Novel Strategies for the Synthesis and Cycloisomerization Reactions of Functionalized Allenes

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Referent:Prof. Dr. Norbert Krause

Korreferent:Prof. Dr. Levent Artok (Izmir Institute of Technology)

Dedicated to my parents and sister

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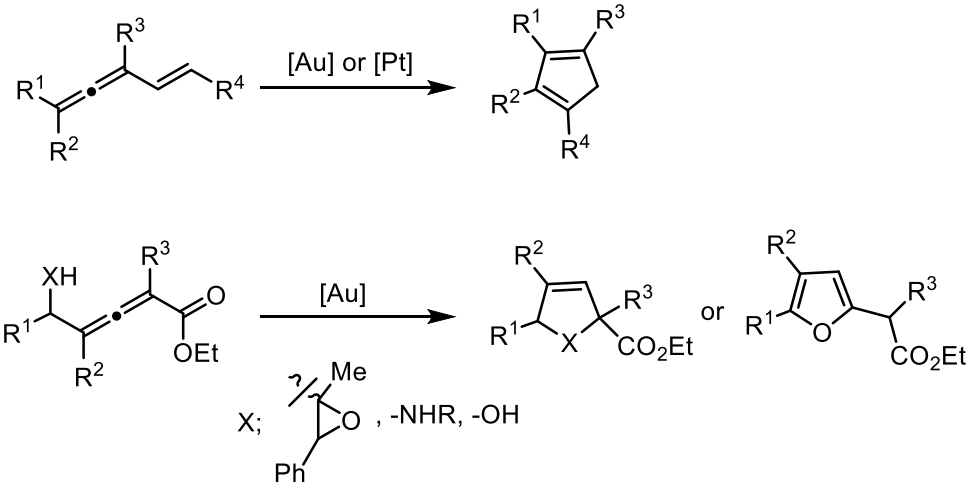
Abstract

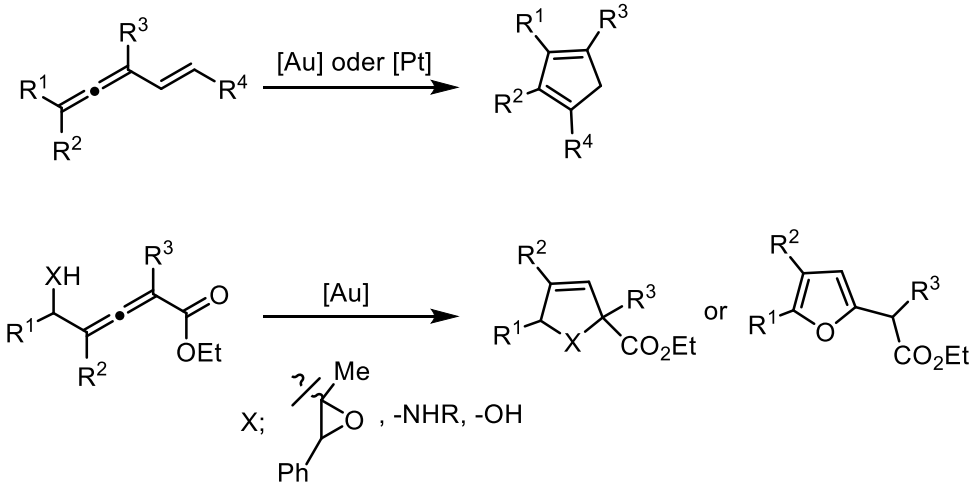
A particular attractive approach toward the synthesis of densely functionalized hetero- and carbocyclic products involves the incorporation of rearrangement steps into transition-metal-catalyzed cycloisomerization cascade reactions. In this context, the diverse reactivity of gold- and platinum-catalyzed transformations has attracted much interest for the development of cascade reaction patterns. The activation of allenes with a homogeneous catalyst sets the stage for a cyclization by intramolecular attack of various nucleophiles, affording highly useful carbo- or heterocyclic products. Among various methods for the synthesis of these heterocycles, the gold- or platinum-catalyzed transformations of allenes play an important role in synthetic organic chemistry.



In this context, we described a novel method for the preparation of highly substituted cyclopentadiene derivatives by gold- and platinum-catalyzed [1,2]-migratory cycloisomerization cascade reactions of 1,1-disubstituted vinylallenes. In addition to this, we have developed a new approach for the synthesis and gold-catalyzed cyclization of difunctionalized allenes, which afford new routes to functionalized heterocyclic products. Those heterocycles are part of many bioactive natural compounds and building blocks in synthetic organic chemistry.

Kurzfassung

Ein besonders attraktiver, synthetischer Zugang zu hoch funktionalisierten hetero- und carbozyklischen Verbindungen ist die Integrierung von Umlagerungsschritten in Übergangsmetallkatalysierte Zykloisomerisierungskaskadenreaktionen. In diesem Zusammenhang hat die vielfältige Reaktivität von Gold- und Platinkatalysatoren ein hohes Interesse in der Entwicklung von Kaskadenreaktionen erhalten. Die Aktivierung von Allenen mit homogenen Katalysatoren schaffte die Voraussetzung für die Zyklisierung, bei der durch intramolekulare Angriffe verschiedenster Nukleophile wertvolle carbo- und heterozyklische Verbindungen entstehen. Neben den bisherigen Synthesemethoden dieser Heterozyklen spielen gold- und platinkatalysierte Reaktionen von Allenen eine wichtige Rolle in der synthetischen, organischen Chemie.



Im Rahmen dieser Arbeit wird eine neue Methode für die Herstellung hochsubstituierter Cyclopentadiene durch gold- und platinkatalysierte Kaskadenreaktionen von 1,1-disubstituierten Vinylallenen vorgestellt. Weiterhin wurde eine neue Methode für die Darstellung und goldkatalysierte Zyklisierung difunktionalisierter Allene entwickelt, welche neue Möglichkeiten für die Synthese funktionalisierte Heterozyklen eröffnet. Diese Heterozyklen sind sowohl Bestandteil bioaktiver Naturstoffe als auch wichtige Synthesebausteine in der organischen Chemie.

Abbreviations

aq.	Aqueous
Ar	Argon
br.s	Broad singlet
Bu	Butyl
Cat.	Catalytic
c-Hex	Cyclohexyl
Cp	Cyclopentadiene
d	Doublet
dba	Dibenzylidene acetone
DCE	Dichloroethane
DCM	Dichloromethane
dd	Doublet of doublets
DHP	3,4-Dihydro-2H-pyran
DIAD	Diisopropylazodicarboxylate
DMAP	4-Dimethylaminopyridin
DMF	N,N-Dimethylformamid
DMSO	Dimethyl sulfoxide
dr	Diastereomeric ratio
dt	Doublet of triplets
e.g.	For example
ee	Enantiomeric excess
Eq.	Equation
eq	Equivalence
ESI	Electrospray ionization
Et	Ethyl
FT-IR	Fourier transform infrared spectroscopy
g	Gram
GC	Gas Chromatography
GC-MS	Gas Chromatography Mass Spectrometry
h	Hour(s)
HRMS	High Resolution Mass Spectra
Hz	Hertz
i-Pr	Iso-propyl
IPr	1,3-Bis-(2,6-diisopropyl phenyl)imidazole
IR	Infrared
J	Coupling constant
LG	Leaving group
M	Molar
m	Multiplet
Me	Methyl
mg	Milligram
MHz	MegaHertz
min	Minutes
mL	Milliliter
mmol	milimole
Mp	Melting point
Ms	Methylsulfonyl
MS	Molecular sieve
NMR	Nuclear Magnetic Resonance
o	Ortho
PG	Protecting group
Ph	Phenyl
p-Ts	*para*-Toluenesulfonyl
q	Quartet
RT	Room Temperature
s	Singlet
Sat.	Saturated
t-Bu	*tert*-butyl
t	Triplet
TBAF	Tetra-n-butlyammonium-fluoride
TBS	*tert*-Butyldimethylsilyl
THF	Tetrahydrofuran

THP	Tetrahydropyran
TLC	Thin layer chromatography
TMS	Trimethylsilyl
μL	Microliter

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Preface

Allenes are an important class of compounds and have gained increasing attraction as interesting building blocks in synthetic organic chemistry. The activation of allenes with a homogeneous catalyst sets the stage for cyclization by intramolecular attack of various nucleophiles, affording highly useful carbo- and heterocyclic products by formation of new C-O, C-N, C-S and C-C bonds.

The results of our investigations in this context form the subject matter of the thesis entitled **"Novel Strategies for the Synthesis and Cycloisomerization Reactions of Functionalized Allenes"**. The thesis is divided into four chapters which are presented as independent units and therefore the structural formulas, schemes, figures and references are numbered chapter-wise. In each chapter, a brief *introduction* of literature examples is followed by *present study*, *conclusion* and *experimental part*.

The thesis starts with a brief introduction into allenes and literature methods for the synthesis of functionalized allenes and further metal-catalyzed cycloisomerization reactions to afford synthetically valuable carbo- and heterocycles depending on the substituents on the nucleophilic moiety. Also, the importance and usage of cyclopentadienes was discussed in this chapter.

In the second chapter, the novel gold- and platinum-catalyzed [1,2]-migratory cycloisomerization cascade reaction of 1,1-disubstituted vinylallenes was discussed. The reaction allows the regioselective formation of highly substituted cyclopentadiene derivatives. The developed gold- and platinum-catalyzed reactions are complement to each other depending on the electronic nature of the substituents in the migrating groups.

In chapter 3, we have demonstrated the efficient Cu(I)-catalyzed cross-coupling reactions of alkynes**,** propargyl alcohols, propargyl amines and propargyl epoxides with diazo compounds. The desired hydroxy-, amino- and epoxy-functionalized allenes were obtained in good yields. The synthesized allene derivatives were subjected to gold-catalyzed cycloisomerization reactions to afford synthetically valuable heterocycles depending on the substituents on the nucleophilic moiety.

A summary of the work, also in German, is given at the end of the thesis as the last chapter.

CHAPTER 1

Introduction

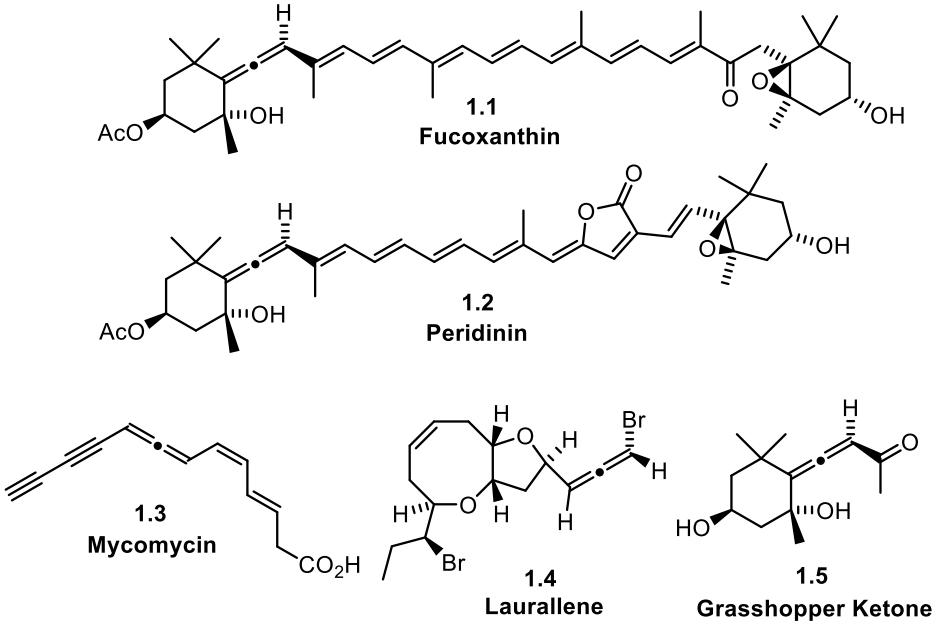
1.1 Allenes

Allenes are of an important class of organic compounds, which are characterized by two cumulated carbon-carbon double bonds. The history of allenes dates back to 1874. At that time, the correct core structure of allenes was predicted for the first time by Jacobus H. Van't Hoff.[1] This predictive work was so extreme for the scientists due to the their unique structure, due to the fact that, allenes have been considered mostly chemical curiosities for a long period. The first report for the synthesis of an allene, pentadienoic acid, was carried out by Burton and Pechmann in 1887[2], which was an attempt to prove the nonexistence of this class of compounds. Nearly 70 years later, the structure of the allene was confirmed by the use of IR and Raman spectroscopy for structural investigation of the characteristic allenic C-C vibration at around 1950 cm^{-1}.[3]

Till today, numerous of natural products and pharmaceuticals containing the allene moiety have been discovered.[4] Selected examples of naturally occurring allenes and pharmaceuticals are shown in Scheme 1.1 and 1.2. For example, the allenic carotenoid Fucoxanthin **1.1** which occurs in brown algae and diatomees and exhibits high energy transfer efficiencies to chlorophyll during the initial process of photosynthesis, was isolated in 1942 by Willstätter and Page.[5] The closely related carotenoid Peridinin **1.2**

[1] H. van't Hoff, *La Chimie dans l'Espace*, Bazendijk: Rotterdam, 1875.
[2] B. S. Burton, H. V. Pechmann, *Ber. Dtsch. Chem. Ges.* **1887**, *20*, 145-149.
[3] E. R. H. Jones, G. H. Mansfield, M. L. H. Whiting, *J. Chem. Soc.* **1954**, 3208-3212.
[4] Review: A. Hoffmann-Röder, N. Krause, *Angew. Chem. Int. Ed*. **2004**, *43*, 1196-1216.
[5] a) R. Willstätter, H. J. Page, *Justus Liebigs Ann. Chem*. **1914**, *404*, 237-271; b) S. Okumura, T. Kajikawa, K. Yano, S. Sakaguchi, D. Kosumi. H. Hashimoto, S. Katsumura, *Tetrahedron Lett.* **2014**, *55*, 407-410; c) T. Kajikawa, S. Okumura, T. Iwashito, D. Kosumi. H. Hashimoto, S. Katsumura, *Org. Lett.* **2012**, *14*, 808-811.

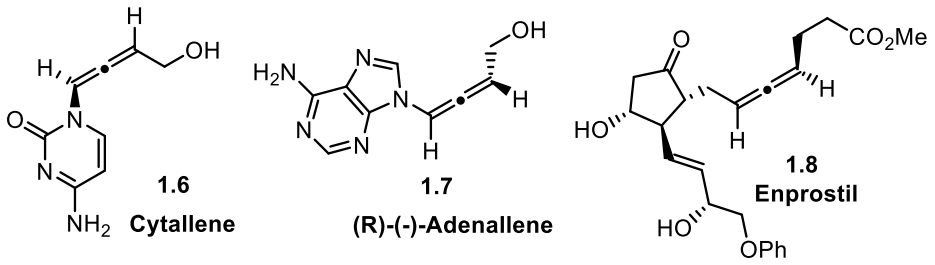
which plays an important role in the photosystem of dinoflagellates was isolated in 1890 by Schütt.[6] The synthesis of these carotenoids is still a fascinating challenge for the organic chemist. Before the discovery of Fucoxanthin **1.1**, Mycomycin **1.3** was the only known natural allene isolated by Johnson and Burdon[7] in 1947 from the Norcardia acidophilus, which shows strong antibiotic activity against Mycobacterium tuberculosis. Naturally occurring bromoallene, Laurallene **1.4** was isolated as a main constituent from the marine red alga Laurencia nipponica Yamada in 1977 by Kurosawa[8] and much attention has been paid to the total synthesis of this type naturally occurring bromoallenes.[9] The grasshopper ketone **1.5**[10] was isolated as a defense substance of the Nord American grasshopper. The first synthesis of racemic grasshopper ketone was described in 1969 and numerous syntheses has also been developed.[11]



Scheme 1.1. Selective examples of allene containing natural products.

[6] F. Schütt, *Ber. Dtsch. Bot. Ges.* **1890**, *8*, 9-32.
[7] a) E. A. Johnson, K. L. Burdon, *J. Bacteriol*. **1947**, *54*, 281-293; b) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc*. **1952**, 74, 2245-2248; c) W. D. Celmer, I. A. Solomons, *J. Am. Chem. Soc*. **1952**, *74*, 3838-3842.
[8] A. Fukuzawa, E. Kurosawa, *Tetrahedron Lett*. **1979**, 2797-2800.
[9] R. Kinnel, A. J. Duggan, T. Eisner, J. Meinwald, *Tetrahedron Lett*. **1977**, 3913-3916; b) K. S. Feldman, C. C. Mechem, L. Nader, *J. Am. Chem. Soc*. **1982**, *104*, 4011-4012; c) M. T. Crimmins, E. A. Tabet, *J. Am. Chem. Soc*. **2000**, *122*, 5473-5476; c) J. lshihara, Y. Shimada, N. Kanoh, Y. Takasugi, A. Fukuzawa, A. Murai, *Tetrahedron* **1997**, *53*, 8371-8382.
[10] M. Ito, Y. Yamano, S. Sumiya, A. Wada, *Pure Appl. Chem*. **1994**, *66*, 939-946.
[11] K. Mori, *Tetrahedron Lett*. **1973**, 723-726; b) K. Mori, *Tetrahedron* **1974**, 1065-1072; c) M. Ito, Y. Hirata, K. Tsukida, N. Tanaka, K. Hamada, R. Hino, T. Fujiwara, *Chem. Pharm. Bull*. **1988**, *36*, 3328-3340.

The potential biological activities of allenic compounds are also of interest in pharmaceutical chemistry. For example, allenic nucleoside Adenallene **1.6** and Cyctallene **1.7** were found efficiently inhibit in vivo replication and cytopathic of human immunodeficiency viruses HIV.[12] Entropstil **1.8**[13] is a potent inhibitor of gastric acid section and effective agent for the treatment of gastrointestinal disease (Scheme 1.2).



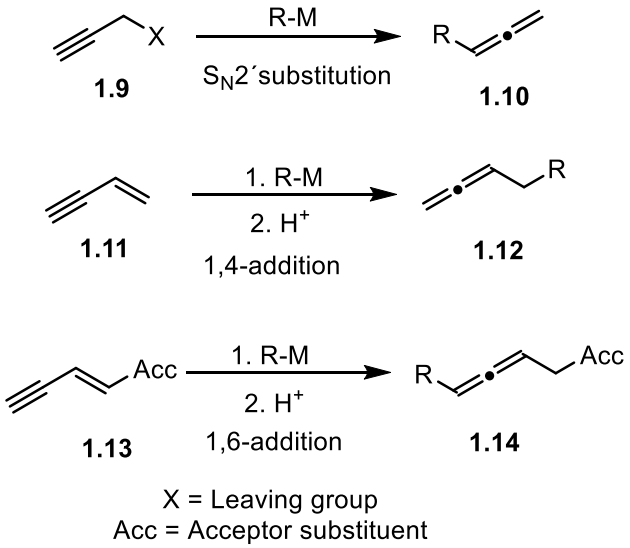
Scheme 1.2. Selective examples of pharmacologically active allenes.

1.2 Synthesis of Allenes

During the last few decades, the chemistry of allenes has witnessed a rapid development in target oriented organic synthesis which mainly include isomerization reaction of alkynes, reaction of aldehydes with terminal alkynes and metal-mediated reactions of propargylic compounds.[14] The earliest methods were mainly based on the isomerization reactions of the corresponding alkynes or propargyl derivatives. Over the past 30 years, the use of organometallic reagents for the synthesis of allenes has been highly developed.[15]

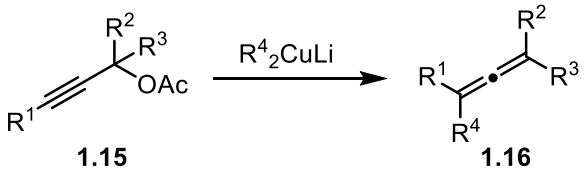
The basic reaction types for metal-mediated syntheses of allenes **1.10, 1.12** and **1.14** are outlined in Scheme 1.3 and consist of S_N2' nucleophilic substitution reactions of propargylic electrophiles **1.9**, furthermore 1,4-additions to unfunctionalized enynes **1.11** and 1,6-addition reactions to acceptor-substituted enynes **1.13**.

[12] J. Zemlicka, *Nucleosides Nucleotides*, **1997**, *16*, 1003-1012; b) J. Zemlicka, *Pharmacol Ther*. **2000**, *85*, 251-266; c) S. Hayashi, S. Phadtare, J. Zemlica, M. Matukura, H. Mitsuya, S. Broder, *Proc. Nat. Acad. Sci*, **1988**, *85*, 6127-6131.
[13] a) H. Carpio, G. F. Cooper, J. A. Edwards, J. H. Fried, G. L. Garay, A. Guzman, J. A. Mendez, J. M. Muchowski, A. P. Roszkowski, A. R. Van Horn, D. Wren, *Prostaglandins* **1987**, *33*, 169-180; b) G. F. Cooper, D. L. Wren, D. Y. Jackson, C. C. Beard, E. Galeazzi, A. R. V. Horn, T. T. Li, *J. Org. Chem.* **1993**, *58*, 4280-4286.
[14] *Modern Allene Chemistry* (Eds.: N. Krause, A. S. K. Hashmi), Wiley-VCH, Weinheim, **2004**.
[15] N. Krause, A. H. Röder, *Tetrahedron* **2004**, *60*, 11671-11694.



Scheme 1.3. Fundamental reaction types in the metal mediated synthesis of allenes.

One of the most developed methods for the synthesis of functionalized allenes is the reaction of propargylic derivatives with organocopper reagents using stoichiometric or catalytic amount of copper salts. The first example of allene synthesis using an organocuprate was documented by Rona and Crabbe[16] in 1968 for the reaction of propargylic acetates **1.15** with lithium dialkylcuprates which afforded allenes **1.16** with moderate to good yields (Scheme 1.4). Besides acetates the method has been successfully applied to benzoate, carbonate, sulfonate, ether, acetal, halide, oxirane and aziridine-substituted propargylic substrates.[14]

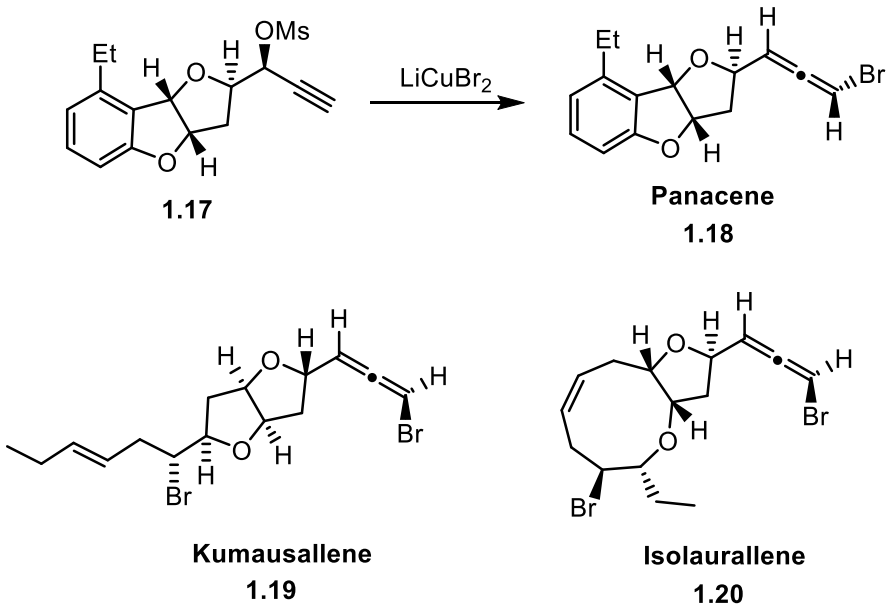


Scheme 1.4. Allene synthesis via S$_N$2´ substitution of propargylic acetates **1.15** with cuprates.

For the synthesis of natural product Panacene **1.18**, the chiral propargyl mesylate **1.17** was treated with lithium dibromocuprate.[17] An analogous protocol was used in the synthesis of Kumausallene **1.19** by

[16] a) P. Rona, P. Crabbe, *J. Am. Chem. Soc*.**1968**, *90*, 4733–4734; b) P. Rona, P. Crabbe, *J. Am. Chem. Soc.* **1969**, *91*, 3289–3292.
[17] K. S. Feldman, C. C. Mechem, L. Nader, *J. Am. Chem. Soc.* **1982**, *104*, 4011-4012.

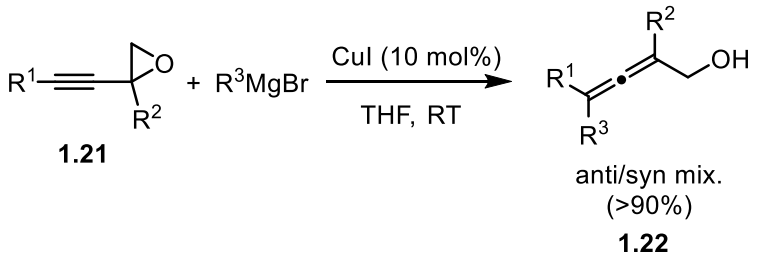
Overman *et al.*[18], as well as by Crimmins and co-workers in their synthesis of Isolaurallene[19] **1.20** (Scheme 1.5).



Scheme 1.5. S_N2' substitution reactions of chiral propargyl mesylates for the synthesis of natural products **1.18**-**20**.

Moreover, the synthesis of hydroxyallenes has a particular important role since they can be transformed into other hetero-substituted allenes and valuable heterocyclic compounds which are extensively used as synthetic building blocks. The S_N2` substitution of the propargylic oxiranes with organometallic reagents is one of the most useful methods for the synthesis of allenic alcohols. In 1974, Vermeer *et al.*[20] described the formation of allenic alcohol **1.22** by the reaction of alkynyl epoxide **1.21** with Grignard reagents in the presence of catalytic amount of copper salts. In the absence of CuI, a complex mixture of products was obtained (Scheme 1.6).

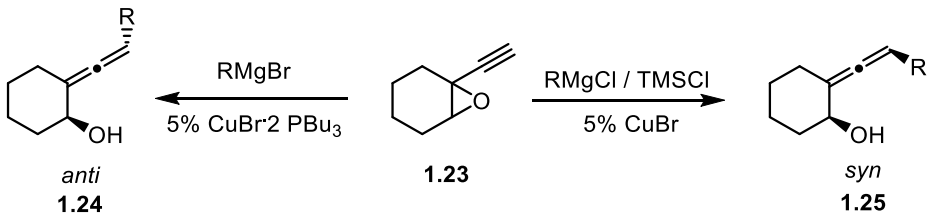
[18] T. A. Grese, K. D. Hutchinson, L. E. Overman, *J. Org. Chem.* **1993**, *58*, 2468-2477.
[19] a) M. T. Crimmins, K. A. Emmintte, *J. Am. Chem. Soc.* **2001**, *123*, 1533-1534; b) M. T. Crimmins, K. A. Emmintte, A. L. Choy, *Tetrahedron* **2002**, *58*, 1817-1834.
[20] P. Vermeer, J. Meijere, C. De Graaf, H. Schreurs, *Recl. Trav. Chim. Pays-Bas* **1974**, *93*, 46-47.



1.21 **1.22**

Scheme 1.6. Cu-catalyzed S_N2' substitution of propargyl oxiranes **1.21**.

Later on, Alexakis *et al.*[21] demonstrated that both diastereoisomers could be obtained by changing the halogen atom of the Grignard reagents in the copper-catalyzed S_N2' substitution reaction (Scheme 1.7).

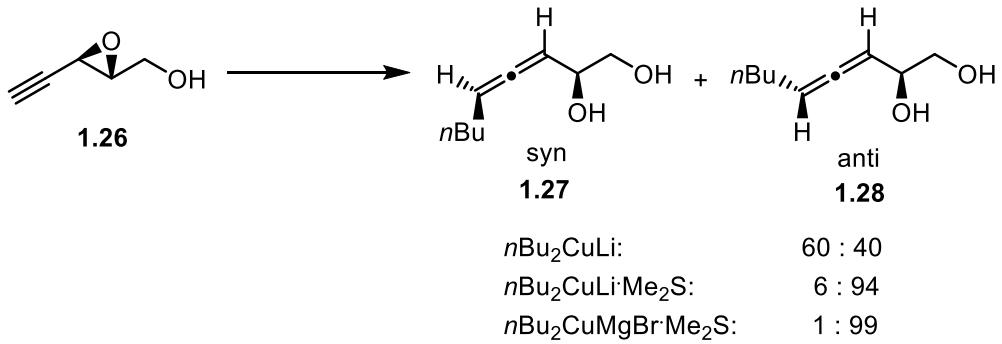


anti **1.24** **1.23** *syn* **1.25**

Scheme 1.7. *Anti/syn* stereoselective S_N2' substitution of propargylic electrophiles **1.23**.

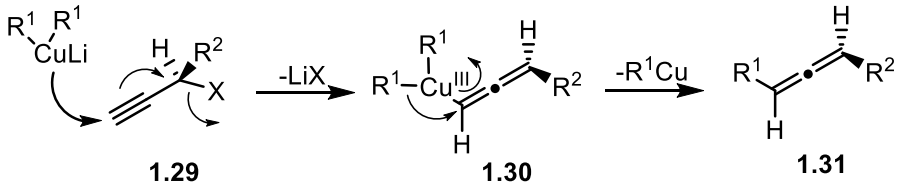
Furthermore, when the strategy was applied to enantiomerically pure or enriched oxiranes, the corresponding α-hydroxyallenes could be obtained easily in stereochemically defined form. In 1983, Oehlschlager *et al.*[22] reported the S_N2' substitution reaction of a chiral propargyl epoxide **1.26** with organocuprates, afforded the allenes **1.27** and **1.28** as *syn–anti* mixtures in the absence of any additives. If, however, the reaction was carried out in the presence of dimethyl sulfide, high *anti*-stereoselectivities were obtained with both lithium and magnesium cuprates (Scheme 1.8).

[21] A. Alexakis, I. Marek, P. Hangeney, J. F. Normant, *Tetrahedron Lett.* **1989**, *30*, 2387-2390.
[22] A. C. Oehlschlager, E. Czyzewska, *Tetrahedron Lett*. **1983**, *24*, 5587–5590.



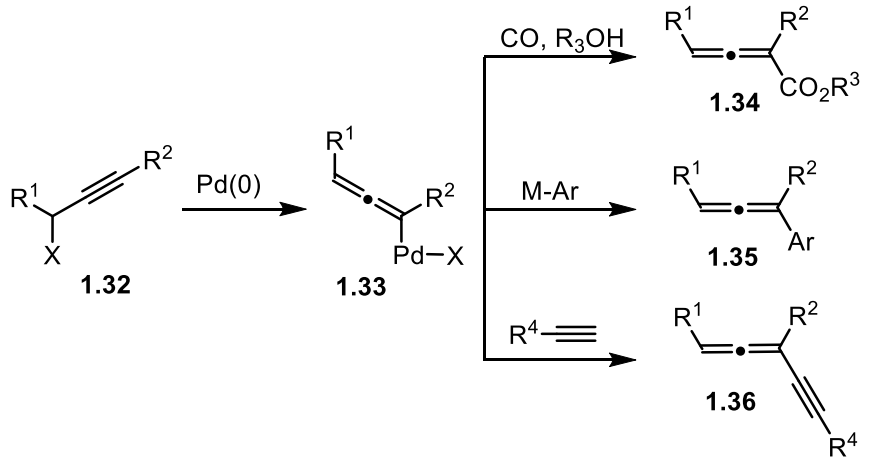
Scheme 1.8. Influence of dimethyl sulfide on the S_N2' substitution of propargyl oxirane **1.26**.

The stereochemical outcome of the reaction is controlled by the interaction of a copper-centered d-orbital with σ and π* orbitals of the substrate. This leads to the formation of a σ-copper(III) species **1.30**, which furnishes the *anti*-substitution product **1.31** after reductive elimination (Scheme 1.9).



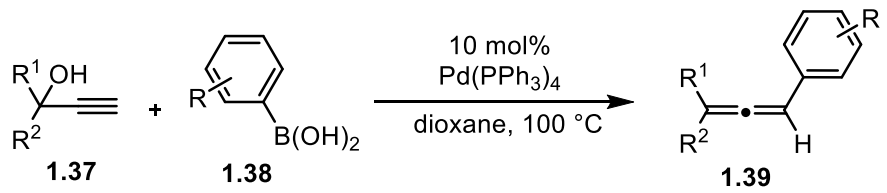
Scheme 1.9. Mechanistical model for the anti-stereoselective S_N2' substitution of propargylic electrophiles.

Propargylic compounds also undergo several transformations in the presence of palladium catalysts. The palladium-catalyzed reactions of propargylic electrophiles can be understood by analyzing the (*σ*-allenyl)palladium intermediate **1.33**. This intermediate is capable of undergoing further transformations such as insertion of alkenes or alkynes, transmetallation of hard carbon nucleophiles such as Grignard reagents or methyl hydrides or insertion of CO to yield allene derivatives (Scheme 1.10).



Scheme 1.10. Palladium-catalyzed reactions of propargylic electrophiles.

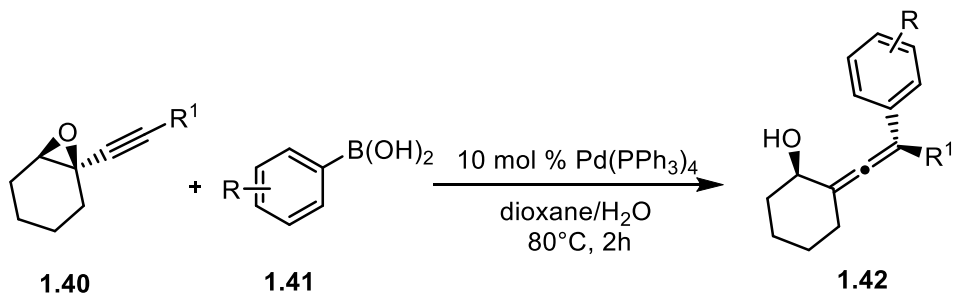
The reactions of propargyl electrophiles with organoboron compounds were investigated by Yoshida *et al*.[23] in the reaction between propargyl alcohols **1.37** and arylboronic acid **1.38** with palladium catalyst (Scheme 1.11).



Scheme 1.11. Palladium-catalyzed reactions of propargyl alcohols **1.37** with arylboronic acids.

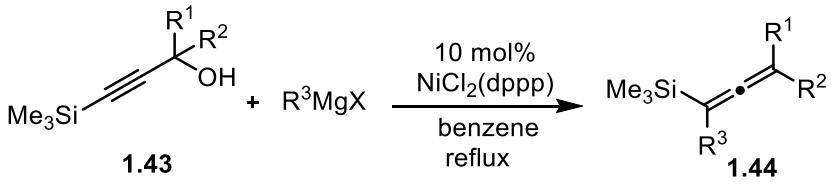
In addition to this, palladium complexes also catalyze the reaction of propargylic oxiranes **1.40** with substituted arylboronic acids **1.41**, in which *anti*-substituted 4-aryl-2,3-allenols **1.42** were obtained in high diastereoselectivity[24] (Scheme 1.12).

[23] M. Yoshida, T. Gotou, M. Ihara, *Tetrahedron Lett*. **2004**, *45*, 5573-5575.
[24] M. Yoshida, H. Ueda, M. Ihara, *Tetrahedron Lett*. **2005**, *46*, 6705-6708.



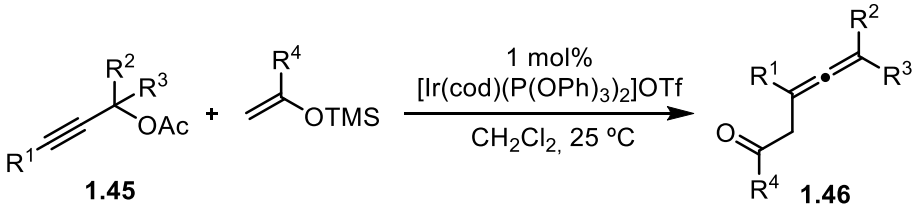
Scheme 1.12. Palladium-catalyzed reactions of propargyl oxiranes **1.40** with arylboronic acids.

In 1985, Wenkert *et al.*[25] published the reaction of Grignard reagents with propargyl alcohols **1.43** in the presence of a nickel catalyst. Excellent yields were obtained with 10 mol % $NiCl_2$(dppp) (Scheme 1.13).



Scheme 1.13. Nickel-catalyzed reaction of propargyl alcohols **1.43** and Grignard reagents.

Iridium complexes also catalyze the reaction of propargyl acetates **1.45** with silyl enol ethers which gives allenic products **1.46** (Scheme 1.14).[26]

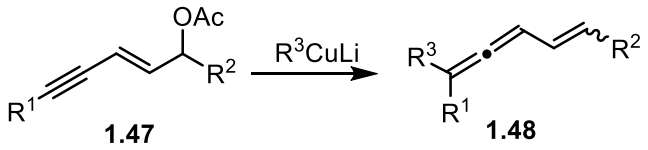


Scheme 1.14. . Iridium-catalyzed substitution of propargyl acetates **1.45** with silyl enol ethers.

[25] E. Wenkert, M. H. Leftin, E. L. Michelotti, *J. Org. Chem.* **1985**, *50*, 1122-1124.
[26] I. Matsuda, K. Komori, K. Itoh, *J. Am. Chem. Soc.* **2002**, *124*, 9072-9073.

Vinyl-substituted allenes are reactive compounds in various cycloaddition and cyclization reactions. They exhibit particularly a higher activity and selectivity in Diels-Alder reactions, because their configurational equilibrium is more on the side of the s-*cis* conformer, a prerequisite for a [4+2] cycloaddition reaction to occur effectively, than in 1,3-dienes.[27] In spite of their synthetic utility in organic reactions, there are only a few methods that can generate vinylallene structures.

