Total Synthesis Of Belizentrin Methyl Ester:

The Polyhydroxylated Sidechain

Dissertation

zur Erlangung des akademischen Grades eines
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vorgelegt von

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Die vorliegende Arbeit entstand unter Anleitung von Herrn Prof. Dr. Alois Fürstner in der Zeit von November 2014 bis Juli 2018 am Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr. Teile dieser Arbeit wurden in folgendem Beitrag veröffentlicht:

„Total Synthesis of Belizentrin Methyl Ester: Report on a Likely Conquest"

F. Anderl*, S. Größl*, C. Wirtz, A. Fürstner, *Angew. Chem. Int. Ed.* **2018**, *57*, 10712-10717

*These authors contributed equally to the project.

Die praktischen Arbeiten entstanden teilweise in Zusammenarbeit mit F. Anderl (Kapitel 3.8) und C. Rustemeier (Kapitel 3.3.2.2, 3.5.1.1, 3.7.1.1 und 3.8). Die beschriebenen Ergebnisse bilden eine vollständige Darstellung dieser gemeinsamen Arbeiten. Die von diesen Mitarbeitern alleinverantwortlich erzielten Ergebnisse wurden als solche an entsprechender Stelle gekennzeichnet.

1. Gutachter: Herr Prof. Dr. Alois Fürstner

2. Gutachter: Herr Prof. Dr. Norbert Krause

for Daniel

"The studio was filled with the rich odour of roses,
and when the light summer wind stirred amidst the trees of the garden,
there came through the open door the heavy scent of the lilac,
or the more delicate perfume of the pink-flowering thorn."
Oscar Wilde, The Picture of Dorian Gray

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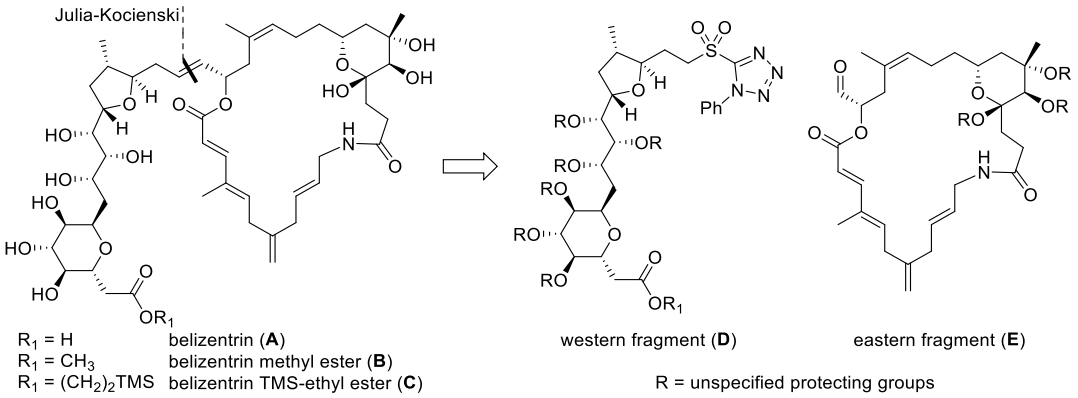
Abstract

Belizentrin (**A**) was isolated in 2014 from the marine dinoflagellate *Prorocentrum belizeanum* as the first member of a group of odd-numbered macrolactamic toxins (Scheme 1). This toxin of marine origin contains a 27-membered macrocycle which bears a high degree of unsaturation. Furthermore, the polyhydroxylated side chain embodies eleven of the 16 stereocentres decorating the core structure of this secondary metabolite.

Belizentrin (**A**) shows significant neurotoxicity when administered to cerebellar cells with an extrapolated EC_{50} value of 193 nM. Experimentally, belizentrin (**A**) was found to be unstable, undergoing observable decomposition during the biological assay. Therefore, we aimed for the total synthesis of both belizentrin methyl ester (**B**) and its congener, belizentrin TMS-ethyl ester (**C**) (Scheme 1). The synthesis of the latter was proposed for the planned release of the natural product **A** by global fluoride-based deprotection.



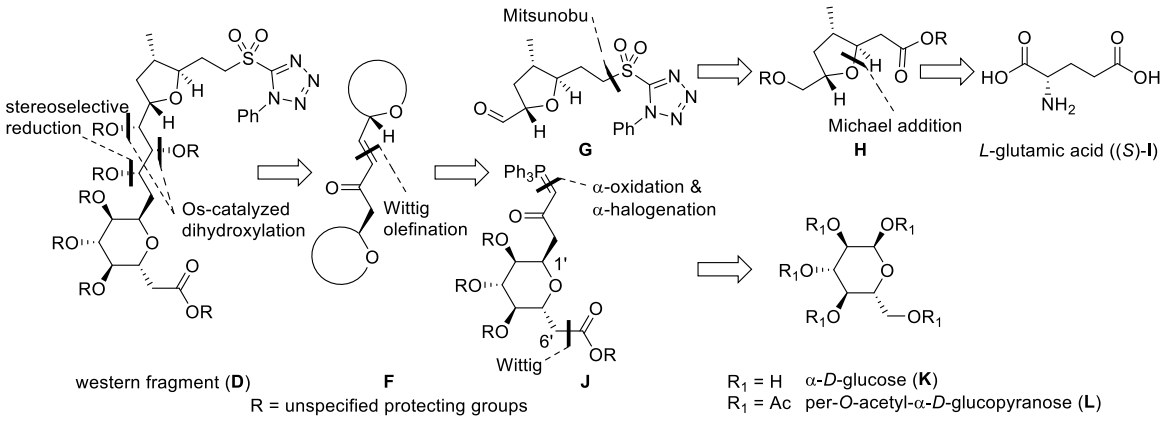
Scheme 1: Retrosynthetic analysis of belizentrin (**A**) and its corresponding esters **B** and **C**.

We sought to synthesize belizentrin (**A**) in a highly convergent manner, with the central *E*-configured C-C double bond of the natural product **A** disconnected via a Julia-Kocienski olefination (Scheme 1). This resulted in a western side chain **D**, bearing a tetrazolylsulfone, and an eastern macrocycle **E**, bearing the required aldehyde.

The eastern belizentrin fragment **E** was prepared in 13 steps (LLS) with an overall yield of ca. 2.5% by Ph.D. student F. Anderl, starting from different commercially available C_3 to C_5 building blocks (for further details, see projected Ph.D. thesis by F. Anderl).

The western belizentrin fragment **D** was accessed in 17 steps (LLS) with an overall yield of 3-5% (regarding both esters) from the commercially available amino acid *L*-glutamic acid ((*S*)-**I**) and the per-*O*-acetyl derivative **L** of α-*D*-glucose (**K**) (Scheme 2).

Based on the literature known synthesis of the enantiomer of 2,5-*trans*-disubstituted ether **H**, tetrazolylsulfone **G** was obtained in 13 steps with an overall yield of 12% (Scheme 2). Key steps included a cyclizing 1,4-addition towards ether **H** and a Mitsunobu reaction to introduce a tetrazolylsulfide. Further functional group modifications led to sulfone **G**.



Scheme 2: Retrosynthetic analysis of western belizentrin fragment **D**.

Phosphorus ylide **J** was obtained via an anomeric allylation, an alkene oxidation, and an α-bromination at the C1' terminus of per-*O*-acetyl-α-*D*-glucopyranose (**L**) (Scheme 2). Selective silyl ether deprotection and oxidation followed by Wittig olefination introduced the ester functionality to the C6' terminus of **J**. Overall, phosphorus ylide **J** was synthesized in eleven steps with an overall yield in the range of 17-18% (regarding both esters).

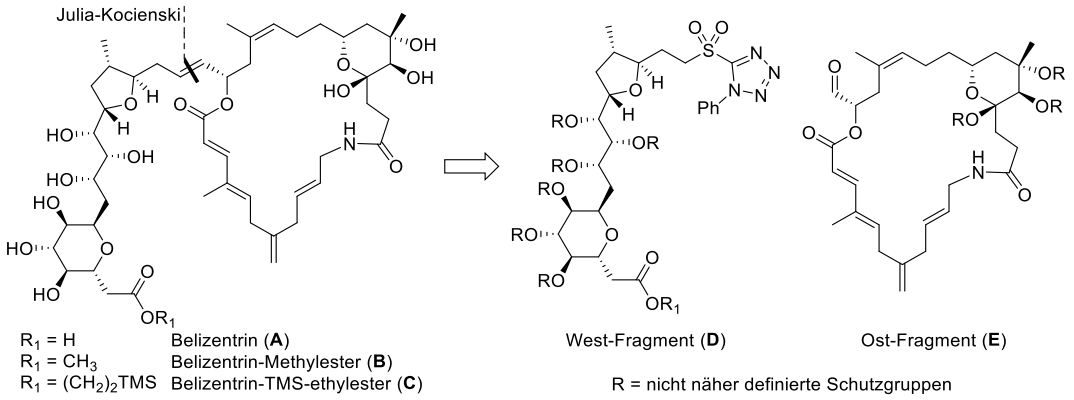
Wittig olefination of aldehyde **G** with phosphorus ylide **J** furnished enone **F**, which was subsequently reduced to the corresponding allylic alcohol by a CBS reduction (Scheme 2). The key step of the synthetic route was a Sharpless dihydoxylation of the allylic alcohol, installing the central triol motif of the western belizentrin fragment **D**. After exhaustive protection with TESOTf, fragment **D** was obtained. The absolute configuration was confirmed by a combination of Mosher ester analyses, derivatization into five-membered carbonate derivatives and NMR comparison of constitutionally isomeric triols, obtained via different synthetic routes.

The final steps towards belizentrin methyl ester (**B**) were carried out by Ph.D. student F. Anderl. The proposed Julia olefination of aldehyde **E** with tetrazolylsulfone **D** proved difficult due to significant base sensitivity of the skipped polyene motif (Scheme 1). This transformation was achieved by transmetallation of deprotonated tetrazolylsulfone **D** from lithium to zinc. Global deprotection with aqueous hydrofluoric acid in acetonitrile finally yielded belizentrin methyl ester (**B**) (in comparison to 3.1 mg of belizentrin (**A**) obtained by the isolation team).

Zusammenfassung

2014 wurde Belizentrin (**A**) aus dem marinen Dinoflagellaten *Prorocentrum belizeanum* als der erste Vertreter einer neuen Klasse von ungeradzahligen, macrolactamischen Toxinen erhalten (Schema 1). Es enthält einen 27-gliedrigen, hochgradig ungesättigten Macrocyclus. Darüber hinaus weist seine polyhydroxylierte Seitenkette elf der insgesamt 16 Stereozentren auf, die zur Komplexität dieses Sekundärmetaboliten beitragen.

Belizentrin (**A**) zeigt mit einem, an Kleinhirn-Nervenzellen ermittelten EC_{50} von 193 nM signifikante Neurotoxizität. Im Rahmen des biologischen Assays war experimentell eine gewisse Instabilität und die damit einhergehende Zersetzung von Belizentrin (**A**) festzustellen. Aus diesem Grund richteten wir unser Augenmerk auf die Totalsynthese von Belizentrin-Methylester (**B**) und den homologen Belizentrin-TMS-ethylester (**C**) (Schema 1). Die Synthese von letzterem wurde zwecks Fluorid-basierter, globaler Entschützung unter Freisetzung des Naturstoffs **A** angestrebt.



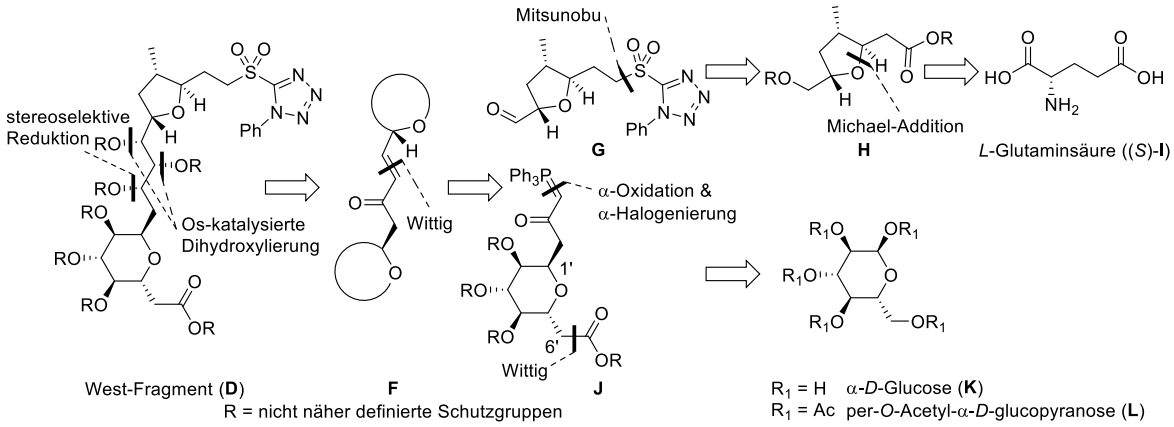
Schema 1: Retrosynthetische Analyse von Belizentrin (**A**) und seinen korrespondierenden Estern **B** und **C**.

Um Belizentrin (**A**) dabei möglichst konvergent aufzubauen, entschieden wir uns für ein Julia-Kocienski-Transform der zentralen, *E*-konfigurierten C-C-Doppelbindung (Schema 1). Dies resultierte in einer westlichen, das Tetrazolsulfon tragenden Seitenkette **D** und einem östlichen Macrocyclus **E**, bestückt mit dem dafür notwendigen Aldehyd.

Das östliche Belizentrin-Fragment **E** wurde in 13 Stufen (LLS) mit einer Gesamtausbeute von ca. 2.5%, ausgehend von kommerziell erhältlichen C_3- bis C_5-Bausteinen von dem Doktoranden F. Anderl synthetisiert (für weiterführende Details, siehe geplante Dissertation von F. Anderl).

Das westliche Belizentrin-Fragment **D** wurde in 17 Stufen (LLS) mit einer Gesamtausbeute von 3-5% (je nach Ester) aus den kommerziell erhältlichen Bausteinen *L*-Glutaminsäure ((*S*)-**I**) und dem per-*O*-Acetyl-Derivat **L** von α-*D*-Glucose (**K**) erhalten (Schema 2).

Gemäß Literatursynthese für das Enantiomer des 2,5-*trans*-disubstituierten Ethers **H** wurde das Tetrazolsulfon **G** in 13 Stufen mit einer Gesamtausbeute von 12% erhalten (Schema 2). Schlüsselschritte waren eine cyclisierende 1,4-Addition zum Ether **H** und eine Mitsunobu-Reaktion zur Einführung des Tetrazolthiols. Anschließende Funktionalisierungen führten zum Sulfon **G**.



Schema 2: Retrosynthetische Analyse des westlichen Belizentrin-Fragments **D**.

Phosphor-Ylid **J** wurde nach Allylierung am anomeren Zentrum, Alken-Oxidation und α-Bromierung am C1‘-Terminus aus per-*O*-Acetyl-α-*D*-glucopyranose (**L**) erhalten (Schema 2). Mit Hilfe selektiver Funktionalisierungen und nachfolgender Wittig-Olefinierung wurde der Ester am C6‘-Terminus von α-*D*-Glucose (**K**) eingeführt. Somit wurde Phosphor-Ylid **J** in elf Stufen mit einer Gesamtausbeute von 17-18% erhalten (je nach Ester).

Wittig-Olefinierung von Aldehyd **G** mit Phosphor-Ylid **J** führte zum Enon **F**, welches anschließend durch CBS-Reduktion in den entsprechenden Allyl-Alkohol überführt wurde (Schema 2). Schlüsselschritt der Synthese war die Sharpless-Dihydroxylierung des Allyl-Alkohols, die zur Einführung des zentralen Triol-Motivs im westlichen Belizentrin-Fragment **D** herangezogen wurde. Nach Schützung mit TESOTf wurde das Fragment **D** erhalten. Die absolute Konfiguration wurde durch eine Kombination von Mosher-Ester-Analysen, Derivatisierung als 5-Ring-Carbonate und NMR-Vergleich konstitutionell isomerer, aus verschiedenen Routen erhaltener Triole bestimmt.

Die abschließenden Schritte zum Belizentrin-Methylester (**B**) wurden von Hr. F. Anderl durchgeführt. Die Julia-Olefinierung von Aldehyd **E** mit Tetrazolsulfon **D** erwies sich in Anbetracht der hohen Basenempfindlichkeit des Polyen-Motivs als schwierig (Schema 1). Die Transformation wurde letztlich durch einen Lithium-Zink-Austausch am deprotonierten Tetrazolsulfon **D** möglich. Globale Entschützung mit Flusssäure in Acetonitril führte zum Belizentrin-Methylester (**B**) (zum Vergleich: 3.1 mg von Belizentrin (**A**) wurden durch das Isolationsteam erhalten).

Table of Contents

1. Introduction

1.1. Natural Products & Total Synthesis

About 13.8 billion years ago, the Big Bang was the starting point for the creation of carbon as the central and essential element of all known lifeforms. Carbon, with its versatility for unsaturation within bonds (*e.g.* along with nitrogen and phosphorus) and the potential of bearing stereochemical information as a quarternary centre (in addition to planar and axial chirality) makes life as we know it not only possible, but also enables complex processes.

The first reported isolation of a natural product was that of morphine (**1**) by F. Sertürner in 1806 (Figure 1.1).[1] With the preparation of urea (**2**), F. Wöhler performed the first reported total synthesis in 1828,[2] and thereby made an entry into this new area of chemical research.

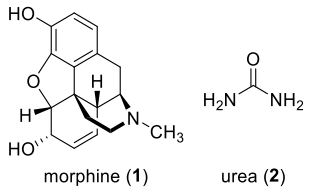
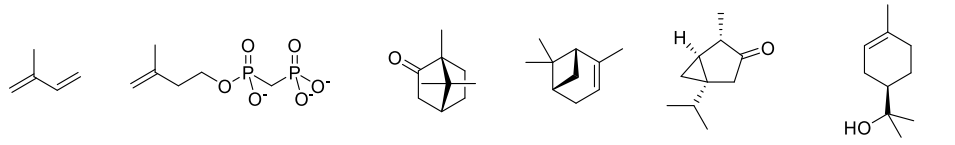


Figure 1.1: Morphine (**1**) and urea (**2**).

O. Wallach made an abundantly important contribution to natural product synthesis by studying terpenes in the late 19th century (Figure 1.2).[3] Terpenes and terpenoids are an important, but also very heterogeneous group of secondary metabolites from many different species. They show great structural diversity but all originate from common building blocks, isoprene (**3**) and *i*-pentenyl pyrophosphate (IPP) (**4**).



isoprene (**3**) *i*-pentenyl pyrophosphate (**4**) (+)-camphor (**5**) (-)-α-pinene (**6**) (+)-α-thujone (**7**) (+)-α-terpineol (**8**)

Figure 1.2: Isoprene (**3**), *i*-pentenyl pyrophosphate (IPP) (**4**) and some representative examples of terpenes.

[1] F. Sertürner, *J. Pharm.* **1806**, *14*, 33-37.
[2] F. Wöhler, *Ann. Phys.* **1828**, *88*, 253-256.
[3] a) O. Wallach, W. Brass, *Liebigs Ann. Chem.* **1884**, *225*, 291-314. b) O. Wallach, *Liebigs Ann. Chem.* **1885**, *227*, 277-302.

Another rich family of natural products can be found in carbohydrates and proteins. Carbohydrates (such as α-*D*-glucose (**9**))[4] and amino acids (such as *L*-glutamic acid ((*S*)-**10**)),[5] which were intensively examined and structurally elucidated by E. Fischer in the late 19th century, are probably the most important structures for understanding biomolecular processes such as the primary metabolism (Figure 1.3). Furthermore, they are involved in membrane processes such as cell recognition, and they are also the foundations of proteinogenic molecules, DNA, and RNA (as ribose and deoxyribose), respectively.

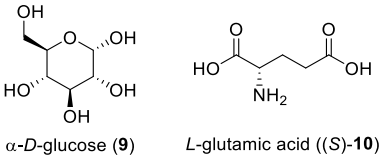


Figure 1.3: α-*D*-Glucose (**9**) and *L*-glutamic acid ((*S*)-**10**).

H. Zahn reported the first total synthesis of the peptide insuline (**11**),[6] a hormone regulating cellular carbohydrate uptake (such as of **9**), in 1963 (Figure 1.4).

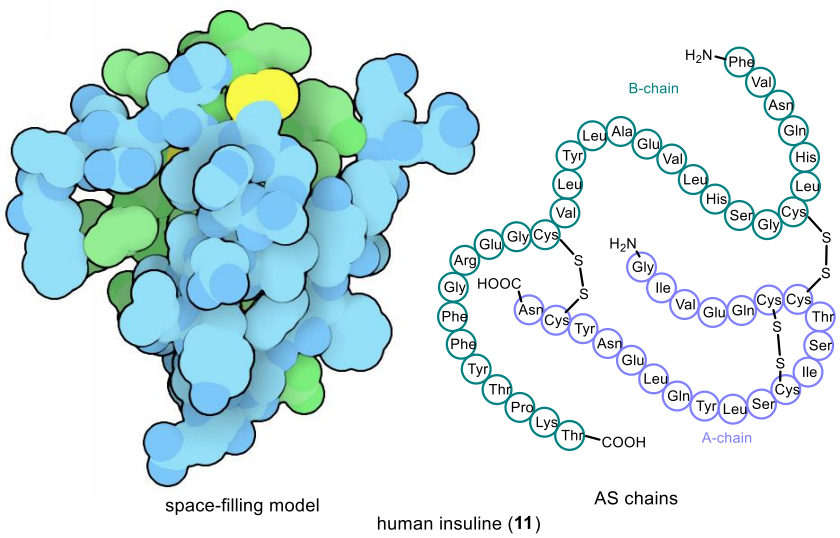


Figure 1.4: Human insuline (**11**) [left: space filling 3D model[7] (green: A-chain, blue: B-chain, yellow: disulfide linkages); right: plain AS chains].

[4] a) E. Fischer, *Chem. Ber.* **1891**, *24*, 1836-1845. b) E. Fischer, *Chem. Ber.* **1891**, *24*, 2683-2687.
[5] E. Fischer, E. Fourneau, *Chem. Ber.* **1901**, *34*, 2868-2877.
[6] J. Meienhofer, E. Schnabel, H. Bremer, O. Brinkhoff, R. Zabel, W. Sroka, H. Klostermeyer, D. Brandenburg, T. Okuda, H. Zahn, *Z. Naturforsch., B: Chem. Sci.* **1963**, *18b*, 1120-1121.
[7] Picture taken from http://pdb101.rcsb.org/motm/14 on 04/25/2018.

The field of natural product synthesis has seen significant advancements since Wöhler´s initial preparation of urea (**2**). Fascinating and structurally complex molecules have been targeted. R. Woodward, for example, did not only accomplish the total synthesis of cholesterol (**12**)[8] (Figure 1.5) simultaneously to R. Robinson,[9] but also the total synthesis of vitamin B_{12} (**13**)[10] with A. Eschenmoser, which are landmark achievements in organic chemistry.

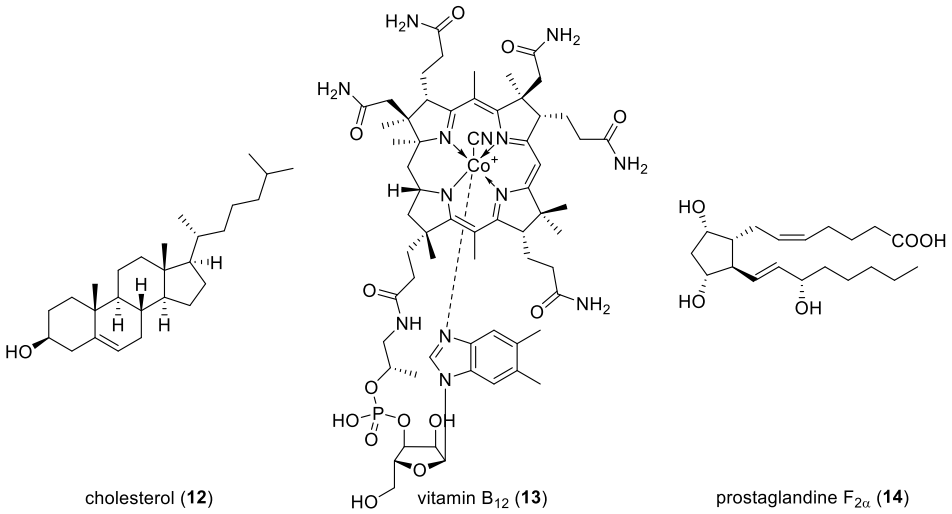


Figure 1.5: Structures of cholesterol (**12**), vitamin B_{12} (**13**) and prostaglandine $F_{2\alpha}$ (**14**).

By developing the concept of retrosynthesis in the middle of the 20th century, E. J. Corey established one of the most versatile and useful tools in organic chemistry.[11] Moreover, his total synthesis of prostaglandine $F_{2\alpha}$ (**14**) remains a benchmark in synthetic chemistry and total synthesis (Figure 1.5).[12]

Natural product total synthesis can be seen as artwork by a creative scientist, or as a helpful tool to train students in synthetic chemistry, but perhaps more interestingly is the spirit behind it. When N. Armstrong set foot on the moon on July 21, 1969, he probably had a similiar feeling to J. Piccard and D. Walsh, when they entered the Mariana trench with their submarine Trieste on January 23, 1960. All of them achieved something for the first time in history.

[8] R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, W. M. McLamore, *J. Am. Chem. Soc.* **1952**, *74*, 4223-4251.
[9] H. M. E. Cardwell, J. W. Cornforth, S. R. Duff, H. Holtermann, R. Robinson, *Chem. Ind.* **1951**, 389-390.
[10] a) A. Eschenmoser, *Q. Rev. Chem. Soc.* **1970**, *24*, 366-415. b) R. B. Woodward, *Pure Appl. Chem.* **1973**, *33*, 145-178.
[11] E. J. Corey, R. D. Cramer, W. J. Howe, *J. Am. Chem. Soc.* **1972**, *94*, 440-459.
[12] E. J. Corey, N. M. Weinshenker, T. K. Schaaf, W. Huber, *J. Am. Chem. Soc.* **1969**, *91*, 5675-5677.

With this in mind, total synthesis embodies the possibility to be the first of your kind. Besides this very adventurous task, the scientific focus of total synthesis remains on the following three major issues:

- structural elucidation,
- chemical method development and application, and
- accessibility of natural products (*e.g.* for medicinal use).

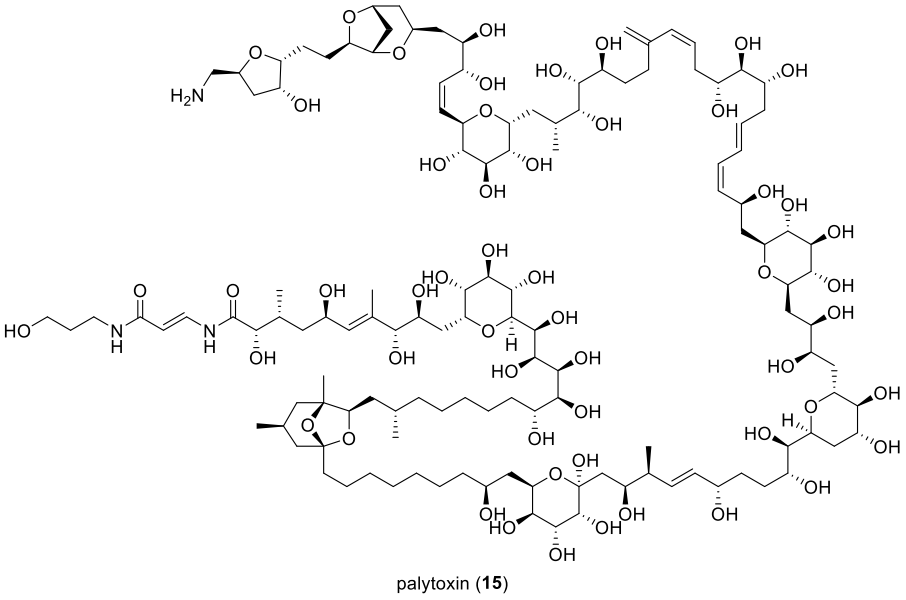


Figure 1.6: Palytoxin (**15**).

Two of the most intriguing total synthesis projects over the past three decades targeted palytoxin (**15**) (Figure 1.6) and maitotoxin (**16**) (Figure 1.7). The first one mentioned, was accomplished by Y. Kishi in the late 80's,[13] and the latter was started by K. C. Nicolaou and is still an ongoing project to date.[14]

[13] R. W. Armstrong, J. M. Beau, S. H. Cheon, W. J. Christ, H. Fujioka, W. H. Ham, L. D. Hawkins, H. Jin, S. H. Kang, Y. Kishi, M. J. Martinelli, J. McWhorter, William W. , M. Mizuno, M. Nakata, A. E. Stutz, F. X. Talamas, M. Taniguchi, J. A. Tino, K. Ueda, J.-i. Uenishi, J. B. White, M. Yonaga, *J. Am. Chem. Soc.* **1989**, *111*, 7525-7530.

[14] a) K. C. Nicolaou, R. J. Aversa, J. Jin, F. Rivas, *J. Am. Chem. Soc.* **2010**, *132*, 6855-6861. b) K. C. Nicolaou, M. O. Frederick, A. C. B. Burtoloso, R. M. Denton, F. Rivas, K. P. Cole, R. J. Aversa, R. Gibe, T. Umezawa, T. Suzuki, *J. Am. Chem. Soc.* **2008**, *130*, 7466-7476. c) K. C. Nicolaou, P. Heretsch, T. Nakamura, A. Rudo, M. Murata, K. Konoki, *J. Am. Chem. Soc.* **2014**, *136*, 16444-16451. d) K. C. Nicolaou, J. H. Seo, T. Nakamura, R. J. Aversa, *J. Am. Chem. Soc.* **2011**, *133*, 214-219.

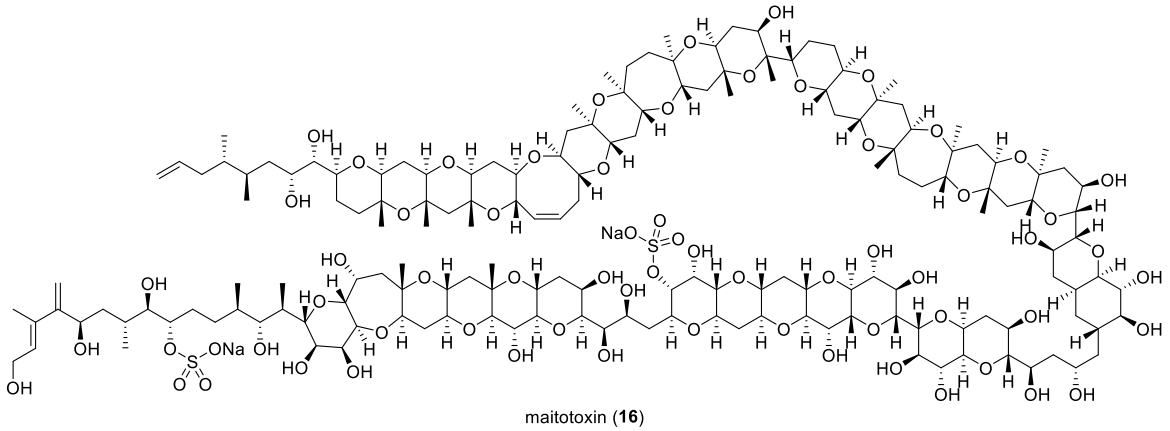


Figure 1.7: Maitotoxin (**16**).

The laboratory synthesis of these extraordinary molecules is a neverending challenge for organic chemists, and once more proves Mother Nature´s unfathomable paths. Beyond mere synthetic curiosity, there are natural products of great complexity which are used as drugs, such as paclitaxel (PTX) (**17**) (Figure 1.8).[15]

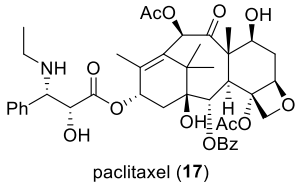


Figure 1.8: Paclitaxel (PTX) (**17**).

Due to the highlighted reasons above, we set out to attempt the synthesis of a highly decorated and challenging, yet very toxic, macrocyclic natural product of marine origin from a tiny dinoflagellate called *Prorocentrum belizeanum*. Some might consider it as a chemist of great talent, while others might see evolution at work...

[15] First total syntheses of Paclitaxel: a) R. A. Holton, C. Somoza, H. B. Kim, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1597-1598. b) R. A. Holton, H. B. Kim, C. Somoza, F. Liang, R. J. Biediger, P. D. Boatman, M. Shindo, C. C. Smith, S. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 1599-1600. c) K. C. Nicolaou, Z. Yang, J. J. Liu, H. Ueno, P. G. Nantermet, R. K. Guy, C. F. Claiborne, J. Renaud, E. A. Couladouros, K. Paulvannan, E. J. Sorensen, *Nature* **1994**, *367*, 630.

2. Aim Of This Thesis

Regarding the previously discussed complexity and beauty of Mother Nature´s diverse chemistry (Chapter 1.1), our goal was to synthesize the highly functionalized natural product belizentrin (**18**) (Figure 2.1). Belizentrin (**18**) is an exciting target to test diverse chemical methodologies such as ring closing alkyne metathesis (RCAM)[16], *trans*-hydroelementation reactions[17] and π-acid catalysis by gold and platinum.[18]

Furthermore, it is very likely that methods like the Nobel Prize winning Sharpless dihydroxylation[19] or the Wittig olefination reaction[20] could once again prove their reliability in a demanding total synthesis of such a complex secondary metabolite.

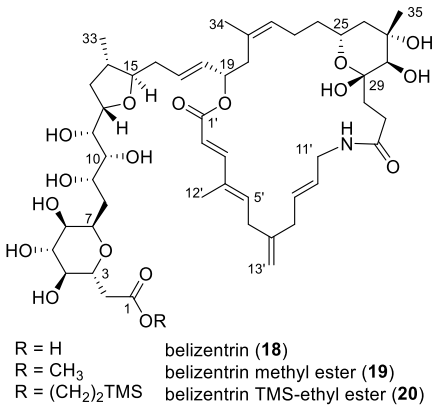


Figure 2.1: Structures of the natural product belizentrin (**18**) and its ester derivatives **19** and **20**.

Major task in this thesis was to synthesize the complete polyhydroxylated western sidechain of belizentrin (**18**).

The natural product **18** itself was to be synthesized to evaluate its structure and biological activity. The synthesis of ester derivatives such as **19** and **20** was envisioned as well, due to the reported instability observed during the biological testing by the isolation team (Chapter 3.1.2).[21]

[16] A. Fürstner, P. W. Davies, *Chem. Commun.* **2005**, *0*, 2307-2320.
[17] a) K. Radkowski, B. Sundararaju, A. Fürstner, *Angew. Chem. Int. Ed.* **2013**, *52*, 355-360. b) B. Sundararaju, A. Fürstner, *Angew. Chem.* **2013**, *125*, 14300-14304. c) S. M. Rummelt, A. Fürstner, *Angew. Chem. Int. Ed.* **2014**, *53*, 3626-3630.
[18] A. Fürstner, *Chem. Soc. Rev.* **2009**, *38*, 3208-3221.
[19] K. B. Sharpless, *The Nobel Prize in Chemistry* **2001**, *Nobelprize.org Nobel Media AB 2014. Web. 14 May 2018. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2001/sharpless-facts.html>*
[20] G. Wittig, *The Nobel Prize in Chemistry* **1979**, *Nobelprize.org Nobel Media AB 2014. Web. 14 May 2018. <http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1979/wittig-lecture.html>*
[21] H. J. Domínguez, J. G. Napolitano, M. T. Fernández-Sánchez, D. Cabrera-García, A. Novelli, M. Norte, J. J. Fernández, A. H. Daranas, *Org. Lett.* **2014**, *16*, 4546-4549.

3. Total Synthesis Of Belizentrin

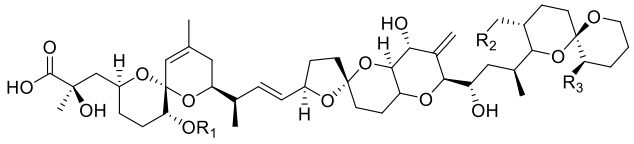
3.1. Introduction

3.1.1. Secondary Metabolites From Marine Dinoflagellates

Dinoflagellates are an interesting taxon of unicellular eukaryotic organisms:[22] many produce marine or freshwater toxins as secondary metabolites, while others are completely non-toxic. The dinoflagellate genus *Prorocentrum* consists of different species. Some of these *Prorocentrum* species live as free floating organisms (plancton), while others live on the sea floor (benthic).[23]

As observed for many highly functionalized and potent toxic entities, they are not necessarily intended to harm a feeding enemy directly. Instead, the dinoflagellate can live in symbiosis with another life form which itself is non-toxic, but becomes unattractive to its own predators by bearing the algae inside. This, however, remains an issue of current biological debate.

Prorocentrum, as well as *Dinophysis* (another dinoflagellate genus), produce secondary metabolites like ocadaic acid (OA) (**21**) and the family of dinophysistoxins (DTX) (**22**) which contain a lipophilic polyether core (Figure 3.1). These compounds are known to cause a gastrointestinal illness in humans, known as diarrhetic shellfish poisoning (DSP).[24]



		R_1	R_2	R_3
OA	**21**	H	CH_3	H
DTX-1	**22a**	H	CH_3	CH_3
DTX-2	**22b**	H	H	CH_3
DTX-3	**22c**	acyl	H or CH_3	H or CH_3

Figure 3.1: Natural products (OA and DTX) from some *Prorocentrum* and *Dinophysis* species.

Dinoflagellates, such as those of the *Prorocentrum* genus, are capable of producing odd-numbered macrocyclic lactone secondary metabolites. Only a few examples of such natural products are

[22] M. A. Faust, *J. Phycol.* **1993**, *29*, 100-107.
[23] a) See footnote 22. b) A. Herrera-Sepúlveda, L. K. Medlin, G. Murugan, A. P. Sierra-Beltrán, A. A. Cruz-Villacorta, N. Y. Hernández-Saavedra, K. Müller, *J. Phycol.* **2015**, *51*, 173-188.
[24] P. Gopalakrishnakone, V. H. Jr., A. Tubaro, E. Kim, W. R. Kem, *Marine and Freshwater Toxins*, SpringerReference (Singapore), **2016**.

known in the literature, such as formosalides A (**23a**) and B (**23b**) from *Prorocentrum sp*.[25] which bear 17-membered lactones, and amphidinolide J (**24**) from *Amphidinium sp*.[26] which has a 15-membered lactone (Figure 3.2).

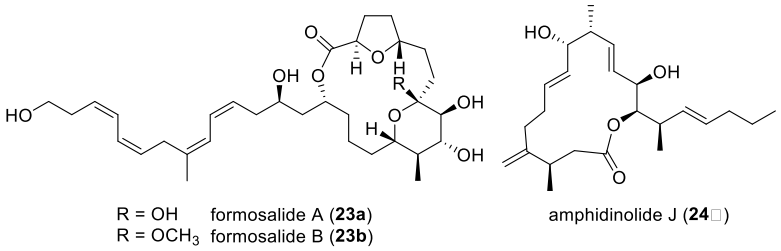


Figure 3.2: Examples for odd-numbered secondary metabolite macrolactones.

Moreover, two complex, yet even-numbered (macrocyclic) natural products were isolated in 2009 by Daranas *et al.* from an extract of *Prorocentrum belizeanum*.[27] Belizeanolide (**25a**) and its *seco* acid belizeanoic acid (**25b**) were found to be very potent neurotoxins with a high density of hydroxy functionalities and *exo*-methylene unsaturations, as well as three 2,5-*trans*-disubstituted tetrahydrofuran rings within the polyketide framework (Figure 3.3).

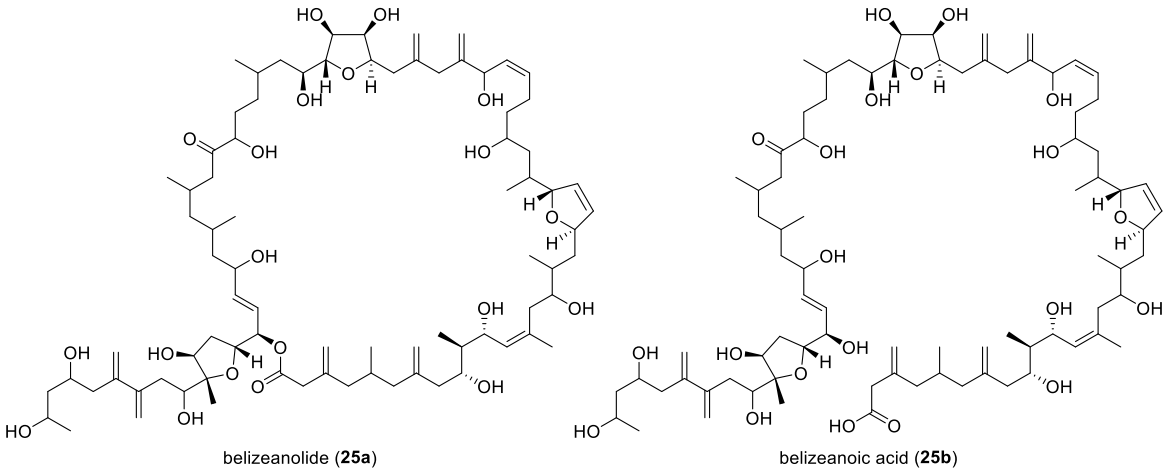


Figure 3.3: Other polyketides from *Prorocentrum belizeanum*.

Both belizeanolide (**25a**) and belizeanoic acid (**25b**) bear no less than 28 stereogenic centres, however the absolute and relative stereochemistry on many centres remained unclear due to the high flexibility and complexicity of these molecules (Figure 3.3). Nevertheless, these two natural products are remarkable examples for highly complex secondary metabolites from dinoflagellates such as *Prorocentrum belizeanum*.

[25] C.-K. Lu, Y.-M. Chen, S.-H. Wang, Y.-Y. Wu, Y.-M. Cheng, *Tetrahedron Lett.* **2009**, *50*, 1825-1827.
[26] J. i. Kobayashi, M. Takahashi, M. Ishibashi, *J. Chem. Soc., Chem. Commun.* **1995**, *16*, 1639-1640.
[27] J. G. Napolitano, M. Norte, J. M. Padrón, J. J. Fernández, A. H. Daranas, *Angew. Chem. Int. Ed.* **2009**, *48*, 796-799.

3.1.2. Isolation, Structure & Biology Of Belizentrin

In 2014, 3.1 mg of belizentrin (**18**) (Figure 3.4) were isolated from a 1000 L culture broth of the Caribbean marine dinoflagellate *Prorocentrum belizeanum* (strain PBMA01) by Daranas *et al.* (Figure 3.5).[28] The methanolic extract of the obtained cell pellet was fractioned by combined gel permeation and reversed-phase chromatography.

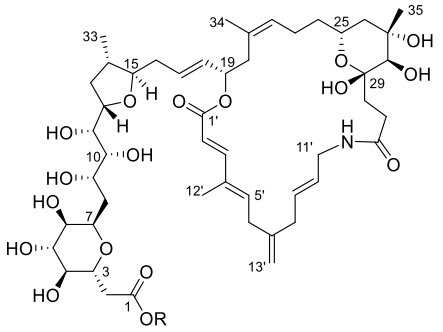


Figure 3.4: Structures of the natural product belizentrin (**18**) and its ester derivatives **19** and **20**.

Belizentrin (**18**) is the first member of a new class of polyhydroxylated and polyunsaturated macrolactamic toxins.[29] A unique feature is the 27-membered macrocycle, which is unusual in view of its origin via the polyketide biosynthesis pathway from acetate and propiolate (C_2 chain elongations).[30]

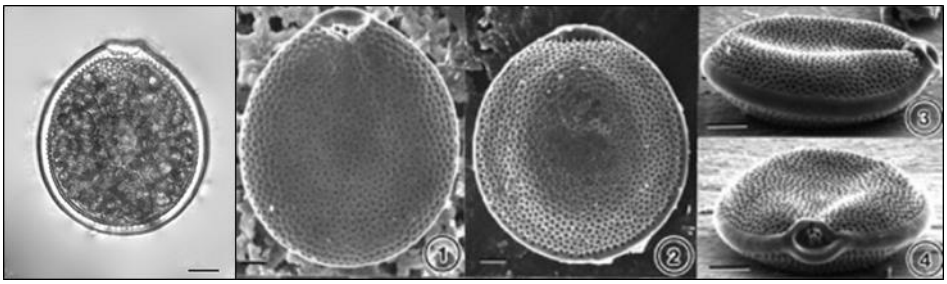


Figure 3.5: *Prorocentrum belizeanum* (optical microscope and SEM).[31]

The isolated natural product **18** exhibits potent neurotoxicity, as it leads to complete disintegration of healthy neurites (*in vitro*) with increasing concentration (Figure 3.6).

[28] H. J. Domínguez, J. G. Napolitano, M. T. Fernández-Sánchez, D. Cabrera-García, A. Novelli, M. Norte, J. J. Fernández, A. H. Daranas, *Org. Lett.* **2014**, *16*, 4546-4549.
[29] R. A. Hill, A. Sutherland, *Nat. Prod. Rep.* **2014**, *33*, 1126-1130.
[30] S. Omura, *Macrolide Antibiotics*, Academic Press (New York), **1984**.
[31] Pictures were taken from http://botany.si.edu/references/dinoflagellates/prorocentrum_be.htm and http://www.revistas.unal.edu.co/index.php/actabiol/article/viewFile/9781/28174/98823 on 03/26/2015

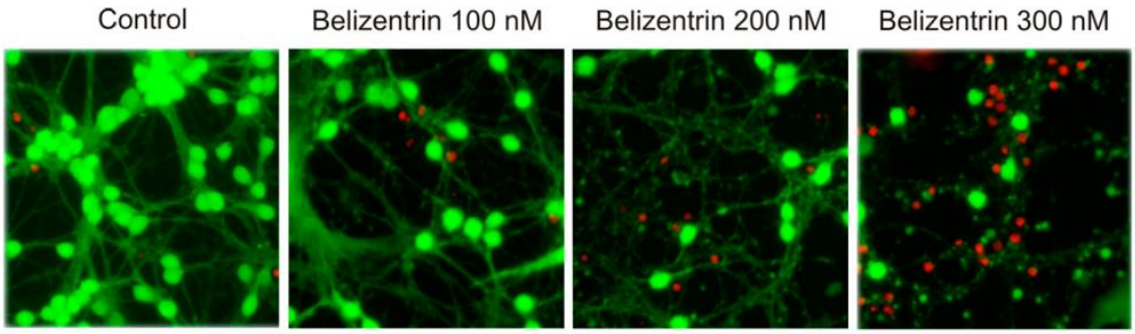


Figure 3.6: Results of the biological assay, part A (fluorescence photomicrographs of neurons before and after exposure to belizentrin (**18**) for 24 h; bright green: vivid neurons; neurites and dead neurons did not retain any fluorescein; red: nuclei stained with ethidium bromide).[32]

When administered at different concentrations to cultured cerebellar cells, belizentrin (**18**) led to massive changes within the neuronal network. Concentrations of 100 nM and higher first resulted in neurite weakness and increasing fragmentation. At concentrations of 300 nM cell death was inevitable. These effects required exposure to belizentrin (**18**) for 24 h. From the corresponding dose-response curve, an EC_{50} value of 193 ± 7 nM was estimated (Figure 3.7).

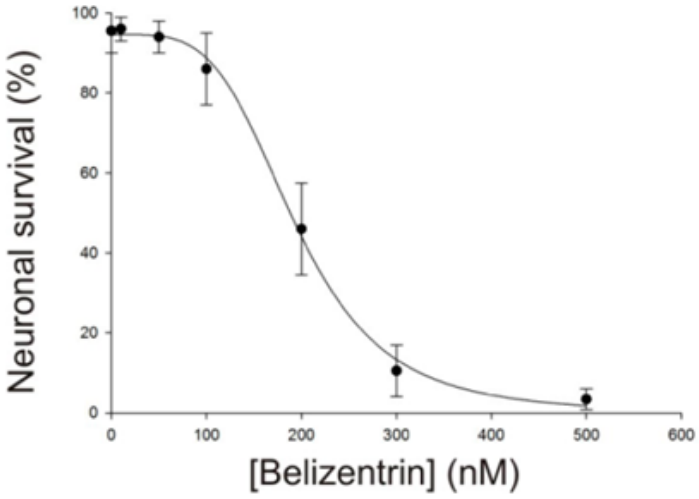


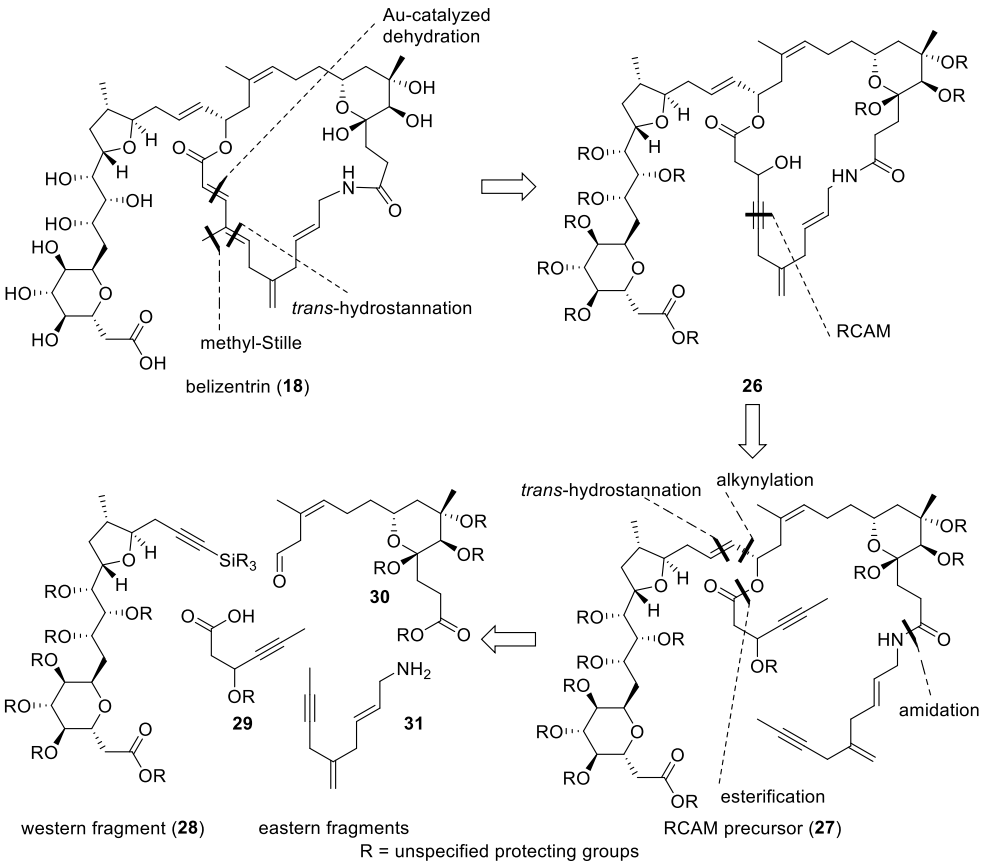
Figure 3.7: Results of the biological assay, part B (dose-response curve (mean ± SD)).[33]

The isolation team reported an intrinsic instability of belizentrin (**18**), and decomposition was observed during their biological assay on neuronal cells. Therefore, the biological activity of the natural product might actually be higher, and it was deemed necessary to synthesize the belizentrin ester derivatives **19** and **20** for the ease of isolation instead of the free carboxylic acid **18** (Figure 2.1).

[32] Pictures were taken from H. J. Domínguez, J. G. Napolitano, M. T. Fernández-Sánchez, D. Cabrera-García, A. Novelli, M. Norte, J. J. Fernández, A. H. Daranas, *Org. Lett.* **2014**, *16*, 4546-4549.
[33] See footnote 32.

3.2. First Retrosynthetic Analysis

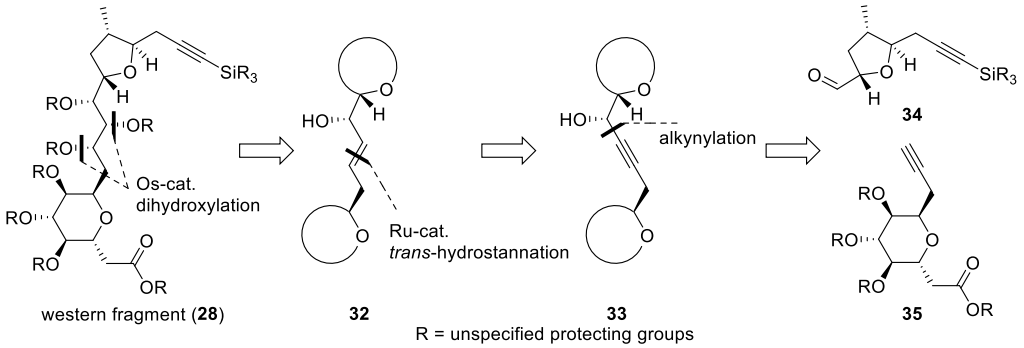
As mentioned earlier, some in house-developed methodologies were included in the retrosynthetic analysis of the target molecule **18** such as gold-catalyzed dehydration, methyl-Stille coupling, and alkyne *trans*-hydrostannation (Scheme 3.1). Applying these disconnections led to macrocyclic propargylic alcohol **26**.



Scheme 3.1: Retrosynthetic analysis of belizentrin (**18**).

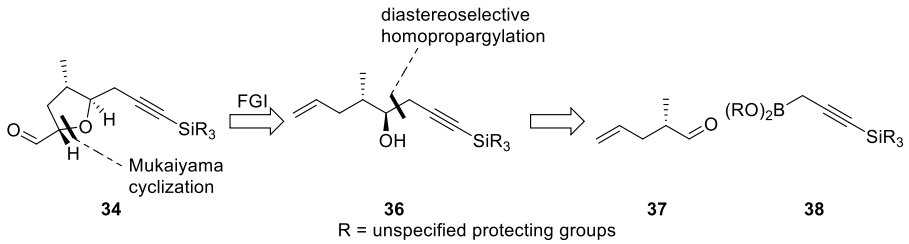
Propargylic alcohol **26** was then disconnected at the central triple bond by ring closing alkyne metathesis (RCAM), leading to open chain precursor **27** (Scheme 3.1). Retron **27** could be obtained by further disconnections such as esterification with carboxylic acid **29** and amidation at its terminus with amine **31**. Diastereoselective aldehyde alkynylation led back to aldehyde **30** and desilylated alkyne **28**. The propargylic alcohol obtained by the coupling process of the western and the northern fragment could then be transformed into the corresponding *E*-configured allylic alcohol by alkyne *trans*-hydrostannation. This was envisioned either before or after ring closure of the two methyl-capped alkynes via RCAM.

The western fragment **28** could come from an osmium-catalyzed stereoselective dihydroxylation (Scheme 3.2). The requisite allylic alcohol **32** could be obtained from the corresponding propargylic alcohol **33** via a sequence of ruthenium-catalyzed *trans*-hydrostannation and subsequent protodestannation. Disconnection of propargylic alcohol **33** via another diastereoselective alkynylation would lead to aldehyde **34** and C-glycosidic alkyne **35**.



Scheme 3.2: Retrosynthetic fragmentation of the western belizentrin fragment **28**.

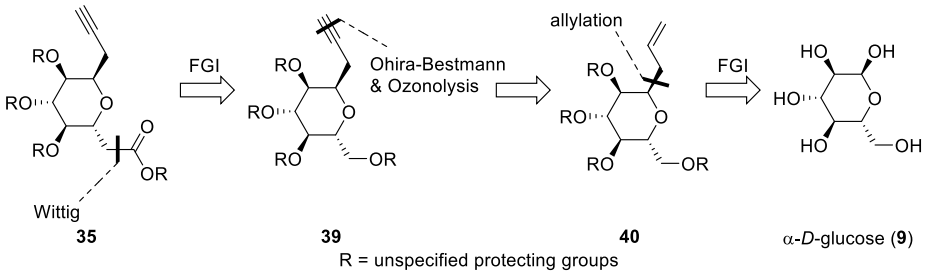
Regarding the 2,5-*trans*-disubstituted ether **34**, a disconnection at one of the C-O ether bonds seemed plausible (Scheme 3.3). The 2,5-*trans*-disubstituted ether **34** could then be derived from bis-homoallylic alcohol **36** by a cobalt-catalyzed oxidative Mukaiyama cyclization.



Scheme 3.3: Retrosynthetic fragmentation of the 2,5-*trans*-disubstituted ether **34**.

Bis-homoallylic alcohol **36** could be further disconnected at the α-position, into the aldehyde (*S*)-**37** and pinacolborane **38** (Scheme 3.3). Both precursors are known to be accessible from commercially available starting materials.

For the retrosynthetic analysis of alkyne **35**, we envisioned a C_1 homologation by a Wittig olefination for the introduction of the ester functionality (Scheme 3.4). After functional group interconversions, protected tetrol **39** could be reached.



Scheme 3.4: Retrosynthetic fragmentation of the sugar-based alkyne **35**.

The alkyne moiety at the C1' terminus could be derived from alkene **40** via ozonolysis and Seyferth-Gilbert homologation (Scheme 3.4). Alkene **40** could then be prepared from α-*D*-glucose (**9**) via allylation at the anomeric position and further protecting group alterations.

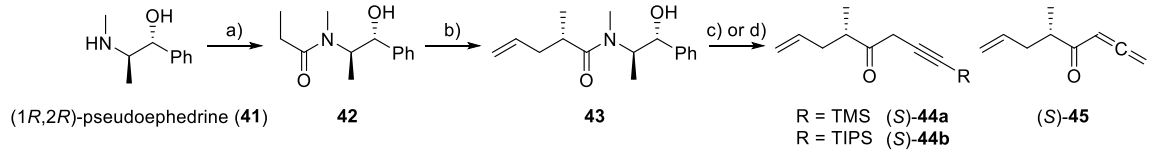
3.3. Western Belizentrin Fragment - Route 1

3.3.1. Successful Synthetic Route

3.3.1.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

3.3.1.1.1. An Auxiliary-Based Entry

The synthesis of the 2,5-*trans*-disubstituted ether **34** (Scheme 3.3) started with an auxiliary-based approach via the stereoselective allylation of pseudoephedrine amides according to Myers *et al.* (90% over two steps) (Scheme 3.5, Figure 3.8).[34]



Scheme 3.5: Synthesis of the 2,5-*trans*-disubstituted ether **34a**, part A. Reagents and conditions: (a) propionic anhydride, TEA, DCM, rt, 70 min, 95%; (b) i. DIPA, *n*-BuLi, LiCl, THF, 0 °C to rt, 45 min, then **42**, -78 °C to rt, 1.5 h; ii. allyl iodide, THF, -78 °C to 0 °C, 2 h, 95%; (c) i. n-BuLi, TMEDA, TMS-propyne, Et_2O, -5 °C, 25 min; ii. add to **43**, THF, -78 °C to 0 °C, 15 min, inseparable mixture of (*S*)-**44a** and (*S*)-**45**; (d) i. *n*-BuLi, TMEDA, TIPS-propyne, Et_2O, -5 °C, 35 min; ii. add to **43**, THF, -78 °C to 0 °C, 25 min, 76%.

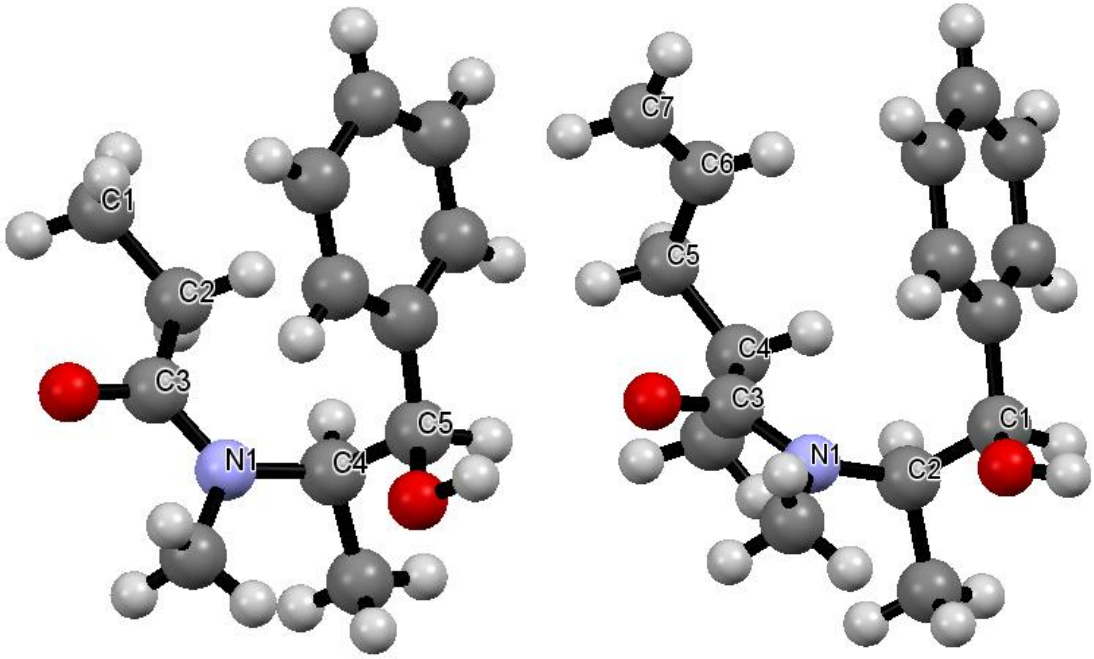


Figure 3.8: X-Ray single crystal structure of pseudoephedrine amides **42** (left) and **43** (right) (numbering of atoms is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue)).

[34] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.

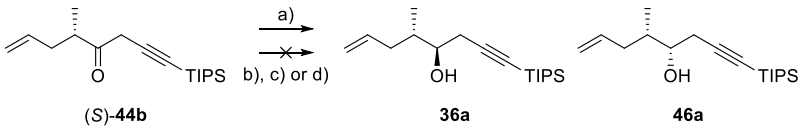
The nucleophilic displacement of such an auxiliary has been previously described for different alkyllithium reagents on pseudoephedrine amides such as **43**. Therefore, we envisioned obtaining homopropargylic ketone (*S*)-**44a** by the displacement of the auxiliary by lithiated TMS-capped propyne according to a procedure reported by Corey *et al.* (Scheme 3.5).[35] The authors stated that they observed only small amounts of an allene species. Unfortunately, in our case we isolated an inseparable mixture (ca. 1:1) of TMS-capped homopropargylic ketone (*S*)-**44a** and allenyl ketone (*S*)-**45**.

We circumvented this problem by using lithiated TIPS-capped propyne for the addition, following another protocol by Corey *et al.*[36] where they reported no detection of the allene species. Indeed, we were able to directly obtain homopropargylic ketone (*S*)-**44b** in 76% yield without allene (*S*)-**45** being formed. Experimentally, double addition was not observed, which might be explained in analogy to Weinreb amides.[37]

3.3.1.1.2. Ketone Reduction

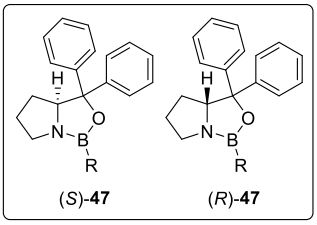
We sought to reduce homopropargylic ketone (*S*)-**44b** to secondary alcohol **36a**. Three methods were selected for a more detailed screening: Corey-Bakshi-Shibata reduction (CBS), Midland´s Alpine® borane, and Noyori reduction (Scheme 3.6). First, we tried to apply different CBS catalyst systems in analogy to procedures by Trost *et al.*[38] (TMS-capped homopropargylic ketone) and Scheidt *et al.*[39] (α-methyl-substituted ketone, Scheme 3.6). This resulted in the formation of secondary alcohols **36a** and **46a** in diastereomeric ratios ranging from 2:1 to 1:3.6, with roughly 10-30% of unreacted starting material (*S*)-**44b**. According to these results, both diastereomers **36a** and **46a** were accessible with moderate selectivity, but conversion and yield were unsatisfactory.

[35] E. J. Corey, H. A. Kirst, *Tetrahedron Lett.* **1968**, *9*, 5041-5043.
[36] E. J. Corey, C. Rücker, *Tetrahedron Lett.* **1982**, *23*, 719-722.
[37] S. Nahm, S. M. Weinreb, *Tetrahedron Lett.* **1981**, *22*, 3815-3818.
[38] B. M. Trost, H. Yang, G. Dong, *Chem. Eur. J.* **2011**, *17*, 9789-9805.
[39] E. A. Crane, T. P. Zabawa, R. L. Farmer, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2011**, *50*, 9112-9115.



(*S*)-**44b** **36a** **46a**

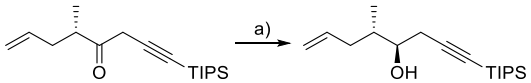
CBS catalyst		recovered SM (*S*)-**44b**	yield **36a**	yield **46a**	*d.r.* (isolated)
R = CH_3	(*S*)-**47a**	27%	45%	23%	1.9:1
	(*R*)-**47a**	24%	20%	50%	1:2.5
R = *o*-Tol	(*S*)-**47b**	23%	40%	24%	1.7:1
	(*R*)-**47b**	34%	11%	40%	1:3.6
R = *n*-Bu	(*S*)-**47c**	7%	35%	26%	1.3:1



(*S*)-**47** (*R*)-**47**

Scheme 3.6: Screening of different reduction methods. Reagents and conditions: (a) 1.5 eq. CatBH, 5 mol% CBS catalyst **47** (see table), DCM, -78°C to 5 °C, 21.5 h, yields shown; (b) 4 eq. (*R*)- or (*S*)-Midland Alpine® borane, THF, rt, 72 h, SM (*S*)-**44b** recovered (99%); (c) H_2 (balloon), 1 mol% $RuCl_2$[(*R*)-DM-BINAP][(*R*)-DAIPEN], 3 mol% KO*t*-Bu, *i*-PrOH, SM (*S*)-**44b** recovered (80%), (d) 1 mol% RuCl(*p*-cymen)[(*S*,*S*)-Ts-DPEN], i-PrOH, rt, 2 d, no reaction.

The reduction of aliphatic, sterically encumbered ketones with Midland´s Alpine® borane was demonstrated by Brown *et al.*[40] and applied to the total synthesis of macrodiolide tartrolon B by Mulzer *et al.*[41] Neither Alpine® borane enantiomer reacted with (*S*)-**44b** to form the diastereomeric products **36a** or **46a** (Scheme 3.6), and the starting material (*S*)-**44b** was fully recovered. Furthermore, a classical Noyori reduction/transfer hydrogenation[42] did not result in the formation of alcohols **36a** and **46a** (Scheme 3.6).



(*S*)-**44b** **36a**

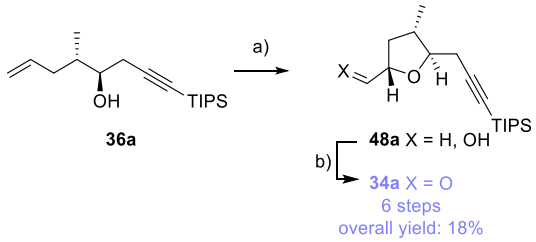
Scheme 3.7: Synthesis of 2,5-*trans*-disubstituted ether **34a**, part B. Reagents and conditions: (a) 6 mol% (*S*)-methyl-CBS-oxazaborolidine (*S*)-**47a**, 2 eq. CatBH, DCM, -78 °C to 0 °C, 22 h, 70% (*d.r.* = 2.9:1).

Based on these results, we chose to use CBS catalyst (*S*)-**47a** to reduce ketone (*S*)-**44b** on gram scale (Scheme 3.7). Fortunately, we found that an increased reaction time and an excess of borane solution led to an improved 70% yield and resulted in a better diastereoselectivity (*d.r.* = 2.9:1). Therefore, no further investigations were deemed necessary.

[40] H. C. Brown, G. G. Pai, *J. Org. Chem.* **1985**, *50*, 1384-1394.
[41] J. Mulzer, M. Berger, *J. Org. Chem.* **2004**, *69*, 891-898.
[42] C. A. Sandoval, Y. Li, K. Ding, R. Noyori, *Chem. Asian J.* **2008**, *3*, 1801-1810.

3.3.1.1.3. The Mukaiyama Cyclization & Beyond

After establishing a successful approach to alcohol **36a**, we investigated the oxidative Mukaiyama cyclization to give the 2,5-*trans*-disubstituted ether **48a** (Scheme 3.8). In 1990, Mukaiyama *et al.*[43] showed that 2,5-*trans*-disubstituted tetrahydrofuran rings can be obtained under cobalt catalysis from bis-homoallylic alcohols such as **36a** (for an overview see Ph.D. thesis of G. Phillips[44]).



Scheme 3.8: Synthesis of 2,5-*trans*-disubstituted ether **34a**, part C. Reagents and conditions: (a) 10 mol% [Co(nmp)$_2$] **49b**, 10 mol% *t*-BuOOH, O_2 (balloon), *i*-PrOH, 55 °C, 15 h, 68%; (b) i. SO_3·py, DMSO, DCM, -20 °C, 2.5 h; ii. DIPEA, 75%, product **34a** obtained as a solution in DCM, which was directly used for alkynylation.

This methodology has been extensively used for challenging substrates. Notable examples include the fragment synthesis of amphidinolide C by Pagenkopf *et al.*[45] in 2011 and the total synthesis of amphidinolide F in 2013 by our group.[46] The design of new catalyst systems by Hartung *et al.*[47] and Pagenkopf *et al.*[48] made this cyclization even more valuable, with improved yields and simplified purifications (Figure 3.9).

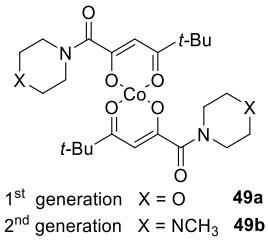


Figure 3.9: 1st and 2nd generation of the Mukaiyama catalyst **49**.

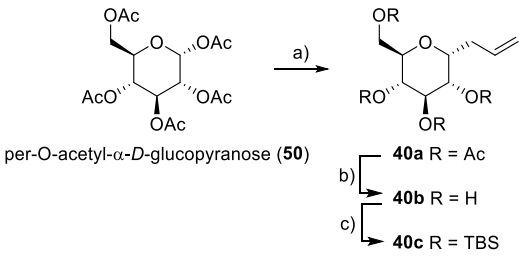
To our delight, this oxidative cyclization indeed led to the 2,5-*trans*-disubstituted ether **48a** in 68% yield (Scheme 3.8).[49] Final Parikh-Doering oxidation[50] of alcohol **48a** yielded the corresponding aldehyde **34a** as the completed northern building block. In summary, aldehyde **34a** was obtained in six steps with an overall yield of 18%; it was not purified but used directly for the fragment coupling via alkynylation.

[43] S. Inoki, T. Mukaiyama, *Chem. Lett.* **1990**, *19*, 67-70.
[44] G. A. Phillips, *Ph.D. Thesis* **2014**, *The University of Western Ontario, Canada*.
[45] N. A. Morra, B. L. Pagenkopf, *Org. Lett.* **2011**, *13*, 572-575.
[46] G. Valot, C. S. Regens, D. P. O'Malley, E. Godineau, H. Takikawa, A. Fürstner, *Angew. Chem. Int. Ed.* **2013**, *52*, 9534-9538.
[47] B. Menendez Perez, D. Schuch, J. Hartung, *Org. Biomol. Chem.* **2008**, *6*, 3532-3541.
[48] C. Palmer, N. A. Morra, A. C. Stevens, B. Bajtos, B. P. Machin, B. L. Pagenkopf, *Org. Lett.* **2009**, *11*, 5614-5617.
[49] A supply of catalyst **49b** for the Mukaiyama cyclization was kindly provided by Dr. M. Ilg.
[50] See footnote 46.

3.3.1.2. The Sugar-Based Alkyne

3.3.1.2.1. Anomeric Allylation & Protecting Group Manipulations

As the sugar-based building block **35** has the same stereochemical configuration as α-*D*-glucose (**9**) (Scheme 3.2), we started its synthesis from the commercially available per-*O*-acetyl derivative **50** (Scheme 3.9). Allylation of **50** was performed with allyl-TMS (**52**) under Lewis acid catalysis as reported by Parkan *et al.*[51] (72% with boron trifluoride diethyletherate), by Deming *et al.*[52] (81% with TMSOTf) and by others[53] (in lower yields). Alkene **40a** was obtained in a comparably good yield and with good stereoselectivity (*d.r.* = 7:1) in favour of the desired α-anomer (X-Ray crystal structure shown in Figure 3.10).



Scheme 3.9: Synthesis of the sugar-based alkyne **35**, Part A. Reagents and conditions: (a) allyl-TMS (**52**), $BF_3{\cdot}OEt_2$, MeCN, rt to 80 °C, 23 h, 79% (α:β = 7:1); (b) 10 mol% NaOEt, MeOH, rt, 4 h, 98%; (c) TBSCl, $AgNO_3$, py, DMF, rt, 16 h, 87%.

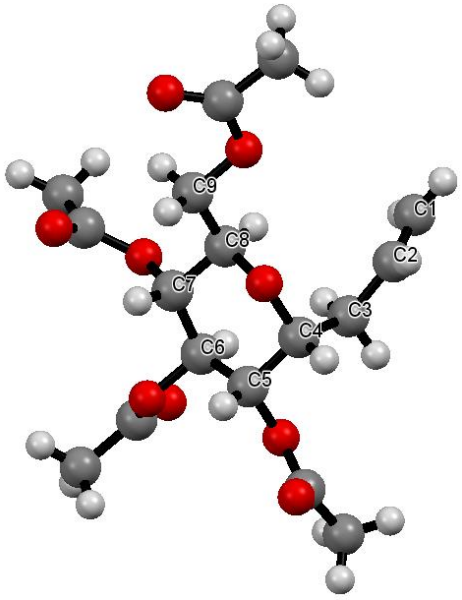
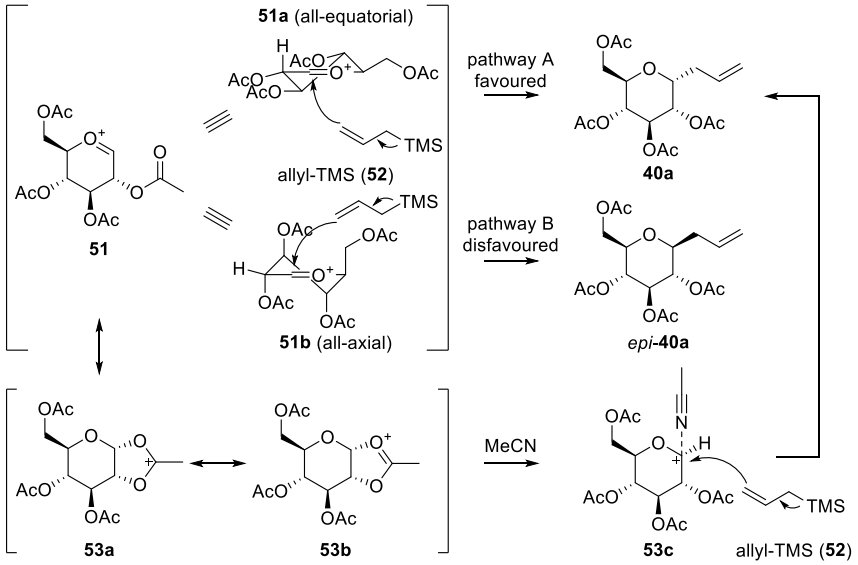


Figure 3.10: X-Ray single crystal structure of alkene **40a** (numbering of atoms is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red)).

[51] K. Parkan, L. Werner, Z. Lövyová, E. Prchalová, L. Kniežo, *Carbohydr. Res.* **2010**, *345*, 352-362.
[52] J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2012**, *134*, 4112-4115.
[53] a) P. Arya, A. Barkley, K. D. Randell, *J. Comb. Chem.* **2002**, *4*, 193-198. b) D. Horton, T. Miyake, *Carbohydr. Res.* **1988**, *184*, 221-229. c) G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730. d) J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.

Mechanistically, the Lewis acid promotes the cleavage of the anomeric functional group and leads to the formation of an oxonium ion **51** (Scheme 3.10). This oxonium ion **51** can then react with an allyl anion equivalent (allyl-TMS (**52**)) in two possible conformations while respecting the *trans*-diaxial effect, also referred to as the Fürst-Plattner rule.[54] If all substituents on the tetrahydropyran ring stand equatorial (**51a**), nucleophilic attack of the allyl anion *trans* to the C2' hydrogen can proceed unhindered giving α-anomer **40a**. If all substituents are axial (**51b**), the attack proceeds *trans* to the acetyl group at C2' under steric repulsion leading to β-anomer **53**. Regarding the 1,3-diaxial repulsions of the acetyl substituents, pathway A seems to be preferred and agrees with the experimental observations.



Scheme 3.10: Mechanistic explanation via the Fürst-Plattner rule (*trans*-diaxial effect) and via the interplay of the anchimeric effect (neighboring group participation) with the solvent effect.

Furthermore, in analogy to other glycosylation reactions[55] an interplay of the anchimeric effect (also referred to as neighboring group participation) towards **53a**/**53b** and the solvent effect (of acetonitrile) via **53c** is conceivable.[56] This double inversion could as well explain the formation of the thermodynamically preferred product **40a**. However, this remains an issue of current debate. This theory is supported by the observation that the use of a less polar solvent like nitromethane inverts the stereochemical outcome of the reaction, as described by Ben *et al*.[57]

[54] A. Fürst, P. A. Plattner, *Helv. Chim. Acta* **1949**, *32*, 275-283.
[55] S. R. R., *Angew. Chem.* **1986**, *98*, 213-236.
[56] a) H. Satoh, H. S. Hansen, S. Manabe, W. F. van Gunsteren, P. H. Hünenberger, *J. Chem. Theory Comput.* **2010**, *6*, 1783-1797. b) S. S. Nigudkar, A. V. Demchenko, *Chem. Sci.* **2015**, *6*, 2687-2704.
[57] R. Y. Tam, S. S. Ferreira, P. Czechura, J. L. Chaytor, R. N. Ben, *J. Am. Chem. Soc.* **2008**, *130*, 17494-17501.

Alkene **40a** was then submitted to a complete deprotection with catalytic sodium ethoxide (10 mol%), according to a procedure by McGarvey *et al.,*[58] which formed the free tetrol **40b** (Scheme 3.9, Figure 3.11). Tetrol **40b** was subsequently submitted to a silver(I) nitrate-promoted global protection with TBSCl, according to a procedure by Kishi *et al.*[59] This resulted in literature known alkene **40c**.[60]

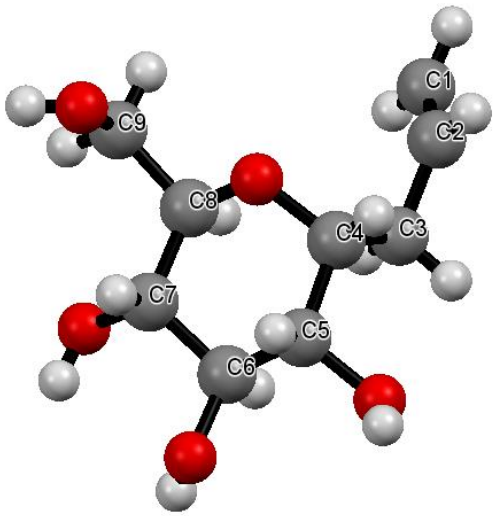
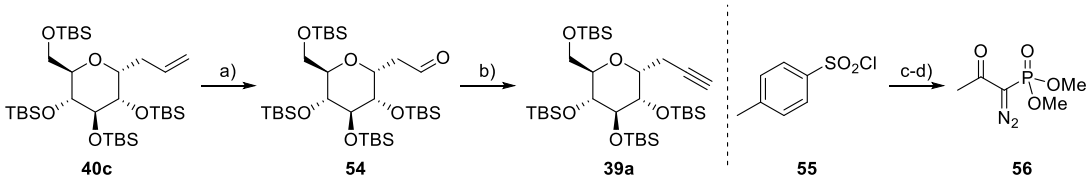


Figure 3.11: X-Ray single crystal structure of alkene **40b** (numbering of atoms is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red)).

[58] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.
[59] Y. Kaburagi, Y. Kishi, *Org. Lett.* **2007**, *9*, 723-726.
[60] See footnote 58.

3.3.1.2.2. Alkene-To-Alkyne-Tranformation

To proceed with the synthesis, a classical ozonolysis of alkene **40c** (in analogy to the procedures by Kishi *et al.*[61] and Nicolaou *et al.*[62] for other hexose derivatives) produced aldehyde **54** in 86% yield (Scheme 3.11). Subsequently, aldehyde **54** was homologated via classical Seyferth-Gilbert conditions with the Ohira-Bestmann reagent **56**. The latter was prepared by a two-step procedure described by Pietruszka *et al.*[63] and others,[64] starting from tosyl chloride **55**.



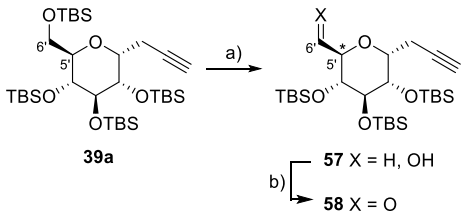
Scheme 3.11: Synthesis of the sugar-based alkyne **35**, Part B. Reagents and conditions: (a) i. O_3, DCM, -78 °C, 8 h; ii. PPh_3 **195a**, DCM, rt, 16 h, 86%; (b) Ohira-Bestmann reagent **56**, K_2CO_3, MeOH, rt, 20 h, 89%; (c) NaN_3, acetone/H_2O (3:1), rt, 2 h 10 min, 98%; (d) dimethyl (2-oxopropyl)phosphonate, NaH, PhMe/THF (7.5:1), 0 °C to rt, 20 h, 86%.

In analogy to the descriptions by Ohira *et al.*,[65] Bestmann *et al.*[66] and Roy *et al.*,[67] the C_1 homologation led to the desired fully TBS-protected alkyne **39a** in 89% yield (Scheme 3.11).

3.3.1.2.3. Selective C6' Manipulation

The synthesis of the C-glucoside **35** continued by the selective cleavage of the C6' TBS group by applying diluted Olah´s reagent (hydrogen fluoride/pyridine) to **39a** following a literature procedure by Murphy *et al.* (Scheme 3.12).[68] After Swern oxidation of the primary alcohol **57** in analogy to a literature procedure by Murai *et al.*,[69] the corresponding aldehyde **58** was obtained in 79% yield (over two steps).

[61] A. Wei, Y. Kishi, *J. Org. Chem.* **1994**, *59*, 88-96.
[62] K. C. Nicolaou, G.-q. Shi, J. L. Gunzner, P. Gärtner, P. A. Wallace, M. A. Ouellette, S. Shi, M. E. Bunnage, K. A. Agrios, C. A. Veale, C.-K. Hwang, J. Hutchinson, C. V. C. Prasad, W. W. Ogilvie, Z. Yang, *Chem. Eur. J.* **1999**, *5*, 628-645.
[63] J. Pietruszka, A. Witt, *Synthesis* **2006**, *24*, 4266-4268.
[64] a) L. Ji, G.-Q. Zhou, C. Qian, X.-Z. Chen, *Eur. J. Org. Chem.* **2014**, *17*, 3622-3636. b) A. Proteau-Gagné, K. Rochon, M. Roy, P.-J. Albert, B. Guérin, L. Gendron, Y. L. Dory, *Biorg. Med. Chem. Lett.* **2013**, *23*, 5267-5269.
[65] S. Ohira, *Synth. Commun.* **1989**, *19*, 561-564.
[66] a) G. J. Roth, B. Liepold, S. G. Müller, H. J. Bestmann, *Synthesis* **2004**, *1*, 59-62. b) S. Müller, B. Liepold, G. J. Roth, H. J. Bestmann, *Synlett* **1996**, *6*, 521-522.
[67] D. Giguère, R. Patnam, M.-A. Bellefleur, C. St-Pierre, S. Sato, R. Roy, *Chem. Commun.* **2006**, *22*, 2379-2381.
[68] G. Anquetin, S. L. Rawe, K. McMahon, E. P. Murphy, P. V. Murphy, *Chem. Eur. J.* **2008**, *14*, 1592-1600.
[69] K. Fujiwaraa, S.-i. Souma, H. Mishima, A. Murai, *Synlett* **2002**, *9*, 1493-1495.



Scheme 3.12: Synthesis of the sugar-based alkyne **35**, Part C. (a) HF·py (12.5%), THF/py (2.5:1), 0 °C to rt, 3 h, 76%; (b) i. $(COCl)_2$, DMSO, DCM, -78°C, 30 min; ii. DIPEA, DCM, -78 °C to rt, 2.5 h, 98%.

During the selective C6' hydroxy deprotection (Figure 3.12), we observed an unexpected epimerization at the C5' stereocentre (Scheme 3.12). The reason remained unclear. Luckily, **57** and *epi*-**57** were easily separable.

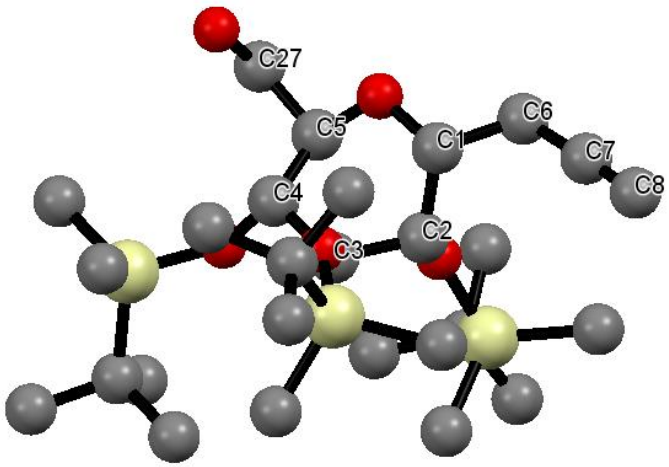
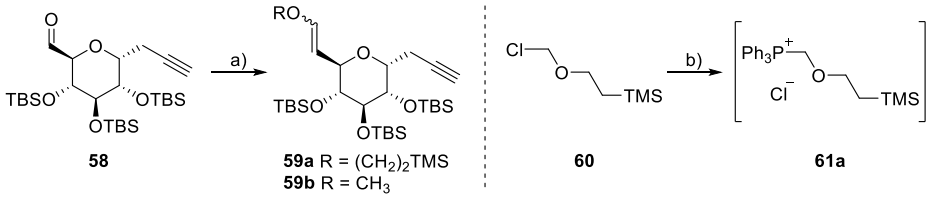


Figure 3.12: X-Ray single crystal structure of primary alcohol **57** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary; colouring of atoms: carbon (grey), oxygen (red), silicon (ivory)).

3.3.1.2.4. Wittig Olefination & E2 Elimination At C4'

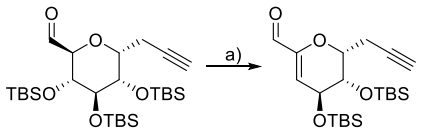
A Swern oxidation of the primary alcohol **57** allowed access to the aldehyde **58**, which was to be a central intermediate to our course (Scheme 3.13).



Scheme 3.13: Synthesis of sugar-based alkyne **35**, Part D. (a) KO*t*-Bu, [R-OCH_2-PPh_3]Cl **61**, 5 Å MS, THF, -50 °C to -78 °C, 2-3.5 h, for R = $(CH_2)_2$TMS (76%), for R = CH_3 (81%), *E*/*Z* mixture not separated; (b) PPh_3 **195a**, PhH, rt to 55 °C, 1 d, 69%.

For the Wittig olefination with commercially available methoxymethyl phosphonium salt **61b**, examples could be found from Takano *et al.*[70] and Kawai *et al.*[71] for sugar-based substrates and from Lazarides *et al.*[72] for tetrahydropyran-based aliphatic aldehydes. Zbiral *et al.* reported a decent example with the TMS-ethoxymethyl phosphonium salt **61a** for a homologation on a steroid core structure.[73] Phosphonium salt **61a** was synthesized from chloromethylether **60**. Both Wittig reactions led to the corresponding enolether **59** as inseparable *E*/*Z* mixtures (Scheme 3.13).

During the first attempts on the performance of the Wittig reaction with aldehyde **58**, we observed the base-driven E2 elimination of the C4' OTBS group to α,β-unsaturated aldehyde **62** (Scheme 3.14).



58 62

Scheme 3.14: Elimination to α,β-unsaturated aldehyde **62**. Reagents and conditions: (a) [Me-OCH_2-PPh_3]Cl **61b**, KO*t*-Bu, THF, -40 °C to -78 °C, 19 h, 85%.

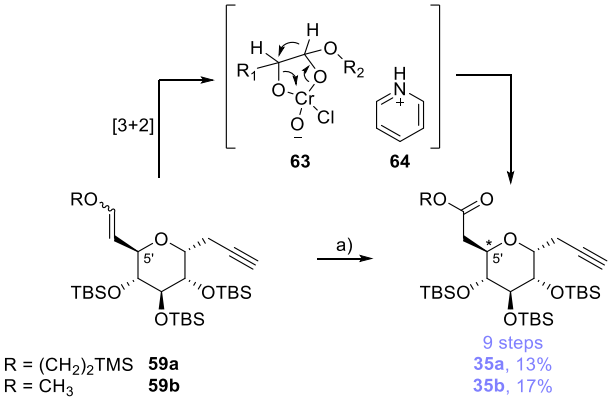
This side reaction could be circumvented by drying the substrate **58** as well as the other reagents (potassium *t*-butoxide and the particular phosphonium salt **61**) over 5 Å molecular sieves as solutions/suspensions in toluene prior to the reaction (Scheme 3.13). In doing so, neither elimination nor epimerization was observed.

3.3.1.2.5. PCC Oxidation & C5'-Epimerization

With enolether **59** in hand, we envisioned the final oxidation to the corresponding ester **35** (Scheme 3.15). The *E*/*Z* mixtures of enolether **59** were subjected to pyridinium chlorochromate (PCC) under literature-known conditions.[74] This reaction is presumed to be mechanistically similiar

[70] S. Hatakeyama, K. Saijo, S. Takano, *Tetrahedron Lett.* **1985**, *26*, 865-868.
[71] A. Kawai, O. Hara, Y. Hamada, T. Shioiri, *Tetrahedron Lett.* **1988**, *29*, 6331-6334.
[72] L. Lazarides, A. S. Smith, R. Stocker, J. C. Theobald, *Patent WO2008101867* **2008**.
[73] K. Schönauer, E. Zbiral, *Liebigs Ann. Chem.* **1983**, *6*, 1031-1042.
[74] a) A. Bianco, A. de Luca, R. Antonio Mazzei, M. Nicoletti, P. Passacantilli, R. Alves De Lima, *Phytochemistry* **1994**, *35*, 1485-1487. b) S. Hatakeyama, K. Saijo, S. Takano, *Tetrahedron Lett.* **1985**, *26*, 865-868.

to the osmium-catalyzed oxidation of alkenes proceeding through a cyclic metallate ester such as **63** after [3+2]-cycloaddition.[75]



Scheme 3.15: Synthesis of the sugar-based alkyne **35**, Part E. Reagents and conditions: (a) PCC, DCM, rt, 2-3 d, for R = $(CH_2)_2$TMS **35a** (68%, d.r. = 2.6:1), for R = CH_3 **35b** (81%, *d.r.* = 3:1).

To our discomfort, partial epimerization at the C5' position once more was observed. Both the desired epimer **35** and its undesired congener *epi*-**35** were isolated (Scheme 3.15, Figure 3.13). Thereby, **35** was accessed in nine steps with an overall yield of 13-17% (referring to each of the ester termini).

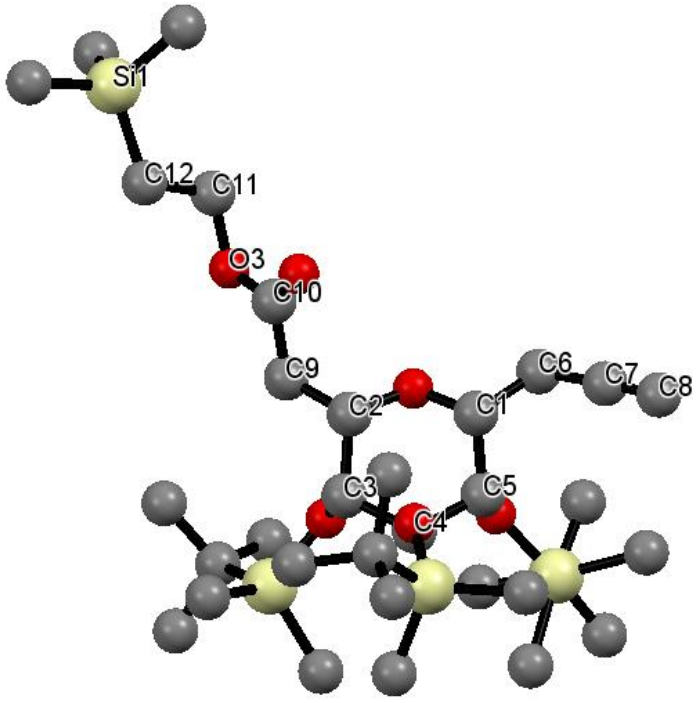
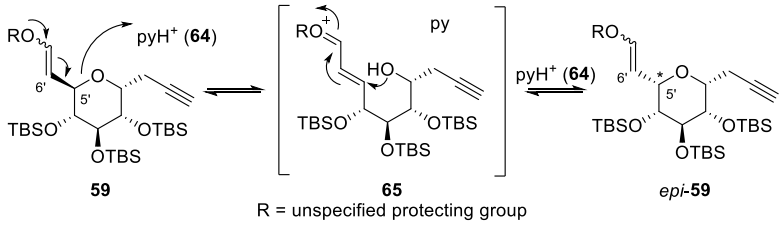


Figure 3.13: X-Ray single crystal structure of ester *epi*-**35a** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary; colouring of atoms: carbon (grey), oxygen (red), silicon (ivory)).

[75] a) G. Piancatelli, A. Scettri, M. D'Auria, *Tetrahedron Lett.* **1977**, *18*, 3483-3484. b) T. D. Michels, M. S. Dowling, C. D. Vanderwal, *Angew. Chem. Int. Ed.* **2012**, *51*, 7572-7576.

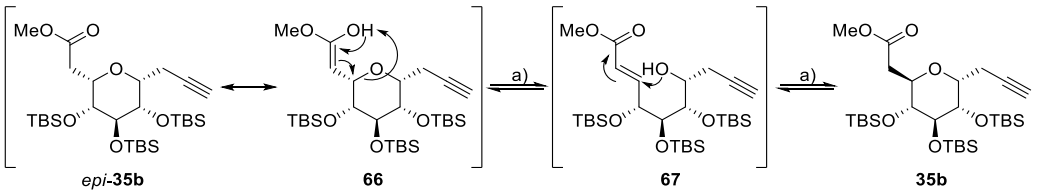
A possible explanation for the epimerization could be the following (Scheme 3.16): by the reaction of enolether **59** with the acidic pyridinium ion **64** present during the reaction, an oxonium ion **65** could be formed. This open chain oxonium species **65** would explain the loss of stereoinformation at the C5' centre, since it is able to recyclize, to give both enolether **59** and *epi*-**59**.



Scheme 3.16: C5' Epimerization occurring during the PCC oxidation of enolether **59** to ester **35**.

To gain further insight into the mechanistic details, we conducted a ^{1}H NMR experiment (Scheme 3.17). Since an *E*/*Z* mixture of **59** would have been difficult to analyze during the course of a reaction, we decided to investigate the less valuable ester *epi*-**35b** instead. Essentially, the observed C5' epimerization could happen either during the oxidation at the stage of the enolether or afterwards with the ester product itself.

For these reasons, pure *epi*-**35b** was treated with TBSOTf in deuterated dichloromethane and the solution was kept at ambient temperature for 4 h (Scheme 3.17). Measurements at different times clearly showed the conversion of *epi*-**35b** into **35b** until an equilibrium was reached. In parallel, however, decomposition ensued. The higher the temperature, the acidity of the medium, or the reaction time, the more epimerization and decomposition were observed.



Scheme 3.17: Epimerization of *epi*-**35b** under Lewis acid catalysis. Reagents and conditions: (a) TBSOTf, CD_2Cl_2, rt, 4 h, NMR tube, result: ca. 1:1 mixture of **35b** and *epi*-**35b** and decomposition.

Based on these observations, we hypothesized that a mechanism took place, which was related to those of either Brønstedt or Lewis acid catalysis (compare Scheme 3.16 vs. Scheme 3.17). Therein, enol tautomer **66** could undergo a ring opening/ring closing sequence via open chain intermediate **67**, giving rise to both ester epimers **35b** and *epi*-**35b**.

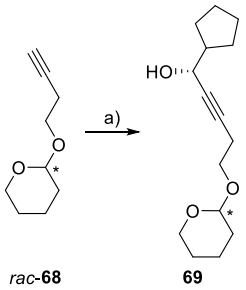
Separation of the observed epimers *epi*-**35** from **35** was possible and the synthesis could proceed.

3.3.1.3. Building Block Coupling & Elaboration

3.3.1.3.1. Preliminary Studies On The Aldehyde Alkynylation

The attempted aldehyde alkynylation involved zinc(II) trifluoromethanesulfonate promotion in the presence of chiral ligands suchs as *N*-methylephedrine. It was originally developed and patented by Carreira *et al.*[76] and used in several total syntheses such as the one of leucascandrolide A.[77] This alkynylation was described for a variety of different substrates such as for silyl-protected alkynes by Yang *et al.*[78] and for alkynyl C-glycosides by Hale *et al.*[79] For 2,5-*trans*-disubstituted tetrahydrofuran ring aldehydes it was previously described by Tanaka *et al.*[80]

Prior to the alkynylation[81] of aldehyde **34** with alkyne **35**, the coupling with simplified model compounds was investigated: racemic alkyne *rac*-**68** was reacted with cyclopentanecarbaldehyde, resulting in the formation of propargylic alcohol **69** in 85% yield as a single diastereomer (Scheme 3.18).

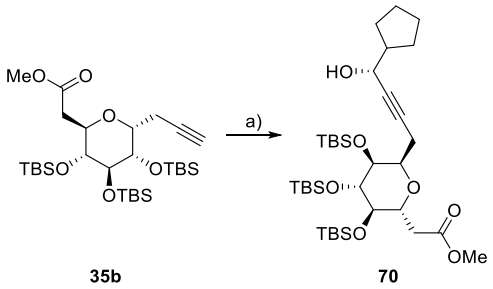


rac-**68** **69**

Scheme 3.18: Alkynylation, preliminiary results, Part A. Reagents and conditions: (a) cyclopentanecarbaldehyde, $Zn(OTf)_2$, (*+*)-NME, TEA, PhMe, rt, 45 h, 85% (only one diasteromer observed).

For propargylic alcohol **70**, the yield dropped slightly (68%), when alkyne **35b** was used for the coupling with cyclopentanecarbaldehyde (again only one diastereomer was observed, Scheme 3.19). In both cases the newly introduced stereocentre was assumed to be of the shown configuration regarding the numerous literature precedents on zinc(II)-mediated alkynylations in the presence of *N*-methylephedrine.

[76] E. M. Carreira, *Patent US2003/0088100* **2003**.
[77] A. Fettes, E. M. Carreira, *J. Org. Chem.* **2003**, *68*, 9274-9283.
[78] X.-W. Chang, D.-W. Zhang, F. Chen, Z.-M. Dong, D. Yang, *Synlett* **2009**, *19*, 3159-3162.
[79] K. J. Hale, Z. Xiong, L. Wang, S. Manaviazar, R. Mackle, *Org. Lett.* **2015**, *17*, 198-201.
[80] a) N. Kojima, Y. Suga, T. Matsumoto, T. Tanaka, A. Akatsuka, T. Yamori, S. Dan, H. Iwasaki, M. Yamashita, *Biorg. Med. Chem.* **2015**, *23*, 1276-1283. b) N. Kojima, N. Maezaki, H. Tominaga, M. Yanai, D. Urabe, T. Tanaka, *Chem. Eur. J.* **2004**, *10*, 672-680. c) N. Kojima, N. Maezaki, H. Tominaga, M. Asai, M. Yanai, T. Tanaka, *Chem. Eur. J.* **2003**, *9*, 4980-4990.
[81] a) See footnote 76. b) See footnote 77.



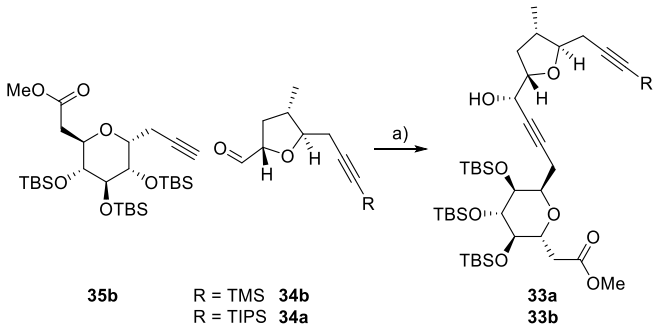
35b 70

Scheme 3.19: Alkynylation, preliminiary results, Part B. Reagents and conditions: (a) cyclopentanecarbaldehyde, $Zn(OTf)_2$, (*+*)-NME, TEA, 4 Å MS, PhMe, rt, 53.5 h, 68%.

Since both test reactions for the fragment coupling were quite promising, the synthesis was pursued as planned.

3.3.1.3.2. Results Of The Fragment Coupling Via Alkynylation

Based on the literature reports, we submitted our fragments to the reaction with zinc(II) trifluoromethanesulfonate, in the presence of (*+*)-*N*-methylephedrine and triethylamine in toluene (Scheme 3.20). Unfortunately, the envisioned zinc-mediated coupling led to the expected products only in 21-25% yield (alkyne starting material **35b** was recovered quantitatively), though the stereoselectivity was very good (*d.r.* > 9.5:1). The reason for the decrease in reactivity remained unclear.



R	time	yield
TMS	70 h	25%
TIPS	71 h	21% (*d.r.* = 9.5:1)

35b R = TMS **34b** R = TIPS **34a** **33a** **33b**

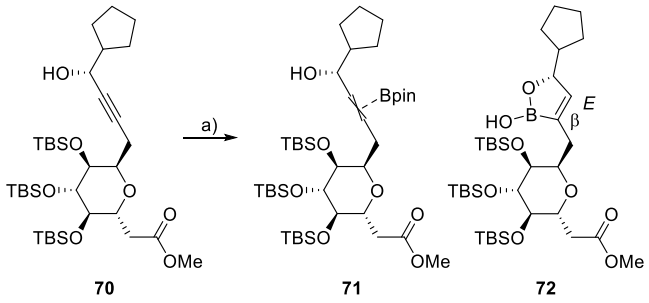
Scheme 3.20: Fragment coupling, Reagents and conditions: (a) $Zn(OTf)_2$, (*+*)-NME, TEA, 4 Å MS, PhMe, rt, yields as shown, alkyne SM **35b** was recovered quantitatively.

Both substrates were predried over 4 Å molecular sieves in toluene and the reaction was carried out in the presence of 4 Å molecular sieves as well, in order to diminish an influence of residual water in the reaction mixture.

Nevertheless, we obtained sufficient amounts (> 100 mg scale) of propargylic alcohol **33** and were able to apply the in house-developed methodology of the ruthenium-catalyzed *trans*-selective hydroelementation of alkynes.

3.3.1.3.3. Alkyne-To-Alkene-Transformation

As demonstrated by our group in 2013, the *trans*-selective hydroboration of internal alkynes under ruthenium catalysis can be a possible entry to *E*-configured alkenes.[82] Based on this precedent, we planned to *trans*-hydroborate propargylic alcohol **70** with pinacolborane (Scheme 3.21). When submitting simplified propargylic alcohol **70** to the literature known conditions, a mixture of borylated products such as **71** was observed. The use of a higher catalyst loading (6 mol% instead of 3 mol%) resulted in a higher conversion, but also in the formation of cyclic boronic acid derivative **72** that lost the pinacol ligand, yet beared an *E*-configured double bond within its five-membered ring.



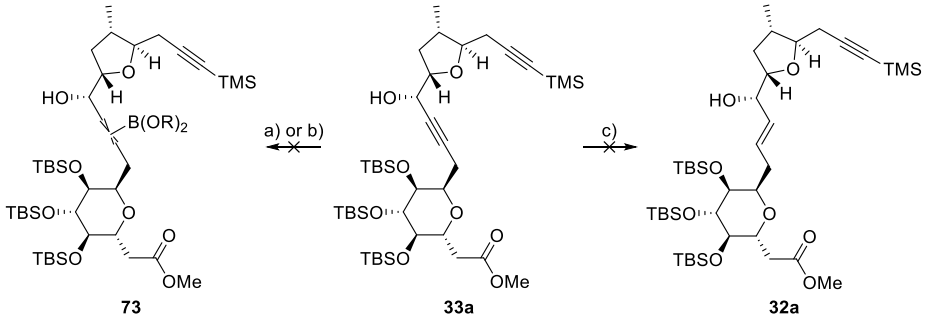
cat. loading	HBpin	time	recovered SM **70**	yield **71**	yield **72**
3 mol-%	1.2 eq.	18 h	40%	51%	-
6 mol-%	2.4 eq.	24 h	10%	8%	67%

Scheme 3.21: *trans*-Hydroboration. Reagents and conditions: (a) $[Cp^*Ru(MeCN)_3]PF_6$, 2.4 eq. HBpin, DCM, 0 °C to rt, catalyst loading and yield as shown.

With these results in hand, the formation of the *E*-configured allylic alcohol **32** by using the ruthenium-catalyzed *trans*-hydroboration seemed possible regarding the high degree of functionalization of the sugar core.

[82] B. Sundararaju, A. Fürstner, *Angew. Chem.* **2013**, *125*, 14300-14304.

In contrast, the results with bis-alkyne substrate **33a** were inconclusive due to the formation of many products and massive decomposition (Scheme 3.22). The use of another borane (4,6,6-trimethyl-1,3,2-dioxaborinane) led to similiar results. Therefore, no further investigations on the *trans*-selective hydroboration were conducted.

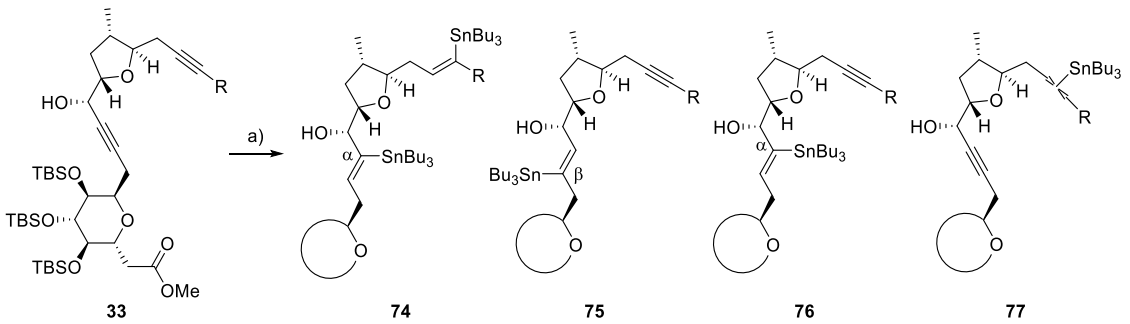


Scheme 3.22: *trans*-Hydroboration and reduction of bis-alkyne **33a**. Reagents and conditions: (a) 2.05-4.8 eq. HBpin, 15-20 mol% $[Cp^*Ru(MeCN)_3]PF_6$, DCM, -40 °C to rt, 22-25.5 h, decomposition; (b) 2.05 eq. 4,6,6-trimethyl-1,3,2-dioxaborinane, 29 mol% $[Cp^*Ru(MeCN)_3]PF_6$, DCM, 0 °C to rt, 21 h, decomposition; (c) 6 eq. Red-Al®, THF, -78 °C to 0 °C, decomposition.

Trost *et al.* previously reported the selective transformation of propargylic alcohols into their allylic alcohol counterparts in the presence of another TMS-capped terminal alkyne with Red-Al® (sodium bis(2-methoxyethoxy)aluminium hydride).[83] According to a publication by Koide *et al.*,[84] the reduction of propargylic alcohols to the corresponding allylic derivatives by Red-Al® is possible also in the presence of a methyl ester. However, administered Red-Al® led to the decomposition of the elaborated substrate **33a** (Scheme 3.22).

As previously shown by our group,[85] the ruthenium-catalyzed *trans*-hydrostannation of propargylic alcohols can be a viable method for the transformation into the corresponding allylic alcohols. Therefore, propargylic alcohol **33** was submitted to the conditions of such a ruthenium-catalyzed *trans*-selective hydrostannation (Scheme 3.23).[86]

[83] B. M. Trost, H. C. Shen, T. Schulz, C. Koradin, H. Schirok, *Org. Lett.* **2003**, *5*, 4149-4151.
[84] C. T. Meta, K. Koide, *Org. Lett.* **2004**, *6*, 1785-1787.
[85] a) S. M. Rummelt, A. Fürstner, *Angew. Chem. Int. Ed.* **2014**, *53*, 3626-3630. b) S. M. Rummelt, K. Radkowski, D.-A. Roşca, A. Fürstner, *J. Am. Chem. Soc.* **2015**, *137*, 5506-5519. c) S. M. Rummelt, J. Preindl, H. Sommer, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 6241-6245.
[86] Both polymeric catalyst $[Cp^*RuCl_2]_n$ and tetrameric catalyst $[Cp^*RuCl]_4$ were kindly provided by either laboratory assistant K. Radkowski, by Dr. D. Roşca or Dr. S. Rummelt.



R	conditions	temperature	time	yield **74**	yield **75**	yield **76**	yield **77**	recovered SM **33**
TMS	5 mol-% $[Cp^*RuCl_2]_n$ 1.15 eq. *n*-Bu_3SnH, DCM	rt	1 h	15%	3%	22%	16%	19%
	30 mol-% $[Cp^*RuCl_2]_n$ 1.4 eq. *n*-Bu_3SnH, pentane	rt	2 h	3%	-	-	-	47%
	5 mol-% $[Cp^*RuCl]_4$ 1.05 eq. *n*-Bu_3SnH, pentane	rt	2 h	7%	-	-	-	44%
	10 mol-% $[Cp^*RuCl_2]_n$ 2.1 eq. *n*-Bu_3SnH, DCM	-78 °C to rt	5 d	-	-	-	-	80%
TIPS	10 mol-% $[Cp^*RuCl_2]_n$ 1.1 eq. *n*-Bu_3SnH, pentane 4 Å MS	rt	1 h	-	38%		-	46%
		rt	1.5 h	-	42%		-	45%
		rt	2.5 h	-	45%		-	52%

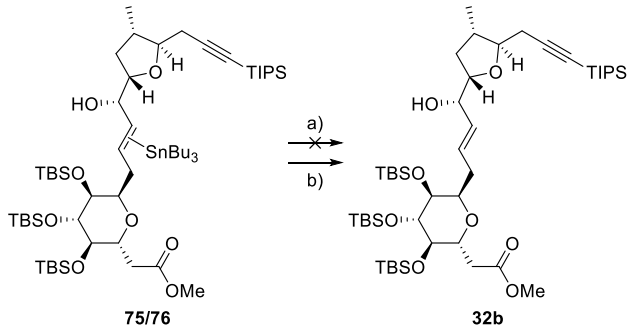
Scheme 3.23: Hydrostannation of bis-alkyne **33**. Reagents and conditions as shown.

Unfortunately, TMS-capped substrate **33a** led to a mixture of regioisomeric products, such as the bis-stannylated product **74a**, as well as to α- and β-isomers on both alkynes (**76a**, **75a** and **77a**), which could be separated; the TMS group did not prevent a reaction at its terminal alkyne site. In the case of the much bulkier TIPS-capped bis-alkyne **33b** however, a reaction with tributylstannane was only observed at the internal alkyne site of the molecule. A mixture of α- and β-stannanes **76b** and **75b** was isolated in 44-45% yield. Additionally, starting material **33** could be recovered in the range of 44-52% in both cases (TMS- and TIPS-capped). Neither increasing the catalyst loading (from 5 mol% to 30 mol%) nor adding more equivalents of stannane (1.05-2.1 eq., right from the beginning on or during the course of the reaction) led to a higher conversion. Nevertheless, we were delighted to see that the desired *E*-configured alkenylstannanes **75** and **76** were formed.

One strategy to transform α-hydroxy vinylstannanes into their corresponding allylic alcohols involves the use of copper(I) thiophene-2-carboxylate (CuTC), also used by our group for the total synthesis of 5,6-dihydrocineromycin B.[87] Interestingly, only the β-isomer **75b** was transformed

[87] S. M. Rummelt, J. Preindl, H. Sommer, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 6241-6245.

under these conditions; the reaction however, remained incomplete (Scheme 3.24). Decomposition was observed after the addition of a catalytic amount of acetic acid (5 mol%), but due to a fast work-up most of the α-isomer **76b** could be recovered in ca. 33%.



Scheme 3.24: Protodestannation. Reagents and conditions: (a) i. 6 eq. CuTC, DMF, rt, 29 h; ii. 5 mol% AcOH, 20 h, decomposition, α-stannane **76b** partly recovered (33%); (b) aq. HI (57%), TBAI, PhMe, 0 °C, 5.5 h, 86%.

A bit more daring for this transformation in the presence of silyl-based protecting groups and an ester though, were conditions reported by Shibasaki *et al.*[88] with aqueous hydroiodic acid under phase transfer catalysis (PTC) with tetrabutylammonium iodide (TBAI, Scheme 3.24). This protodestannation with a protic acid in a bisphasic mixture gave the *E*-configured allylic alcohol **32b** in 86% yield.

3.3.1.3.4. Dihydroxylation Strategies & Global Protection

With allylic alcohol **32b** in hand, we investigated the osmium-mediated dihydroxylation to obtain the central triol motif of western belizentrin fragment **28** (Scheme 3.25).

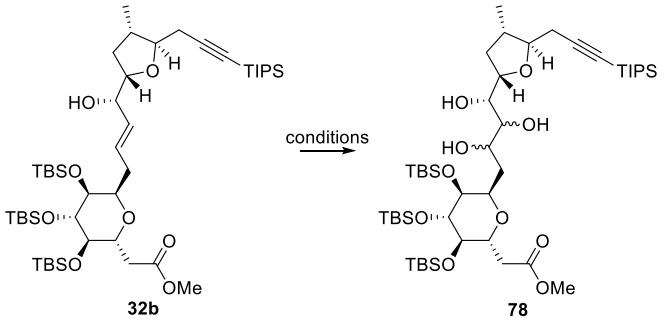
One procedure was the classical ligand-controlled Sharpless dihydroxylation protocol of alkenes, using a catalytic amount of osmate(VI) which is (re)oxidized to osmium(VIII) tetroxide *in situ* by a stoichiometrically added primary oxidant.[89]

In cases of allylic alcohols, where substrate control is inevitable, the empirical stereochemical rule by Kishi *et al.* states that the attack of osmium(VIII) tetroxide proceeds preferentially *trans* to the

[88] M. Mori, N. Kaneta, M. Shibasaki, *J. Organomet. Chem.* **1994**, *464*, 35-40.
[89] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483-2547.

preexisting hydroxy group resulting in a stereochemical outcome which refers to *erythro*.[90] Such a behaviour was for example observed in the total synthesis of palytoxin.[91]

Another procedure, reported by Donohoe *et al.*, makes use of stoichiometric amounts of an OsO_4·TMEDA complex which is capable of inverting the Kishi selectivity by altering the course of the attack (Scheme 3.25).[92] These authors argued that the selectivity changes due to hydrogen bonding of the free hydroxy group to the OsO_4·TMEDA complex. Therefore, the attack of osmium(VIII) tetroxide takes place on the same side as the preinstalled hydroxy group and leads to the *threo* product. Based on these options, we hoped to get access to both diastereomers of triol **78**.



DH	conditions	L* (ligand)	yield	*d.r.* (isolated)
Sharpless	K_2OsO_4 $MeSO_2NH_2$ $K_3[Fe(CN)_6]$, K_2CO_3 *t*-BuOH/H_2O 1:2 0 °C to rt	$(DHQ)_2PHAL$	77%	1:3 [a]
			87%	1:1.2 [b]
			28%	1:2.5 [c]
		$(DHQD)_2PHAL$	58%	1:4.8 [b]
Donohoe	stoich. OsO_4 DCM -78 °C to rt	TMEDA	56%	1:1.3
			87%	1:1.2

[a] 9 mol-% [Os], 24 mol-% L*
[b] 10 mol-% [Os], 25 mol-% L*
[c] 50 mol-% [Os], 100 mol-% L*

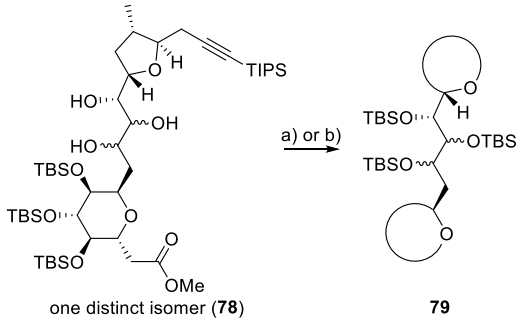
Scheme 3.25: Os-promoted dihydroxylations (Sharpless and Donohoe conditions). Reagents and conditions as shown.

The Sharpless dihydroxylation of allylic alcohol **32b** indeed led to one distinct triol **78a** as the *major* isomer and to **78b** as the *minor* compound with a *d.r.* in the range of 1:1.2 to 1:4.8 (Scheme 3.25). In all cases investigated, substrate control seemed to be a dominant course of action during the dihydroxylation, since different ligands did not change the course of induction.

[90] J. K. Cha, W. J. Christ, Y. Kishi, *Tetrahedron* **1984**, *40*, 2247-2255.
[91] a) E. M. Suh, Y. Kishi, *J. Am. Chem. Soc.* **1994**, *116*, 11205-11206. b) Y. Kishi, *Pure & Appl. Chem.* **1989**, *61*, 313-324.
[92] a) T. J. Donohoe, K. Blades, P. R. Moore, M. J. Waring, J. J. G. Winter, M. Helliwell, N. J. Newcombe, G. Stemp, *J. Org. Chem.* **2002**, *67*, 7946-7956. b) K. Blades, T. J. Donohoe, J. J. G. Winter, G. Stemp, *Tetrahedron Lett.* **2000**, *41*, 4701-4704. c) T. J. Donohoe, R. Garg, P. R. Moore, *Tetrahedron Lett.* **1996**, *37*, 3407-3410. d) T. J. Donohoe, N. J. Newcombe, M. J. Waring, *Tetrahedron Lett.* **1999**, *40*, 6881-6885. e) T. J. Donohoe, P. R. Moore, M. J. Waring, N. J. Newcombe, *Tetrahedron Lett.* **1997**, *38*, 5027-5030. f) T. J. Donohoe, L. Mitchell, M. J. Waring, M. Helliwell, A. Bell, N. J. Newcombe, *Org. Biomol. Chem.* **2003**, *1*, 2173-2186.

Unfortunately, it turned out that the same result was obtained when the Donohoe conditions were applied instead. Again, the same distinct isomer was isolated as the *major* and the other one as the *minor* compound of the dihydroxylation. The absolute configuration of the newly formed hydroxy groups remained unclear and was subsequently examined as shown in the next chapter.

Both diastereomers of triol **78** were reached separately. By protection with TBSOTf in the presence of 2,6-lutidine, according to McGarvey *et al.*[93] and Deming *et al.*[94] (for a simple methylglucoside), **79** was obtained in 73%-quant. yield as the western belizentrin fragment and its diastereomer (Scheme 3.26).



Scheme 3.26: TBS Protection of diastereomeric triols **78**. Reagents and conditions: (a) TBSOTf, 2,6-lutidine, DCM, 0 °C to rt, 24 h, 27%, performed with the *minor* isomer of the dihydroxylation; (b) TBSOTf, 2,6-lutidine, DCM, 0 °C to rt, 17 h, 73%, performed with the *major* isomer of the dihydroxylation.

Due to the low yield of the alkynylation, final TIPS cleavage was never conducted, yet envisioned according to the literature reports describing silver-mediated deprotections of silyl-protected terminal alkynes *e.g.* by Kim *et al.*[95] with silver(I) fluoride or by Carreira *et al.*[96] and Arens *et al.*[97] with silver(I) nitrate.

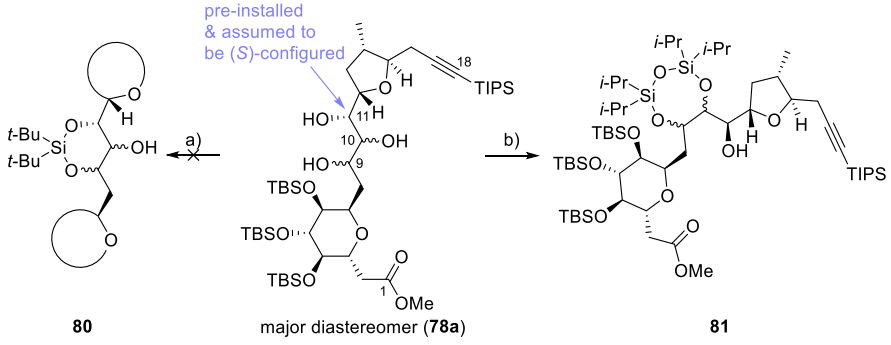
[93] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.
[94] J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.
[95] S. Kim, B. Kim, J. In, *Synthesis* **2009**, *12*, 1963-1968.
[96] E. M. Carreira, J. Du Bois, *J. Am. Chem. Soc.* **1995**, *117*, 8106-8125.
[97] H. M. Schmidt, J. F. Arens, *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1138-1142.

3.3.1.4. Stereochemical Elucidation & Cyclization Trials

In order to determine the stereochemical outcome of the dihydroxylation (Scheme 3.25), it was planned to derive the absolute configuration of the newly formed stereocentres at C-9 and C-10 via NMR analysis.

For such a NMR-based approach, it was necessary to cyclize one of the hydroxy groups formed during the dihydroxylation with the one at C-11, originating from the alkynylation (Scheme 3.27). The absolute configuration of the latter was assigned based on the tremendous amount of literature examples showing the reliability of this method in terms of stereocontrol. Therefore, the hydroxy groups were assumed to be (*R*)-configured for **69** and **70**, and (*S*)-configured for **33** due to the use of (*+*)-*N*-methylephedrine in these reactions (Scheme 3.20).[98] Based on this assumption for the configuration of C-11, its relative configuration to the other two stereocentres at C-9 and C-10 was investigated.

The *major* triol isomer **78a** was submitted to di-*t*-butyldichlorosilane in an attempt to synthesize siloxane **80**, but this reagent turned out to be sterically too hindered to react at all (Scheme 3.27). Therefore, sterically less hindered di-*i*-propyldichlorosilane was administered to *major* triol isomer **78a**, which resulted in a cyclized product. Unfortunately, this cyclization gave only siloxane **81**, in which both hydroxy groups introduced via the dihydroxylation (at C-9 and C-10) were part of a newly formed 7-membered ring. Regarding this particular attachment and the flexibility of the 7-membered ring, this compound was not suitable for a stereochemical analysis by NMR.

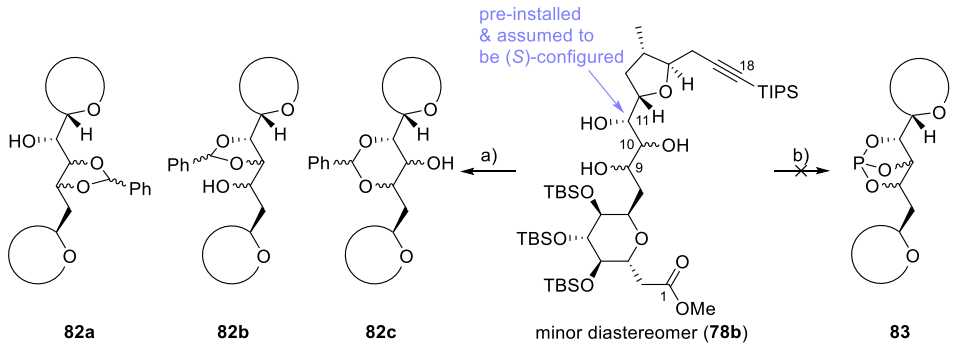


Scheme 3.27: Triol cyclization, part A. Reagents and conditions: (a) 2.4 eq. $(t\text{-Bu})_2SiCl_2$, 2 eq. $AgNO_3$, 10 eq. im, DMF, rt, 2 d, no reaction observed; (b) $(i\text{-Pr})_2SiCl_2$, $AgNO_3$, im, DMF, rt, 2 d, 32%.

Since these attempts remained unsuccessful, other cyclization methods such as acetalization and phosphorylation were applied (Scheme 3.28). 1,3-Acetalizations are either used as protecting

[98] a) E. M. Carreira, *Patent US2003/0088100* **2003**. b) A. Fettes, E. M. Carreira, *J. Org. Chem.* **2003**, *68*, 9274-9283.

groups or for structural elucidation purposes.[99] Acetalization of the *minor* triol isomer **78b** resulted in the formation of no less than six regio- and stereoisomers such as **82**.



Scheme 3.28: Triol cyclization, part B. Reagents and conditions: (a) 1.2 eq. Ph-CH(OMe)$_2$, 20 mol% CSA, DCM, rt, 17 h, minimum 6 different isomers observed on TLC, not separated or isolated; (b) 1.05 eq. P(NMe$_2$)$_3$ (HMTP), 1,4-dioxane, 90-100 °C, 4 d, no reaction observed.

Alternatively, the synthesis of tricyclic phosphite **83** was examined (Scheme 3.28). A method to obtain such fused and strained polycyclic systems was published by Nifantyev *et al.*[100] and was applied to *minor* triol isomer **78b.** Unfortunately, with tris(dimethylamino)phosphine (HMPT) no reaction was observed under the reported conditions.

These results clearly showed the difficulty of determining the absolute configuration of the stereocentres in question. Further attempts for the stereochemical determination by derivatization were not performed due to the lack of material at this stage of the synthesis.

[99] a) C. Cai, J. Liu, Y. Du, R. J. Linhardt, *J. Org. Chem.* **2010**, *75*, 5754-5756. b) K. Tatsuta, M. Kitagawa, T. Horiuchi, K. Tsuchiya, N. Shimada, *J. Antibiot.* **1995**, *48*, 741-744. c) H. Takamura, H. Wada, M. Ogino, T. Kikuchi, I. Kadota, D. Uemura, *J. Org. Chem.* **2015**, *80*, 3111-3123. d) V. Navickas, M. E. Maier, *Tetrahedron* **2010**, *66*, 94-101.

[100] a) M. P. Koroteev, S. A. Lysenko, N. M. Pugashova, A. M. Il´inets, É. E. Nifant´ev, *Russ. J. Gen. Chem.* **1989**, *59*, 2116-2123. b) E. E. Nifantyev, A. M. Koroteev, M. P. Koroteev, S. V. Meshkov, V. K. Belsky, A. R. Bekker, *Phosphorus, Sulfur Silicon Relat. Elem.* **1996**, *113*, 1-13. c) A. M. Koroteev, M. P. Koroteev, A. R. Bekker, V. K. Belskii, E. E. Nifantyev, *Phosphorus, Sulfur Silicon Relat. Elem.* **1996**, *111*, 168-168.

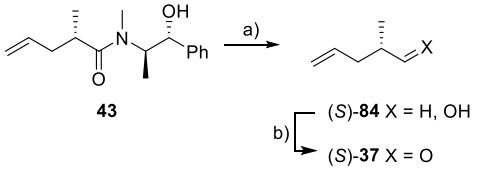
3.3.2. Investigations On Alternative Pathways

3.3.2.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

Alternative pathways towards the 2,5-*trans*-disubstituted ether **34** included key steps similiar to the ones of the successful route described earlier (Chapter 3.3.1.1). Differences mostly appeared in the preparation of the starting materials as well as in the substitution pattern of the alkynyl side chain.

3.3.2.1.1. Auxiliary Reduction & Alternative Alkyne Substitution

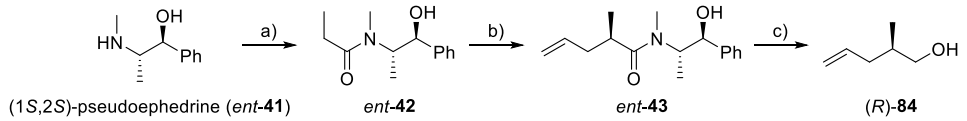
We first envisioned a synthesis of northern building block **34** by starting similarly with the known pseudoephedrine amide **43** (Scheme 3.29). In contrast to the auxiliary displacement with a nucleophile (Chapter 3.3.1.1.1), volatile alcohol (*S*)-**84** was obtained by a reductive cleavage of the auxiliary with lithium amidoborane.[101] Subsequent Swern oxidation led to very volatile aldehyde (*S*)-**37**.[102] Both steps were performed according to the reported two-step procedure by De Brabander *et al.*[103]



Scheme 3.29: Synthesis of the 2,5-*trans*-disubstituted ether **34b**, part A. Reagents and conditions: (a) i. DIPA, *n*-BuLi, THF, 0 °C, 10 min ; ii. $NH_3 \cdot BH_3$, THF, 0 °C to rt, 1 h; iii. add **43**, THF, 0 °C to rt, 2 h, 91%, 99%*ee*; (b) i. $(COCl)_2$, DMSO, DCM, -78 °C, 35 min; ii. DIPEA, -78 °C to rt, 1.5 h, 97% (as a solution in MTBE).

In order to determine the enantiomeric excess (*ee*) of (*S*)-**84**, it was necessary to prepare the enantiomeric alcohol (*R*)-**84** in an analogous fashion starting with commercially available (1*S*,2*S*)-pseudoephedrine *ent*-**41** (Scheme 3.30, Figure 3.14).[104] GC on chiral stationary phase was used for the determination of the *ee*, reporting values of 98-99%.[105]

[101] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.
[102] N.-H. Lin, L. E. Overman, M. H. Rabinowitz, L. A. Robinson, M. J. Sharp, J. Zablocki, *J. Am. Chem. Soc.* **1996**, *118*, 9062-9072.
[103] S. Lebreton, J. Jaunbergs, M. G. Roth, D. A. Ferguson, J. K. De Brabander, *Biorg. Med. Chem. Lett.* **2008**, *18*, 5879-5883.
[104] a) See footnote 101. b) A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511. c) See footnote 103.
[105] The calibration was performed with the racemate *rac*-**84**.



Scheme 3.30: Synthesis of enantiomeric alcohol *ent*-**78**. Reagents and conditions: (a) propionic anhydride, TEA, DCM, rt, 1 h 10 min, 89%; (b) i. DIPA, *n*-BuLi, LiCl, THF, 0 °C to rt, 35 min, then *ent*-**42**, -78 °C to 0 °C, 1.5 h; ii. allyl iodide, THF, -78 °C to 0 °C, 2 h, 64%; (c) i. DIPA, *n*-BuLi, THF, 0 °C to rt; ii. $NH_3 \cdot BH_3$, 0 °C to rt, 1 h; iii. add *ent*-**43**, THF, 0 °C to rt, 2 h, 80%, 98%*ee*; (d) $(COCl)_2$, DMSO, DIPEA, DCM, 2 h, -78 °C to rt.

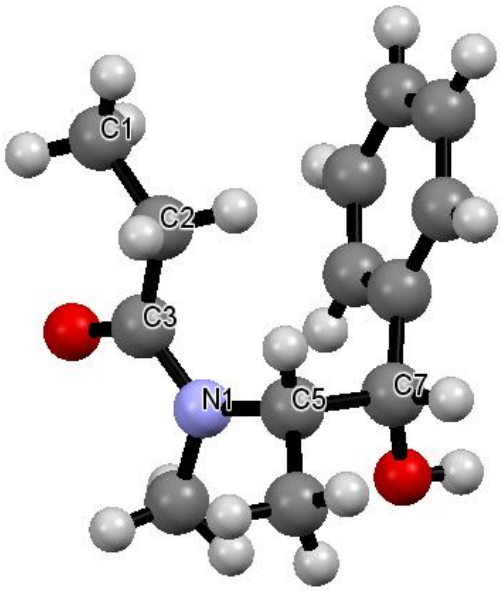
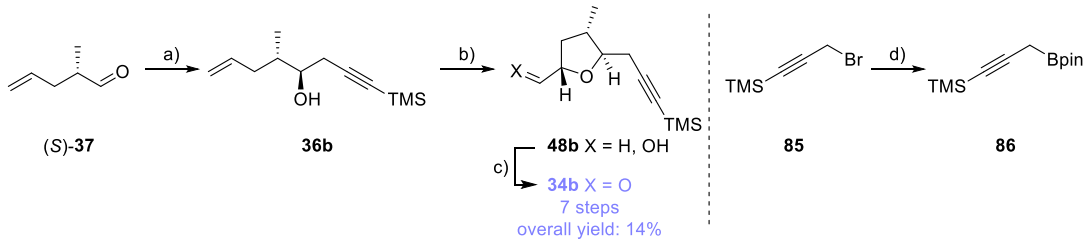


Figure 3.14: X-Ray single crystal structure of pseudoephedrine amide *ent*-**42** (numbering of atoms is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue)).

Enantiomerically pure aldehyde (*S*)-**37** was then submitted to a propargylation reported by Fandrick *et al.* (Scheme 3.31).[106] This reaction was conducted with TMS-capped pinacolborane **86**, which was synthesized according to a procedure by Hoffmann *et al.*[107]



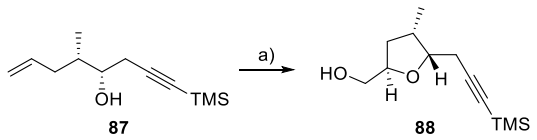
Scheme 3.31: Synthesis of the 2,5-*trans*-disubstituted ether **34b**, part B. Reagents and conditions: (a) TMS-propargyl pinacolborane **86**, 20 mol% Et_2Zn, 4 Å MS, THF, PhMe, rt, 19 h, 83% (*d.r.* = 1.2:1); (b) 10 mol% $[Co(nmp)_2]$ **49b**, 10 mol% *t*-BuOOH, O_2 (balloon), *i*-PrOH, rt to 55 °C, 15.5 h, 62%; (c) i. $SO_3 \cdot$py, DMSO, DCM, -20 °C, 25 min; ii. DIPEA, 2 h, 61%, product obtained as a solution in DCM, directly used for alkynylation; (d) i. Mg turnings, I_2, Et_2O, rt to -5 °C, 5.5 h; ii. *i*-propoxy pinacolborane, -70 °C to rt, 16 h, 32%.

[106] D. R. Fandrick, K. R. Fandrick, J. T. Reeves, Z. Tan, C. S. Johnson, H. Lee, J. J. Song, N. K. Yee, C. H. Senanayake, *Org. Lett.* **2010**, *12*, 88-91.

[107] a) R. W. Hoffmann, H. Brinkmann, G. Frenking, *Chem. Ber.* **1990**, *123*, 2387-2394. b) A first supply of pinacolborane **86** was kindly provided by Dr. M.-A. Müller.

Bis-homoallylic alcohol **36b** was obtained with a *d.r.* of 1.2:1 (Scheme 3.31). After separation of the diastereomers, alcohol **36b** was submitted to the previously described aerobic oxidative Mukaiyama cyclization,[108] resulting in the formation of 2,5-*trans*-disubstituted ether **48b**. This primary alcohol **48b** was subsequently transformed to the corresponding aldehyde **34b** by Parikh-Doering oxidation.[109] In summary, aldehyde **34b** was obtained in seven steps with an overall yield of 14%; it was directly used for the attempted alkynylation as well (Scheme 3.20).

In order to confirm the 2,5-*trans*-configuration of **48b** by NMR comparison, the diastereomeric alcohol **87** was also converted into the corresponding 2,5-*trans*-disubstituted ether **88** by the oxidative Mukaiyama cyclization (Scheme 3.32). By a combination of coupling constant and nOe signal correlation, NMR analysis confirmed the proposed structures of both 2,5-*trans*-disubstituted ether diastereomers **48b** and **88**.



87 **88**

Scheme 3.32: Synthesis of the diastereomeric 2,5-*trans*-disubstituted ether **88**. Reagents and conditions: (a) 10 mol% $[Co(nmp)_2]$ **49b**, 10 mol% *t*-BuOOH, O_2 (balloon), *i*-PrOH, 55 °C, 18.5 h, 76%.

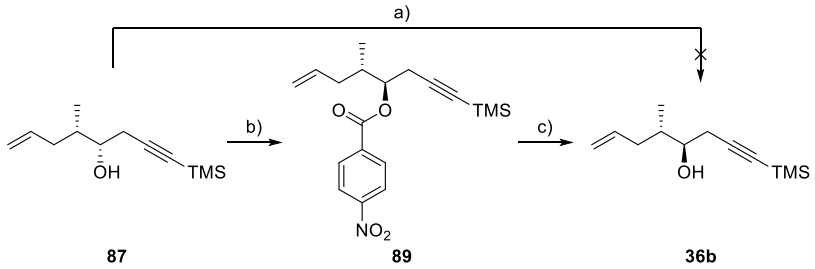
Since the *trans*-selective hydrostannation had resulted in mixtures of stannane products even at the TMS-alkyne site (Chapter 3.3.1.3.3), we chose the TIPS-capped substrate **33b** instead. In terms of step count, yield and manageability (volatile aldehyde (*S*)-**37**) to access TIPS-capped alkyne **34a**, the direct auxiliary displacement proved more practical. Therefore, the route via aldehyde (S)-**37** was not investigated any further.

[108] a) S. Inoki, T. Mukaiyama, *Chem. Lett.* **1990**, *19*, 67-70. b) G. A. Phillips, *Ph.D. Thesis* **2014**, *The University of Western Ontario, Canada*. c) B. Menendez Perez, D. Schuch, J. Hartung, *Org. Biomol. Chem.* **2008**, *6*, 3532-3541. d) C. Palmer, N. A. Morra, A. C. Stevens, B. Bajtos, B. P. Machin, B. L. Pagenkopf, *Org. Lett.* **2009**, *11*, 5614-5617.

[109] G. Valot, C. S. Regens, D. P. O'Malley, E. Godineau, H. Takikawa, A. Fürstner, *Angew. Chem. Int. Ed.* **2013**, *52*, 9534-9538.

3.3.2.1.2. Mitsunobu Recycling Strategy

Attempts were made to recycle propargylation byproduct **87** (Scheme 3.33). The crude ester **89**, obtained from a Mitsunobu reaction of alcohol **87** with *p*-nitrobenzoic acid, was directly reacted with DIBAL (Scheme 3.33). This one-pot reaction resulted in decomposition.

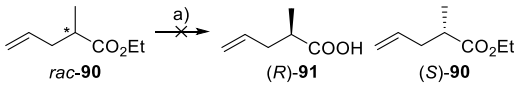


Scheme 3.33: Recycling via Mitsunobu inversion of homopropargylic alcohol **87**. Reagents and conditions: (a) i. 3.6 eq. DIAD, 3.75 eq. PPh_3 **195a**, 3 eq. *p*-nitro benzoic acid, PhMe, rt, 2 h, not isolated; ii. 5 eq. DIBAL, DCM, -78 °C to rt, 24 h, decomposition; (b) DIAD, PPh_3 **195a**, *p*-nitro benzoic acid, PhMe, rt, 20 h, 24%; (c) DIBAL, DCM, -78 °C to rt, 18 h, 70%.

Stepwise procedures for such a transformation were described by Trost *et al.*,[110] McDonald *et al.*[111] and Johnson *et al.*[112] in the presence of TMS-capped alkynes, or for related ester hydrolyses by McDonald *et al.*[113] and Ley *et al.*[114] Such a two-step approach led to alcohol **36b**, but only in 17% yield (over two steps). Therefore, recycling was deemed inappropriate.

3.3.2.1.3. Other Approaches For The Aldehyde Precursor

In terms of the accessibility of the small chiral building block (*S*)-**37**, alternative approaches were investigated (Scheme 3.29). Wong *et al.* for example had reported the use of *Candida cylindracea* lipase (CCL) to transform *rac*-**90** into enantiomerically enriched carboxylic acid (*R*)-**91** and enantiomerically enriched ester (*S*)-**90** (Scheme 3.34).[115]

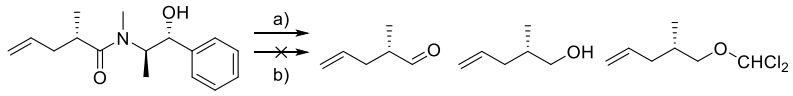


Scheme 3.34: Kinetic enzymatic resolution approach. Reagents and conditions: (a) lipase (CRL, PCL or BCL), 200 mM pH 7 aq. phosphate buffer solution, rt to 50 °C, 5 h.

[110] B. M. Trost, S. T. Wrobleski, J. D. Chisholm, P. E. Harrington, M. Jung, *J. Am. Chem. Soc.* **2005**, *127*, 13589-13597.
[111] F. E. McDonald, K. S. Reddy, Y. Díaz, *J. Am. Chem. Soc.* **2000**, *122*, 4304-4309.
[112] S. N. Greszler, J. T. Malinowski, J. S. Johnson, *Org. Lett.* **2011**, *13*, 3206-3209.
[113] S. A. Burova, F. E. McDonald, *J. Am. Chem. Soc.* **2002**, *124*, 8188-8189.
[114] S. Newton, C. F. Carter, C. M. Pearson, L. de C. Alves, H. Lange, P. Thansandote, S. V. Ley, *Angew. Chem. Int. Ed.* **2014**, *53*, 4915-4920.
[115] T. D. Machajewski, C.-H. Wong, *Synthesis* **1999**, *S1*, 1469-1472.

Major drawbacks of this approach included the non-accessibility of CCL and the unknown exact enzyme loading used by Wong *et al*. Therefore, different lipases were used such as from *Candida rugosa*, *Penicillinum camemberti* or *Burkholderia cepacia*, but these enzymes failed to transform *rac*-**90** into (*R*)-**91** and (*S*)-**90** (Scheme 3.34).