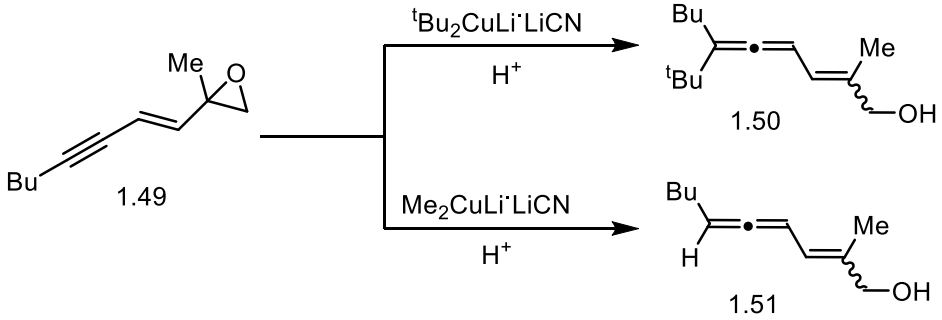
In 1999, Krause *et al*.[28] developed a regioselective 1,5-$S_N2´´$ type reaction of (*E*)-2,4-enyne acetates **1.47** with various lithium dialkylcuprates affording the vinylallenes **1.48** as a mixture of *E*- and *Z*-isomers (Scheme 1.15).



R^1=R^2=Me, R^3=Bu	90% (E:Z = 67:33)
R^1=R^2=Me, R^3=^{t}Bu	93% (E:Z = 25:75)
R^1=Me_3Si, R^2=^{t}Bu, R^3=Me	96% (E:Z = 40:60)
R^1=Bu, R^2=^{t}Bu, R^3=Me	92% (E:Z > 99:1)

Scheme 1.15. 1,5-$S_N2´´$ type Substitution reaction of enyne acetates **1.47** with dialkylcuprates.

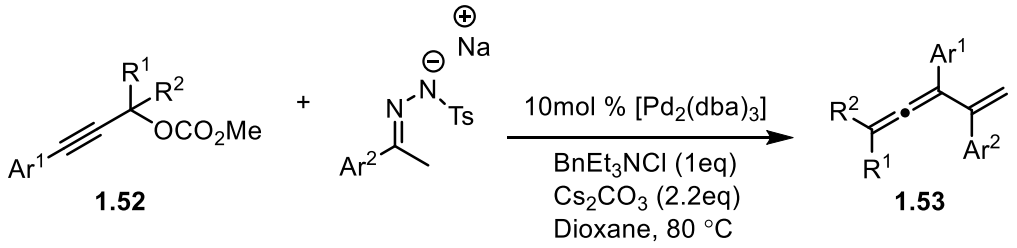
The method was also applied to (*E*)-2,4-enyne oxirane **1.49**, which was treated with $Me_2CuLi{\cdot}LiI$ or *t*-$Bu_2CuLi{\cdot}LiCN$. The substrate reacted cleanly with the *tert*-butylcuprate to afford the alkylated vinylallene **1.50** with a primary hydroxyl group, whereas its reaction with the lithium dimethylcuprate reagent proceeded without coupling and led to exclusive reduction to a vinylallene **1.51** (Scheme 1.16). [28]



Scheme 1.16. 1,5-$S_N2´´$ type substitution reaction of enyne oxiranes **1.49** with dialkyl cuprates.

[27] D. Bond, *J. Org. Chem.* **1990**, *55*, 661-665.
[28] a) N. Krause, M. Purpura, *Eur. J. Org. Chem.* **1999**, *1*, 265-275; b) N. Krause, M. Purpura, *Angew. Chem. Int. Ed.* **2000**, *39*, 4355-4356.

In 2011, Chen *et al*.[29] reported that diazo compounds generated *in-situ* from *N*-tosylhydrazone salts in the presence of a base, act as a nucleophile and react with the propargylic carbonates **1.52** to form vinylallenes **1.53** in the presence of [$Pd_2(dba)_3$] (Scheme 1.17).



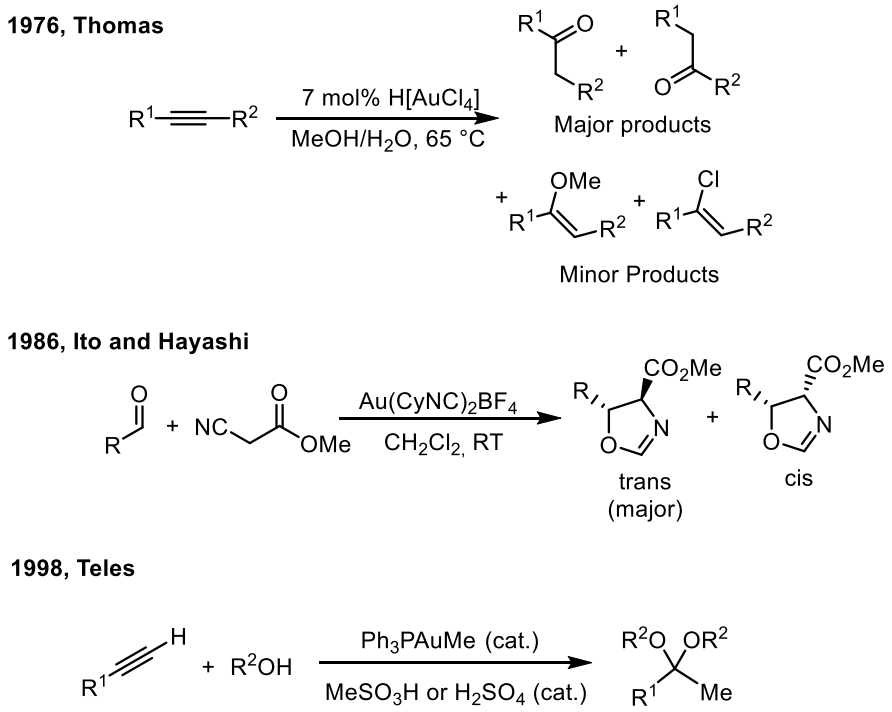
Scheme 1.17. Synthesis of vinylallene **1.53** by *N*-tosylhydrazone salt.

1.3 Homogeneous Gold Catalysis

Gold has been used for thousands of years in jewelry and currency with the advantage of impressive durability. Gold has also found application as precious metal for the industrial processes due to its resistance against oxidation from air and moisture. Gold has an excellent conductivity which makes it a key component in electronics and many other high-tech applications. It is well-known that gold has been used in the field of medicine and dentistry due to its non-allergenic and non-toxic characteristic properties. However, gold had not been recognized as a catalyst for the chemists until last few decades. Obviously, this can be attributed to the fact that chemists used to consider gold as a chemically inert and very expensive metal.

In 1976, Thomas *et al.*[30] reported the first homogeneous gold-catalyzed reaction for the hydration of alkynes promoted by tetrachloroauric acid in aqueous methanol and obtained the corresponding ketones by Markovnikov addition as major products. After one decade, in 1986, Ito and Hayashi[31] described an aldol-type reaction between aldehydes and isocyanate using a chiral ferrocenylphosphine-gold(I) complex that afforded substituted, nonracemic oxazolines with high diastereoselectivity and enantioselectivity. In 1998, Teles *et al.*[32] demonstrated the extraordinary high reactivity of cationic Au(I)-phosphine complexes in the hydroalkoxylation of alkynes which was the actual turning point for homogeneous gold catalysis and the potential of gold salts to act as soft carbophilic Lewis acids caught the attention of the scientific community (Scheme 1.18).

[29] Z. Chen, X. Duan, L. Wu, S. Ali, K. Ji, P. Zhou, X. Liu, Y. Liang, *Chem. Eur. J*. **2011**, *17*, 6918-6921.
[30] R. O. C. Norman, W. J. E. Parr, C. B. Thomas, *J. Chem. Soc. Perkin. Trans. 1*, **1976**, 1983-1987.
[31] Y. Ho, M. Sawamura, T. Hayashi, *J. Am. Chem. Soc*. **1986**, *108*, 6405-6406.
[32] J. H. Teles, S. Brode, M. Chabanas, *Angew. Chem. Int. Ed*. **1998**, *37*, 1415-1418.



Scheme 1.18. Early investigations on homogeneous gold catalysis.

Since these pioneering works, the area of homogeneous gold catalysis finally undergoes widespread investigations, covering a broad spectrum of transformations in organic synthesis. The last decade has been the "booming time" for homogeneous gold catalysis. The ability of gold catalysts to act as carbophilic Lewis acids and hence to chemoselectively activate π-bonds towards nucleophilic attack initiates numerous investigations of incredible variety to form different carbo- and heterocyclic motifs that are now easily accessible.[33]

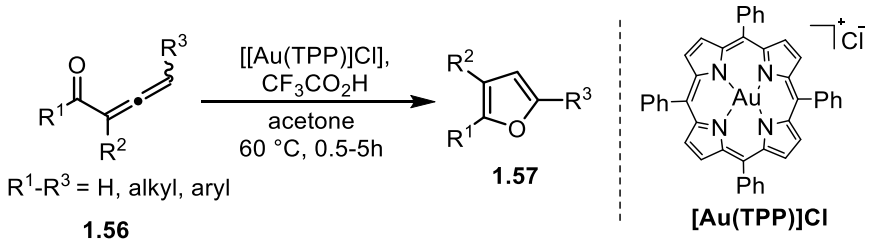
1.4 Gold-Catalyzed Cycloisomerization Reactions of Functionalized Allenes

The homogeneous catalysis of organic reactions by gold complexes has received significant attention in recent years due to its extraordinary reactivities and selectivities in various transformations. The activation of allenes with a homogeneous gold catalyst sets the stage for a cyclization by intramolecular

[33] a) Reviews; A. Corman, A. Leyva-Perez, M. J. Sabater, *Chem. Rev.* **2011**, *111*, 1657-1712; b) M. Rudolph, A. S. K. Hashmi, *Chem. Commun*. **2011**, *47*, 6536–6544; c) H. C. Shen, *Tetrahedron* **2008**, *64*, 3885-3903.

attack of various nucleophiles, affording highly useful carbo- and heterocyclic products by formation of new C-O, C-N, C-S and C-C bonds[34].

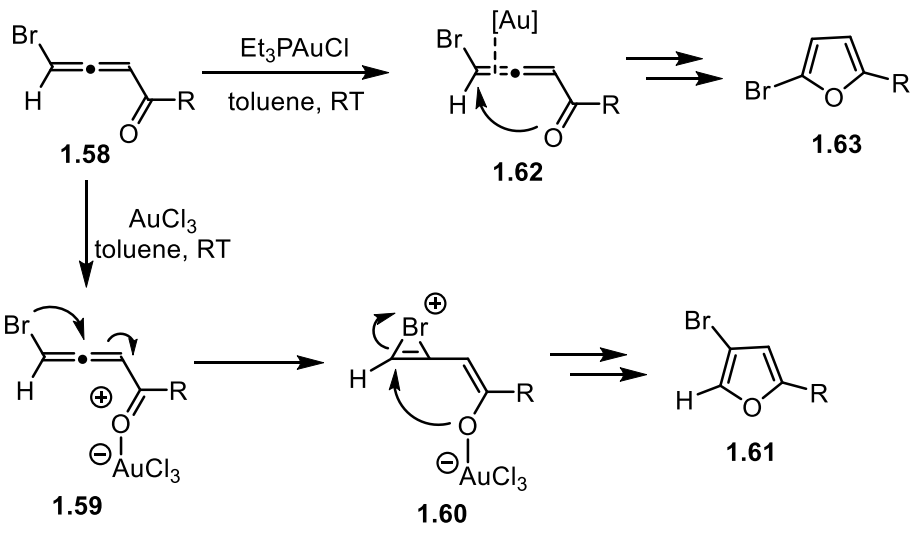
In 2000, the first gold-catalyzed addition of heteroatom nucleophiles was reported by Hashmi,[34] who reported the cycloisomerization of allenyl ketones to the corresponding furans by the use of only 1 mol% $AuCl_3$ in acetonitrile. The use of the gold catalyst entails a number of advantages to operate the reaction in shorter reaction time, milder reaction conditions and very low catalyst loading compared with the other transition metal-catalyzed reactions (silver[35] and palladium[36]). Despite of a number of advantages of Hashmi´s[34] pioneering report, variable amounts of undesired dimerization product were also obtained. In 2006, Che *et al*.[37] described the first gold(III) porphyrin-catalyzed cycloisomerization reaction of allenyl ketones in excellent yield with preventing the formation of undesired dimerization products (Scheme 1.19).



Scheme 1.19. [Au(TPP)]Cl-catalyzed cycloisomerization of allenyl ketones **1.56**.

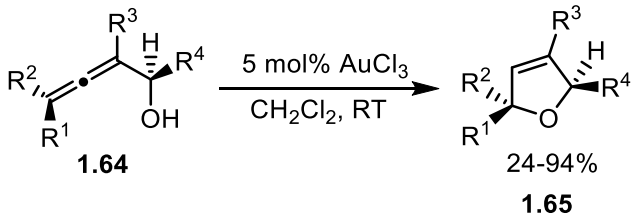
Along this line, Gevorgyan and co-workers[38] reported the gold-catalyzed regiodivergent cycloisomerization of bromoallenyl ketones to isomeric bromofurans **1.61** and **1.63**, in which the structure of the product is highly dependent on the oxidation state of the gold catalyst (Scheme 1.20).

[34] A. S. K. Hashmi, L. Schwarz, J. H. Choi, T. M. Trost, *Angew. Chem. Int. Ed.* **2000**, *39*, 2285-2288.
[35] a) J. A. Marshall, E. D. J. Robinson, *J. Org. Chem*. **1990**, *55*, 3450-3451; (b) J. A. Marshall, G. S. Bartley, *J. Org. Chem*. **1994**, *59*, 7169-7171; (c) J. A. Marshall, C. A. Sehon, *J. Org. Chem*. **1995**, *60*, 5966-5968.
[36] (a) A. S. K. Hashmi, *Angew. Chem., Int. Ed*. **1995**, *34*, 1581-1583. (b) A. S. K. Hashmi, T. L. Ruppert, T. Knöfel, J. W. Bats, *J. Org. Chem*. **1997**, *62*, 7295-7304.
[37] C. Y. Zhou, P. W. H. Chan, C. M. Che, *Org. Lett*. **2006**, *8*, 325-328.
[38] A. W. Sromek, M. Rubina, V. J. Gevorgyan, *J. Am. Chem. Soc.* **2005**, *127*, 10500-10501.



Scheme 1.20. Gold-catalyzed cycloisomerization of bromoallenones **1.58**.

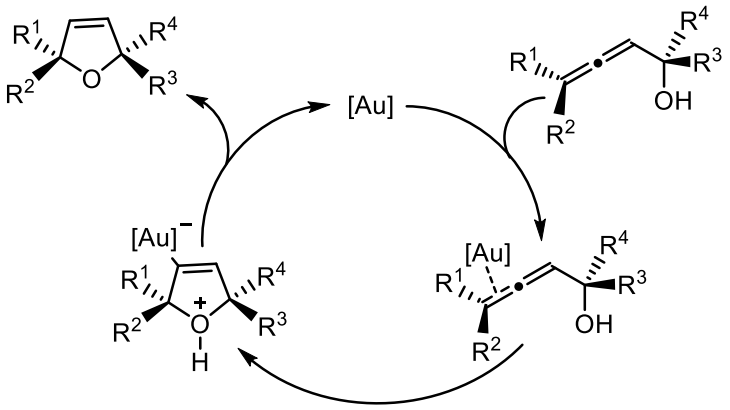
The possibility of using chiral substrates was achieved by replacing the keto with a hydroxy group by Krause *et al*.[39] They reported the highly efficient synthesis of chiral 2,5-dihydrofurans **1.65** from α-hydroxyallenes **1.64** by using 5 mol% $AuCl_3$ in dichloromethane, which takes place with complete axis-to-center chirality transfer, and is therefore, ideally suited for target oriented stereoselective synthesis (Scheme 1.21).



Scheme 1.21. Gold(III) chloride-catalyzed cyclization of α-hydroxyallenes **1.64**.

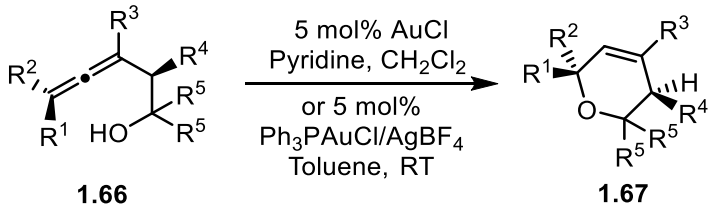
The mechanism of this transformation proceeds through the coordination of the carbophilic gold catalyst to an allenic double bond to afford a π-complex, which undergoes a 5-*endo*-cyclization resulting in the formation of a vinylgold intermediate. Subsequent protodeauration leads to the desired product with regeneration of the gold catalyst (Scheme 1.22).

[39] A. Hoffmann-Röder, N. Krause, *Org. Lett.* **2001**, *3*, 2537-2538.



Scheme 1.22. Mechanism of the gold-catalyzed cycloisomerization of α-hydroxysubstituted allenes.

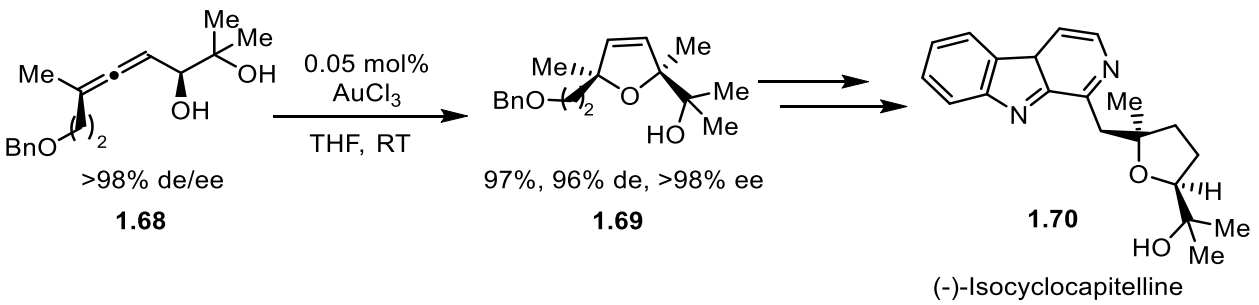
The method was also extended to an efficient gold-catalyzed 6-*endo*-*trig* cycloisomerization of β-hydroxyallenes **1.66** to dihydropyrans **1.67** where both Au(I) and Au(III) were found to be efficient precatalysts (Scheme 1.23).[40]



Scheme 1.23. Gold(I)-chloride-catalyzed cyclization of β-hydroxyallenes **1.66**.

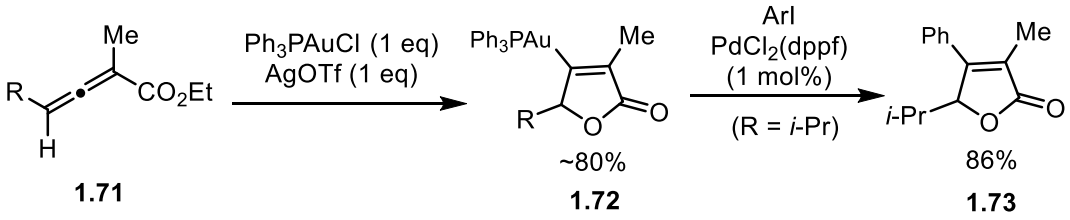
This method is compatible with various functional groups present in the substrate and found many applications in natural product synthesis. For example, Volz and Krause reported the synthesis of chiral dihydrofuran **1.69** as a subunit of β-carboline alkaloids (–)-isocyclocapitelline **1.70** from the corresponding allenic diol **1.68** by using only 0.05 mol % of $AuCl_3$ in THF (Scheme 1.24).[41]

[40] B. Gockel, N. Krause, *Org. Lett*. **2006**, *8*, 4485-4488.
[41] F. Volz, N. Krause, *Org. Biomol. Chem*. **2007**, *5*, 1519-1521.



Scheme 1.24. Synthesis of β-carboline alkaloid (–)-Isocyclocapitelline **1.70**.

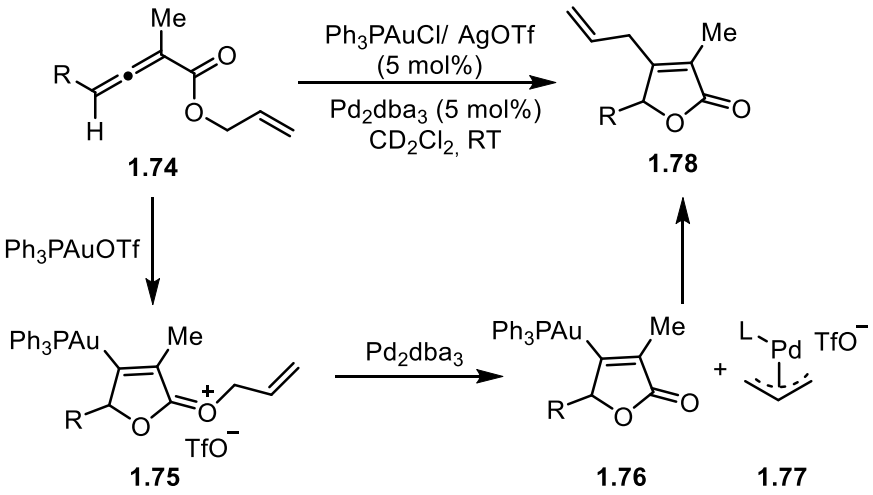
In 2008, Hammond *et al*.[42] found that stable vinylgold complexes **1.72** can be isolated from the reaction of cationic gold species with allenoates **1.71** which provides a direct evidence for the proposed mechanism of the gold-catalyzed allene cyclization. By combining the high reactivity of gold for cycloisomerization reactions together with its transmetallation ability with palladium, Hashmi *et al*.[43] showed that organogold complexes participates in Pd/Au dual-metal catalyzed cross-coupling reactions which provides C-C bond formation as an alternative to protodemetallation (Scheme 1.25).



Scheme 1.25. Synthesis and transmetallation of organogold(I) complexes **1.72**.

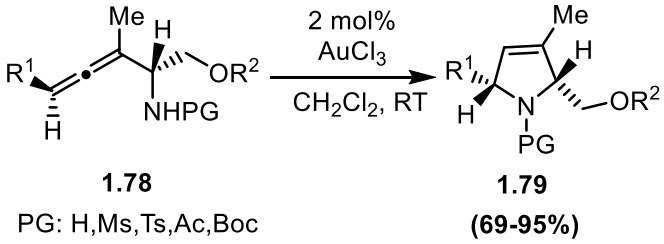
With the success of palladium-catalyzed cross-coupling reactions of organogold compounds, Blum *et al*.[44] established the dual-metal catalyzed transformation of allylic allenoates **1.74** to allylated butenolides **1.78** with catalytic amount of Pd and Au complexes. The allyl oxonium intermediates **1.75** undergo deallylation in the presence of the Pd(0) catalyst. The subsequent nucleophilic attack of the resulting σ-vinylgold intermediate **1.76** at the π-allyl palladium species **1.77** and reductive elimination afforded the final product **1.78** with the regeneration of the cationic gold species (Scheme 1.26).

[42] L. P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc.* **2008**, *130*, 17642-17643.
[43] A. S. K. Hashmi, C. Lothschütz, R. Döpp, M. Rudolph, T. D. Ramamurthi, F. Rominger, *Angew. Chem. Int. Ed.* **2009**, *48*, 8243-8247.
[44] Y. Shi, K. E. Roth, S. D. Ramgren, S. A. Blum, *J. Am. Chem. Soc.* **2009**, *131*, 18022-18023.



Scheme 1.26. Tandem Au/Pd-catalyzed cycloisomerization of allenoates **1.74**.

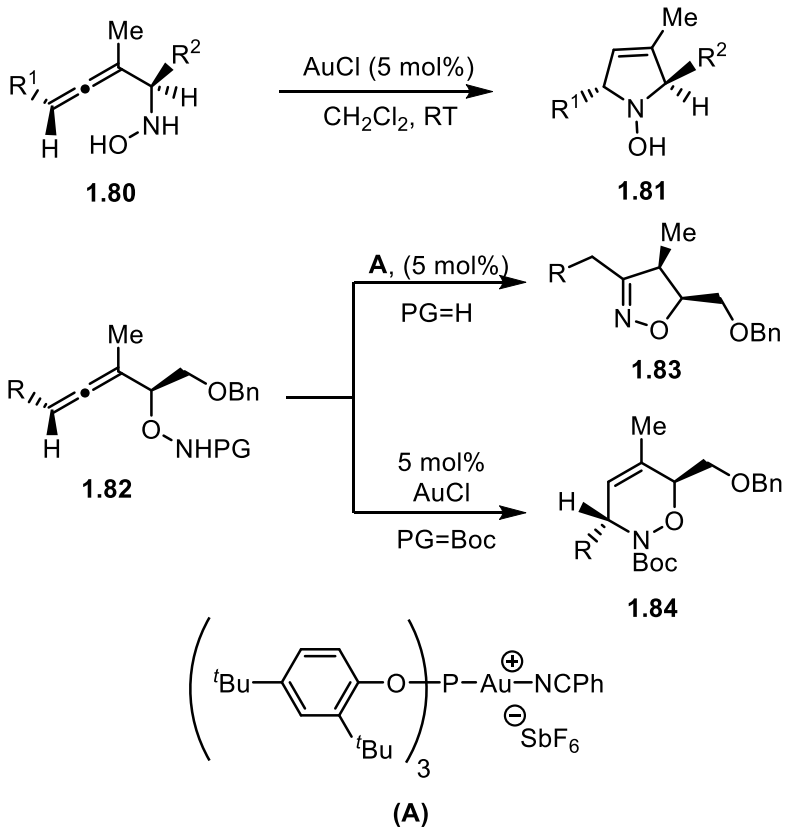
The activation of allenes by gold catalysts toward nucleophilic attack has also opened a new route to C-N bond formation. In 2004, Morita and Krause[45] reported the first intramolecular *endo*-selective hydroamination of α-aminoallenes **1.78** to 3-pyrrolines **1.79** by using $AuCl_3$ with complete axis-to-center chirality transfer. Gold(I) precatalyst such as AuCl and AuI showed a higher reactivity in case of hydroamination of unprotected α-aminoallenes (Scheme 1.27).



Scheme 1.27. Gold-catalyzed cycloisomerization of α-aminoallenes **1.78**.

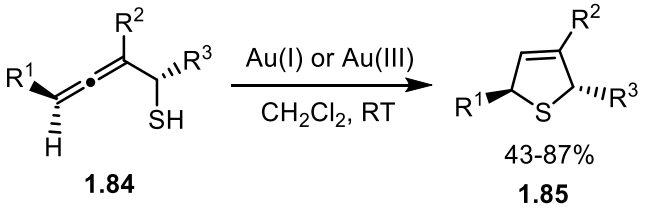
Encouraged by the observation on the gold-catalyzed cycloisomerization of hydroxy- and amino-functionalized allenes, Krause *et al*.[46] extended the method to gold-catalyzed synthesis of heterocycles with two heteroatoms from the allenic precursors such as hydroxylamines and hydroxylamine ethers. In all cases, the nitrogen atom acts as a nucleophile and attacks the allene in 5- or 6-*endo* mode depending on the gold catalyst and the protecting group at nitrogen (Scheme 1.28).

[45] a) N. Morita, N. Krause, *Org. Lett.* **2004**, *6*, 4121-4123; b) N. Morita, N. Krause, *Eur. J. Org. Chem.* **2006**, 4634-4641.
[46] C. Winter, N. Krause, *Angew. Chem. Int. Ed.* **2009**, *48*, 6339-6342.



Scheme 1.28. Gold-catalyzed cycloisomerization of allenic hydroxylamines **1.80** and hydroxylamine ethers **1.82**.

Later on, the same group extended the method to the cycloisomerization of α-thioallenes **1.84** which was the first example of a gold-catalyzed C-S bond formation.[47] The coordination of the gold catalyst to the sulfur atom of the α-thioallenes is probably more pronounced than its coordination to the other heteroatoms, which is responsible for a lower reactivity (Scheme 1.29).

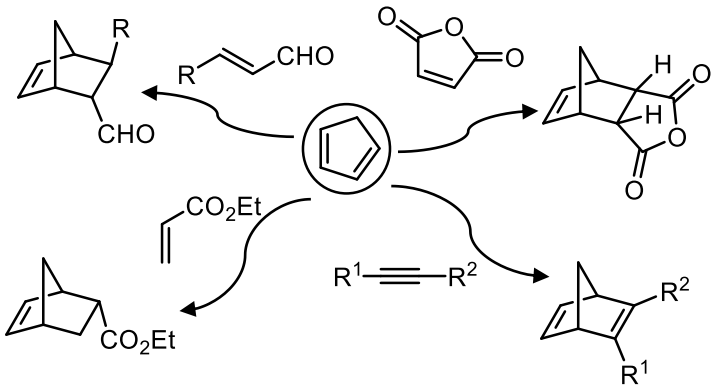


Scheme 1.29. Gold-catalyzed cycloisomerization of α-thioallenes **1.84**.

[47] N. Morita, N. Krause, *Angew. Chem. Int. Ed.* **2006**, *45*, 1897–1899.

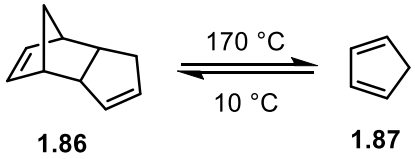
1.5 Cyclopentadienes

Cyclopentadienes (Cps) are very useful synthetic intermediates in organic and organometallic chemistry. They display a wide reactivity for the construction of fused ring systems via inter- and intramolecular Diels-Alder reactions (Scheme 1.30).[48]



Scheme 1.30. Diels-Alder reaction of Cp with various dienophiles.

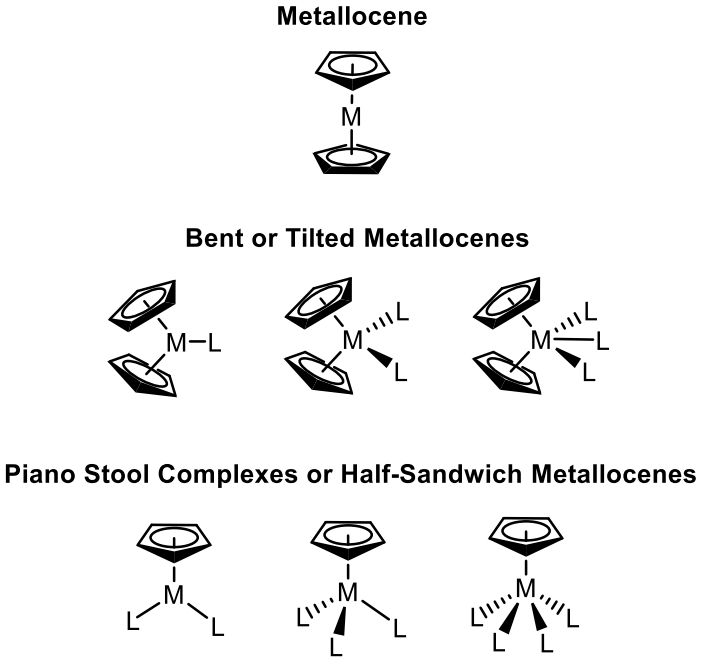
In addition to this, cyclopentadienes are used as precursors for the preparation of transition-metal complexes in coordination chemistry.[49] Therefore, methods to access these substrates are highly desirable. Cyclopentadiene **1.87** can be obtained by thermal decomposition of dicyclopentadiene **1.86** at high temperature (Scheme 1.31).[50] Apart from unsubstituted cyclopentadiene, the preparation of substituted cyclopentadienes is not easy due to their low stability, and the facile migration of the endocyclic double bonds. Consequently, synthesis of highly substituted cyclopentadienes is an important subject of synthetic chemistry.



Scheme 1.31. Thermal decomposition of dicyclopentadiene **1.86**.

[48] a) G. O. Jones, V. A. Guner, K. N. Houk, *J. Phys. Chem. A* **2006**, *110*, 1216-1224; b) H. Yoon, W. Chae, *Tetrahedron Lett*. **1997**, *38*, 5169 – 5172.
[49] Reviews: a) R. L. Halterman, *Chem. Rev*. **1992**, *92*, 965-994; b) U. Siemeling, *Chem. Rev*. **2000**, *100*, 1495 – 1526.
[50] B. Moffett, *Org. Synth. Coll*. **1963**, *4*, 238.

After the discovery of ferrocene in the area of coordination chemistry, Cps have been among the most important ligands because minor modification on the Cp ligands can provide a significant change in the structure and reactivity of the metallocence complexes.[51] Scheme 1.32 illustrates some of the common transition metal Cp structures. Complexes having two Cp ligands are classified as metallocenes, and those bearing one, two, or three additional ligands are termed tilted or bent metallocenes. Compounds having one Cp ligand but two, three, or four additional ligands are called half-sandwich or piano stool complexes.

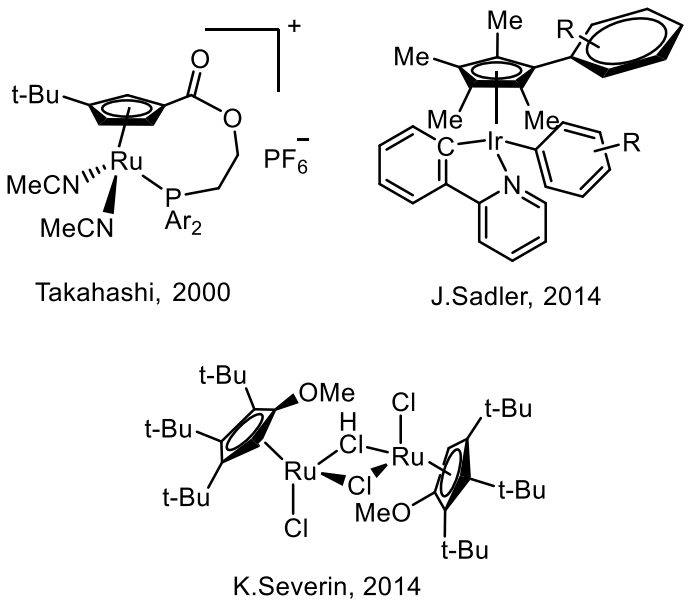


Scheme 1.32. Examples of Cp complexes.

Electron-donating or electron withdrawing groups influence the properties and reactivities of Cp metal complexes. Electron-donating groups increase the electron density around the metal center, making the metal less electrophilic. Electron-withdrawing groups decrease the electron density of the metal center, making the metal more electrophilic. Steric effects occur when the Cp substituent is bulky enough to control the orientation of reacting molecules as they approach the metal (Scheme 1.33).[52]

[51] M. Horacek, J. Pinkas, J. Merna, R. Gyepes, P. Meunier, *J. Organomet. Chem*. **2009**, *694*, 173-178; b) W. C. Finch, E. V. Anslyn, R. H. Grubbs, *J. Am. Chem. Soc.* **1988**, *110*, 2406-2414; c) M. Koller, W. von Philipsborn, *Organometallics* **1992**, *11*, 467-472; d) M. E. Rerek, F. Basolo, *J. Am. Chem. Soc.* **1984**, *106*, 5908-5912.

[52] a) N. Dodo, Y. Matsushima, M. Uno, K. Onitsuka, S. Takahashi, *J. Chem. Soc., Dalton Trans*. **2000**, 35-41; b) Z. Liu, I. R. Canelon, A. Habtemariam, G. J. Clarkson, P. J. Sadler, *Organometallics* **2014**, *33*, 5324−5333; c) J. Risse, B. Dutta, E. Solari, R. Scopelliti, K. Severin, *Z. Anorg. Allg. Chem*. **2014**, *640*, 1322-1329.

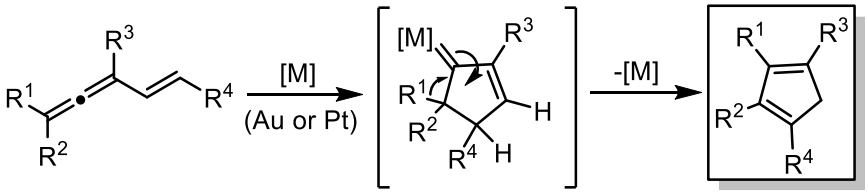


Scheme 1.33. Selected examples of Cp-ligated transition-metal complexes.

1.6. Definition of the Research Problem

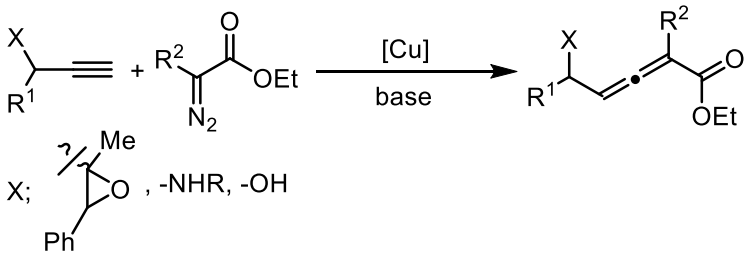
In recent years, homogeneous transition metal-catalyzed organic reactions have received significant attention due to their extraordinary reactivities and selectivities. One of these transformations is the activation of allenes with homogeneous gold catalyst which promotes the cyclization by intramolecular attack of various nucleophiles, affording highly useful carbo- and heterocyclic products by formation of new C-O, C-N, C-S and C-C bonds. As a consequence, the development of practical synthetic approaches to access these target molecules is of our major interest.

In the first part, we developed gold- or platinum-catalyzed [1,2]-migratory cycloisomerization cascade reaction of 1,1-disubstituted vinylallenes which provides a regioselective access to highly substituted cyclopentadiene derivatives.



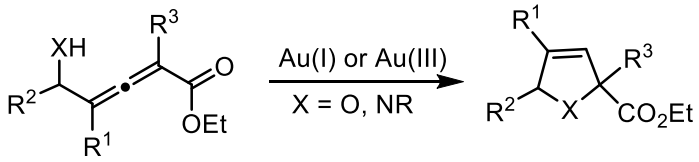
Scheme 1.34. Transition metal-catalyzed 1,2-migratory cycloisomerization of vinylallenes.

Extensive investigations of the transition metal-catalyzed reactions of diazo compounds have led to the development of valuable synthetic method. Although significant progress has been made in this field, the development of highly efficient catalytic transformations via transition metal carbene intermediates is still an important and attractive area in modern synthesis. In the second part, we perform the Cu(I)-catalyzed cross-coupling reaction of alkynes with diazo compounds for the synthesis of functionalized allenes.



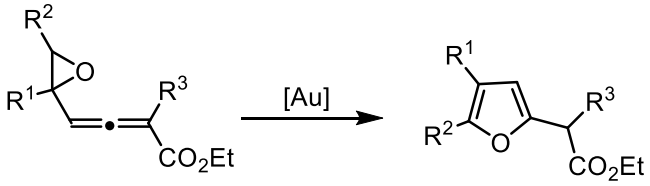
Scheme 1.35. Cu(I)-catalyzed cross-coupling reaction of alkynes with diazo compounds.

The new allene derivatives thus formed are subjected to gold-catalyzed cycloisomerization reaction to afford heterocyclic products by formation of new C-O and C-N bonds depending on the substituents on the nucleophilic moiety.



Scheme 1.36. Gold-catalyzed cycloisomerization of functionalized allenes.

Also, we have developed a gold-catalyzed cycloisomerization reaction of epoxy-functionalized allenic ester to afford functionalized furan derivatives containing a stereogenic center.



Scheme 1.37. Gold-catalyzed cycloisomerization of epoxy-functionalized allenic ester.

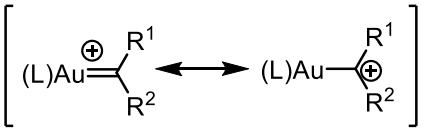
CHAPTER 2

Gold- and Platinum-Catalyzed [1,2]-Migratory Cycloisomerization Cascade Reactions of Vinylallenes

2.1 Introduction

2.1.1 Recent Developments on Gold-Carbenoid Structures

The use of gold complexes as carbophilic π-acids has become a powerful tool for building molecular complexity in a number of reactions. Gold carbenes or gold carbenoids, which indicates the carbocationic nature of this species, have been widely proposed as key and reactive intermediates in a range of gold(I)-catalyzed transformations.[53] Recent theoretical and experimental investigations polarized the discussion about the nature of carbene or cationic character of organogold species (Scheme 2.1).[54] Although some of the mechanistic pathways have been investigated by DFT calculations, labeling and kinetic studies, isolation of the key intermediates still one of the most important challenges in this field of research.

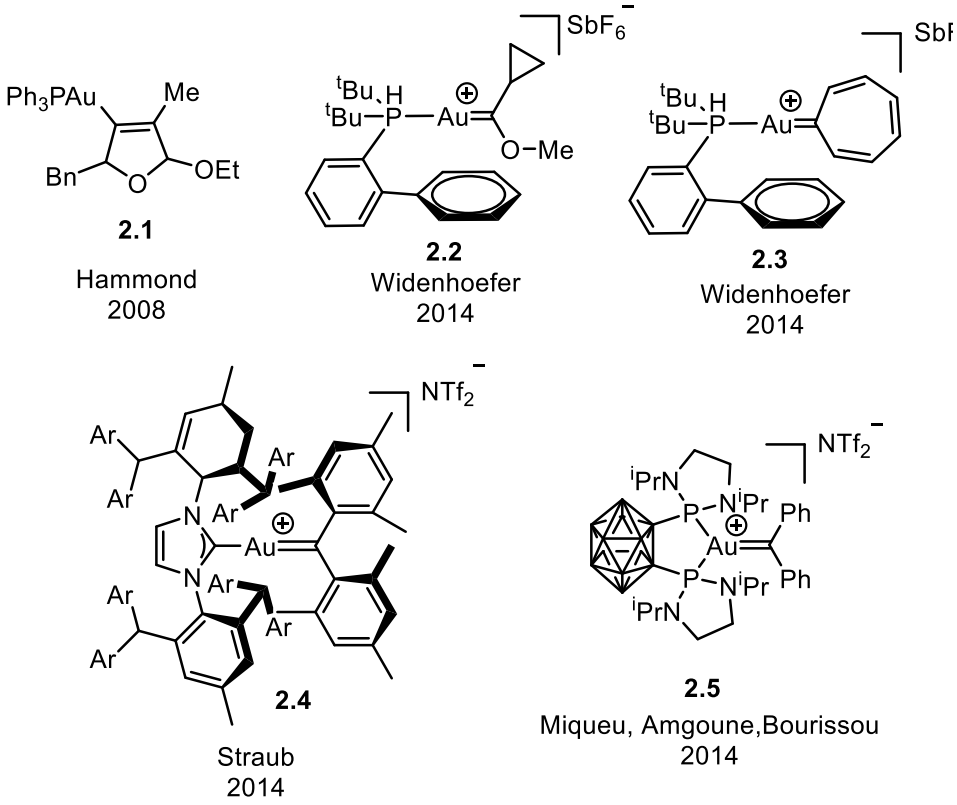


Scheme 2.1. Carbene and carbocation resonance forms of gold carbenes.

Recently, the isolation and structural characterization of gold carbenoids has provided a new insight into the nature of the key gold(I) species. In 2008, Hammond and coworkers [55] were the first to report the isolation of vinylgold intermediate **2.1** and provided experimental evidence to support the postulated mechanisms of many Au-catalyzed reactions (Scheme 2.2). Since then, a number of cationic gold carbenoid complexes have been isolated. For example, Brooner and Widenhoefer[56] reported the first example of a heteroatom stabilized gold cyclopropylcarbene complex **2.2.** Later the non-heteroatom stabilized complex **2.3**[57] was also reported in which the carbene moiety is incorporated into an aromatic cycloheptatrienylidene framework and stabilized by π-delocalization. In 2014, Straub[58] reported a fully characterized non-heteroatom stabilized gold-carbene complex **2.4**. In this complex, the dimesityl carbene moiety is combined

[53] a) E. J. Numez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326-3350.
[54] a) D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Gaddord, F. D. Toste, *Nature Chem.* **2009**, *1*, 482-486; b) Y. Wang, M. E. Muratore, A. M. Echavarren, *Chem. Eur. J.* **2015**, *21*, 7332-7339.
[55] L. P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc.* **2008**, *130*, 17642-17643.
[56] R. E. M. Brooner, R. A. Widenhoefer, *Chem. Commun*. **2014**, *50*, 2420-2423.
[57] R. J. Harris, R. A. Wiedenhoefer, *Angew. Chem. Int. Ed.* **2014**, *53*, 9369-9371.
[58] M. W. Hussong, F. Romiger, P. Krämer, B. F. Straub, *Angew. Chem. Int. Ed.* **2014**, *53*, 9372-9375.

with a bulky NHC fragment, resulting in very strong steric shielding of gold carbenoid structure. Another example of gold-carbenoid complex **2.5** was reported by Miqueu, Amgoune and Bourissou[59] by taking the advantage of peculiar electronic properties of the $[(DPCb)Au]^+$ (DPCb = o-carborane diphosphines) fragment which stabilized the carbene complexes with participation of gold fragment via π-backdonation.



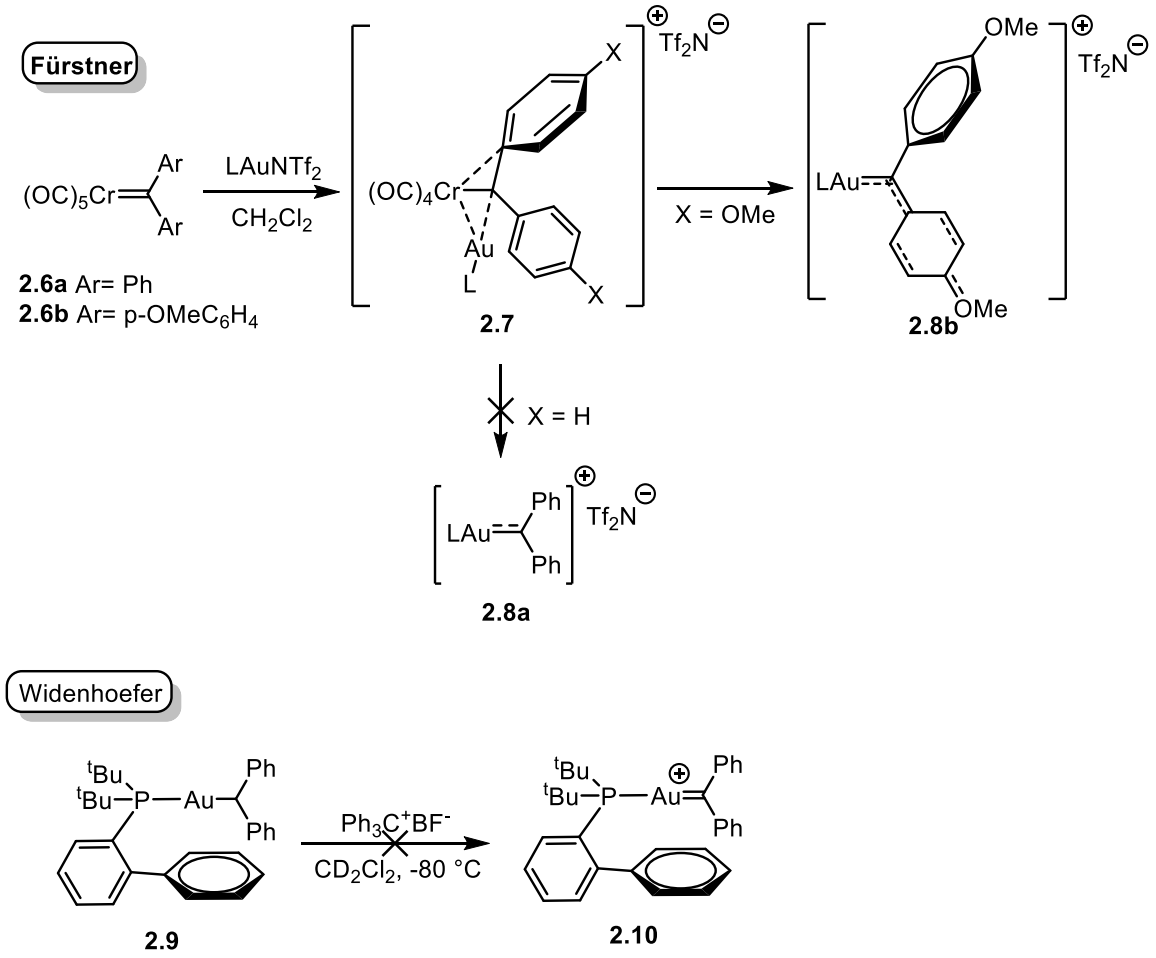
Scheme 2.2. Examples of gold-carbenoids.

In this context, Fürstner[60] have developed an efficient method for the synthesis of gold carbenoids from Fischer carbene complexes which are known to undergo a facile carbene transfer upon treatment with appropriate Au(I) sources (Scheme2.3).[61] They have found that in the reaction of **2.6a** ($Ph_2C{=}Cr(CO)_5$) with $[(Cy_3P)Au]NTf_2$, the formation of gold carbenoid **2.8a** could not be observed, whereas the reaction of *p*-methoxy-substituted carbene **2.6b** afforded the gold carbenoids **2.8b**. Similarly, Widenhoefer [57] reported

[59] M. Joost, L. Estevez, S. M. Ladeira, K. Miqueu, A. Amgoune, D. Bourissou, *Angew. Chem. Int. Ed.* **2014**, *53*, 14512-14516.
[60] G. Seidel, A. Fürstner, *Angew. Chem. Int. Ed.* **2014**, *53*, 4807-4811.
[61] R. Auman, E. O. Fischer, *Chem. Ber*. **1983**, *114*, 1853-1857.

a failed attempt to form gold carbenoid complex **2.10** through the hydride abstraction from gold diphenyl methane precursor **2.9** (Scheme2.3).

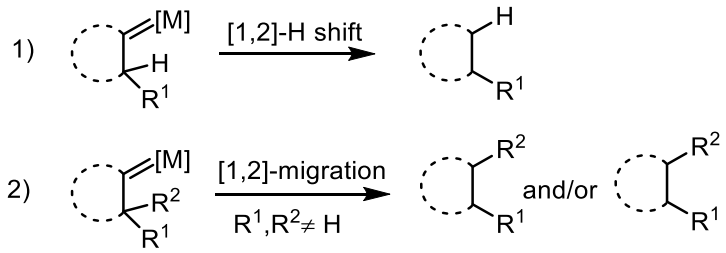
These results demonstrate the importance of strongly electron-donating substituents for the stabilization of gold-carbenoid intermediates by resonance delocalization and indicate that the [LAu] fragment alone is not able to impart sufficient stability onto a gold carbenoid center (Scheme 2.3).



Scheme 2.3. Synthesis of gold-carbenoids.

2.1.2 Migratory Cycloisomerization Reactions of Allenes

A particular attractive approach toward the synthesis of densely functionalized hetero- and carbocyclic products involves the incorporation of molecular rearrangement steps into transition-metal-catalyzed migrative cycloisomerization cascade reactions.[62] In this context, the diverse reactivity of gold- and platinum-catalyzed transformations have attracted much interest in the development of cascade reaction patterns. Most of these transformations include 1,2-migration to an adjacent metal-carbenoid center. Generally, the migratory aptitude follows the order H > aryl > alkyl. In the presence of available hydrogen atoms in the adjacent position, mostly a clean 1,2-hydride shift takes place to the metal-carbenoid center (Scheme 2.4, eq 1). Alternatively, introduction of a migratory group other than hydrogen provides an easy route for the synthesis of diverse functionalized products (Scheme 2.4, eq 2). Furthermore, the reactive metal-carbenoid intermediates could undergo further cascade transformations such as cyclopropanation or cyclization depending on the substituent pattern.



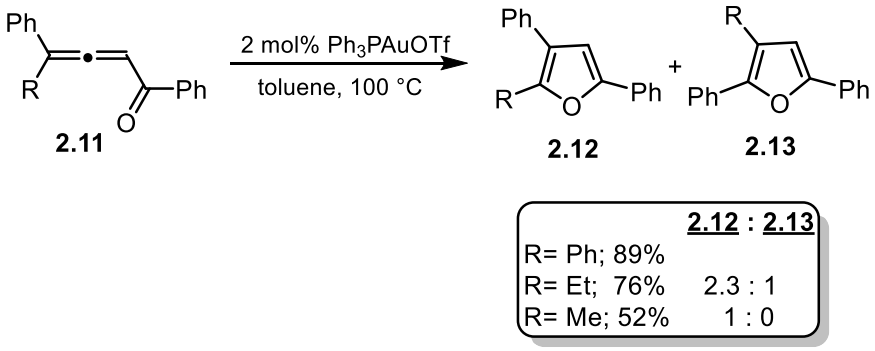
Scheme 2.4. Migration in metal-carbene.

Cycloisomerization of allenes provides highly efficient routes toward hetero- and carbocycles which in many cases involves a 1,2-hydrogen shift.[63] A migratory cycloisomerization sequence towards multisubstituted furans has been developed by Gevorgyan and co-workers[64] by introducing a migratory group other than hydrogen into the allenic terminus.

They have found that the reaction of 4,4-diphenyl-substituted allenyl ketone **2.11** in the presence of $Ph_3PAuOTf$ proceeded smoothly to provide furans **2.12** and **2.13** through a cycloisomerization-migration sequence. The issue of selectivity with regard to aryl and alkyl group migration was also studied by the authors. Selective migration of the phenyl over the methyl group was observed. In contrast to the disfavored

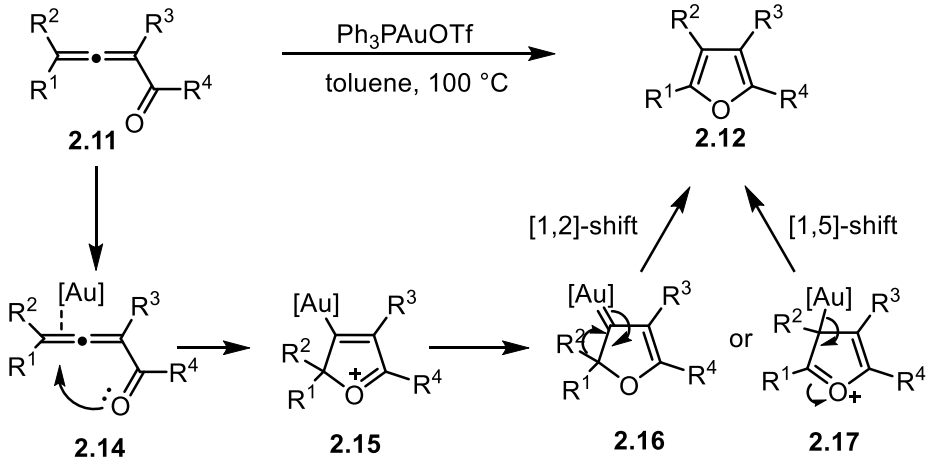
[62] a) J. Sun, M. P. Conley, L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2006**, *127*, 9705-9710; b) H. Kusama, H. Funami, J. Takaya, N. Iwasawa, *Org. Lett.* **2004**, *6*, 605-608; c) G. Li, X. Huang, L. Zhang, *Angew. Chem. Int. Ed.* **2008**, *47*, 346-349.
[63] N. Krause, C. Winter, *Chem. Rev*. **2011**, *111*, 1994-2009.
[64] a) A. W. Sromek, M. Rubina, V. Gevorgyan, *J. Am. Chem. Soc.* **2005**, *127*, 10500-10501; b) J. T. Kim, A. V Kel'in, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2003,** *42*, 98-101; c) A. S. Dudnik, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2007**, *46*, 5195-5197; d) A. S. Dudnik, A. W. Srorek, M. Rubina, J. T. Kim, A. V. Kel'in, V. Gevorgyan, *J. Am. Chem. Soc.* **2008,** *130*, 1440-1452.

methyl group migration, migration of the ethyl group competed with the phenyl group which resulted in the formation of 2.3:1 mixture of the corresponding furans (Scheme 2.5).



Scheme 2.5. Gold(I)-catalyzed migratory cycloisomerization of allenones **2.11**.

According to their proposed mechanism, the reaction proceeded through the activation of a carbon-carbon double bond of the allene **2.11** with π-philic cationic gold complexes toward the nucleophilic attack of a carbonyl oxygen lone pair to form cyclic oxonium intermediate **2.15**. The furan **2.12** was obtain via subsequent [1,5]- and/or [1,2]- alkyl shift with the regeneration of the gold precatalyst (Scheme 2.6).



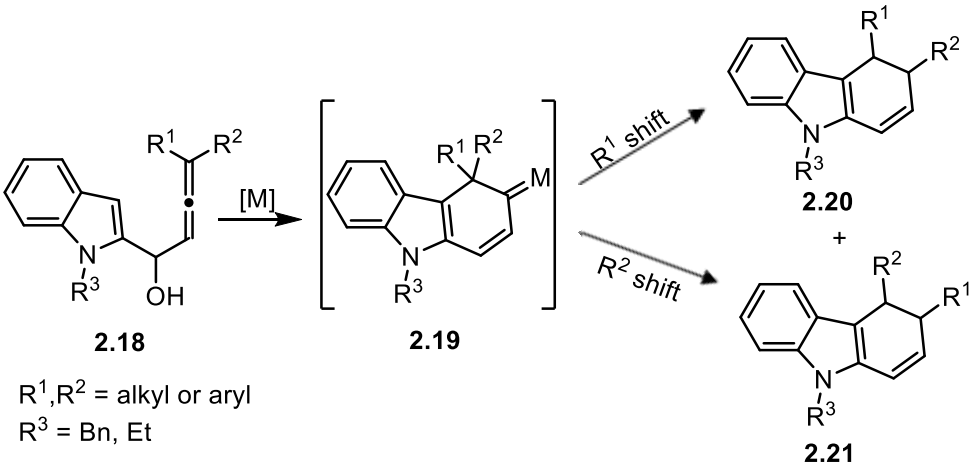
Scheme 2.6. Proposed mechanism for the synthesis of furans **2.12**.

More recently, Ma and co-workers[65] reported the gold- and platinum-catalyzed reaction of 1-(indol-2-yl)-2,3-allenols **2.18** which provides an efficient route to substituted carbazoles involving 1,2-alkyl

[65] a) W. Kong, Y. Qui, X. Zhang, C. Fu, S. Ma, *Adv. Synth. Catal.* **2012**, *354*, 2339-2347; b) Y. Qui, C. Fu, X. Zhang, S. Ma, *Chem. Eur. J.* **2014**, *20*, 10314-10322.

or -aryl migration via metal-carbene intermediate **2.19** (Scheme 2.7). Their investigations were mainly focused on the competition between the aryl/alkyl and alkyl/alkyl group migration. Selective 1,2-migration was achieved by using non-equivalent 4,4-dialkyl-substituted allenols, equivalent 4,4-dialkyl-substituted allenols and 4-alkyl-4-aryl-substituted allenols providing the formation of desired carbazoles in moderate to high yield with both catalytic systems (Au(I) and Pt(II)). However, they have found that no reaction occurred when 4,4-diphenyl-substituted allenols were subjected to the Pt(II)-catalyzed reaction procedure whereas with the Au(I)-catalyzed procedure 4,4-diphenyl-substituted allenols had not been tested.

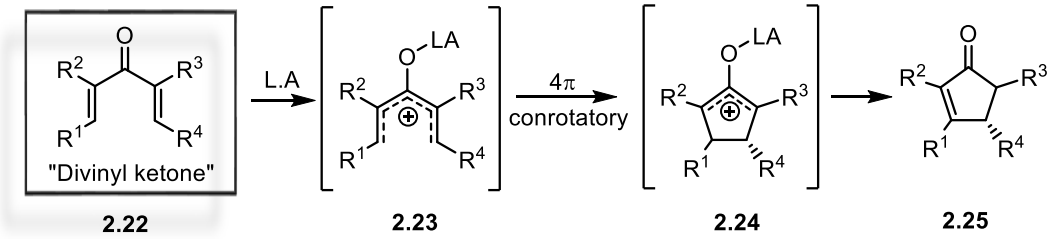
Their DFT calculations indicated that the energy barrier of the aryl migration is lower than the that of the competing methyl and ethyl group migration, which is in accordance with their experimental results. Also the energy barrier of the methyl group migration was calculated as higher than the competing ethyl, propyl, isopropyl, and cyclopropyl migration.



Scheme 2.7. 1,2-Migratory cyclization reactions of 1-indol-2,3-allenols.

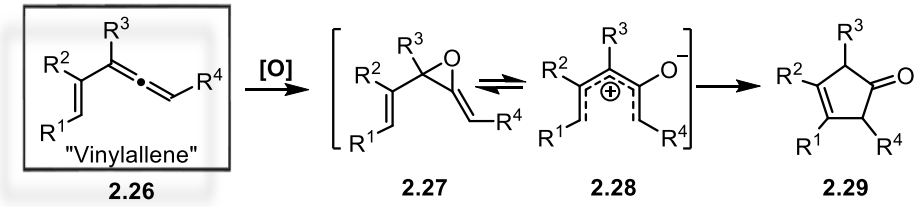
2.1.3 Vinylallenes as Nazarov Precursor

The Nazarov cyclization is a 4π electrocyclization process used for the synthesis of five-membered rings that are part of the many biologically active natural products.[66] In the classical Nazarov cyclization a divinyl ketone **2.22** converts to a cyclopentenone derivative by activation with a Lewis acid or Brønsted acid. A 4-π electrocyclic conrotatory ring closure of the pentadienyl cation **2.23** yields the oxoallyl cation **2.24** which undergoes a deprotonation and tautomerization to yield the cyclopentenone derivative **2.25** (Scheme 2.8).



Scheme 2.8. Representative pathway of classical Nazarov cyclization.

Several research groups have discovered important advances of the Nazarov cyclization by taking the advantage of vinylallene derivatives **2.26** as an alternative precursor to access the key pentadienyl cation intermediate **2.27** (Scheme 2.9).[67]

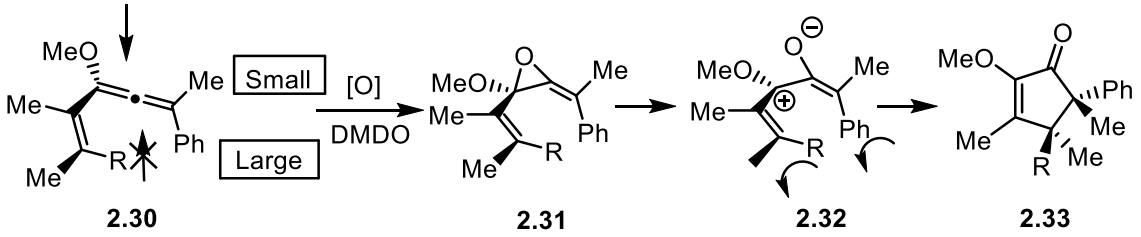


Scheme 2.9. Oxidation-initiated Nazarov cyclization pathway of vinylallenes.

For example, the group of Frontier developed an oxidation-initiated cyclization method of alkoxy-substituted vinylallenes **2.30** to produce cyclopentenones **2.33** with high diastereoselectivity (Scheme 2.10).[68] They showed that the regio- and stereoselectivity of the oxidation can be controlled by using

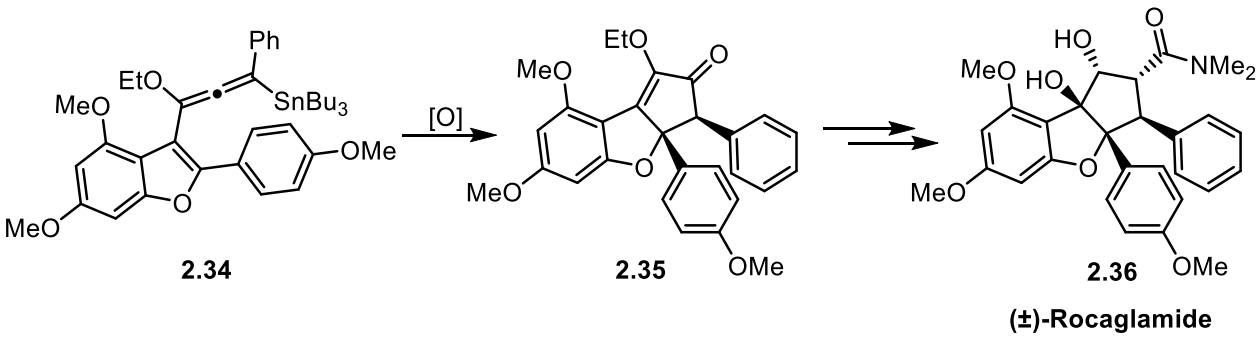
[66] a) N. Shimada, C. Stewart, M. A. Tius, *Tetrahedron*, **2011**, *67*, 5851-5870; b) A. J. Frontier, C. Collison, *Tetrahedron*, **2005**, *61*, 7577-7606; c) M. A. Tius, *Eur. J. Org. Chem.* **2005**, 2193-2206; c) T. N. Grant, C. J. Reider, F. G. West, *Chem. Commun*. **2009** 5676-5688; d) W. T. Spencer, T. Vaidya, A. J. Frontier, *Eur, J. Org. Chem*. **2013**, 3621-3633.
[67] a) P. E. Harrington, M. A. Tius, *J. Am. Chem. Soc*. **200**1, *123*, 8509-8514; b) M. A. Tius, *Chem. Soc. Rev*. **2014**, *43*, 2979-3002; c) M. A. Tius, *Acc. Chem. Res.* **2003**, *36*, 284-290. d) Z. Li, R. J. Boyd, D. J. Burnell, *J. Org. Chem.* **2015**, *80*, 12535-12544.
[68] W.T.Spencer, M.D.Levin, A.J.Frontier, *Org Lett.* **2013**, 13, 414-417.

alkoxy-substituted vinylallenes, which occurred on the more electron-rich internal allene double bond and through the less sterically demanding face.



Scheme 2.10. Oxidation-initiated Nazarov cyclization of vinylallenes.

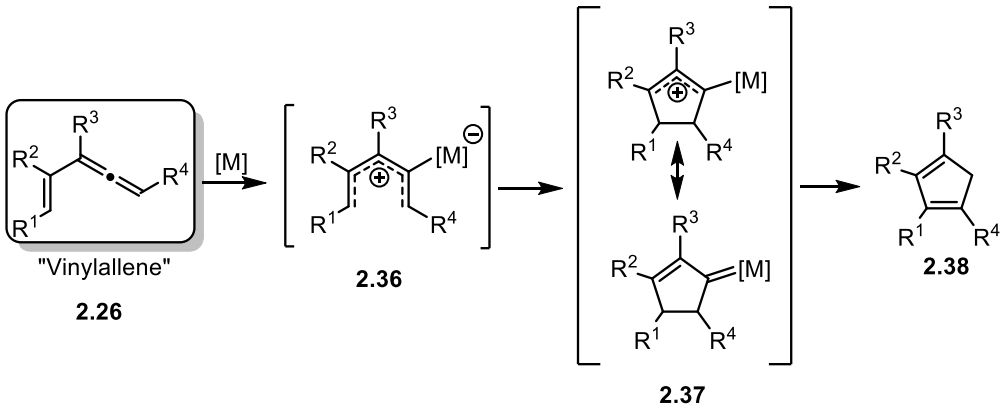
The method was applied in a total synthesis of (±)-Rocaglamide (Scheme 2.11).[69]



Scheme 2.11. Key step in the Frontier`s synthesis of (±)-Rocaglamide.

Furthermore, the transition metal-catalyzed cyclization of vinylallene derivatives **2.26** has been reported as an efficient way to access cyclopentadiene derivatives **2.36,** which are key intermediates in organic synthesis and useful ligands in organometallic chemistry (Scheme 2.12).[70]

[69] J. A. Malona, K. Coriou, A. J. Frontier, *J. Am. Chem. Soc.* **2009**, *131*, 7560-7561.
[70] a) J. H. Lee, F. D. Toste, *Angew. Chem. Int. Ed.* **2007**, *46*, 912-914; b) H. Funami, H. Kusama, N. Iwasawa, *Angew. Chem. Int. Ed.* **2007**, *46*, 909-911.

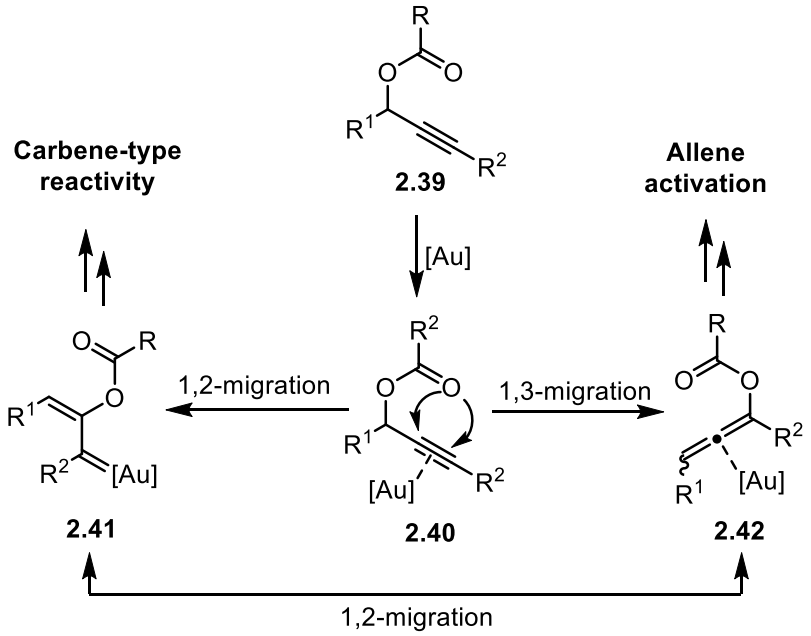


Scheme 2.12. Metalla-Nazarov cyclization of vinylallenes.

2.1.4 Transition Metal-Catalyzed Cyclization of Vinylallenes

At the beginning of the 2000's, the synthetic potential of the metal-assisted acetoxy-group migration in propargylic carboxylates came to the surface which offers a mild and selective access to a variety of products.[71] In particular, gold-catalyzed migratory cycloisomerization reactions of propargylic carboxylates have attracted considerable attention. The Toste group was the first to report that propargylic esters **2.39** could undergo an Au-catalyzed [2,3]-rearrangement via 1,2-acyl migration leading to alkenyl gold carbenoids **2.41**.[72] The group of Zhang reported the possibility of [3,3]-rearrangements through either 1,2- or 1,3-acyl migration leading to the generation of allenic intermediates **2.42**.[73] These intermediates contain multiple reaction sites and can undergo various useful transformations which allow to synthesis of diverse organic products (Scheme 2.13).[74]

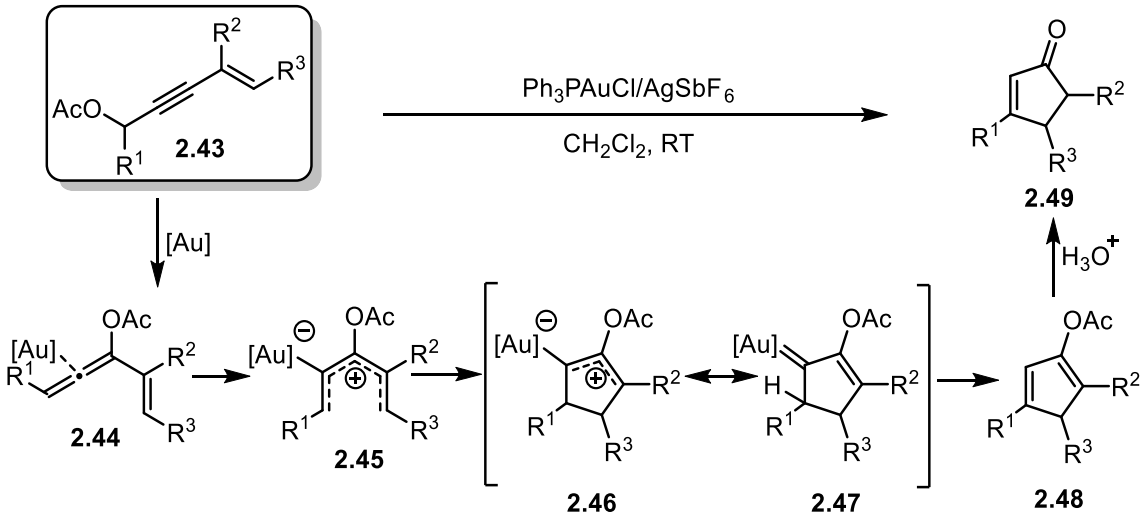
[71] a) A. Fürstner, P. Hannen, *Chem. Commun.* **2004**, 2546-2547; b) M. J. Johansson, D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc*. **2005**, 127, 18002-18003; c) V. Mamane, T. Gress, H. Krause, A. Fürstner, *J. Am. Chem. Soc*. **2004**, 126, 8654-8655; d) A. Fürstner, A. Hannen, *Chem. Eur. J.* **2006**, 13, 3006-3019.
[72] X. Shi, D. J. Gorin, F. D. Toste, *J. Am. Chem. Soc*. **2005**, *127*, 5802-5803.
[73] L. Zhang, *J. Am. Chem. Soc*. **2005**, *127*, 16804-16805;
[74] S. Wang, G. Zhang, L. Zhang, *Synlett*, **2010**, 692-706; c) M. Yu, G. Zhang, L. Zhang, *Adv. Synth. Catal*. **2007**, *349*, 871–875.



Scheme 2.13. Gold-catalyzed propargylic ester rearrangements.

In 2006, Zhang and co-workers took advantage of this method and developed a highly efficient method for the synthesis of cyclopentenones.[75] The proposed reaction mechanism involves an 1,3-acyloxy migration for the in situ generation of vinylallene **2.44**, which in the presence of a gold catalyst transforms into the pentadienyl cation **2.45**. The Metalla-Nazarov 4π-electrocyclic ring closure of the pentadienyl cation **2.45** affords Au-containing cyclopentenylic cation **2.46**, which is in resonance with Au carbenoid species **2.47**. Subsequent 1,2-hydrogen shift and further hydrolysis yields the cyclopentenone **2.49** with the regeneration of cationic gold catalyst. This reaction proceeds well with various cyclic and acyclic substrates providing an access to synthetically useful cyclopentenones in good to excellent yields.

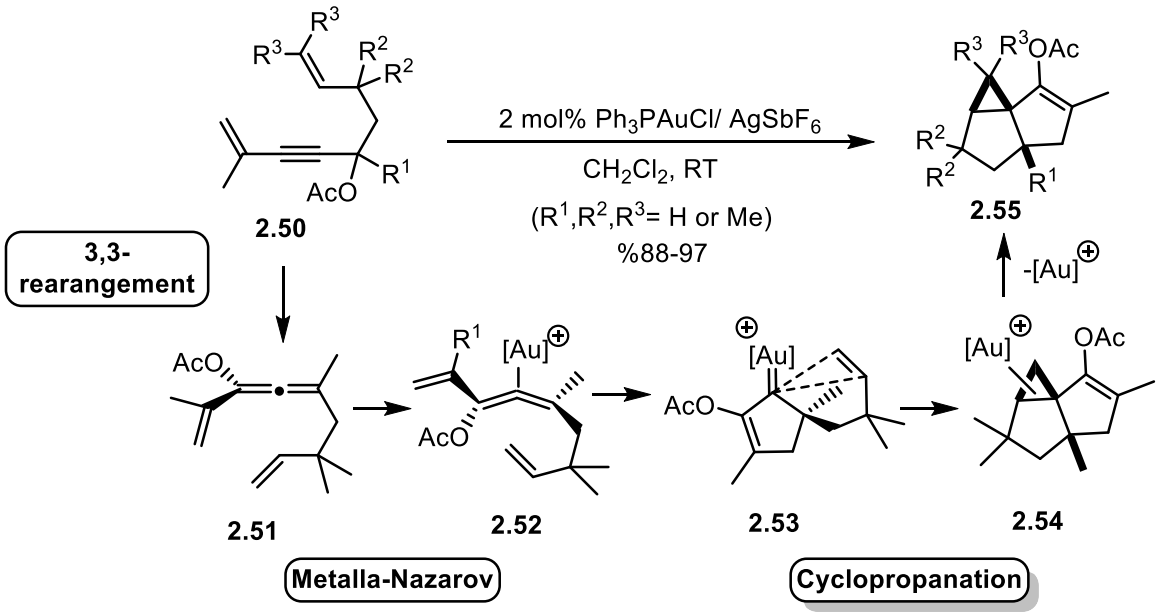
[75] L.Zhang, S.Wang, *J. Am. Chem. Soc*. **2006**, *128*, 1442-1443.



Scheme 2.14. Tandem Au(I)-catalyzed 3,3-reaarangement and Nazarov cyclization.