Another approach to enantiomerically pure (*S*)-**37** involved cleavage of the auxiliary of pseudoephedrine amide **43** with di-*i*-butylaluminium hydride (DIBAL) and analogues thereof (Scheme 3.35). These reagents with the general formula $LiAlH(OR)_3$ as reported by Myers *et al.* are less reactive then DIBAL.[116]



43 (*S*)-**37** (*S*)-**84** (*S*)-**92**

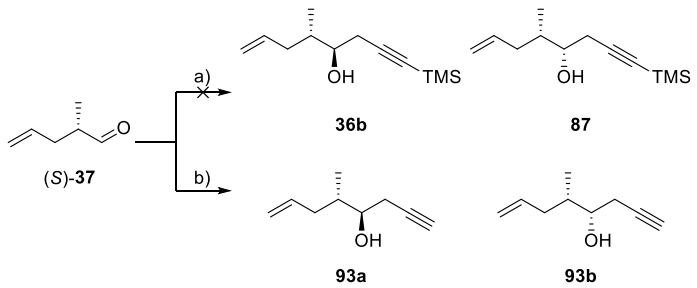
Scheme 3.35: Direct reductive cleavage of the auxiliary. Reagents and conditions: (a) 2.82 eq. DIBAL, DCM, -78 °C, 1 h, 25% alcohol (*S*)-**84** and 13% of ether (*S*)-**92**; (b) 2.3 eq. $LiAlH(OR)_3$, (R = Et, *t*-Bu), THF, pentane, -78 °C to 0 °C, 1 h, no reaction observed.

These attempts only resulted in either unreacted starting material **43** or in the formation of (*S*)-**84** along with ethers like (*S*)-**92**. For these reasons, no further investigations were undertaken.

3.3.2.1.4. Aldehyde Propargylations

With the propargylation[117] of aldehyde (*S*)-**37**, we already had a viable, but unsatisfying (*d.r.* = 1.6:1) strategy in hand (Scheme 3.29). Alternatively, we planned the introduction of a TMS-capped propargyl group by a Barbier-type reaction with propargyl bromide **85** as reported by Loh *et al.* with indium/indium(III) bromide on a steroid substrate[118] and by others on simpler substrates with either indium[119] or zinc[120] metal (Scheme 3.36). Unfortunately, no reaction was observed under these conditions.

[116] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.
[117] D. R. Fandrick, K. R. Fandrick, J. T. Reeves, Z. Tan, C. S. Johnson, H. Lee, J. J. Song, N. K. Yee, C. H. Senanayake, *Org. Lett.* **2010**, *12*, 88-91.
[118] M.-J. Lin, T.-P. Loh, *J. Am. Chem. Soc.* **2003**, *125*, 13042-13043.
[119] a) L. C. Hirayama, K. K. Dunham, B. Singaram, *Tetrahedron Lett.* **2006**, *47*, 5173-5176. c) T.-P. Loh, M.-J. Lin, K.-L. Tan, *Tetrahedron Lett.* **2003**, *44*, 507-509.
[120] a) T. Mukaiyama, T. Harada, *Chem. Lett.* **1981**, *10*, 621-624. b) Z. Pakulski, A. Zamojski, *Tetrahedron* **1997**, *53*, 2653-2666. c) C. V. Ramana, S. B. Narute, R. G. Gonnade, R. S. Patil, *Synthesis* **2008**, *11*, 1783-1787.



Scheme 3.36: Diastereoselective homopropargylation attempts. Reagents and conditions: (a) 2 eq. TMS-propargylbromide **85**, 2 eq. In, 10 mol% $InBr_3$, THF, rt to 66 °C, 16 h, no reaction observed; (b) 2 eq. allenylpinacolborane, 20 mol% Et_2Zn, THF, PhMe, rt, 18 h, 6% (*d.r.* = 1:1.3).

With allenylpinacolborane in the presence of diethylzinc, according to Fandrick *et al.*,[121] we observed 6% conversion to a 1:1.3 mixture of **93** (Scheme 3.36). Further investigations were not undertaken. For a more comprehensive overview on catalytic asymmetric propargylations see Hou *et al.*[122]

[121] D. R. Fandrick, K. R. Fandrick, J. T. Reeves, Z. Tan, W. Tang, A. G. Capacci, S. Rodriguez, J. J. Song, H. Lee, N. K. Yee, C. H. Senanayake, *J. Am. Chem. Soc.* **2010**, *132*, 7600-7601.
[122] C.-H. Ding, X.-L. Hou, *Chem. Rev.* **2011**, *111*, 1914-1937.

3.3.2.2. The Sugar-Based Alkyne

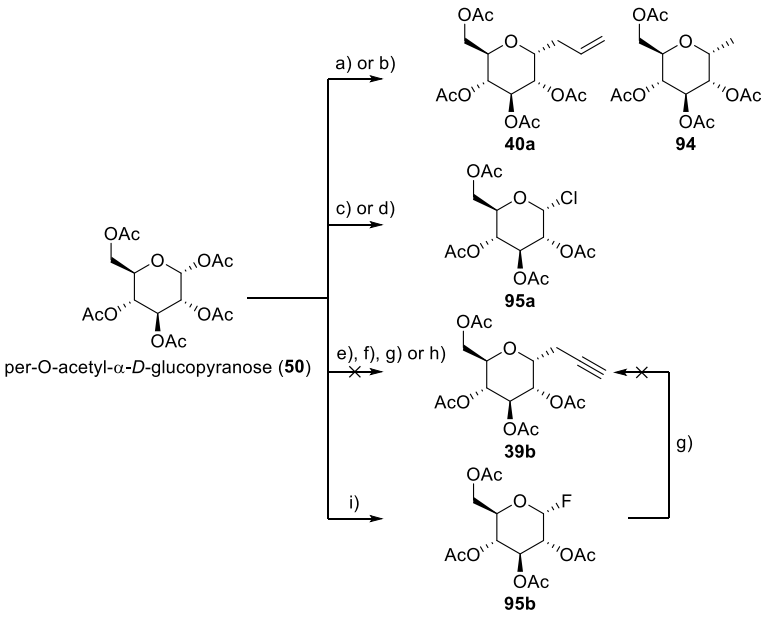
Alkyne **35** as a central part of route 1 was successfully accessed after intensive investigations. These studies on a variety of functional group modifications, not always directly correlating to the finally successful route, are shown herein.

3.3.2.2.1. Anomeric Allylation & Propargylation Studies

The anomeric allylation of sugars such as α-*D*-glucose (**9**) and its derivatives is extensively described in the literature (Chapter 3.3.1.2). All of these procedures have in common that they make use of allyl-TMS (**52**) as the pro-nucleophile as well as of a Lewis acid (*e.g.* boron trifluoride diethyl etherate or TMSOTf) for the activation of the anomeric position. Some of them use our substrate **50**,[123] while others were closely related (such as galactose,[124] fucose[125] and other sugars with different protecting groups[126]) or of more general character.[127] When per-*O*-acetyl-α-*D*-glucopyranose (**50**) was reacted with allyl-TMS (**52**) and TMSOTf, alkene **40a** was isolated in 36% yield (Scheme 3.37). When DCM was added or used as a solvent, the yield massively dropped (7%) and **94** was isolated as well (1%). In both cases the reaction mixture became dark brown and some decomposition occurred, which rendered purification problematic.

Using other Lewis acids suchs as tin(IV) chloride or tin(II) chloride (inspired by general investigations on anomeric allylations by Kozikowski *et al.*[128]), we observed the formation of chloro compound **95a** instead (Scheme 3.37).

[123] a) P. Arya, A. Barkley, K. D. Randell, *J. Comb. Chem.* **2002**, *4*, 193-198. b) D. Horton, T. Miyake, *Carbohydr. Res.* **1988**, *184*, 221-229. c) G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730. d) J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.
[124] a) R. N. Ben, A. A. Eniade, L. Hauer, *Org. Lett.* **1999**, *1*, 1759-1762. b) R. Y. Tam, S. S. Ferreira, P. Czechura, J. L. Chaytor, R. N. Ben, *J. Am. Chem. Soc.* **2008**, *130*, 17494-17501.
[125] T. Uchiyama, V. P. Vassilev, T. Kajimoto, W. Wong, C.-C. Lin, H. Huang, C.-H. Wong, *J. Am. Chem. Soc.* **1995**, *117*, 5395-5396.
[126] D. V. Jarikote, C. O'Reilly, P. V. Murphy, *Tetrahedron Lett.* **2010**, *51*, 6776-6778.
[127] A. P. Kozikowski, K. L. Sorgi, B. C. Wang, Z.-b. Xu, *Tetrahedron Lett.* **1983**, *24*, 1563-1566.
[128] See footnote 127.



Scheme 3.37: Direct allylation/propargylation strategy. Reagents and conditions: (a) 2 eq. allyl-TMS (**52**), 1 eq. TMSOTf, MeCN, 0 °C to rt, 23 h, 36% (α:β = 12:1); (b) 5 eq. allyl-TMS (**52**), 2 eq. TMSOTf, MeCN, DCM, 0 °C to rt, 7 d, 7% of **40a** and 1% of **94**; (c) 2 eq. allyl-TMS (**52**), 1 eq. $SnCl_2$, MeCN, rt, 5 d, 42%; (d) 2 eq. allenylpinacolborane, 1 eq. $SnCl_4$, DCM, rt, 3 d, 42%; (e) 2 eq. allenylpinacolborane, 0.5 eq. 9-MeO-BBN, 10 mol% InOTf, DCM, hexane, decomposition; (f) 2 eq. allenylpinacolborane, 0.5 eq. 9-MeO-BBN, 10 mol% InOTf **96**, DCM, rt to 45 °C, 4 d, decomposition; (g) 1.46 eq. allenyltributylstannane, 5.3 eq. TMSOTf, DCM, rt, 20 h, decomposition; (h) 1.46 eq. allenyltributylstannane, 1.04 eq. $BF_3{\cdot}OEt_2$, DCM, -15 °C to rt to 140 °C (mw), 2 d, decomposition; (i) 8.7 eq. HF·py, rt, 24 h, 59%.

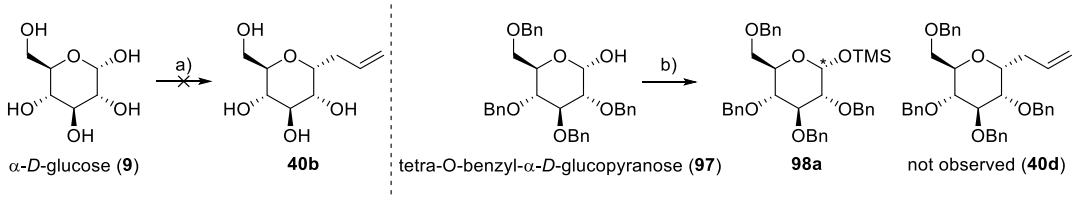
Next, we envisioned a more direct anomeric propargylation approach. According to a literature report, a propargyl group can be introduced into per-*O*-acetyl-β-*D*-glucopyranose (*epi*-**50**) with allenylstannane as the nucleophilic reagent and Lewis acids such as TMSOTf or boron trifluoride diethyl etherate as described by Wyatt *et al*.[129] Jamison *et al.* reported a closely related example during the total synthesis of amphidinolides T1 and T4 for the propargylation of five-membered lactols.[130] Unfortunately, we could not reproduce these results for the α-anomer **50** using allenylstannane, as this resulted in decomposition (Scheme 3.37).

Wyatt *et al.* stated that glucosyl fluorides like **95b** were observed to be even more reactive (Scheme 3.37). Therefore, glucosyl fluoride **95b** was prepared according to a procedure by Hayashi *et al.* for similar galactose substrates[131] and it was submitted to the conditions with allenylstannane. Again, only decomposition was observed, while propargyl-substituted product **39b** was not formed.

[129] K. L. Chan, G. S. Coumbarides, S. Islam, P. B. Wyatt, *Tetrahedron Lett.* **2005**, *46*, 61-65.
[130] E. A. Colby, K. C. O'Brie, T. F. Jamison, *J. Am. Chem. Soc.* **2005**, *127*, 4297-4307.
[131] J. T. Zacharia, M. Hayashi, *Carbohydr. Res.* **2012**, *348*, 91-94.

Another approach based on a precedent by Kobayashi *et al.*[132] for the propargylation of glycosides with allenylboranes under 9-methoxy-9-borabicyclo[3.3.1]nonane (9-MeO-BBN) co-catalysis either with or without indium(I) trifluoromethanesulfonate **96** as the catalyst only led to decomposition in our hands as well (Scheme 3.37).

According to Dussault *et al*., it is possible to catalyze the reaction of hemiacetals with C-nucleophiles (as well as other nucleophiles) by rhenium(VII) oxide.[133] α-*D*-Glucose (**9**) consists of such a hemiacetal substructure and was reacted under similiar conditions (Scheme 3.38).

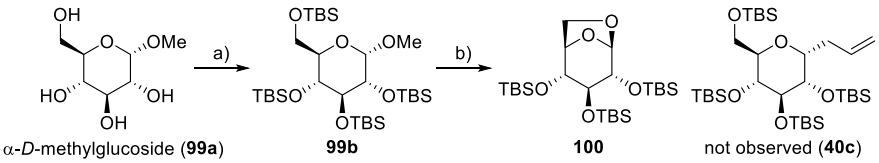


Scheme 3.38: Anomeric allylations with Re_2O_7. Reagents and conditions: (a) 1 mol% Re_2O_7, allyl-TMS (**52**), DCM, rt, 7 d, no reaction observed; (b) 1 mol% Re_2O_7, allyl-TMS (**52**), DCM, rt, 6 d, 49% (α:β = 1.9:1).

Unfortunately, both attempts, either with unprotected α-*D*-glucose (**9**) or with tetra-O-benzyl-α-*D*-glucopyranose (**97**) did not result in the formation of alkenes **40b** or **40d** (Scheme 3.38). While the unprotected sugar **9** did not react at all, tetra-O-benzylated hemiacetal **97** gave both anomers of derivative **98** in 49% yield (α:β = 1.9:1).

Furthermore, Bernardi *et al.* showed that methylglycosides such as α-methylgalactoside could also be activated directly by using *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA), followed by allyl-TMS (**52**) and a catalytic amount of a Lewis acid.[134] α-*D*-Methylglucoside **99b** was obtained in analogy to the procedures of McGarvey *et al.*[135] and Deming *et al.*[136] (Scheme 3.39). For the aimed allylation, we found that an intramolecular reaction to anhydro sugar **100** took place, while alkene **40c** was not observed.

[132] a) H. T. Dao, U. Schneider, S. Kobayashi, *Chem. Asian J.* **2011**, *6*, 2522-2529. b) Preparation of InOTf according to: C. L. B. Macdonald, A. M. Corrente, C. G. Andrews, A. Taylor, B. D. Ellis, *Chem. Commun.* **2004**, *2*, 250-251.
[133] W. Sittiwong, M. W. Richardson, C. E. Schiaffo, T. J. Fisher, P. H. Dussault, *Beilstein J. Org. Chem.* **2013**, *9*, 1526-1532.
[134] S. Mari, F. J. Cañada, J. Jiménez-Barbero, A. Bernardi, G. Marcou, I. Motto, I. Velter, F. Nicotra, B. La Ferla, *Eur. J. Org. Chem.* **2006**, *13*, 2925-2933.
[135] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.
[136] J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.



Scheme 3.39: Allylation on globally TBS-protected α-*D*-methylglucoside **99b** and reaction to anhydro sugar **100**. Reagents and conditions: (a) TBSOTf, 2,6-lutidine, DCM, 0 °C to rt, 3.5 h, 99%; (b) TMSOTf, allyl-TMS (**52**), 2,6-lutidine, DCM, 0 °C to rt, 20 h, 39%.

Further investigations on anomeric allylations and propargylations were not undertaken, since boron trifluoride diethyl etherate yielded alkene **40a** in 79% yield and good *d.r.* (α:β = 7:1, Scheme 3.9).

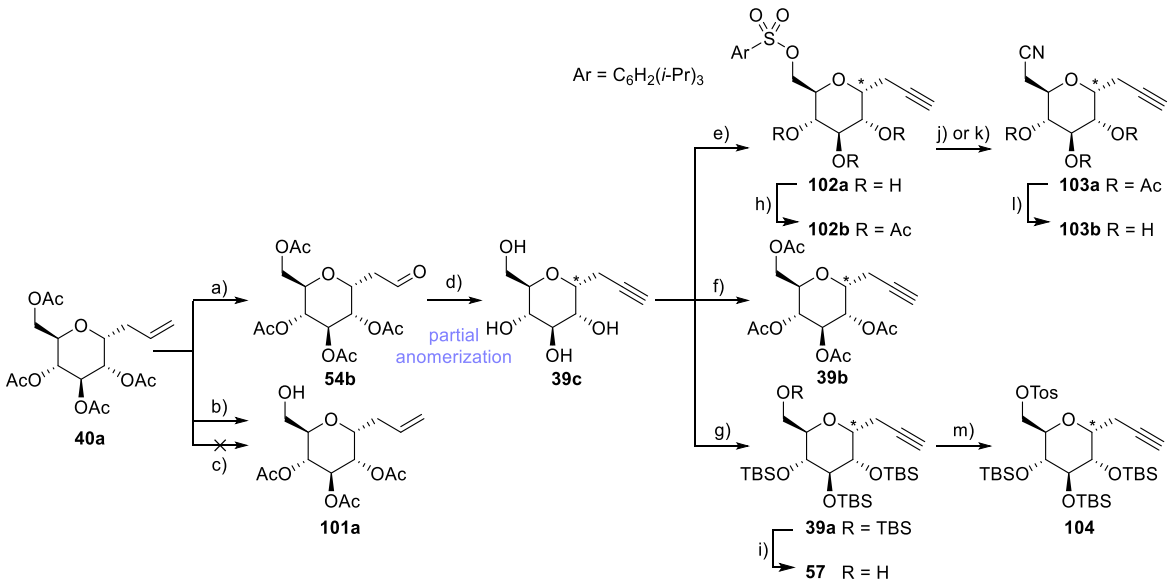
3.3.2.2.2. General Functional Group Manipulations At C6'

In parallel to the previously shown C-glucosidation reactions, we investigated the introduction of the required ester functionality at C6´ of retron **35** by various strategies.

At first, alkene **40a** was submitted to an enzyme-catalyzed selective cleavage of the C6' acetyl group based on literature examples for acetyl-protected methyl glycosides (Scheme 3.40).[137] This resulted in the formation of primary alcohol **101a** in 31% yield. Other products with cleaved acetyl groups at different positions around the tetrahydropyran ring were also obtained as an inseparable mixture. In terms of selectivity, these enzymatic approaches were not comparable to the C6'-TBS group deprotection with Olah´s reagent (hydrofluoric acid/pyridine, Scheme 3.12).

Alkene **40a** was transformed into aldehyde **54b** by ozonolysis according to Randell *et al.*[138] with a subsequent work-up with zinc (Scheme 3.40). Aliphatic aldehyde **54b** was then submitted to the classical basic Seyferth-Gilbert conditions[139] giving rise to alkyne **39c** due to complete deprotection of all hydroxy groups. A partial anomerization (ca. 50%) of the previously α-anomerically pure substrate **54b** occurred during the Seyferth-Gilbert homologation as well.

[137] a) K.-F. Hsiao, F.-L. Yang, S.-H. Wu, K.-T. Wang, *Biotechnol. Lett* **1995**, *17*, 963-968. b) G. Fernandez-Lorente, J. M. Palomo, J. Cocca, C. Mateo, P. Moro, M. Terreni, R. Fernandez-Lafuente, J. M. Guisan, *Tetrahedron* **2003**, *59*, 5705-5711. c) M. Kloosterman, E. W. J. Mosmuller, H. E. Schoemaker, E. M. Meijer, *Tetrahedron Lett.* **1987**, *28*, 2989-2992. d) R. Sundell, L. T. Kanerva, *Eur. J. Org. Chem.* **2013**, *22*, 4971-4978. e) E. Levoirier, Y. Canac, S. Norsikian, A. Lubineau, *Carbohydr. Res.* **2004**, *339*, 2737-2747.
[138] P. Arya, A. Barkley, K. D. Randell, *J. Comb. Chem.* **2002**, *4*, 193-198.
[139] a) G. J. Roth, B. Liepold, S. G. Müller, H. J. Bestmann, *Synthesis* **2004**, *1*, 59-62. b) S. Müller, B. Liepold, G. J. Roth, H. J. Bestmann, *Synlett* **1996**, *6*, 521-522.



Scheme 3.40: First attempts for the synthesis of the sugar-based building block **35**. Reagents and conditions: (a) i. O_3, MeOH, DCM, -78 °C, 6 h; ii. Zn, AcOH, -78 °C to rt, 17 h, 90%; (b) 182.000 U CRL, pH 7 aq. phosphate buffer solution, rt, 3 d, 31%; (c) 182.000 U CRL, EtOH/hexane (1:55), rt, 1 month, no reaction observed; (d) Ohira-Bestmann reagent **56**, K_2CO_3, MeOH, rt, 82% (α:β = 1:1); (e) $ArSO_2Cl$, py, 0 °C, 5 h, 38%; (f) Ac_2O, $BF_3{\cdot}OEt_2$, DCM, rt, 1 h, 48%; (g) TBSCl, $AgNO_3$, py, DMF, rt, 2 d, 17%; (h) Ac_2O, $BF_3{\cdot}OEt_2$, rt, 1 h, 74% (*d.r.* = 1.25:1); (i) HF·py, THF, 0 °C to rt, 4 h, 28%; (j) NaCN, DMSO, rt to 80 °C, 2 d, quant.; (k) NaCN, DMA, rt to 80 °C, 2 d, quant.; (l) HCl in MeOH, Et_2O/MeOH (1:1), 0 °C to reflux, 4 d, 67% (*d.r.* = 1.5:1); (m) TosCl, TEA, 4-DMAP, DCM, rt, 16 h, 38% (α:β = 3.2:1).

The epimeric mixture of alkyne **39c** was the starting point for a number of investigations of different reaction pathways such as sulfonylation, reacetylation and TBS protection (anomers were not separated, Scheme 3.40).

Sulfonylation with a sterically hindered sulfonyl chloride (Ar = $C_6H_2(i\text{-Pr})_3$) according to a procedure for simple tosylates by Macmillan *et al.*[140] and Koskinen *et al.*[141] led to product **102a** (Scheme 3.40). Sulfonate **102a** was reprotected with acetic anhydride in the presence of boron trifluoride diethyl etherate (as reported by Sandoval-Ramírez *et al.* for alcoholic substrates in general[142]) giving sulfonate **102b**. The S_N2 reaction of sulfonate **102b** with sodium cyanide in dimethylsulfoxide in analogy to precedents both for sugar derivatives[143] as well as for sugar-related substrates[144] resulted in the formation of nitrile **103a**. This compound was then submitted to Pinner reaction conditions with hydrochloric acid in methanol reported by Ogawa *et*

[140] S. Marchesan, D. Macmillan, *Chem. Commun.* **2008**, *36*, 4321-4323.
[141] A. J. Pihko, K. C. Nicolaou, A. M. P. Koskinen, *Tetrahedron: Asymmetry* **2001**, *12*, 937-942.
[142] R. Martinez-Pascual, O. Viñas-Bravo, S. Meza-Reyes, M. A. Iglesias-Arteaga, J. Sandoval-Ramírez, *Synth. Commun.* **2004**, *34*, 4591-4596.
[143] a) T. Heidelberg, J. Thiem, *Carbohydr. Res.* **1997**, *301*, 145-153. b) L. V. Dunkerton, K. T. Brady, F. Mohamed, B. P. McKillican, *J. Carbohydr. Chem.* **1988**, *7*, 49-65.
[144] K. Zhu, J. S. Panek, *Org. Lett.* **2011**, *13*, 4652-4655.

al. for a glucose derivative with benzyl protecting groups.[145] In our case, this led to product **103b** as a result of cleaving the previously introduced acetyl groups.

Acetyl reprotection of tetrol **39c** was possible by using the acetylation protocol with boron trifluoride diethyl etherate as before[146] resulting in alkyne **39b** (Scheme 3.40, Figure 3.15). Since further transformations were originally planned, reintroduction of the acetyl protecting groups was performed. As other synthetic approaches were found to be much more suitable (by the introduction of TBS protecting groups), acetyl-protected sugars (Scheme 3.37, Scheme 3.40) were not investigated any further.

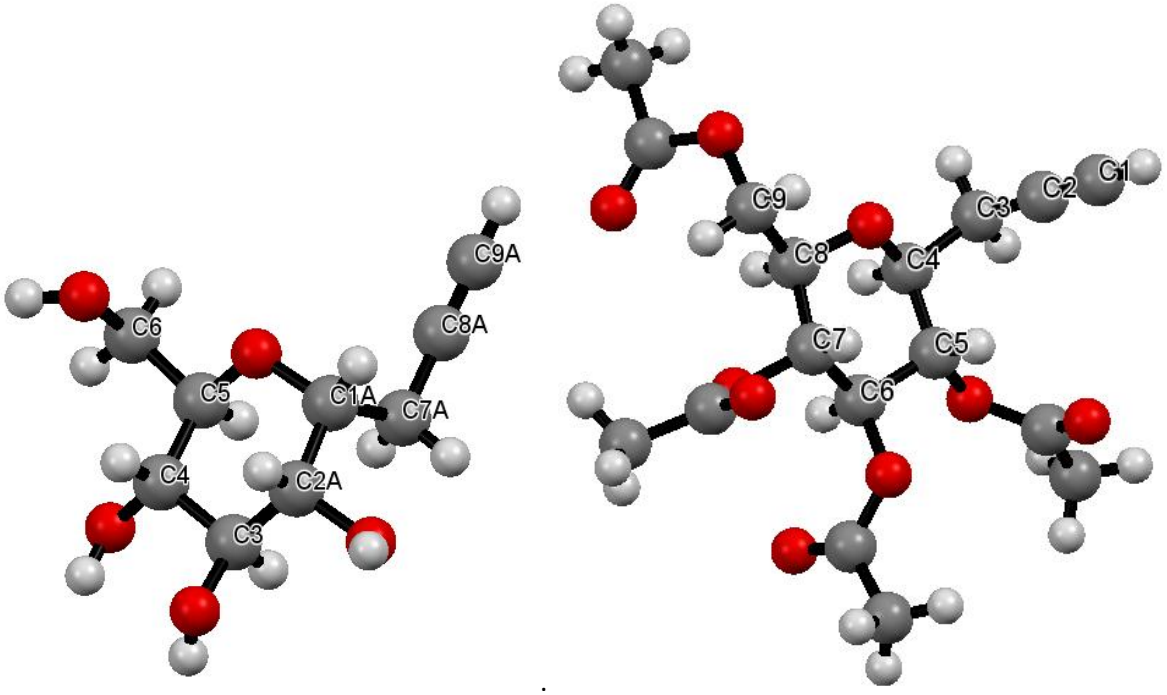


Figure 3.15: X-Ray single crystal structure of alkynes **39c** and *epi*-**39b** (numbering of atoms is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red)).

In contrast, global TBS protection of tetrol **39c** with TBSCl/silver nitrate was possible by the protocol by Kishi *et al.*[147] giving rise to alkyne **39a** (Scheme 3.40). Selective cleavage of the C6' TBS group by administering diluted Olah´s reagent (hydrogen fluoride/pyridine) to **39a** according to the procedure by Murphy *et al.*[148] gave primary alcohol **57**. This alcohol was sulfonylated by the

[145] Y. Nakahara, A. Fujita, K. Beppu, T. Ogawa, *Tetrahedron* **1986**, *42*, 6465-6476.
[146] R. Martinez-Pascual, O. Viñas-Bravo, S. Meza-Reyes, M. A. Iglesias-Arteaga, J. Sandoval-Ramírez, *Synth. Commun.* **2004**, *34*, 4591-4596.
[147] Y. Kaburagi, Y. Kishi, *Org. Lett.* **2007**, *9*, 723-726.
[148] G. Anquetin, S. L. Rawe, K. McMahon, E. P. Murphy, P. V. Murphy, *Chem. Eur. J.* **2008**, *14*, 1592-1600.

previously described protocols[149] resulting in pure tosylate **104** (at this stage, the epimeric mixture could finally be separated by flash chromatography).

These selective C6' functionalizations led to useful observations either regarding the sulfonylation, the nucleophilic substitution with cyanide or the selective C6' TBS cleavage with Olah´s reagent (hydrofluoric acid/pyridine). Based on the repetitive cleavage of the acetyl groups, TBS protection was deemed necessary. Furthermore, tosylate **104** seemed to be an attractive intermediate to access the aimed carboxylic acid (ester) **35** via its nitrile analogue.

3.3.2.2.3. C_1 Homologations At The C6' Terminus (Towards Carboxy Derivatives)

C6' tosylate **104** was isolated as a very stable and crystalline intermediate that is easily accessible by tosylation of primary alcohol **57** (Scheme 3.41, Figure 3.16).[150] Therefore, it was an important entry into different approaches for the introduction of the required carboxy functionality at C6'.

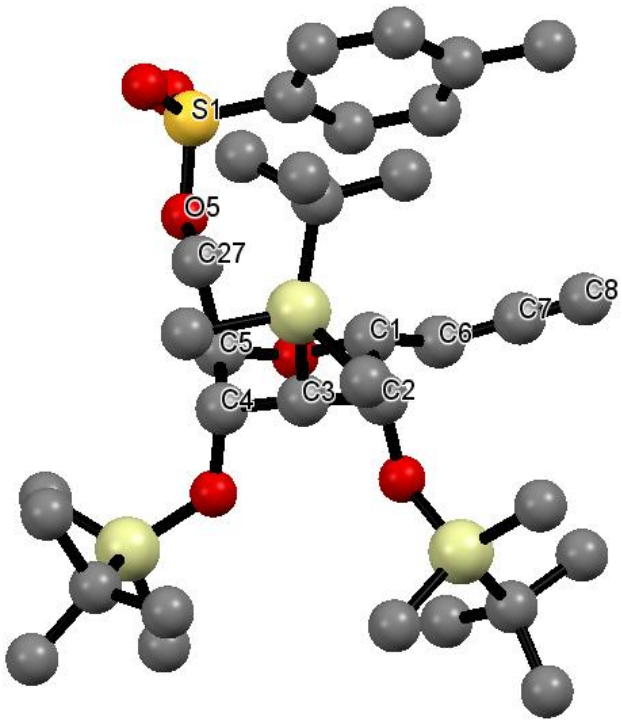
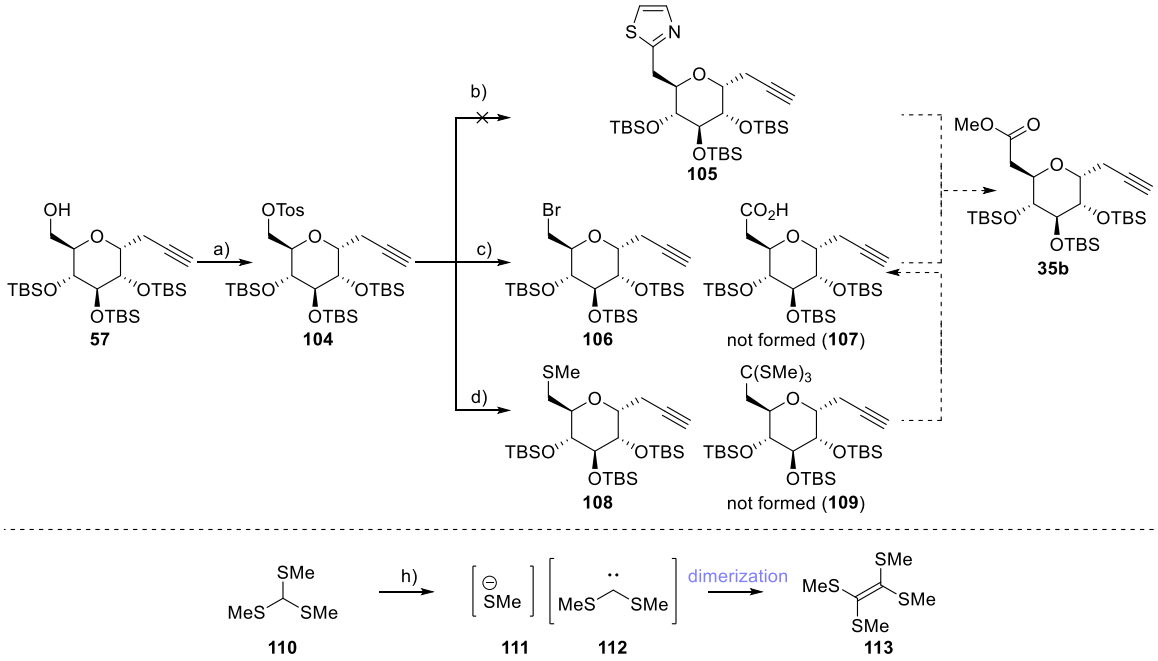


Figure 3.16: X-Ray single crystal structure of tosylate **104** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary; colouring of atoms: carbon (grey), oxygen (red), silicon (ivory), sulfur (yellow)).

[149] a) S. Marchesan, D. Macmillan, *Chem. Commun.* **2008**, *36*, 4321-4323. b) A. J. Pihko, K. C. Nicolaou, A. M. P. Koskinen, *Tetrahedron: Asymmetry* **2001**, *12*, 937-942.
[150] See footnote 149.

2-TMS-thiazole is reported as a viable nucleophile for aldehydes[151] and other electrophiles.[152] The introduction of a thiazole unit as formyl anion equivalent[153] via direct S_N2 reaction of tosylate **104** with 2-TMS-thiazole was unsuccessful using conditions reported by Field *et al.*[154] (Scheme 3.41).



Scheme 3.41: Attempts for the introduction of the ester functionality. Reagents and conditions: (a) TosCl, 4-DMAP, TEA, DCM, rt, 16 h, 98%; (b) 4 eq. 2-TMS-thiazole, DMSO, 80 °C, 22 h, no reaction observed; (c) 10 mol% $NiBr_2$·glyme, CO_2 (balloon), 2.4 eq. Mn, 26 mol%, DMF, 70 °C, 22 h, 9% of **106**, SM **104**mainly recovered (90%); (d) $HC(SiMe)_3$, *n*-BuLi, DMPU, THF, -78 °C to -50 °C to -40 °C to rt, 1 d, 19% of **108**.

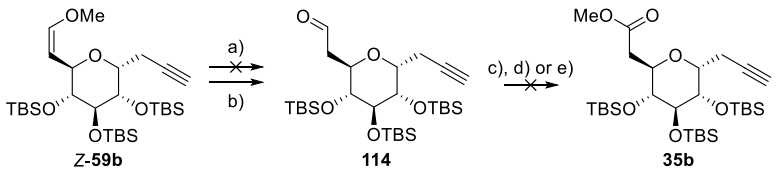
Interestingly, Martin *et al.* reported the transformation of a simple primary aliphatic tosylate into the corresponding C_1-homologated carboxylic acid by a nickel-catalyzed carboxylation.[155] With this report in mind, we planned to access carboxylic acid **107** directly from tosylate **104** via carbon dioxide insertion, but only observed the undesired formation of small amounts of bromide **106** (9%) by the reaction of the nickel(II) bromide-based catalyst with tosylate **104** (Scheme 3.41). Most of the unreacted starting material **104** was recovered (90%).

Another idea was the introduction of an orthothioester functionality resulting in intermediate **109** using methods described by Wipf *et al.*[156] and Hiyama *et al.*[157] (Scheme 3.41). In both reports, a primary alkyl trifluoromethanesulfonate or even a primary alkyl chloride underwent a S_N2 reaction

[151] K. C. Nicolaou, H. J. Mitchell, K. C. Fylaktakidou, R. M. Rodríguez, H. Suzuki, *Chem. Eur. J.* **2000**, *6*, 3116-3148.
[152] A. Dondoni, A. Marra, *Chem. Rev.* **2004**, *104*, 2557-2600.
[153] A. Kirschning, C. Kujat, S. Luiken, E. Schaumann, *Eur. J. Org. Chem.* **2007**, *15*, 2387-2400.
[154] N. A. Jones, S. A. Nepogodiev, C. J. MacDonald, D. L. Hughes, R. A. Field, *J. Org. Chem.* **2005**, *70*, 8556-8559.
[155] a) Y. Liu, J. Cornella, R. Martin, *J. Am. Chem. Soc.* **2014**, *136*, 11212-11215. b) X. Wang, Y. Liu, R. Martin, *J. Am. Chem. Soc.* **2015**, *137*, 6476-6479.
[156] P. Wipf, Y. Uto, S. Yoshimura, *Chem. Eur. J.* **2002**, *8*, 1670-1681.
[157] S. Furuta, M. Kuroboshi, T. Hiyama, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1939-1951.

with lithiated orthothioester **110**. Unfortunately, such a nucleophilic substitution did not take place with tosylate **104**. Instead, thioether **108** was isolated in 19% yield. This thioether was formed by the reaction of the orthothioester anion to thiomethyl anion **111** and carbene **112** which itself can dimerize to **113** as described by the groups of Seebach[158] and Fochi.[159]

Knowing that the introduction of enolethers by the Wittig reaction on aldehyde **58** worked quite well (Chapter 3.3.1.2.4), enolether *Z*-**59b** was taken to investigate the transformation into aldehyde **114** (Scheme 3.42). Kobayashi *et al.* reported the reaction of an aromatic enolether into a benzylic aldehyde, making use of TMSCl and sodium iodide.[160] In our case, this method was unsuccessful. Another method, described for a steroidal substrate by Strnad *et al.*, made use of pyridinium *p*-toluenesulfonate (PPTS) as a catalyst and directly led from *Z*-**59b** to aldehyde **114** in 63% yield.[161]



Scheme 3.42: Further attempts to access the ester **35b**. Reagents and conditions: (a) 1.1 eq. NaI, 0.9 eq. TMSCl, 3 Å MS, MeCN, -18 °C to 0 °C to rt, 30 min, no reaction observed, SM *Z*-**59b** recovered (quant.); (b) PPTS, acetone/H_2O (10:1), rt to 60 °C, 17 h, 63%; (c) 20 mol% 1,4-dimethyl-4*H*-1,2,4-triazol-1-ium iodide, 5 eq. MnO_2, 1.1 eq. DBU, MeOH, 3 Å MS, DCM, rt, 17 h, decomposition; (d) i. 5.25 eq. KOH, MeOH, 0 °C, 5 min; ii. I_2, 0 °C, 1.5 h, decomposition; (e) $KHSO_5 \cdot 0.5KHSO_4 \cdot 0.5K_2SO_4$ (OXONE®), MeOH, rt, several hours, decomposition.

Our original plan was to convert aldehyde **114** (C_1-elongated intermediate) into ester **35b** by an oxidation similar to the original Corey-Gilman-Ganem reaction (Scheme 3.42).[162] Different protocols were tested, such as a modern version of this method published by Scheidt *et al.*[163] and Studer *et al.*[164] Making use of a triazolinium-based catalyst and maganese dioxide as the oxidant in alcoholic solution, we found that this protocol worked quite well on simple substrates (not shown). In contrast, aldehyde **114** did not undergo the attempted transformation.

[158] D. Seebach, K. H. Geiß, A. K. Beck, B. Graf, H. Daum, *Chem. Ber.* **1972**, *105*, 3280-3300.
[159] M. Barbero, S. Cadamuro, I. Degani, S. Dughera, R. Fochi, *J. Chem. Soc., Perkin Trans. 1* **1993**, *17*, 2075-2080.
[160] Y. Takashima, Y. Kobayashi, *J. Org. Chem.* **2009**, *74*, 5920-5926.
[161] K. Sidoryk, A. Korda, L. Rárová, J. Oklešťková, M. Strnad, P. Cmoch, Z. Pakulski, K. Gwardiak, R. Karczewski, R. Luboradzki, *Tetrahedron* **2015**, *71*, 2004-2012.
[162] E. J. Corey, N. W. Gilman, B. E. Ganem, *J. Am. Chem. Soc.* **1968**, *90*, 5616-5617.
[163] a) B. E. Maki, K. A. Scheidt, *Org. Lett.* **2008**, *10*, 4331-4334. b) B. E. Maki, A. Chan, E. M. Phillips, K. A. Scheidt, *Tetrahedron* **2009**, *65*, 3102-3109.
[164] S. D. Sarkar, S. Grimme, A. Studer, *J. Am. Chem. Soc.* **2010**, *132*, 1190-1191.

Next, we envisioned to oxidize an *in situ* formed hemiacetal with iodine, which also did not result in the formation of ester **35b** (Scheme 3.42). Another method tested on aldehyde **114**, was the oxidation with OXONE® ($KHSO_5 \cdot 0.5KHSO_4 \cdot 0.5K_2SO_4$) in an alcoholic solution as described by Borhan *et al.*,[165] but no conversion was observed.

Starting again from alcohol intermediate **57**, it was investigated to directly form nitrile **115** (Scheme 3.43, Figure 3.17). This transformation was reported by a TMSCl-facilitated S_N2 reaction with sodium cyanide or by the Mitsunobu reaction of alcohol **57** with acetone cyanohydrin.

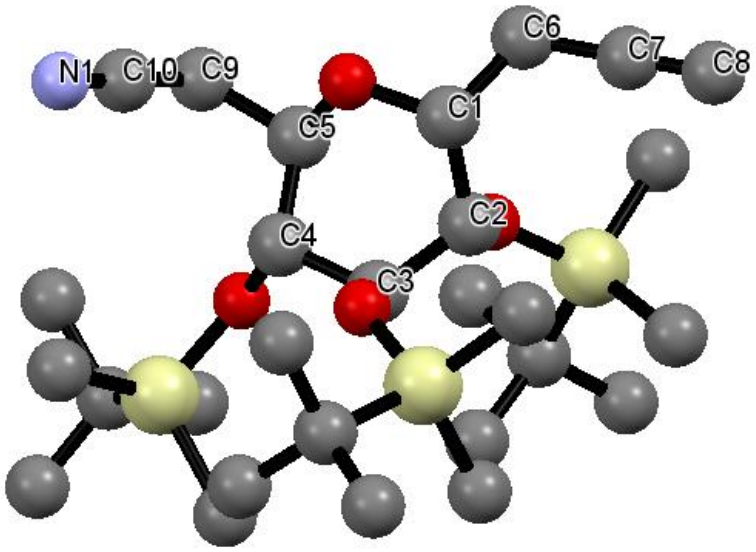
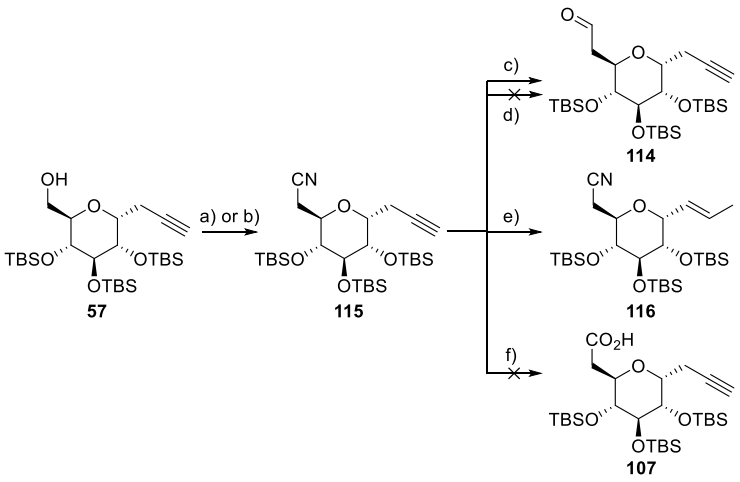


Figure 3.17: X-Ray single crystal structure of nitrile **115** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary; colouring of atoms: carbon (grey), oxygen (red), nitrogen (blue), silicon (ivory)).

The first procedure, reported by Untch *et al.*,[166] involved the *in situ* formation of a bis-TMS-substituted oxonium ion which then reacts with the cyanide anion. The Mitsunobu variant was reported for a variety of primary, as well as for secondary alcohols by Tsunoda *et al.*[167] and Ricci *et al.*[168] In fact, both pathways led to the expected product **115**, but only in 12-40% yield (Scheme 3.43).

[165] B. R. Travis, M. Sivakumar, G. O. Hollist, B. Borhan, *Org. Lett.* **2003**, *5*, 1031-1034.
[166] R. Davis, K. G. Untch, *J. Org. Chem.* **1981**, *46*, 2985-2987.
[167] T. Tsunoda, K. Uemoto, C. Nagino, M. Kawamura, H. Kaku, S. Itô, *Tetrahedron Lett.* **1999**, *40*, 7355-7358.
[168] C. Gioia, A. Hauville, L. Bernardi, F. Fini, A. Ricci, *Angew. Chem. Int. Ed.* **2008**, *47*, 9236-9239.



Scheme 3.43: Further attempts to access other sugar-based carboxylic acid derivatives. Reagents and conditions: (a) NaCN, TMSCl, 10 mol% NaI, DMF/MeCN (1:1), rt to 60 °C, 5 h, 12%; (b) acetone cyanohydrin, DEAD, PPh_3 **195a**, THF/Et_2O (1:2), 0 °C to rt, 20 h, 40%; (c) DIBAL, DCM, -95 °C to -90 °C, 40% of **114**, some SM **115** recovered (17%); (d) 20 eq. $(HSiMe_2)_2O$, 1 eq. $VO(O\textit{i}\text{-}Pr)_3$, PhMe, 60 °C, 18 h, decomposition; (e) 3 mol% $Ru(H_2)(PPh_3)_4$, H_2O, MeOH, 1,2-DME, 140 °C, 22 h, 23%; (f) [bmim]HSO_4 (1-butyl-3-methylimidazolium hydrogensulfate), 70 °C, 60 h, no reaction observed, SM **115** not recovered.

Nevertheless, experiments were conducted to transform nitrile **115** into ester **35b** either via previously shown aldehyde **114**, or by the direct condensation with an alcohol under transition metal catalysis (Scheme 3.43). Applying di-*i*-butylaluminium hydride (DIBAL) for the reduction of nitrile **115**,[169] gave aldehyde **114** in 40% yield, together with some unreacted starting material **115** (17%). Corey *et al.* had previously shown that DIBAL can be safely used with TBS-protected substrates.[170] Due to the observed lack in reactivity with DIBAL, tempered analogues, as reported by An *et al.*,[171] were not used.

The vanadium-catalyzed transfer hydrogenation with a disiloxane according to Lemaire *et al.*[172] only led to decomposition (Scheme 3.43).

A ruthenium-catalyzed condenstion of nitrile **115** with methanol, following general solvolysis procedures of nitriles by Murahashi *et al.*[173] did not result in the desired ester **35b**. Instead, alkyne **115** was reduced and isomerized to the undesired *E*-configured alkenyl product **116**, whereas the nitrile functionality remained intact.

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[169] a) Y. Anami, T. Itoh, D. Egawa, N. Yoshimoto, K. Yamamoto, *J. Med. Chem.* **2014**, *57*, 4351-4367. b) A. P. Kozikowski, J. Lee, *J. Org. Chem.* **1990**, *55*, 863-870. c) L. Thijs, E. H. M. Stokkingreef, J. M. Lemmens, B. Zwanenburg, *Tetrahedron* **1985**, *41*, 2949-2956. d) M. Ball, M. J. Gaunt, D. F. Hook, A. S. Jessiman, S. Kawahara, P. Orsini, A. Scolaro, A. C. Talbot, H. R. Tanner, S. Yamanoi, S. V. Ley, *Angew. Chem. Int. Ed.* **2005**, *44*, 5433-5438. e) H. Kusama, R. Hara, S. Kawahara, T. Nishimori, H. Kashima, N. Nakamura, K. Morihira, I. Kuwajima, *J. Am. Chem. Soc.* **2000**, *122*, 3811-3820.

[170] E. J. Corey, A. Venkateswarlu, *J. Am. Chem. Soc.* **1972**, *94*, 6190-6191.

[171] Y. R. Kim, D. K. An, *Bull. Korean Chem. Soc.* **2012**, *33*, 4194-4196.

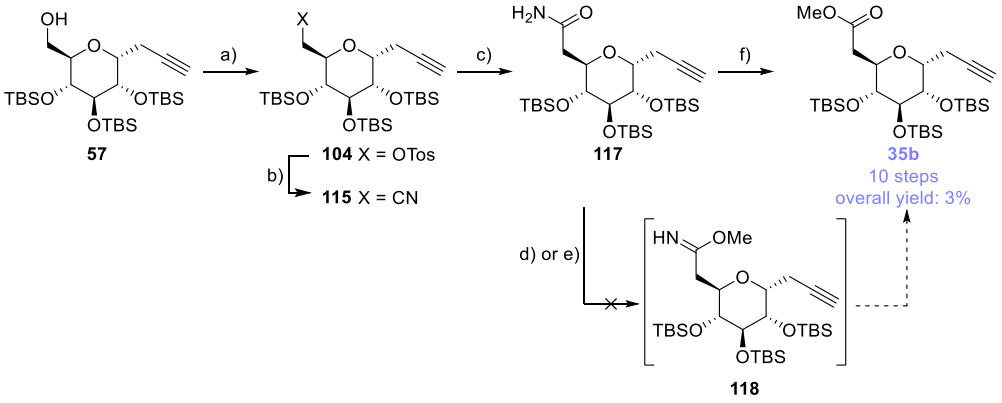
[172] S. Laval, W. Dayoub, L. Pehlivan, E. Métay, D. Delbrayelle, G. Mignani, M. Lemaire, *Tetrahedron Lett.* **2014**, *55*, 23-26.

[173] a) T. Naota, Y. Shichijo, S.-I. Murahashi, *J. Chem. Soc., Chem. Commun.* **1994**, *11*, 1359-1360. b) S.-I. Murahashi, T. Naota, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1805-1824.

Moreover, Awasthi *et al.* had previously shown the transformation of aromatic nitriles into their corresponding carboxylic acids by simply heating them in an ionic liquid such as 1-butyl-3-methylimidazolium hydrogensulfate.[174] We observed no reaction under these conditions (Scheme 3.43).

3.3.2.2.4. First Viable Introductions Of The Ester Functionality At C6'

We accessed tosylate **104** starting from alcohol **57** by the afore-mentioned methods (Scheme 3.44).[175] Nitrile **115** was obtained through a subsequent S_N2 reaction with sodium cyanide as described above.[176] As direct reduction and alcoholysis of nitrile **115** did not yield any positive results (Scheme 3.43), we sought another method, such as its basic hydrolysis with aqueous hydrogen peroxide and sodium hydroxide as reported by Montero *et al*., for a fully unprotected sugar derivative.[177] This procedure led to the formation of amide **117** in moderate but reproducible 70% yield (Scheme 3.44).



Scheme 3.44: First successful route towards the alkyne **35b**. Reagents and conditions: (a) TosCl, 4-DMAP, TEA, DCM, 0 °C to rt, 16 h, 98%; (b) NaCN, DMSO, rt to 80 °C, 16 h, 97%; (c) aq. H_2O_2 (35%), NaOH, EtOH, rt, 22 h, 70%; (d) 1.3 eq. [Me_3OBF_4], DCM, rt, 6 h, degradation; (e) 5 eq. [Me_3OBF_4], 12 eq. PVP (poly(4-vinylpyridine)), DCM, rt, 1.5 h, starting decomposition, SM **117** mostly recovered (77%); (f) DMF·DMA, MeOH, 65 °C, 7 d, 30%.

Amide **117** was then submitted to different conditions to perform the transformation into ester **35b** (Scheme 3.44). First, we tried to access the corresponding imidoester **118** by

[174] S. Kumar, S. K. Dixit, S. K. Awasthi, *Tetrahedron Lett.* **2014**, *55*, 3802-3804.
[175] a) S. Marchesan, D. Macmillan, *Chem. Commun.* **2008**, *36*, 4321-4323. b) A. J. Pihko, K. C. Nicolaou, A. M. P. Koskinen, *Tetrahedron: Asymmetry* **2001**, *12*, 937-942.
[176] a) T. Heidelberg, J. Thiem, *Carbohydr. Res.* **1997**, *301*, 145-153. b) L. V. Dunkerton, K. T. Brady, F. Mohamed, B. P. McKillican, *J. Carbohydr. Chem.* **1988**, *7*, 49-65. c) K. Zhu, J. S. Panek, *Org. Lett.* **2011**, *13*, 4652-4655.
[177] V. Barragan-Montero, A. Awwad, S. Combemale, P. de Santa Barbara, B. Jover, J.-P. Molès, J.-L. Montero, *ChemMedChem* **2011**, *6*, 1771-1774.

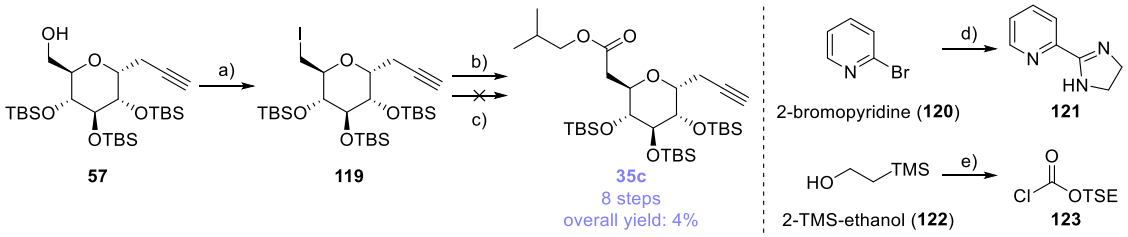
methylation. The use of Meerwein´s salt on its own according to Ogawa *et al.*[178] and Kocieński *et al.*,[179] or in the presence of poly(4-vinylpyridine) (PVP) as an additive according to De Brabander *et al.*,[180] resulted only in decomposition of our C-glucoside (due to the successive cleavage of its TBS groups).

Only after treatment of amide **117** with *N*,*N*-dimethylformamide dimethyl acetal in methanol (according to a precedent by Hansen *et al.* used for a sugar derivative as well[181]) could we obtain methyl ester **35b** (Scheme 3.44). A major drawback was the 30% yield of this reaction, which we were unable to improve.

Nevertheless, this resulted in another pathway to alkyne building block **35b** in ten steps starting from per-*O*-acetyl-α-*D*-glucopyranose (**50**) with an overall yield of roughly 3%.

Another way in which we were able to introduce an ester functionality into substrate **35** at its C6' position also started with alcohol **57** that was first submitted to an Appel reaction (Scheme 3.45). In analogy to reports by Isobe *et al.*[182] and Jensen *et al.*[183] on benzyl-protected sugars, this operation resulted in alkyl iodide **119** in 99% yield.[184] Iodide **119** was then submitted to a nickel-catalyzed reductive coupling of alkyl halides with chloroformates recently reported by Gong *et al.*[185] The introduction of an *i*-butyl ester functionality starting with the corresponding *i*-butyl chloroformate and ending with **35c** succeeded with 25% yield. Therefore, a second pathway to alkyne **35** in eight steps starting from per-*O*-acetyl-α-*D*-glucopyranose (**50**) with an overall yield of roughly 4% was found.

[178] Y. Nakahara, A. Fujita, K. Beppu, T. Ogawa, *Tetrahedron* **1986**, *42*, 6465-6476.
[179] P. Kocieński, K. Jarowicki, S. Marczak, *Synthesis* **1991**, *12*, 1191-1200.
[180] Y. Feng, X. Jiang, J. K. De Brabander, *J. Am. Chem. Soc.* **2012**, *134*, 17083-17093.
[181] S. U. Hansen, M. Baráth, B. A. B. Salameh, R. G. Pritchard, W. T. Stimpson, J. M. Gardiner, G. C. Jayson, *Org. Lett.* **2009**, *11*, 4528-4531.
[182] S. Hosokawa, M. Isobe, *J. Org. Chem.* **1999**, *64*, 37-48.
[183] A. H. Viuff, L. M. Besenbacher, A. Kamori, M. T. Jensen, M. Kilian, A. Kato, H. H. Jensen, *Org. Biomol. Chem.* **2015**, *13*, 9637-9658.
[184] Laboratory apprentice C. Rustemeier once synthesized alkyl iodide **119** (ca. 110 mg).
[185] M. Zheng, W. Xue, T. Xue, H. Gong, *Org. Lett.* **2016**, *18*, 6152-6155.



Scheme 3.45: Reductive cross coupling for the introduction of the ester functionality and ligand synthesis. Reagents and conditions: (a) I_2, PPh_3 **195a**, PhH, rt, 1 h, 99%; (b) *i*-butyl chloroformate, 5 mol% $Ni(COD)_2$, 5 mol% ligand **121**, Zn, 50 mol% TBAI, 4 Å MS, DMA/THF (7:3), rt, 20.5 h, 25%; (c) chloroformate **123**, 5 mol% $Ni(COD)_2$, 5 mol% ligand **121**, Zn, 50 mol% TBAI, 4 Å MS, DMA/THF (7:3), rt, several hours, decomposition; (d) 1,2-ethylene diamine, *t*-BuNC, 10 mol% dppp (bis(1,3-diphenylphosphino)-propane), 5 mol% $PdCl_2$, Cs_2CO_3, PhMe, 120 °C, 3 d, 51%; (e) *phosgene*, PhMe, 0 °C, 3 h, 48%.

The ligand **121**, essential for the nickel-catalyzed reductive coupling, was prepared according to a procedure by Himeda *et al.*,[186] but proved to be unstable over the course of a few months (Scheme 3.45). Furthermore, the reductive coupling proved to be very dependant on the catalyst loading. A catalyst loading of 5 mol% was found to be most useful, since lower amounts (2 mol%) did not result in any reductive coupling, while higher catalyst loadings (10-90 mol%) led to decomposition of the starting materials. Literature-known chloroformate **123**, prepared according to a procedure by Gerlach *et al.*,[187] finally proved to be unsuitable for the reductive coupling since this resulted in decomposition. In contrast to the *i*-butyl derivative **35c** TMS-ethyl ester **35a** was not directly accessible by this method.

In summary, two successful routes to access the sugar-based fragment **35** are herein described. Because both pathways had specific drawbacks (low yield, undesired *i*-butyl ester, difficulty with catalyst loading), the direct PCC oxidation of enolether **59** into ester **35** was used to secure material supply as necessary for the total synthesis (Chapter 3.3.1.2.5).

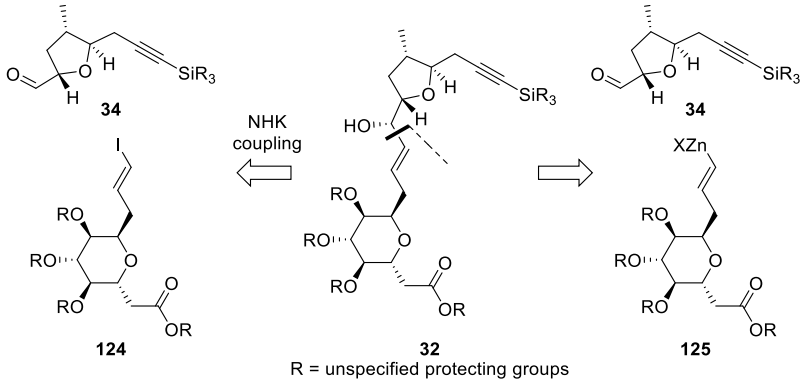
[186] S. Xu, N. Onishi, A. Tsurusaki, Y. Manaka, W.-H. Wang, J. T. Muckerman, E. Fujita, Y. Himeda, *Eur. J. Inorg. Chem.* **2015**, *34*, 5591-5594.
[187] A. B. Shenvi, H. Gerlach, *Helv. Chim. Acta* **1980**, *63*, 2426-2433.

3.3.2.3. Building Block Coupling & Elaboration

Regarding the low yielding alkynylation of the sugar-derived aldehydes described earlier (Chapter 3.3.1.3.2), a different fragment coupling strategy was considered.

3.3.2.3.1. Nozaki-Hiyama-Kishi Coupling & Related Alkenyl-Zinc Additions

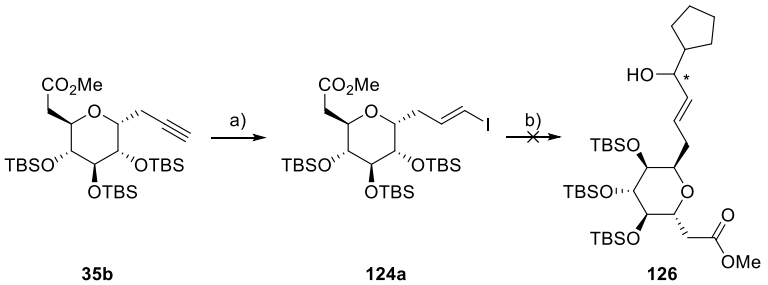
Instead of the addition of alkynes to aldehydes, we envisaged the use of a Nozaki-Hiyama-Kishi coupling (NHK) or a related coupling with an alkenyl-zinc species (Scheme 3.46). This leads back to the exact same aldehyde **34** and a new alkenyl iodide **124** or an alkenyl-zinc species **125**.



Scheme 3.46: Alternative disconnection approach by NHK or related B/Zn-mediated cross coupling.

Based on this central NHK disconnection (Scheme 3.46), we planned to synthesize alkenyl iodide **124a** starting from alkyne **35b** (Scheme 3.47). Alkyne **35b** was submitted a hydrozirconation reported by Johnson *et al.* in the total synthesis of alternaric acid[188] and by our group in the total synthesis of 16-*epi*-latrunculin B[189] for ester-bearing substrates. In this short sequence, the Schwartz reagent reacts with the alkyne **35b** to give an alkenyl-zirconium species. As planned, reaction with iodine gave the desired alkenyl iodide **124a**, although in only 33% yield.

[188] M. C. Slade, J. S. Johnson, *Beilstein J. Org. Chem.* **2013**, *9*, 166-172.
[189] A. Fürstner, D. De Souza, L. Turet, M. D. B. Fenster, L. Parra-Rapado, C. Wirtz, R. Mynott, C. W. Lehmann, *Chem. Eur. J.* **2007**, *13*, 115-134.



Scheme 3.47: Synthesis of the attempted NHK precursor. Reagents and conditions: (a) i. Cp_2ZrHCl, THF, 0 °C, 30 min; ii. I_2, THF, 0 °C, 30 min, 53%; (b) 1 eq. cyclopentanecarbaldehyde, 10 mol% $CrCl_2$·THF, 2 mol% $NiCl_2$, 25 mol% $BnBu_3NCl$, 2 eq.LiCl, 2 eq. Mn, 2 eq. TMSCl, THF, rt, 7 d, no reaction observed, SM **124a** mainly recovered (66%).

The obtained alkenyl iodide **124a** was submitted to a ligand-free NHK reaction according to a procedure used by our group during an approach to the higher sugar core of hikizimycin,[190] but the attempted product **126** could not be obtained (Scheme 3.47). Most of the unreacted starting material **124a** was recovered (66%).

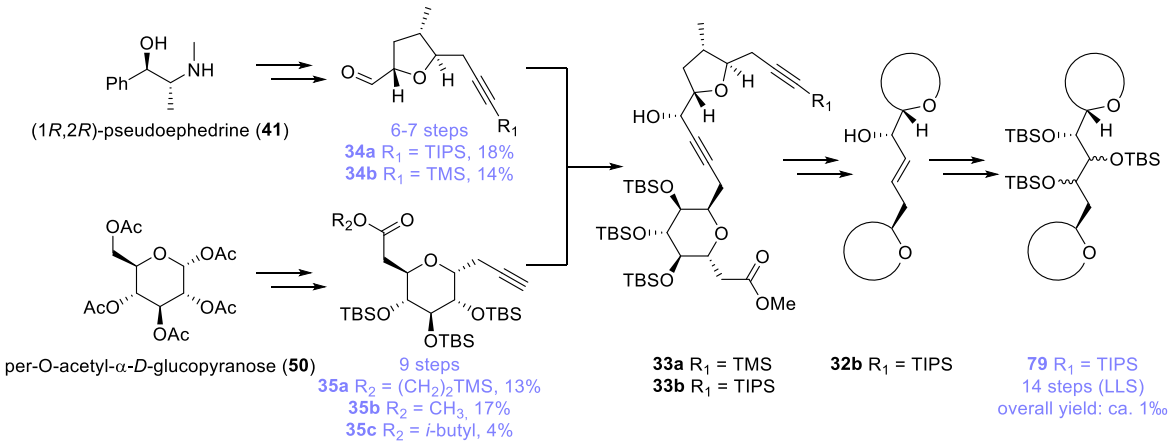
Since the reaction towards alkenyl iodide **124a** was low-yielding and a ligand-free version of the NHK reaction did not result in product formation, we did not proceed any further. For the coupling of our fragments, we focused on the alkynylation strategy with zinc(II) trifluoromethanesulfonate and *N*-methylephedrine, since it was already giving access to the desired material **33** (> 100 mg), and thus was to be optimized.

[190] A. Fürstner, M. Wuchrer, *Chem. Eur. J.* **2006**, *12*, 76-89.

3.3.3. Interim Summary

Auxiliary-based chemistry, in combination with CBS reduction and an aerobic oxidative Mukaiyama cyclization, was used to forge the 2,5-*trans*-disubstituted tetrahydrofuran ring **34** (Scheme 3.48). Starting from (1*R*,2*R*)-pseudoephedrine **41**, this goal was accomplished in six steps with an overall yield of 18%.

Alkyne **35** was accessed from per-*O*-acetyl-α-*D*-glucopyranose (**50**) in nine steps with an overall yield of 13-17% (Scheme 3.48). Initial C-glycosidation and a sequence of ozonolysis and Seyferth-Gilbert homologation introduced the alkynyl side chain. A Wittig olefination at the C6' terminus made different esters available such as the TMS-ethyl (**35a**) and the methyl ester (**35b**). In contrast, preliminary studies showed, that the corresponding *i*-butyl ester derivative **35c** could be synthesized via a nickel-catalyzed reductive cross coupling with a chloroformate.



Scheme 3.48: First synthetic route to western belizentrin fragment **79**. Reagents and conditions: as shown before.

The obtained fragments were coupled by a stereoselective alkynylation giving propargylic alcohol **33** in 21-25% yield (Scheme 3.48). For the aimed *trans*-selective hydrostannation, only the TIPS-capped substrate **33b** was a useful candidate due to its sterically protected second alkyne moiety. Protodestannation proceeded cleanly to give rise to desired allylic alcohol **32b**.

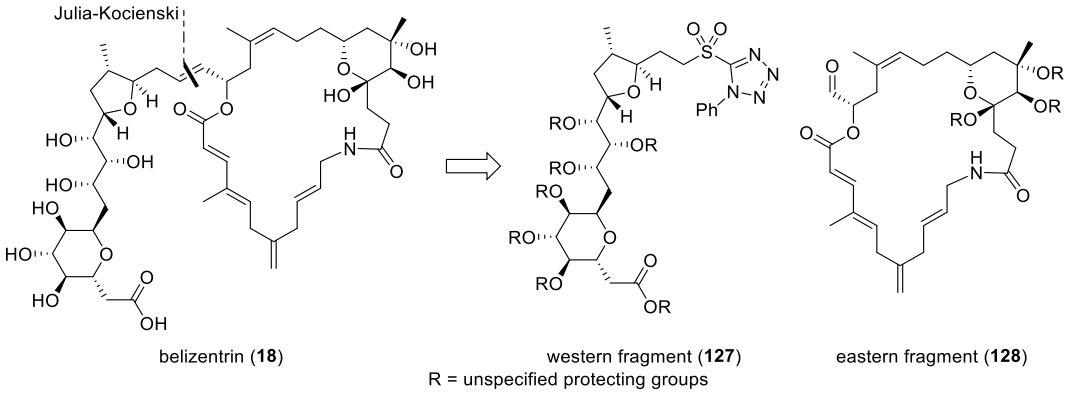
A major drawback arose during the osmium-promoted dihydroxylation. Under all conditions investigated, the same distinct diastereomer of **79** was formed as the *major* product. Neither Sharpless dihydroxylation nor the conditions described by Donohoe reversed this selectivity. Unfortunately, the stereochemical outcome could not be elucidated at this point, leaving undetermined which of the diastereomers was preferred. Nevertheless, the reaction sequence

(14 steps LLS, ca. 1‰) provided a first tiny crop of both globally protected diastereomers of triol **79**.

In light of these results, the originally envisioned central alkynylation of both belizentrin fragments **79** and **30** seemed unsuitable for the completion of the natural product **18** or its congeners **19** or **20**. Thus we considered a first retrosynthetic revision, while maintaining most of the major transformations for the introduction of the triol motif.

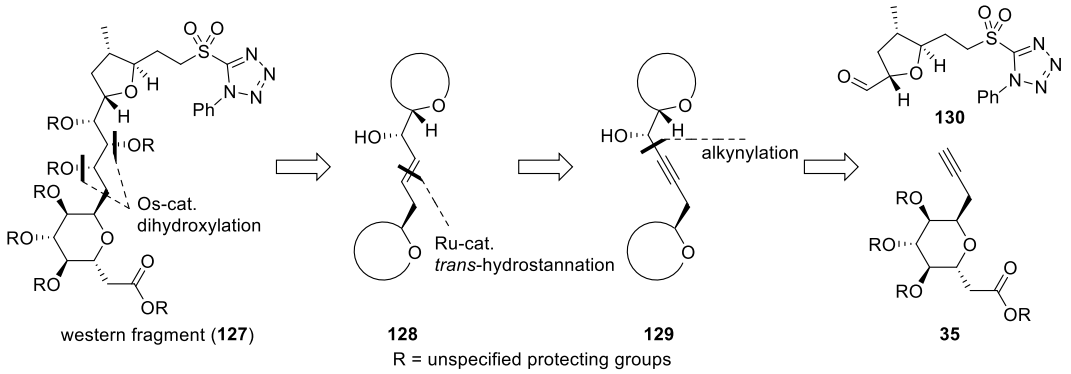
3.4. First Retrosynthetic Revision

In order to synthesize belizentrin (**18**) in a more convergent manner without major changes to the single parts, the molecule was disconnected at the central *E*-configured double bond (Scheme 3.49). A Julia-Kocienski olefination retron led back to western side chain **127** bearing the required tetrazolylsulfone and an eastern macrocyclic aldehyde **128**.



Scheme 3.49: New retrosynthetic analysis of belizentrin (**18**).

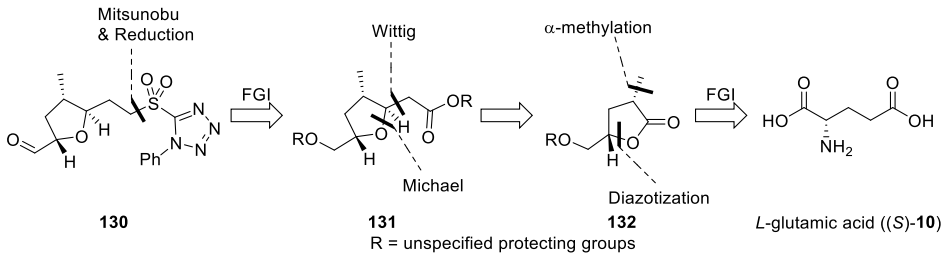
The western belizentrin fragment **127** should be approached by maintaining an osmium-catalyzed dihydroxylation giving rise to allylic alcohol **128** (Scheme 3.50). In order to obtain the allylic alcohol **128**, we wanted to make use of our in house-developed methodology of the ruthenium-catalyzed *trans*-hydrostannation originating from propargylic alcohol substrate **129**. Propargylic alcohol **129** was disconnected at the α-position via an aldehyde alkynylation, requiring aldehyde **130** and the unmodified alkyne **35**.



Scheme 3.50: New retrosynthetic analysis of the western belizentrin fragment **127**.

The retrosynthetic analysis of aldehyde **130** started with simple functional group interconversions (Scheme 3.51). It was aimed to introduce the tetrazolylsulfone group by a reduction and Mitsunobu inversion at the terminus, bringing forth the functionalized 2,5-*trans*-disubstituted

tetrahydrofuran ring **130**. The major disconnection of the five-membered ring **131** was a ring-closing Michael addition. The necessary α,β-unsaturated ketone was disconnected by a Wittig olefination, resulting in lactone **132** after a functional group interconversion from the corresponding lactol.



Scheme 3.51: New retrosynthetic analysis of the 2,5-*trans*-disubstituted ether **130**.

A final α-methylation (and the inversion of this methyl group), as well as preliminary diazotization were pointing to *L*-glutamic acid ((*S*)-**10**) as the commercial starting point of the synthesis (Scheme 3.51).

3.5. Western Belizentrin Fragment - Route 2

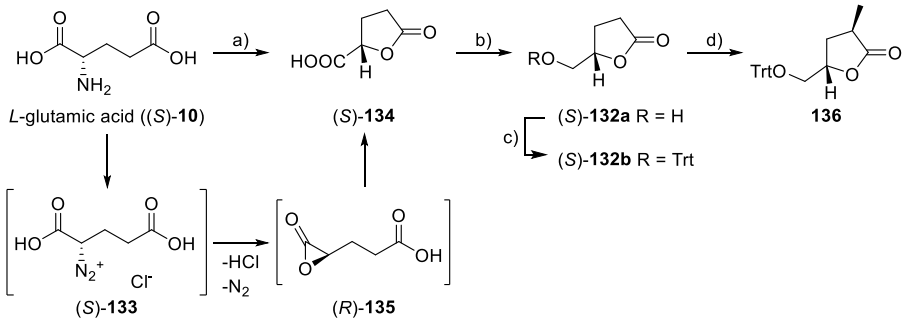
3.5.1. Successful Synthetic Route

3.5.1.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring - A New Synthesis

3.5.1.1.1. From *L*-Glutamic Acid To The 2,5-*trans*-Disubstituted Tetrahydrofuran Core

The new synthesis is based on a literature known pathway for the enantiomer of 2,5-*trans*-disubstituted ether **131a** involved in the total synthesis of amphidinolides C and F published by our group (Scheme 3.52).[191] The sequence started with the diazotization of *L*-glutamic acid ((*S*)-**10**) at low temperature according to a large scale synthesis of (*S*)-**134** reported by Chorghade *et al.*[192] and Rouessac *et al.*[193]

During the reaction, the three-membered lactone (*R*)-**135** was first generated by the intramolecular S_N2 reaction of *in situ* formed diazo compound (*S*)-**133** with the more proximate carboxylic acid under inversion (Scheme 3.52). After nucleophilic attack of the second carboxylic acid of (*R*)-**135** on its three-membered lactone cycle (S_N2 again) the new five-membered lactone (*S*)-**134** was generated. This sequence explains the overall retention of the configuration at the stereocentre.



Scheme 3.52: Synthesis of the 2,5-*trans*-disubstituted ether **130**, Part A. Reagents and conditions: (a) $NaNO_2$, conc. aq. HCl, H_2O, 0 °C to rt, 1 d, 79%; (b) $BH_3{\cdot}SMe_2$, THF, 0 °C to rt, 18 h, 69%; (c) TrtCl, py, rt, 16 h, 73%; (d) DIPA, *n*-BuLi, MeI, 4 Å MS, THF, -78 °C to -30 °C, 4.5 h, 99%.

[191] G. Valot, D. Mailhol, C. S. Regens, D. P. O'Malley, E. Godineau, H. Takikawa, P. Philipps, A. Fürstner, *Chem. Eur. J.* **2015**, *21*, 2398-2408.
[192] X. Cai, M. S. Chorghade, A. Fura, G. S. Grewal, K. A. Jauregui, H. A. Lounsbury, R. T. Scannell, C. G. Yeh, M. A. Young, S. Yu, L. Guo, R. M. Moriarty, R. Penmasta, M. S. Rao, R. K. Singhal, Z. Song, J. P. Staszewski, S. M. Tuladhar, S. Yang, *Org. Process Res. Dev.* **1999**, *3*, 73-76.
[193] O. H. Gringore, F. P. Rouessac, M. F. Schlecht, H. Drossman, C. H. Heathcock, *Organic Syntheses*, John Wiley & Sons, Inc. (New York), **2003**.

The synthesis was accomplished according to the procedure by Fürstner *et al.* for the enantiomer of **131a** unless otherwise stated (Scheme 3.52).[194] The carboxylic acid side chain of lactone (*S*)-**134** was reduced with borane dimethylsulfide to generate the corresponding alcohol (*S*)-**132a**. Tritylation of (*S*)-**132a** led to protected lactone (*S*)-**132b**, which was α-methylated giving rise to lactone **136** (Figure 3.18).

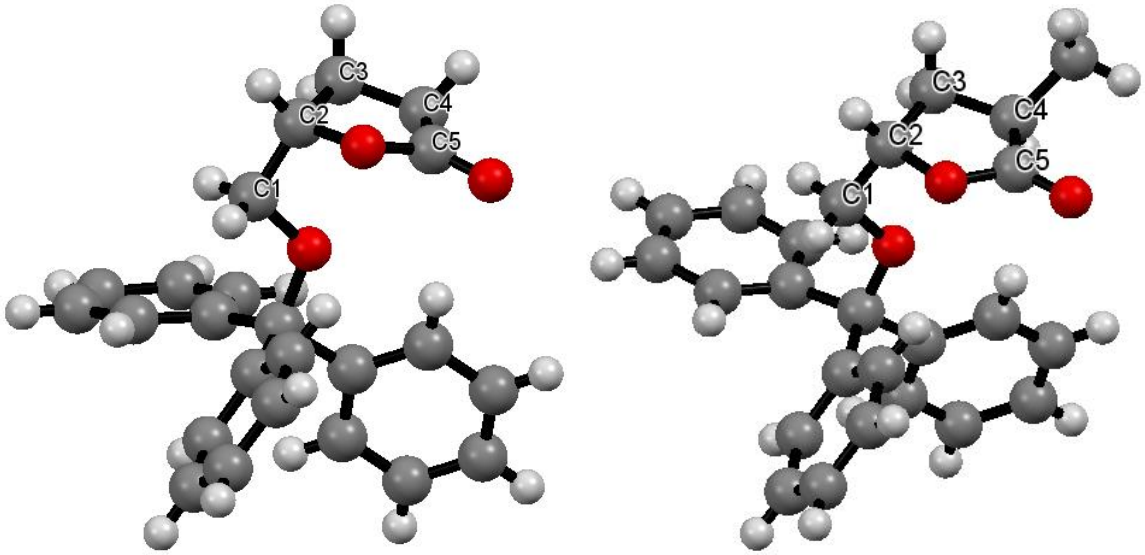
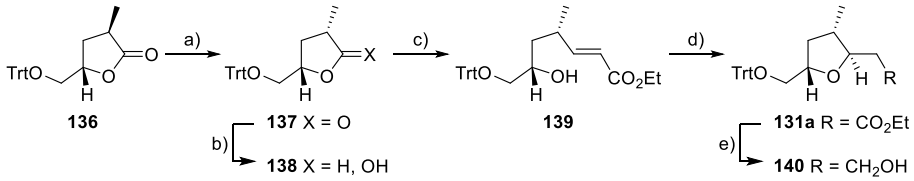


Figure 3.18: X-Ray single crystal structure of lactones (*S*)-**132b** and **136** (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red)).

The methyl group of intermediate **136** was inverted by deprotonation in α-position with LDA and reprotonation during the work-up (Scheme 3.53, Figure 3.19). The lactone functionality of **137** was reduced, using di-*i*-butylaluminium hydride (DIBAL) resulting in a diastereomeric mixture of lactol **138**. After Wittig olefination of hemiacetal **138**, secondary alcohol **139** was obtained. Subsequent intramolecular 1,4-addition of the hydroxy group to the enone functionality of **139** resulted in the 2,5-*trans*-disubstituted ether **131a** (*ent*-**131a** is literature known) (Figure 3.19).



Scheme 3.53: Synthesis of the 2,5-*trans*-disubstituted ether **130**, Part B. Reagents and conditions: (a) DIPA, *n*-BuLi, THF, -78 °C to 0 °C, 45 min, 96%; (b) DIBAL, DCM, PhMe, -78 °C, 3 h, 98%; (c) Ph_3P=CH-COOEt, PhMe, rt to 80 °C, 17 h, 69%; (d) TBAF·$3H_2O$, THF, 0 °C, 3 h, 82%; (e) $LiAlH_4$, THF, -20 °C to 0 °C, 2.25 h, quant.

[194]G. Valot, D. Mailhol, C. S. Regens, D. P. O'Malley, E. Godineau, H. Takikawa, P. Philipps, A. Fürstner, *Chem. Eur. J.* **2015**, *21*, 2398-2408.

The ester group of **131a** was reduced to the corresponding alcohol **140** with lithium aluminium hydride according to a literature precedent by Noyori *et al.* on a tritylated ribose derivative (Scheme 3.53).[195]

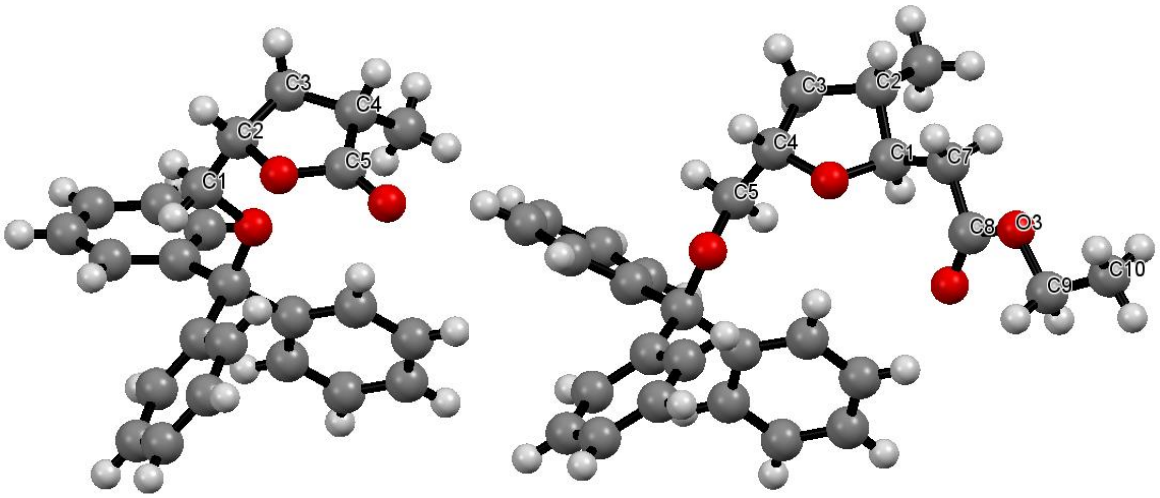
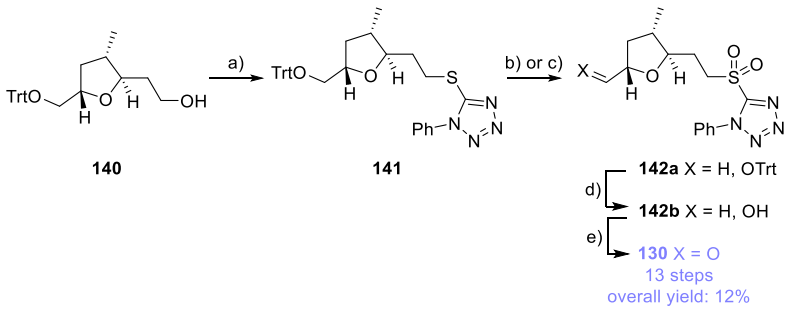


Figure 3.19: X-Ray single crystal structure of lactone **137** and 2,5-*trans*-disubstituted ether **131a** (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red)).

[195] T. Sato, R. Noyori, *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2700-2705.

3.5.1.1.2. Introduction Of The Tetrazolylsulfone

Primary alcohol **140** was submitted to a Mitsunobu reaction with 1-phenyl-1*H*-tetrazole-5-thiol **168** in analogy to the procedures for similar substitutions by Wicha *et al.*[196] and Helmchen *et al.*[197] (Scheme 3.54). This resulted in sulfide intermediate **141**,[198] which was subsequently oxidized to the corresponding sulfone **142a** based on another literature precedent by Bera *et al.* for a comparable aliphatic substrate.[199]



Scheme 3.54: Synthesis of the 2,5-*trans*-disubstituted ether **130**, Part C. Reagents and conditions: (a) 1-phenyl-1*H*-tetrazole-5-thiol **168**, DIAD, PPh_3 **195a**, THF, 0 °C to rt, 17 h, 87%; (b) $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, aq. H_2O_2 (35%), EtOH, rt, 5 d, 71%; (c) *m*-CPBA, DCM, rt, 1 d, quenched cautiously, 67%; (d) TFA, DCM, 0 °C, 1 h, 98%; (e) i. $(COCl)_2$, DMSO, DCM, -78 °C, 30 min; ii. DIPEA, -78 °C to rt, 1 h, 94%.

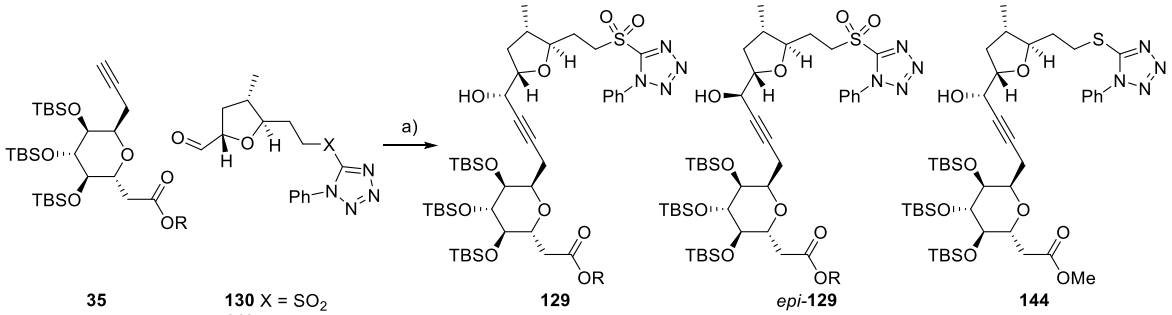
Compound **142a** was detritylated by the treatment with TFA regarding a procedure by Xie *et al.* on tritylated sugar derivatives[200] resulting in primary alcohol **142b** (Scheme 3.54). The synthesis sequence was completed by the oxidation of the obtained alcohol **142b** to aldehyde **130** under Swern conditions according to a report by Mohapatra *et al.* for another 2,5-*trans*-disubstituted ether derivative.[201] Thus, the new building block **130** was obtained in 13 steps with an overall yield of 12%.

[196] P. R. Blakemore, P. J. Kocienski, S. Marzcak, J. Wicha, *Synthesis* **1999**, *7*, 1209-1215.
[197] T. Hübscher, G. Helmchen, *Synlett* **2006**, *9*, 1323-1326.
[198] Laboratory apprentice C. Rustemeier helped with the synthesis and purification of thioether **141** (on a scale of ca. 1 g).
[199] B. Chatterjee, D. Mondal, S. Bera, *Tetrahedron: Asymmetry* **2012**, *23*, 1170-1185.
[200] S. Peyrat, K. Cheng, J. Xie, *Synthesis* **2013**, *45*, 2737-2744.
[201] D. K. Mohapatra, P. Dasari, H. Rahaman, R. Pal, *Tetrahedron Lett.* **2009**, *50*, 6276-6279.

3.5.1.2. Building Block Coupling & Elaboration

3.5.1.2.1. Aldehyde Akynylation

For fusing the alkyne **35** with the 2,5-*trans*-disubstituted ether **130**, we still relied on the zinc-mediated aldehyde alkynylation (Scheme 3.55).[202]



L*	R	time	yield **129**	yield *epi*-**129**	yield **145**	recovered SM **35**
(+)-NME	CH_3	3 d	19%*	-	5%***	51%
			26%**	-	6%***	68%
(-)-NME	CH_3	5 d	-	31%	-	57%
	$(CH_2)_2TMS$		-	16%	-	78%

* with 4 Å MS in reaction vessel
** $Zn(OTf)_2$ dried for 5 h at 120°C at HV; no MS in reaction, only for prior drying of SM **35** and **130**
*** isolated as a result of incomplete oxidation of thiol **141**; enrichment during subsequent transformations

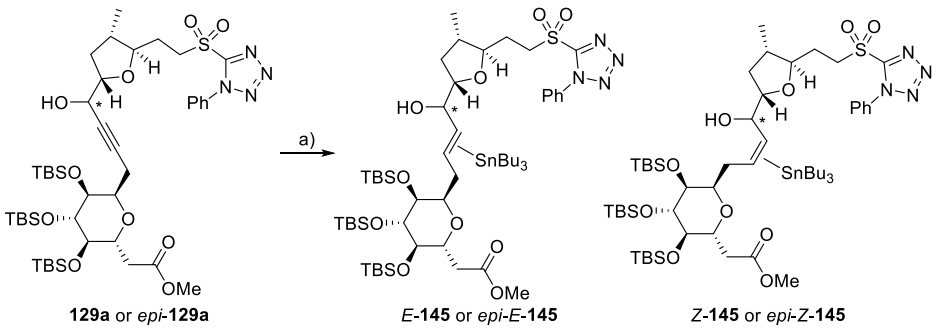
Scheme 3.55: Fragment coupling. Reagents and conditions: (a) $Zn(OTf)_2$, L*, TEA or DIPEA, PhMe, rt, yield and reaction time as shown.

The coupling resulted in the stereoselective formation of both diastereomers **129** and *epi*-**129** by using the two different enantiomers of *N*-methylephedrine (Scheme 3.55). The yields ranged between 18-31%. When zinc(II) trifluoromethanesulfonate was especially dried prior to its use (200 °C under high vacuum for 5 h) and molecular sieves was not present during the reaction, the yield did not increase (from 19-26%). Besides, undesired thioether **144** was isolated as a byproduct, originating from the incomplete oxidation of thioether **141** to sulfone **142a** in small amounts (5-6%, Scheme 3.54).

[202] a) E. M. Carreira, *Patent US2003/0088100* **2003**. b) A. Fettes, E. M. Carreira, *J. Org. Chem.* **2003**, *68*, 9274-9283.

3.5.1.2.2. Alkene-To-Alkyne-Tranformation

Subsequently, we performed the *trans*-selective ruthenium-catalyzed hydrostannation on the propargylic alcohol diastereomers **129** and *epi*-**129** (Scheme 3.56).[203] The main difference to the previous investigation on the *trans*-hydrostannation (Chapter 3.3.1.3.3) lied within the newly introduced sulfonic side chain instead of a second alkyne moiety. Therefore, we hoped for an intrinsically higher selectivity.

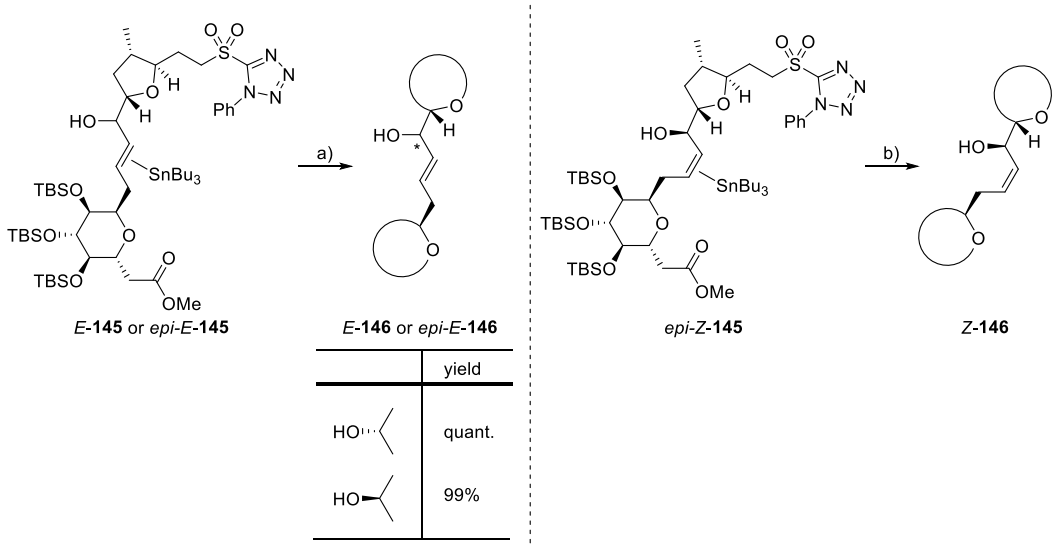


stereocentre	yield *E*-**145**/*epi*-*E*-**145**	yield *Z*-**145**/*epi*-*Z*-**145**	recovered SM **129a**/*epi*-**129a**
HO	67%	-	18%
HO	59%	9%	21%

Scheme 3.56*: trans*-Hydrostannation. Reagents and conditions: (a) 10 mol% $[Cp^*RuCl]_4$, *n*-Bu_3SnH, 4 Å MS, DCM, -50 °C to rt to -50 °C, 30 min, yield and selectivity as shown.

When the *trans*-hydrostannation was performed on propargylic alcohol **129** with the tetrameric ruthenium catalyst $[Cp^*RuCl]_4$, we observed the exclusive formation of the stannane *E*-**145**. When the diastereomeric propargylic alcohol *epi*-**129** was used, *epi*-*E*-**145** was formed as the major product of the reaction with an *E*/*Z* selectivity of 6.6:1 (Scheme 3.56). The α:β selectivity was not determined, since subsequent protodestannation was planned. In both cases, a complete conversion could not be reached and starting material **129** or *epi*-**129** was partially recovered (18-21%).

[203] a) S. M. Rummelt, A. Fürstner, *Angew. Chem. Int. Ed.* **2014**, *53*, 3626-3630. b) S. M. Rummelt, K. Radkowski, D.-A. Roşca, A. Fürstner, *J. Am. Chem. Soc.* **2015**, *137*, 5506-5519. c) S. M. Rummelt, J. Preindl, H. Sommer, A. Fürstner, *Angew. Chem. Int. Ed.* **2015**, *54*, 6241-6245.



Scheme 3.57: Protodestannation in a biphasic mixture under PTC. Reagents and conditions: (a) aq. HI (57%), TBAI, PhMe, 0 °C, 4 h, yield as shown; (b) aq. HI (57%), TBAI, PhMe, 0 °C, 6 h, 98%.

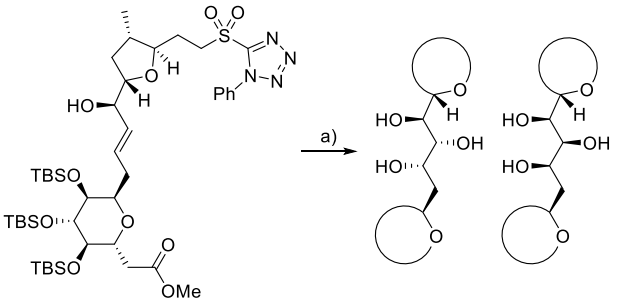
Stannane **145** was submitted to the previously described conditions for the protodestannation with aqueous hydroiodic acid under phase transfer catalysis (PTC, Scheme 3.57) to give the allylic alcohol **146** in 98%-quant. yield.[204]

3.5.1.2.3. Sharpless Dihydroxylation

With allylic alcohol **146** accessible, we were able to perform the osmium-promoted dihydroxylation to install the central triol motif of the western belizentrin fragment **127** (Scheme 3.58, Scheme 3.59).

Sharpless dihydroxylation of allylic alcohol *epi-E*-**146** with different ligands gave both diastereomeric triols **147** and **148** in acceptable selectivities ranging between 2.7:1 and 1:1.7 (Scheme 3.58).[205] Ligand control was achieved with this particular substrate. This was in stark contrast to the dihydroxylation previously described for the alkyne-bearing substrate **32b**, where one diastereomer was preferentially formed in all cases investigated (Scheme 3.25).

[204] M. Mori, N. Kaneta, M. Shibasaki, *J. Organomet. Chem.* **1994**, *464*, 35-40.
[205] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483-2547.



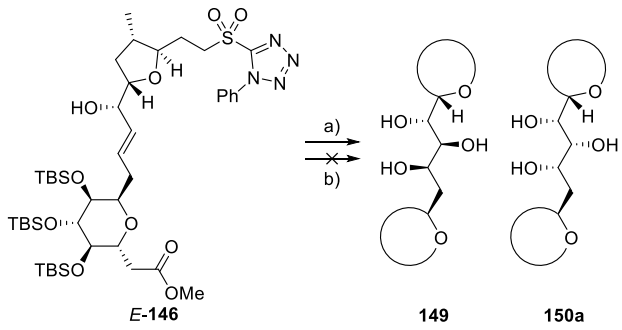
L*	*d.r.*** (*anti*:*syn*)
$(DHQ)_2PHAL$	2.6:1
$(DHQD)_2PHAL$	1:2.1
$(DHQ)_2PYR$	2.7:1
$(DHQD)_2PYR$	1.1:1
$(DHQ)_2AQN$	2.1:1
$(DHQD)_2AQN$	1:1.7

** determined by HPLC

Scheme 3.58: Ligand screening for the Sharpless dihydroxylation of the allylic alcohol *epi*-*E*-**146**. Reagents and conditions: (a) 40 mol% K_2OsO_4, 100 mol% L*, $MeSO_2NH_2$, $K_3[Fe(CN)_6]$, K_2CO_3, *t*-BuOH/H_2O (1:1), 0 °C to rt, 21 h, 80% (for both diastereomers) and some recovered SM *epi*-*E*-**146** (8%).

In parallel, *desired* diastereomer *E*-**146** was also prepared and tested in the osmium-promoted Sharpless dihydroxylation[206] and under Donohoe conditions[207] (Scheme 3.59).

In this case, however, the use of different chiral ligands resulted in the formation of the same *major* isomer (Scheme 3.59). No matter which pseudoenantiomeric ligand L* was used, the stereoselectivities ranged between 7:1 and 9.3:1 in favour of the *undesired* triol **149** (stereochemical assignment shown in Chapter 3.5.1.3 and Chapter 3.7.1.3).



L*	*d.r.*** (*anti*:*syn*)
$(DHQ)_2PHAL$	7:1
$(DHQD)_2PHAL$	9.3:1
$(DHQ)_2PYR$	9.3:1
$(DHQD)_2PYR$	7.4:1
$(DHQ)_2AQN$	8:1
$(DHQD)_2AQN$	8.1:1

** determined by HPLC

Scheme 3.59: Ligand screening for the Sharpless dihydroxylation of the allylic alcohol *E*-**146** and dihydroxylation under Donohoe conditions. Reagents and conditions: (a) 10 mol% K_2OsO_4, 12.5 mol% L*, $MeSO_2NH_2$, $K_3[Fe(CN)_6]$, K_2CO_3, *t*-BuOH/H_2O (1:1), 0 °C to rt, 1 d, 40% (for both diastereomers) and recovered SM *E*-**146** (47%); (b) i. 2.1 eq. OsO_4, 2.2 eq. TMEDA, DCM, -78°C, 80 min; ii. 40 eq. 1,2-ethylene diamine, -78 °C to rt, 2 d, stable adduct was not cleaved; then 96 eq. $NaHSO_5$, H_2O, rt, 20 min, decomposition.

An experiment applying the conditions decribed by Donohoe *et al.* with OsO_4·TMEDA looked promising, since the thin-layer chromatogram (TLC) clearly showed the formation of a new product and the complete consumption of the starting material *E*-**146**. The major drawback was

[206] See footnote 205.

[207] a) T. J. Donohoe, K. Blades, P. R. Moore, M. J. Waring, J. J. G. Winter, M. Helliwell, N. J. Newcombe, G. Stemp, *J. Org. Chem.* **2002**, *67*, 7946-7956. b) K. Blades, T. J. Donohoe, J. J. G. Winter, G. Stemp, *Tetrahedron Lett.* **2000**, *41*, 4701-4704. c) T. J. Donohoe, R. Garg, P. R. Moore, *Tetrahedron Lett.* **1996**, *37*, 3407-3410. d) T. J. Donohoe, N. J. Newcombe, M. J. Waring, *Tetrahedron Lett.* **1999**, *40*, 6881-6885. e) T. J. Donohoe, P. R. Moore, M. J. Waring, N. J. Newcombe, *Tetrahedron Lett.* **1997**, *38*, 5027-5030. f) T. J. Donohoe, L. Mitchell, M. J. Waring, M. Helliwell, A. Bell, N. J. Newcombe, *Org. Biomol. Chem.* **2003**, *1*, 2173-2186.

the unexpectedly high stability of this adduct primarily formed. A typical work-up procedure with 1,2-ethylenediamine did not achieve the cleavage of this intermediate, even after several hours. Administering additional sodium sulfite (typically used for the work-up of Sharpless dihydroxylations) did also not result in any of the desired triols **149** or **150a**, but led to decomposition.

Since such a behavior was not observed with allylic alcohol **32b**, we concluded that the tetrazole sulfone moiety present in the molecule could be a problem in the presence of stoichiometric amounts of osmium(VIII) tetroxide due to its coordinating properties. The structure of this very stable adduct remained unclear, and thus no further experimentation was undertaken.

3.5.1.3. Stereochemical Elucidation

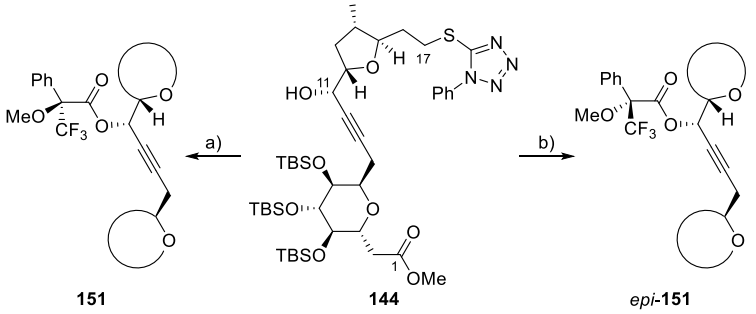
Mosher ester analysis[208] was applied to some of the isolated allylic and propargylic alcohols to determine the absolute configuration of newly introduced stereocentres. All Mosher esters shown herein were prepared and structurally elucidated according to procedures of Kakisawa *et al.*[209] and Hoye *et al.*[210]

Several attempts were undertaken to elucidate the stereochemical configuration of the triol motif by crystallization. Furthermore, cyclic carbonate derivatives of different triols were prepared for the structural elucidation by NMR.

3.5.1.3.1. Mosher Ester Analysis (Propargylic Alcohols)

As briefly mentioned earlier (Chapter 3.5.1.1.2), incomplete oxidation of sulfide **141** to sulfone **142a** (Scheme 3.54) led to the enrichment of an undesired thioether byproduct during the subsequent steps. It could be isolated in small amounts as thioether-bearing alcohol **144** at the stage of the alkynylation (Scheme 3.55).

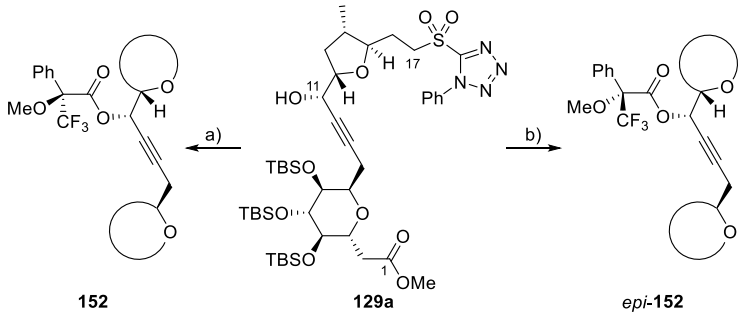
This undesired, yet very elaborated byproduct was submitted to Mosher ester analysis resulting in esters **151** and *epi*-**151** (Scheme 3.60). Thereby, it was a valuable indication of the (*S*)-configured stereocentre at C-11 correctly installed during the alkynylation in the presence of (*+*)-*N*-methylephedrine.



Scheme 3.60: Preparation of Mosher esters of propargylic alcohol **144a**. Reagents and conditions: (a) (*R*)-Mosher acid chloride, py, DCM, rt, 20.5 h, 97%; (b) (*S*)-Mosher acid chloride, py, DCM, rt, 20.5 h, 78%.

[208] J. A. Dale, D. L. Dull, H. S. Mosher, *J. Org. Chem.* **1969**, *34*, 2543-2549.
[209] I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc.* **1991**, *113*, 4092-4096.
[210] T. R. Hoye, C. S. Jeffrey, F. Shao, *Nat. Protocols* **2007**, *2*, 2451-2458.

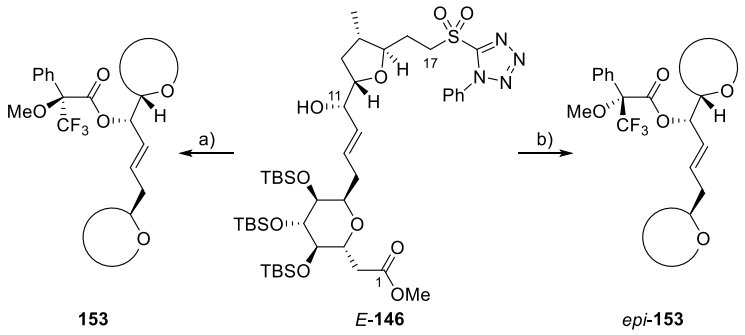
We also prepared Mosher esters **152** and *epi*-**152** starting from propargylic alcohol **129a** (Scheme 3.61). The assumed (*S*)-configuration of stereocentre C-11 could be confirmed as well by comparative analysis.



Scheme 3.61: Preparation of Mosher esters of propargylic alcohol **129a**. Reagents and conditions: (a) (*R*)-Mosher acid chloride, py, DCM, rt, 3 d, 98%; (b) (*S*)-Mosher acid chloride, py, DCM, rt, 3 d, 98%.

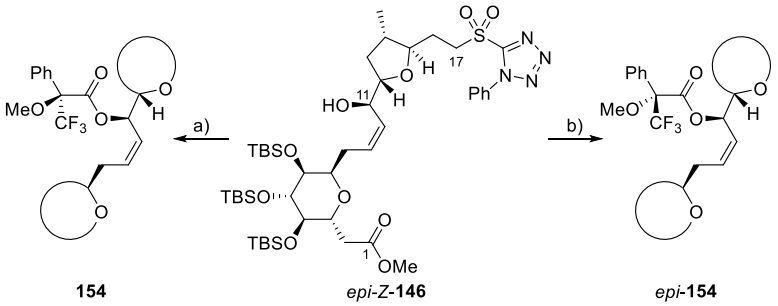
3.5.1.3.2. Mosher Ester Analysis (Allylic Alcohols)

The allylic alcohol *E*-**146** was converted into the corresponding Mosher esters **153** and *epi*-**153** (Scheme 3.62). Their analysis revealed the correctly installed (*S)*-configured stereocentre at C-11 of allylic alcohol *E*-**146** originating from the alkynylation in the presence of (*+*)-*N*-methylephedrine.



Scheme 3.62: Preparation of Mosher esters of allylic alcohol *E*-**146**. Reagents and conditions: (a) (*R*)-Mosher acid chloride, py, DCM, rt, 25 h, 98%; (b) (*S*)-Mosher acid chloride, py, DCM, rt, 25 h, 98%.

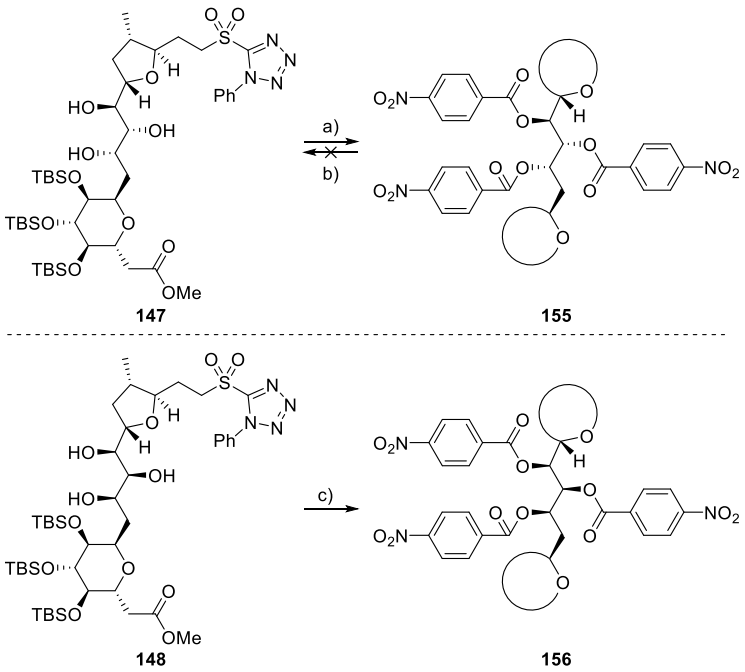
Mosher ester analysis was also performed with the allylic alcohol *epi-Z*-**146**, thus confirming the assumed (*R*)-configuration of its stereocentre at C-11, originating from the use of (-)-*N*-methylephedrine during the alkynylation (Scheme 3.63).



Scheme 3.63: Preparation of Mosher esters of allylic alcohol *epi-Z*-**146**. Reagents and conditions: (a) (*R*)-Mosher acid chloride, py, DCM, rt, 3 d, 90%; (b) (*S*)-Mosher acid chloride, py, DCM, rt, 2 d, 90%.

3.5.1.3.3. Tris-Nitrobenzoic Acid Esters For Crystallization

We wanted to unveal the absolute configuration of triols **147** and **148** by crystallization. It is known in the literature that benzoic acid derivatives often crystallize well due to π-stacking interactions. According to a literature precedent for such an esterification on TBS-protected substrates by Ohfune *et al.*,[211] we prepared both tris-nitrobenzoic acid esters **155** and **156** (Scheme 3.64).



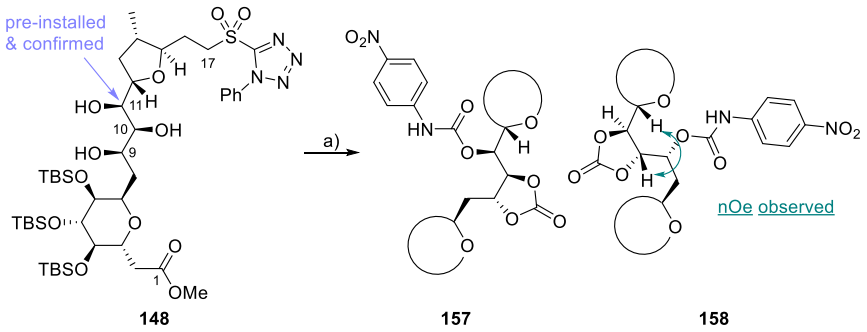
Scheme 3.64: Preparation of the tris-nitrobenzoic acid esters of triols **147** and **148**. Reagents and Conditions: (a) *p*-nitrobenzoic acid, EDC·HCl, 4-DMAP, DCM, rt, 4 d, 79%; (b) 15 eq. NaN_3, MeOH, 40 °C, 4 d, triol deprotection and degradation of sulfone side chain, product remained unknown;[212] (c) *p*-nitrobenzoic acid, EDC·HCl, 4-DMAP, DCM, rt, 21 h, 95%.

Crystallization studies using different solvents (pentane, benzene, etc.) at low temperature or by slow solvent evaporation remained unsuccessful.

[211] M. Higashino, N. Ikeda, T. Shinada, K. Sakaguchi, Y. Ohfune, *Tetrahedron Lett.* **2011**, *52*, 422-425.
[212] J. A. Gómez-Vidal, M. T. Forrester, R. B. Silverman, *Org. Lett.* **2001**, *3*, 2477-2479.

3.5.1.3.4. Cyclic Carbonates & nOe Signal Correlations

Another attempt to obtain triol derivatives suitable for crystallization led to an unexpected, yet very fortunate result. An attempt to derivatize *e.g.* triol **148** as its corresponding *p*-nitrobenzoic acid amide by the use of *p*-nitrophenyl isocyanate according to Carreira *et al.*,[213] led to the formation of different regioisomers **157** and **158** of a mixed carbamate/carbonate (Scheme 3.65).



Scheme 3.65: Structure and nOe correlation of cyclic carbonates **157** and **158**. Reagents and conditions: (a) *p*-nitrophenyl isocyanate, TEA, DCM, rt, 5 d, 93% (*d.r.* = 3:5).

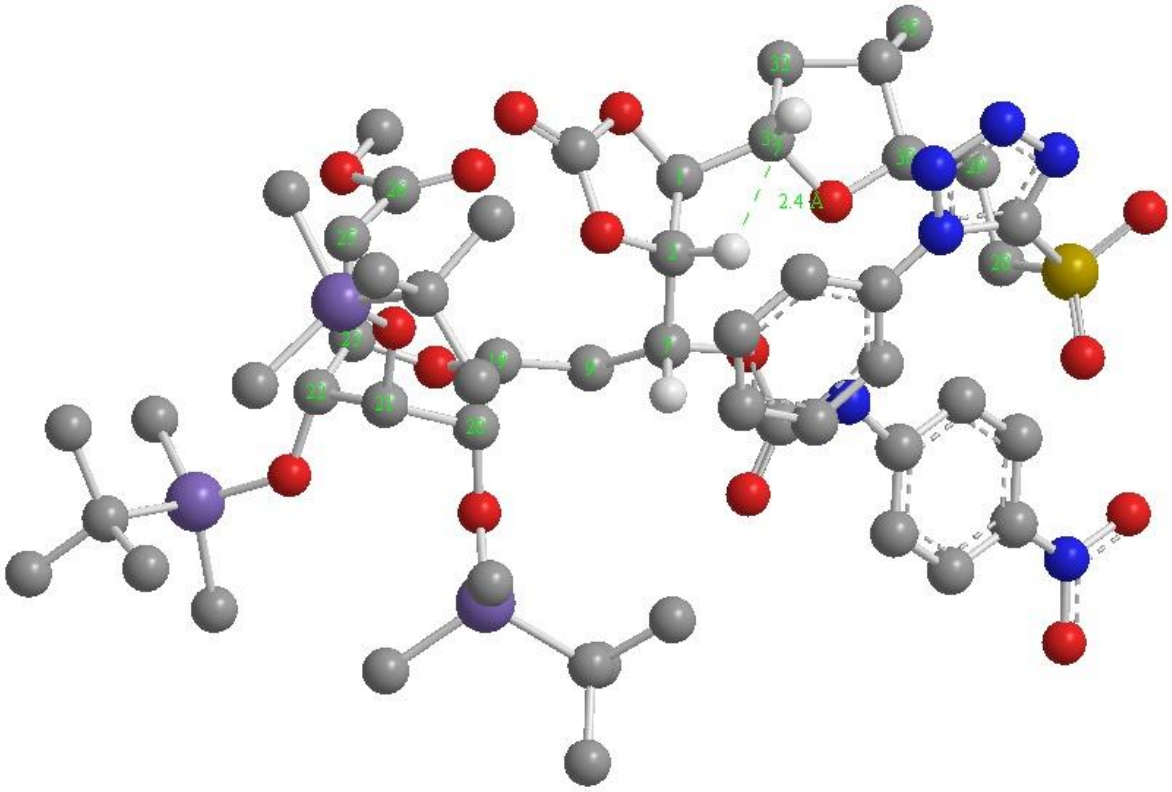
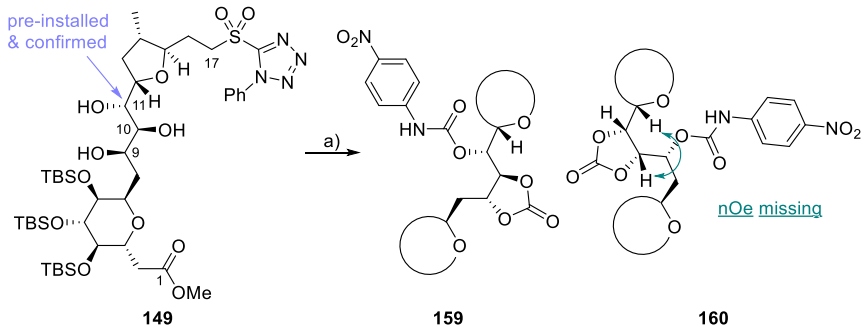


Figure 3.20: Calculated 3D model of cyclic carbonate **158** based on MM2 optimization with Chem3D (total energy: 241 kcal/mol), measured distance between H-10 and H-12: 2.4 Å (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue), silicon (lilac), sulfur (yellow)).

[213] T. Sandmeier, S. Krautwald, H. F. Zipfel, E. M. Carreira, *Angew. Chem. Int. Ed.* **2015**, *54*, 14363-14367.

Reasoning that the new five-membered carbonate ring introduced a certain degree of rigidity into the molecule, analysis of nOe signal correlations should allow the absolute configuration present within the triol motif to be unveiled.

As a result, we synthesized two more mixtures of the regioisomeric carbonates **159** and **160** (Scheme 3.66) and their diastereomeric congeners **161** and **162** (Scheme 3.67).



Scheme 3.66: Structure and nOe correlation of cyclic carbonates **159** and **160**. Reagents and conditions: (a) *p*-nitrophenyl isocyanate, TEA, DCM, rt, 48 h, 50% (*d.r.* = 14:1).

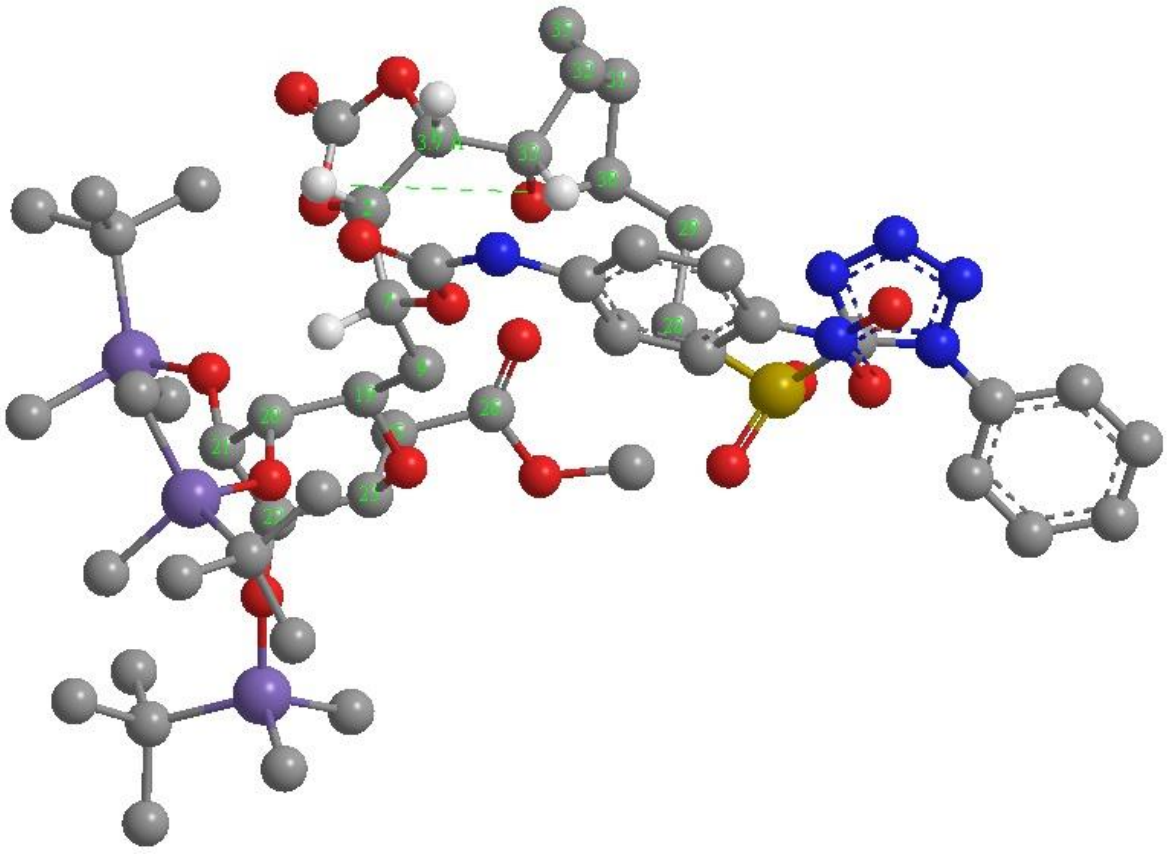
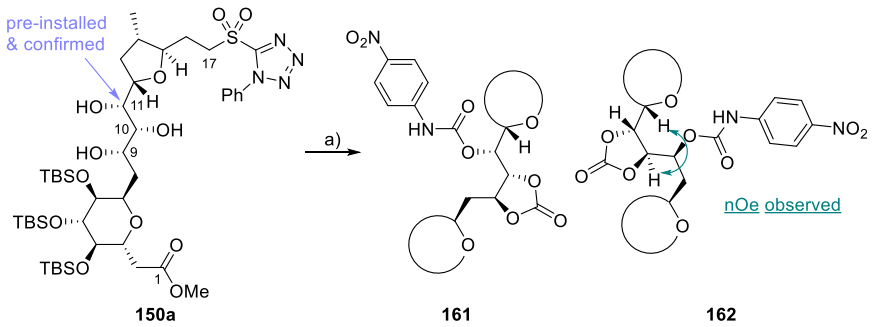


Figure 3.21: Calculated 3D model of cyclic carbonate **160** based on MM2 optimization with Chem3D (total energy: 230 kcal/mol), measured distance between H-10 and H-12: 3.7 Å (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue), silicon (lilac), sulfur (yellow)).



Scheme 3.67: Structure and nOE correlation of cyclic carbonates **161** and **162**. Reagents and conditions: (a) *p*-nitrophenyl isocyanate, TEA, DCM, rt, 5 d, 84% (*d.r.* = 2:5).

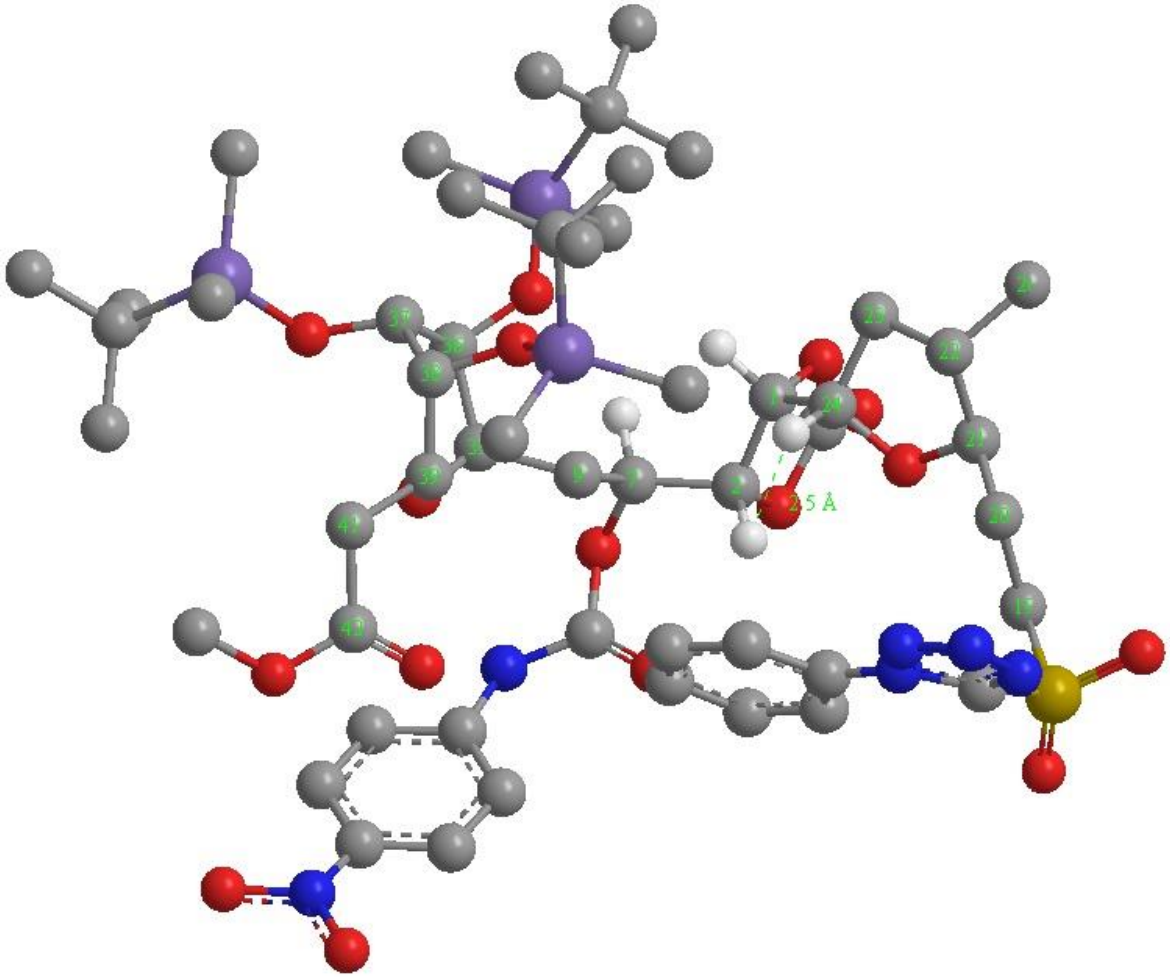


Figure 3.22: Calculated 3D model of cyclic carbonate **162** based on MM2 optimization with Chem3D (total energy: 349 kcal/mol), measured distance between H-10 and H-12: 2.5 Å (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue), silicon (lilac), sulfur (yellow)).

The substitution patterns of each component of the three regioisomeric mixtures were determined by extensive examination of their 2D NMR spectra. Careful interpretation of $^{1}H,^{1}H$-COSY, $^{1}H,^{13}C$-HSQC and $^{1}H,^{13}C$-HMBC cross peaks led to the complete assignment of the regioisomers. For example, the HMBC cross peaks of either H-9 and H-10 or H-10 and H-11 to the

carbonate carbon atom and the one of C-11 or C-9 to the carbamate carbon atom (dependant on the distinct regioisomer) were valuable evidence for the assigned connectivity.

3D conformational analysis was mainly based on measured ^{1}H,^{1}H-NOESY data. For the carbonates **157**, **159** and **161** it did neither make sense to investigate their ^{1}H coupling constants nor their nOe signal correlation due to the fact that the carbonate cycle only attached the two hydroxy groups at C-9 and C-10, simultaneously formed by dihydroxylation. Only ^{1}H coupling constants and nOe signal correlations of carbonates **158**, **160** and **162** were of further interest, due to the connection of the preinstalled hydroxy group at C-11 with the one at C-10, newly introduced during the dihydroxylation.

Unfortunately ^{1}H coupling constants were ambiguous, since their magnitude was neither confirming a *cis*- nor a *trans*-configuration. A plausible explanation could be a twisted five-membered ring. Therefore, we were focusing on the nOe signal correlations observed by NMR.

3D models of carbonates **158**, **160** and **162** (generated by MM2 optimization with Chem3D) show the approximate distances between the hydrogen atoms in question of an observable nOe interaction, such as between H-10 an H-12 (Figure 3.20, Figure 3.21, Figure 3.22).

According to these models, nOe correlations between proton H-10 and H-12 in the cases of carbonates **158** and **162** (Scheme 3.65, Scheme 3.67) were very likely, regarding the calculated approximate proton distances of 2.4 Å for carbonate **158** and 2.5 Å for carbonate **162**. In fact, such nOe correlations were experimentally observed.

In contrast, a nOe interaction between H-10 and H-12 was unlikely for carbonate **160** regarding the approximated proton distance of 3.7 Å between H-10 and H-12. Indeed, the measured spectra lacked any cross peaks, and thus underlined this assumption.

Based on these results, we had reason to believe in the consistent assignment of the two stereocentres at C-9 and C-10 in question. Later on, this was confirmed by another even more definite approach (Chapter 3.7.1.3).

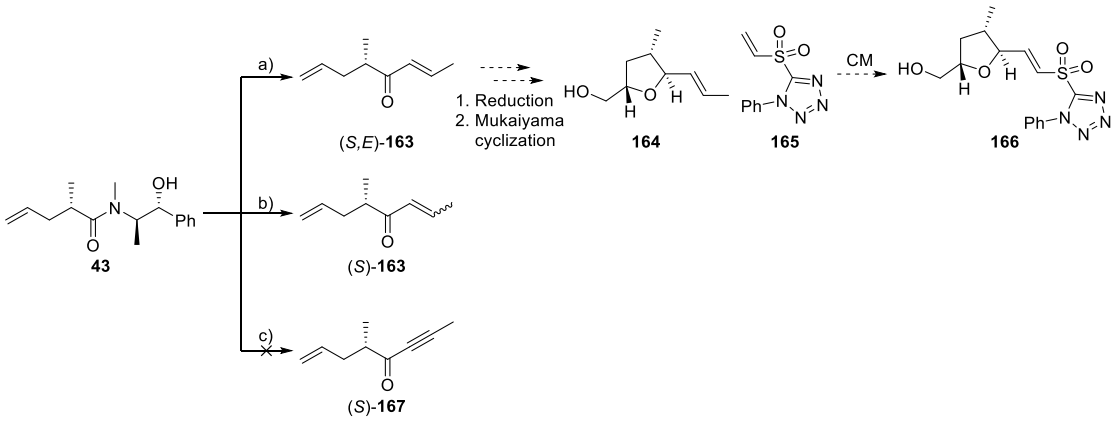
3.5.2. Investigations On Alternative Pathways

3.5.2.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

3.5.2.1.1. Introduction Of The Tetrazolylsulfone Via Alkene Cross Metathesis (CM)

Since the direct auxiliary displacement could be performed with nucleophiles[214] such as lithiated propyne (Chapter 3.3.1.1.1), we sought to introduce an alkene substituent instead (Scheme 3.68).

α,β-Unsaturated ketone (*S*,*E*)-**163** was accessed by lithiation of (*E*)-bromopropene according to a procedure by Moeller *et al.* for a similiar pseudoephedrine amide (Scheme 3.68).[215] Enone (*S,E*)-**163** seemed to be a suitable candidate for further elaboration by subsequent reduction, Mukaiyama cyclization and an alkene cross metathesis (CM).

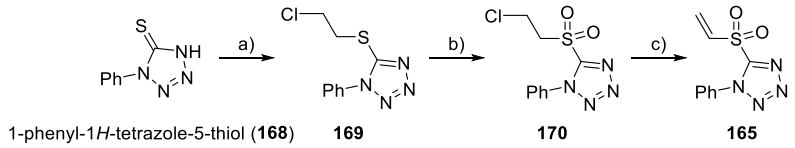


Scheme 3.68: Attempted Synthesis of the 2,5-*trans*-disubstituted THF-ring **166** bearing the sulfone. Reagents and conditions: (a) i. *n*-BuLi, THF, -78 °C, 5 min; ii. (*E*)-1-bromoprop-1-ene, TMEDA, *t*-BuLi, Et_2O, -78 °C, 45 min; iii. add propenyl-Li to **43**, -78 °C to 0 °C, 2.25 h, 74%; (b) i. *n*-BuLi, THF, -78 °C, 5 min; ii. 1-bromoprop-1-ene (*E*:*Z* = 1:1), TMEDA, *t*-BuLi, Et_2O, -78 °C, 45 min, iii. add propenyl-Li to **43**, -78 °C to 0 °C, 2 h, 10% of (*S*)-**163**, SM **43** mostly recovered (74%); (c) i. 1 eq. *n*-BuLi, Et_2O, -78 °C, 5 min; ii. 1.1 eq. propynyl-Li ethylene diamine complex, 1.1 eq. TMEDA, Et_2O, -78 °C to 0 °C, 1 h; iii. -20 °C, 16 h, solubility issues, SM **43** recovered (quant.).

Whenever an *E*/*Z* mixture of 1-bromoprop-1-ene was used, only less than 10% of product (*S*)-**163** were formed. Auxiliary displacement with propinyllithium, according to a procedure by Jacobi *et al.* for the reaction of alkyne nucleophiles with Weinreb amides, was also performed, but failed to give (*S*)-**167** (Scheme 3.68).[216]

[214] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.
[215] H.-C. Xu, J. D. Brandt, K. D. Moeller, *Tetrahedron Lett.* **2008**, *49*, 3868-3871.
[216] P. A. Jacobi, J. I. Kravitz, W. Zheng, *J. Org. Chem.* **1995**, *60*, 376-385.

In parallel, sulfone **165** was synthesized in three steps starting from 1-phenyl-*1H*-tetrazole-5-thiol **168** according to a procedure by Cid *et al.*[217] (Scheme 3.69, Figure 3.23).



Scheme 3.69: Synthesis of the sulfone precursor **165** for cross metathesis. Reagents and conditions: (a) K_2CO_3, 1,2-DCE, rt to 84 °C, 4 d, 98%; (b) *m*-CPBA, DCM, rt, 3 d, 76%; (c) TEA, THF, rt, 30 min, 38%.

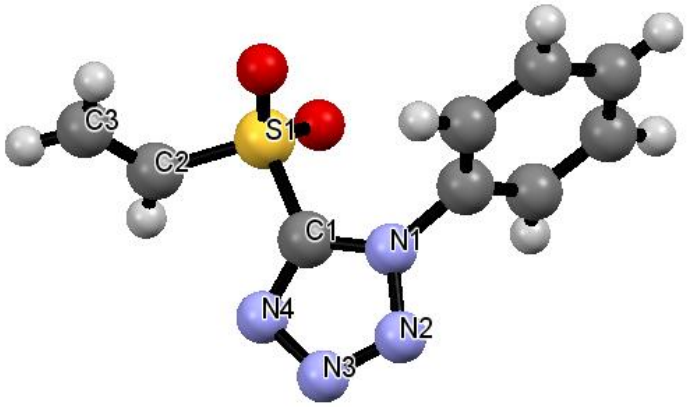
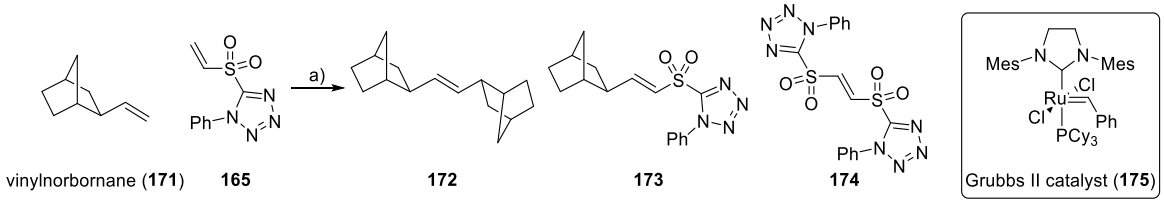


Figure 3.23: X-Ray single crystal structure of tetrazolylvinylsulfone **165** (atom numbering is arbitrary; colouring of atoms: carbon (grey), hydrogen (white), oxygen (red), nitrogen (blue), sulfur (yellow)).

With vinylsulfone **165** in hand, a CM was conducted with vinylnorbornane (**171**) and Grubbs II catalyst (**175**) following a procedure by Grela *et al.* for the CM of various alkenes with comparable vinylsulfones (Scheme 3.70).[218]



Scheme 3.70: Introduction of the sulfone by CM and some of the possible products. Reagents and conditions: (a) 5 mol% Grubbs-II catalyst **175**, DCM, 45 °C, 2 d, complex mixture.

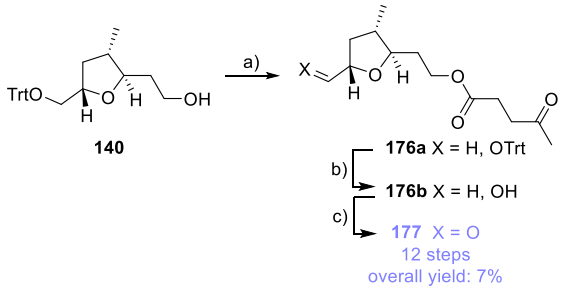
A complex and inseparable mixture of multiple alkenes such as **172** or **174** and the desired **173** was isolated (Scheme 3.70). Based on this experimental result and the poor yielding synthesis of α,β-unsaturated ketone (*S*,*E*)-**163**, further investigations were not undertaken.

[217] E. Rodrigo, S. Morales, S. Duce, J. L. G. Ruano, M. B. Cid, *Chem. Commun.* **2011**, *47*, 11267-11269.
[218] A. Michrowska, M. Bieniek, M. Kim, R. Klajn, K. Grela, *Tetrahedron* **2003**, *59*, 4525-4531.

3.5.2.2. Building Block Coupling & Elaboration

3.5.2.2.1. Levulinic Ester Protecting Group

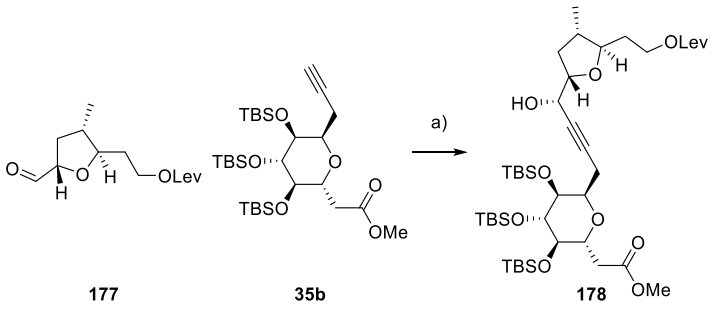
Regarding the all silyl-based protecting groups of fragment **127**, we envisioned the use of an orthogonal substituent. According to van Boom *et al.*, levulinic esters can be cleaved selectively with hydrazine hydrate which is intrinsically compatible with the methyl ester of **35b**.[219] The levulinic ester was introduced at the stage of **140** using standard esterification conditions with *N*,*N*'-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (4-DMAP) (Scheme 3.71).[220]



Scheme 3.71: Introduction of the Lev group. Reagents and conditions: (a) levulinic acid, DCC, 4-DMAP, DCM, 0 °C to rt, 15 h, 77%; (b) TFA, DCM, 0 °C, 1 h, 82%; (c) i. $(COCl)_2$, DMSO, DCM, -78 °C, 35 min; ii. DIPEA, 2.5 h, -78 °C to rt, 67%.

176a was detritylated with trifluoroacetic acid,[221] leading to alcohol **176b** in 82% yield (Scheme 3.71), which was subsequently oxidized to aldehyde **177** under Swern conditions in 67% yield.[222]

Aldehyde **177** was coupled with alkyne **35b** in the presence of zinc(II) trifluoromethanesulfonate[223] giving rise to the propargylic alcohol **178** in only 14% yield (Scheme 3.72). We reasoned that the presence of two additional carbonyl groups rendered the alkynylation more difficult. Therefore, we did not further proceed with this route.



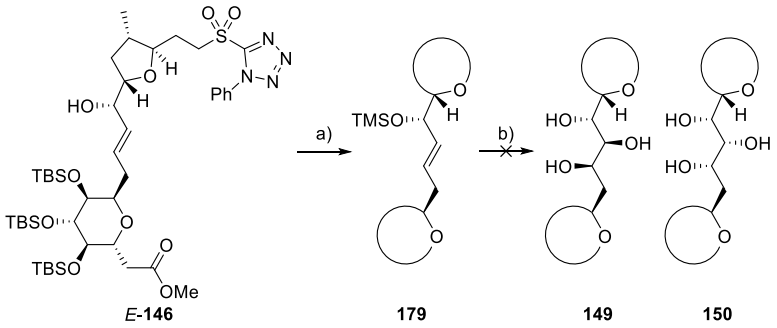
Scheme 3.72: Fragment coupling via alkynylation, with Lev PG. Reagents and conditions: (a) $Zn(OTf)_2$, TEA; (+)-NME, PhMe, 4 Å MS, rt, 3 d, 14% of **178**, recovered SM **35b** (69%).

[219] J. H. van Boom, P. M. J. Burgers, *Tetrahedron Lett.* **1976**, *17*, 4875-4878.
[220] B. Neises, W. Steglich, *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 522-524.
[221] S. Peyrat, K. Cheng, J. Xie, *Synthesis* **2013**, *45*, 2737-2744.
[222] D. K. Mohapatra, P. Dasari, H. Rahaman, R. Pal, *Tetrahedron Lett.* **2009**, *50*, 6276-6279.
[223] a) E. M. Carreira, *Patent US2003/0088100* **2003**. b) A. Fettes, E. M. Carreira, *J. Org. Chem.* **2003**, *68*, 9274-9283.

3.5.2.2.2. TMS-Capped Allylic Alcohol

In the 90's, Koskinen *et al.* reported a dramatic influence of protecting groups on the selectivity of Sharpless dihydroxylations.[224] They stated that protecting groups on the allylic alcohol (no matter of their size) were able to shift the selectivity of the dihydroxylation towards an *all-syn*-triol by surpressing hydrogen bonding between the allylic alcohol and the osmium catalyst.

Regarding the *all-syn*-triol motif of our target **18**, we introduced a TMS group on the alcohol *E*-**146** with TMSOTf (similiarly to previous TBS protections[225]) resulting in alkene **179** (Scheme 3.73).



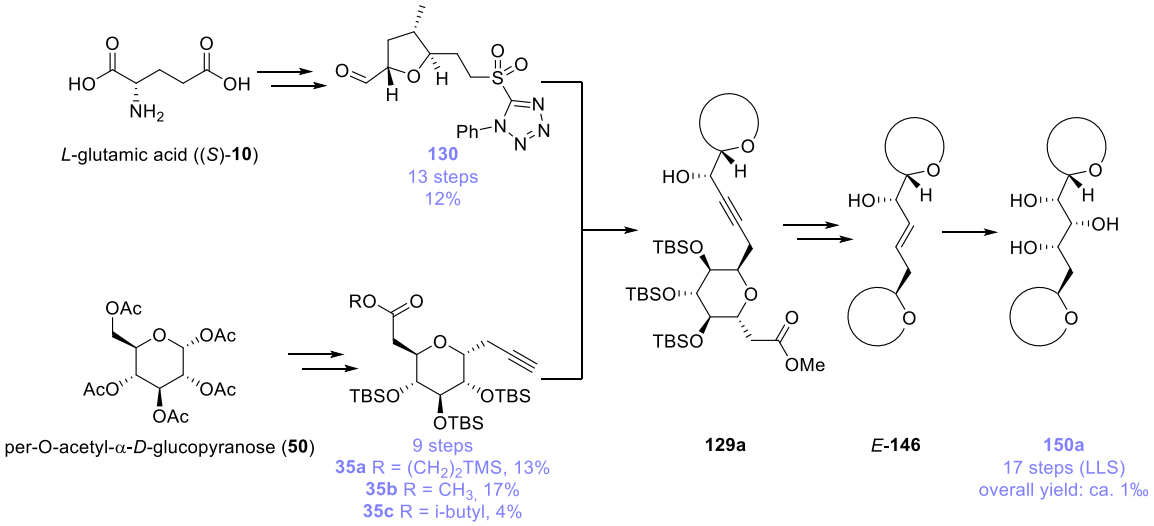
Scheme 3.73: Preparation of TMS-capped allylic alcohol **179** for an alternative Sharpless dihydroxylation. Reagents and conditions: (a) TMSOTf, 2,6-lutidine, DCM, 0 °C to rt, 2 h, 86%; (b) i. 80 mol% K_2OsO_4, 200 mol% L* (corresponds to $(DHQ)_2R$ and $(DHQD)_2R$ with R = AQN, PYR and PHAL), $MeSO_2NH_2$, $K_3[Fe(CN)_6]$, K_2CO_3, *t*-BuOH/H_2O (1:1), 0 °C to rt, 20 h, (*d.r.* not determined due to attempted *in situ* TMS deprotection); ii. 12 eq. K_2CO_3, MeOH, rt, decomposition.