The group of Malacria and Fensterbank developed an efficient strategy for the synthesis of polycyclic compounds starting from propargyl acetates or vinylallenes (Scheme 2.15).[76] The method involves three consecutive gold-catalyzed elemental steps which are the [3,3]-rearrangements of propargyl acetates **2.50** to corresponding vinylallenes **2.51**, a subsequent Metalla-Nazarov cyclization and the electrophilic cyclopropanation by trapping the gold-carbene intermediates with a pendant double bond. This reaction provides an excellent chirality transfer by using enantioenriched propargyl acetates or vinylallenes.

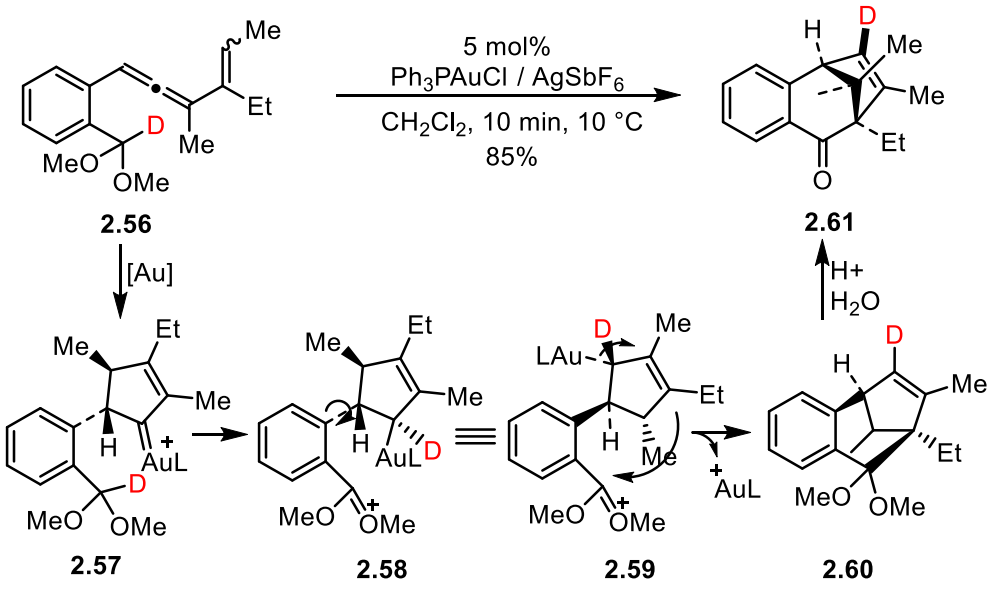
[76] G. Lemiere, V. Gandon, K. Cariou, T. Fukuyama, A. L. Dhimane, L. Fensterbank, M. Malacria, *Org. Lett.* **2007**, *9*, 2207-2209.



Scheme 2.15. Gold-catalyzed synthesis of polycyclic products via vinylallenes.

A related work was reported by Liu and Bhunia[77] for the synthesis of tricyclic ketone **2.61** .The reaction sequence involves an atypical gold-carbenoid-induced 1,5-hydride shift from the acetal moiety. On the basis of their deuterium-labeling and crossover experiments, they proposed that the substrate, initiated by the activation of the allene **2.56** with the gold catalyst, undergoes a Nazarov-type cyclization to give intermediate **2.57** that has a phenyl group *trans* to the adjacent methyl group to minimize steric hindrance. A following 1,5-hydride shift from the acetal moiety to the metal carbene center provides intermediate **2.59**. Subsequent cyclization of the allyl gold intermediate **2.59** with the oxonium cation furnished the tricyclic bridged product **2.61** (Scheme 2.16).

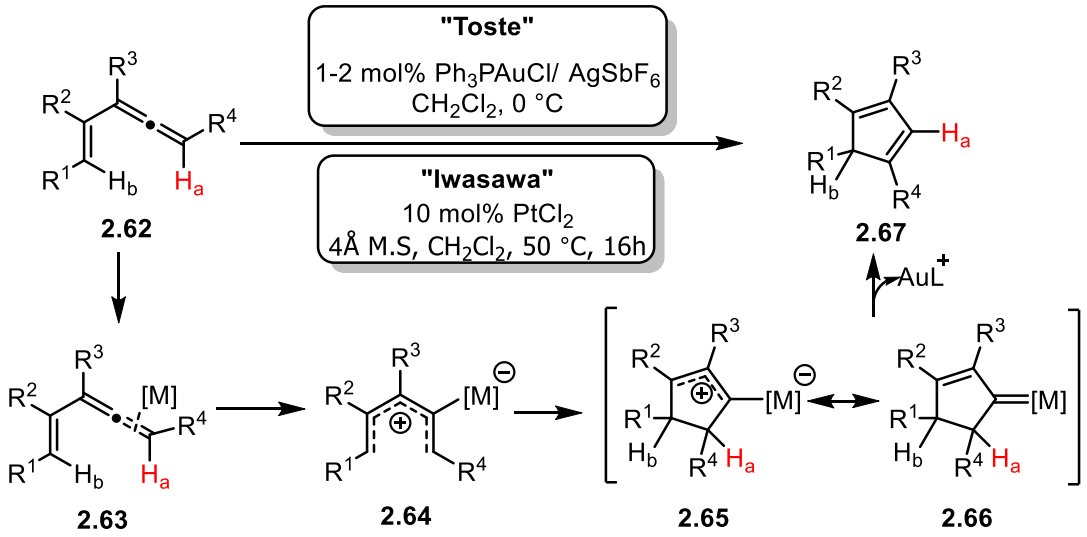
[77] S. Bhunia, R. S. Liu, *J. Am. Chem. Soc.* **2008,** *130,* 16488-16489.



Scheme 2.16. Gold-catalyzed cascade synthesis of tricyclic compounds.

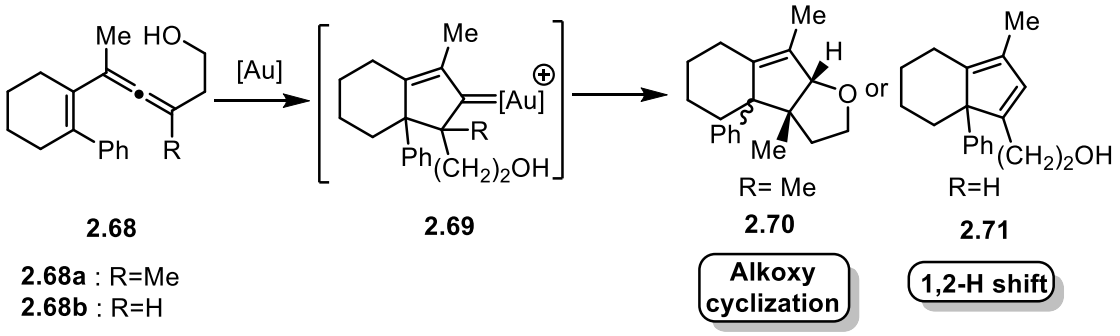
In 2007, Toste and Iwasawa independently reported a significant process for the synthesis of cyclopentadienes **2.67** from the vinylallenes **2.62**.[71] According to their experimental evidence, treatment of the vinylallenes with Au(I)- or Pt(II)-catalysts provides a regioselective access to functionalized cyclopentadienes **2.67** in good to excellent yields.

They proposed that coordination of the catalyst to the allene moiety produces a pentadienyl cation intermediate **2.64** which undergoes a Nazarov-type 4π-electrocyclization to give the allyl cation **2.65** and/or its carbene counterpart **2.66**. Then, a formal 1,2-H shift in the metal-carbenoid intermediate **2.66** furnished the cyclopentadiene **2.67** with the regeneration of active metal catalyst (Scheme 2.17).



Scheme 2.17. Gold-catalyzed conversion of vinylallenes into cyclopentadienes.

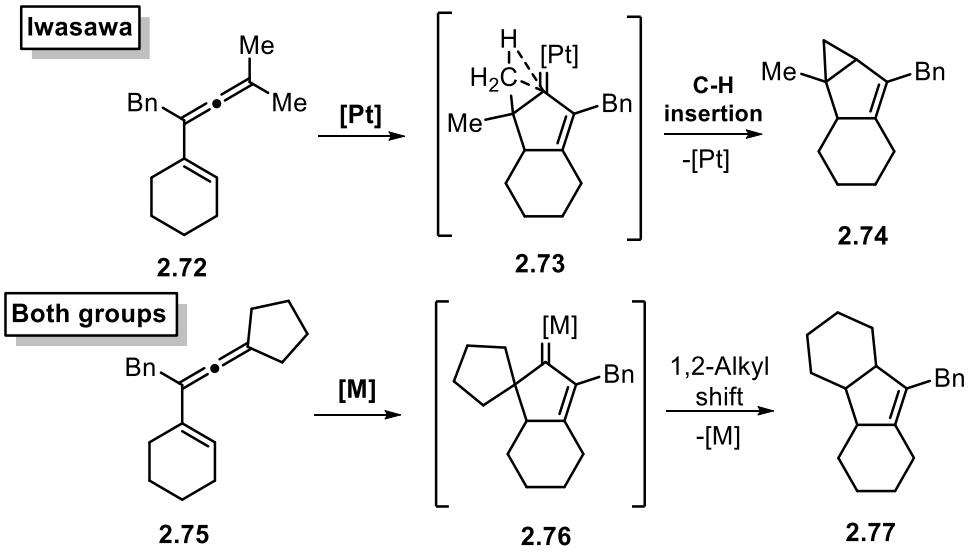
The possibility of trapping the cationic intermediate was studied by both groups in different ways such as using an additional alcohol functionality in the absence of hydrogen at the allene terminus, a 1,1-disubstituted vinylallene or a bicyclic vinylallene. In the case of an additional alcohol functionality, the gold-catalyzed cycloisomerization reaction of vinylallene **2.68a**, which bears a methyl group at the allene terminus instead of hydrogen, afforded the formation of tetrahydrofuranyl product **2.70**, whereas the hydrogen-bearing vinylallene **2.68b** undergoes a formal 1,2-hydrogen shift to give the cyclopentadiene **2.71** (Scheme 2.18).



Scheme 2.18. Trapping strategies of intermediate **2.69**.

Furthermore, the Pt(II)-catalyzed cyclization of 1,1-dimethyl-substituted vinylallene **2.72** afforded cyclopropanation product **2.74**. The platinum carbene intermediate **2.73** inserted into a neighboring C-H bond of the methyl group rather than undergoing a 1,2-methyl migration. Also, a ring-enlargement process

was observed when the method was applied to the bicyclic vinylallene **2.75** (Scheme 2.19). At this point it can be concluded that these results prove the presence of metal-carbene intermediates.



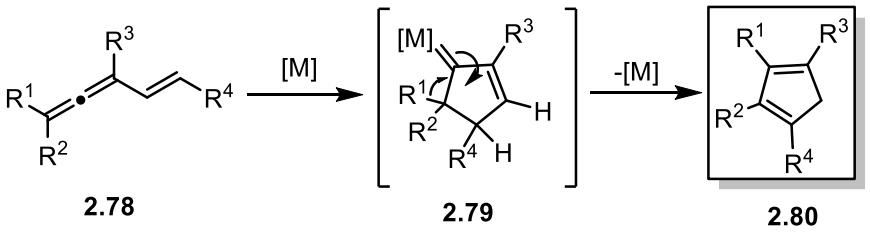
Scheme 2.19. C-H insertion and 1,2-alkyl shift in metal-carbenoids.

2.2 Present study

A survey of the literature reveals that the migratory cycloisomerization cascade reaction sequence is a challenging approach for the synthesis of densely functionalized carbo- and heterocyclic products. In this context, the diverse reactivity of gold- and platinum-catalyzed transformations has attracted much interest in the development of cascade reaction patterns. Most of these cascade reactions involve a 1,2-migration in the metal-carbenoid intermediates. However, various factors controlling the 1,2-migration of the different groups in metal-carbenoid intermediates have not been established systematically. Therefore, the development of new strategies for further understanding the migratory aptitude and the reactivities of the metal carbenoid intermediates is of major interest.

Furthermore, cyclopentadienes are useful substrates for Diels-Alder reactions and also important ligands in organometallic chemistry for the preparation of transition-metal complexes. Although there have been numerous reports in the literature, the synthesis of highly substituted cyclopentadienes is still an important subject of organometallic chemistry, in which an even minor modification on the Cp ligands can provide a significant change in the catalytic activities of the metallocene complexes.

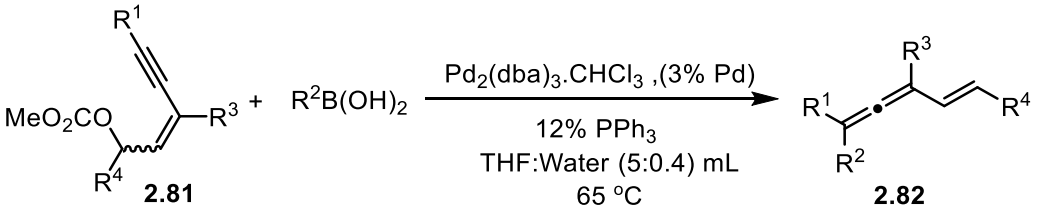
Herein, we have developed a metal-catalyzed 1,2-migratory cycloisomerization cascade reaction of vinylallenes providing a regioselective access to highly substituted cyclopentadiene derivatives (Scheme 2.20). In this part of our studies, the effects on the 1,2-migratory cycloisomerization process such as electronic properties of the migrating group and also the nature of the metal catalysts will be discussed.



Scheme 2.20. Transition metal-catalyzed 1,2-migratory cycloisomerization of vinylallenes.

2.3 Result and Discussion

The 1,1-disubstituted vinylallenes **2.82** required for our studies were prepared according to a procedure previously established by Artok and co-workers.[78] Palladium-catalyzed 1,5-substitution reactions of 2-en-4-yne carbonates **2.81** with arylboronic acids allowed the introduction of different substituents in the allenic system. The method is applicable for both (*E*)- and (*Z*)-configured enyne substrates and gave the 1,1-disubstituted vinylallenes with an exclusively (*E*)-configuration. The method tolerates various arylboronic acids having different electron-withdrawing or electron-donating substituents.



Scheme 2.21. Pd-catalyzed reaction of the enyne carbonate with organoboronic acids.

2.3.1 Gold(I)-Catalyzed 1,2-Migrative Cycloisomerization Reactions of Vinylallenes.

The vinylallene **2.82a** was initially chosen as a model substrate to determine appropriate reaction conditions for the formation of the desired cyclopentadiene derivatives. For initial experiments, treatment of vinylallene **2.82a** with the Au(III) salts, such as $AuBr_3$ and $AuCl_3$ in various solvents, such as DCM, THF or toluene at room temperature showed no catalytic activity (Table 2.1, entries 1-2), whereas employment of the Au(I) salt AuCl in the presence of DCM resulted in decomposition of the starting vinylallene **2.82a** into a complex product mixture (Table 2.1, entry 3). Similarly, when the catalytic system was modified to Ph_3PAuCl in combination with silver salts such as AgOTf, $AgBF_4$ and $AgSbF_6$ in DCM, the starting compound **2.82a** was consumed in 10-15 min to afford an inseparable mixture of unassigned products (Table 2.1, entries 4-6), whereas THF and toluene gave no conversion even at higher reaction temperature (Table 2.1, entries 7,8).

[78] M. Ucuncu, E. Karakus, M. Kus, G. E. Akpinar, O. A. Artok, N. Krause, S. Karaca, N. Elmaci, L. Artok, *J. Org. Chem.* **2011**, *76*, 5959-5971.

Vinylallene **2.82b**, bearing a butyl substituent in the R^1 position was also subjected to the same reaction conditions. Similar to the reactions of **2.82a**, in the presence of a catalytic amount of Ph_3PAuCl in combination with different silver salts in DCM inseparable mixture of unassigned structures with no desired cyclization products were obtained (Table 2.1, entries 9-11).

Furthermore, 1,1-diphenyl substituted vinylallene **2.82c** was also subjected to the same reaction conditions. This also resulted in the formation of non-separable product mixtures (Table 2.1, entries 12-15).

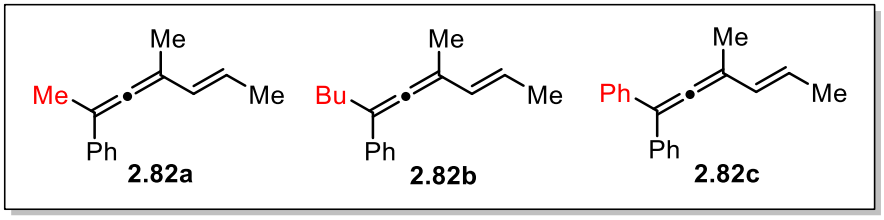
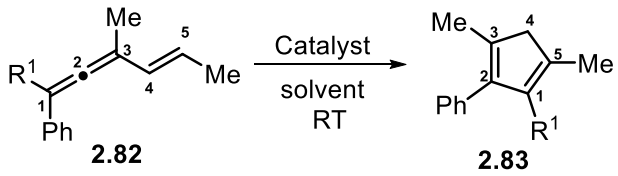


Table 2.1. Attempted cycloisomerization reactions of **2.82a-c**.[a]



Entry	Compound	R^1	Catalyst	Cat. [%]	Solvent	Time	Yield[%]
1	**2.82a**	Me	$AuCl_3$	5	-[b]	1 d	-[c]
2	**2.82a**	Me	$AuBr_3$	5	-[b]	1 d	-[c]
3	**2.82a**	Me	AuCl	5	CH_2Cl_2	20 min	-[d]
4	**2.82a**	Me	Ph_3PAuCl / $AgSbF_6$	10	CH_2Cl_2	15 min	-[d]
5	**2.82a**	Me	Ph_3PAuCl / AgOTf	10	CH_2Cl_2	15 min	-[d]
6	**2.82a**	Me	Ph_3PAuCl / $AgBF_4$	5	CH_2Cl_2	15 min	-[d]
7	**2.82a**	Me	Ph_3PAuCl/ $AgSbF_6$	10	THF	1 d	-[c]
8	**2.82a**	Me	Ph_3PAuCl / $AgSbF_6$	10	Toluene	1 d	-[c]
9	**2.82b**	Bu	Ph_3PAuCl / $AgSbF_6$	10	CH_2Cl_2	15 min	-[d]
10	**2.82b**	Bu	Ph_3PAuCl / AgOTf	10	CH_2Cl_2	15 min	-[d]
11	**2.82b**	Bu	Ph_3PAuCl / $AgBF_4$	5	CH_2Cl_2	15 min	-[d]
12	**2.82c**	Ph	AuCl	5	CH_2Cl_2	20 min	-[d]
13	**2.82c**	Ph	Ph_3PAuCl / $AgSbF_6$	10	CH_2Cl_2	15 min	-[d]
14	**2.82c**	Ph	Ph_3PAuCl / AgOTf	10	CH_2Cl_2	15 min	-[d]
15	**2.82c**	Ph	Ph_3PAuCl / $AgBF_4$	5	CH_2Cl_2	15 min	-[d]

[a] The reaction was carried out using 0.3 mmol of **2.82a-c** in 5.0 mL of solvent at RT under argon. [b] CH_2Cl_2, THF, and toluene were tested. [c] No conversion of starting material. [d] Decomposition of the starting material to unassigned products.

In spite of all these disappointing results obtained with vinylallenes **2.82a-c** which contained at least one unsubstituted phenyl group on the terminal allenyl carbon, an additional attempt was performed with the vinylallene **2.82e** bearing an *ortho*-methoxy phenyl group. We were pleased to find that the treatment of vinylallene **2.82e** gave promising results; although AuCl, $AuCl_3$ and $AuBr_3$ failed to convert **2.82e** (Table 2.2, entries 1-3), its treatment with the Ph_3PAuCl (5 mol%)/AgOTf (5 mol%) combination in DCM afforded the corresponding cyclopentadiene product **2.83e** in 30% isolated yield after 30 min at room temperature (Table 2.2, entry 4). Encouraged by this promising result, different silver salts were also tested. The yield of **2.83e** could be increased to 67% by the use of $AgBF_4$ in a relatively short reaction time, 10 min, at room temperature (Table 2.2, entry 5). The substitution of the silver salt with $AgSbF_6$, gratifyingly, further improved the process and thus led the formation of the product **2.83e** in 83% yield in 5 min (Table 2.2, entry 6).

It seems that DCM is a suitable solvent type for the reaction system. When the reaction was carried out in the presence of 1,2-dichloroethane (DCE), the desired cyclopentadiene was obtained in relatively low yield, 65% in 5 min (Table 2.2 entry 7), whereas tetrahydrofuran (THF) and toluene were found to be inefficient at room temperature (Table 2.2, entries 8,9). A complete decomposition to unidentified products was observed when the reaction was performed at 100 °C in toluene, (Table 2.2, entry 10).

A reduction of the catalyst loading to 2% or increasing to 10% resulted in similar yields (78% and 80%, respectively) (Table 2.2, entries 11,12). The control experiments revealed that Ph_3PAuCl and $AgSbF_6$ have no activity when they are used individually (Table 2.2, entries 13,14).

An N-heterocyclic carbene ligated gold(I) complex, IPrAuCl (**A**), in combination with $AgSbF_6$ also afforded cyclopentadiene **2.83e** in a good yield (69%) after 15 min at room temperature (Table 2.2, entry 15). Similarly, catalyst **B** also catalyzed the reaction and cyclopentadiene **2.83e** was obtained in moderate yield of 61% within 20 min (Table 2.2, entry 16). However, complex **C** failed to catalyze the reaction (Table 2.2, entry 17).

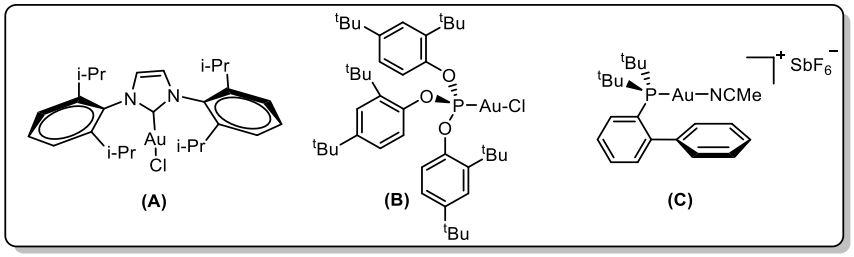
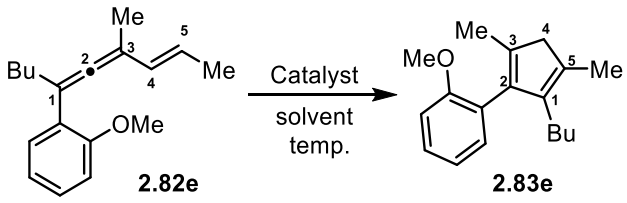


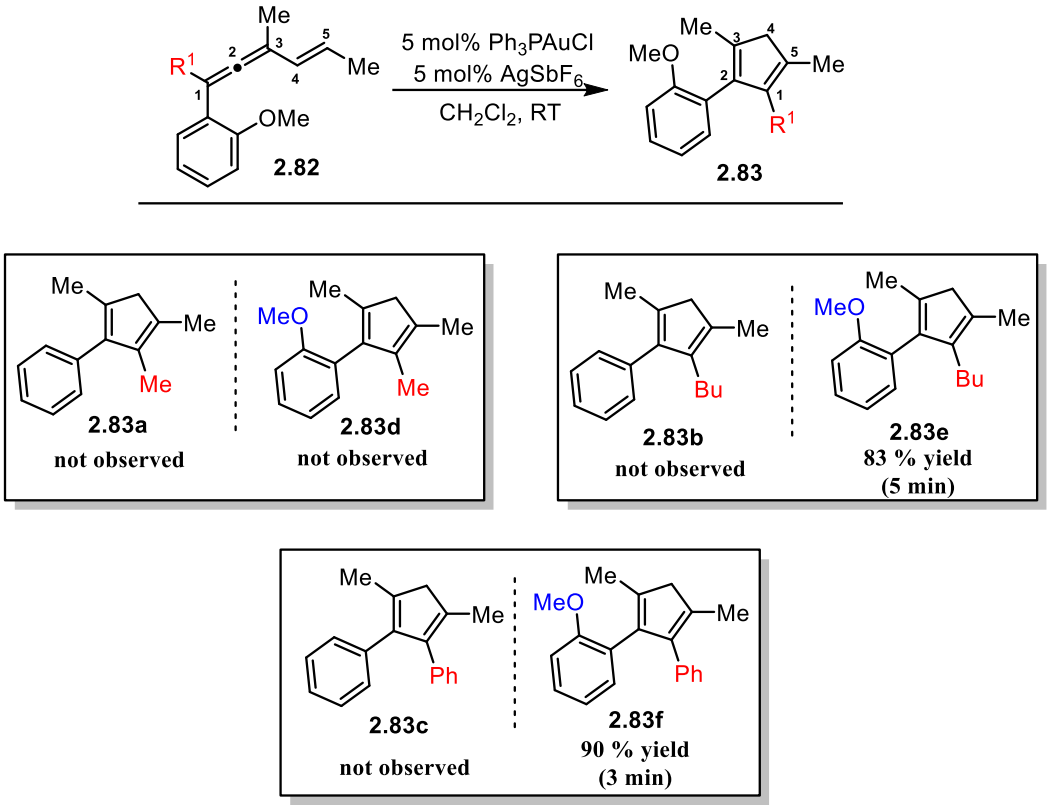
Table 2.2. Effect of Au precatalysts on the cycloisomerization of. [a]



Entry	Catalyst	Cat. [%]	Solvent	Time	Yield[b]
1	$AuCl_3$	5	-[c]	5 h	-[d]
2	$AuBr_3$	5	-[c]	5 h	-[d]
3	AuCl	5	CH_2Cl_2	5 h	-[e]
4	Ph_3PAuCl / AgOTf	5	CH_2Cl_2	30 min	30
5	Ph_3PAuCl / $AgBF_4$	5	CH_2Cl_2	10 min	67
6	Ph_3PAuCl / $AgSbF_6$	5	CH_2Cl_2	5 min	83
7	Ph_3PAuCl / $AgSbF_6$	5	DCE	5 min	65
8	Ph_3PAuCl / $AgSbF_6$	5	THF	1 d	-[d]
9	Ph_3PAuCl / $AgSbF_6$	5	toluene	1 d	-[d]
10[f]	Ph_3PAuCl / $AgSbF_6$	5	toluene	1 d	-[e]
11	Ph_3PAuCl / $AgSbF_6$	10	CH_2Cl_2	5 min	78
12	Ph_3PAuCl / $AgSbF_6$	2	CH_2Cl_2	10 min	80
13	Ph_3PAuCl	5	CH_2Cl_2	1 d	-[d]
14	$AgSbF_6$	5	CH_2Cl_2	1 d	-[d]
15	**A**/ $AgSbF_6$	5	CH_2Cl_2	15 min	69
16	**B**/ $AgSbF_6$	5	CH_2Cl_2	20 min	61
17	**C**	5	CH_2Cl_2	1 d	-[d]

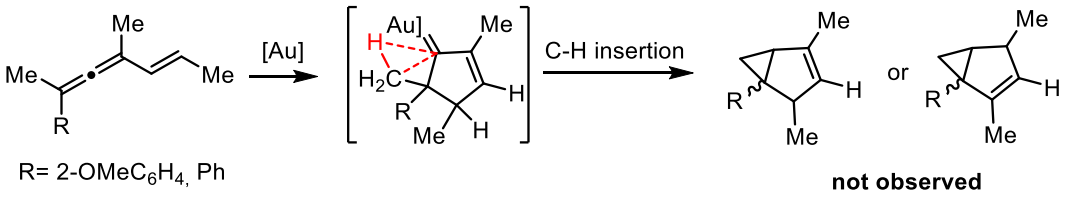
[a] The reaction was carried out using 0.3 mmol of **2.82e** and in 5.0 mL of solvent at RT under nitrogen. [b] Isolated Yield [c] THF, toluene, CH_2Cl_2 were tested. [d] No conversion [e] Decomposition of the starting material to unassigned products. [f] Reaction was conducted at 100 °C.

Having determined that the vinylallene is reactive in the cycloisomerization process provided that its allenyl terminus is substituted with a highly electron rich phenyl ring, we next investigated the effect of other groups on the scope of the process for vinylallenes containing a 2-$MeOC_6H_4$ group. The method was also well applicable to the vinylallene **2.82f** carrying a phenyl group (R^1) on the allenyl carbon that is common to the 2-methoxyphenyl group, which afforded the corresponding product **2.83f** in a high yield (90%) within 3 min (Scheme 2.22).



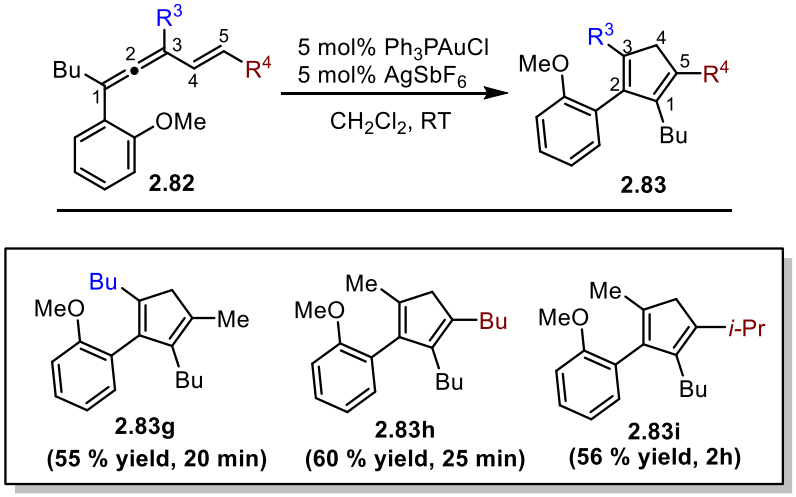
Scheme 2.22. Effect of variation of R^1 group on the gold(I)-catalyzed [1,2]-migration/cycloisomerization reaction.

Interestingly however, the vinylallene **2.82d** having a methyl group on R^1 converted to a complex mixture and thus revealed no selectivity toward the desired product **2.83f** or any cyclopropanated product which was reported to form via the insertion of the metal-carbenoid intermediates into neighboring carbon-hydrogen bond of the methyl group (Scheme 2.23).



Scheme 2.23. Possible cyclopropanation pathway in gold-carbenoid intermediates.

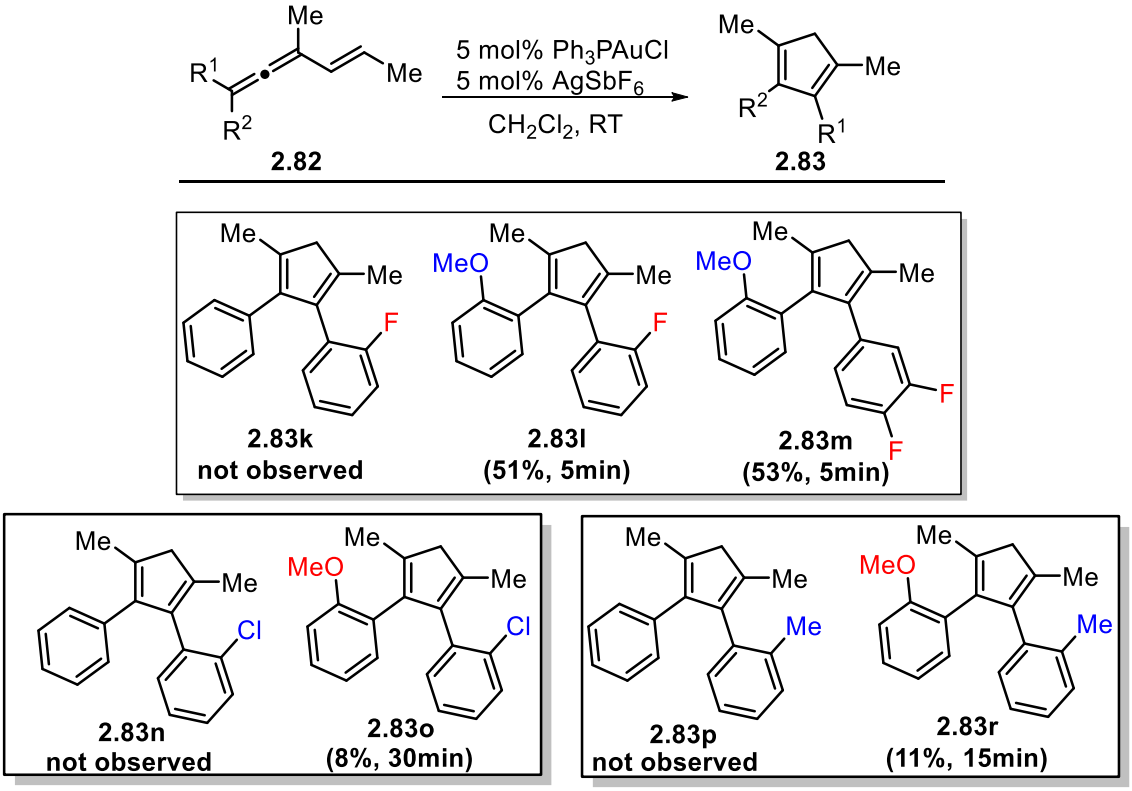
The reactions with vinylallenes having butyl or isopropyl groups on internal allenyl carbon R^3 or alkenyl carbon R^4 proceeded evidently with selective [1,2]-migration of methoxy-substituted phenyl ring but at a lower rate, affording the corresponding products in moderate yields, typically in the range of 50-60% (Scheme 2.24). These results could be explained by steric repulsion of the bulky groups in the Nazarov-type cyclization step.



Scheme 2.24. Effect of R^3 and R^4 substituents on the reaction.

Inspired from these results, a variety of vinylallenes bearing non-equivalent two aryl groups (R^1, R^2) on the allenyl carbon was examined. The importance of the methoxy substituent on the phenyl group was also obvious for the success of the method. While the vinylallenes with a Ph/EWG-C_6H_4 (EWG: electron withdrawing group) combination of substituents (**2.82k**, **2.82n**) and even the one with moderately electron rich phenyl ring (2-MeC_6H_4, **2.82p**) were all inert to gold-catalysis procedure (resulted in complex product mixtures), those with a 2-$MeOC_6H_4$ group were found to be suitable for the synthesis of cyclopentadienes (Scheme 2.25). The vinylallenes **2.82l** and **2.82m** having a fluorine-substituted phenyl

group along with its 2-$MeOC_6H_4$ partner provided cyclopentadiene products **2.823l** and **2.83m** in moderate yields. However, relatively low yields of products were obtained from the reactions of chloro-substituted phenyl ring (**2.82o**) and ortho-tolyl group (**2.82p**).



Scheme 2.25. Effect of the methoxy substituent on the gold(I)-catalyzed [1,2]-migratory cycloisomerization reactions.

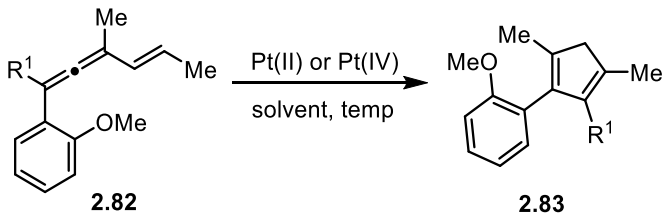
2.3.2. Platinum(II)-Catalyzed [1,2]-Migratory Cycloisomerization Reactions of Vinylallenes

After having determined the importance of electron-rich aryl groups on the [1,2]-migration aptitude in gold-catalyzed reactions, we also wanted to explore the cycloisomerization of vinylallenes in the presence of a platinum catalyst.

We began our investigations relying on our findings from the gold(I)-catalyzed [1,2]-migratory cascade cycloisomerization reaction. Throughout the initial stages of our work on the platinum-catalyzed method, all our attempts for the optimization using vinylallenes **2.82e** and **2.82f** which were suitable substrates for the gold-catalyzed cyclization, unfortunately failed. Both Pt(II) and Pt(IV) catalysts were

used. DCM, THF, and toluene were the solvents tested and the reactions were performed either at room temperature or elevated temperatures up to 100 °C. But in each case, either the substrate was recovered or resulted in decomposition (Table 2.3).

Table 2.3 Screening of conditions[a]



2.82 **2.83**

Entry	Compound	Cataylst	Solvent	Temp[°C]	Time	Yield[%]
1	**2.82e**	$PtCl_4$	CH_2Cl_2	RT	1 d	-[b]
2	**2.82e**	$PtCl_4$	THF	RT	1 d	-[b]
3	**2.82e**	$PtCl_4$	THF	65	1 d	-[b]
4	**2.82e**	$PtCl_4$	toluene	RT	1 d	-[b]
5	**2.82e**	$PtCl_4$	toluene	100	1 d	-[c]
6	**2.82e**	$PtCl_2$	toluene	RT	1 d	-[b]
7	**2.82e**	$PtCl_2$	toluene	80	30 min	-[c]
8	**2.82e**	$PtCl_2$	toluene	100	10 min	-[c]
9	**2.82f**	$PtCl_4$	toluene	100	1 d	-[c]
10	**2.82f**	$PtCl_2$	CH_2Cl_2	RT	1 d	-[b]
11	**2.82f**	$PtCl_2$	THF	65	1 d	-[b]
12	**2.82f**	$PtCl_2$	toluene	RT	1 d	-[b]
13	**2.82f**	$PtCl_2$	toluene	80	30 min	-[c]
14	**2.82f**	$PtCl_2$	toluene	100	10 min	-[c]
15	**2.82e**	-	toluene	100	1 d	-[b]

a] The reaction was carried out using 0.3 mmol of **2.82** in 5.0 mL of solvent under argon. [b] No conversion. [c] Decomposition of starting material.

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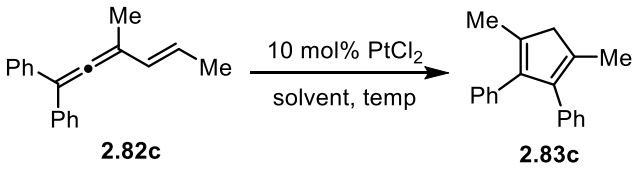
However, we have realized later that the incompatibility of the platinum-catalyzed method, on contrary to its gold-catalyzed version, is specific to vinylallenes **2.82e** and **2.82f**. We have found upon further study that, in fact vinylallenes, whether or not bearing a methoxyphenyl group, are applicable substrates.

1,1-Diphenyl-substituted vinylallene **2.82c** also did not show any activity in DCM, THF, and toluene at room temperature, and in refluxing THF in the presence of $PtCl_2$ (Table 2.4, entries 1-4). Nevertheless, increasing the reaction temperature to 80 °C in toluene led to the formation of the desired cyclopentadiene **2.83c** in 45% yield within 5h (Table 2.4, entry 5). A higher reaction temperature of 100 °C gave the same yield (45%) in shorter reaction time (2h) (Table 2.4, entry 6).

Table 2.4 Screening the conditions.

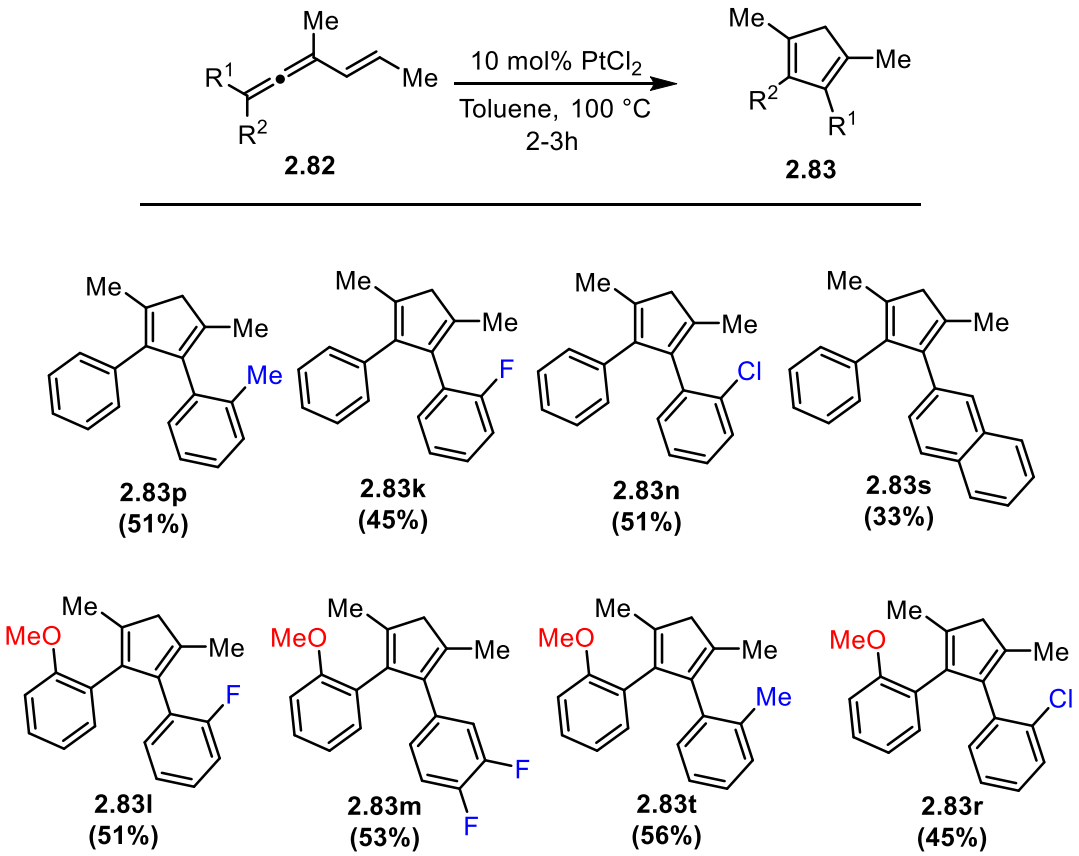


2.82c **2.83c**

Entry	Solvent	Temp [°C]	Time	Yield[%]
1	CH_2Cl_2	r.t	1 d	-[c]
2	THF	r.t	1 d	-[c]
3	THF	65	1 d	-[c]
4	toluene	r.t	1 d	trace
5	toluene	80	5 h	45[b]
6	toluene	100	2 h	45[b]

[a] The reaction was carried out using 0.3 mmol of **2.82c** and in 5.0 mL of solvent under argon. [b] Isolated Yield [c] No conversion.

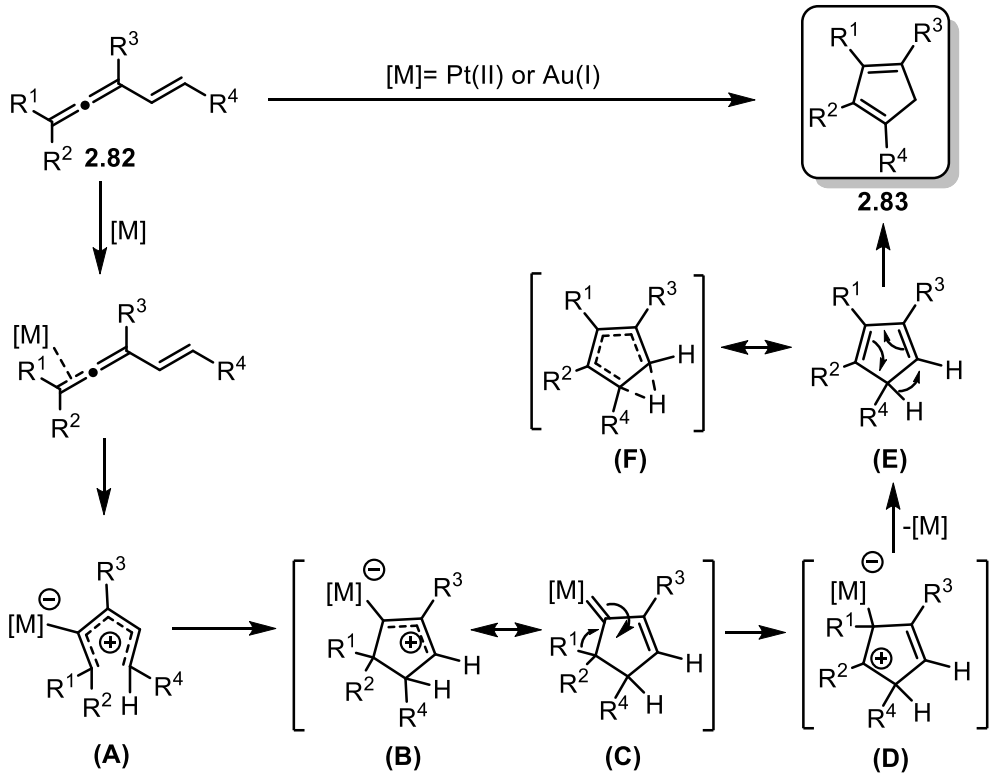
The reaction tolerates both electron rich (**2.82p**) and electron deficient (**2.82k, 2.82n)** R^1 and R^2 aryl groups, which led to cyclopentadienes **2.83p** (51%), **2.83k** (45%) and **2.83n** (51%) in moderate yields, whereas the gold(I)-catalyzed method had not tolerated these vinylallenes. Furthermore, in contrast to **2.82f** a number of methoxyphenyl-substituted vinylallenes was also tolerated by the method and produced cyclopentadienes **2.83l**, **2.83m**, **2.83r**, and **2.83t** in 45-56% yield. In addition, the Pt(II)-catalyzed cyclization of the **2.83s**, bearing a bulky 2-naphtyl substituent, afforded the cyclopentadiene **2.83r** in 33% isolated yield within 2h.



Scheme 2.26. The scope of the Pt(II)-catalyzed reaction of vinylallenes.

On the basis of these results, a plausible reaction mechanism for the Au(I)- and Pt(II)-catalyzed [1,2]-migratory cycloisomerization cascade reaction of vinylallenes is proposed in the Scheme 2.27. The reaction should proceed through the coordination of the metal to the allenyl moiety which results in the formation of pentadienyl cation intermediate **A**. This undergoes a Nazarov-type 4π-electrocyclization to give the cationic intermediate **B** in resonance with the metal-carbenoid intermediates **C**. The metal-carbenoid intermediate **C** is assumed to undergo a 1,2-aryl migration to give the cyclopentadiene **D** with the regeneration of the metal catalyst. The formation of only a single regioisomer of the cyclopentadienes **2.83** clearly proved a formal [1,5]- sigmatropic hydrogen shift as illustrated in the intermediate **F**.

The effect of the methoxy substituent for the gold-catalyzed cycloisomerization reaction can be explained by the importance of the aryl rings for the stabilization of the gold-carbenoid intermediates by resonance delocalization in accordance with the reports by Fürstner[61] and Widenhoefer[57].



Scheme 2.27. Proposed reaction mechanism.

2.4 Conclusion

In this part of our study, we have developed a metal-catalyzed [1,2]-migratory cycloisomerization cascade reaction of 1,1-disubstituted vinylallenes which provides a regioselective access to highly substituted cyclopentadiene derivatives. Although there have been numerous reports for the synthesis of cyclopentadienes, the efficient preparation of highly substituted derivatives is still an important subject of organometallic chemistry, in which an even minor modification on the cyclopentadienyl ligands can provide a significant change in the structure and catalytic activity of metallocene complexes.

Based on our experimental evidence, it was found that the method involves a metalla-Nazarov 4π-electrocyclization sequence, a subsequent [1,2]-aryl migration to afford a metal-carbenoid species and a [1,5]-sigmatropic hydrogen shift.

Our results show that the substituents on the migrating aryl group have a strong impact on the Au(I)-catalyzed cascade cycloisomerization procedure. The method provides a selective 1,2-aryl migration profile where the migrating aryl group contains a strongly electron-donating methoxy substituent. The effect of the substituents provides an interesting input for further understanding of the nature of the gold-carbenoid species and their reactivity in [1,2]-migration sequences. Furthermore, the gold-catalyzed method tolerates a variety of substituents on the alkenyl allenyl moieties which allows the synthesis of differently substituted cyclopentadiene derivatives.

In contrast to the Au(I)-catalyzed method, the Pt(II)-catalyzed cyclization has a wider substrate scope and shows no limitation on the electronic properties of the migrating group.

2.5 Experimental Part

General Remarks:

Reactions were performed under an argon atmosphere unless noted otherwise. Gold and silver salts were purchased from Sigma-Aldrich, Chempur, and Fluorochem. 1,2-Dichloroethane, dichloromethane, toluene, and tetrahydrofuran were dried with a solvent purification system MBraun SPS-800. $Pd_2(dba)_3$-$CHCl_3$ complex was synthesized in the laboratory.[79] All boronic acid reagents were purchased from ABCR, Across Organics, Sigma Aldrich, Carbolution Chemicals, and TCI. (*E*)-3-Methylpent-2-en-4-in-1-ol and (*Z*)-3-Methylpent-2-en-4-in-1-ol were obtained from DSM. Column chromatography was carried out with silica gel 60 Å (0.040-0.063), which was purchased from Macherey-Nagel.

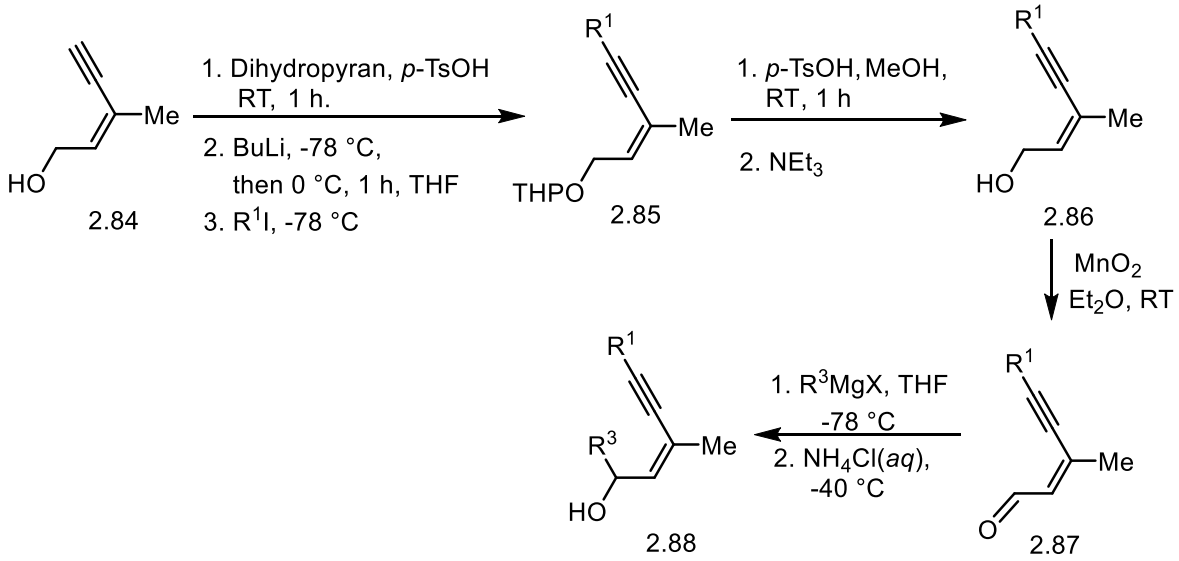
Proton (^1H) and carbon (^{13}C) NMR spectra were recorded on a Bruker DPX300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon nuclei, a Bruker DRX400 spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei, a Bruker DRX500 and a Varian Inova 500 spectrometers operating at 500 MHz for proton and 125 MHz for carbon nuclei. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$: δ=7.26 for protons, δ=77.16 for carbon atoms; C_6H_6: δ=7.16 for protons, δ=128.06 for carbon atoms). The signals of the major component of a product mixture are marked with an asterisk (*). Reactions were monitored by thin layer chromatography.

Low resolution mass spectra were recorded with a Thermo TSQ spectrometer. High resolution mass spectrometry (ESI) was performed on an Thermo LTQ Orbitrap coupled with a Accela HPLC system.

[79] T. Ukai, H. Kawazura, Y. Ishu, *J. Organomet. Chem*. **1974**, *6*5, 253-266.

2.5.1 Synthesis of (*Z*)-enyne carbonates 2.81a-g[80]

2.5.1.1 General procedure for the synthesis of (*Z*)-enyne alcohols 2.88a-d



Scheme 2.28. Synthesis of *Z*-enyne alcohols **2.88a-d**

To the mixture of (*Z*)-pent-2-en-4-yn-1-ol **2.84** (1.0 eq) and 3,4-dihydropyran (1.15 eq) was added *p*-toluenesulfonic acid monohydrate (0.01 eq) and stirred for 1 h at room temperature. The mixture was diluted with dry THF (2 mL/1 mmol) and cooled to -78 °C. At that temperature n-BuLi (2.5 M solution in hexane, 2.0 eq) was added via syringe. After stirring the reaction mixture for 1 h at 0 °C, alkyl iodide (2.0 eq) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for overnight. The reaction was quenched with sat. NH_4Cl solution and extracted with Et_2O. The organic phase was washed with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was used in the following step without any other purification. [81]

A solution of the preceding crude compound **2.85** (1 eq) in methanol (3 mL/1 mmol) was treated with *p*-toluenesulfonic acid (0.3 eq) and stirred at RT for 60 min. Then, trimethylamine was added (0.6 eq), and the solution was concentrated under reduced pressure. The mixture was taken into dichloromethane and washed with water. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and

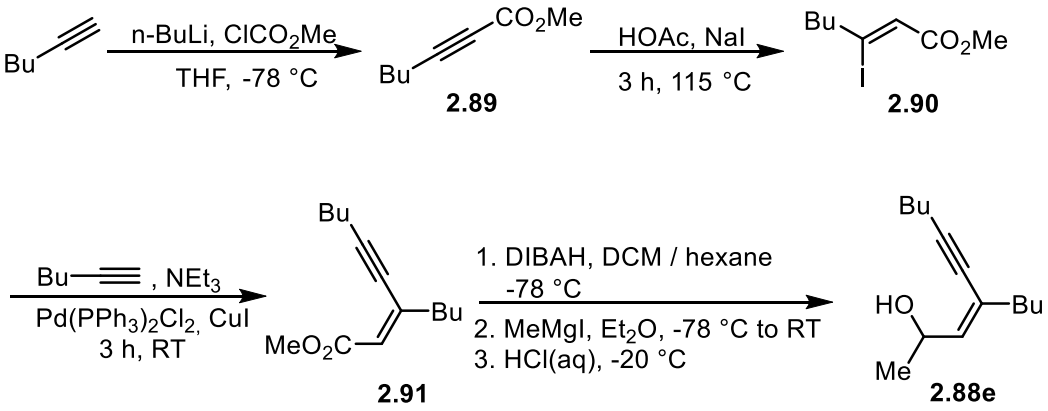
[80] a) G. E. Akpinar, M. Kus, M. Ucuncu, E. Karakus, L. Artok, *Org. Lett*. **2011**, *13*, 748-751; b) E. S. Karagoz, M. Kus, G. E. Akpinar, L. Artok, *J. Org. Chem*. **2014**, *79*, 9222-9230.
[81] J. F. Betzer, F. Delaloge, B. Muller, A. Pancrazi, J. Prunet, *J. Org. Chem.* **1997**, *62*, 7768-7780.

concentrated under reduced pressure. The product **2.86** was purified by column chromatography on silica gel.[82]

To the solution of **2.86** (1 eq) in dry diethyl ether (3 mL/1 mmol), activated MnO_2 (30 eq) was added, and the mixture was stirred for overnight at room temperature. After filtration through celite, the solution was concentrated under reduced pressure. [83]

The crude aldehyde **2.87** (1 eq) was dissolved in anhydrous THF (3 mL/1 mmol) and ethereal solution of R^3MgCl (1.2 eq) was added dropwise at -78 °C. The cooling bath was removed and the reaction was allowed to warm room temperature in 2 h. The mixture was hydrolyzed at -40 °C by dropwise addition of sat. NH_4Cl solution. After extraction with diethyl ether, the combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The product **2.88** was purified by column chromatography on silica gel.

2.5.1.2 General procedure for the synthesis of Z-Enyne alcohols 2.88e



Scheme 2.29. Synthesis of *Z*-enyne alcohols **2.88e-f.**

To a solution of 1-hexyne (5.7 mL, 50 mmol) in THF (100 mL) under a nitrogen atmosphere, n-BuLi (22.5 mL, 2.5 M solution in hexane, 56.25 mmol) was added dropwise at -78 °C. After stirring 30 min. at -78 °C, methylchloroformate (5.2 mL, 66.5 mmol) was added in one portion. The reaction was stirred for 30 min at -78 °C and allowed to reach room temperature over a period of three hours. The reaction was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The combined organic extracts were

[82] M. Purpura, N. Krause, *Eur. J. Org. Chem*. **1999**, 267-275.

dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (pentane: Et_2O = 100:1) to give **2.89** as a pale yellow oil (5.1 g, 72% yield).[83]

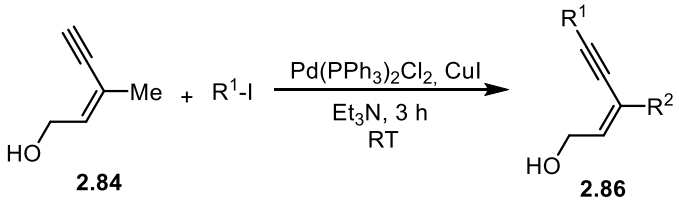
To a solution of alkynoic ester **2.89** (36 mmol) and acetic acid (230 mmol, 13.2 mL) was added sodium iodide (8.6 g, 57.6 mmol.) and stirred for 3 h at 115 °C. After completion of the reaction, the brown mixture was transferred while hot to a separatory funnel containing water (200 mL). The reaction flask was washed with a mixture of water (50 mL) and diethyl ether (100 mL). The washings were combined in a separatory funnel. The phases were separated and the aqueous phase was extracted with diethyl ether. The combined organic phases were treated sequentially with saturated aqueous sodium bicarbonate, aqueous sodium thiosulfate (1 M), and brine, then were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was purified by column chromatography on silica gel (8.4 g, 87%;).[84]

A mixture of **2.90** (8.4 g, 31.3 mmol), $PdCl_2(PPh_3)_2$ (220 mg, 0.313 mmol), and CuI (0.16 mmol, 30 mg) in Et_3N (4 mL/1 mmol) was stirred for 10 min at room temperature under Ar, and then, to this mixture was added 1-hexyne (2.7 mL, 32.9 mmol). The mixture was stirred at room temperature for 3h. Water was added to the reaction mixture and then extracted with Et_2O. The combined organic layers were dried over $MgSO_4$. The solvent was evaporated in vacuo and the product was purified by column chromatography on silica gel to give **2.91** (6.4 g, 92%).[85]

A dry, three-necked, round-bottomed 250-mL flask equipped with an internal thermometer, a rubber septum, and a nitrogen atmosphere, was charged with **2.91** (6.4 g, 28.8 mmol) and dry dichloromethane (60 mL). The stirred solution was cooled to -78 °C and diisobutylaluminum hydride (31.7 mL, 31.7 mmol, 1M in hexane solution) was added dropwise with a syringe at such a rate that the temperature would not exceed -75 °C. After stirring for 30 min at -78 °C, MeMgCl (10.6 mL, 31.7 mmol, 3.0 M in THF) was added dropwise at -78 °C with a syringe. The cooling bath was removed and the reaction mixture was allowed to warm to room temperature. The mixture was hydrolyzed at -20 °C by dropwise addition of 1 M aqueous solution of hydrochloric acid (57 mL), followed by addition of diethylether (85 mL). The organic layer was separated, the aqueous layer was extracted with ether, and the combined extracts were dried over $MgSO_4$. The solvent was evaporated in vacuo. The product was purified by column chromatography on silica gel. (82%).[86]

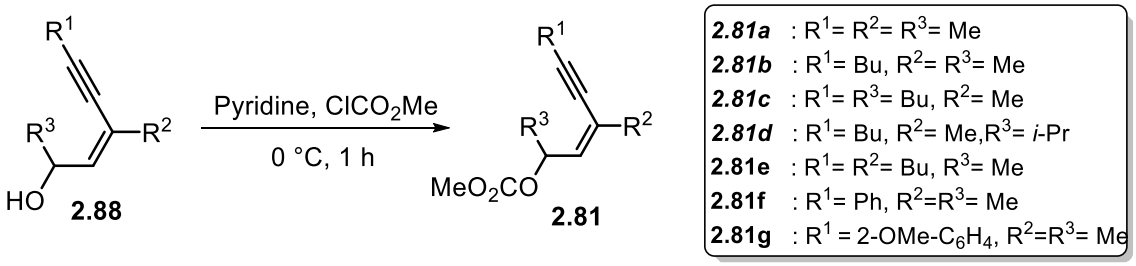
[83] I. N. Michaelides, B. Darses, D. J. Dixon, *Org. Lett.* **2011**, *13*, 664-667.
[84] E. Piers, T. Wong, P. Coish, C. Rogers, *Can. J. Chem.* **1994**, *72*, 1816.
[85] R. Takeuchi, K. Tanabe, S. Tanaka, *J. Org. Chem*. **2000**, *65*, 1558-1561.
[86] I. Marek, C. Meyer, J. F. Normant, *Org. Synth*. **1998**, *Coll. Vol*. *9*, 510.

2.5.1.3 General procedure for the synthesis of *Z*-Enyne alcohols 2.88f-g



To a solution of aryl iodide (1 eq.), *Z*- or *E*-enyne alcohol (1.1 eq) in Et_3N (3 eq) was stirred for 10 min at room temperature under Ar then, to this mixture $PdCl_2(PPh_3)_2$ (1 mol%), and CuI (5 mol%) was added. The mixture was stirred at room temperature for 3 h. Water was added to the reaction mixture and then extracted with Et_2O. The combined organic layers were dried over $MgSO_4$. The solvent was evaporated in vacuo and the product was purified by column chromatography on silica gel. (yields: R^1= Ph, R^2= Me, 72%; R^1= 2-OMe-C_6H_4, R^2= Me, 68%).

2.5.1.4 General Procedure for the Preparation of Enyne Carbonates 2.81a-h.[88]

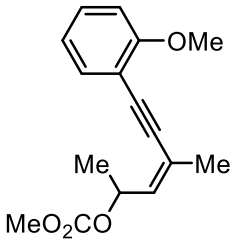


To a mixture of propargylic alcohol **2.88** (1.0 eq) in DCM (1.5 mL/1 mmol) was added pyridine (8 eq) and methylchloroformate (3 eq) at 0 °C. The reaction mixture was stirred at 0 °C for 3 h. The reaction was quenched by the addition of water, extracted with DCM and dried over $MgSO_4$. The solvents were removed in vacuo, and the residue was purified by column chromatography (cyclohexane/NEt_3 (1 vol. %)). yields: **2.81a**, 82%; **2.81b**, 85%; **2.81c**, %77; **2.81d**, %72, **2.81e**, %82; **2.81f**, %90; **2.81g**, %92).[87]

The spectrometric data of the starting enyne carbonates 2.81a-f can be found elsewhere.[81]

[87] S. C. Zhao, K. G. Ji, L. Lu, T. He, A. X. Zhou, R. L. Yan, S. Ali, X. Yuan, Y. M. Liang, *J. Org. Chem*. **2012**, *77*, 2763−2772.

(Z)-6-(2-Methoxyphenyl)-4-methylhex-3-en-5-yn-2-yl methyl carbonate 2.81h.

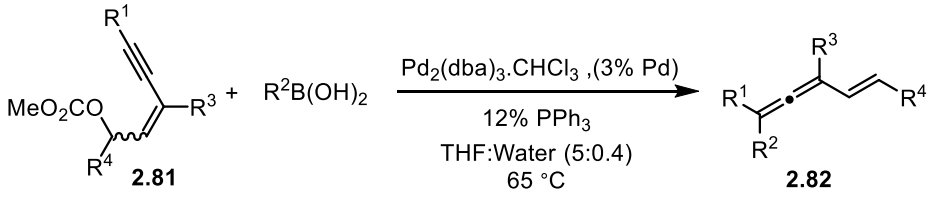


2.81h

^{1}H NMR (500 MHz, C_6D_6) δ: 7.45 (dd, *J* = 7.6, 1.9 Hz, 1 H), 6.97 (dt, *J* = 8.2, 1.5 Hz, 1 H), 6.68 (t, *J* = 7.5 Hz, 1 H), 6.42 (d, *J* = 8.4 Hz, 1 H), 6.00 (m, 1 H), 5.48 (m, 1 H), 3.31 (s, 3H), 3.28 (s, 3 H), 1.93 (d, *J* = 1.5 Hz, 3 H), 1.07 (d, *J* = 6.5 Hz, 3 H).

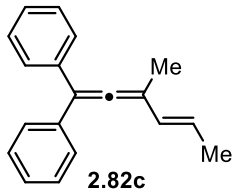
^{13}C NMR (125 MHz, C_6D_6) δ: 160.7, 155.7, 135.7, 133.9, 129.8, 128.3, 128.0, 122.7, 120.6, 113.4, 111.0, 95.9, 85.8, 71.3, 55.2, 54.1, 20.2, 18.1.

2.5.2 General Procedure for the Synthesis of Vinylallenes 2.82a-t[79]



A mixture of $Pd_2(dba)_3CHCl_3$ (3% Pd) and PPh_3 (12%) in dry THF (5 mL/1 mmol) was stirred for 15 min under Ar. Then, the dry THF (10 mL/1 mmol) solution of enyne carbonate (1 eq), boronicacid (2 eq), and degassed water (1.2 mL/1 mmol) was added successively. The mixture was stirred magnetically in a preheated oil bath at 65 °C. After the TLC control indicated complete consumption of the starting material, the THF was evaporated, and the residue, which contains proper amount of water was taken into Et_2O and removed by extraction. The extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Then, the residue was purified by column chromatography (cyclohexane/ethyl acetate) to give desired vinylallenes.

(E)-(3-Methylhexa-1,2,4-triene-1,1-diyl)dibenzene (2.82c)

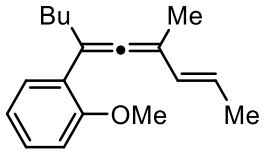


2.82c

Following the general procedure **2.5.2**, from **2.81f** (2.44 g, 10 mmol) and phenyl boronicacid (2.42 g, 20 mmol), **2.64c** was obtained (1.97 g, 8 mmol, 80 %) as white solid after column chromatography (cyclohexane:EtOAc =100:2).

^{1}H NMR (400 MHz, C_6D_6) δ: 7.63 - 7.57 (m, 4 H), 7.30 - 7.24 (m, 4 H), 7.22 - 7.16 (m, 2 H), 6.27 (dq, *J*= 15.6, 1.6 Hz,1H), 5.60 (dq, *J* = 15.6, 6.7 Hz, 1 H), 1.94 (s, 3 H), 1.71 (dd, *J* = 6.8, 1.8 Hz, 3 H).
^{13}C NMR (100 MHz , C_6D_6) δ: 209.5, 137.9, 129.2, 129.1, 128.8, 128.2, 127.9, 127.5, 127.4, 125.4, 110.1, 103.5, 18.4, 15.6.;
HRMS (ESI, m/z, $[M+H]^+$): 247.14813 (calculated), 247.14813 (found).

(E)-1-Methoxy-2-(7-methyldeca-5,6,8-trien-5-yl)benzene (2.82e)

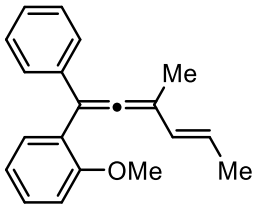


2.82e

Following the general procedure **2.5.2**, starting from **2.81b** (2.24 g, 10 mmol), of 2-Methoxybenzeneboronic acid (3.04 g, 20 mmol), **2.82e** (2.1 g, 8 mmol, 80 %) was obtained as colorless oil after column chromatography (cyclohexane: EtOAc = 100:2).

^{1}H NMR (500 MHz, C_6D_6): δ 7.37 (dd, *J* = 7.3, 1.9 Hz, 1 H), 7.07 (ddd, *J* = 7.8, 1.5, 0.5 Hz, 1H), 6.87 (td, *J* = 7.5, 1.1 Hz, 1 H), 6.57 (d, *J* = 8.0 Hz, 1 H), 6.33 (qd, *J* = 16.0, 1.5 Hz, 1H), 5.46 (dq, *J* = 15.6, 6.5 Hz, 1 H), 3.34 (s, 3 H), 2.62 (td, *J* = 7.5, 1.5 Hz, 2 H), 1.89 (s, 3 H), 1.65 (dd, *J* =6.7, 1.7 Hz, 3 H), 1.58 (quin, *J* = 7.5 Hz, 2 H), 1.41 (sxt, J = 7.5 Hz, 2 H), 0.88 (t, *J* = 7.5 Hz, 3 H).
^{13}C NMR (125 MHz, C_6D_6): δ 207.3, 157.6, 131.0, 130.5, 128.5, 128.4, 123.3, 121.0, 111.6, 103.5, 100.3, 55.2, 33.1, 30.8, 22.8, 18.4, 16.0, 14.2.
HRMS (ESI, m/z, M+): 257.18999 (calculated), 257.18991 (found).

(E)-1-Methoxy-2-(3-methyl-1-phenylhexa-1,2,4-trien-1-yl)benzene (2.82f)

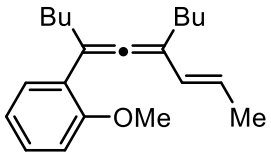


2.82f

Following the general procedure **2.5.2**, starting from **2.81f** (2.44 g, 10 mmol), of 2-Methoxybenzeneboronic acid (3.04 g, 20 mmol), **2.82f** (2.15 g, 7.8 mmol, 78 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:2).

^{1}H NMR (400 MHz, C_6D_6): δ 7.48 (d, *J* = 7.3 Hz, 1 H), 7.43 (dd, *J* = 7.4, 1.6 Hz, 1 H), 7.15 - 7.10 (m, 3 H), 7.03 (tt, *J* = 7.4, 1.2 Hz, 1H), 6.89 (td, *J* = 7.5, 1.1 Hz, 1 H), 6.59 (d, *J* = 8.3 Hz, 1 H), 6.27 (dq, *J* =15.6, 1.4 Hz, 1H), 5.48 (dq, *J* =15.6, 6,6 Hz, 1 H), 3.20 (s, 3 H), 1.88 (s, 3 H), 1.61 (dd, *J* = 6.7, 1.9 Hz, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ 209.1, 157.9, 138.3, 132.1, 129.6, 129.1, 128.5, 128.2, 127.9, 127.5, 126.8, 126.7, 124.8, 121.0, 111.5, 106.1, 102.7, 55.1, 18.4, 15.6.
HRMS (ESI, m/z, $[M]^+$): 276.15087 (calculated), 276.15029 (found)

(E)-1-Methoxy-2-(7-(prop-1-en-1-yl)undeca-5,6-dien-5-yl)benzene (2.82g)



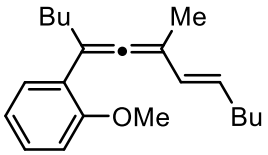
2.82g

Following the general procedure **2.5.2**, starting from **2.81e** (1.3 g, 5 mmol), of 2-Methoxybenzeneboronic acid (1.52 g, 10 mmol), **2.82g** (1.15 g, 3.8 mmol, 76 %) was obtained as colorless oil after column chromatography (cyclohexane:EtOAc = 100:2).

^{1}H NMR (400 MHz, C_6D_6): δ 7.39 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.07(td, *J* = 7.8, 1.8 Hz, 1H), 6.88(td, *J* = 7.5, 1.1 Hz, 1H), 6.56(d, *J* = 8.3 Hz, 1H), 6.36(d, *J* = 15.6 Hz, 1H), 5.55(dt, *J* = 15.6, 7.0 Hz, 1H), 3.34(s, 3H), 2.65(t, *J* = 7.6 Hz, 2H), 2.06(q, *J* = 6.8 Hz, 2H), 1.94 (s, 3H), 1.59(quin, *J* = 7.5 Hz, 2H), 1.41(spt, *J* = 15.0 Hz, 2H), 1.19-1.36(m,4H), 0.86(dt, *J* = 16.6, 7.2 Hz, 6H).
^{13}C NMR (100 MHz, C_6D_6): δ 207.6, 157.6, 130.6, 129.8, 129.1, 128.5, 128.3, 128.0, 121.0, 111.6, 103.5, 100.4, 55.2, 33.2, 32.3, 30.9, 22.9, 22.8, 16.2, 14.4, 14.3.

HRMS (ESI, *m/z*, [M+H]$^+$): 299.23694 (calculated), 299.23677 (found).

(E)-1-Methoxy-2-(7-methyltrideca-5,6,8-trien-5-yl)benzene (2.82h)

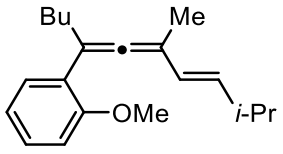


2.82h

Following the general procedure **2.5.2**, starting from **2.81c** (2.1 g, 8 mmol), of 2-Methoxybenzeneboronic acid (2.43 g, 16 mmol), **2.82h** (1.8 g, 6 mmol, 75 %) was obtained as colorless oil after column chromatography (cyclohexane:EtOAc = 100:2).

^{1}H NMR (400 MHz, C_6D_6): δ 7.40 (dd, *J* = 7.40, 1.6 Hz, 1H), 7.21 - 7.15 (m, 3 H), 6.88 (td, *J* = 7.6, 1.2 Hz, 1H), 6.56 (d, *J* = 8.3 Hz, 1H), 6.37 (d, *J* = 5.8 Hz, 1H), 5.55 (dt, *J* = 15.5, 6.9 Hz, 1H), 3.34 (s, 3H), 2.65 (t, *J* = 7.4 Hz, 3H), 2.06 (dq, *J* = 13.3, 6.8 Hz, 2H), 1.59 (quint, *J* = 7.4 Hz, 2H), 1.41 (sext, *J* = 15.3 Hz, 2H), 1.19-1.36 (m, 4H), 0.862 (dt, *J* = 7.3,16.6 Hz, 4H).
^{13}C NMR (100 MHz, C_6D_6): δ 207.5, 157.5, 130.5, 129.7, 129.0, 128.4, 128.2, 127.9, 120.9, 111.5, 103.4, 100.3, 55.1, 33.1, 32.2, 30.8, 22.8, 22.7, 16.1, 14.3, 14.2.
HRMS (ESI, *m/z*, M$^+$): 299.23694 (calculated), 299.23724 (found).

(E)-1-(7,10-Dimethylundeca-5,6,8-trien-5-yl)-2-methoxybenzene (2.82i)



2.82i

Following the general procedure **2.5.2**, starting from **2.81d** (2.1 g, 8 mmol), of 2-Methoxybenzeneboronic acid (2.43 g, 16 mmol), **2.82i** (1.45 g, 5 mmol, 63 %) was obtained as colorless oil after column chromatography (cyclohexane:EtOAc = 100:2).

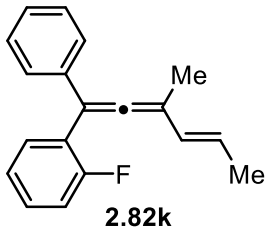
^{1}H NMR (500 MHz, C_6D_6): δ 7.40-7.37 (m, 1 H), 7.06 (dt, *J* = 7.7, 1.7 Hz, 1 H), 6.87 (t, *J* = 7.5 Hz, 1 H), 6.56 (d, *J* = 8.4 Hz, 1 H), 6.33 (td, *J* = 16.0, 1.5 Hz, 1 H), 5.54 (dd, *J* = 15.7, 6.9 Hz, 1 H), 3.34 (s, 3 H),

2.64 (tt, *J* = 7.5, 1.8 Hz, 2 H), 2.29 (dsext, *J* = 6.5, 0.5 Hz, 1 H), 1.94 (s, 3 H), 1.58 (quin, *J* = 7.5 Hz, 2 H), 1.41 (sxt, *J* = 7.5 Hz, 2 H), 0.96 (dd, *J* = 6.9, 3.8 Hz, 6 H), 0.88 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, C_6D_6): δ 207.6, 157.6, 135.9, 130.5, 128.5, 128.3, 127.0, 120.9, 111.6, 103.3, 100.2, 55.2, 33.1, 31.9, 30.8, 22.9, 22.9, 22.8, 16.1, 14.2.

HRMS (ESI, m/z, [M+H]$^+$): 285.22129 (calculated), 285.22120 (found).