According to Koert *et al.* for a bis-homoallylic alcohol, Sharpless dihydroxylations are possible without loosing a preinstalled TMS group.[226] Full conversion was not reached during the dihydroxylation with a catalyst loading of 10 mol% (as in the case without the TMS group), and could only be obtained with a catalyst loading of 80 mol% (Scheme 3.73). Unfortunately, a subsequent addition of excess potassium carbonate led to decomposition.

[224] O. A. Kallatsa, A. M. P. Koskinen, *Tetrahedron Lett.* **1997**, *38*, 8895-8898.
[225] a) G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730. b) J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.
[226] H. Wagner, K. Harms, U. Koert, S. Meder, G. Boheim, *Angew. Chem.* **1996**, *108*, 2836-2839.

3.5.3. Interim Summary

Based on the synthesis of the literature-known enantiomer of **131a**, we started the synthesis of tetrazolylsulfone **130** with *L*-glutamic acid ((*S*)-**10**) (Scheme 3.74). After lactonization, opening of the corresponding hemiacetal **138** by a Wittig olefination, and recyclization by an oxa-Michael process, the tetrazolylthiol moiety was introduced via a Mitsunobu reaction. Simple functional group modifications led to aldehyde **130** in 13 steps with an overall yield of 12%.



Scheme 3.74: Second synthetic route to western belizentrin fragment **150a**. Reagents and conditions: as shown before.

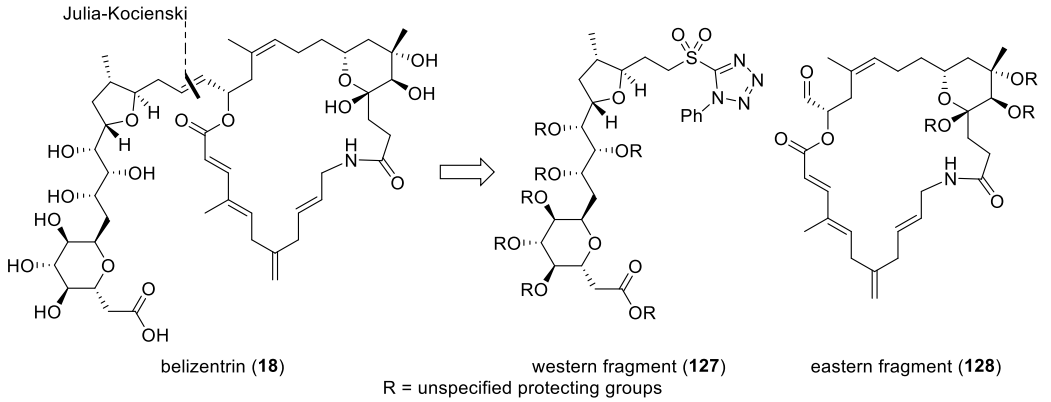
Coupling of aldehyde **130** with known alkyne **35b** mediated by zinc(II) trifluoromethanesulfonate led to propargylic alcohol **129a** in poor yield (Scheme 3.74). *trans*-Selective hydrostannation accessed allylic alcohol *E*-**146** after protodestannation.

The final osmium-catalyzed dihydroxylation proved to be a reluctant transformation, since substrate control was dominant, regardless of the ligands used and for the introduction of a TMS protecting group on the remaining free hydroxy group. A stoichiometric osmylation led to the unfortunate formation of a stable, yet unidentified, adduct.

Triol **150a** was isolated in 17 steps (LLS, 1‰). Alkynylation and dihydroxylation remained problematic bottlenecks to the synthesis. Based on these results, we entered a second retrosynthetic revision mainly focusing on the exchange of the central fragment coupling and the dihydroxylation (Chapter 3.6).

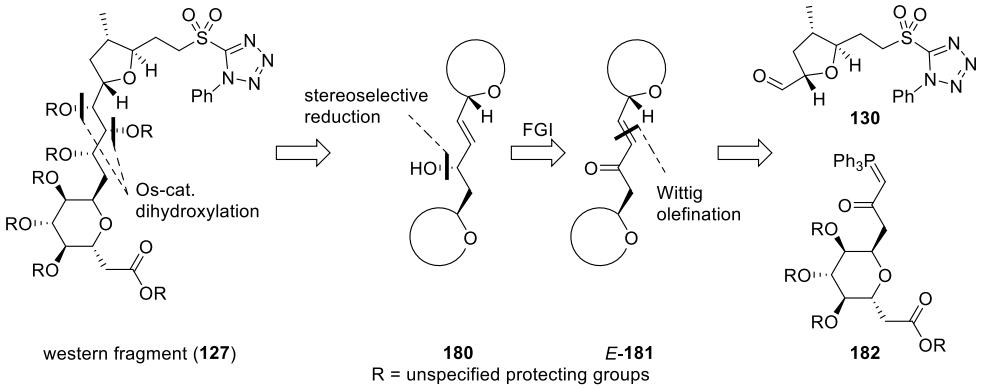
3.6. Second Retrosynthetic Revision

As before, the natural product **18** was disconnected at the central *E*-configured double bond, by a Julia-Kocienski olefination retron (Scheme 3.75).



Scheme 3.75: Latest retrosynthetic analysis of belizentrin (**18**).

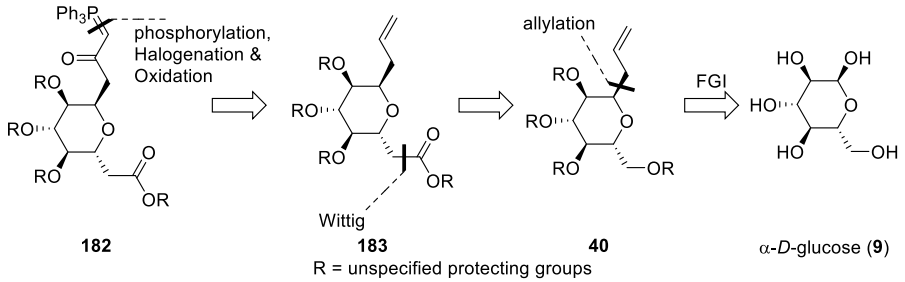
Since the previous dihydroxylation resulted in the formation of the desired diastereomer **150a** as the *minor* product, the retrosynthetic analysis of belizentrin´s western fragment **127** had to be changed (Scheme 3.76).



Scheme 3.76: Latest retrosynthetic analysis of the western belizentrin fragment **127**.

To this end an inverse disconnection of triol **127** was envisaged. An osmium-catalyzed dihydroxylation led to the constitutionally isomeric allylic alcohol **180** (Scheme 3.76). The hydroxy group was identified as a possible target originating from the corresponding enone *E*-**181**. A central disconnection at the *E*-configured double bond (Wittig olefination) resulted in the unmodified aldehyde **130** and a new phosphorus ylide **182**.

The latter could be assembled by a sequence of phosphorylation, halogenation and oxidation at the α-position of the C1' terminus of alkene **183** (Scheme 3.77).



Scheme 3.77: Retrosynthetic analysis of the phosphorus ylide **182**.

The ester was introduced as described before (oxidation and Wittig olefination) starting from unchanged alkene **40** (Scheme 3.77). After a few protecting group alterations, this resulted again in α-*D*-glucose (**9**) as the starting point of the reaction sequence.

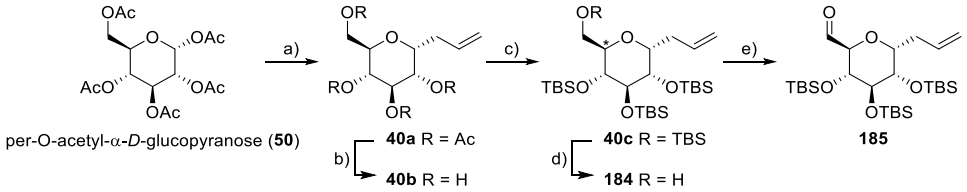
3.7. Western Belizentrin Fragment - Final Route

3.7.1. Successful Synthetic Route

3.7.1.1. The C-Glucoside Building Block - A New Synthesis

3.7.1.1.1. Introducing The Ester First

The new synthetic route of building block **182** again started with the allylation of commercially available per-*O*-acetyl-α-*D*-glucopyranose (**50**) (Scheme 3.78).[227] Following previous synthetic approaches, alkene **40a** was globally deprotected. Tetrol **40b** was then submitted to the protection with TBSOTf instead of the previously used TBSCl, in analogy to procedures by Schmidtmann *et al.*[228] and Deming *et al.*,[229] giving access to alkene **40c** in higher yields (96%, compared to 87%).[230]

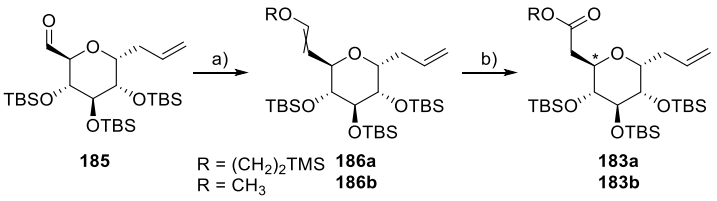


Scheme 3.78: Synthesis of the phosphorus ylide **182**, Part A. Reagents and conditions: (a) allyl-TMS (**52**), $BF_3{\cdot}OEt_2$, MeCN, rt to 80 °C, 1 d, 79% (α:β = 7:1); (b) 10 mol% NaOEt, MeOH, rt, 4 h, 98%; (c) TBSOTf, 2,6-lutidine, DCM, 0 °C to rt, 20 h, 96%; (d) HF·py, 12.5% THF/py (2.5:1), 0 °C to rt, 16.5 h, 97% (*d.r.* = 8:1); (e) i. $(COCl)_2$, DMSO, DCM, -78 °C, 25 min; ii. DIPEA, -78 °C to rt, 40 min, 90%.

After selective O6' deprotection of **40c** with diluted Olah´s reagent (hydrogen fluoride/pyridine), we obtained primary alcohol **184** (Scheme 3.78).[231] Subsequent Swern oxidation of alcohol **184** furnished aldehyde **185** in 92% yield,[232] which was the central intermediate for the introduction of both the methyl and the TMS-ethyl ester functionality.

[227] a) K. Parkan, L. Werner, Z. Lövyová, E. Prchalová, L. Kniežo, *Carbohydr. Res.* **2010**, *345*, 352-362. b) J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2012**, *134*, 4112-4115.
[228] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.
[229] J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.
[230] The first three steps of the reaction sequence towards aldehyde **185** were also carried out by laboratory apprentice C. Rustemeier on a scale above 5 g (Scheme 3.78). Therefore, material supply was always assured, when in parallel the focus lay on the introduction of the subsequent steps of the new synthetic route towards phosphorus ylide **182**.
[231] G. Anquetin, S. L. Rawe, K. McMahon, E. P. Murphy, P. V. Murphy, *Chem. Eur. J.* **2008**, *14*, 1592-1600.
[232] K. Fujiwaraa, S.-i. Souma, H. Mishima, A. Murai, *Synlett* **2002**, *9*, 1493-1495.

Aldehyde **185** was submitted to a Wittig olefination with phosphorus ylide **61**,[233] in analogy to the previous route leading to the formation of inseparable *E*/*Z* mixtures of both derivatives of enolether **186** in 84-88% yield (Scheme 3.79).



Scheme 3.79: Synthesis of the phosphorus ylide **182**, Part B. Reagents and conditions: (a) [R-OCH_2-PPh_3]Cl **61**, KO*t*-Bu, 5 Å MS, THF, -50 °C to -78 °C, for R = $(CH_2)_2$-TMS (16.5 h, 83%), for R = CH_3 (18.5 h, 88%), *E*/*Z* mixture not separated; (b) PCC, DCM, rt, for R = $(CH_2)_2$-TMS (17 h, 82%, *d.r.* = 2.7:1), for R = CH_3 (23 h, 79%, *d.r.* = 3.4:1).

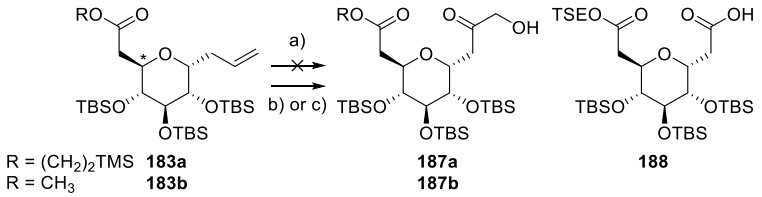
After PCC oxidation of these enolether compounds, ester **183** was isolated with good diastereoselectivity (*d.r.* = 3.4:1 to 4.1:1, due to epimerization at C5', for a possible explanation see Chapter 3.3.1.2.5) in 79-96% yield (regarding both ester moieties) (Scheme 3.79).

3.7.1.1.2. Alkene Oxidation

With alkene **183** in hand, we started investigating the oxidation into the corresponding α-hydroxyketone **187** (Scheme 3.80). Murahashi *et al.* had reported the osmium(III) chloride-catalyzed transformation of simple alkenes into α-hydroxyketones with peracetic acid.[234] These conditions did not result in the formation of α-hydroxyketone **187a** and the unreacted starting material **183a** was reisolated.

In contrast, other reports made use of superstoichiometric amounts of potassium permanganate in (un)buffered aqueous acetone solutions.[235] Based on these procedures, we submitted substrate **183a** to the reaction in the presence of sodium acetate (buffer), as reported by Schmid *et al.* for simple alkene substrates (Scheme 3.80).[236] We encountered the problem of diol scission and the subsequent oxidation of the corresponding primary alcohol to carboxylic acid **188** in an unacceptably high amount (31%).

[233] a) S. Hatakeyama, K. Saijo, S. Takano, *Tetrahedron Lett.* **1985**, *26*, 865-868. b) A. Kawai, O. Hara, Y. Hamada, T. Shioiri, *Tetrahedron Lett.* **1988**, *29*, 6331-6334. c) L. Lazarides, A. S. Smith, R. Stocker, J. C. Theobald, *Patent WO2008101867* **2008**. d) K. Schönauer, E. Zbiral, *Liebigs Ann. Chem.* **1983**, *6*, 1031-1042.
[234] S.-I. Murahashi, T. Naota, H. Hanaoka, *Chem. Lett.* **1993**, *22*, 1767-1770.
[235] a) C. Schmölzer, M. Fischer, W. Schmid, *Eur. J. Org. Chem.* **2010**, *25*, 4886-4892. b) C. Bonini, L. Chiummiento, M. Funicello, P. Lupattelli, M. Pullez, *Eur. J. Org. Chem.* **2006**, *1*, 80-83.
[236] See footnote 235 a).



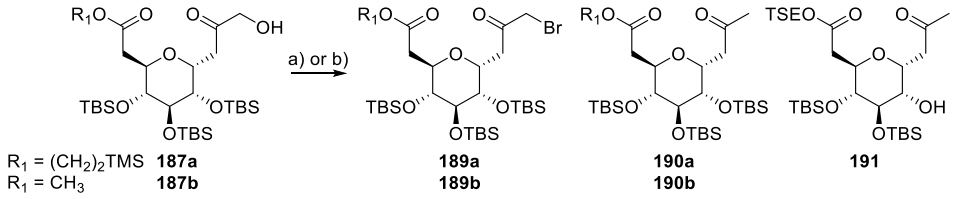
Scheme 3.80: Synthesis of the phosphorus ylide **182**, Part C. Reagents and conditions: (a) 1 mol% $OsCl_3 \cdot 3H_2O$, 2 eq. AcOOH, H_2O/MeCN/DCM (1:1:1), rt, 7 d, SM recovered (quant., with R = $(CH_2)_2$TMS); (b) $KMnO_4$, aq. acetate buffer (pH 3), acetone/H_2O (4:1), rt to 40 °C, 44 h, 45% of **187a**, 31% of **188** (with R = $(CH_2)_2$TMS); (c) $KMnO_4$, AcOH, acetone/H_2O (4:1), rt, for R = $(CH_2)_2$TMS (4.75 h, 72%), for R = CH_3 (3.25 h, 77%).

More counterintuitively, without a sodium acetate buffer (according to a procedure by Bonini *et al.*,[237] also simple alkene substrates), the desired α-hydroxyketone **187** was formed in 72-77% yield (Scheme 3.80).

3.7.1.1.3. α-Bromination

We wanted to access the α-bromoketone **189** by an Appel reaction according to the reports by Kobayashi *et al.*[238] and Aponick *et al.*[239] for much simpler substrates (Scheme 3.81).

To this end triphenylphosphine (**195a**) and tetrabromomethane were added as a solution in dichloromethane to the substrate, resulting in only poor conversion. Therefore, additional triphenylphosphine (**195a**) and tetrabromomethane (excess) were added as a solid to the reaction mixture which resulted in the formation of the methylketone **190a** as a major byproduct which was isolated in 16% yield.

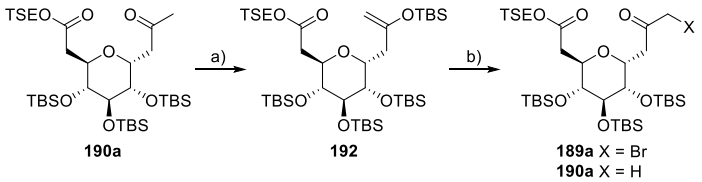


Scheme 3.81: Synthesis of the phosphorus ylide **182**, Part D. Reagents and conditions: (a) 1.65 eq. CBr_4, 1.65 eq. PPh_3 **195a**, DCM, rt, 2 h, 81% of **189a**, 16% of **190a**, 4% of **191**, both reagents were added successively (R = $(CH_2)_2$TMS); (b) 2 eq. CBr_4, 2 eq. PPh_3 **195a**, DCM, rt, reagents added at once, for R = $(CH_2)_2$TMS (55 min, 99%), for R = CH_3 (40 min, 81%).

[237] C. Bonini, L. Chiummiento, M. Funicello, P. Lupattelli, M. Pullez, *Eur. J. Org. Chem.* **2006**, *1*, 80-83.
[238] S. Kobayashi, M. Ueno, R. Suzuki, H. Ishitani, H.-S. Kim, Y. Wataya, *J. Org. Chem.* **1999**, *64*, 6833-6841.
[239] N. V. Borrero, A. Aponick, *J. Org. Chem.* **2012**, *77*, 8410-8416.

When all reagents (still in excess) were added as a solid at once to a solution of substrate **187** in dichloromethane, this undesired side reaction was not observed, affording α-bromoketone **189** in 81-99% yield (Scheme 3.81).

As considerable amounts of ketone **190a** were formed, we investigated a possible recycling strategy for this material. To this end, we were following a literature precedent for the transformation of a simple methylketone into an α-bromoketone via its corresponding silyl enolether as reported by Leighton *et al.*[240] (Scheme 3.82).



Scheme 3.82: Recycling of the methylketone **190a**. Reagents and conditions: (a) TBSOTf, 2,6-lutidine, DCM, -78 °C to -20 °C to rt, 28.5 h, 87%; (b) NBS, THF, -78 °C to -20 °C, 1 h, 63% of **189a**, 17% of **190a**.

Methylketone **190a** was successfully transformed into silyl enolether **192** in 87% yield (Scheme 3.82). Alkene **192** was submitted to a *N*-bromosuccinimide solution to give α-bromoketone **189a** in 63% yield (together with 17% of **190a**).

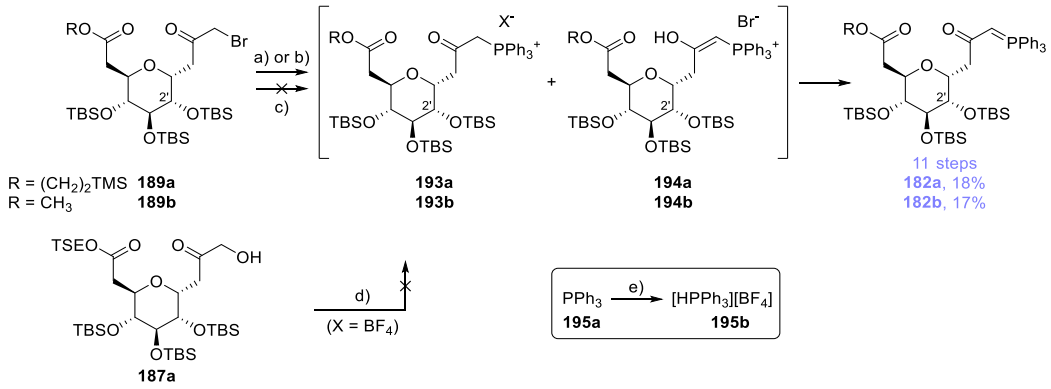
3.7.1.1.4. The Phosphorus Ylide & Reactions In Frozen Solutions

The addition of triphenylphosphine (**195a**) to the alkylbromide **189a** under reflux conditions in an aprotic solvent (Scheme 3.83) led to decomposition (via methylketone **190a** and other species, at reflux in acetonitrile) or partial degradation (loss of O2' TBS protecting group, at 55 °C in benzene).[241]

A possible explanation for the instability of phosphonium salt **193a** could be the formation of an intermediate enolphosphonium species as postulated by Moorhoff *et al.*[242] These authors had made a similiar observation (debromination and formation of the corresponding methylketone) during the reaction of a simple α-bromoketone to its corresponding phosphonium salt under comparable conditions.

[240] S. Ho, C. Bucher, J. L. Leighton, *Angew. Chem. Int. Ed.* **2013**, *52*, 6757-6761.
[241] H. J. Bestmann, K. H. Koschatzky, W. Schätzke, J. Süß, O. Vostrowsky, *Liebigs Ann. Chem.* **1981**, *9*, 1705-1720.
[242] C. M. Moorhoff, *J. Chem. Soc., Perkin Trans. 1* **1997**, *13*, 1987-1996.

Alternatively, phosphonium salt **193a** could be obtained from the α-hydroxyketone **187a** via a Mitsunobu reaction, as previously described by Mazurkiewicz *et al.* for simple primary alcohols with triphenylphosphonium tetrafluoroborate (**195b**) (Scheme 3.83).[243] The latter was prepared from triphenylphosphine (**195a**) with tetrafluoroboric acid according to Grubbs *et al*.[244] An attempted Mitsunobu reaction of alcohol **187a** with this salt did not furnish desired phosphonium salt **193a**; rather, the starting material **187a** was almost completely recovered.



Scheme 3.83: Synthesis of the phosphorus ylide **182**, Part E. Reagents and conditions: (a) i. PPh_3 **195a**, PhH, -20 °C, 4 Å MS, 49-52 h, quant.; ii. DIPEA, PhH, rt, 30 min, quant.; (b) i. PPh_3 **195a**, PhH, rt to 55 °C, 5 d, 91% (ca. 1:1 mixture with C2'-deprotected byproduct); ii. KO*t*-Bu, THF, 5 Å MS, -50 °C, 10 min, quant. (R = $(CH_2)_2$TMS); (c) PPh_3 **195a**, MeCN, rt to 85 °C, 2.5 h, decomposition (R = $(CH_2)_2$TMS); (d) triphenylphosphonium tetrafluoroborate **195b**, DEAD, PPh_3 **195a**, THF, 0 °C to rt, 3 h, SM recovered (95%); (e) aq. HBF_4, Et_2O, rt, 5 min, 23%.

Ultimately, both phosphonium salt species **193** and **194** were formed *in situ* by freezing the reagents in dry benzene at -20 °C according to Kiovsky *et al.* (Scheme 3.83).[245] These authors had reported such counterintuitive conditions for the bimolecular reaction of iodomethane with triethylamine in benzene glass. Such nucleophilic substitutions can be accelerated under these conditions. A plausible explanation for this phenomenon is the following: due to the occurance of microscopic regions of liquid eutectic mixtures of high concentration, an enhancement of the reaction can be observed until a specific minimum temperature below which the whole mixture freezes and reactions are in fact surpressed.

The enolphosphonium species postulated by Moorhoff *et al.* is closely related to the experimentally observed enolate **194** (Scheme 3.83), which could explain the sensitivity of phosphonium salt **193**.

[243] R. Mazurkiewicz, T. Gorewoda, A. Kuźnik, M. Grymel, *Tetrahedron Lett.* **2006**, *47*, 4219-4220.
[244] C. S. Daeffler, R. H. Grubbs, *Org. Lett.* **2011**, *13*, 6429-6431.
[245] R. E. Pincock, T. E. Kiovsky, *J. Am. Chem. Soc.* **1966**, *88*, 51-55.

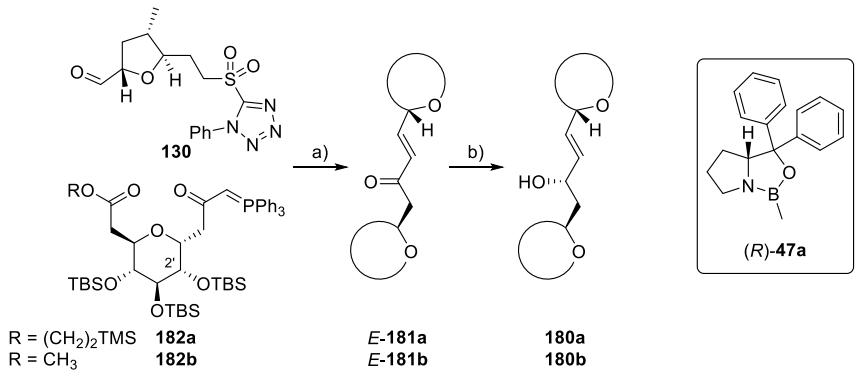
Deprotonation of readily enolizable phosphonium salt **193** with di-*i*-propylethylamine led to the formation of phosphorus ylide **182** (Scheme 3.83).[246] These species were used directly for the Wittig olefination of aldehyde **130**. The completion of both reactions (phosphorylation and deprotonation) was confirmed by ^{1}H NMR measurements of aliquots taken from the reaction mixture at different times.

[246] Based on the results shown in Chapter 3.3.1.2 and with the aimed phosphorus ylide **182** in mind, Dr. J. Novacek proposed an order of events which in fact helped to pave a way to this important intermediate.

3.7.1.2. Building Block Coupling & Elaboration

3.7.1.2.1. Wittig Olefination & CBS Reduction

Phosphorus ylide **182** (obtained in benzene glass at -20 °C) reacted with aldehyde **130** to give enone **181** in 76-79% yield with high *E*/*Z* selectivity (*E*/*Z* > 16:1).[247]



Scheme 3.84: Fragment coupling and elaboration. Reagents and conditions: (a) PhH, rt, 4 Å MS, for R = $(CH_2)_2$TMS (17 h, 76%, *E*/*Z* = 16:1), for R = CH_3 (19 h, 79%, *E*/*Z* = 18:1); (b) (*R*)-(*+*)-2-Methyl-CBS-oxazaborolidine (*R*)-**47a**, $BH_3{\cdot}SMe_2$, DCM, -20 °C, for R = $(CH_2)_2$TMS (3 h 10 min, 97%), for R = CH_3 (1 h 50 min, 91%).

The obtained α,β-unsaturated ketone *E*-**181** was reduced in a stereoselective manner under CBS conditions (Scheme 3.84). Such transformations were precedented for sulfone-bearing substrates by Sawa *et al.*[248] and for different enone substrates, with either TBS-protected alcohols by Sabitha *et al.*[249] or with ester moieties by Rao *et al.*[250] In analogy to these protocols, we obtained allylic alcohol **180** almost exclusively in 91-97% yield with (*R*)-**47a** as the catalyst.

3.7.1.2.2. Sharpless Dihydroxylation & Global Protection

Originally, we had envisioned a route involving *E*-**146** as a constitutional isomer of allylic alcohol **180** which initially showed substrate control for all dihydroxylation attempts (Chapter 3.3.1.3.4, Chapter 3.5.1.2.3). Our hope was that the constitutional difference between these allylic alcohols would give better access to the desired triols.

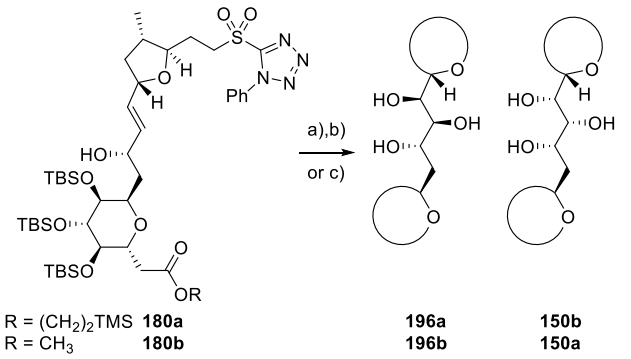
[247] A preliminary experiment revealed the following: Using a mixture (ca. 1:1) of partially degraded phosphonium salts (loss of the O2' TBS group), led to enone **181** and a partially deprotected enone **209** (without C2' TBS group) in yields of 33% for **181** and 42% for **209**, respectively (see Supporting Information, Chapter 5.2.3.2).

[248] M. Sawa, K. Mizuno, H. Harada, H. Tateishi, Y. Arai, S. Suzuki, M. Oue, H. Tsujiuchi, Y. Furutani, S. Kato, *Biorg. Med. Chem. Lett.* **2005**, *15*, 1061-1064.

[249] G. Sabitha, C. Gurumurthy, J. S. Yadav, *Synthesis* **2014**, *46*, 110-118.

[250] A. Venkanna, E. Sreedhar, B. Siva, K. S. Babu, K. R. Prasad, J. M. Rao, *Tetrahedron: Asymmetry* **2013**, *24*, 1010-1022.

With constitutional isomer **180** in hand (compared to *E*-**146** in Scheme 3.59), we again performed the Sharpless dihydroxylation with a set of different ligands (Scheme 3.85).[251]



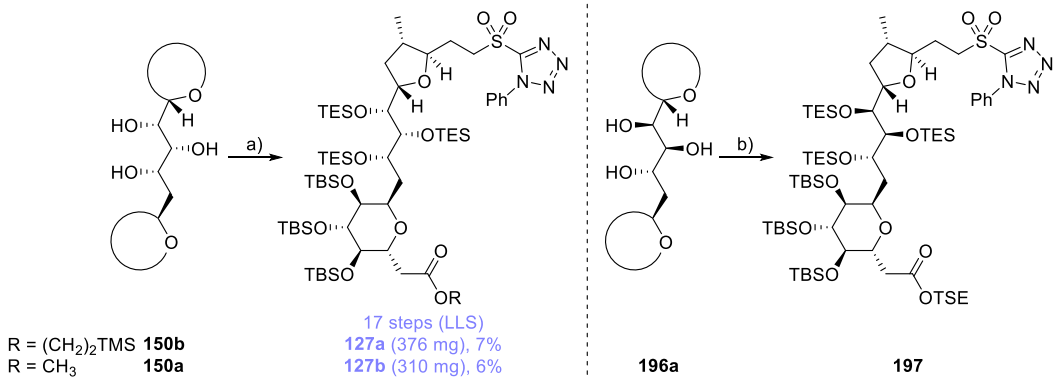
R	L*	*d.r.*** (*anti*:*syn*)
$(CH_2)_2TMS$	$(DHQ)_2PHAL$	3.2:1
	$(DHQD)_2PHAL$	1:1.8
	$(DHQ)_2PYR$	3.7:1
	$(DHQD)_2PYR$	1:3.3
	$(DHQ)_2AQN$	3.5:1
	$(DHQD)_2AQN$	1:6.7
Me	$(DHQD)_2AQN$	1:4.2

** determined by HPLC

Scheme 3.85: Ligand screening for the Sharpless dihydroxylation of the allylic alcohols **180**. Reagents and conditions: (a) 20 mol% K_2OsO_4, 25 mol% L*, $MeSO_2NH_2$, $K_3[Fe(CN)_6]$, K_2CO_3, *t*-BuOH/H_2O (1:1), 0 °C to rt, 1 d, 96% on small scale (6x 2 mg SM) diastereoselectivity shown; (b) same conditions as before, 78% (*d.r.* = 1:7.1) on larger scale (25 mg SM **180a**) for R = $(CH_2)_2$TMS; (c) same conditions as before, 59% (*d.r.* = 1:4.2) on larger scale (30 mg SM **180b**) for R = CH_3.

We observed ligand control with diastereoselectivities ranging between 3.7:1 and 1:6.7 for the diastereomeric triols **196a** and **150b** with the TMS-ethyl ester side chain (78%, isolated *d.r.* = 1:7.1, Scheme 3.85). For the allylic alcohol **180b**, only the ligands were screened which worked best for its TMS-ethyl ester analogue **180a** and found a comparable result in favour of our desired diastereomer **150a** (59%, isolated *d.r.* = 1:4.2).

However, when the reaction scale was increased, the yield decreased, probably because of diol scission.



Scheme 3.86: Global TES protection. Reagents and conditions: (a) TESOTf, 2,6-lutidine, DCM, 0 °C to rt, for R = $(CH_2)_2$TMS (2 h, 79%), for R = CH_3 (1 h, 82%), total amount of isolated material as shown; (b) TESOTf, 2,6-lutidine, DCM, 0 °C to rt, 2 h, 76%.

[251] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483-2547.

The final step was the protection of triols **150** and **196a** with TESOTf,[252] resulting in the formation of the fully protected western belizentrin fragment **127** and a diastereomer **197** (Scheme 3.86).

In conclusion, tetrazolylsulfone **127** was synthesized in 17 steps (LLS) and an overall yield of 6% for the methyl ester **127b** and 7% for the TMS-ethyl ester **127a** starting from α-*D*-glucose (**9**) and *L*-glutamic acid ((*S*)-**10**).

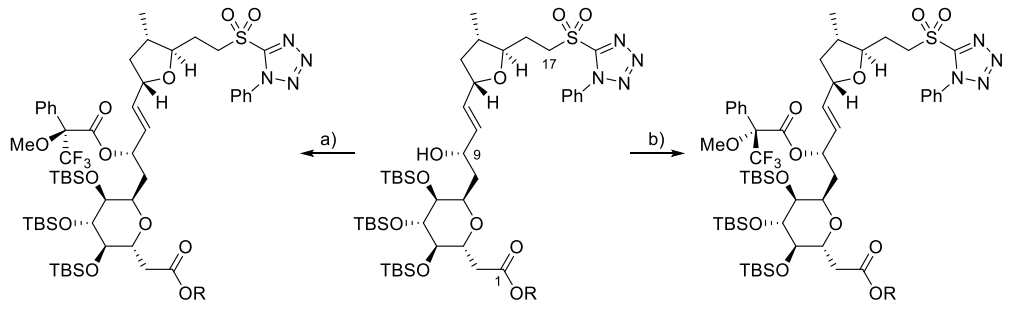
[252] a) G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730. b) J. R. Kramer, T. J. Deming, *J. Am. Chem. Soc.* **2010**, *132*, 15068-15071.

3.7.1.3. Stereochemical Proof

Some intermittently obtained triol isomers (such as **147**, **148**, **149** and **150a**) were previously elucidated by a combination of Mosher ester analysis and nOe correlation experiments on cyclic carbonate derivatives (Chapter 3.5.1.3). We finally established the absolute configuration of triols **196** and **150** by a combination of Mosher ester analysis and NMR comparison with constitutional isomers as following.

3.7.1.3.1. Mosher Ester Analysis

In order to determine the absolute configuration, allylic alcohol **180** was derivatized according to the Mosher ester analysis[253] resulting in the formation of ester **198** and its diastereomer *epi*-**198** (Scheme 3.87). Both analyses confirmed that the (*S*)-configured stereocentre at C-9 had been correctly installed.



Scheme 3.87: Preparation of Mosher esters **198** and *epi*-**198**. Reagents and conditions: (a) (*R*)-Mosher acid chloride, py, DCM, rt, for R = $(CH_2)_2$TMS (25 h, 96%), for R = CH_3 (3 d, 95%); (b) (*S*)-Mosher acid chloride, py, DCM, rt, for R = $(CH_2)_2$TMS (24 h, 96%), R = CH_3 (3 d, 95%).

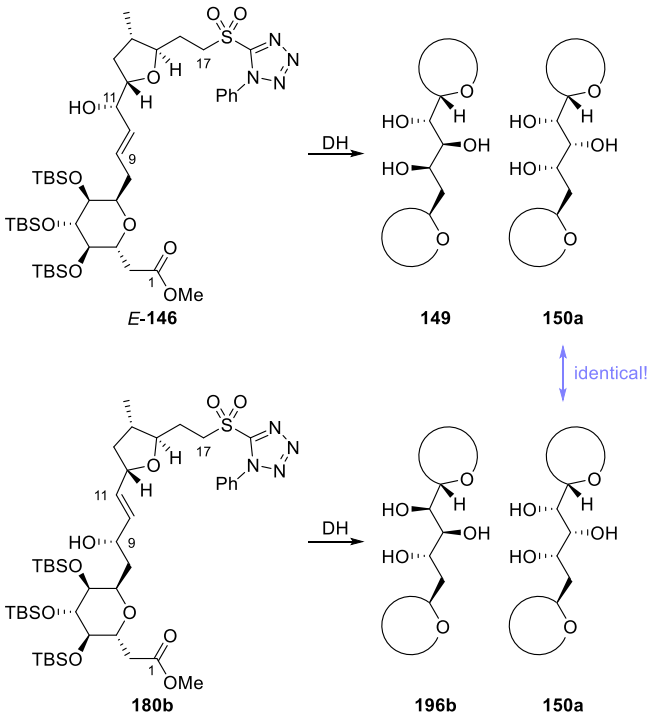
3.7.1.3.2. Stereochemical Proof Through NMR Comparison Of Constitutional Isomers

In theory, the Sharpless dihydroxylation of allylic alcohol *E*-**146** leads to two possible diastereomers (Scheme 3.88). At the same time, the dihydroxylation of allylic alcohol **180b** also leads to two possible diastereomers. Since *E*-**146** and **180b** are constitutional isomers,[254] two of the four possible diastereomeric triol products are in fact the same (**150a**). This particular

[253] a) I. Ohtani, T. Kusumi, Y. Kashman, H. Kakisawa, *J. Am. Chem. Soc.* **1991**, *113*, 4092-4096. b) T. R. Hoye, C. S. Jeffrey, F. Shao, *Nat. Protocols* **2007**, *2*, 2451-2458.

[254] The stereochemistry of allylic alcohol *E*-**146** was proven by Mosher esters **153** and *epi*-**153** (Scheme 3.62), the one of constitutionally isomeric allylic alcohol **180b** by Mosher esters **198b** and *epi*-**198b** (Scheme 3.87).

diastereomer **150a** should also match the stereochemistry of our desired *all-syn*-triol motif within the western belizentrin fragment **127**.



Scheme 3.88: Constitutionally isomeric allylic alcohols *E*-**146** and **180b** and possible diastereomeric dihydroxylation products **149**, **150a** and **196b**.

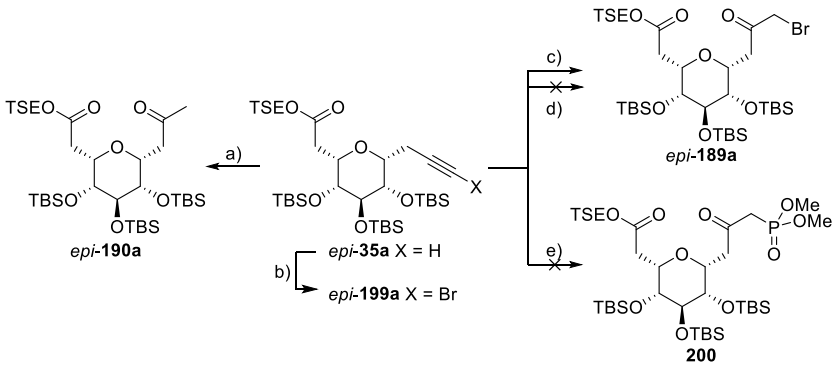
Finally, the careful comparison of the obtained NMR datasets proved two of the four isolated compounds obtained via different synthetic routes to be identical (compare Chapter 3.3 vs. Chapter 3.5) and led to the shown stereochemical assignment (Scheme 3.88).

The confirmed stereochemistry of diastereomers **149**, **150a** and **196b** also paved the way to the retrospective identification of structures which, until then, remained unclear such as **147** and **148**. Importantly, this conclusion was indeed matching the assignment of cyclic carbonate derivatives **158**, **160** and **162** earlier obtained by the interpretation of nOe signal correlations (Chapter 3.5.1.3.4).

3.7.2. Investigations On Alternative Pathways

3.7.2.1. Reactivity Differences Between C5'-Epimeric Glucosides

We tried to convert alkyne *epi*-**35a**[255] directly into α-haloketone *epi*-**189a** or β-ketophosphonate **200** (Scheme 3.89). A gold-catalyzed one-step approach from *epi*-**35a** towards *epi*-**189a**, as described by Xing *et al.* for simple terminal alkynes,[256] was unsuccessful as was the transformation of *epi*-**35a** into **200**, following a report by Zhao *et al.* for aromatically substituted alkynes.[257]



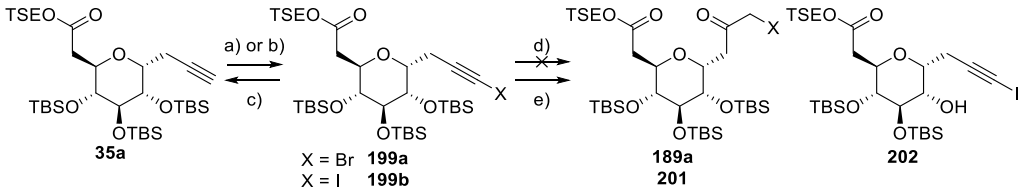
Scheme 3.89: Preliminary C5' epimer modification studies. Reagents and conditions: (a) 3 mol% XPhosAuNTf$_2$, H_2O, 1,2-DCE, 1.5 h, rt, 88% (with X = H); (b) NBS, 10 mol% $AgNO_3$, acetone, rt, 2.5 d, 86% (with X = H); (c) 3 mol% XPhosAuNTf$_2$, H_2O, 1,2-DCE, rt, 2.5 h, 41% (with X = Br); (d) i. 2.6 mol% $AuCl_3$, 7.6 mol% $AgNTf_2$, MeOH/1,4-dioxane (1:3), rt to 45 °C, 1 d; ii. 1 eq. NBS, rt, 1 d, mainly decomposition, some recovered SM *epi*-**199a** (20%, with X = Br); (e) diethylphosphite, air, 10 mol% $AgNO_3$, 20 mol% $CuSO_4{\cdot}5H_2O$, 12 eq. $KHSO_5{\cdot}0.5KHSO_4{\cdot}0.5K_2SO_4$ (OXONE®), DCM/H_2O (1:1), rt, 2 d, no reaction, SM *epi*-**35a** recovered (quant., with X = H).

The gold-catalyzed hydration of alkyne *epi*-**35a** resulted in the expected methylketone *epi*-**190a**, as described by He *et al.* (as part of a general two-step procedure from alkynes to α-haloketones) (Scheme 3.89).[258] Alkyne *epi*-**35a** was submitted to a silver-mediated bromination[259] and resulted in *epi*-**199a** in 86% yield. Bromoalkyne *epi*-**199a** was subsequently transformed into α-bromoketone *epi*-**189a** by the above mentioned gold-catalyzed hydration, yet in only 41% yield.

Based on these results, epimer **35a** was submitted to the same bromination conditions and bromoalkyne **199a** was successfully obtained in 98% yield (Scheme 3.90). When **199a** was submitted to the hydration that had previously worked for *epi*-**199a** only decomposition was observed.

---

[255] Preliminary studies were undertaken with the less valuable C5' epimer *epi*-**35a** (Chapter 3.3.1.2).
[256] Y. Xing, M. Zhang, S. Ciccarelli, J. Lee, B. Catano, *Eur. J. Org. Chem.* **2017**, *4*, 781-785.
[257] X. Chen, X. Li, X.-L. Chen, L.-B. Qu, J.-Y. Chen, K. Sun, Z.-D. Liu, W.-Z. Bi, Y.-Y. Xia, H.-T. Wu, Y.-F. Zhao, *Chem. Commun.* **2015**, *51*, 3846-3849.
[258] L. Xie, Y. Wu, W. Yi, L. Zhu, J. Xiang, W. He, *J. Org. Chem.* **2013**, *78*, 9190-9195.
[259] Also reported by He *et al.* as part of the before mentioned two-step procedure.



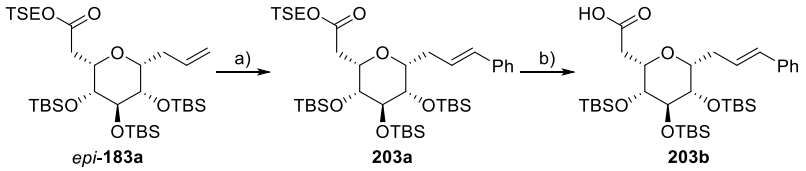
Scheme 3.90: Alkyne manipulations with the C-glucoside **199**. Reagents and conditions: (a) NBS, 10 mol% $AgNO_3$, acetone, rt, 20.5 h, 98% (X = Br); (b) NIS, 10 mol% $AgNO_3$, acetone, rt, 5 d, 97% (X = I); (c) 10 mol% $PdCl_2(P(2\text{-furyl})_3)_2$, 8 eq. diethylphosphite, 6 eq. TEA, DMF, rt, 7 d, 59% (X = I); (d) 3 mol% XPhosAuNTf$_2$, H_2O, 1,2-DCE, rt, 10 min, degradation (successive loss of TBS groups, X = Br); (e) 6 mol% XPhosAuNTf$_2$, H_2O, 1,2-DCE, rt to 0 °C, 5.5 h, 16% of **202**, 32% of an inseparable mixture of mono-deprotected byproducts, some recovered SM **199b** (10%, X = I).

Iodoalkyne **199b** was prepared analogously from **35a** with *N*-iodosuccinimide and silver(I) in 97% yield (Scheme 3.90). Submitted to the gold-catalyzed hydration, rapid degradation occurred. A palladium-catalyzed cross coupling only gave protodeiodinated alkyne **35a** in 59% yield.[260]

In stark contrast to the epimeric series (Scheme 3.89), it was impossible to isolate **189a** or **201** (Scheme 3.90). The addition of the gold catalyst immediately resulted in the (visible) formation of elemental halogen (colouring: brown with bromoalkyne **199a**, purple with iodoalkyne **199b**).

3.7.2.2. Cross Metathesis & TMS-Ethyl Ester Cleavage

The cleavage for a final release of belizentrin (**18**) from derivative **20** was tested. Cross metathesis (CM) of *epi*-**183a** and styrene with the Grubbs II catalyst (**175**), as reported by Pohmakotr *et al.* for simple terminal alkenes,[261] gave UV-active test substrate **203a** in 36% yield (Scheme 3.91).



Scheme 3.91: TMS-ethyl ester functionalization and deprotection. Reagents and conditions: (a) styrene, 5 mol% Grubbs II catalyst **175**, DCM, 4 Å MS, rt to 45 °C, 21 h, 36%; (b) TASF, DMF, 0 °C to rt, 5 h, 77%.

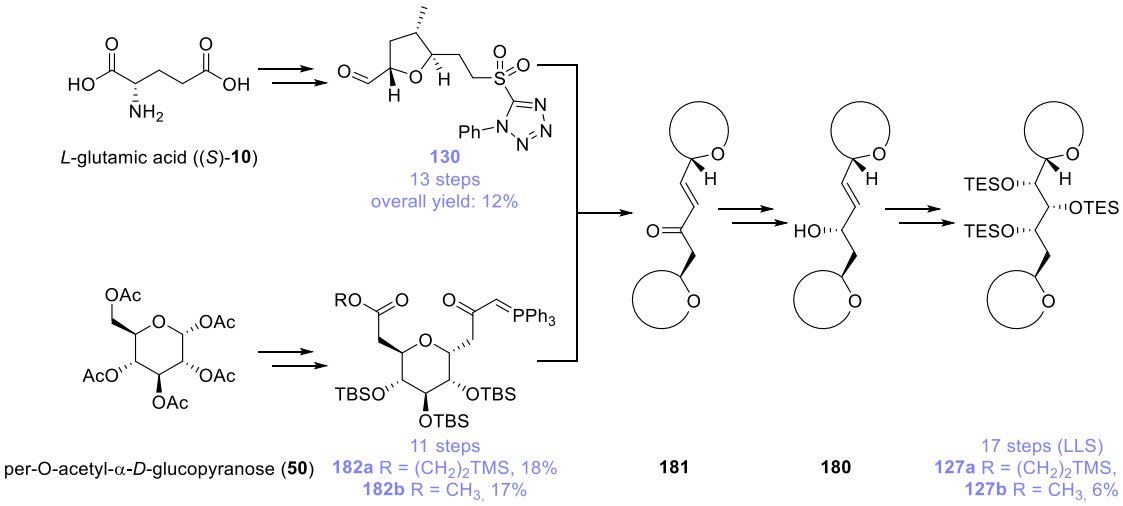
epi-**183a** was submitted to tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) in *N*,*N*'-dimethylformamide according to a procedure used in the total synthesis of putative orevactaene reported by our group[262] to give carboxylic acid **203b** in 77% yield (Scheme 3.91).

Based on these results, we were hoping to release target molecule **18** under similiar conditions.

[260] A supply of catalyst $PdCl_2(P(2\text{-furyl})_3)_2$ was kindly provided by F. Anderl.
[261] K. Peewasan, C. Kuhakarn, D. Soorukram, P. Tuchinda, V. Reutrakul, M. Pohmakotr, *J. Fluorine Chem.* **2012**, *135*, 367-372.
[262] J. Preindl, S. Schulthoff, C. Wirtz, J. Lingnau, A. Fürstner, *Angew. Chem. Int. Ed.* **2017**, *56*, 7525-7530.

3.7.3. Interim Summary

The C-glucoside moiety **182** was synthesized by a series of events that started again with the allylation of per-O-acetyl-α-*D*-glucopyranose (**50**) at the anomeric position which was followed by protecting group manipulations. After introduction of the ester functionality, alkene **183** was obtained as a suitable candidate for a sequence of α-oxidation and α-halogenation towards **189**. Intriguingly, the substitution of the bromine with triphenylphosphine (**195a**) was not as straightforward as anticipated, due to the lability of the phosphonium salt **193**. Finally, the reaction of α-bromoketone **189** with triphenylphosphine (**195a**) succeeded smoothly in benzene glass at -20 °C. Deprotonation of the readily enolizable phosphonium salt **193** resulted in desired phosphorus ylide **182** in nine steps in an estimated (due to the *in situ* formation of the ylide) overall yield of 17-18% (Scheme 3.92).



Scheme 3.92: Final synthetic route to the western belizentrin fragment **127**. Reagents and conditions: as shown before.

Aldehyde **130** and phosphorus ylide **182** were coupled by a Wittig olefination which proceeded with high *E* selectivity (*E*/*Z* > 16:1) in 76-79% yield (Scheme 3.92). CBS reduction of enone **181** resulted in allylic alcohol **180**. Its altered constitution (in comparison to allylic alcohol *E*-**146**) finally paved the way to a ligand-controlled Sharpless dihydroxylation. The desired triol **150** was obtained in good diastereoselectivity (*d.r.* > 6.7:1). Final protection with TESOTf resulted in the western belizentrin fragment **127** in 17 steps (LLS) in an overall yield of 6-7%.

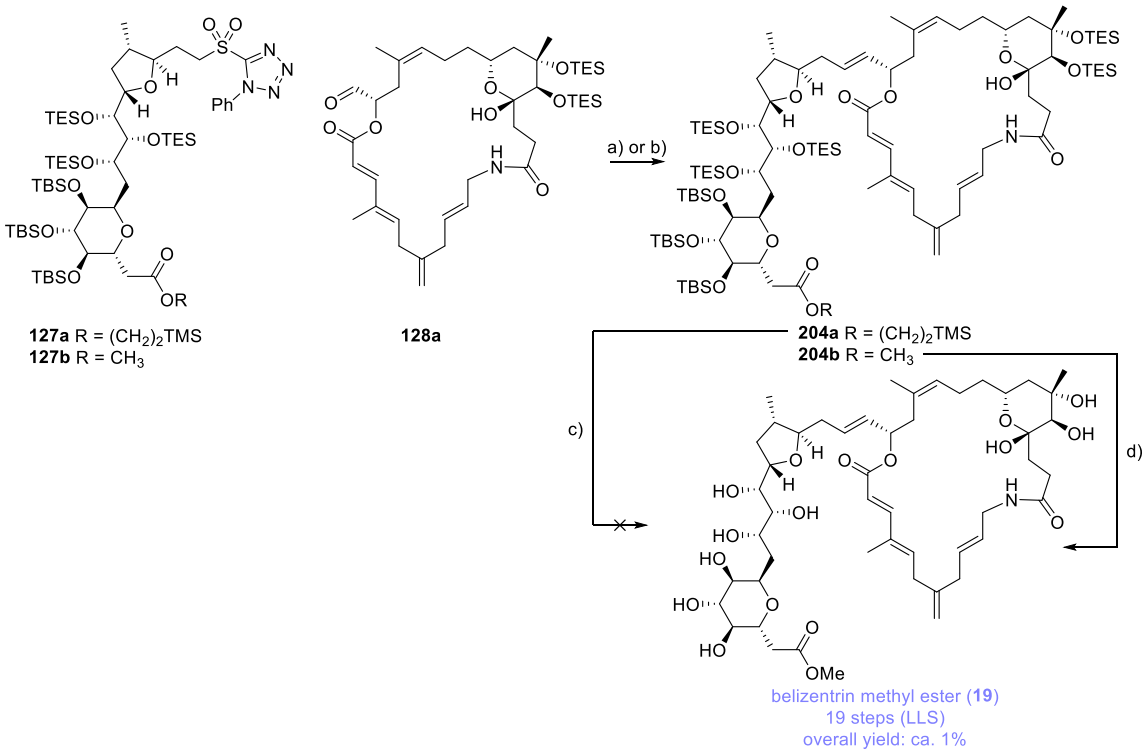
During the course of some preliminary studies, we observed a very interesting difference in the reactivity between alkyne **35a** and its C5' epimer *epi*-**35a**. Moreover, carboxylic acid deprotection performed on the TMS-ethyl ester-bearing test substrate **203a** with tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) proceeded cleanly.

In summary, we found a suitable route towards western belizentrin fragment **127** available on a 300 mg scale both as the methyl, as well as the TMS-ethyl, ester. The absolute configuration of the triol motif was unambiguously confirmed by the NMR comparison of triols obtained through two different routes, originating from constitutionally isomeric allylic alcohol *E*-**146** and **180b** (Chapter 3.7.1.3.2).

3.8. The Belizentrin Esters

3.8.1. Final Fragment Coupling & Elaboration Towards Belizentrin Esters

During the Julia-Kocienski olefination of western belizentrin fragment **127** and its eastern counterpart **128a**,[263] a severe base-lability of aldehyde **128a** in the presence of lithiated **127** was encountered (Scheme 3.93). We were inspired by literature reports to improve the outcome of a Julia-Kocienski olefination for enolizable ketones by transmetalation to cerium(III) chloride, as reported by Sasaki *et al*.[264] After different attempts, finally transmetalation to zinc was of great assistance, and prevented the decomposition of aldehyde **128a**.



Scheme 3.93: Synthetic pathway to the belizentrin methyl ester (**19**). Reagents and conditions: (a) **127a**, LiHMDS, $ZnCl_2$, then **128a**, DMF/DMPU (3:1), -40 °C to rt, 3 d, 25-30%; (b) excess **127b**, LiHMDS, $ZnCl_2$, then **128a**, DMF/DMPU (3:1), -40 °C to rt, 72 h, 25-30%; (c) TASF, DMF, rt, decomposition; (d) i. aq. HF, MeCN, rt, 6 h; ii. Me_3SiOH, rt, 30 min, 36%.

The fragments were coupled in a reproducible yield of 25-30% in DMF/DMPU (3:1)[265] yielding globally protected **204** (Scheme 3.93). This was a satisfying result, regarding the targeted chemical

[263] All experiments discussed in this chapter were conducted and optimized by Ph.D. student F. Anderl. Laboratory assistant P. Ortsack and laboratory assistant apprentice C. Rustemeier contributed to his success. Further details on the total synthesis of belizentrin methyl ester (**18**) and the synthesis of the macrocyclic scaffold **128a** can be found in the projected Ph.D. thesis of F. Anderl.

[264] a) K. Ishigai, H. Fuwa, K. Hashizume, R. Fukazawa, Y. Cho, M. Yotsu-Yamashita, M. Sasaki, *Chem. Eur. J.* **2013**, *19*, 5276-5288. b) K. Tsubone, K. Hashizume, H. Fuwa, M. Sasaki, *Tetrahedron* **2011**, *67*, 6600-6615.

[265] P. Liu, E. N. Jacobsen, *J. Am. Chem. Soc.* **2001**, *123*, 10772-10773.

problem. Lithiated tetrazolylsulfone **127** was used in excess (ca. 3 eq.) due to the free hydroxy group within the aldehyde partner **128a**. Fortunately, unreacted sulfone **127** could be recovered almost quantitatively, whereas remaining aldehyde **128a** could not be reisolated.

Final deprotection of globally protected substrate **204a** led to the cleavage of all silyl-based protecting groups but the TMS-ethyl ester. This ester could neither be cleaved with Olah´s reagent (hydrofluoric acid/pyridine) nor with aqueous hydrofluoric acid. Due to the previously observed base-lability of the polyene motif, tetra-*n*-butylammonium fluoride (TBAF) and other fluoride reagents were not suitable. According to HPLC measurements, tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) achieved the ester cleavage, but decomposition was taking place as well, making it impossible to isolate belizentrin (**18**).

Therefore, we prepared methyl ester **204b**, which was globally deprotected with aqueous hydrofluoric acid[266] resulting in belizentrin methyl ester (**19**) and only volatile byproducts which were removed under vacuum (Scheme 3.93). After final HPLC purification, belizentrin methyl ester (**19**) was isolated in 36% yield (2.2 mg, in comparison to 3.1 mg obtained by the isolation team).

[266] a) Y. Ogawa, M. Nunomoto, M. Shibasaki, *J. Org. Chem.* **1986**, *51*, 1625-1627. b) A. Fürstner, M. Bindl, L. Jean, *Angew. Chem. Int. Ed.* **2007**, *46*, 9275-9278. c) Y. Kwon, S. Schulthoff, Q. M. Dao, C. Wirtz, A. Fürstner, *Chem. Eur. J.* **2018**, *24*, 109-114.

4. Final Summary & Conclusion

Herein, we present the first total synthesis of belizentrin methyl ester (**19**) that is concise and convergent in terms of step count and fragment couplings.

In 2014, belizentrin (**18**) was isolated from the marine dinoflagellate *Prorocentrum belizeanum* as the first member of a class of odd-numbered, polyunsaturated and polyhydroxylated macrolactamic neurotoxins (EC_{50} value of 193 ± 7 nM) (Figure 4.1). Belizentrin (**18**) is a target of interest within total synthesis due to the possible application of diverse chemical methodology, the purposes of structural elucidation and biological evaluation. Since belizentrin (**18**) proved unstable during the biological assay, methyl ester derivative **19** was deemed a suitable target.

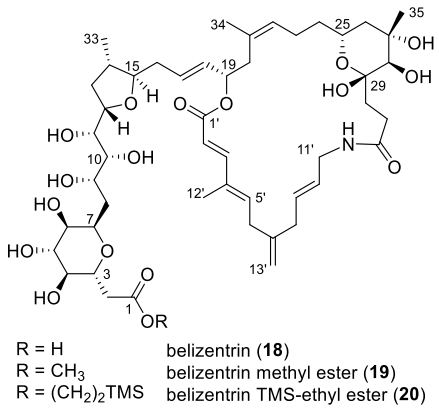
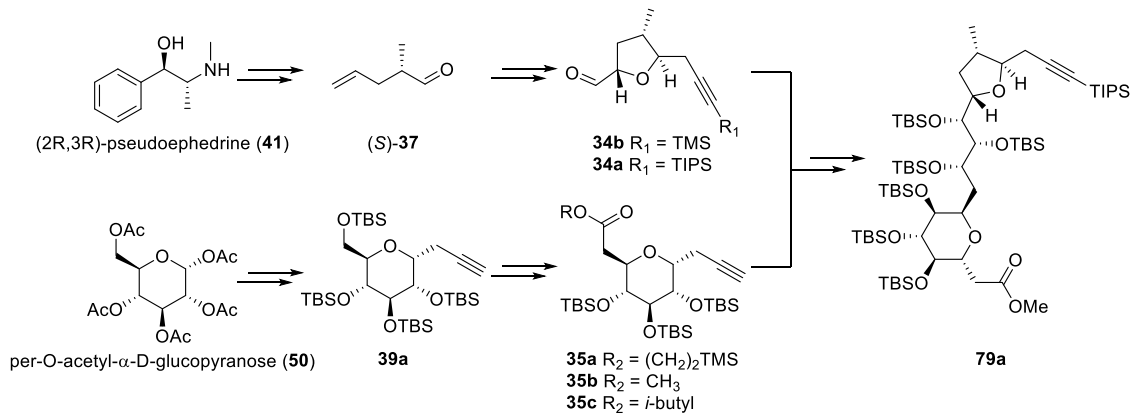


Figure 4.1: Structures of the natural product belizentrin (**18**) and its ester derivatives **19** and **20**.

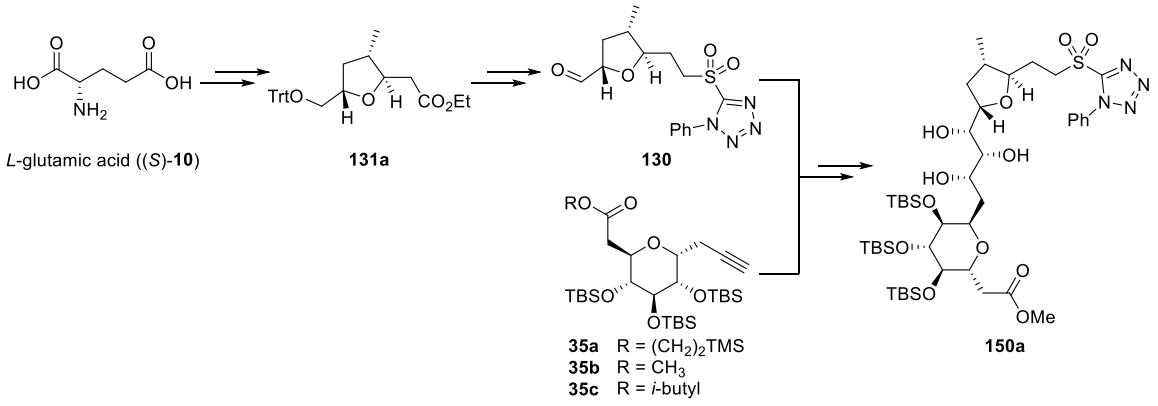
Our first approach to western belizentrin fragment **79a** started with auxiliary-based chemistry leading to alkynyl-bearing 2,5-*trans*-disubstituted ether **34** (Scheme 4.1). Challenging volatile aldehyde (*S*)-**37** paved the way to an oxidative aerobic Mukaiyama cyclization which successfully provided access to the core structure of the 2,5-*trans*-disubstituted tetrahydrofuran ring **34**. The synthetic access to alkyne **35** was guaranteed by C-glycosidation of **50** with allyl-TMS (**52**) and further transformation into the alkyne substituent of **39a**. Enolether formation via Wittig reaction and subsequent oxidation ensured the installation of different esters in **35**.



Scheme 4.1: Synthesis of western belizentrin fragment **79a**, via route 1.

The coupling of both building blocks was performed under zinc(II) mediation and led to the corresponding allylic alcohol in a straightforward sense via the in house-developed methodology of the ruthenium-catalyzed *trans*-selective hydrostannation (Scheme 4.1). A major drawback was the low-yielding alkynylation in combination with an overall substrate-controlled osmium-mediated dihydroxylation towards triol **78**.

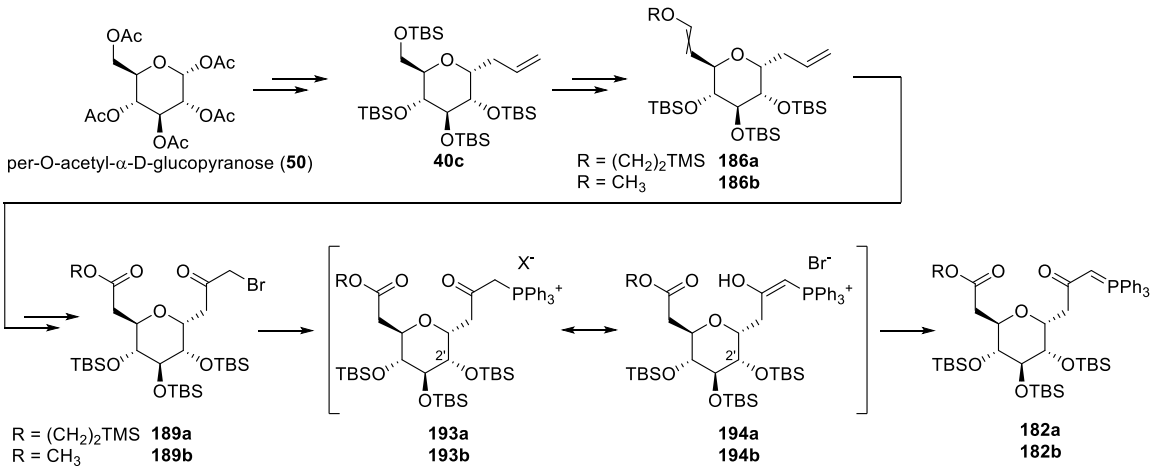
As a consequence, a second route was envisioned. Major change was the attempted use of a Julia olefination instead of an alkynylation as the central coupling of belizentrin´s western and eastern parts. Therefore, the preparation of a completely new northern 2,5-*trans*-disubstituted tetrahydrofuran building block **130** was necessary (Scheme 4.2). Starting from *L*-glutamic acid ((*S*)-**10**) and based on a literature precedent for the elaborated enantiomer of 2,5-*trans*-disubstituted tetrahydrofuran system **131a**, we achieved the synthesis of the new building block **130**, whereas the alkynylation and the Sharpless dihydroxylation were maintained within the western belizentrin fragment **150a**, the C-glucoside fragment´s synthesis did not change.



Scheme 4.2: Synthesis of western belizentrin fragment **150a**, via route 2.

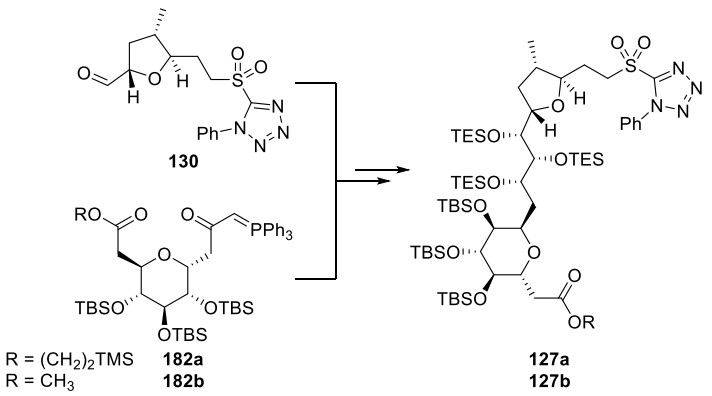
Unfortunately, the alkynylation remained as unsatisfying as before, as it only proceeded in low yield (Scheme 4.2). Even more renitent was the attempted Sharpless dihydroxylation, which remained substrate-controlled. Therefore, we only obtained tiny amounts of the desired diastereomer **150a** and had to develop a third synthetic approach.

The final pathway to globally protected western belizentrin fragment **127** involved the previous route to 2,5-*trans*-disubstituted ether **130** as well as a new route to phosphorus ylide **182** (Scheme 4.3). After anomeric allylation and functional group alterations of **50**, we again installed an ester moiety at the C6' terminus of the C-glucoside **40c** by Wittig olefination and subsequent oxidation of the corresponding enolether **186**. The allyl side chain was α-oxidized by an interesting method with stoichiometric potassium permanganate in acidic medium, followed by an Appel reaction to access the α-bromoketone **189**. Most fascinating about the phosphorus ylide synthesis remained the transformation of this α-bromoketone **189** into the corresponding phosphorus salt **193** by freezing a solution of the substrate and triphenylphosphine (**195a**) in benzene at -20 °C. Previous attempts to observe the phosphorus salt **193** resulted in degradation and decomposition, probably due to an enolization to **194** which finally could even be characterized by ^{1}H NMR analysis.



Scheme 4.3: Synthesis of phsphorus ylide **182**.

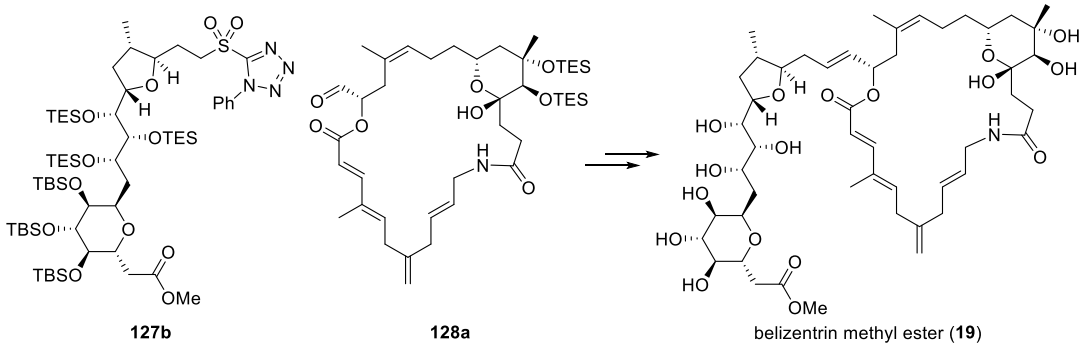
Aldehyde **130** and phosphorus ylide **182** were coupled by a highly *E*-selective Wittig olefination (Scheme 4.4). After transformation into the corresponding allylic alcohol **180** by CBS reduction, the osmium-catalyzed dihydroxylation proceeded under ligand control (or with a matching effect) and finally yielded the desired triol **127** in acceptable yield after protection with TESOTf.



Scheme 4.4: Synthesis of western belizentrin fragment **127**, via (final) route 3.

The most important observation we made was the change from substrate control to ligand control during the Sharpless dihydroxylation by altering the constitution of our central intermediate allylic alcohol *E*-**146**. Thereby, we did not only manage to isolate desired triol **150** as the *major* isomer, but we also secured definite proof for the absolute configuration of the stereocentres of the central triol motif.

Moreover, western belizentrin fragment **127** and its eastern counterpart **128a** were successfully coupled in a modified Julia-Kocienski olefination, despite the base sensitivity of the skipped polyene motif (Scheme 4.5). Global deprotection led to belizentrin methyl ester (**19**) as a reasonably stable derivative of the natural product **18**. NMR data suggested that the isolated natural product and our own material are likely of the same relative and absolute configuration (an NMR comparison of belizentrin (**18**) with belizentrin methyl ester (**19**) can be found in Chapter 5.2.4). Release of the natural product **18** from its globally protected TMS-ethyl ester **20** (via fluoride-based chemistry) or (enzymatically) from its methyl ester congener **19** was not achieved.



Scheme 4.5: Final coupling of western and eastern fragment and global deprotection under the release of belizentrin methyl ester (**19**).

5. Experimental Procedures

5.1. General Experimental Details

All reactions were carried out under Ar in flame-dried glassware dried under vacuum (Schlenk line) using anhydrous solvents, unless water was used as a solvent or it is stated otherwise. The solvents were purified by distillation over the indicated drying agents and were transferred under Ar: THF, Et_2O (Mg/anthracene), acetone (B_2O_3), DCM, hexane, pentane, PhMe (Na/K), MeOH (Mg, stored over 3 Å MS), ethanol (3 Å MS), EtOAc (P_2O_5, filtered through dry Al_2O_3, stored over 4 Å MS); 1,4-dioxane, DMF, MeCN, TEA, py and DMSO were dried by an adsorbtion solvent purification system (SPS) based on MS. DIPEA was distilled over CaH_2 under Ar prior to its use. Thin layer chromatography (TLC): Macherey-Nagel precoated plates (POLYGRAM® SIL/UV254); Flash chromatography: Merck silica gel 60 (40-63 µm or 15-40 µm (fine)) or VWR silica gel (40-64 µm) with pre-distilled or HPLC grade solvents. TLC plates were visualized by UV and stained by exposure to either an ethanolic solution of *p*-anisaldehyde, AcOH and conc. H_2SO_4 or a solution of $Ce(NH_4)_2(NO_3)_6$ and $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ in conc. H_2SO_4 followed by development with a heat gun (>300 °C). IR: ALPHA (Bruker) spectrometer, wavenumbers ($\tilde{\nu}$) in cm^{-1}. MS (EI): Finnigan MAT 8200 (70 eV), MS (ESI): ESQ 3000 (Bruker), accurate mass determinations: Bruker APEX III FT-MS (7 T magnet) or Mat 95 (Finnigan). Optical rotation ($[\alpha]_D^{20}$): A-KRÜSS Optronic Model P8000-t polarimeter. Melting point (m.p.): BÜCHI Melting Point B-540.

NMR: Spectra were recorded on a Bruker DPX 300, AV 400, AV 500 or AV 600 spectrometer in the solvents indicated; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (*J*) in Hz. The solvent signals were used as references and the chemical shifts converted to the TMS scale ($CDCl_3$ at 7.26 and 77.16 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; C_6D_6 at 7.16 ppm and 128.06 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; CD_3OD at 3.31 ppm and 49.00 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; CD_2Cl_2 at 5.32 ppm and 54.00 ppm for ^1H and ^{13}C NMR spectroscopy, respectively; D_2O at 4.79 ppm for ^1H and spectroscopy, respectively; DMSO-d_6 at 2.50 and 39.52 ppm for ^1H and ^{13}C NMR spectroscopy, respectively). ^{13}C NMR spectra were recorded with broadband ^1H decoupling. Where indicated, the signal assignments in the NMR spectra are unambiguous; the numbering scheme is arbitrary and shown in the inserts. The assignments are based upon 1D and 2D spectra recorded using the following pulse sequences from the Bruker standard pulse program library: DEPT; COSY (*cosygpmfphpp*);

HSQC (*hsqcedetgpsisp2.2*) optimized for $^{1}J_{C,H}$ = 145 Hz; HMBC (*hmbcetgpl3nd*) for correlations via $^{n}J_{C,H}$; HSQC-TOCSY (*invietgsml*) using an MLEV17 mixing time of 120 ms; NOESY (*noesygpph*).

Important key fragments or complex byproducts were analyzed by the NMR department of our institute, especially by Mrs. Cornelia Wirtz, Mrs. Petra Philipps, Mrs. Julia Lingnau and Dr. Christophe Farès.

LC-MS analyses were conducted with a LC-MS2020 instrument from Shimadzu (pumps LC-20 AD, autosampler SIL-20AC, column oven CTO-20AC, diode array detector SPD-M20A, controller CBM-20A, ESI detector and software LCMS-solution) with an ZORBAX Eclipse Plus C18 1.8 µm, 3.0 mm or 4.6 mm ID × 50 mm (Agilent). A binary gradient of MeCN or MeOH in water or aq. triethylammonium acetate (TEAA) buffer (10 mmol. pH 8) was used at flow rates of 0.5 (3.0 mm ID) mL/min or 0.8 (4.6 mm ID) mL/min. The oven temperature was kept at 35 °C and a detection wave length of 254 nm was used.

Unless stated otherwise, all commercially available compounds (abcr, ACROS, Sigma-Aldrich (Merck), Alfa Aesar, Fluka, Oakwood, Strem, TCI, VWR) were used as received. Conditions for the synthesis of each compound are described in the experimental below.

A supply of catalyst **49b** for the Mukaiyama cyclization was kindly provided by Dr. M. Ilg. Both polymeric catalyst $[Cp^*RuCl_2]_n$ and tetrameric catalyst $[Cp^*RuCl]_4$ for the *trans*-hydrostannation were kindly provided by either laboratory assistant K. Radkowski, by Dr. D. Roşca or Dr. S. Rummelt. Within the reaction sequence towards the 2,5-*trans*-disubstituted ether **130**, laboratory apprentice C. Rustemeier helped with the synthesis and purification of thioether **141** (on a scale of ca. 1 g, Scheme 3.54). The first three steps of the reaction sequence towards aldehyde **185** were also carried out by laboratory apprentice C. Rustemeier on a scale above 5 g (Scheme 3.78). Therefore, material supply was always assured, when in parallel the focus lay on the introduction of the subsequent steps of the new synthetic route towards phosphorus ylide **182**. Based on the results shown in Chapter 3.3.1.2 and with the aimed phosphorus ylide **182** in mind, Dr. J. Novacek proposed an order of events which in fact helped to pave a way to this important intermediate. A supply of catalyst $PdCl_2(P(2\text{-furyl})_3)_2$ was kindly provided by F. Anderl. All experiments discussed in Chapter 3.8 were conducted and optimized by Ph.D. student F. Anderl. Laboratory assistant P. Ortsack and laboratory assistant apprentice C. Rustemeier contributed to his success. Further details on the total synthesis of belizentrin methyl ester (**18**)

and the synthesis of the macrocyclic scaffold **128a** can be found in the projected Ph.D. thesis of F. Anderl.

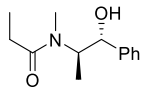
Their help and contribution is therefore thankfully acknowledged.

5.2. Total Synthesis Of Belizentrin

5.2.1. The Western Belizentrin Fragment - Route 1

5.2.1.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

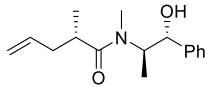
N-((1R,2R)-1-Hydroxy-1-phenylpropan-2-yl)-N-methylpropionamide (42)



Propionic anhydride (21.3 mL, 165 mmol) was added to a stirred solution of (1*R*,2*R*)-(-)-pseudoephedrine (**41**) (25.9 g, 154 mmol) and TEA (23.6 mL, 169 mmol) in DCM (300 mL) at rt over the course of 10 min and stirring was continued for 1 h. The reaction was quenched with sat. aq. $NaHCO_3$ (200 mL). The organic extract was subsequently washed with aq. HCl (1.0 M, 200 mL) and brine (200 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by recrystallization from boiling PhMe (120 mL) affording compound **42** as a colourless crystalline solid (32.3 g, 95%).

^{1}H NMR (2.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 400 MHz, C_6D_6): δ = 7.37 - 6.94 (m, 5H), 7.37 – 6.94* (m, 5H), 5.02 (br s, 1H), 4.53 (t, J = 7.2 Hz, 1H), 4.25 (br s, 1H), 4.21* (dd, J = 8.9, 3.0 Hz, 1H), 3.71* (dq J = 9.1, 6.8 Hz, 1H), 3.44* (br s, 1H), 2.83* (s, 3H), 2.49* (dq, J = 15.1, 7.5 Hz, 1H), 2.14 – 2.09* (m, 1H), 2.08 (s, 3H), 1.84 – 1.64 (m, 2H), 1.23* (t, J = 7.4 Hz, 3H), 1.02 (t, J = 7.4 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H), 0.55* (d, J = 6.8 Hz, 3H) ppm; **^{13}C NMR** (2.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 101 MHz, C_6D_6): δ = 175.3, 174.3*, 143.9, 142.8*, 128.7*, 128.6, 128.4 (2C), 128.2*, 128.0* (2C), 127.5* (2C), 127.4, 126.9 (2C), 76.6, 75.3*, 59.4, 58.5*, 27.5, 27.0*, 15.2*, 14.4, 10.0*, 9.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{13}H_{19}NO_2Na^+$: 244.1308, found: 244.1307. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[267]

(S)-N-((1R,2R)-1-Hydroxy-1-phenylpropan-2-yl)-N,2-dimethylpent-4-enamide (43)



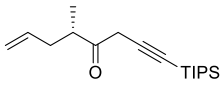
n-BuLi (1.6 M in hexane, 176 mL, 282 mmol) was slowly added to a stirred solution of flame-dried LiCl (34.5 g, 813 mmol) and DIPA (42.7 mL, 305 mmol) in THF (180 mL) at 0 °C giving a white suspension, and stirring was continued for 15 min. The reaction mixture was warmed to rt and stirring was continued for 30 min. Propionamide **42**

[267] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.

(30.0 g, 136 mmol) as a solution in THF (370 mL) was slowly added to the stirred reaction mixture at -78 °C over the course of 30 min and stirring was continued for 45 min. Afterwards the reaction mixture was warmed to 0 °C and stirring was continued for 20 min. Then the reaction mixture was warmed to rt and stirring was continued for 15 min. Allyl iodide (19.0 mL, 203 mmol) was added dropwise at -78 °C to the reaction mixture and stirring was continued for 1 h. Finally the reaction mixture was warmed to 0 °C and stirring was continued for 1 h. The reaction was quenched with sat. aq. NH_4Cl (200 mL) and sat. aq. $Na_2S_2O_3$ (15 mL) and the aq. phase was extracted with EtOAc (2 x 400 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 2:1 to 1:1) affording compound **43** as an orange oil (33.7 g, 95%).

^{1}H NMR (3.3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 400 MHz, C_6D_6): δ = 7.37 – 7.05 (m, 5H), 7.37 – 7.05* (m, 5H), 5.98 – 5.85* (m, 1H), 5.69 – 5.56 (m, 1H), 5.22 – 5.14* (m, 1H), 5.09 – 5.04* (m, 1H), 5.03 (br s, 1H), 5.02 – 4.91 (m, 2H), 4.55 (t, J = 7.2 Hz, 1H), 4.32 (br s, 1H), 4.27* (dd, J = 8.4, 3.2 Hz, 1H), 3.94 – 3.85* (m, 1H), 3.39 – 3.35* (m, 1H), 2.87 – 2.75* (m, 2H), 2.84* (s, 3H), 2.46 – 2.37 (m, 1H), 2.35 – 2.29* (m, 1H), 2.27 (dd, J = 12.8, 5.9 Hz, 1H), 2.24 (s, 3H), 2.02 – 1.93 (m, 1H), 1.07* (d, J = 6.5 Hz, 3H), 0.97 (d, J = 6.8 Hz, 3H), 0.965 (d, J = 6.8 Hz, 3H), 0.68* (d, J = 6.7 Hz, 1H) ppm; **^{13}C NMR** (3.3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 101 MHz, C_6D_6): δ = 177.4, 176.5*, 143.7, 142.8*, 137.6*, 136.7, 128.7*, 128.6, 128.4 (2C), 128.2*, 127.9* (2C), 127.4* (2C), 127.3, 126.9 (2C), 116.41, 116.36*, 76.3, 75.4*, 59.1, 58.2*, 38.7*, 38.5, 36.6, 35.9*, 17.8*, 17.2, 15.5*, 14.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{16}H_{23}NO_2Na^+$: 284.1621, found: 284.1621. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[268]

(S)-5-Methyl-1-(triisopropylsilyl)oct-7-en-1-yn-4-one (44b)



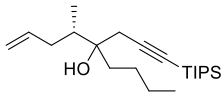
n-BuLi (1.6 M in hexane, 6.51 mL, 10.4 mmol) was slowly added to a stirred solution of 1-(triisopropylsilyl)-1-propyne (95%, 2.62 mL, 10.4 mmol) and TMEDA (1.56 mL, 10.4 mmol) in Et_2O (10 mL) at -5 °C over the course of 5 min and stirring was continued for 30 min. In parallel *n*-BuLi (1.6 M in hexane, 5.42 mL, 8.67 mmol) was slowly added to a stirred solution of amide **43** (2.27 g, 8.67 mmol) as a solution in THF (55 mL) at -78 °C over the

[268] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.

course of 10 min. Afterwards the previously prepared solution of lithiated 1-(triisopropylsilyl)-1-propyne was slowly added to the stirred reaction mixture at -78 °C over the course of 10 min. The reaction mixture was warmed to 0 °C and stirring was continued for 20 min. The reaction was quenched with sat. aq. NH_4Cl (100 mL) and diluted with EtOAc (100 mL). After phase separation the aq. phase was extracted with EtOAc (50 mL). The combined organic extracts were subsequently washed with sat. aq. NH_4Cl (100 mL) and water (100 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography twice (first column: SiO_2, hexane/EtOAc, 75:1; second column: SiO_2, hexane/EtOAc 80:1) affording both major product **44b** (1.93 g, 76%) and minor byproduct **205** (60 mg, 2%, *d.r.* = 1:1) as a colourless oil.

Analytical and spectral data of the major product **44b**: $[\alpha]_D^{20}$: +20.9 (c = 1.01, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.77 – 5.67 (m, 1H), 5.08 – 5.01 (m, 2H), 3.36 (d, J = 22.8 Hz, 1H), 3.32 (d, J = 22.8 Hz, 1H), 3.11 (sex, J = 7.0 Hz, 1H), 2.46 (dtt, J = 14.2, 6.4, 1.4 Hz, 1H), 2.13 (dtt, J = 14.5, 7.4, 1.2 Hz, 1H), 1.13 (d, J = 7.0 Hz, 3H), 1.09 – 1.05 (m, 21H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 207.6, 135.5, 117.2, 100.2, 85.8, 43.9, 36.9, 34.7, 18.7 (6C), 16.1, 11.4 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3079, 2942, 2892, 2865, 2175, 1920, 1719, 1642, 1461, 1382, 1270, 1242, 1197, 1073, 1034, 1017, 993, 916, 882, 675, 660, 621, 528, 502, 452, 417 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{18}H_{32}OSiNa^+$: 315.2116, found: 315.2115.

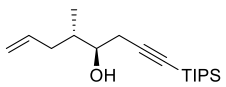
Analytical and spectral data of the minor byproduct **205**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.84 – 5.62



(m, 1H), 5.10 – 4.94 (m, 2H), 2.55 – 2.39 (m, 2H), 1.90 – 1.53 (m, 4H), 1.43 – 1.20 (m, 4H), 1.17 – 0.96 (m, 23H), 0.91 (t, J = 7.0 Hz, 3H), 0.91 (d, J = 6.7 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 138.5, 138.4*, 115.92*, 115.89, 105.1*, 105.0, 84.4*, 84.3, 75.5, 75.4*, 40.4, 39.7*, 37.0*, 36.1, 35.9*, 35.7, 29.6, 29.1*, 25.7, 25.5*, 23.6, 23.5*, 18.79 (6C), 18.78* (6C), 14.24, 14.23*, 13.9, 13.7*, 11.4 (3C), 11.4* (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3433, 3076, 2942, 2892, 2865, 2171, 1713, 1640, 1462, 1382, 1367, 1242, 1071, 1017, 993, 912, 882, 738, 675, 494, 460, 412 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{22}H_{42}OSiNa^+$: 373.2897, found: 373.2900.

(4R,5S)-5-Methyl-1-(triisopropylsilyl)oct-7-en-1-yn-4-ol (36a)

Representative Procedure A (CBS Reduction)

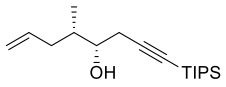


L* (0.5 M in PhMe, 5 mol%, 34.2 µL, 17.1 µmol) was added to a stirred solution of ketone **44b** (100 mg, 342 µmol) in DCM (2.5 mL) at -78 °C and stirring was continued for 20 min. Then, catecholborane (72.9 µL, 684 µmol) as added to the reaction mixture and stirring was continued at -78 °C for 4 h. The reaction mixture was warmed to 5 °C and stirring was continued for 17 h. The reaction was quenched with aq. NaH_2PO_4 (1.0 M, 10 mL) at 0 °C and the aq. phase was extracted with EtOAc (2 x 10 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 75:1) affording desired *anti*-isomer **36a**, *syn*-isomer **46a** and some unreacted starting material **44b** as a colourless oil.

Herein, L* corresponds to: (*R*)- or (*S*)-CBS-oxazaborolidine **47** with R = CH_3, tolyl and *n*-butyl. The reaction was conducted on a 300 mg scale for R = CH_3 following the conditions as described. Yields and corresponding *d.r.* are shown in Scheme 3.6.

Analytical and spectral data of the *anti*-diastereomer **36a**: $[\alpha]_D^{20}$: +8.3 (c = 1.02, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.80 (dddd, J = 16.8, 10.1, 7.9, 6.4 Hz, 1H), 5.08 – 5.00 (m, 2H), 3.53 (tt, J = 7.1, 4.5 Hz, 1H), 2.55 (dd, J = 16.8, 4.2 Hz, 1H), 2.43 (dd, J = 16.8, 7.4 Hz, 1H), 2.42 – 2.34 (m, 1H), 2.06 (d, J = 4.9 Hz, 1H), 1.99 – 1.88 (m, 1H), 1.82 – 1.70 (m, 1H), 1.10 – 1.01 (m, 21H), 0.89 (d, J = 6.8 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.2, 116.4, 105.0, 83.9, 73.6, 37.9, 36.9, 26.4, 18.8 (6C), 15.4, 11.3 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3419, 3077, 2942, 2892, 2865, 2172, 1727, 1641, 1462, 1382, 1242, 1117, 1045, 1017, 989, 913, 882, 663, 607, 527, 490, 460, 417 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{18}H_{34}OSiNa^+$: 317.2271, found: 317.2269.

Analytical and spectral data of the *syn*-diastereomer **46a**: $[\alpha]_D^{20}$: -11.5 (c = 0.97, $CHCl_3$);



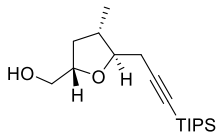
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.78 (ddt, J = 17.0, 10.1, 7.0 Hz, 1H), 5.09 – 4.99 (m, 2H), 3.68 (tt, J = 6.3, 4.6 Hz, 1H), 2.47 (d, J = 6.3 Hz, 2H), 2.24 (dddt, J = 13.8, 6.9, 5.6, 1.4 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.90 (d, J = 4.6 Hz, 1H), 1.78 (ddqd, J = 10.1, 8.3, 6.8, 4.7 Hz, 1H), 1.10 – 1.01 (m, 21H), 0.94 (d, J = 6.8 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.1, 116.4, 105.1, 83.6, 72.9, 38.0, 37.3, 26.6, 18.8 (6C), 13.8, 11.3 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3435, 3077, 2942, 2892, 2865, 2171, 1726, 1641, 1462, 1382, 1242, 1123, 1018, 993, 911, 882,

675, 663, 528, 491, 460, 416 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{18}H_{34}OSiNa^+$: 317.2271, found: 317.2271.

Procedure B

(*S*)-2-Methyl-CBS-oxazaborolidine (*S*)-**47a** (1.0 M in PhMe, 5 mol%, 239 µL, 239 µmol) was added to a stirred solution of ketone **44b** (1.40 g, 4.79 mmol) in DCM (35.3 mL) at -78 °C and stirring continued for 20 min. Then, catecholborane (765 µL, 7.18 mmol) was added to the reaction mixture and stirring was continued at -78 °C for 6.5 h. (*S*)-2-methyl-CBS-oxazaborolidine (*S*)-**47a** (1.0 M in PhMe, 1 mol%, 47.9 µL, 47.9 µmol) and catecholborane (255 µL, 2.39 mmol) were again added to the stirred reaction mixture at -78 °C and stirring was continued for 1 h. The reaction mixture was warmed to 5 °C and stirring was continued for 14 h. The reaction was quenched with aq. NaH_2PO_4 (1.0 M, 50 mL) at 0 °C and the aq. phase was extracted with EtOAc (2 x 50 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 80:1 to 50:1) affording both desired major *anti*-isomer **36a** (735 mg, 52%) and minor *syn*-isomer **46a** (247 mg, 18%) as a colourless oil. The analytical and spectroscopic data of the isolated compounds were identical with those shown above.

((2S,4S,5R)-4-Methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)methanol (48a)



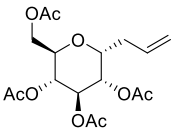
Alcohol **36a** (700 mg, 2.38 mmol) as a solution in *i*-PrOH (23.7 mL) was added to $Co(nmp)_2$ **49b** (10 mol%, 134 mg, 238 µmol) and O_2 was bubbled through the stirred solution for 10 min. *t*-BuOOH (5.5 M in decane, 43.2 µL, 23.8 µmol) was added to the stirred reaction mixture at rt. The resulting reaction mixture was warmed to 55 °C resulting in a colour change from orange to green and stirring was continued for 15 h under an atmosphere of O_2 (balloon). The solvent was evaporated and the residue was dissolved in hexane (60 mL). The resulting solution was washed with aq. phosphate buffer (200 mM, pH 7, 30 mL) and the aq. phase was extracted with hexane (3 x 30 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 7:1 to 3:1) affording compound **48a** as a colourless oil (503 mg, 68%).

$[\alpha]_D^{20}$: +0.4 (c = 1.05, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.18 – 4.11 (m, 1H), 3.68 (ddd, J = 11.6, 6.5, 3.1 Hz, 1H), 3.60 (dt, J = 8.3, 5.2 Hz, 1H), 3.49 (dt, J = 11.7, 5.9 Hz, 1H), 2.57 (dd, J = 17.0, 5.7 Hz, 1H), 2.53 (dd, J = 17.0, 4.8 Hz, 1H), 2.33 – 2.20 (m, 1H), 2.11 (ddd, J = 12.3, 7.2, 6.1 Hz, 1H), 1.91 (t, J = 6.3 Hz, 1H), 1.43 (ddd, J = 12.2, 10.6, 9.6 Hz, 1H), 1.11 (d, J = 6.5 Hz, 3H), 1.09 – 1.00 (m, 21H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 104.9, 83.4, 82.5, 79.1, 65.1, 39.4, 36.8, 25.2, 18.8 (6C), 17.3, 11.4 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3425, 2958, 2942, 2892, 2865, 2174, 1781, 1732, 1462, 1422, 1382, 1366, 1328, 1243, 1169, 1113, 1031, 1017, 996, 971, 919, 883, 840, 822, 676, 661, 632, 605, 527, 460 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{18}H_{34}O_2SiNa^+$: 333.2220, found: 333.2221.

5.2.1.2. The Sugar-Based Alkyne

(2R,3R,4R,5S,6R)-2-(Acetoxymethyl)-6-allyltetrahydro-2H-pyran-3,4,5-triyl triacetate (40a)

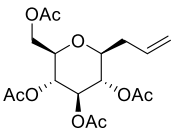
Procedure A (MeCN, $BF_3{\cdot}OEt_2$)



Allyl-TMS (**52**) (30.5 mL, 192 mmol) and $BF_3{\cdot}OEt_2$ (23.7 mL, 192 mmol) were subsequently added to a stirred solution of per-*O*-acetyl-α-*D*-glucopyranose (**50**) (15.0 g, 38.4 mmol) in MeCN (250 mL) at rt. The resulting reaction mixture was stirred for 23 h at 80 °C. Then the reaction mixture was cooled to rt and the solvent was evaporated. The crude product was dissolved in $CHCl_3$ (150 mL) and the organic phase was subsequently washed with water (2 x 100 mL), sat. aq. $NaHCO_3$ (100 mL) and brine (100 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography twice (first column: SiO_2, hexane/EtOAc, 4:1 to 2:1; second column: SiO_2, PhMe/EtOAc, 20:1 to 5:1) affording compound **40a** as an anomeric mixture (11.3 g, 79%, α:β = 7:1). The anomers **40a** and **53** were separated by recrystallization from boiling $CHCl_3$ (7.8 mL) and forced precipitation with hexane (130 mL) affording the major α-anomer **40a** as precipitate whereas the minor β-anomer **53** remained in solution. The crystalline precipitate was washed with ice-cold hexane and dried under vacuum, the solution was evaporated and yielded a light yellow solid.

Analytical and spectral data of the major α-anomer **40a**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.75 (dddd, J = 17.5, 10.2, 7.5, 6.1 Hz, 1H), 5.37 – 5.31 (m, 1H), 5.19 – 5.05 (m, 3H), 4.98 (dd, J = 9.5, 8.8 Hz, 1H), 4.28 (ddd, J = 10.7, 5.6, 4.5 Hz, 1H), 4.21 (dd, J = 12.2, 5.4 Hz, 1H), 4.08 (dd, J = 12.2, 2.6 Hz, 1H), 3.86 (ddd, J = 9.5, 5.4, 2.6 Hz, 1H), 2.61 – 2.50 (m, 1H), 2.38 – 2.29 (m, 1H), 2.08 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.9, 170.3, 169.8, 169.7, 133.1, 118.0, 72.0, 70.5, 70.4, 68.92, 68.90, 62.4, 30.7, 20.9, 20.89, 20.87, 20.8 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{17}H_{24}O_9Na^+$: 395.1313, found: 395.1313.

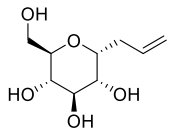
Analytical and spectral data of the minor β-anomer **53**: **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.86 – 5.74



(m, 1H), 5.16 (t, J = 9.4 Hz, 1H), 5.09 – 5.01 (m, 3H), 4.91 (t, J = 9.6 Hz, 1H), 4.23 (dd, J = 12.3, 5.0 Hz, 1H), 4.08 (dd, J = 12.2, 2.3 Hz, 1H), 3.62 (ddd, J = 10.0, 5.0, 2.3 Hz, 1H), 3.49 (ddd, J = 9.7, 7.0, 4.2 Hz, 1H), 2.35 – 2.21 (m, 2H), 2.07 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.9, 170.6, 169.73, 169.66, 133.1, 117.9, 77.3, 75.7, 74.5, 71.7, 68.6, 62.4, 36.0, 20.93, 20.89, 20.82, 20.79 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{17}H_{24}O_9Na^+$: 395.1313, found: 395.1316. For both anomers the

analytical and spectroscopic data are in agreement with those previously reported in the literature.[269]

(2R,3R,4R,5S,6R)-2-Allyl-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol (40b)



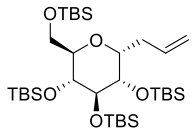
NaOEt (165 mg, 2.42 mmol) was added to a stirred solution of C-glucoside **40a** (9.00 g, 24.2 mmol) in MeOH (110 mL) at rt and the resulting reaction mixture was stirred for 4 h. The reaction was quenched and neutralized with the weakly acidic ion exchange resin Amberlite®. The resin was filtered off and washed with MeOH, the filtrate was dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording crude compound **40b** as a colourless crystalline solid (4.84 g, 98%).

^{1}H NMR (400 MHz, CD_3OD): δ = 5.88 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H), 5.12 (dq, J = 17.1, 1.5 Hz, 1H), 5.04 (ddt, J = 10.2, 2.2, 1.1 Hz, 1H), 3.95 (ddd, J = 10.5, 5.6, 4.3 Hz, 1H), 3.74 (dd, J = 11.8, 2.5 Hz, 1H), 3.64 (dd, J = 11.7, 5.2 Hz, 1H), 3.60 (dd, J = 9.4, 5.7 Hz, 1H), 3.53 (dd, J = 9.5, 8.4 Hz, 1H), 3.45 (ddd, J = 9.6, 5.3, 2.6 Hz, 1H), 3.28 (dd, J = 9.6, 8.4 Hz, 1H), 2-53 – 2.36 (m, 2H) ppm; **^{13}C NMR** (101 MHz, CD_3OD): δ = 136.6, 116.9, 77.1, 75.1, 74.4, 72.9, 72.2, 62.9, 30.5 ppm; **^{1}H NMR** (400 MHz, D_2O): δ = 5.78 – 5.65 (m, 1H), 5.09 (dq, J = 17.3, 1.5 Hz, 1H), 5.05 – 5.00 (m, 1H), 3.97 (ddd, J = 11.5, 5.8, 4.0 Hz, 1H), 3.69 (dd, J = 12.3, 2.3 Hz, 1H), 3.62 (dd, J = 9.7, 5.7 Hz, 1H), 3.58 (dd, J = 11.9, 5.2 Hz, 1H), 3.55 (dd, J = 9.8, 8.7 Hz, 1H), 3.47 (ddd, J = 10.1, 5.3, 2.3 Hz, 1H), 3.25 (dd, J = 10.0, 8.7 Hz, 1H), 2.45 – 2.26 (m, 2H) ppm; **^{13}C NMR** (101 MHz, D_2O): δ = 134.3, 117.4, 75.2, 73.0, 72.2, 70.9, 70.0, 60.6, 28.7 ppm; **HRMS** (ESI): *m/z* calcd. for $C_9H_{16}O_5Na^+$: 227.0890, found: 227.0891. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[270]

[269] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.
[270] R. Y. Tam, S. S. Ferreira, P. Czechura, J. L. Chaytor, R. N. Ben, *J. Am. Chem. Soc.* **2008**, *130*, 17494-17501.

(((2R,3S,4R,5R,6R)-2-Allyl-6-(((tert-butyldimethylsilyl)oxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (40c)

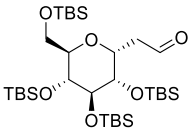
Procedure A (TBSCl, $AgNO_3$)



TBSCl (32.8 g, 218 mmol) as a solution in DMF (60 mL), py (31.3 mL, 387 mmol) and $AgNO_3$ (32.8 g, 193 mmol) were subsequently added to a stirred solution of C-glucoside **40b** (5.10 g, 23.7 mmol) in DMF (60 mL) at rt. The resulting reaction mixture was stirred for 16 h under protection of light. The reaction was quenched with sat. aq. $NaHCO_3$ (100 mL) and diluted with MTBE (150 mL). The resulting mixture was filtered through a plug of Celite® to remove all insoluble materials, and washed with MTBE (3 x 50 mL). The organic extract was subsequently washed with water (2 x 75 mL) and brine (75 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 20:1) affording compound **40c** as a colourless oil (13.6 g, 87%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (dddd, J = 17.5, 10.2, 7.5, 6.0 Hz, 1H), 5.10 (dq, J = 17.3, 1.7 Hz, 1H), 5.05 – 5.01 (m, 1H), 3.91 – 3.70 (m, 5H), 3.69 – 3.66 (m, 1H), 3.46 – 3.43 (m, 1H), 2.44 (dddt, J = 11.9, 7.8, 5.9, 1.7 Hz, 1H), 2.10 (dddt, J = 14.1, 7.6, 5.2, 1.3 Hz, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (s, 18H), 0.10 (s, 6H), 0.08 (s, 3H), 0.07 (s, 3H), 0.065 (s, 3H), 0.06 (s, 3H), 0.03 (s, 3H), 0.025 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 136.1, 116.3, 78.2, 74.3, 71.5, 70.6, 69.4, 62.5, 36.0, 26.34 (3C), 26.2 (3C), 26.1 (3C), 25.9 (3C), 18.5, 18.5, 18.3, 18.0, -3.3, -4.0, -4.2, -4.48, -4.50, -4.9, -5.0, -5.2 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{72}O_5Si_4Na^+$: 683.4349, found: 683.4352. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[271]

2-((2R,3S,4R,5R,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(((tert-butyldimethylsilyl)oxy)methyl)tetrahydro-2H-pyran-2-yl)acetaldehyde (54a)



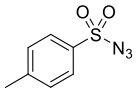
O_3 was bubbled through a stirred solution of C-glucoside **40c** (14.5 g, 22.0 mmol) in DCM (190 mL) at -78 °C until the solution became blue after 8 h. Then Ar was bubbled through the solution until it turned colourless again. PPh_3 (**195a**) (9.51 g, 36.3 mmol) was added at -78 °C. The reaction mixture was allowed to reach rt over 1 h and stirring was continued for 15 h. The solvent was evaporated and the crude product was

[271] G. J. McGarvey, C. A. LeClair, B. A. Schmidtmann, *Org. Lett.* **2008**, *10*, 4727-4730.

purified by flash chromatography (SiO_2, PhMe) affording compound **54a** as a glassy colourless solid (12.6 g, 86%).

$[\alpha]_D^{20}$: +26.9 (c = 1.17, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.85 (t, J = 2.1 Hz, 1H), 4.32 (ddd, J = 9.0, 4.3, 2.2 Hz, 1H), 3.86 – 3.75 (m, 4H), 3.72 – 3.68 (m, 1H), 3.50 (tt, J = 2.2, 0.9 Hz, 1H), 2.81 (ddd, J = 16.6, 9.0, 2.0 Hz, 1H), 2.34 (ddd, J = 16.6, 4.3, 2.3 Hz, 1H), 0.91 (s, 9H), 0.89 (s, 18H), 0.87 (s, 9H), 0.11 (s, 3H), 0.09 (s, 9H), 0.07 (s, 3H), 0.02 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 202.9, 78.2, 74.0, 71.6, 70.2, 65.6, 62.1, 45.8, 26.3 (3C), 26.2 (3C), 26.0 (3C), 25.8 (3C), 18.50, 18.45, 18.3, 18.0, -3.6, -4.0, -4.2, -4.51, -4.54, -5.0 (2C), -5.2 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2887, 2857, 2712, 1728, 1472, 1463, 1407, 1389, 1361, 1325, 1253, 1217, 1187, 1139, 1085, 1033, 1005, 981, 938, 879, 834, 812, 790, 729, 669, 617, 574, 531, 476, 418 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{32}H_{70}O_6Si_4Na^+$: 685.4141, found: 685.4142.

4-Methylbenzenesulfonyl azide (206)

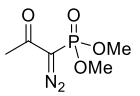


TosCl (**55**) (26.0 g, 136 mmol) as a solution in acetone (70 mL) was slowly added to a stirred solution of NaN_3 (9.75 g, 150 mmol) in a mixture of acetone (70 mL) and water (46 mL) at rt over the course of 10 min and stirring was continued for 2 h. The solvent was evaporated, the aq. phase was diluted with water (10 mL) and extracted with DCM (3 x 50 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **206** as a colourless crystalline solid (26.2 g, 98%).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.91 – 7.87 (m, 2H), 7.55 – 7.50 (m, 2H), 2.43 (s, 3H) ppm; **^{13}C NMR** (101 MHz, DMSO-d_6): δ = 146.5, 134.6, 130.6 (2C), 127.3 (2C), 21.1 ppm; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.80 – 7.75 (m, 2H), 7.37 – 7.31 (m, 2H), 2.42 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 146.4, 135.6, 130.4 (2C), 127.7 (2C), 21.9 ppm; **HRMS** (ESI): *m/z* calcd. for $C_7H_7N_3O_2SNa^+$: 220.0151, found: 220.0151. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[272]

[272] L. Ji, G.-Q. Zhou, C. Qian, X.-Z. Chen, *Eur. J. Org. Chem.* **2014**, *17*, 3622-3636.

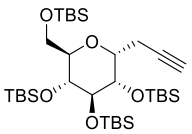
Dimethyl (1-diazo-2-oxopropyl)phosphonate (Ohira-Bestmann reagent) (56)



NaH (3.03 g, 126 mmol) was added portionwise to a stirred solution of dimethyl-2-oxopropylphosphonate (20 g, 0.120 mol) in a mixture of THF (70 mL) and PhMe (430 mL) at 0 °C regarding the evolution of gas, and stirring of the resulting suspension was continued for 1 h. $TosN_3$ (24.9 g, 126 mmol) as a solution in PhMe (120 mL) was slowly added at 0 °C to the reaction mixture. The reaction mixture was warmed to rt and stirring was continued for 19 h. The reaction mixture was filtered through Celite® and the filter cake was washed with EtOAc (2 x 400 mL). The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 1:1 to 1:3) affording compound **56** as a yellow oil (20.0 g, 86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3H), 3.78 (s, 3H), 2.21 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 181.0, 180.8, 53.63, 53.57, 27.2 ppm; **^{31}P NMR** (162 MHz, $CDCl_3$): δ = 13.91 ppm; **IR** (film): $\tilde{\nu}$ = 2959, 2855, 2223, 2116, 1654, 1450, 1364, 1264, 1241, 1178, 1010, 969, 928, 833, 801, 780, 647, 612, 577, 548, 475, 452 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_5H_9N_2O_4PNa^+$: 215.0192, found: 215.0192. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[273]

(((2R,3R,4R,5S,6R)-2-(((Tert-butyldimethylsilyl)oxy)methyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (39a)



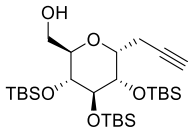
Ohira-Bestmann reagent (**56**) (2.92 g, 15.2 mmol) was added to a stirred suspension of aldehyde **54a** (8.40 g, 12.7 mmol) and K_2CO_3 (3.50 g, 25.3 mmol) in MeOH (190 mL) at rt resulting in a colour change from colourless to yellow, and stirring was continued for 20 h. The reaction was neutralized with Amberlite® (weakly acidic cation exchange resin). The resin was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, PhMe) affording compound **39a** as a colourless oil (7.43 g, 89%).

$[\alpha]_D^{20}$: +15.0 (c = 1.19, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.92 (ddd, J = 9.0, 5.7, 1.9 Hz, 1H), 3.86 – 3.69 (m, 6H), 2.50 (ddd, J = 16.3, 9.0, 2.6 Hz, 1H), 2.41 (ddd, J = 16.4, 5.8, 2.8 Hz, 1H), 1.95 (t, J = 2.6 Hz, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.885 (s, 9H), 0.875 (s, 9H), 0.125 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.6,

[273] J. Pietruszka, A. Witt, *Synthesis* **2006**, *24*, 4266-4268.

78.2, 74.6, 71.0, 70.2, 70.0, 69.0, 62.6, 26.3 (3C), 26.2 (3C), 26.1 (3C), 25.9 (3C), 21.4, 18.50, 18.48, 18.3, 18.0, -3.5, -3.9, -4.1, -4.5, -4.6, -4.9 (2C), -5.2 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2953, 2929, 2896, 2857, 1472, 1463, 1430, 1407, 1389, 1361, 1320, 1252, 1219, 1187, 1140, 1084, 1057, 1024, 1005, 983, 939, 881, 832, 813, 788, 729, 671, 637, 627, 572, 529, 475 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_5Si_4Na^+$: 681.4189, found: 681.4193.

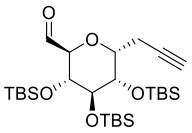
((2R,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)methanol (57)



HF·py (12.5% in THF/py 2.5:1, 28.7 mL, 39.8 mmol) was added to a stirred solution of TBS-protected alcohol **39a** (7.00 g, 10.6 mmol) in THF (57.4 mL) at 0 °C. The resulting reaction mixture was allowed to reach rt over 30 min and stirring was continued for 2.5 h. The reaction was quenched with sat. aq. $NaHCO_3$ (200 mL) and the aq. phase was extracted with MTBE (3x 200 mL). The combined extracts were washed with brine (200 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 30:1) affording compound **57** as a colourless oil which crystallized upon storage at -20 °C (4.39 g, 76%).

m.p.: 38-39 °C; $[\alpha]_D^{20}$: +11.8 (c = 1.07, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.03 (td, J = 7.3, 2.2 Hz, 1H), 3.96 (ddd, J = 8.4, 5.1, 3.4 Hz, 1H), 3.82 (dd, J = 11.4, 8.3 Hz, 1H), 3.81 (dd, J = 3.3, 1.5 Hz, 1H), 3.72 (tt, J = 2.3, 0.9 Hz, 1H), 3.56 (dd, J = 11.5, 3.5 Hz, 1H), 3.51 (dt, J = 5.1, 1.2 Hz, 1H), 2.53 (ddd, J = 16.5, 7.1, 2.7 Hz, 1H), 2.40 (ddd, J = 16.4, 7.4, 2.7 Hz, 1H), 2.11 (br s, 1H), 1.99 (t, J = 2.6 Hz, 1H), 0.92 (s, 9H), 0.885 (s, 9H), 0.88 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.5, 77.1, 74.5, 72.0, 70.7, 70.1, 68.8, 61.5, 26.2 (3C), 26.1 (3C), 25.9 (3C), 21.5, 18.4, 18.3, 18.0, -3.6, -3.9, -4.0, -4.6, -4.8, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3474, 3314, 2953, 2929, 2896, 2858, 1743, 1472, 1463, 1389, 1373, 1361, 1319, 1252, 1188, 1134, 1088, 1006, 977, 939, 923, 879, 851, 812, 772, 671, 636, 574, 529, 477 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{56}O_5Si_3Na^+$: 567.3326, found: 567.3328.

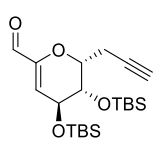
(2S,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-carbaldehyde (58)



DMSO (1.43 mL, 20.2 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (867 µL, 10.1 mmol) in DCM (35 mL) at -78 °C and the reaction mixture was stirred for 5 min. Then alcohol **57** (2.50 g, 4.59 mmol) as a solution in DCM (8 mL, rinsed with 2 x 8 mL) was added dropwise and stirring was continued for 20 min. DIPEA (7.99 mL, 45.9 mmol) was slowly added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 2.5 h. The reaction was quenched with water (50 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 2 x 40 mL) and with brine (35 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **58** as a colourless oil (2.44 g, 98%).

$[\alpha]_D^{20}$: +47.4 (c = 1.58, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 9.80 (s, 1H), 4.19 – 4.13 (m, 2H), 4.03 (dt, J = 2.4, 1.2 Hz, 1H), 3.85 (t, J = 2.9 Hz, 1H), 3.58 (dt J = 2.9, 1.3 Hz, 1H), 2.61 (ddd, J = 16.3, 6.1, 2.8 Hz, 1H), 2.55 (ddd, J = 16.4, 8.3, 2.7 Hz, 1H), 2.00 (t, J = 2.7 Hz, 1H), 0.94 (s, 9H), 0.92 (s, 9H), 0.85 (s, 9H), 0.135 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.075 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 200.8, 84.0, 80.8, 71.2, 70.4, 70.3, 70.2, 68.5, 26.5 (3C), 26.2 (3C), 25.7 (3C), 21.4, 18.8, 18.4, 17.9, -3.3, -4.2, -4.57, -4.63, -4.7, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2953, 2929, 2896, 2858, 1735, 1472, 1470, 1390, 1375, 1362, 1303, 1252, 1190, 1138, 1087, 1053, 1003, 975, 939, 918, 884, 835, 813, 785, 673, 638, 536, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{54}O_5Si_3Na^+$: 565.3178, found: 565.3171.

(2R,3S,4S)-3,4-Bis((tert-butyldimethylsilyl)oxy)-2-(prop-2-yn-1-yl)-3,4-dihydro-2H-pyran-6-carbaldehyde (62)

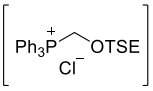


KO*t*-Bu (22 mg, 0.20 mmol) was added to a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (**61b**) (67 mg, 0.20 µmol) in THF (0.25 mL) at -40 °C and stirring was continued for 45 min. Then the reaction mixture was cooled to -78 °C and aldehyde **58** (53 mg, 98 µmol) as a solution in THF (146 µL, rinsed with 146 µL) was slowly added over the course of 5 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 18 h. The reaction was quenched with ice (10 g)

and the aq. phase was extracted with MTBE (2 x 20 mL). The combined extracts were washed with brine (10 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **62** as a colourless oil (34 mg, 85%).

$[\alpha]_D^{20}$: +31.0 (c = 0.98, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 9.20 (s, 1H), 5.75 (dd, J = 5.2, 1.6 Hz, 1H), 4.09 – 4.01 (m, 2H), 3.92 (ddd, J = 2.7, 1.6, 1.0 Hz, 1H), 2.76 (ddd, J = 16.5, 5.5, 2.7 Hz, 1H), 2.66 (ddd, J = 16.4, 9.9, 2.7 Hz, 1H), 2.04 (t, J = 2.7 Hz, 1H), 0.90 (s, 9H), 0.84 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 187.3, 152.2, 117.9, 79.5, 73.0, 71.0, 68.7, 65.1, 25.84 (3C), 25.79 (3C), 20.4, 18.10, 18.07, -4.0, -4.37, -4.40, -4.7 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2930, 2896, 2858, 1741, 1641, 1472, 1464, 1432, 1408, 1390, 1362, 1309, 1254, 1216, 1085, 1005, 978, 939, 904, 834, 812, 776, 756, 667, 629, 443, 431 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{21}H_{38}O_4Si_2Na^+$: 433.2207, found: 433.2201.

Triphenyl((2-(trimethylsilyl)ethoxy)methyl)phosphonium chloride (61a)



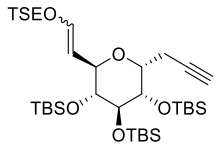
PPh_3 (**195a**) (3.00 g, 11.4 mmol) was added to a stirred solution of 2-(trimethylsilyl)ethoxymethyl chloride (**60**) (95%, 2.24 mL, 12.0 mmol) in PhH (21 mL) at rt. The resulting reaction mixture was stirred for 24 h at 55 °C resulting in a white precipitate. The precipitate was filtered off and washed with EtOAc (3 x 25 mL), and dried under vacuum affording compound **61a** as a white solid (3.40 g, 69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 – 7.83 (m, 6H), 7.82 – 7.76 (m, 3H), 7.72 – 7.64 (m, 6H), 5.98 (d, $J_{31P,1H}$ = 3.9 Hz, 2H), 4.01 – 3.93 (m, 2H), 0.96 – 0.88 (m, 2H), -0.09 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 135.3 (d, $J_{31P,13C}$ = 3.0 Hz, 3C), 134.4 (d, $J_{31P,13C}$ = 10.0 Hz, 6C), 130.4 (d, $J_{31P,13C}$ = 12.2 Hz, 6C), 117.2 (d, $J_{31P,13C}$ = 85.3 Hz, 3C), 73.2 (d, $J_{31P,13C}$ = 12.2 Hz), 64.1 (d, $J_{31P,13C}$ = 67.7 Hz), 18.4, -1.3 (3C) ppm; **^{31}P NMR** (162 MHz, $CDCl_3$): δ = 18.1 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{24}H_{30}O_1P_1Si_1^+$: 393.1798, found: 393.1795. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[274]

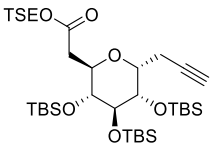
[274] K. Schönauer, E. Zbiral, *Liebigs Ann. Chem.* **1983**, *6*, 1031-1042.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (35a)

Procedure A (Wittig reaction)



A solution of KO*t*-Bu (504 mg, 4.49 mmol) in THF (4 mL, rinsed with 4 mL) was dried over 5 Å MS before it was slowly added to a stirred suspension of phosphonium chloride **61a** (1.89 g, 4.40 mmol) in THF (8 mL) with 5 Å MS at -50 °C over the course of 5 min resulting in a fast colour change from colourless to deep red. Stirring was continued for 15 min. Then the reaction mixture was cooled to -78 °C and aldehyde **58** (1.22 g, 2.25 mmol) as a solution in THF (4 mL, rinsed with 4 mL) over 5 Å MS was slowly added over the course of 5 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 3 h. The reaction was quenched with water (20 mL) and the aq. phase was extracted with MTBE (2 x 45 mL). The combined extracts were washed with brine (45 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 20:1) affording intermediate **59a** as a yellow oil (95%, 1.18 g, 76%, *E*/*Z* = 1:1).

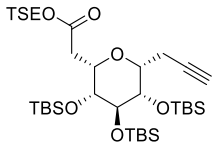


PCC (728 mg, 3.38 mmol) was added to a stirred solution of the *E*/*Z* mixture of enolether **59a** (95%, 1.17 g, 1.69 mmol) in DCM (100 mL) at rt and the reaction mixture was stirred for 4 d. Celite® was added and the solvent was evaporated. The loaded Celite® was added on top of a silica gel column and the crude product was purified by flash chromatography (fine SiO_2, hexane/EtOAc, 100:1 to 50:1) affording minor isomer *epi*-**35a** (209 mg, 18%), a mixture of both isomers (27 mg, 2%, *d.r.* = 2:1) and major isomer **35a** (541 mg, 48%) as a colourless oil.

Analytical and spectral data of the major epimer **35a**: $[\alpha]_D^{20}$: +15.5 (c = 1.04, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.33 (ddd, J = 8.6, 5.8, 4.3 Hz, 1H), 4.20 – 4.13 (m, 2H), 4.02 (ddd, J = 8.5, 6.1, 2.2 Hz, 1H), 3.85 – 3.82 (m, 1H), 3.75 (ddd, J = 3.2, 2.2, 0.9 Hz, 1H), 3.50 (ddd, J = 4.3, 1.6, 1.0 Hz, 1H), 2.72 – 2.60 (m, 2H), 2.49 (ddd, J = 16.4, 8.6, 2.7 Hz, 1H), 2.41 (ddd, J = 16.4, 6.1, 2.7 Hz, 1H), 1.93 (t, J = 2.7 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 6H), 0.11 (s, 6H), 0.10 (s, 3H), 0.07 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 81.4, 74.5, 74.2, 74.1, 70.1, 69.9, 68.8, 62.8, 37.9, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.1, 18.5, 18.3, 18.0, 17.5, -1.4 (3C), -3.4, -3.9, -4.1, -4.58, -4.61, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2858, 1735, 1472, 1463, 1389, 1361, 1250, 1167, 1128, 1083, 1056, 1005, 977, 939, 831,

813, 773, 694, 672, 637, 547, 469, 449 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{68}O_6Si_4Na^+$: 695.3985, found: 695.3982.

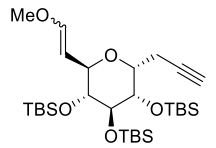
Analytical and spectral data of the minor epimer *epi*-**35a**: $[\alpha]_D^{20}$: +2.9 (c = 1.04, $CHCl_3$);



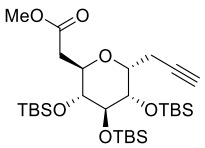
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.20 – 4.09 (m, 3H), 3.84 – 3.78 (m, 2H), 3.54 – 3.50 (m, 1H), 3.44 – 3.40 (m, 1H), 2.67 (dd, J = 16.1, 8.2 Hz, 1H), 2.48 – 2.44 (m, 2H), 2.43 (dd, J = 16.1, 5.1 Hz, 1H), 1.93 (t, J = 2.7 Hz, 1H), 1.02 – 0.96 (m, 2H), 0.923 (s, 9H), 0.921 (s, 9H), 0.91 (s, 9H), 0.12 (s, 3H), 0.115 (s, 9H), 0.09 (s, 3H), 0.03 (s, 9H), 0.02 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 81.6, 75.7, 73.8, 73.0, 71.4, 70.1, 69.9, 62.7, 37.1, 26.50 (3C), 26.47 (3C), 25.8 (3C), 21.3, 18.53, 18.47, 18.0, 17.4, -1.3 (3C), -2.7, -3.1, -4.3, -4.4, -4.9, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2858, 1735, 1472, 1463, 1406, 1389, 1361, 1348, 1285, 1251, 1175, 1144, 1083, 1058, 1006, 985, 938, 892, 858, 831, 812, 771, 694, 674, 637, 553, 457 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{68}O_6Si_4Na^+$: 695.3985, found: 695.3983.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (35b)

Procedure A (Wittig Reaction)



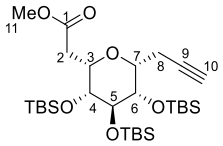
A solution of KO*t*-Bu (909 mg, 8.10 mmol) in THF (6 mL, rinsed with 6 mL) was dried over 5 Å MS before it was slowly added to a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (**61b**) (2.78 g, 8.10 mmol) in THF (12 mL) over 5 Å MS at -50 °C over the course of 5 min resulting in a fast colour change from colourless to bright orange, and stirring was continued for 15 min. Then the reaction mixture was cooled to -78 °C and aldehyde **58** (2.20 g, 4.05 mmol) as a solution in THF (6 mL, rinsed with 6 mL) over 5 Å MS was slowly added over the course of 5 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 50 min. The reaction was quenched with water (25 mL) and the aq. phase was extracted with MTBE (2 x 50 mL). The combined extracts were washed with brine (50 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 40:1) affording intermediate **59b** as a colourless oil (1.88 g, 81%, *E*/*Z* = 1:1).



PCC (1.36 g, 6.30 mmol) was added to a stirred solution of the *E*/*Z* mixture of enolether **59b** (1.80 g, 3.15 mmol) in DCM (200 mL) at rt and the reaction mixture was stirred for 20 h. PCC (1.36 g, 6.30 mmol) was again added to the reaction mixture and stirring was continued for 24 h. Celite® was added and the solvent was evaporated. The loaded Celite® was added on top of a silica gel column and the crude product was purified by flash chromatography twice (first column: SiO_2, hexane/EtOAc, 100:1 to 75:1, second column: fine SiO_2, hexane/EtOAc, 100:1) affording minor isomer *epi*-**35b** (316 mg, 17%), a mixture of both isomers (*d.r.* = 1:2, 199 mg, 11%) and major isomer **35b** (980 mg, 53%) as a colourless oil.

Analytical and spectral data of the major epimer **35b**: $[\alpha]_D^{20}$: +14.9 (c = 1.04, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.33 (td, J = 7.2, 4.0 Hz, 1H), 4.01 (ddd, J = 8.3, 6.4, 2.2 Hz, 1H), 3.85 – 3.81 (m, 1H), 3.74 – 3.70 (m, 1H), 3.68 (s, 3H), 3.50 (dt, J = 4.0, 1.4 Hz, 1H), 2.74 – 2.66 (m, 2H), 2.47 (ddd, J = 16.3, 8.0, 2.6 Hz, 1H), 2.41 (ddd, J = 16.2, 6.4, 2.7 Hz, 1H), 1.94 (t, J = 2.6 Hz, 1H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 6H), 0.11 (s, 6H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 81.4, 74.4, 74.2, 74.0, 70.1, 69.9, 68.7, 51.8, 37.5, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.1, 18.5, 18.3, 18.0, -3.4, -3.9, -4.1, -4.60, -4.63, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2953, 2929, 2896, 2858, 1743, 1472, 1463, 1436, 1389, 1361, 1253, 1168, 1128, 1083, 1056, 1005, 976, 939, 878, 831, 813, 773, 672, 636, 545, 467 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{58}O_6Si_3Na^+$: 609.3434, found: 609.3434.

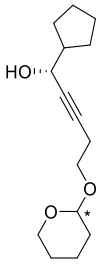
Analytical and spectral data of the minor epimer *epi*-**35b**: $[\alpha]_D^{20}$: +2.4 (c = 1.10, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.13 (ddd, J = 8.3, 5.2, 1.9 Hz, 1H, H-3), 3.83 – 3.79 (m, 2H, H-5 and H-7), 3.67 (s, 3H, H-11), 3.52 – 3.50 (m, 1H, H-6), 3.43 – 3.42 (m, 1H, H-4), 2.70 (dd, J = 16.2, 8.3 Hz, 1H, H-2a), 2.51 – 2.40 (m, 3H, H-2b and H-8), 1.94 (t, J = 2.6 Hz, 1H, H-10), 0.92 (s, 18H, *t*-Bu), 0.91 (s, 9H, *t*-Bu), 0.11 (s, 12H, Si-Me), 0.09 (s, 3H, Si-Me), 0.01 (s, 3H, Si-Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.2 (C-1), 81.6 (C-9), 75.8 (C-7), 73.7 (C-3), 73.0 (C-5), 71.3 (C-4), 70.2 (C-6), 69.8 (C-10), 51.7 (C-11), 36.7 (C-2), 26.5 (6C, *t*-Bu), 25.8 (3C, *t*-Bu), 21.3, 18.5 (*t*-Bu), 18.4 (*t*-Bu), 18.0 (*t*-Bu), -2.7 (Me), -3.1 (Me), -4.36 (Me), -4.41 (Me), -4.9 (Me), -5.2 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3315, 2952, 2930, 2894, 2858, 1741, 1472, 1463, 1436, 1361, 1287, 1254, 1175, 1143, 1082, 1056, 1006, 984, 963, 938, 917, 904, 829, 812, 771, 674, 636, 553, 464, 417 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{58}O_6Si_3Na^+$: 609.3438, found: 425.2087.

5.2.1.3. Building Block Coupling & Elaboration

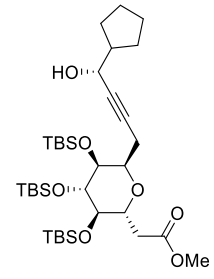
(1R)-1-Cyclopentyl-5-((tetrahydro-2H-pyran-2-yl)oxy)pent-2-yn-1-ol (69)



TEA (78.3 µL, 562 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (187 mg, 515 µmol) and (*+*)-N-methylephedrine (101 mg, 562 µmol) in PhMe (0.8 mL) at rt and stirring was continued for 2 h. Then 2-(but-3-yn-1-yloxy)tetrahydro-2*H*-pyran (*rac*-**68**) (88.0 µL, 562 µmol) was added to the reaction mixture at rt and stirring was continued for 1 h. Then cyclopentanecarbaldehyde (50.0 µL, 468 µmol) was added to the stirred reaction mixture at rt and stirring was continued for 18 h. Cyclopentanecarbaldehyde (20.0 µL, 187 µmol) was added again to the stirred reaction mixture at rt and stirring was continued for 24 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 15 mL) and the aq. phase was extracted with MTBE (3 x 20 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 15 mL) and brine (15 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 10:1) affording compound **69** as a colourless oil (121 mg, 85%).

$[\alpha]_D^{20}$: +2.9 (c = 1.11, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.64 (dd, J = 4.1, 2.8 Hz, 1H), 4.22 (br s, 1H), 3.88 (ddd, J = 11.2, 8.3, 3.2 Hz, 1H), 3.81 (dt, J = 9.6, 7.1 Hz, 1H), 3.55 – 3.48 (m, 1H), 3.53 (dt, J = 9.6, 7.2 Hz, 1H), 2.51 (td, J = 7.1, 2.0 Hz, 2H), 2.20 – 2.08 (m, 1H), 1.88 – 1.34 (m, 15H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 98.9, 82.4, 81.8, 66.6, 65.9, 62.3, 46.5 30.7, 28.9, 28.4, 25.83, 25.82, 25.6, 20.4, 19.5 ppm; **IR** (film): $\tilde{\nu}$ = 3427, 2944, 2868, 2214, 1732, 1670, 1453, 1442, 1385, 1352, 1323, 1260, 1201, 1182, 1158, 1135, 1121, 1069, 1031, 984, 906, 869, 846, 813, 572, 542, 462, 433, 414 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{15}H_{24}O_3Na^+$: 275.1620, found: 275.1618.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R)-4-cyclopentyl-4-hydroxybut-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (70)

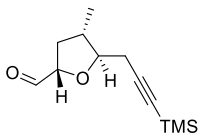


TEA (54.1 µL, 388 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (129 mg, 356 µmol) and (*+*)-N-methylephedrine (70 mg, 0.39 mmol) over 4 Å MS in PhMe (300 µL) at rt and stirring was continued for 4 h. Then alkyne **35b** (76 mg, 0.13 mmol) as a solution in PhMe (150 µL, rinsed with 2x 150 µL) over 4 Å MS was added to the reaction mixture at rt and stirring was continued for 1.5 h. Then cyclopentanecarbaldehyde (13.8 µL, 130 µmol) was added to the stirred

reaction mixture at rt and stirring was continued for 2 h. Afterwards cyclopentanecarbaldehyde (5.5 µL, 52 µmol) was added again to the stirred reaction mixture at rt and stirring was continued for 46 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with MTBE (3 x 15 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 10:1) affording both compound **70** (60 mg, 68%) and some unreacted starting material **35b** (9 mg, 12%) as a colourless oil.

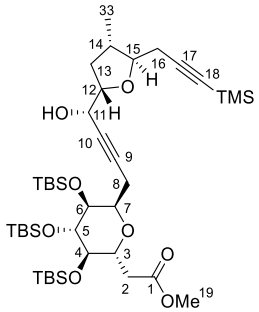
$[\alpha]_D^{20}$: +1.9 (c = 1.12, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.33 (ddd, J = 9.1, 5.1, 3.3 Hz, 1H), 4.17 (ddt, J = 7.4, 5.4, 2.0 Hz, 1H), 3.97 (td, J = 7.2, 2.0 Hz, 1H), 3.82 (t, J = 2.5 Hz, 1H), 3.69 (s, 3H), 3.66 – 3.63 (m, 1H), 3.49 (ddd, J = 3.0, 1.9, 1.0 Hz, 1H), 2.77 (dd, J = 14.6, 9.5 Hz, 1H), 2.67 (dd, J = 14.6, 5.3 Hz, 1H), 2.46 (dd, J = 7.2, 2.1 Hz, 2H), 2.11 (h, J = 7.9 Hz, 1H), 1.97 (d, J = 5.4 Hz, 1H), 1.81 – 1.69 (m, 2H), 1.66 – 1.58 (m, 2H), 1.57 – 1.48 (m, 2H), 1.46 – 1.35 (m, 2H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 6H), 0.11 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 82.4, 82.3, 74.6, 74.1, 73.5, 70.3, 68.5, 66.6, 51.9, 46.6, 37.3, 29.0, 28.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 25.8 (2C), 21.6, 18.5, 18.3, 18.0, -3.4, -4.0, -4.2, -4.6 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3467, 2952, 2929, 2896, 2858, 1740, 1472, 1463, 1437, 1389, 1361, 1322, 1253, 1168, 1128, 1083, 1054, 1005, 973, 938, 925, 888, 831, 813, 774, 671, 545, 467 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{35}H_{68}O_7Si_3Na^+$: 707.4171, found: 707.4165.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)but-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (33a)



DMSO (157 µL, 2.21 mmol) was added dropwise to a stirred solution of SO_3·py (88 mg, 0.55 mmol) in DCM (0.75 mL) at -20 °C and stirring was continued for 5 min. Then alcohol **48b** (50 mg, 0.22 mmol) as a solution in DCM (0.75 mL, rinsed with 2 x 0.75 mL) was added dropwise to the reaction mixture at -20 °C and stirring was continued for 20 min. Afterwards DIPEA (192 µL, 1.10 mmol) was slowly added to the reaction mixture at -20 °C over the course of 5 min and stirring was continued for 2 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) at -20 °C and the aq. phase was extracted with MTBE (3 x 15 mL). The combined organic extracts were subsequently washed with

aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **34b** as a yellow oil (30 mg, 61%) which was used in the next step without further purification.

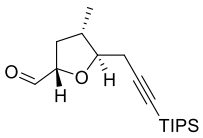


TEA (93.2 µL, 669 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (223 mg, 613 µmol) and (*+*)-N-methylephedrine (110 mg, 613 µmol) over 4 Å MS in PhMe (400 µL) at rt and stirring was continued for 4 h. Then alkyne **35b** (109 mg, 186 µmol) as a solution in PhMe (200 µL, rinsed with 2 x 150 µL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1 h. Then crude aldehyde **34b** (30 mg, 0.13 mmol) as a solution in PhMe (200 µL, rinsed with 2 x 150 µL) was dried over 4 Å MS before it was added to the stirred reaction mixture at rt and stirring was continued for 65 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with MTBE (3 x 15 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 10:1) affording both compound **33a** (37 mg, 25%) and some unreacted starting material **35b** (79 mg, 73%) as a colourless oil.

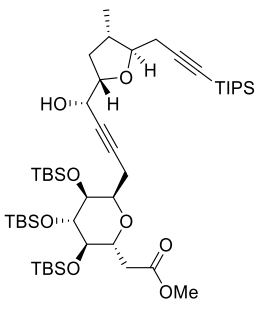
$[\alpha]_D^{20}$: -1.4 (c = 0.80, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.32 (ddd, J = 9.1, 5.4, 3.6 Hz, 1H, H-3), 4.18 (td, J = 4.3, 2.0 Hz, 1H, H-11), 4.05 – 3.95 (m, 2H, H-7 and H-12), 3.82 (ddd, J = 2.9, 1.8, 0.8 Hz, 1H, H-5), 3.68 (s, 3H, H-19), 3.67 – 3.62 (m, 1H, H-6), 3.59 (ddd, J = 8.6, 6.5, 4.6 Hz, 1H, H-15), 3.49 (ddd, J = 3.5, 1.8, 0.9 Hz, 1H, H-4), 2.74 (dd, J = 14.7, 9.3 Hz, 1H, H-2a), 2.68 (dd, J = 14.7, 5.4 Hz, 1H, H-2b), 2.55 (dd, J = 17.1, 4.7 Hz, 1H, H-16a), 2.53 (d, J = 4.6 Hz, 1H, OH), 2.48 (dd, J = 17.0, 6.6 Hz, 1H, H-16b), 2.49 – 2.44 (m, 2H, H-8), 2.24 (ddd, J = 12.4, 7.4, 6.2 Hz, 1H, H-13a), 2.19 – 2.08 (m, 1H, H-14), 1.45 (ddd, J = 12.5, 10.6, 9.0 Hz, 1H, H-13b), 1.11 (d, J = 6.5 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu-6), 0.90 (s, 9H, *t*-Bu-5), 0.89 (s, 9H, *t*-Bu-4), 0.14 (s, 9H, TMS), 0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.11 (s, 3H, Me), 0.11 (s, 3H, Me), 0.09 (s, 3H, Me-4), 0.07 (s, 3H, Me-4) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.7 (C-1), 103.1 (C-17), 86.6 (C-18), 83.3 (C-9), 83.2 (C-15), 81.6 (C-12), 79.5 (C-10), 74.3 (C-3), 74.0 (C-5), 73.5 (C-4), 70.1 (C-6), 68.3 (C-7), 66.0 (C-11), 51.7 (C-19), 39.6 (C-14), 37.8 (C-13), 37.2 (C-2), 26.2 (3C, *t*-Bu-4), 26.0 (3C, *t*-Bu-6), 25.7 (3C, *t*-Bu-5), 25.1 (C-16), 21.4 (C-8), 18.4 (*t*-Bu-4), 18.2 (*t*-Bu-6), 17.9 (*t*-Bu-5), 17.1 (C-33), 0.0 (3C, TMS), -3.5 (Me), -4.1 (Me-4), -4.3 (Me), -4.7 (2C, Me-4 and Me), -5.0 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3492, 2954, 2929, 2897, 2858, 2177, 1741, 1472, 1463, 1436, 1408, 1389, 1361, 1250, 1168, 1128, 1083, 1055, 1005,

972, 938, 924, 832, 814, 775, 759, 698, 671, 645, 544, 468 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{41}H_{78}O_8Si_4Na^+$: 833.4674, found: 833.4666.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)but-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (33b)



DMSO (1.03 mL, 14.5 mmol) was added dropwise to a stirred solution of SO_3·py (577 mg, 3.62 mmol) in DCM (14 mL) at -20 °C and stirring was continued for 5 min. Then alcohol **48a** (450 mg, 1.45 mmol) as a solution in DCM (2 mL, rinsed with 2 x 2 mL) was added dropwise to the reaction mixture at -20 °C and stirring was continued for 20 min. Afterwards DIPEA (1.26 mL, 7.25 mmol) was slowly added to the reaction mixture at -20 °C over the course of 5 min and stirring was continued for 2 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 45 mL) at -20 °C and the aq. phase was extracted with MTBE (3 x 60 mL). The combined organic extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 45 mL) and brine (45 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **34a** as a yellow oil (ca. 60%, 562 mg, 75%) which was used in the next step without further purification.

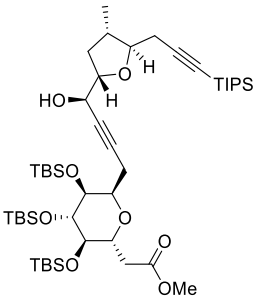


TEA (470 µL, 3.37 mmol) was added to a stirred suspension of $Zn(OTf)_2$ (1.12 g, 3.09 mmol) and (*+*)-N-methylephedrine (554 mg, 3.09 mmol) was dried over 4 Å MS in PhMe (2.7 mL) at rt and stirring was continued for 4.25 h. Then alkyne **35b** (550 mg, 937 µmol) as a solution in PhMe (1 mL, rinsed with 2 x 0.6 mL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1 h. Then crude aldehyde **34a** (ca. 60%, 562 mg, 1.09 mmol) as a solution in PhMe (1 mL, rinsed with 2 x 0.6 mL) was dried over 4 Å MS before it was added to the stirred reaction mixture at rt and stirring was continued for 65 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 30.0 mL) and the aq. phase was extracted with MTBE (3 x 45 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 30 mL) and brine (30 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 5:1)

affording minor isomer *epi*-**33b** (14 mg, 2%), major isomer **33b** (156 mg, 19%) and some unreacted starting material **35b** (429 mg, 78%) as a colourless oil.

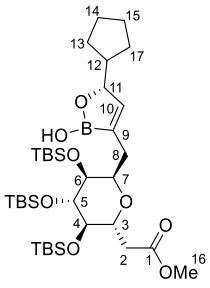
Analytical and spectral data of the major diastereomer **33b**: $[\alpha]_D^{20}$: -4.5 (c = 1.01, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.32 (ddd, J = 9.2, 5.7, 3.5 Hz, 1H), 4.17 (ddd, J = 7.1, 4.1, 2.0 Hz, 1H), 4.01 (dt, J = 8.9, 6.3 Hz, 1H), 3.97 (td, J = 7.1, 2.0 Hz, 1H), 3.82 (t, J = 2.4 Hz, 1H), 3.68 (s, 3H), 3.64 (t, J = 2.1 Hz, 1H), 3.59 (ddd, J = 8.2, 6.0, 4.6 Hz, 1H), 3.51 – 3.48 (m, 1H), 2.74 (dd, J = 14.7, 9.2 Hz, 1H), 2.68 (dd, J = 14.8, 5.7 Hz, 1H), 2.56 (dd, J = 17.0, 4.6 Hz, 1H), 2.55 (dd, J = 17.0, 6.0 Hz, 1H), 2.52 (d, J = 4.3 Hz, 1H), 2.46 (dd, J = 7.3, 2.0 Hz, 2H), 2.28 – 2.14 (m, 2H), 1.49 – 1.39 (m, 1H), 1.11 (d, J = 6.2 Hz, 3H), 1.09 – 0.99 (m, 21H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 104.7, 83.6, 83.4, 82.6, 81.7, 79.6, 74.5, 74.1, 73.6, 70.2, 68.5, 66.2, 51.9, 39.4, 37.8, 37.3, 26.3 (3C), 26.2 (3C), 25.9 (3C), 25.0, 21.6, 18.8 (6C), 18.5, 18.3, 18.0, 17.1, 11.4 (3C), -3.4, -4.0, -4.1, -4.6 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3469, 2929, 2893, 2861, 2174, 1742, 1463, 1436, 1383, 1361, 1254, 1168, 1128, 1083, 1057, 1038, 1005, 973, 938, 919, 883, 833, 813, 775, 675, 607, 547, 530, 459, 422 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{90}O_8Si_4Na^+$: 917.5605, found: 917.5608.