(E)-1-Fluoro-2-(3-methyl-1-phenylhexa-1,2,4-trien-1-yl)benzene (2.82k)



2.82k

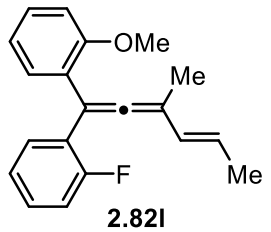
Following the general procedure **2.5.2**, starting from **2.81f** (2.44 g, 10 mmol), of 2-Fluorophenylboronic acid (2.8 g, 20 mmol), **2.82k** (1.8 g, 7 mmol, 70 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:3).

^{1}H NMR (500 MHz, C_6D_6): δ 7.42 (d, *J* = 7.6 Hz, 2 H), 7.29 (dt, *J* = 7.4, 1.7 Hz, 1 H), 7.13 (t, *J* = 7.6 Hz, 2 H), 7.06-7.01 (m, 1H), 6.90 - 6.79 (m, 3 H), 6.18 (dq, *J* = 16.0, 1.5, 1H), 1.83 (s, 3 H), 1.58 (dd, *J* = 1.9, 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, C_6D_6): δ 209.5, 162.0, 160.1, 158.6, 137.5, 132.1, 132.1, 129.4, 129.3, 128.8, 128.4, 127.7, 127.3, 125.8, 125.6, 125.5, 124.4, 124.3, 116.3, 116.2, 103.7, 103.6, 18.4, 15.4.;

HRMS (ESI, m/z, [M+H]$^+$): 265.13871 (calculated), 265.13870 (found).

(E)-1-Fluoro-2-(1-(2-methoxyphenyl)-3-methylhexa-1,2,4-trien-1-yl)benzene (2.82l)

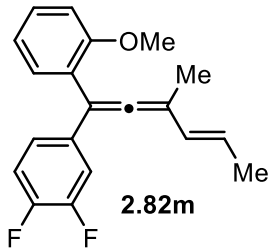


2.82l

Following the general procedure **2.5.2**, starting from **2.81g** (1.92 g, 7 mmol), of 2-Fluorophenylboronic acid (1.96 g, 14 mmol), **2.82l** (1.18 g, 4 mmol, 57 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.41 (dt, *J* = 7.6,1.6 Hz, 1H), 7.30 - 7.24 (m, 1 H), 7.09 (dt, *J* = 7.8 Hz, 1 H), 6.89 - 6.75 (m, 4 H), 6.55 (dd, *J* = 8.4, 1.2 Hz, 1 H), 6.30 (dq, 15.5, 1.4 Hz, 1H), 5.46 (dq, *J* = 15.6, 6.7 Hz, 1 H), 3.20 (s, 3 H), 1.89 (s, 3 H), 1.59 (dd, *J* = 6.8, 1.8 Hz, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ 211.2, 162.1, 159.7, 157.7, 131.4, 130.8, 130.7, 129.4, 128.9, 128.4, 127.1, 127.0, 126.9, 124.8, 124.0, 124.0, 121.0, 116.2, 115.9, 111.6, 101.1, 55.2, 18.4, 15.6.;
HRMS (ESI, m/z, [M+H]$^+$): 295.14927 (calculated), 295.14942 (found).

(E)-1,2-Difluoro-4-(1-(2-methoxyphenyl)-3-methylhexa-1,2,4-trien-1-yl)benzene (2.82m)

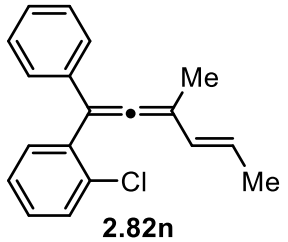


2.82m

Following the general procedure **2.5.2**, starting from **2.81g** (1.92 g, 7 mmol), of 3,4-difluorophenylboronic acid (2.2 g, 14 mmol), **2.82m** (1.38 g, 4.4 mmol, 63%) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.32 (dd, *J* = 1.8, 7.5 Hz, 1 H), 7.23 (ddd, *J* = 11.8, 7.8, 2.3 Hz, 1 H), 7.11 (ddd, *J* = 8.2, 7.5, 1.9 Hz, 1 H), 6.93-6.89 (m, 1 H), 6.86 (td, *J* = 7.4, 1.2 Hz, 1 H), 6.69 (dt, *J* = 10.1, 8.5 Hz, 1 H), 6.54 (d, *J* = 8.3 Hz, 1 H), 6.15 (dq, *J* = 15.5, 1.6 Hz, 1 H), 5.46 (dq, *J* = 15.6, 6.7 Hz, 1 H), 3.17 (s, 3 H), 1.79 (s, 3 H), 1.59 (dd, *J* = 6.7, 1.6 Hz, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ: 208.9, 157.7, 152.2, 152.0, 150.9, 149.7, 149.6, 148.4, 135.6, 131.9, 129.5, 128.8, 125.8, 123.2, 123.2, 121.1, 117.1, 117.0, 116.0, 115.9, 111.6, 104.8, 103.4, 55.0, 27.3, 18.4, 15.4.;
HRMS (ESI, *m/z*, [M+H]$^+$): 313.13985 (calculated), 313.13999 (found).

(E)-1-Chloro-2-(3-methyl-1-phenylhexa-1,2,4-trien-1-yl)benzene (2.82n)

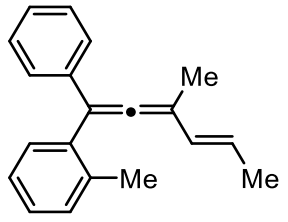


2.82n

Following the general procedure **2.5.2**, starting from **2.81f** (1.7 g, 7 mmol), of 2-chlorophenylboronic acid (2.19 g, 14 mmol), **2.82m** (1.2 g, 4.4 mmol, 63 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:2).

^{1}H NMR (400 MHz, C_6D_6): δ 7.37 (dd, *J* = 8.3, 1.3 Hz, 2 H), 7.26 (ddd, *J* = 9.2, 7.7, 1.6 Hz, 2 H), 7.14 - 7.09 (m, 2 H), 7.02 (1H, *J* = 7.4, 1.4 Hz, 1H), 6.88 (dt, *J* = 7.5, 1.3 Hz, 1 H), 6.80 (dt, *J* = 7.8, 1.8 Hz, 1 H), 6.25 (qd, *J* = 15.6, 1.7 Hz, 1 H), 5.49 (qd, *J* = 15.6, 6.7 Hz, 1 H), 1.85 (s, 3 H), 1.59 (dd, *J* = 6.5, 1.8 Hz, 3 H).;
^{13}C NMR (100 MHz, C_6D_6): δ 208.2, 137.3, 136.6, 134.6, 132.3, 130.2, 128.9, 128.8, 128.7, 128.3, 127.4, 127.2, 127.0, 125.9, 106.8, 104.2, 27.3, 18.4, 15.2.
HRMS (ESI, m/z, [M+H]$^+$): 281.10914 (calculated), 281.10915 (found).

(E)-1-Methyl-2-(3-methyl-1-phenylhexa-1,2,4-trien-1-yl)benzene (2.82p)



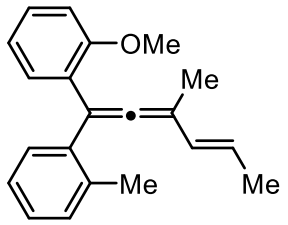
2.82p

Following the general procedure **2.5.2**, starting from **2.81f** (1.22 g, 5 mmol), of 2-methylphenylboronic acid (1.35 g, 10 mmol), **2.82p** (1.2 g, 3.4 mmol, 67 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:1).

^{1}H NMR (400 MHz, C_6D_6): δ 7.40 - 7.35 (m, 3 H), 7.13 - 7.08 (m, 5 H), 7.01 (tt, *J* = 7.2, 1.2 Hz, 1H), 6.20 (qd, *J* = 15.6, 1.8 Hz, 1 H), 5.48 (qd, *J* = 15.6, 6.7 Hz, 1 H), 2.25 (s, 3 H), 1.82 (s, 3 H), 1.61 (dd, *J* = 6.5, 1.8 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 207.6, 138.0, 137.0, 137.0, 130.9, 130.7, 129.1, 128.8, 128.3, 127.9, 127.4, 127.1, 126.4, 125.3, 108.0, 103.0, 20.5, 18.4, 15.5.
(ESI, *m/z*): 261.1, 233.1, 219.1, 181.1, 146.0, 105.1, 100.1.

(E)-1-Methoxy-2-(3-methyl-1-(o-tolyl)hexa-1,2,4-trien-1-yl)benzene (2.82r)

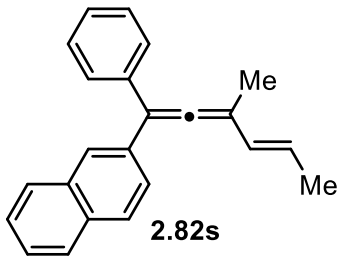


2.82r

Following the general procedure **2.5.2**, starting from **2.81g** (1.65 g, 6 mmol), of 2-methylphenylboronic acid (1.6 g, 12 mmol), **2.82r** (1.28 g, 3.8 mmol, 63 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.40 - 7.35 (m, 1 H), 7.26 (dd, *J* = 7.5, 1.8 Hz, 1 H), 7.12 - 7.01 (m, 4 H), 6.80 (dt, *J* = 7.5, 1.3 Hz, 1 H), 6.55 (d, *J* = 8.0 Hz, 1 H), 6.34 (qd, *J* = 15.6, 1.6 Hz, 1H), 5.46 (qd, *J* = 15.6, 6.6 Hz, 1 H), 3.25 (s, 3 H), 2.39 (s, 3 H), 1.87 (s, 3 H), 1.63 (dd, *J* = 6.7, 1.6 Hz, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ 209.8, 157.7, 138.6, 136.6, 130.8, 130.8, 130.1, 130.0, 128.5, 128.3, 127.2, 126.1, 124.1, 120.9, 111.8, 103.8, 100.0, 55.4, 21.0, 18.5, 15.7.
HRMS (ESI, m/z, $[M+H]^+$): 291.17434 (calculated), 291.17455 (found).

(E)-2-(3-Methyl-1-phenylhexa-1,2,4-trien-1-yl)naphthalene (2.82s)



2.82s

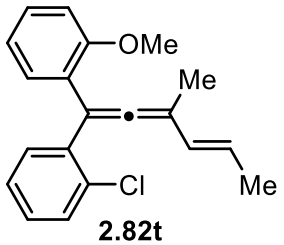
Following the general procedure **2.5.2**, starting from **2.81f** (1.22 g, 5 mmol), of 2-Naphthylboronic acid (1.7 g, 10 mmol), **2.82s** (0.92 g, 3.1 mmol, 62 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 8.20 (d, *J* = 7.6 Hz, 1 H), 7.68 - 7.61 (m, 2 H), 7.54 (dd, *J* = 6.9, 1.1 Hz, 1 H), 7.41 - 7.38 (m, 2 H), 7.28 (dd, *J* = 8.2, 7.1 Hz, 1 H), 7.20 (dquin, *J* = 7.6, 1.5 Hz, 2 H), 7.08 - 7.04 (m, 2 H), 6.99 (tt, *J* = 7.3, 1,0 Hz, 1H), 6.24 (m, 1H), 5.47 (dq, *J* = 15.6, 6.6 Hz, 1 H), 1.84 (s, 3 H), 1.59 (dd, *J* = 6.7, 1.7 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 208.6, 138.3, 135.4, 134.6, 132.9, 129.1, 128.8, 128.7, 128.3, 128.3, 128.3, 127.9, 127.5, 127.1, 126.7, 126.4, 126.1, 126.0, 125.5, 107.4, 103.2, 18.4, 15.6.

HRMS (ESI, m/z, $[M+H]^+$): 297.16378 (calculated), 297.16395 (found).

(E)-1-Chloro-2-(1-(2-methoxyphenyl)-3-methylhexa-1,2,4-trien-1-yl)benzene (2.82t)



2.82t

Following the general procedure **2.5.2**, starting from **2.81h** (1.92 g, 7 mmol), of 2-chlorophenylboronic acid (2.19 g, 14 mmol), **2.82t** (1.37 g, 4.4 mmol, 63 %) was obtained as white solid after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.32 (dt, *J* = 7.6, 1.9 Hz, 2 H), 7.26 (dd, *J* = 7.9, 1.1 Hz, 1 H), 7.06 (ddd, *J* = 8.5, 7.5, 1.8 Hz, 1H), 6.84 (dtd, *J* = 10.4, 7.5, 1.1 Hz, 2 H), 6.77 (dt, *J* = 7.6, 1.6 Hz, 1H), 6.54 (d, *J* = 8.3 Hz, 1 H), 6.34 (qd, *J* = 15.6, 1.8 Hz, 1 H), 5.47 (qd, *J* = 15.6, 6.7 Hz, 1 H), 3.23 (s, 3 H), 1.90 (s, 3 H), 1.60 (dd, *J* = 6.7, 1.6 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 210.5, 157.7, 138.0, 133.8, 131.4, 131.0, 130.3, 129.4, 128.8, 128.2, 127.9, 126.7, 124.8, 121.0, 111.8, 102.9, 101.3, 55.4, 18.5, 15.4.

HRMS (ESI, m/z, $[M+H]^+$): 311.11972 (calculated), 311.11988 (found).

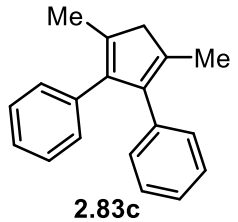
2.5.3 General Procedure A; The Gold-Catalyzed [1,2]-Migratory Cycloisomerization of Vinylallenes

To a solution of vinylallene (0.3 mmol) in 4 ml of dry DCM were added Ph_3PAuCl (5 mol%) and (5 mol%) $AgSbF_6$ under nitrogen atmosphere. The reaction mixture was stirred at room temperature and monitored by TLC. After completion, the reaction mixture was filtered over celite, washed with Et_2O. The solvents were evaporated under reduced pressure. The residue was purified by column chromatography (cyclohexane/dichloromethane) to give the cyclopentadiene **2.83.**

2.5.4 General Procedure B; The Platinum-Catalyzed [1,2]-Migratory Cycloisomerization of Vinylallenes.

To a solution of vinylallene (0.3 mmol) in 5 ml of dry toluene were added 10 mol% $PtCl_2$ under nitrogen atmosphere. The mixture was stirred magnetically in a preheated oil bath at 100 °C and monitored by TLC. After completion, the reaction mixture was cooled down to room temperature and filtered over celite, washed with Et_2O and solvent was evaporated under reduced pressure. The solvents were evaporated under reduced pressure and the residue was purified by column chromatography (cyclohexane/ DCM) to give the cyclopentadiene **2.83.**

(3,5-Dimethylcyclopenta-2,5-diene-1,2-diyl)dibenzene (2.83c)



2.83c

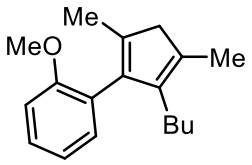
Following the general procedure **B**, starting from **2.82c** (73.9 mg, 0.3 mmol), **2.83c** (35 mg, 0.14 mmol, 45 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5) and slowly crystallized in cyclohexane.

^{1}H NMR (400 MHz, C_6D_6): δ 7.14 - 7.05 (m, 8 H), 7.00 (tt, *J* = 7.2, 1.8 Hz, 2H), 2.73 (s, 2 H), 1.95 (s, 6 H).

^{13}C NMR (100 MHz, C_6D_6): δ 142.2, 137.3, 136.3, 130.0, 128.4, 128.2, 128.1, 127.9, 126.4, 49.9, 14.5.

Spectral data agreed with previous data.[88]

1-(5-Butyl-2,4-dimethylcyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83e)

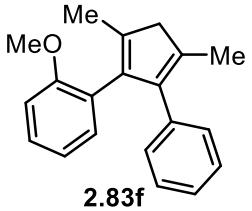


2.83e

Following the general procedure **A**, starting from **2.82e** (76,9 mg, 0.3 mmol), **2.83e** (65.3 mg, 0.25 mmol, 83 %) was obtained as yellow oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.22 (dd, *J* = 7.3, 1.8 Hz, 1 H), 7.14(m, 1H), 6.93 (td, *J* = 7.4, 1.2 Hz, 1 H), 6.64 (d, *J* = 8.0 Hz, 1 H), 3.30 (s, 3 H), 2.72 (s, 2 H), 2.40-2.34 (m, 2 H), 1.94 (s, 3 H), 1.89 (s, 3 H), 1.34 (quin, *J* = 7.3 Hz, 2 H), 1.23 (sxt, *J* = 7.4 Hz, 2 H), 0.77 (t, *J* = 7.3 Hz, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ 157.9, 141.6, 140.4, 135.9, 132.2, 131.7, 128.4, 128.3, 128.2, 127.9 120.7, 111.0, 54.8, 49.0, 32.0, 26.4, 22.9, 14.5, 14.2, 13.7.
FTIR (ν_{max}/cm^{-1}): 3050, 1996, 1968, 1639, 1476, 1434, 1359, 1286, 1156, 1103, 1002, 931, 755, 691.
HRMS (ESI, m/z, [M+H]$^+$): 257.18999 (calculated), 257.19033 (found).

1-(2,4-Dimethyl-5-phenylcyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83f)



2.83f

Following the general procedure **A**, starting from **2.82f** (82.9 mg, 0.3 mmol), **2.83f** (75 mg, 0.27 mmol, 90 %) was obtained as colorless solid after column chromatography (cyclohexane:CH_2Cl_2 = 100:5) and slowly crystallized in cyclohexane.

[88] M. Horacek, J. Dinkas, J. Merna, R. Gyepes, P. Meunier, *J. Organomet. Chem*. **2009**, *694*, 173-178.

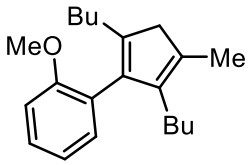
^{1}H NMR (500 MHz, C_6D_6): δ 7.21 - 7.17 (m, 3 H), 7.09 - 7.04 (m, 3 H), 6.97 (tt, *J* = 7.5, 1.5 Hz, 1 H), 6.86 (dt, *J* = 7.4, 1.0 Hz, 1 H), 6.47 (d, *J* = 8.0 Hz, 1 H), 3.00 (s, 3 H), 2.76 (ABq, *J* = 5.6, 5.5 Hz, 2H), 2.00 (s, 3 H), 1.94 (s, 3 H).

^{13}C NMR (125MHz, C_6D_6): δ 157.7, 143.0, 139.9, 138.1, 136.5, 135.0, 131.7, 129.1, 128.4, 127.7, 127.0, 126.0, 120.6, 111.2, 54.5, 49.7, 14.6, 14.5.

FTIR (ν_{max}/cm^{-1}): 3073, 3051, 2989, 2932, 2904, 2868, 2855, 2831, 1607, 1597, 1585, 1578, 1488, 1462, 1431, 1380, 1247, 1142, 1116, 1023, 756, 700.

HRMS (ESI, m/z, [M+H]$^+$): 277.15869 (calculated), 277.15888 (found).

1-(2,5-Dibutyl-4-methylcyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83g)



2.83g

Following the general procedure **A**, starting from **2.82g** (89.5 mg, 0.3 mmol), **2.83g** (49 mg, 0.17 mmol, 55 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

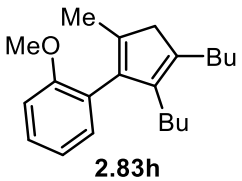
^{1}H NMR (400 MHz, C_6D_6): δ 7.22 (dd, *J* = 7.3, 1.8 Hz, 1 H), 7.12 - 7.15 (m, 1 H), 6.93 (td, *J* = 7.4, 1.2 Hz, 1 H), 6.64 (d, *J* = 8.3 Hz, 1 H), 3.31 (s, 3 H), 2.81 (s, 2 H), 2.36 - 2.46 (m, 4 H), 1.92 (s, 3 H), 1.47 (quin, *J* = 7.6 Hz, 2 H), 1.35 (sxt, *J* = 7.3 Hz, 4 H), 1.23 (sxt, *J* = 7.2 Hz, 2 H), 0.92 (t, *J* = 7.2 Hz, 3 H), 0.78 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 158.0, 141.6, 140.3, 137.5, 136.3, 131.8, 128.5, 127.6, 120.8, 111.1, 54.9, 46.8, 33.5, 32.4, 28.7, 26.5, 23.4, 23.1, 14.7, 14.5, 14.3.

FTIR (ν_{max}/cm^{-1}): 3073, 2996, 2954, 2926, 2870, 2856, 2833, 1642, 1579, 1489, 1456, 1434, 1378, 1244, 1116, 1051, 1030, 751.

HRMS (ESI, *m/z*, [M+H]$^+$): 299.23694 (calculated), 299.23726 (found).

1-(4,5-Dibutyl-2-methylcyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83h)



2.83h

Following the general procedure **A**, starting from **2.82h** (89.5 mg, 0.3 mmol), **2.83h** (53 mg, 0.18 mmol, 60 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

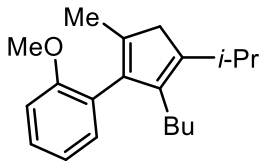
^{1}H NMR (400 MHz, C_6D_6): δ7.21 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.14 (dd, *J* = 8.2, 1,8 Hz, 1H), 6.93(td, *J* = 7.4 Hz, 1H), 6.65(d, *J* = 8.0 Hz, 1H), 3.31(s, 3H), 2.80(s, 2H), 2.35-2.45(m, 4H), 1.92(s, 3H), 1.46 (sxt, *J* = 7.6 Hz, 2H), 1.35(spt, *J* = 7.5 Hz, 4H), 1.23(sxt, *J* = 7.5 Hz, 2H), 0.92(t, *J* = 7.3 Hz, 3H) , 0.77(t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, C_6D_6): δ 158.0, 141.5, 140.2, 137.4, 136.2, 131.7, 128.4, 127.5, 120.7, 111.0, 54.8, 46.7, 33.4, 32.3, 28.6, 26.4, 23.3, 23.0, 14.6, 14.4, 14.2.

FTIR (ν_{max}/cm^{-1}): 3415, 2955, 2931, 2870, 2861, 2835, 1708, 1597, 1579, 1490, 1460, 1434, 1241, 1116, 1049, 1026, 752.;

HRMS (ESI, m/z, [M+H]$^+$): 299.23694 (calculated), 299.23719 (found).

1-(5-Butyl-4-isopropyl-2-methylcyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83i)



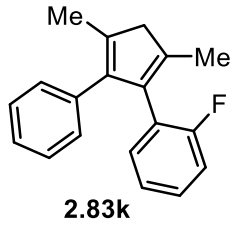
2.83i

Following the general procedure **A**, starting from **2.82i** (85.3 mg, 0.3 mmol), **2.83i** (48.3 mg, 0.17 mmol, 56 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (500 MHz, C_6D_6): δ 7.20 (dd, *J* = 7.5, 2.1 Hz, 1 H), 7.13 (dd, *J* = 8.0, 1.9 Hz, 1 H), 6.92 (t, *J* = 7.5 Hz, 1 H), 6.64 (d, *J* = 8.4 Hz, 1 H), 3.30 (s, 3 H), 2.99 (spt, *J* = 7.0 Hz, 1 H), 2.80 (s, 2 H), 2.45 - 2.31 (m, 2 H), 1.92 (s, 3 H), 1.35 (quin, *J* = 7.5 Hz, 2 H), 1.23 (sxt, *J* = 7.5 Hz, 2 H), 1.11 (dd, *J* = 12.6, 6.9 Hz, 6 H), 0.78 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (125 MHz, C_6D_6): δ 158.0, 143.3, 140.1, 140.0, 136.0, 131.7, 128.4, 127.5, 120.7, 111.0, 54.8, 42.4, 32.5, 27.6, 26.3, 24.3, 23.9, 23.0, 14.6, 14.1.
HRMS (ESI, m/z, [M+H]$^+$): 285.22129 (calculated), 285.22108 (found).

1-(2,4-Dimethyl-5-phenylcyclopenta-1,4-dien-1-yl)-2-fluorobenzene (2.83k)

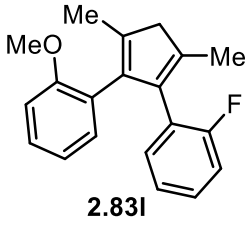


2.83k

Following the general procedure **B**, starting from **2.82k** (79.3 mg, 0.3 mmol), **2.83k** (40.5 mg, 0.15 mmol, 51 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (500 MHz, C_6D_6): δ 7.18 - 7.13 (m, 2 H), 7.07 (t, *J* = 7.6 Hz, 2 H), 7.01 - 6.94 (m, 2 H), 6.82 - 6.78 (m, 2 H), 6.74 - 6.69 (m, 1 H), 2.71 (s, 2 H), 1.93 (s, 3 H), 1.90 (s, 3 H).
^{13}C NMR (125 MHz, C_6D_6): δ 161.6, 159.7, 142.2, 138.9, 137.1, 136.4, 136.2, 132.2, 132.1, 129.5, 128.7, 128.6, 128.3, 128.1, 126.5, 125.3, 125.2, 123.8, 123.7, 115.9, 115.7, 49.8, 14.6, 14.4.
HRMS (ESI, m/z, [M+H]$^+$): 265.13871 (calculated), 265.13845 (found)

1-Fluoro-2-(5-(2-methoxyphenyl)-2,4-dimethylcyclopenta-1,4-dien-1-yl)benzene (2.83l)



2.83l

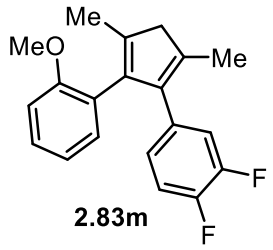
Following the general procedure **A** or **B**, starting from **2.82l** (88.3 mg, 0.3 mmol), **2.83l** (45.0 mg, 0.15 mmol, Yield; procedure A=B= 51 %) was obtained as white solid after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (400 MHz, C_6D_6) δ: 7.25 (dd, *J* = 7.4, 1.9 Hz, 1 H), 7.03 (dt, *J* = 7.8, 1.8 Hz, 1 H), 6.86 (t, *J* = 7.4 Hz, 2 H), 6.80 - 6.73 (m, 1 H), 6.64 (br.s, 1H), 6.41 (d, *J* = 8.3 Hz, 1 H), 3.05 (s, 3 H), 2.71 (s, 2 H), 1.96 (s, 3 H), 1.93 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 161.7, 157.5, 139.7, 137.8, 136.6, 131.5, 126.4, 126.5, 125.8, 123.2, 120.4, 115.4, 115.2, 110.8, 54.3, 49.5, 14.8, 14.5.

HRMS (ESI, m/z, $[M+H]^+$): 295.14927 (calculated), 295.14877 (found).

1,2-Difluoro-4-(5-(2-methoxyphenyl)-2,4-dimethylcyclopenta-1,4-dien-1-yl)benzene (2.83m)



2.83m

Following the general procedure **A** or **B**, starting from **2.82m** (93.7 mg, 0.3 mmol), **2.83m** (49.7 mg, 0.16 mmol, yields; procedure A=B=53 %) was obtained as white solid after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

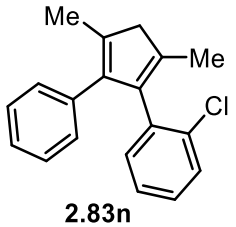
^{1}H NMR (400 MHz, C_6D_6): δ 7.11 (dd, *J* = 7.3, 1.8 Hz, 1 H), 7.06 (dt, *J* = 7.8, 1.9 Hz, 1 H), 6.95 (ddd, *J* = 11.9, 8.0, 1.8 Hz, 1 H), 6.86 (dt, *J* = 7.4, 1.0 Hz, 1 H), 6.64 - 6.52 (m, 2 H), 6.41 (d, *J* = 8.3 Hz, 1 H), 2.94 (s, 3 H), 2.67 (d, *J* = 5.0 Hz, 2 H), 1.87 (s, 3 H), 1.84 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 157.4, 151.4(d), 147.8(d), 140.8, 139.2, 136.8, 136.0, 135.1, 131.5, 128.7, 126.1, 125.0, 124.9, 120.7, 117.7(d), 116.4(d), 111.0, 54.3, 49.6, 14.4, 14.3.

FTIR (ν_{max}/cm^{-1}): 3065, 2970, 2927, 2869, 1715, 1001, 1515, 1491, 1433, 1273, 1246, 1116, 1026, 757.

HRMS (ESI, m/z, $[M+H]^+$): 313.13985 (calculated), 313.13987 (found).

1-Chloro-2-(2,4-dimethyl-5-phenylcyclopenta-1,4-dien-1-yl)benzene (2.83n)



2.83n

Following the general procedure **B**, starting from **2.82m** (84.2 mg, 0.3 mmol), **2.83m** (43.0 mg, 0.15 mmol, 51 %) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

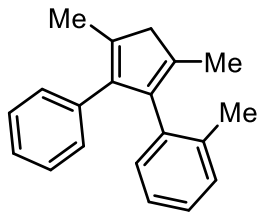
^{1}H NMR (500 MHz, C_6D_6): δ 7.17 (tt, *J* = 8.0, 1.5 Hz, 3H), 7.06 (t, *J* = 7.6 Hz, 2 H), 7.00 - 6.94 (m, 2 H), 6.78 (dt, *J* = 7.5, 1.5 Hz, 1 H), 6.72 (dt, *J* = 7.5, 1.5 Hz, 1 H), 2.77 (ABq, *J* = 5.6, 3.6 Hz, 2H), 1.95 (s, 3 H), 1.85 (s, 3 H).

^{13}C NMR (125 MHz, C_6D_6): δ 142.3, 140.3, 138.1, 137.1, 136.9, 136.0, 134.6, 132.0, 129.7, 129.5, 128.4, 128.2, 128.0, 126.5, 126.4, 49.6, 14.5.

FTIR (ν_{max}/cm^{-1}): 3056, 1964, 2923, 2854, 1713, 1606, 1491, 1471, 1430, 1376, 1258, 1125, 1062, 1032, 842, 747, 697.

HRMS (ESI, m/z, [M+H]$^+$): 281.10903 (calculated), 281.10915 (found).

1-(2,4-Dimethyl-5-phenylcyclopenta-1,4-dien-1-yl)-2-methylbenzene (2.83p)



2.83p

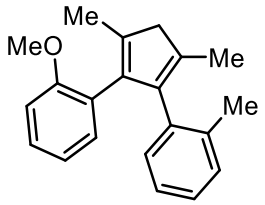
Following the general procedure **B**, starting from **2.82p** (78.3 mg, 0.3 mmol), **2.83p** (39.2 mg, 0.15 mmol, 51 %) was obtained as yellow oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.18 - 7.11 (m, 3 H), 7.06 - 7.01 (m, 4 H), 7.00 - 6.97 (m, 1 H), 6.97 - 6.92 (m, 1 H), 2.78 (ABq, *J* = 7.1, 6.8, Hz, 2H), 2.03 (s, 3 H), 1.98 (s, 3 H), 1.81 (s, 3 H).

^{13}C NMR (100 MHz, C_6D_6): δ 142.5, 137.5, 137.3, 137.0, 136.1, 135.9, 130.6, 130.2, 129.4, 128.3, 128.0, 127.2, 126.4, 125.8, 49.6, 20.1, 14.7, 14.3.

HRMS (ESI, m/z, [M+H]$^+$): 261.16378 (calculated), 261.16412(found).

1-(2,4-Dimethyl-5-(o-tolyl)cyclopenta-1,4-dien-1-yl)-2-methoxybenzene (2.83r)



2.83r

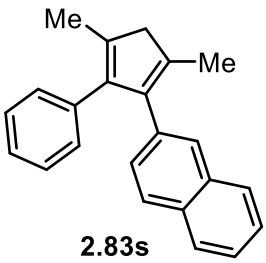
Following the general procedure **A** or **B**, starting from **2.82r** (87.0 mg, 0.3 mmol), **2.83r** (Procedure A; 9.5 mg, 0.033mmol, 11 %; Procedure B; 44.4 mg, 0.15 mmol, 51 %,) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (400 MHz, C_6D_6): δ 7.35-6.86 (m, 6H), 6.79 (td, *J* = 7.2, 1.2 Hz, 1H), 3.10 (br.s., 3H), 2.95-2.67 (m, 2H), 2.28 (s, 3H), 1.95 (s, 3H), 1.84 (s, 3H).

^{13}C NMR (100 MHz, C_6D_6): 157.4, 143.0, 137.8, 136.6, 135.1, 131.7, 129.8, 126.7, 125.1, 120.2, 110.7, 54.3, 49.2, 20.1, 14.7(br)

HRMS (ESI, m/z, [M+H]$^+$): 291.17394 (calculated), 291.17434(found).

2-(2,4-Dimethyl-5-phenylcyclopenta-1,4-dien-1-yl)naphthalene (2.83s)



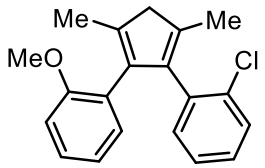
2.83s

Following the general procedure **B**, starting from **2.82s** (89.1 mg, 0.3 mmol), **2.83s** (29.6 mg, 0.1 mmol, 33 %) was obtained as yellow oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

^{1}H NMR (400 MHz, C_6D_6) δ: 8.03 (d, *J* = 8.4 Hz, 1 H), 7.61 (d, *J* = 7.7 Hz, 1 H), 7.54 (d, *J* = 7.7 Hz, 1 H), 7.27 (ddd, *J* = 8.4, 6.6, 1.8 Hz, 1 H), 7.22 - 7.17 (m, 3 H), 7.09 - 7.06 (m, 2 H), 6.89 - 6.86 (m, 2 H), 6.80 (tt, *J* = 7.5, 1.2 Hz, 1 H), 2.88 (ABq, *J* = 4.9, 4.7 Hz, 2H), 2.03 (s, 3 H), 1.75 (s, 3 H).
^{13}C NMR (100 MHz, C_6D_6): δ 143.3, 141.0, 138.0, 137.1, 136.1, 135.7, 134.2, 132.9, 129.3, 128.7, 128.4, 127.9, 127.8, 127.4, 126.8, 126.4, 125.9, 125.8, 125.6, 49.8, 14.7, 14.6.

HRMS (ESI, m/z, $[M]^+$): 296.15595 (calculated), 296.15582 (found).

1-Chloro-2-(5-(2-methoxyphenyl)-2,4-dimethylcyclopenta-1,4-dien-1-yl)benzene (2.83t)



2.83t

Following the general procedure **A or B**, starting from **2.82t** (93.0 mg, 0.3 mmol), **2.83t** (Procedure A; 7.7 mg, 0.025 mmol, 8 %; Procedure B; 47.5 mg, 0.15 mmol, 51 %,) was obtained as colorless oil after column chromatography (cyclohexane:CH_2Cl_2 = 100:5).

HRMS (ESI, m/z, $[M^{\cdot}]^+$): 310.11189 (calculated), 310.11301(found).

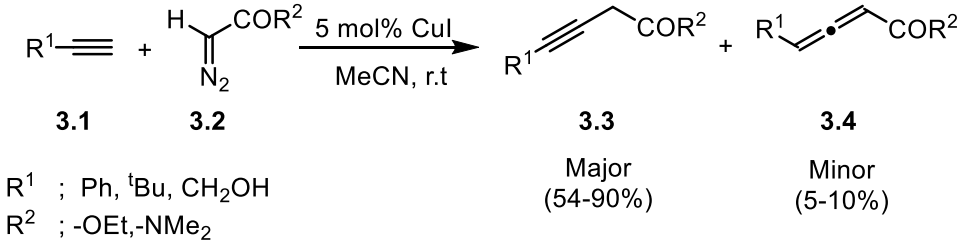
CHAPTER 3

Synthesis and Gold-Catalyzed Cycloisomerization Reactions of Difunctionalized Allenes

3.1 Copper-Catalyzed Cross-Coupling Reaction of Diazo Compounds

The rich chemistry of diazo compounds has been extensively explored in a variety of organic transformations and has found many applications in synthetic organic chemistry.[89] They can be dediazonized to highly reactive free carbene intermediates or metal carbenoids under transition metal catalysts.[90]

Recently, the use of diazo compounds as a coupling partner in transition metal-catalyzed cross-coupling reactions has attracted much interest. It is well known that the Cu(I)-catalyzed carbene transfer reaction of unsaturated compounds usually provide cyclopropanation products.[91] On the contrary, in 2004, Fu *et al*.[92] developed an efficient method for the synthesis of 3-alkynoates **3.3** by Cu(I)-catalyzed cross-coupling reaction of terminal alkynes with diazo compounds under mild reaction condition. They showed that 5 mol% CuI in the presence of CH_3CN was an efficient catalytic system to access 3-alkynoates **3.3** with high yield (Scheme 3.1). Although, in this coupling reaction, 3-allenoate derivatives **3.4** were formed as minor products, later on the method became important work for the synthesis of allene derivatives.



Scheme 3.1. Cu(I)-catalyzed cross-coupling reaction of alkynes with diazo compounds.

Inspired by this report, over the last five year enormous efforts have been devoted to the synthesis of allenes by Cu(I)-catalyzed cross-coupling reaction of alkynes and diazo compounds. [93]

[89] Rewievs; a) T. Ye, M. A. McKervey, *Chem. Rev*. **1994**, *94*, 1091-1160; b) M. P. Doyle, M. A. McKervey, T. Ye, *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds; Wiley-Interscience, New York;* **1998**; c) D. M. Hodgson, F. Y. T. M. Pierrard, P. A. Stupple, *Chem. Soc. Rev.* **2001**, 30, 50-61; d) X. Zhao, Y. Zhang, J. Wang, *Chem. Commun.* **2012**, *48*, 10162-10173; e) N. R. Candeias, P. Paterna, P. M. P. Gois, *Chem. Rev*. **2016**, *116*, 2937-2981.

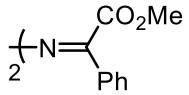
[90] Rewievs; a) H. M. L. Davies, R. E. J. Beckwith, *Chem. Rev*. **2003**, *103*, 2861-2903; b) M. P. Doyle, D. C. Forbes, *Chem. Rev*. **1998**, *98*, 911-935; c) H. M. L. Davies, J. R. Manning, *Nature* **2008**, *451*, 417-424; d) A. Padwa, M. D. Weingarten, *Chem. Rev*. **1996**, *96*, 223-269; e) P. M. P. Gois, C. A. M. Afonso, *Eur. J. Org. Chem.* **2004**, 3773-3788; f) M. P. Doyle, R. Duffy, M. Ratnikov, L.Zhou, *Chem. Rev*. **2010**, *110*, 704-724; g) S. F. Zhu, Q.L. Zhou, *Acc. Chem. Res.* **2012**, *45*, 1365-1377; h) H. M. L. Davies, D. Morton, *Chem. Soc. Rev.* ***2011***, *40*, 1857-1869.

[91] G. Bartoli, G. Bencivenni, R. Dalpozzo, *Synthesis*, **2014**, *46*, 979-1029.

[92] A. Suarez, G. C. Fu, *Angew. Chem. Int. Ed*. **2004**, *43*, 3580-3582.

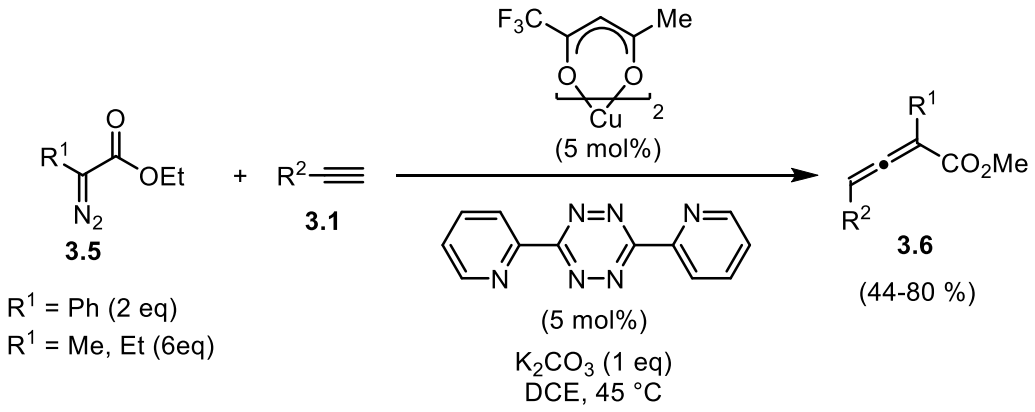
[93] a) Y. Tang, Q. Chen, X. Liu, G. Wang, L. Lin, X. Feng, **2015**, *54*, 9512-9516; b) K. Liu, C. Zhu, J. Min, S. Peng, G. Xu, J. Sun, *Angew. Chem. Int. Ed*, **2015**, *127*, 13154-13159; c) C. Wang, F. Ye, C. Wu, Y. Zhang, J. Wang, *J. Org. Chem*, **2015**, *80*, 8748-8757.

In 2011, Fox and co-workers[94] reported a one pot method directly 2,4-disubstituted allenoates **3.6** by coupling reaction of terminal alkynes **3.1** with α-substituted diazoesters **3.5** (Scheme 3.2). The success of this relied on using a base and an excess amount of the diazo compound, which were necessary for the isomerization of alkynoate to allenoate products. The desired 2,4-disubstituted allenoates **3.6** were obtained as major products with high selectivity over alkynoates when at least 2 eq of the α-diazoester and 1 eq of base were used. The effect of using an excess amount of the diazo compound was explained by isolating one of the side products which was characterized as azine.



Azine dimer

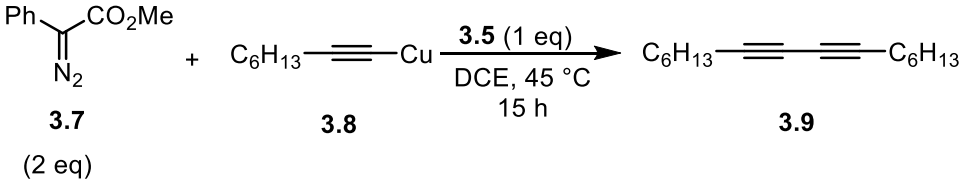
In order to probe the function of the azine, a control experiment was conducted by adding the azine into the reaction medium which gave rise to an isomerization of the alkynoate to the allenoate. This result showed that, the azine acted as a base and promoted this isomerization. Accordingly, it was that the addition of a base improved the selectivity of the one pot reaction. Furthermore, the substituents on the α-diazoester showed a strong influence on this reaction. A larger amount of the diazo compound (6 eq) was necessary when methyl- or ethyl-substituted diazo compounds were used, which were more susceptible to azine formation, whereas the addition of 2 eq of the phenyl-substituted diazo compound was sufficient.



Scheme 3.2. Cu(I)-catalyzed one pot synthesis of allenoates **3.6**.

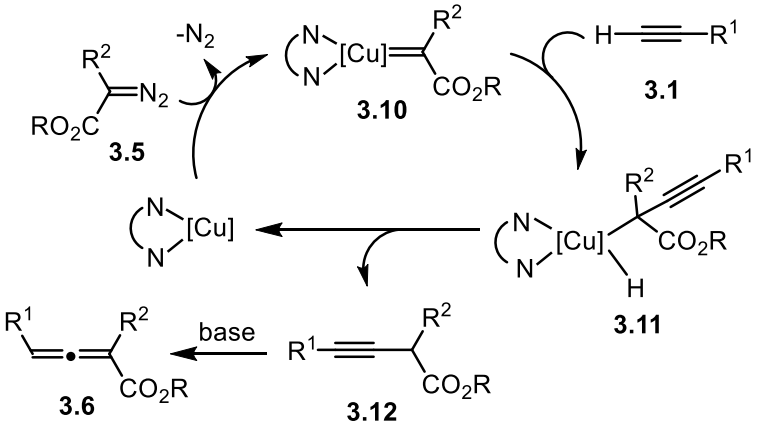
[94] M. Hassink, X. Liu, J. M. Fox, *Org. Lett*. **2011**, 13, 2388-2391.

A plausible reaction mechanism was proposed based on the results obtained from the reaction of copper acetylide **3.8** with diazo compound **3.7**. The acetylide was transformed into hexadeca-7,9-diyne **3.9** and neither allenoate nor alkynoate products were detected, which showed that the initial formation of the copper acetylide is not involved in the reaction pathway (Scheme 3.3).



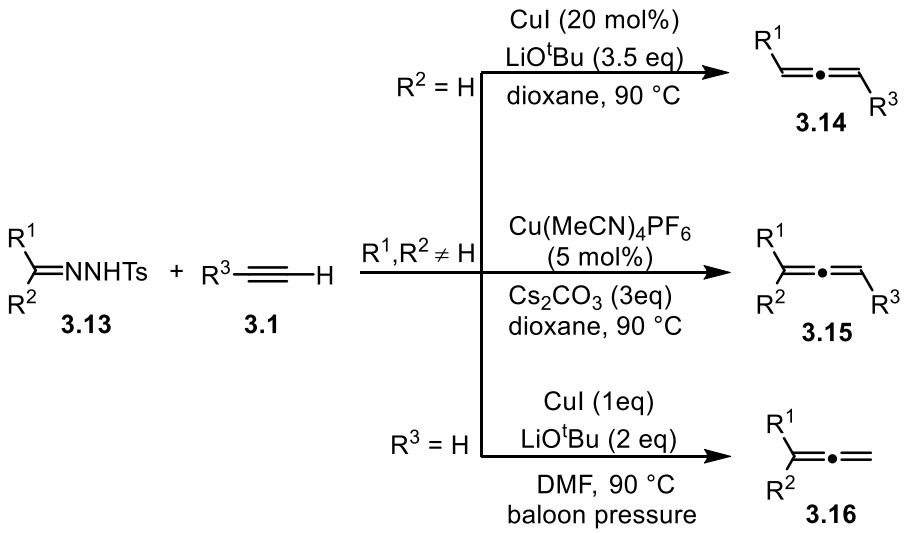
Scheme 3.3. Reaction of copper acetylide with diazo compound.

Therefore, the plausible reaction mechanism should involve the formation of a carbenoid intermediate **3.10** from the reaction of the Cu-chelate with α-diazoester **3.5**. Then, insertion of the copper carbenoid **3.10** into the C-H bond of the terminal acetylene **3.1** to generate the intermediate **3.11** and subsequent reductive elimination gives alkynoate **3.12** with the regeneration of the Cu-chelate. At the final stage, the alkynoate **3.12** is converted to allenoate **3.6** via base mediated isomerization (Scheme 3.4).



Scheme 3.4. Proposed mechanism of the Cu(I)-catalyzed one pot synthesis of allenoates.

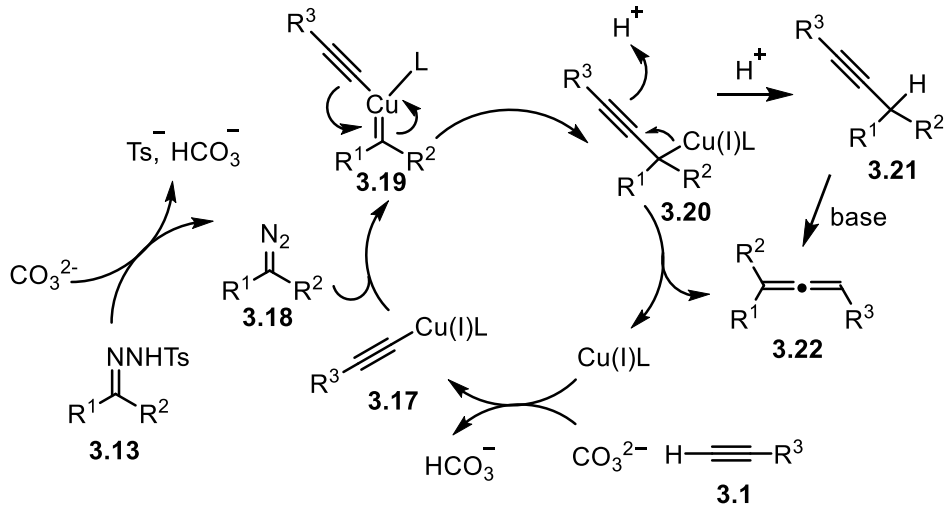
Furthermore, Wang *et al.*[95] developed an efficient protocol for the synthesis of allenes via Cu(I)-catalyzed coupling of alkynes with diazo compounds generated in situ from N-tosylhydrazones **3.13** in the presence of a base. Depending on whether N-tosylhydrazones derived from an aldehyde or a ketone were used, the Cu-catalyzed cross-coupling reaction with alkynes provides a convenient route for the synthesis of di- and trisubstituted allenes.[96a,b] The method was also extended to the synthesis of terminal allenes **3.16** by using ethyne as a coupling partner (Scheme 3.5).[96c]



Scheme 3.5. Cu(I)-catalyzed coupling of alkynes and N-tosylhydrazones.

Mechanistically, the reaction of Cu-acetylide **3.17** (formed from the terminal alkyne **3.1**) with diazo compound **3.18** (generated in situ from the N-tosylhydrazone **3.13**) provided the formation of Cu-carbene species **3.19**. Migratory insertion of the alkynyl group to the carbene, followed by protonation of intermediate **3.20**, resulted in the formation of allene **3.22** with the regeneration of the Cu(I) catalyst (Scheme 3.6). Alternatively, if the protonation occurs at the carbon atom attached to copper, the alkyne product **3.21** would be formed and isomerized to allene **3.22** with the assistance of a base (Scheme 3.6).

[95] a) M. L. Hossain, F. Ye, Y. Zhang, J. Wang, *J. Org. Chem.* **2013**, *78*, 1236-1241; b) Q. Xiao, Y. Xia, H. Li, Y. Zhang, J. Wang, *Angew. Chem. Int. Ed.* **2011**, *50*, 1114-1117; c) F. Ye, C. Wang, X. Ma, M. L. Hossain, Y. Xia, Y. Zhang, J. Wang, *J. Org. Chem.* **2015**, *80*, 647-652.

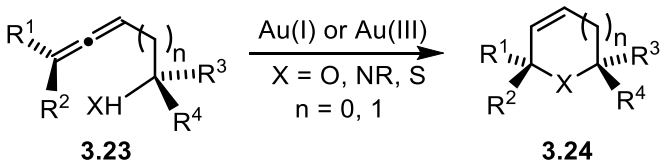


Scheme 3.6. Proposed mechanism of the Cu(I)-catalyzed coupling of alkynes and N-tosylhydrazones.

3.2 Gold-catalyzed Cycloisomerization Reactions of Allenes

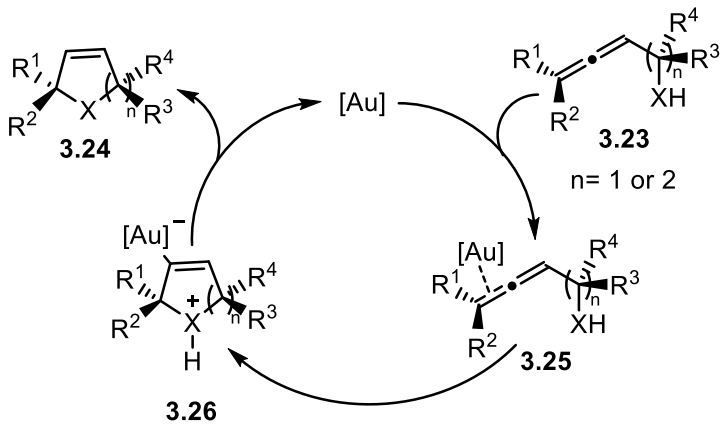
Heterocycles are an important class of compounds which are mostly used in pharmaceutical industry, and found as structural units in a variety of natural products. Among various methods for the synthesis of heterocycles, gold-catalyzed transformations of allenes play an important role in synthetic organic chemistry. Gold catalysts selectively activate allenes because of their soft and carbophilic character. The gold-catalyzed cycloisomerization of functionalized allenes is a valuable method for the synthesis of five- or six-membered oxygen-, nitrogen- and sulfur-containing heterocycles. These heterocycles can be obtained in a stereoselective manner either from chiral allenes by axis-to-center chirality transfer or from achiral allenes by using chiral gold catalysts.

In this area, Krause *et. al.*[64] reported highly regio- and stereo-selective gold-catalyzed cycloisomerization reactions of allenes **3.23** bearing nucleophilic substituents in the α- or β-position to afford the desired five- or six-membered heterocycles **3.24** (Scheme 3.7).



Scheme 3.7. Gold-catalyzed cycloisomerization of α- or β-heterosubstituted allenes.

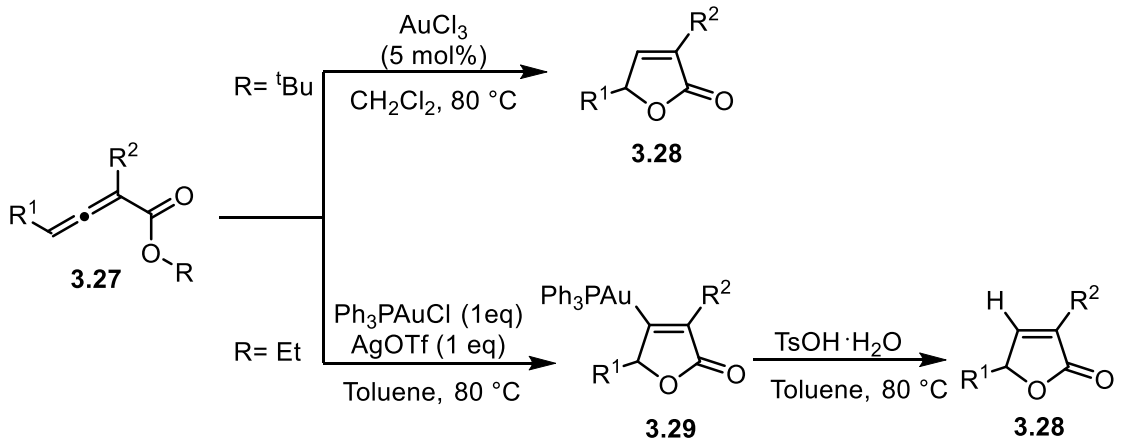
The mechanism of these transformations proceed through the coordination of the carbophilic gold catalyst to an allenic double bond to afford π-complex **3.25**, which undergoes a 5-endo-cyclization resulting in the formation of **3.26**. Subsequent protodeauration leads to the desired product **3.24** with regeneration of the gold catalyst (Scheme 3.8).



Scheme 3.8. Mechanism of the gold-catalyzed cycloisomerization of α- or β-heterosubstituted allenes.

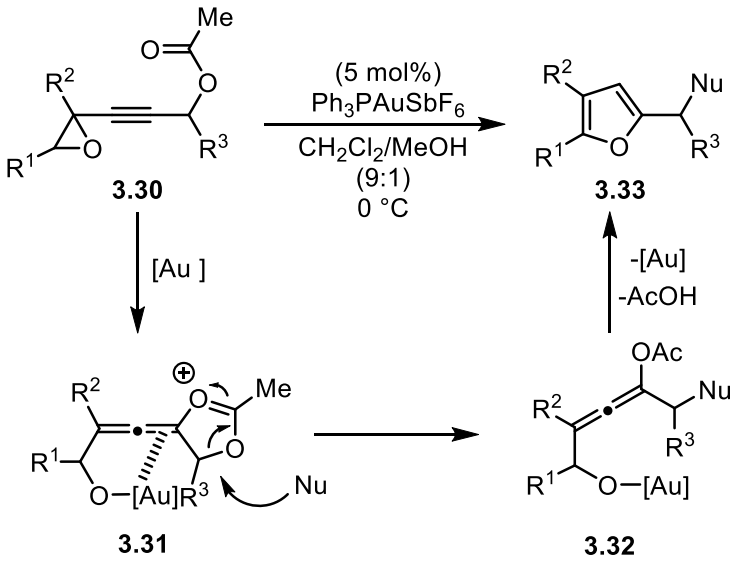
Allenoates **3.27** can also undergo a gold-catalyzed cycloisomerization to afford γ-lactones **3.28** or stable vinyl gold species **3.29** depending on the substituents in the ester moiety. Hammond *et. al.*[96] reported that cationic gold compounds can react with primary alkyl-substituted allenoates to form stable organogold complexes **3.29** which are converted to the desired γ -lactones **3.28** after treatment with acid. In contrast to this, Shin *et. al.*[97] reported that if the reaction was carried out with tertiary alkyl-substituted allenoates, γ -lactones **3.28** were formed directly (Scheme 3.9).

[96] L. P. Liu, B. Xu, M. S. Mashuta, G. B. Hammond, *J. Am. Chem. Soc*. **2008**, *130*, 17642-17643.
[97] J. E. Kang, E. S. Lee, S. Park. S. Shin, *Tetrahedron. Lett.* **2005**, *46*, 7431-7433.



Scheme 3.9. Gold-catalyzed cycloisomerization of allenoates.

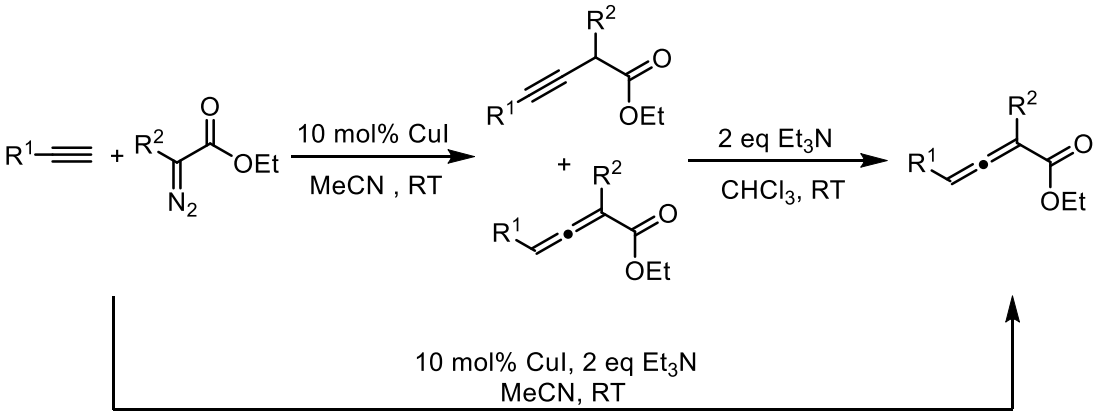
Although several methods have been reported for the gold-catalyzed cyclization of functionalized allenes, epoxy-functionalized allenes have not been explored well. Only in the gold-catalyzed cascade reaction of acetoxylated alkynyloxiranes **3.30**, oxirane-substituted allene intermediate were discussed.



Scheme 3.10. Gold(I)-catalyzed cycloisomerization of acyloxylated alkynyl oxiranes.

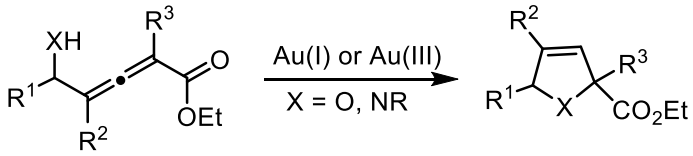
3.3 Definition of Research Problems

Due to their easy conversion to furans and the other heterocyclic compounds, functionalized allenes are of great importance in synthetic chemistry. The development of synthetic routes that allow the facile assembly of substituted allenes under mild conditions still remains an important objective. As a consequence, the development of practical synthetic approaches to access these target molecules is of major interest. Extensive investigations of transition metal-catalyzed reactions of diazo compounds have led to the development of valuable synthetic method. Although significant progress has been made in this field, the development of highly efficient catalytic transformations via transition metal carbene intermediates is still an important and attractive area in modern synthesis. In the first part of this study, we performed Cu(I)-catalyzed cross-coupling reaction of alkynes with diazo compounds for the synthesis of functionalized allenes (Scheme 3.11).



Scheme 3.11. Cu(I)-catalyzed cross-coupling reaction of alkynes with diazo compounds.

In the second part of this study, the gold-catalyzed cycloisomerization of hetero-substituted allenes have been described (Scheme 3.12). Because of their soft and carbophilic character, gold catalysts are particularly well suited for the selective activation of allenes in the presence of other reactive functionalities. The gold-catalyzed cyclization reactions of allenes by intramolecular nucleophilic attack has received more attention and allows the formation of C-O, C-N, and C-S bonds.



Scheme 3.12. Gold-catalyzed cycloisomerization of functionalized allenes.

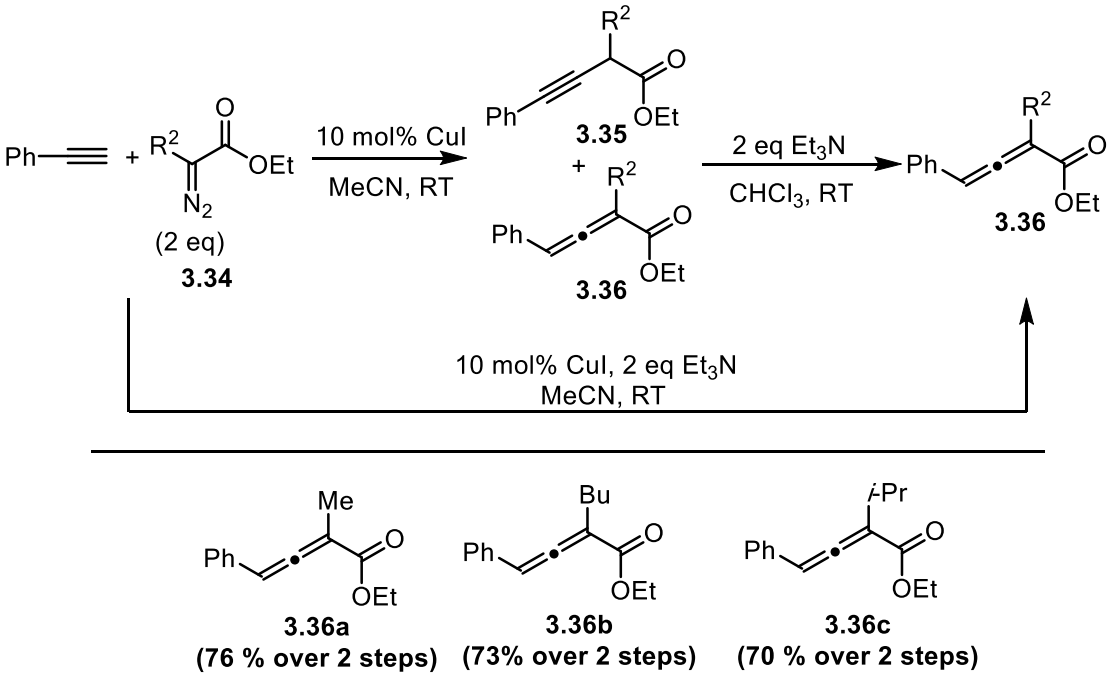
3.4 Results and Discussion

3.4.1 Synthesis of Substrates

3.4.1.1 Synthesis of Tetrasubstituted Hydroxyallenoates

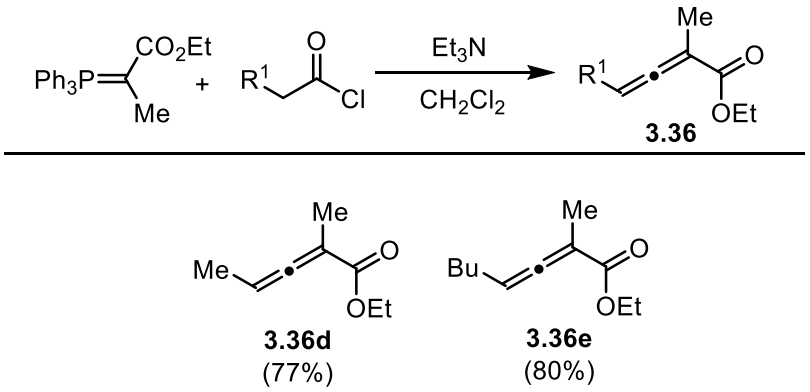
The 2,4-disubstituted allenoates **3.36a-c** were synthesized by Cu(I)-catalyzed cross-coupling reaction of terminal alkynes with α-diazoesters according to slightly modified literature condition.[79] Based on the original procedure, when a 1:1-mixture of terminal alkyne and ethyl diazoacetate is subjected to the Cu(I)-catalyzed cross-coupling reaction in the absence of a base, the formation of the 3-alkynoate would be favored over the formation of the 3-allenoate. On the other hand, Fox *et al* described that the use of diazo compounds in excess amounts in the presence of a base would bring about the isomerization of alkynoates to allenoates.

Accordingly, application of Fu`s Cu(I)-catalyzed cross-coupling procedure for the reaction of phenyl acetylene and α-methyl-α-diazoester (1.1 eq, **3.34)** in the presence of 10 mol% CuI in CH_3CN at room temperature afforded predominantly alkynoate **3.35a** and allenoate **3.36a** in a ratio of 9:1 in 66% combined yield, which could not be separated by column chromatography. Increasing the amount of α-methyl-α-diazoester to 1.5 eq or 2.0 eq had no influence on the product distribution, albeit improved the combined yields (79 and 85%, respectively). Finally, addition of 2 eq of triethylamine into the reaction medium, increased the selectivity of the process in the favor of allenoate **3.36a** and only small amount of alkynoate **3.35a** was observed. A further treatment of this mixture in the presence of 2 eq triethylamine in chloroform, led to complete disappearance of **3.35a** and thus the allenoate **3.36a** could be isolated in pure form in 90% yield. The allenoates **3.36b** and **3.36c** were also synthesized according to the same procedure (Scheme 3.13).



Scheme 3.13. Synthesis of allenoates **3.36a-c**.

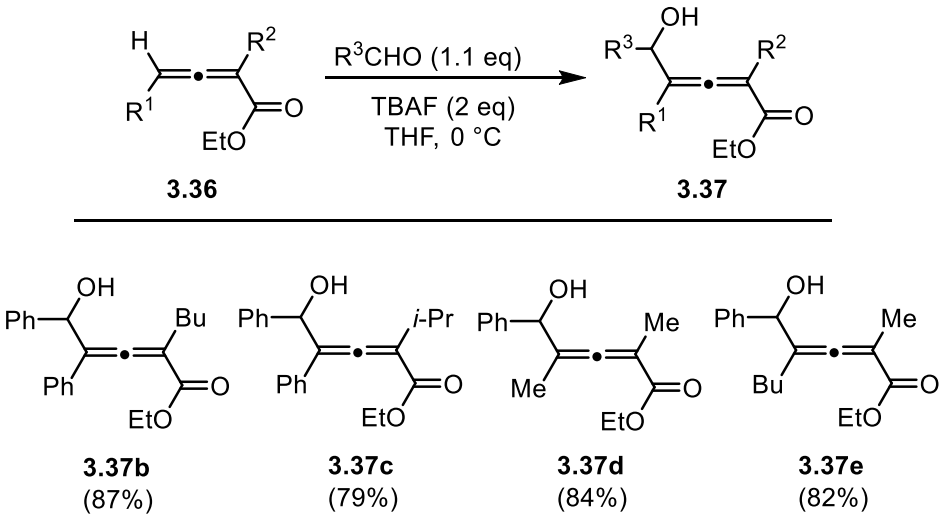
The allenoates **3.36d** and **3.36e** were synthesized according to the literature procedure by Wittig reaction of acyl chlorides in good yields (Scheme 3.14).[98]



Scheme 3.14. Synthesis of allenoates **3.36d-e**.

[98] R. W. Lang, H. J. Hansen, *Org. Synth.* **1990**, *7*, 232-236.

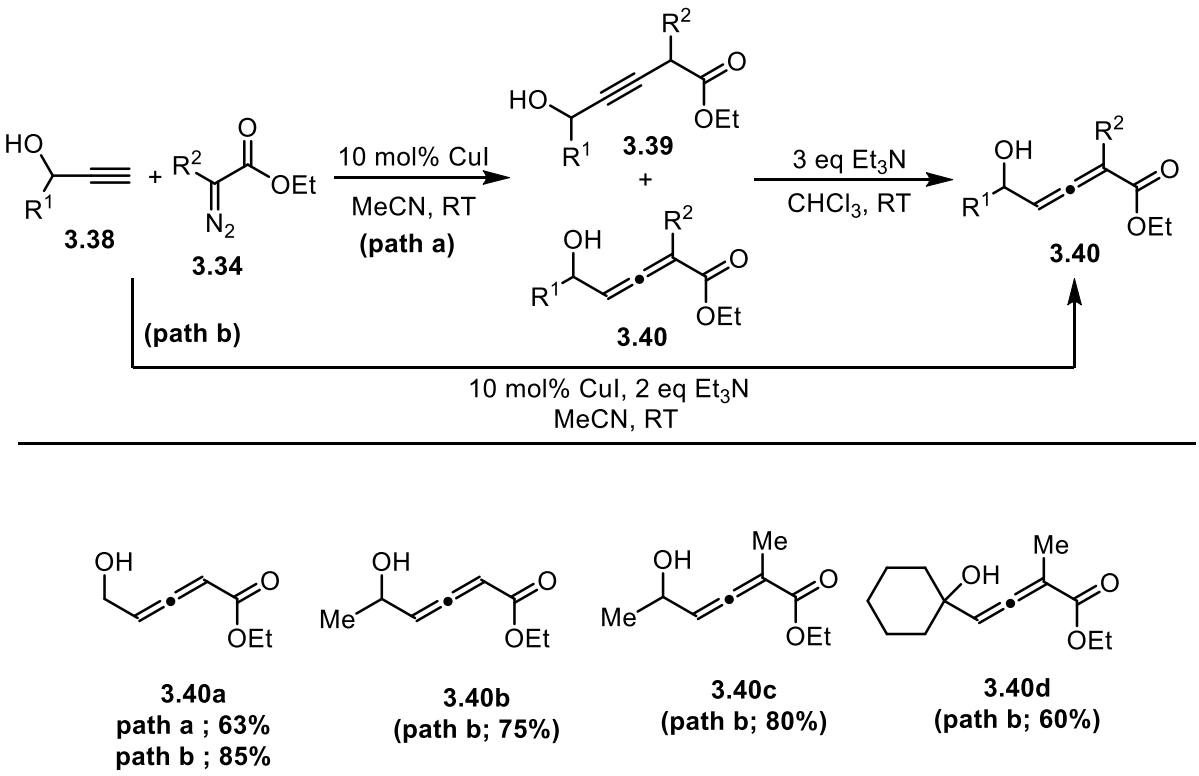
The tetrasubstituted allenes **3.37b-e** were synthesized from trisubstituted allenoates **3.36b-e**, which bear a γ-hydrogen at the allenic carbon.[99] The allenes **3.37b-e** were obtained in good yields by aldol reaction of allenoates **3.36b-e** with aldehydes in the presence of TBAF (Scheme 3.15).



Scheme 3.15. Synthesis of tetrasubstituted allenes **3.37b-e**.

Furthermore, for the synthesis of di- and trisubstituted allenoates **3.40a-d**, propargyl alcohols **3.38** were subjected to the Cu(I)-catalyzed cross-coupling reaction with diazo compounds **3.34** (Scheme 3.16). The coupling reaction of ethyl diazoacetate with propargyl alcohol, gave alkynoate **3.39a** as a major product with small amount of the desired allene **3.40a** (<10%) in 16 h (70% combined yield). Subsequent treatment of the isolated mixture with triethylamine at room temperature in chloroform gave the desired allene **3.40a** in 90% yield after 16 h. Alternatively, direct addition of 2 eq triethylamine into the reaction medium, provided a one pot access to desired allene **3.40a** in 85% yield. Di- and trisubstituted allenoates **3.40b-d** were also synthesized according to the same procedure.

[99] B. Xu, G. B. Hammond, *Angew. Chem. Int. Ed.* **2008**, *47*, 689-692.

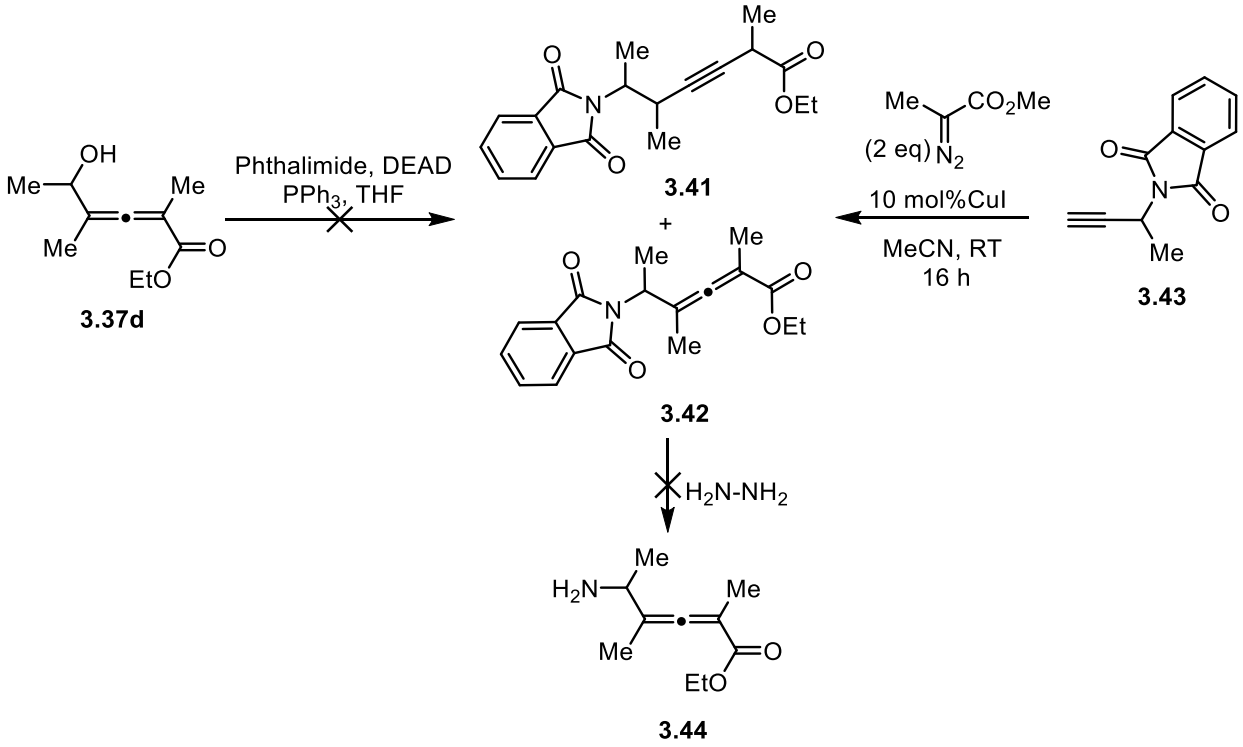


Scheme 3.16. Synthesis of di- and trisubstituted allenes **3.40a-d.**

3.4.1.2 Synthesis of Amino-functionalized Allenoates

Our initial attempts for the synthesis of amino-functionalized allenoate **3.44** from alkoxy-functionalized allenoate **3.37d** by Mitsunobu reaction[100] was disappointing, resulting in the decomposition of the starting material at the first stage of the method which involved treatment of **3.37d** with DEAD, PPh_3, and phthalimide. Therefore, we tried to synthesize the allene **3.42** by applying the Cu(I)-catalyzed cross-coupling condition to N-protected amine **3.43**. Reaction with α-methyl-α-diazoester afforded allene **3.42**. Reaction together with alkynoate **3.41** (10:3). Unfortunately, attempts for the phthalimide deprotection with hydrazine hydrate to obtain allene **3.43** resulted in decomposition of starting material (Scheme 3.17).

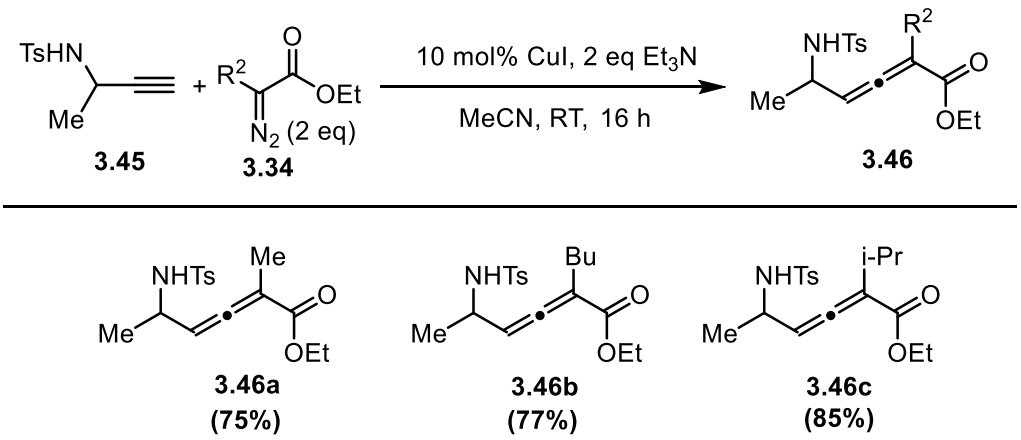
[100] B. Gockel, Dissertation, Dortmund University of Technology, **2006**.