Analytical and spectral data of the minor diastereomer *epi*-**33b**: $[\alpha]_D^{20}$: +17.1 (c = 1.40, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.50 – 4.45 (m, 1H), 4.32 (td, J = 7.4, 3.8 Hz, 1H), 4.08 (ddd, J = 8.3, 4.8, 3.1 Hz, 1H), 4.01 – 3.94 (m, 1H), 3.82 (t, J = 2.3 Hz, 1H), 3.71 – 3.66 (m, 1H), 3.68 (s, 3H), 3.58 – 3.52 (m, 1H), 3.51 – 3.47 (m, 1H), 2.76 – 2.68 (m, 2H), 2.68 – 2.56 (m, 2H), 2.54 (s, 1H), 2.51 – 2.40 (m, 2H), 2.36 – 2.16 (m, 2H), 1.66 – 1.55 (m, 1H), 1.12 – 0.98 (m, 24H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 104.8, 84.1, 83.3, 83.2, 81.0, 79.6, 74.4, 74.3, 73.7, 70.1, 68.5, 64.8, 51.8, 37.6, 37.4, 34.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 24.7, 21.5, 18.8 (6C), 18.5, 18.3, 18.0, 17.4, 11.4 (3C), -3.4, -4.0, -4.2, -4.59, -4.60, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3501, 2952, 2929, 2893, 2861, 2175, 1742, 1471, 1463, 1436, 1382, 1361, 1323, 1253, 1171, 1129, 1083, 1056, 1040, 1018, 1005, 996, 973, 939, 921, 883, 833, 813, 775, 675, 663, 606, 583, 541, 524, 466, 441, 428, 419 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{90}O_8Si_4Na^+$: 917.5605, found: 917.5612.

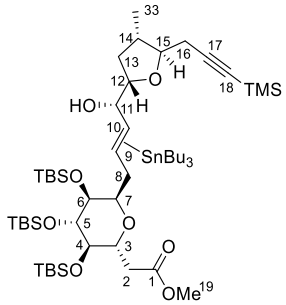
Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(((R)-5-cyclopentyl-2-hydroxy-2,5-dihydro-1,2-oxaborol-3-yl)methyl)tetrahydro-2H-pyran-2-yl)acetate (72)



Pinacolborane (5.1 µL, 35 µmol) was slowly added to a stirred solution of propargylic alcohol **70** (10 mg, 15 µmol) and $[Cp^*Ru(MeCN)_3]PF_6$ (6 mol%, 0.4 mg, 0.8 µmol) in DCM (200 µL) at 0 °C over the course of 5 min and stirring was continued. The reaction mixture was allowed to reach rt and stirring was continued for 24 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 10:1) affording compound **72** (7 mg, 67%), an inseparable mixture of borylation products (1 mg, 8%) and some unreacted starting material **70** (1 mg, 10%) as a colourless oil.

$[\alpha]_D^{20}$: +16.1 (c = 0.70, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 6.80 (s, 1H, H-9), 6.41 (s, 1H, OH), 4.46 (dt, J = 7.4, 1.3 Hz, 1H, H-11), 4.42 (ddd, J = 8.7, 5.5, 5.0 Hz, 1H, H-3), 3.86 (dt, J = 10.6, 2.2 Hz, 1H, H-7), 3.79 (dd, J = 3.1, 1.6 Hz, 1H, H-5), 3.67 (s, 3H, H-16), 3.54 (t, J = 5.0 Hz, 1H, H-4), 3.53 (dd, J = 2.2, 2.1 Hz, 1H, H-6), 2.78 (dd, J = 15.4, 8.7 Hz, 1H, H-2a), 2.67 (dd, J = 15.4, 5.5 Hz, 1H, H-2b), 2.63 (ddt, J = 15.2, 10.6, 2.1 Hz, 1H, H-8a), 2.15 (dd, J = 15.2, 2.2 Hz, 1H, H-8b), 1.88 (h, J = 8.0 Hz, 1H, H-12), 1.79 – 1.64 (m, 2H, H-13a and H-17a), 1.64 – 1.46 (m, 4H, H-14 and H-15), 1.45 – 1.30 (m, 2H, H-13b and H-17b), 0.94 (s, 9H, *t*-Bu-6), 0.90 (s, 9H, *t*-Bu-4), 0.87 (s, 9H, *t*-Bu-5), 0.11 (s, 3H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$): δ = 171.7 (C-1), 153.3 (C-10), 136.3 (C-9), 85.1 (C-11), 74.4 (C-5), 73.7 (C-4), 73.6 (C-3), 72.3 (C-6), 71.4 (C-7), 51.8 (C-16), 44.3 (C-12), 36.9 (C-2), 32.3 (C-8), 28.6 (C-13), 28.4 (C-17), 26.10 (3C, *t*-Bu), 26.06 (3C, *t*-Bu), 25.74 (C-14), 25.70 (3C, *t*-Bu), 25.5 (C-15), 18.3 (*t*-Bu), 18.2 (*t*-Bu), 17.8 (*t*-Bu), -3.7 (Me), -4.0 (Me), -4.3 (Me), -4.7 (Me), -4.8 (Me), -5.0 (Me) ppm; **^{11}B NMR** (160 MHz, $CDCl_3$): δ = 32.0 ppm; **IR** (film): $\tilde{\nu}$ = 3354, 2852, 2929, 2896, 2857, 1741, 1631, 1472, 1463, 1434, 1389, 1361, 1253, 1169, 1124, 1086, 1005, 972, 926, 867, 832, 812, 774, 672, 540, 473, 452, 419 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{35}H_{69}O_8BSi_3Na^+$: 735.4286, found: 735.4287.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R,Z)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)-3-(tributylstannyl)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (76a)

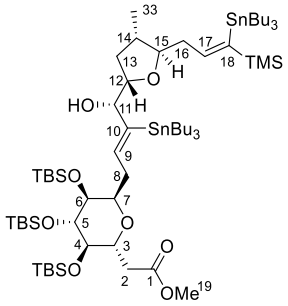


A solution of *n*-Bu_3SnH (10.3 µL, 38.3 µmol) in DCM (350 µL) was slowly added to a stirred solution of bis-alkyne **33a** (27 mg, 33 µmol) and $[Cp^*RuCl_2]_n$ (5 mol%, 1 mg, 2 µmol) in DCM (0.9 mL) at rt over the course of 40 min resulting in a colour change from brown to rose. Stirring was continued for 2 h, the solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 10:1) affording affording bis-stannane **74** (7 mg, 15%), minor β-stannane **75a** (1 mg, 3%), major α-stannane **76a** (8 mg, 22%), an inseparable mixture of TMS-alkenyl-stannanes (6 mg, 16%) and some unreacted starting material **33a** (5 mg, 19%) as a colourless oil.

Analytical and spectral data of the major α-regioisomer **76a**: $[\alpha]_D^{20}$: +16.8 (c = 0.80, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 6.33 (dd, $J_{H,H}$ = 8.4, 5.8 Hz, $J_{119\text{-}Sn,H\text{-}10}$ = 133 Hz, $J_{117\text{-}Sn,H\text{-}10}$ = 116 Hz, 1H, H-9), 4.33 – 4.29 (m, 1H, H-3), 3.95 (d, J = 8.0 Hz, 1H, H-11), 3.84 – 3.81 (m, 1H, H-12), 3.81 – 3.78 (m, 1H, H-5), 3.71 – 3.68 (m, 1H, H-7), 3.67 (s, 3H, H-19), 3.58 – 3.54 (m, 1H, H-15), 3.54 – 3.52 (m, 1H, H-4), 3.48 – 3.46 (m, 1H, H-6), 2.80 (dd, J = 14.8, 6.4 Hz, 1H, H-2a), 2.64 (dd, J = 14.8, 8.3 Hz, 1H, H-2b), 2.54 (dd, J = 16.9, 4.9 Hz, 1H, H-16a), 2.52 (s, 1H, OH), 2.52 – 2.49 (m, 1H, H-8a), 2.47 (dd, J = 16.9, 6.6 Hz, 1H, H-16b), 2.11 – 2.-05 (m, 1H, H-14), 1.98 – 1.91 (m, 2H, H-13a and H-8b), 1.54 – 1.39 (m, 6H, CH_2), 1.37 – 1.24 (m, 6H, CH_2), 1.35 – 1.32 (m, 1H, H-13b), 1.09 (d, J = 6.5 Hz, 3H, H-33), 1.00 – 0.93 (m, 6H, $SnCH_2$), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 6H, Me), 0.87 (s, 3H, Me), 0.15 (s, 9H, TMS), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.08 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7 (C-1), 144.7 (C-10), 140.8 (C-9), 103.4 (C-17), 86.4 (C-18), 84.0 (C-11), 82.7 (C-15), 81.7 (C-12), 74.2 (C-3), 74.0 (C-5), 73.0 (C-4), 71.6 (C-6), 69.7 (C-7), 51.6 (C-19), 39.9 (C-14), 38.0 (C-13), 37.1 (C-2), 35.8 (C-8), 29.4 (3C, CH_2), 27.4 (3C, CH_2), 26.20 (3C, *t*-Bu), 26.16 (3C, *t*-Bu), 25.7 (3C, *t*-Bu), 25.2 (C-16), 18.4 (*t*-Bu), 18.2 (*t*-Bu), 17.8 (*t*-Bu), 17.1 (C-33), 13.7 (3C, Me), 11.2 (3C, $SnCH_2$), -0.1 (3C, TMS), -3.4 (Me), -4.2 (Me), -4.4 (Me), -4.66 (Me), -4.68 (Me), -4.73 (Me) ppm; **^{119}Sn NMR** (149 MHz, $CDCl_3$): δ = -55.3 ppm; **IR** (film): $\tilde{\nu}$ = 3467, 2954, 2928, 2857, 2178, 1741, 1620, 1463, 1437, 1376, 1361, 1250, 1169, 1125, 1081, 1038, 1006, 971, 938, 911, 833, 813, 774, 672, 593, 494, 466, 419 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{53}H_{106}O_8Si_4SnNa^+$: 1125.5896, found: 1125.5878.

Analytical and spectral data of the minor β-regioisomer **75a**: $[\alpha]_D^{20}$: +9.0 (c = 0.10, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.01 (dd, $J_{H,H}$ = 8.3, 5.8 Hz, $J_{119\text{-}Sn,H\text{-}10}$ = 136 Hz, $J_{117\text{-}Sn,H\text{-}10}$ = 120 Hz, 1H), 4.24 (td, J = 6.9, 2.8 Hz, 1H), 3.91 (dt, J = 9.1, 6.1 Hz, 1H), 3.77 – 3.71 (m, 2H), 3.66 (s, 3H), 3.65 – 3.60 (m, 1H), 3.60 – 3.55 (m, 1H), 3.52 – 3.49 (m, 1H), 3.45 – 3.42 (m, 1H), 2.83 (dd, J = 15.1, 6.8 Hz, 1H), 2.62 – 2.54 (m, 3H), 2.52 (dd, J = 15.1, 7.6 Hz, 1H), 2.47 (dd, J = 17.0, 7.0 Hz, 1H), 2.15 – 2.05 (m, 3H), 1.53 – 1.43 (m, 6H), 1.36 – 1.25 (m, 7H), 1.11 (d, J = 6.0 Hz, 3H), 0.96 – 0.90 (m, 6H) 0.93 (s, 9H), 0.89 (s, 18H), 0.88 (s, 9H), 0.14 (s, 9H), 0.105 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.075 (s, 3H), 0.06 (s, 3H) ppm; **^{119}Sn NMR** (149 MHz, $CDCl_3$): δ = -54.1 ppm; **IR** (film): $\tilde{\nu}$ = 3359, 2955, 2925, 2854, 2176, 2124, 1740, 1659, 1463, 1376, 1362, 1251, 1175, 1125, 1082, 1033, 971, 923, 834, 811, 774, 671, 646, 582, 543, 448, 417 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{53}H_{106}O_8Si_4SnNa^+$: 1125.5892, found: 1125.5878.

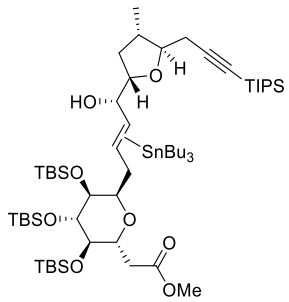
Analytical and spectral data of the major byproduct **74**: $[\alpha]_D^{20}$: +16.1 (c = 0.70, $CHCl_3$);



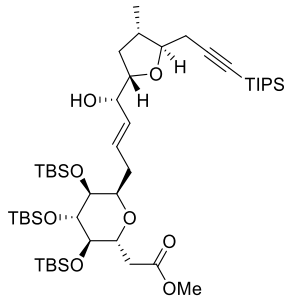
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.80 (t, $J_{H,H}$ = 6.3 Hz, $J_{119\text{-}Sn,H\text{-}2}$ = 179 Hz, $J_{117\text{-}Sn,H\text{-}2}$ = 171 Hz, 1H, H-17), 6.33 (dd, $J_{H,H}$ = 8.4, 5.8 Hz, $J_{119\text{-}Sn,H\text{-}10}$ = 133 Hz, $J_{117\text{-}Sn,H\text{-}10}$ = 117 Hz, 1H, H-9), 4.34 – 4.29 (m, 1H, H-3), 3.94 (d, $J_{H,H}$ = 8.3 Hz, $J_{Sn,H}$ = 61 Hz, 1H, H-11), 3.82 – 3.80(m, 1H, H-5), 3.80 – 3.77 (m, 1H, H-12), 3.69 (ddd, J = 9.6, 3.9, 2.1 Hz, 1H, H-7), 3.67 (s, 3H, H-19), 3.55 – 3.53 (m, 1H, H-4), 3.50 (dt, J = 8.7, 5.8 Hz, 1H, H-15), 3.48 – 3.47 (m, 1H, H-6), 2.82 (dd, J = 14.8, 6.5 Hz, 1H, H-2a), 2.63 (dd, J = 14.8, 8.2 Hz, 1H, H-2b), 2.63 (s, 1H, OH), 2.51 (ddd, J = 14.4, 9.6, 5.7 Hz, 1H, H-8a), 2.40 – 2.36 (m, 2H, H-16), 1.99 – 1.95 (m, 1H, H-8b), 1.95 – 1.90 (m, 1H, H-13a), 1.90 – 1.85 (m, 1H, H-14), 1.53 – 1.39 (m, 12H, CH_2), 1.35 – 1.27 (m, 12H, CH_2), 1.30 (m, 1H, H-13b), 1.00 (d, J = 6.3 Hz, 3H, H-33), 1.00 – 0.91 (m, 12H, $SnCH_2$), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 3H, Me), 0.89 (s, 12H, *t*-Bu and Me), 0.885 (s, 3H, Me), 0.88 (s, 3H, Me), 0.875 (s, 3H, Me), 0.87 (s, 3H, Me), 0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Si-CH_3), 0.08 (s, 3H, Si-CH_3), 0.05 (s, 9H, TMS) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.7 (C-1), 151.6 (C-17), 145.2 (C-18), 144.7 (C-10), 140.7 (C-9), 84.24 (C-15), 84.15 (C-11), 81.3 (C-12), 74.2 (C-3), 74.0 (C-5), 73.0 (C-4), 71.6 (C-6), 69.7 (C-7), 51.6 (C-19), 43.2 (C-16), 40.2 (C-14), 37.8 (C-13), 37.1 (C-2), 35.7 (C-8), 29.3 (3C, CH_2), 29.2 (3C, CH_2), 27.43 (3C, CH_2), 27.37 (3C, CH_2), 27.0 (3C, *t*-Bu), 26.1 (3C, *t*-Bu), 25.7 (3C, *t*-Bu), 18.4 (*t*-Bu), 18.2 (*t*-Bu), 17.8 (*t*-Bu), 16.5 (C-33), 13.8 (3C, Me), 13.7 (3, Me), 11.4 (3C, $SnCH_2$), 11.2 (3C, $SnCH_2$), -0.2 (3C, TMS), -3.4 (Me), -4.1 (Me), -4.4 (Me), -4.66 (Me), -4.68 (Me), -5.0 (Me) ppm; **^{119}Sn NMR** (149 MHz, $CDCl_3$): δ = -54.2, -55.1 ppm; **IR** (film): $\tilde{\nu}$ = 3469, 2954, 2928, 2856, 1787,

1742, 1572, 1463, 1417, 1376, 1361, 1340, 1286, 1252, 1170, 1125, 1082, 1005, 884, 861, 833, 814, 775, 746, 673, 621, 593, 534, 466, 412 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{65}H_{134}O_8Si_4Sn_2Na^+$: 1417.7106, found: 1417.7091.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S,E)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (32b)



A solution of *n*-Bu_3SnH (31.1 µL, 116 µmol) in pentane (1.7 mL) was slowly added to a stirred solution of bis-alkyne **33b** (94 mg, 105 µmol), $[Cp^*RuCl_2]_n$ (10 mol%, 3 mg, 11 µmol) and 4 Å MS in pentane (3.5 mL) at rt over the course of 1 h resulting in a colour change from rose to yellow, and stirring was continued for 20 min. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 5:1) both affording a mixture of intermediates **75b** and **76b** (52 mg, 42%) and some unreacted starting material **33b** (42 mg, 45%) as a colourless oil. The mixture of stannanes **75b** and **76b** was used in the next step without further purification.



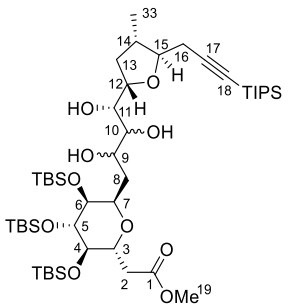
Aq. HI (57%, 28.9 µL, 219 µmol) was added to a stirred suspension of the mixture of stannanes **75b/76b** (52 mg, 22 µmol) and TBAI (8 mg, 22 µmol) in PhMe (1.4 mL) at 0 °C and stirring was continued for 2 h. Then aq. HI (57%, 28.9 µL, 219 µmol) was added to the stirred reaction mixture at 0 °C and stirring was continued for 1 h. Afterwards TBAI (8 mg, 22 µmol) was added to the stirred reaction mixture at 0 °C and stirring was continued for 30 min. Then aq. HI (57%, 28.9 µL, 219 µmol) was added again to the stirred reaction mixture at 0 °C and stirring was continued for 2 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (2.5 mL) and the aq. phase was extracted with EtOAc (2 x 5 mL). The combined extracts were washed with aq. $Na_2S_2O_3$ (10%, 2.5 mL) and brine (2.5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 5:1) affording compound **32b** as a colourless oil (34 mg, 86%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.79 (dt, J = 15.6, 6.9 Hz, 1H), 5.48 (dd, J = 15.5, 5.2 Hz, 1H), 4.34 – 4.28 (m, 1H), 3.93 – 3.85 (m, 2H), 3.84 – 3.79 (m, 1H), 3.80 – 3.76 (m, 1H), 3.68 (s, 3H), 3.59 (dt,

J = 8.3, 5.4 Hz, 1H), 3.50 – 3.46 (m, 2H), 2.68 (dd, J = 7.4, 2.3 Hz, 2H), 2.54 (dd, J = 5.4, 1.3 Hz, 2H), 2.47 (d, J = 2.6 Hz, 1H), 2.51 – 2.40 (m, 1H), 2.25 – 2.14 (m, 1H), 2.13 – 2.05 (m, 1H), 2.04 – 1.97 (m, 1H), 1.43 – 1.31 (m, 1H), 1.10 (d, J = 6.5 Hz, 3H), 1.09 – 0.99 (m, 21H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.09 (s, 6H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 131.2, 130.4, 105.1, 83.4, 82.4, 81.7, 76.0, 74.5, 74.0, 73.9, 71.8, 69.6, 51.8, 39.7, 37.8, 37.6, 34.4, 26.3 (3C), 26.2 (3C), 25.9 (3C), 25.2, 18.8 (6C), 18.5, 18.3, 18.0, 17.2, 11.4 (3C), -3.4, -3.9, -4.1, -4.5 (2C), -4.9 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{92}O_8Si_4Na^+$: 919.5762, found: 919.5764.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((4S)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (78)

Representative Procedure A (Sharpless Dihydroxylation)



Aq. $Me_5O_2NH_2$ (0.05 M, 228.8 µL, 11.1 µmol), $K_3[Fe(CN)_6]$ (0.15 M, 33.4 µmol) and K_2CO_3 (0.15 M, 33.4 µmol) and aq. $K_2OsO_2(OH)_4$ (0.01 M, 5 mol%, 55.7 µL, 557 nmol) were subsequently added to a stirred solution of allylic alcohol **32b** (10 mg, 11 µmol) and $(DHQ)_2PHAL$ (12.5 mol%, 1 mg, 1.4 µmol) in *t*-BuOH (0.6 mL) and water (50 µL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 19 h. Then, aq. $K_2OsO_2(OH)_4$ (0.01 M, 5 mol%, 55.7 µL, 557 nmol) and $(DHQ)_2PHAL$ (12.5 mol%, 1 mg, 1.4 µmol) were again subsequently added to the reaction mixture, and stirring was continued for 2 d. The reaction mixture was diluted with water (1 mL) and the reaction was quenched with EtOAc (1 mL) and $NaHSO_3$ (14 mg, 134 µmol). The aq. phase was extracted with EtOAc (10 x 2.5 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 5:1) affording a major isomer **78a** (4 mg, 39%), a mixture of both isomers (2 mg, 19%, *d.r.* = 1:1) and a minor isomer **78b** (3 mg, 29%) as a colourless oil.

For other ligands and different loadings, the procedure was conducted in a similiar fashion with one half of the ligand/catalyst loading added in the beginning, and the other half added after 19 h.

Analytical and spectral data of the major isomer **78a** (the sample contained traces of the minor diastereomer **78b**): $[\alpha]_D^{20}$: +21.0 (c = 0.1, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.31 – 4.22 (m, 2H, H-3 and H-12), 4.15 (dt, J = 11.0, 1.9 Hz, 1H, H-7), 4.06 (dddd, J = 10.3, 8.0, 5.2, 2.8 Hz, 1H, H-9), 3.80 – 3.77 (m, 1H, H-5), 3.69 (s, 3H, H-19), 3.63 – 3.57 (m, 1H, H-15), 3.54 – 2.49 (m, 1H, H-11), 3.51 (d, J = 5.2 Hz, 1H, OH-9), 3.47 – 3.44 (m, 1H, H-4), 3.42 – 3.40 (m, 1H, H-6), 3.36 (ddd, J = 9.1, 6.7, 2.4 Hz, 1H, H-10), 3.03 (dd, J = 14.1, 11.1 Hz, 1H, H-2a), 2.67 (d, J = 9.0 Hz, 1H, OH-10), 2.61 (d, J = 7.9 Hz, 1H, OH-11), 2.59 – 2.46 (m, 3H, H-16 and H-2b), 2.22 – 2.09 (m, 2H, H-13a and H-14), 1.88 (ddd, J = 14.0, 11.0, 2.9 Hz, 1H, H-8a), 1.74 – 1.60 (m, 1H, H-13b), 1.55 – 1.48 (m, 1H, H-8b), 1.12 (d, J = 6.1 Hz, 3H, H-33), 1.09 – 1.00 (m, 21H, TIPS), 0.92 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.10 (s, 6H, Me), 0.092 (s, 3H, Me), 0.089 (s, 3H, Me), 0.08 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 173.1 (C-1), 105.1 (C-17), 84.0 (C-15), 82.4 (C-18), 78.5 (C-12), 75.2 (C-10), 75.1 (C-3), 74.0 (C-11), 73.8 (C-5), 73.1 (C-4), 72.4 (C-6), 67.0 (C-9), 64.7 (C-7), 52.2 (C-19), 40.0 (C-14), 37.9 (C-13), 37.1 (C-2), 35.9 (C-8), 26.4 (3C, *t*-Bu), 26.3 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 25.6 (C-16), 18.8 (6C, TIPS), 18.7 (*t*-Bu), 18.4 (*t*-Bu), 18.0 (*t*-Bu), 17.2 (C-33), 11.4 (3C, TIPS), -3.6 (Me), -4.1 (Me), -4.2 (Me), -4.48 (Me), -4.54 (Me), -4.8 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3357, 2953, 2929, 2892, 2860, 2174, 1741, 1635, 1463, 1388, 1361, 1343, 1255, 1170, 1125, 1084, 1037, 1005, 970, 920, 882, 833, 812, 774, 674, 457 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{94}O_{10}Si_4Na^+$: 953.5816, found: 953.5825.

Analytical and spectral data of the minor isomer **78b** (the sample contained traces of the major diastereomer **78a**): $[\alpha]_D^{20}$: +11.5 (c = 0.2, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.32 (dt, J = 10.2, 4.2 Hz, 1H, H-3), 4.17 (ddd, J = 10.1, 6.0, 5.3 Hz, 1H, H-12), 4.09 (dt, J = 10.7, 1.9 Hz, 1H, H-7), 3.96 (dtd, J = 9.0, 3.3, 2.0 Hz, 1H, H-9), 3.78 (d, J = 2.6 Hz, 1H, H-5), 3.75 (d, J = 1.9 Hz, 1H, OH-9), 3.69 (s, 3H, H-19), 3.65 – 3.61 (m, 2H, H-11 and H-15), 3.49 – 3.47 (m, 2H, H-10 and H-4), 3.47 – 3.45 (m, 1H, H-6), 3.13 (d, J = 4.8 Hz, 1H, OH-11), 3.12 (d, J = 6.8 Hz, 1H, OH-10), 2.82 (dd, J = 15.0, 9.9 Hz, 1H, H-2a), 2.65 (dd, J = 15.0, 4.6 Hz, 1H, H-2b), 2.58 – 2.50 (m, 2H, H-16), 2.23 – 2.11 (m, 3H, H-14 and H-13a and H-8a), 1.61 – 1.55 (m, 1H, H-13b), 1.45 (ddd, J = 14.9, 3.0, 2.4 Hz, 1H, H-8b), 1.12 (d, J = 6.3 Hz, 3H, H-33), 1.08 – 0.99 (m, 21H, TIPS), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.895 (s, 9H, *t*-Bu), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.095 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.075 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.9 (C-1), 104.9 (C-17), 83.6 (C-15), 82.2 (C-18), 80.0 (C-12), 74.1 (C-11), 73.91 (C-3), 73.89 (C-5), 73.44 (C-10), 73.41 (C-4), 73.1 (C-9), 72.1 (C-6), 69.3 (C-7), 51.8 (C-19), 39.3 (C-14), 37.2 (C-13), 37.0 (C-2), 34.3 (C-8), 26.12 (3C, *t*-Bu), 26.06 (3C, *t*-Bu), 25.8 (3C, *t*-Bu), 25.1 (C-16), 18.6 (6C, TIPS), 18.3 (*t*-Bu), 18.2 (*t*-Bu), 17.8 (*t*-Bu), 16.9 (C-33),

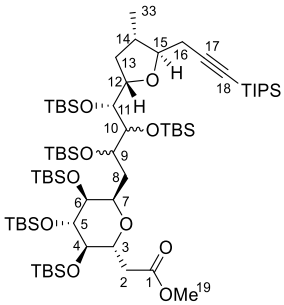
11.3 (3C, TIPS), -3.7 (Me), -4.0 (Me), -4.3 (Me), -4.7 (Me), -4.8 (Me), -5.0 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3397, 2953, 2928, 2895, 2859, 2172, 1737, 1644, 1463, 1438, 1387, 1362, 1255, 1172, 1124, 1081, 1037, 1006, 920, 883, 833, 813, 774, 674, 461, 428 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{94}O_{10}Si_4Na^+$: 953.5816, found: 953.5828.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4S)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (78)

Procedure B (Donohoe Conditions)

TMEDA (0.2 M in DCM, 61.3 µL, 53.1 µmol) was added to a stirred solution of allylic alcohol **32b** (10 mg, 11 µmol) in DCM (1.0 mL) at rt. The stirred reaction mixture was cooled to -78 °C and OsO_4 (0.22 M in DCM, 53.2 µL, 11.7 µmol) was added resulting in an immediate colour change to orange, and stirring was continued for 1 h. Then, TMEDA (0.2 M in DCM, 61.3 µL, 53.1 µmol) and OsO_4 (0.22 M in DCM, 53.2 µL, 11.7 µmol) were subsequently added once again to the stirred reaction mixture at -78 °C resulting in an immediate colour change to red, and stirring was continued for 30 min. The reaction was quenched with 1,2-ethylenediamine (7.4 µL, 111 µmol) at -78 °C and the reaction mixture was allowed to reach rt, and stirring was continued for 4 d. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 5:1) affording both the major isomer ***78a*** (5 mg, 48%) and the minor isomer **78b** (4 mg, 39%) as a colourless oil. The analytical and spectroscopic data of the isolated compounds were identical with those shown above.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4R)-2,3,4-tris((tert-butyldimethylsilyl)oxy)-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (79a)

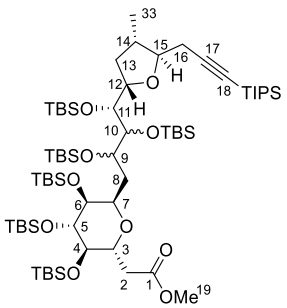


TBSOTf (12.2 µL, 53.1 µmol) was added to a stirred solution of *major* triol **78a** (11 mg, 12 µmol) and 2,6-lutidine (8.3 µL, 71 µmol) in DCM (0.6 mL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 4 h. Then 2,6-lutidine (0.9 µL, 8 µmol) and TBSOTf (1.4 µL, 5.9 µmol) were subsequently added at rt and stirring was continued for 20 h. The reaction was diluted with MTBE (10 mL) and quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL). The organic extract was washed with water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 50:1) affording compound **79a** as a colourless oil (4 mg, 27%).

$[\alpha]_D^{20}$: +24.0 (c = 0.40, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.23 (td, J = 6.6, 5.2 Hz, 1H, H-3), 4.08 (dt, J = 10.0, 4.5 Hz, 1H, H-12), 3.99 (ddd, J = 9.5, 4.4, 2.5 Hz, 1H, H-9), 3.90 (dt, J = 11.4, 1.7 Hz, 1H, H-7), 3.79 (dd, J = 2.9, 2.0 Hz, 1H, H-5), 3.76 – 3.73 (m, 2H, H-10 and H-11), 3.70 (ddd, J = 6.2, 2.0, 0.8 Hz, 1H, H-4), 3.63 (s, 3H, H-19), 3.54 (td, J = 7.7, 4.4 Hz, 1H, H-15), 3.51 – 3.47 (m, 1H, H-6), 2.87 (dd, J = 14.8, 6.8 Hz, 1H, H-2a), 2.59 (dd, J = 16.9, 4.5 Hz, 1H, H-16a), 2.46 (dd, J = 14.8, 5.2 Hz, 1H, H-2b), 2.38 (dd, J = 16.9, 7.5 Hz, 1H, H-16b), 2.07 (ddd, J = 13.9, 11.2, 2.5 Hz, 1H, H-8a), 2.04 – 1.95 (m, 2H, H-13a and H-14), 1.50 – 1.47 (m, 1H, H-13b), 1.21 – 1.18 (m, 1H, H-8b), 1.13 (d, J = 6.2 Hz, 3H, H-33), 1.07 – 1.03 (m, 18H, TIPS), 1.03 – 0.99 (m, 3H, TIPS), 0.92 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.895 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.875 (s, 9H, *t*-Bu), 0.12 (s, 3H, Me),0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.08 (s, 3H, Me), 0.08 (s, 3H, Me), 0.07 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 172.0 (C-1), 105.8 (C-17), 82.6 (C-15), 81.8 (C-18), 78.5 (C-10), 78.1 (C-12), 76.1 (C-5), 75.7 (C-11), 74.6 (C-4), 74.1 (C-6), 72.0 (C-3), 71.4 (C-9), 66.8 (C-7), 51.4 (C-19), 40.7 (C-14), 38.9 (C-13), 37.7 (C-2), 36.0 (C-8), 26.7 (3C, *t*-Bu), 26.6 (3C, *t*-Bu), 26.5 (3C, *t*-Bu), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 26.1 (3C, *t*-Bu), 26.0 (C-16), 18.78 (6C, TIPS), 18.77 (*t*-Bu), 18.6 (*t*-Bu), 18.4 (*t*-Bu), 18.28 (*t*-Bu), 18.26 (*t*-Bu), 18.1 (*t*-Bu), 17.2 (C-33), 11.5 (3C, TIPS), -2.9 (Me), -3.0 (Me), -3.1 (Me), -3.4 (2C, Me), -3.5 (Me), -3.6 (Me), -3.8 (Me), -4.2 (Me), -4.5 (Me), -4.6 (Me), -4.7 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2928, 2894, 2857, 2177, 1742, 1646, 1472, 1463, 1437, 1408, 1388,

1361, 1252, 1123, 1084, 1041, 1005, 938, 882, 831, 812, 773, 674, 663, 585, 486, 473, 465, 459, 449, 430 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{65}H_{136}O_{10}Si_7Na^+$: 1295.8411, found: 1295.8407.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2R,3S,4R)-2,3,4-tris((tert-butyldimethylsilyl)oxy)-4-((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (79b)



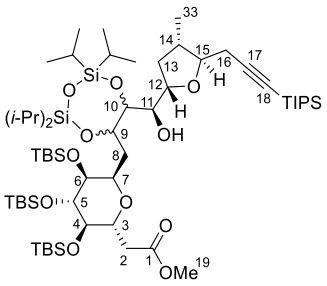
TBSOTf (6.2 µL, 27 µmol) was added to a stirred solution of *minor* triol **78b** (5 mg, 5 µmol) and 2,6-lutidine (4.4 µL, 37.6 µmol) in DCM (0.5 mL) at rt and stirring was continued for 1 h. Then 2,6-lutidine (4.4 µL, 38 µmol) and TBSOTf (6.2 µL, 27 µmol) were subsequently added at rt and stirring was continued for 16 h. The reaction was diluted with MTBE (10 mL) and quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL). The extract was washed with water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 50:1) affording compound **79b** as a colourless oil (5 mg, 73%).

$[\alpha]_D^{20}$: +8.8 (c = 0.50, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.28 – 4.21 (m, 2H, H-9 and H-3), 4.01 (ddd, J = 9.9, 8.5, 5.3 Hz, 1H, H-12), 3.80 – 3.77 (m, 1H, H-7), 3.76 (t, J = 2.3 Hz, 1H, H-5), 3.65 (s, 3H, H-19), 3.62 (d, J = 8.8 Hz, 1H, H-10), 3.57 (dd, J = 8.5, 3.7 Hz, 1H, H-11), 3.53 (ddd, J = 4.7, 1.8, 0.9 Hz, 1H, H-4), 3.45 (td, J = 7.7, 4.5 Hz, 1H, H-15), 3.41 (t, J = 2.3 Hz, 1H, H-6), 3.03 (dd, J = 15.1, 7.4 Hz, 1H, H-2a), 2.54 (dd, J = 16.8, 4.6 Hz, 1H, H-16a), 2.42 – 2.36 (m, 2H, H-16b and H-2b), 2.30 – 2.24 (m, 1H, H-13a), 2.04 – 1.93 (m, 1H, H-14), 1.93 – 1.87 (m, 1H, H-8a), 1.53 – 1.49 (m, 1H, 8b), 1.40 – 1.33 (m, 1H, H-13b), 1.08 (d, J = 6.5 Hz, 3H, H-33), 1.07 – 1.00 (m, 21H, TIPS), 0.92 (s, 9H, t-Bu), 0.91 (s, 9H, t-Bu), 0.89 (s, 9H, t-Bu), 0.88 (s, 9H, t-Bu), 0.875 (s, 9H, t-Bu), 0.86 (s, 9H, t-Bu), 0.13 (s, 3H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.075 (s, 3H, Me), 0.07 (s, 6H, Me), 0.065 (s, 3H, Me), 0.055 (s, 3H, Me), 0.05 (s, 3H, Me), 0.03 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 172.0 (C-1), 105.7 (C-17), 81.9 (C-15), 81.4 (C-18),79.8 (C-12), 77.2 (C-11), 75.2 (C-5), 74.6 (C-10), 73.8 (C-4), 73.3 (C-6), 72.6 (C-3), 68.1 (C-9), 66.4 (C-7), 51.3 (C-19), 40.3 (C-14), 38.9 (C-13), 37.8 (C-2), 36.4 (C-8), 26.3 (3C, t-Bu), 26.22 (3C, t-Bu), 26.16 (3C, t-Bu), 26.13 (3C, t-Bu), 26.08 (3C, t-Bu), 25.9 (4C, t-Bu and C-16), 18.6 (6C, TIPS), 18.2 (t-Bu), 18.16 (t-Bu), 18.15 (t-Bu), 18.12 (2C, t-Bu), 18.11 (t-Bu), 17.7 (C-33), 11.3 (3C, TIPS), -3.0 (Me), -3.52 (Me), -3.54

(Me), -3.60 (Me), -3.61 (Me), -3.7 (Me), -3.8 (Me), -4.0 (Me), -4.5 (Me), -4.7 (Me), -4.8 (Me), -4.9 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2927, 2856, 2173, 1742, 1463, 1438, 1407, 1388, 1361, 1253, 1216, 1084, 1039, 1006, 974, 937, 921, 885, 833, 810, 773, 673, 628, 462, 438 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{65}H_{136}O_{10}Si_7Na^+$: 1295.8411, found: 1295.8404.

5.2.1.4. Stereochemical Elucidation & Cyclization Trials

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((7-((R)-hydroxy((2S,4S,5R)-4-methyl-5-(3-(triisopropylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)methyl)-2,2,4,4-tetraisopropyl-1,3,5,2,4-trioxadisilepan-6-yl)methyl)tetrahydro-2H-pyran-2-yl)acetate (81)



t-Bu_2SiCl_2 (2.8 µL, 13 µmol) was added to a stirred solution of triol **78a** (10 mg, 11 µmol) and imidazole (3.7mg, 54 µmol) in DMF (0.5 mL) at rt and stirring was continued for 17 h. Then imidazole (3.7mg, 54 µmol) and *t*-Bu_2SiCl_2 (2.8 µL, 13 µmol) were subsequently added at rt and stirring was continued for 2 h. The $AgNO_3$ (3.7 mg, 22 µmol) was added to the stirred reaction mixture at rt immediately resulting in a white precipitate, and stirring was continued for 1.5 h. Then *i*-Pr_2SiCl_2 (2.3 µL, 13 µmol) was added at rt with the precipitate dissolving again and stirring was continued for 2 h. Then imidazole (7 mg, 0.1 mmol) and *i*-Pr_2SiCl_2 (2.3 µL, 13 µmol) were subsequently added at rt and stirring was continued for 10 h. Then *i*-Pr_2SiCl_2 (2.3 µL, 13 µmol) and $AgNO_3$ (3.7 mg, 22 µmol) were subsequently added at rt resulting in a white precipitate again and stirring was continued for 1 h. The reaction was diluted with MTBE (10 mL) and quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL). The aq. phase was extracted with MTBE (2 x 5 mL) and the combined extracts were washed with water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 50:1) affording compound **81** as a colourless oil (4 mg, 32%).

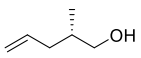
$[\alpha]_D^{20}$: +6.2 (c = 0.40, $CHCl_3$); **^{1}H NMR** (OH not visible, 600 MHz, $CDCl_3$): δ = 4.36 – 4.28 (m, 2H, H-9 and H-12), 4.24 (m, 1H, H-3), 4.23 (ddd, J = 9.0, 6.1, 3.3 Hz, 1H, H-10), 4.17 (dt, J = 11.4, 1.7 Hz, 1H, H-7), 3.81 – 3.75 (m, 1H, H-5), 3.66 (s, 3H, H-19), 3.64 – 3.59 (m, 1H, H-15), 3.59 (dd, J = 9.1, 1.6 Hz, 1H, H-11), 3.54 (ddd J = 3.0, 1.9, 0.9 Hz, 1H, H-4), 3.45 – 3.41 (m, 1H, H-6), 2.84 (dd, J = 15.4, 6.7 Hz, 1H, H-2a), 2.76 (dd, J = 15.4, 7.5 Hz, 1H, H-2b), 2.57 (dd, J = 17.0, 4.7 Hz, 1H, H-16a), 2.49 (dd, J = 17.0, 6.3 Hz, 1H, H-16b), 2.28 (ddd, J = 14.4, 11.1, 1.7 Hz, 1H, H-8a), 2.20 – 2.08 (m, 1H, H-14), 2.03 (dt, J = 11.6, 7.1 Hz, 1H, H-13a), 1.88 (ddd, J = 11.8, 10.5, 8.9 Hz, 1H, H-13b), 1.16 (dd, J = 14.1, 11.0 Hz, 1H, H-8b), 1.12 (d, J = 6.5 Hz, 3H, H-33), 1.07 – 1.04 (m, 18H, TIPS), 1.03 – 0.95 (m, 27H, *i*-Pr and TIPS), 0.96 – 0.86 (m, 4H, *i*-Pr), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.10 (s, 3H, Me), 0.08 (s, 3H, Me), 0.08 (s, 3H, Me), 0.08 (s, 3H, Me), 0.06 (s, 3H, Me), 0.03 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 172.2 (C-1), 104.7 (C-17), 84.1 (C-15), 82.0 (C-18),

76.9 (C-12), 74.3 (C-5), 73.9 (C-11), 73.6 (C-3), 72.9 (C-4), 72.8 (C-6), 71.6 (C-9), 69.7 (C-10), 65.1 (C-7), 51.4 (C-19), 39.6 (C-14), 36.7 (C-2), 34.9 (C-13), 33.0 (C-8), 26.07 (3C, *t*-Bu), 26.06 (3C, *t*-Bu), 25.7 (3C, *t*-Bu), 25.2 (C-16), 18.6 (6C, TIPS), 18.21 (*t*-Bu), 18.19 (*t*-Bu), 17.8 (*t*-Bu), 17.23 (*i*-Pr), 17.18 (*i*-Pr), 17.16 (2C, *i*-Pr), 17.15 (*i*-Pr), 17.1 (*i*-Pr), 16.84 (2C, *i*-Pr), 16.83 (C-33), 13.4 (*i*-Pr), 13.2 (*i*-Pr), 12.9 (*i*-Pr), 12.3 (*i*-Pr), 11.3 (3C, TIPS) -3.7 (Me), -4.0 (Me), -4.5 (Me), -4.8 (Me), -4.9 (Me), -5.1 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3325, 2954, 2926, 2894, 2857, 2178, 1740, 1630, 1464, 1383, 1363, 1259, 1082, 1039, 1011, 938, 920, 884, 834, 801, 775, 677, 624, 596, 532, 525 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{59}H_{120}O_{11}Si_6Na^+$: 1195.7339, found: 1195.7350.

5.2.1.5. Investigations On Alternative Pathways

5.2.1.5.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

(S)-2-Methylpent-4-en-1-ol ((S)-84)

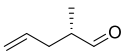


n-BuLi (1.6 M in hexane, 66.5 mL, 106 mmol) was slowly added to a stirred solution of DIPA (15.7 mL, 112 mmol) in THF (39 mL) at 0 °C. The reaction mixture was warmed to rt and stirring was continued for 10 min. Then the reaction mixture was cooled to 0 °C and $NH_3 \cdot BH_3$ (90%, 3.83 g, 112 mmol) was added portionwise at such a rate as to the development of gas. Then the reaction mixture was warmed to rt and stirring was continued for 1 h. The reaction mixture was again cooled to 0 °C. Amide **43** (6.95 g, 26.6 mmol) as a solution in THF (39 mL) was added dropwise to the reaction mixture. Finally the reaction mixture was allowed to reach rt and stirring was continued for 2 h. The reaction was quenched at 0 °C with aq. HCl (2.0 M, 250 mL) and the aq. phase was extracted with MTBE (3 x 200 mL). The combined organic extracts were washed with aq. HCl (1.5 M, 200 mL) and brine (200 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated until 400 mbar at 40 °C bath temperature. Aq. KOH (1.0 M, 200 mL) was added to the stirred solution of the crude at rt and stirring was continued for 1 h. The resulting mixture was neutralized with aq. HCl (2.0 M) and the aq. phase was extracted with MTBE (3 x 150 mL). The combined organic extracts were washed with brine (150 mL) and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound (*S*)-**84** as a yellow oil (2.44 g, 91%, 99%*ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.80 (ddt, J = 17.2, 10.1, 7.3 Hz, 1H), 5.07 – 4.98 (m, 2H), 3.50 (dd, J = 10.6, 6.2 Hz, 1H), 3.44 (dd, J = 10.6, 6.1 Hz, 1H), 2.17 (dddt, J = 14.2, 7.1, 5.9, 1.3 Hz, 1H), 1.92 (dtt, J = 13.8, 7.3, 1.2 Hz, 1H), 1.73 (dp, J = 13.4, 6.7 Hz, 1H), 1.67 (br s, 1H), 0.91 (d, J = 6.7 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 131.1, 116.2, 68.0, 38.0, 35.7, 16.5 ppm; **HRMS** (CI): *m/z* calcd. for $C_6H_{13}O^+$: 101.0966, found: 101.0966. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[275]

[275] A. Fettes, E. M. Carreira, *J. Org. Chem.* **2003**, *68*, 9274-9283.

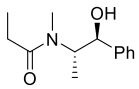
(S)-2-Methylpent-4-enal ((S)-37)



DMSO (312 µL, 4.39 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (189 µL, 2.20 mmol) in DCM (6 mL) at -78 °C and the reaction mixture was stirred for 5 min. Then alcohol (*S*)-**84** (200 mg, 2.00 mmol) as a solution in DCM (1 mL, rinsed with 1 mL) was added dropwise and stirring was continued for 20 min. DIPEA (1.74 mL, 9.98 mmol) was slowly added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 1.5 h. The reaction was quenched with water (15 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 4 x 10 mL) and with brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, pentane/MTBE, 20:1) affording compound (*S*)-**37** as solution in MTBE/pentane (38%, 500 mg, 97%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.64 (d, J = 1.3 Hz, 1H), 5.74 (ddt, J = 17.0, 10.1, 6.9 Hz, 1H), 5.11 – 5.04 (m, 2H), 2.50 – 2.39 (m, 2H), 2.17 – 2.09 (m, 1H), 1.09 (d, J = 6.9 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 204.8, 135.0, 117.4, 45.9, 34.9, 13.1 ppm; The analytical and spectroscopic data are in agreement with those previously reported in the literature.[276]

N-((1S,2S)-1-Hydroxy-1-phenylpropan-2-yl)-N-methylpropionamide (ent-42)



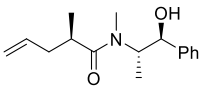
Propionic anhydride (2.08 mL, 16.2 mmol) was added to a stirred solution of (1*S*,2*S*)-(*+*)-pseudoephedrine (*ent*-**41**) (2.50 g, 15.1 mmol) and TEA (2.32 mL, 16.6 mmol) in DCM (27.5 mL) at rt over the course of 10 min and stirring was continued for 1 h. The reaction was quenched with sat. aq. $NaHCO_3$ (20 mL). The organic extract was washed with aq. HCl (1.0 M, 20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by recrystallization from boiling PhMe (14 mL) affording compound *ent*-**42** as a colourless crystalline solid (2.99 g, 89%).

^{1}H NMR (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 400 MHz, C_6D_6): δ = 7.37 – 6.95 (m, 5H), 7.37 – 6.95* (m, 5H), 4.84 (br s, 1H), 4.52 (t, J = 7.0 Hz, 1H), 4.26 – 4.07 (m, 1H), 4.06* (d, J = 8.8 Hz, 1H), 3.72 – 3.62* (m, 1H), 2.78* (s, 3H), 2.41* (dq, J = 14.9, 7.3 Hz, 1H), 2.17* (s, 1H), 2.07 (s, 3H), 2.05 – 1.99* (m, 1H), 1.82 – 1.65 (m, 2H), 1.24* (t, J = 7.4 Hz, 3H), 1.02 (t, J = 7.4 Hz,

[276] C. Lentsch, U. Rinner, *Org. Lett.* **2009**, *11*, 5326-5328.

3H), 0.98 (d, J = 7.0 Hz, 3H), 0.54* (d, J = 6.8 Hz, 3H) ppm; **^{13}C NMR** (3:1 rotamer ratio, asterisk denotes minor rotamer peaks, 101 MHz, C_6D_6): δ = 175.3, 174.1*, 144.0, 142.6*, 128.7*, 128.6, 128.4 (2C), 128.2*, 127.9* (2C), 127.4* (2C), 127.3, 126.8 (2C), 76.8, 75.5*, 60.1, 58.1*, 27.5, 26.9*, 15.1*, 14.5, 10.0*, 9.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{13}H_{19}NO_2Na^+$: 244.1308, found: 244.1307. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[277]

(R)-N-((1S,2S)-1-Hydroxy-1-phenylpropan-2-yl)-N,2-dimethylpent-4-enamide (ent-43)



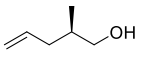
n-BuLi (1.6 M in hexane, 16.2 mL, 25.8 mmol) was slowly added to a stirred solution of flame-dried LiCl (3.16 g, 74.6 mmol) and DIPA (3.92 mL, 28.0 mmol) in THF (14 mL) at 0 °C giving a white suspension, and stirring was continued for 15 min. The reaction mixture was warmed to rt and stirring was continued for 20 min. A solution of propionamide *ent*-**42** (2.75 g, 12.4 mmol) in THF (36 mL) was slowly added to the stirred reaction mixture at -78 °C over the course of 30 min and stirring was continued for 45 min. The reaction mixture was warmed to 0 °C and stirring was continued for 15 min. Then the reaction mixture was warmed to rt and stirring was continued for 15 min. Allyl iodide (1.71 mL, 18.6 mmol) was added dropwise at -78 °C to the reaction mixture and stirring was continued for 1 h. Finally the reaction mixture was warmed to 0 °C and stirring was continued for 1 h. The reaction was quenched with sat. aq. NH_4Cl (35 mL) and sat. aq. $Na_2S_2O_3$ (2 mL) and the aq. phase was extracted with EtOAc (2 x 35 mL). The combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 2:1) affording compound *ent*-**43** as a colourless oil (2.07 g, 64%).

^{1}H NMR (3.5:1 rotamer ratio, asterisk denotes minor rotamer peaks, 400 MHz, C_6D_6): δ = 7.37 – 7.05 (m, 5H), 7.37 – 7.05* (m, 5H), 5.98 – 5.84* (m, 1H), 5.64 (dddd, J = 16.7, 10.2, 7.6, 6.3 Hz, 1H), 5.22 – 5.13* (m, 1H), 5.09 – 5.03* (m, 1H), 5.02 – 4.91 (m, 2H), 4.90 (br s, 1H), 4.55 (t, J = 7.2 Hz, 1H), 4.29 (br s, 1H), 4.23* (dd, J = 8.4, 3.2 Hz, 1H), 3.93 – 3.84* (m, 1H), 3.00* (br s, 1H), 2.82* (s, 3H), 2.85 – 2.74* (m, 2H), 2.47 – 2.37 (m, 1H), 2.35 – 2.29* (m, 1H), 2.28 (dd, J = 13.0, 6.2 Hz, 1H), 2.25 (s, 3H), 2.03 – 1.93 (m, 1H), 1.07* (d, J = 6.4 Hz, 3H), 0.975 (d, J = 6.8 Hz, 3H), 0.97 (d, J = 6.7 Hz, 3H), 0.68* (dd, J = 6.9, 1.2 Hz, 3H) ppm; **^{13}C NMR** (3.5:1 rotamer ratio, asterisk denotes

[277] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.

minor rotamer peaks, 101 MHz, C_6D_6): δ = 177.5, 176.4*, 143.8, 142.7*, 137.6*, 136.7, 128.7*, 128.6, 128.4 (2C), 128.2*, 127.9* (2C), 127.4* (2C), 127.3, 126.8 (2C), 116.4, 116.3*, 76.4, 75.5*, 59.3, 58.2*, 38.7*, 38.5, 36.7, 35.9*, 17.8*, 17.2, 15.5*, 14.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{16}H_{23}NO_2Na^+$: 284.1621, found: 284.1619. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[278]

(R)-2-Methylpent-4-en-1-ol ((R)-84)



n-BuLi (1.6 M in hexane, 18.5 mL, 29.5 mmol) was slowly added to a stirred solution of DIPA (4.35 mL, 31.0 mmol) in THF (11 mL) at 0 °C. The reaction mixture was warmed to rt and stirring was continued for 10 min. Then the reaction mixture was cooled to 0 °C and $NH_3{\cdot}BH_3$ (90%, 1.06 g, 31.0 mmol) was added portionwise regarding the development of gas. Then the reaction mixture was warmed to rt and stirring was continued for 1 h. The reaction mixture was again cooled to 0 °C. Amide *ent*-**43** (1.93 g, 7.38 mmol) as a solution in THF (11 mL) was added dropwise to the reaction mixture. Finally the reaction mixture was allowed to reach rt and stirring was continued for 2 h. The reaction was quenched at 0 °C with aq. HCl (2.0 M, 80 mL) and the aq. phase was extracted with MTBE (3 x 70 mL). The combined organic extracts were washed with aq. HCl (1.5 M, 70 mL) and brine (70 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated until 400 mbar at 40 °C bath temperature. KOH (1.0 M, 50.0 mL) was added to the stirred solution of the crude at rt and stirring was continued for 1 h. The resulting mixture was neutralized with aq. HCl (2.0 M) and the aq. phase was extracted with MTBE (3 x 50 mL). The combined organic extracts were washed with brine (50 mL) and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound (*R*)-**84** as a yellow oil (592 mg, 80%, 98%*ee*).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (ddt, J = 17.2, 10.1, 7.1 Hz, 1H), 5.08 – 4.98 (m, 2H), 3.51 (dd, J = 10.6, 6.1 Hz, 1H), 3.45 (dd, J = 10.6, 6.1 Hz, 1H), 2.17 (dddt, J = 14.2, 7.2, 5.9, 1.2 Hz, 1H), 1.94 (dtt, J = 13.9, 7.3, 1.3 Hz, 1H), 1.74 (dp, J = 13.3, 6.5 Hz, 1H), 1.53 (br s, 1H), 0.92 (d, J = 6.8 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.1, 116.3, 68.0, 38.0, 35.7, 16.5 ppm; **HRMS** (EI): *m/z* calcd. for $C_6H_{12}O$: 100.0888, found: 100.0888. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[279]

[278] A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason, *J. Am. Chem. Soc.* **1997**, *119*, 6496-6511.
[279] N.-H. Lin, L. E. Overman, M. H. Rabinowitz, L. A. Robinson, M. J. Sharp, J. Zablocki, *J. Am. Chem. Soc.* **1996**, *118*, 9062-9072.

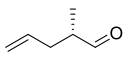
Trimethyl(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)prop-1-yn-1-yl)silane (86)

A solution of I_2 (311 mg, 1.22 mmol) in Et_2O (4 mL) was added to a stirred suspension of Mg turnings (15.3 g, 627 mmol) in Et_2O (42 mL) at rt. Then a few drops of 3-(TMS)-propargylbromide (**85**) (11.5 mL, 70.4 mmol) in Et_2O (20 mL) were added to the stirred suspension. As soon as the reaction started the reaction mixture was cooled to -5 °C and the residual solution of 3-(TMS)-propargylbromide (**85**) was added dropwise to the stirred suspension over the course of 5.5 h. Then the resulting suspension was cooled to -70 °C and was slowly added to 2-isopropoxyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (12.0 mL, 58.8 mmol) as a solution in Et_2O (14 mL) at -70 °C. Then the reaction mixture was allowed to reach rt and stirring was continued for 16 h. The reaction was quenched at -60 °C by slow addition of HCl (2.0 M in Et_2O, 35 mL). After reaching rt the mixture was filtered and the filtrate washed with water (2 x 15 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by distillation ($4.3 \cdot 10^{-2}$ mbar, bath: 85-115 °C, head: 44-56 °C) affording compound **86** as a yellow oil (7.61 g, 32%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.88 (s, 2H), 1.27 (s, 12H), 0.13 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 103.3, 84.2 (2C), 83.3, 24.8 (4C), 24.70, 0.35 (3C) ppm; **^{11}B NMR** (101 MHz, $CDCl_3$): δ = 20.3; $C_{12}H_{23}BO_2Si$. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[280]

(4S,5S)-5-Methyl-1-(trimethylsilyl)oct-7-en-1-yn-4-ol (36b)

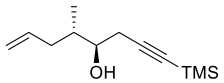
Procedure B (Propargylation)



DMSO (3.84 mL, 54.0 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (2.32 mL, 27.0 mmol) in DCM (36 mL) at -78 °C and the reaction mixture was stirred for 5 min. A solution of alcohol (*S*)-**84** (1.23 g, 12.3 mmol) in DCM (6 mL, rinsed with 6 mL) was added dropwise and stirring was continued for 20 min. DIPEA (21.4 mL, 123 mmol) was slowly added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 1.5 h. The reaction was quenched with water (50 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 4 x 50 mL) and with brine (50 mL), and dried over anhydrous Na_2SO_4. The drying

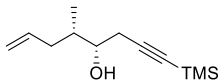
[280] R. W. Hoffmann, H. Brinkmann, G. Frenking, *Chem. Ber.* **1990**, *123*, 2387-2394.

agent was filtered off and the solvent was evaporated yielding the crude product (*S*)-**37** as a solution in DCM (6.3%, 15.9g, 83%) which was used in the next step without further purification.



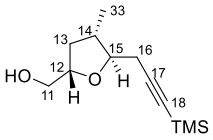
A solution of boronic acid ester **86** (70%, 4.51 mL, 12.2 mmol) in THF (8.75 mL, rinsed with 8.75 mL) was added to a stirred solution of aldehyde (*S*)-**37** (6.3% in DCM, 15.9 g, 10.2 mmol) in THF (50 mL) with 4 Å MS at rt. Et_2Zn (15% in PhMe, 1.67 mL, 2.45 mmol) was added to the stirred reaction mixture at rt and stirring was continued for 19 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 100 mL) and the aq. phase was extracted with MTBE (3 x 150 mL). The combined extracts were washed with aq. phosphate buffer (200 mM, pH 7, 100 mL) and brine (100 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography twice (first column: fine SiO_2, pentane/Et_2O, 75:1 to 20:1; second column: fine SiO_2, pentane/Et_2O, 80:1) affording both desired minor isomer **36b** (755 mg, 35%), a mixture of both isomers (88 mg, 4%, *d.r.* = 1:1) and undesired major isomer **87** (950 mg, 44%) as a colourless oil.

Analytical and spectral data of the minor diastereomer **36b**: $[\alpha]_D^{20}$: +14.4 (c = 1.08, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.80 (dddd, J = 16.8, 10.1, 7.8, 6.5 Hz, 1H), 5.10 – 4.97 (m, 2H), 3.54 (ddd, J = 7.7, 6.5, 4.3 Hz, 1H), 2.50 (dd, J = 16.8, 4.1 Hz, 1H), 2.40 – 2.27 (m, 1H), 2.37 (dd, J = 16.9, 7.8 Hz, 1H), 2.04 (d, J = 4.6 Hz, 1H), 1.96 (dddt, J = 14.0, 8.8, 7.7, 1.2 Hz, 1H), 1.81 – 1.64 (m, 1H), 0.89 (d, J = 6.8 Hz, 3H), 0.16 (s, 9H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 137.2, 116.4, 103.6, 87.9, 73.4, 38.0, 36.9, 26.2, 15.4, 0.2 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3412, 3077, 2961, 2934, 2902, 2880, 2175, 1641, 1458, 1446, 1420, 1380, 1340, 1203, 1124, 1037, 994, 959, 912, 841, 760, 699, 651, 637, 588, 522 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{12}H_{22}OSiNa^+$: 233.1332, found: 233.1331.



Analytical and spectral data of the major diastereomer **87**: $[\alpha]_D^{20}$: -14.1 (c = 0.94, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.84 – 5.73 (m, 1H), 5.08 – 5.01 (m, 2H), 3.68 (td, J = 6.4, 4.4 Hz, 1H), 2.42 (d, J = 6.3 Hz, 2H), 2.23 (dddt, J = 13.9, 7.0, 5.7, 1.4 Hz, 1H), 1.99 – 1.91 (m, 1H), 1.82 (s, 1H), 1.72 (dqdd, J = 8.1, 6.8, 5.6, 4.5 Hz, 1H), 0.92 (d, J = 6.8 Hz, 3H), 0.15 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 137.1, 116.4, 103.8, 87.6, 72.7, 37.9, 37.4, 26.5, 13.8, 0.2 (3C) ppm; **IR** (film): $\tilde{\nu}$ = 3413, 3078, 2962, 2934, 2901, 2879, 2175, 1641, 1460, 1443, 1419, 1379, 1250, 1118, 1040, 1020, 990, 958, 913, 841, 760, 699, 651, 638, 556, 518 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{12}H_{22}OSiNa^+$: 233.1332, found: 233.1333.

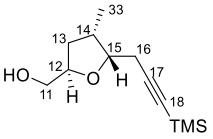
((2S,4S,5R)-4-Methyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)methanol (48b)



A solution of alcohol **36b** (733 mg, 3.48 mmol) in *i*-PrOH (35 mL) was added to $Co(nmp)_2$ (**49b**) (10 mol%, 197 mg, 348 µmol) and O_2 was bubbled through the stirred solution for 10 min. *t*-BuOOH (5.5 M in decane, 63.3 µL, 348 µmol) was added at rt and stirring was continued for 15 min resulting in a colour change from orange to green. The resulting reaction mixture was warmed to 55 °C and stirring was continued for 15 h under an atmosphere of O_2 (balloon). The solvent was evaporated and the resulting residue was dissolved in hexane (50 mL). The resulting solution was washed with aq. phosphate buffer (200 mM, pH 7, 25 mL) and the aq. phase was extracted with hexane (3 x 15 mL). The combined organic extracts were washed with aq. phosphate buffer (200 mM, pH 7, 25 mL) and brine (25 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated after filtration through Celite®. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 7:1 to 5:1) affording compound **48b** as a colourless oil (490 mg, 62%).

$[\alpha]_D^{20}$: +4.0 (c = 1.10, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.13 (dddd, J = 9.7, 5.8, 5.6, 3.1 Hz, 1H, H-12), 3.69 (dd, J = 11.6, 3.1 Hz, 1H, H-11a), 3.60 (dt, J = 8.3, 5.5 Hz, 1H, H-15), 3.50 (dd, J = 11.6, 5.6 Hz, 1H, H-11b), 2.51 (d, J = 5.5 Hz, 2H, H-16), 2.18 (dddq, J = 10.6, 8.3, 7.2, 6.5 Hz, 1H, H-14), 2.10 (ddd, J = 12.0, 7.2, 5.8 Hz, 1H, H-13a), 2.0 (s, 1H, OH), 1.44 (ddd, J = 12.0, 10.6, 9.7 Hz, 1H, H-13b), 1.11 (d, J = 6.5 Hz, 3H, H-33), 0.15 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 103.5 (C-17), 86.7 (C-18), 83.3 (C-15), 79.3 (C-12), 65.0 (C-11), 39.7 (C-14), 36.9 (C-13), 25.4 (C-16), 17.3 (C-33), 0.20 (3C, TMS) ppm; **IR** (film): $\tilde{\nu}$ = 3444, 2960, 2933, 2901, 2876, 2177, 1781, 1728, 1602, 1456, 1418, 1381, 1331, 1249, 1199, 1167, 1114, 1080, 1019, 934, 912, 838, 759, 698, 642, 527, 476 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{12}H_{22}O_2SiNa^+$: 249.1281, found: 249.1280.

((2R,4S,5S)-4-Methyl-5-(3-(trimethylsilyl)prop-2-yn-1-yl)tetrahydrofuran-2-yl)methanol (88)

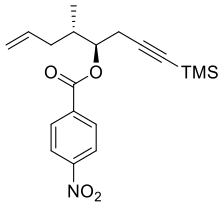


A solution of alcohol **87** (50 mg, 0.24 mmol) in *i*-PrOH (2.38 mL) was added to $Co(nmp)_2$ (**49b**) (10 mol%, 13 mg, 24 µmol) and O_2 was bubbled through the stirred solution for 10 min. *t*-BuOOH (5.5 M in decane, 4.3 µL, 24 µmol) was added to the stirred reaction mixture at rt and stirring was continued for 15 min resulting in a colour change from orange to green. The resulting reaction mixture was warmed to 55 °C and stirring was continued for 18 h under an atmosphere of O_2 (balloon). The solvent was evaporated

and the resulting residue was dissolved in hexane (20 mL). The resulting solution was washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with hexane (3 x 5 mL). The combined organic extracts were washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated after filtration through Celite®. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 5:1) affording compound **88** as a colourless oil (41 mg, 76%).

$[\alpha]_D^{20}$: -5.8 (c = 1.07, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.28 – 4.22 (m, 1H, H-12), 4.09 (dt, J = 8.0, 5.5 Hz, 1H, H-15), 3.62 (dd, J = 11.5, 3.2 Hz, 1H, H-11a), 3.47 (dd, J = 11.5, 6.3 Hz, 1H, H-11b), 2.49 (dd, J = 16.7, 5.8 Hz, 1H, H-16a), 2.48 – 2.37 (m, 1H, H-14), 2.36 (dd, J = 16.7, 8.1 Hz, 1H, H-16b), 1.88 (dt, J = 12.4, 7.3 Hz, 1H, H-13a), 1.87 (s, 1H, OH), 1.73 (ddd, J = 12.4, 7.3, 4.1 Hz, 1H, H-13b), 1.02 (d, J = 7.1 Hz, 3H, H-33), 0.14 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 103.9 (C-17), 86.1 (C-18), 80.2 (C-15), 78.4 (C-12), 65.7 (C-11), 36.1 (C-14), 35.3 (C-13), 22.4 (C-16), 14.0 (C-33), 0.2 (3C, TMS) ppm; **IR** (film): $\tilde{\nu}$ = 3425, 2961, 2937, 2901, 2878, 2177, 1777, 1730, 1634, 1596, 1455, 1423, 1383, 1364, 1341, 1249, 1203, 1171, 1090, 1072, 1029, 982, 949, 927, 903, 838, 759, 698, 642, 569, 530, 478 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{12}H_{22}O_2SiNa^+$: 249.1281, found: 249.1281.

(4R,5S)-5-Methyl-1-(trimethylsilyl)oct-7-en-1-yn-4-yl 4-nitrobenzoate (89)

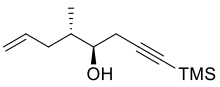


PPh_3 (**195a**) (1.16 g, 4.40 mmol) and *p*-nitrobenzoic acid (589 mg, 3.52 mmol) were subsequently added to a stirred solution of alcohol **87** (247 mg, 1.17 mmol) in PhMe (23 mL) at rt. Then, DIAD (94%, 0.89 mL, 4.22 mmol) was added to the stirred reaction mixture at rt, and stirring was continued for 20 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 4:1) affording compound **89** as a colourless oil (100 mg, 24%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 – 8.20 (m, 4H), 5.84 – 5.72 (m, 1H), 5.15 (dt, J = 6.1, 6.1 Hz, 1H), 5.08 – 5.00 (m, 2H), 2.75 – 2.58 (m, 2H), 2.36 – 2.27 (m, 1H), 2.19 – 2.09 (m, 1H), 2.04 – 1.95 (m, 1H), 1.00 (d, J = 6.9 Hz, 3H), 0.06 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 164.2, 150.7, 136.1, 135.9, 130.9 (2C), 123.7 (2C), 117.0, 101.9, 87.6, 76.8, 36.8, 35.8, 23.1, 15.5, 0.0 (3C) ppm; $C_{19}H_{25}NO_4Si$.

(4S,5S)-5-Methyl-1-(trimethylsilyl)oct-7-en-1-yn-4-ol (36b)

Procedure B (Recycling)

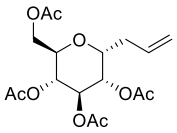


DIBAL (1.0 M in DCM, 14 mL, 14 mmol) was added to a stirred solution of ester **89** (330 mg, 918 µmol) in DCM (13.4 mL) at -78 °C and stirring was continued for 2 h. Then, the reaction mixture was warmed to rt and stirring was continued for 16 h. The reaction was cooled to -78 °C and quenched with EtOAc (20 mL). Then, the mixture was warmed to rt, diluted with sat. aq. Na/K tartrate solution (40 mL) and stirring was continued for 15 min. After dilution with water (15 mL), the aq. phase was extracted with MTBE (2 x 50 mL). The combined extracts were washed with brine (100 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, pentane/MTBE, 20:1) affording compound **36b** as a colourless oil (136 mg, 70%). The analytical and spectroscopic data of the isolated compound were identical with those shown above.

5.2.1.5.2. The Sugar-Based Alkyne

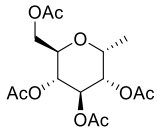
(2R,3R,4R,5S,6R)-2-(Acetoxymethyl)-6-methyltetrahydro-2H-pyran-3,4,5-triyl triacetate (40a)

Procedure B (DCM, TMSOTf)



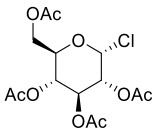
per-*O*-Acetyl-α-*D*-glucopyranose (**50**) (20.2 g, 51.7 mmol) was reacted with allyl-TMS (**52**) (41.1 mL, 258 mmol) in a similiar fashion as before (Chapter 5.2.1.2), but with TMSOTf (18.7 mL, 103 mmol) in MeCN/DCM (1:1, 200 mL) as the solvent. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 3:1 to 2:1) affording major compound **40a** as an anomeric mixture (1.36 g, 7%, α:β = 7:1) and minor byproduct **94** (130 mg, 1%). After recrystallization, the analytical and spectroscopic data of the isolated major compound were identical with those shown above.

Analytical and spectral data of the minor byproduct **94**: $[\alpha]_D^{20}$: +52.6 (c = 1.10, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.34 (t, J = 9.3 Hz, 1H), 5.05 (dd, J = 9.7, 5.8 Hz, 1H), 4.99 (dd, J = 9.7, 9.0 Hz, 1H), 4.44 – 4.36 (m, 1H), 4.23 (dd, J = 12.2, 4.8 Hz, 1H), 4.09 (dd, J = 12.2, 2.5 Hz, 1H), 3.90 (ddd, J = 9.6, 4.8, 2.5 Hz, 1H), 2.10 (s, 3H), 2.05 (s, 3H), 2.035 (s, 3H), 2.03 (s, 3H), 1.30 (d, J = 6.9 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.0, 170.5, 169.9, 169.8, 70.6, 70.3, 69.0, 68.9, 68.7, 62.4, 21.0, 20.9 (2C), 20.8, 12.6 ppm; **IR** (film): $\tilde{\nu}$ = 2958, 1741, 1433, 1368, 1218, 1145, 1106, 1033, 976, 909, 757, 718, 633, 602, 526, 500, 484, 444, 422 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{15}H_{22}O_9Na^+$: 369.1156, found: 369.1157. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[281]

(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-chlorotetrahydro-2H-pyran-3,4,5-triyl triacetate (95a)



4,4,5,5-Tetramethyl-2-(propa-1,2-dien-1-yl)-1,3,2-dioxaborolane (2.20 mL, 12.2 mmol) was added to a stirred solution of per-*O*-acetyl-α-*D*-glucopyranose (**50**) (2.39 g, 6.12 mmol) and $SnCl_4$ (6.12 mL, 6.12 mmol) in DCM (24.5 mL) at rt and stirring was continued for 3 d. The reaction mixture was cautiously quenched with aq. K_2CO_3 (1.0 M, 50 mL) and water (17.5 mL). The aq. phase was extracted with DCM (2 x 105 mL) and the combined extracts were washed with water (70 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash

[281] R. Bihovsky, C. Selick, I. Giusti, *J. Org. Chem.* **1988**, *53*, 4026-4031.

chromatography (SiO_2, hexane/EtOAc, 3:1) affording compound **95a** as a yellow crystalline solid (950 mg, 42%).

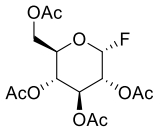
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.29 (d, J = 4.0 Hz, 1H), 5.55 (t, J = 9.8 Hz, 1H), 5.13 (t, J = 9.7 Hz, 1H), 5.00 (dd, J = 10.1, 4.0 Hz, 1H), 4.34 – 4.28 (m, 2H), 4.15 – 4.08 (m, 1H), 2.098 (s, 3H), 2.096 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.7, 170.07, 170.05, 169.6 90.2, 70.8, 70.4, 69.5, 67.4, 61.2, 20.9, 20.79, 20.76, 20.7 ppm; **IR** (film): $\tilde{\nu}$ = 1738, 1430, 1365, 1328, 1220, 1164, 1115, 1075, 1032, 976, 923, 910, 891, 847, 768, 675, 646, 597, 514, 485, 447, 420 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{14}H_{19}ClO_9Na^+$: 389.0610, found: 389.0610. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[282]

Indium(I) trifluoromethanesulfonate (96)

TfOH (0.62 mL, 6.98 mmol) was added to a stirred suspension of InCl (1.0 g, 6.7 mmol) in PhMe (30 mL) at rt and stirring was continued for 2 h, first resulting in a clear colourless solution and later on in a white precipitate. The crude precipitate was filtered under Ar and washed with pentane (5 x 20 mL). The solvent was removed under vacuum affording compound **96** as a white amorphous solid (1.54 g, 88%).

^{19}F-NMR (377 MHz, PhMe-d_8): δ = -77.6 ppm (3F); CF_3InO_3S. The analytical and spectroscopic data is in agreement with those previously reported in the literature.[283]

(2R,3R,4S,5R,6R)-2-(Acetoxymethyl)-6-fluorotetrahydro-2H-pyran-3,4,5-triyl triacetate (95b)

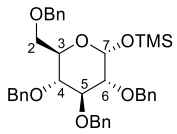


per-*O*-Acetyl-α-*D*-glucopyranose (**50**) (5.00 g, 12.8 mmol) was added to stirred HF·py (10.0 mL, 111 mmol) at rt and stirring was continued for 24 h. The reaction mixture was diluted with DCM (80 mL) and water (80 mL), and neutralized with solid Na_2CO_3. The aq. phase was extracted with DCM (3 x 50 mL). The combined extracts were washed with water (50 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 4:1 to 3:1) affording compound **95b** as a colourless crystalline solid (2.67 g, 59%).

[282] A. Steinmann, J. Thimm, J. Thiem, *Eur. J. Org. Chem.* **2007**, *33*, 5506-5513.
[283] C. L. B. Macdonald, A. M. Corrente, C. G. Andrews, A. Taylor, B. D. Ellis, *Chem. Commun.* **2004**, *2*, 250-251.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.76 (dd, $J_{H,F}$ = 52.8 Hz, $J_{H,H}$ = 2.8 Hz, 1H), 5.50 (t, J = 9.9 Hz, 1H), 5.16 (t, J = 9.9 Hz, 1H), 4.96 (ddd, $J_{H,F}$ = 24.2 Hz, $J_{H,H}$ = 10.2, 2.8 Hz, 1H), 4.29 (dd, J = 12.3, 3.9 Hz, 1H), 4.19 (ddd, J = 10.4, 4.1, 2.1 Hz, 1H), 4.15 (dd, J = 12.3, 2.1 Hz, 1H), 2.111 (s, 3H), 2.108 (s, 3H), 2.05 (s, 3H), 2.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.8, 170.19, 170.16, 169.6, 103.9 (d, $J_{C,F}$ = 229.6 Hz), 70.3 (d, $J_{C,F}$ = 24.4 Hz), 69.9 (d, $J_{C,F}$ = 4.5 Hz), 69.5, 67.4, 61.3, 20.9, 20.8, 20.74, 20.73 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -149.7 ppm; **IR** (film): $\tilde{\nu}$ = 1732, 1433, 1376, 1220, 1166, 1108, 1064, 1034, 984, 919, 902, 886, 835, 773, 672, 654, 611, 572, 553, 532, 488, 476, 454, 439 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{14}H_{19}O_9FNa^+$: 373.0905, found: 373.0902. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[284]

Trimethyl(((2S,3R,4S,5R,6R)-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)tetrahydro-2H-pyran-2-yl)oxy)silane (98a)



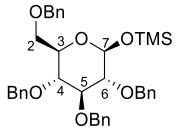
Allyl-TMS (**52**) (147 µL, 925 µmol) was added to a stirred solution of 2,3,4,6-tetra-O-benzyl-α-*D*-glucopyranose (**97**) (100 mg, 185 µmol) and Re_2O_7 (1 mol%, 1 mg, 2 µmol) in DCM (5 mL) at rt and the resulting reaction mixture was stirred for 6 d. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 20:1) affording both minor β-anomer *epi*-**98a** (19 mg, 17%) and major α-isomer **98a** (36 mg, 32%) as a colourless solid.

Analytical and spectral data of the major α-anomer **98a**: **m.p.**: 135-136 °C; **$[\alpha]_D^{20}$**: +28.3 (c = 1.27, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.38 – 7.23 (m, 18H, Ph), 7.15 – 7.09 (m, 2H, Ph), 5.17 (d, J = 3.3 Hz, 1H, H-7), 4.98 (d, J = 10.8 Hz, 1H, CH_2Ph), 4.83 (d, J = 10.5 Hz, 1H, CH_2Ph), 4.82 (d, J = 10.9 Hz, 1H, CH_2Ph), 4.74 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.65 (d, J = 12.2 Hz, 1H, CH_2Ph), 4.64 (d, J = 11.9 Hz, 1H, CH_2Ph), 4.45 (d, J = 10.6 Hz, 1H, CH_2Ph), 4.44 (d, J = 12.1 Hz, 1H, CH_2Ph), 4.00 (t, J = 9.3 Hz, 1H, H-5), 3.90 (dt, J = 9.9, 2.7 Hz, 1H, H-3), 3.77 (dd, J = 10.5, 3.2 Hz, 1H, H-2a), 3.69 (dd, J = 10.1, 9.0 Hz, 1H, H-4), 3.59 (dd, J = 10.5, 2.1 Hz, 1H, H-2b), 3.51 (dd, J = 9.6, 3.2 Hz, 1H, H-6), 0.16 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 138.9 (*i*-Ph), 138.3 (*i*-Ph), 138.2 (*i*-Ph), 137.9 (*i*-Ph), 128.4 (6C, *m*-Ph), 128.3 (2C, *m*-Ph), 128.01 (2C, *o*-Ph), 127.97 (2C, *o*-Ph), 127.93 (2C, *o*-Ph), 127.91 (2C, *o*-Ph), 127.8 (*p*-Ph), 127.71 (*p*-Ph), 127.65 (*p*-Ph), 127.5 (*p*-Ph), 91.7 (C-7), 81.8 (C-5), 80.8 (C-6), 77.7 (C-4), 75.6 (CH_2Ph), 75.2 (CH_2Ph), 73.4 (CH_2Ph), 73.0 (CH_2Ph), 69.9 (H-3), 68.4 (C-2), -0.0 (3C, TMS) ppm; **IR** (film): $\tilde{\nu}$ = 3089, 3062, 3031, 2920, 2869, 1723, 1713, 1603, 1584, 1497,

[284] M. H. E. Griffith, O. Hindsgaul, *Carbohydr. Res.* **1991**, *211*, 163-166.

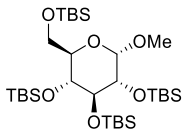
1453, 1362, 1315, 1271, 1267, 1207, 1150, 1090, 1070, 1028, 909, 878, 846, 739, 736, 701, 697, 648, 609, 578, 532, 481, 461, 413 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{37}H_{44}O_6SiNa^+$: 635.2799, found: 635.2799. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[285]

Analytical and spectral data of the minor β-anomer *epi*-**98a**: **m.p.**: 142-143 °C; $[\alpha]_D^{20}$: +20.1



(c = 0.49, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.37 – 7.25 (m, 18H, Ph), 7.21 – 7.16 (m, 2H, Ph), 4.94 (d, J = 10.9 Hz, 1H, CH_2Ph), 4.92 (d, J = 10.9 Hz, 1H, CH_2Ph), 4.82 (d, J = 10.8 Hz, 1H, CH_2Ph), 4.78 (d, J = 10.9 Hz, 1H, CH_2Ph), 4.73 (d, J = 11.0 Hz, 1H, CH_2Ph), 4.66 (d, J = 7.5 Hz, 1H, H-7), 4.61 (d, J = 12.2 Hz, 1H, CH_2Ph), 4.55 (d, J = 10.8 Hz, 1H, CH_2Ph), 4.54 (d, J = 12.2 Hz, 1H, CH_2Ph), 3.73 – 3.66 (m, 2H, H-2), 3.65 – 3.56 (m, 2H, H-4 and H-5), 3.47 (ddd, J = 9.4, 4.4, 2.2 Hz, 1H, H-3), 3.43 – 3.37 (m, 1H, H-6), 0.22 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 138.8 (*i*-Ph), 138.6 (*i*-Ph), 138.4 (*i*-Ph), 138.3 (*i*-Ph), 128.53 (2C, *m*-Ph), 128.51 (4C, *m*-Ph), 128.46 (2C, *m*-Ph), 128.3 (2C, *o*-Ph), 128.1 (2C, *o*-Ph), 128.0 (2C, *o*-Ph), 127.9 (*p*-Ph), 127.8 (3C, *p*-Ph and *o*-Ph), 127.73 (*p*-Ph), 127.65 (*p*-Ph), 98.2 (C-7), 84.8 (C-5), 84.1 (C-6), 78.1 (C-4), 75.8 (CH_2Ph), 75.11 (CH_2Ph), 75.06 (CH_2Ph), 75.0 (C-3), 73.6 (CH_2Ph), 69.2 (C-2), 0.4 (3C, TMS) ppm; **IR** (film): $\tilde{\nu}$ = 3087, 3063, 3030, 2918, 2861, 1725, 1603, 1584, 1496, 1452, 1399, 1361, 1326, 1274, 1269, 1213, 1147, 1086, 1073, 1045, 1027, 1001, 940, 905, 858, 830, 743, 695, 626, 608, 547, 463, 438, 429, 416, 406 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{37}H_{44}O_6SiNa^+$: 635.2799, found: 635.2797.

(((2R,3R,4S,5R,6S)-2-(((Tert-butyldimethylsilyl)oxy)methyl)-6-methoxytetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (99b)

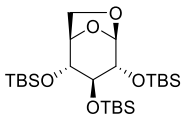


TBSOTf (17.7 mL, 77.2 mmol) was added to a stirred suspension of α-*D*-methylglucoside (**99a**) (2.50 g, 12.9 mmol) and 2,6-lutidine (12.1 mL, 104 mmol) in DCM (64.4 mL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 3.5 h. The reaction was diluted with MTBE (100 mL) and poured into aq. HCl (1.0 M, 100 mL). The organic extract was washed with water (50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, PhMe) affording compound **99b** as a colourless oil (8.27 g, 99%).

[285] L. F. Tietze, R. Fischer, H.-J. Guder, *Synthesis* **1982**, *11*, 946-948.

[α]$_D^{20}$: +55.9 (c = 1.09, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.62 (d, J = 3.3 Hz, 1H), 3.85 – 3.78 (m, 3H), 3.75 (dd, J = 5.4, 3.4 Hz, 1H), 3.67 – 3.61 (m, 1H), 3.58 (dd, J = 8.5, 3.2 Hz, 1H), 3.38 (s, 3H), 0.89 (s, 9H), 0.885 (s, 9H), 0.88 (s, 18H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 6H), 0.054 (s, 6H), 0.048 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 97.8, 76.1, 74.3, 72.8, 72.5, 63.4, 54.7, 26.3 (3C), 26.21 (3C), 26.17 (3C), 26.0 (3C), 18.6, 18.5, 18.2, 18.1, -2.8, -3.0, -3.5, -3.6, -4.3, -4.4, -4.8, -5.2 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2895, 2857, 1472, 1463, 1407, 1389, 1361, 1252, 1216, 1190, 1163, 1087, 1073, 1003, 981, 938, 914, 883, 831, 814, 773, 758, 668, 626, 572, 491, 442 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{31}H_{70}O_6Si_4Na^+$: 673.4142, found: 673.4144. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[286]

(((1R,2R,3S,4R,5R)-6,8-Dioxabicyclo[3.2.1]octane-2,3,4-triyl)tris(oxy))tris(tert-butyldimethylsilane) (100)



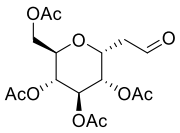
Allyl-TMS (**52**) (244 µL, 1.54 mmol) and TMSOTf (167 µL, 921 µmol) were subsequently added to a stirred solution of methylglucoside **99b** (0.50 g, 768 µmol) and 2,6-lutidine (143 µL, 1.23 µmol) in DCM (5 mL) at 0 °C. The reaction mixture was warmed to rt and stirring was continued for 20 h. The reaction was diluted with MTBE (20 mL) and poured into aq. HCl (1.0 M, 20 mL). The organic extract was washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, PhMe) affording compound **100** as a colourless oil (150 mg, 39%).

m.p.: 57-58 °C; **[α]$_D^{20}$**: -24.7 (c = 1.18, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.25 (t, J = 1.9 Hz, 1H), 4.36 – 4.32 (m, 1H), 4.08 (dd, J = 6.8, 1.1 Hz, 1H), 3.65 (t, J = 6.4 Hz, 1H), 3.58 (p, J = 1.5 Hz, 1H), 3.47 (td, J = 2.0, 1.1 Hz, 1H), 3.42 (dq, J = 1.6, 1.0 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 3H), 0.074 (s, 3H), 0.071 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 102.2, 76.5, 75.4, 72.9, 71.9, 64.6, 26.0 (3C), 25.9 (3C), 25.8 (3C), 18.3, 18.2, 17.9, -4.3, -4.4 (3C), -4.5, -4.6 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2928, 2894, 2857, 1634, 1472, 1463, 1389, 1361, 1328, 1252, 1189, 1100, 1083, 1031, 1006, 991, 964, 946, 918, 892, 869, 831, 813, 772, 705, 669, 569, 513, 458 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{24}H_{52}O_5Si_3Na^+$: 527.3015, found: 527.3018. The

[286] M.-Y. Chen, L. N. Patkar, K.-C. Lu, A. S.-Y. Lee, C.-C. Lin, *Tetrahedron* **2004**, *60*, 11465-11475.

analytical and spectroscopic data are in agreement with those previously reported in the literature.[287]

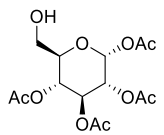
(2R,3R,4R,5S,6R)-2-(Acetoxymethyl)-6-(2-oxoethyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (54b)



O_3 was bubbled through a stirred solution of alkene **40a** (2.73 g, 7.33 mmol) in DCM (39 mL) at -78 °C until the solution became blue after 6 h. Then Ar was bubbled through the solution until it turned colourless again. Zn dust (8.0 g) and AcOH (8 mL) were added at -78 °C and the reaction mixture was warmed to rt and stirring was continued for 17 h. The suspension was filtered through Celite® and the filter cake was washed with DCM (2 x 25 mL). The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 2:1 to 1:1) affording compound **54b** as a glassy colourless solid (2.48 g, 90%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.73 (dd, J = 2.5, 1.5 Hz, 1H), 5.26 (t, J = 8.6 Hz, 1H), 5.13 (dd, J = 9.0, 5.5 Hz, 1H), 4.98 (t, J = 8.6 Hz, 1H), 4.86 (dt, J = 8.0, 5.9 Hz, 1H), 4.26 (dd, J = 12.2, 5.5 Hz, 1H), 4.07 (dd, J = 12.1, 2.7 Hz, 1H), 3.87 (ddd, J = 8.6, 5.5, 2.8 Hz, 1H), 2.83 (ddd, J = 16.6, 8.0, 2.6 Hz, 1H), 2.78 (ddd, J = 16.6, 6.1, 1.4 Hz, 1H), 2.08 (s, 3H), 2.044 (s, 3H), 2.041 (s, 3H), 2.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 198.1, 170.8, 170.1, 169.61, 169.60, 70.3, 70.0, 69.4, 68.2, 67.5, 61.9, 41.8, 20.9, 20.83, 20.79, 20.77 ppm; **IR** (film): $\tilde{\nu}$ = 2972, 1738, 1432, 1367, 1212, 1090, 1031, 982, 901, 846, 723, 644, 601, 537, 484, 457, 416 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{16}H_{22}O_{10}Na^+$: 397.1105, found: 397.1105. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[288]

(2R,3R,4S,5R,6R)-6-(Hydroxymethyl)tetrahydro-2H-pyran-2,3,4,5-tetrayl tetraacetate (101a)



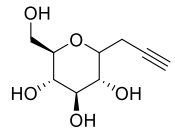
CRL (>700 U/mg, 260 mg, 182.000 U) was added to a stirred suspension of per-*O*-acetyl-α-*D*-glucopyranose (**50**) (1.00 g, 2.56 mmol) in aq. phosphate buffer (100 mM, pH 7, 50 mL) at rt and stirring was continued for 3 d. The reaction mixture was filtered through Celite® and the filter cake was washed with water (2 x 30 mL). The aq. phase was extracted with EtOAc (4x 50 mL) and the combined extracts were dried over

[287] J. P. Henschke, P.-Y. Wu, C.-W. Lin, S.-F. Chen, P.-C. Chiang, C.-N. Hsiao, *J. Org. Chem.* **2015**, *80*, 2295-2309.
[288] P. Arya, A. Barkley, K. D. Randell, *J. Comb. Chem.* **2002**, *4*, 193-198.

anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, EtOAc) affording compound **101a** as a colourless solid (279 mg, 31%)

$[\alpha]_D^{20}$: +55.5 (c = 0.95, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.33 (d, J = 3.7 Hz, 1H), 5.52 (dd, J = 10.2, 9.6 Hz, 1H), 5.10 (dd, J = 10.0, 9.7 Hz, 1H), 5.06 (dd, J = 10.2, 3.7 Hz, 1H), 3.91 (ddd, J = 10.2, 3.0, 2.2 Hz, 1H), 3.71 (dd, J = 12.9, 2.2 Hz, 1H), 3.57 (dd, J = 12.8, 4.0 Hz, 1H), 2.24 (s, 1H), 2.17 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.5, 170.4, 169.9, 169.1, 89.2, 72.1, 69.6, 69.4, 68.3, 60.8, 21.1, 20.9, 20.8, 20.6 ppm; **IR** (film): $\tilde{\nu}$ = 3444, 2927, 1739, 1433, 1369, 1217, 1151, 1072, 1034, 939, 917, 854, 775, 746, 689, 603, 544, 523, 483 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{14}H_{20}O_{10}Na^+$: 371.0949, found: 371.0948. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[289]

(2R,3S,4R,5R,6R)-2-(Hydroxymethyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triol (39c)



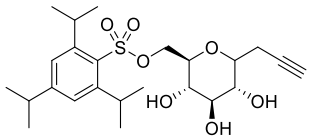
Ohira Bestmann reagent (**56**) (1.32 g, 6.88 mmol) was added to a stirred suspension of aldehyde **54b** (2.15 g, 5.73 mmol) and K_2CO_3 (1.58 g, 11.5 mmol) in MeOH (86 mL) at rt resulting in a colour change from colourless to yellow, and stirring was continued for 8 h. The reaction was quenched and neutralized with aq. $NaHCO_3$ (5%, 28 mL) and water was evaporated. The resulting residue was washed with MeCN (5 x 50 mL) and MeOH (5 x 50 mL), and the combined organic filtrates were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, DCM/MeOH, 3:1) affording compound **39c** as a colourless oil (1.14 g, 98%, *d.r.* = 1:1).

^{1}H NMR (signal set corresponds to the anomeric mixture, 400 MHz, CD_4OD): δ = 3.98 (ddd, J = 8.1, 6.6, 5.5 Hz, 1H), 3.78 – 3.60 (m, 7H), 3.59 – 3.48 (m, 3H), 3.44 – 3.34 (m, 3H), 3.29 – 3.24 (m, 4H), 3.20 – 3.13 (m, 4H), 2.60 (dt, J = 17.3, 2.6 Hz, 1H), 2.50 (d, J = 2.7 Hz, 1H), 2.48 (dd, J = 2.7, 1.4 Hz, 1H), 2.39 (ddd, J = 17.0, 5.7, 2.5 Hz, 1H), 2.19 (t, J = 2.7 Hz, 1H), 2.17 (t, J = 2.7 Hz, 1H) ppm; **^{13}C NMR** (signal set corresponds to the anomeric mixture, 101 MHz, CD_4OD): δ = 82.0, 81.8, 81.7, 79.6, 79.0, 75.9, 75.1, 74.7, 74.0, 72.4, 71.8, 71.6, 70.9, 70.8, 63.0, 62.5, 22.5, 16.8 ppm; **IR** (film): $\tilde{\nu}$ = 3432, 3389, 3275, 2944, 2933, 2904, 2888, 1645, 1458, 1441, 1422, 1337, 1360, 1304, 1257,

[289] T. Rodríguez-Pérez, I. Lavandera, S. Fernández, Y. S. Sanghvi, M. Ferrero, V. Gotor, *Eur. J. Org. Chem.* **2007**, *17*, 2769-2778.

1224, 1214, 1120, 1099, 1063, 1040, 1026, 932, 911, 887, 831, 704, 686, 651, 631, 610, 539, 491 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_9H_{14}O_5Na^+$: 225.0733, found: 225.0734.

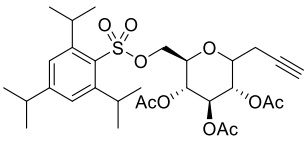
((2R,3S,4R,5R,6R)-3,4,5-Trihydroxy-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)methyl 2,4,6-triisopropylbenzenesulfonate (102a)



2,4,6-Triisopropylbenzenesulfonyl chloride (165 mg, 544 µmol) was added to a stirred solution of tetrol **39c** (100 mg, 495 µmol) in py (1.1 mL) at 0 °C and stirring was continued for 5 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, DCM/MeOH, 20:1) affording compound **102a** as a colourless oil (89 mg, 38%).

$[\alpha]_D^{20}$: -0.5 (c = 0.60, $CHCl_3$); **^{1}H NMR** (signal set corresponds to the anomeric mixture, 400 MHz, CD_4OD): δ = 7.29 (s, 4H), 4.31 (dd, J = 10.6, 1.8 Hz, 1H), 4.24 (dd, J = 10.6, 6.1 Hz, 1H), 4.16 (dd, J = 10.8, 2.4 Hz, 1H), 4.15 (dd, J = 13.6, 2.9 Hz, 1H), 4.13 (dd, J = 13.7, 2.7 Hz, 1H), 4.12 (dd, J = 13.5, 2.9 Hz, 1H), 4.06 (dd, J = 10.6, 6.6 Hz, 1H), 3.92 (dt, J = 9.7, 5.0 Hz, 1H), 3.80 (dd, J = 11.2, 3.6 Hz, 1H), 3.77 (dd, J = 10.8, 2.5 Hz, 1H), 3.70 (ddd, J = 8.4, 6.2, 2.7 Hz, 1H), 3.54 (dd, J = 8.3, 4.9 Hz, 1H), 3.49 (dd, J = 8.8, 7.1 Hz, 1H), 3.40 (ddd, J = 9.8, 6.6, 1.8 Hz, 1H), 3.26 – 3.18 (m, 2H), 3.18 – 3.09 (m, 2H), 2.97 – 2.85 (m, 2H), 2.54 – 2.45 (m, 2H), 2.37 (dd, J = 17.1, 2.8 Hz, 1H), 2.35 (ddd, J = 17.4, 4.9, 2.7 Hz, 1H), 2.15 (t, J = 2.7 Hz, 2H), 1.41 – 1.05 (m, 6H), 1.23 (d, J = 6.8 Hz, 36H) ppm; **^{13}C NMR** (signal set corresponds to the anomeric mixture, 101 MHz, CD_4OD): δ = 155.4 (2C), 152.3 (2C), 152.2 (2C), 130.7, 130.6, 125.0 (4C), 81.5, 81.3, 79.4, 78.98, 78.96, 74.8, 73.8, 73.61, 73.57, 71.8, 71.5, 71.4, 71.3, 71.03, 70.97, 70.8, 70.5, 69.7, 35.5 (2C), 30.81 (2C), 30.78 (2C), 25.12 (4C), 25.07 (2C), 24.0 (4C), 22.4, 17.4 ppm; **IR** (film): $\tilde{\nu}$ = 3336, 2954, 2929, 2898, 2857, 1733, 1678, 1641, 1499, 1471, 1463, 1408, 1389, 1348, 1286, 1252, 1152, 1092, 1042, 1006, 979, 937, 834, 813, 776, 762, 689, 674, 635, 542, 504, 468, 440, 429 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{24}H_{36}O_7SNa^+$: 491.2074, found: 491.2074.

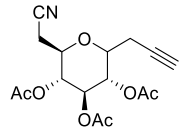
(2R,3S,4R,5R,6R)-2-(Prop-2-yn-1-yl)-6-((((2,4,6-triisopropylphenyl)sulfonyl)oxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (102b)



Ac_2O (182 µL, 1.92 mmol) and $BF_3{\cdot}OEt_2$ (50 µL, 405 µmol) were subsequently added to a stirred solution of triol **102a** (80 mg, 170 µmol) in DCM (0.5 mL) at rt and stirring was continued for 1 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:3) affording compound **102b** as a colourless amorphous solid (75 mg, 74%, *d.r.* = 1.25:1).

^{1}H NMR (1.25:1 anomer ratio, asterisk denotes minor anomer, 400 MHz, $CDCl_3$): δ = 7.18 (br s, 2H), 7.18* (br s, 2H), 5.31* (t, J = 8.1 Hz, 1H), 5.18 (t, J = 9.4 Hz, 1H), 5.03* (dd, J = 8.3, 5.2 Hz, 1H), 5.01 (t, J = 9.6 Hz, 1H), 4.93 (dd, J = 10.1, 9.4 Hz, 1H), 4.86* (dd, J = 8.5, 7.9 Hz, 1H), 4.29* (td, J = 7.2, 5.1 Hz, 1H), 4.17 – 4.00 (m, 4H), 4.17 – 4.00* (m, 5H), 3.77 (ddd, J = 10.1, 5.8, 3.1 Hz, 1H), 3.55 (dt, J = 9.9, 5.1 Hz, 1H), 2.97 – 2.84 (m, 1H), 2.97 – 2.84* (m, 1H), 2.53* (d, J = 2.7 Hz, 1H), 2.51* (dd, J = 2.8, 1.1 Hz, 1H), 2.45 (ddd, J = 17.5, 5.2, 2.8 Hz, 1H), 2.39 (ddd, J = 17.2, 5.3, 2.9 Hz, 1H), 2.06* (s, 3H), 2.03* (s, 3H), 2.02 (s, 3H), 2.02* (s, 3H), 2.01 (s, 3H), 2.00* (t, J = 2.7 Hz, 1H), 1.99 (s, 3H), 1.97 (t, J = 2.7 Hz, 1H), 1.28 – 1.26* (m, 18H), 1.26 – 1.22 (m, 18H) ppm; **^{13}C NMR** (signal set corresponds to the anomeric mixture, 101 MHz, CD_4OD): δ = 170.5, 170.0, 169.8, 169.6 (3C), 154.1 (2C), 151.1 (2C), 148.3 (2C), 129.3, 129.2, 124.0 (4C), 78.7, 78.6, 75.9, 75.7, 74.0, 71.3, 70.9 (2C), 70.5, 70.2, 70.12, 70.10, 69.51, 69.47, 68.9, 68.6, 67.4, 66.8, 34.4 (2C), 29.81 (2C), 29.78 (2C), 24.9 (4C), 23.7 (4C), 22.2 (2C), 20.9, 20.84 (2C), 20.78 (2C), 20.7, 20.5, 18.5 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{30}H_{42}O_{10}SNa^+$: 617.2391, found: 617.2391.

(2R,3R,4R,5S)-2-(Cyanomethyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (103a)

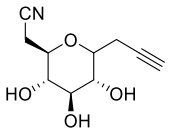


NaCN (6 mg, 126 µmol) was added to a stirred solution of sulfonate **102b** (50 mg, 84 µmol) in DMA or DMSO (200 µL) at rt and stirring was continued for 8 h. Then, the reaction mixture was heated to 80 °C and stirring was again continued for 8 h. The crude reaction mixture was purified by flash chromatography (SiO_2, hexane/EtOAc, 3:1) affording compound **103a** as a colourless amorphous solid (23 mg, 81%, *d.r.* = 2:1).

^{1}H NMR (2:1 anomer ratio, asterisk denotes minor anomer, 400 MHz, $CDCl_3$): δ = 5.34* (t, J = 8.7 Hz, 1H), 5.20 (t, J = 9.4 Hz, 1H), 5.13* (dd, J = 9.1, 5.6 Hz, 1H), 5.05 (t, J = 9.6 Hz, 1H), 4.04 (t,

J = 9.6 Hz, 1H), 4.88* (t, J = 8.8 Hz, 1H), 4.38* (dt, J = 9.0, 5.8 Hz, 1H), 4.00* (dt, J = 9.1, 5.9 Hz, 1H), 3.75 (dt, J = 9.8, 5.9 Hz, 1H), 3.65 (ddd, J = 10.1, 5.7, 4.6 Hz, 1H), 2.71 – 2.58 (m, 2H), 2.71 – 2.58* (m, 4H), 2.55 (ddd, J = 17.4, 4.6, 2.7 Hz, 1H), 2.48 (ddd, J = 17.3, 5.7, 2.7 Hz, 1H), 2.10* (t, J = 2.6 Hz, 1H), 2.08 (s, 3H), 2.08* (s, 3H), 2.07* (s, 3H), 2.05 (t, J = 2.6 Hz, 1H), 2.04 (s, 3H), 2.04* (s, 3H), 2.01 (s, 3H) ppm; **^{13}C NMR** (signal set corresponds to the anomeric mixture, 101 MHz, CD_4OD): δ = 170.4, 170.0, 169.90, 169.85, 169.63, 169.60, 128.5, 126.5, 78.5, 78.3, 77.5, 77.4, 76.8, 76.0, 73.5, 73.4, 71.73, 71.68, 71.2, 71.1, 69.7, 69.6, 67.5, 38.2, 36.7, 22.2, 21.5 (2C), 20.9, 20.8 (2C), 20.7 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{16}H_{19}NO_7Na^+$: 360.1052, found: 360.1054.

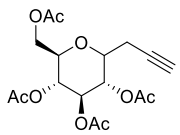
2-((2R,3S,4R,5R)-3,4,5-Trihydroxy-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetonitrile (103b)



Nitrile **103a** (21 mg, 61 µmol) was suspended in methanolic HCl (1.25 M, 1.25 mL) at 0 °C and stirring was continued for 4 d. Then, Et_2O/MeOH (1:1, 2 mL) was added and the reaction mixture was heated to 35 °C and stirring was again continued for 1 d. The solvents were evaporated and the crude was dissolved in MTBE (5 mL). The organic phase was washed with water (5 mL) and brine (5 mL), and was dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, DCM/MeOH, 20:1) affording compound **103b** as a colourless oil (9 mg, 67%, *d.r.* = 1.5:1).

^{1}H NMR (1.5:1 anomer ratio, asterisk denotes minor anomer, OH not visible, 400 MHz, CD_3OD): δ = 3.99* (dt, J = 8.4, 6.1 Hz, 1H), 3.65 –3.56* (m, 1H), 3.58 –3.50 (m, 1H), 3.40* (t, J = 8.8 Hz, 1H), 3.34 (ddd, J = 9.7, 6.4, 3.4 Hz, 1H), 3.27 – 3.23 (m, 2H), 3.18* (d, J = 8.5 Hz, 1H), 3.12 (t, J = 8.8 Hz, 1H), 3.10* (t, J = 9.0 Hz, 1H), 2.82 (dd, J = 17.1, 3.5 Hz, 1H), 2.77* (dd, J = 17.1, 3.9 Hz, 1H), 2.70* (dd, J = 17.0, 5.9 Hz, 1H), 2.64 (dd, J = 16.9, 6.2 Hz, 1H), 2.59 (dt, J = 17.2, 2.8 Hz, 1H), 2.52* (d, J = 2.7 Hz, 1H), 2.50* (dd, J = 2.7, 1.5 Hz, 1H), 2.37 (ddd, J = 17.4, 6.2, 2.8 Hz, 1H), 2.19* (t, J = 2.8 Hz, 1H), 2.18 (t, J = 2.7 Hz, 1H) ppm; **^{13}C NMR** (1.5:1 anomer ratio, asterisk denotes minor anomer, 101 MHz, CD_3OD): δ = 118.6, 118.5*, 81.3*, 81.2, 79.3*, 78.9, 76.4, 76.2*, 74.4*, 74.3, 74.2*, 73.9, 72.3, 71.2*, 70.9, 70.4*, 22.4, 21.6*, 21.5, 16.9* ppm; **IR** (film): $\tilde{\nu}$ = 3358, 3284, 2974, 2903, 2258, 1693, 1663, 1576, 1415, 1368, 1298, 1255, 1219, 1190, 1079, 1047, 1008, 928, 878, 806, 636, 595, 556, 526 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{10}H_{12}NO_4^-$: 210.0772, found: 210.0772.

(2R,3R,4R,5S,6R)-2-(Acetoxymethyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (39b)

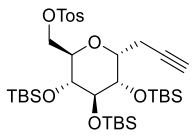


Ac_2O (468 µL, 4.95 mmol) and $BF_3{\cdot}OEt_2$ (50 µL, 405 µmol) were subsequently added to a stirred solution of tetrol **39c** (50 mg, 247 µmol) in DCM (0.5 mL) at rt and stirring was continued for 1 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:3) affording compound **39b** as a colourless amorphous oil (44 mg, 48%, *d.r.* = 1.25:1).

(The sample contained traces of Ac_2O) **^{1}H NMR** (1.25:1 anomer ratio, asterisk denotes minor anomer, 400 MHz, $CDCl_3$): δ = 5.30 (t, J = 8.7 Hz, 1H), 5.18* (t, J = 9.4 Hz, 1H), 5.15 – 5.05 (m, 1H), 5.15 – 5.05* (m, 1H), 5.03* (t, J = 9.5 Hz, 1H), 4.97 (dd, J = 9.1, 8.4 Hz, 1H), 4.37 (dt, J = 9.0, 5.7 Hz, 1H), 4.26* (dd, J = 12.3, 5.4 Hz, 1H), 4.23 (dd, J = 13.3, 5.2 Hz, 1H), 4.12 (dd, J = 5.2, 2.6 Hz, 1H), 4.09* (dd, J = 5.2, 2.6 Hz, 1H), 3.91 (ddd, J = 9.1, 5.4, 2.7 Hz, 1H), 3.67* (ddd, J = 9.9, 4.9, 2.3 Hz, 1H), 3.60* (ddd, J = 9.7, 5.8, 4.8 Hz, 1H), 2.65 (ddd, J = 17.4, 9.0, 2.7 Hz, 1H), 2.54 (ddd, J = 17.1, 5.7, 2.6 Hz, 1H), 2.52* (ddd, J = 17.2, 4.6, 2.4 Hz, 1H), 2.46* (ddd, J = 17.3, 5.7, 2.7 Hz, 1H), 2.21 (s, 3H), 2.21 (t, J = 3.3 Hz, 1H), 2.21* (t, J = 3.3 Hz, 1H), 2.08 (s, 3H), 2.07* (s, 3H), 2.05 (s, 3H), 2.03* (s, 3H), 2.025 (s, 3H), 2.01* (s, 3H), 1.99* (s, 3H) ppm; **^{13}C NMR** (1.25:1 anomer ratio, asterisk denotes minor anomer, 101 MHz, $CDCl_3$): δ = 170.92*, 170.89, 170.6*, 170.2, 169.8, 169.8*, 169.7, 169.6*, 78.9, 78.81, 78.79*, 78.2*, 75.84*, 75.78*, 74.1*, 71.4*, 71.1, 70.8, 70.7*, 69.9, 69.8, 69.6, 68.4*, 68.3, 62.2*, 62.0, 22.33*, 22.28, 20.89 (2C), 20.85*, 20.83, 20.78*, 20.7* ppm; **IR** (film): $\tilde{\nu}$ = 3281, 2956, 1738, 1432, 1367, 1201, 1142, 1093, 1031, 980, 907, 735, 651, 602, 541, 485, 457, 425 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{17}H_{22}O_9Na^+$: 393.1155, found: 393.1156.

((2R,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)methyl 4-methylbenzenesulfonate (104)

Procedure A (only α)



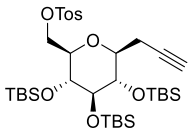
TosCl (136 mg, 716 µmol) was added to a stirred solution of alcohol **57** (300 mg, 551 µmol), TEA (92.1 µL, 661 µmol) and 4-DMAP (67.3 mg, 551 µmol) in DCM (1.77 mL) at rt and stirring was continued for 16 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 20:1) affording compound **104** as a colourless crystalline solid (377 mg, 98%).

Procedure B (anomeric mixture)

TosCl (161 mg, 845 µmol) was added to a stirred solution of an anomeric mixture of alcohol **57** (355 mg, 651 µmol), TEA (109 µL, 782 µmol) and 4-DMAP (79.6 mg, 651 µmol) in DCM (2.1 mL) at rt and stirring was continued for 16 h resulting in a colour change from colourless to brown. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 30:1) affording both major α-anomer **104** (132 mg, 29%) and minor β-anomer *epi*-**104** (39 mg, 9%) as a colourless crystalline solid.

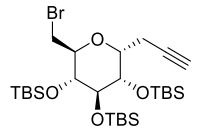
Analytical and spectral data of the major α-anomer **104**: **m.p.**: 90-91 °C; $[\alpha]_D^{20}$: +17.9 (c = 1.06, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.81 – 7.78 (m, 2H), 7.35 – 7.31 (m, 2H), 4.30 – 4.25 (m, 1H), 4.07 – 4.02 (m, 2H), 3.76 (dd, J = 3.1, 1.9 Hz, 1H), 3.65 – 3.62 (m, 1H), 3.60 (ddd, J = 9.9, 5.0, 2.0 Hz, 1H), 3.45 (ddd, J = 3.0, 2.0, 1.0 Hz, 1H), 2.44 (s, 3H), 2.43 (ddd, J = 16.3, 9.7, 2.7 Hz, 1H), 2.16 (ddd, J = 16.2, 5.0, 2.8 Hz, 1H), 1.93 (t, J = 2.7 Hz, 1H), 0.89 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.063 (s, 3H), 0.057 (s, 3H), 0.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 144.9, 133.1, 130.0 (2C), 128.1 (2C), 80.8, 75.4, 73.3, 70.9, 70.3, 69.4, 68.2, 68.1, 26.2 (3C), 26.1 (3C), 25.8 (3C), 21.8, 20.9, 18.5, 18.3, 17.9, -3.5, -4.0, -4.3, -4.6, -4.8, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3313, 2953, 2929, 2896, 2857, 1599, 1471, 1468, 1362, 1254, 1189, 1177, 1139, 1110, 1087, 1055, 1021, 1005, 978, 931, 901, 878, 830, 812, 785, 665, 636, 553, 529, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{34}H_{62}O_7SSi_3Na^+$: 721.3416, found: 721.3424.

Analytical and spectral data of the minor β-anomer *epi*-**104**: $[\alpha]_D^{20}$: +15.7 (c = 1.12, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83 – 7.76 (m, 2H), 7.35 – 7.28 (m, 2H), 4.17 (dd, J = 10.2, Hz, 1H), 4.06 (dd, J = 10.2, 6.7 Hz, 1H), 3.91 – 3.84 (m, 2H), 3.75 (t, J = 1.8 Hz, 1H), 3.69 (ddd, J = 8.5, 5.5, 3.3 Hz, 1H), 3.59 (dt, J = 6.1, 1.4 Hz, 1H), 2.50 (ddd, J = 17.0, 8.1, 2.8 Hz, 1H), 2.43 (s, 3H), 2.33 (ddd, J = 16.8, 5.5, 2.7 Hz, 1H), 1.96 (t, J = 2.7 Hz, 1H), 0.87 (s, 9H), 0.86 (s, 9H), 0.84 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H), 0.085 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.04 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 144.7, 133.3, 129.9 (2C), 128.2 (2C), 81.1, 78.0, 76.0, 72.6, 72.2, 71.0, 70.3, 27.1, 25.91 (3C), 25.87 (3C), 25.86 (3C), 23.8, 21.8, 18.0 (3C), -3.7, -3.99, -4.03, -4.4, -4.5, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2954, 2929, 2887, 2857, 1599, 1472, 1362, 1253, 1189, 1177, 1117, 1086, 1006, 982, 931, 880, 835, 811, 770, 664, 627, 572, 554, 535, 502, 452, 413 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{34}H_{62}O_7SSi_3Na^+$: 721.3416, found: 721.3417.

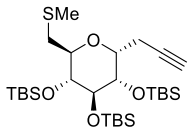
(((2S,3R,4R,5S,6R)-2-(Bromomethyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (106)



CO_2 (wet, evolved from dry ice) was bubbled through a stirred suspension of tosylate **104** (25 mg, 36 µmol), $NiBr_2$·glyme (10 mol%, 1 mg, 4 µmol), Mn dust (5 mg, 86 µmol) and neocuproine (26 mol%, 2 mg, 9 µmol) in DMF (142 µL) at rt. The reaction mixture was warmed to 70 °C and stirring was continued for 22 h under an atmosphere of CO_2. The crude reaction mixture was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording both compound **106** (2 mg, 9%) and some unreacted starting material **104** (23 mg, 90%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.04 (ddd, J = 12.8, 6.3, 4.5 Hz, 1H), 3.99 (ddd, J = 8.3, 6.6, 2.0 Hz, 1H), 3.88 – 3.85 (m, 1H), 3.78 – 3.74 (m, 2H), 3.71 (dd, J = 10.4, 6.1 Hz, 1H), 3.57 (dd, J = 10.4, 6.4 Hz, 1H), 2.51 (t, J = 2.9 Hz, 1H), 2.49 (dd, J = 2.7, 1.6 Hz, 1H), 1.96 (t, J = 2.7 Hz, 1H), 0.93 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.14 (s, 6H), 0.13 (s, 3H), 0.125 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.2, 74.5, 72.2, 70.2, 70.1, 68.9, 33.2, 26.3 (3C), 26.2 (3C), 25.9 (3C), 22.5, 21.3, 18.5, 18.3, 18.0, 14.2, -3.7, -4.1, -4.5, -4.8, -4.9 ppm; $C_{27}H_{55}BrO_4Si_3$.

(((2S,3R,4R,5S,6R)-2-((Methylthio)methyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (108)



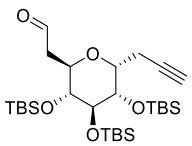
n-BuLi (1.6 M in hexane, 69.3 µL, 111 µmol) was slowly added to a stirred solution of tris(methylthio)methane (**110**) (15.2 µL, 114 µmol) in THF (0.5 mL) at -78 °C over the course of 5 min and stirring was continued for 20 min. In parallel tosylate **104** (50 mg, 72 µmol) was dissolved in THF (1.25 mL) and the solution was cooled to -78 °C. The previously prepared solution of lithiated tris(methylthio)methane (**110**) in THF (rinsed with 0.25 mL) was slowly added to the stirred reaction mixture at -78 °C over the course of 5 min and stirring was continued for 1 h. Then the reaction mixture was warmed to -50 °C and stirring was continued for 1.5 h. Then DMPU (13.4 µL, 111 µmol) were added to the stirred reaction mixture at -50 °C and stirring was continued for 5 min. The reaction mixture was warmed to -40 °C and stirring was continued for 1 h. In parallel *n*-BuLi (1.6 M in hexane, 69.3 µL, 111 µmol) was slowly added to a stirred solution of tris(methylthio)methane (**110**) (15.2 µL, 114 µmol) and DMPU (13.4 µL, 111 µmol) in THF (0.5 mL) at -78 °C over the course of 5 min and stirring was continued for 20 min. This solution of lithiated tris(methylthio)methane (**110**) in THF was added to

the stirred reaction mixture at -40 °C. The reaction mixture was warmed to rt and stirring was continued for 16 h. In parallel *n*-BuLi (1.6 M in hexane, 434 µL, 694 µmol) was slowly added to a stirred solution of tris(methylthio)methane (**110**) (95.1 µL, 715 µmol) and DMPU (83.9 µL, 694 µmol) in THF (5 mL) at -78 °C over the course of 5 min and stirring was continued for 20 min. This solution of lithiated tris(methylthio)methane (**110**) in THF was added to the stirred reaction mixture at rt and stirring was continued for 5 h. The reaction was quenched with sat. aq. NH_4Cl (5 mL) and the aq. phase was extracted with MTBE (2 x 10 mL). The combined organic extracts were subsequently washed with sat. aq. $NaHCO_3$ (5 mL) and brine (5 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 75:1) affording compound **108** as a colourless oil (8 mg, 19%).

$[\alpha]_D^{20}$: +6.1 (c = 0.80, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.00 – 3.94 (m, 2H), 3.86 – 3.82 (m, 1H), 3.71 – 3.67 (m, 2H), 2.96 (dd, J = 13.4, 6.9 Hz, 1H), 2.73 (dd, J = 13.4, 7.1 Hz, 1H), 2.51 (ddd, J = 16.4, 8.4, 2.7 Hz, 1H), 2.46 (ddd, J = 16.3, 6.3, 2.8 Hz, 1H), 2.12 (s, 3H), 1.96 (t, J = 2.7 Hz, 1H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 6H), 0.12 (s, 3H), 0.11 (s, 6H), 0.09 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.4, 76.9, 74.2, 72.4, 70.1, 69.9, 68.3, 35.8, 26.4 (3C), 26.2 (3C), 25.9 (3C), 21.3, 18.6, 18.3, 18.0, 16.1, -3.4, -3.8, -4.2, -4.5, -4.6, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3312, 2954, 2929, 2896, 2857, 1471, 1463, 1430, 1389, 1361, 1317, 1257, 1216, 1189, 1125, 1089, 1053, 1006, 976, 939, 882, 831, 812, 773, 753, 666, 637, 571, 546, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{28}H_{58}O_4SSi_3Na^+$: 597.3256, found: 597.3262.

2-((2R,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetaldehyde (114)

Procedure A



PPTS (31 mg, 0.12 µmol) was added to a stirred solution of enolether *Z*-**59b** (26 mg, 46 µmol) in a mixture of acetone (1.5 mL) and water (150 µL) at rt. The reaction mixture was warmed to 60 °C and stirring was continued for 17 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **114** as a colourless oil (16 mg, 63%).

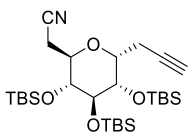
Procedure B

DIBAL (1.0 M in DCM, 75.8 µL, 75.8 µmol) was slowly added to a stirred solution of nitrile **115** (30 mg, 54 µmol) in DCM (520 µL) at -95 °C/-90 °C and stirring was continued for 30 min. The reaction was cautiously quenched with MeOH (0.5 mL) and sat. aq. NH_4Cl (0.5 mL), and the resulting mixture was diluted with MTBE (15 mL) and warmed to rt. The resulting gelatinous mixture was filtered through Celite® and the filter cake was washed with MTBE (2 x 15 mL). The combined filtrates were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording both compound **114** (12 mg, 40%) and some unreacted starting material **115** (5 mg, 17%) as a colourless oil.

$[\alpha]_D^{20}$: +18.4 (c = 0.65, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.75 (dd, J = 3.2, 1.7 Hz, 1H), 4.44 (dt, J = 9.6, 4.6 Hz, 1H), 4.02 (td, J = 7.3, 2.2 Hz, 1H), 3.83 (dd, J = 3.2, 1.6 Hz, 1H), 3.76 (tt, J = 2.3, 1.0 Hz, 1H), 3.48 (dt, J = 4.8, 1.2 Hz, 1H), 2.78 (ddd, J = 16.2, 9.7, 3.2 Hz, 1H), 2.64 (ddd, J = 16.2, 4.5, 1.8 Hz, 1H), 2.52 – 2.38 (m, 2H), 1.96 (t, J = 2.7 Hz, 1H), 0.93 (s, 9H), 0.892 (s, 9H), 0.885 (s, 9H), 0.128 (s, 3H), 0.125 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 201.7, 81.1, 74.7, 74.5, 72.2, 70.3, 70.2, 68.9, 46.0, 26.2 (3C), 26.1 (3C), 25.9 (3C), 21.2, 18.4, 18.3, 18.0, -3.5, -3.8, -4.0, -4.6, -4.7, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2954, 2929, 2896, 2858, 1713, 1472, 1463, 1409, 1390, 1362, 1253, 1131, 1087, 1056, 1005, 975, 939, 875, 832, 813, 774, 668, 666, 636, 633, 546, 467 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{28}H_{56}O_5Si_3Na^+$: 579.3327, found: 579.3328.

2-((2R,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetonitrile (115)

Procedure A



TMSCl (46.6 µL, 367 µmol) was added to a stirred solution of alcohol **57** (100 mg, 184 µmol), NaCN (18 mg, 0.37 mmol) and NaI (3 mg, 0.02 mmol) in a mixture of DMF (1 mL) and MeCN (1 mL) at rt resulting in a colour change from colourless to yellow. The reaction mixture was warmed to 60 °C and stirring was continued for 6 h. Then the reaction mixture was allowed to reach rt and stirring was continued for 16 h. MeCN was evaporated and the remaining crude was purified by flash chromatography (SiO_2, hexane/EtOAc, 40:1) affording compound **115** as a colourless crystalline solid (12 mg, 12%).

Procedure B

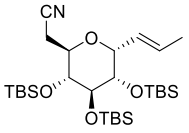
NaCN (13 mg, 0.26 mmol) was added to a stirred solution of tosylate **104** (120 mg, 172 µmol) in DMSO (0.35 mL) at rt. The reaction mixture was warmed to 80 °C and stirring was continued for 16 h. The crude reaction mixture was purified by flash chromatography (SiO_2, hexane/EtOAc, 40:1) affording compound **115** as a colourless crystalline solid (92 mg, 97%).

Procedure C (Mitsunobu)

PPh_3 (**195a**) (193 mg, 734 µmol) and DEAD (134 µL, 734 µmol) were subsequently added to a stirred solution of alcohol **57** (100 mg, 184 µmol) in THF/Et_2O (1:2, 2 mL) at 0 °C and stirring was continued for 15 min. Then, acetone cyanhydrine (83.8 µL, 917 µmol) was added to the stirred reaction mixture at 0 °C and stirring was continued for 5 min. The reaction mixture was allowed to reach rt and stirring was continued for 21.5 h. The solvents were evaporated and the crude reaction mixture was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 30:1) affording compound **115** as a colourless crystalline solid (41 mg, 40%).

m.p.: 75-76 °C; $[\alpha]_D^{20}$: +16.9 (c = 1.14, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.15 (td, J = 6.6, 5.1 Hz, 1H), 3.98 (ddd, J = 8.4, 6.3, 2.0 Hz, 1H), 3.85 (dd, J = 3.1, 1.7 Hz, 1H), 3.79 (tt, J = 2.1, 0.9 Hz, 1H), 3.61 (dq, J = 5.0, 0.9 Hz, 1H), 2.85 (dd, J = 16.5, 6.3 Hz, 1H), 2.65 (dd, J = 16.6, 6.9 Hz, 1H), 2.52 (ddd, J = 16.4, 8.5, 2.7 Hz, 1H), 2.47 (ddd, J = 16.5, 6.4, 2.8 Hz, 1H), 1.98 (t, J = 2.7 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.14 (s, 6H), 0.13 (s, 3H), 0.125 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 117.7, 80.8, 74.4, 73.8, 72.5, 70.5, 70.0, 69.2, 26.2 (3C), 26.1 (3C), 25.9 (3C), 21.23, 21.17, 18.4, 18.3, 18.0, -3.6, -3.8, -4.0, -4.6, -4.7, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3283, 2956, 2929, 2900, 2857, 1472, 1463, 1412, 1390, 1361, 1330, 1254, 1189, 1133, 1085, 1052, 1007, 966, 880, 800, 790, 750, 700, 673, 553, 537, 464, 433 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{28}H_{55}NO_4Si_3Na^+$: 576.3336, found: 576.3331.

2-((2R,3R,4S,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-((E)-prop-1-en-1-yl)tetrahydro-2H-pyran-2-yl)acetonitrile (116)

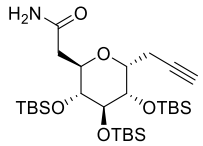


MeOH (13.7 µL, 339 µmol) was added to a stirred solution of nitrile **115** (47 mg, 85 µmol), water (3.05 µL, 170 µmol) and $RuH_2(PPh_3)_4$ (3 mol%, 3 mg, 3 µmol) as a solution in 1,2-DME (0.5 mL) at rt. The resulting reaction mixture was warmed to 140 °C in a sealed Schlenk tube and stirring was continued for 22 h. Then the reaction mixture was warmed to 160 °C and stirring for continued for 3 h. The solvent was evaporated and the crude

product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 2:1) affording compound **116** as a colourless oil (11 mg, 23%).

$[\alpha]_D^{20}$: +15.7 (c = 1.10, $CHCl_3$); **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 5.77 – 5.64 (m, 1H), 5.63 – 5.53 (m, 1H), 4.28 (dd, J = 6.9, 2.5 Hz, 1H), 4.23 – 4.15 (m, 1H), 3.80 (dd, J = 3.3, 1.5 Hz, 1H), 3.66 – 3.57 (m, 2H), 2.84 (dd, J = 16.5, 5.7 Hz, 1H), 2.59 (dd, J = 16.5, 6.7 Hz, 1H), 1.71 (dd, J = 6.3, 1.2 Hz, 3H), 0.91 (s, 18H), 0.90 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.07 (s, 3H), 0.03 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 129.4, 127.8, 117.8, 75.3, 74.6, 73.4, 72.3, 71.9, 26.11 (3C), 26.05 (3C), 25.9 (3C), 21.8, 18.28, 18.25, 18.0, 17.9, -3.7, -3.99, -4.02, -4.5, -4.7, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2930, 2895, 2858, 1729, 1616, 1472, 1464, 1410, 1389, 1362, 1254, 1187, 1092, 1006, 967, 938, 874, 832, 812, 775, 672, 572, 472 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{28}H_{57}NO_4Si_3Na^+$: 578.3488, found: 578.3489.

2-((2R,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetamide (117)



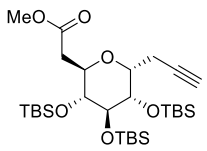
NaOH (25 mg, 630 µmol) was added to a stirred solution of nitrile **115** (50 mg, 90 µmol) in aq. H_2O_2 (35%, 230 µL, 6.77 mmol) and EtOH (685 µL) at rt resulting in an emulsion, and stirring was continued for 22 h. The reaction mixture was diluted with EtOH (10 mL) and neutralized with Dowex® (acidic cation exchange resin). The resin was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 4:1) affording compound **117** as a colourless oil (36 mg, 70%).

$[\alpha]_D^{20}$: +30.1 (c = 0.71, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.93 (d, J = 3.5 Hz, 1H), 5.33 (d, J = 3.6 Hz, 1H), 4.19 (ddd, J = 10.9, 4.6, 2.2 Hz, 1H), 4.10 (J = 8.4, 5.8, 2.6 Hz, 1H), 3.80 (dd, J = 3.3, 1.6 Hz, 1H), 3.66 (tt, J = 2.5, 0.9 Hz, 1H), 3.46 (dt, J = 4.7, 1.2 Hz, 1H), 2.80 (dd, J = 16.4, 10.9 Hz, 1H), 2.61 (ddd, J = 16.6, 8.3, 2.7 Hz, 1H), 2.38 (dd, J = 16.4, 2.4 Hz, 1H), 2.34 (ddd, J = 16.7, 5.7, 2.6 Hz, 1H), 2.00 (t, J = 2.6 Hz, 1H), 0.92 (s, 9H), 0.893 (s, 9H), 0.885 (s, 9H), 0.11 (s, 6H), 0.10 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 173.7, 81.6, 74.9, 74.0, 73.9, 70.7, 70.5, 69.0, 38.2, 26.3 (3C), 26.1 (3C), 25.9 (3C), 21.5, 18.5, 18.3, 18.0, -3.6, -3.8, -4.1, -4.5, -4.7, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3433, 3310, 3170, 3053, 2954, 2930, 2896, 2858, 1681, 1604, 1472, 1464, 1389, 1362, 1329, 1257, 1131, 1089, 1055, 1006, 972, 939, 830, 812, 774, 736, 703,

672, 639, 561, 543, 468 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{28}H_{57}NO_5Si_3Na^+$: 594.3444, found: 594.3437.

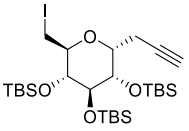
Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (35b)

Procedure B (DMF·DMA)



DMF·DMA (30.2 µL, 227 µmol) was added to a stirred solution of carboxamide **117** (26 mg, 46 µmol) in MeOH (0.5 mL) at rt and stirring was continued for 7 d. A second portion of DMF·DMA (30.2 µL, 227 µmol) was added to the stirred reaction mixture at rt and the reaction mixture was warmed to 65 °C, and stirring was continued for 5 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with EtOAc (3 x 15 mL). The combined organic extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 15 mL) and brine (15 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **35b** as a colourless oil (8 mg, 30%). The analytical and spectroscopic data of the isolated compound were identical with those shown above.

(((2S,3R,4R,5S,6R)-2-(Iodomethyl)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (119)

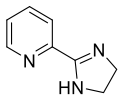


PPh_3 (**195a**) (120 mg, 459 µmol) and I_2 (93 mg, 370 µmol) were subsequently added to a stirred solution of alcohol **57** (100 mg, 184 µmol) in PhH (2 mL) at rt and stirring was continued for 1 h. The reaction was quenched with sat. aq. Na_2SO_3 (5 mL), the aq. phase was extracted with Et_2O (2 x 10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 90:1) affording compound **119** as a colourless oil (119 mg, 99%).

$[\alpha]_D^{20}$: +14.1 (c = 1.07, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.00 (ddd, J = 8.3, 6.6, 2.1 Hz, 1H), 3.88 (ddd, J = 7.2, 5.8, 4.0 Hz, 1H), 3.84 (dd, J = 3.2, 1.7 Hz, 1H), 3.74 (ddd, J = 3.0, 2.1, 0.9 Hz, 1H), 3.70 (ddd, J = 4.0, 1.7, 0.9 Hz, 1H), 3.54 (dd, J = 10.2, 5.8 Hz, 1H), 3.40 (dd, J = 10.2, 7.2 Hz, 1H), 2.53

(ddd, J = 16.5, 8.1, 2.7 Hz, 1H), 2.48 (ddd, J = 16.3, 6.5, 2.7 Hz, 1H), 1.97 (t, J = 2.7 Hz, 1H), 0.92 (s, 9H), 0.90 (s, 9H), 0.895 (s, 9H), 0.13 (s, 6H), 0.125 (s, 3H), 0.120 (s, 3H), 0.115 (s, 3H), 0.110 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.2, 77.0, 74.5, 73.2, 70.3, 70.0, 68.6, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.3, 18.5, 18.3, 18.0, 7.9, -3.4, -3.6, -4.1, -4.3, -4.5, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 2854, 2929, 2896, 2858, 1472, 1408, 1389, 1361, 1258, 1186, 1140, 1124, 1093, 1054, 1005, 977, 938, 914, 877, 834, 813, 776, 674, 631, 550, 539, 474, 444, 407 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{55}O_4Si_3INa^+$: 677.2345, found: 677.2345.

2-(4,5-Dihydro-1H-imidazol-2-yl)pyridine (121)

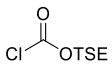


t-BuNC (1.07 mL, 94.9 mmol) was added to a stirred suspension of 2-bromopyridine (**120**) (1.00 g, 6.33 mmol), Cs_2CO_3 (2.68 g, 8.23 mmol), 1,2-ethylene diamine (2.12 mL, 31.6 mmol), dppp (10 mol%, 261 mg, 633 µmol) and $PdCl_2$ (5 mol%, 56 mg, 0.32 mmol) in PhMe (35 mL) at rt and the resulting reaction mixture was warmed to 120 °C and stirring was continued for 3 d. The reaction mixture was cooled to rt and filtered through Celite®. The filter cake was washed with PhMe (2 x 10 mL) and the organic phase was washed with water (3 x 25 mL). The aq. phase was extracted with DCM (3 x 50 mL) and the combined extracts were washed with brine (3 x 50 mL), and were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, DCM/MeOH, 10:1) affording compound **121** as a colourless solid (476 mg, 51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.59 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 8.17 (dt, J = 7.9, 1.1, Hz, 1H), 7.79 (td, J = 7.7, 1.8 Hz, 1H), 7.37 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 6.07 (br s, 1H), 3.87 (br s, 4H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 164.5, 148.8, 148.7, 136.7, 125.2, 122.4, 49.1 (2C) ppm; **HRMS** (ESI): *m/z* calcd. for $C_8H_{10}N_3^+$: 148.0869, found: 148.0869. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[290]

[290] S. Xu, N. Onishi, A. Tsurusaki, Y. Manaka, W.-H. Wang, J. T. Muckerman, E. Fujita, Y. Himeda, *Eur. J. Inorg. Chem.* **2015**, *34*, 5591-5594.

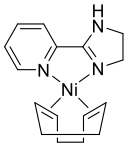
2-(Trimethylsilyl)ethyl carbonochloridate (123)



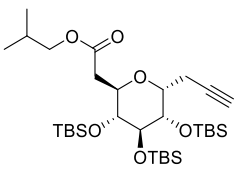
TMS-ethanol (**122**) (5.00 mL, 34.9 mmol) was added to a stirred solution of phosgene (20% in PhMe, 1.00 g, 6.33 mmol) at 0 °C and stirring was continued for 3 h. The solvent and unreacted phosgene were removed under vacuum with an extra cooling trap. The crude product was purified by distillation at HV affording compound **123** as a colourless oil (3.01 g, 48%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.45 – 4.38 (m, 2H), 1.17 – 1.10 (m, 2H), 0.07 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 150.7, 71.5, 17.6, -1.5 (3C) ppm; **HRMS** (ESI): *m/z* calcd. for $C_6H_{14}O_2ClSi^+$: 181.0452, found: 181.0451. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[291]

Isobutyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (35c)



2-(4,5-Dihydro-1*H*-imidazol-2-yl)pyridine (**121**) (47 mg, 0.32 mmol) was added to a stirred solution of $Ni(COD)_2$ (82 mg, 298 µmol) in DMA/THF (7:3, 2.5 mL) at rt resulting in a deep blue mixture which had to be freshly prepared prior to its use.



Catalyst **207** (0.12 M, 5 mol%, 15.9 µL, 1.91 µmol) was added to a stirred suspension of alkyl iodide **119** (25 mg, 38 µmol), Zn dust (8 mg, 115 µmol) and TBAI (50 mol%, 7 mg, 19 µmol) in DMA/THF (7:3, 395 µL) at rt, and stirring was continued for 5 min. Then, isobutylchloroformate (10.0 µL, 76.3 µmol) was added to the stirred reaction mixture at rt and stirring was continued for 20.5 h. The reaction was quenched with aq. $KHSO_4$ (1.0 M, 2 mL) and the aq. phase was extracted with Et_2O (2 x 5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1) affording compound **35c** as a colourless oil (6 mg, 25%).

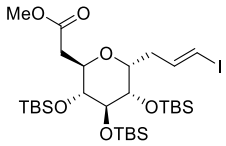
$[\alpha]_D^{20}$: +14.7 (c = 0.60, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.34 (dt, J = 9.4, 4.9 Hz, 1H), 4.02 (ddd, J = 8.6, 5.9, 2.2 Hz, 1H), 3.86 (d, J = 6.7 Hz, 2H), 3.84 (dd, J = 3.2, 1.6 Hz, 1H), 3.77 – 3.75 (m, 1H), 3.51 (dt, J = 4.6, 1.3 Hz, 1H), 2.75 (dd, J = 14.7, 5.2 Hz, 1H), 2.64 (dd, J = 14.8, 9.1 Hz, 1H), 2.49 (ddd,

[291] F. Gille, A. Kirschning, *Beilstein J. Org. Chem.* **2016**, *12*, 564-570.

J = 16.3, 8.7, 2.7 Hz, 1H), 2.40 (ddd, J = 16.3, 6.0, 2.7 Hz, 1H), 1.98 – 1.86 (m, 2H), 0.935 (s, 3H), 0.930 (s, 9H), 0.92 (s, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.13 (s, 6H), 0.11 (s, 6H), 0.10 (s, 3H), 0.08 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 81.4, 74.6, 74.4, 74.0, 70.8, 70.2, 70.0, 68.9, 38.0, 27.8, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.1, 19.30, 19.28, 18.5, 18.3, 18.0, -3.4, -3.8, -4.1, -4.56, -4.63, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3314, 2955, 2929, 2895, 2858, 1737, 1472, 1463, 1389, 1378, 1361, 1252, 1167, 1128, 1083, 1056, 1005, 977, 939, 877, 832, 813, 774, 672, 638, 634, 572, 547, 471, 447, 425 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{32}H_{65}O_6Si_3^+$: 629.4084, found: 629.4084.

5.2.1.5.3. Building Block Coupling & Elaboration

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((E)-3-iodoallyl)tetrahydro-2H-pyran-2-yl)acetate (124a)



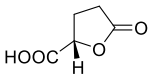
$Cp_2Zr(H)Cl$ (15 mg, 59 µmol) was added to a stirred solution of alkyne **35b** (30 mg, 51 µmol) in THF (0.25 mL) at 0 °C resulting in a white suspension. The reaction mixture was stirred for 30 min. before a solution of I_2 (15 mg, 59 µmol) in THF (125 µL) was added dropwise at 0 °C and stirring was continued for 30 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 17 h. The reaction was quenched with sat. aq. $Na_2S_2O_3$ (0.5 mL) and water (5 mL). The aq. phase was extracted with MTBE (2 x 10 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1) affording both compound **124a** (12.0 mg, 33%) and some unreacted starting material **35b** (16 mg, 53%) as a colourless oil.

$[\alpha]_D^{20}$: +14.2 (c = 0.80, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 6.53 (dt, J = 14.4, 7.2 Hz, 1H), 6.06 (dt, J = 14.4, 1.3 Hz, 1H), 4.31 (dt, J = 9.6, 4.5 Hz, 1H), 3.89 – 3.84 (m, 1H), 3.79 – 3.76 (m, 1H), 3.72 (s, 3H), 3.50 – 3.45 (m, 2H), 2.74 (dd, J = 14.6, 10.0 Hz, 1H), 2.61 (dd, J = 14.6, 4.8 Hz, 1H), 2.50 (dddd, J = 14.7, 9.8, 7.0, 1.5 Hz, 1H), 1.98 (dddd, J = 14.6, 7.4, 3.5, 1.3 Hz, 1H), 0.92 (s, 9H), 0.89 (s, 18H), 0.10 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H), 0.07 (s, 3H), 0.05 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 143.6, 76.5, 74.4, 74.0, 73.9, 71.7, 68.6, 52.1, 37.9, 37.5, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.3, 18.0, -3.4, -4.0, -4.1, -4.5, -4.6, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2952, 2929, 2894, 2857, 1742, 1646, 1472, 1463, 1436, 1389, 1361, 1327, 1253, 1168, 1127, 1085, 1005, 972, 939, 919, 891, 864, 832, 812, 773, 666, 563, 487, 459, 426 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{59}O_6ISi_3Na^+$: 737.2559, found: 737.2556.

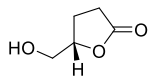
5.2.2. The Western Belizentrin Fragment - Route 2

5.2.2.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring - A New Synthesis

(S)-5-(Hydroxymethyl)dihydrofuran-2(3H)-one ((S)-132a)



Conc. aq. HCl (25 mL) was slowly added to a stirred solution of *L*-glutamic acid ((*S*)-**10**) (25.0 g, 170 mmol) in water (60 mL) at rt. The resulting solution was cooled to 0 °C and a solution of $NaNO_2$ (15.2 g, 221 mmol) in water (80 mL) was added dropwise over the course 45 min causing a gentle evolution of N_2 gas. Once the addition of $NaNO_2$ was complete the colourless reaction mixture was warmed to rt and stirring was continued for 23 h. The solvents were evaporated and the resulting white solid was washed with EtOAc (100 mL), and filtered. The filter cake was washed with EtOAc (2 x 100 mL) and the combined filtrates were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording intermediate (*S*)-**134** as a white solid (17.5 g, 79%) which was used in the next step without further purification.

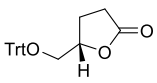


$BH_3{\cdot}SMe_2$ (15.2 mL, 170 mmol) was slowly added to a stirred solution of crude carboxylic acid (*S*)-**134** (17.5 g, 170 mmol) in THF (280 mL) at 0 °C over the course of 15 min. Once the addition of $BH_3{\cdot}SMe_2$ was complete the resulting reaction mixture was allowed to reach rt and stirring was continued for 18 h. Then the reaction mixture was cooled to 0 °C and the reaction was quenched with MeOH (70 mL). The solvents were evaporated and the resulting oil was filtered through a plug of Celite®, and washed with EtOAc. Evaporation of the solvent afforded compound (*S*)-**132a** as a white solid (10.8 g, 69%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.63 (ddd, J = 7.5, 6.9, 4.6 Hz, 1H), 3.91 (dd, J = 12.4, 2.9 Hz, 1H), 3.66 (dd, J = 12.5, 4.7 Hz, 1H), 2.67 – 2.50 (m, 2H), 2.27 (dddd, J = 13.2, 9.6, 7.6, 5.8 Hz, 1H), 2.15 (dddd, J = 12.9, 10.0, 8.4, 7.0 Hz, 1H), 2.03 (s, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 177.4, 80.7, 64.4, 28.8, 23.3 ppm; **HRMS** (ESI): m/z calcd. for $C_5H_8O_3Na^+$: 139.0366, found: 139.0365. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[292]

[292] S. Höck, H. J. Borschberg, *Helv. Chim. Acta* **2003**, *86*, 1397-1409.

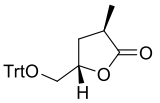
(S)-5-((Trityloxy)methyl)dihydrofuran-2(3H)-one ((S)-132b)



TrtCl (8.48 g, 30.4 mmol) was added to a stirred solution of alcohol (*S*)-**132a** (2.94 g, 25.4 mmol) in py (13.5 mL, 167 mmol) at rt and the resulting reaction mixture was stirred for 16 h. The reaction was quenched with water (110 mL), the aq. phase was extracted with EtOAc (3 x 45 mL). The combined extracts were subsequently washed with water (45 mL) and brine (45 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 9:1 to 2:1), followed by recrystallization from boiling hexane/EtOAc (5:1) to give compound (*S*)-**132b** as a colourless crystalline solid (6.62 g, 73%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.40 (m, 6H), 7.34 – 7.28 (m, 6H), 7.27 – 7.26 (m, 1H), 7.25 – 7.22 (m, 2H), 4.65 (dddd, J = 7.9, 5.8, 4.3, 3.5 Hz, 1H), 3.42 (dd, J = 10.4, 3.5 Hz, 1H), 3.16 (dd, J = 10.4, 4.3 Hz, 1H), 2.69 (ddd, J = 17.9, 10.1, 6.6 Hz, 1H), 2.51 (ddd, J = 17.8, 10.1, 6.9 Hz, 1H), 2.25 (dddd, J = 12.8, 10.1, 7.9, 6.6 Hz, 1H), 2.04 (dddd, J = 12.8, 10.1, 6.9, 5.8 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 177.6, 143.6 (3C), 128.8 (6C), 128.1 (6H), 127.3 (3C), 87.1, 79.2, 65.4, 28.6, 24.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{24}H_{22}O_3Na^+$: 381.1461, found: 381.1459. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[293]

(3R,5S)-3-Methyl-5-((trityloxy)methyl)dihydrofuran-2(3H)-one (136)

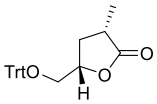


n-BuLi (1.6 M in hexane, 20.9 mL, 33.5 mmol) was slowly added to a stirred solution of DIPA (5.47 mL, 39.1 mmol) in THF (130 mL) at -78 °C. Once the addition of *n*-BuLi was complete the resulting reaction mixture was warmed to 0 °C and stirring was continued for 15 min. The reaction mixture was cooled to -78 °C and a solution of lactone (*S*)-**132b** in THF (65 mL) predried over 4 Å MS was slowly added. Stirring was continued for 15 min before MeI (2.08 mL, 33.5 mmol) as a solution in THF (30 mL) was slowly added to the reaction mixture, which was allowed to reach -30 °C over the course of 4 h. The reaction was quenched with sat. aq. Na_2SO_4 (100 mL) and the aq. phase was extracted with MTBE (4 x 100 mL). The combined extracts were washed with water (75 mL) and brine (75 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **136** as a colourless crystalline solid (10.2 g, 99%).

[293] S. Höck, H. J. Borschberg, *Helv. Chim. Acta* **2003**, *86*, 1397-1409.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.38 (m, 6H), 7.34 – 7.28 (m, 6H), 7.27 – 7.26 (m, 1H), 7.25 – 7.22 (m, 2H), 4.60 (dq, J = 8.6, 3.7 Hz, 1H), 3.42 (dd, J = 10.4, 3.7 Hz, 1H), 3.13 (dd, J = 10.4, 4.1 Hz, 1H), 2.87 (tq, J = 9.2, 7.3 Hz, 1H), 2.26 (ddd, J = 12.8, 9.4, 3.5 Hz, 1H), 1.93 (dt, J = 12.9, 8.8 Hz, 1H), 1.28 (d, J = 7.3 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 180.5, 143.6 (3C), 128.8 (6C), 128.1 (6C), 127.3 (3C), 87.2, 76.8, 65.4, 34.3, 32.7, 16.5 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{25}H_{24}O_3Na^+$: 395.1618; found: 395.1616. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[294]

(3S,5S)-3-Methyl-5-((trityloxy)methyl)dihydrofuran-2(3H)-one (137)

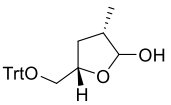


n-BuLi (1.6 M in hexane, 42.3 mL, 67.6 mmol) was slowly added to a stirred solution of DIPA (11.1 mL, 78.9 mmol) in THF (260 mL) at -78 °C. Once the addition of *n*-BuLi was complete the resulting reaction mixture was warmed to 0 °C and stirring was continued for 15 min. The reaction mixture was cooled to -78 °C and a solution of lactone **136** in THF (155 mL) was slowly added, and stirring was continued for 30 min. The reaction was quenched with sat. aq. Na_2SO_4 (200 mL) and the aq. phase was extracted with MTBE (4 x 125 mL). The combined extracts were washed with water (150 mL) and brine (150 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 9:1 to 2:1) affording compound **137** as a colourless crystalline solid (20.1 g, 96%).

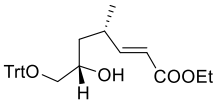
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 – 7.43 (m, 6H), 7.34 – 7.29 (m, 6H), 7.27 – 7.22 (m, 3H), 4.52 (dddd, J = 10.1, 6.0, 5.3, 3.9 Hz, 1H), 3.30 (dd, J = 10.4, 4.0 Hz, 1H), 3.26 (dd, J = 10.4, 5.4 Hz, 1H), 2.68 (ddq, J = 11.7, 8.9, 7.0 Hz, 1H), 2.37 (ddd, J = 12.6, 9.0, 6.1 Hz, 1H), 1.69 (ddd, J = 12.6, 11.8, 10.2 Hz, 1H), 1.28 (d, J = 7.1 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 179.5, 143.7 (3C), 128.8 (6C), 128.0 (6C), 127.3 (3C), 86.9, 77.3, 65.2, 35.5, 33.2, 15.5 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{25}H_{24}O_3Na^+$: 395.1618, found: 395.1617. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[295]

[294] M. Kögl, L. Brecker, R. Warrass, J. Mulzer, *Eur. J. Org. Chem.* **2008**, *16*, 2714-2730.
[295] See footnote 294.

Ethyl (4S,6S,E)-6-hydroxy-4-methyl-7-(trityloxy)hept-2-enoate (139)



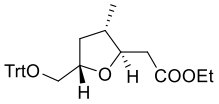
DIBAL (1.2 M in PhMe, 48.0 mL, 57.6 mmol) was slowly added to a stirred solution of lactone **137** (18.7 g, 50.1 mmol) in DCM (200 mL) at -78 °C over the course of 15 min and the resulting reaction mixture was stirred for 3 h. The reaction was quenched with MeOH (40 mL) at -78 °C. The resulting mixture was transferred into an Erlenmeyer flask with sat. aq. Rochelle (200 mL) and was vigorously stirred for 16 h at rt. The resulting biphasic mixture was diluted with water (400 mL) and the aq. phase was extracted with DCM (3 x 200 mL). The combined extracts were subsequently washed with water (200 mL) and brine (200 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **138** as a mixture of diastereomers as a colourless oil (18.4 g, 98%) which was used in the next step without further purification.



Ethyl (triphenylphosphoranylidene)acetate (18.1 g, 50.8 mmol) was added to a stirred solution of crude lactol **138** (18.2 g, 48.7 mmol) in PhMe (250 mL) at rt. The resulting reaction mixture was stirred for 17 h at 80 °C. Then the reaction mixture was cooled to rt and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1 to 9:1) affording compound **139** as a colourless oil (15.0 g, 69%).

$[\alpha]_D^{20}$: +24.8 (c = 1.21, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.46 – 7.40 (m, 6H), 7.35 – 7.29 (m, 6H), 7.28 – 7.27 (m, 1H), 7.26 – 7.23 (m, 2H), 6.86 (dd, J = 15.7, 7.7 Hz, 1H), 5.70 (dd, J = 15.7, 1.2 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 3.82 (tq, J = 8.0, 3.8 Hz, 1H), 3.20 (dd, J = 9.5, 3.2 Hz, 1H), 3.02 (dd, J = 9.4, 7.4 Hz, 1H), 2.44 (dtd, J = 8.0, 6.6, 5.3 Hz, 1H), 2.28 (d, J = 3.8 Hz, 1H), 1.58 (ddd, J = 13.6, 8.5, 6.3 Hz, 1H), 1.35 – 1.30 (m, 1H), 1.29 (t, J = 7.2 Hz, 3H), 1.03 (d, J = 6.7 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 166.9, 154.2, 143.9 (3C), 128.8 (6C), 128.1 (6C), 127.3 (3C), 119,7, 86.9, 68.7, 67.8, 60.4, 39.3, 32.9, 19.0, 14.4 ppm; **IR** (film): $\tilde{\nu}$ = 3486, 3058, 3022, 2962, 2930, 2871, 1714, 1651, 1597, 1490, 1448, 1368, 1302, 1277, 1211, 1180, 1153, 1072, 1033, 985, 948, 900, 869, 775, 763, 747, 706, 703, 667, 649, 633, 618, 528, 407 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{32}O_4Na^+$: 467.2193, found: 467.2189.

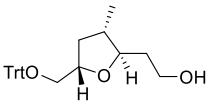
Ethyl 2-((2R,3S,5S)-3-methyl-5-((trityloxy)methyl)tetrahydrofuran-2-yl)acetate (131a)



A solution of TBAF·3H_2O (14.5 g, 45.8 mmol) in THF (45 mL) was slowly added to a stirred solution of α,β-unsaturated ester **139** (13.6 g, 30.5 mmol) in THF (155 mL) at 0 °C. The resulting reaction mixture was stirred for 3 h, the solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **131a** as a colourless crystalline solid (11.2 g, 82%).

m.p.: 113-114 °C; $[\alpha]_D^{20}$: +5.0 (c = 1.01, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.48 – 7.44 (m, 6H), 7.32 – 7.26 (m, 6H), 7.25 – 7.19 (m, 3H), 4.27 – 4.19 (m, 1H), 4.18 (qd, J = 7.1, 1.6 Hz, 2H), 3.90 (ddd, J = 9.0, 8.1, 4.1 Hz, 1H), 3.16 (dd, J = 9.4, 5.3 Hz, 1H), 3.02 (dd, J = 9.4, 4.8 Hz, 1H), 2.57 (dd, J = 14.8, 4.2 Hz, 1H), 2.49 (dd, J = 14.8, 8.1 z, 1H), 2.19 (dt, J = 12.3, 7.0 Hz, 1H), 2.00 – 1.88 (m, 1H), 1.43 (ddd, J = 12.3, 10.8, 8.9 Hz, 1H), 1.25 (t, J = 7.2 Hz, 3H), 1.03 (d, J = 6.5 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7, 144.3 (3C), 128.9 (6C), 127.9, (6C), 127.0 (3C), 86.5, 81.6, 77.4, 66.8, 60.6, 40.0, 39.6, 37.9, 16.3, 14.4 ppm; **IR** (film): $\tilde{\nu}$ = 3059, 3022, 2961, 2928, 2871, 1733, 1597, 1490, 1448, 1382, 1318, 1276, 1250, 1196, 1152, 1091, 1074, 1031, 1002, 991, 946, 914, 899, 850, 816, 746, 697, 667, 646, 632, 561, 537, 493 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{32}O_4Na^+$: 467.2193, found: 467.2193.

2-((2R,3S,5S)-3-Methyl-5-((trityloxy)methyl)tetrahydrofuran-2-yl)ethan-1-ol (140)

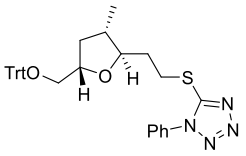


A solution of $LiAlH_4$ (1.0 M in THF, 23.4 mL, 23.4 mmol) was slowly added to a stirred solution of ester **131a** (9.91 g, 22.3 mmol) in THF (27 mL) at -20 °C over the course of 15 min and the resulting reaction mixture was stirred for 1 h. The reaction mixture was warmed to rt and stirring was continued for 1 h. Then the reaction mixture was diluted with Et_2O (100 mL) and the reaction was quenched with sat. aq. NH_4Cl (20 mL). The resulting mixture was filtered through a plug of Celite® and washed with EtOAc (3 x 100 mL). The combined filtrates were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **140** as a colourless oil (8.96 g, quant.).

$[\alpha]_D^{20}$: +0.8 (c = 1.02, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.49 – 7.44 (m, 6H), 7.33 – 7.27 (m, 6H), 7.25 – 7.20 (m, 3H), 4.25 (dddd, J = 9.3, 6.7, 5.4, 4.2 Hz, 1H), 3.88 – 3.82 (m, 2H), 3.62 (td, J = 9.3, 2.7 Hz, 1H), 3.11 (dd, J = 9.6, 5.3 Hz, 1H), 3.06 (dd, J = 9.6, 4.2 Hz, 1H), 3.05 (t, J = 5.8 Hz, 1H), 2.13 (dt, J = 12.2, 6.9 Hz, 1H), 1.97 – 1.85 (m, 2H), 1.74 – 1.63 (m, 1H), 1.41 (ddd, J = 12.3, 11.0, 9.1 Hz, 1H), 1.02 (d, J = 6.6 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 144.3 (3C), 128.9 (6C), 127.9 (6C),

127.1 (3C), 86.5, 86.0, 77.6, 66.9, 62.3, 40.3, 37.2, 35.4, 16.0 ppm; **IR** (film): $\tilde{\nu}$ = 3416, 3086, 3059, 3031, 2959, 2927, 2870, 1596, 1491, 1449, 1380, 1321, 1221, 1182, 1154, 1092, 1067, 1034, 1002, 990, 947, 899, 872, 776, 765, 747, 702, 646, 633, 619, 557, 536, 513, 493, 478, 462, 454, 443, 425, 420, 413, 404 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{30}O_3Na^+$: 425.2087, found: 425.2087.

5-((2-((2R,3S,5S)-3-Methyl-5-((trityloxy)methyl)tetrahydrofuran-2-yl)ethyl)thio)-1-phenyl-1H-tetrazole (141)

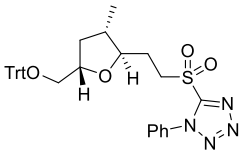


1-Phenyl-1*H*-tetrazole-5-thiol (**168**) (0.76 g, 4.29 mmol) and PPh_3 (**195a**) (1.24 g, 4.71 mmol) were added to a stirred solution of alcohol **140** (1.15 g, 2.86 mmol) in THF (23 mL) at rt. The resulting reaction mixture was cooled to 0 °C and a solution of DIAD (0.84 mL, 4.29 mmol) in THF (7 mL) was slowly added over the course of 15 min, and stirring was continued for 1 h. Then the reaction mixture was allowed to reach rt and stirring was continued for 16 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **141** as a colourless oil (1.39 g, 87%).

$[\alpha]_D^{20}$: +5.0 (c = 1.15, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.57 – 7.44 (m, 11H), 7.31 – 7.18 (m, 9H), 4.21 (dddd, J = 9.0, 6.6, 5.3, 4.1 Hz, 1H), 3.69 – 3.50 (m, 3H), 3.11 (dd, J = 9.6, 5.4 Hz, 1H), 3.04 (dd, J = 9.6, 4.1 Hz, 1H), 2.24 (dddd, J = 14.0, 8.5, 7.4, 2.7 Hz, 1H), 2.16 (dt, J = 12.2, 7.0 Hz, 1H), 1.97 – 1.83 (m, 2H), 1.42 (ddd, J = 12.4, 10.9, 9.0 Hz, 1H), 1.02 (d, J = 6.5 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 154.7, 144.3 (3C), 133.9, 130.1, 129.9 (2C), 128.9 (6C), 127.9 (6C), 127.1 (3C), 124.0 (2C), 86.5, 83.5, 77.3, 67.0, 39.9, 37.8, 33.5, 30.8, 16.2 ppm; **IR** (film): $\tilde{\nu}$ = 3058, 3023, 2957, 2927, 2871, 1739, 1596, 1499, 1448, 1412, 1386, 1318, 1277, 1243, 1221, 1183, 1156, 1089, 1074, 1044, 1016, 988, 942, 900, 841, 760, 689, 667, 645, 632, 551, 495 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{34}H_{34}N_4O_2S_1Na^+$: 585.2295, found: 585.2289.

5-((2-((2R,3S,5S)-3-Methyl-5-((trityloxy)methyl)tetrahydrofuran-2-yl)ethyl)sulfonyl)-1-phenyl-1H-tetrazole (142a)

Procedure A (molybdate)



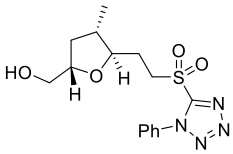
A mixture of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (175 mg, 141 µmol) and conc. aq. H_2O_2 (35% in water, 481 µL, 14.1 mmol) was added to a stirred solution of thioether **141** (795 mg, 1.41 mmol) in EtOH (10.3 mL) at rt and the reaction mixture was stirred for 5 d. The reaction was quenched with water (50 mL) and the aq. phase was extracted with EtOAc (5 x 50 mL). The combined extracts were subsequently washed with water (150 mL) and brine (150 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 6:1) affording compound **142a** as a colourless oil (593 mg, 71%).

$[\alpha]_D^{20}$: -1.9 (c = 1.06, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.43 (m, 11H), 7.34 – 7.27 (m, 6H), 7.25 – 7.20 (m, 3H), 4.19 (ddd, J = 11.5, 9.2, 5.2 Hz, 1H), 4.01 (ddd, J = 14.6, 11.3, 3.8 Hz, 1H), 3.83 (ddd, J = 14.6, 11.1, 4.8 Hz, 1H), 3.55 (td, J = 8.9, 2.9 Hz, 1H), 3.12 (dd, J = 9.7, 5.3 Hz, 1H), 3.05 (dd, J = 9.6, 4.3 Hz, 1H), 2.30 (dddd, J = 14.0, 11.3, 4.8, 2.9 Hz, 1H), 2.19 (dt, J = 12.4, 7.0 Hz, 1H), 2.01 (dddd, J = 13.6, 11.1, 8.8, 4.7 Hz, 1H), 1.96 – 1.83 (m, 1H), 1.46 (ddd, J = 12.4, 10.9, 9.0 Hz, 1H), 1.04 (d, J = 6.5 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 153.7, 144.2 (3C), 133.2, 131.6, 129.9 (2C), 128.9 (6C), 127.9 (6C), 127.1 (3C), 125.3 (2C), 86.6, 82.8, 77.6, 66.9, 53.9, 40.0, 37.8, 26.4, 16.2 ppm; **IR** (film): $\tilde{\nu}$ = 3060, 3023, 2959, 2927, 2871, 1735, 1596, 1495, 1448, 1382, 1342, 1270, 1219, 1151, 1093, 1075, 1039, 1002, 989, 941, 916, 900, 825, 760, 749, 701, 667, 633, 561, 536, 509, 423 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{34}H_{34}N_4O_4S_1Na^+$: 617.2193, found: 617.2197.

Procedure B (m-CPBA)

A solution of *m*-CPBA (72.5%, 1.23 g, 5.15 mmol) in DCM (3 mL) was added to a stirred solution of the thioether **141** (580 mg, 1.03 mmol) in DCM (2 mL) at rt, and stirring was continued for 1 d. The reaction mixture was filtered and the filter cake was washed with DCM (2 x 10 mL). The combined organic phases were subsequently (cautious, mind the very strong gas evolution!) washed with aq. $NaHSO_3$ (40%, 15 mL) and additional water (10 mL), sat. aq. $NaHCO_3$ (3 x 15 mL) and brine (15 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 6:1) affording compound **142a** as a colourless oil (412 mg, 67%). The analytical and spectroscopic data of the isolated compound were identical with those shown above.

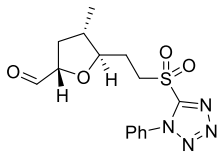
((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)methanol (142b)



TFA (2.41 mL, 31.5 mmol) was added to a stirred solution of protected alcohol **142a** (750 mg, 1.26 mmol) in DCM (26.7 mL) at 0 °C and the resulting reaction mixture was stirred for 1 h. The reaction was quenched and neutralized with sat. aq. $NaHCO_3$ (ca. 26 mL) and the aq. phase was extracted with EtOAc (3x 20 mL). The combined extracts were washed with brine (15 mL) and the solvent was evaporated. The crude product was dissolved in EtOAc (60 mL), sat. aq. K_2CO_3 (25 mL) was added and the resulting mixture was stirred at rt for 15 min. The aq. phase was extracted with EtOAc (20 mL). The organic extract was subsequently washed with water (20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 2:1 to 1:3) affording compound **142b** as a colourless oil (435 mg, 98%).

$[\alpha]_D^{20}$: +22.3 (c = 1.03, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.56 (m, 5H), 4.10 (dtd, J = 9.3, 6.0, 3.1 Hz, 1H), 3.97 (ddd, J = 14.6, 10.7, 4.90 Hz, 1H), 3.83 (ddd, J = 14.7, 10.5, 5.3 Hz, 1H), 3.70 – 3.63 (m, 1H), 3.56 (td, J = 8.7, 3.0 Hz, 1H), 3.48 (dd, J = 11.7, 5.9 Hz, 1H), 2.30 (dddd, J = 13.8, 10.7, 5.3, 3.0 Hz, 1H), 2.12 (ddd, J = 12.2, 7.1, 6.2 Hz, 1H), 2.06 – 1.90 (m, 2H), 1.85 (s, 1H), 1.43 (ddd, J = 12.2, 10.7, 9.5 Hz, 1H), 1.06 (d, J = 6.5 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 153.7, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 82.9, 79.1, 65.1, 53.7, 40.1, 36.5, 26.6, 16.3 ppm; **IR** (film): $\tilde{\nu}$ = 3426, 3068, 2960, 2929, 2873, 1595, 1498, 1461, 1399, 1339, 1295, 1236, 1153, 1112, 1078, 1041, 1015, 982, 917, 874, 826, 764, 689, 633, 536, 508, 437, 420 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{15}H_{20}N_4O_4S_1Na^+$: 375.1098, found: 375.1098.

(2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-carbaldehyde (130)



DMSO (279 µL, 3.93 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (169 µL, 1.97 mmol) in DCM (8.2 mL) at -78 °C and the reaction mixture was stirred for 5 min. Then alcohol **142b** (315 mg, 894 µmol) as a solution in DCM (3.3 mL) was added dropwise and stirring was continued for 20 min. DIPEA (1.56 mL, 8.94 mmol) was slowly added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 1 h.

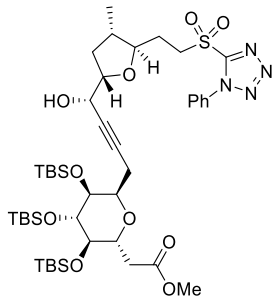
The reaction was quenched with water (50 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 2 x 50 mL) and with brine (50 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 2:1 to 1:1) affording compound **130** as a colourless oil (295 mg, 94%).

$[\alpha]_D^{20}$: -12.4 (c = 1.01, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.63 (d, J = 1.9 Hz, 1H), 7.72 – 7.57 (m, 5H), 4.33 (ddd, J = 8.6, 7.8, 2.0 Hz, 1H), 4.02 (ddd, J = 14.7, 10.8, 4.9 Hz, 1H), 3.85 (ddd, J = 14.7, 10.6, 5.2 Hz, 1H), 3.66 (td, J = 8.7, 2.9 Hz, 1H), 2.45 – 2.30 (m, 2H), 2.13 – 2.05 (m, 1H), 2.04 – 1.93 (m, 1H), 1.64 (ddd, J = 12.8, 9.7, 8.6 Hz, 1H), 1.07 (d, J = 6.7 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 202.0, 153.6, 133.1, 131.7, 129.9 (2C), 125.2 (2C), 84.5, 82.0, 53.6, 39.4, 35.9, 26.7, 16.2 ppm; **IR** (film): $\tilde{\nu}$ = 3701, 2962, 2928, 2875, 2814, 1730, 1659, 1595, 1497, 1461, 1440, 1385, 1340, 1295, 1236, 1150, 1105, 1087, 1077, 1040, 1015, 982, 918, 903, 762, 688, 666, 633, 532, 508, 473, 408 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{15}H_{17}N_4O_4S_1^-$: 349.0976, found: 349.0980.

5.2.2.2. Building Block Coupling & Elaboration

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (129a)

Procedure A (TEA, only MS)

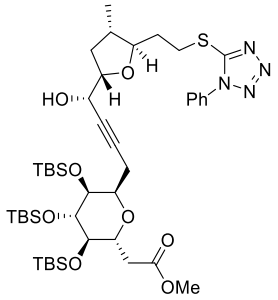


TEA (256 µL, 1.84 mmol) was added to a stirred suspension of $Zn(OTf)_2$ (613 mg, 1.69 mmol) and (*+*)-N-methylephedrine (302 mg, 1.69 mmol) with 4 Å MS in PhMe (1.35 mL) at rt and stirring was continued for 3 h. A solution of alkyne **35b** (360 mg, 613 µmol) in PhMe (0.5 mL, rinsed with 2 x 0.4 mL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1.5 h. A solution of aldehyde **130** (290 mg, 828 µmol) in PhMe (0.5 mL, rinsed with 2x 0.4 mL) was dried over 4 Å MS before ot was added to the stirred reaction mixture at rt and stirring was continued for 64 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 20 mL) and the aq. phase was extracted with MTBE (3 x 30 mL) and EtOAc (3 x 20 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 3:1) affording the desired major product **129a** (109 mg, 19%), minor byproduct **144** (25 mg, 5%) and some unreacted starting material **35b** (183 mg, 51%) as a colourless oil.

Analytical and spectral data of the major product **129a**: $[\alpha]_D^{20}$: +9.6 (c = 1.05, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 4.32 (dt, J = 9.2, 4.6 Hz, 1H), 4.18 (dt, J = 7.0, 1.9 Hz, 1H), 4.04 – 3.90 (m, 3H), 3.87 – 3.78 (m, 2H), 3.69 (s, 3H), 3.63 (t, J = 2.2 Hz, 1H), 3.57 (td, J = 8.6, 3.2 Hz, 1H), 3.49 (ddd, J = 3.7, 1.8, 0.9 Hz, 1H), 2.76 (dd, J = 14.6, 9.5 Hz, 1H), 2.67 (dd, J = 14.6, 5.2 Hz, 1H), 2.49 (ddd, J = 16.5, 6.9, 2.2 Hz, 1H), 2.42 (ddd, J = 16.5, 7.3, 2.0 Hz, 1H), 2.35 – 2.27 (m, 1H), 2.27 (ddd, J = 19.2, 12.3, 6.0 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.98 – 1.88 (m, 1H), 1.48 (ddd, J = 12.7, 10.9, 9.0 Hz, 1H), 1.28 (dd, J = 12.4, 6.8 Hz, 1H), 1.05 (d, J = 6.5 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.115 (s, 3H), 0.11 (s, 6H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 152.5, 133.5, 131.6, 129.9 (2C), 125.3 (2C), 83.8, 83.1, 81.7, 79.4, 74.5, 74.2, 73.6, 70.4, 68.5, 66.1, 53.5, 51.9, 39.8, 37.5, 37.4, 26.31 (3C), 26.26, 26.2 (3C), 25.9 (3C), 21.6, 18.5, 18.3, 18.0, 16.1, -3.4, -4.0, -4.1, -4.57, -4.58, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3569,

2954, 2929, 2895, 2857, 1738, 1498, 1467, 1463, 1437, 1389, 1348, 1345, 1255, 1149, 1129, 1088, 1055, 1006, 974, 860, 813, 776, 688, 673, 634, 537, 508, 474 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{76}N_4O_{10}SSi_3Na^+$: 959.4482, found: 959.4481.

Analytical and spectral data of the minor byproduct **144**: $[\alpha]_D^{20}$: +15.7 (c = 0.85, $CHCl_3$);



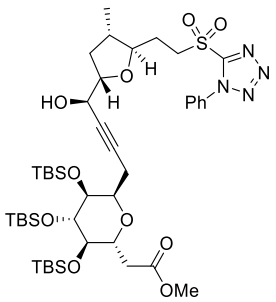
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.50 (m, 5H), 4.32 (ddd, J = 9.2, 5.6, 3.4 Hz, 1H), 4.19 – 4.12 (m, 1H), 4.03 – 3.94 (m, 2H), 3.84 – 3.79 (m, 1H), 3.68 (s, 3H), 3.64 (t, J = 2.1 Hz, 1H), 3.60 – 3.40 (m, 4H), 2.74 (dd, J = 14.7, 9.1 Hz, 1H), 2.68 (dd, J = 14.8, 5.5 Hz, 1H), 2.58 – 2.59 (m, 1H), 2.48 – 2.42 (m, 2H), 2.27 – 2.14 (m, 2H), 1.98 – 1.85 (m, 2H), 1.42 (ddd, J = 12.5, 10.8, 8.9 Hz, 1H), 1.03 (d, J = 6.6 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.88 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.105 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 154.5, 133.9, 130.2, 129.9 (2C), 124.0 (2C), 84.0, 83.5, 81.6, 79.6, 74.5, 74.2, 73.6, 70.3, 68.5, 66.2, 51.9, 39.7, 37.7, 37.4, 33.4, 30.3, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.6, 18.5, 18.3, 18.0, 16.2, -3.4, -4.0, -4.1, -4.6 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3466, 2954, 2930, 2882, 2857, 1738, 1597, 1500, 1466, 1463, 1444, 1409, 1389, 1361, 1254, 1128, 1092, 1055, 1007, 980, 865, 815, 789, 777, 694, 525, 501, 474, 448, 428 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{76}N_4O_8SSi_3Na^+$: 927.4584, found: 927.4588.

Procedure B (DIPEA, MS and $Zn(OTf)_2$ predried at HV)

DIPEA (96.9 µL, 557 µmol) and (*+*)-N-methylephedrine (86.5 mg, 482 µmol) dried over 4 Å MS in PhMe (0.4 mL, rinsed with 2 x 0.4 mL) were subsequently added to $Zn(OTf)_2$ (155 mg, 427 µmol, predried at 120 °C at HV for 5 h) at rt, and the reaction mixture was stirred for 1.5 h. A solution of alkyne **35b** (270 mg, 460 µmol) in PhMe (0.4 mL, rinsed with 2 x 0.4 mL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 30 min. A solution of aldehyde **130** (100 mg, 285 µmol) in PhMe (0.4 mL, rinsed with 2 x 0.4 mL) was dried over 4 Å MS before it was added to the stirred reaction mixture at rt, and stirring was continued for 64 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 20 mL) and the aq. phase was extracted with EtOAc (3 x 30 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 20 mL) and brine (20 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 3:1) affording desired major product **129a** (110 mg, 26%), minor byproduct **144** (23 mg, 6%) and some unreacted starting material **35b**

(183 mg, 68%) as a colourless oil. The analytical and spectroscopic data of the isolated compounds were identical with those shown above.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (epi-129a)

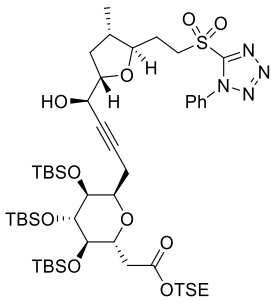


TEA (71.6 µL, 514 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (176 mg, 484 µmol) and (-)-N-methylephedrine (88 mg, 0.49 mmol) over 4 Å MS in PhMe (0.7 mL) at rt and stirring was continued for 3.25 h. A solution of alkyne **35b** (274 mg, 467 µmol) in PhMe (300 µL, rinsed with 2 x 300 µL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1 h. A solution of aldehyde **130** (180 mg, 514 µmol) in PhMe (300 µL, rinsed with 2 x 300 µL) was dried over 4 Å MS before it was added to the stirred reaction mixture at rt and stirring was continued for 5 d. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with MTBE (3 x 15 mL) and EtOAc (2 x 15 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 2:1) and preparative TLC (DCM/MeOH, 100:1) affording both compound *epi*-**129a** (134 mg, 31%) and some unreacted starting material **35b** (155 mg, 57%) as a colourless oil.

$[\alpha]_D^{20}$: +5.1 (c = 0.88, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 4.40 (ddt, J = 5.5, 3.9, 2.1 Hz, 1H), 4.33 (dt, J = 9.2, 4.3 Hz, 1H), 4.07 (ddd, J = 9.6, 6.3, 3.5 Hz, 1H), 3.98 (td, J = 7.0, 2.3 Hz, 1H), 3.94 (dd, J = 11.1, 4.8 Hz, 1H), 3.86 – 3.77 (m, 2H), 3.69 (s, 3H), 3.65 (td, J = 8.8, 3.1 Hz, 1H), 3.60 (t, J = 2.5 Hz, 1H), 3.49 (ddd, J = 3.7, 1.8, 0.9 Hz, 1H), 2.78 (dd, J = 14.6, 9.8 Hz, 1H), 2.65 (dd, J = 14.6, 5.0 Hz, 1H), 2.52 (d, J = 5.1 Hz, 1H), 2.50 (ddd, J = 16.6, 7.2, 2.1 Hz, 1H), 2.39 (ddd, J = 16.6, 6.9, 2.2 Hz, 1H), 2.29 (tdd, J = 10.9, 5.0, 2.9 Hz, 1H), 2.16 (dt, J = 12.8, 6.7 Hz, 1H), 2.06 – 1.96 (m, 1H), 1.95 – 1.86 (m, 1H), 1.75 (ddd, J = 12.3, 11.1, 9.3 Hz, 1H), 1.07 (d, J = 6.5 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 84.1, 83.8, 81.0, 79.3, 74.6, 74.2, 73.6, 70.5, 68.5, 64.5, 53.7, 51.9, 39.9, 37.4, 35.3, 26.5, 26.3 (3C), 26.2

(3C), 25.9 (3C), 21.7, 18.5, 18.3, 18.0, 16.0, -3.4, -4.0, -4.2, -4.55, -4.57, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3464, 2954, 2929, 2894, 2857, 1737, 1596, 1498, 1471, 1463, 1437, 1389, 1344, 1254, 1148, 1130, 1085, 1054, 1006, 974, 938, 920, 889, 833, 813, 775, 756, 688, 668, 631, 533, 507, 469, 438, 424, 407 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{76}N_4O_{10}SSi_3Na^+$: 959.4482, found: 959.4490.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (epi-129b)

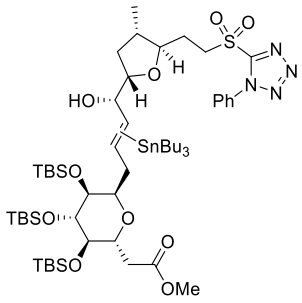


TEA (70.6 µL, 507 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (176 mg, 484 µmol) and (-)-N-methylephedrine (87 mg, 0.48 mmol) over 4 Å MS in PhMe (0.7 mL) at rt and stirring was continued for 3.25 h. A solution of alkyne **35a** (310 mg, 461 µmol) in PhMe (300 µL, rinsed with 2 x 300 µL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1 h. A solution of aldehyde **130** (178 mg, 507 µmol) in PhMe (300 µL, rinsed with 2 x 300 µL) was dried over 4 Å MS before it was added to the stirred reaction mixture at rt and stirring was continued for 5 d. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with MTBE (3 x 15 mL) and EtOAc (2 x 15 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 2:1) and preparative TLC (DCM/MeOH, 100:1) affording both compound *epi*-**129b** (73 mg, 16%) and some unreacted starting material **35a** (241 mg, 78%) as a colourless oil.

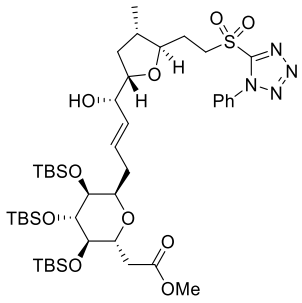
$[\alpha]_D^{20}$: +5.8 (c = 0.97, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.96 – 7.42 (m, 5H), 4.43 – 4.36 (m, 1H), 4.32 (dt, J = 9.3, 4.5 Hz, 1H), 4.23 – 4.11 (m, 2H), 4.06 (ddd, J = 9.6, 6.3, 3.5 Hz, 1H), 4.02 – 3.96 (m, 1H), 3.93 (dd, J = 11.0, 4.7 Hz, 1H), 3.87 – 3.76 (m, 2H), 3.68 – 3.59 (m, 2H), 3.48 (d, J = 2.2 Hz, 1H), 2.71 (dd, J = 14.5, 9.6 Hz, 1H), 2.62 (dd, J = 14.5, 5.0 Hz, 1H), 2.56 – 2.36 (m, 3H), 2.28 (dddd, J = 12.5, 9.5, 4.4, 2.3 Hz, 1H), 2.15 (dt, J = 12.8, 6.7 Hz, 1H), 2.06 – 1.95 (m, 1H), 1.95 – 1.85 (m, 1H), 1.75 (td, J = 11.6, 9.3 Hz, 1H), 1.06 (d, J = 6.5 Hz, 3H), 0.98 (dd, J = 9.6, 7.4 Hz, 2H), 0.92 (s, 9H), 0.895 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 6H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 153.6, 133.2, 131.6, 129.8 (2C), 125.3 (2C), 84.0,

83.8, 80.9, 79.4, 74.5, 74.2, 73.8, 70.4, 68.5, 64.4, 62.9, 53.7, 39.9, 37.8, 35.3, 26.5, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.6, 18.5, 18.3, 18.0, 17.4, 15.9, -1.3 (3C), -3.4, -4.0, -4.2, -4.55, -4.59, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3480, 2954, 2929, 2896, 2858, 1733, 1596, 1499, 1469, 1463, 1389, 1345, 1252, 1145, 1130, 1093, 1056, 1006, 976, 841, 835, 828, 776, 689, 631, 530, 506, 469 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{86}N_4O_{10}SSi_4Na^+$: 1045.5034, found: 1045.5043.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S,E)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (E-146)



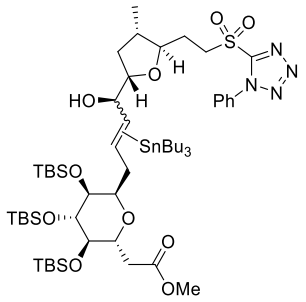
A solution of $[Cp^*RuCl]_4$ (10 mol%, 3 mg, 11 µmol) in DCM (0.6 mL) was added to a stirred solution of propargylic alcohol **129a** (100 mg, 107 µmol) in DCM (6 mL) was dried over 4 Å MS at -50 °C. The reaction mixture was warmed to rt and stirring was continued for 2 min. A solution of *n*-Bu_3SnH (31.6 µL, 117 µmol) in DCM (6 mL) was slowly added to the reaction mixture at -50 °C over the course of 30 min resulting in a colour change from brown to yellow. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:1) affording both a mixture of stannanes **145** (88 mg, 67%) and some unreacted starting material **129a** (18 mg, 18%) as a colourless oil. The mixture of stannanes *E*-**145** was used in the next step without further purification.



Aq. HI (57%, 47.3 µL, 358 µmol) was added to a stirred suspension of the mixture of stannanes *E*-**145** (88 mg, 36 µmol) and TBAI (27 mg, 72 µmol) in PhMe (2.3 mL) at 0 °C and stirring was continued for 2.5 h. Then aq. HI (57%, 47.3 µL, 358 µmol) was added to the stirred reaction mixture at 0 °C and stirring was continued for 1 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (5 mL) and the aq. phase was extracted with EtOAc (2 x 10 mL). The combined extracts were washed with aq. $Na_2S_2O_3$ (10%, 5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 3:1) affording compound *E*-**146** as a colourless oil (67 mg, quant.).

Analytical and spectral data of the allylic alcohol *E*-**146**: $[\alpha]_D^{20}$: +23.5 (c = 0.93, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 5.80 (dt, J = 15.7, 6.9 Hz, 1H), 5.47 (dd, J = 15.5, 6.4 Hz, 1H), 4.31 (dt, J = 9.2, 4.5 Hz, 1H), 4.00 – 3.76 (m, 6H), 3.68 (s, 3H), 3.56 (td, J = 8.6, 3.1 Hz, 1H), 3.50 – 3.45 (m, 2H), 2.71 (dd, J = 14.6, 9.4 Hz, 1H), 2.65 (dd, J = 14.5, 5.3 Hz, 1H), 2.51 – 2.43 (m, 1H), 2.42 (d, J = 2.6 Hz, 1H), 2.31 (dddd, J = 16.4, 10.8, 5.5, 2.8 Hz, 1H), 2.14 – 2.06 (m, 1H), 2.06 – 1.98 (m, 2H), 1.97 – 1.85 (m, 1H), 1.43 – 1.31 (m, 1H), 1.04 (d, J = 6.6 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.09 (s, 6H), 0.075 (s, 3H), 0.065 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 153.7, 133.2, 131.7, 131.6, 130.1, 129.9 (2C), 125.3 (2C), 82.8, 81.8, 76.1, 74.4, 74.1, 73.9, 71.8, 69.5, 53.6, 51.9, 40.0, 37.6, 37.5, 34.4, 26.4, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.2, -3.4, -4.0, -4.1, -4.50, -4.51, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3470, 2954, 2929, 2893, 2857, 1739, 1596, 1498, 1471, 1463, 1437, 1389, 1344, 1254, 1149, 1126, 1085, 1043, 1006, 972, 924, 833, 813, 774, 688, 673, 634, 535, 507, 474 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{78}N_4O_{10}SSi_3Na^+$: 961.4639, found: 961.4624.

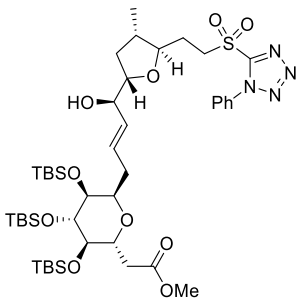
*trans-Hydrostannation to stannanes epi-**145***



A solution of $[Cp^*RuCl]_4$ (10 mol%, 3 mg, 11 µmol) in DCM (1 mL) was added to a stirred solution of propargylic alcohol *epi*-**129a** (100 mg, 107 µmol) in DCM (9 mL) with 4 Å MS at -50 °C. The reaction mixture was warmed to rt and stirring was continued for 2 min. Then *n*-Bu_3SnH (33.0 µL, 123 µmol) as a solution in DCM (9 mL) was slowly added to the reaction mixture at -50 °C over the course of 30 min resulting in a colour change from brown to green. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:1 to 2:1) affording both a mixture of stannanes *epi-Z*-**145** (12 mg, 12%) and a mixture of stannanes *epi-E*-**145** (77 mg, 74%) as a colourless oil which was used in the next step without further purification.

Procedure A (E-isomer)

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R,E)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (epi-E-146)

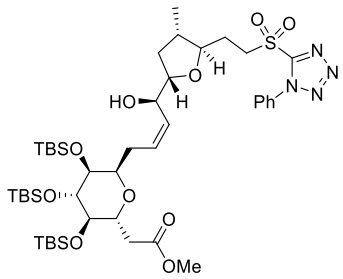


Aq. HI (57%, 41.3 µL, 313 µmol) was added to a stirred suspension of the mixture of stannanes *epi-E*-**145** (77 mg, 31 µmol) and TBAI (23 mg, 63 µmol) in PhMe (2 mL) at 0 °C and stirring was continued for 1 h. Then aq. HI (57%, 41.3 µL, 313 µmol) was again added to the stirred reaction mixture at 0 °C and stirring was continued for 3 h. By that time aq. HI (57%, 41.3 µL, 313 µmol) was once more added to the stirred reaction mixture at 0 °C and stirring was continued for 1.5 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (5 mL) and the aq. phase was extracted with EtOAc (2 x 10 mL). The combined extracts were washed with aq. $Na_2S_2O_3$ (10%, 5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 3:1) affording compound *epi-E*-**146** as a colourless oil (59 mg, 99%).

$[\alpha]_D^{20}$: +10.7 (c = 0.94, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 5.79 (dt, J = 15.5, 6.9 Hz, 1H), 5.47 (dd, J = 15.6, 6.8 Hz, 1H), 4.35 – 4.29 (m, 1H), 4.18 (dt, J = 6.7, 2.8 Hz, 1H), 4.01 – 3.91 (m, 2H), 3.87 – 3.80 (m, 2H), 3.80 – 3.76 (m, 1H), 3.67 (s, 3H), 3.58 (td, J = 8.6, 3.1 Hz, 1H), 3.49 – 3.43 (m, 2H), 2.82 (dd, J = 14.5, 10.3 Hz, 1H), 2.59 (dd, J = 14.5, 4.9 Hz, 1H), 2.46 (ddd, J = 15.5, 9.7, 6.3 Hz, 1H), 2.35 (d, J = 2.9 Hz, 1H), 2.28 (dddd, J = 13.8, 10.9, 5.2, 3.0 Hz, 1H), 2.07 – 1.95 (m, 3H), 1.92 (ddt, J = 10.9, 8.9, 6.5 Hz, 1H), 1.67 – 1.60 (m, 1H), 1.05 (d, J = 6.4 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.105 (s, 3H), 0.10 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 153.7, 133.2, 131.6 (2C), 130.0, 129.9 (2C), 125.3 (2C), 83.5, 81.5, 74.6, 74.2, 73.7, 73.3, 71.8, 69.4, 53.7, 51.8, 39.9, 37.3, 34.8, 34.4, 26.7, 26.4 (3C), 26.2 (3C), 25.9 (3C), 18.6, 18.4, 18.0, 16.2, -3.4, -4.0, -4.2, -4.49, -4.53, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3520, 2954, 2930, 2888, 2857, 1739, 1596, 1498, 1463, 1437, 1389, 1345, 1254, 1151, 1127, 1085, 1042, 1006, 972, 921, 833, 813, 774, 688, 671, 632, 535, 507, 422 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{78}N_4O_{10}SSi_3Na^+$: 961.4639, found: 961.4645.

Procedure B (Z-isomer)

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R,Z)-4-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (Z-146)

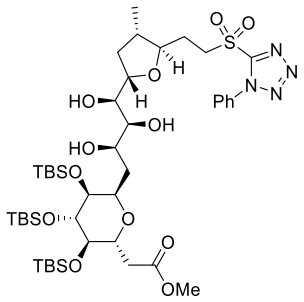


Aq. HI (57%, 12.9 µL, 97.7 µmol) was added to a stirred suspension of the mixture of stannanes *epi-Z*-**145** (12 mg, 5 µmol) and TBAI (4 mg, 10 µmol) in PhMe (1 mL) at 0 °C and stirring was continued for 2.5 h. Then aq. HI (57%, 6.4 µL, 49 µmol) was added to the stirred reaction mixture at 0 °C and stirring was continued for 5 h. Then aq. HI (57%, 6.4 µL, 49 µmol) was added again to the stirred reaction mixture at 0 °C and stirring was continued for 1 h. The reaction mixture was quenched with sat. aq. $NaHCO_3$ (5 mL) and the aq. phase was extracted with EtOAc (2 x 10 mL). The combined extracts were washed with aq. $Na_2S_2O_3$ (10%, 5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 3:1) affording compound *Z*-**146** as a colourless oil (9 mg, 98%).

$[\alpha]_D^{20}$: -2.4 (c = 0.66, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.56 (m, 5H), 5.64 (td, J = 10.9, 5.6 Hz, 1H), 5.53 (dd, J = 11.1, 8.5 Hz, 1H), 4.42 (ddd, J = 7.8, 4.2, 2.4 Hz, 1H), 4.27 (dt, J = 9.5, 4.9 Hz, 1H), 4.03 – 3.90 (m, 2H), 3.85 – 3.76 (m, 3H), 3.55 (td, J = 8.4, 3.1 Hz, 1H), 3.52 (t, J = 2.6 Hz, 1H), 3.46 (dt, J = 4.2, 1.4 Hz, 1H), 3.02 (d, J = 2.4 Hz, 1H), 2.76 (dt, J = 14.8, 10.0 Hz, 1H), 2.70 (dd, J = 15.1, 9.4 Hz, 1H), 2.63 (dd, J = 15.1, 5.4 Hz, 1H), 2.28 (tdd, J = 14.3, 6.5, 4.1 Hz, 1H), 2.13 (dt, J = 12.6, 6.6 Hz, 1H), 2.00 (dddd, J = 14.1, 8.5, 5.7, 2.8 Hz, 1H), 1.92 (tdd, J = 10.9, 7.5, 5.3 Hz, 1H), 1.83 (ddt, J = 13.9, 4.3, 2.1 Hz, 1H), 1.56 (ddd, J = 12.4, 10.9, 9.7 Hz, 1H), 1.05 (d, J = 6.5 Hz, 3H), 0.94 (s, 9H), 0.895 (s, 9H), 0.89 (s, 9H), 0.105 (s, 6H), 0.095 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.065 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.2, 153.7, 133.2, 131.6, 131.2, 130.7, 129.9 (2C), 125.3 (2C), 83.4, 81.2, 74.6, 74.0, 73.7, 72.1, 69.3, 68.9, 53.7, 52.0, 39.7, 37.4, 36.3, 30.1, 26.5, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.3, -3.5, -3.9, -4.2, -4.5, -4.6, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3455, 2954, 2929, 2895, 2857, 1739, 1597, 1499, 1462, 1449, 1388, 1345, 1254, 1152, 1102, 1089, 1044, 1006, 918, 835, 814, 776, 695, 633, 534, 507 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{78}N_4O_{10}SSi_3Na^+$: 961.4639, found: 961.4642.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2R,3S,4R)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (148)

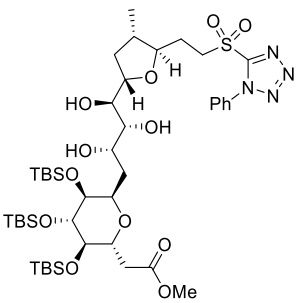
Representative Procedure (Sharpless Dihydroxylation)



Aq. $Me_SO_2NH_2$ (0.1 M, 106 µL, 10.6 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 31.9 µmol), K_2CO_3 (0.3 M, 31.9 µmol) and aq. $K_2OsO_2(OH)_4$ (0.05 M, 5 mol%, 10.6 µL, 532 nmol) were subsequently added to a stirred solution of allylic alcohol *epi-E*-**146** (10 mg, 11 µmol) and L* (12.5 mol%, 1 mg, 1.3 µmol) in *t*-BuOH (250 µL) and water (133 µL) at 0 °C, and stirring was continued for 15 min. The reaction mixture was warmed to rt and stirring was continued for 17 h. Then, aq. $Me_SO_2NH_2$ (0.1 M, 106 µL, 10.6 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 31.9 µmol) and K_2CO_3 (0.3 M, 31.9 µmol), *t*-BuOH (181µL), aq. $K_2OsO_2(OH)_4$ (0.05 M, 35 mol%, 74.5 µL, 3.73 µmol) and L* (87.5 mol%, 9 mg, 10 µmol) were again subsequently added to the reaction mixture, and stirring was continued for 3.5 h.

Herein, L* corresponds to: $(DHQ)_2R$ and $(DHQD)_2R$ with R = AQN, PHAL and PYR. HPLC analyses to determine the *d.r.* were carried out on each of the six reactions (Chapter 6.3.1), the work-up and purificiation was conducted with the mixture of all six reaction setups as following:

The mixture was diluted with water (5 mL) and the reaction was quenched with EtOAc (5 mL) and $NaHSO_3$ (200 mg, 1.92 mmol). The aq. phase was extracted with EtOAc (10 x 5 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 4:3) affording the *syn*,*anti*-isomer **147** (19 mg, 31%), a mixture of both isomers (11 mg, 18%), the *all-syn*-isomer **148** (19 mg, 31%) and some unreacted starting material *epi-E*-**146** (5 mg, 8%) as a colourless oil each.



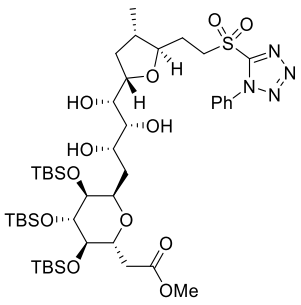
Analytical and spectral data of the *syn*,*anti*-isomer **147**: $[\alpha]_D^{20}$: -5.0 (c = 0.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.56 (m, 5H), 4.34 (dt, J = 10.1, 4.1 Hz, 1H), 4.20 – 4.10 (m, 3H), 3.95 (s, 1H), 3.92 (dt, J = 9.4, 4.6 Hz, 1H), 3.82 (dt, J = 9.4, 4.9 Hz, 1H), 3.77 (dd, J = 3.2, 1.9 Hz, 1H), 3.72 – 3.67 (m, 1H), 3.69 (s, 3H), 3.58 (td, J = 8.6, 2.9 Hz, 1H), 3.50 – 3.45 (m, 2H), 3.41 (td, J = 7.4, 1.5 Hz, 1H), 3.15 (d, J = 4.2 Hz, 1H), 3.06 (d, J = 7.3 Hz, 1H), 2.85 (dd, J = 15.1, 10.2 Hz, 1H), 2.63 (dd, J = 15.1, 4.4 Hz,

1H), 2.34 – 2.19 (m, 3H), 2.08 – 1.88 (m, 2H), 1.64 (ddd, J = 12.4, 10.9, 9.5 Hz, 1H), 1.43 (dt, J = 14.7, 2.1 Hz, 1H), 1.07 (d, J = 6.5 Hz, 3H), 0.94 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 6H), 0.09 (s, 3H), 0.08 (s, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.5, 80.4, 74.1, 74.1, 74.0, 73.7, 73.6, 72.3, 71.9, 70.4, 53.7, 52.0, 39.7, 37.1, 36.6, 34.3, 26.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.5, -3.6, -3.9, -4.1, -4.55, -4.60, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3461, 2954, 2930, 2894, 2858, 1738, 1596, 1499, 1463, 1438, 1390, 1345, 1257, 1151, 1129, 1088, 1007, 921, 835, 814, 776, 688, 633, 539, 506, 461, 422 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{80}N_4O_{12}SSi_3Na^+$: 995.4694, found: 995.4694.

Analytical and spectral data of the *all-syn*-isomer **148**: $[\alpha]_D^{20}$: -7.0 (c = 0.1, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 4.24 (dt, J = 12.3, 2.8 Hz, 1H), 4.18 (dt, J = 11.0, 1.8 Hz, 1H), 4.08 (d, J = 4.8 Hz, 1H), 4.04 (dt, J = 9.2, 6.4 Hz, 1H), 3.95 – 3.86 (m, 2H), 3.80 – 3.78 (m, 1H), 3.78 (ddd, J = 15.0, 11.1, 5.0 Hz, 1H), 3.69 (s, 3H), 3.61 (ddd, J = 6.9, 3.5, 1.1 Hz, 1H), 3.58 (d, J = 3.5 Hz, 1H), 3.57 – 3.54 (m, 1H), 3.50 (td, J = 8.8, 3.0 Hz, 1H), 3.45 (dt, J = 2.8, 1.4 Hz, 1H), 3.42 (t, J = 2.2 Hz, 1H), 3.12 (dd, J = 13.8, 12.0 Hz, 1H), 2.72 (d, J = 7.6 Hz, 1H), 2.44 (dd, J = 13.8, 3.5 Hz, 1H), 2.32 – 2.21 (m, 2H), 2.04 – 1.87 (m, 3H), 1.58 (ddd, J = 12.0, 10.9, 9.4 Hz, 1H), 1.54 – 1.47 (m, 1H), 1.06 (d, J = 6.4 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.095 (s, 3H), 0.09 (s, 3H), 0.085 (s, 3H), 0.08 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 173.6, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.0, 78.3, 75.8, 75.2, 73.6, 73.0, 72.7, 72.1, 70.2, 64.2, 53.7, 52.4, 40.1, 38.1, 36.9, 35.5, 26.6, 26.4 (3C), 26.3 (3C), 25.9 (3C), 18.7, 18.4, 18.0, 16.4, -3.6, -4.1, -4.2, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3472, 2954, 2930, 2896, 2857, 1736, 1596, 1498, 1471, 1463, 1438, 1389, 1345, 1256, 1151, 1086, 1042, 1006, 918, 894, 835, 813, 774, 759, 688, 668, 633, 537, 507, 458, 433, 421, 407 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{80}N_4O_{12}SSi_3Na^+$: 995.4694, found: 995.4694.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4S)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (150a)

Representative Procedure (Sharpless Dihydroxylation)



Aq. $MeSO_2NH_2$ (0.1 M, 79.8 µL, 7.98 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 24.0 µmol), K_2CO_3 (0.3 M, 24.0 µmol) and aq. $K_2OsO_2(OH)_4$ (0.05 M, 5 mol%, 8.0 µL, 399 nmol) were subsequently added to a stirred solution of allylic alcohol *E*-**146** (7.5 mg, 8 µmol) and L* (12.5 mol%, 1 mg, 1.0 µmol) in *t*-BuOH (250 µL) and water (140 µL) at 0 °C, and stirring was continued for 15 min. The reaction mixture was warmed to rt and stirring was continued for 24 h. Then, aq. $K_2OsO_2(OH)_4$ (0.05 M, 5 mol%, 8.0 µL, 399 nmol) was again added to the reaction mixture, and stirring was continued for 4 d.

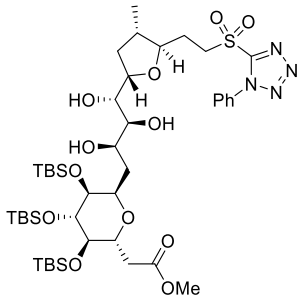
Herein, L* corresponds to: $(DHQ)_2R$ and $(DHQD)_2R$ with R = AQN, PHAL and PYR. HPLC analyses to determine the *d.r.* were carried out on each of the six reactions (Chapter 6.3.2), the work-up and purificiation was conducted with the mixture of all six reaction setups as following:

The mixture was diluted with water (5 mL) and the reaction was quenched with EtOAc (5 mL) and $NaHSO_3$ (60 mg, 574 µmol). The aq. phase was extracted with EtOAc (10 x 5 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 4:3) affording the major *syn*,*anti*-isomer **149** (15 mg, 32%), a mixture of both isomers (1 mg, 2%), the desired minor *all-syn*-isomer **150a** (3 mg, 6%) and some unreacted starting material *E*-**146** (21 mg, 47%) as a colourless oil each.

Analytical and spectral data of the minor *all-syn*-isomer **150a**: $[\alpha]_D^{20}$: +16.4 (c = 1.00, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.57 (m, 5H), 4.32 (dt, J = 10.1, 4.1 Hz, 1H), 4.16 (dt, J = 9.6, 5.9 Hz, 1H), 4.12 (dt, J = 10.9, 2.1 Hz, 1H), 4.01 – 3.94 (m, 1H), 3.91 (dd, J = 10.8, 4.8 Hz, 1H), 3.86 – 3.84 (m, 1H), 3.83 (ddd, J = 14.8, 10.6, 5.4 Hz, 1H), 3.79 – 3.76 (m, 1H), 3.69 (s, 3H), 3.66 – 3.62 (m, 1H), 3.60 (td, J = 8.7, 3.0 Hz, 1H), 3.50 – 3.42 (m, 3H), 3.29 (d, J = 3.4 Hz, 1H), 3.05 (d, J = 6.5 Hz, 1H), 2.85 (dd, J = 15.0, 10.2 Hz, 1H), 2.63 (dd, J = 15.0, 4.4 Hz, 1H), 2.30 (tdd, J = 10.8, 5.2, 3.1 Hz, 1H), 2.24 – 2.12 (m, 2H), 2.02 (dddd, J = 13.2, 10.4, 8.1, 4.9 Hz, 1H), 1.94 (dtd, J = 10.4, 8.8, 6.6 Hz, 1H), 1.61 – 1.51 (m, 1H), 1.42 (dt, J = 14.4, 2.3 Hz, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.93 (s, 9H), 0.90 (s, 18H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0,

153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.1, 80.2, 74.9, 74.1, 74.0, 73.7, 73.6, 73.4, 72.3, 69.6, 53.6, 52.0, 39.8, 37.14, 37.11, 34.5, 26.5, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.1, -3.6, -3.9, -4.2, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3480, 2954, 2930, 2893, 2858, 1737, 1597, 1499, 1463, 1438, 1389, 1339, 1256, 1150, 1130, 1087, 1044, 1006, 916, 834, 813, 775, 689, 667, 632, 529, 507, 452, 420 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{80}N_4O_{12}Si_3SNa^+$: 995.4694, found: 995.4700.

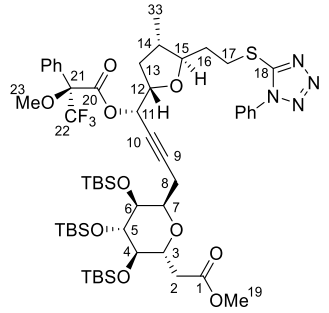
Analytical and spectral data of the major *syn*,*anti*-isomer **149**: $[\alpha]_D^{20}$: +13.9 (c = 1.42, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73 – 7.56 (m, 5H), 4.35 – 4.22 (m, 2H), 4.19 – 4.12 (m, 1H), 4.12 – 4.04 (m, 1H), 3.95 (ddd, J = 15.3, 10.5, 4.8 Hz, 1H), 3.83 (ddd, J = 15.3, 10.2, 5.2 Hz, 1H), 3.80 – 3.76 (m, 1H), 3.69 (s, 3H), 3.63 (d, J = 5.3 Hz, 1H), 3.58 (td, J = 8.6, 2.9 Hz, 1H), 3.54 – 3.47 (m, 1H), 3.45 (t, J = 2.1 Hz, 1H), 3.41 (t, J = 2.3 Hz, 1H), 3.40 – 3.33 (m, 1H), 3.07 (dd, J = 14.0, 11.4 Hz, 1H), 2.64 (d, J = 9.1 Hz, 1H), 2.57 (d, J = 8.1 Hz, 1H), 2.49 (dd, J = 14.0, 3.9 Hz, 1H), 2.30 (dddd, J = 13.5, 10.5, 5.3, 2.9 Hz, 1H), 2.15 (dt, J = 12.4, 6.3 Hz, 1H), 2.07 – 1.93 (m, 2H), 1.90 (ddd, J = 14.1, 11.2, 3.1 Hz, 1H), 1.74 – 1.59 (m, 1H), 1.55 (ddd, J = 14.1, 10.1, 1.9 Hz, 1H), 1.06 (d, J = 6.5 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.09 (s, 6H), 0.08 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 173.2, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.4, 78.6, 75.2, 74.9, 74.2, 73.7, 73.0, 72.3, 66.8, 64.5, 53.6, 52.3, 40.1, 37.6, 37.0, 36.0, 26.7, 26.4 (3C), 26.3 (3C), 25.9 (3C), 18.7, 18.4, 18.0, 16.1, -3.6, -4.1, -4.2, -4.48, -4.54, -4.7 ppm; **IR** (film): $\tilde{\nu}$ = 3459, 2954, 2929, 2895, 2857, 1736, 1596, 1499, 1463, 1438, 1390, 1342, 1255, 1150, 1100, 1084, 1040, 1006, 921, 894, 863, 833, 813, 774, 761, 688, 669, 632, 540, 507, 477 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{80}N_4O_{12}SSi_3Na^+$: 995.4694, found: 995.4696.

5.2.2.3. Stereochemical Elucidation

(S)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)thio)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-yn-1-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (151)



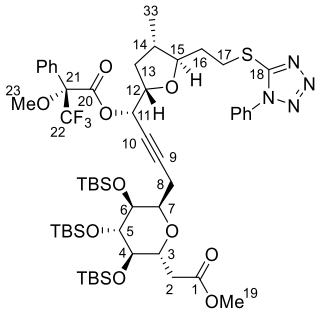
(*R*)-Mosher acid chloride (10.3 µL, 55.2 µmol) was added to a stirred solution of propargylic alcohol **144** (13 mg, 14 µmol) and py (5.6 µL, 69 µmol) in DCM (0.5 mL) at rt and the reaction mixture was stirred for 1.5 h. Then, py (2.2 µL, 28 µmol) and (*R*)-Mosher acid chloride (2.6 µL, 14 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 19 h. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1) affording compound **151** as a colourless oil (15 mg, 97%).[296]

$[\alpha]_D^{20}$: +9.4 (c = 1.50, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.63 – 7.50 (m, 7H, Ph), 7.40 – 7.34 (m, 3H, Ph), 5.53 (ddd, J = 8.6, 2.3, 1.8 Hz, 1H, H-11), 4.29 (ddd, J = 8.8, 5.6, 4.0 Hz, 1H, H-3), 4.18 (td, J = 8.4, 7.0 Hz, 1H, H-12), 3.93 (ddd, J = 8.4, 6.2, 2.2 Hz, 1H, H-7), 3.81 (dd, J = 3.0, 2.0 Hz, 1H, H-5), 3.66 (s, 3H, H-19), 3.63 (ddd, J = 3.0, 2.2, 1.0 Hz, 1H, H-6), 3.59 (s, 3H, H-23), 3.56 (td, J = 9.2, 2.8 Hz, 1H, H-15), 3.50 (ddd, J = 4.0, 1.7, 1.0 Hz, 1H, H-4), 3.48 (ddd, J = 13.4, 8.7, 4.7 Hz, 1H, H-17a), 3.30 (ddd, J = 13.4, 8.4, 7.5 Hz, 1H, H-17b), 2.75 (dd, J = 14.9, 5.7 Hz, 1H, H-2a), 2.64 (dd, J = 14.9, 8.8 Hz, 1H, H-2b), 2.50 (ddd, J = 16.6, 8.5, 1.8 Hz, 1H, H-8a), 2.41 (ddd, J = 16.5, 5.9, 2.4 Hz, 1H, H-8b), 2.31 (ddd, J = 12.9, 7.5, 7.1 Hz, 1H, H-13a), 2.20 (dddd, J = 14.0, 8.7, 7.5, 2.8 Hz, 1H, H-16a), 1.96 – 1.84 (m, 2H, H-14 and H-16b), 1.48 (ddd, J = 13.0, 10.8, 8.2 Hz, 1H, H-13b), 1.04 (d, J = 6.5 Hz, 3H, H-33), 0.89 (s, 18H, *t*-Bu), 0.885 (s, 9H, *t*-Bu), 0.11 (s, 3H, Me), 0.095 (s, 3H, Me), 0.09 (s, 3H, Me), 0.085 (s, 3H, Me), 0.07 (s, 3H, Me), 0.03 (s, 3H, Me) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.6 (C-1), 165.8 (C-20), 154.4 (C-18), 133.9 (*i*-Ph), 132.4 (*i*-Ph), 130.2 (*p*-Ph), 129.9 (2C, *m*-Ph), 129.7 (*p*-Ph), 128.4 (2C, *o*-Ph), 127.6 (2C, *m*-Ph), 123.9 (2C, *o*-Ph), 123.4 (q, J = 289 Hz, C-22), 85.4 (C-9), 85.0 (q, J = 25.7 Hz, C-21), 83.6 (C-15), 78.8 (C-12), 75.1 (C-10), 74.23 (C-5), 74.15 (C-3), 73.7 (C-4), 70.1 (C-6), 68.9 (C-11), 68.6 (C-7), 55.7 (C-23), 51.8 (C-19), 39.7 (C-14), 38.0 (C-13), 37.4 (C-2), 33.3 (C-16), 30.1 (C-17), 26.3 (3C, *t*-Bu), 26.1 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 21.4 (C-8), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 16.0 (C-33), -3.4 (Me), -3.9 (Me), -4.2 (Me), -4.6 (2C, Me), -5.0

[296] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.1.

(Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.5 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2857, 1745, 1598, 1500, 1472, 1463, 1436, 1388, 1361, 1335, 1251, 1186, 1168, 1126, 1082, 1055, 1015, 993, 939, 832, 813, 775, 759, 722, 695, 667, 547, 508, 454, 432, 419 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{83}N_4O_{10}F_3SSi_3Na^+$: 1143.4982, found: 1143.4991.

(S)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)thio)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-yn-1-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-151)



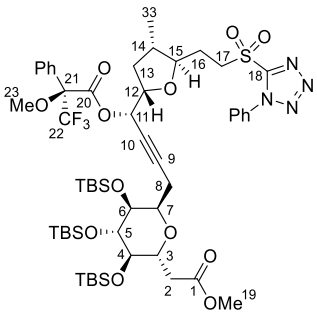
(*S*)-Mosher acid chloride (10.3 µL, 55.2 µmol) was added to a stirred solution of propargylic alcohol **144** (13 mg, 14 µmol) and py (5.6 µL, 69 µmol) in DCM (0.5 mL) at rt and the reaction mixture was stirred for 1.5 h. Then, py (2.2 µL, 28 µmol) and (*S*)-Mosher acid chloride (2.6 µL, 14 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 19 h. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1) affording compound *epi*-**151**as a colourless oil (12 mg, 78%).[297]

$[\alpha]_D^{20}$: +24.2 (c = 1.20, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 7.60 – 7.51 (m, 7H, Ph), 7.41 – 7.33 (m, 3H, Ph), 5.54 (ddd, J = 7.6, 2.4, 1.9 Hz, 1H, H-11), 4.30 (ddd, J = 9.1, 5.5, 4.2 Hz, 1H, H-3), 4.11 (ddd, J = 8.3, 7.4, 7.0 Hz, 1H, H-12), 3.94 (ddd, J = 8.5, 6.3, 2.2 Hz, 1H, H-7), 3.82 (dd, J = 2.9, 1.7 Hz, 1H, H-5), 3.66 (s, 3H, H-19), 3.65 – 3.63 (m, 1H, H-6), 3.55 (s, 3H, H-23), 3.54 – 3.49 (m, 2H, H-15 and H-4), 3.44 (ddd, J = 13.4, 8.8, 4.7 Hz, 1H, H-17a), 3.29 (ddd, J = 13.4, 8.3, 7.6 Hz, 1H, H-17b), 2.75 (dd, J = 14.9, 5.7 Hz, 1H, H-2a), 2.63 (dd, J = 14.9, 9.0 Hz, 1H, H-2b), 2.52 (ddd, J = 16.6, 8.1, 1.8 Hz, 1H, H-8a), 2.46 (ddd, J = 16.6, 6.3, 2.4 Hz, 1H, H-8b), 2.23 (dt, J = 12.9, 7.3 Hz, 1H, H-13a), 2.16 (dddd, J = 13.9, 8.7, 7.3, 2.7 Hz, 1H, H-16a), 1.93 – 1.85 (m, 1H, H-14), 1.83 (ddd, J = 13.7, 8.6, 4.8 Hz, 1H, H-16b), 1.44 (ddd, J = 12.7, 10.7, 8.4 Hz, 1H, H-13b), 0.99 (d, J = 6.6 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.115 (s, 3H, Me), 0.105 (s, 3H, Me), 0.095 (s, 3H, Me), 0.09 (s, 3H, Me), 0.085 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.8 (C-1), 165.7

[297] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.1.

(C-21), 154.5 (C-18), 133.9 (*i*-Ph), 132.4 (*i*-Ph), 130.2 (*p*-Ph), 129.9 (2C, *m*-Ph), 129.7 (*p*-Ph), 128.4 (2C, *o*-Ph), 127.7 (2C, *m*-Ph), 123.9 (2C, *o*-Ph), 123.4 (q, J = 289 Hz, C-22), 85.5 (C-9), 84.5 (q, J = 28.3 Hz, C-21), 83.6 (C-15), 78.6 (C-12), 75.4 (C-10), 74.3 (C-5), 74.1 (C-3), 73.8 (C-4), 70.3 (C-6), 68.8 (C-7), 68.6 (C-11), 55.6 (C-23), 51.8 (C-19), 39.6 (C-14), 37.7 (C-13), 37.4 (C-2), 33.3 (C-16), 30.1 (C-17), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.8 (3C, *t*-Bu), 21.5 (C-8), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 15.9 (C-33), -3.3 (Me), -3.9 (Me), -4.1 (Me), -4.60 (Me), -4.61 (Me), -4.9 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.9 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2897, 2857, 1749, 1598, 1500, 1472, 1463, 1410, 1388, 1361, 1333, 1251, 1185, 1169, 1126, 1083, 1056, 1015, 994, 973, 938, 891, 833, 813, 776, 762, 719, 695, 672, 552, 460, 406 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{83}N_4O_{10}F_3SSi_3Na^+$: 1143.4982, found: 1143.4988.

(S)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-yn-1-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (152)



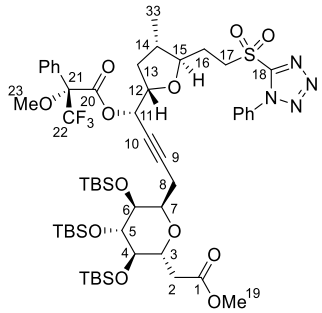
(*R*)-Mosher acid chloride (1.5 µL, 8.0 µmol) was added to a stirred solution of propargylic alcohol **129a** (5 mg, 5 µmol) and py (1.3 µL, 16 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 1 h. By that time py (0.9 µL, 11 µmol) and (*R*)-Mosher acid chloride (2.5 µL, 13 µmol) were again subsequently added to the reaction mixture at rt and stirring was continued for 3 h. Then py (2.2 µL, 27 µmol) and (*R*)-Mosher acid chloride (4.0 µL, 21 µmol) were once more subsequently added to the reaction mixture at rt and stirring was continued for 3 d. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 6:1) affording compound **152** as a colourless oil (6 mg, 98%).[298]

$[\alpha]_D^{20}$: +7.1 (c = 0.80, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.50 (m, 7H, Ph), 7.44 – 7.34 (m, 3H, Ph), 5.54 (dt, J = 8.4, 2.0 Hz, 1H, H-11), 4.29 (dt, J = 9.3, 5.2 Hz, 1H, H-3), 4.19 (td, J = 8.3, 6.9 Hz, 1H, H-12), 3.93 (ddd, J = 8.2, 6.1, 2.2 Hz, 1H, H-7), 3.83 – 3.78 (m, 1H, H-5), 3.77 (dd, J = 11.4, 4.8 Hz, 1H, H-17a), 3.68 (dd, J = 11.4, 4.7 Hz, 1H, H-17b), 3.66 (s, 3H, H-19), 3.64 – 3.62 (m,

[298] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.2.

1H, H-6), 3.61 (s, 3H, H-23), 3.58 – 3.52 (m, 1H, H-15), 3.51 – 3.49 (m, 1H, H-4), 2.75 (dd, J = 14.9, 5.6 Hz, 1H, H-2a), 2.63 (dd, J = 14.9, 8.8 Hz, 1H, H-2b), 2.49 (ddd, J = 16.6, 8.2, 1.7 Hz, 1H, H-8a), 2.42 (ddd, J = 16.6, 6.2, 2.3 Hz, 1H, H-8b), 2.34 (dt, J = 12.7, 7.2 Hz, 1H, H-13a), 2.28 (dddd, J = 12.7, 11.3, 4.7, 2.7 Hz, 1H, H-16a), 2.05 – 1.95 (m, 1H, H-16a), 1.95 – 1.85 (m, 1H, H-14), 1.52 (ddd, J = 12.9, 10.5, 8.2 Hz, 1H, H-13b), 1.07 (d, J = 6.5 Hz, 3H, H-33), 0.895 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.885 (s, 9H, *t*-Bu), 0.11 (s, 3H, Me), 0.095 (s, 6H, Me), 0.09 (s, 3H, Me), 0.07 (s, 3H, Me), 0.04 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8 (C-1), 165.8 (C-20), 153.5 (C-18), 133.2, 132.3 (Ph), 131.6 (Ph), 129.9 (2C, Ph), 129.8 (Ph), 128.5 (2C, Ph), 127.6 (2C, Ph), 125.2 (2C, Ph), 122.7 (q, J = 283 Hz, C-22), 85.7 (C-9), 84.8 (q, J = 27.3 Hz, C-21), 82.8 (C-15), 79.0 (C-12), 74.8 (C-10), 74.3 (C-5), 74.1 (C-3), 73.8 (C-4), 70.2 (C-6), 68.7 (C-7), 68.6 (C-11), 55.7 (C-23), 53.7 (C-17), 51.8 (C-19), 39.9 (C-14), 37.8 (C-13), 37.4 (C-2), 26.3 (4C, C-16 and *t*-Bu), 26.1 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 21.4 (C-8), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 15.8 (C-33), -3.4 (Me), -3.9 (Me), -4.2 (Si-Me), -4.59 (Me), -4.61 (Me), -5.0 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.4 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2955, 2930, 2895, 2857, 1747, 1499, 1469, 1463, 1344, 1257, 1180, 1169, 1160, 1096, 1088, 1069, 1015, 834, 777, 688, 543, 505, 460, 411 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{83}N_4O_{12}F_3SSi_3Na^+$: 1175.4880, found: 1175.4893.

(S)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-yn-1-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-152)



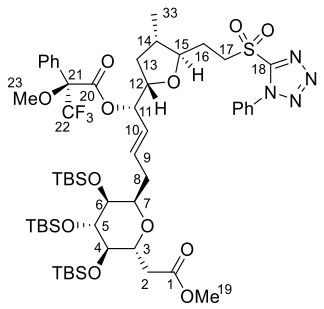
(*S*)-Mosher acid chloride (1.5 µL, 8.0 µmol) was added to a stirred solution of propargylic alcohol **129a** (5 mg, 5 µmol) and py (1.3 µL, 16 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 1 h. Then py (0.9 µL, 11 µmol) and (*S*)-Mosher acid chloride (2.5 µL, 13 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 3 h. Then py (2.2 µL, 27 µmol) and (*S*)-Mosher acid chloride (4.0 µL, 21 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 3 d. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was

purified by flash chromatography (SiO_2, hexane/EtOAc, 6:1) affording compound *epi*-**152** as a colourless oil (6 mg, 98%).[299]

$[\alpha]_D^{20}$: +24.9 (c = 0.80, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.51 (m, 7H, Ph), 7.44 – 7.35 (m, 3H, Ph), 5.55 (dt, J = 7.5, 2.0 Hz, 1H, H-11), 4.30 (dt, J = 9.4, 5.0 Hz, 1H, H-3), 4.11 (dt, J = 8.4, 7.0 Hz, 1H, H-12), 3.95 (td, J = 7.1, 2.3 Hz, 1H, H-7), 3.82 (dd, J = 3.3, 1.6 Hz, 1H, H-5), 3.77 (ddd, J = 14.7, 11.4, 4.8 Hz, 1H, H-17a), 3.70 – 3.61 (m, 2H, H-17b and H-6), 3.66 (s, 3H, H-19), 3.57 (s, 3H, H-23), 3.53 – 3.47 (m, 2H, H-4 and H-15), 2.75 (dd, J = 14.9, 5.6 Hz, 1H, H-2a), 2.62 (dd, J = 14.9, 8.9 Hz, 1H, H-2b), 2.49 (dt, J = 6.8, 1.9 Hz, 2H, H-8), 2.30 – 2.19 (m, 2H, H-16a and H-13a), 2.00 – 1.91 (m, 1H, H-16b), 1.91 – 1.82 (m, 1H, H-14), 1.49 (ddd, J = 12.8, 10.8, 8.6 Hz, 1H, H-13b), 1.01 (d, J = 6.6 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.095 (s, 3H, Si-Me), 0.09 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8 (C-1), 165.8 (C-20), 153.5 (C-18), 133.2 (Ph), 132.3 (Ph), 131.6 (Ph), 129.87 (2C, Ph), 129.85 (Ph), 128.5 (2C, Ph), 127.6 (2C, Ph), 125.2 (2C, Ph), 123.3 (q, J = 304 Hz, C-22), 85.8 (C-9), 85.6 (q, J = 28.1 Hz, C-21), 82.9 (C-15), 78.7 (C-12), 75.2 (C-10), 74.3 (C-5), 74.0 (C-3), 73.9 (C-4), 70.3 (C-6), 68.9 (C-7), 68.4 (C-11), 55.7 (C-23), 53.6 (C-17), 51.8 (C-19), 39.7 (C-14), 37.5 (C-13), 37.4 (C-2), 26.3 (4C, C-16 and *t*-Bu), 26.2 (3C, *t*-Bu), 25.8 (3C, *t*-Bu), 21.5 (C-8), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 15.8 (C-33), -3.4 (Me), -3.9 (Me), -4.1 (Me), -4.59 (Me), -4.61 (Me), -4.9 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.8 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2895, 2857, 1747, 1498, 1469, 1463, 1347, 1256, 1178, 1170, 1160, 1097, 1086, 1076, 1015, 917, 834, 776, 770, 720, 687, 528, 503, 482, 460, 427, 411 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{83}N_4O_{12}F_3SSi_3Na^+$: 1175.4880, found: 1175.4877.

[299] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.2.

(S,E)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-en-1-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (153)



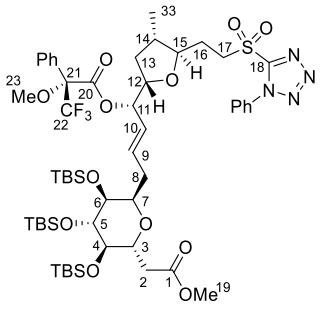
(*R*)-Mosher acid chloride (4.0 µL, 21 µmol) was added to a stirred solution of allylic alcohol *E*-**146** (5 mg, 5 µmol) and py (2.2 µL, 27 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 6 h. Then py (0.4 µL, 5.3 µmol) and (*R*)-Mosher acid chloride (1.0 µL, 5.3 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 19 h. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **153** as a colourless oil (6 mg, 98%).[300]

$[\alpha]_D^{20}$: +7.9 (c = 0.81, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.48 (m, 7H, Ph), 7.42 – 7.32 (m, 3H, Ph), 5.88 (dtd, J = 18.7, 7.2, 4.7 Hz, 1H, H-9), 5.43 – 5.31 (m, 2H, H-10 and H-11), 4.29 (ddd, J = 9.3, 5.6, 3.7 Hz, 1H, H-3), 4.14 – 4.07 (m, 1H, H-12), 3.86 – 3.74 (m, 3H, H-17a and H-5 and H-7), 3.73 – 3.67 (m, 1H, H-17b), 3.66 (s, 3H, H-19), 3.61 (s, 3H, H-23), 3.58 – 3.51 (m, 1H, H-15), 3.51 – 3.48 (m, 1H, H-4), 3.47 (t, J = 2.3 Hz, 1H, H-6), 2.74 (dd, J = 14.9, 5.7 Hz, 1H, H-2a), 2.60 (dd, J = 14.9, 8.9 Hz, 1H, H-2b), 2.45 (ddd, J = 15.2, 8.7, 6.5 Hz, 1H, H-8a), 2.27 (dddd, J = 14.0, 11.4, 4.6, 2.9 Hz, 1H, H-16a), 2.16 (dt, J = 12.6, 7.0 Hz, 1H, H-13a), 2.05 – 1.94 (m, 2H, H-8b and H-16b), 1.93 – 1.84 (m, 1H, H-14), 1.36 (ddd, J = 12.6, 10.8, 8.9 Hz, 1H, H-13b), 1.04 (d, J = 6.5 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu), 0.895 (s, 9H, *t*-Bu), 0.885 (s, 9H, *t*-Bu), 0.105 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.085 (s, 3H, Me), 0.07 (s, 3H, Me), 0.05 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8 (C-1), 165.9 (C-20), 153.5 (C-18), 135.7 (C-9), 133.2 (Ph), 132.7 (Ph), 131.6 (Ph), 129.9 (2C, Ph), 129.6 (Ph), 128.4 (2C, Ph), 127.6 (2C, Ph), 125.3 (2C, Ph), 124.7 (C-10), 124.3 (q, J = 286 Hz, C-22), 84.5 (q, J = 27.0 Hz, C-21), 82.6 (C-15), 79.4 (C-11), 78.8 (C-12), 74.4 (C-5), 73.8 (C-3), 73.7 (C-4), 71.8 (C-6), 69.3 (C-7), 55.7 (H-23), 53.7 (C-17), 51.8 (H-19), 40.0 (C-14), 37.7 (C-13), 37.4 (C-2), 34.4 (C-8), 26.34 (C-16), 26.31 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 15.9 (C-33), -3.4 (Me), -3.9 (Me), -4.2 (Me), -4.51 (Me), -4.54 (Me), -4.9 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.4 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2930, 2895, 2857,

[300] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.3.

1743, 1596, 1498, 1472, 1463, 1438, 1390, 1346, 1256, 1184, 1167, 1124, 1084, 1040, 1014, 993, 923, 866, 835, 813, 775, 721, 689, 673, 637, 534, 508, 471, 453, 438, 406 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}F_3SSi_3Na^+$: 1177.5037, found: 1177.5044.

(S,E)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-en-1-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-153)



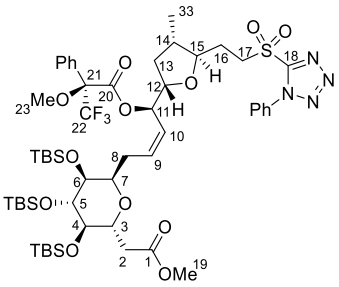
(*S*)-Mosher acid chloride (4 µL, 21 µmol) was added to a stirred solution of allylic alcohol *E*-**146** (5 mg, 5 µmol) and py (2.2 µL, 27 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 6 h. Then py (0.4 µL, 5.3 µmol) and (*S*)-Mosher acid chloride (1.0 µL, 5.3 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 19 h. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound *epi*-**153** as a colourless oil (6 mg, 98%).[301]

$[\alpha]_D^{20}$: +25.9 (c = 0.82, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.48 (m, 7H, Ph), 7.42 – 7.32 (m, 3H, Ph), 5.96 (dt, J = 15.4, 7.0 Hz, 1H, H-9), 5.55 (ddt, J = 15.7, 8.5, 1.4 Hz, 1H, H-10), 5.39 (dd, J = 8.4, 6.3 Hz, 1H, H-11), 4.29 (dt, J = 9.5, 5.1 Hz, 1H, H-3), 4.06 (dt, J = 9.0, 6.5 Hz, 1H, H-12), 3.84 – 3.75 (m, 3H, H-17a and H-5 and H-7), 3.70 – 3.64 (m, 1H, H-17b), 3.64 (s, 3H, H-19), 3.54 (s, 3H, H-23), 3.52 – 3.47 (m, 2H, H-6 and H-4), 3.43 (td, J = 9.0, 3.0 Hz, 1H, H-15), 2.75 (dd, J = 14.9, 5.5 Hz, 1H, H-2a), 2.59 (dd, J = 14.9, 8.9 Hz, 1H, H-2b), 2.54 – 2.44 (m, 1H, H-8a), 2.22 (dddd, J = 14.1, 11.6, 4.6, 3.0 Hz, 1H, H-16a), 2.08 (dt, J = 12.6, 7.1 Hz, 1H, H-13a), 2.06 – 1.99 (m, 1H, H-8b), 1.98 – 1.89 (m, 1H, H-16b), 1.88 – 1.78 (m, 1H, H-14), 1.30 (ddd, J = 12.6, 10.9, 9.2 Hz, 1H, H-13b), 0.95 (d, J = 6.7 Hz, 3H, H-33), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.085 (s, 3H, Me), 0.075 (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9 (C-1), 166.0 (C-20), 153.5 (C-18), 136.0 (C-9), 133.2 (Ph), 132.6 (Ph), 131.6 (Ph), 129.9 (2C, Ph), 129.7 (Ph), 128.5 (2C, Ph), 127.7 (2C, Ph), 125.4 (C-10),

[301] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.3.

125.3 (2C, Ph), 123.8 (q, J = 291 Hz, C-22), 84.6 (J = 27.4 Hz, C-21), 82.6 (C-15), 79.1 (C-11), 78.8 (C-12), 74.5 (C-5), 73.9 (C-3), 73.7 (C-4), 71.9 (C-6), 69.6 (C-7), 55.6 (C-23), 53.7 (C-17), 51.8 (C-19), 39.8 (C-14), 37.5 (C-2), 37.2 (C-13), 34.4 (C-8), 26.5 (C-16), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.5 (*t*-Bu), 18.4 (*t*-Bu), 18.0 (*t*-Bu), 15.7 (C-33), -3.4 (Me), -3.9 (Me), -4.2 (Me), -4.5 (Me), -4.6 (Me), -4.9 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.5 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2930, 2894, 2857, 1743, 1596, 1498, 1472, 1463, 1438, 1390, 1346, 1254, 1168, 1162, 1123, 1083, 1040, 1015, 992, 923, 866, 834, 813, 774, 763, 720, 689, 669, 635, 533, 507, 470, 424 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}F_3SSi_3Na^+$: 1177.5037, found: 1177.5045.

(R,Z)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-en-1-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (154)



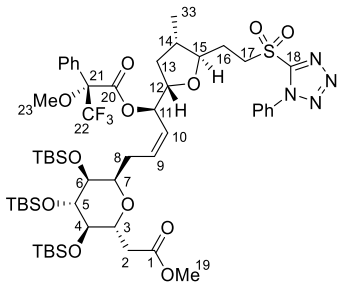
(*R*)-Mosher acid chloride (3.6 µL, 19 µmol) was added to a stirred solution of allylic alcohol *epi-Z*-**146** (5 mg, 5 µmol) and py (1.9 µL, 24 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 3 d. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **154** as a colourless oil (5 mg, 90%).[302]

(the sample contained some cleaved off 2,5-*trans*-disubstituted ether) $[\alpha]_D^{20}$: +9.0 (c = 0.63, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.31 – 7.44 (m, 7H, Ph), 7.42 – 7.35 (m, 3H, Ph), 5.99 – 5.81 (m, 2H, H-9 and H-11), 5.42 – 5.28 (m, 1H, H-10), 4.34 (ddd, J = 9.2, 5.6, 3.6 Hz, 1H, H-3), 4.02 (ddd, J = 9.6, 6.2, 3.2 Hz, 1H, H-12), 3.83 – 3.73 (m, 3H, H-7 and H-5 and H-17a), 3.65 (s, 3H, H-19), 3.64 – 3.56 (m, 2H, H-17b and H-15), 3.55 (s, 3H, H-23), 3.54 – 3.51 (m, 1H, H-6), 3.51 – 3.48 (m, 1H, H-4), 2.74 (dd, J = 14.7, 9.2 Hz, 1H, H-2a), 2.67 (dd, J = 14.8, 5.6 Hz, 1H, H-2b), 2.59 (ddd, J = 15.8, 10.1, 5.6 Hz, 1H, H-8a), 2.34 – 2.03 (m, 3H, H-8b and H-16a and H-13a), 1.96 – 1.77 (m, 2H, H-16b and H-14), 1.59 – 1.52 (m, 1H, H-13b), 1.02 (d, J = 6.5 Hz, 3H, H-33), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.12 (s, 6H, Me), 0.11 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9 (C-1), 165.4 (C-20), 153.6 (C-18), 135.3 (C-9), 133.2 (Ph), 132.7 (Ph), 131.6 (Ph), 129.9 (2C, Ph), 129.7 (Ph), 128.5 (2C, Ph), 127.4 (2C, Ph), 125.3 (2C, Ph), 123.6 (C-10), 123.0 (q, J = 287 Hz, C-22), 86.5 (C-15), 84.4 (q, J = 24.8 Hz, C-21), 79.1 (C-12), 74.3 (C-5), 74.2 (C-3), 73.7 (C-4), 73.0 (C-11), 71.8 (C-6), 69.6 (C-7), 55.6 (C-23), 53.6 (C-17), 51.7 (C-19), 39.9 (C-14), 37.4 (C-2), 35.2 (C-13), 33.5 (C-16), 30.2 (C-8), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 16.2 (C-33), -3.5 (Me), -4.0 (Me), -4.2 (Me), -4.5 (2C, Me), -4.9 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.5 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2895, 2856, 1744, 1636, 1597, 1499, 1472, 1463, 1450, 1409, 1389, 1360, 1347, 1253, 1169, 1154, 1121, 1085, 1041, 1015, 993, 964, 938, 918, 865, 834, 813, 775, 762, 709, 695, 688, 670, 666, 633, 550,

[302] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.4.

535, 507, 493, 474, 461, 415 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}SSi_3F_3Na^+$: 1177.5037, found: 1177.5039.

(R,Z)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-en-1-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-154)



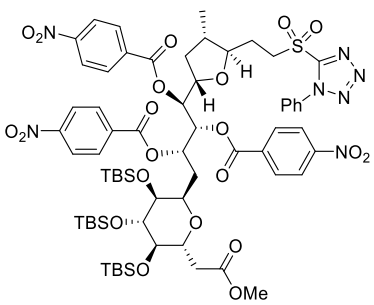
(*S*)-Mosher acid chloride (3.6 µL, 19 µmol) was added to a stirred solution of allylic alcohol *epi-Z*-**146** (5 mg, 5 µmol) and py (1.9 µL, 24 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 1 d. Then py (0.4 µL, 5 µmol) and (*S*)-Mosher acid chloride (0.9 µL, 5 µmol) were subsequently added to the reaction mixture at rt and stirring was continued for 2 d. The reaction was quenched with water (2 mL) and the aq. phase was extracted with DCM (3 x 3 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound *epi*-**154** as a colourless oil (5 mg, 90%).[303]

(the sample contained some cleaved off 2,5-*trans*-disubstituted ether) $[\alpha]_D^{20}$: +12.8 (c = 0.58, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.45 (m, 7H, Ph), 7.44 – 7.34 (m, 3H, Ph), 5.90 – 5.80 (m, 2H, H-9 and H-11), 5.27 (dd, J = 11.2, 9.3 Hz, 1H, H-10), 4.34 (ddd, J = 9.2, 5.4, 3.8 Hz, 1H, H-3), 4.09 (ddd, J = 9.5, 6.1, 3.0 Hz, 1H, H-12), 3.91 (ddd, J = 15.5, 11.5, 4.5 Hz, 1H, H-17a), 3.83 – 3.77 (m, 2H, H-7 and H-5), 3.74 – 3.67 (m, 1H, H-17b), 3.65 (s, 3H, H-19), 3.63 – 3.57 (m, 1H, H-15), 3.57 – 3.53 (m, 1H, H-6), 3.52 – 3.48 (m, 1H, H-4), 3.50 (s, 3H, H-23), 2.73 (dd, J = 14.8, 9.1 Hz, 1H, H-2a), 2.67 (dd, J = 15.0, 5.9 Hz, 1H, H-2b), 2.59 (ddd, J = 14.6, 10.3, 5.7 Hz, 1H, H-8a), 2.34 – 2.08 (m, 3H, H-8b and H-16a and H-13a), 2.00 – 1.82 (m, 2H, H-16b and H-14), 1.67 – 1.57 (m, 1H, H-13b), 1.02 (d, J = 6.5 Hz, 3H, H-33), 0.93 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.12 (s, 6H, Me), 0.11 (s, 3H, Me), 0.105 (s, 3H, Me), 0.10 (s, 3H, Me), 0.08 (s, 3H, Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9 (C-1), 165.9 (C-20), 153.6 (C-18), 134.7 (C-9), 133.2 (Ph), 132.5 (Ph), 131.6 (Ph), 129.9 (2C, Ph), 129.8 (Ph), 128.6 (2C, Ph), 127.8 (2C, Ph), 125.3 (2C, Ph), 123.5 (C-10), 123.4 (q, J = 290 Hz, C-22), 86.5 (C-15), 84.5 (q, J = 28.3 Hz, C-21), 79.1 (C-12), 74.4 (C-5), 74.1 (C-3), 73.8 (C-

[303] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.4.

4), 73.5 (C-11), 71.8 (C-6), 69.8 (C-7), 55.4 (C-23), 53.7 (C-17), 51.7 (C-19), 39.9 (C-14), 37.5 (C-2), 35.3 (C-13), 33.5 (C-16), 30.2 (C-8), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.5 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 16.2 (C-33), -3.5 (Me), -4.0 (Me), -4.2 (Me), -4.5 (2C, Me), -4.8 (Me) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.3 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2928, 2895, 2856, 1742, 1597, 1499, 1471, 1463, 1450, 1410, 1388, 1360, 1347, 1252, 1183, 1169, 1123, 1085, 1040, 1015, 1006, 964, 939, 916, 865, 834, 813, 775, 762, 709, 696, 688, 672, 668, 633, 539, 506, 473, 412 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}SSi_3F_3Na^+$: 1177.5037, found: 1177.5038.

(1S,2R,3S)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)butane-1,2,3-triyl tris(4-nitrobenzoate) (155)

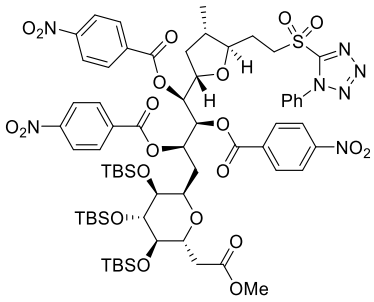


EDC·HCl (45 mg, 234 µmol) was added to a stirred solution of *p*-nitrobenzoic acid (22 mg, 129 µmol), 4-DMAP (4 mg, 29 µmol) and triol **147** (19 mg, 20 µmol) in DCM (1 mL) at rt and stirring was continued for 4 d. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 9:2) affording compound **155** as a colourless oil (22 mg, 79%).

$[\alpha]_D^{20}$: +6.1 (c = 1.37, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.37 – 8.23 (m, 8H), 8.15 – 8.08 (m, 4H), 7.69 – 7.65 (m, 5H), 5.88 (dd, J = 7.4, 3.3 Hz, 1H), 5.81 (td, J = 6.3, 3.2 Hz, 1H), 5.64 (dd, J = 7.4, 6.0 Hz, 1H), 4.33 (dt, J = 9.8, 6.0 Hz, 1H), 4.18 (ddd, J = 9.0, 5.9, 3.3 Hz, 1H), 4.01 (dt, J = 9.1, 3.0 Hz, 1H), 3.76 – 3.67 (m, 2H), 3.62 – 3.51 (m, 1H), 3.55 (s, 3H), 3.48 – 3.44 (m, 1H), 3.43 (td, J = 8.9, 2.8 Hz, 1H), 3.40 – 3.37 (m, 1H), 2.72 (dd, J = 14.8, 6.0 Hz, 1H), 2.64 (dd, J = 14.8, 8.3 Hz, 1H), 2.29 – 2.19 (m, 2H), 2.14 (tdd, J = 10.6, 5.0, 2.8 Hz, 1H), 1.97 – 1.84 (m, 2H), 1.77 – 1.62 (m, 2H), 0.99 (d, J = 6.4 Hz, 3H), 0.85 (s, 9H), 0.84 (s, 9H), 0.82 (s, 9H), 0.06 (s, 3H), 0.04 (s, 6H), 0.02 (s, 3H), 0.01 (s, 3H), -0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7, 164.0, 163.9, 163.5, 153.4, 151.1, 150.9, 150.7, 135.6, 135.0, 134.5, 133.1, 131.6, 131.2 (2C), 131.0 (2C), 130.8 (2C), 129.9 (2C), 125.1 (2C), 124.1 (2C), 123.8 (2C), 123.7 (2C), 83.8, 76.8, 74.1, 74.0, 73.8, 73.0, 72.6, 71.6, 70.6, 65.8, 53.3, 51.7, 39.6, 37.4, 36.9, 32.9, 26.7, 26.2 (3C), 26.1 (3C), 25.8 (3C), 18.4, 18.2, 17.9, 16.2, -3.3, -4.0, -4.4, -4.6 (2C), -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2857, 1730, 1608, 1528, 1498, 1463,

1438, 1410, 1389, 1346, 1320, 1266, 1257, 1151, 1096, 1042, 1014, 915, 872, 834, 813, 776, 758, 718, 688, 668, 632, 538, 507 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{65}H_{89}N_7O_{21}SSi_3Na^+$: 1442.5032, found: 1442.5026.

(1S,2S,3R)-1-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)butane-1,2,3-triyl tris(4-nitrobenzoate) (156)

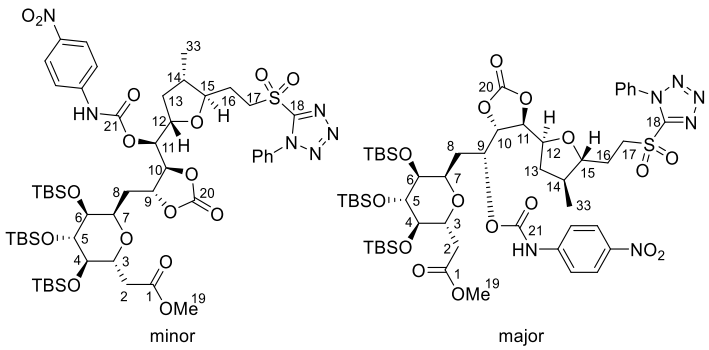


EDC·HCl (11 mg, 56 µmol) was added to a stirred solution of *p*-nitrobenzoic acid (5 mg, 31 µmol), 4-DMAP (1 mg, 7 µmol) and triol **148** (9 mg, 9 µmol) in DCM (0.5 mL) at rt and stirring was continued for 17 h. Then *p*-nitrobenzoic acid (5 mg, 31 µmol), 4-DMAP (1 mg, 7 µmol) and EDC·HCl (11 mg, 56 µmol) were subsequently added to the stirred reaction mixture at rt and stirring was continued for 4 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 9:2) affording compound **156** as a colourless oil (13 mg, 95%).

$[\alpha]_D^{20}$: +31.7 (c = 1.25, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.35 – 8.03 (m, 12H), 7.73 – 7.54 (m, 5H), 5.88 (ddd, J = 10.2, 4.4, 2.3 Hz, 1H), 5.81 (dd, J = 6.4, 4.3 Hz, 1H), 5.61 (t, J = 6.0 Hz, 1H), 4.36 (dt, J = 9.5, 6.0 Hz, 1H), 4.08 (td, J = 7.2, 3.5 Hz, 1H), 3.87 (ddd, J = 15.2, 10.8, 4.7 Hz, 1H), 3.78 (dt, J = 11.2, 1.8 Hz, 1H), 3.72 – 3.64 (m, 2H), 3.62 (s, 3H), 3.50 – 3.41 (m, 2H), 3.32 (t, J = 2.7 Hz, 1H), 2.75 (dd, J = 15.5, 7.1 Hz, 1H), 2.50 (dd, J = 15.4, 7.2 Hz, 1H), 2.36 – 2.24 (m, 2H), 2.19 (tdd, J = 10.8, 5.1, 2.8 Hz, 1H), 1.98 – 1.82 (m, 2H), 1.77 – 1.67 (m, 1H), 1.57 (dd, J = 13.7, 10.2 Hz, 1H), 1.04 (d, J = 6.5 Hz, 3H), 0.86 (s, 9H), 0.855 (s, 9H), 0.66 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.04 (s, 3H), -0.09 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 164.1, 163.9, 163.7, 153.5, 150.92, 150.85, 150.8, 135.0, 134.8, 134.5, 133.2, 131.6, 131.0 (2C), 130.94 (2C), 130.87 (2C), 129.9 (2C), 125.2 (2C), 123.9 (2C), 123.79 (2C), 123.76 (2C), 83.7, 76.7, 74.7, 74.2, 73.9, 73.6, 72.9, 72.2, 71.1, 65.3, 53.5, 51.6, 40.1, 37.5, 36.7, 34.3, 26.8, 26.3 (3C), 26.2 (3C), 25.6 (3C), 18.4, 18.3, 17.7, 16.2, -3.6, -4.0, -4.5, -4.6, -4.7, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2959, 2929, 2896, 2857, 1733, 1608, 1528, 1498, 1471, 1463, 1437, 1411, 1390, 1347, 1320, 1283, 1258, 1217, 1150, 1092, 1014,

921, 871, 832, 800, 776, 753, 717, 688, 667, 633, 539, 532, 506, 473, 447 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{65}H_{89}N_7O_{21}SSi_3Na^+$: 1442.5032, found: 1442.5030.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(((4R,5S)-5-((S)-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)(((4-nitrophenyl)carbamoyl)oxy)methyl)-2-oxo-1,3-dioxolan-4-yl)methyl)tetrahydro-2H-pyran-2-yl)acetate (157) and Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R)-2-((4S,5S)-5-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxo-1,3-dioxolan-4-yl)-2-(((4-nitrophenyl)carbamoyl)oxy)ethyl)tetrahydro-2H-pyran-2-yl)acetate (158)



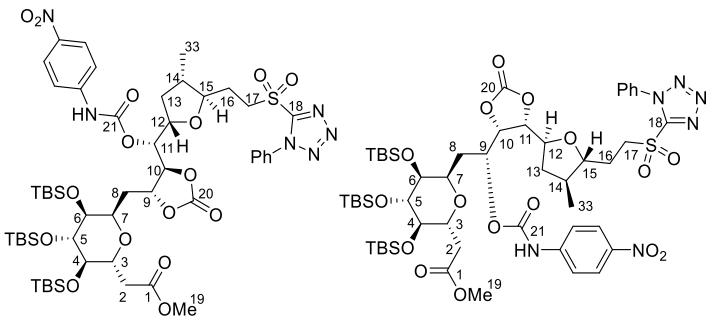
p-Nitrophenyl isocyanate (6 mg, 33 µmol) was added to a stirred solution of triol **148** (9 mg, 9 µmol) and TEA (4.1 µL, 29 µmol) in DCM (0.5 mL) at rt resulting in the formation of a yellow precipitate. Stirring was continued for 5 d, the solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 4:1 to 3:1) affording a mixture of regioisomeric cyclic carbonates **157** and **158** as a colourless oil (10 mg, 93%, *d.r.* = 3:5).

(the sample contained some 1,3-*bis*(4-nitrophenyl)urea) **^{1}H NMR** (3:5 regioisomer ratio, asterisk denotes minor regioisomer peaks,[304] 600 MHz, $CDCl_3$): δ = 8.24 – 8.19 (m, 2H, Ph), 8.24 – 8.19* (m, 2H, Ph), 8.04* (br s, 1H, NH), 7.72 – 7.67 (m, 2H, Ph), 7.72 – 7.67* (m, 2H, Ph), 7.65 – 7.58* (m, 5H, Ph), 7.65 – 7.54 (m, 5H, Ph), 7.22 (br s, 1H, NH), 5.28 (dt, J = 9.6, 2.7 Hz, 1H, H-9), 5.13* (dd, J = 6.8, 2.8 Hz, 1H, H-11), 4.86* (dt, J = 9.5, 4.0 Hz, 1H, H-9), 4.65 (dd, J = 4.3, 2.2 Hz, 1H, H-10), 4.61* (dd, J = 4.4, 2.8 Hz, 1H, H-10), 4.46 (dd, J = 5.5, 4.2 Hz, 1H, H-11), 4.31 – 4.26 (m, 1H, H-3), 4.31 – 4.26* (m, 1H, H-3), 4.24* (dt, J = 9.6, 6.3 Hz, 1H, H-12), 4.14 (dt, J = 9.6, 5.8 Hz, 1H, H-12), 4.09* (dt, J = 11.4, 2.3 Hz, 1H, H-7), 3.96 – 3.87 (m, 2H, H-17a and H-7), 3.96 – 3.87* (m, 1H, H-17a), 3.85 – 3.80 (m, 1H, H-17b), 3.80 – 3.76 (m, 1H, H-5), 3.80 – 3.76* (m, 2H, H-17b and H-5), 3.68* (s, 3H, H-19), 3.65 (s, 3H, H-19), 3.64 – 3.60 (m, 1H, H-15), 3.64 – 3.60* (m, 1H, H-15), 3.60 – 3.58* (m, 1H,

[304] The assignment is based on 2D-NMR data; ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC and ^{1}H,^{13}C-HMBC respectively.

H-6), 3.53 – 3.51 (m, 1H, H-4), 3.50 – 3.48* (m, 1H, H-4), 3.47 – 3.45 (m, 1H, H-6), 2.76 (dd, J = 15.8, 6.1 Hz, 1H, H-2a), 2.72* (dd, J = 15.6, 3.8 Hz, 1H, H-2a), 2.64 (dd, J = 15.8, 8.3 Hz, 1H, H-2b), 2.57* (dd, J = 15.6, 9.9 Hz, 1H, H-2b), 2.37 – 2.26 (m, 2H, H-13a and H-16a), 2.37 – 2.26* (m, 2H, H-16a and H-13a), 2.22 (ddd, J = 14.4, 11.0, 3.0 Hz, 1H, H-8a), 2.15* (ddd, J = 14.5, 11.0, 3.9 Hz, 1H, H-8a), 2.07 – 1.99 (m, 2H, H-16b and H-14), 2.07 – 1.99* (m, 1H, H-16b), 1.98 – 1.93* (m, 1H, H-14), 1.72 – 1.65 (m, 1H, H-8b), 1.72 – 1.65* (m, 1H, H-13b), 1.56 – 1.51* (m, 1H, H-8b), 1.47 (ddd, J = 12.5, 11.0, 9.7 Hz, 1H, H-13b), 1.10 (d, J = 6.6 Hz, 3H, H-33), 1.08* (d, J = 6.5 Hz, 3H, H-33), 0.94 (s, 9H, *t*-Bu), 0.895* (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.885* (s, 9H, *t*-Bu), 0.84* (s, 9H, *t*-Bu), 0.77 (s, 9H, *t*-Bu), 0.12* (s, 3H, Me), 0.11 (s, 3H, Me), 0.10* (s, 3H, Me), 0.095 (s, 3H, Me), 0.09 (s, 3H, Me), 0.085 (s, 3H, Me), 0.08* (s, 3H, Me), 0.075* (s, 3H, Me), 0.065* (s, 3H, Me), 0.06 (s, 3H, Me), 0.055 (s, 3H, Me), 0.04* (s, 3H, Me) ppm; **^{13}C NMR** (3:5 regioisomer ratio, asterisk denotes minor regioisomer peaks, 151 MHz, $CDCl_3$): δ = 173.1* (C-1), 172.1 (C-1), 154.6* (C-20), 154.3 (C-20), 153.59 (C-18), 153.57* (C-18), 152.2 (C-21), 151.7* (C-21), 143.8* (*i*-Ph), 143.6 (*p*-Ph), 143.5* (*p*-Ph), 143.4 (*i*-Ph), 133.21* (*i*-Ph), 133.17 (*i*-Ph), 131.7 (*p*-Ph), 131.6* (*p*-Ph), 129.91 (2C, *m*-Ph), 129.87* (2C, *m*-Ph), 125.4 (2C, *m*-Ph), 125.33* (2C, *o*-Ph), 125.32* (2C, *m*-Ph), 125.32 (2C, *o*-Ph), 118.23 (2C, *o*-Ph), 118.21* (2C, *o*-Ph), 84.1 (C-15), 83.7* (C-15), 80.0 (C-10), 79.69 (C-11), 79.69* (C-10), 77.6 (C-12), 76.6* (C-12), 76.2* (C-9), 75.4* (C-4), 75.1* (C-5), 74.1 (C-5), 74.0* (C-11), 73.53 (C-3), 73.47 (C-4), 72.6 (C-9), 72.3 (C-6), 72.23* (C-3), 72.20* (C-6), 67.2* (C-7), 65.8 (C-7), 53.58* (C-17), 53.55 (C-17), 52.0* (C-19), 51.8 (C-19), 40.0 (C-14), 39.9* (C-14), 38.5* (C-13), 37.6* (C-2), 37.2* (C-8), 36.72 (C-13), 36.69 (C-2), 33.4 (C-8), 26.9* (C-16), 26.8 (C-16), 26.3 (3C, *t*-Bu), 26.23 (3C, *t*-Bu), 26.17* (3C, *t*-Bu), 26.0* (3C, *t*-Bu), 25.9* (3C, *t*-Bu), 25.7 (3C, *t*-Bu), 18.5 (*t*-Bu), 18.4 (*t*-Bu), 18.3* (*t*-Bu), 18.2* (*t*-Bu), 18.0* (*t*-Bu), 17.8 (*t*-Bu), 16.06 (C-33), 16.05* (C-33), -3.57* (Me), -3.58 (Me), -3.7* (Me), -3.92* (Me), -3.93 (Me), -4.4 (Me), -4.47 (Me), -4.47* (Me), -4.53 (Me), -4.7* (Me), -4.8 (Me), -5.0* (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3311, 2956, 2929, 2857, 1799, 1737, 1614, 1599, 1554, 1512, 1463, 1438, 1413, 1334, 1305, 1259, 1215, 1177, 1151, 1083, 1038, 1008, 917, 833, 797, 775, 736, 688, 632, 504, 459 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{52}H_{82}N_6O_{16}SSi_3Na^+$: 1185.4708, found: 1185.4725.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(((4R,5S)-5-((R)-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)(((4-nitrophenyl)carbamoyl)oxy)methyl)-2-oxo-1,3-dioxolan-4-yl)methyl)tetrahydro-2H-pyran-2-yl)acetate (159) and Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((R)-2-((4S,5R)-5-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxo-1,3-dioxolan-4-yl)-2-(((4-nitrophenyl)carbamoyl)oxy)ethyl)tetrahydro-2H-pyran-2-yl)acetate (160)



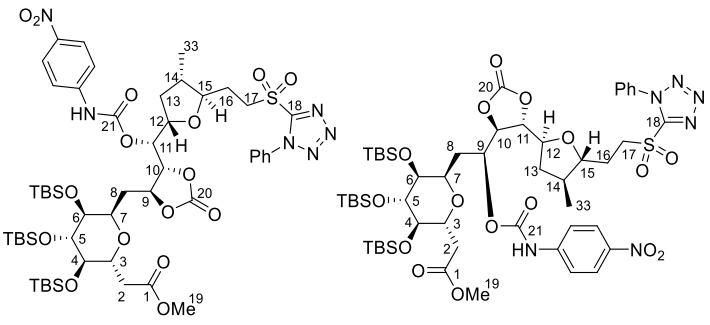
p-Nitrophenyl isocyanate (9 mg, 56 µmol) was added to a stirred solution of triol **149** (15 mg, 15 µmol) and TEA (6.8 µL, 49 µmol) in DCM (0.8 mL) at rt resulting in the formation of a yellow precipitate. Stirring was continued for 24 h, TEA (2.3 µL, 16 µmol) and *p*-nitrophenyl isocyanate (3 mg, 19 µmol) were subsequently added to the stirred reaction mixture at rt and stirring was continued for 24 h. The solvent was evaporated and the crude product was purified by flash chromatography twice (SiO_2, hexane/EtOAc, 5:1) affording a mixture of regioisomeric cyclic carbonates **159** and **160** as a colourless oil (9 mg, 50%, *d.r.* = 14:1).

^{1}H NMR (14:1 regioisomer ratio, asterisk denotes minor regioisomer peaks,[305] 600 MHz, $CDCl_3$): δ = 8.61 (br s, 1H, NH), 8.21 – 8.17 (m, 2H, Ph), 8.21 – 8.17* (m, 2H, Ph), 7.84* (br s, 1H, NH), 7.79 – 7.74 (m, 2H, Ph), 7.70 – 7.58 (m, 5H, Ph), 7.70 – 7.58* (m, 7H, Ph), 5.31 (ddd, J = 10.3, 4.8, 2.0 Hz, 1H, H-9), 5.22 (t, J = 3.1 Hz, 1H, H-11), 5.11* (dd, J = 7.8, 2.5 Hz, 1H, H-11), 5.04* (ddd, J = 9.7, 6.5, 2.7 Hz, 1H, H-9), 4.75* (dd, J = 6.5, 2.5 Hz, 1H, H-10), 4.50 (ddd, J = 15.2, 9.0, 5.4 Hz, 1H, H-17a), 4.43 (dd, J = 6.4, 3.3 Hz, 1H, H-10), 4.31 (ddd, J = 9.7, 5.0, 2.3 Hz, 1H, H-3), 4.32 – 4.28* (m, 1H, H-3), 4.17 (ddd, J = 9.7, 7.0, 3.0 Hz, 1H, H-12), 4.18 – 4.14* (m, 1H, H-12), 4.12 – 4.09* (m, 1H, H-7), 4.07 (dt, J = 11.2, 2.0 Hz, 1H, H-7), 3.82 – 3.80* (m, 1H, H-5), 3.79 (t, J = 2.5 Hz, 1H, H-5), 3.75 – 3.67 (m, 2H, H-17b and H-15), 3.66* (s, 3H, H-19), 3.59 (s, 3H, H-19), 3.56 – 3.54* (m, 1H, H-17a) 3.55 – 3.53* (m, 1H, H-15), 3.53 – 3.51* (m, 1H, H-17b), 3.52 – 3.50* (m, 2H, H-4 and H-6), 3.48 (t, J = 2.3 Hz, 1H, H-4), 3.37 (t, J = 2.4 Hz, 1H, H-6), 2.88 (dd, J = 15.3, 9.9 Hz, 1H, H-2a), 2.81* (dd, J = 15.0, 9.4 Hz, 1H, H-2a), 2.74* (dd, J = 15.1, 5.0 Hz, 1H, H-2b), 2.51 (dd, J = 15.3, 5.0 Hz, 1H, H-

[305] The assignment is based on 2D-NMR data; ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC and ^{1}H,^{13}C-HMBC respectively.

2b), 2.43 – 2.33 (m, 2H, H-16a and H-8a), 2.34 – 2.31* (m, 1H, H-16a), 2.28 (dt, J = 12.5, 6.9 Hz, 1H, H-13a), 2.20* (ddd, J = 14.5, 11.3, 3.0 Hz, 1H, H-8a), 2.15* (ddd, J = 13.2, 8.0, 4.8 Hz, 1H, H-13a), 2.06 – 2.00* (m, 1H, H-16b), 2.03 – 1.96* (m, 1H, H-14), 1.86 (ddt, J = 15.8, 10.9, 5.6 Hz, 1H, H-16b), 1.82 – 1.72 (m, 1H, H-14), 1.82 – 1.72* (m, 1H, H-13b), 1.69 – 1.62* (m, 1H, H-8b), 1.55 – 1.45 (m, 2H, H-13b and H-8b), 1.06* (d, J = 6.6 Hz, 3H, H-33), 0.99 (d, J = 6.4 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu), 0.90* (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.885* (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.87* (s, 9H, *t*-Bu), 0.115 (s, 3H, Me), 0.115* (s, 3H, Me), 0.11* (s, 3H, Me), 0.10 (s, 3H, Me), 0.10* (s, 3H, Me), 0.095 (s, 3H, Me), 0.095* (s, 3H, Me), 0.09 (s, 3H, Me), 0.08 (s, 3H, Me), 0.07* (s, 6H, Me), 0.06 (s, 3H, Me) ppm; **^{13}C NMR** (some carbons of the minor compound are missing and carbon shifts were partially taken from 2D spectra, 14:1 regioisomer ratio, asterisk denotes minor regioisomer peaks, 151 MHz, $CDCl_3$): δ = 172.0 (C-1), 154.4 (C-18), 154.1 (C-20), 152.4 (C-21), 144.2 (*i*-Ph), 143.3 (*p*-Ph), 133.3 (*i*-Ph), 131.6 (*p*-Ph), 129.8 (2C, *m*-Ph), 125.7 (2C, *o*-Ph), 125.3 (2C, *m*-Ph), 118.1 (2C, *o*-Ph), 84.3* (C-15), 82.9 (C-15), 82.2 (C-10), 80.2* (C-10), 75.37 (C-9), 75.35* (C-9), 75.22 (C-12), 75.22* (C-12), 74.5 (C-3), 74.3* (C-11), 74.1* (C-5), 74.0* (C-3), 73.7* (C-4), 73.5 (C-5), 73.1 (C-11), 72.6 (C-4), 71.9* (C-6), 71.7 (C-6), 65.8* (C-7), 64.4 (C-7), 53.7 (C-17), 51.9* (C-19), 51.8 (C-19), 40.0 (C-14), 38.1* (C-14), 37.43 (C-13), 37.35 (C-8), 37.1* (C-2), 36.8* (C-13), 36.5* (C-8), 36.3 (C-2), 27.4* (C-16), 27.1 (C-16), 26.4 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 25.8 (3C, *t*-Bu), 18.6 (*t*-Bu), 18.3 (*t*-Bu), 17.9 (*t*-Bu), 16.4* (C-33), 15.0 (C-33), -3.3 (Me), -4.2 (Me), -4.4 (Me), -4.55 (Me), -4.56 (Me), -5.0 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3317, 2955, 2929, 2897, 2857, 1803, 1741, 1614, 1599, 1553, 1512, 1499, 1471, 1463, 1439, 1413, 1389, 1376, 1342, 1332, 1305, 1259, 1212, 1178, 1150, 1087, 1066, 1036, 1005, 936, 913, 865, 831, 813, 774, 762, 751, 735, 703, 688, 672, 668, 664, 633, 552, 530, 504, 462, 438, 406 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{52}H_{82}N_6O_{16}SSi_3Na^+$: 1185.4708, found: 1185.4713.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(((4S,5R)-5-((R)-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)(((4-nitrophenyl)carbamoyl)oxy)methyl)-2-oxo-1,3-dioxolan-4-yl)methyl)tetrahydro-2H-pyran-2-yl)acetate (161) and Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S)-2-((4R,5R)-5-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxo-1,3-dioxolan-4-yl)-2-(((4-nitrophenyl)carbamoyl)oxy)ethyl)tetrahydro-2H-pyran-2-yl)acetate (162)



p-Nitrophenyl isocyanate (2 mg, 11 µmol) was added to a stirred solution of triol **150a** (3 mg, 3 µmol) and TEA (1.4 µL, 9.7 µmol) in DCM (200 µL) at rt resulting in the formation of a yellow precipitate, and stirring was continued for 24 h. Then TEA (0.5 µL, 3 µmol) and *p*-nitrophenyl isocyanate (1 mg, 4 µmol) were subsequently added to the stirred reaction mixture at rt and stirring was continued for 24 h. The solvent was evaporated and the crude product was purified by flash chromatography twice (both columns: SiO_2, hexane/EtOAc, 5:1) affording a mixture of regioisomeric cyclic carbonates **161** and **162** as a colourless oil (3 mg, 84%, *d.r.* = 2:5).

^{1}H NMR (2:5 regioisomer ratio, asterisk denotes minor regioisomer peaks,[306] 600 MHz, $CDCl_3$): δ = 8.59 (br s, 1H, NH), 8.23 – 8.18 (m, 2H, Ph), 8.23 – 8.18* (m, 2H, Ph), 7.85 (br s, 1H, NH), 7.70 – 7.68 (m, 2H, Ph), 7.67 – 7.65* (m, 2H, Ph), 7.64 – 7.58 (m, 5H, Ph), 7.64 – 7.58* (m, 5H, Ph), 5.16 – 5.12 (m, 1H, H-9), 5.06 (dd, J = 5.6, 4.7 Hz, 1H, H-10), 5.01* (dd, J = 7.4, 2.4 Hz, 1H, H-11), 4.86* (dt, J = 8.0, 3.4 Hz, 1H, H-9), 4.77* (dd, J = 4.3, 2.4 Hz, 1H, H-10), 4.39 (dd, J = 4.7, 1.2 Hz, 1H, H-11), 4.38 – 4.35 (m, 1H, H-3), 4.34 – 4.32* (m, 1H, H-3), 4.31 – 4.27 (m, 1H, H-12), 4.31 – 4.27* (m, 1H, H-12), 4.04 – 4.02* (m, 1H, H-7), 4.00 (dt, J = 10.7, 2.1 Hz, 1H, H-7), 3.96 (ddd, J = 14.6, 11.8, 4.5 Hz, 1H, H-17a), 3.83 – 3.81*(m, 1H, H-17a), 3.80 (s, 3H, H-19), 3.79 – 3.77* (m, 1H, H-5), 3.77 – 3.75 (m, 2H, H-17b and H-5), 3.75 – 3.72* (m, 1H, H-17b), 3.70* (s, 3H, H-19), 3.59 – 3.58* (m, 1H, H-15), 3.58 (td, J = 8.8, 2.9 Hz, 1H, H-15), 3.48 – 3.46* (m, 1H, H-4), 3.45 – 3.44* (m, 1H, H-6), 3.39 – 3.37 (m, 2H, H-4 and H-6), 3.04 (dd, J = 14.9, 11.9 Hz, 1H, H-2a), 2.73* (dd, J = 15.4, 9.4 Hz, 1H, H-2a), 2.66* (dd, J = 15.4, 4.8 Hz, 1H, H-2b), 2.52 (dd, J = 14.9, 3.8 Hz, 1H, H-2b), 2.38 – 2.34* (m, 1H,

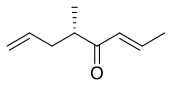
[306] The assignment is based on 2D-NMR data; ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC and ^{1}H,^{13}C-HMBC respectively.

H-13a), 2.33 – 2.29 (m, 1H, H-16a), 2.33 – 2.29* (m, 1H, H-8a), 2.28 – 2.25* (m, 1H, H-16a), 2.18 (dt, J = 12.3, 6.9 Hz, 1H, H-13a), 2.10 (ddd, J = 15.0, 10.5, 4.4 Hz, 1H, H-8a), 2.03 – 2.01 (m, 1H, H-16b), 1.99 – 1.93 (m, 1H, H-14), 1.99 – 1.93* (m, 2H, H-16b and H-14), 1.78 – 1.72 (m, 2H, H-13b and H-8b), 1.67 – 1.64* (m, 1H, H-8b), 1.50 – 1.46* (m, 1H, H-13b), 1.08 (d, J = 6.5 Hz, 3H, H-33), 1.08* (d, J = 6.5 Hz, 3H, H-33), 0.92 (s, 9H, *t*-Bu), 0.91* (s, 9H, *t*-Bu), 0.90* (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.86* (s, 9H, *t*-Bu), 0.80 (s, 9H, *t*-Bu), 0.11* (s, 3H, Me), 0.10 (s, 3H, Me), 0.09* (s, 3H, Me), 0.085* (s, 3H, Me), 0.08* (s, 3H, Me), 0.075 (s, 3H, Me), 0.07 (s, 3H, Me), 0.07* (s, 3H, Me), 0.065* (s, 3H, Me), 0.06 (s, 3H, Me), 0.055 (s, 3H, Me), 0.05 (s, 3H, Si-Me) ppm; **^{13}C NMR** (2:5 regioisomer ratio, asterisk denotes minor regioisomer peaks, 151 MHz, $CDCl_3$): δ = 173.1 (C-1), 172.1* (C-1), 145.5* (C-20), 154.4 (C-20), 152.5 (C-21), 152.2* (C-21), 144.3 (*i*-Ph), 143.7* (*i*-Ph), 143.5* (*p*-Ph), 143.2 (*p*-Ph), 133.18 (*i*-Ph), 133.16* (*i*-Ph), 131.64 (*p*-Ph), 131.61* (*p*-Ph), 129.90 (2C, *m*-Ph), 129.86* (2C, *m*-Ph), 125.4* (2C, *m*-Ph), 125.3 (2C, *m*-Ph), 125.2 (4C, *o*-Ph), 125.2* (4C, *o*-Ph), 118.13* (2C, *m*-Ph), 118.07 (2C, *m*-Ph), 83.9 (C-15), 82.6* (C-15), 79.4 (C-10), 78.7 (C-11), 78.2* (C-10), 76.6* (C-9), 76.0* (C-12), 75.1* (C-11), 74.7 (C-3), 73.9* (C-5), 73.71* (C-3), 73.65* (C-4), 73.5 (C-5), 73.1 (C-9), 72.74 (C-4), 72.67* (C-6), 71.5 (C-6), 65.2 (C-7), 64.7* (C-7), 53.6 (C-17), 53.6* (C-17), 52.7 (C-19), 52.1* (C-19), 40.3 (C-14), 40.2* (C-14), 37.5 (C-2), 37.0* (C-13), 36.9* (C-2), 35.8 (C-13), 35.0* (C-8), 30.6 (C-8), 25.5 (C-16), 26.24 (3C, *t*-Bu), 26.23* (C-16), 26.19 (3C, *t*-Bu), 26.17* (3C, *t*-Bu), 26.0* (3C, *t*-Bu), 25.8* (3C, *t*-Bu), 25.7 (3C, *t*-Bu), 18.4* (*t*-Bu), 18.3 (*t*-Bu), 18.1 (*t*-Bu), 18.1* (*t*-Bu), 17.8* (*t*-Bu), 17.7 (*t*-Bu), 15.9* (C-33), 15.5 (C-33), -3.3 (Me), -3.5* (Me), -3.9* (Me), -4.0 (Me), -4.3* (Me), -4.41* (Me), -4.43 (Me), -4.5 (Me), -4.60 (Me), -4.61* (Me), -4.9* (Me), -5.0 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3362, 2955, 2923, 2853, 1798, 1737, 1640, 1599, 1555, 1510, 1463, 1412, 1377, 1332, 1308, 1259, 1218, 1178, 1084, 1021, 833, 799, 775, 752, 495, 443 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{52}H_{82}N_6O_{16}SSi_3Na^+$: 1185.4708, found: 1185.4714.

5.2.2.4. Investigations On Alternative Pathways

5.2.2.4.1. The 2,5-*trans*-Disubstituted Tetrahydrofuran Ring

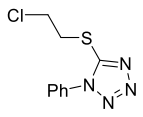
(S,E)-5-Methylocta-2,7-dien-4-one (E-163)



t-BuLi (1.7 M in pentane, 11.8 mL, 20.0 mmol) was slowly added to a stirred solution of *trans*-1-bromo-1-propene (1.76 mL, 20.5 mmol) and TMEDA (3.0 mL, 20.0 mmol) in Et_2O (20 mL) at -78 °C and stirring was continued for 45 min. In parallel, *n*-BuLi (1.6 M, 11.6 mL, 18.6 mmol) was slowly added to a stirred solution of amide **43** in THF (105 mL) at -78 °C over the course of 5 min. Then, the previously prepared solution of propenyllithium was slowly added to the stirred solution of deprotonated amide **43** via cannula at -78 °C over the course of 15 min. When the addition was complete, the reaction mixture was warmed to 0 °C and stirring was continued for 2 h. The reaction was quenched with sat. aq. NH_4Cl (200 mL) at 0 °C and the mixture diluted with Et_2O (100 mL). The aq. phase was extracted with Et_2O (100 mL) and the combined extracts were washed with sat. aq. NH_4Cl (200 mL) and water (200 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 4:1) affording compound *E*-**163** as a colourless oil (ca. 90%, 2.12 g, 74%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (dq, J = 15.6, 6.9 Hz, 1H), 6.19 (dq, J = 15.6, 1.7 Hz, 1H), 5.72 (dddd, J = 16.8, 10.1, 7.5, 6.6 Hz, 1H), 5.06 – 4.98 (m, 2H), 2.80 (h, J = 6.9 Hz, 1H), 2.42 (dtt, J = 14.3, 6.5, 1.4 Hz, 1H), 2.13 – 2.05 (m, 1H), 1.90 (dd, J = 6.9, 1.7 Hz, 3H), 1.09 (d, J = 7.0 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 203.1, 142.8, 136.0, 130.6, 116.7, 43.6, 37.3, 18.4, 16.4 ppm; **HRMS** (ESI): *m/z* calcd. for $C_9H_{14}O$: 138.1045, found: 138.1046.

5-((2-Chloroethyl)thio)-1-phenyl-1H-tetrazole (169)

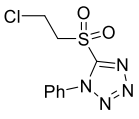


K_2CO_3 (3.88 g, 28.1 mmol) was added to a stirred solution of 1-Phenyl-1*H*-tetrazole-5-thiol (**168**) (2.50 g, 14.0 mmol) as a solution in 1,2-DCE (65 mL) at rt and the resulting suspension was warmed to 84 °C and refluxed for 4 d. The reaction was quenched with water (60 mL) and the aq. phase was extracted with DCM (2 x 70 mL). The combined organic extracts were washed with water (60 mL) and brine (60 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was

evaporated affording intermediate **169** as a yellow solid (ca. 90%, 3.66 g, 98%) which was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 – 7.53 (m, 5H), 3.96 (t, J = 6.7 Hz, 2H), 3.73 (t, J = 6.7 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 153.4, 133.6, 130.5, 130.1 (2C), 123.9 (2C), 42.3, 35.4 ppm; **IR** (film): $\tilde{\nu}$ = 3058, 2958, 2222, 1805, 1775, 1731, 1596, 1498, 1462, 1439, 1413, 1386, 1316, 1299, 1274, 1242, 1224, 1176, 1159, 1090, 1074, 1056, 1041, 1014, 980, 952, 915, 863, 759, 734, 686, 614, 551, 500, 465 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_9H_9N_4ClSNa^+$: 263.0129, found: 263.0129. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[307]

5-((2-Chloroethyl)sulfonyl)-1-phenyl-1H-tetrazole (170)

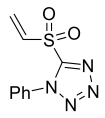


A solution of *m*-CPBA (77%, 15.7 g, 70.1 mmol) in DCM (30 mL) was added to a stirred solution of the crude sulfide **169** (ca. 90%, 3.66 g, 13.7 mmol) in DCM (15 mL) at rt, and stirring was continued for 3 d. The reaction mixture was filtered and the filter cake was washed with DCM (2 x 25 mL). The combined organic phases were subsequently (cautious, mind the very strong gas evolution!) washed with aq. $NaHSO_3$ (40%, 40 mL), sat. aq. $NaHCO_3$ (3 x 40 mL) and brine (40 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording intermediate **170** as a yellow solid (ca. 90%, 2.83 g, 76%) which was used in the next step without further purification.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.59 (m, 5H), 4.16 (ddd, J = 7.8, 6.7, 0.9 Hz, 2H), 4.03 (ddd, J = 7.8, 6.8, 0.9 Hz, 2H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 153.4, 132.9, 131.8, 130.0 (2C), 125.2 (2C), 58.0, 35.1 ppm; **IR** (film): $\tilde{\nu}$ = 3065, 2982, 2928, 2223, 1805, 1728, 1595, 1497, 1462, 1422, 1385, 1349, 1314, 1266, 1234, 1201, 1154, 1136, 1106, 1076, 1046, 1015, 984, 920, 870, 762, 733, 687, 662, 610, 568, 539, 512, 460, 431 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_9H_9N_4O_2ClSNa^+$: 295.0027, found: 295.0024.

[307] E. Rodrigo, S. Morales, S. Duce, J. L. G. Ruano, M. B. Cid, *Chem. Commun.* **2011**, *47*, 11267-11269.

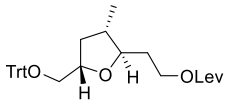
1-Phenyl-5-(vinylsulfonyl)-1H-tetrazole (165)



TEA (2.93 mL, 21.0 mmol) was added to a stirred solution of the crude alkyl chloride **170** (ca. 90%, 2.83 g, 9.34 mmol) as a solution in THF (75 mL) at rt and stirring was continued for 30 min. The reaction mixture was filtered and the filter cake was washed with THF (2 x 25 mL). The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 4:1) affording compound **165** as a crystalline solid (845 mg, 38%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 – 7.59 (m, 5H), 7.15 (dd, J = 16.5, 9.9 Hz, 1H), 6.68 (dd, J = 16.5, 1.1 Hz, 1H), 6.50 (dd, J = 9.9, 1.1 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 154.3, 135.4, 134.7, 133.2, 131.7, 129.9 (2C), 125.3 (2C) ppm; **IR** (film): $\tilde{\nu}$ = 3109, 3068, 2985, 2939, 1727, 1713, 1597, 1551, 1498, 1462, 1444, 1376, 1346, 1295, 1243, 1152, 1076, 1044, 1015, 948, 921, 847, 762, 746, 689, 661, 627, 607, 567, 521, 508, 485 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_9H_8N_4O_2SNa^+$: 237.0441, found: 237.0439. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[308]

2-((2R,3S,5S)-3-Methyl-5-((trityloxy)methyl)tetrahydrofuran-2-yl)ethyl 4-oxopentanoate (176a)



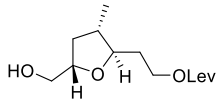
DCC (1.03 g, 4.97 mmol) was added to a stirred solution of levulinic acid (577 mg, 4.97 mmol), 4-DMAP (10 mol%, 30.4 mg, 249 µmol) and alcohol **140** (1.00 g, 2.48 mmol) as a solution in DCM (25 mL) at 0 °C and stirring was continued for 5 min. The reaction mixture was warmed to rt and stirring was continued for 15 h yielding a suspension. The reaction mixture was filtered and the filtrate was washed with aq. phosphate buffer (200 mM, pH 7, 2 x 15 mL) and brine (15 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc 4:1) affording compound **176a** as a colourless oil (963 mg, 77%).

$[\alpha]_D^{20}$: +13.5 (c = 1.10, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.50 – 7.45 (m, 6H), 7.32 – 7.26 (m, 6H), 7.25 – 7.19 (m, 3H), 4.35 (ddd, J = 10.8, 7.5, 5.1 Hz, 1H), 4.29 – 4.16 (m, 2H), 3.55 (td, J = 9.2, 2.7 Hz, 1H), 3.11 – 3.03 (m, 2H), 2.76 – 2.61 (m, 2H), 2.60 – 2.43 (m, 2H), 2.15 (dt, J = 12.1, 7.0 Hz, 1H), 2.10 (s, 3H), 1.97 (dtd, J = 13.8, 7.6, 2.7 Hz, 1H), 1.87 (ddt, J = 10.7, 9.1, 6.6 Hz, 1H), 1.74 (dddd, J = 14.2, 9.1, 6.8, 5.2 Hz, 1H), 1.44 (ddd, J = 12.2, 10.9, 8.8 Hz, 1H), 1.03 (d, J = 6.5 Hz,

[308] E. Rodrigo, S. Morales, S. Duce, J. L. G. Ruano, M. B. Cid, *Chem. Commun.* **2011**, *47*, 11267-11269.

3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 206.8, 172.9, 144.4 (3C), 128.9 (6C), 127.9 (6C), 127.0 (3C), 86.5, 81.9, 77.2, 67.1, 62.7, 40.2, 38.1, 37.7, 33.0, 29.9, 28.2, 16.1 ppm; **IR** (film): $\tilde{\nu}$ = 3085, 3058, 3023, 2958, 2923, 2871, 1732, 1719, 1597, 1491, 1448, 1409, 1356, 1318, 1209, 1181, 1156, 1116, 1103, 1072, 1026, 990, 969, 927, 900, 869, 748, 700, 667, 645, 632, 606, 563, 534, 486, 444, 424 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{32}H_{36}O_5Na^+$: 523.2455, found: 523.2456.

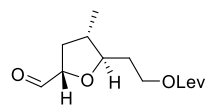
2-((2R,3S,5S)-5-(Hydroxymethyl)-3-methyltetrahydrofuran-2-yl)ethyl 4-oxopentanoate (176b)



TFA (2.81 mL, 36.7 mmol) was added to a stirred solution of protected alcohol **176a** (735 mg, 1.47 mmol) in DCM (31 mL) at 0 °C and stirring was continued for 1 h. The reaction was quenched and neutralized with sat. aq. $NaHCO_3$ and the aq. phase was extracted with EtOAc (3 x 25 mL). The combined extracts were washed with brine (25 mL) and the solvent was evaporated. The crude product was dissolved in EtOAc (100 mL), sat. aq. K_2CO_3 (25 mL) was added and the resulting mixture was stirred at rt for 15 min. The aq. phase was extracted with EtOAc (50 mL). The organic extract was subsequently washed with water (50 mL) and brine (50 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 1:1 to 1:3) affording compound **176b** as a colourless oil (310 mg, 82%).

$[\alpha]_D^{20}$: +38.6 (c = 0.50, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.29 – 4.18 (m, 2H), 4.08 (dtd, J = 9.3, 6.1, 3.1 Hz, 1H), 3.64 (ddd, J = 11.6, 6.8, 3.1 Hz, 1H), 3.51 – 3.42 (m, 2H), 2.79 – 2.71 (m, 2H), 2.60 – 2.53 (m, 2H), 2.19 (s, 3H), 2.14 (t, J = 6.4 Hz, 1H), 2.12 – 2.05 (m, 1H), 1.97 – 1.84 (m, 2H), 1.76 – 1.66 (m, 1H), 1.38 (ddd, J = 12.2, 10.7, 9.2 Hz, 1H), 1.03 (d, J = 6.6 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 207.0, 173.0, 82.1, 78.6, 65.2, 62.4, 40.3, 38.1, 36.5, 33.1, 30.0, 28.2, 16.3 ppm; **IR** (film): $\tilde{\nu}$ = 3384, 2965, 2926, 1715, 1637, 1460, 1405, 1362, 1304, 1212, 1161, 1114, 1064, 1025, 946, 764, 611, 571 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{13}H_{22}O_5Na^+$: 281.1359, found: 281.1355.

2-((2R,3S,5S)-5-Formyl-3-methyltetrahydrofuran-2-yl)ethyl 4-oxopentanoate (177)



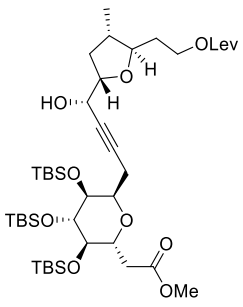
DMSO (50.8 µL, 715 µmol) was added dropwise to a stirred solution of $(COCl)_2$ (30.7 µL, 358 µmol) in DCM (1.1 mL) at -78 °C and stirring was continued for 5 min. Then alcohol **176b** (42 mg, 0.16 mmol) as a solution in DCM (0.5 mL, rinsed with 0.5 mL) was added dropwise and stirring was continued for 30 min. DIPEA (283 µL, 1.63 mmol) was slowly

added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 2.5 h. The reaction was quenched with water (10 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 2 x 10 mL) and with brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 3:1 to 2:1) affording compound **177** as a colourless oil (28 mg, 67%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.65 (d, J = 2.1 Hz, 1H), 4.33 – 4.25 (m, 2H), 4.24 – 4.17 (m, 1H), 3.58 (td, J = 8.6, 3.1 Hz, 1H), 2.78 – 2.73 (m, 2H), 2.60 – 2.55 (m, 2H), 2.36 (dt, J = 12.6, 7.6 Hz, 1H), 2.19 (s, 3H), 2.01 – 1.90 (m, 2H), 1.82 – 1.72 (m, 1H), 1.59 (ddd, J = 12.7, 9.7, 8.5 Hz, 1H), 1.04 (d, J = 6.6 Hz, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 206.8, 203.0, 172.8, 83.9, 81.9, 62.1, 39.4, 38.1, 36.1, 32.9, 30.0, 28.1, 16.3 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{13}H_{20}O_5Na^+$: 279.1203, found: 279.1202.

5.2.2.4.2. Building Block Coupling & Elaboration

2-((2R,3S,5S)-5-((S)-1-Hydroxy-4-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-2-yn-1-yl)-3-methyltetrahydrofuran-2-yl)ethyl 4-oxopentanoate (178)

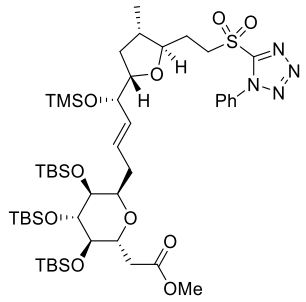


TEA (43.5 µL, 312 µmol) was added to a stirred suspension of $Zn(OTf)_2$ (104 mg, 286 µmol) and (*+*)-*N*-methylephedrine (51 mg, 0.29 mmol) with 4 Å MS in PhMe (250 µL) at rt and stirring was continued for 3 h. Then alkyne **35b** (61 mg, 0.10 mmol) as a solution in PhMe (200 µL, rinsed with 150 µL) was dried over 4 Å MS before it was added to the reaction mixture at rt and stirring was continued for 1.5 h. Then aldehyde **177** (28 mg, 0.11 mmol) as a solution in PhMe (200 µL, rinsed with 150 µL) over 4 Å MS was added to the stirred reaction mixture at rt and stirring was continued for 3 d. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL) and the aq. phase was extracted with MTBE (3 x 10 mL) and EtOAc (3 x 15 mL). The combined extracts were subsequently washed with aq. phosphate buffer (200 mM, pH 7, 10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by

flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 2:1) affording both compound **178** (12 mg, 14%) and some unreacted starting material **35b** (42 mg, 69%) as a colourless oil.

$[\alpha]_D^{20}$: +8.3 (c = 1.20, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.32 (ddd, J = 9.1, 6.1, 3.5 Hz, 1H), 4.28 – 4.17 (m, 2H), 4.16 – 4.10 (m, 1H), 4.01 – 3.92 (m, 2H), 3.82 (t, J = 2.4 Hz, 1H), 3.68 (s, 3H), 3.65 (t, J = 2.4 Hz, 1H), 3.51 – 3.49 (m, 1H), 3.46 (td, J = 9.0, 3.0 Hz, 1H), 2.77 – 2.66 (m, 5H), 2.59 – 2.54 (m, 2H), 2.48 – 2.44 (m, 2H), 2.26 – 2.20 (m, 1H), 2.19 (s, 3H), 1.97 – 1.83 (m, 2H), 1.72 (ddt, J = 14.3, 8.5, 5.9 Hz, 1H), 1.39 (ddd, J = 12.6, 10.7, 8.6 Hz, 1H), 1.02 (d, J = 6.5 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.12 (s, 6H), 0.115 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 206.9, 173.0, 171.9, 83.2, 82.3, 81.5, 79.7, 74.5, 74.2, 73.6, 70.2, 68.5, 66.1, 62.3, 51.9, 40.1, 38.1, 37.6, 37.4, 32.9, 30.0, 28.2, 26.3 (3C), 26.2 (3C), 25.9 (3C), 21.6, 18.5, 18.3, 18.0, 16.1, -3.4, -4.0, -4.1, -4.6 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3499, 2954, 2929, 2896, 2857, 1737, 1726, 1472, 1463, 1436, 1400, 1360, 1256, 1159, 1128, 1093, 1056, 1006, 974, 925, 890, 849, 813, 776, 674, 471, 438, 420, 408 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{78}O_{11}Si_3Na^+$: 865.4744, found: 865.4744.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S,E)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-4-((trimethylsilyl)oxy)but-2-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (179)



TMSOTf (7.5 µL, 42 µmol) was added to a stirred solution of allylic alcohol *E*-**146** (26 mg, 28 µmol) and 2,6-lutidine (6.5 µL, 55 µmol) in DCM (0.6 mL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 2 h. The reaction was diluted with MTBE (10 mL) and quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL). The organic extract was subsequently washed with water (5 mL) and brine (5 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **179** as a colourless oil (24 mg, 86%).

$[\alpha]_D^{20}$: +20.4 (c = 1.20, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.56 (m, 5H), 5.67 (dt, J = 15.5, 6.8 Hz, 1H), 5.48 (dd, J = 15.7, 6.5 Hz, 1H), 4.31 (ddd, J = 9.2, 5.7, 3.7 Hz, 1H), 3.99 – 3.90 (m, 2H), 3.89 – 3.74 (m, 4H), 3.66 (s, 3H), 3.53 – 3.45 (m, 3H), 2.77 (dd, J = 14.8, 5.8 Hz, 1H), 2.63 (dd, J = 14.8, 8.7 Hz, 1H), 2.39 (dt, J = 14.1, 6.7 Hz, 1H), 2.25 (dddd, J = 14.0, 11.3, 4.8, 3.0 Hz, 1H), 2.12

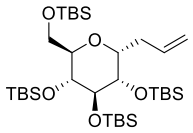
(dt, J = 13.7, 6.7 Hz, 1H), 2.07 – 1.91 (m, 2H), 1.85 (ddt, J = 10.7, 8.8, 6.7 Hz, 1H), 1.37 (ddd, J = 12.2, 10.9, 9.2 Hz, 1H), 1.01 (d, J = 6.5 Hz, 3H), 0.93 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.11 (s, 3H), 0.10 (s, 12H), 0.09 (s, 3H), 0.08 (s, 3H), 0.075 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 153.6, 133.2, 131.6, 131.1, 129.8 (2C), 129.6, 125.3 (2C), 82.8, 81.9, 76.4, 74.4, 73.9, 73.8, 71.5, 69.9, 53.8, 51.7, 39.8, 37.5, 37.2, 34.3, 26.4, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.0, 0.6 (3C), -3.2, -3.9, -4.2, -4.51, -4.54, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2888, 2857, 1741, 1596, 1498, 1472, 1463, 1437, 1389, 1362, 1346, 1250, 1157, 1126, 1084, 1044, 1006, 975, 869, 832, 813, 774, 688, 673, 634, 532, 507, 475, 423 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{86}N_4O_{10}Si_4SNa^+$: 1033.5034, found: 1033.5047.

5.2.3. The Western Belizentrin Fragment - Final Route

5.2.3.1. The C-Glucoside Building Block - A New Synthesis

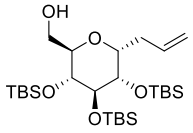
(((2R,3S,4R,5R,6R)-2-Allyl-6-(((tert-butyldimethylsilyl)oxy)methyl)tetrahydro-2H-pyran-3,4,5-triyl)tris(oxy))tris(tert-butyldimethylsilane) (40c)

Procedure B (TBSOTf, 2,6-lutidine)



TBSOTf (36.7 mL, 160 mmol) was slowly added to a stirred suspension of C-glucoside **40b** (5.44 g, 26.6 mmol) and 2,6-lutidine (24.8 mL, 213 mmol) in DCM (135 mL) at 0 °C over the course of 30 min. The reaction mixture was allowed to reach rt and stirring was continued for 2.25 h. Then 2,6-lutidine (6.20 mL, 53.2 mmol) and TBSOTf (6.11 mL, 26.6 mmol) were subsequently added to the stirred reaction mixture at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 17 h. The reaction was diluted with MTBE (200 mL) and cautiously poured into aq. HCl (1.0 M, 100 mL). The extract was washed with water (100 mL) and brine (100 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 20:1) affording compound **40c** as a colourless oil (16.9 g, 96%). The analytical and spectroscopic data of the isolated compound were identical with those shown above.

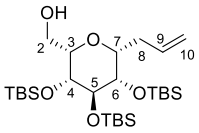
((2R,3R,4R,5S,6R)-6-Allyl-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)methanol (184)



HF·py (12.5% in THF/py 2.5:1, 13.8 mL, 19.2 mmol) was added to a stirred solution of TBS-protected alcohol **40c** (911 mg, 1.38 mmol) in THF (29 mL) at 0 °C. The resulting reaction mixture was allowed to reach rt over 30 min and stirring was continued for 16 h. The reaction was quenched with sat. aq. $NaHCO_3$ (100 mL) and the aq. phase was extracted with MTBE (3 x 75 mL). The combined extracts were washed with brine (75 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 40:1 to 20:1) affording both minor isomer *epi*-**184** (81 mg, 11%) and desired major isomer **184** (647 mg, 86%) as a colourless oil.

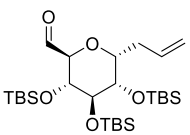
Analytical and spectral data of the major epimer **184**: $[\alpha]_D^{20}$: +18.5 (c = 1.23, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.87 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H), 5.14 (dq, J = 17.2, 1.6 Hz, 1H), 5.09 (ddt, J = 10.3, 2.2, 1.1 Hz, 1H), 3.95 (ddd, J = 8.6, 5.1, 3.5 Hz, 1H), 3.88 (ddd, J = 9.1, 4.5, 2.4 Hz, 1H), 3.80 – 3.78 (m, 1H), 3.78 (ddd, J = 11.5, 8.5, 3.5 Hz, 1H), 3.60 – 3.55 (m, 1H), 3.55 (ddd, J = 11.4, 8.6, 3.5 Hz, 1H), 3.49 (dt, J = 5.1, 1.2 Hz, 1H), 2.49 (dddt, J = 14.3, 8.7, 7.1, 1.3 Hz, 1H), 2.11 (dddt, J = 14.2, 7.0, 4.5, 1.3 Hz, 1H), 2.04 (dd, J = 8.6, 3.5 Hz, 1H), 0.93 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.115 (s, 3H), 0.105 (s, 3H), 0.085 (s, 6H), 0.075 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 135.8, 117.2, 76.6, 74.8, 72.3, 72.0, 69.7, 61.9, 35.8, 26.2 (3C), 26.2 (3C), 25.9 (3C), 18.4, 18.3, 18.0, -3.5, -3.9, -4.0, -4.5, -4.7, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3485, 2953, 2929, 2886, 2858, 1642, 1472, 1463, 1433, 1406, 1389, 1361, 1322, 1253, 1187, 1130, 1088, 1005, 963, 939, 911, 881, 858, 833, 813, 774, 670, 666, 568, 494, 479, 466, 448, 434, 426, 413 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{58}O_5Si_3Na^+$: 569.3484, found: 569.3487.

Analytical and spectral data of the minor epimer *epi*-**184**:$[\alpha]_D^{20}$: -1.5 (c = 1.05, $CHCl_3$); **^{1}H NMR**



(600 MHz, C_6D_6): δ = 5.99 (ddt, J = 17.2, 10.3, 6.9 Hz, 1H, H-9), 5.18 (ddt, J = 17.2, 2.2, 1.5 Hz, 1H, H-10a), 5.08 (ddt, J = 10.3, 2.3, 1.2 Hz, 1H, H-10b), 3.99 (ddd, J = 5.0, 2.1, 1.2 Hz, 1H, H-4), 3.94 (t, J = 2.2 Hz, 1H, H-5), 3.88 – 3.82 (m, 3H, H-7 and H-3 and H-1a), 3.80 (ddd, J = 4.7, 2.1, 1.3 Hz, 1H, H-6), 3.76 – 3.70 (m, 1H, H-1b), 2.62 – 2.56 (m, 1H, H-8a), 2.53 – 2.47 (m, 1H, H-8b), 1.86 (t, J = 6.0 Hz, 1H, H-1), 0.98 (s, 9H, *t*-Bu), 0.97 (s, 9H, *t*-Bu), 0.96 (s, 9H, *t*-Bu), 0.17 (s, 3H, Me), 0.155 (s, 3H, Me), 0.15 (s, 3H, Me), 0.14 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, C_6D_6): δ = 135.6 (C-9), 117.1 (C-10), 80.8 (C-3), 80.0 (C-7), 78.2 (C-5), 75.1 (C-6), 72.3 (C-4), 64.0 (C-2), 39.2 (C-8), 26.1 (6C *t*-Bu), 26.0 (3C *t*-Bu), 18.2 (2C *t*-Bu), 18.1 (*t*-Bu), -3.6 (Me), -3.8 (Me), -4.0 (Me), -4.1 (Me), -4.4 (Me), -4.6 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 3484, 2953, 2929, 2894, 2857, 1642, 1472, 1463, 1389, 1361, 1342, 1251, 1085, 1005, 938, 914, 880, 853, 831, 813, 772, 670, 576, 520, 472, 418 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{58}O_5Si_3Na^+$: 569.3484, found: 569.3488.

(2S,3R,4R,5S,6R)-6-Allyl-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-carbaldehyde (185)

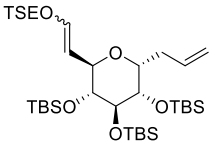


DMSO (377 µL, 5.31 mmol) was added dropwise to a stirred solution of $(COCl)_2$ (228 µL, 2.65 mmol) in DCM (8.0 mL) at -78 °C and the reaction mixture was stirred for 5 min. A solution of alcohol **184** (660 mg, 1.21 mmol) in DCM (2.5 mL,

rinsed with 2 x 2.5 mL) was added dropwise and stirring was continued for 20 min. DIPEA (2.10 mL, 12.1 mmol) was slowly added over the course of 5 min and stirring was continued for 5 min. Then the reaction mixture was allowed to reach rt and stirring was again continued for 30 min. The reaction was quenched with water (20 mL) and the organic extract was subsequently washed with aq. phosphate buffer (200 mM, pH 7, 2 x 15 mL) and with brine (15 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **185** as a colourless oil (589 mg, 90%).

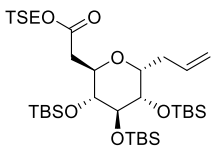
$[\alpha]_D^{20}$: +67.9 (c = 1.11, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.78 (s, 1H), 5.95 (ddt, J = 17.1, 10.3, 6.7 Hz, 1H), 5.18 (dq, J = 17.3, 1.7 Hz, 1H), 5.11 (dq, J = 10.3, 1.4 Hz, 1H), 4.17 – 4.14 (m, 1H), 4.05 – 3.99 (m, 2H), 3.81 (t, J = 2.9 Hz, 1H), 3.37 – 3.33 (m, 1H), 2.57 (dddt, J = 14.8, 8.2, 6.4, 1.5 Hz, 1H), 2.19 (dddt, J = 14.7, 7.3, 4.9, 1.4 Hz, 1H), 0.94 (s, 9H), 0.93 (s, 9H), 0.84 (s, 9H), 0.12 (s, 3H), 0.115 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 201.3, 135.4, 116.9, 84.0, 71.4, 71.1, 70.2, 70.1, 36.0, 26.5 (3C), 26.3 (3C), 25.7 (3C), 18.8, 18.4, 17.9, -3.2, -4.2, -4.5, -4.6, -4.7, -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 2952, 2929, 2886, 2858, 1734, 1643, 1472, 1463, 1390, 1362, 1305, 1252, 1131, 1086, 1041, 1005, 968, 939, 914, 882, 831, 812, 773, 673, 666, 600, 573, 538, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{56}O_5Si_3Na^+$: 567.3328, found: 567.3331.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-6-allyl-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (183a)



A solution of KO*t*-Bu (206 mg, 1.84 mmol) in THF (1.0 mL, rinsed with 1.0 mL) was dried over 5 Å MS before it was slowly added to a stirred suspension of phosphonium salt **61a** (787 mg, 1.84 mmol) in THF (3.5 mL) with 5 Å MS at -50 °C over the course of 5 min resulting in a fast colour change from colourless to deep red. Stirring was continued for 15 min. Then the reaction mixture was cooled to -78 °C and a solution of aldehyde **185** (500 mg, 917 μmol) in THF (1.5 mL, rinsed with 2 x 1.5 mL) with 5 Å MS was slowly added over the course of 5 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 16 h. The reaction was quenched with water (20 mL) and the aq. phase was extracted with MTBE (3 x 30 mL). The combined extracts were washed with brine (2 x 5.0 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated.

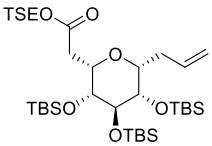
The crude product was purified by flash chromatography (fine SiO_2, hexane/EtOAc, 100:1 to 75:1) affording intermediate **186a** as an inseparable mixture of *E*/*Z* isomers (502 mg, 83%).



PCC (315 mg, 1.46 mmol) was added to a stirred solution of the *E*/*Z* mixture of enolether **186a** (502 mg, 731 μmol) in DCM (42 mL) at rt and the reaction mixture was stirred for 16 h. PCC (78.8 mg, 366 μmol) was added to the reaction mixture and stirring was continued for 1 h. Celite® was added and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1) affording both minor isomer *epi*-**183a** (109 mg, 22%) and desired major isomer **183a** (298 mg, 60%) as a colourless oil.

Analytical and spectral data of the major epimer **183a**: $[\alpha]_D^{20}$: +24.6 (c = 1.08, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.83 (dddd, J = 17.4, 10.2, 7.3, 6.2 Hz, 1H), 5.07 (dq, J = 17.2, 1.6 Hz, 1H), 5.01 (ddt, J = 10.2, 2.3, 1.2 Hz, 1H), 4.34 (td, J = 7.5, 4.0 Hz, 1H), 4.19 – 4.12 (m, 2H), 3.85 (ddd, J = 8.8, 4.7, 2.3 Hz, 1H), 3.79 (dd, J = 2.8, 1.3 Hz, 1H), 3.52 – 3.50 (m, 1H), 3.50 – 3.47 (m, 1H), 2.45 (m, 2H), 2.45 (dddt, J = 14.9, 9.1, 6.3, 1.6 Hz, 1H), 2.09 (dddt, J = 14.5, 7.2, 4.6, 1.2 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.095 (s, 3H), 0.09 (s, 3H), 0.075 (s, 3H), 0.07 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.7, 136.0, 116.4, 74.6, 74.1, 74.0, 71.7, 69.5, 62.7, 37.9, 35.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 17.5, -1.4 (3C), -3.3, -3.9, -4.1, -4.5 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2895, 2858, 1735, 1642, 1472, 1463, 1408, 1389, 1361, 1324, 1250, 1168, 1120, 1080, 1005, 972, 939, 910, 859, 830, 813, 772, 694, 672, 669, 608, 559, 472, 428, 419 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_6Si_4Na^+$: 697.4142, found: 697.4145.

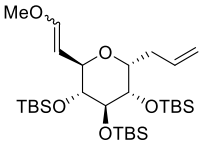
Analytical and spectral data of the minor epimer *epi*-**183a**: $[\alpha]_D^{20}$: +17.4 (c = 1.04, $CHCl_3$);



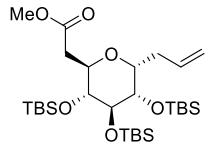
^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (dddd, J = 17.4, 10.2, 7.3, 5.5 Hz, 1H), 5.07 (dq, J = 17.3, 1.8 Hz, 1H), 4.99 (dq, J = 10.2, 1.5 Hz, 1H), 4.20 – 4.12 (m, 2H), 4.09 (ddd, J = 8.4, 5.0, 1.8 Hz, 1H), 3.78 (t, J = 2.5 Hz, 1H), 3.65 (ddd, J = 9.4, 3.9, 1.7 Hz, 1H), 3.43 – 3.40 (m, 1H), 3.34 – 3.31 (m, 1H), 2.68 (dd, J = 15.9, 8.4 Hz, 1H), 2.47 (dddt, J = 11.3, 9.3, 5.8, 1.7 Hz, 1H), 2.40 (dd, J = 15.9, 5.1 Hz, 1H), 2.02 (ddd, J = 14.9, 7.4, 3.9 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.92 (s, 9H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.035 (s, 9H), 0.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 136.3, 115.8, 76.7, 73.5, 73.9, 72.0, 71.6, 62.6, 37.3, 35.9, 26.52 (3C), 26.50 (3C), 25.9 (3C), 18.6, 18.5, 18.0, 17.5, -1.3 (3C), -2.9, -3.1, -4.31, -4.34, -4.8, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2895,

2858, 1735, 1642, 1545, 1472, 1463, 1407, 1389, 1361, 1347, 1285, 1251, 1217, 1174, 1086, 1079, 1019, 1005, 983, 938, 913, 892, 858, 830, 813, 770, 694, 674, 611, 586, 563, 503, 463, 408 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_6Si_4Na^+$: 697.4142, found: 697.4145.

Methyl 2-((2R,3R,4R,5S,6R)-6-allyl-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (183b)



A solution of KO*t*-Bu (824 mg, 7.34 mmol) in THF (4.0 mL, rinsed with 4.0 mL) was dried over 5 Å MS before it was slowly added to a stirred suspension of phosphonium salt **61b** (2.52 g, 7.34 mmol) in THF (17 mL) with 5 Å MS at -50 °C over the course of 25 min resulting in a fast colour change from colourless to deep orange. Stirring was continued for 10 min. Then the reaction mixture was cooled to -78 °C and after 10 min aldehyde **185** (2.00 g, 3.67 mmol) as a solution in THF (4.0 mL, rinsed with 4.0 mL) over 5 Å MS was slowly added over the course of 15 min. The resulting reaction mixture was allowed to reach rt and stirring was continued for 17.5 h. The reaction was quenched with water (25 mL) and the aq. phase was extracted with MTBE (2 x 50 mL). The combined extracts were washed with brine (50 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 20:1) affording intermediate **186b** as an inseparable mixture of *E*/*Z* isomers (1.85 g, 88%).

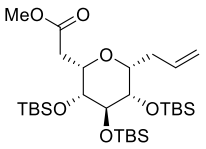


PCC (1.39 g, 6.44 mmol) was added to a stirred solution of the *E*/*Z* mixture of enolether **186b** (1.85 g, 3.22 mmol) in DCM (185 mL) at rt and the reaction mixture was stirred for 6 h. PCC (347 mg, 1.61 mmol) was added to the reaction mixture and stirring was continued for 17 h. PCC (347 mg, 1.61 mmol) was added to the reaction mixture and stirring was continued for 30 min. Celite® was added and the solvent was evaporated. The crude product was purified by flash chromatography (fine SiO_2, hexane/EtOAc, 100:1 to 40:1) affording both minor isomer *epi*-**183b** (340 mg, 18%) and desired major isomer **183b** (1.16 g, 61%) as a colourless oil each.

Analytical and spectral data of the major epimer **183b**: $[\alpha]_D^{20}$: +22.9 (c = 1.02, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.82 (ddt, J = 17.1, 10.2, 6.8 Hz, 1H), 5.08 (dq, J = 17.2, 1.7 Hz, 1H), 5.03 (ddt, J = 10.2, 2.2, 1.2 Hz, 1H), 4.33 (ddd, J = 9.2, 5.8, 3.7 Hz, 1H), 3.85 (ddd, J = 9.0, 4.5, 2.2 Hz, 1H), 3.80 (t, J = 2.5 Hz, 1H), 3.67 (s, 3H), 3.52 – 3.47 (m, 2H), 2.73 (dd, J = 14.6, 8.9 Hz, 1H), 2.68 (dd, J = 14.5, 5.8 Hz, 1H), 2.45 (dddt, J = 14.5, 9.3, 6.4, 1.5 Hz, 1H), 2.07 (dddt, J = 14.3, 7.2,

4.5, 1.3 Hz, 1H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (s, 6H), 0.09 (s, 6H), 0.075 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 135.9, 116.4, 74.5, 74.1, 73.9, 71.7, 69.5, 51.7, 37.5, 35.8, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, -3.3, -4.0, -4.1, -4.5 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 2952, 2929, 2886, 2858, 1743, 1472, 1463, 1436, 1409, 1390, 1361, 1339, 1253, 1124, 1082, 1005, 939, 911, 833, 813, 774, 673, 666, 559, 486, 427 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{60}O_6Si_3Na^+$: 611.3590, found: 611.3593.

Analytical and spectral data of the minor epimer *epi*-**183b**: **$[\alpha]_D^{20}$**: +10.5 (c = 1.03, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87 (dddd, J = 17.5, 10.3, 7.3, 5.6 Hz, 1H), 5.07 (dq, J = 17.3, 1.8 Hz, 1H), 5.01 (dq, J = 10.4, 1.5 Hz, 1H), 4.08 (ddd, J = 8.5, 5.1, 1.8 Hz, 1H), 3.78 (t, J = 2.5 Hz, 1H), 3.67 (s, 3H), 3.65 (ddd, J = 9.7, 3.9, 1.8 Hz, 1H), 3.43 – 3.41 (m, 1H), 3.34 – 3.31 (m, 1H), 2.72 (dd, J = 15.9, 8.5 Hz, 1H), 2.48 (dddt, J = 15.0, 9.2, 5.6, 1.7 Hz, 1H), 2.43 (dd, J = 15.9, 5.1 Hz, 1H), 2.02 (dddt, J = 15.0, 7.3, 4.0, 1.2 Hz, 1H), 0.925 (s, 9H), 0.92 (s, 9H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.06 (s, 3H), 0.02 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.4, 136.2, 115.8, 76.7, 73.5, 73.3, 72.0, 71.5, 51.6, 36.9, 35.8, 26.51 (3C), 26.48 (3C), 25.9 (3C), 18.6, 18.5, 18.0, -2.9, -3.1, -4.32, -4.34, -4.8, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2952, 2929, 2887, 2858, 1742, 1473, 1463, 1436, 1406, 1390, 1379, 1361, 1349, 1288, 1252, 1195, 1162, 1137, 1121, 1085, 1071, 1005, 982, 939, 914, 869, 830, 813, 770, 674, 593, 564, 509, 463 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{60}O_6Si_3Na^+$: 611.3590, found: 611.3593.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(3-hydroxy-2-oxopropyl)tetrahydro-2H-pyran-2-yl)acetate (187a)

Procedure A

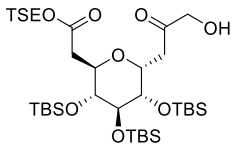
A solution of $KMnO_4$ (47 mg, 0.30 mmol) as a solution in acetone (0.75 mL) and aq. acetate buffer (1.0 M, pH 3, 0.75 mL) was added to a stirred solution of alkene **183a** (100 mg, 148 μmol) in acetone (1.5 mL) and aq. acetate buffer (1.0 M, pH 3, 1.5 mL) at rt. The reaction mixture was warmed to 40 °C and stirring was continued for 20 h. A solution of $KMnO_4$ (47 mg, 0.30 mmol) in acetone (0.75 mL) and aq. acetate buffer (1.0 M, pH 3, 0.75 mL) was added to the reaction mixture at 40 °C and stirring was continued for 1 d. The reaction mixture was filtered through a plug of SiO_2 which was washed with acetone. The solvent was evaporated and the crude product was purified by flash chromatography twice (first column: SiO_2, hexane/EtOAc, 20:1 to 10:1, second column:

SiO_2, hexane/EtOAc, 20:1 to 7:1) affording both the desired major compound **187a** (47 mg, 45%) and a minor byproduct **188** (32 mg, 31%) as a colourless oil.

Procedure B

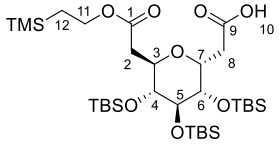
A solution of $KMnO_4$ (187 mg, 1.18 mmol) in acetone (2.45 mL) and water (0.8 mL) was added to a stirred solution of alkene **183a** (500 mg, 741 μmol) in acetone (6.25 mL), water (1.4 mL) and AcOH (302 μL) at rt and the reaction mixture was stirred for 3.5 h. $KMnO_4$ (23 mg, 0.15 mmol) was added to the reaction mixture and stirring was continued for 1.25 h. The reaction was quenched with EtOH (1.0 mL) and the resulting mixture was filtered through a plug of SiO_2 which was washed with MTBE. The filtrate was washed with sat. aq. $NaHCO_3$ (2 x 30 mL) and the aq. phase was extracted with MTBE (2 x 30 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording the desired compound **187a** as a colourless oil (375 mg, 72%).

Analytical and spectral data of the major product **187a**: $[\alpha]_D^{20}$: +33.2 (c = 1.13, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.36 – 4.32 (m, 1H), 4.31 (dd, J = 9.0, 4.5 Hz, 1H), 4.30 (dd, J = 19.4, 5.0 Hz, 1H), 4.20 (dd, J = 19.2, 5.0 Hz, 1H), 4.18 – 4.12 (m, 2H), 3.80 (dd, J = 3.2, 1.5 Hz, 1H), 3.62 (td, J = 3.0, 1.0 Hz, 1H), 3.48 (dt, J = 4.8, 1.2 Hz, 1H), 3.09 (t, J = 5.0 Hz, 1H), 2.94 (dd, J = 15.3, 8.9 Hz, 1H), 2.69 (dd, J = 15.3, 4.9 Hz, 1H), 2.58 (dd, J = 15.3, 9.2 Hz, 1H), 2.31 (dd, J = 15.4, 4.0 Hz, 1H), 1.00 – 0.95 (m, 2H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.115 (s, 6H), 0.11 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 9H), 0.02 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 209.5, 171.7, 74.5, 74.1, 73.4, 71.8, 69.3, 67.2, 62.9, 40.7, 37.6, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.4, 18.3, 18.0, 17.4, -1.4 (3C), -3.5, -3.8, -4.1, -4.5, -4.6, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 3496, 2954, 2929, 2896, 2858, 1731, 1472, 1463, 1407, 1389, 1361, 1325, 1251, 1171, 1122, 1087, 1042, 1005, 977, 938, 883, 860, 833, 813, 775, 694, 671, 633, 611, 576, 551, 545, 508, 499, 466, 459, 440, 433, 425, 418, 403 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_8Si_4Na^+$: 729.4040, found: 729.4040.

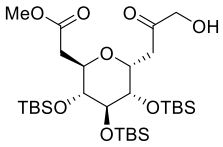
Analytical and spectral data of the minor byproduct **188**: $[\alpha]_D^{20}$: +31.6 (c = 0.82, $CHCl_3$);



^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.75 (br s, 1H, H-10), 4.33 (ddd, J = 9.6, 5.2, 4.2 Hz, 1H, H-3), 4.31 (dt, J = 9.7, 3.6, 3.3 Hz, 1H, H-7), 4.22 – 4.17 (m, 2H, H-11), 3.81 (dd, J = 3.3, 1.4 Hz, 1H, H-5), 3.65 (td, J = 3.0, 0.9 Hz, 1H, H-6), 3.51 (dt, J = 5.5, 1.2 Hz, 1H, H-4), 2.85 (dd, J = 15.6, 9.7 Hz, 1H, H-8a), 2.74 (dd, J = 16.0,

4.2 Hz, 1H, H-2a), 2.61 (dd, J = 16.0, 9.6 Hz, 1H, H-2b), 2.35 (dd, J = 15.6, 3.5 Hz, 1H, H-8b), 1.01 – 0.97 (m, 2H, H-12), 0.93 (s, 9H, *t*-Bu), 0.89 (s, 18H, *t*-Bu), 0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.105 (s, 3H, Me), 0.10 (s, 3H, Me), 0.09 (s, 3H, Me), 0.06 (s, 3H, Me), 0.03 (s, 9H, TMS) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 173.6 (C-9), 172.2 (C-1), 74.8 (C-4), 74.5 (C-5), 72.8 (C-3), 71.6 (C-6), 67.8 (C-7), 63.4 (C-11), 37.4 (C-2), 36.7 (C-8), 26.2 (3C *t*-Bu), 26.2 (3C *t*-Bu), 25.9 (3C *t*-Bu), 18.4 (*t*-Bu), 18.3 (*t*-Bu), 18.0 (*t*-Bu), 17.4 (C-12), -1.4 (3C, TMS), -3.6 (Me), -3.7 (Me), -4.1 (Me), -4.5 (Me), -4.7 (Me), -5.2 (Me) ppm; **^{1}H NMR** (600 MHz, C_6D_6): δ = 10.27 (br s, 1H), 4.69 (ddd, J = 8.1, 5.9, 4.4 Hz, 1H, H-3), 4.62 (ddd, J = 7.5, 6.0, 2.5 Hz, 1H, H-7), 4.26 – 4.21 (m, 2H, H-11), 4.01 (dd, J = 3.2, 1.6 Hz, 1H, H-5), 3.88 – 3.86 (m, 1H, H-6), 3.82 (ddd, J = 4.5, 1.6, 0.9 Hz, 1H, CH-4), 3.07 (dd, J = 15.4, 6.0 Hz, 1H, H-2a), 2.91 (dd, J = 16.4, 7.5 Hz, 1H, H-8a), 2.86 (dd, J = 15.4, 8.1 Hz, 1H, H-2b), 2.70 (dd, J = 16.5, 6.1 Hz, 1H, H-8b), 1.02 (s, 9H, *t*-Bu), 0.99 (s, 9H, *t*-Bu), 0.98 (s, 9H, *t*-Bu), 0.96 – 0.93 (m, 2H, H-12), 0.20 (s, 3H, Me), 0.19 (s, 3H, Me), 0.17 (s, 3H, Me), 0.16 (s, 6H, Me), 0.07 (s, 3H, Me), -0.07 (s, 9H, TMS) ppm; **^{13}C NMR** (151 MHz, C_6D_6): δ = 175.4 (C-9), 171.4 (C-1), 75.1 (C-5), 74.3 (C-4), 73.9 (C-3), 71.5 (C-6), 67.1 (C-7), 62.7 (C-11), 37.7 (C-2), 36.5 (C-8), 26.4 (3C *t*-Bu), 26.3 (3C *t*-Bu), 26.0 (3C *t*-Bu), 18.5 (*t*-Bu), 18.4 (*t*-Bu), 18.1 (*t*-Bu), 17.6 (C-12), -1.4 (3C, TMS), -3.3 (Me), -3.7 (Me), -4.2 (Me), -4.48 (Me), -4.50 (Me), -5.2 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2858, 1733, 1711, 1472, 1463, 1407, 1390, 1362, 1251, 1170, 1126, 1084, 1063, 1005, 977, 938, 858, 831, 813, 773, 756, 693, 666, 553, 471 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{32}H_{68}O_8Si_4Na^+$: 715.3884, found: 715.3886.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(3-hydroxy-2-oxopropyl)tetrahydro-2H-pyran-2-yl)acetate (187b)



A solution of $KMnO_4$ (159 mg, 1.01 mmol) in acetone (2.45 mL) and water (0.8 mL) was added to a stirred solution of alkene **183b** (370 mg, 628 μmol) in acetone (6.25 mL), water (1.4 mL) and AcOH (302 μL) at rt and the reaction mixture was stirred for 3.25 h. The reaction was quenched with EtOH (1.0 mL) and the resulting mixture was filtered through a plug of silica gel which was washed with MTBE. The filtrate was washed with sat. aq. $NaHCO_3$ (2 x 30 mL) and the aq. phase was extracted with MTBE (2 x 30 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 5:1) affording compound **187b** as a colourless oil (301 mg, 77%).

$[\alpha]_D^{20}$: +34.5 (c = 1.10, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.36 – 4.25 (m, 3H), 4.21 (dd, J = 19.3, 5.0 Hz, 1H), 3.80 (dd, J = 3.2, 1.6 Hz, 1H), 3.67 (s, 3H), 3.62 – 3.60 (m, 1H), 3.48 (dt, J = 4.4, 1.3 Hz, 1H), 3.09 (t, J = 4.9 Hz, 1H), 2.94 (dd, J = 15.2, 9.1 Hz, 1H), 2.71 (dd, J = 15.3, 5.2 Hz, 1H), 2.63 (dd, J = 15.3, 9.1 Hz, 1H), 2.29 (dd, J = 15.3, 3.9 Hz, 1H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.115 (s, 3H), 0.11 (s, 3H), 0.105 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 209.5, 172.0, 74.4, 73.9, 73.5, 71.8, 69.4, 67.1, 51.8, 40.7, 37.2, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.4, 18.3, 18.0, -3.5, -3.9, -4.1, -4.5, -4.6, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 3505, 2953, 2929, 2896, 2858, 1739, 1472, 1463, 1437, 1390, 1361, 1341, 1253, 1171, 1122, 1083, 1005, 938, 893, 867, 831, 812, 773, 672, 547, 475 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{60}O_8Si_3Na^+$: 643.3488, found: 643.3489.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-6-(3-bromo-2-oxopropyl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (189a)

*Procedure A (PPh_3 (**195a**) as solution, successive addition and excess of reagents)*

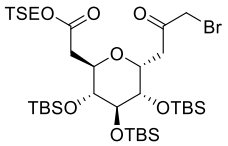
A solution of PPh_3 (**195a**) (82 mg, 312 µmol) in DCM (0.81 mL) was added to a stirred solution of α-hydroxyketone **187a** (210 mg, 297 µmol) and CBr_4 (103 mg, 312 µmol) in DCM (3.0 mL) at rt over the course of 15 min, and stirring was continued for 30 min. Then CBr_4 (49 mg, 149 µmol) and PPh_3 (**195a**) (39 mg, 149 µmol) were subsequently added to the reaction mixture and stirring was continued for 30 min. Then, CBr_4 (10 mg, 30 µmol) and PPh_3 (**195a**) (8 mg, 30 µmol) were subsequently added to the reaction mixture and stirring was continued for 15 min. The reaction mixture was filtered through a plug of silica gel, and washed with MTBE. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording the desired major compound **189a** (185 mg, 81%) and both a major byproduct **190a** (32 mg, 16%) and a minor byproduct **191** (7 mg, 4%) as a colourless oil.

Procedure B (2 eq. of both reagents right from the start)

PPh_3 (**195a**) (15 mg, 0.06 mmol) was added to a stirred solution of α-hydroxyketone **187a** (38 mg, 54 µmol) and CBr_4 (19 mg, 0.06 mmol) in DCM (0.7 mL) at rt and the reaction mixture was stirred for 35 min. Then CBr_4 (9 mg, 27 µmol) and PPh_3 (**195a**) (7 mg, 27 µmol) were subsequently added to the reaction mixture and stirring was continued for 20 min. The reaction mixture was filtered through a plug of silica gel, and washed with MTBE. The solvent was evaporated and the crude

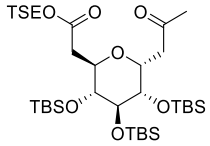
product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **189a** as a colourless oil (41 mg, 99%).

Analytical and spectral data of the major product **189a**: $[\alpha]_D^{20}$: +51.0 (c = 0.96, $CHCl_3$);



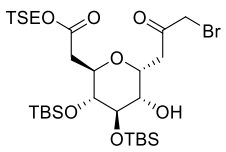
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.35 – 4.26 (m, 2H), 4.19 – 4.12 (m, 2H), 4.06 – 3.98 (m, 2H), 3.80 (dd, J = 3.2, 1.5 Hz, 1H), 3.62 (td, J = 2.9, 1.0 Hz, 1H), 3.48 (dt, J = 4.9, 1.9 Hz, 1H), 3.13 (dd, J = 15.7, 8.8 Hz, 1H), 2.70 (dd, J = 15.3, 4.9 Hz, 1H), 2.58 (dd, J = 15.3, 9.2 Hz, 1H), 2.51 (dd, J = 15.8, 4.1 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.94 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 6H), 0.105 (s, 3H), 0.10 (s, 3H), 0.08 (s, 3H), 0.04 (s, 12H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 201.05, 171.77, 74.52, 74.22, 73.32, 71.71, 67.54, 62.91, 42.12, 37.62, 36.31, 26.26 (3C), 26.18 (3C), 25.90 (3C), 18.42, 18.31, 18.00, 17.47, -1.34 (3C), -3.51, -3.82, -4.09, -4.52, -4.60, -5.04 ppm; **^{1}H NMR** (400 MHz, C_6D_6): δ = 4.68 (ddd, J = 8.5, 5.5, 4.2 Hz, 1H), 4.63 (ddd, J = 7.8, 4.8, 2.4 Hz, 1H), 4.29 – 4.21 (m, 2H), 3.99 (dd, J = 3.2, 1.6 Hz, 1H), 3.81 – 3.76 (m, 2H), 3.58 (d, J = 13.4 Hz, 1H), 3.48 (d, J = 13.4 Hz, 1H), 3.09 (dd, J = 16.2, 8.2 Hz, 1H), 2.99 (dd, J = 15.5, 5.7 Hz, 1H), 2.89 (dd, J = 15.5, 8.5 Hz, 1H), 2.52 (dd, J = 16.3, 4.8 Hz, 1H), 1.05 (s, 9H), 0.99 (s, 9H), 0.97 (s, 9H), 0.97 – 0.92 (m, 2H), 0.19 (s, 3H), 0.18 (s, 3H), 0.165 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.03 (s, 3H), -0.06 (s, 9H) ppm; **^{13}C NMR** (101 MHz, C_6D_6): δ = 199.5, 171.3, 75.0, 74.3, 73.9, 72.0, 67.4, 62.7, 41.8, 37.6, 36.0, 26.4 (3C), 26.4 (3C), 26.0 (3C), 18.6, 18.5, 18.1, 17.6, -1.5 (3C), -3.3, -3.7, -4.2, -4.46, -4.47, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2858, 1731, 1472, 1463, 1390, 1361, 1327, 1250, 1171, 1084, 1040, 1006, 973, 938, 859, 831, 812, 773, 694, 672, 608, 573, 551, 473 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{69}O_7Br_1Si_4Na^+$: 791.3196, found: 791.3197.

Analytical and spectral data of the major byproduct **190a**: $[\alpha]_D^{20}$: +25.9 (c = 1.01, $CHCl_3$);



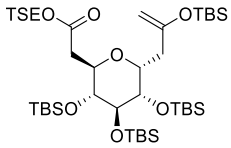
^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.34 – 4.26 (m, 2H), 4.17 – 4.11 (m, 2H), 3.79 (dd, J = 3.2, 1.6 Hz, 1H), 3.67 – 3.64 (m, 1H), 3.50 (dt, J = 4.5, 1.3 Hz, 1H), 2.82 (dd, J = 16.8, 7.2 Hz, 1H), 2.74 (dd, J = 15.2, 5.3 Hz, 1H), 2.61 (dd, J = 15.2, 8.9 Hz, 1H), 2.53 (dd, J = 16.7, 5.8 Hz, 1H), 2.15 (s, 3H), 1.00 – 0.95 (m, 2H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 (s, 9H), 0.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 207.7, 171.8, 74.5, 74.1, 73.6, 71.4, 66.6, 62.7, 45.3, 37.7, 31.0, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 17.5, -1.4 (3C), -3.4, -3.9, -4.1, -4.5, -4.6, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2857, 1733, 1472, 1463, 1389, 1361, 1250, 1168, 1125, 1086, 1006, 980, 939, 859, 831, 812, 773, 694, 672, 606, 468 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_7Si_4Na^+$: 713.4091, found: 713.4089.

Analytical and spectral data of the minor byproduct **191**: $[\alpha]_D^{20}$: +20.8 (c = 0.95, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.43 – 4.35 (m, 2H), 4.20 – 4.13 (m, 2H), 3.98 (s, 2H), 3.93 – 3.89 (m, 1H), 3.66 (d, J = 11.4 Hz, 1H), 3.55 – 3.51 (m, 1H), 3.45 – 3.39 (m, 1H), 3.05 (dd, J = 15.8, 8.9 Hz, 1H), 3.02 (dd, J = 15.6, 9.4 Hz, 1H), 2.64 (dd, J = 15.6, 5.5 Hz, 1H), 2.57 (dd, J = 15.8, 4.2 Hz, 1H), 1.01 - 0.96 (m, 2H), 0.95 (s, 9H), 0.91 (s, 9H), 0.16 (s, 3H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.04 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 200.4, 171.4, 75.8, 72.1, 70.6, 70.4, 65.2, 63.0, 42.0, 35.6, 29.9, 25.94 (3C), 25.90 (3C), 18.2, 18.1, 17.4, -1.3 (3C), -4.2, -4.7 (2C), -4.9 ppm; **IR** (film): $\tilde{\nu}$ = 3523, 2954, 2929, 2898, 2858, 1731, 1472, 1463, 1408, 1390, 1362, 1251, 1219, 1168, 1091, 1037, 1006, 964, 938, 858, 835, 777, 693, 670, 607, 540, 472, 428, 418 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{55}O_7Si_3BrNa^+$: 677.2331, found: 677.2333.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-((tert-butyldimethylsilyl)oxy)allyl)tetrahydro-2H-pyran-2-yl)acetate (192)



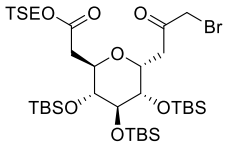
TBSOTf (31.4 µL, 137 µmol) was added dropwise to a stirred solution of methylketone **190a** (86 mg, 0.12 mmol) and 2,6-lutidine (31.9 µL, 274 µmol) in DCM (1 mL) at -78 °C and stirring was continued for 5 min. The reaction mixture was allowed to warm to -20 °C and stirring was continued for 7 h. Then 2,6-lutidine (5.8 µL, 49.8 µmol) and TBSOTf (5.7 µL, 25 µmol) were again subsequently added to the stirred reaction mixture at -20 °C and stirring was continued for 16 h. Then 2,6-lutidine (15.9 µL, 137 µmol) and TBSOTf (15.7 µL, 68.4 µmol) were again subsequently added to the stirred reaction mixture at -20 °C and stirring was continued for 3.5 h. The reaction mixture was warmed to rt and stirring was continued for 1.5 h. Then 2,6-lutidine (15.9 µL, 137 µmol) and TBSOTf (15.7 µL, 68.4 µmol) were again subsequently added to the stirred reaction mixture at rt and stirring was continued for 30 min. The reaction was diluted with MTBE (10 mL) and quenched with aq. phosphate buffer (200 mM, pH 7, 10 mL). The aq. phase was extracted with MTBE (10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/TEA, 75:1) affording compound **192** as a colourless oil (87 mg, 87%).

$[\alpha]_D^{20}$: +11.6 (c = 1.14, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.36 – 4.27 (m, 1H), 4.18 – 4.06 (m, 5H), 3.82 – 3.77 (m, 1H), 3.56 – 3.48 (m, 2H), 2.84 (dd, J = 14.9, 6.3 Hz, 1H), 2.52 (dd, J = 14.8,

7.8 Hz, 1H), 2.41 (dd, J = 14.6, 8.7 Hz, 1H), 2.00 (dd, J = 14.6, 3.8 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (s, 18H), 0.16 (s, 3H), 0.15 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.085 (s, 3H), 0.07 (s, 3H), 0.065 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 156.4, 91.8, 74.8, 73.9, 73.7, 72.1, 66.8, 62.6, 39.1, 38.0, 26.32 (3C), 26.25 (3C), 25.92 (3C), 25.87 (3C), 25.85, 18.5, 18.4, 18.1, 18.0, 17.4, -1.4 (3C), -3.3, -3.9, -4.1, -4.4, -4.5, -4.6, -4.7, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2858, 1735, 1639, 1472, 1463, 1408, 1389, 1361, 1324, 1298, 1250, 1208, 1167, 1126, 1082, 1062, 1019, 1005, 975, 939, 919, 860, 830, 812, 772, 695, 672, 665, 609, 570, 543, 518, 472, 424, 412 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{39}H_{84}O_7Si_5Na^+$: 827.4956, found: 827.4961.

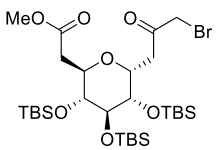
2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-6-(3-bromo-2-oxopropyl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (189a)

Procedure C



A solution of NBS (23 mg, 130 µmol) in THF (0.25 mL, rinsed with 0.25 mL) was slowly added to a stirred solution of silyl enolether **192** (87 mg, 108 µmol) in THF (0.5 mL) at -78 °C over the course of 10 min resulting in a colour change from colourless to dark brown, and stirring was continued for 50 min. The mixture was diluted with DCM (5 mL) and the reaction quenched with sat. aq. $NaHCO_3$ (5 mL). The aq. phase was extracted with DCM (2 x 5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 10:1) affording both desired compound **189a** (52 mg, 63%) and minor byproduct **190a** (13 mg, 17%) as a colourless oil. The analytical and spectroscopic data of the isolated compounds were identical with those shown above.

Methyl 2-((2R,3R,4R,5S,6R)-6-(3-bromo-2-oxopropyl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (189b)

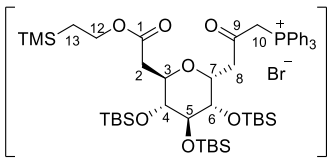


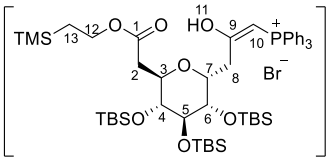
PPh_3 (**195a**) (129 mg, 490 µmol) was added to a stirred solution of α-hydroxyketone **187b** (290 mg, 467 µmol) and CBr_4 (163 mg, 490 µmol) in DCM (6.0 mL) at rt and the reaction mixture was stirred for 40 min. Then CBr_4

(77 mg, 234 µmol) and PPh_3 (**195a**) (61 mg, 234 µmol) were subsequently added to the reaction mixture and stirring was continued for 40 min. The reaction mixture was filtered through a plug of SiO_2 which was washed with MTBE. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 40:1 to 30:1) affording compound **189b** as a colourless oil (257 mg, 81%).

$[\alpha]_D^{20}$: +43.7 (c = 1.07, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.35 – 4.26 (m, 2H), 4.01 (s, 2H), 3.80 (dd, J = 3.2, 1.6 Hz, 1H), 3.67 (s, 3H), 3.62 – 3.59 (m, 1H), 3.49 (dt, J = 4.5, 1.3 Hz, 1H), 3.13 (dd, J = 15.8, 8.9 Hz, 1H), 2.72 (dd, J = 15.3, 5.3 Hz, 1H), 2.65 (dd, J = 15.3, 9.1 Hz, 1H), 2.50 (dd, J = 15.8, 4.0 Hz, 1H), 0.94 (s, 9H), 0.90 (s, 9H), 0.89 (s, 9H), 0.11 (s, 3H), 0.105 (s, 6H), 0.09 (s, 3H), 0.08 (s, 3H), 0.04 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 201.0, 172.0, 74.4, 73.9, 73.5, 71.6, 67.3, 51.8, 42.1, 37.1, 36.2, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.4, 18.3, 18.0, -3.5, -3.9, -4.1, -4.5, -4.6, -5.0 ppm; **^{1}H NMR** (400 MHz, C_6D_6): δ = 4.63 – 4.55 (m, 2H) 3.98 – 3.95 (m, 1H), 3.77 – 3.74 (m, 1H), 3.72 (ddd, J = 4.0, 1.8, 1.0 Hz, 1H), 3.51 (d, J = 13.3 Hz, 1H), 3.44 (d, J = 13.3 Hz, 1H), 3.39 (s, 3H), 3.05 (dd, J = 16.2, 8.3 Hz, 1H), 2.92 (dd, J = 15.5, 6.0 Hz, 1H), 2.81 (dd, J = 15.5, 8.3 Hz, 1H), 2.47 (dd, J = 16.3, 4.8 Hz, 1H), 1.04 (s, 9H), 0.97 (s, 9H), 0.95 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.03 (s, 3H) ppm; **^{13}C NMR** (101 MHz, C_6D_6): δ = 199.4, 171.6, 74.8, 74.0, 73.9, 71.9, 67.2, 51.3, 41.8, 37.1, 35.9, 26.4 (3C), 26.3 (3C), 25.9 (3C), 18.53, 18.45, 18.1, -3.4, -3.8, -4.3, -4.5 (2C), -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2952, 2929, 2895, 2857, 1739, 1472, 1463, 1437, 1390, 1361, 1253, 1172, 1124, 1084, 1042, 1005, 970, 938, 893, 870, 832, 813, 774, 673, 575, 551, 475 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{29}H_{59}O_7Br_1Si_3Na^+$: 705.2644, found: 705.2650.

(2-Oxo-3-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)tetrahydro-2H-pyran-2-yl)propyl)triphenylphosphonium bromide (193a) and ((Z)-2-Hydroxy-3-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)tetrahydro-2H-pyran-2-yl)prop-1-en-1-yl)triphenylphosphonium bromide (194a)





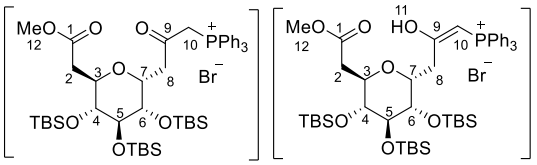
A solution of PPh_3 (**195a**) (122 mg, 464 µmol) in PhH (2.0 mL, rinsed with 2.0 mL) was dried for 1.5 h over 4 Å MS at rt before it was combined with a solution of α-bromoketone **189a** (340 mg, 442 µmol) in PhH (4.0 mL) which was dried for 1.5 h

over 4 Å MS at rt. The reaction mixture was stirred for 5 min before it was stored as a frozen solid at -20 °C for 52 h. Then the reaction mixture was allowed to reach rt and the afforded mixture of intermediates **193a** and **194a** was used in the next step without purification or removal of the solvent.

(the sample contained some unreacted PPh_3 (**195a**)) **^{1}H NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peaks, 600 MHz, C_6D_6): δ = 14.03* (d, J = 2.3 Hz, 1H, H-11), 7.94 (dd, J = 18.4, 10.4 Hz, 1H, H-10a), 7.86 – 7.80 (m, 6H, *o*-Ph), 7.41 – 7.35* (m, 6H, *o*-Ph), 7.10 – 7.06 (m, 6H, *m*-Ph), 7.05 – 7.02 (m, 3H, *p*-Ph), 7.05 – 7.02* (m, 3H, *p*-Ph), 7.01 – 6.96* (m, 6H, *m*-Ph) 6.07 (dd, J = 18.0, 12.7 Hz, 1H, H-10b), 5.44 (dt, J = 11.3, 2.6 Hz, 1H, H-7), 5.36* (ddd, J = 10.5, 3.3, 1.4 Hz, 1H, H-7), 4.86* (dt, J = 7.9, 5.6 Hz, 1H, H-3), 4.80* (dd, J = 20.9, 2.4 Hz, 1H, H-10), 4.72 (ddd, J = 10.2, 6.2, 3.8 Hz, 1H, H-3), 4.69* (dd, J = 3.1, 1.1 Hz, 1H, H-6), 4.37 (td, J = 3.3, 1.0 Hz, 1H, H-6), 4.19* (dd, J = 3.2, 1.1 Hz, 1H, H-5), 4.15* (dt, J = 13.6, 1.8 Hz, 1H, H-8a), 4.12 – 4.07 (m, 3H, H-5 and H-12), 4.07 – 4.02* (m, 1H, H-12a), 3.96* (dt, J = 6.1, 1.2 Hz, 1H, H-4), 3.90 (dd, J = 15.2, 2.3 Hz, 1H, H-8a), 3.78 (dt, J = 6.2, 1.1 Hz, 1H, H-4), 3.77 – 3.73* (m, 1H, H-12b), 3.45 (ddd, J = 14.9, 11.2, 3.5 Hz, 1H, H-8b), 3.39* (dd, J = 15.7, 5.3 Hz, 1H, H-2a), 3.26* (ddd, J = 12.7, 10.5, 1.5 Hz, 1H, H-8b), 3.00 (dd, J = 14.4, 3.7 Hz, 1H, H-2a), 2.85 (dd, J = 14.4, 10.1 Hz, 1H, H-2b), 2.73* (dd, J = 15.6, 8.0 Hz, 1H, H-2b), 1.15* (s, 9H, *t*-Bu), 1.125* (s, 9H, *t*-Bu), 1.12 (s, 9H, *t*-Bu), 1.07 (s, 9H, *t*-Bu), 1.00* (s, 9H, *t*-Bu), 0.98 (s, 9H, *t*-Bu), 0.94 – 0.87 (m, 2H, H-13), 0.82* (ddd, J = 9.8, 6.5, 4.8 Hz, 2H, H-13), 0.67* (s, 3H, Me), 0.58 (s, 3H, Me), 0.51* (s, 3H, Me), 0.36* (s, 3H, Me), 0.33* (s, 3H, Me), 0.32 (s, 3H, Me), 0.30* (s, 3H, Me), 0.26 (s, 3H, Me), 0.25 (s, 3H, Me), 0.19 (s, 3H, Me), 0.18* (s, 3H, Me), 0.10 (s, 3H, Me), -0.06 (s, 9H, TMS), -0.13* (s, 9H, TMS) ppm; **^{13}C NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peaks, 151 MHz, C_6D_6): δ = 203.4 (d, $J_{31P,13C}$ = 7.1 Hz, C-9), 184.8* (d, $J_{31P,13C}$ = 2.2 Hz, C-9), 172.1* (C-1), 171.9 (C-1), 134.5 (d, $J_{31P,13C}$ = 10.7 Hz, 6C, *o*-Ph), 134.0 (d, $J_{31P,13C}$ = 3.1 Hz, 3C, *p*-Ph), 133.5* (d, $J_{31P,13C}$ = 10.7 Hz, 6C, *o*-Ph), 133.5* (d, $J_{31P,13C}$ = 3.1 Hz, 3C, *p*-Ph), 129.8 (d, $J_{31P,13C}$ = 12.9 Hz, 6C, *m*-Ph), 129.6* (d, $J_{31P,13C}$ = 12.8 Hz, 6C, *m*-Ph), 122.6* (d, $J_{31P,13C}$ = 91.6 Hz, 3C, *i*-Ph), 119.8 (d, J = 88.6 Hz, 3C, *i*-Ph), 76.8 (C-4), 76.3* (C-4), 76.0* (C-5), 75.9 (C-5), 73.2 (C-3), 72.8* (C-3), 71.9* (C-6), 71.6 (C-6), 71.4* (C-7), 71.1* (d, $J_{31P,13C}$ = 96.2 Hz, C-10), 69.4 (C-7), 62.7 (C-12), 62.1* (C-12), 47.9 (d, $J_{31P,13C}$ = 5.8 Hz, C-8), 40.1 (d, $J_{31P,13C}$ = 57.9 Hz, C-10), 39.8* (d, $J_{31P,13C}$ = 12.1 Hz, C-8), 39.7 (C-2), 39.0* (C-2), 26.60* (3C, t-Bu), 26.58* (3C, t-Bu), 26.53 (3C, t-Bu), 26.50 (3C, t-Bu), 26.4* (3C, t-Bu), 26.3 (3C, t-Bu), 18.6* (t-Bu), 18.50* (2C, t-Bu), 18.46 (t-Bu), 18.44 (t-Bu), 18.42 (t-Bu), 17.5* (C-13), 17.4 (C-13), -1.4 (3C, Me), -1.5* (3C, Me), -2.6* (Me), -2.7 (Me), -3.36* (Me), -3.44* (Me), -3.60 (Me), -3.61 (Me), -4.1* (Me), -4.3* (Me), -4.47

(Me), -4.50* (Me), -4.53 (Me), -4.6 (Me) ppm; **^{31}P NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peak, 162 MHz, C_6D_6): δ = 21.0, 13.4* ppm; **HRMS** (ESI): *m/z* calcd. for $C_{51}H_{84}O_7P_1Si_4^+$: 951.5026, found: 951.5036.

(2-Oxo-3-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)propyl)triphenylphosphonium bromide (193b) and ((Z)-2-Hydroxy-3-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)prop-1-en-1-yl)triphenylphosphonium bromide (194b)



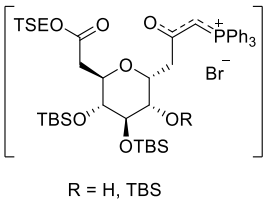
A solution of PPh_3 (**195a**) (101 mg, 384 μmol) as a solution in PhH (2.0 mL, rinsed with 2.0 mL) was dried for 1 h over 4 Å MS before it was combined with a solution of α-bromoketone **189b** (250 mg, 366 μmol) in PhH (4.0 mL) which was dried for 1 h over 4 Å MS at rt. The reaction mixture was stirred for 5 min before it was stored as a frozen solid at -20 °C for 49 h. Then the reaction mixture was allowed to reach rt and the afforded mixture of intermediates **193b** and **194b** was used in the next step without purification or removal of the solvent.

(the sample contained some unreacted PPh_3 (**195a**)) **^{1}H NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peaks, 600 MHz, C_6D_6): δ = 14.16* (d, J = 2.5 Hz, 1H, H-11), 7.88 (dd, J = 18.1, 10.5 Hz, 1H, H-10a), 7.85 – 7.80 (m, 6H, *o*-Ph), 7.33 – 7.26* (m, 6H, *o*-Ph), 7.04 – 6.98 (m, 6H, *m*-Ph), 6.97 – 6.93 (m, 3H, *p*-Ph), 6.97 – 6.93* (m, 3H, *p*-Ph), 6.91 – 6.87* (m, 6H, *m*-Ph), 6.21 (dd, J = 18.0, 12.8 Hz, 1H, H-10b), 5.40 (dt, J = 11.1, 2.1 Hz, 1H, H-7), 5.33* (d, J = 10.6 Hz, 1H, H-7), 4.82* (dt, J = 8.4, 5.7 Hz, 1H, H-3), 4.72* (dd, J = 21.1, 2.4 Hz, 1H, H-10), 4.72* (t, J = 2.6 Hz, 1H, H-6), 4.66 (dt, J = 8.4, 5.6 Hz, 1H, H-3), 4.34 – 4.31 (m, 1H, H-6), 4.17* (d, J = 12.9 Hz, 1H, H-8a), 4.17* (d, J = 3.8 Hz, 1H, H-5), 4.07 (dd, J = 3.3, 1.3 Hz, 1H, H-5), 3.92 – 3.90* (m, 1H, H-4), 3.92 (dd, J = 15.3, 2.3 Hz, 1H, H-8a), 3.74 (dt, J = 5.5, 1.0 Hz, 1H, H-4), 3.46 (ddd, J = 14.8, 11.1, 3.4 Hz, 1H, H-8b), 3.30* (dd, J = 15.7, 5.2 Hz, 1H, H-2a), 3.25 (s, 3H, Me), 3.25* (dd, J = 12.9, 10.6 Hz, 1H, H-8b), 3.00* (s, 3H, Me), 2.92 – 2.86 (m, 2H, H-2), 2.67* (dd, J = 15.7, 8.2 Hz, 1H, H-2b), 1.13* (s, 9H, *t*-Bu), 1.11* (s, 9H, *t*-Bu), 1.09 (s, 9H, *t*-Bu), 1.05 (s, 9H, *t*-Bu), 0.97* (s, 9H, *t*-Bu), 0.95 (s, 9H, *t*-Bu), 0.67* (s, 3H, Me), 0.54 (s, 3H, Me), 0.52* (s, 3H, Me), 0.35* (s, 3H, Me), 0.34 (s, 3H, Me), 0.31* (s, 3H, Me), 0.24 (s, 3H, Me), 0.23 (s, 3H, Me), 0.22* (s, 3H, Me), 0.16 (s, 3H, Me), 0.13* (s, 3H, Me), 0.07 (s, 3H, Me) ppm; **^{13}C NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peaks,

151 MHz, C_6D_6): δ = 203.5 (d, $J_{31P,13C}$ = 7.2 Hz, C-9), 185.0* (C-9), 172.4* (C-1), 172.3 (C-1), 134.5 (d, $J_{31P,13C}$ = 10.9 Hz, 6C, *o*-Ph), 133.9 (d, $J_{31P,13C}$ = 2.9 Hz, 3C, *p*-Ph), 133.5* (d, $J_{31P,13C}$ = 10.7 Hz, 6C, *o*-Ph), 133.4* (d, $J_{31P,13C}$ = 2.2 Hz, 3C, *p*-Ph), 129.7 (d, $J_{31P,13C}$ = 13.0 Hz, 6C, *m*-Ph), 129.5* (d, $J_{31P,13C}$ = 12.9 Hz, 6C, *m*-Ph), 122.6* (d, $J_{31P,13C}$ = 91.4 Hz, 3C, *i*-Ph), 119.8 (d, $J_{31P,13C}$ = 88.7 Hz, 3C, *i*-Ph), 76.4* (C-4), 76.2 (C-4), 76.0* (C-5), 75.6 (C-5), 73.5 (C-3), 72.6* (C-3), 71.9* (C-6), 71.6* (C-7), 71.5 (C-6), 71.1* (d, $J_{31P,13C}$ = 97.1 Hz, C-10), 68.9 (C-7), 51.3 (C-12), 50.6* (C-12), 48.0 (d, $J_{31P,13C}$ = 5.7 Hz, C-8), 40.2 (d, $J_{31P,13C}$ = 58.0 Hz, C-10), 39.6* (d, $J_{31P,13C}$ = 11.8 Hz, C-8), 39.0 (C-2), 38.6* (C-2), 26.6* (3C, *t*-Bu), 26.53* (3C, *t*-Bu), 26.50 (3C, *t*-Bu), 26.45 (3C, *t*-Bu), 26.4* (3C, *t*-Bu), 26.3 (3C, *t*-Bu), 18.6* (*t*-Bu), 18.47* (2C, *t*-Bu), 18.47 (*t*-Bu), 18.45 (*t*-Bu), 18.4 (*t*-Bu), -2.6* (Me), -2.8 (Me), -3.4* (Me), -3.5* (Me), -3.6 (Me), -3.7 (Me), -4.1* (Me), -4.36* (Me), -4.39 (Me), -4.56* (Me), -4.57 (Me), -4.59 (Me) ppm; **^{31}P NMR** (4:1 tautomer ratio, asterisk denotes minor tautomer peak, 162 MHz, C_6D_6): δ = 20.9, 13.4* ppm; **HRMS** (ESI): *m/z* calcd. for $C_{47}H_{74}O_7PSi_3^+$: 865.4475, found: 865.4472.

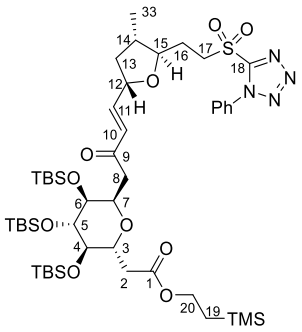
5.2.3.2. Building Block Coupling & Elaboration

2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((E)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxobut-3-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (E-181a)



R = H, TBS

PPh_3 (**195a**) (7 mg, 26 µmol) was added to a stirred solution of α-bromoketone **189a** (20 mg, 26 µmol) in PhH (200 µL) at rt. The reaction mixture was warmed to 55 °C and stirring was continued for 5 d. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, DCM/MeOH, 20:1) affording a mixture of phosphonium salts **193a**/**194a** and **208** as a colourless oil (23 mg, 91%, ca. 1:1).

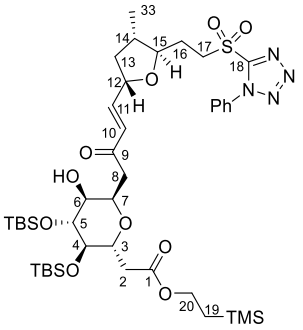


A solution of KO*t*-Bu (3 mg, 22 µmol) in THF (200 µL, rinsed with 200 µL) was dried over 5 Å MS before it was added to a stirred solution of phosphonium salts **193a**/**194a** and **208** (23 mg, 24 µmol) in THF (400 µL) over 5 Å MS at -50 °C and stirring was continued for 10 min. Then the reaction mixture was cooled to -78 °C and a solution of aldehyde **130** (21 mg, 60 µmol) in THF (200 µL, rinsed with 200 µL) which had been dried over 5 Å MS was slowly added to the reaction mixture. The resulting reaction mixture was allowed to reach rt and stirring was continued for 1.25 h. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 5 mL) and the aq. phase was extracted with MTBE (2 x 10 mL). The combined extracts were washed with aq. phosphate buffer (200 mM, pH 7, 5 mL) and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 5:1) affording both desired compound *E*-**181a** (8 mg, 33%) and byproduct **209** (9 mg, 42%) as a colourless oil each. Yields are based on the ratios of the phosphonium salt starting materials **193a**/**194a** and **208**.

Analytical and spectral data of the desired compound *E*-**181a**: $[\alpha]_D^{20}$: -3.9 (c = 0.67, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.71 – 7.67 (m, 2H, Ph), 7.65 – 7.58 (m, 3H, Ph), 6.70 (dd, J = 15.9, 5.4 Hz, 1H, H-11), 6.21 (dd, J = 15.9, 1.5 Hz, 1H, H-10), 4.57 (dddd, J = 9.4, 6.7, 5.5, 1.4 Hz, 1H, H-12), 4.19 (ddd, J = 7.5, 6.1, 1.8 Hz, 1H, H-7), 4.15 – 4.10 (m, 3H, H-3 and H-20), 3.97 (ddd, J = 14.6, 11.2, 4.7 Hz, 1H, H-17a), 3.81 (ddd, J = 14.7, 11.0, 5.0 Hz, 1H, H-17b), 3.80 – 3.77 (m, 1H, H-5), 3.61 (td, J = 8.7, 2.9 Hz, 1H, H-15), 3.49 – 3.47 (m, 1H, H-6), 3.46 – 3.43 (m, 1H, H-4), 2.98 (dd, J = 16.7,

7.1 Hz, 1H, H-8a), 2.65 (dd, J = 16.8, 5.9 Hz, 1H, H-8b), 2.59 (dd, J = 16.1, 7.9 Hz, 1H, H-2a), 2.43 (dd, J = 16.1, 5.6 Hz, 1H, H-2b), 2.36 (dt, J = 12.9, 6.8 Hz, 1H, H-13a), 2.30 (dddd, J = 12.4, 9.4, 7.8, 4.8 Hz, 1H, H-16a), 2.04 (dddd, J = 11.9, 9.3, 7.9, 3.8 Hz, 1H, H-16b), 1.98 (ddt, J = 10.4, 8.5, 5.8 Hz, 1H, H-14), 1.41 (ddd, J = 12.6, 10.6, 9.4 Hz, 1H, H-13b), 1.06 (d, J = 6.6 Hz, 3H, H-33), 0.98 – 0.94 (m, 2H, H-19), 0.93 (s, 18H, *t*-Bu), 0.92 (s, 9H, *t*-Bu), 0.13 (s, 3H, Me), 0.12 (s, 3H, Me), 0.095 (s, 3H, Me), 0.09 (s, 3H, Me), 0.03 (s, 9H, TMS), 0.025 (s, 3H, Me), -0.01 (s, 3H, Me) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 198.6 (C-9), 171.6 (C-1), 153.6 (C-18), 146.3 (C-11), 133.2 (*i*-Ph), 131.6 (*p*-Ph), 129.88 (2C, *m*-Ph), 129.87 (C-10), 125.3 (2C, *o*-Ph), 83.3 (C-15), 77.4 (C-12), 73.3 (C-3), 73.1 (C-7), 73.0 (C-5), 71.34 (C-6), 71.30 (C-4), 62.7 (C-20), 53.7 (C-17), 42.2 (C-8), 41.3 (C-13), 40.3 (C-14), 37.2 (C-2), 26.7 (C-16), 26.54 (3C, *t*-Bu), 26.52 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.54 (*t*-Bu), 18.51 (*t*-Bu), 18.0 (*t*-Bu), 17.4 (C-19), 16.3 (C-33), -1.3 (3C, TMS), -3.0 (Me), -3.1 (Me), -4.3 (Me), -4.4 (Me), -4.9 (Me), -5.1 (Me) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2928, 2896, 2857, 1733, 1679, 1641, 1596, 1499, 1472, 1463, 1407, 1381, 1361, 1348, 1286, 1252, 1175, 1151, 1088, 1045, 1006, 984, 934, 924, 859, 834, 813, 773, 731, 688, 675, 632, 542, 523, 508, 488, 481, 475, 466, 458, 432, 430, 423, 415 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{86}N_4O_{10}Si_4SNa^+$: 1045.5034, found: 1045.5041.

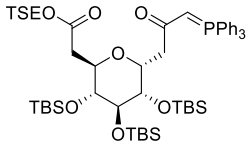
Analytical and spectral data of the byproduct **209**: **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.71 – 7.67 (m,



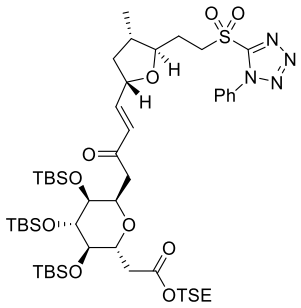
2H, Ph), 7.65 – 7.58 (m, 3H, Ph), 6.74 (dd, J = 15.8, 5.3 Hz, 1H, H-11), 6.23 (dd, J = 15.9, 1.5 Hz, 1H, H-10), 4.56 (dt, J = 10.0, 6.0 Hz, 1H, H-12), 4.35 – 4.31 (m, 1H, H-7), 4.28 – 4.23 (m, 1H, H-3), 4.18 – 4.10 (m, 2H, H-20), 4.00 – 3.91 (m, 2H, H-17a and H-5), 3.80 (ddd, J = 15.2, 10.9, 4.9 Hz, 1H, H-17b), 3.61 (td, J = 8.8, 3.0 Hz, 1H, H-15), 3.58 – 3.55 (m, 1H, H-4), 3.39 (d, J = 11.9 Hz, 1H, OH), 3.35 (dd, J = 11.9, 2.9 Hz, 1H, H-6), 2.93 (dd, J = 17.0, 6.5 Hz, 1H, H-8a), 2.88 (dd, J = 16.9, 6.6 Hz, 1H, H-8b), 2.56 (dd, J = 16.0, 7.1 Hz, 1H, H-2a), 2.44 (dd, J = 16.0, 6.7 Hz, 1H, H-2b), 2.35 (dt, J = 12.5, 6.5 Hz, 1H, H-13a), 2.30 (dddd, J = 18.8, 12.5, 5.7, 3.0 Hz, 1H, H-16a), 2.07 – 1.95 (m, 2H, H-16b and H-14), 1.46 – 1.38 (m, 1H, H-13b), 1.06 (d, J = 6.6 Hz, 3H, H-33), 0.99 – 0.96 (m, 2H, H-19), 0.94 (s, 9H, *t*-Bu), 0.92 (s, 9H, *t*-Bu), 0.15 (s, 3H, Me), 0.12 (s, 3H, Me), 0.11 (s, 3H, Me), 0.07 (s, 3H, Me), 0.04 (s, 9H, TMS) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 198.2 (C-9), 171.1 (C-1), 153.6 (C-18), 146.2 (C-11), 133.2 (*i*-Ph), 131.6 (*p*-Ph), 129.9 (2C, *m*-Ph), 128.8 (C-10), 125.3 (2C, *o*-Ph), 83.3 (C-15), 77.4 (C-12), 72.2 (C-3), 70.1 (C-7), 71.9 (C-4), 70.8 (C-6), 69.7 (C-5), 62.9 (C-20), 53.7 (C-17), 41.7 (C-8), 41.4 (C-13), 40.4 (C-14), 36.9 (C-2), 26.8 (C-16), 26.0 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.2 (*t*-Bu), 18.1 (*t*-

Bu), 17.5 (C-19), 16.3 (C-33), -1.3 (3C, TMS), -4.4 (Me), -4.67 (Me), -4.72 (Me), -5.1 (Me) ppm; **HRMS** (ESI): *m/z* calcd. for $C_{42}H_{72}N_4O_{10}Si_3SNa^+$: 931.4169, found: 931.4173.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((E)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxobut-3-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (E-181a)

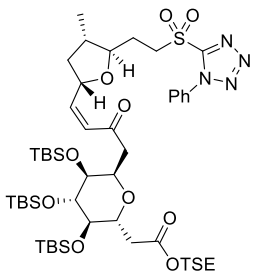


DIPEA (169 µL, 971 µmol) was added to a solution of the crude mixture of phosphonium salts **193a** and **194a** (456 mg, 442 µmol) in PhH (8.0 mL) at rt and the reaction mixture was stirred for 1 h resulting in the formation of a white precipitate. The afforded intermediate **182a** was used in the next step without purification or removal of the solvent.



A solution of aldehyde **130** (170 mg, 486 µmol) in PhH (2.0 mL, rinsed with 2.0 mL) was dried for 1 h over 4 Å MS before it was added to the crude phosphorus ylide **182a** (420 mg, 442 µmol) as a solution in PhH (8.0 mL) at rt and the reaction mixture was stirred for 16 h. The mixture was diluted with MTBE (50 mL) and the resulting mixture was washed with aq. phosphate buffer (200 mM, pH 7, 2 x 25 mL). The combined aq. phases were extracted with MTBE (2 x 25 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1 to 5:1) affording both the minor isomer *Z*-**181a** (20 mg, 4%) and the desired major isomer *E*-**181a** (322 mg, 71%) as a colourless oil. The analytical and spectroscopic data of the isolated major compound *E*-**181a** were identical with those shown above.

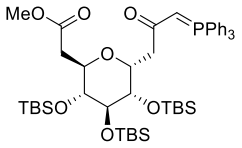
Analytical and spectral data of the minor isomer *Z*-**181a**: $[\alpha]_D^{20}$: +5.8 (c = 1.30, $CHCl_3$);



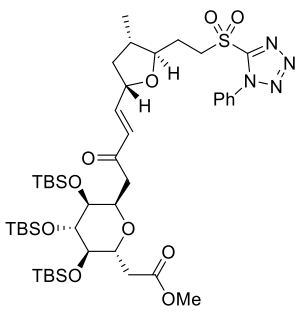
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.56 (m, 5H), 6.17 (dd, J = 11.5, 1.4 Hz, 1H), 6.05 (dd, J = 11.6, 7.0 Hz, 1H), 5.26 – 5.18 (m, 1H), 4.34 (ddd, J = 7.7, 5.0, 2.4 Hz, 1H), 4.29 (dt, J = 9.1, 5.2 Hz, 1H), 4.18 – 4.10 (m, 2H), 3.94 (ddd, J = 15.3, 10.7, 4.9 Hz, 1H), 3.82 – 3.77 (m, 1H), 3.79 (ddd, J = 15.3, 10.8, 5.1 Hz, 1H), 3.65 – 3.58 (m, 2H), 3.53 – 3.48 (m, 1H), 2.89 (dd, J = 16.6, 7.7 Hz, 1H), 2.80 (dd, J = 15.3, 5.7 Hz, 1H), 2.64 – 2.55 (m, 2H), 2.52 (dd, J = 16.7, 5.0 Hz, 1H), 2.27 (tdd, J = 10.8, 5.1, 3.0 Hz, 1H), 2.05 – 1.92 (m, 2H), 1.34 – 1.28 (m,

1H), 1.04 (d, J = 6.5 Hz, 3H), 0.99 – 0.94 (m, 2H), 0.92 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 6H), 0.07 (s, 3H), 0.03 (s, 9H), 0.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 199.1, 171.8, 153.7, 148.8, 133.2, 131.6, 129.9 (2C), 126.7, 125.3 (2C), 83.3, 76.1, 74.5, 73.9, 73.6, 71.6, 66.8, 62.7, 53.7, 45.4, 41.1, 40.0, 37.6, 26.6, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.4, 18.3, 18.0, 17.5, 16.4, -1.3 (3C), -3.4, -3.9, -4.1, -4.56, -4.58, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2928, 2898, 2856, 1731, 1691, 1619, 1498, 1472, 1463, 1408, 1389, 1346, 1251, 1153, 1084, 1038, 1005, 973, 938, 859, 832, 812, 774, 759, 688, 667, 628, 536, 507, 472, 441, 424 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{86}N_4O_{10}Si_4S_1Na^+$: 1045.5034, found: 1045.5038.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((E)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2-oxobut-3-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (E-181b)



DIPEA (140 µL, 804 µmol) was added to a solution of the crude mixture of phosphonium salts **193b** and **194b** (346 mg, 366 µmol) in PhH (8.0 mL) at rt and the reaction mixture was stirred for 1 h resulting in the formation of a white precipitate. The afforded intermediate **182b** was used in the next step without purification or removal of the solvent.

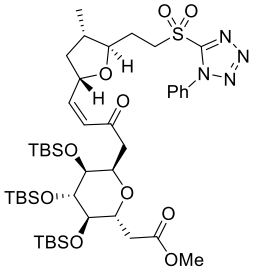


A solution of aldehyde **130** (141 mg, 402 µmol) in PhH (2.0 mL, rinsed with 1.0 mL) was dried for 1 h over 4 Å MS before it was added to the crude phosphorus ylide **182b** (316 mg, 366 µmol) as a solution in PhH (8.0 mL) at rt and the reaction mixture was stirred for 18 h. The mixture was diluted with MTBE (50 mL) and the resulting mixture was washed with aq. phosphate buffer (200 mM, pH 7, 2 x 25 mL). The combined aq. phases were extracted with MTBE (2 x 25 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:1 to 3:1) affording both the minor isomer *Z*-**181b** (14 mg, 4%) and the desired major isomer *E*-**181b** (256 mg, 75%) as a colourless oil.

Analytical and spectral data of the major isomer *E*-**181b**: **$[\alpha]_D^{20}$**: +3.3 (c = 0.95, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 6.71 (dd, J = 15.9, 5.3 Hz, 1H), 6.23 (dd, J = 15.9, 1.5 Hz, 1H), 4.57 (dddd, J = 9.5, 6.7, 5.2, 1.5 Hz, 1H), 4.39 (td, J = 6.5, 2.4 Hz, 1H), 4.28 (ddd, J = 9.3,

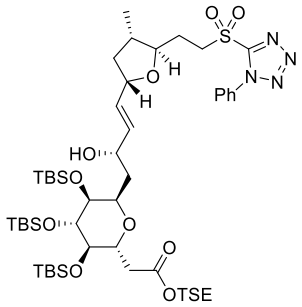
5.7, 3.8 Hz, 1H), 3.97 (ddd, J = 14.7, 11.1, 4.8 Hz, 1H), 3.82 – 3.79 (m, 1H), 3.81 (ddd, J = 14.8, 11.0, 5.1 Hz, 1H), 3.70 – 3.67 (m, 1H), 3.66 (s, 3H), 3.61 (td, J = 8.8, 2.5 Hz, 1H), 3.51 (ddd, J = 4.0, 1.8, 1.0 Hz, 1H), 2.94 (dd, J = 17.0, 6.6 Hz, 1H), 2.79 (dd, J = 15.2, 5.8 Hz, 1H), 2.73 (dd, J = 17.0, 6.3 Hz, 1H), 2.69 (dd, J = 15.2, 8.6 Hz, 1H), 2.41 – 2.25 (m, 2H), 2.10 – 1.93 (m, 2H), 1.42 (ddd, J = 12.4, 10.5, 9.4 Hz, 1H), 1.06 (d, J = 6.6 Hz, 3H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), -0.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 198.6, 172.1, 153.6, 146.2, 133.2, 131.6, 129.9 (2C), 128.6, 125.3 (2C), 83.3, 77.3, 74.3, 73.9, 73.73, 71.2, 66.2, 53.7, 51.7, 42.0, 41.3, 40.3, 37.2, 26.8, 26.3 (3C), 26.3 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 16.3, -3.4, -3.9, -4.2, -4.58, -4.60, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2955, 2929, 2894, 2857, 1737, 1673, 1632, 1596, 1498, 1472, 1463, 1437, 1407, 1389, 1344, 1258, 1216, 1153, 1124, 1083, 1043, 1005, 973, 938, 894, 866, 832, 812, 773, 752, 688, 667, 633, 536, 506, 467, 448, 436, 418 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{76}N_4O_{10}Si_3SNa^+$: 959.4482, found: 959.4487.

Analytical and spectral data of the minor isomer *Z*-**181b**: **$[\alpha]_D^{20}$**: +5.3 (c = 1.11, $CHCl_3$);



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 – 7.56 (m, 5H), 6.17 (dd, J = 11.5, 1.4 Hz, 1H), 6.06 (dd, J = 11.6, 7.0 Hz, 1H), 5.27 – 5.18 (m, 1H), 4.34 (ddd, J = 7.6, 4.6, 2.4 Hz, 1H), 4.28 (ddd, J = 9.4, 5.7, 3.9 Hz, 1H), 3.94 (ddd, J = 14.7, 10.8, 5.0 Hz, 1H), 3.81 – 3.78 (m, 1H), 3.80 (ddd, J = 14.6, 10.4, 5.2 Hz, 1H), 3.65 (s, 3H), 3.64 – 3.60 (m, 1H), 3.60 – 3.57 (m, 1H), 3.50 (ddd, J = 4.1, 1.7, 1.0 Hz, 1H), 2.90 (dd, J = 16.5, 8.0 Hz, 1H), 2.81 (dd, J = 15.2, 5.8 Hz, 1H), 2.66 (dd, J = 15.2, 8.6 Hz, 1H), 2.59 (dt, J = 12.9, 6.6 Hz, 1H), 2.48 (dd, J = 16.6, 4.7 Hz, 1H), 2.27 (tdd, J = 10.7, 5.2, 3.0 Hz, 1H), 2.06 – 1.92 (m, 2H), 1.29 (ddd, J = 12.5, 10.6, 9.5 Hz, 1H), 1.04 (d, J = 6.6 Hz, 3H), 0.92 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 199.1, 172.1, 153.7, 148.8, 133.2, 131.6, 129.9 (2C), 126.8, 125.3 (2C), 83.3, 76.1, 74.4, 73.74, 73.66, 71.6, 66.7, 53.7, 51.7, 45.4, 41.1, 40.0, 37.2, 26.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 16.4, -3.4, -3.9, -4.1, -4.57, -4.58, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2894, 2857, 1739, 1690, 1618, 1498, 1472, 1463, 1437, 1409, 1389, 1346, 1257, 1154, 1125, 1084, 1038, 1005, 971, 938, 889, 868, 833, 813, 774, 762, 688, 673, 630, 536, 508, 473, 466, 438, 429, 420 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{76}N_4O_{10}Si_3SNa^+$: 959.4482, found: 959.4487.

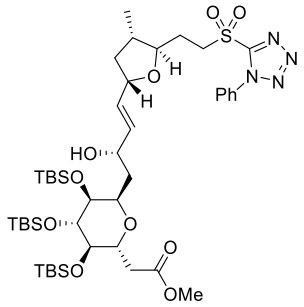
2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S,E)-2-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-3-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (180a)



(*R*)-(*+*)-2-Methyl-CBS-oxazaborolidine ((*R*)-**47a**) (68 mg, 246 µmol) was added to a stirred solution of α,β-unsaturated ketone *E*-**181a** (240 mg, 235 µmol) in THF (3.8 mL) at -20 °C and the reaction mixture was stirred for 30 min. Then $BH_3{\cdot}SMe_2$ (31.4 µL, 352 µmol) was added to the reaction mixture and stirring was continued for 2 h 40 min at -20 °C. The reaction was quenched with aq. NaH_2PO_4 (1.0 M, 20 mL) at 0 °C and the aq. phase was extracted with EtOAc (3 x 20 mL). The combined extracts were washed with aq. phosphate buffer (200 mM, pH 7, 2 x 10 mL) and the aq. phase was extracted with EtOAc (10 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (fine SiO_2, hexane/EtOAc, 10:1 to 4:1) affording compound **180a** as a colourless oil (232 mg, 97%).

$[\alpha]_D^{20}$: +8.6 (c = 1.09, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.73 – 7.54 (m, 5H), 5.72 – 5.63 (m, 2H), 4.42 – 4.28 (m, 3H), 4.23 – 4.15 (m, 2H), 4.04 (dt, J = 10.7, 2.3 Hz, 1H), 3.94 (ddd, J = 14.8, 11.0, 4.9 Hz, 1H), 3.78 – 3.75 (m, 1H), 3.77 (ddd, J = 14.7, 10.8, 5.0 Hz, 1H), 3.57 (td, J = 8.7, 3.0 Hz, 1H), 3.49 (ddd, J = 4.1, 1.8, 0.9 Hz, 1H), 3.46 – 3.43 (m, 1H), 3.30 (s, 1H), 2.72 (dd, J = 15.1, 8.9 Hz, 1H), 2.66 (dd, J = 15.1, 5.3 Hz, 1H), 2.37 – 2.16 (m, 2H), 2.08 – 1.98 (m, 2H), 1.97 – 1.84 (m, 1H), 1.44 – 1.84 (m, 2H), 1.04 (d, J = 6.5 Hz, 3H), 1.01 – 0.95 (m, 2H), 0.92 (s, 9H), 0.89 (s, 18H), 0.11 (s, 3H), 0.095 (s, 6H), 0.09 (s, 3H), 0.08 (s, 3H), 0.06 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 153.6, 134.1, 133.2, 131.6, 130.9, 129.8 (2C), 125.4 (2C), 82.9, 78.8, 74.2, 73.8 (2C), 72.4, 71.6, 70.0, 63.1, 53.9, 42.0, 40.3, 38.6, 37.7, 26.9, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 17.4, 16.5, -1.3 (3C), -3.5, -3.9, -4.2, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3501, 2954, 2928, 2896, 2857, 1731, 1596, 1499, 1472, 1463, 1408, 1389, 1360, 1345, 1251, 1151, 1125, 1086, 1040, 1006, 973, 938, 916, 859, 833, 813, 774, 689, 673, 634, 506, 464, 427 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{88}N_4O_{10}Si_4S_1Na^+$: 1047.5191, found: 1047.5196.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((S,E)-2-hydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)but-3-en-1-yl)tetrahydro-2H-pyran-2-yl)acetate (180b)

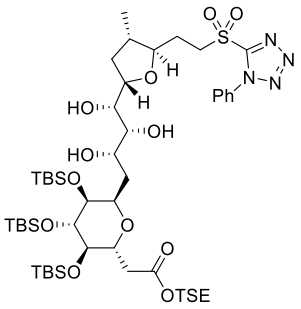


(*R*)-(+)-2-Methyl-CBS-oxazaborolidine ((*R*)-**47a**) (68 mg, 0.25 mmol) was added to a stirred solution of α,β-unsaturated ketone *E*-**181b** (220 mg, 235 µmol) in THF (3.8 mL) at -20 °C and the reaction mixture was stirred for 20 min. Then $BH_3 \cdot SMe_2$ (31.5 µL, 352 µmol) was added to the reaction mixture and stirring was continued for 1.5 h at -20 °C. The reaction was quenched with aq. NaH_2PO_4 (1.0 M, 20 mL) at 0 °C and the aq. phase was extracted with EtOAc (3 x 20 mL). The combined extracts were washed with aq. phosphate buffer (200 mM, pH 7, 2 x 10 mL) and the aq. phase was extracted with EtOAc (10 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 4:1 to 2:1) affording compound **180b** as a colourless oil (200 mg, 91%).

$[\alpha]_D^{20}$: +6.2 (c = 1.03, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.73 – 7.56 (m, 5H), 5.73 – 5.62 (m, 2H), 4.42 – 4.27 (m, 3H), 4.04 (dt, J = 10.7, 2.2 Hz, 1H), 3.94 (ddd, J = 14.8, 10.9, 4.9 Hz, 1H), 3.78 – 3.76 (m, 1H), 3.77 (ddd, J = 14.7, 10.7, 5.0 Hz, 1H), 3.70 (s, 3H), 3.57 (td, J = 8.7, 3.0 Hz, 1H), 3.49 (ddd, J = 3.9, 1.9, 1.0 Hz, 1H), 3.46 – 3.42 (m, 1H), 3.24 (d, J = 1.7 Hz, 1H), 2.78 (dd, J = 15.0, 9.6 Hz, 1H), 2.67 (dd, J = 15.0, 5.0 Hz, 1H), 2.31 – 2.18 (m, 2H), 2.08 – 1.88 (m, 3H), 1.44 – 1.32 (m, 2H), 1.05 (d, J = 6.6 Hz, 3H), 0.92 (s, 9H), 0.90 (s, 18H), 0.11 (s, 3H), 0.09 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 153.7, 134.0, 133.2, 131.6, 131.0, 129.9 (2C), 125.4 (2C), 82.9, 78.8, 74.1, 74.0, 73.6, 72.4, 71.6, 69.8, 53.9, 52.0, 42.0, 40.3, 38.6, 37.3, 26.9, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 16.5, -3.5, -3.9, -4.2, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3502, 2953, 2929, 2887, 2857, 1738, 1596, 1498, 1472, 1463, 1437, 1389, 1345, 1253, 1150, 1127, 1083, 1006, 972, 939, 916, 833, 813, 774, 761, 688, 668, 633, 506, 466, 424 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{78}N_4O_{10}Si_3SNa^+$: 961.4639, found: 961.4645.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4S)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (150b)

Representative Procedure A (Sharpless Dihydroxylation)



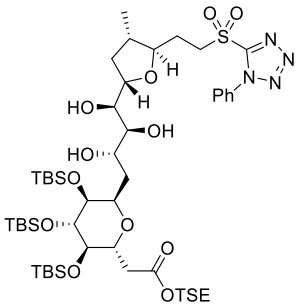
Aq. $Me_SO_2NH_2$ (0.1 M, 39.0 µL, 3.90 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 11.7 µmol), K_2CO_3 (0.3 M, 11.7 µmol) and aq. $K_2OsO_2(OH)_4$ (0.05 M, 20 mol%, 7.8 µL, 390 nmol) were subsequently added to a stirred solution of allylic alcohol **180a** (2 mg, 2 µmol) and L* (25 mol%, 0.5 mg, 488 nmol) in *t*-BuOH (125 µL) and water (70 µL) at rt, and stirring was continued for 23 h.

Herein, L* corresponds to: $(DHQ)_2R$ and $(DHQD)_2R$ with R = AQN, PHAL and PYR. HPLC analyses to determine the *d.r.* were carried out on each of the six reactions (Chapter 6.3.3), the work-up and purificiation was conducted with the mixture of all six reaction setups as following:

The mixture was filtered through a pad of SiO_2 which was washed with EtOAc (5 mL). After removal of the solvent, the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 2:1) affording both the *syn*,*anti*-isomer **196a** (6 mg, 48%) and the desired *all-syn*-isomer **150b** (6 mg, 48%) as a colourless oil.

Analytical and spectral data of the major *all-syn*-isomer **150b**: $[\alpha]_D^{20}$: +9.2 (c = 0.78, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.57 (m, 5H), 4.32 (dt, J = 9.5, 4.2 Hz, 1H), 4.22 – 4.14 (m, 3H), 4.13 – 4.08 (m, 1H), 4.01 – 3.96 (m, 1H), 3.95 – 3.89 (m, 1H), 3.88 (s, 1H), 3.87 – 3.79 (m, 1H), 3.79 – 3.75 (m, 1H), 3.67 – 3.61 (m, 1H), 3.59 (td, J = 8.4, 2.9 Hz, 1H), 3.50 – 3.46 (m, 2H), 3.46 – 3.42 (m, 1H), 3.25 (d, J = 3.4 Hz, 1H), 3.04 (d, J = 6.4 Hz, 1H), 2.77 (dd, J = 15.0, 10.0 Hz, 1H), 2.61 (dd, J = 15.1, 4.4 Hz, 1H), 2.37 – 2.25 (m, 1H), 2.24 – 2.11 (m, 2H), 2.07 – 1.99 (m, 1H), 1.98 – 1.87 (m, 1H), 1.61 – 1.52 (m, 1H), 1.41 (dt, J = 14.7, 2.6 Hz, 1H), 1.06 (d, J = 6.5 Hz, 3H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.89 (s, 18H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 6H), 0.08 (s, 6H), 0.03 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.1, 80.2, 74.8, 74.1, 73.9, 73.8, 73.7, 73.4, 72.4, 69.8, 63.2, 53.6, 39.8, 37.5, 37.1, 34.5, 26.4, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 17.4, 16.1, -1.3 (3C), -3.6, -3.9, -4.1, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3488, 2954, 2928, 2897, 2857, 1731, 1596, 1498, 1472, 1463, 1389, 1344, 1251, 1149, 1129, 1085, 1041, 1006, 979, 917, 859, 834, 813, 775, 688, 670, 635, 507, 472, 420 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{90}N_4O_{12}Si_4SNa^+$: 1081.5245, found: 1081.5255.

Analytical and spectral data of the minor *syn*,*anti*-isomer **196a**: $[\alpha]_D^{20}$: +6.3 (c = 0.71, $CHCl_3$);

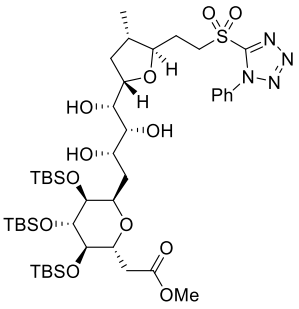


^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.73 – 7.53 (m, 5H), 4.33 (dt, J = 9.4, 4.1 Hz, 1H), 4.21 – 4.04 (m, 5H), 4.04 (dd, J = 9.7, 5.2 Hz, 1H), 3.90 (ddd, J = 15.7, 10.9, 4.9 Hz, 1H), 3.79 (ddd, J = 15.7, 10.7, 5.0 Hz, 1H), 3.79 – 3.76 (m, 1H), 3.71 (t, J = 5.8 Hz, 1H), 3.57 – 3.50 (m, 2H), 3.50 – 3.45 (m, 2H), 3.36 (d, J = 4.5 Hz, 1H), 2.94 (d, J = 8.5 Hz, 1H), 2.80 (dd, J = 15.3 Hz, 1H), 2.61 (dd, J = 15.2, 4.2 Hz, 1H), 2.34 – 2.28 (m, 1H), 2.28 – 2.21 (m, 1H), 2.09 – 1.98 (m, 2H), 1.98 – 1.89 (m, 1H), 1.66 – 1.57 (m, 1H), 1.53 – 1.49 (m, 1H), 1.06 (d, J = 6.5 Hz, 3H), 1.01 – 0.96 (m, 2H), 0.94 (s, 9H), 0.90 (s, 18H), 0.11 (s, 3H), 0.105 (s, 3H), 0.10 (s, 6H), 0.09 (s, 3H), 0.08 (s, 3H), 0.03 (s, 9H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.8, 153.6, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.2, 78.8, 75.5, 74.01, 73.95, 73.9, 73.7, 73.2, 72.4, 70.9, 63.2, 53.6, 39.9, 38.7, 37.4, 34.9, 26.6, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.4, 18.0, 17.4, 16.5, -1.3 (3C), -3.6, -3.9, -4.1, -4.5, -4.6, -4.8 ppm; **IR** (film): $\tilde{\nu}$ = 3339, 2954, 2928, 2896, 2856, 1731, 1631, 1596, 1499, 1472, 1463, 1389, 1345, 1251, 1148, 1130, 1089, 1042, 1006, 977, 920, 857, 834, 812, 775, 689, 673, 632, 512, 471, 413 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{48}H_{90}N_4O_{12}Si_4SNa^+$: 1081.5245, found: 1081.5258.

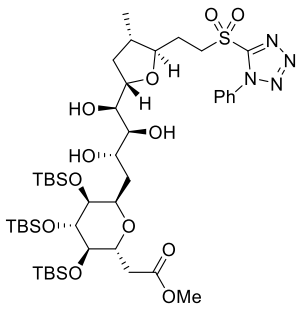
Procedure B (large scale)

Aq. $Me_5O_2NH_2$ (0.1 M, 488 µL, 48.8 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 146 µmol) and K_2CO_3 (0.3 M, 146 µmol) and aq. $K_2OsO_2(OH)_4$ (0.05 M, 20 mol%, 4.87 µmol, 97.5 µL) were subsequently added to a stirred solution of allylic alcohol **180a** (25 mg, 24 µmol) and $(DHQD)_2AQN$ (25 mol%, 6 mg, 6 µmol) in *t*-BuOH (1.54 mL) and water (954 µL) at rt and the reaction mixture was stirred for 18 h. The reaction mixture was filtered through a plug of SiO_2, and the mixture washed with EtOAc (10 mL). Then a solution of $NaHSO_3$ (30 mg, 0.29 mmol) in water (10 mL) was added. The aq. phase was extracted with EtOAc (10 x 10 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 5:1 to 2:1) affording both the minor *syn,anti*-isomer **196a** (3 mg, 10%) and the desired major *all-syn*-isomer **150b** (18 mg, 68%) as a colourless oil each. The analytical and spectroscopic data of the isolated compounds **196a** and **150b** were identical with those shown above.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4S)-2,3,4-trihydroxy-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)butyl)tetrahydro-2H-pyran-2-yl)acetate (150a)

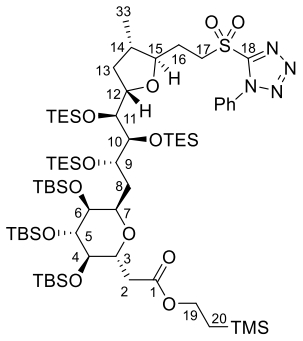


Aq. $MeSO_2NH_2$ (0.1 M, 639 µL, 64 µmol), $K_3[Fe(CN)_6]$ (0.3 M, 192 µmol) and K_2CO_3 (0.3 M, 192 µmol) and aq. $K_2OsO_2(OH)_4$ (0.05 M, 20 mol%, 6.4 µmol, 128 µL) were subsequently added to a stirred solution of allylic alcohol **180b** (30 mg, 32 µmol) and $(DHQD)_2AQN$ (0.05 M in *t*-BuOH, 160 µL, 8 µmol) in *t*-BuOH (1.85 mL) and water (1.27 mL) at rt, and the reaction mixture was stirred for 21 h. The reaction mixture was diluted with EtOAc (2.5 mL) and water (2.5 mL) and the reaction was quenched with aq. $NaHSO_3$ (2.5 M, 153 µL). The aq. phase was extracted with EtOAc (8 x 2.5 mL), and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 3:1 to 1:1) to give both the minor *syn*,*anti*-isomer **196b** (4 mg, 11%) and the desired major *all-syn*-isomer **150a** (15 mg, 48%) as a colourless oil. The analytical and spectroscopic data of the major compound **150a** were identical with those shown above.

Analytical and spectral data of the minor *syn,anti*-isomer **196b** (the sample contained traces of $(DHQD)_2AQN$): 

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 – 7.54 (m, 5H), 4.34 (dt, J = 9.7, 4.1 Hz, 1H), 4.21 – 4.09 (m, 2H), 4.08 – 3.97 (m, 2H), 3.96 – 3.85 (m, 1H), 3.83 – 3.74 (m, 2H), 3.72 – 3.68 (m, 1H), 3.69 (s, 3H), 3.62 (s, 1H), 3.59 – 3.51 (m, 2H), 3.50 – 3.44 (m, 3H), 2.88 (dd, J = 15.0, 10.2, 4.8 Hz, 1H), 3.63 (dd, J = 15.0, 4.3 Hz, 1H), 2.40 – 2.13 (m, 3H), 2.07 – 1.84 (m, 2H), 1.63 – 1.49 (m, 1H), 1.47 – 1.36 (m, 1H), 1.07 (d, J = 6.5 Hz, 3H), 0.93 (s, 9H), 0.89 (s, 18H), 0.11 (s, 3H), 0.105 (s, 3H), 0.095 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.075 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.0, 153.7, 133.2, 131.6, 129.9 (2C), 125.3 (2C), 83.2, 78.9, 75.3, 74.2 (2C), 73.9, 73.5, 73.2, 72.2, 70.4, 53.9, 52.0, 39.9, 38.4, 37.1, 34.8, 26.3 (3C), 26.2 (3C), 25.93, 25.90 (3C), 18.5, 18.4, 18.0, 16.5, -3.6, -3.9, -4.1, -4.5, -4.56, -4.59 ppm; **IR** (film): $\tilde{\nu}$ = 3433, 2953, 2929, 2894, 2857, 1736, 1598, 1501, 1462, 1438, 1388, 1345, 1256, 1149, 1128, 1083, 1043, 1006, 964, 938, 917, 833, 813, 775, 737, 689, 673, 634, 567, 536, 506, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{44}H_{80}N_4O_{12}Si_3SNa^+$: 995.4694, found: 995.4700.

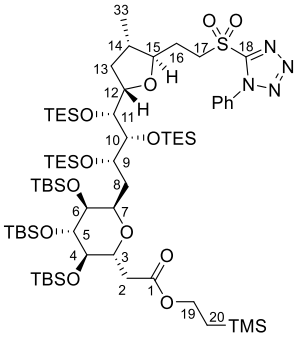
2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6S)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4S)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2,3,4-tris((triethylsilyl)oxy)butyl)tetrahydro-2H-pyran-2-yl)acetate (197)



TESOTf (4.8 µL, 21 µmol) was added to a stirred solution of triol **196a** (5 mg, 5 µmol) and 2,6-lutidine (3.3 µL, 28 µmol) in DCM (160 µL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 2 h. The reaction was diluted with EtOAc (3.0 mL) and the reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 3.0 mL). The organic extract was washed with brine (3.0 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 30:1) affording compound **197** as a colourless oil (5 mg, 76%).

$[\alpha]_D^{20}$: +3.2 (c = 0.50, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.68 (m, 2H, Ph), 7.64 – 7.57 (m, 3H, Ph), 4.24 – 4.20 (m, 2H, H-12 and H-3), 4.13 – 4.09 (m, 2H, H-19), 3.91 (ddd, J = 15.0, 11.5, 4.7 Hz, 1H, H-17a), 3.88 – 3.84 (m, 1H, H-9), 3.83 – 3.75 (m, 3H, H-17b and H-11 and H-5), 3.70 (t, J = 6.6 Hz, 1H, H-7), 3.57 – 3.55 (m, 1H, H-4), 3.51 – 3.48 (m, 1H, H-10), 3.49 (td, J = 9.3, 8.6, 2.8 Hz, 1H, H-15), 3.35 – 3.33 (m, 1H, H-6), 2.98 (dd, J = 15.2, 7.7 Hz, 1H, H-2a), 2.47 (dd, J = 15.2, 6.0 Hz, 1H, H-2b), 2.23 – 2.17 (m, 1H, H-16a), 2.00 – 1.90 (m, 3H, H-16b and H-14 and H-13a), 1.83 (dd, J = 8.3, 4.1 Hz, 2H, H-8), 1.76 (d, J = 10.3 Hz, 1H, 13b), 1.03 (d, J = 6.0 Hz, 3H, H-33), 0.98 (s, 3H, Me), 0.96 (s, 6H, Me), 0.95 (s, 6H, Me), 0.945 (s, 3H, Me), 0.93 (s, 6H, Me), 0.92 (s, 3H, Me), 0.915 (s, 9H, *t*-Bu), 0.89 (s, 18H, *t*-Bu), 0.68 – 0.56 (m, 18H, CH_2), 0.09 (s, 3H, Si-Me), 0.085 (s, 3H, Si-Me), 0.08 (s, 3H, Si-Me), 0.07 (s, 6H, Si-Me), 0.05 (s, 3H, Si-Me), 0.01 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8 (C-1), 153.7 (C-18), 133.3 (*i*-Ph), 131.5 (*p*-Ph), 129.8 (2C, *m*-Ph), 125.3 (2C, *o*-Ph), 82.7 (C-15), 79.5 (C-12), 77.6 (C-10), 74.8 (C-11), 74.4 (C-5), 73.8 (C-3), 72.5 (C-6), 72.2 (C-4), 71.7 (C-9), 66.3 (C-7), 62.6 (C-19), 53.9 (C-17), 40.1 (C-14), 37.2 (C-2), 36.0 (C-8), 34.2 (C-13), 26.9 (C-16), 26.3 (3C, *t*-Bu), 26.2 (3C, *t*-Bu), 26.0 (3C, *t*-Bu), 18.4 (*t*-Bu), 18.3 (*t*-Bu), 18.1 (*t*-Bu), 17.5 (C-20), 16.5 (C-33), 7.4 (3C, Me), 7.23 (3C, Me), 7.15 (3C, Me), 5.5 (3C, CH_2), 5.2 (3C, CH_2), 5.0 (3C, CH_2), -1.4 (3C, TMS), -3.4 (Si-Me), -3.7 (Si-Me), -4.3 (Si-Me), -4.6 (Si-Me), -4.8 (Si-Me), -4.9 (Si-Me) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2928, 2877, 2857, 1733, 1661, 1634, 1499, 1463, 1416, 1379, 1344, 1251, 1154, 1082, 1044, 1005, 976, 940, 834, 813, 775, 761, 742, 739, 687, 670, 666, 635, 610, 535, 507, 468 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{66}H_{132}N_4O_{12}Si_7SNa^+$: 1423.7840, found: 1423.7858.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4R)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2,3,4-tris((triethylsilyl)oxy)butyl)tetrahydro-2H-pyran-2-yl)acetate (127a)

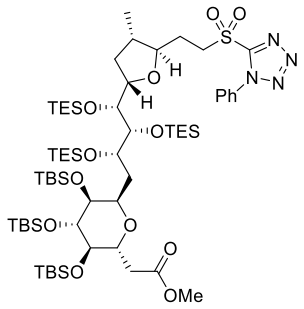


TESOTf (346 µL, 1.53 mmol) was added to a stirred solution of triol **150b** (360 mg, 340 µmol) and 2,6-lutidine (237 µL, 2.04 mmol) in DCM (13 mL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 2 h. The reaction was diluted with MTBE (25 mL) and the reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 25 mL). The organic extract was washed with water (10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1) affording compound **127a** as a colourless oil (376 mg, 79%).

$[\alpha]_D^{20}$: +12.5 (c = 1.10, $CHCl_3$); **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 7.71 – 7.68 (m, 2H, Ph), 7.64 – 7.58 (m, 3H, Ph), 4.20 – 4.15 (m, 2H, H-9 and H-3), 4.14 – 4.10 (m, 2H, H-19), 4.06 (ddd, J = 9.9, 8.0, 5.6 Hz, 1H, H-12), 3.94 (ddd, J = 14.5, 11.7, 4.7 Hz, 1H, H-17a), 3.83 – 3.76 (m, 3H, H-17b and H-7 and H-5), 3.69 – 3.61 (m, 2H, H-10 and H-11), 3.60 – 3.58 (m, 1H, H-4), 3.45 (td, J = 8.5, 3.1 Hz, 1H, H-15), 3.36 – 3.33 (m, 1H, H-6), 3.25 (dd, J = 15.5, 9.9 Hz, 1H, H-2a), 2.38 (dd, J = 15.4, 3.8 Hz, 1H, H-2b), 2.25 (dddd, J = 13.5, 11.8, 4.5, 3.2 Hz, 1H, H-16a), 2.21 (dd, J = 12.4, 6.2 Hz, 1H, H-13a), 1.99 (dddd, J = 13.2, 11.4, 8.2, 4.8 Hz, 1H, H-16b), 1.92 (dd, J = 14.9, 10.8 Hz, 1H, H-8a), 1.83 (ddt, J = 11.2, 8.9, 6.5 Hz, 1H, H-14), 1.51 (dd, J = 14.4, 8.6 Hz, 1H, H-8b), 1.39 (dt, J = 12.8, 11.1 Hz, 1H, H-13b), 1.02 (d, J = 6.5 Hz, 3H, H-33), 0.99 (s, 3H, Me), 0.98 (s, 3H, Me), 0.97 (s, 3H, Me), 0.96 (s, 3H, Me), 0.95 (s, 3H, Me), 0.945 (s, 6H, Me), 0.935 (s, 6H, Me), 0.93 (s, 9H, *t*-Bu), 0.92 (s, 3H, Me), 0.895 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.66 – 0.55 (m, 18H, CH_2), 0.105 (s, 3H, Si-Me), 0.10 (s, 3H, Si-Me), 0.09 (s, 3H, Si-Me), 0.075 (s, 3H, Si-Me), 0.07 (s, 3H, Si-Me), 0.06 (s, 3H, Si-Me), 0.03 (s, 9H, TMS) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.9 (C-1), 153.7 (C-18), 133.3 (*i*-Ph), 131.6 (*p*-Ph), 129.8 (2C, *m*-Ph), 125.3 (2C, *o*-Ph), 81.9 (C-15), 81.1 (C-12), 77.0 (C-11), 75.4 (C-10), 74.4 (C-5), 73.8 (C-3), 73.1 (C-6), 71.6 (C-4), 70.0 (C-9), 65.3 (C-7), 62.6 (C-19), 53.9 (C-17), 40.0 (C-14), 37.9 (C-13), 37.2 (C-2), 36.2 (C-8), 26.4 (C-16), 26.33 (3C, *t*-Bu), 26.30 (3C, *t*-Bu), 25.9 (3C, *t*-Bu), 18.39 (*t*-Bu), 18.36 (*t*-Bu), 18.0 (*t*-Bu), 17.5 (C-20), 16.4 (C-33), 7.29 (3C, Me), 7.25 (3C, Me), 7.2 (3C, Me), 5.68 (3C, CH_2), 5.66 (3C, CH_2), 5.5 (3C, CH_2), -1.4 (3C, TMS), -3.3 (Si-Me), -3.6 (Si-Me), -4.4 (Si-Me), -4.6 (Si-Me), -4.7 (Si-Me), -4.8 (Si-Me) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2930, 2877, 2858, 1732, 1597, 1500, 1463, 1414, 1389,

1363, 1346, 1251, 1150, 1115, 1088, 1043, 1005, 974, 918, 900, 861, 834, 813, 775, 761, 740, 730, 687, 673, 634, 532, 507, 465, 443, 430, 407 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{66}H_{132}N_4O_{12}Si_7SNa^+$: 1423.7840, found: 1423.7849.

Methyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-((2S,3R,4R)-4-((2S,4S,5R)-4-methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-2,3,4-tris((triethylsilyl)oxy)butyl)tetrahydro-2H-pyran-2-yl)acetate (127b)

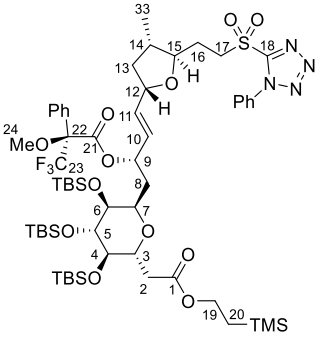


TESOTf (293 µL, 1.29 mmol) was added to a stirred solution of triol **150a** (280 mg, 288 µmol) and 2,6-lutidine (201 µL, 1.73 mmol) in DCM (11 mL) at 0 °C. The reaction mixture was allowed to reach rt and stirring was continued for 1 h. The reaction was diluted with MTBE (25 mL) and the reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 25 mL). The organic extract was washed with water (10 mL) and brine (10 mL), and dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 30:1) affording compound **127b** as a colourless oil (310 mg, 82%).

$[\alpha]_D^{20}$: +24.3 (c = 0.98, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.74 – 7.67 (m, 2H), 7.65 – 7.57 (m, 3H), 4.22 – 4.13 (m, 2H), 4.06 (ddd, J = 9.8, 7.8, 5.5 Hz, 1H), 3.95 (ddd, J = 14.5, 11.6, 4.8 Hz, 1H), 3.85 – 3.74 (m, 3H), 3.68 – 3.63 (m, 1H), 3.65 (s, 3H), 3.63 – 3.60 (m, 1H), 3.60 – 3.57 (m, 1H), 3.45 (td, J = 8.5, 3.1 Hz, 1H), 3.38 – 3.34 (m, 1H), 3.23 (dd, J = 15.4, 9.5 Hz, 1H), 2.41 (dd, J = 15.4, 4.1 Hz, 1H), 2.31 – 2.16 (m, 2H), 2.05 – 1.96 (m, 1H), 1.92 (ddd, J = 14.8, 10.7, 1.8 Hz, 1H), 1.83 (ddt, J = 11.1, 8.7, 6.5 Hz, 1H), 1.51 (dd, J = 14.5, 8.4 Hz, 1H), 1.45 – 1.33 (m, 1H), 1.02 (d, J = 6.4 Hz, 3H), 0.99 (s, 3H), 0.97 (s, 6H), 0.955 (s, 3H), 0.95 (s, 6H), 0.935 (s, 6H), 0.93 (s, 9H), 0.91 (s, 3H), 0.895 (s, 9H), 0.89 (s, 9H), 0.67 – 0.54 (m, 18H), 0.10 (s, 6H), 0.09 (s, 3H), 0.07 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 172.2, 153.7, 133.3, 131.6, 129.8 (2C), 125.3 (2C), 81.9, 81.1, 77.0, 75.4, 74.5, 73.6, 73.1, 71.8, 69.8, 65.5, 53.9, 51.5, 40.0, 38.0, 36.9, 36.2, 26.5, 26.30 (3C), 26.27 (3C), 25.8 (3C), 18.36, 18.35, 18.0, 16.3, 7.3 (3C), 7.2 (6C), 5.7 (6C), 5.5 (3C), -3.3, -3.6, -4.3, -4.6, -4.8 (2C) ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2931, 2910, 2877, 2858, 1740, 1597, 1499, 1462, 1437, 1414, 1389, 1345, 1252, 1149, 1126, 1078, 1044, 1005, 972, 919, 899, 872, 833, 813, 774, 760, 738, 726, 687, 673, 636, 536, 507, 465, 434 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{62}H_{122}N_4O_{12}Si_6SNa^+$: 1337.7288, found: 1337.7290.

5.2.3.3. Stereochemical Proof

(S,E)-4-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-1-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (198a)



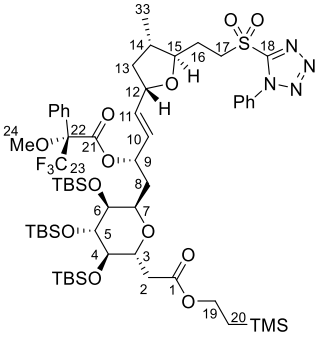
(*R*)-Mosher acid chloride (3.3 µL, 18 µmol) was added to a stirred solution of allylic alcohol **180a** (6 mg, 6 µmol) and py (2.4 µL, 30 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 1 h. Then py (2.4 µL, 30 µmol) and (*R*)-Mosher acid chloride (3.3 µL, 18 µmol) were subsequently added to the reaction mixture and stirring was continued for 5 h. Afterwards py (2.4 µL, 30 µmol) and (*R*)-Mosher acid chloride (3.3 µL, 18 µmol) were again subsequently added to the reaction mixture and stirring was continued for 18 h. The reaction was quenched with water (2.0 mL) and the aq. phase was extracted with MTBE (3 x 3.0 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **198a** as a colourless oil (7 mg, 96%).[309]

$[\alpha]_D^{20}$: +3.9 (c = 0.71, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.50 (m, 7H, Ph), 7.41 – 7.33 (m, 3H, Ph), 5.89 (dd, J = 14.6, 6.1 Hz, 1H, H-11), 5.67 (ddd, J = 15.2, 8.0, 1.1 Hz, 1H, H-10), 5.65 – 5.59 (m, 1H, H-9), 4.39 (dt, J = 9.2, 6.1 Hz, 1H, H-12), 4.32 (ddd, J = 8.8, 5.7, 3.6 Hz, 1H, H-3), 4.23 – 4.16 (m, 2H, H-19), 3.93 (ddd, J = 14.7, 11.2, 4.6 Hz, 1H, H-17a), 3.83 – 3.73 (m, 3H, H-17b and H-5 and H-7), 3.55 (td, J = 8.6, 3.0 Hz, 1H, H-15), 3.52 – 3.48 (m, 1H, H-4), 3.50 (s, 3H, H-24), 3.40 (t, J = 2.5 Hz, 1H, H-6), 2.76 (dd, J = 15.0, 5.9 Hz, 1H, H-2a), 2.51 (dd, J = 15.0, 8.3 Hz, 1H, H-2b), 2.32 – 2.16 (m, 3H, H-16a and H-8a and H-13a), 2.06 – 1.89 (m, 2H, H-16b and H-14), 1.47 (ddd, J = 13.5, 9.7, 2.2 Hz, 1H, H-8b), 1.36 (ddd, J = 12.3, 10.7, 9.4 Hz, 1H, H-13b), 1.03 (d, J = 6.6 Hz, 3H, H-33), 1.02 – 0.97 (m, 2H, H-20), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.86 (s, 9H, *t*-Bu), 0.09 (s, 6H, Si-Me), 0.08 (s, 6H, Si-Me), 0.06 (s, 3H, Si-Me), 0.03 (s, 9H, TMS), 0.01 (s, 3H, Si-Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 165.2, 153.6, 137.3, 133.2, 132.6, 131.6, 129.9 (2C), 129.6, 128.5 (2C), 127.7 (2C), 126.9, 125.3 (2C), 123.5 (q, $J_{13C,19F}$ = 290 Hz), 84.4, 83.0, 78.2, 74.9, 74.2, 73.9, 73.6, 72.3, 65.8, 62.9, 55.4, 53.8, 42.1, 40.2, 37.8, 36.4, 26.8, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 17.5, 16.5, -1.4 (3C), -3.5, -4.0, -4.3, -4.5 (2C), -5.0 ppm; **^{19}F NMR** (282 MHz,

[309] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.5.

$CDCl_3$): δ = -71.6 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2857, 1733, 1596, 1498, 1472, 1463, 1408, 1390, 1361, 1345, 1251, 1217, 1169, 1156, 1121, 1081, 1038, 1024, 1006, 993, 973, 938, 917, 901, 881, 859, 833, 812, 773, 757, 720, 695, 688, 666, 669, 635, 537, 525, 506 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{58}H_{95}N_4O_{12}F_3Si_4S_1Na^+$: 1263.5589, found: 1263.5597.

(S,E)-4-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-1-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-oxo-2-(2-(trimethylsilyl)ethoxy)ethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-198a)



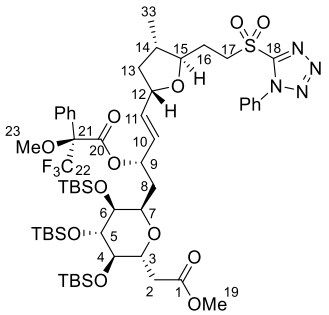
(*S*)-Mosher acid chloride (3.3 µL, 18 µmol) was added to a stirred solution of allylic alcohol **180a** (6 mg, 6 µmol) and py (2.4 µL, 29 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 1 h. Then py (2.4 µL, 29 µmol) and (*S*)-Mosher acid chloride (3.3 µL, 18 µmol) were subsequently added to the reaction mixture and stirring was continued for 5 h. Afterwards py (2.4 µL, 29 µmol) and (*S*)-Mosher acid chloride (3.3 µL, 18 µmol) were again subsequently added to the reaction mixture and stirring was continued for 15 h. Then py (2.4 µL, 29 µmol) and (*S*)-Mosher acid chloride (33 µL, 18 µmol) were again subsequently added to the reaction mixture and stirring was continued for 3 h. The reaction was quenched with water (2.0 mL) and the aq. phase was extracted with MTBE (3 x 3.0 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound *epi*-**198a** as a colourless oil (7 mg, 96%).[310]

$[\alpha]_D^{20}$: +30.0 (c = 0.68, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.71 – 7.50 (m, 7H, Ph), 7.45 – 7.33 (m, 3H, Ph), 5.77 (dd, J = 15.2, 6.1 Hz, 1H, H-11), 5.62 (ddd, J = 9.7, 7.7, 4.4 Hz, 1H, H-9), 5.54 (ddd, J = 15.2, 7.6, 1.2 Hz, 1H, H-10), 4.38 – 4.29 (m, 2H, H-12 and H-3), 4.22 – 4.15 (m, 2H, H-19), 3.91 (ddd, J = 14.7, 11.3, 4.7 Hz, 1H, H-17a), 3.80 (dt, J = 10.8, 2.4 Hz, 1H, H-5), 3.79 – 3.75 (m, 1H, H-7), 3.74 (ddd, J = 14.6, 11.1, 4.9 Hz, 1H, H-17b), 3.57 (s, 3H, H-24), 3.52 – 3.47 (m, 2H, H-15 and H-4), 3.42 (t, J = 2.5 Hz, 1H, H-6), 2.74 (dd, J = 15.1, 5.8 Hz, 1H, H-2a), 2.55 (dd, J = 15.1, 8.5 Hz, 1H, H-2b), 2.36 – 2.16 (m, 3H, H-8a and H-16a and H-13a), 2.06 – 1.86 (m, 2H, H-16b and H-14), 1.53

[310] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.5.

(ddd, J = 19.6, 9.8, 2.5 Hz, 1H, H-8b), 1.31 (ddd, J = 12.3, 10.7, 9.4 Hz, 1H, H-13b), 1.03 (d, J = 6.5 Hz, 3H, H-33), 1.02 – 0.97 (m, 2H, H-20), 0.91 (s, 9H, *t*-Bu), 0.90 (s, 9H, *t*-Bu), 0.86 (s, 9H, *t*-Bu), 0.09 (s, 9H, Si-Me), 0.08 (s, 3H, Si-Me), 0.07 (s, 3H, Si-Me), 0.05 (s, 3H, Si-Me), 0.02 (s, 9H, TMS) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 165.1, 153.6, 136.6, 133.2, 132.7, 131.6, 129.9 (2C), 129.6, 128.4 (2C), 127.6 (2C), 126.9, 125.3 (2C), 124.2 (q, $J_{13C,19F}$ = 285 Hz), 84.5, 82.9, 78.1, 74.5, 74.2, 73.9, 73.5, 72.2, 65.9, 63.0, 55.7, 53.8, 42.0, 40.2, 37.7, 36.5, 26.7, 26.3 (3C), 26.2 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 17.5, 16.4, -1.4 (3C), -3.4, -4.0, -4.3, -4.50, -4.51, -5.0 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.5 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2898, 2857 1746, 1632, 1597, 1498, 1472, 1463, 1452, 1390, 1360, 1346, 1251, 1167, 1122, 1081, 1038, 1023, 1015, 1006, 991, 938, 917, 902, 884, 859, 833, 812, 774, 760, 720, 695, 688, 667, 636, 575, 525, 506, 469 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{58}H_{95}N_4O_{12}F_3Si_4S_1Na^+$: 1263.5589, found: 1263.5594.

(S,E)-4-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-1-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (198b)



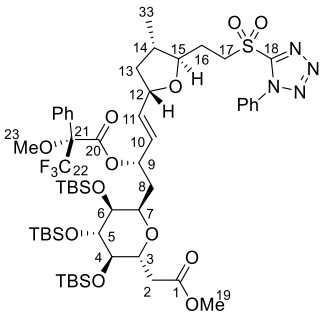
(*R*)-Mosher acid chloride (3.6 µL, 19 µmol) was added to a stirred solution of allylic alcohol **180b** (6 mg, 6 µmol) and py (2.6 µL, 32 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 4 h. Then py (2.6 µL, 32 µmol) and (*R*)-Mosher acid chloride (3.6 µL, 19 µmol) were subsequently added to the reaction mixture and stirring was continued for 3 d. The reaction was quenched with water (2.0 mL) and the aq. phase was extracted with MTBE (3 x 3.0 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:1) affording compound **198b** as a colourless oil (7 mg, 95%).[311]

$[\alpha]_D^{20}$: +0.9 (c = 0.71, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.72 – 7.34 (m, 10H, Ph), 5.88 (dd, J = 14.5, 6.0 Hz, 1H, H-11), 5.66 (ddd, J = 12.2, 8.1, 1.2 Hz, 1H, H-10), 5.62 (ddd, J = 14.5, 8.0, 4.0 Hz, 1H, H-9), 4.39 (dt, J = 9.4, 6.1 Hz, 1H, H-12), 4.32 (ddd, J = 9.1, 5.7, 3.7 Hz, 1H, H-3), 3.93 (ddd, J = 14.6, 11.1, 4.7 Hz, 1H, H-17a), 3.83 – 3.72 (m, 3H, H-17b and H-7 and H-5), 3.70 (s, 3H, H-19),

[311] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.6.

3.55 (td, J = 8.7, 3.0 Hz, 1H, H-15), 3.53 (s, 3H, H-23), 3.51 – 3.49 (m, 1H, H-4), 3.43 – 3.39 (m, 1H, H-6), 2.78 (dd, J = 15.1, 5.7 Hz, 1H, H-2a), 2.57 (dd, J = 15.1, 8.6 Hz, 1H, H-2b), 2.29 (ddd, J = 13.7, 8.1, 3.1 Hz, 1H, H-16a), 2.28 – 2.22 (m, 1H, H-8a), 2.23 (dd, J = 12.5, 6.2 Hz, 1H, H-13a), 2.01 (dddd, J = 12.2, 9.7, 7.8, 4.1 Hz, 1H, H-16b), 1.94 (ddt, J = 10.5, 8.5, 6.9 Hz, 1H, H-14), 1.47 (ddd, J = 13.5, 9.9, 2.5 Hz, 1H, H-8b), 1.36 (ddd, J = 12.4, 10.6, 9.4 Hz, 1H, H-13b), 1.03 (d, J = 6.6 Hz, 3H, H-33), 0.89 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.86 (s, 9H, *t*-Bu), 0.09 (s, 6H, Si-Me), 0.08 (s, 3H, Si-Me), 0.07 (s, 3H, Si-Me), 0.06 (s, 3H, Si-Me), 0.01 (3H, Si-Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 165.3, 153.6, 137.4, 133.2, 132.6, 131.6, 129.9 (2C), 129.6, 128.5 (2C), 127.7 (2C), 126.8, 125.3 (2C), 124.6 (q, $J_{13C,19F}$ = 288 Hz), 84.6, 83.0, 78.1, 75.0, 74.2, 73.74, 73.65, 72.2, 65.9, 55.4, 53.8, 51.9, 42.0, 40.2, 37.4, 36.3, 26.8, 26.3 (3C), 26.1 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 16.4, -3.5, -4.0, -4.3, -4.52, -4.53, -5.0 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.6 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2857, 1743, 1596, 1498, 1463, 1439, 1390, 1346, 1254, 1167, 1121, 1082, 1015, 938, 917, 897, 833, 813, 774, 761, 720, 696, 668, 636, 524, 506, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}F_3Si_3SNa^+$: 1177.5037, found: 1177.5047.

(S,E)-4-((2S,4S,5R)-4-Methyl-5-(2-((1-phenyl-1H-tetrazol-5-yl)sulfonyl)ethyl)tetrahydrofuran-2-yl)-1-((2R,3S,4R,5R,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-methoxy-2-oxoethyl)tetrahydro-2H-pyran-2-yl)but-3-en-2-yl (R)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (epi-198b)



(*S*)-Mosher acid chloride (3.6 µL, 19 µmol) was added to a stirred solution of allylic alcohol **180b** (6 mg, 6 µmol) and py (2.6 µL, 32 µmol) in DCM (200 µL) at rt and the reaction mixture was stirred for 4 h. Then py (2.6 µL, 32 µmol) and (*S*)-Mosher acid chloride (3.6 µL, 19 µmol) were subsequently added to the reaction mixture and stirring was continued for 3 d. The reaction was quenched with water (2.0 mL) and the aq. phase was extracted with MTBE (3 x 3.0 mL). The combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 7:1) affording compound *epi*-**198b** as a colourless oil (7 mg, 95%).[312]

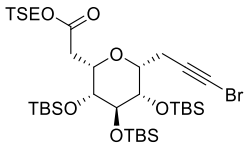
[312] A detailed graphical evaluation (complete Mosher ester analysis) can be found in chapter 6.1.6.

$[\alpha]_D^{20}$: +33.9 (c = 0.70, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.70 – 7.35 (m, 10H, Ph), 5.77 (dd, J = 15.1, 6.1 Hz, 1H, H-11), 5.61 (ddd, J = 9.8, 7.7, 4.2 Hz, 1H, H-9), 5.54 (ddd, J = 15.1, 7.7, 1.2 Hz, 1H, H-10), 4.39 – 4.30 (m, 2H, H-12 and H-3), 3.91 (ddd, J = 14.7, 11.3, 4.7 Hz, 1H, H-17a), 3.81 (dt, J = 11.4, 2.8 Hz, 1H, H-7), 3.79 – 3.76 (m, 1H, H-5), 3.74 (ddd, J = 14.8, 9.8, 4.9 Hz, 1H, H-17b), 3.69 (s, 3H, H-19), 3.57 (s, 3H, H-23), 3.53 – 3.50 (m, 1H, H-4), 3.50 (dd, J = 9.2, 3.0 Hz, 1H, H-15), 3.45 – 3.41 (m, 1H, H-6), 2.75 (dd, J = 15.1, 5.6 Hz, 1H, H-2a), 2.60 (dd, J = 15.1, 8.8 Hz, 1H, H-2b), 2.31 (ddd, J = 13.6, 10.6, 4.3 Hz, 1H, H-8a), 2.26 (ddd, J = 11.4, 8.7, 5.6 Hz, 1H, H-16a), 2.21 (dt, J = 12.5, 6.2 Hz, 1H, H-13a), 2.00 (dddd, J = 14.1, 11.7, 9.0, 5.0 Hz, 1H, H-16b), 1.92 (ddt, J = 10.5, 8.6, 6.0 Hz, 1H, H-14), 1.52 (ddd, J = 13.6, 9.9, 2.4 Hz, 1H, H-8b), 1.32 (ddd, J = 12.3, 10.7, 9.5 Hz, 1H, H-13b), 1.04 (d, J = 6.6 Hz, 3H, H-33), 0.91 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.86 (s, 9H, *t*-Bu), 0.09 (s, 9H, Si-Me), 0.08 (s, 3H, Si-Me), 0.07 (s, 3H, Si-Me), 0.05 (s, 3H, Si-Me) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 165.2, 153.6, 136.8, 133.2, 132.7, 131.6, 129.9 (2C), 129.6, 128.4 (2C), 127.6 (2C), 126.7, 125.3 (2C), 123.3 (q, $J_{13C,19F}$ = 289 Hz), 84.5, 82.9, 78.1, 74.6, 74.2, 73.8, 73.6, 72.2, 66.1, 55.7, 53.8, 51.9, 42.0, 40.2, 37.3, 36.5, 26.7, 26.3 (3C), 26.1 (3C), 25.9 (3C), 18.5, 18.3, 18.0, 16.4, -3.4, -4.0, -4.3, -4.51, -4.54, -5.0 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -71.5 (3F) ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2896, 2857, 1745, 1597, 1498, 1463, 1452, 1390, 1346, 1257, 1167, 1122, 1081, 1015, 992, 939, 917, 897, 833, 813, 775, 762, 720, 703, 635, 526, 506, 466, 445, 432 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{54}H_{85}N_4O_{12}F_3Si_3SNa^+$: 1177.5037, found: 1177.5046.

5.2.3.4. Alternative Pathways

5.2.3.4.1. Reactivity Differences Between C5'-Epimeric Glucosides

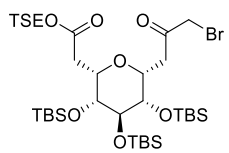
2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6R)-6-(3-bromoprop-2-yn-1-yl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (epi-199a)



$AgNO_3$ (10 mol%, 1 mg, 7 µmol) and NBS (15 mg, 82 µmol) were subsequently added to a stirred solution of alkyne *epi*-**35a** (50 mg, 74 µmol) in acetone (0.45 mL) at rt and stirring was continued for 2.5 d. The reaction mixture was filtered through a pad of SiO_2 and the filtrate was diluted with water (5 mL). The aq. phase was extracted with Et_2O (3 x 5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 50:1) affording compound *epi*-**199a** as a colourless oil (48 mg, 86%).

$[\alpha]_D^{20}$: +1.7 (c = 1.03, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.21 – 4.15 (m, 2H), 4.13 (ddd, J = 8.3, 4.8, 1.6 Hz, 1H), 3.84 – 3.76 (m, 2H), 3.52 – 3.48 (m, 1H), 3.44 – 3.40 (m, 1H), 2.66 (dd, J = 16.1, 8.3 Hz, 1H), 2.47 (d, J = 7.3 Hz, 2H), 2.41 (dd, J = 16.1, 5.0 Hz, 1H), 1.02 – 0.96 (m, 2H), 0.92 (s, 9H), 0.915 (s, 9H), 0.91 (s, 9H), 0.12 (s, 3H), 0.115 (s, 6H), 0.11 (s, 3H), 0.09 (s, 3H), 0.04 (s, 9H), 0.02 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.8, 77.4, 75.4, 73.8, 73.0, 71.4, 70.2, 62.8, 39.5, 37.2, 26.5 (3C), 26.4 (3C), 25.8 (3C), 22.4, 18.53, 18.46, 18.0, 17.4, -1.3 (3C), -2.7, -3.1, -4.3, -4.4, -5.0, -5.08 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2858, 1735, 1472, 1463, 1406, 1382, 1361, 1348, 1285, 1251, 1216, 1174, 1143, 1083, 1006, 983, 923, 985, 831, 812, 770, 693, 674, 562, 518, 462 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{67}O_6Si_4BrNa^+$: 773.3091, found: 773.3096.

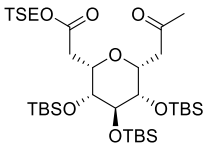
2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6R)-6-(3-bromo-2-oxopropyl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (epi-189a)



Water (3.45 µL, 192 µmol) and $XPhosAuNTf_2$ (3 mol%, 2 mg, 2 µmol) were subsequently added to a stirred solution of bromo alkyne *epi*-**199a** (48 mg, 84 µmol) in 1,2-DCE (0.5 mL) at rt and stirring was continued for 2.5 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 30:1) affording compound *epi*-**189a** as a colourless oil (20 mg, 41%).

$[\alpha]_D^{20}$: +18.1 (c = 0.97, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.22 – 4.11 (m, 2H), 4.12 – 4.06 (m, 2H), 4.08 (d, J = 13.6 Hz, 1H), 4.02 (d, J = 13.7 Hz, 1H), 3.78 (t, J = 2.5 Hz, 1H), 3.42 – 3.39 (m, 1H), 3.38 – 3.34 (m, 1H), 3.08 (dd, J = 15.0, 9.8 Hz, 1H), 2.65 (dd, J = 15.9, 9.1 Hz, 1H), 2.41 (dd, J = 15.1, 3.4 Hz, 1H), 2.33 (dd, J = 15.9, 4.4 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 18H), 0.91 (s, 9H), 0.11 (s, 6H), 0.095 (s, 3H), 0.09 (s, 3H), 0.04 (s, 9H), 0.035 (s, 6H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 201.2, 171.7, 73.7, 73.4, 72.9, 71.7, 71.3, 63.0, 42.9, 37.3, 36.4, 26.49 (3C), 26.47 (3C), 25.9 (3C), 18.53, 18.51, 18.0, 17.4, -1.3 (3C), -3.10, -3.14, -4.3 (2C), -4.9, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2895, 2858, 1734, 1472, 1463, 1389, 1362, 1345, 1251, 1173, 1141, 1084, 1006, 984, 924, 833, 813, 773, 675, 666, 535, 470, 424, 411 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{69}O_7Si_4BrNa^+$: 791.3196, found: 791.3199.

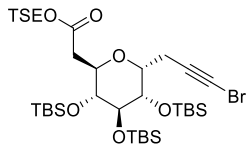
2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(2-oxopropyl)tetrahydro-2H-pyran-2-yl)acetate (epi-190a)



Water (0.80 µL, 44.6 µmol) and $XPhosAuNTf_2$ (3 mol%, 0.4 mg, 0.5 µmol) were subsequently added to a stirred solution of alkyne *epi*-**35a** (10 mg, 15 µmol) in 1,2-DCE (0.15 mL) at rt and stirring was continued for 1.5 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 20:1) affording compound *epi*-**190a** as a colourless oil (9 mg, 88%).

$[\alpha]_D^{20}$: +3.6 (c = 0.90, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.17 – 4.10 (m, 3H), 4.09 (ddd, J = 8.5, 4.7, 1.8 Hz, 1H), 3.78 (t, J = 2.5 Hz, 1H), 3.44 – 3.37 (m, 2H), 2.84 (dd, J = 15.9, 8.5 Hz, 1H), 2.64 (dd, J = 16.0, 8.5 Hz, 1H), 2.37 (dd, J = 16.0, 5.3 Hz, 1H), 2.36 (dd, J = 16.0, 5.1 Hz, 1H), 2.15 (s, 3H), 1.00 – 0.95 (m, 2H), 0.93 (s, 9H), 0.92 (s, 9H), 0.91 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.09 (s, 3H), 0.085 (s, 3H), 0.035 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 208.1, 171.8, 73.35, 73.34, 73.0, 71.6, 71.4, 62.7, 45.9, 37.3, 30.8, 26.5 (6C), 25.9 (3C), 18.54, 18.51, 18.0, 17.4, -1.3 (3C), -3.0, -3.1, -4.3 (2C), -4.95, -5.03 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2930, 2896, 2858, 1735, 1730, 1473, 1463, 1409, 1381, 1361, 1251, 1171, 1141, 1087, 1062, 1023, 1006, 983, 924, 833, 813, 772, 675, 532, 466 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{70}O_7Si_4Na^+$: 713.4091, found: 713.4094.

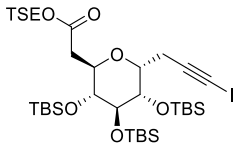
2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-6-(3-bromoprop-2-yn-1-yl)-3,4,5-tris((tert-butyldimethylsilyl)oxy)tetrahydro-2H-pyran-2-yl)acetate (199a)



$AgNO_3$ (10 mol%, 3 mg, 0.02 mmol) and NBS (29 mg, 0.16 mmol) were subsequently added to a stirred solution of alkyne **35a** (100 mg, 149 µmol) in acetone (0.9 mL) at rt and stirring was continued for 20.5 h. The reaction mixture was filtered through a pad of SiO_2 and the filtrate was diluted with water (5 mL). The aq. phase was extracted with Et_2O (3 x 5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1) affording compound **199a** as a colourless oil (109 mg, 98%).

$[\alpha]_D^{20}$: +12.7 (c = 1.03, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.33 (td, J = 7.2, 4.4 Hz, 1H), 4.23 – 4.11 (m, 2H), 4.01 (ddd, J = 8.6, 6.1, 2.2 Hz, 1H), 3.83 (dd, J = 3.2, 1.6 Hz, 1H), 3.75 – 3.71 (m, 1H), 3.52 – 3.47 (m, 1H), 2.68 – 2.61 (m, 2H), 2.51 (dd, J = 16.3, 8.7 Hz, 1H), 2.42 (dd, J = 16.3, 6.1 Hz, 1H), 1.02 – 0.96 (m, 2H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.12 (s, 6H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 77.3, 74.5, 74.3, 74.0, 70.2, 68.6, 62.8, 39.7, 37.9, 26.3 (3C), 26.2 (3C), 25.9 (3C), 22.2, 18.5, 18.3, 18.0, 17.5, -1.3 (3C), -3.4, -3.9, -4.1, -4.5, -4.6, -5.1 ppm; **IR** (film): $\tilde{\nu}$ = 2954, 2929, 2897, 2858, 1735, 1472, 1463, 1389, 1361, 1251, 1167, 1130, 1092, 1057, 1006, 974, 939, 827, 832, 813, 774, 694, 670, 666, 549, 500, 469 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{67}O_6BrSi_4Na^+$: 773.3091, found: 773.3096.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(3-iodoprop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (199b)

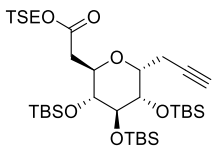


$AgNO_3$ (10 mol%, 3 mg, 0.02 mmol) and NIS (37 mg, 0.16 mmol) were subsequently added to a stirred solution of alkyne **35a** (100 mg, 149 µmol) in acetone (0.9 mL) at rt and stirring was continued for 5 d. The reaction mixture was filtered through a pad of SiO_2 and the filtrate was diluted with water (5 mL). The aq. phase was extracted with Et_2O (3 x 5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated. The crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 100:1 to 50:1) affording compound **199b** as a colourless oil (115 mg, 97%).

$[\alpha]_D^{20}$: +14.9 (c = 1.02, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.33 (ddd, J = 8.9, 6.5, 4.3 Hz, 1H), 4.22 – 4.11 (m, 2H), 4.01 (ddd, J = 8.7, 5.9, 2.2 Hz, 1H), 3.83 (dd, J = 3.2, 1.6 Hz, 1H), 3.76 – 3.72 (m, 1H), 3.51 – 3.47 (m, 1H), 2.67 (dd, J = 16.4, 9.0 Hz, 1H), 2.66 – 2.62 (m, 2H), 2.57 (dd, J = 16.4, 5.9 Hz, 1H), 1.01 – 0.96 (m, 2H), 0.93 (s, 9H), 0.91 (s, 9H), 0.89 (s, 9H), 0.13 (s, 3H), 0.12 (s, 6H), 0.11 (s, 3H), 0.09 (s, 3H), 0.07 (s, 3H), 0.04 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.6, 91.4, 74.5, 74.3, 74.1, 70.1, 68.8, 62.8, 37.9, 26.3 (3C), 26.2 (3C), 25.9 (3C), 23.3, 18.5, 18.3, 18.0, 17.5, -1.3 (3C), -3.4, -3.9, -4.1, -4.5, -4.6, -4.9, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 2953, 2929, 2896, 2857, 1734, 1472, 1463, 1389, 1361, 1250, 1167, 1139, 1091, 1056, 1005, 973, 939, 854, 841, 831, 813, 773, 694, 673, 547, 491, 472 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{33}H_{67}O_6Si_4INa^+$: 821.2952, found: 821.2957.

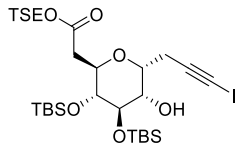
2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-(prop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (35a)

Procedure B (Protodeiodination)



A solution of iodo alkyne **199b** (10 mg, 13 µmol) in DMF (100 µL) was added to $PdCl_2(P(2\text{-furyl})_3)_2$ (5 mol%, 0.4 mg, 0.6 µmol) and TEA (5.2 µL, 37.5 µmol) in DMF (100 µL, rinsed with 2 x 100 µL) at rt, and stirring was continued for 5 min. Then, diethylphosphite (3.2 µL, 25 µmol) was added to the stirred reaction mixture at rt and stirring was continued for 2.5 h. Diethylphosphite (9.7 µL, 75 µmol), $PdCl_2(P(2\text{-furyl})_3)_2$ (5 mol%, 0.4 mg, 0.6 µmol) and TEA (5.2 µL, 37.5 µmol) were again subsequently added to the stirred reaction mixture at rt, and stirring was continued for 7 d. The reaction was quenched with aq. phosphate buffer (200 mM, pH 7, 5 mL). The aq. phase was extracted with MTBE (5 mL) and the combined extracts were dried over anhydrous Na_2SO_4. The drying agent was filtered off and the solvent was evaporated affording compound **35a** as a colourless oil (5 mg, 59%) which was not further purified. The analytical and spectroscopic data of the isolated compound **35a** were identical with those shown above.

2-(Trimethylsilyl)ethyl 2-((2R,3R,4R,5S,6R)-3,4-bis((tert-butyldimethylsilyl)oxy)-5-hydroxy-6-(3-iodoprop-2-yn-1-yl)tetrahydro-2H-pyran-2-yl)acetate (202)



Water (7.8 µL, 0.43 mmol) and XPhosAuNTf$_2$ (3 mol%, 4 mg, 4 µmol) were subsequently added to a stirred solution of iodo alkyne **199b** (115 mg, 144 µmol) in 1,2-DCE (1.15 mL) at rt resulting in a fast colour change from colourless to deep violet. The reaction mixture was immediately cooled to 0 °C and stirring was continued for 3.25 h. Then water (7.8 µL, 0.43 mmol) and XPhosAuNTf$_2$ (1.5 mol%, 2 mg, 2 µmol) were subsequently added to the stirred reaction mixture at 0 °C and stirring was continued for 2 h. Then XPhosAuNTf$_2$ (1.5 mol%, 2 mg, 2 µmol) was added again to the stirred reaction mixture at 0 °C and stirring was continued for 15 min. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 50:1 to 5:1) affording both major compound **202** (16 mg, 16%), a mixture of other inseparable mono-deprotected byproducts (31 mg, 32%) and some unreacted starting material **199b** (9 mg, 10%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.43 (dd, J = 9.7, 5.6 Hz, 1H), 4.26 – 4.12 (m, 2H), 4.10 – 4.04 (m, 1H), 3.99 – 3.95 (m, 1H), 3.75 (d, J = 11.8 Hz, 1H), 3.72 – 3.68 (m, 1H), 3.42 (ddt, J = 11.8, 3.0, 1.4 Hz, 1H), 3.08 (dd, J = 15.1, 9.7 Hz, 1H), 2.63 (dd, J = 15.1, 5.5 Hz, 1H), 2.62 (dd, J = 16.4, 8.7 Hz, 1H), 2.57 (dd, J = 16.3, 6.2 Hz, 1H), 1.03 – 0.97 (m, 2H), 0.93 (s, 9H), 0.92 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.04 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.3, 90.5, 76.5, 70.6, 70.4, 70.2, 66.6, 63.0, 35.8, 25.93 (3C), 25.86 (3C), 23.4, 18.2, 18.1, 17.5, -1.3 (3C), -4.1, -4.7, -4.8, -4.9 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{27}H_{53}IO_6Si_3Na^+$: 707.2087, found: 707.2089.

Triphenylphosphonium tetrafluoroborate (195b)

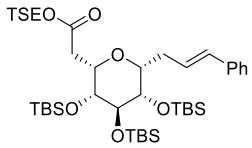
Aq. HBF_4 (48%, 2.00 mL, 15.4 mmol) was slowly added to a stirred solution of PPh_3 (**195a**) (4.45 g, 17.0 mmol) in Et_2O (22 mL) at rt and stirring was continued for 5 min resulting in the formation of a white precipitate. The precipitate was filtered off and the crude product was purified by recrystallization from boiling $CHCl_3$ (3.6 mL) affording compound **195b** as a white crystalline solid (1.22 g, 23%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.24 (d, J = 537.1 Hz, 1H), 7.93 – 7.54 (m, 15H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 135.6 (d, J = 3.0 Hz, 3C), 134.2 (d, J = 11.6 Hz, 6C), 130.6 (d, J = 13.4 Hz, 6C), 115.9 (d, J = 83.9 Hz, 3C) ppm; **^{11}B NMR** (96 MHz, $CDCl_3$): δ = -0.7 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): δ = -150.2 ppm; **^{31}P NMR** (162 MHz, $CDCl_3$): δ = 3.3 ppm; **HRMS** (ESI):

m/z calcd. for $C_{18}H_{16}P^+$: 263.0984, found: 263.0984. The analytical and spectroscopic data are in agreement with those previously reported in the literature.[313]

5.2.3.4.2. Cross Metathesis and TMS-ethyl Ester Cleavage

2-(Trimethylsilyl)ethyl 2-((2S,3R,4R,5S,6R)-3,4,5-tris((tert-butyldimethylsilyl)oxy)-6-cinnamyltetrahydro-2H-pyran-2-yl)acetate (203a)

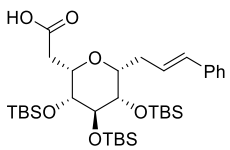


Grubbs II catalyst (**175**) (5 mol%, 3 mg, 4 µmol) was added to a stirred solution of alkene *epi*-**183a** (50 mg, 74 µmol), styrene (42.6 µL, 370 µmol) and 4 Å MS in DCM (1 mL) at rt. The resulting reaction mixture was warmed to 45 °C under an atmosphere of Ar and stirring was continued for 21 h. The solvent was evaporated and the crude product was purified by flash chromatography (SiO_2, hexane/EtOAc, 125:1) affording compound **203a** as a colourless oil (20 mg, 36%).

$[\alpha]_D^{20}$: +15.9 (c = 0.95, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.36 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 7.19 – 7.14 (m, 1H), 6.45 (d, J = 16.1 Hz, 1H), 6.29 (ddd, J = 16.0, 7.5, 5.6 Hz, 1H), 4.16 – 4.06 (m, 3H), 3.80 (t, J = 2.5 Hz, 1H), 3.74 (ddd, J = 9.6, 3.8, 1.8 Hz, 1H), 3.45 – 3.43 (m, 1H), 3.39 – 3.36 (m, 1H), 2.70 (dd, J = 16.0, 8.4 Hz, 1H), 2.64 (dddd, J = 15.1, 9.7, 5.5, 1.7 Hz, 1H), 2.42 (dd, J = 16.0, 5.1 Hz, 1H), 2.16 (dddd, J = 15.2, 7.5, 3.9, 1.2 Hz, 1H), 0.94 (s, 9H), 0.93 (s, 9H), 0.90 (s, 9H), 0.89 - 0.86 (m, 2H), 0.12 (s, 6H), 0.11 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H), 0.01 (s, 9H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.9, 138.1, 131.1, 128.6 (2C), 128.2, 126.9, 126.1 (2C), 76.8, 73.5, 73.3, 72.1, 71.6, 62.6, 37.3, 35.1, 26.54 (3C), 26.51 (3C), 25.9 (3C), 18.6, 18.5, 18.0, 17.4, -1.4 (3C), -2.9, -3.1, -4.30, -4.31, -4.8, -5.0 ppm; **IR** (film): $\tilde{\nu}$ = 3025, 2953, 2929, 2895, 2857, 1735, 1599, 1495, 1472, 1463, 1449, 1406, 1382, 1361, 1347, 1283, 1251, 1217, 1172, 1142, 1084, 1006, 984, 965, 922, 858, 832, 811, 771, 692, 674, 666, 562, 542, 526, 493, 462, 431, 421, 406 cm^{-1}; **HRMS** (ESI): *m/z* calcd. for $C_{39}H_{74}O_6Si_4Na^+$: 773.4455, found: 773.4459.

[313] P. J. C. Hausoul, A. N. Parvulescu, M. Lutz, A. L. Spek, P. C. A. Bruijnincx, B. M. Weckhuysen, R. J. M. K. Gebbink, *Angew. Chem. Int. Ed.* **2010**, *49*, 7972-7975.

2-((2S,3R,4R,5S,6R)-3,4,5-Tris((tert-butyldimethylsilyl)oxy)-6-cinnamyltetrahydro-2H-pyran-2-yl)acetic acid (203b)



A solution of TASF (19 mg, 70 µmol) in DMF (125 µL) was slowly added to a stirred solution of ester **203a** (6 mg, 8 µmol) in DMF (125 µL) at 0 °C and the resulting reaction mixture was allowed to reach rt, and stirring was continued for 5 h. The reaction mixture was purified by preparative thin layer chromatography (SiO_2, hexane/EtOAc, 10:1) affording compound **203b** as a colourless oil (4 mg, 77%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.36 – 7.33 (m, 2H), 7.31 – 7.28 (m, 2H), 7.23 – 7.19 (m, 1H), 6.50 (dd, J = 38.7, 15.9 Hz, 1H), 6.18 (dt, J = 15.9, 7.2 Hz, 1H), 3.99 (ddd, J = 8.2, 5.6, 4.1 Hz, 1H), 3.83 (dt, J = 8.6, 4.5 Hz, 1H), 3.80 (t, J = 2.1 Hz, 1H), 3.74 (ddd, J = 3.8, 2.5, 1.3 Hz, 1H), 3.62 (dt, J = 5.6, 1.6 Hz, 1H), 2.74 (dd, J = 16.1, 4.2 Hz, 1H), 2.70 (dd, J = 16.1, 8.2 Hz, 1H), 2.62 – 2.57 (m, 1H), 2.54 (dddd, J = 14.3, 8.5, 7.3, 1.3 Hz, 1H), 0.92 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.135 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H) ppm; **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 189.9, 137.3, 133.2, 128.7 (2C), 127.4, 126.3 (2C), 125.9, 81.0, 75.5, 74.3, 72.6, 71.7, 39.1, 38.1, 25.98 (6C), 25.96 (3C), 18.10, 18.08, 18.07, -3.7, -3.8, -3.9, -4.2, -4.6, -4.7 ppm; **HRMS** (ESI): *m/z* calcd. for $C_{34}H_{61}O_6Si_3^+$: 649.3782, found: 649.3784.

5.2.4. NMR Data Of Belizentrin & Belizentrin Methyl Ester

Herein, the NMR datasets of the isolated natural product **18** and of our synthesized sample of belizentrin methyl ester (**19**) can be found. Aside from a systematic shift, the NMR data matches reasonably good, and thus the absolute as well as the relative stereochemical assignment of the isolation team could be confirmed.

Table 5.1: Comparison of ^{1}H NMR (CD_3OD) shifts of belizentrin (**18**) with belizentrin methyl ester (**19**) in ppm.

Position	Natural product Belizentrin (18)	Belizentrin Methyl Ester (19)	Belizentrin Methyl Ester (19) (after correction)	Deviation Δδ (before Correction)
2a	2.67	2.87	2.68	0.19
2b	2.16	2.42	2.17	0.25
3	3.85	3.92	3.86	0.06
4	2.97	3.10	2.98	0.12
5	3.43	3.54	3.44	0.10
6	3.48	3.57	3.49	0.08
7	3.94	4.05	3.95	0.10
8a	1.89	2.04	1.90	0.14
8b	1.89	1.92	1.90	0.02
9	3.83	3.99	3.84	0.15
10	3.48	3.52	3.49	0.03
11	3.56	3.57	3.57	0.00
12	3.97	4.12	3.98	0.14
13a	2.09	2.10	2.10	0.00
13b	1.45	1.56	1.46	0.10
14	1.83	1.91	1.84	0.07
15	3.38	3.50	3.39	0.11
16a	2.23	2.35	2.24	0.11
16b	2.14	2.20	2.15	0.05
17	5.71	5.81	5.72	0.09
18	5.51	5.59	5.52	0.07
19	5.36	5.45	5.37	0.08
20a	2.64	2.69	2.65	0.04
20b	1.92	2.09	1.93	0.16
22	5.12	5.28	5.13	0.15
23a	2.10	2.13	2.11	0.02
23b	1.96	2.10	1.97	0.13
24a	1.42	1.52	1.43	0.09
24b	1.26	1.45	1.27	0.18
25	3.78	3.90	3.79	0.11
26a	1.64	1.73	1.65	0.08

26b	1.30	1.45	1.31	0.14
28	3.18	3.28	3.19	0.09
30a	1.93	2.09	1.94	0.15
30b	1.82	1.88	1.83	0.05
31a	2.42	2.52	2.43	0.09
31b	2.26	2.35	2.27	0.08
33	0.92	1.02	0.93	0.09
34	1.61	1.71	1.62	0.09
35	1.29	1.38	1.30	0.08
36 (Me)		3.67		
2’	5.72	5.79	5.73	0.06
3’	7.17	7.27	7.18	0.09
5’	5.83	5.93	5.84	0.09
6’a	2.86	3.04	2.87	0.17
6’b	2.86	2.92	2.87	0.05
8’	2.66	2.77	2.67	0.10
9’	5.45	5.53	5.46	0.07
10’	5.39	5.46	5.40	0.06
11’a	3.84	3.75	3.85	-0.10
11’b	3.41	3.65	3.42	0.23
12’	1.67	1.78	1.68	0.10
13’a	4.75	4.84	4.76	0.08
13’b	4.72		4.73	

Table 5.2: *Comparison of ^{13}C NMR (CD_3OD) shifts of belizentrin (**18**) with belizentrin methyl ester (**19**) in ppm.*

Position	Natural product Belizentrin (18)	Belizentrin Methyl Ester (19)	Belizentrin Methyl Ester (19) (after correction)	Deviation Δδ (before Correction)
1	179.4	173.9	179.4	-5.5
2	41.7	38.4	41.7	-3.3
3	71.4	71.4	71.4	0.0
4	75.6	75.3	75.6	-0.3
5	74.5	74.7	74.5	0.2
6	72.8	73.0	72.8	0.2
7	76.2	74.8	76.2	-1.4
8	29.8	30.4	29.8	0.6
9	73.3	71.5	73.3	-1.8
10	72.8	73.6	72.8	0.8
11	76.0	75.8	76.0	-0.2
12	78.9	80.2	78.9	1.3
13	38.2	38.3	38.2	0.1
14	40.0	40.5	40.0	0.5
15	85.5	86.2	85.5	0.7

16	85.5	86.2	85.5	0.7
17	130.6	131.1	130.6	0.5
18	131.2	132.1	131.2	0.9
19	73.0	73.7	73.0	0.7
20	38.0	38.4	38.0	0.4
21	131.5	131.9	131.5	0.4
22	129.2	129.2	129.2	0.0
23	25.5	24.8	25.5	-0.7
24	37.0	37.0	37.0	0.0
25	68.4	68.0	68.4	-0.4
26	46.5	46.5	46.5	0.0
27	72.2	72.8	72.2	0.6
28	78.8	79.4	78.8	0.6
29	97.9	98.5	97.9	0.6
30	35.8	36.6	35.8	0.8
31	30.5	31.0	30.5	0.5
32	175.7	176.3	175.7	0.6
33	16.4	16.7	16.4	0.3
34	23.2	23.9	23.2	0.7
35	21.4	21.8	21.4	0.4
36 (Me)		52.3		
1’	167.8	168.3	167.8	0.5
2’	116.8	117.2	116.8	0.4
3’	150.1	170.7	150.1	0.6
4’	134.9	135.1	134.9	0.2
5’	139.8	140.9	139.8	1.1
6’	35.2	36.2	35.2	1.0
7’	146.7	147.3	146.7	0.6
8’	40.1	40.6	40.1	0.5
9’	130.8	131.3	130.8	0.5
10’	129.1	129.4	129.1	0.3
11’	41.3	41.9	41.3	0.6
12’	12.4	12.8	12.4	0.4
13’	112.4	113.1	112.4	0.7

6. Appendix

6.1. Mosher Ester Analyses

6.1.1. Stereochemical Assignment Of 151 & *epi*-151

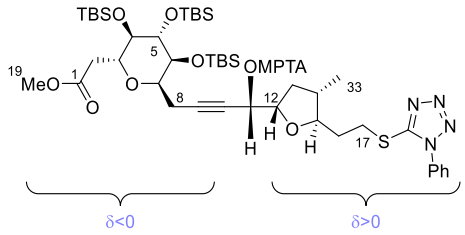


Figure 6.1: Molecular structure of **151** and *epi*-**151** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.1: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **151** and *epi*-**151** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester **151**	*R*-configured Ester ***epi*-151**	Deviation Δδ (*S* - *R*)
2a	2.75	2.75	0.00
2b	2.64	2.63	0.01
3	4.29	4.30	-0.01
4	3.57-3.42	3.60-3.48	<0
5	3.84-3.79	3.84-3.79	0.00
6	3.64-3.61	3.67-3.63	<0
7	3.93	3.94	-0.01
8a	2.50	2.53	-0.03
8b	2.41	2.46	-0.05
11	5.53	5.54	-0.01
12	4.18	4.15-4.07	>0
13a	2.31	2.28-2.20	>0
13b	1.48	1.44	0.04
14	1.96-1.83	1.91-1.78	>0
15	3.57-3.42	3.60-3.48	<0
16a	2.20	2.19-2.12	>0
16b	1.96-1.83	1.91-1.78	>0
17a	3.57-3.42	3.44	>0
17b	3.30	3.29	0.01
19	3.66	3.66	0.00
33	1.04	0.99	0.05

6.1.2. Stereochemical Assignment Of 152 & *epi*-152

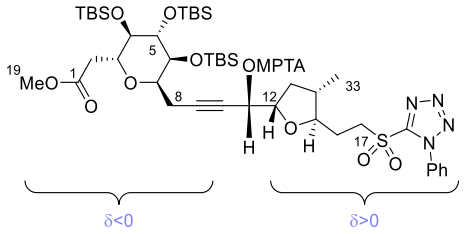


Figure 6.2: Molecular structure of **152** and *epi*-**152** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.2: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **152** and *epi*-**152** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester **152**	*R*-configured Ester *epi*-**152**	Deviation Δδ (*S* - *R*)
2a	2.75	2.75	0.00
2b	2.63	2.62	0.01
3	4.29	4.30	-0.01
4	3.51-3.49	3.53-3.47	0.00
5	3.83-3.78	3.82	-0.02 (Ø)
6	3.64-3.62	3.70-3.61	-0.05 (Ø)
7	3.93	3.95	-0.02
8a	2.49	2.49	0.00
8b	2.42	2.49	-0.07
11	5.54	5.55	-0.01
12	4.19	4.11	0.08
13a	2.34	2.30-2.19	0.10 (Ø)
13b	1.52	1.49	0.03
14	1.95-1.85	1.91-1.82	0.04 (Ø)
15	3.58-3.52	3.53-3.47	0.05 (Ø)
16a	2.28	2.30-2.19	0.04 (Ø)
16b	2.05-1.95	2.00-1.91	0.05 (Ø)
17a	3.77	3.77	0.00
17b	3.68	3.70-3.61	0.03 (Ø)
19	3.66	3.66	0.00
33	1.07	1.01	0.06

6.1.3. Stereochemical Assignment Of 153 & *epi*-153

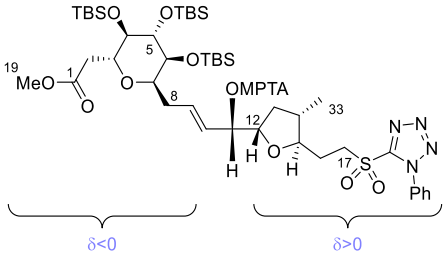


Figure 6.3: Molecular structure of **153** and *epi*-**153** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.3: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **153** and *epi*-**153** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester **153**	*R*-configured Ester *epi*-**153**	Deviation Δδ (*S* - *R*)
2a	2.74	2.75	-0.01
2b	2.60	2.59	0.01
3	4.29	4.29	0.00
4	3.51-3.48	3.52-3.47	<0
5	3.86-3.74	3.84-3.75	>0
6	3.47	3.52-3.47	<0
7	3.86-3.74	3.84-3.75	>0
8a	2.45	2.54-2.44	<0
8b	2.05-1.94	2.06-1.99	<0
9	5.88	5.96	-0.08
10	5.43-5.31	5.55	<0
11	5.43-5.31	5.39	<0
12	4.14-4.07	4.06	>0
13a	2.16	2.08	0.08
13b	1.36	1.30	0.06
14	1.93-184	1.88-1.78	>0
15	3.58-3.51	3.43	>0
16a	2.27	2.22	0.05
16b	2.05-1.94	1.98-1.89	>0
17a	3.86-3.74	3.84-3.75	>0
17b	3.73-3.67	3.70-3.64	>0
19	3.66	2.64	0.02
33	1.04	0.95	0.09

6.1.4. Stereochemical Assignment Of 154 & *epi*-154

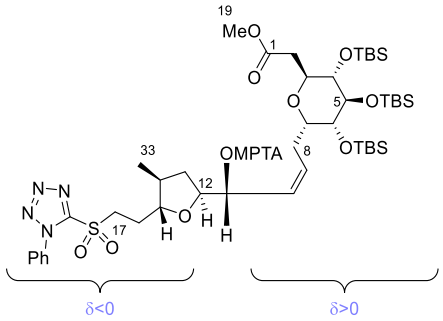


Figure 6.4: Molecular structure of **154** and *epi*-**154** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.4: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **154** and *epi*-**154** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester **154**	*R*-configured Ester *epi*-**154**	Deviation Δδ (*S* - *R*)
2a	2.74	2.73	0.01
2b	2.67	2.67	0.00
3	4.34	4.34	0.00
4	3.51-3.48	3.52-3.48	-0.01 (Ø)
5	3.83-3.73	3.83-3.77	-0.02 (Ø)
6	3.64-3.56	3.57-3.53	0.05 (Ø)
7	3.83-3.73	3.83-3.77	-0.02 (Ø)
8a	2.59	2.59	0.00
8b	2.34-2.03	2.34-2.08	-0.03 (Ø)
9	5.99-5.81	5.90-5.80	0.05 (Ø)
10	5.42-5.28	5.27	0.08 (Ø)
11	5.99-5.81	5.90-5.80	0.05 (Ø)
12	4.02	4.09	-0.07 (Ø)
13a	2.34-2.03	2.34-2.08	-0.03 (Ø)
13b	1.59-1.52	1.62	-0.07 (Ø)
14	1.96-1.77	2.00-1.82	-0.05 (Ø)
15	3.64-3.56	3.63-3.57	0.00
16a	2.34-2.03	2.34-2.08	-0.03 (Ø)
16b	1.96-1.77	2.00-1.82	-0.05 (Ø)
17a	3.83-3.73	3.91	-0.03 (Ø)
17b	3.64-3.56	3.74-3.67	-0.11 (Ø)
19	3.65	3.65	0.00
33	1.02	1.02	0.00

6.1.5. Stereochemical Assignment Of 198a & *epi*-198a

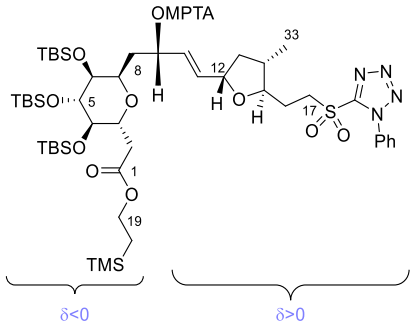


Figure 6.5: Molecular structure of **198a** and *epi*-**198a** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.5: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **198a** and *epi*-**198a** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester 198a	*R*-configured Ester *epi*-198a	Deviation Δδ (*S* - *R*)
2a	2.76	2.74	0.02
2b	2.51	2.55	-0.04
3	4.32	4.38-4.29	-0.02 (Ø)
4	3.52-3.48	3.52-3.47	0.01 (Ø)
5	3.83-3.73	3.80	-0.02 (Ø)
6	3.40	3.42	-0.02
7	3.83-3.73	3.79-3.75	0.01 (Ø)
8a	2.32-2.16	2.36-2.16	-0.02 (Ø)
8b	1.47	1.53	-0.06
9	5.65-5.59	5.62	0.00
10	5.67	5.54	0.13
11	5.89	5.77	0.12
12	4.39	4.38-4.29	0.06
13a	2.32-2.16	2.36-2.16	-0.02 (Ø)
13b	1.36	1.31	0.05
14	2.06-1.89	2.06-1.86	0.02 (Ø)
15	3.55	3.52-3.47	0.06 (Ø)
16a	2.32-2.16	2.36-2.16	-0.02 (Ø)
16b	2.06-1.89	2.06-1.86	0.02 (Ø)
17a	3.93	3.91	0.02
17b	3.83-3.72	3.74	0.04 (Ø)
19	4.23-4.16	4.22-4.15	0.01 (Ø)
20	1.02-0.97	1.02-0.97	0.00 (Ø)
33	1.03	1.03	0.00

6.1.6. Stereochemical Assignment Of 198b & *epi*-198b

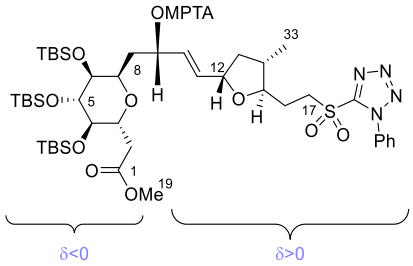


Figure 6.6: Molecular structure of **198b** and *epi*-**198b** and graphical representation of the deviation necessary for the assignment (lilac).

Table 6.6: Comparison of ^{1}H NMR ($CDCl_3$) shifts of **198b** and *epi*-**198b** in ppm (lilac: important shifts for the assignment).

Position	*S*-configured Ester **198b**	*R*-configured Ester ***epi*-198b**	Deviation Δδ (*S* - *R*)
2a	2.78	2.75	0.03
2b	2.57	2.60	-0.03
3	4.32	4.38-4.30	-0.02 (Ø)
4	3.51-3.49	3.53-3.50	-0.01 (Ø)
5	3.83-3.72	3.79-3.76	0.00 (Ø)
6	3.43-3.39	3.45-3.41	-0.02 (Ø)
7	3.83-3.72	3.81	-0.04 (Ø)
8a	2.28-2.22	2.31	-0.06 (Ø)
8b	1.47	1.52	-0.05
9	5.62	5.61	0.01
10	5.66	5.54	0.12
11	5.88	5.77	0.11
12	4.39	4.38-4.30	0.05 (Ø)
13a	2.23	2.21	0.02
13b	1.36	1.32	0.04
14	1.94	1.92	0.02
15	3.55	3.50	0.05
16a	2.29	2.26	0.03
16b	2.01	2.00	0.01
17a	3.93	3.91	0.02
17b	3.83-3.72	3.74	0.04 (Ø)
19	3.70	3.69	0.01
33	1.03	1.04	-0.01

6.2. GC Data

6.2.1. *ee* Determination Of 84

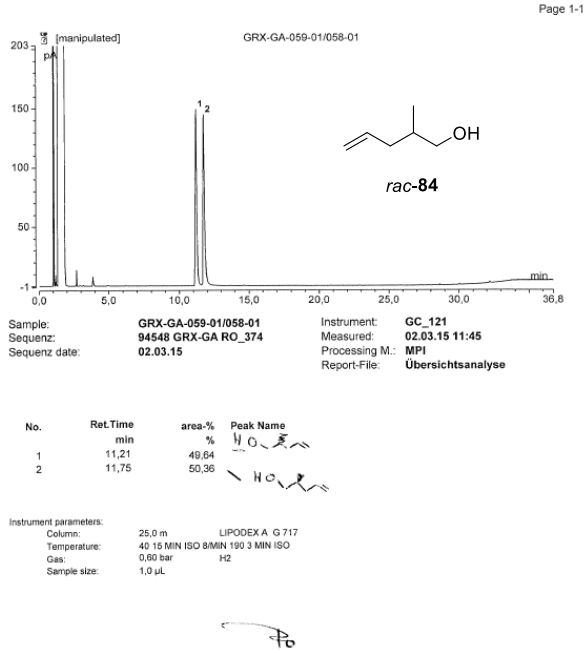


Figure 6.7: GC-MS chromatogram of the measurement of the racemic mixture of alcohol *rac*-**84** (chiral stationary phase).

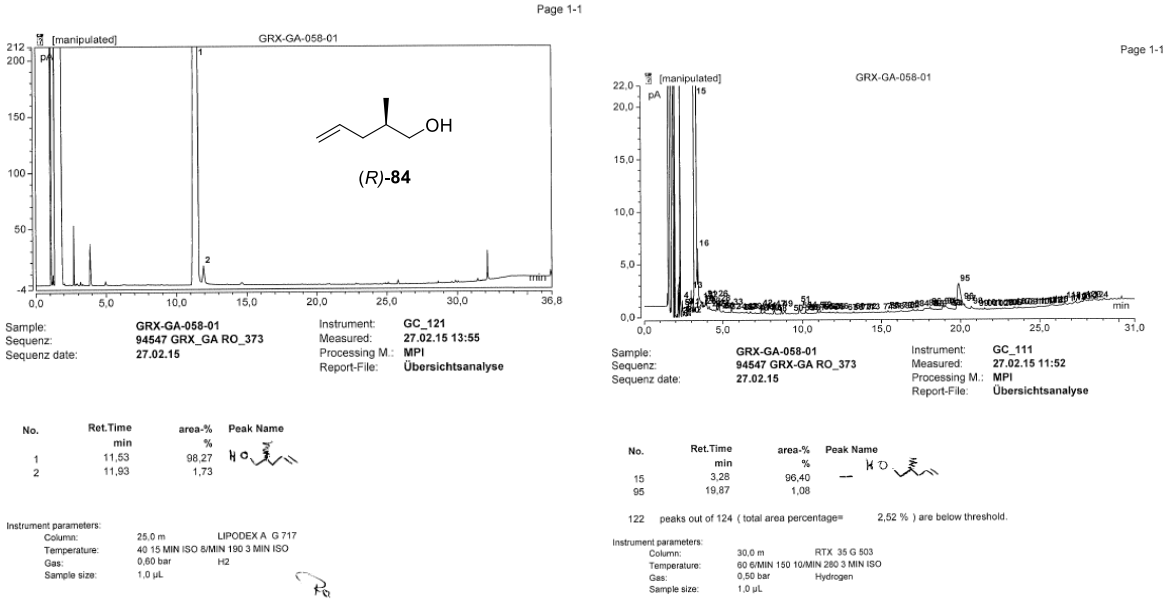


Figure 6.8: Chiral GC-MS chromatograms of the measurements of the enantio-enriched alcohol (*R*)-**84** (chiral stationary phase).

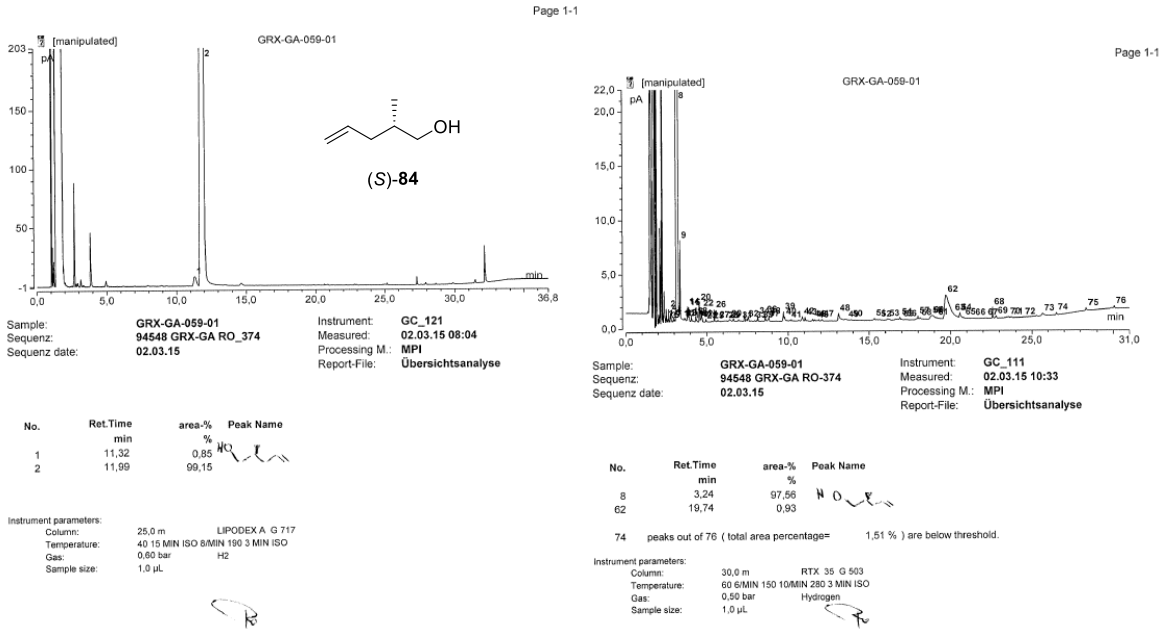


Figure 6.9: GC-MS chromatograms of the measurements of the enantio-enriched alcohol (*S*)-**84** (chiral stationary phase).

6.3. HPLC Data

6.3.1. *d.r.* Determination Of 147 & 148

L*	*d.r.* (*anti*:*syn*)
$(DHQ)_2PHAL$	2.6:1
$(DHQD)_2PHAL$	1:2.1
$(DHQ)_2PYR$	2.7:1
$(DHQD)_2PYR$	1.1:1
$(DHQ)_2AQN$	2.1:1
$(DHQD)_2AQN$	1:1.7

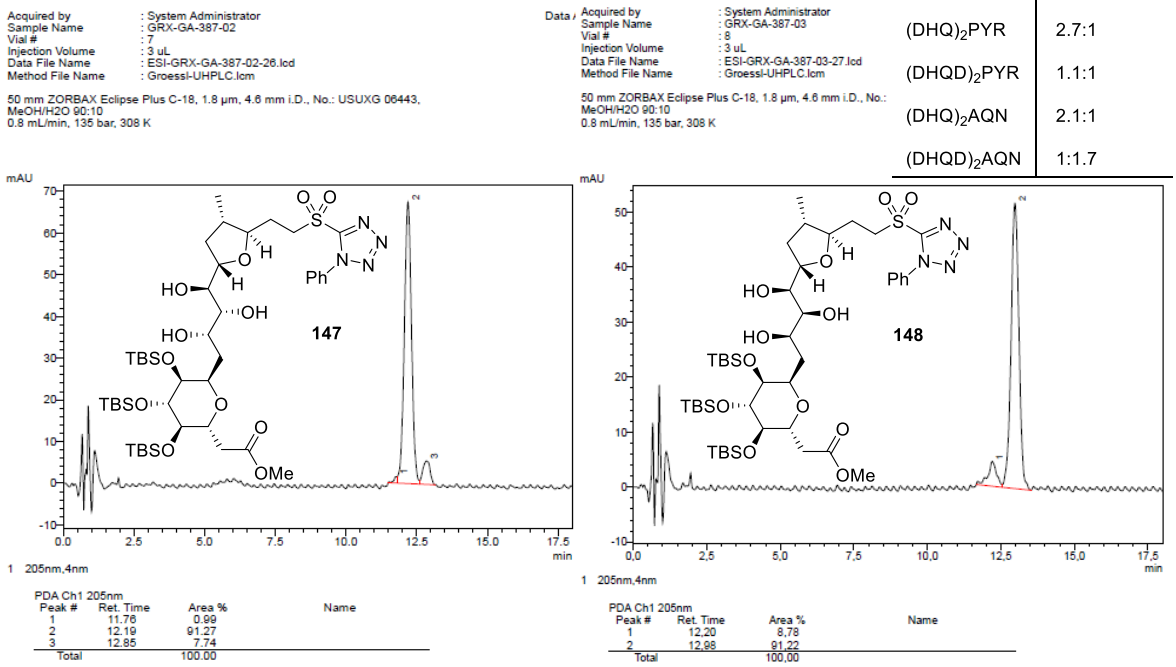


Figure 6.10: HPLC-MS chromatograms of the isolated diastereo-enriched triols from the Sharpless dihydroxylation of allylic alcohol *epi-E*-**146** with different ligands (left: diastereomer **147**, right: diastereomer **148**).

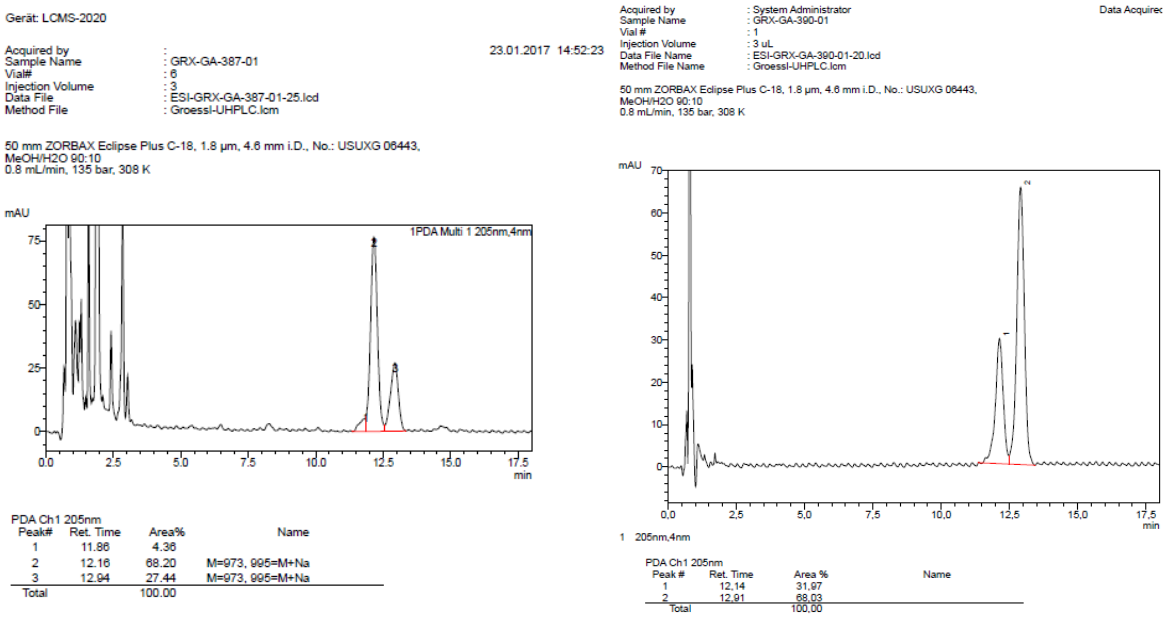


Figure 6.11: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *epi-E*-**146** with different ligands resulting in diastereomeric triols **147** and **148** (left: $(DHQ)_2PHAL$, right: $(DHQD)_2PHAL$).

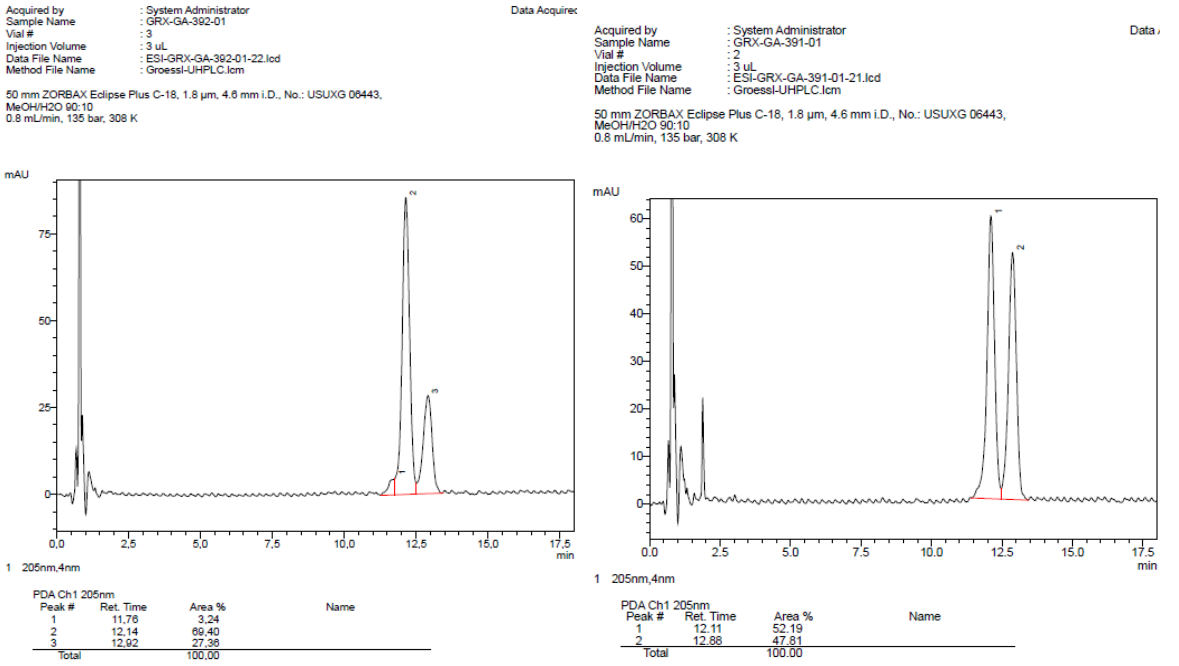


Figure 6.12: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *epi-E*-**146** with different ligands resulting resulting in diastereomeric triols **147** and **148** (left: $(DHQ)_2PYR$, right: $(DHQD)_2PYR$).

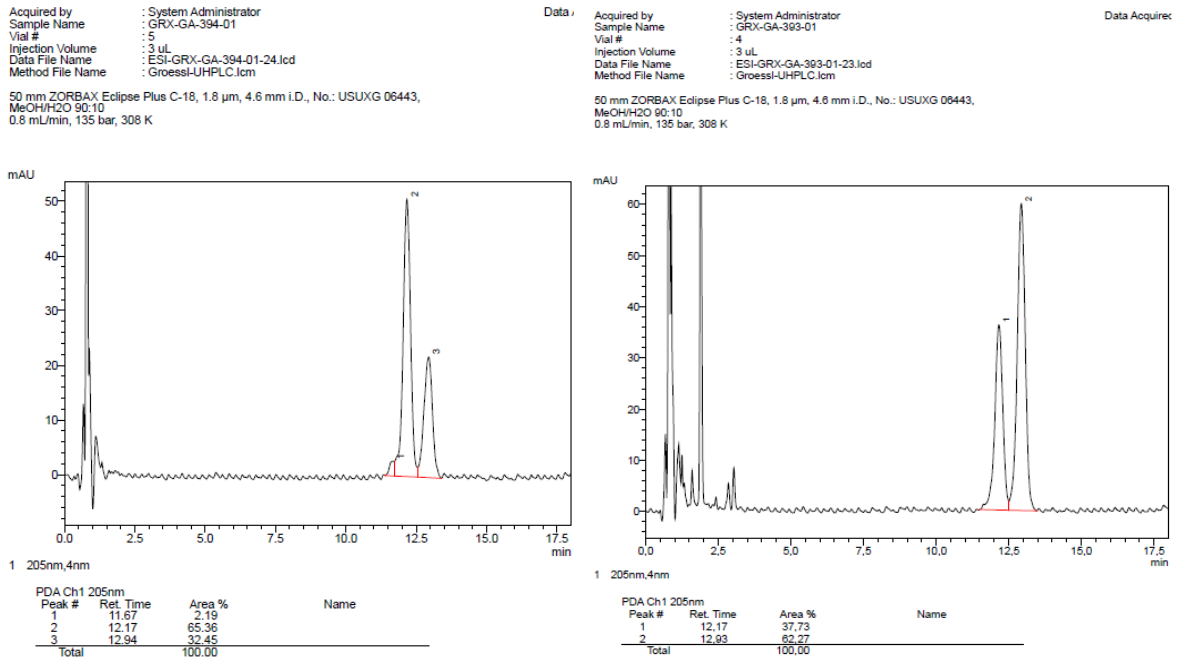


Figure 6.13: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *epi-E*-**146** with different ligands resulting in diastereomeric triols **147** and **148** (left: $(DHQ)_2AQN$, right: $(DHQD)_2AQN$).

6.3.2. *d.r.* Determination Of 149 & 150a

L*	*d.r.* (*anti*:*syn*)
$(DHQ)_2PHAL$	7:1
$(DHQD)_2PHAL$	9.3:1
$(DHQ)_2PYR$	9.3:1
$(DHQD)_2PYR$	7.4:1
$(DHQ)_2AQN$	8:1
$(DHQD)_2AQN$	8.1:1

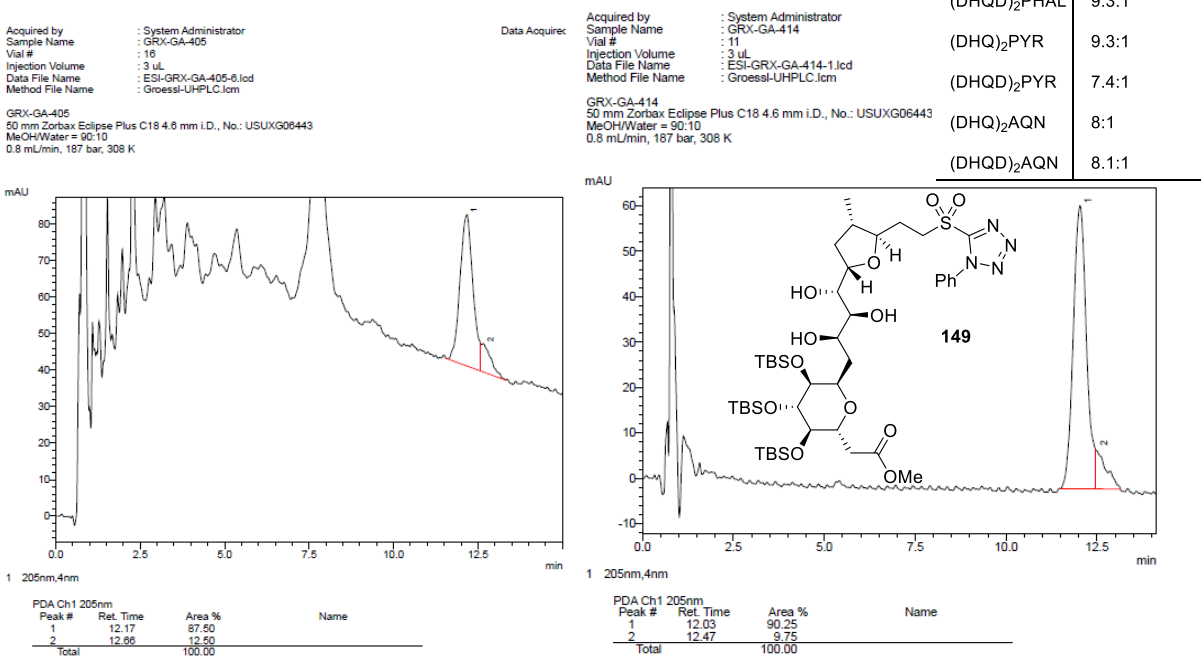


Figure 6.14: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *E*-**146** with different ligands resulting in diastereomeric triols **149** and **150a** (left: $(DHQ)_2PHAL$, right: $(DHQD)_2PHAL$).

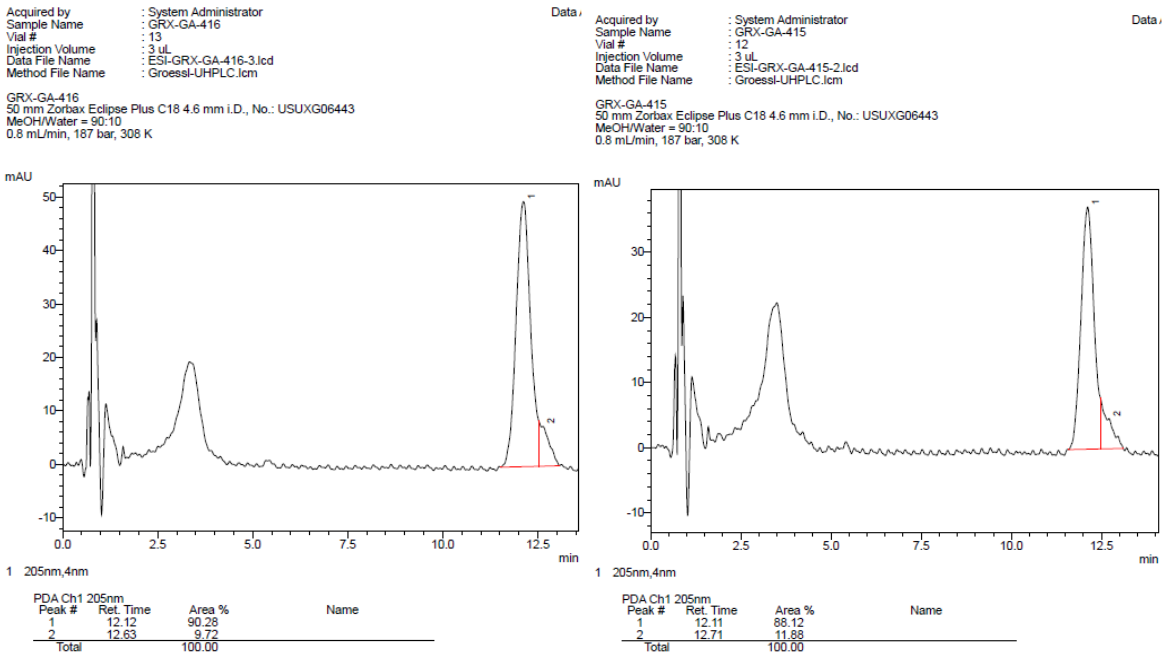


Figure 6.15: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *E*-**146** with different ligands resulting resulting in diastereomeric triols **149** and **150a** (left: $(DHQ)_2PYR$, right: $(DHQD)_2PYR$).

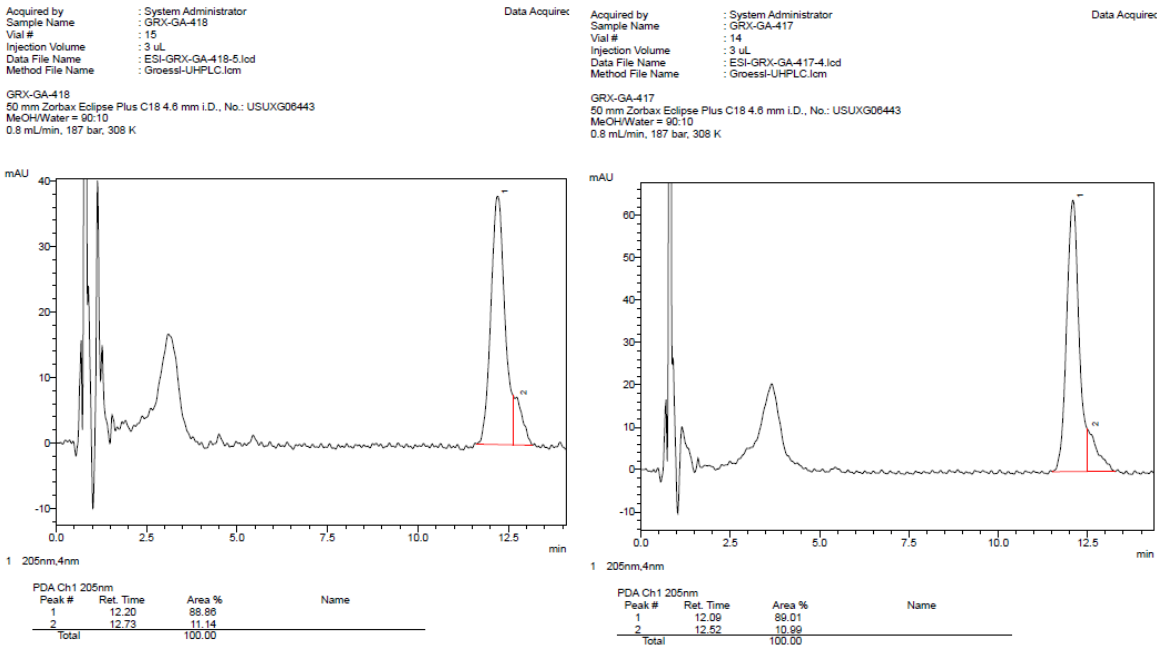


Figure 6.16: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol *E*-**146** with different ligands resulting in diastereomeric triols **149** and **150a** (left: $(DHQ)_2AQN$, right: $(DHQD)_2AQN$).

6.3.3. *d.r.* Determination Of 150b & 196a

L*	*d.r.* (*anti*:*syn*)
$(DHQ)_2PHAL$	3.2:1
$(DHQD)_2PHAL$	1:1.8
$(DHQ)_2PYR$	3.7:1
$(DHQD)_2PYR$	1:3.3
$(DHQ)_2AQN$	3.5:1
$(DHQD)_2AQN$	1:6.7

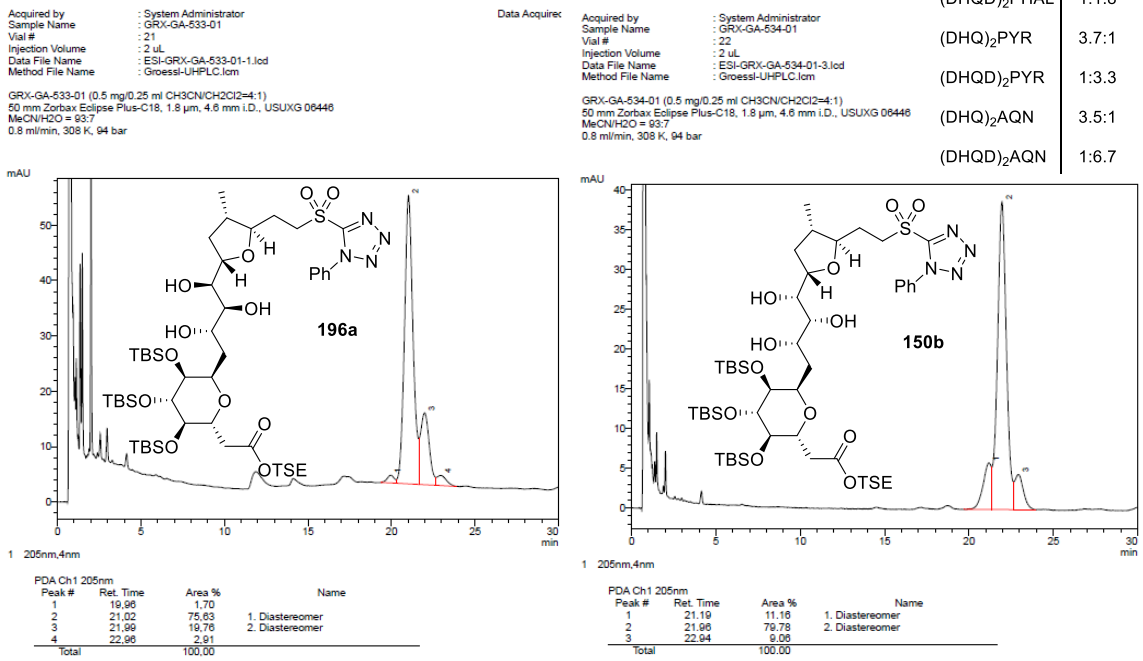


Figure 6.17: HPLC-MS chromatograms of the isolated diastereo-enriched triols from the Sharpless dihydroxylation of allylic alcohol **180a** with different ligands (left: diastereomer **196a**, right: diastereomer **150b**).

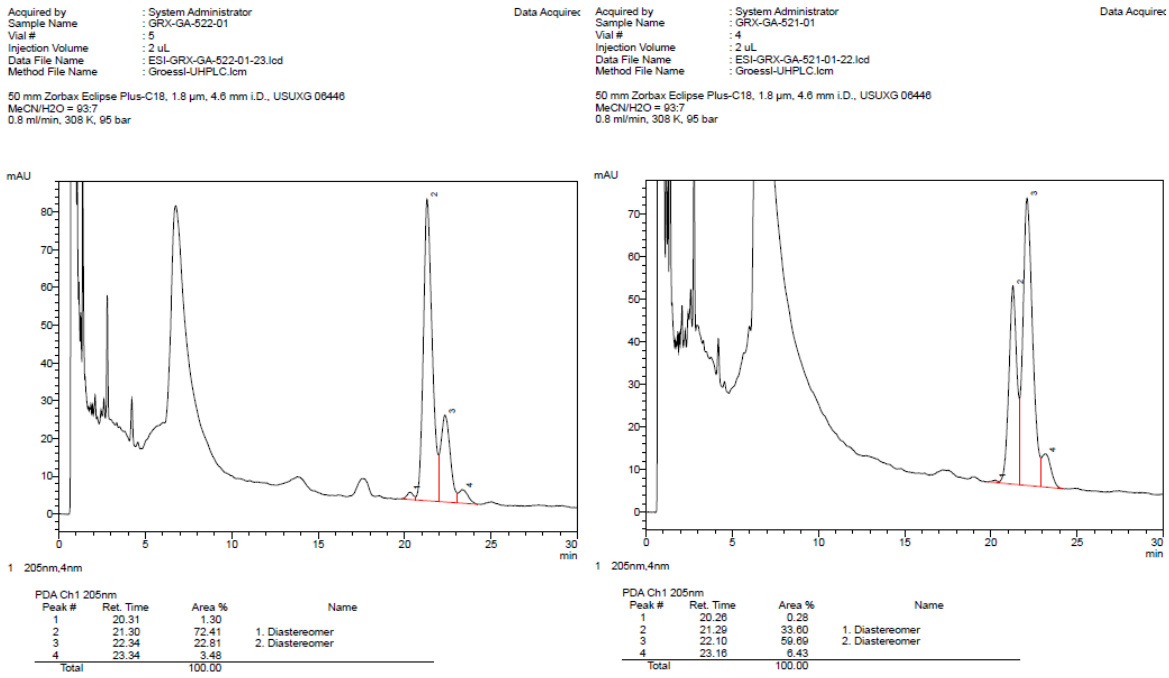


Figure 6.18: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol **180a** with different ligands resulting in diastereomeric triols **150b** and **196a** (left: $(DHQ)_2PHAL$, right: $(DHQD)_2PHAL$).

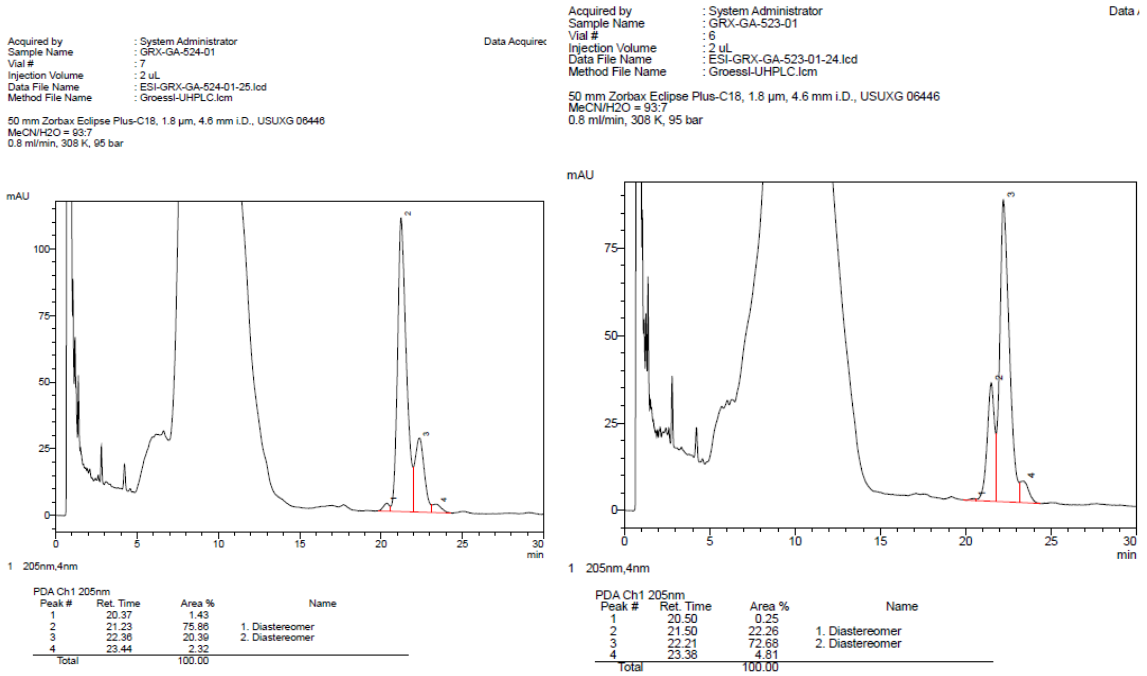


Figure 6.19: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol **180a** with different ligands resulting resulting in diastereomeric triols **150b** and **196a** (left: $(DHQ)_2PYR$, right: $(DHQD)_2PYR$).

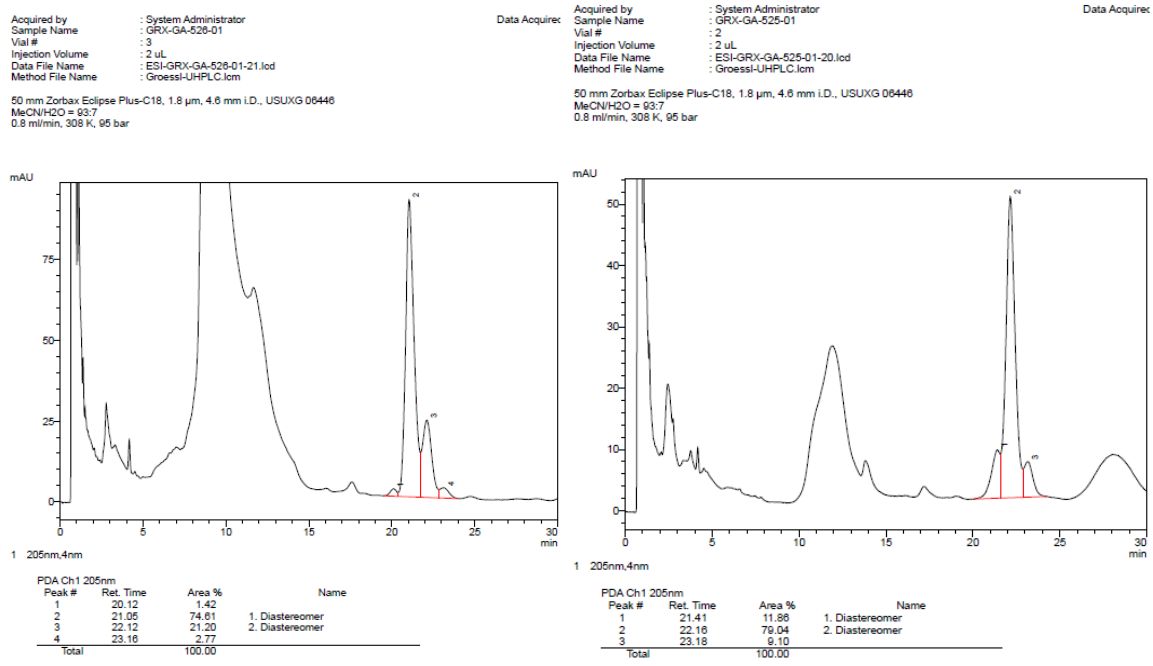


Figure 6.20: HPLC-MS chromatograms of the reaction mixtures of the Sharpless dihydroxylation of allylic alcohol **180a** with different ligands resulting in diastereomeric triols **150b** and **196a** (left: $(DHQ)_2AQN$, right: $(DHQD)_2AQN$).

6.4. X-Ray Crystallographic Data

6.4.1. Crystallographic Data Of 42

Crystal Data & Structure Refinement

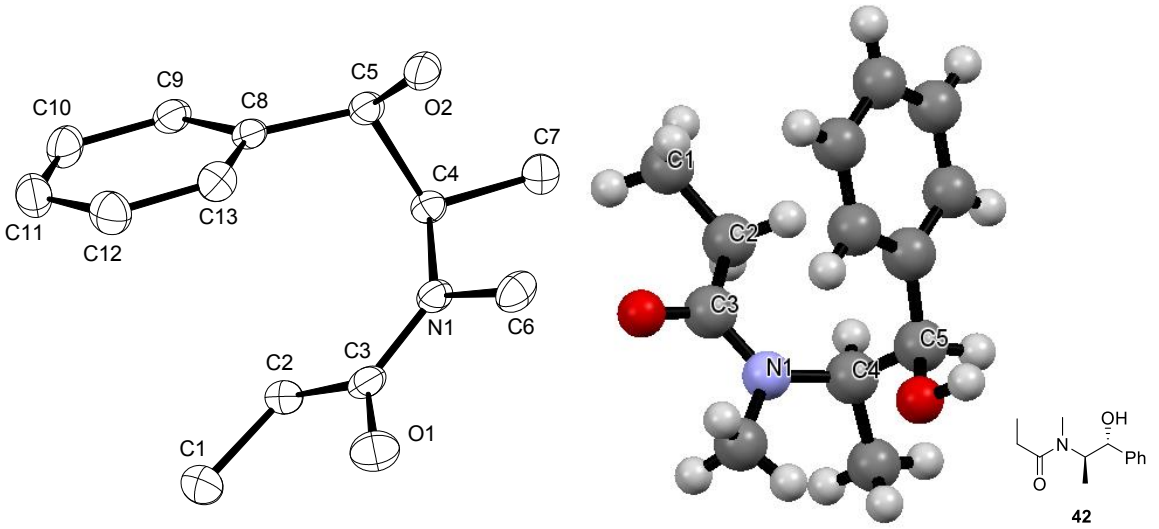


Figure 6.21: X-Ray single crystal structure and molecular structure of pseudoephedrine amide **42** (numbering of atoms is arbitrary).

Identification code	9847	
Empirical formula	$C_{13}H_{19}NO_2$	
Color	colorless	
Formula weight	221.29 g·mol^{-1}	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 5.4556(2) Å	α = 90°.
	b = 13.0941(4) Å	β = 98.2940(10)°.
	c = 8.5866(3) Å	γ = 90°.
Volume	606.98(4) Å^3	
Z	2	
Density (calculated)	1.211 Mg·m^{-3}	
Absorption coefficient	0.647 mm^{-1}	
F(000)	240 e	
Crystal size	0.550 x 0.249 x 0.070 mm^3	

θ range for data collection	5.205 to 67.372°.	
Index ranges	$-6 \leq h \leq 6$, $-15 \leq k \leq 15$, $-10 \leq l \leq 10$	
Reflections collected	14323	
Independent reflections	2033 [R_{int} = 0.0391]	
Reflections with I>2σ(I)	1936	
Completeness to θ = 67.372°	100.0%	
Absorption correction	Gaussian	
Max. and min. transmission	0.96 and 0.84	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	2033/1/153	
Goodness-of-fit on F^2	1.074	
Final R indices [I>2σ(I)]	R_1 = 0.0357	wR^2 = 0.0870
R indices (all data)	R_1 = 0.0384	wR^2 = 0.0888
Absolute structure parameter	0.04(14)	
Extinction coefficient	0.014(2)	
Largest diff. peak and hole	0.162 and -0.141 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(2)-C(5)	1.426(3)	O(1)-C(3)	1.244(3)
N(1)-C(3)	1.353(3)	N(1)-C(4)	1.469(3)
N(1)-C(6)	1.467(3)	C(8)-C(9)	1.392(3)
C(8)-C(13)	1.392(3)	C(8)-C(5)	1.505(3)
C(3)-C(2)	1.511(3)	C(9)-C(10)	1.387(3)
C(4)-C(5)	1.543(3)	C(4)-C(7)	1.529(3)
C(13)-C(12)	1.386(3)	C(2)-C(1)	1.515(4)
C(10)-C(11)	1.386(4)	C(12)-C(11)	1.388(4)
C(3)-N(1)-C(4)	124.11(19)	C(3)-N(1)-C(6)	116.6(2)
C(6)-N(1)-C(4)	119.27(19)	C(9)-C(8)-C(13)	118.6(2)
C(9)-C(8)-C(5)	119.9(2)	C(13)-C(8)-C(5)	121.4(2)
O(1)-C(3)-N(1)	119.5(2)	O(1)-C(3)-C(2)	119.8(2)
N(1)-C(3)-C(2)	120.7(2)	C(10)-C(9)-C(8)	120.8(2)
N(1)-C(4)-C(5)	112.24(17)	N(1)-C(4)-C(7)	111.9(2)
C(7)-C(4)-C(5)	111.1(2)	C(12)-C(13)-C(8)	120.7(2)
O(2)-C(5)-C(8)	112.72(19)	O(2)-C(5)-C(4)	107.80(19)
C(8)-C(5)-C(4)	112.22(19)	C(3)-C(2)-C(1)	112.8(2)
C(11)-C(10)-C(9)	120.2(2)	C(13)-C(12)-C(11)	120.2(2)
C(10)-C(11)-C(12)	119.5(2)		

6.4.2. Crystallographic Data Of 43

Crystal Data & Structure Refinement

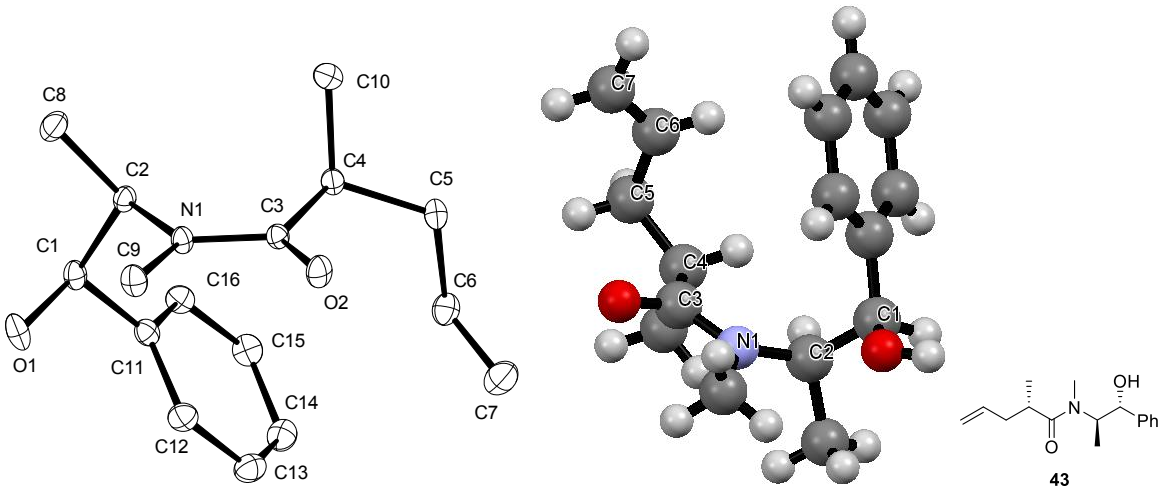


Figure 6.22: X-Ray single crystal structure and molecular structure of pseudoephedrine amide **43** (numbering of atoms is arbitrary).

Identification code	9834	
Empirical formula	$C_{16}H_{23}NO_2$	
Color	colorless	
Formula weight	261.35 g·mol^{-1}	
Temperature	100.15 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$ (No. 19)	
Unit cell dimensions	a = 6.2777(3) Å	α = 90°.
	b = 15.0357(11) Å	β = 90°.
	c = 15.1634(10) Å	γ = 90°.
Volume	1431.27(16) Å^3	
Z	4	
Density (calculated)	1.213 Mg·m^{-3}	
Absorption coefficient	0.079 mm^{-1}	
F(000)	568 e	
Crystal size	0.41 x 0.16 x 0.06 mm^3	
θ range for data collection	3.765 to 36.093°.	
Index ranges	$-10 \leq h \leq 10$, $-24 \leq k \leq 24$, $-24 \leq l \leq 25$	

Reflections collected	50631	
Independent reflections	6804 [R_{int} = 0.0278]	
Reflections with I>2σ(I)	6525	
Completeness to θ = 27.500°	99.2%	
Absorption correction	Gaussian	
Max. and min. transmission	0.7471 and 0.6765	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	6804/0/185	
Goodness-of-fit on F^2	1.105	
Final R indices [I>2σ(I)]	R_1 = 0.0287	wR^2 = 0.0775
R indices (all data)	R_1 = 0.0312	wR^2 = 0.0794
Absolute structure parameter	0.1(6)	
Largest diff. peak and hole	0.315 and -0.188 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(1)-C(1)	1.4174(10)	O(2)-C(3)	1.2408(9)
N(1)-C(2)	1.4730(9)	N(1)-C(3)	1.3535(9)
N(1)-C(9)	1.4666(10)	C(1)-C(2)	1.5470(11)
C(1)-C(11)	1.5156(11)	C(2)-C(8)	1.5282(11)
C(3)-C(4)	1.5270(11)	C(4)-C(5)	1.5315(11)
C(4)-C(10)	1.5369(12)	C(5)-C(6)	1.4975(12)
C(6)-C(7)	1.3262(13)	C(7)-H(7A)	1.002(16)
C(7)-H(7B)	0.998(18)	C(11)-C(12)	1.3947(11)
C(11)-C(16)	1.3984(11)	C(12)-C(13)	1.3927(12)
C(13)-C(14)	1.3900(13)	C(14)-C(15)	1.3939(13)
C(15)-C(16)	1.3932(12)	C(3)-N(1)-C(2)	124.96(6)
C(3)-N(1)-C(9)	115.88(6)	C(9)-N(1)-C(2)	118.91(6)
O(1)-C(1)-C(2)	108.97(6)	O(1)-C(1)-C(11)	112.38(7)
C(11)-C(1)-C(2)	111.05(6)	N(1)-C(2)-C(1)	112.42(6)
N(1)-C(2)-C(8)	111.91(6)	C(8)-C(2)-C(1)	111.55(6)
O(2)-C(3)-N(1)	119.61(7)	O(2)-C(3)-C(4)	120.82(7)
N(1)-C(3)-C(4)	119.34(6)	C(3)-C(4)-C(5)	112.55(6)
C(3)-C(4)-C(10)	107.52(6)	C(5)-C(4)-C(10)	110.70(6)
C(6)-C(5)-C(4)	113.44(7)	C(7)-C(6)-C(5)	124.84(8)
C(6)-C(7)-H(7A)	120.3(9)	C(6)-C(7)-H(7B)	120.4(11)
H(7A)-C(7)-H(7B)	119.0(14)	C(12)-C(11)-C(1)	121.41(7)
C(12)-C(11)-C(16)	118.80(7)	C(16)-C(11)-C(1)	119.77(7)
C(13)-C(12)-C(11)	120.49(7)	C(14)-C(13)-C(12)	120.40(8)
C(13)-C(14)-C(15)	119.62(8)	C(16)-C(15)-C(14)	119.88(8)
C(15)-C(16)-C(11)	120.80(7)		

6.4.3. Crystallographic Data Of 40a

Crystal Data & Structure Refinement

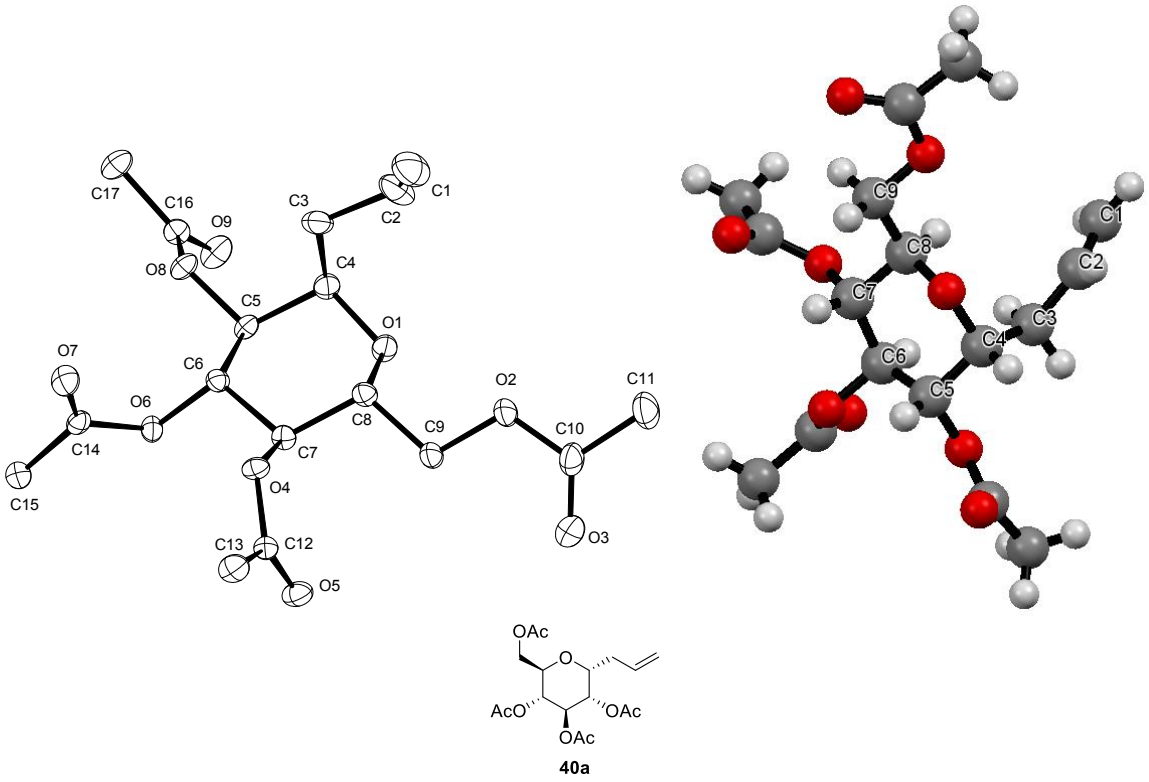


Figure 6.23: X-Ray single crystal structure and molecular structure of alkene **40a** (numbering of atoms is arbitrary).

Identification code	9875	
Empirical formula	$C_{17}H_{24}O_9$	
Color	colorless	
Formula weight	372.36 g·mol^{-1}	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$ (No. 19)	
Unit cell dimensions	a = 5.4396(2) Å	α = 90°.
	b = 14.3397(6) Å	β = 90°.
	c = 24.1983(10) Å	γ = 90°.
Volume	1887.52(13) Å^3	
Z	4	
Density (calculated)	1.310 Mg·m^{-3}	

Absorption coefficient	0.907 mm^{-1}	
F(000)	792 e	
Crystal size	0.640 x 0.130 x 0.070 mm^3	
θ range for data collection	3.583 to 67.487°.	
Index ranges	$-6 \leq h \leq 6$, $-17 \leq k \leq 17$, $-28 \leq l \leq 28$	
Reflections collected	85906	
Independent reflections	3403 [R_{int} = 0.0458]	
Reflections with I>2σ(I)	3321	
Completeness to θ = 67.487°	100.0%	
Absorption correction	Gaussian	
Max. and min. transmission	0.94 and 0.76	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	3403/0/239	
Goodness-of-fit on F^2	1.065	
Final R indices [I>2σ (I)]	R_1 = 0.0270	wR^2 = 0.0685
R indices (all data)	R_1 = 0.0278	wR^2 = 0.0692
Absolute structure parameter	-0.01(4)	
Largest diff. peak and hole	0.1 and -0.2 $e \cdot Å^{-3}$	

Bond Lengths [Å] & Angles [°]

O(1)-C(4)	1.433(2)	O(1)-C(8)	1.427(2)
O(2)-C(9)	1.444(2)	O(2)-C(10)	1.342(2)
O(3)-C(10)	1.204(3)	O(4)-C(7)	1.447(2)
O(4)-C(12)	1.358(2)	O(5)-C(12)	1.206(2)
O(6)-C(6)	1.4448(19)	O(6)-C(14)	1.353(2)
O(7)-C(14)	1.200(2)	O(8)-C(5)	1.450(2)
O(8)-C(16)	1.353(2)	O(9)-C(16)	1.204(2)
C(1)-C(2)	1.310(3)	C(2)-C(3)	1.500(3)
C(3)-C(4)	1.532(3)	C(4)-C(5)	1.532(2)
C(5)-C(6)	1.516(2)	C(6)-C(7)	1.519(2)
C(7)-C(8)	1.534(2)	C(8)-C(9)	1.505(2)
C(10)-C(11)	1.499(3)	C(12)-C(13)	1.488(3)
C(14)-C(15)	1.495(2)	C(16)-C(17)	1.494(3)
C(8)-O(1)-C(4)	113.88(12)	C(10)-O(2)-C(9)	114.91(14)
C(12)-O(4)-C(7)	118.52(14)	C(14)-O(6)-C(6)	118.11(12)
C(16)-O(8)-C(5)	117.08(14)	C(1)-C(2)-C(3)	124.0(2)
C(2)-C(3)-C(4)	113.52(18)	O(1)-C(4)-C(3)	114.36(14)
O(1)-C(4)-C(5)	107.96(14)	C(3)-C(4)-C(5)	112.71(16)
O(8)-C(5)-C(4)	109.65(14)	O(8)-C(5)-C(6)	105.37(13)

C(6)-C(5)-C(4)	110.95(13)	O(6)-C(6)-C(5)	107.61(13)
O(6)-C(6)-C(7)	107.51(13)	C(5)-C(6)-C(7)	111.81(13)
O(4)-C(7)-C(6)	105.34(14)	O(4)-C(7)-C(8)	108.81(13)
C(6)-C(7)-C(8)	112.32(13)	O(1)-C(8)-C(7)	109.77(13)
O(1)-C(8)-C(9)	106.59(14)	C(9)-C(8)-C(7)	109.92(14)
O(2)-C(9)-C(8)	108.14(14)	O(2)-C(10)-C(11)	111.65(17)
O(3)-C(10)-O(2)	123.12(17)	O(3)-C(10)-C(11)	125.23(18)
O(4)-C(12)-C(13)	110.72(15)	O(5)-C(12)-O(4)	123.07(16)
O(5)-C(12)-C(13)	126.20(16)	O(6)-C(14)-C(15)	109.98(14)
O(7)-C(14)-O(6)	124.11(15)	O(7)-C(14)-C(15)	125.91(16)
O(8)-C(16)-C(17)	111.19(15)	O(9)-C(16)-O(8)	123.20(16)
O(9)-C(16)-C(17)	125.57(17)		

6.4.4. Crystallographic Data Of 40b

Crystal Data & Structure Refinement

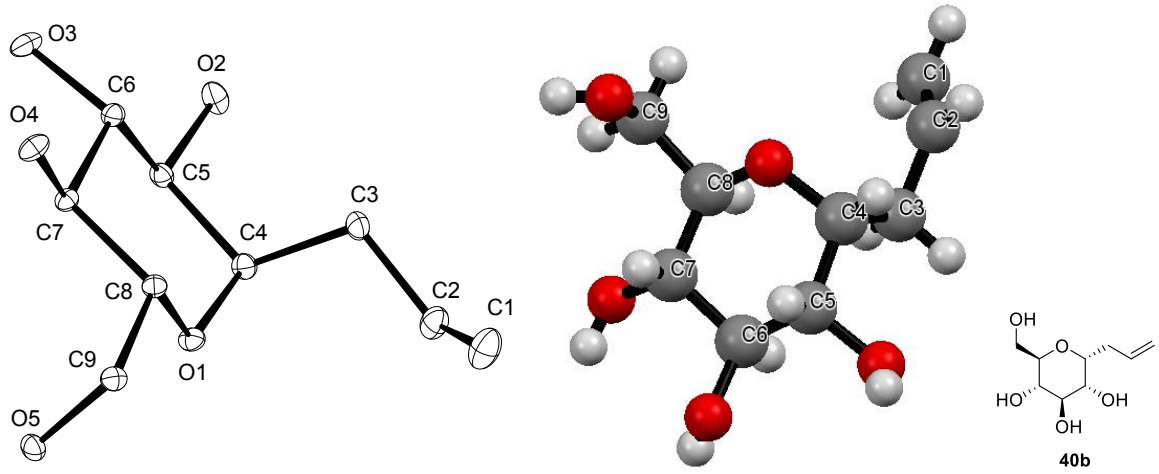


Figure 6.24: X-Ray single crystal structure and molecular structure of alkene **40b** (numbering of atoms is arbitrary).

Identification code	9888sadabs	
Empirical formula	$C_9H_{16}O_5$	
Color	colourless	
Formula weight	204.22 g·mol$_{-1}$	
Temperature	100.15 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_1\ 2_1\ 2_1$ (No. 19)	
Unit cell dimensions	a = 6.1229(3) Å	α = 90°.
	b = 11.0919(7) Å	β = 90°.
	c = 14.4098(8) Å	γ = 90°.
Volume	978.64(10) Å^3	
Z	4	
Density (calculated)	1.386 Mg·m^{-3}	
Absorption coefficient	0.113 mm^{-1}	
F(000)	440 e	
Crystal size	0.26 x 0.10 x 0.05 mm^3	
θ range for data collection	2.827 to 33.092°.	
Index ranges	$-9 \le h \le 9, -17 \le k \le 17, -22 \le l \le 22$	
Reflections collected	21965	
Independent reflections	3674 [R_{int} = 0.0337]	

Reflections with I>2σ(I)	3250	
Completeness to θ = 25.242°	99.8%	
Absorption correction	Gaussian	
Max. and min. transmission	0.99502 and 0.97396	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	3674/0/151	
Goodness-of-fit on F^2	1.201	
Final R indices [I>2σ (I)]	R_1 = 0.0402	wR^2 = 0.0924
R indices (all data)	R_1 = 0.0522	wR^2 = 0.0979
Absolute structure parameter	0.2(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.336 and -0.272 e·$Å^{-3}$	

Bond lengths [Å] & Angles [°]

O(1)-C(4)	1.4421(19)	O(1)-C(8)	1.4351(19)
O(2)-H(2)	0.78(3)	O(2)-C(5)	1.4318(19)
O(3)-H(3)	0.78(3)	O(3)-C(6)	1.4247(19)
O(4)-H(4)	0.85(3)	O(4)-C(7)	1.4308(19)
O(5)-H(5)	0.80(3)	O(5)-C(9)	1.434(2)
C(1)-C(2)	1.325(3)	C(2)-C(3)	1.501(2)
C(3)-C(4)	1.535(2)	C(4)-C(5)	1.539(2)
C(5)-C(6)	1.525(2)	C(6)-C(7)	1.531(2)
C(7)-C(8)	1.525(2)	C(8)-C(9)	1.521(2)
C(9)-H(9A)	0.98(2)	C(9)-H(9B)	1.01(2)
C(8)-O(1)-C(4)	114.99(12)	C(6)-O(3)-H(3)	108(2)
C(7)-O(4)-H(4)	111.3(19)	C(9)-O(5)-H(5)	108.3(18)
C(1)-C(2)-C(3)	125.12(17)	C(2)-C(3)-C(4)	109.93(14)
O(1)-C(4)-C(3)	111.72(13)	O(1)-C(4)-C(5)	108.86(12)
C(3)-C(4)-C(5)	115.76(13)	O(2)-C(5)-C(4)	109.28(13)
O(2)-C(5)-C(6)	110.65(13)	C(6)-C(5)-C(4)	112.29(13)
O(3)-C(6)-C(5)	107.84(13)	O(3)-C(6)-C(7)	109.86(13)
C(5)-C(6)-C(7)	109.89(12)	O(4)-C(7)-C(6)	111.45(13)
O(4)-C(7)-C(8)	106.85(12)	C(8)-C(7)-C(6)	110.79(13)
O(1)-C(8)-C(7)	108.94(12)	O(1)-C(8)-C(9)	106.30(12)
C(9)-C(8)-C(7)	114.59(13)	O(5)-C(9)-C(8)	111.23(12)
O(5)-C(9)-H(9A)	105.7(14)	O(5)-C(9)-H(9B)	111.7(14)
C(8)-C(9)-H(9A)	111.3(14)	C(8)-C(9)-H(9B)	110.3(14)
H(9A)-C(9)-H(9B)	106.3(19)		

6.4.5. Crystallographic Data Of 57

Crystal Data & Structure Refinement

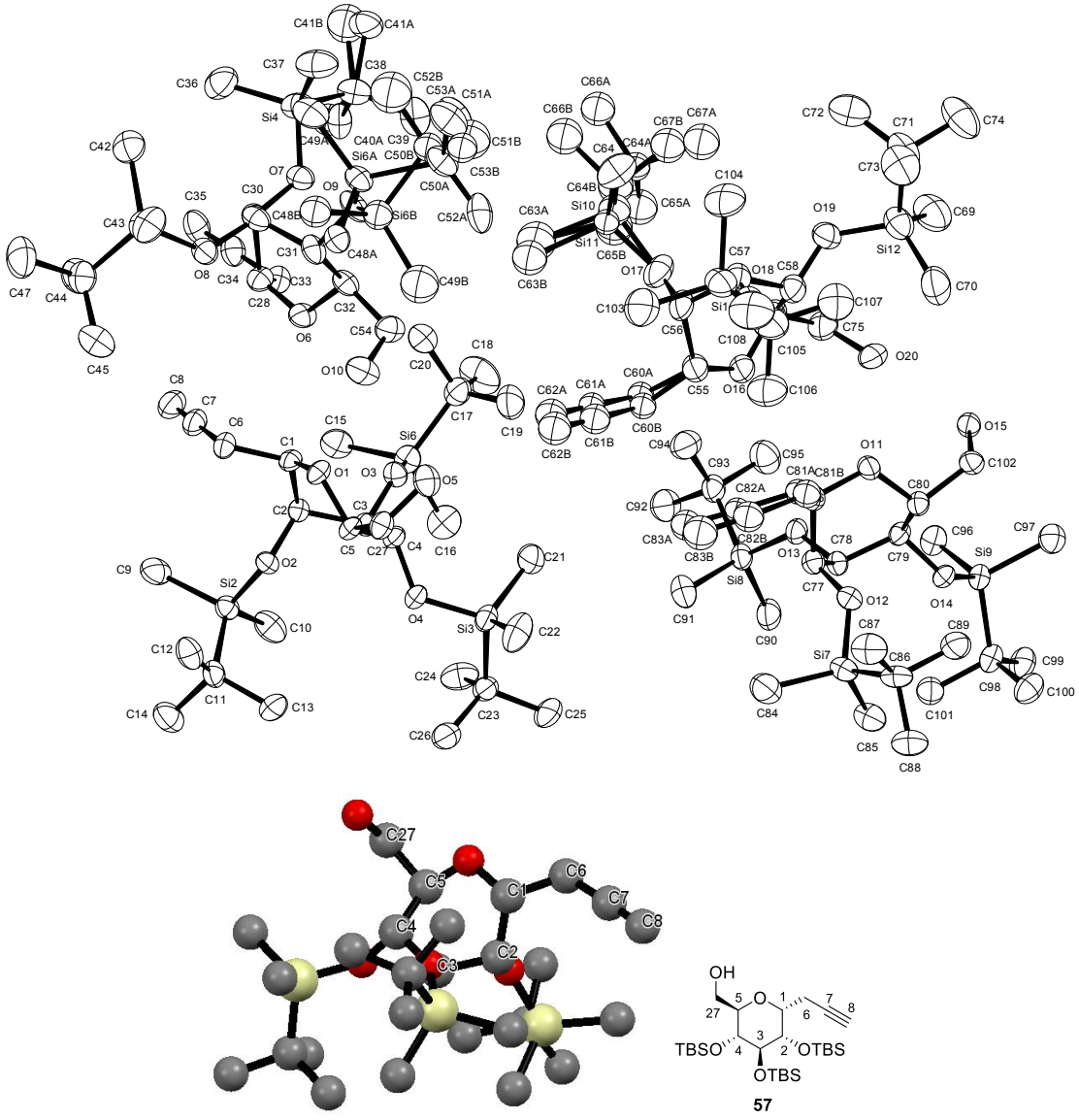


Figure 6.25: X-Ray single crystal structure and molecular structure of primary alcohol **57** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary).

Identification code	9540sadabs
Empirical formula	$C_{27}H_{56}O_5Si_3$
Color	colourless
Formula weight	544.98 g·mol^{-1}
Temperature	100 K
Wavelength	1.54178 Å

Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 20.9651(9) Å	α = 90°.
	b = 11.2610(5) Å	β = 91.742(2)°.
	c = 29.2979(13) Å	γ = 90°.
Volume	6913.7(5) $Å^3$	
Z	8	
Density (calculated)	1.047 $Mg·m^{-3}$	
Absorption coefficient	1.492 mm^{-1}	
F(000)	2400 e	
Crystal size	0.20 x 0.20 x 0.13 mm^3	
θ range for data collection	1.508 to 67.831°.	
Index ranges	$-24 \leq h \leq 24$, $-13 \leq k \leq 13$, $-32 \leq l \leq 34$	
Reflections collected	163068	
Independent reflections	24037 [R_{int} = 0.0902]	
Reflections with I>2σ(I)	19755	
Completeness to θ = 67.679°	97.7%	
Absorption correction	Gaussian	
Max. and min. transmission	0.84407 and 0.76252	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	24037/9/1360	
Goodness-of-fit on F^2	1.089	
Final R indices [I>2σ(I)]	R_1 = 0.0684	wR^2 = 0.1709
R indices (all data)	R_1 = 0.0829	wR^2 = 0.1812
Absolute structure parameter	0.03(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.758 and -0.956 $e·Å^{-3}$	

Bond Lengths [Å] & Angles [°]

Si(11)-O(17)	1.610(6)	Si(11)-C(63B)	1.909(18)
Si(11)-C(64B)	1.704(17)	Si(11)-C(64)	1.798(9)
Si(10)-O(17)	1.705(7)	Si(10)-C(63A)	1.89(2)
Si(10)-C(64A)	1.691(17)	Si(10)-C(64)	2.027(9)
Si(12)-O(19)	1.642(5)	Si(12)-C(70)	1.839(9)
Si(12)-C(71)	1.888(8)	Si(12)-C(69)	1.840(9)
Si(1)-O(18)	1.647(5)	Si(1)-C(105)	1.884(9)

Si(1)-C(104)	1.860(8)	Si(1)-C(103)	1.862(9)
O(16)-C(59)	1.459(8)	O(16)-C(55)	1.436(8)
O(20)-H(20)	0.8400	O(20)-C(75)	1.427(8)
O(17)-C(56)	1.413(9)	O(18)-C(57)	1.425(8)
O(19)-C(58)	1.418(7)	C(70)-H(70A)	0.9800
C(70)-H(70B)	0.9800	C(70)-H(70C)	0.9800
C(105)-C(107)	1.541(11)	C(105)-C(106)	1.526(11)
C(105)-C(108)	1.539(11)	C(71)-C(72)	1.550(12)
C(71)-C(73)	1.554(11)	C(71)-C(74)	1.517(10)
C(72)-H(72A)	0.9800	C(72)-H(72B)	0.9800
C(72)-H(72C)	0.9800	C(59)-H(59)	1.0000
C(59)-C(75)	1.503(9)	C(59)-C(58)	1.520(9)
C(73)-H(73A)	0.9800	C(73)-H(73B)	0.9800
C(73)-H(73C)	0.9800	C(74)-H(74A)	0.9800
C(74)-H(74B)	0.9800	C(74)-H(74C)	0.9800
C(75)-H(75A)	0.9900	C(75)-H(75B)	0.9900
C(63B)-H(63A)	0.9800	C(63B)-H(63B)	0.9800
C(63B)-H(63C)	0.9800	C(63A)-H(63D)	0.9800
C(63A)-H(63E)	0.9800	C(63A)-H(63F)	0.9800
C(60B)-H(60A)	0.9900	C(60B)-H(60B)	0.9900
C(60B)-C(61B)	1.47(2)	C(60B)-C(55)	1.516(15)
C(61B)-C(62B)	1.17(3)	C(62B)-H(62B)	0.9500
C(107)-H(10A)	0.9800	C(107)-H(10B)	0.9800
C(107)-H(10C)	0.9800	C(64B)-C(66B)	1.64(2)
C(64B)-C(65B)	1.61(2)	C(64B)-C(67B)	1.49(2)
C(64A)-C(65A)	1.53(2)	C(64A)-C(67A)	1.60(2)
C(64A)-C(66A)	1.56(2)	C(106)-H(10D)	0.9800
C(106)-H(10E)	0.9800	C(106)-H(10F)	0.9800
C(57)-H(57)	1.0000	C(57)-C(58)	1.549(9)
C(57)-C(56)	1.515(8)	C(65A)-H(65A)	0.9800
C(65A)-H(65B)	0.9800	C(65A)-H(65C)	0.9800
C(61A)-C(60A)	1.48(2)	C(61A)-C(62A)	1.19(3)
C(108)-H(10G)	0.9800	C(108)-H(10H)	0.9800
C(108)-H(10I)	0.9800	C(67A)-H(67A)	0.9800
C(67A)-H(67B)	0.9800	C(67A)-H(67C)	0.9800
C(104)-H(10J)	0.9800	C(104)-H(10K)	0.9800
C(104)-H(10L)	0.9800	C(66A)-H(66A)	0.9800
C(66A)-H(66B)	0.9800	C(66A)-H(66C)	0.9800
C(103)-H(10M)	0.9800	C(103)-H(10N)	0.9800
C(103)-H(10O)	0.9800	C(66B)-H(66D)	0.9800
C(66B)-H(66E)	0.9800	C(66B)-H(66F)	0.9800
C(58)-H(58)	1.0000	C(60A)-H(60C)	0.9900
C(60A)-H(60D)	0.9900	C(60A)-C(55)	1.569(15)
C(62A)-H(62A)	0.9500	C(64)-H(64D)	0.9800
C(64)-H(64E)	0.9800	C(64)-H(64F)	0.9800
C(64)-H(64A)	0.9800	C(64)-H(64B)	0.9800
C(64)-H(64C)	0.9800	C(55)-H(55A)	1.0000
C(55)-H(55)	1.0000	C(55)-C(56)	1.523(8)
C(56)-H(56)	1.0000	C(65B)-H(65D)	0.9800

C(65B)-H(65E)	0.9800	C(65B)-H(65F)	0.9800
C(67B)-H(67D)	0.9800	C(67B)-H(67E)	0.9800
C(67B)-H(67F)	0.9800	C(69)-H(69A)	0.9800
C(69)-H(69B)	0.9800	C(69)-H(69C)	0.9800
Si(6B)-O(9)	1.777(6)	Si(6B)-C(49B)	1.85(2)
Si(6B)-C(50B)	1.89(3)	Si(6B)-C(48B)	1.76(2)
Si(5)-O(8)	1.643(4)	Si(5)-C(42)	1.868(8)
Si(5)-C(43)	1.862(7)	Si(5)-C(44)	1.878(7)
Si(4)-O(7)	1.636(4)	Si(4)-C(36)	1.859(8)
Si(4)-C(37)	1.841(8)	Si(4)-C(38)	1.874(7)
Si(6A)-O(9)	1.639(4)	Si(6A)-C(50A)	1.924(17)
Si(6A)-C(48A)	1.845(10)	Si(6A)-C(49A)	1.844(12)
O(10)-H(10)	0.8400	O(10)-C(54)	1.442(8)
O(7)-C(29)	1.437(7)	O(6)-C(28)	1.443(7)
O(6)-C(32)	1.439(6)	O(9)-C(31)	1.428(6)
O(8)-C(30)	1.435(7)	C(49B)-H(49A)	0.9800
C(49B)-H(49B)	0.9800	C(49B)-H(49C)	0.9800
C(53A)-H(53A)	0.9800	C(53A)-H(53B)	0.9800
C(53A)-H(53C)	0.9800	C(53A)-C(50A)	1.50(2)
C(28)-H(28)	1.0000	C(28)-C(29)	1.525(7)
C(28)-C(33)	1.522(8)	C(29)-H(29)	1.0000
C(29)-C(30)	1.529(8)	C(30)-H(30)	1.0000
C(30)-C(31)	1.544(8)	C(31)-H(31)	1.0000
C(31)-C(32)	1.517(8)	C(32)-H(32)	1.0000
C(32)-C(54)	1.518(8)	C(52A)-H(52A)	0.9800
C(52A)-H(52B)	0.9800	C(52A)-H(52C)	0.9800
C(52A)-C(50A)	1.43(2)	C(33)-H(33A)	0.9900
C(33)-H(33B)	0.9900	C(33)-C(34)	1.466(8)
C(54)-H(54A)	0.9900	C(54)-H(54B)	0.9900
C(34)-C(35)	1.184(9)	C(52B)-H(52D)	0.9800
C(52B)-H(52E)	0.9800	C(52B)-H(52F)	0.9800
C(52B)-C(50B)	1.49(4)	C(40B)-H(40A)	0.9800
C(40B)-H(40B)	0.9800	C(40B)-H(40C)	0.9800
C(40B)-C(38)	1.61(5)	C(35)-H(35)	0.9500
C(41B)-H(41A)	0.9800	C(41B)-H(41B)	0.9800
C(41B)-H(41C)	0.9800	C(41B)-C(38)	1.60(4)
C(36)-H(36A)	0.9800	C(36)-H(36B)	0.9800
C(36)-H(36C)	0.9800	C(37)-H(37A)	0.9800
C(37)-H(37B)	0.9800	C(37)-H(37C)	0.9800
C(50A)-C(51A)	1.68(2)	C(51A)-H(51A)	0.9800
C(51A)-H(51B)	0.9800	C(51A)-H(51C)	0.9800
C(38)-C(39)	1.528(10)	C(38)-C(40A)	1.50(3)
C(38)-C(41A)	1.526(17)	C(39)-H(39A)	0.9800
C(39)-H(39B)	0.9800	C(39)-H(39C)	0.9800
C(50B)-C(51B)	1.39(4)	C(50B)-C(53B)	1.68(4)
C(40A)-H(40D)	0.9800	C(40A)-H(40E)	0.9800
C(40A)-H(40F)	0.9800	C(41A)-H(41D)	0.9800
C(41A)-H(41E)	0.9800	C(41A)-H(41F)	0.9800
C(42)-H(42A)	0.9800	C(42)-H(42B)	0.9800

C(42)-H(42C)	0.9800	C(51B)-H(51D)	0.9800
C(51B)-H(51E)	0.9800	C(51B)-H(51F)	0.9800
C(53B)-H(53D)	0.9800	C(53B)-H(53E)	0.9800
C(53B)-H(53F)	0.9800	C(43)-H(43A)	0.9800
C(43)-H(43B)	0.9800	C(43)-H(43C)	0.9800
C(48B)-H(48A)	0.9800	C(48B)-H(48B)	0.9800
C(48B)-H(48C)	0.9800	C(44)-C(45)	1.541(11)
C(44)-C(46)	1.527(9)	C(44)-C(47)	1.549(10)
C(45)-H(45A)	0.9800	C(45)-H(45B)	0.9800
C(45)-H(45C)	0.9800	C(46)-H(46A)	0.9800
C(46)-H(46B)	0.9800	C(46)-H(46C)	0.9800
C(47)-H(47A)	0.9800	C(47)-H(47B)	0.9800
C(47)-H(47C)	0.9800	C(48A)-H(48D)	0.9800
C(48A)-H(48E)	0.9800	C(48A)-H(48F)	0.9800
C(49A)-H(49D)	0.9800	C(49A)-H(49E)	0.9800
C(49A)-H(49F)	0.9800	Si(9)-O(14)	1.655(4)
Si(9)-C(97)	1.846(6)	Si(9)-C(96)	1.862(6)
Si(9)-C(98)	1.886(6)	Si(7)-O(12)	1.643(4)
Si(7)-C(85)	1.861(7)	Si(7)-C(84)	1.850(7)
Si(7)-C(86)	1.887(7)	Si(8)-O(13)	1.643(4)
Si(8)-C(91)	1.842(7)	Si(8)-C(93)	1.872(6)
Si(8)-C(90)	1.855(6)	O(13)-C(78)	1.433(6)
O(12)-C(77)	1.432(6)	O(15)-H(15)	0.8400
O(15)-C(102)	1.427(7)	O(14)-C(79)	1.427(6)
O(11)-C(76)	1.441(6)	O(11)-C(80)	1.446(6)
C(78)-H(78)	1.0000	C(78)-C(79)	1.545(7)
C(78)-C(77)	1.530(7)	C(91)-H(91A)	0.9800
C(91)-H(91B)	0.9800	C(91)-H(91C)	0.9800
C(83A)-H(83A)	0.9500	C(83A)-C(82A)	1.21(2)
C(99)-H(99A)	0.9800	C(99)-H(99B)	0.9800
C(99)-H(99C)	0.9800	C(99)-C(98)	1.539(8)
C(82B)-C(81B)	1.47(3)	C(82B)-C(83B)	1.18(2)
C(87)-H(87A)	0.9800	C(87)-H(87B)	0.9800
C(87)-H(87C)	0.9800	C(87)-C(86)	1.522(9)
C(95)-H(95A)	0.9800	C(95)-H(95B)	0.9800
C(95)-H(95C)	0.9800	C(95)-C(93)	1.524(9)
C(76)-H(76A)	1.0000	C(76)-H(76)	1.0000
C(76)-C(81A)	1.47(2)	C(76)-C(77)	1.524(7)
C(76)-C(81B)	1.58(2)	C(79)-H(79)	1.0000
C(79)-C(80)	1.523(7)	C(81A)-H(81A)	0.9900
C(81A)-H(81B)	0.9900	C(81A)-C(82A)	1.46(2)
C(85)-H(85A)	0.9800	C(85)-H(85B)	0.9800
C(85)-H(85C)	0.9800	C(89)-H(89A)	0.9800
C(89)-H(89B)	0.9800	C(89)-H(89C)	0.9800
C(89)-C(86)	1.526(9)	C(93)-C(92)	1.537(8)
C(93)-C(94)	1.540(9)	C(97)-H(97A)	0.9800
C(97)-H(97B)	0.9800	C(97)-H(97C)	0.9800
C(101)-H(10P)	0.9800	C(101)-H(10Q)	0.9800
C(101)-H(10R)	0.9800	C(101)-C(98)	1.547(8)

C(77)-H(77)	1.0000	C(81B)-H(81C)	0.9900
C(81B)-H(81D)	0.9900	C(80)-H(80)	1.0000
C(80)-C(102)	1.515(7)	C(83B)-H(83B)	0.9500
C(84)-H(84A)	0.9800	C(84)-H(84B)	0.9800
C(84)-H(84C)	0.9800	C(86)-C(88)	1.538(8)
C(88)-H(88A)	0.9800	C(88)-H(88B)	0.9800
C(88)-H(88C)	0.9800	C(90)-H(90A)	0.9800
C(90)-H(90B)	0.9800	C(90)-H(90C)	0.9800
C(92)-H(92A)	0.9800	C(92)-H(92B)	0.9800
C(92)-H(92C)	0.9800	C(94)-H(94A)	0.9800
C(94)-H(94B)	0.9800	C(94)-H(94C)	0.9800
C(96)-H(96A)	0.9800	C(96)-H(96B)	0.9800
C(96)-H(96C)	0.9800	C(98)-C(100)	1.527(8)
C(100)-H(10S)	0.9800	C(100)-H(10T)	0.9800
C(100)-H(10U)	0.9800	C(102)-H(10V)	0.9900
C(102)-H(10W)	0.9900	Si(2)-O(2)	1.650(3)
Si(2)-C(9)	1.855(6)	Si(2)-C(11)	1.863(6)
Si(2)-C(10)	1.857(7)	Si(3)-O(4)	1.648(4)
Si(3)-C(21)	1.859(8)	Si(3)-C(23)	1.885(6)
Si(3)-C(22)	1.838(7)	Si(6)-O(3)	1.636(4)
Si(6)-C(15)	1.850(7)	Si(6)-C(17)	1.884(7)
Si(6)-C(16)	1.851(7)	O(5)-H(5)	0.8400
O(5)-C(27)	1.423(7)	O(4)-C(4)	1.429(6)
O(1)-C(1)	1.430(6)	O(1)-C(5)	1.449(6)
O(3)-C(3)	1.433(6)	O(2)-C(2)	1.432(6)
C(1)-H(1)	1.0000	C(1)-C(2)	1.513(7)
C(1)-C(6)	1.536(7)	C(3)-H(3)	1.0000
C(3)-C(2)	1.533(7)	C(3)-C(4)	1.535(7)
C(5)-H(5A)	1.0000	C(5)-C(27)	1.525(7)
C(5)-C(4)	1.515(7)	C(7)-C(6)	1.462(8)
C(7)-C(8)	1.188(9)	C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800	C(9)-H(9C)	0.9800
C(11)-C(13)	1.542(8)	C(11)-C(12)	1.549(9)
C(11)-C(14)	1.544(8)	C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800	C(13)-H(13C)	0.9800
C(15)-H(15A)	0.9800	C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800	C(17)-C(19)	1.509(9)
C(17)-C(18)	1.515(10)	C(17)-C(20)	1.521(9)
C(19)-H(19A)	0.9800	C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800	C(21)-H(21A)	0.9800
C(21)-H(21B)	0.9800	C(21)-H(21C)	0.9800
C(23)-C(25)	1.510(8)	C(23)-C(24)	1.534(9)
C(23)-C(26)	1.530(9)	C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800	C(25)-H(25C)	0.9800
C(27)-H(27A)	0.9900	C(27)-H(27B)	0.9900
C(2)-H(2)	1.0000	C(4)-H(4)	1.0000
C(6)-H(6A)	0.9900	C(6)-H(6B)	0.9900
C(8)-H(8)	0.9500	C(10)-H(10X)	0.9800
C(10)-H(10Y)	0.9800	C(10)-H	0.9800

C(12)-H(12A)	0.9800	C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800	C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800	C(14)-H(14C)	0.9800
C(16)-H(16A)	0.9800	C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800	C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800	C(18)-H(18C)	0.9800
C(20)-H(20A)	0.9800	C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800	C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800	C(22)-H(22C)	0.9800
C(24)-H(24A)	0.9800	C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800	C(26)-H(26A)	0.9800
C(26)-H(26B)	0.9800	C(26)-H(26C)	0.9800
O(17)-Si(11)-C(63B)	112.0(6)	O(17)-Si(11)-C(64B)	97.7(7)
O(17)-Si(11)-C(64)	115.9(4)	C(64B)-Si(11)-C(63B)	112.0(9)
C(64B)-Si(11)-C(64)	110.5(7)	C(64)-Si(11)-C(63B)	108.5(7)
O(17)-Si(10)-C(63A)	104.0(7)	O(17)-Si(10)-C(64)	101.2(4)
C(63A)-Si(10)-C(64)	101.6(8)	C(64A)-Si(10)-O(17)	114.9(6)
C(64A)-Si(10)-C(63A)	117.1(10)	C(64A)-Si(10)-C(64)	115.8(6)
O(19)-Si(12)-C(70)	111.4(3)	O(19)-Si(12)-C(71)	104.8(3)
O(19)-Si(12)-C(69)	108.8(3)	C(70)-Si(12)-C(71)	112.4(4)
C(70)-Si(12)-C(69)	109.6(4)	C(69)-Si(12)-C(71)	109.8(4)
O(18)-Si(1)-C(105)	103.2(3)	O(18)-Si(1)-C(104)	110.0(3)
O(18)-Si(1)-C(103)	112.5(3)	C(104)-Si(1)-C(105)	111.8(4)
C(104)-Si(1)-C(103)	109.2(4)	C(103)-Si(1)-C(105)	110.2(4)
C(55)-O(16)-C(59)	116.1(4)	C(75)-O(20)-H(20)	109.5
C(56)-O(17)-Si(11)	122.8(5)	C(56)-O(17)-Si(10)	139.6(5)
C(57)-O(18)-Si(1)	130.2(4)	C(58)-O(19)-Si(12)	130.6(4)
Si(12)-C(70)-H(70A)	109.5	Si(12)-C(70)-H(70B)	109.5
Si(12)-C(70)-H(70C)	109.5	H(70A)-C(70)-H(70B)	109.5
H(70A)-C(70)-H(70C)	109.5	H(70B)-C(70)-H(70C)	109.5
C(107)-C(105)-Si(1)	109.4(6)	C(106)-C(105)-Si(1)	109.9(5)
C(106)-C(105)-C(107)	109.2(7)	C(106)-C(105)-C(108)	109.0(7)
C(108)-C(105)-Si(1)	111.3(6)	C(108)-C(105)-C(107)	108.1(7)
C(72)-C(71)-Si(12)	110.2(5)	C(72)-C(71)-C(73)	107.7(7)
C(73)-C(71)-Si(12)	109.2(6)	C(74)-C(71)-Si(12)	111.4(6)
C(74)-C(71)-C(72)	108.6(7)	C(74)-C(71)-C(73)	109.7(6)
C(71)-C(72)-H(72A)	109.5	C(71)-C(72)-H(72B)	109.5
C(71)-C(72)-H(72C)	109.5	H(72A)-C(72)-H(72B)	109.5
H(72A)-C(72)-H(72C)	109.5	H(72B)-C(72)-H(72C)	109.5
O(16)-C(59)-H(59)	108.8	O(16)-C(59)-C(75)	106.7(5)
O(16)-C(59)-C(58)	108.2(5)	C(75)-C(59)-H(59)	108.8
C(75)-C(59)-C(58)	115.5(5)	C(58)-C(59)-H(59)	108.8
C(71)-C(73)-H(73A)	109.5	C(71)-C(73)-H(73B)	109.5
C(71)-C(73)-H(73C)	109.5	H(73A)-C(73)-H(73B)	109.5
H(73A)-C(73)-H(73C)	109.5	H(73B)-C(73)-H(73C)	109.5
C(71)-C(74)-H(74A)	109.5	C(71)-C(74)-H(74B)	109.5
C(71)-C(74)-H(74C)	109.5	H(74A)-C(74)-H(74B)	109.5
H(74A)-C(74)-H(74C)	109.5	H(74B)-C(74)-H(74C)	109.5
O(20)-C(75)-C(59)	113.7(6)	O(20)-C(75)-H(75A)	108.8

O(20)-C(75)-H(75B)	108.8	C(59)-C(75)-H(75A)	108.8
C(59)-C(75)-H(75B)	108.8	H(75A)-C(75)-H(75B)	107.7
Si(11)-C(63B)-H(63A)	109.5	Si(11)-C(63B)-H(63B)	109.5
Si(11)-C(63B)-H(63C)	109.5	H(63A)-C(63B)-H(63B)	109.5
H(63A)-C(63B)-H(63C)	109.5	H(63B)-C(63B)-H(63C)	109.5
Si(10)-C(63A)-H(63D)	109.5	Si(10)-C(63A)-H(63E)	109.5
Si(10)-C(63A)-H(63F)	109.5	H(63D)-C(63A)-H(63E)	109.5
H(63D)-C(63A)-H(63F)	109.5	H(63E)-C(63A)-H(63F)	109.5
H(60A)-C(60B)-H(60B)	107.1	C(61B)-C(60B)-H(60A)	107.8
C(61B)-C(60B)-H(60B)	107.8	C(61B)-C(60B)-C(55)	118.2(12)
C(55)-C(60B)-H(60A)	107.8	C(55)-C(60B)-H(60B)	107.8
C(62B)-C(61B)-C(60B)	176(2)	C(61B)-C(62B)-H(62B)	180.0
C(105)-C(107)-H(10A)	109.5	C(105)-C(107)-H(10B)	109.5
C(105)-C(107)-H(10C)	109.5	H(10A)-C(107)-H(10B)	109.5
H(10A)-C(107)-H(10C)	109.5	H(10B)-C(107)-H(10C)	109.5
C(66B)-C(64B)-Si(11)	115.3(12)	C(65B)-C(64B)-Si(11)	116.7(14)
C(65B)-C(64B)-C(66B)	101.1(13)	C(67B)-C(64B)-Si(11)	118.9(12)
C(67B)-C(64B)-C(66B)	96.1(14)	C(67B)-C(64B)-C(65B)	105.6(15)
C(65A)-C(64A)-Si(10)	107.1(12)	C(65A)-C(64A)-C(67A)	107.9(13)
C(65A)-C(64A)-C(66A)	112.9(12)	C(67A)-C(64A)-Si(10)	107.8(10)
C(66A)-C(64A)-Si(10)	116.9(11)	C(66A)-C(64A)-C(67A)	103.9(14)
C(105)-C(106)-H(10D)	109.5	C(105)-C(106)-H(10E)	109.5
C(105)-C(106)-H(10F)	109.5	H(10D)-C(106)-H(10E)	109.5
H(10D)-C(106)-H(10F)	109.5	H(10E)-C(106)-H(10F)	109.5
O(18)-C(57)-H(57)	108.6	O(18)-C(57)-C(58)	109.5(5)
O(18)-C(57)-C(56)	109.2(6)	C(58)-C(57)-H(57)	108.6
C(56)-C(57)-H(57)	108.6	C(56)-C(57)-C(58)	112.3(5)
C(64A)-C(65A)-H(65A)	109.5	C(64A)-C(65A)-H(65B)	109.5
C(64A)-C(65A)-H(65C)	109.5	H(65A)-C(65A)-H(65B)	109.5
H(65A)-C(65A)-H(65C)	109.5	H(65B)-C(65A)-H(65C)	109.5
C(62A)-C(61A)-C(60A)	177.3(16)	C(105)-C(108)-H(10G)	109.5
C(105)-C(108)-H(10H)	109.5	C(105)-C(108)-H(10I)	109.5
H(10G)-C(108)-H(10H)	109.5	H(10G)-C(108)-H(10I)	109.5
H(10H)-C(108)-H(10I)	109.5	C(64A)-C(67A)-H(67A)	109.5
C(64A)-C(67A)-H(67B)	109.5	C(64A)-C(67A)-H(67C)	109.5
H(67A)-C(67A)-H(67B)	109.5	H(67A)-C(67A)-H(67C)	109.5
H(67B)-C(67A)-H(67C)	109.5	Si(1)-C(104)-H(10J)	109.5
Si(1)-C(104)-H(10K)	109.5	Si(1)-C(104)-H(10L)	109.5
H(10J)-C(104)-H(10K)	109.5	H(10J)-C(104)-H(10L)	109.5
H(10K)-C(104)-H(10L)	109.5	C(64A)-C(66A)-H(66A)	109.5
C(64A)-C(66A)-H(66B)	109.5	C(64A)-C(66A)-H(66C)	109.5
H(66A)-C(66A)-H(66B)	109.5	H(66A)-C(66A)-H(66C)	109.5
H(66B)-C(66A)-H(66C)	109.5	Si(1)-C(103)-H(10M)	109.5
Si(1)-C(103)-H(10N)	109.5	Si(1)-C(103)-H(10O)	109.5
H(10M)-C(103)-H(10N)	109.5	H(10M)-C(103)-H(10O)	109.5
H(10N)-C(103)-H(10O)	109.5	C(64B)-C(66B)-H(66D)	109.5
C(64B)-C(66B)-H(66E)	109.5	C(64B)-C(66B)-H(66F)	109.5
H(66D)-C(66B)-H(66E)	109.5	H(66D)-C(66B)-H(66F)	109.5
H(66E)-C(66B)-H(66F)	109.5	O(19)-C(58)-C(59)	110.6(5)

O(19)-C(58)-C(57)	110.6(5)	O(19)-C(58)-H(58)	108.3
C(59)-C(58)-C(57)	110.5(5)	C(59)-C(58)-H(58)	108.3
C(57)-C(58)-H(58)	108.3	C(61A)-C(60A)-H(60C)	110.1
C(61A)-C(60A)-H(60D)	110.1	C(61A)-C(60A)-C(55)	107.9(11)
H(60C)-C(60A)-H(60D)	108.4	C(55)-C(60A)-H(60C)	110.1
C(55)-C(60A)-H(60D)	110.1	C(61A)-C(62A)-H(62A)	180.0
Si(11)-C(64)-H(64A)	109.5	Si(11)-C(64)-H(64B)	109.5
Si(11)-C(64)-H(64C)	109.5	Si(10)-C(64)-H(64D)	109.5
Si(10)-C(64)-H(64E)	109.5	Si(10)-C(64)-H(64F)	109.5
H(64D)-C(64)-H(64E)	109.5	H(64D)-C(64)-H(64F)	109.5
H(64E)-C(64)-H(64F)	109.5	H(64A)-C(64)-H(64B)	109.5
H(64A)-C(64)-H(64C)	109.5	H(64B)-C(64)-H(64C)	109.5
O(16)-C(55)-C(60B)	110.1(7)	O(16)-C(55)-C(60A)	102.4(7)
O(16)-C(55)-H(55A)	110.1	O(16)-C(55)-H(55)	105.2
O(16)-C(55)-C(56)	112.6(6)	C(60B)-C(55)-H(55)	105.2
C(60B)-C(55)-C(56)	117.4(8)	C(60A)-C(55)-H(55A)	110.1
C(56)-C(55)-C(60A)	111.2(7)	C(56)-C(55)-H(55A)	110.1
C(56)-C(55)-H(55)	105.2	O(17)-C(56)-C(57)	110.9(6)
O(17)-C(56)-C(55)	109.1(5)	O(17)-C(56)-H(56)	109.2
C(57)-C(56)-C(55)	109.3(5)	C(57)-C(56)-H(56)	109.2
C(55)-C(56)-H(56)	109.2	C(64B)-C(65B)-H(65D)	109.5
C(64B)-C(65B)-H(65E)	109.5	C(64B)-C(65B)-H(65F)	109.5
H(65D)-C(65B)-H(65E)	109.5	H(65D)-C(65B)-H(65F)	109.5
H(65E)-C(65B)-H(65F)	109.5	C(64B)-C(67B)-H(67D)	109.5
C(64B)-C(67B)-H(67E)	109.5	C(64B)-C(67B)-H(67F)	109.5
H(67D)-C(67B)-H(67E)	109.5	H(67D)-C(67B)-H(67F)	109.5
H(67E)-C(67B)-H(67F)	109.5	Si(12)-C(69)-H(69A)	109.5
Si(12)-C(69)-H(69B)	109.5	Si(12)-C(69)-H(69C)	109.5
H(69A)-C(69)-H(69B)	109.5	H(69A)-C(69)-H(69C)	109.5
H(69B)-C(69)-H(69C)	109.5	O(9)-Si(6B)-C(49B)	116.0(8)
O(9)-Si(6B)-C(50B)	95.9(9)	C(49B)-Si(6B)-C(50B)	111.8(11)
C(48B)-Si(6B)-O(9)	110.0(7)	C(48B)-Si(6B)-C(49B)	107.5(11)
C(48B)-Si(6B)-C(50B)	115.6(11)	O(8)-Si(5)-C(42)	110.6(3)
O(8)-Si(5)-C(43)	109.9(3)	O(8)-Si(5)-C(44)	105.1(2)
C(42)-Si(5)-C(44)	111.8(3)	C(43)-Si(5)-C(42)	108.2(3)
C(43)-Si(5)-C(44)	111.3(3)	O(7)-Si(4)-C(36)	110.9(3)
O(7)-Si(4)-C(37)	110.3(3)	O(7)-Si(4)-C(38)	105.2(3)
C(36)-Si(4)-C(38)	111.6(3)	C(37)-Si(4)-C(36)	108.6(4)
C(37)-Si(4)-C(38)	110.2(4)	O(9)-Si(6A)-C(50A)	105.1(5)
O(9)-Si(6A)-C(48A)	107.1(4)	O(9)-Si(6A)-C(49A)	114.5(4)
C(48A)-Si(6A)-C(50A)	108.5(7)	C(49A)-Si(6A)-C(50A)	112.2(7)
C(49A)-Si(6A)-C(48A)	109.1(5)	C(54)-O(10)-H(10)	109.5
C(29)-O(7)-Si(4)	128.3(4)	C(32)-O(6)-C(28)	115.1(4)
C(31)-O(9)-Si(6B)	117.7(4)	C(31)-O(9)-Si(6A)	129.0(4)
C(30)-O(8)-Si(5)	128.2(4)	Si(6B)-C(49B)-H(49A)	109.5
Si(6B)-C(49B)-H(49B)	109.5	Si(6B)-C(49B)-H(49C)	109.5
H(49A)-C(49B)-H(49B)	109.5	H(49A)-C(49B)-H(49C)	109.5
H(49B)-C(49B)-H(49C)	109.5	H(53A)-C(53A)-H(53B)	109.5
H(53A)-C(53A)-H(53C)	109.5	H(53B)-C(53A)-H(53C)	109.5

C(50A)-C(53A)-H(53A)	109.5	C(50A)-C(53A)-H(53B)	109.5
C(50A)-C(53A)-H(53C)	109.5	O(6)-C(28)-H(28)	107.4
O(6)-C(28)-C(29)	113.4(4)	O(6)-C(28)-C(33)	108.0(4)
C(29)-C(28)-H(28)	107.4	C(33)-C(28)-H(28)	107.4
C(33)-C(28)-C(29)	112.9(5)	O(7)-C(29)-C(28)	111.1(5)
O(7)-C(29)-H(29)	108.7	O(7)-C(29)-C(30)	110.2(4)
C(28)-C(29)-H(29)	108.7	C(28)-C(29)-C(30)	109.4(5)
C(30)-C(29)-H(29)	108.7	O(8)-C(30)-C(29)	107.2(4)
O(8)-C(30)-H(30)	109.3	O(8)-C(30)-C(31)	109.4(5)
C(29)-C(30)-H(30)	109.3	C(29)-C(30)-C(31)	112.4(5)
C(31)-C(30)-H(30)	109.3	O(9)-C(31)-C(30)	110.5(5)
O(9)-C(31)-H(31)	109.2	O(9)-C(31)-C(32)	107.2(4)
C(30)-C(31)-H(31)	109.2	C(32)-C(31)-C(30)	111.5(4)
C(32)-C(31)-H(31)	109.2	O(6)-C(32)-C(31)	109.2(4)
O(6)-C(32)-H(32)	109.4	O(6)-C(32)-C(54)	105.8(4)
C(31)-C(32)-H(32)	109.4	C(31)-C(32)-C(54)	113.5(5)
C(54)-C(32)-H(32)	109.4	H(52A)-C(52A)-H(52B)	109.5
H(52A)-C(52A)-H(52C)	109.5	H(52B)-C(52A)-H(52C)	109.5
C(50A)-C(52A)-H(52A)	109.5	C(50A)-C(52A)-H(52B)	109.5
C(50A)-C(52A)-H(52C)	109.5	C(28)-C(33)-H(33A)	109.1
C(28)-C(33)-H(33B)	109.1	H(33A)-C(33)-H(33B)	107.9
C(34)-C(33)-C(28)	112.3(5)	C(34)-C(33)-H(33A)	109.1
C(34)-C(33)-H(33B)	109.1	O(10)-C(54)-C(32)	112.4(5)
O(10)-C(54)-H(54A)	109.1	O(10)-C(54)-H(54B)	109.1
C(32)-C(54)-H(54A)	109.1	C(32)-C(54)-H(54B)	109.1
H(54A)-C(54)-H(54B)	107.8	C(35)-C(34)-C(33)	178.5(7)
H(52D)-C(52B)-H(52E)	109.5	H(52D)-C(52B)-H(52F)	109.5
H(52E)-C(52B)-H(52F)	109.5	C(50B)-C(52B)-H(52D)	109.5
C(50B)-C(52B)-H(52E)	109.5	C(50B)-C(52B)-H(52F)	109.5
H(40A)-C(40B)-H(40B)	109.5	H(40A)-C(40B)-H(40C)	109.5
H(40B)-C(40B)-H(40C)	109.5	C(38)-C(40B)-H(40A)	109.5
C(38)-C(40B)-H(40B)	109.5	C(38)-C(40B)-H(40C)	109.5
C(34)-C(35)-H(35)	180.0	H(41A)-C(41B)-H(41B)	109.5
H(41A)-C(41B)-H(41C)	109.5	H(41B)-C(41B)-H(41C)	109.5
C(38)-C(41B)-H(41A)	109.5	C(38)-C(41B)-H(41B)	109.5
C(38)-C(41B)-H(41C)	109.5	Si(4)-C(36)-H(36A)	109.5
Si(4)-C(36)-H(36B)	109.5	Si(4)-C(36)-H(36C)	109.5
H(36A)-C(36)-H(36B)	109.5	H(36A)-C(36)-H(36C)	109.5
H(36B)-C(36)-H(36C)	109.5	Si(4)-C(37)-H(37A)	109.5
Si(4)-C(37)-H(37B)	109.5	Si(4)-C(37)-H(37C)	109.5
H(37A)-C(37)-H(37B)	109.5	H(37A)-C(37)-H(37C)	109.5
H(37B)-C(37)-H(37C)	109.5	C(53A)-C(50A)-Si(6A)	108.9(12)
C(53A)-C(50A)-C(51A)	101.4(13)	C(52A)-C(50A)-Si(6A)	113.1(10)
C(52A)-C(50A)-C(53A)	119.7(15)	C(52A)-C(50A)-C(51A)	110.8(14)
C(51A)-C(50A)-Si(6A)	100.7(11)	C(50A)-C(51A)-H(51A)	109.5
C(50A)-C(51A)-H(51B)	109.5	C(50A)-C(51A)-H(51C)	109.5
H(51A)-C(51A)-H(51B)	109.5	H(51A)-C(51A)-H(51C)	109.5
H(51B)-C(51A)-H(51C)	109.5	C(40B)-C(38)-Si(4)	107(2)
C(41B)-C(38)-Si(4)	106.4(15)	C(41B)-C(38)-C(40B)	96(2)

C(39)-C(38)-Si(4)	110.1(5)	C(39)-C(38)-C(40B)	114.2(19)
C(39)-C(38)-C(41B)	121.5(13)	C(40A)-C(38)-Si(4)	113.4(12)
C(40A)-C(38)-C(39)	105.8(13)	C(40A)-C(38)-C(41A)	112.5(15)
C(41A)-C(38)-Si(4)	110.8(7)	C(41A)-C(38)-C(39)	103.5(10)
C(38)-C(39)-H(39A)	109.5	C(38)-C(39)-H(39B)	109.5
C(38)-C(39)-H(39C)	109.5	H(39A)-C(39)-H(39B)	109.5
H(39A)-C(39)-H(39C)	109.5	H(39B)-C(39)-H(39C)	109.5
C(52B)-C(50B)-Si(6B)	109.5(19)	C(52B)-C(50B)-C(53B)	102(2)
C(51B)-C(50B)-Si(6B)	120(2)	C(51B)-C(50B)-C(52B)	109(3)
C(51B)-C(50B)-C(53B)	110(2)	C(53B)-C(50B)-Si(6B)	105.9(17)
C(38)-C(40A)-H(40D)	109.5	C(38)-C(40A)-H(40E)	109.5
C(38)-C(40A)-H(40F)	109.5	H(40D)-C(40A)-H(40E)	109.5
H(40D)-C(40A)-H(40F)	109.5	H(40E)-C(40A)-H(40F)	109.5
C(38)-C(41A)-H(41D)	109.5	C(38)-C(41A)-H(41E)	109.5
C(38)-C(41A)-H(41F)	109.5	H(41D)-C(41A)-H(41E)	109.5
H(41D)-C(41A)-H(41F)	109.5	H(41E)-C(41A)-H(41F)	109.5
Si(5)-C(42)-H(42A)	109.5	Si(5)-C(42)-H(42B)	109.5
Si(5)-C(42)-H(42C)	109.5	H(42A)-C(42)-H(42B)	109.5
H(42A)-C(42)-H(42C)	109.5	H(42B)-C(42)-H(42C)	109.5
C(50B)-C(51B)-H(51D)	109.5	C(50B)-C(51B)-H(51E)	109.5
C(50B)-C(51B)-H(51F)	109.5	H(51D)-C(51B)-H(51E)	109.5
H(51D)-C(51B)-H(51F)	109.5	H(51E)-C(51B)-H(51F)	109.5
C(50B)-C(53B)-H(53D)	109.5	C(50B)-C(53B)-H(53E)	109.5
C(50B)-C(53B)-H(53F)	109.5	H(53D)-C(53B)-H(53E)	109.5
H(53D)-C(53B)-H(53F)	109.5	H(53E)-C(53B)-H(53F)	109.5
Si(5)-C(43)-H(43A)	109.5	Si(5)-C(43)-H(43B)	109.5
Si(5)-C(43)-H(43C)	109.5	H(43A)-C(43)-H(43B)	109.5
H(43A)-C(43)-H(43C)	109.5	H(43B)-C(43)-H(43C)	109.5
Si(6B)-C(48B)-H(48A)	109.5	Si(6B)-C(48B)-H(48B)	109.5
Si(6B)-C(48B)-H(48C)	109.5	H(48A)-C(48B)-H(48B)	109.5
H(48A)-C(48B)-H(48C)	109.5	H(48B)-C(48B)-H(48C)	109.5
C(45)-C(44)-Si(5)	109.4(5)	C(45)-C(44)-C(47)	109.3(7)
C(46)-C(44)-Si(5)	109.9(5)	C(46)-C(44)-C(45)	110.3(6)
C(46)-C(44)-C(47)	108.0(6)	C(47)-C(44)-Si(5)	109.9(5)
C(44)-C(45)-H(45A)	109.5	C(44)-C(45)-H(45B)	109.5
C(44)-C(45)-H(45C)	109.5	H(45A)-C(45)-H(45B)	109.5
H(45A)-C(45)-H(45C)	109.5	H(45B)-C(45)-H(45C)	109.5
C(44)-C(46)-H(46A)	109.5	C(44)-C(46)-H(46B)	109.5
C(44)-C(46)-H(46C)	109.5	H(46A)-C(46)-H(46B)	109.5
H(46A)-C(46)-H(46C)	109.5	H(46B)-C(46)-H(46C)	109.5
C(44)-C(47)-H(47A)	109.5	C(44)-C(47)-H(47B)	109.5
C(44)-C(47)-H(47C)	109.5	H(47A)-C(47)-H(47B)	109.5
H(47A)-C(47)-H(47C)	109.5	H(47B)-C(47)-H(47C)	109.5
Si(6A)-C(48A)-H(48D)	109.5	Si(6A)-C(48A)-H(48E)	109.5
Si(6A)-C(48A)-H(48F)	109.5	H(48D)-C(48A)-H(48E)	109.5
H(48D)-C(48A)-H(48F)	109.5	H(48E)-C(48A)-H(48F)	109.5
Si(6A)-C(49A)-H(49D)	109.5	Si(6A)-C(49A)-H(49E)	109.5
Si(6A)-C(49A)-H(49F)	109.5	H(49D)-C(49A)-H(49E)	109.5
H(49D)-C(49A)-H(49F)	109.5	H(49E)-C(49A)-H(49F)	109.5

O(14)-Si(9)-C(97)	109.7(2)	O(14)-Si(9)-C(96)	110.7(2)
O(14)-Si(9)-C(98)	105.7(2)	C(97)-Si(9)-C(96)	109.9(3)
C(97)-Si(9)-C(98)	110.3(3)	C(96)-Si(9)-C(98)	110.3(3)
O(12)-Si(7)-C(85)	110.5(3)	O(12)-Si(7)-C(84)	110.6(3)
O(12)-Si(7)-C(86)	103.0(2)	C(85)-Si(7)-C(86)	110.4(3)
C(84)-Si(7)-C(85)	109.5(3)	C(84)-Si(7)-C(86)	112.8(3)
O(13)-Si(8)-C(91)	110.5(3)	O(13)-Si(8)-C(93)	103.6(2)
O(13)-Si(8)-C(90)	111.0(2)	C(91)-Si(8)-C(93)	112.0(3)
C(91)-Si(8)-C(90)	107.4(3)	C(90)-Si(8)-C(93)	112.4(3)
C(78)-O(13)-Si(8)	129.5(3)	C(77)-O(12)-Si(7)	130.7(3)
C(102)-O(15)-H(15)	109.5	C(79)-O(14)-Si(9)	125.1(3)
C(76)-O(11)-C(80)	117.6(4)	O(13)-C(78)-H(78)	109.2
O(13)-C(78)-C(79)	108.1(4)	O(13)-C(78)-C(77)	108.7(4)
C(79)-C(78)-H(78)	109.2	C(77)-C(78)-H(78)	109.2
C(77)-C(78)-C(79)	112.3(4)	Si(8)-C(91)-H(91A)	109.5
Si(8)-C(91)-H(91B)	109.5	Si(8)-C(91)-H(91C)	109.5
H(91A)-C(91)-H(91B)	109.5	H(91A)-C(91)-H(91C)	109.5
H(91B)-C(91)-H(91C)	109.5	C(82A)-C(83A)-H(83A)	180.0
H(99A)-C(99)-H(99B)	109.5	H(99A)-C(99)-H(99C)	109.5
H(99B)-C(99)-H(99C)	109.5	C(98)-C(99)-H(99A)	109.5
C(98)-C(99)-H(99B)	109.5	C(98)-C(99)-H(99C)	109.5
C(83B)-C(82B)-C(81B)	176(2)	H(87A)-C(87)-H(87B)	109.5
H(87A)-C(87)-H(87C)	109.5	H(87B)-C(87)-H(87C)	109.5
C(86)-C(87)-H(87A)	109.5	C(86)-C(87)-H(87B)	109.5
C(86)-C(87)-H(87C)	109.5	H(95A)-C(95)-H(95B)	109.5
H(95A)-C(95)-H(95C)	109.5	H(95B)-C(95)-H(95C)	109.5
C(93)-C(95)-H(95A)	109.5	C(93)-C(95)-H(95B)	109.5
C(93)-C(95)-H(95C)	109.5	O(11)-C(76)-H(76A)	109.3
O(11)-C(76)-H(76)	106.6	O(11)-C(76)-C(81A)	110.3(9)
O(11)-C(76)-C(77)	112.0(4)	O(11)-C(76)-C(81B)	104.3(9)
C(81A)-C(76)-H(76)	106.6	C(81A)-C(76)-C(77)	114.2(9)
C(77)-C(76)-H(76A)	109.3	C(77)-C(76)-H(76)	106.6
C(77)-C(76)-C(81B)	112.5(10)	C(81B)-C(76)-H(76A)	109.3
O(14)-C(79)-C(78)	111.0(4)	O(14)-C(79)-H(79)	108.2
O(14)-C(79)-C(80)	109.5(4)	C(78)-C(79)-H(79)	108.2
C(80)-C(79)-C(78)	111.7(4)	C(80)-C(79)-H(79)	108.2
C(76)-C(81A)-H(81A)	108.8	C(76)-C(81A)-H(81B)	108.8
H(81A)-C(81A)-H(81B)	107.7	C(82A)-C(81A)-C(76)	113.9(14)
C(82A)-C(81A)-H(81A)	108.8	C(82A)-C(81A)-H(81B)	108.8
Si(7)-C(85)-H(85A)	109.5	Si(7)-C(85)-H(85B)	109.5
Si(7)-C(85)-H(85C)	109.5	H(85A)-C(85)-H(85B)	109.5
H(85A)-C(85)-H(85C)	109.5	H(85B)-C(85)-H(85C)	109.5
H(89A)-C(89)-H(89B)	109.5	H(89A)-C(89)-H(89C)	109.5
H(89B)-C(89)-H(89C)	109.5	C(86)-C(89)-H(89A)	109.5
C(86)-C(89)-H(89B)	109.5	C(86)-C(89)-H(89C)	109.5
C(95)-C(93)-Si(8)	109.7(4)	C(95)-C(93)-C(92)	109.4(6)
C(95)-C(93)-C(94)	108.5(5)	C(92)-C(93)-Si(8)	110.3(4)
C(92)-C(93)-C(94)	108.7(5)	C(94)-C(93)-Si(8)	110.2(4)
Si(9)-C(97)-H(97A)	109.5	Si(9)-C(97)-H(97B)	109.5

Si(9)-C(97)-H(97C)	109.5	H(97A)-C(97)-H(97B)	109.5
H(97A)-C(97)-H(97C)	109.5	H(97B)-C(97)-H(97C)	109.5
H(10P)-C(101)-H(10Q)	109.5	H(10P)-C(101)-H(10R)	109.5
H(10Q)-C(101)-H(10R)	109.5	C(98)-C(101)-H(10P)	109.5
C(98)-C(101)-H(10Q)	109.5	C(98)-C(101)-H(10R)	109.5
O(12)-C(77)-C(78)	110.4(4)	O(12)-C(77)-C(76)	109.9(4)
O(12)-C(77)-H(77)	109.1	C(78)-C(77)-H(77)	109.1
C(76)-C(77)-C(78)	109.2(4)	C(76)-C(77)-H(77)	109.1
C(82B)-C(81B)-C(76)	111.9(15)	C(82B)-C(81B)-H(81C)	109.2
C(82B)-C(81B)-H(81D)	109.2	C(76)-C(81B)-H(81C)	109.2
C(76)-C(81B)-H(81D)	109.2	H(81C)-C(81B)-H(81D)	107.9
O(11)-C(80)-C(79)	108.5(4)	O(11)-C(80)-H(80)	109.3
O(11)-C(80)-C(102)	107.5(4)	C(79)-C(80)-H(80)	109.3
C(102)-C(80)-C(79)	113.0(4)	C(102)-C(80)-H(80)	109.3
C(82B)-C(83B)-H(83B)	180.0	C(83A)-C(82A)-C(81A)	176.7(18)
Si(7)-C(84)-H(84A)	109.5	Si(7)-C(84)-H(84B)	109.5
Si(7)-C(84)-H(84C)	109.5	H(84A)-C(84)-H(84B)	109.5
H(84A)-C(84)-H(84C)	109.5	H(84B)-C(84)-H(84C)	109.5
C(87)-C(86)-Si(7)	110.6(5)	C(87)-C(86)-C(89)	109.2(5)
C(87)-C(86)-C(88)	109.0(5)	C(89)-C(86)-Si(7)	109.8(4)
C(89)-C(86)-C(88)	108.3(5)	C(88)-C(86)-Si(7)	110.0(4)
C(86)-C(88)-H(88A)	109.5	C(86)-C(88)-H(88B)	109.5
C(86)-C(88)-H(88C)	109.5	H(88A)-C(88)-H(88B)	109.5
H(88A)-C(88)-H(88C)	109.5	H(88B)-C(88)-H(88C)	109.5
Si(8)-C(90)-H(90A)	109.5	Si(8)-C(90)-H(90B)	109.5
Si(8)-C(90)-H(90C)	109.5	H(90A)-C(90)-H(90B)	109.5
H(90A)-C(90)-H(90C)	109.5	H(90B)-C(90)-H(90C)	109.5
C(93)-C(92)-H(92A)	109.5	C(93)-C(92)-H(92B)	109.5
C(93)-C(92)-H(92C)	109.5	H(92A)-C(92)-H(92B)	109.5
H(92A)-C(92)-H(92C)	109.5	H(92B)-C(92)-H(92C)	109.5
C(93)-C(94)-H(94A)	109.5	C(93)-C(94)-H(94B)	109.5
C(93)-C(94)-H(94C)	109.5	H(94A)-C(94)-H(94B)	109.5
H(94A)-C(94)-H(94C)	109.5	H(94B)-C(94)-H(94C)	109.5
Si(9)-C(96)-H(96A)	109.5	Si(9)-C(96)-H(96B)	109.5
Si(9)-C(96)-H(96C)	109.5	H(96A)-C(96)-H(96B)	109.5
H(96A)-C(96)-H(96C)	109.5	H(96B)-C(96)-H(96C)	109.5
C(99)-C(98)-Si(9)	108.9(4)	C(99)-C(98)-C(101)	108.2(5)
C(101)-C(98)-Si(9)	110.2(4)	C(100)-C(98)-Si(9)	110.2(4)
C(100)-C(98)-C(99)	110.3(5)	C(100)-C(98)-C(101)	109.0(5)
C(98)-C(100)-H(10S)	109.5	C(98)-C(100)-H(10T)	109.5
C(98)-C(100)-H(10U)	109.5	H(10S)-C(100)-H(10T)	109.5
H(10S)-C(100)-H(10U)	109.5	H(10T)-C(100)-H(10U)	109.5
O(15)-C(102)-C(80)	114.4(4)	O(15)-C(102)-H(10V)	108.7
O(15)-C(102)-H(10W)	108.7	C(80)-C(102)-H(10V)	108.7
C(80)-C(102)-H(10W)	108.7	H(10V)-C(102)-H(10W)	107.6
O(2)-Si(2)-C(9)	110.3(2)	O(2)-Si(2)-C(11)	103.5(2)
O(2)-Si(2)-C(10)	109.4(2)	C(9)-Si(2)-C(11)	111.3(3)
C(9)-Si(2)-C(10)	109.7(3)	C(10)-Si(2)-C(11)	112.4(3)
O(4)-Si(3)-C(21)	109.8(3)	O(4)-Si(3)-C(23)	105.9(2)

O(4)-Si(3)-C(22)	110.2(3)	C(21)-Si(3)-C(23)	111.1(3)
C(22)-Si(3)-C(21)	109.3(4)	C(22)-Si(3)-C(23)	110.6(3)
O(3)-Si(6)-C(15)	111.3(3)	O(3)-Si(6)-C(17)	103.6(2)
O(3)-Si(6)-C(16)	111.7(3)	C(15)-Si(6)-C(17)	111.9(3)
C(15)-Si(6)-C(16)	106.9(3)	C(16)-Si(6)-C(17)	111.5(3)
C(27)-O(5)-H(5)	109.5	C(4)-O(4)-Si(3)	126.4(3)
C(1)-O(1)-C(5)	117.6(4)	C(3)-O(3)-Si(6)	129.7(3)
C(2)-O(2)-Si(2)	126.7(3)	O(1)-C(1)-H(1)	107.5
O(1)-C(1)-C(2)	113.1(4)	O(1)-C(1)-C(6)	107.4(4)
C(2)-C(1)-H(1)	107.5	C(2)-C(1)-C(6)	113.7(4)
C(6)-C(1)-H(1)	107.5	O(3)-C(3)-H(3)	109.0
O(3)-C(3)-C(2)	108.6(4)	O(3)-C(3)-C(4)	108.7(4)
C(2)-C(3)-H(3)	109.0	C(2)-C(3)-C(4)	112.3(4)
C(4)-C(3)-H(3)	109.0	O(1)-C(5)-H(5A)	109.2
O(1)-C(5)-C(27)	106.0(4)	O(1)-C(5)-C(4)	110.7(4)
C(27)-C(5)-H(5A)	109.2	C(4)-C(5)-H(5A)	109.2
C(4)-C(5)-C(27)	112.4(4)	C(8)-C(7)-C(6)	178.0(7)
Si(2)-C(9)-H(9A)	109.5	Si(2)-C(9)-H(9B)	109.5
Si(2)-C(9)-H(9C)	109.5	H(9A)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9C)	109.5	H(9B)-C(9)-H(9C)	109.5
C(13)-C(11)-Si(2)	109.6(4)	C(13)-C(11)-C(12)	108.6(5)
C(13)-C(11)-C(14)	108.8(5)	C(12)-C(11)-Si(2)	109.7(4)
C(14)-C(11)-Si(2)	111.2(4)	C(14)-C(11)-C(12)	108.9(5)
C(11)-C(13)-H(13A)	109.5	C(11)-C(13)-H(13B)	109.5
C(11)-C(13)-H(13C)	109.5	H(13A)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13C)	109.5	H(13B)-C(13)-H(13C)	109.5
Si(6)-C(15)-H(15A)	109.5	Si(6)-C(15)-H(15B)	109.5
Si(6)-C(15)-H(15C)	109.5	H(15A)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15C)	109.5	H(15B)-C(15)-H(15C)	109.5
C(19)-C(17)-Si(6)	110.8(5)	C(19)-C(17)-C(18)	109.6(6)
C(19)-C(17)-C(20)	108.4(6)	C(18)-C(17)-Si(6)	111.0(5)
C(18)-C(17)-C(20)	107.2(6)	C(20)-C(17)-Si(6)	109.8(4)
C(17)-C(19)-H(19A)	109.5	C(17)-C(19)-H(19B)	109.5
C(17)-C(19)-H(19C)	109.5	H(19A)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19C)	109.5	H(19B)-C(19)-H(19C)	109.5
Si(3)-C(21)-H(21A)	109.5	Si(3)-C(21)-H(21B)	109.5
Si(3)-C(21)-H(21C)	109.5	H(21A)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21C)	109.5	H(21B)-C(21)-H(21C)	109.5
C(25)-C(23)-Si(3)	110.7(4)	C(25)-C(23)-C(24)	108.1(5)
C(25)-C(23)-C(26)	109.6(5)	C(24)-C(23)-Si(3)	110.1(4)
C(26)-C(23)-Si(3)	110.3(4)	C(26)-C(23)-C(24)	107.9(5)
C(23)-C(25)-H(25A)	109.5	C(23)-C(25)-H(25B)	109.5
C(23)-C(25)-H(25C)	109.5	H(25A)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25C)	109.5	H(25B)-C(25)-H(25C)	109.5
O(5)-C(27)-C(5)	113.8(5)	O(5)-C(27)-H(27A)	108.8
O(5)-C(27)-H(27B)	108.8	C(5)-C(27)-H(27A)	108.8
C(5)-C(27)-H(27B)	108.8	H(27A)-C(27)-H(27B)	107.7
O(2)-C(2)-C(1)	110.5(4)	O(2)-C(2)-C(3)	109.3(4)
O(2)-C(2)-H(2)	109.5	C(1)-C(2)-C(3)	108.5(4)

C(1)-C(2)-H(2)	109.5	C(3)-C(2)-H(2)	109.5
O(4)-C(4)-C(3)	111.2(4)	O(4)-C(4)-C(5)	107.5(4)
O(4)-C(4)-H(4)	108.5	C(3)-C(4)-H(4)	108.5
C(5)-C(4)-C(3)	112.5(4)	C(5)-C(4)-H(4)	108.5
C(1)-C(6)-H(6A)	109.4	C(1)-C(6)-H(6B)	109.4
C(7)-C(6)-C(1)	111.2(5)	C(7)-C(6)-H(6A)	109.4
C(7)-C(6)-H(6B)	109.4	H(6A)-C(6)-H(6B)	108.0
C(7)-C(8)-H(8)	180.0	Si(2)-C(10)-H(10X)	109.5
Si(2)-C(10)-H(10Y)	109.5	Si(2)-C(10)-H	109.5
H(10X)-C(10)-H(10Y)	109.5	H(10X)-C(10)-H	109.5
H(10Y)-C(10)-H	109.5	C(11)-C(12)-H(12A)	109.5
C(11)-C(12)-H(12B)	109.5	C(11)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12B)	109.5	H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5	C(11)-C(14)-H(14A)	109.5
C(11)-C(14)-H(14B)	109.5	C(11)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14B)	109.5	H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5	Si(6)-C(16)-H(16A)	109.5
Si(6)-C(16)-H(16B)	109.5	Si(6)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16B)	109.5	H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5	C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5	C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18B)	109.5	H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5	C(17)-C(20)-H(20A)	109.5
C(17)-C(20)-H(20B)	109.5	C(17)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20B)	109.5	H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5	Si(3)-C(22)-H(22A)	109.5
Si(3)-C(22)-H(22B)	109.5	Si(3)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22B)	109.5	H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5	C(23)-C(24)-H(24A)	109.5
C(23)-C(24)-H(24B)	109.5	C(23)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24B)	109.5	H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5	C(23)-C(26)-H(26A)	109.5
C(23)-C(26)-H(26B)	109.5	C(23)-C(26)-H(26C)	109.5
H(26A)-C(26)-H(26B)	109.5	H(26A)-C(26)-H(26C)	109.5
H(26B)-C(26)-H(26C)	109.5		

6.4.6. Crystallographic Data Of *epi*-35a

Crystal Data & Structure Refinement

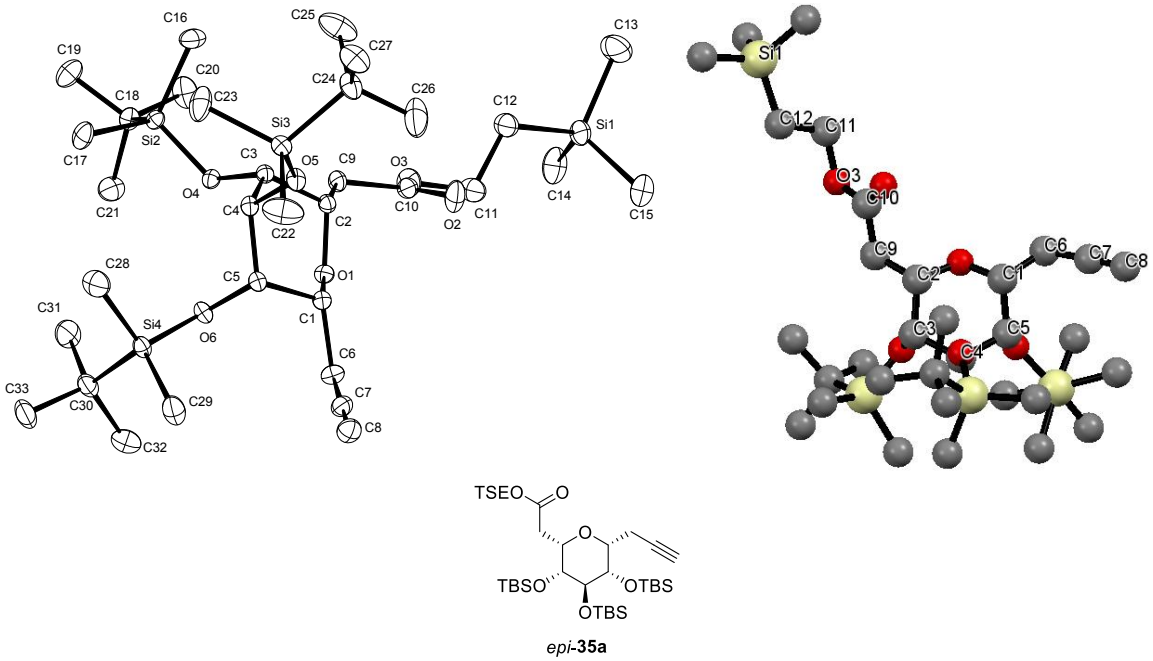


Figure 6.26: X-Ray single crystal structure and molecular structure of ester *epi*-**35a** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary).

Identification code	10221	
Empirical formula	$C_{33}H_{68}O_6Si_4$	
Color	colorless	
Formula weight	673.23 g·mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 2_1 2_1 2_1 (No. 19)	
Unit cell dimensions	a = 11.8299(8) Å	α = 90°.
	b = 13.3897(9) Å	β = 90°.
	c = 25.9735(16) Å	γ = 90°.
Volume	4114.2(5) Å^3	
Z	4	
Density (calculated)	1.087 Mg·m^{-3}	
Absorption coefficient	0.181 mm^{-1}	
F(000)	1480 e	

Crystal size	0.31 x 0.24 x 0.23 mm^3	
θ range for data collection	2.782 to 36.017°.	
Index ranges	$-19 \leq h \leq 19$, $-22 \leq k \leq 22$, $-42 \leq l \leq 42$	
Reflections collected	178854	
Independent reflections	19462 [R_{int} = 0.0323]	
Reflections with I>2σ(I)	18370	
Completeness to θ = 25.242°	99.5%	
Absorption correction	Gaussian	
Max. and min. transmission	0.96 and 0.95	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	19462 / 0 / 406	
Goodness-of-fit on F^2	1.165	
Final R indices [I>2σ(I)]	R_1 = 0.0357	wR^2 = 0.1074
R indices (all data)	R_1 = 0.0404	wR^2 = 0.1140
Absolute structure parameter	-0.014(9)	
Largest diff. peak and hole	0.8 and -0.7 $e \cdot Å^{-3}$	

Bond Lengths [Å] & Angles [°]

Si(1)-C(12)	1.9004(16)	Si(1)-C(13)	1.868(2)
Si(1)-C(14)	1.859(2)	Si(1)-C(15)	1.864(2)
Si(2)-O(4)	1.6630(10)	Si(2)-C(16)	1.8679(15)
Si(2)-C(17)	1.8658(15)	Si(2)-C(18)	1.8838(14)
Si(3)-O(5)	1.6541(10)	Si(3)-C(22)	1.871(2)
Si(3)-C(23)	1.8548(18)	Si(3)-C(24)	1.8752(15)
Si(4)-O(6)	1.6643(10)	Si(4)-C(28)	1.8726(18)
Si(4)-C(29)	1.8630(16)	Si(4)-C(30)	1.8825(15)
O(1)-C(1)	1.4262(15)	O(1)-C(2)	1.4305(15)
O(2)-C(10)	1.197(2)	O(3)-C(10)	1.3543(19)
O(3)-C(11)	1.459(2)	O(4)-C(3)	1.4206(15)
O(5)-C(4)	1.4206(15)	O(6)-C(5)	1.4215(15)
C(1)-C(5)	1.5306(17)	C(1)-C(6)	1.5281(18)
C(2)-C(3)	1.5306(17)	C(2)-C(9)	1.5172(18)
C(3)-C(4)	1.5437(17)	C(4)-C(5)	1.5418(17)
C(6)-C(7)	1.463(2)	C(7)-C(8)	1.204(2)
C(9)-C(10)	1.5121(18)	C(11)-C(12)	1.505(2)
C(18)-C(19)	1.538(2)	C(18)-C(20)	1.535(2)
C(18)-C(21)	1.540(2)	C(24)-C(25)	1.556(3)
C(24)-C(26)	1.522(3)	C(24)-C(27)	1.534(2)
C(30)-C(31)	1.535(2)	C(30)-C(32)	1.543(3)
C(30)-C(33)	1.539(2)	C(13)-Si(1)-C(12)	107.21(9)

C(14)-Si(1)-C(12)	110.43(9)	C(14)-Si(1)-C(13)	110.29(13)
C(14)-Si(1)-C(15)	108.20(11)	C(15)-Si(1)-C(12)	110.38(9)
C(15)-Si(1)-C(13)	110.34(12)	O(4)-Si(2)-C(16)	109.51(6)
O(4)-Si(2)-C(17)	110.47(6)	O(4)-Si(2)-C(18)	107.71(5)
C(16)-Si(2)-C(18)	110.21(7)	C(17)-Si(2)-C(16)	108.76(8)
C(17)-Si(2)-C(18)	110.18(7)	O(5)-Si(3)-C(22)	109.35(9)
O(5)-Si(3)-C(23)	109.81(7)	O(5)-Si(3)-C(24)	103.36(6)
C(22)-Si(3)-C(24)	111.72(11)	C(23)-Si(3)-C(22)	110.36(13)
C(23)-Si(3)-C(24)	112.01(9)	O(6)-Si(4)-C(28)	110.89(7)
O(6)-Si(4)-C(29)	110.88(7)	O(6)-Si(4)-C(30)	104.63(6)
C(28)-Si(4)-C(30)	111.46(9)	C(29)-Si(4)-C(28)	107.86(10)
C(29)-Si(4)-C(30)	111.14(8)	C(1)-O(1)-C(2)	111.28(9)
C(10)-O(3)-C(11)	117.29(14)	C(3)-O(4)-Si(2)	122.85(8)
C(4)-O(5)-Si(3)	127.79(8)	C(5)-O(6)-Si(4)	122.26(8)
O(1)-C(1)-C(5)	110.54(10)	O(1)-C(1)-C(6)	106.46(10)
C(6)-C(1)-C(5)	113.85(10)	O(1)-C(2)-C(3)	111.46(10)
O(1)-C(2)-C(9)	107.17(10)	C(9)-C(2)-C(3)	111.85(10)
O(4)-C(3)-C(2)	110.87(10)	O(4)-C(3)-C(4)	112.00(10)
C(2)-C(3)-C(4)	110.57(10)	O(5)-C(4)-C(3)	106.01(10)
O(5)-C(4)-C(5)	107.39(10)	C(5)-C(4)-C(3)	114.24(9)
O(6)-C(5)-C(1)	110.74(9)	O(6)-C(5)-C(4)	110.71(10)
C(1)-C(5)-C(4)	109.26(9)	C(7)-C(6)-C(1)	111.96(11)
C(8)-C(7)-C(6)	178.30(16)	C(10)-C(9)-C(2)	114.09(11)
O(2)-C(10)-O(3)	124.72(14)	O(2)-C(10)-C(9)	125.73(14)
O(3)-C(10)-C(9)	109.55(13)	O(3)-C(11)-C(12)	112.79(13)
C(11)-C(12)-Si(1)	112.84(11)	C(19)-C(18)-Si(2)	109.07(10)
C(19)-C(18)-C(21)	109.39(13)	C(20)-C(18)-Si(2)	110.40(10)
C(20)-C(18)-C(19)	108.70(13)	C(20)-C(18)-C(21)	108.92(13)
C(21)-C(18)-Si(2)	110.32(10)	C(25)-C(24)-Si(3)	107.44(12)
C(26)-C(24)-Si(3)	110.89(14)	C(26)-C(24)-C(25)	108.7(2)
C(26)-C(24)-C(27)	109.65(16)	C(27)-C(24)-Si(3)	111.82(11)
C(27)-C(24)-C(25)	108.27(15)	C(31)-C(30)-Si(4)	110.51(11)
C(31)-C(30)-C(32)	108.63(15)	C(31)-C(30)-C(33)	109.01(14)
C(32)-C(30)-Si(4)	109.32(11)	C(33)-C(30)-Si(4)	109.96(12)
C(33)-C(30)-C(32)	109.37(14)		

6.4.7. Crystallographic Data Of *ent*-42

Crystal Data & Structure Refinement

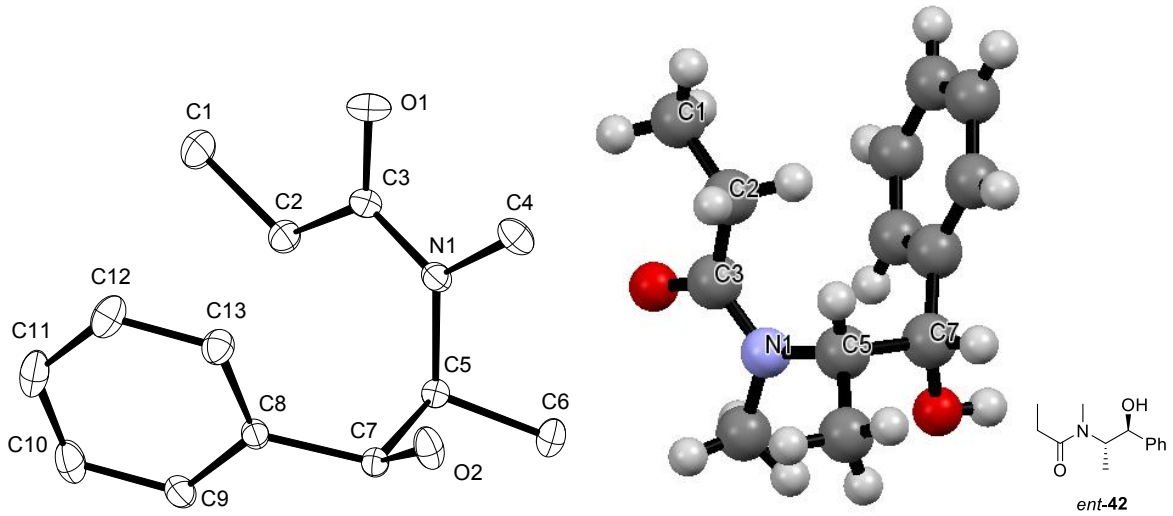


Figure 6.27: X-Ray single crystal structure and molecular structure of pseudoephedrine amide *ent*-**42** (numbering of atoms is arbitrary).

Identification code	9880	
Empirical formula	$C_{13}H_{19}NO_2$	
Color	colorless	
Formula weight	221.29 g·mol^{-1}	
Temperature	100.15 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 5.4570(8) Å	α = 90°.
	b = 13.106(2) Å	β = 98.357(7)°.
	c = 8.5932(4) Å	γ = 90°.
Volume	608.04(14) Å^3	
Z	2	
Density (calculated)	1.209 Mg·m^{-3}	
Absorption coefficient	0.081 mm^{-1}	
F(000)	240 e	
Crystal size	0.19 x 0.17 x 0.13 mm^3	
θ range for data collection	2.856 to 38.118°.	
Index ranges	$-9 \leq h \leq 9$, $-22 \leq k \leq 22$, $-14 \leq l \leq 14$	

Reflections collected	56002	
Independent reflections	6679 [R_{int} = 0.0489]	
Reflections with I>2σ(I)	5993	
Completeness to θ = 25.242°	99.9%	
Absorption correction	Gaussian	
Max. and min. transmission	0.99 and 0.98	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	6679/1/152	
Goodness-of-fit on F^2	1.117	
Final R indices [I>2σ(I)]	R_1 = 0.0378	wR^2 = 0.1032
R indices (all data)	R_1 = 0.0463	wR^2 = 0.1096
Absolute structure parameter	0.0(3)	
Largest diff. peak and hole	0.3 and -0.2 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(2)-C(7)	1.4226(14)	O(1)-C(3)	1.2388(13)
N(1)-C(3)	1.3527(14)	N(1)-C(5)	1.4696(13)
N(1)-C(4)	1.4690(14)	C(3)-C(2)	1.5194(16)
C(5)-C(7)	1.5458(14)	C(5)-C(6)	1.5307(14)
C(8)-C(9)	1.3967(14)	C(8)-C(7)	1.5132(14)
C(8)-C(13)	1.3930(15)	C(9)-C(10)	1.3930(16)
C(2)-C(1)	1.5239(17)	C(13)-C(12)	1.3945(16)
C(10)-C(11)	1.393(2)	C(11)-C(12)	1.393(2)
C(3)-N(1)-C(5)	124.26(9)	C(3)-N(1)-C(4)	116.47(9)
C(4)-N(1)-C(5)	119.22(9)	O(1)-C(3)-N(1)	119.80(11)
O(1)-C(3)-C(2)	120.04(11)	N(1)-C(3)-C(2)	120.13(9)
N(1)-C(5)-C(7)	112.29(8)	N(1)-C(5)-C(6)	111.90(8)
C(6)-C(5)-C(7)	110.70(8)	C(9)-C(8)-C(7)	119.69(9)
C(13)-C(8)-C(9)	119.05(9)	C(13)-C(8)-C(7)	121.15(9)
C(10)-C(9)-C(8)	120.57(10)	O(2)-C(7)-C(5)	108.17(8)
O(2)-C(7)-C(8)	112.57(9)	C(8)-C(7)-C(5)	111.75(8)
C(3)-C(2)-C(1)	112.39(11)	C(8)-C(13)-C(12)	120.48(10)
C(11)-C(10)-C(9)	120.13(11)	C(10)-C(11)-C(12)	119.54(10)
C(11)-C(12)-C(13)	120.23(11)		

6.4.8. Crystallographic Data Of 39c/*epi*-39c

Crystal Data & Structure Refinement

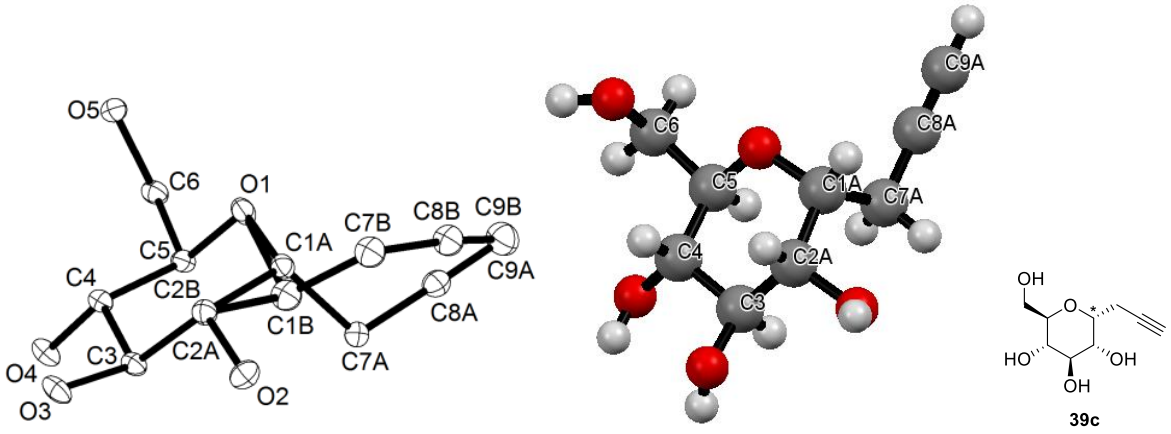


Figure 6.28: X-Ray single crystal structure and molecular structure of tetrol **39c**/*epi*-**39c** (anomeric mixture, numbering of atoms is arbitrary).

Identification code	9814	
Empirical formula	$C_9H_{14}O_5$	
Color	colourless	
Formula weight	202.20 g·mol^{-1}	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	orthorhombic	
Space group	P 2_1 2_1 2_1 (No. 19)	
Unit cell dimensions	a = 6.0462(17) Å	α = 90°.
	b = 10.418(3) Å	β = 90°.
	c = 14.579(4) Å	γ = 90°.
Volume	918.3(4) Å^3	
Z	4	
Density (calculated)	1.463 Mg·m^{-3}	
Absorption coefficient	0.120 mm^{-1}	
F(000)	432 e	
Crystal size	0.274 x 0.116 x 0.046 mm^3	
θ range for data collection	3.411 to 33.427°.	
Index ranges	$-9 \leq h \leq 8$, $-15 \leq k \leq 16$, $-22 \leq l \leq 22$	
Reflections collected	29506	
Independent reflections	3535 [R_{int} = 0.0966]	

Reflections with I>2σ(I)	2790	
Completeness to θ = 25.242°	99.8%	
Absorption correction	Gaussian	
Max. and min. transmission	0.99456 and 0.97333	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	3535/0/145	
Goodness-of-fit on F^2	1.060	
Final R indices [I>2σ(I)]	R_1 = 0.0476	wR^2 = 0.1006
R indices (all data)	R_1 = 0.0716	wR^2 = 0.1103
Absolute structure parameter	0.8(7)	
Extinction coefficient	0	
Largest diff. peak and hole	0.288 and -0.276 e·Å^{-3}	

Anisotropic Atomic Coordinates & Equivalent Isotropic Displacement Parameters (Å2)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(3)	0.4979(3)	0.4702(2)	0.2267(1)	0.013(1)
C(4)	0.3800(3)	0.5249(2)	0.1432(1)	0.012(1)
C(5)	0.1816(3)	0.6060(2)	0.1716(1)	0.013(1)
C(6)	0.0483(4)	0.6553(2)	0.0915(2)	0.014(1)
O(1)	0.0353(2)	0.5297(2)	0.2267(1)	0.016(1)
O(2)	0.4380(3)	0.3629(2)	0.3723(1)	0.017(1)
O(3)	0.6615(3)	0.3799(1)	0.1988(1)	0.017(1)
O(4)	0.5219(2)	0.6078(1)	0.0920(1)	0.016(1)
O(5)	-0.0541(3)	0.5519(1)	0.0433(1)	0.015(1)
C(1A)	0.1280(4)	0.4798(3)	0.3102(2)	0.013(1)
C(2A)	0.3343(3)	0.4003(2)	0.2884(1)	0.014(1)
C(7A)	0.1648(4)	0.5873(2)	0.3807(2)	0.014(1)
C(8A)	-0.0459(5)	0.6438(2)	0.4086(2)	0.016(1)
C(9A)	-0.2240(4)	0.6832(2)	0.4332(2)	0.024(1)
C(1B)	0.173(4)	0.525(2)	0.3144(15)	0.020
C(2B)	0.3343(3)	0.4003(2)	0.2884(1)	0.014(1)
C(7B)	0.004(3)	0.4856(19)	0.3825(13)	0.020
C(8B)	-0.137(4)	0.596(2)	0.4124(14)	0.020
C(9B)	-0.2240(4)	0.6832(2)	0.4332(2)	0.024(1)

Bond Lengths [Å] & Angles [°]

C(3)-O(3)	1.425(2)	C(3)-C(4)	1.521(3)
C(3)-C(2B)	1.523(3)	C(3)-C(2A)	1.523(3)
C(3)-H(3)	1.0000	C(4)-O(4)	1.428(2)
C(4)-C(5)	1.525(3)	C(4)-H(4)	1.0000
C(5)-O(1)	1.434(2)	C(5)-C(6)	1.509(3)
C(5)-H(5)	1.0000	C(6)-O(5)	1.428(2)
C(6)-H(6A)	0.9900	C(6)-H(6B)	0.9900
O(1)-C(1A)	1.438(3)	O(1)-C(1B)	1.53(2)
O(2)-C(2B)	1.428(2)	O(2)-C(2A)	1.428(2)
O(2)-H(2)	0.77(3)	O(3)-H(3A)	0.82(3)
O(4)-H(4A)	0.89(3)	O(5)-H(5A)	0.91(3)
C(1A)-C(2A)	1.530(3)	C(1A)-C(7A)	1.536(4)
C(1A)-H(1A)	1.0000	C(2A)-H(2A)	1.0000
C(7A)-C(8A)	1.461(3)	C(7A)-H(7AA)	0.9900
C(7A)-H(7AB)	0.9900	C(8A)-C(9A)	1.207(4)
C(9A)-H(9A)	0.9500	C(1B)-C(7B)	1.49(3)
C(1B)-C(2B)	1.67(2)	C(1B)-H(1B)	1.0000
C(2B)-H(2B)	1.0000	C(7B)-C(8B)	1.50(3)
C(7B)-H(7B1)	0.9900	C(7B)-H(7B2)	0.9900
C(8B)-C(9B)	1.09(2)	C(9B)-H(9B)	0.9500
O(3)-C(3)-C(4)	110.13(16)	O(3)-C(3)-C(2B)	107.70(16)
C(4)-C(3)-C(2B)	110.35(16)	O(3)-C(3)-C(2A)	107.70(16)
C(4)-C(3)-C(2A)	110.35(16)	O(3)-C(3)-H(3)	109.5
C(4)-C(3)-H(3)	109.5	C(2A)-C(3)-H(3)	109.5
O(4)-C(4)-C(3)	111.30(16)	O(4)-C(4)-C(5)	106.25(15)
C(3)-C(4)-C(5)	111.03(16)	O(4)-C(4)-H(4)	109.4
C(3)-C(4)-H(4)	109.4	C(5)-C(4)-H(4)	109.4
O(1)-C(5)-C(6)	107.00(16)	O(1)-C(5)-C(4)	109.29(15)
C(6)-C(5)-C(4)	113.49(17)	O(1)-C(5)-H(5)	109.0
C(6)-C(5)-H(5)	109.0	C(4)-C(5)-H(5)	109.0
O(5)-C(6)-C(5)	110.82(16)	O(5)-C(6)-H(6A)	109.5
C(5)-C(6)-H(6A)	109.5	O(5)-C(6)-H(6B)	109.5
C(5)-C(6)-H(6B)	109.5	H(6A)-C(6)-H(6B)	108.1
C(5)-O(1)-C(1A)	115.71(17)	C(5)-O(1)-C(1B)	98.5(9)
C(2A)-O(2)-H(2)	109.5	C(3)-O(3)-H(3A)	109.5
C(4)-O(4)-H(4A)	109.5	C(6)-O(5)-H(5A)	109.5
O(1)-C(1A)-C(2A)	109.74(18)	O(1)-C(1A)-C(7A)	111.0(2)
C(2A)-C(1A)-C(7A)	114.6(2)	O(1)-C(1A)-H(1A)	107.0
C(2A)-C(1A)-H(1A)	107.0	C(7A)-C(1A)-H(1A)	107.0
O(2)-C(2A)-C(3)	110.57(17)	O(2)-C(2A)-C(1A)	109.10(17)
C(3)-C(2A)-C(1A)	113.15(18)	O(2)-C(2A)-H(2A)	108.0
C(3)-C(2A)-H(2A)	108.0	C(1A)-C(2A)-H(2A)	108.0
C(8A)-C(7A)-C(1A)	110.75(19)	C(8A)-C(7A)-H(7AA)	109.5
C(1A)-C(7A)-H(7AA)	109.5	C(8A)-C(7A)-H(7AB)	109.5
C(1A)-C(7A)-H(7AB)	109.5	H(7AA)-C(7A)-H(7AB)	108.1
C(9A)-C(8A)-C(7A)	176.0(3)	C(8A)-C(9A)-H(9A)	180.0
C(7B)-C(1B)-O(1)	101.0(16)	C(7B)-C(1B)-C(2B)	109.7(16)

O(1)-C(1B)-C(2B)	98.8(13)	C(7B)-C(1B)-H(1B)	115.1
O(1)-C(1B)-H(1B)	115.1	C(2B)-C(1B)-H(1B)	115.1
O(2)-C(2B)-C(3)	110.57(17)	O(2)-C(2B)-C(1B)	105.9(8)
C(3)-C(2B)-C(1B)	98.0(8)	O(2)-C(2B)-H(2B)	113.7
C(3)-C(2B)-H(2B)	113.7	C(1B)-C(2B)-H(2B)	113.7
C(1B)-C(7B)-C(8B)	111.8(17)	C(1B)-C(7B)-H(7B1)	109.3
C(8B)-C(7B)-H(7B1)	109.3	C(1B)-C(7B)-H(7B2)	109.3
C(8B)-C(7B)-H(7B2)	109.3	H(7B1)-C(7B)-H(7B2)	107.9
C(9B)-C(8B)-C(7B)	174(2)	C(8B)-C(9B)-H(9B)	180.0

Anisotropic Displacement Parameters (Å2)

Symmetry transformations used to generate equivalent atoms:

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11} + ... + 2\ h\ k\ a^*\ b^*\ U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(3)	0.010(1)	0.012(1)	0.017(1)	0.000(1)	0.000(1)	0.001(1)
C(4)	0.010(1)	0.012(1)	0.014(1)	0.000(1)	0.000(1)	-0.001(1)
C(5)	0.010(1)	0.014(1)	0.014(1)	-0.001(1)	0.000(1)	0.000(1)
C(6)	0.010(1)	0.014(1)	0.018(1)	0.000(1)	-0.001(1)	0.001(1)
O(1)	0.011(1)	0.024(1)	0.013(1)	0.003(1)	0.001(1)	0.002(1)
O(2)	0.020(1)	0.015(1)	0.015(1)	0.001(1)	-0.004(1)	0.001(1)
O(3)	0.010(1)	0.015(1)	0.025(1)	0.001(1)	0.003(1)	0.002(1)
O(4)	0.011(1)	0.015(1)	0.021(1)	0.003(1)	0.003(1)	0.000(1)
O(5)	0.014(1)	0.019(1)	0.013(1)	-0.001(1)	-0.001(1)	-0.002(1)
C(1A)	0.012(1)	0.015(1)	0.012(1)	0.001(1)	0.001(1)	0.000(1)
C(2A)	0.013(1)	0.016(1)	0.014(1)	0.000(1)	0.000(1)	0.001(1)
C(7A)	0.013(1)	0.015(1)	0.014(1)	-0.002(1)	0.000(1)	0.000(1)
C(8A)	0.018(1)	0.015(1)	0.016(1)	-0.001(1)	-0.001(1)	-0.001(1)
C(9A)	0.022(1)	0.020(1)	0.029(1)	-0.004(1)	0.003(1)	0.000(1)
C(2B)	0.013(1)	0.016(1)	0.014(1)	0.000(1)	0.000(1)	0.001(1)
C(9B)	0.022(1)	0.020(1)	0.029(1)	-0.004(1)	0.003(1)	0.000(1)

Hydrogen Coordinates & Isotropic Displacement Parameters (Å2)

	x	y	z	U_{eq}
H(3)	0.5696	0.5414	0.2618	0.015
H(4)	0.3291	0.4530	0.1030	0.015
H(5)	0.2346	0.6806	0.2088	0.015
H(6A)	-0.0668	0.7151	0.1140	0.017
H(6B)	0.1464	0.7032	0.0493	0.017
H(2)	0.446(5)	0.289(3)	0.3743(10)	0.025

H(3A)	0.782(5)	0.4160(15)	0.195(2)	0.025
H(4A)	0.640(5)	0.5643(17)	0.0736(18)	0.024
H(5A)	-0.031(4)	0.5616(14)	-0.018(2)	0.023
H(1A)	0.0163	0.4197	0.3369	0.016
H(2A)	0.2858	0.3206	0.2559	0.017
H(7AA)	0.2413	0.5520	0.4352	0.017
H(7AB)	0.2602	0.6546	0.3536	0.017
H(9A)	-0.3643	0.7142	0.4525	0.028
H(1B)	0.2542	0.6064	0.3294	0.024
H(2B)	0.2540	0.3288	0.2570	0.017
H(7B1)	0.0782	0.4481	0.4368	0.024
H(7B2)	-0.0916	0.4185	0.3552	0.024
H(9B)	-0.3000	0.7589	0.4513	0.028

6.4.9. Crystallographic Data Of *epi*-39b

Crystal Data & Structure Refinement

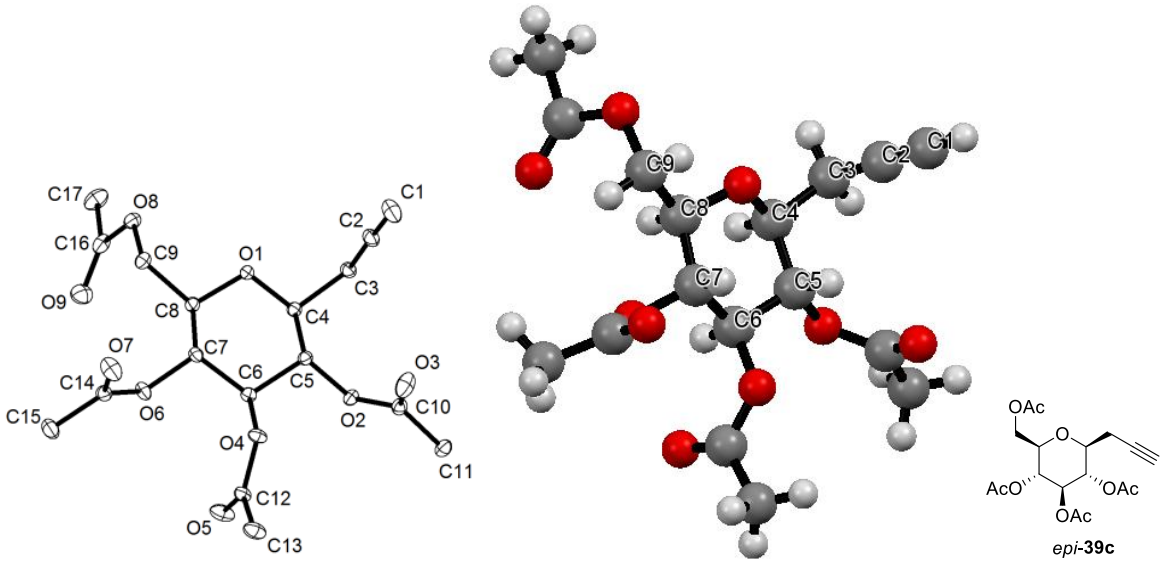


Figure 6.29: X-Ray single crystal structure and molecular structure of alkyne *epi*-**39b** (numbering of atoms is arbitrary).

Identification code	GRX-GA-014 (9810)	
Empirical formula	$C_{17}H_{22}O_9$	
Color	colourless	
Formula weight	370.34 g·mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 10.6718(11) Å	α = 90°.
	b = 7.4951(8) Å	β = 108.3476(18)°.
	c = 11.8592(12) Å	γ = 90°.
Volume	900.35(16) Å^3	
Z	2	
Density (calculated)	1.366 Mg·m^{-3}	
Absorption coefficient	0.111 mm^{-1}	
F(000)	392 e	
Crystal size	0.280 x 0.083 x 0.065 mm^3	
θ range for data collection	3.100 to 36.226°.	
Index ranges	$-17 \leq h \leq 17$, $-12 \leq k \leq 12$, $-19 \leq l \leq 19$	

Reflections collected	33320	
Independent reflections	8643 [R_{int} = 0.0297]	
Reflections with I>2σ(I)	7737	
Completeness to θ = 25.242°	99.8%	
Absorption correction	Gaussian	
Max. and min. transmission	0.99497 and 0.97830	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	8643/1/239	
Goodness-of-fit on F^2	1.015	
Final R indices [I>2σ(I)]	R_1 = 0.0343	wR^2 = 0.0843
R indices (all data)	R_1 = 0.0418	wR^2 = 0.0884
Absolute structure parameter	-0.16(18)	
Extinction coefficient	0	
Largest diff. peak and hole	0.360 and -0.193 e·Å^{-3}	

Atomic Coordinates & Equivalent Isotropic Displacement Parameters (Å2)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	0.0531(2)	0.2042(2)	0.8249(1)	0.023(1)
C(2)	0.1373(1)	0.1563(2)	0.7849(1)	0.016(1)
C(3)	0.2368(1)	0.0896(2)	0.7338(1)	0.013(1)
C(4)	0.3331(1)	0.2300(2)	0.7183(1)	0.011(1)
C(5)	0.2675(1)	0.3843(2)	0.6371(1)	0.011(1)
C(6)	0.3730(1)	0.5142(2)	0.6275(1)	0.011(1)
C(7)	0.4603(1)	0.5727(2)	0.7500(1)	0.012(1)
C(8)	0.5115(1)	0.4080(2)	0.8271(1)	0.012(1)
C(9)	0.5910(1)	0.4591(2)	0.9527(1)	0.013(1)
C(10)	0.0721(1)	0.3505(2)	0.4705(1)	0.014(1)
C(11)	0.0171(1)	0.2696(2)	0.3496(1)	0.015(1)
C(12)	0.3504(1)	0.7285(2)	0.4725(1)	0.014(1)
C(13)	0.2733(1)	0.8888(2)	0.4147(1)	0.020(1)
C(14)	0.6034(1)	0.8284(2)	0.7788(1)	0.013(1)
C(15)	0.7290(1)	0.8890(2)	0.7606(1)	0.020(1)
C(16)	0.7690(1)	0.2551(2)	0.9907(1)	0.017(1)
C(17)	0.8275(2)	0.0901(2)	1.0574(1)	0.024(1)
O(1)	0.4018(1)	0.3037(1)	0.8321(1)	0.012(1)
O(2)	0.2025(1)	0.3137(1)	0.5199(1)	0.012(1)
O(3)	0.0102(1)	0.4409(2)	0.5175(1)	0.024(1)
O(4)	0.3082(1)	0.6689(1)	0.5624(1)	0.013(1)

O(5)	0.4389(1)	0.6604(2)	0.4449(1)	0.022(1)
O(6)	0.5722(1)	0.6630(1)	0.7328(1)	0.014(1)
O(7)	0.5396(1)	0.9105(1)	0.8285(1)	0.022(1)
O(8)	0.6602(1)	0.3053(1)	1.0164(1)	0.015(1)
O(9)	0.8112(1)	0.3339(2)	0.9214(1)	0.023(1)

Bond Lengths [Å] & Angles [°]

C(1)-C(2)	1.1960(18)	C(2)-C(3)	1.4657(17)
C(3)-C(4)	1.5229(16)	C(4)-O(1)	1.4285(13)
C(4)-C(5)	1.5271(16)	C(5)-O(2)	1.4435(13)
C(5)-C(6)	1.5200(15)	C(6)-O(4)	1.4427(14)
C(6)-C(7)	1.5230(15)	C(7)-O(6)	1.4417(14)
C(7)-C(8)	1.5311(16)	C(8)-O(1)	1.4253(13)
C(8)-C(9)	1.5131(15)	C(9)-O(8)	1.4466(15)
C(10)-O(3)	1.1988(15)	C(10)-O(2)	1.3579(14)
C(10)-C(11)	1.4953(16)	C(12)-O(5)	1.2051(15)
C(12)-O(4)	1.3577(14)	C(12)-C(13)	1.4952(18)
C(14)-O(7)	1.2012(14)	C(14)-O(6)	1.3529(15)
C(14)-C(15)	1.4946(16)	C(16)-O(9)	1.2090(16)
C(16)-O(8)	1.3441(15)	C(16)-C(17)	1.495(2)
C(1)-C(2)-C(3)	177.16(14)	C(2)-C(3)-C(4)	114.73(10)
O(1)-C(4)-C(3)	108.55(9)	O(1)-C(4)-C(5)	107.49(9)
C(3)-C(4)-C(5)	113.98(9)	O(2)-C(5)-C(6)	107.78(8)
O(2)-C(5)-C(4)	108.40(9)	C(6)-C(5)-C(4)	109.18(8)
O(4)-C(6)-C(5)	108.23(8)	O(4)-C(6)-C(7)	108.96(9)
C(5)-C(6)-C(7)	110.97(8)	O(6)-C(7)-C(6)	106.58(8)
O(6)-C(7)-C(8)	107.89(9)	C(6)-C(7)-C(8)	109.50(9)
O(1)-C(8)-C(9)	108.10(9)	O(1)-C(8)-C(7)	108.88(9)
C(9)-C(8)-C(7)	111.57(9)	O(8)-C(9)-C(8)	110.37(9)
O(3)-C(10)-O(2)	123.59(11)	O(3)-C(10)-C(11)	124.61(11)
O(2)-C(10)-C(11)	111.78(10)	O(5)-C(12)-O(4)	123.78(11)
O(5)-C(12)-C(13)	125.54(11)	O(4)-C(12)-C(13)	110.68(10)
O(7)-C(14)-O(6)	124.18(11)	O(7)-C(14)-C(15)	126.04(11)
O(6)-C(14)-C(15)	109.77(10)	O(9)-C(16)-O(8)	123.45(12)
O(9)-C(16)-C(17)	125.53(12)	O(8)-C(16)-C(17)	111.01(11)
C(8)-O(1)-C(4)	110.83(8)	C(10)-O(2)-C(5)	117.25(9)
C(12)-O(4)-C(6)	117.54(9)	C(14)-O(6)-C(7)	118.87(9)
C(16)-O(8)-C(9)	116.10(9)		

Anisotropic Displacement Parameters (Å2)

Symmetry transformations used to generate equivalent atoms:

The anisotropic displacement factor exponent takes the form:
$-2\pi^2[h^2a^{*2}U_{11} + ... + 2 h k a^* b^* U_{12}]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	0.022(1)	0.021(1)	0.030(1)	-0.007(1)	0.014(1)	-0.006(1)
C(2)	0.018(1)	0.014(1)	0.018(1)	-0.002(1)	0.007(1)	-0.004(1)
C(3)	0.014(1)	0.012(1)	0.013(1)	0.000(1)	0.005(1)	-0.002(1)
C(4)	0.012(1)	0.011(1)	0.010(1)	0.000(1)	0.004(1)	-0.001(1)
C(5)	0.011(1)	0.012(1)	0.010(1)	0.000(1)	0.003(1)	0.000(1)
C(6)	0.012(1)	0.010(1)	0.012(1)	0.001(1)	0.004(1)	0.001(1)
C(7)	0.011(1)	0.012(1)	0.013(1)	-0.001(1)	0.005(1)	-0.001(1)
C(8)	0.012(1)	0.013(1)	0.011(1)	-0.001(1)	0.004(1)	-0.001(1)
C(9)	0.014(1)	0.014(1)	0.012(1)	-0.002(1)	0.003(1)	0.000(1)
C(10)	0.013(1)	0.013(1)	0.014(1)	0.001(1)	0.002(1)	0.000(1)
C(11)	0.015(1)	0.015(1)	0.013(1)	0.001(1)	0.001(1)	0.001(1)
C(12)	0.016(1)	0.013(1)	0.015(1)	0.003(1)	0.006(1)	-0.001(1)
C(13)	0.022(1)	0.017(1)	0.023(1)	0.009(1)	0.011(1)	0.004(1)
C(14)	0.014(1)	0.012(1)	0.013(1)	0.000(1)	0.005(1)	-0.001(1)
C(15)	0.019(1)	0.020(1)	0.022(1)	-0.003(1)	0.010(1)	-0.006(1)
C(16)	0.015(1)	0.021(1)	0.014(1)	-0.003(1)	0.002(1)	0.002(1)
C(17)	0.026(1)	0.025(1)	0.019(1)	0.003(1)	0.001(1)	0.009(1)
O(1)	0.012(1)	0.013(1)	0.009(1)	-0.001(1)	0.003(1)	-0.003(1)
O(2)	0.011(1)	0.014(1)	0.011(1)	-0.001(1)	0.002(1)	0.001(1)
O(3)	0.015(1)	0.033(1)	0.022(1)	-0.009(1)	0.003(1)	0.006(1)
O(4)	0.015(1)	0.012(1)	0.015(1)	0.004(1)	0.008(1)	0.003(1)
O(5)	0.024(1)	0.022(1)	0.024(1)	0.007(1)	0.016(1)	0.006(1)
O(6)	0.014(1)	0.012(1)	0.018(1)	-0.003(1)	0.009(1)	-0.003(1)
O(7)	0.025(1)	0.016(1)	0.032(1)	-0.007(1)	0.017(1)	-0.003(1)
O(8)	0.015(1)	0.017(1)	0.012(1)	0.001(1)	0.003(1)	0.001(1)
O(9)	0.019(1)	0.030(1)	0.022(1)	0.002(1)	0.010(1)	0.004(1)

Hydrogen Coordinates & Isotropic Displacement Parameters (Å2)

	x	y	z	U_{eq}
H(1)	-0.0138	0.2422	0.8567	0.028
H(3A)	0.1908	0.0363	0.6553	0.016
H(3B)	0.2876	-0.0066	0.7855	0.016
H(4)	0.3985	0.1716	0.6855	0.013
H(5)	0.2024	0.4461	0.6686	0.013
H(6)	0.4285	0.4563	0.5838	0.013
H(7)	0.4111	0.6535	0.7883	0.014

H(8)	0.5678	0.3355	0.7910	0.014
H(9A)	0.6555	0.5531	0.9507	0.016
H(9B)	0.5313	0.5077	0.9943	0.016
H(11A)	-0.0729	0.2273	0.3384	0.023
H(11B)	0.0726	0.1690	0.3421	0.023
H(11C)	0.0157	0.3594	0.2892	0.023
H(13A)	0.2666	0.8909	0.3304	0.030
H(13B)	0.3181	0.9970	0.4535	0.030
H(13C)	0.1846	0.8834	0.4224	0.030
H(15A)	0.7420	1.0164	0.7792	0.029
H(15B)	0.7242	0.8691	0.6776	0.029
H(15C)	0.8032	0.8212	0.8129	0.029
H(17A)	0.9038	0.0525	1.0340	0.037
H(17B)	0.7613	-0.0051	1.0392	0.037
H(17C)	0.8560	0.1148	1.1429	0.037

6.4.10. Crystallographic Data Of 104

Crystal Data & Structure Refinement

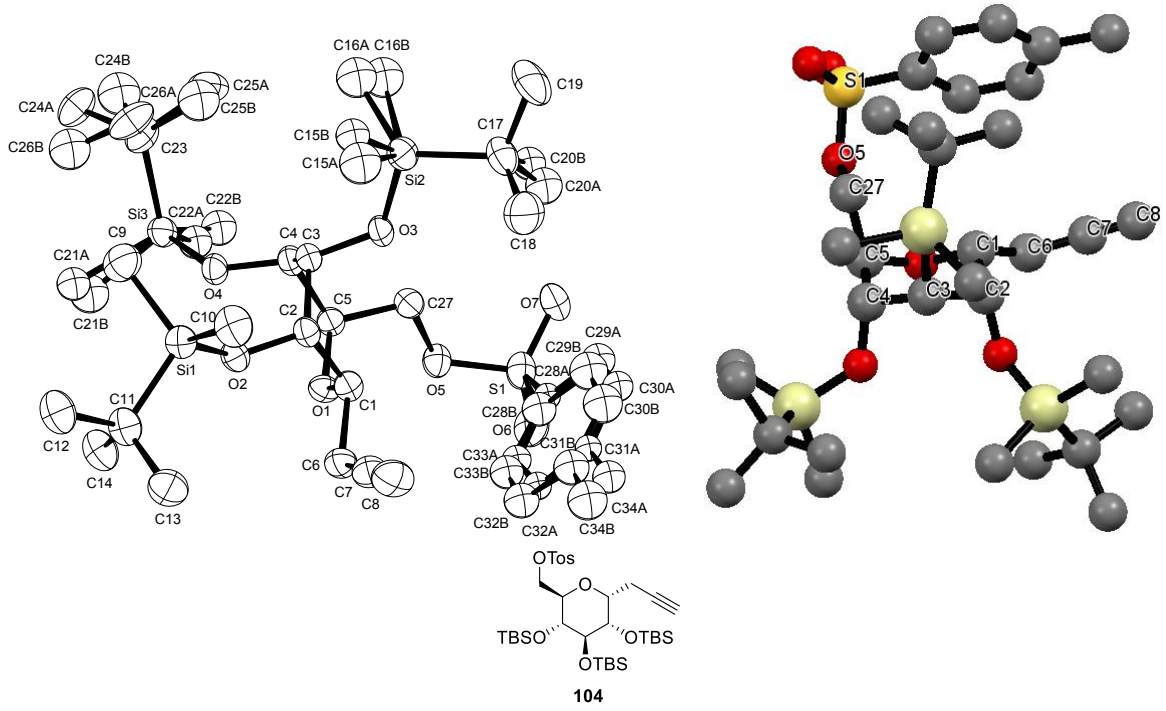


Figure 6.30: X-Ray single crystal structure and molecular structure of tosylate **104** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary).

Identification code	9643sadabs	
Empirical formula	$C_{34}H_{62}O_7SSi_3$	
Color	colourless	
Formula weight	699.16 g·mol^{-1}	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	orthorhombic	
Space group	P 2_1 2_1 2_1 (No. 19)	
Unit cell dimensions	a = 11.5486(7) Å	α = 90°.
	b = 14.7788(8) Å	β = 90°.
	c = 23.7438(13) Å	γ = 90°.
Volume	4052.5(4) Å^3	
Z	4	
Density (calculated)	1.146 Mg·m^{-3}	
Absorption coefficient	1.886 mm^{-1}	

F(000)	1520 e	
Crystal size	0.24 x 0.13 x 0.05 mm^3	
θ range for data collection	3.523 to 67.883°.	
Index ranges	$-13 \leq h \leq 11$, $-17 \leq k \leq 17$, $-28 \leq l \leq 28$	
Reflections collected	183456	
Independent reflections	7291 [R_{int} = 0.0789]	
Reflections with I>2σ(I)	6870	
Completeness to θ = 67.679°	99.5%	
Absorption correction	Gaussian	
Max. and min. transmission	0.91016 and 0.66204	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	7291/0/431	
Goodness-of-fit on F^2	1.044	
Final R indices [I>2σ(I)]	R_1 = 0.0530	wR^2 = 0.1356
R indices (all data)	R_1 = 0.0561	wR^2 = 0.1383
Absolute structure parameter	0.013(7)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.360 and -0.676 e·$Å^{-3}$	

Bond Lengths [Å] & Angles [°]

Si(3)-O(4)	1.644(3)	Si(3)-C(23)	1.887(5)
Si(3)-C(22A)	1.770(11)	Si(3)-C(21B)	1.795(12)
Si(3)-C(21A)	1.923(10)	Si(3)-C(22B)	1.988(12)
S(1)-O(5)	1.570(3)	S(1)-O(6)	1.423(4)
S(1)-O(7)	1.434(4)	S(1)-C(28B)	1.852(16)
S(1)-C(28A)	1.657(12)	Si(1)-O(2)	1.651(3)
Si(1)-C(9)	1.863(6)	Si(1)-C(11)	1.887(5)
Si(1)-C(10)	1.852(5)	Si(2)-O(3)	1.652(3)
Si(2)-C(17)	1.859(5)	Si(2)-C(15A)	2.028(14)
Si(2)-C(16A)	1.806(13)	Si(2)-C(16B)	1.916(13)
Si(2)-C(15B)	1.772(10)	O(1)-C(1)	1.437(5)
O(1)-C(5)	1.436(5)	O(2)-C(2)	1.415(5)
O(5)-C(27)	1.462(5)	C(4)-O(4)	1.428(5)
C(4)-C(5)	1.524(6)	C(4)-C(3)	1.529(6)
O(3)-C(3)	1.434(5)	C(1)-C(2)	1.510(6)
C(1)-C(6)	1.520(6)	C(2)-C(3)	1.542(6)
C(5)-C(27)	1.523(6)	C(23)-C(24A)	1.537(8)
C(23)-C(26B)	1.676(19)	C(23)-C(25A)	1.584(9)
C(23)-C(26A)	1.511(8)	C(23)-C(25B)	1.479(19)

C(23)-C(24B)	1.49(2)	C(33B)-C(32B)	1.363(19)
C(33B)-C(28B)	1.37(2)	C(29B)-C(28B)	1.43(2)
C(29B)-C(30B)	1.42(2)	C(6)-C(7)	1.463(6)
C(7)-C(8)	1.193(7)	C(17)-C(19)	1.535(7)
C(17)-C(20A)	1.539(12)	C(17)-C(18)	1.510(9)
C(17)-C(20B)	1.578(11)	C(11)-C(14)	1.540(7)
C(11)-C(13)	1.517(7)	C(11)-C(12)	1.538(7)
C(31B)-C(32B)	1.395(18)	C(31B)-C(34B)	1.489(17)
C(31B)-C(30B)	1.37(2)	C(28A)-C(33A)	1.388(19)
C(28A)-C(29A)	1.369(17)	C(33A)-C(32A)	1.413(16)
C(32A)-C(31A)	1.396(15)	C(31A)-C(30A)	1.361(16)
C(31A)-C(34A)	1.508(14)	C(30A)-C(29A)	1.418(17)
O(4)-Si(3)-C(23)	111.49(19)	O(4)-Si(3)-C(22A)	113.3(4)
O(4)-Si(3)-C(21B)	106.7(4)	O(4)-Si(3)-C(21A)	102.0(3)
O(4)-Si(3)-C(22B)	107.0(4)	C(23)-Si(3)-C(21A)	106.0(4)
C(23)-Si(3)-C(22B)	105.1(4)	C(22A)-Si(3)-C(23)	112.3(4)
C(22A)-Si(3)-C(21A)	111.1(5)	C(21B)-Si(3)-C(23)	119.6(4)
C(21B)-Si(3)-C(22B)	106.2(6)	O(5)-S(1)-C(28B)	100.4(5)
O(5)-S(1)-C(28A)	106.2(4)	O(6)-S(1)-O(5)	104.37(19)
O(6)-S(1)-O(7)	119.7(2)	O(6)-S(1)-C(28B)	107.4(5)
O(6)-S(1)-C(28A)	111.2(4)	O(7)-S(1)-O(5)	109.8(2)
O(7)-S(1)-C(28B)	113.1(5)	O(7)-S(1)-C(28A)	104.9(5)
O(2)-Si(1)-C(9)	109.5(2)	O(2)-Si(1)-C(11)	105.01(18)
O(2)-Si(1)-C(10)	111.2(2)	C(9)-Si(1)-C(11)	110.4(2)
C(10)-Si(1)-C(9)	109.7(3)	C(10)-Si(1)-C(11)	110.9(2)
O(3)-Si(2)-C(17)	105.4(2)	O(3)-Si(2)-C(15A)	103.4(5)
O(3)-Si(2)-C(16A)	112.6(4)	O(3)-Si(2)-C(16B)	108.0(4)
O(3)-Si(2)-C(15B)	113.6(4)	C(17)-Si(2)-C(15A)	106.5(5)
C(17)-Si(2)-C(16B)	105.9(5)	C(16A)-Si(2)-C(17)	122.3(5)
C(16A)-Si(2)-C(15A)	105.1(6)	C(15B)-Si(2)-C(17)	115.7(4)
C(15B)-Si(2)-C(16B)	107.8(6)	C(5)-O(1)-C(1)	114.2(3)
C(2)-O(2)-Si(1)	129.1(3)	C(27)-O(5)-S(1)	117.4(3)
O(4)-C(4)-C(5)	110.1(3)	O(4)-C(4)-C(3)	108.5(3)
C(5)-C(4)-C(3)	112.1(3)	C(4)-O(4)-Si(3)	127.6(3)
C(3)-O(3)-Si(2)	124.5(3)	O(1)-C(1)-C(2)	112.2(3)
O(1)-C(1)-C(6)	104.5(3)	C(2)-C(1)-C(6)	113.4(4)
O(2)-C(2)-C(1)	110.3(3)	O(2)-C(2)-C(3)	111.7(3)
C(1)-C(2)-C(3)	109.7(3)	O(1)-C(5)-C(4)	112.0(3)
O(1)-C(5)-C(27)	112.2(3)	C(27)-C(5)-C(4)	112.6(3)
C(24A)-C(23)-Si(3)	111.1(4)	C(24A)-C(23)-C(25A)	105.3(5)
C(26B)-C(23)-Si(3)	97.9(7)	C(25A)-C(23)-Si(3)	107.8(4)
C(26A)-C(23)-Si(3)	114.0(4)	C(26A)-C(23)-C(24A)	110.6(5)
C(26A)-C(23)-C(25A)	107.5(6)	C(25B)-C(23)-Si(3)	112.9(8)
C(25B)-C(23)-C(26B)	108.1(10)	C(25B)-C(23)-C(24B)	115.6(12)
C(24B)-C(23)-Si(3)	111.4(8)	C(24B)-C(23)-C(26B)	109.4(11)
O(5)-C(27)-C(5)	106.9(3)	C(32B)-C(33B)-C(28B)	120.9(14)
C(4)-C(3)-C(2)	113.8(3)	O(3)-C(3)-C(4)	107.5(3)
O(3)-C(3)-C(2)	106.7(3)	C(30B)-C(29B)-C(28B)	115.2(15)
C(7)-C(6)-C(1)	111.9(4)	C(8)-C(7)-C(6)	179.7(6)

C(19)-C(17)-Si(2)	111.0(4)	C(19)-C(17)-C(20A)	112.3(6)
C(19)-C(17)-C(20B)	104.5(6)	C(20A)-C(17)-Si(2)	114.8(5)
C(18)-C(17)-Si(2)	110.6(4)	C(18)-C(17)-C(19)	109.1(5)
C(18)-C(17)-C(20A)	98.3(7)	C(18)-C(17)-C(20B)	119.2(7)
C(20B)-C(17)-Si(2)	102.2(5)	C(14)-C(11)-Si(1)	109.3(3)
C(13)-C(11)-Si(1)	111.1(4)	C(13)-C(11)-C(14)	108.4(5)
C(13)-C(11)-C(12)	108.8(4)	C(12)-C(11)-Si(1)	109.8(4)
C(12)-C(11)-C(14)	109.4(4)	C(32B)-C(31B)-C(34B)	119.4(13)
C(30B)-C(31B)-C(32B)	118.9(12)	C(30B)-C(31B)-C(34B)	121.6(12)
C(33B)-C(32B)-C(31B)	120.6(14)	C(33B)-C(28B)-S(1)	121.6(11)
C(33B)-C(28B)-C(29B)	121.4(14)	C(29B)-C(28B)-S(1)	116.9(13)
C(31B)-C(30B)-C(29B)	122.9(13)	C(33A)-C(28A)-S(1)	116.3(9)
C(29A)-C(28A)-S(1)	122.9(11)	C(29A)-C(28A)-C(33A)	120.7(12)
C(28A)-C(33A)-C(32A)	119.6(12)	C(31A)-C(32A)-C(33A)	119.6(11)
C(32A)-C(31A)-C(34A)	118.6(11)	C(30A)-C(31A)-C(32A)	119.8(9)
C(30A)-C(31A)-C(34A)	121.6(9)	C(31A)-C(30A)-C(29A)	121.0(10)
C(28A)-C(29A)-C(30A)	119.3(13)		

6.4.11. Crystallographic Data Of 115

Crystal Data & Structure Refinement

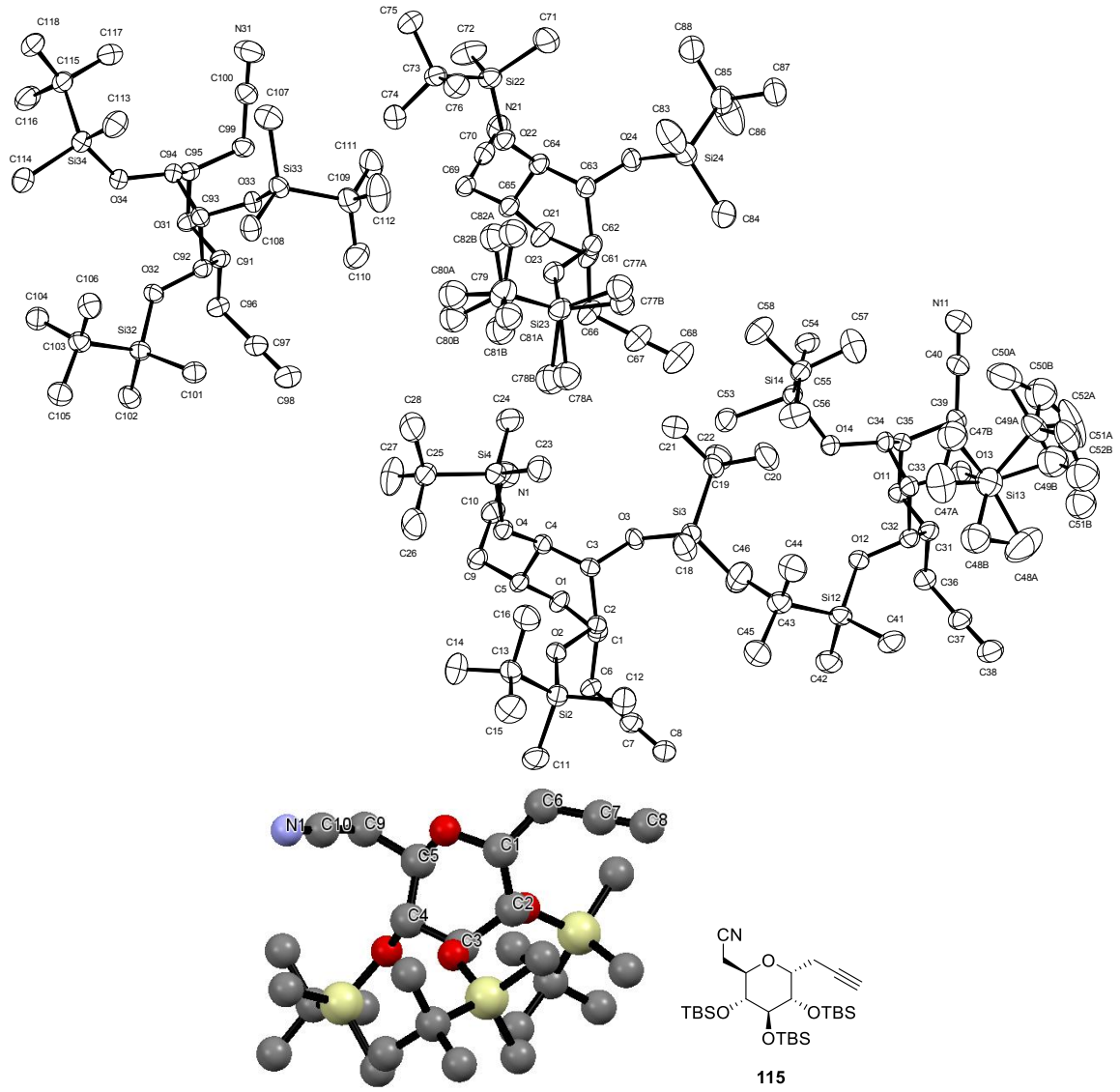


Figure 6.31: X-Ray single crystal structure and molecular structure of nitrile **115** (hydrogen atoms not shown for better visibility, numbering of atoms is arbitrary).

Identification code	9887
Empirical formula	$C_{28}H_{55}NO_4Si_3$
Color	colorless
Formula weight	554.00 g·mol^{-1}
Temperature	100 K
Wavelength	1.54178 Å
Crystal system	monoclinic

Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 21.2571(6) Å	α = 90°.
	b = 11.4919(3) Å	β = 104.2930(10)°.
	c = 29.2028(8) Å	γ = 90°.
Volume	6913.0(3) $Å^3$	
Z	8	
Density (calculated)	1.065 $Mg·m^{-3}$	
Absorption coefficient	1.487 mm^{-1}	
F(000)	2432 e	
Crystal size	0.400 x 0.249 x 0.100 mm^3	
θ range for data collection	1.561 to 67.529°.	
Index ranges	$-25 \leq h \leq 25$, $-13 \leq k \leq 11$, $-34 \leq l \leq 34$	
Reflections collected	220531	
Independent reflections	22775 [R_{int} = 0.0855]	
Reflections with I>2σ(I)	19511	
Completeness to θ = 67.529°	98.4%	
Absorption correction	Gaussian	
Max. and min. transmission	0.92 and 0.71	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	22775/1/1404	
Goodness-of-fit on F^2	1.024	
Final R indices [I>2σ(I)]	R_1 = 0.0542	wR^2 = 0.1313
R indices (all data)	R_1 = 0.0675	wR^2 = 0.1418
Absolute structure parameter	0.02(2)	
Extinction coefficient	0.00172(12)	
Largest diff. peak and hole	1.4 and -0.4 $e·Å^{-3}$	

Bond Lengths [Å] & Angles [°]

Si(2)-O(2)	1.662(3)	Si(2)-C(11)	1.849(6)
Si(2)-C(12)	1.854(5)	Si(2)-C(13)	1.889(5)
Si(3)-O(3)	1.652(3)	Si(3)-C(17)	1.860(5)
Si(3)-C(18)	1.860(6)	Si(3)-C(19)	1.882(5)
Si(4)-O(4)	1.650(3)	Si(4)-C(23)	1.856(5)
Si(4)-C(24)	1.851(6)	Si(4)-C(25)	1.886(5)
O(1)-C(1)	1.446(5)	O(1)-C(5)	1.434(5)
O(2)-C(2)	1.418(5)	O(3)-C(3)	1.432(5)

O(4)-C(4)	1.425(5)	N(1)-C(10)	1.151(7)
C(1)-C(2)	1.534(6)	C(1)-C(6)	1.525(6)
C(2)-C(3)	1.534(6)	C(3)-C(4)	1.540(6)
C(4)-C(5)	1.517(6)	C(5)-C(9)	1.542(6)
C(6)-C(7)	1.472(6)	C(7)-C(8)	1.189(7)
C(9)-C(10)	1.457(8)	C(13)-C(14)	1.531(7)
C(13)-C(15)	1.534(7)	C(13)-C(16)	1.533(7)
C(19)-C(20)	1.537(7)	C(19)-C(21)	1.529(7)
C(19)-C(22)	1.525(7)	C(25)-C(26)	1.540(9)
C(25)-C(27)	1.515(7)	C(25)-C(28)	1.510(7)
Si(22)-O(22)	1.647(3)	Si(22)-C(71)	1.848(6)
Si(22)-C(72)	1.865(6)	Si(22)-C(73)	1.880(5)
Si(23)-O(23)	1.650(4)	Si(23)-C(77A)	1.953(13)
Si(23)-C(77B)	1.775(12)	Si(23)-C(78A)	1.776(14)
Si(23)-C(78B)	1.947(16)	Si(23)-C(79)	1.875(6)
Si(24)-O(24)	1.657(3)	Si(24)-C(83)	1.853(7)
Si(24)-C(84)	1.853(7)	Si(24)-C(85)	1.881(6)
O(21)-C(61)	1.439(5)	O(21)-C(65)	1.428(5)
O(22)-C(64)	1.434(5)	O(23)-C(62)	1.431(6)
O(24)-C(63)	1.429(5)	N(21)-C(70)	1.147(7)
C(61)-C(62)	1.522(6)	C(61)-C(66)	1.524(7)
C(62)-C(63)	1.536(6)	C(63)-C(64)	1.551(6)
C(64)-C(65)	1.525(6)	C(65)-C(69)	1.531(6)
C(66)-C(67)	1.458(7)	C(67)-C(68)	1.190(8)
C(69)-C(70)	1.469(7)	C(73)-C(74)	1.540(7)
C(73)-C(75)	1.537(6)	C(73)-C(76)	1.532(7)
C(79)-C(80A)	1.445(15)	C(79)-C(80B)	1.618(15)
C(79)-C(81A)	1.561(16)	C(79)-C(81B)	1.521(17)
C(79)-C(82A)	1.641(15)	C(79)-C(82B)	1.465(15)
C(85)-C(86)	1.518(9)	C(85)-C(87)	1.534(7)
C(85)-C(88)	1.538(8)	Si(32)-O(32)	1.662(3)
Si(32)-C(101)	1.865(5)	Si(32)-C(102)	1.856(5)
Si(32)-C(103)	1.875(5)	Si(33)-O(33)	1.655(3)
Si(33)-C(107)	1.859(6)	Si(33)-C(108)	1.849(5)
Si(33)-C(109)	1.869(5)	Si(34)-O(34)	1.662(3)
Si(34)-C(113)	1.851(5)	Si(34)-C(114)	1.855(6)
Si(34)-C(115)	1.892(5)	O(31)-C(91)	1.436(5)
O(31)-C(95)	1.430(5)	O(32)-C(92)	1.420(5)
O(33)-C(93)	1.433(5)	O(34)-C(94)	1.425(5)
N(31)-C(100)	1.144(7)	C(91)-C(92)	1.522(6)
C(91)-C(96)	1.530(6)	C(92)-C(93)	1.534(6)
C(93)-C(94)	1.540(6)	C(94)-C(95)	1.533(6)
C(95)-C(99)	1.548(6)	C(96)-C(97)	1.465(6)
C(97)-C(98)	1.189(7)	C(99)-C(100)	1.465(6)
C(103)-C(104)	1.532(6)	C(103)-C(105)	1.547(7)
C(103)-C(106)	1.540(7)	C(109)-C(110)	1.526(8)
C(109)-C(111)	1.531(7)	C(109)-C(112)	1.540(7)
C(115)-C(116)	1.536(7)	C(115)-C(117)	1.524(7)
C(115)-C(118)	1.539(6)	Si(12)-O(12)	1.664(3)

Si(12)-C(41)	1.854(5)	Si(12)-C(42)	1.854(5)
Si(12)-C(43)	1.884(5)	Si(13)-O(13)	1.670(4)
Si(13)-C(47A)	1.837(9)	Si(13)-C(47B)	1.92(3)
Si(13)-C(48A)	1.858(9)	Si(13)-C(48B)	1.66(4)
Si(13)-C(49A)	1.860(8)	Si(13)-C(49B)	1.74(3)
Si(14)-O(14)	1.656(3)	Si(14)-C(53)	1.855(5)
Si(14)-C(54)	1.846(5)	Si(14)-C(55)	1.884(5)
O(11)-C(31)	1.432(5)	O(11)-C(35)	1.438(5)
O(12)-C(32)	1.428(5)	O(13)-C(33)	1.431(5)
O(14)-C(34)	1.425(5)	N(11)-C(40)	1.148(7)
C(31)-C(32)	1.521(6)	C(31)-C(36)	1.520(6)
C(32)-C(33)	1.535(6)	C(33)-C(34)	1.534(6)
C(34)-C(35)	1.530(6)	C(35)-C(39)	1.546(6)
C(36)-C(37)	1.452(7)	C(37)-C(38)	1.201(8)
C(39)-C(40)	1.463(7)	C(43)-C(44)	1.538(7)
C(43)-C(45)	1.528(8)	C(43)-C(46)	1.518(7)
C(49A)-C(50A)	1.544(13)	C(49A)-C(51A)	1.540(10)
C(49A)-C(52A)	1.519(12)	C(49B)-C(50B)	1.85(5)
C(49B)-C(51B)	1.67(4)	C(49B)-C(52B)	1.58(4)
C(55)-C(56)	1.536(8)	C(55)-C(57)	1.517(7)
C(55)-C(58)	1.534(6)	O(2)-Si(2)-C(11)	108.4(2)
O(2)-Si(2)-C(12)	109.5(2)	O(2)-Si(2)-C(13)	107.02(19)
C(11)-Si(2)-C(12)	110.0(3)	C(11)-Si(2)-C(13)	110.2(2)
C(12)-Si(2)-C(13)	111.6(2)	O(3)-Si(3)-C(17)	109.1(2)
O(3)-Si(3)-C(18)	110.2(2)	O(3)-Si(3)-C(19)	105.66(19)
C(17)-Si(3)-C(18)	110.3(3)	C(17)-Si(3)-C(19)	110.3(2)
C(18)-Si(3)-C(19)	111.3(2)	O(4)-Si(4)-C(23)	110.3(2)
O(4)-Si(4)-C(24)	110.5(2)	O(4)-Si(4)-C(25)	103.24(19)
C(23)-Si(4)-C(25)	111.6(2)	C(24)-Si(4)-C(23)	109.3(3)
C(24)-Si(4)-C(25)	111.8(2)	C(5)-O(1)-C(1)	113.9(3)
C(2)-O(2)-Si(2)	130.1(3)	C(3)-O(3)-Si(3)	128.7(3)
C(4)-O(4)-Si(4)	127.3(3)	O(1)-C(1)-C(2)	113.1(3)
O(1)-C(1)-C(6)	107.6(3)	C(6)-C(1)-C(2)	113.8(4)
O(2)-C(2)-C(1)	111.6(4)	O(2)-C(2)-C(3)	108.7(3)
C(1)-C(2)-C(3)	109.6(3)	O(3)-C(3)-C(2)	110.1(3)
O(3)-C(3)-C(4)	108.2(3)	C(2)-C(3)-C(4)	111.7(4)
O(4)-C(4)-C(3)	112.4(3)	O(4)-C(4)-C(5)	107.1(3)
C(5)-C(4)-C(3)	111.1(3)	O(1)-C(5)-C(4)	108.8(3)
O(1)-C(5)-C(9)	107.1(3)	C(4)-C(5)-C(9)	113.9(4)
C(7)-C(6)-C(1)	113.6(4)	C(8)-C(7)-C(6)	178.8(5)
C(10)-C(9)-C(5)	114.3(4)	N(1)-C(10)-C(9)	178.5(6)
C(14)-C(13)-Si(2)	109.8(4)	C(14)-C(13)-C(15)	108.5(5)
C(14)-C(13)-C(16)	109.0(4)	C(15)-C(13)-Si(2)	110.2(4)
C(16)-C(13)-Si(2)	110.5(3)	C(16)-C(13)-C(15)	108.8(5)
C(20)-C(19)-Si(3)	110.8(4)	C(21)-C(19)-Si(3)	110.7(4)
C(21)-C(19)-C(20)	109.1(4)	C(22)-C(19)-Si(3)	109.2(3)
C(22)-C(19)-C(20)	108.4(4)	C(22)-C(19)-C(21)	108.6(4)
C(26)-C(25)-Si(4)	109.9(4)	C(27)-C(25)-Si(4)	109.2(4)
C(27)-C(25)-C(26)	106.4(6)	C(28)-C(25)-Si(4)	110.8(4)

C(28)-C(25)-C(26)	110.9(5)	C(28)-C(25)-C(27)	109.7(5)
O(22)-Si(22)-C(71)	111.0(2)	O(22)-Si(22)-C(72)	110.5(2)
O(22)-Si(22)-C(73)	103.79(19)	C(71)-Si(22)-C(72)	108.8(3)
C(71)-Si(22)-C(73)	111.7(2)	C(72)-Si(22)-C(73)	111.0(2)
O(23)-Si(23)-C(77A)	110.2(4)	O(23)-Si(23)-C(77B)	110.6(4)
O(23)-Si(23)-C(78A)	113.7(5)	O(23)-Si(23)-C(78B)	104.8(5)
O(23)-Si(23)-C(79)	105.3(2)	C(77B)-Si(23)-C(78B)	109.6(6)
C(77B)-Si(23)-C(79)	117.9(5)	C(78A)-Si(23)-C(77A)	107.7(7)
C(78A)-Si(23)-C(79)	115.0(5)	C(79)-Si(23)-C(77A)	104.6(5)
C(79)-Si(23)-C(78B)	107.8(5)	O(24)-Si(24)-C(83)	110.1(2)
O(24)-Si(24)-C(84)	111.2(3)	O(24)-Si(24)-C(85)	104.9(2)
C(83)-Si(24)-C(84)	109.5(4)	C(83)-Si(24)-C(85)	110.9(3)
C(84)-Si(24)-C(85)	110.3(3)	C(65)-O(21)-C(61)	117.1(3)
C(64)-O(22)-Si(22)	127.4(3)	C(62)-O(23)-Si(23)	129.0(3)
C(63)-O(24)-Si(24)	127.2(3)	O(21)-C(61)-C(62)	112.4(3)
O(21)-C(61)-C(66)	106.6(4)	C(62)-C(61)-C(66)	113.4(4)
O(23)-C(62)-C(61)	111.2(4)	O(23)-C(62)-C(63)	108.6(3)
C(61)-C(62)-C(63)	110.2(4)	O(24)-C(63)-C(62)	110.0(3)
O(24)-C(63)-C(64)	109.0(4)	C(62)-C(63)-C(64)	111.8(4)
O(22)-C(64)-C(63)	110.5(3)	O(22)-C(64)-C(65)	107.6(3)
C(65)-C(64)-C(63)	111.1(4)	O(21)-C(65)-C(64)	110.6(4)
O(21)-C(65)-C(69)	105.4(4)	C(64)-C(65)-C(69)	114.2(4)
C(67)-C(66)-C(61)	113.5(5)	C(68)-C(67)-C(66)	177.9(7)
C(70)-C(69)-C(65)	113.0(4)	N(21)-C(70)-C(69)	179.1(5)
C(74)-C(73)-Si(22)	110.3(3)	C(75)-C(73)-Si(22)	109.6(3)
C(75)-C(73)-C(74)	109.0(4)	C(76)-C(73)-Si(22)	110.1(3)
C(76)-C(73)-C(74)	109.5(4)	C(76)-C(73)-C(75)	108.3(4)
C(80A)-C(79)-Si(23)	115.8(7)	C(80A)-C(79)-C(81A)	119.0(9)
C(80A)-C(79)-C(82A)	107.3(9)	C(80B)-C(79)-Si(23)	105.4(6)
C(81A)-C(79)-Si(23)	111.8(6)	C(81A)-C(79)-C(82A)	94.7(8)
C(81B)-C(79)-Si(23)	110.3(6)	C(81B)-C(79)-C(80B)	94.3(9)
C(82A)-C(79)-Si(23)	104.7(6)	C(82B)-C(79)-Si(23)	113.9(7)
C(82B)-C(79)-C(80B)	108.4(9)	C(82B)-C(79)-C(81B)	121.5(9)
C(86)-C(85)-Si(24)	111.0(5)	C(86)-C(85)-C(87)	109.6(5)
C(86)-C(85)-C(88)	109.3(7)	C(87)-C(85)-Si(24)	110.6(4)
C(87)-C(85)-C(88)	107.1(5)	C(88)-C(85)-Si(24)	109.2(4)
O(32)-Si(32)-C(101)	110.3(2)	O(32)-Si(32)-C(102)	108.3(2)
O(32)-Si(32)-C(103)	106.43(18)	C(101)-Si(32)-C(103)	110.4(2)
C(102)-Si(32)-C(101)	110.5(2)	C(102)-Si(32)-C(103)	110.7(2)
O(33)-Si(33)-C(107)	110.2(2)	O(33)-Si(33)-C(108)	109.6(2)
O(33)-Si(33)-C(109)	103.59(19)	C(107)-Si(33)-C(109)	110.4(3)
C(108)-Si(33)-C(107)	110.6(2)	C(108)-Si(33)-C(109)	112.2(2)
O(34)-Si(34)-C(113)	110.20(19)	O(34)-Si(34)-C(114)	106.4(2)
O(34)-Si(34)-C(115)	109.8(2)	C(113)-Si(34)-C(114)	109.7(3)
C(113)-Si(34)-C(115)	110.8(2)	C(114)-Si(34)-C(115)	109.8(2)
C(95)-O(31)-C(91)	113.8(3)	C(92)-O(32)-Si(32)	127.1(3)
C(93)-O(33)-Si(33)	126.2(3)	C(94)-O(34)-Si(34)	123.1(3)
O(31)-C(91)-C(92)	111.1(3)	O(31)-C(91)-C(96)	104.8(3)
C(92)-C(91)-C(96)	114.4(4)	O(32)-C(92)-C(91)	111.2(3)

O(32)-C(92)-C(93)	110.4(3)	C(91)-C(92)-C(93)	109.5(4)
O(33)-C(93)-C(92)	106.2(3)	O(33)-C(93)-C(94)	107.7(3)
C(92)-C(93)-C(94)	114.5(4)	O(34)-C(94)-C(93)	109.8(4)
O(34)-C(94)-C(95)	109.3(3)	C(95)-C(94)-C(93)	112.0(3)
O(31)-C(95)-C(94)	111.5(4)	O(31)-C(95)-C(99)	109.4(3)
C(94)-C(95)-C(99)	114.5(4)	C(97)-C(96)-C(91)	112.0(4)
C(98)-C(97)-C(96)	178.9(6)	C(100)-C(99)-C(95)	112.7(4)
N(31)-C(100)-C(99)	179.3(6)	C(104)-C(103)-Si(32)	109.8(3)
C(104)-C(103)-C(105)	108.6(4)	C(104)-C(103)-C(106)	109.2(4)
C(105)-C(103)-Si(32)	111.0(3)	C(106)-C(103)-Si(32)	110.2(3)
C(106)-C(103)-C(105)	108.1(4)	C(110)-C(109)-Si(33)	109.8(4)
C(110)-C(109)-C(111)	108.8(5)	C(110)-C(109)-C(112)	109.1(5)
C(111)-C(109)-Si(33)	110.1(4)	C(111)-C(109)-C(112)	109.5(5)
C(112)-C(109)-Si(33)	109.6(4)	C(116)-C(115)-Si(34)	108.4(3)
C(116)-C(115)-C(118)	109.4(4)	C(117)-C(115)-Si(34)	111.1(3)
C(117)-C(115)-C(116)	108.9(5)	C(117)-C(115)-C(118)	109.3(4)
C(118)-C(115)-Si(34)	109.7(4)	O(12)-Si(12)-C(41)	111.2(2)
O(12)-Si(12)-C(42)	107.4(2)	O(12)-Si(12)-C(43)	107.0(2)
C(41)-Si(12)-C(42)	109.1(2)	C(41)-Si(12)-C(43)	110.6(2)
C(42)-Si(12)-C(43)	111.5(2)	O(13)-Si(13)-C(47A)	111.7(3)
O(13)-Si(13)-C(47B)	104.1(11)	O(13)-Si(13)-C(48A)	108.7(4)
O(13)-Si(13)-C(49A)	106.2(3)	O(13)-Si(13)-C(49B)	108.6(10)
C(47A)-Si(13)-C(48A)	109.3(6)	C(47A)-Si(13)-C(49A)	110.1(4)
C(48A)-Si(13)-C(49A)	110.9(5)	C(48B)-Si(13)-O(13)	115.4(12)
C(48B)-Si(13)-C(47B)	100.3(17)	C(48B)-Si(13)-C(49B)	119.0(16)
C(49B)-Si(13)-C(47B)	107.8(15)	O(14)-Si(14)-C(53)	104.60(19)
O(14)-Si(14)-C(54)	109.78(19)	O(14)-Si(14)-C(55)	111.16(19)
C(53)-Si(14)-C(55)	109.9(2)	C(54)-Si(14)-C(53)	111.6(3)
C(54)-Si(14)-C(55)	109.7(2)	C(31)-O(11)-C(35)	113.7(3)
C(32)-O(12)-Si(12)	127.1(3)	C(33)-O(13)-Si(13)	123.1(3)
C(34)-O(14)-Si(14)	123.5(3)	O(11)-C(31)-C(32)	111.2(3)
O(11)-C(31)-C(36)	105.1(4)	C(36)-C(31)-C(32)	114.1(4)
O(12)-C(32)-C(31)	110.5(3)	O(12)-C(32)-C(33)	109.8(3)
C(31)-C(32)-C(33)	110.1(4)	O(13)-C(33)-C(32)	108.2(3)
O(13)-C(33)-C(34)	107.3(4)	C(34)-C(33)-C(32)	114.0(4)
O(14)-C(34)-C(33)	109.2(4)	O(14)-C(34)-C(35)	109.5(3)
C(35)-C(34)-C(33)	112.7(3)	O(11)-C(35)-C(34)	112.0(4)
O(11)-C(35)-C(39)	109.7(3)	C(34)-C(35)-C(39)	113.5(4)
C(37)-C(36)-C(31)	111.8(4)	C(38)-C(37)-C(36)	177.9(6)
C(40)-C(39)-C(35)	111.1(4)	N(11)-C(40)-C(39)	179.0(6)
C(44)-C(43)-Si(12)	109.1(4)	C(45)-C(43)-Si(12)	110.0(4)
C(45)-C(43)-C(44)	107.8(5)	C(46)-C(43)-Si(12)	110.8(3)
C(46)-C(43)-C(44)	109.3(5)	C(46)-C(43)-C(45)	109.7(5)
C(50A)-C(49A)-Si(13)	109.3(6)	C(51A)-C(49A)-Si(13)	110.8(6)
C(51A)-C(49A)-C(50A)	111.1(7)	C(52A)-C(49A)-Si(13)	110.9(6)
C(52A)-C(49A)-C(50A)	106.8(9)	C(52A)-C(49A)-C(51A)	107.7(7)
Si(13)-C(49B)-C(50B)	98.5(18)	C(51B)-C(49B)-Si(13)	104.1(19)
C(51B)-C(49B)-C(50B)	121(2)	C(52B)-C(49B)-Si(13)	111(2)
C(52B)-C(49B)-C(50B)	121(2)	C(52B)-C(49B)-C(51B)	100(2)

C(56)-C(55)-Si(14)	110.1(4)	C(57)-C(55)-Si(14)	112.6(3)
C(57)-C(55)-C(56)	108.6(5)	C(57)-C(55)-C(58)	108.1(5)
C(58)-C(55)-Si(14)	108.9(3)	C(58)-C(55)-C(56)	108.3(4)

6.4.12. Crystallographic Data Of (*S*)-132b

Crystal Data & Structure Refinement

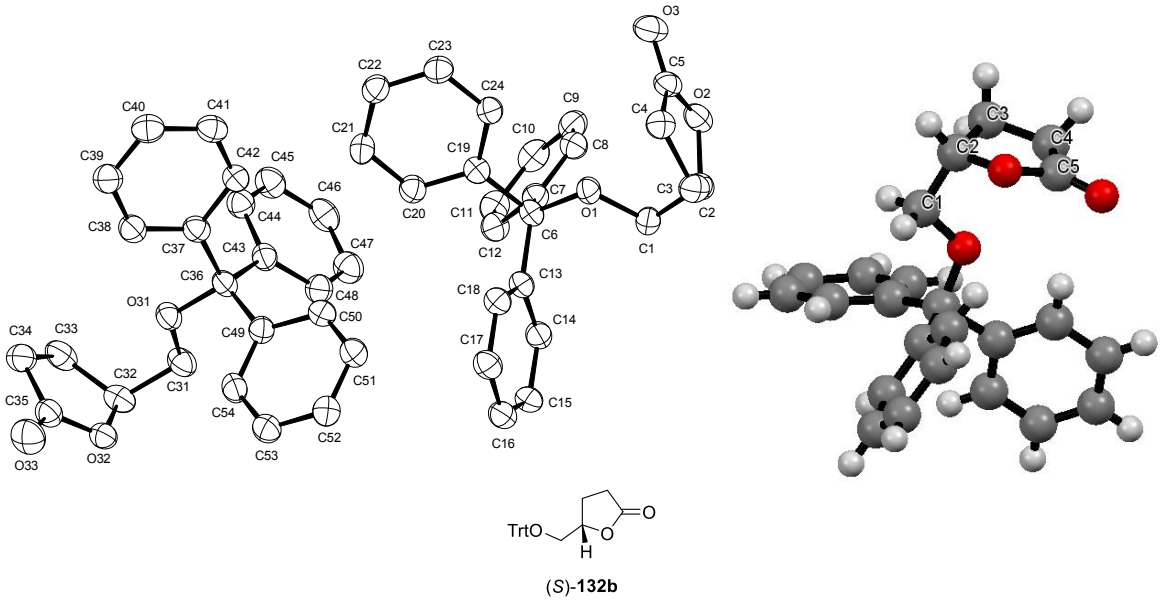


Figure 6.32: X-Ray single crystal structure and molecular structure of lactone (*S*)-**132b** (numbering of atoms is arbitrary).

Identification code	10220	
Empirical formula	$C_{24}H_{22}O_3$	
Color	colorless	
Formula weight	358.41 g·mol^{-1}	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 8.9299(11) Å	α = 90°.
	b = 11.6265(14) Å	β = 94.042(5)°.
	c = 18.063(2) Å	γ = 90°.
Volume	1870.7(4) Å^3	
Z	4	
Density (calculated)	1.273 Mg·mm^{-3}	
Absorption coefficient	0.659 mm^{-1}	
F(000)	760 e	
Crystal size	0.200 x 0.090 x 0.080 mm^3	
θ range for data collection	2.452 to 68.357°.	

Index ranges	$-10 \leq h \leq 10$, $-13 \leq k \leq 13$, $-21 \leq l \leq 21$	
Reflections collected	78376	
Independent reflections	6655 [R_{int} = 0.1421]	
Reflections with I>2σ(I)	5814	
Completeness to θ = 67.679°	99.4%	
Absorption correction	Gaussian	
Max. and min. transmission	0.95 and 0.89	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	6655/1/488	
Goodness-of-fit on F^2	1.137	
Final R indices [I>2σ(I)]	R_1 = 0.0727	wR^2 = 0.1996
R indices (all data)	R_1 = 0.0889	wR^2 = 0.2260
Absolute structure parameter	-0.2(2)	
Extinction coefficient	0.016(3)	
Largest diff. peak and hole	0.7 and -0.4 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(1)-C(1)	1.427(6)	O(1)-C(6)	1.447(6)
O(2)-C(2)	1.455(6)	O(2)-C(5)	1.365(7)
O(3)-C(5)	1.210(7)	C(1)-C(2)	1.512(7)
C(2)-C(3)	1.529(8)	C(3)-C(4)	1.524(8)
C(4)-C(5)	1.486(8)	C(6)-C(7)	1.538(7)
C(6)-C(13)	1.535(7)	C(6)-C(19)	1.536(7)
C(7)-C(8)	1.390(7)	C(7)-C(12)	1.400(7)
C(8)-C(9)	1.395(8)	C(9)-C(10)	1.380(8)
C(10)-C(11)	1.380(9)	C(11)-C(12)	1.393(8)
C(13)-C(14)	1.398(7)	C(13)-C(18)	1.402(8)
C(14)-C(15)	1.388(7)	C(15)-C(16)	1.390(8)
C(16)-C(17)	1.398(8)	C(17)-C(18)	1.378(8)
C(19)-C(20)	1.394(7)	C(19)-C(24)	1.385(7)
C(20)-C(21)	1.391(7)	C(21)-C(22)	1.384(8)
C(22)-C(23)	1.373(8)	C(23)-C(24)	1.410(7)
O(31)-C(31)	1.431(6)	O(31)-C(36)	1.446(5)
O(32)-C(32)	1.453(7)	O(32)-C(35)	1.340(7)
O(33)-C(35)	1.217(7)	C(31)-C(32)	1.515(7)
C(32)-C(33)	1.534(9)	C(33)-C(34)	1.521(9)
C(34)-C(35)	1.481(8)	C(36)-C(37)	1.538(7)
C(36)-C(43)	1.527(7)	C(36)-C(49)	1.547(7)
C(37)-C(38)	1.385(7)	C(37)-C(42)	1.390(7)
C(38)-C(39)	1.388(8)	C(39)-C(40)	1.387(8)
C(40)-C(41)	1.378(8)	C(41)-C(42)	1.384(8)

C(43)-C(44)	1.395(8)	C(43)-C(48)	1.395(7)
C(44)-C(45)	1.384(8)	C(45)-C(46)	1.392(9)
C(46)-C(47)	1.380(9)	C(47)-C(48)	1.399(8)
C(49)-C(50)	1.397(7)	C(49)-C(54)	1.389(7)
C(50)-C(51)	1.388(8)	C(51)-C(52)	1.390(8)
C(52)-C(53)	1.386(8)	C(53)-C(54)	1.393(8)
C(1)-O(1)-C(6)	116.0(4)	C(5)-O(2)-C(2)	109.6(4)
O(1)-C(1)-C(2)	106.2(4)	O(2)-C(2)-C(1)	108.0(4)
O(2)-C(2)-C(3)	105.4(4)	C(1)-C(2)-C(3)	115.3(4)
C(4)-C(3)-C(2)	103.8(4)	C(5)-C(4)-C(3)	104.9(5)
O(2)-C(5)-C(4)	110.9(4)	O(3)-C(5)-O(2)	120.8(5)
O(3)-C(5)-C(4)	128.3(5)	O(1)-C(6)-C(7)	110.8(4)
O(1)-C(6)-C(13)	108.4(4)	O(1)-C(6)-C(19)	104.3(4)
C(13)-C(6)-C(7)	115.2(4)	C(13)-C(6)-C(19)	112.3(4)
C(19)-C(6)-C(7)	105.3(4)	C(8)-C(7)-C(6)	119.6(5)
C(8)-C(7)-C(12)	118.1(5)	C(12)-C(7)-C(6)	121.9(4)
C(7)-C(8)-C(9)	120.9(5)	C(10)-C(9)-C(8)	120.4(5)
C(11)-C(10)-C(9)	119.5(5)	C(10)-C(11)-C(12)	120.4(5)
C(11)-C(12)-C(7)	120.6(5)	C(14)-C(13)-C(6)	123.8(5)
C(14)-C(13)-C(18)	117.6(5)	C(18)-C(13)-C(6)	118.5(4)
C(15)-C(14)-C(13)	121.1(5)	C(14)-C(15)-C(16)	120.5(5)
C(15)-C(16)-C(17)	118.9(5)	C(18)-C(17)-C(16)	120.3(5)
C(17)-C(18)-C(13)	121.5(5)	C(20)-C(19)-C(6)	119.9(4)
C(24)-C(19)-C(6)	121.1(4)	C(24)-C(19)-C(20)	118.8(5)
C(21)-C(20)-C(19)	120.9(5)	C(22)-C(21)-C(20)	119.8(5)
C(23)-C(22)-C(21)	120.2(5)	C(22)-C(23)-C(24)	120.1(5)
C(19)-C(24)-C(23)	120.1(5)	C(31)-O(31)-C(36)	115.6(4)
C(35)-O(32)-C(32)	110.2(4)	O(31)-C(31)-C(32)	107.1(4)
O(32)-C(32)-C(31)	108.7(5)	O(32)-C(32)-C(33)	106.6(5)
C(31)-C(32)-C(33)	114.4(4)	C(34)-C(33)-C(32)	103.9(5)
C(35)-C(34)-C(33)	104.6(5)	O(32)-C(35)-C(34)	112.3(5)
O(33)-C(35)-O(32)	120.1(5)	O(33)-C(35)-C(34)	127.5(5)
O(31)-C(36)-C(37)	104.7(4)	O(31)-C(36)-C(43)	108.3(4)
O(31)-C(36)-C(49)	109.6(4)	C(37)-C(36)-C(49)	107.1(4)
C(43)-C(36)-C(37)	111.7(4)	C(43)-C(36)-C(49)	115.0(4)
C(38)-C(37)-C(36)	122.0(4)	C(38)-C(37)-C(42)	118.0(5)
C(42)-C(37)-C(36)	120.0(5)	C(37)-C(38)-C(39)	121.0(5)
C(40)-C(39)-C(38)	120.1(5)	C(41)-C(40)-C(39)	119.3(5)
C(40)-C(41)-C(42)	120.3(5)	C(41)-C(42)-C(37)	121.2(5)
C(44)-C(43)-C(36)	118.5(5)	C(44)-C(43)-C(48)	118.6(5)
C(48)-C(43)-C(36)	122.3(5)	C(45)-C(44)-C(43)	121.0(5)
C(44)-C(45)-C(46)	120.3(5)	C(47)-C(46)-C(45)	119.3(5)
C(46)-C(47)-C(48)	120.8(5)	C(43)-C(48)-C(47)	120.1(5)
C(50)-C(49)-C(36)	121.0(5)	C(54)-C(49)-C(36)	121.3(4)
C(54)-C(49)-C(50)	117.7(5)	C(51)-C(50)-C(49)	121.2(5)
C(50)-C(51)-C(52)	120.7(5)	C(53)-C(52)-C(51)	118.5(5)
C(52)-C(53)-C(54)	120.9(5)	C(49)-C(54)-C(53)	121.1(5)

6.4.13. Crystallographic Data Of 136

Crystal Data & Structure Refinement

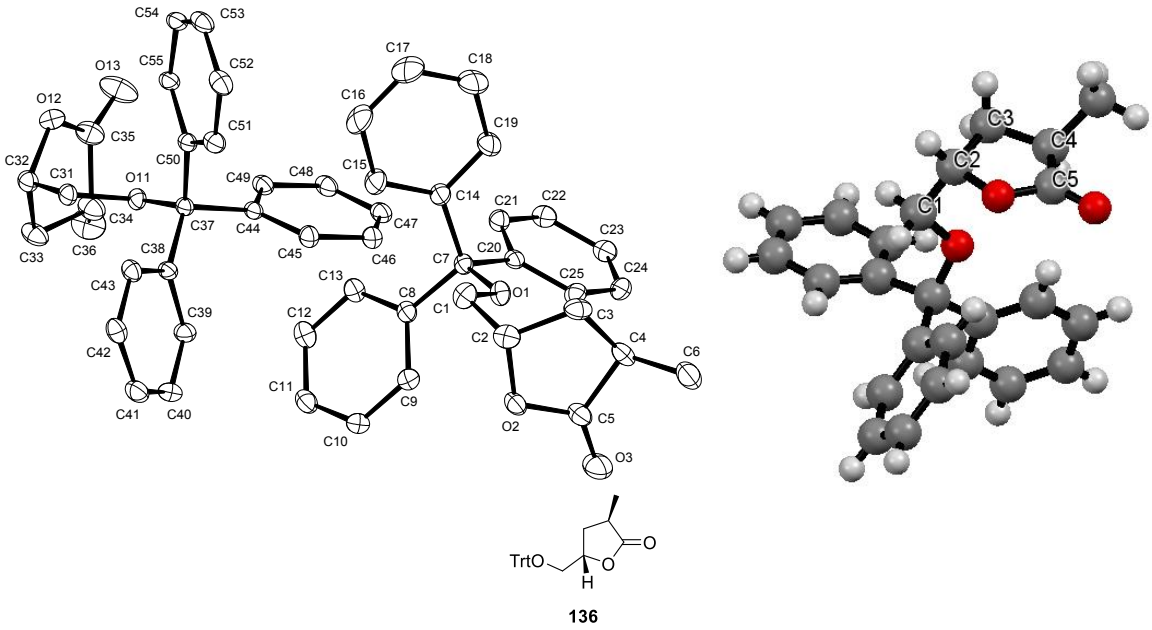


Figure 6.33: X-Ray single crystal structure and molecular structure of lactone **136** (numbering of atoms is arbitrary).

Identification code	10230	
Empirical formula	$C_{25}H_{24}O_3$	
Color	colorless	
Formula weight	372.44 g·mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	monclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 8.8667(18) Å	α = 90°.
	b = 11.936(2) Å	β = 94.816(4)°.
	c = 18.687(4) Å	γ = 90°.
Volume	1970.7(7) Å^3	
Z	4	
Density (calculated)	1.255 Mg·m^{-3}	
Absorption coefficient	0.081 mm^{-1}	
F(000)	792 e	
Crystal size	0.185 x 0.072 x 0.012 mm^3	
θ range for data collection	1.094 to 32.388°.	

Index ranges	$-13 \leq h \leq 13, -17 \leq k \leq 17, -28 \leq l \leq 28$	
Reflections collected	60158	
Independent reflections	14075 [R_{int} = 0.1002]	
Reflections with I>2σ(I)	11068	
Completeness to θ = 25.242°	100.0%	
Absorption correction	Gaussian	
Max. and min. transmission	1.00 and 0.99	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	14075/1/507	
Goodness-of-fit on F^2	0.990	
Final R indices [I>2σ(I)]	R_1 = 0.0576	wR^2 = 0.1457
R indices (all data)	R_1 = 0.0777	wR^2 = 0.1637
Absolute structure parameter	0.3(6)	
Largest diff. peak and hole	0.6 and -0.4 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(1)-C(1)	1.426(3)	O(1)-C(7)	1.437(3)
O(2)-C(2)	1.452(3)	O(2)-C(5)	1.344(3)
O(3)-C(5)	1.201(3)	C(1)-C(2)	1.508(4)
C(2)-C(3)	1.533(4)	C(3)-C(4)	1.516(4)
C(4)-C(5)	1.510(4)	C(4)-C(6)	1.525(4)
C(7)-C(8)	1.542(4)	C(7)-C(14)	1.529(3)
C(7)-C(20)	1.536(3)	C(8)-C(9)	1.391(4)
C(8)-C(13)	1.398(4)	C(9)-C(10)	1.397(4)
C(10)-C(11)	1.380(4)	C(11)-C(12)	1.387(4)
C(12)-C(13)	1.390(4)	C(14)-C(15)	1.387(4)
C(14)-C(19)	1.400(4)	C(15)-C(16)	1.396(4)
C(16)-C(17)	1.383(5)	C(17)-C(18)	1.388(5)
C(18)-C(19)	1.390(4)	C(20)-C(21)	1.398(3)
C(20)-C(25)	1.393(3)	C(21)-C(22)	1.397(4)
C(22)-C(23)	1.391(4)	C(23)-C(24)	1.384(4)
C(24)-C(25)	1.396(4)	O(11)-C(31)	1.431(3)
O(11)-C(37)	1.440(3)	O(12)-C(32)	1.453(3)
O(12)-C(35)	1.346(3)	O(13)-C(35)	1.199(4)
C(31)-C(32)	1.509(4)	C(32)-C(33)	1.525(3)
C(33)-C(34)	1.516(4)	C(34)-C(35)	1.518(4)
C(34)-C(36)	1.495(4)	C(37)-C(38)	1.530(3)
C(37)-C(44)	1.536(3)	C(37)-C(50)	1.531(3)
C(38)-C(39)	1.393(3)	C(38)-C(43)	1.395(3)
C(39)-C(40)	1.382(4)	C(40)-C(41)	1.387(4)
C(41)-C(42)	1.383(4)	C(42)-C(43)	1.388(4)

C(44)-C(45)	1.397(3)	C(44)-C(49)	1.391(3)
C(45)-C(46)	1.393(4)	C(46)-C(47)	1.385(4)
C(47)-C(48)	1.390(4)	C(48)-C(49)	1.393(4)
C(50)-C(51)	1.400(3)	C(50)-C(55)	1.396(3)
C(51)-C(52)	1.390(3)	C(52)-C(53)	1.384(4)
C(53)-C(54)	1.385(4)	C(54)-C(55)	1.393(3)
C(1)-O(1)-C(7)	115.22(19)	C(5)-O(2)-C(2)	110.9(2)
O(1)-C(1)-C(2)	107.4(2)	O(2)-C(2)-C(1)	108.7(2)
O(2)-C(2)-C(3)	106.2(2)	C(1)-C(2)-C(3)	114.5(2)
C(4)-C(3)-C(2)	104.6(2)	C(3)-C(4)-C(6)	115.4(2)
C(5)-C(4)-C(3)	103.9(2)	C(5)-C(4)-C(6)	111.1(2)
O(2)-C(5)-C(4)	111.4(2)	O(3)-C(5)-O(2)	121.8(3)
O(3)-C(5)-C(4)	126.8(3)	O(1)-C(7)-C(8)	110.1(2)
O(1)-C(7)-C(14)	107.61(18)	O(1)-C(7)-C(20)	105.26(19)
C(14)-C(7)-C(8)	114.9(2)	C(14)-C(7)-C(20)	111.0(2)
C(20)-C(7)-C(8)	107.49(17)	C(9)-C(8)-C(7)	119.9(2)
C(9)-C(8)-C(13)	118.2(2)	C(13)-C(8)-C(7)	121.8(2)
C(8)-C(9)-C(10)	120.6(2)	C(11)-C(10)-C(9)	120.7(3)
C(10)-C(11)-C(12)	119.1(2)	C(11)-C(12)-C(13)	120.5(3)
C(12)-C(13)-C(8)	120.8(3)	C(15)-C(14)-C(7)	122.9(2)
C(15)-C(14)-C(19)	118.5(2)	C(19)-C(14)-C(7)	117.9(2)
C(14)-C(15)-C(16)	120.6(3)	C(17)-C(16)-C(15)	120.5(3)
C(16)-C(17)-C(18)	119.4(3)	C(17)-C(18)-C(19)	120.2(3)
C(18)-C(19)-C(14)	120.8(3)	C(21)-C(20)-C(7)	119.7(2)
C(25)-C(20)-C(7)	121.6(2)	C(25)-C(20)-C(21)	118.6(2)
C(22)-C(21)-C(20)	120.6(2)	C(23)-C(22)-C(21)	120.2(2)
C(24)-C(23)-C(22)	119.4(2)	C(23)-C(24)-C(25)	120.6(2)
C(20)-C(25)-C(24)	120.6(2)	C(31)-O(11)-C(37)	116.05(17)
C(35)-O(12)-C(32)	110.4(2)	O(11)-C(31)-C(32)	106.85(19)
O(12)-C(32)-C(31)	108.9(2)	O(12)-C(32)-C(33)	104.8(2)
C(31)-C(32)-C(33)	115.4(2)	C(34)-C(33)-C(32)	104.1(2)
C(33)-C(34)-C(35)	102.5(2)	C(36)-C(34)-C(33)	117.4(3)
C(36)-C(34)-C(35)	112.8(3)	O(12)-C(35)-C(34)	111.0(2)
O(13)-C(35)-O(12)	121.4(3)	O(13)-C(35)-C(34)	127.5(3)
O(11)-C(37)-C(38)	108.31(18)	O(11)-C(37)-C(44)	104.79(18)
O(11)-C(37)-C(50)	110.59(19)	C(38)-C(37)-C(44)	112.24(19)
C(38)-C(37)-C(50)	115.28(19)	C(50)-C(37)-C(44)	105.13(18)
C(39)-C(38)-C(37)	119.0(2)	C(39)-C(38)-C(43)	117.9(2)
C(43)-C(38)-C(37)	123.0(2)	C(40)-C(39)-C(38)	121.3(2)
C(39)-C(40)-C(41)	120.1(2)	C(42)-C(41)-C(40)	119.4(2)
C(41)-C(42)-C(43)	120.4(2)	C(42)-C(43)-C(38)	120.8(2)
C(45)-C(44)-C(37)	119.8(2)	C(49)-C(44)-C(37)	121.3(2)
C(49)-C(44)-C(45)	118.8(2)	C(46)-C(45)-C(44)	120.7(2)
C(47)-C(46)-C(45)	120.1(3)	C(46)-C(47)-C(48)	119.7(2)
C(47)-C(48)-C(49)	120.1(2)	C(44)-C(49)-C(48)	120.6(2)
C(51)-C(50)-C(37)	121.8(2)	C(55)-C(50)-C(37)	119.6(2)
C(55)-C(50)-C(51)	118.3(2)	C(52)-C(51)-C(50)	120.9(2)
C(53)-C(52)-C(51)	120.0(2)	C(52)-C(53)-C(54)	119.8(2)
C(53)-C(54)-C(55)	120.4(2)	C(54)-C(55)-C(50)	120.5(2)

6.4.14. Crystallographic Data Of 137

Crystal Data & Structure Refinement

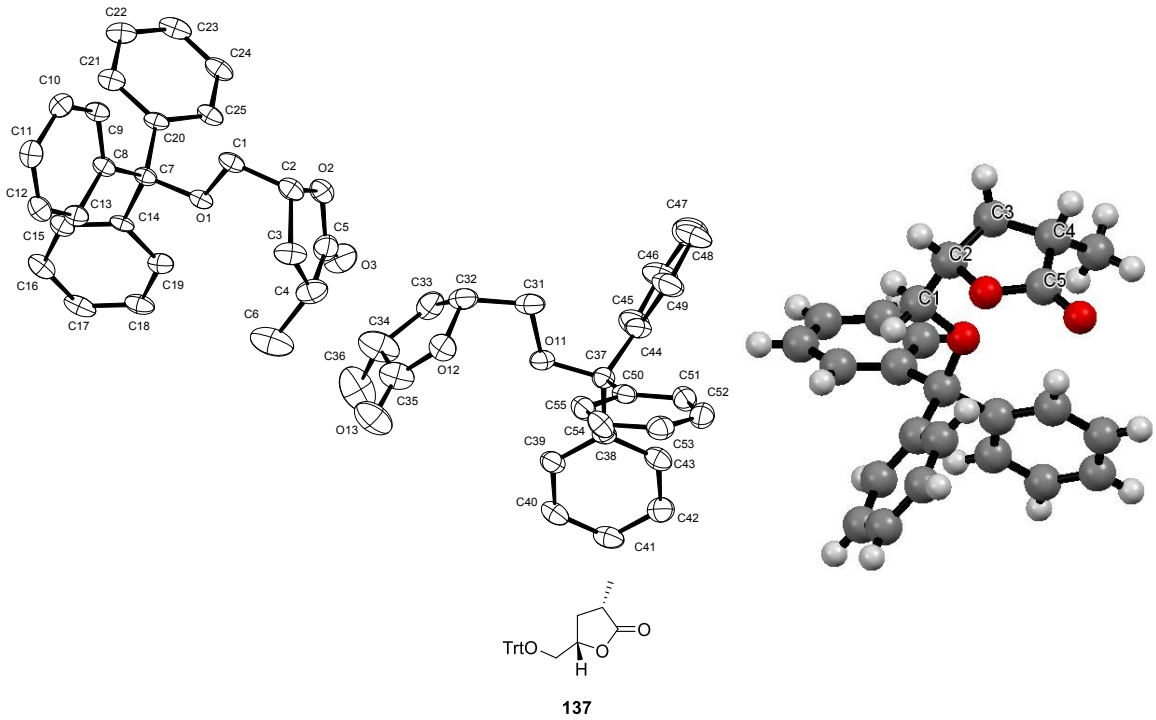


Figure 6.34: X-Ray single crystal structure and molecular structure of lactone **137** (numbering of atoms is arbitrary).

Identification code	10251	
Empirical formula	$C_{25}H_{24}O_3$	
Color	colorless	
Formula weight	372.44 g·mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 8.850(3) Å	α = 90°.
	b = 12.205(5) Å	β = 92.758(7)°.
	c = 18.397(7) Å	γ = 90°.
Volume	1984.7(13) Å^3	
Z	4	
Density (calculated)	1.246 Mg·m^{-3}	
Absorption coefficient	0.081 mm^{-1}	
F(000)	792 e	

Crystal size	0.261 x 0.215 x 0.020 mm^3	
θ range for data collection	1.108 to 26.506°.	
Index ranges	$-11 \leq h \leq 11$, $-15 \leq k \leq 15$, $-22 \leq l \leq 22$	
Reflections collected	41274	
Independent reflections	8154 [R_{int} = 0.0869]	
Reflections with I>2σ(I)	5934	
Completeness to θ = 25.242°	100.0%	
Absorption correction	Gaussian	
Max. and min. transmission	1.00 and 0.98	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	8154/1/507	
Goodness-of-fit on F^2	1.068	
Final R indices [I>2σ(I)]	R_1 = 0.0564	wR^2 = 0.1464
R indices (all data)	R_1 = 0.0912	wR^2 = 0.1760
Absolute structure parameter	0.6(9)	
Largest diff. peak and hole	0.428 and -0.319 e·$Å^{-3}$	

Bond Lengths [Å] & Angles [°]

O(1)-C(7)	1.438(6)	O(1)-C(1)	1.439(5)
O(11)-C(37)	1.435(6)	O(11)-C(31)	1.425(6)
O(2)-C(2)	1.451(6)	O(2)-C(5)	1.350(7)
O(12)-C(35)	1.340(7)	O(12)-C(32)	1.464(6)
O(3)-C(5)	1.198(7)	O(13)-C(35)	1.210(7)
C(20)-C(7)	1.545(6)	C(20)-C(21)	1.396(7)
C(20)-C(25)	1.397(6)	C(17)-C(16)	1.373(8)
C(17)-C(18)	1.386(8)	C(7)-C(14)	1.534(6)
C(7)-C(8)	1.525(6)	C(22)-C(21)	1.398(7)
C(22)-C(23)	1.379(7)	C(15)-C(14)	1.390(7)
C(15)-C(16)	1.391(7)	C(14)-C(19)	1.390(7)
C(10)-C(11)	1.376(7)	C(10)-C(9)	1.386(6)
C(38)-C(43)	1.394(7)	C(38)-C(37)	1.526(7)
C(38)-C(39)	1.386(7)	C(11)-C(12)	1.367(7)
C(25)-C(24)	1.380(7)	C(12)-C(13)	1.387(7)
C(13)-C(8)	1.393(6)	C(24)-C(23)	1.369(8)
C(8)-C(9)	1.390(6)	C(53)-C(52)	1.377(8)
C(53)-C(54)	1.380(8)	C(50)-C(37)	1.536(7)
C(50)-C(51)	1.391(7)	C(50)-C(55)	1.385(7)
C(43)-C(42)	1.384(8)	C(18)-C(19)	1.394(7)
C(52)-C(51)	1.387(8)	C(42)-C(41)	1.383(8)
C(2)-C(1)	1.489(7)	C(2)-C(3)	1.534(7)

C(37)-C(44)	1.533(6)	C(54)-C(55)	1.378(8)
C(39)-C(40)	1.390(7)	C(5)-C(4)	1.502(7)
C(3)-C(4)	1.503(8)	C(41)-C(40)	1.375(8)
C(44)-C(49)	1.386(8)	C(44)-C(45)	1.398(9)
C(33)-C(32)	1.518(8)	C(33)-C(34)	1.510(9)
C(35)-C(34)	1.513(8)	C(32)-C(31)	1.507(8)
C(4)-C(6)	1.511(9)	C(49)-C(48)	1.429(8)
C(45)-C(46)	1.387(8)	C(48)-C(47)	1.348(10)
C(46)-C(47)	1.377(10)	C(34)-C(36)	1.443(10)
C(7)-O(1)-C(1)	115.6(3)	C(31)-O(11)-C(37)	116.3(4)
C(5)-O(2)-C(2)	110.2(4)	C(35)-O(12)-C(32)	110.7(4)
C(21)-C(20)-C(7)	121.8(4)	C(21)-C(20)-C(25)	118.0(4)
C(25)-C(20)-C(7)	119.7(4)	C(16)-C(17)-C(18)	119.4(5)
O(1)-C(7)-C(20)	110.2(3)	O(1)-C(7)-C(14)	105.4(3)
O(1)-C(7)-C(8)	108.7(3)	C(14)-C(7)-C(20)	104.6(3)
C(8)-C(7)-C(20)	115.0(4)	C(8)-C(7)-C(14)	112.5(3)
C(23)-C(22)-C(21)	120.1(5)	C(14)-C(15)-C(16)	120.9(5)
C(15)-C(14)-C(7)	121.0(4)	C(19)-C(14)-C(7)	120.5(4)
C(19)-C(14)-C(15)	118.4(4)	C(11)-C(10)-C(9)	119.8(5)
C(17)-C(16)-C(15)	120.5(5)	C(43)-C(38)-C(37)	120.1(4)
C(39)-C(38)-C(43)	117.6(5)	C(39)-C(38)-C(37)	122.3(4)
C(20)-C(21)-C(22)	120.3(5)	C(12)-C(11)-C(10)	119.8(4)
C(24)-C(25)-C(20)	121.1(5)	C(11)-C(12)-C(13)	120.8(4)
C(12)-C(13)-C(8)	120.4(4)	C(23)-C(24)-C(25)	120.3(5)
C(13)-C(8)-C(7)	118.6(4)	C(9)-C(8)-C(7)	123.3(4)
C(9)-C(8)-C(13)	117.8(4)	C(10)-C(9)-C(8)	121.3(4)
C(52)-C(53)-C(54)	118.7(5)	C(24)-C(23)-C(22)	120.2(4)
C(51)-C(50)-C(37)	122.7(4)	C(55)-C(50)-C(37)	119.6(4)
C(55)-C(50)-C(51)	117.6(5)	C(42)-C(43)-C(38)	121.8(5)
C(17)-C(18)-C(19)	120.3(5)	C(53)-C(52)-C(51)	120.5(5)
C(14)-C(19)-C(18)	120.5(5)	C(41)-C(42)-C(43)	119.6(5)
O(2)-C(2)-C(1)	107.7(4)	O(2)-C(2)-C(3)	105.8(4)
C(1)-C(2)-C(3)	115.1(4)	O(11)-C(37)-C(38)	104.8(4)
O(11)-C(37)-C(50)	110.2(4)	O(11)-C(37)-C(44)	107.1(4)
C(38)-C(37)-C(50)	108.1(4)	C(38)-C(37)-C(44)	110.4(4)
C(44)-C(37)-C(50)	115.7(4)	O(1)-C(1)-C(2)	107.2(4)
C(55)-C(54)-C(53)	121.0(5)	C(52)-C(51)-C(50)	121.1(5)
C(38)-C(39)-C(40)	120.7(5)	O(2)-C(5)-C(4)	111.5(5)
O(3)-C(5)-O(2)	120.9(5)	O(3)-C(5)-C(4)	127.6(5)
C(54)-C(55)-C(50)	121.2(5)	C(4)-C(3)-C(2)	106.1(4)
C(40)-C(41)-C(42)	119.4(5)	C(49)-C(44)-C(37)	121.6(5)
C(49)-C(44)-C(45)	118.8(5)	C(45)-C(44)-C(37)	119.2(5)
C(34)-C(33)-C(32)	105.3(5)	C(41)-C(40)-C(39)	120.8(5)
O(12)-C(35)-C(34)	111.3(5)	O(13)-C(35)-O(12)	121.7(5)
O(13)-C(35)-C(34)	127.0(6)	O(12)-C(32)-C(33)	106.0(4)
O(12)-C(32)-C(31)	107.6(4)	C(31)-C(32)-C(33)	114.6(5)
C(5)-C(4)-C(3)	104.2(4)	C(5)-C(4)-C(6)	114.0(5)
C(3)-C(4)-C(6)	117.0(5)	O(11)-C(31)-C(32)	107.0(4)
C(44)-C(49)-C(48)	118.9(6)	C(46)-C(45)-C(44)	120.9(6)

C(47)-C(48)-C(49)	121.1(6)	C(47)-C(46)-C(45)	120.1(6)
C(48)-C(47)-C(46)	120.2(6)	C(33)-C(34)-C(35)	103.4(5)
C(36)-C(34)-C(33)	121.7(6)	C(36)-C(34)-C(35)	112.3(6)

6.4.15. Crystallographic Data Of 131a

Crystal Data & Structure Refinement

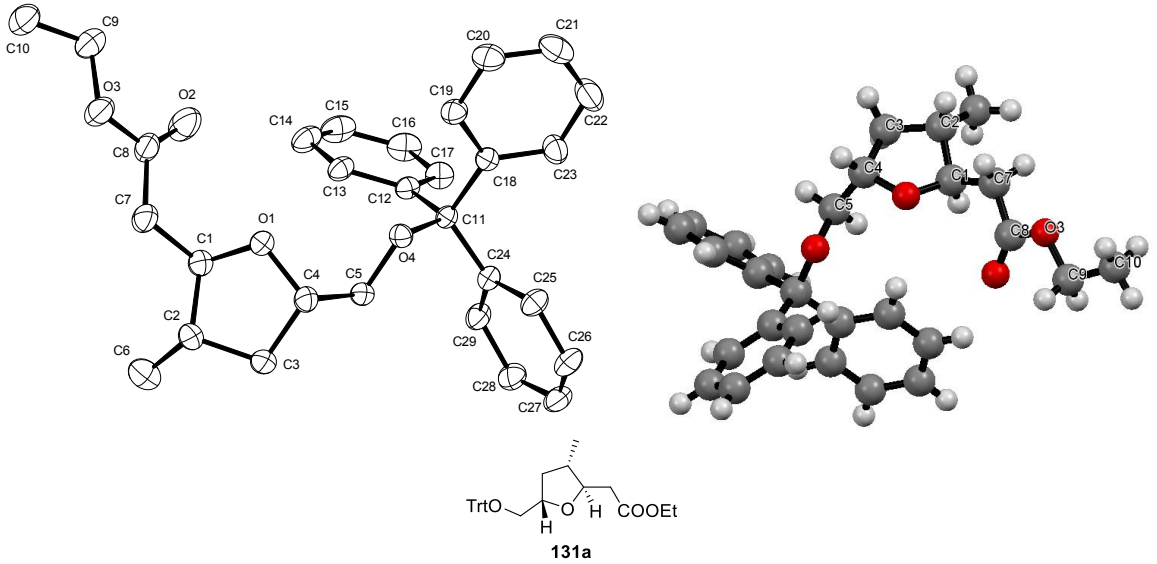


Figure 6.35: X-Ray single crystal structure and molecular structure of 2,5-*trans*-disubstituted ether **131a** (numbering of atoms is arbitrary).

Identification code	10245	
Empirical formula	$C_{29}H_{32}O_4$	
Color	colorless	
Formula weight	444.54 g·mol^{-1}	
Temperature	200 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1$ (No. 4)	
Unit cell dimensions	a = 8.5623(4) Å	α = 90°.
	b = 16.4804(8) Å	β = 98.122(4)°.
	c = 8.6025(4) Å	γ = 90°.
Volume	1201.72(10) Å^3	
Z	2	
Density (calculated)	1.229 Mg·m^{-3}	
Absorption coefficient	0.080 mm^{-1}	
F(000)	476 e	
Crystal size	0.29 x 0.15 x 0.15 mm^3	
θ range for data collection	3.440 to 33.129°.	

Index ranges	$-13 \leq h \leq 13$, $-25 \leq k \leq 25$, $-13 \leq l \leq 13$	
Reflections collected	26607	
Independent reflections	9025 [R_{int} = 0.0424]	
Reflections with I>2σ(I)	8105	
Completeness to θ = 25.242°	99.2%	
Absorption correction	Gaussian	
Max. and min. transmission	0.99 and 0.98	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	9025/1/301	
Goodness-of-fit on F^2	1.112	
Final R indices [I>2σ(I)]	R_1 = 0.0555	wR^2 = 0.1446
R indices (all data)	R_1 = 0.0823	wR^2 = 0.1612
Absolute structure parameter	0.3(5)	
Extinction coefficient	0.37(3)	
Largest diff. peak and hole	0.9 and -1.1 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

O(1)-C(1)	1.428(3)	O(1)-C(4)	1.428(2)
O(2)-C(8)	1.201(3)	O(3)-C(8)	1.347(3)
O(3)-C(9)	1.449(3)	O(4)-C(5)	1.427(2)
O(4)-C(11)	1.448(2)	C(1)-C(2)	1.534(3)
C(1)-C(7)	1.516(3)	C(2)-C(3)	1.534(3)
C(2)-C(6)	1.517(4)	C(3)-C(4)	1.538(3)
C(4)-C(5)	1.515(3)	C(7)-C(8)	1.502(3)
C(9)-C(10)	1.490(4)	C(11)-C(12)	1.540(2)
C(11)-C(18)	1.532(2)	C(11)-C(24)	1.532(2)
C(12)-C(13)	1.396(3)	C(12)-C(17)	1.400(3)
C(13)-C(14)	1.401(3)	C(14)-C(15)	1.382(4)
C(15)-C(16)	1.385(4)	C(16)-C(17)	1.395(3)
C(18)-C(19)	1.398(3)	C(18)-C(23)	1.397(3)
C(19)-C(20)	1.389(3)	C(20)-C(21)	1.385(4)
C(21)-C(22)	1.384(4)	C(22)-C(23)	1.392(3)
C(24)-C(25)	1.404(2)	C(24)-C(29)	1.393(3)
C(25)-C(26)	1.391(3)	C(26)-C(27)	1.384(3)
C(27)-C(28)	1.385(3)	C(28)-C(29)	1.397(3)
C(4)-O(1)-C(1)	109.16(16)	C(8)-O(3)-C(9)	116.6(2)
C(5)-O(4)-C(11)	114.64(14)	O(1)-C(1)-C(2)	105.55(17)
O(1)-C(1)-C(7)	108.75(19)	C(7)-C(1)-C(2)	113.08(18)
C(1)-C(2)-C(3)	101.47(16)	C(6)-C(2)-C(1)	113.5(2)
C(6)-C(2)-C(3)	114.7(2)	C(2)-C(3)-C(4)	104.83(18)
O(1)-C(4)-C(3)	106.95(17)	O(1)-C(4)-C(5)	111.91(17)

C(5)-C(4)-C(3)	110.27(19)	O(4)-C(5)-C(4)	109.60(16)
C(8)-C(7)-C(1)	115.38(19)	O(2)-C(8)-O(3)	123.4(2)
O(2)-C(8)-C(7)	127.1(2)	O(3)-C(8)-C(7)	109.5(2)
O(3)-C(9)-C(10)	107.7(3)	O(4)-C(11)-C(12)	110.11(13)
O(4)-C(11)-C(18)	104.51(13)	O(4)-C(11)-C(24)	107.84(13)
C(18)-C(11)-C(12)	106.16(13)	C(24)-C(11)-C(12)	113.99(13)
C(24)-C(11)-C(18)	113.82(14)	C(13)-C(12)-C(11)	120.45(15)
C(13)-C(12)-C(17)	118.86(16)	C(17)-C(12)-C(11)	120.50(16)
C(12)-C(13)-C(14)	120.08(19)	C(15)-C(14)-C(13)	120.6(2)
C(14)-C(15)-C(16)	119.49(18)	C(15)-C(16)-C(17)	120.6(2)
C(16)-C(17)-C(12)	120.3(2)	C(19)-C(18)-C(11)	118.74(16)
C(23)-C(18)-C(11)	122.96(16)	C(23)-C(18)-C(19)	118.22(18)
C(20)-C(19)-C(18)	120.8(2)	C(21)-C(20)-C(19)	120.5(2)
C(22)-C(21)-C(20)	119.3(2)	C(21)-C(22)-C(23)	120.6(2)
C(22)-C(23)-C(18)	120.6(2)	C(25)-C(24)-C(11)	118.58(15)
C(29)-C(24)-C(11)	123.00(15)	C(29)-C(24)-C(25)	117.85(17)
C(26)-C(25)-C(24)	120.94(19)	C(27)-C(26)-C(25)	120.28(19)
C(26)-C(27)-C(28)	119.77(19)	C(27)-C(28)-C(29)	120.0(2)
C(24)-C(29)-C(28)	121.19(18)		

6.4.16. Crystallographic Data Of 165

Crystal Data & Structure Refinement

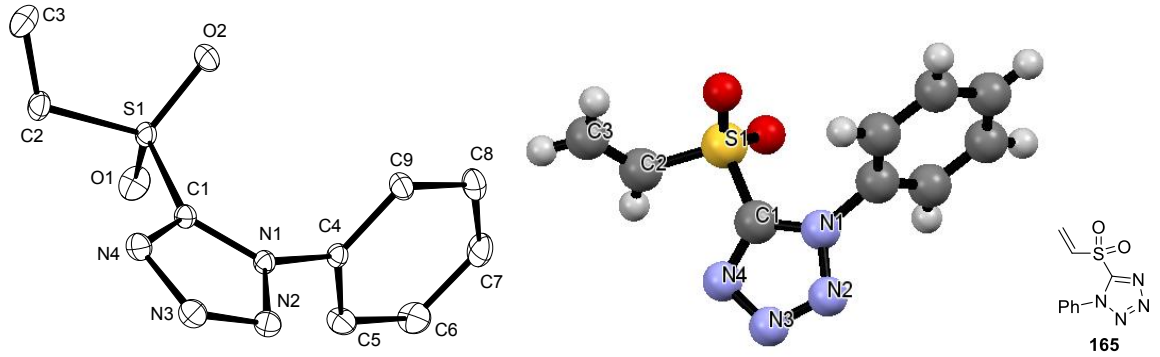


Figure 6.36: X-Ray single crystal structure and molecular structure of tetrazolylvinylsulfone **165** (numbering of atoms is arbitrary).

Identification code	10229	
Empirical formula	$C_9H_8N_4O_2S$	
Color	colorless	
Formula weight	236.25 g·mol^{-1}	
Temperature	100 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	C2 (No. 5)	
Unit cell dimensions	a = 15.7115(19) Å	α = 90°.
	b = 5.4826(7) Å	β = 90.526(2)°.
	c = 11.8473(15) Å	γ = 90°.
Volume	1020.5(2) Å^3	
Z	4	
Density (calculated)	1.538 Mg·m^{-3}	
Absorption coefficient	0.307 m^{-1}	
F(000)	488 e	
Crystal size	0.364 x 0.285 x 0.142 mm^3	
θ range for data collection	1.719 to 36.317°.	
Index ranges	$-26 \leq h \leq 26$, $-9 \leq k \leq 9$, $-19 \leq l \leq 19$	
Reflections collected	19793	
Independent reflections	4870 [R_{int} = 0.0216]	
Reflections with I>2σ(I)	4723	

Completeness to θ = 25.242°	99.9 %	
Absorption correction	Gaussian	
Max. and min. transmission	0.97 and 0.93	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4870/1/145	
Goodness-of-fit on F^2	1.130	
Final R indices [I>2σ(I)]	R_1 = 0.0241	wR^2 = 0.0691
R indices (all data)	R_1 = 0.0256	wR^2 = 0.0753
Absolute structure parameter	-0.008(19)	
Largest diff. peak and hole	0.5 and -0.3 e·Å^{-3}	

Bond Lengths [Å] & Angles [°]

S(1)-O(1)	1.4360(10)	S(1)-O(2)	1.4347(10)
S(1)-C(1)	1.7780(10)	S(1)-C(2)	1.7430(10)
N(1)-N(2)	1.3534(12)	N(1)-C(1)	1.3427(13)
N(1)-C(4)	1.4408(13)	N(2)-N(3)	1.2955(14)
N(3)-N(4)	1.3655(15)	N(4)-C(1)	1.3187(13)
C(2)-C(3)	1.3221(19)	C(4)-C(5)	1.3833(15)
C(4)-C(9)	1.3882(16)	C(5)-C(6)	1.3951(16)
C(6)-C(7)	1.389(2)	C(7)-C(8)	1.3923(18)
C(8)-C(9)	1.3965(15)	O(1)-S(1)-C(1)	105.76(5)
O(1)-S(1)-C(2)	109.77(6)	O(2)-S(1)-O(1)	119.49(6)
O(2)-S(1)-C(1)	107.62(5)	O(2)-S(1)-C(2)	110.78(6)
C(2)-S(1)-C(1)	101.78(5)	N(2)-N(1)-C(4)	121.27(8)
C(1)-N(1)-N(2)	107.38(8)	C(1)-N(1)-C(4)	131.33(9)
N(3)-N(2)-N(1)	106.70(9)	N(2)-N(3)-N(4)	111.21(9)
C(1)-N(4)-N(3)	104.83(9)	N(1)-C(1)-S(1)	124.19(7)
N(4)-C(1)-S(1)	125.72(8)	N(4)-C(1)-N(1)	109.88(9)
C(3)-C(2)-S(1)	119.31(10)	C(5)-C(4)-N(1)	117.89(9)
C(5)-C(4)-C(9)	122.76(9)	C(9)-C(4)-N(1)	119.32(9)
C(4)-C(5)-C(6)	118.52(11)	C(7)-C(6)-C(5)	119.91(11)
C(6)-C(7)-C(8)	120.62(10)	C(7)-C(8)-C(9)	120.16(11)
C(4)-C(9)-C(8)	118.03(10)		

6.5. Abbreviations

3D	three-dimensional
9-BBN	9-Borabicyclo[3.3.1]nonan
Å	Ångström, 1 Å = 10^{-10} m
Ac	acetyl
Alpine® borane	9-(2,6,6-trimethylbicyclo[3.1.1]hept-3-yl)-9-bora-bicyclo[3.3.1]nonane
aq.	aqueous
AQN	anthraquinone-1,4-diyl diether
Ar	aromatic group/ arene/ aryl
AS	amino acid
BCL	*Burkholderia cepacia* lipase
Bn	benzyl
bmim	1-butyl-3-methylimidazolium
br	broad
BSTFA	*N*,*O*-bis(trimethylsilyl)trifluoroacetamide
DM-BINAP	1,1'-binaphthalene-2,2'-diyl)bis[bis(3,5-dimethylphenyl)phosphine]
Bu	butyl
ca.	circa
calcd.	calculated
Cat	catechol
cat.	catalytic
CBS	Corey-Bakshi-Shibata
CCL	*Candida cylindracea* lipase
conc.	concentrated
Cp	cyclopentadienyl
Cp*	1,2,3,4,5-pentamethylcyclopentadienyl
CSA	camphorsulfonic acid
CM	alkene cross metathesis
COD	bis(1,5-cyclooctadiene)
Cy	cyclohexane

δ	chemical shift
d	day
d	doublet
D	right (Lat. *dextro*)
DBU	1,8-diazabicycloundec-7-ene
DCC	*N*,*N*´-dicyclohexylcarbodiimide
DCE	dichloroethane
DCM	dichloromethane
DHQ	hydroquinine
DHQD	dihydroquinidin
DIAD	di-*i*-propyl azodicarboxylate
DIBAL	di-*i*-butylaluminium hydride
DIPA	di-*i*-propylamine
DIPEA	di-*i*-propylethylamine
DEAD	diethyl azodicarboxylate
DMA	*N*,*N*'-dimethylacetamide
DMAP	(dimethylamino)-pyridine
DMF	*N*,*N*'-dimethylformamide
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
dppp	(bis(1,3-diphenylphosphino)-propane)
d.r.	diastereomeric ratio
Dr.	doctor
DSP	diarrhetic shellfish poisoning
DTX	dinophysistoxin
E	entgegen
E2	bimolecular elimination
EC_{50}	half maximal effective concentration 24 h
ee	enantiomeric excess
e.g.	for example (Lat. *exempli gratia*)
EI	electron ionization

epi	epimer
ESI	electronspray ionization
Et	ethyl
et al.	and others (Lat. *et alli*, *et aliae*, *et alia*)
eq.	equivalent
eV	electronvolt
FGI	functional group interconversion
g	gram
GC	gas chromatography
Grubbs II	(1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene) dichloro(phenylmethylene)
h	hour
HMDS	hexamethyldisilamide
HMPT	tris(dimethylamino)phosphine
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectroscopy
Hz	Hertz, 1 Hz = 1 s^{-1}
HV	high vacuum
i	*iso*
ibid.	in the same place (Lat. *ibidem*)
im	imidazol
i-Ph	*ipso* (position in Ph ring)
IPP	*i*-pentenyl pyrophosphate
IR	infrared spectroscopy
J	coupling constant
L	ligand
L	left (Lat. *levo*)
L	liter
Lat.	Latinum
Lev	levulinyl
LLS	longest linear sequence
m	*meta*

m	multiplet
m	10^{-3}
µ	10^{-6}
M	molar: mol·l^{-1}
m/z	mass per charge
Me	methyl
Mes	mesityl/ (1,3,5-trimethylphenyl)
MIB	3-*exo*-morpholinoisoborneol
min	minute
MS	mass spectrometry
MS	molecular sieves
MTBE	methyl-*t*-butylether
n	10^{-9}
NBS	*N*-bromosuccinimide
NHK	Nozaki-Hiyama-Kishi
NIS	*N*-iodosuccinimide
NME	*N*-methylephedrine
nmp	(*Z*)-2-hydroxy-5,5-dimethyl-1-(4-methyl-1-piperazinyl)-2-hexene-1,4-dione
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
o	*ortho*
OA	ocadaic acid
OTf	trifluoromethanesulfonate
OXONE®	$KHSO_5 \cdot 0.5KHSO_4 \cdot 0.5K_2SO_4$
p	*para*
PCC	pyridinium chlorochromate
PCL	*Penicillinum camemberti* lipase
Ph	phenyl
pH	potential of hydrogen
Ph.D.	doctor of philosophy
PHAL	1,4-phthalazinediyl diether

ppm	parts per million
PPTS	pyridinium *p*-toluenesulfonate
PTC	phase transfer catalysis
PTX	paclitaxel
PVP	poly(4-vinylpyridine)
Py	pyridine
PYR	2,5-diphenyl-4,6-pyrimidinediyl diether
q	quartet
quant.	quantitative
R	unspecified protecting group/ organic substituent
R	right (Lat. *rectus*)
®	registered trade mark
rac	*racemic*
RCAM	ring closing alkyne metathesis
RCM	ring closing olefin metathesis
Red-Al®	sodium bis(2-methoxyethoxy)aluminum hydride
RNA	ribonucleic acid
rt	room temperature/ ambient temperature
s	singlet
S	left (Lat. *sinister*)
sat.	saturated
SD	standard deviation
sm	starting material
S_N2	bimolecular nucleophilic substitution
t	tertiary
t	triplet
TASF	tris(dimethylamino)sulfonium difluorotrimethylsilicate
TBAF	tetra-*n*-butylammonium fluoride
TBAI	tetra-*n*-butyammonium iodide
TBS	*t-b*utyldimethylsilyl
TC	thiophene-2-carboxylate
TEA	triethylammonium

TEMPO	2,2,6,6-tetramethyl-1-piperidinyloxy
TES	triethylsilyl
TFA	trifluoro acetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine
TMS	trimethylsilyl
Tos	tosyl
Ts-DPEN	1-amino-2-tosylamino-1,2-diphenylethane
U	enzymatic units
UV	ultra violet
vs.	versus
Z	zusammen

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