Scheme 3.17. Attempts for the synthesis of allene **3.44**.

Then, we tested whether the Cu(I)-catalyzed cross-coupling method could be applied to propargyl amines for the synthesis of the amino-functionalized allenoates **3.46**. The N-protected propargyl amine **3.45** was synthesized from the corresponding propargyl alcohol and subjected to the Cu(I)-catalyzed cross-coupling reaction in the presence of a base.

The treatment of N-protected propargyl amine **3.45** with of α-methyl-α-diazoester **3.34a** under our standard condition afforded allene **3.46a** in 75% yield after 16 h. The method was also effective in the synthesis of α-butyl- and α-isopropyl-substituted diazoesters and allenes **3.46b** and **3.46c** were obtained in good yields (**3.46b**, 77%; **3.46c**, 85%) (Scheme 3.18).



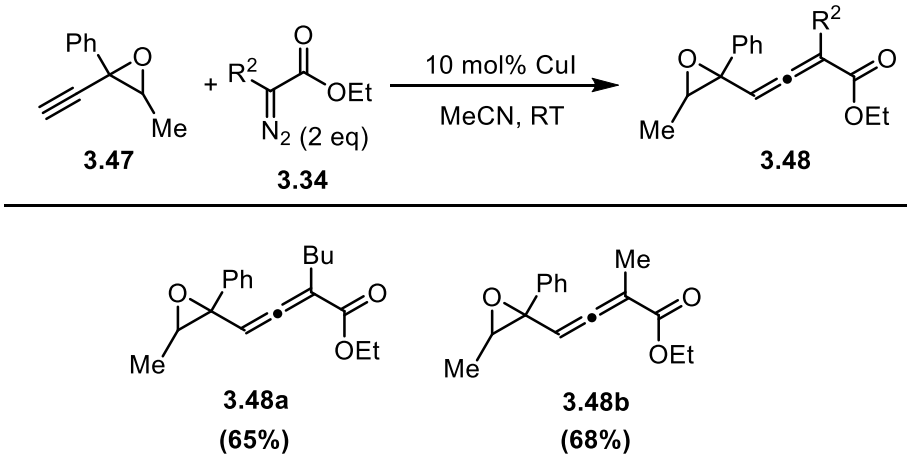
Scheme 3.18. Synthesis of amino-functionalized allenoates **3.46a-c.**

3.4.1.3 Synthesis of Allenyl Oxiranes

For the scope of the method, the study was extended for the synthesis of epoxy-functionalized allenes. Although several methods have been reported for the functionalization of allenes, epoxy-functionalized allenes have not been explored well and only few examples have been revealed in the literature.[101] Therefore, the development of synthetic routes for epoxy-functionalized allenes, which are also found in nature[102], would be highly valuable.

The Cu(I)-catalyzed cross-coupling reaction of propargylic oxirane **3.47** with α-methyl-α-diazoester **3.34a** led to the formation of corresponding epoxy-functionalized allene **3.48a** in 65% yield. Interestingly, the method could also be applied in the absence of a base and no alkynoate product formation was observed. Allene **3.34b** was also synthesized in 68% according to the same procedure by using α-butyl-α-diazoester **3.34b** (Scheme 3.19).

[101] M. Sasaki, Y. Kondo, T. Moro-ishi, M. Kawahata, K. Yamaguchi, *Org. Lett*. **2015**, *17*, 1280-1283.
[102] C. J. Tang, Y. Wu, *Tetrahedron* **2007**, *63*, 4887-4906.



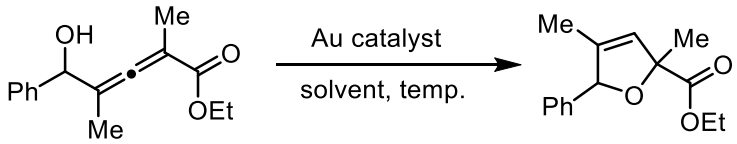
Scheme 3.19. Synthesis of allenyl oxiranes **3.48**.

3.4.2 Gold-Catalyzed Cycloisomerization of Functionalized Allenes

In order to optimize the reaction conditions, tetrasubstituted hydroxyallenoate **3.37d** was treated with various gold catalysts in different solvents and at varying temperatures (Table 3.1). Treatment of allene **3.37d** with 10 mol% of $AuCl_3$ in DCM at room temperature afforded 2,5-dihydrofuran **3.49a** in 55% yield after 2 days (Table 3.1, entry 1). Similarly, the use of 10 mol% of $AuBr_3$ gave slightly higher yield of **3.49a** (67%) after 2 days (Table 3.1, entry 2). When the same reaction was carried out in diethyl ether, the desired product could be obtained in 56% yield within 2 days (Table 3.1, entry 3). Only trace amounts of the product were produced when the reaction was carried out in THF at room temperature (Table 3.1, entry 4). A complete conversion was achieved with 66% yield at an elevated temperature (60 °C) after 30 min (Table 3.1, entry 5). Cationic gold complexes exhibited better catalytic activities. Treatment of allene **3.37d** with 5 mol% of $Ph_3PAuCl/AgOTf$ in DCM gave the desired product in 78% yield after 3 h at room temperature (Table 3.1, entry 6). A comparable result was obtained when the reaction was carried out in toluene which gave the **3.49a** in 80% yield after 3h (Table 3.1, entry 7). Changing the silver salt to $AgBF_4$ did not affect the reaction but using $AgSbF_6$ decreased the reaction time to 1 h and provided 2,5-dihydrofuran carboxylate **3.49a** in a yield of 83% (Table 3.1, entries 8-9). Increasing the temperature to 50 °C accelerated the reaction considerably (15 min) and gave a slightly higher yield (90%) (Table 3.1, entry 10). The highest yield was achieved when the reaction was carried out by using $Ph_3PAuCl/AgSbF_6$ in toluene at 70 °C, which gave the desired product **3.49a** in excellent yield (95%) after only 3 min of reaction time (Table 3.1, entry 11). The effect of the catalyst loading on the reaction duration and yield was also examined. The amount of catalyst could be reduced to 2

mol% which only increased the reaction time to 25 min for complete conversion and did not cause a significant decrease of the yield (92%) (Table 3.1, entry 12). Not surprisingly, neither Ph_3PAuCl nor $AgSbF_6$ alone catalyzed the reaction. (Table 3.1, entries 13-14).

Table 3.1 Optimization of the gold-catalyzed cycloisomerization of **3.37d**[a]



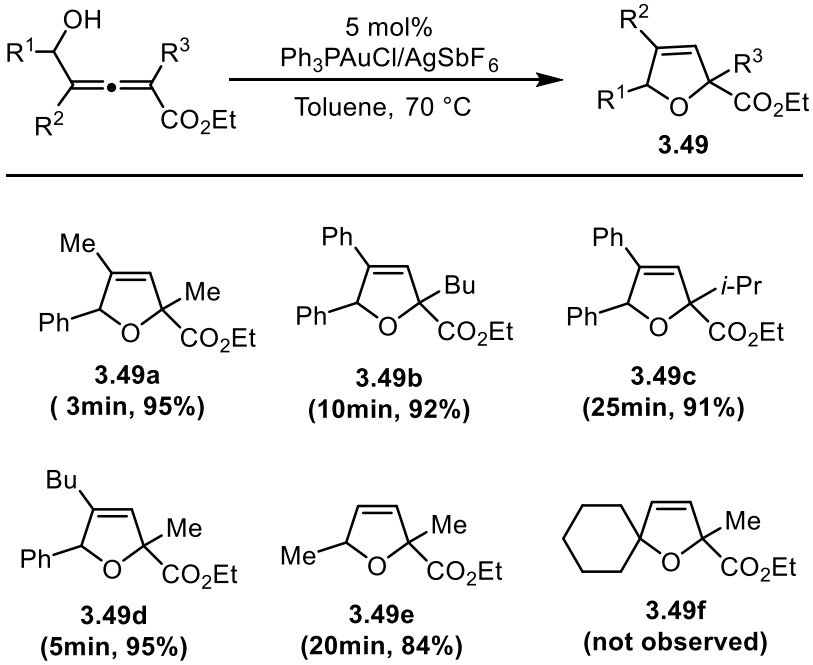
3.37d **3.49a**

Entry	Catalyst	Cat.[%]	Solvent	Temp[°C]	Time	Yield[b]
1	$AuCl_3$	10	DCM	RT	2 d	55
2	$AuBr_3$	10	DCM	RT	2 d	67
3	$AuBr_3$	10	Et_2O	RT	2 d	56
4	$AuBr_3$	10	THF	RT	1 d	trace
5	$AuBr_3$	10	THF	60	30 min	66
6	Ph_3PAuCl/ AgOTf	5	DCM	RT	3 h	78
7	Ph_3PAuCl/ AgOTf	5	toluene	RT	3 h	80
8	Ph_3PAuCl/ $AgBF_4$	5	toluene	RT	3 h	73
9	$Ph_3PAuCl/AgSbF_6$	5	toluene	RT	1 h	83
10	$Ph_3PAuCl/AgSbF_6$	5	toluene	50	15 min	90
11	$Ph_3PAuCl/AgSbF_6$	5	toluene	70	3 min	95
12	$Ph_3PAuCl/AgSbF_6$	2	toluene	70	25 min	92
13	Ph_3PAuCl	5	toluene	70	1 d	-[c]
14	$AgSbF_6$	5	toluene	70	1 d	-[c]

[a] The reaction was carried out using 0.3 mmol of **3.37d** and in 5.0 mL of solvent under nitrogen. [b] Isolated yield. [c] No conversion.

With the optimized conditions in hand, the scope of the gold-catalyzed cycloisomerization was investigated. The hydroxyallenoates were converted to the corresponding 2,5-dihydrofuran carboxylate derivatives **3.49a-e** in excellent yields (91-95%), (Scheme 3.20). The reactions were generally completed within 3 to 20 min depending on the size of the substituents. Varying the substituents in the R^3 position from methyl (**3.37d**), butyl (**3.37b**) to isopropyl (**3.37c**), the reaction required slightly longer reaction time to achieve complete conversion but the yields were still

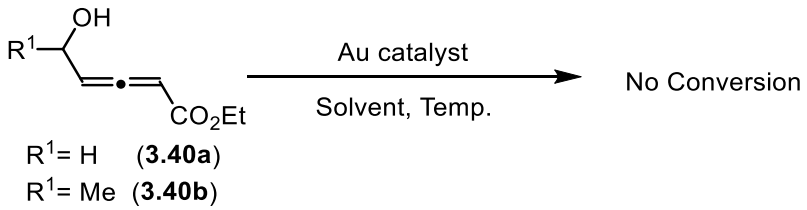
excellent (**3.49b**, 92%; **3.49c**, 91%). The method was also suitable for trisubstituted allene **3.40c** providing the desired furan **3.49e** in 84% yield after 20 min reaction time. The attempts for the cycloisomerization of the cyclohexyl-substituted allene **3.40d** resulted in the formation of a complex product mixture. It is important to note that when the reaction was conducted with diastereomerically enriched allene **3.37b (**90:10) complete axis-to-center chirality transfer was observed and the product **3.49d** was obtained diasteroselectively (90:10).



Scheme 3.20. Scope of the gold-catalyzed cycloisomerization.

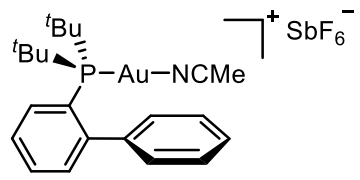
However, under the optimized reaction conditions, the gold-catalyzed cycloisomerization reaction of disubstituted hydroxyallene esters **3.40a** and **3.40b** did not give the corresponding dihydrofuran derivatives and resulted in the formation of complex product mixtures. Various gold catalysts in different solvents were tested (Table 3.2). Treatment of these compounds with 10 mol% AuCl in DCM, THF or toluene at various temperatures did not afford any conversion even after 5 d reaction time (Table 3.2, entries 1-3,10,11). Employment of Au(III) salts such as $AuCl_3$ or $AuBr_3$ under various conditions also failed to catalyze the reaction (Table 3.2, entries 4-9, 12-14). Addition of 2,2′-bipyridine, which may activate the allene by partial deprotonation, also did not afford any conversion (Table 3.2, entries 15-16). Furthermore, the use of cationic gold catalysts PPh_3AuNTf_2 and **A** did not show any catalytic activity even at a pro-longed reaction time (Table 3.2, entries 17-19).

Table 3.2 Attempt to optimize gold-catalyzed cycloisomerization of **3.40a** [a]



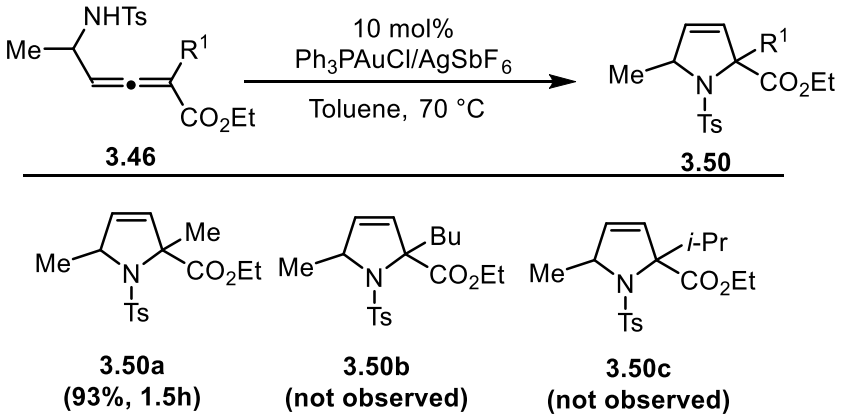
Entry	Compounds	Catalyst	Cat. [%]	Solvent	Temp	Time	Yield[b]
1	**3.40a**	AuCl	10	DCM	RT	5d	-
2	**3.40a**	AuCl	10	THF	60	2d	-
3	**3.40a**	AuCl	10	toluene	75	2d	-
4	**3.40a**	$AuCl_3$	10	DCM	RT	2d	-
5	**3.40a**	$AuCl_3$	10	DCM	40	1d	-
6	**3.40a**	$AuCl_3$	10	THF	RT	2d	-
7	**3.40a**	$AuBr_3$	10	DCM	RT	1d	-
8	**3.40a**	$AuBr_3$	10	THF	50	1d	-
9	**3.40a**	$AuBr_3$	10	toluene	70	1d	-
10	**3.40b**	AuCl	10	DCM	RT	5d	-
11	**3.40b**	AuCl	10	toluene	75	2d	-
12	**3.40b**	$AuCl_3$	10	DCM	RT	2d	-
13	**3.40b**	$AuBr_3$	10	DCM	RT	1d	-
14	**3.40b**	$AuBr_3$	10	toluene	70	1d	-
15	**3.40a**	$AuCl_3$/2,2′-bipyridine	10	DCM	RT	1d	-
16	**3.40a**	$AuBr_3$/2,2′-biyridine	10	DCM	RT	2d	-
17	**3.40a**	$Ph_3PAuNTf_2$	5	DCM	RT	2d	-
18	**3.40a**	$Ph_3PAuNTf2$	5	THF	50	2d	-
19	**3.40a**	**A**	5	DCM	RT	2d	-

[a] The reaction was carried out using 0.3 mmol of **3.40** and in 5.0 mL of solvent under nitrogen. [b] No conversion.



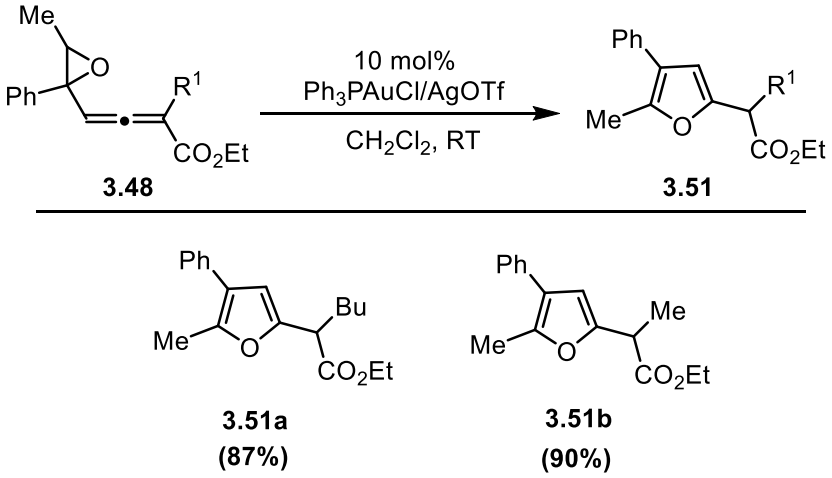
(A)

Furthermore, when the α-amino functionalized allene **3.46a** was subjected to the optimized reaction conditions, the desired 2,5-dihydropyrrole **3.50a** was obtained in excellent yield, 93%, after 1.5 h. Interestingly, the method did not tolerate substituents in the R^1 position. The reactions of the allenes **3.46b** (R^1 = Bu) and **3.46c** (R^1 = *i*-Pr) resulted in the formation of complex product mixtures.



Scheme 3.21. Gold-catalyzed cycloisomerization of amino-functionalized allenoates **3.46**.

In addition to this, compared to Au(I)-catalyzed cycloisomerization reactions of hydroxy- and amino-functionalized allenes, the cycloisomerization of epoxy-functionalized derivatives take place under milder conditions. When the epoxy-functionalized allene **3.48a** was treated with 10 mol% $Ph_3PAuCl/AgSbF_6$ in DCM at room temperature the furan **3.51a** was obtained in good yield (87%) after only 5 min of reaction time (Scheme 3.22). The method was also suitable for allene **3.48b** providing the furan **3.51b** in 90% yield after 5 min reaction time. Mechanistically, the reaction should proceed through the activation of the allene by the coordination of the carbophilic gold catalyst to an allenic double bond. Nucleophilic attack of the epoxide oxygen at the central allenic carbon atom followed by a cyclization-elimination process affords the furan **3.51** with the regeneration of the gold catalyst.



Scheme 3.22. Gold-catalyzed cycloisomerization of α-epoxy functionalized allene **3.48**

3.5 Conclusion

In the first part of this study, we have developed the Cu(I)-catalyzed cross-coupling reactions of alkynes**,** propargyl alcohols, propargyl amines and propargyl epoxides with diazo compounds. The reactions tolerate diverse functionalities and the desired functionalized allenes were obtained in good yields. The synthesized allene derivatives were subjected to gold-catalyzed cycloisomerization reactions to afford synthetically valuable heterocycles depending on the substituents on the nucleophilic moiety.

3.6 Experimental

General Remarks:

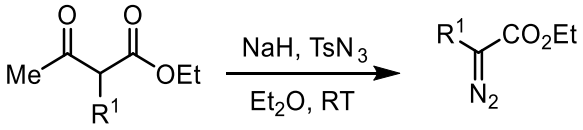
Unless otherwise stated, all reactions were carried out in heat dried glassware under nitrogen atmosphere. Gold and silver salts were purchased from Sigma-Aldrich, Chempur and Fluorochem. 1,2-Dichloroethane, dichloromethane, toluene, and tetrahydrofuran were dried with a solvent purification system MBraun SPS-800. Column chromatography was carried out with silica gel 60 Å (0.040-0.063), which purchased from Macherey-Nagel. Reactions were monitored by thin layer chromatography on Silica Gel 60 F254 from Merck.

Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a Bruker DPX300 spectrometer operating at 300 MHz for proton and 75 MHz for carbon nuclei, a Bruker DRX400 spectrometer operating at 400 MHz for proton and 100 MHz for carbon nuclei, a Bruker DRX500 and a Varian Inova 500 spectrometer operating at 500 MHz for proton and 125 MHz for carbon nuclei. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$: δ=7.26 for protons, δ=77.16 for carbon atoms; C_6H_6: δ=7.16 for protons, δ=128.06 for carbon atoms). The signals of the major component of a product mixture are marked with an asterisk (*).

Low resolution mass spectra were recorded with a Thermo TSQ spectrometer. High resolution mass spectrometry (ESI) was performed on an Thermo LTQ Orbitrap coupled with a Accela HPLC system.

3.6.1 Synthesis of Diazoesters

3.6.1.1 General Procedure for Synthesis of α-alkyl-α-diazoester 3.34a-c

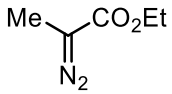


3.53 **3.34**

The **3.34** was synthesized according to literature procedure.[103] A solution of corresponding acetoacetate (1.0 eq) in diethylether (1 mL/3 mmol) was added dropwise to a suspension of NaH (2.0 eq) in dry Et_2O (1 mL/1 mmol) at room temperature. The solution was cooled in water bath and TsN_3 (1.2 eq) was added dropwise. The reaction mixture was diluted with Et_2O (1 mL/1 mmol) and stirred for 45 min. The precipitates were filtered over celite by washing with Et_2O and the filtrate was extracted with water. The organic layer was dried over $MgSO_4$ and concentrated under vacuum without applying heat. If necessary, the desired compound can be purified by column chromatography (pentane/Et_2O = 8/1).

[103] S. Bachman, D. Fielenbach, K. A. Jorgensen, *Org. Biomol. Chem.* **2004**, 2, 3044-3049.

Synthesis of α-methyl-α-diazoester 3.34a

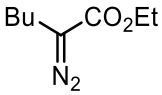


3.34a

Following the general procedure **3.6.1.1**, α-methyl-α-diazoester **3.34a** was synthesized starting from commercially available ethyl 2-methylacetoacetate (50 mmol, 7.21 g). The crude product was purified by column chromatography (pentane:Et_2O = 8:1) to afford α-methyl-α-diazoester **3.34a** (3.46 g, 27 mmol, %54) as a yellow oil.
Spectral data agreed with previous data.[103]

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.20 (q, *J* = 7.3 Hz, 2 H), 1.94 (s, 3 H), 1.28 - 1.23 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 168.1, 60.9, 14.6, 8.5.

Synthesis of α-butyl-α-diazoester 3.34b

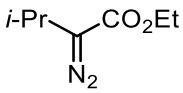


3.34b

Following the general procedure **3.6.1.1**, α-butyl-α-diazoester **3.34b** was synthesized starting from ethyl 2-butylacetoacetate (30 mmol, 5.7 g). The crude product was purified by column chromatography (pentane:Et_2O = 8:1) to afford α-butyl-α-diazoester **3.34b** (3.57 g, 21 mmol, 70 %) as a yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.20 (q, *J* = 7.1 Hz, 2 H), 2.29 (t, *J* = 7.5 Hz, 2 H), 1.51 - 1.44 (sept, *J* = 7.5Hz, 2 H), 1.41 - 1.32 (sept, *J* = 7.5Hz, 2 H), 1.26 (t, *J* = 7.1 Hz, 3 H), 0.92 (t, *J* = 7.3 Hz, 3 H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 167.7, 60.8, 29.8, 22.8, 22.0, 14.6, 13.8.

Synthesis of α-*iso*-propyl-α-diazoester 3.34c



3.34c

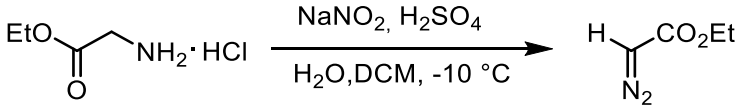
Following the general procedure **3.6.1.1**, α-*iso*-propyl-α-diazoester **3.34c** was synthesized starting from ethyl 2-isopropylacetoacetate (28 mmol, 4.8 g). The crude product was purified by column chromatography (pentane:Et_2O = 8:1) to afford α-*iso*-propyl-α-diazoester **3.34c** (2.34 g, 15 mmol, 53 %) as a yellow oil.

Spectral data agreed with previous data.[103]

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (q, *J* = 7.2 Hz, 2H), 2.74 (sept, *J* = 6.8 Hz, 1H), 1,26 (t, *J* = 7.2, 3H), 1.14 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 60.7, 29.8, 20.6, 14.6.

3.6.1.2 Synthesis of Ethyl diazoacetate 3.34d



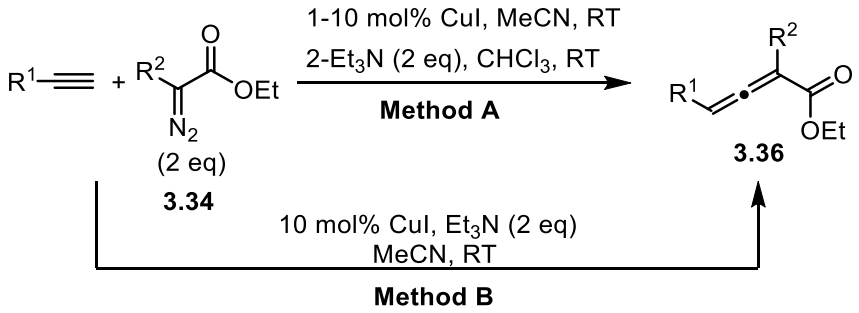
3.34d

Ethyl diazoacetate was synthesized according to the literature procedure.[104] Glycine ethyl ester hydrochloride (50 mmol, 7 g) was dissolved in water (15 mL) and dichloromethane (30 mL), and cooled to -10 °C. Aqueous sodium nitrite solution (1.15 eq, 4.43 M) was prepared and cooled to 0 °C in an ice bath, then was added to the solution of glycine ethyl ester hydrochloride. To this solution, 5% H_2SO_4 (4.6 mL) was added dropwise, and the solution was stirred for 10 min at -10 °C. The organic layer was poured into 5% sodium carbonate at 0 °C. The aqueous layer was extracted with dichloromethane, and the organic extracts were combined. Then, the combined solution was shaken thoroughly and the pH was checked to be ensure that it was alkaline. The solution was dried over $MgSO_4$ and concentrated under reduced pressure without applying heat. The product was obtained as a pale yellow oil (3.6 g, 32mmol, 64 %).

Spectral data agreed with previous data.[104]

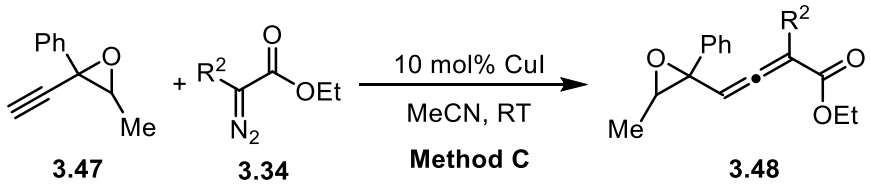
[104] S. A. Moore, D. E. G. Shuker, *J. Label. Compd. Radiopharm.* **2011**, *54*, 855-858.

3.6.2 General Procedure for Cu(I)-Catalyzed Cross-Coupling Reaction



Method A: To a stirred solution of corresponding alkyne (1 eq) in CH_3CN (3 mL/1 mmol) was added corresponding diazo compound (2 eq) and CuI (10 mol%). After stirring for 5 h at room temperature, the reaction mixture was directly filtrated over celite and washed with Et_2O. After removal of solvent, the residue was purified by column chromatography to give the mixture of corresponding 2,3-alkynoate and 2,3-allenoate. Then, the mixture diluted in $CHCl_3$ (3 mL/1 mmol) and Et_3N (3 eq) was added. After stirring for 12 h, the reaction mixture was concentrated under reduced pressure and purified by column chromatography to give the corresponding allene.

Method B: To a stirred solution of corresponding alkyne (1 eq) in dry CH_3CN (3 mL/1 mmol) was added corresponding diazo compound (2 eq), CuI (10 mol%) and Et_3N (2 eq) subsequently. After stirring for 12 h at room temperature, the reaction mixture directly filtrated over celite and washed with Et_2O. The solvents were removed reduced pressure. The residue was purified by column chromatography to give the corresponding allene.

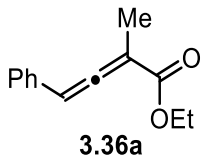


Method C: To a stirred solution of propargyl oxirane **3.47**[105] (1 eq) in dry CH_3CN (5 mL/1 mmol) was added corresponding diazo compound (2 eq). After stirring for 2 h at room temperature, the reaction mixture directly filtrated over celite and washed with Et_2O. The solvents were removed

[105] C. Gronniert, S. Kramer, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2012**, *134*, 828-831.

reduced pressure. The residue was purified by column chromatography (cyclohexane/NEt_3 (1 vol. %): EtOAc: 100/2) to give the corresponding allene.

Ethyl 2-methyl-4-phenylbuta-2,3-dienoate 3.36a

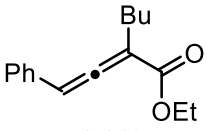


3.36a

Following the general procedure **3.6.2-Method A** using **3.34a** (2.56 g, 20 mmol), phenyl acetylene (1.02 g, 10 mmol), and CuI (190 mg, 10 mol%), a mixture of alkynoate **3.35a** and allenoate **3.36a** (4:1) was obtained (8 mmol, 85 % combined yield). Then, the mixture was diluted in $CHCl_3$ (24 ml) and Et_3N (3.3 mL, 24 mmol) was added to afford **3.36a** (1.31 g, 6.5 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 - 7.18 (m, 5 H), 6.46 (q, *J* = 2.9 Hz, 1 H), 4.20 (m, 2 H), 1.99 (d, *J* = 2.9 Hz, 3 H), 1.25 (t, *J* = 7.1 Hz, 3 H)
^{13}C NMR (75 MHz, $CDCl_3$): δ 212.4, 167.2, 132.6, 128.9, 127.7, 127.6, 127.4, 99.5, 97.3, 61.2, 15.2, 14.4.

Ethyl 2-butyl-4-phenylbuta-2,3-dienoate 3.36b

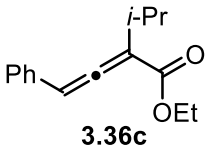


3.36b

Following the general procedure **3.6.2-Method A** using **3.34b** (3.40 g, 20 mmol), phenyl acetylene (1.02 g, 10 mmol), and CuI (190 mg, 10 mol%), a mixture of alkynoate **3.35b** and allenoate **3.36b** (4:1) was obtained (8.3 mmol, 83 % combined yield). Then, the mixture was diluted in $CHCl_3$ (18 mL) and Et_3N (3.42 mL, 24.9 mmol) was added to afford **3.36b** (1.83 g, 7.5 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 - 7.20 (m, 5 H), 6.51 (t, *J* = 2.9 Hz, 1 H), 4.24 - 4.15 (m, 2 H), 2.41 - 2.31 (m, 2 H), 1.51 - 1.29 (m, 4 H), 1.24 (t, *J* = 7.2 Hz, 3 H), 0.88(t, *J* = 7.2, 3 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 212.1, 166.9, 132.8, 128.9, 127.7, 127.3, 104.7, 98.4, 61.1, 30.3, 28.7, 22.5, 14.4, 14.0.

Ethyl 2-isopropyl-4-phenylbuta-2,3-dienoate 3.36c

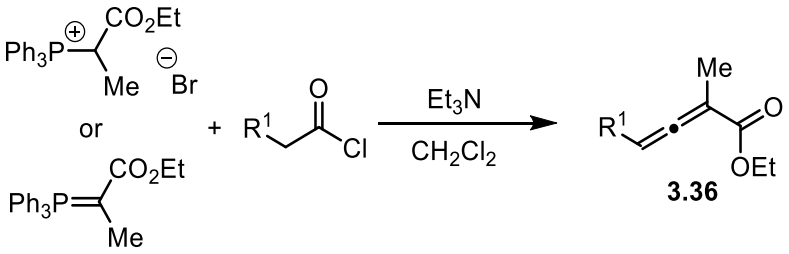


3.36c

Following the general procedure **3.6.2-Method A** using **3.34c** (2.1 g, 13.5 mmol), phenyl acetylene (685 mg, 6.7 mmol), and CuI (127.3 mg, 10 mol%), a mixture of alkynoate **3.35c** and allenoate **3.36c** (4:1) was obtained (6 mmol, 78 % yield). Then, the mixture was diluted in $CHCl_3$ (18 mL) and Et_3N (2.47 mL, 18 mmol) was added to afford **3.36c** (1.73 g, 7.5 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 - 7.19 (m, 5 H), 6.57 (d, *J* = 2.2 Hz, 1 H), 4.21 (dq, *J* = 2.4, 7.1 Hz, 2 H), 2.86 (dspt, *J* = 2.1 Hz, 1 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.13 (dd, *J* = 7.0, 8.1 Hz, 6 H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 210.9, 166.5, 132.8, 128.9, 127.7, 127.1, 111.4, 99.6, 61.1, 28.4, 22.4, 22.1, 14.4.

3.6.3 General Procedure for Synthesis of 3.36d-e



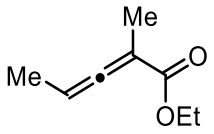
3.36

The 2,3-allenoates **3.36d-e** were prepared according to the literature procedure.[106]
The appropriate ylide or phosphonium salt (1 eq) was dissolved in dichloromethane (2 mL/1 mmol) and flushed with nitrogen. The yellow solution was cooled to 0 °C and triethylamine (1.3 eq) was added slowly. After 10 min, the solution of acyl chloride (1.1 eq) in dichloromethane (1 mL/1 mmol) was added dropwise to the vigorously stirred solution. The solution was allowed to warm RT. Progress of the reaction was monitored by TLC and approximately after 12 h, the mixture was evaporated under reduced pressure. The precipitate was removed by filtration over celite and the

[106] G. Chai, Z. Lu, C. Fu, S. Ma, *Adv. Synth. Catal*. **2009,** 351, 1946-1954.

filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (cyclohexane:EtOAc = 100:4) to afford 2,3-allenoates **3.36d-e**.

Ethyl 2-methylpenta-2,3-dienoate 3.36d

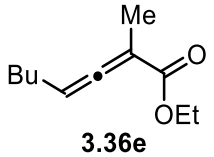


3.36d

Following the general procedure **3.6.3**, the reaction of [1-(ethoxycarbonyl)ethyl]-triphenylphosphonium bromide (17.7 g, 40 mmol), NEt_3 (7.25 mL, 5.3 g, 52 mmol), and propionyl chloride (3.85 mL, 4.07 g, 44 mmol) afforded **3.36d** (4.2 g, 30 mmol, 77%) as a yellow oil.
Spectral data agreed with previous data.[107]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45 - 5.37 (m, 1H), 4.17 (q, *J* = 7.0 Hz, 2 H), 1.84 (d, *J* = 3.0 Hz, 3 H), 1.73 (d, *J* = 7.3 Hz, 3 H), 1.26 (t, *J* = 7.0 Hz, 3 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 210.7, 168.1, 95.2, 88.6, 60.9, 15.4, 14.4, 13.4.

Ethyl 2-methylocta-2,3-dienoate 3.36e



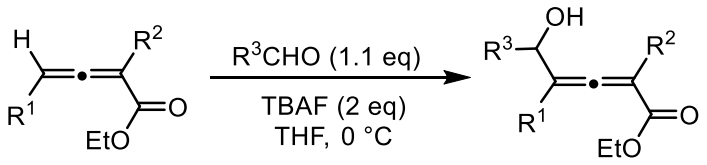
3.36e

Following the general procedure **3.6.3**, the reaction of ethyl(triphenylphosphoranylidene)propionate (11.6 g, 32 mmol), NEt_3 (7.25 mL, 5.3 g, 52 mmol), and hexanoyl chloride (4.92 mL, 4.74 g, 35.2 mmol) afforded **3.36e** (4.74 g, 26 mmol, 80%) as a yellow oil.
Spectral data agreed with previous data.[106]

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45 - 5.38 (m, 1 H), 4.21 - 4.11 (m, 2 H), 2.09 (q, *J* = 6.8 Hz, 2 H), 1.84 (d, *J* = 3.0 Hz, 3 H), 1.46 - 1.29 (m, 4 H), 1.25 (t, *J* = 7.2 Hz, 3 H), 0.88 (t, *J* = 7.2 Hz, 4 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 168.2, 95.6, 93.8, 60.9, 31.0, 27.7, 22.0, 15.4, 14.4, 13.9.

[107] P. Selig, W. Raven, *Org. Lett*. **2014,** 16, 5192-5195.

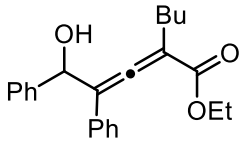
3.6.4 General Procedure for Synthesis of Tetrasubstituted Allenes 3.37b-e



3.36 **3.37**

The tetrasubstituted allenes **3.37b-e** were prepared according to the literature procedure.[100]
To a mixture of corresponding 2,3-allenoate **3.36** (1 eq) and THF (1 mL/1 mmol) at 0 °C, a solution of TBAF (2 eq, 1 M solution in THF) was added dropwise. The reaction mixture was stirred for 1,5 h at 0 °C. Then, aldehyde (1.15 eq) was added dropwise. Progress of the reaction was monitored by TLC and approximately after 3 h of stirring at 0 °C, the reaction mixture was quenched with saturated NH_4Cl solution and stirred for an additional 10 min at 0 °C. The resulting mixture was extracted with Et_2O, washed with brine, and dried over $MgSO_4$. The solvent was concentrated under reduced pressure and the crude product was purified by column chromatography (cyclohexane:EtOAc) to afford the allene **3.37**.

Ethyl 2-(3-hydroxy-2,3-diphenylprop-1-en-1-ylidene)hexanoate 3.37b



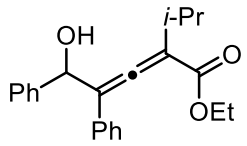
3.37b

Following the general procedure **3.6.4** using **3.36b** (1.22 g, 5 mmol), TBAF (10.0 mL, 10 mmol, 1 M solution in THF), and benzaldehyde (610.2 mg, 0.58 mL, 5.75 mmol), **3.37b** was obtained (1.4 g, 4 mmol, 87 %, *dr* = 48:52) after column chromatography (cyclohexane:EtOAc = 7:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 - 7.56 (m, 1 H), 7.54 - 7.49 (m, 1 H), 7.45 - 7.40 (m, 1 H), 7.38 - 7.20 (m, 7 H), 5.85* (s, 1 H), 5.79 (s, 1 H), 4.35 - 4.18 (m, 2 H), 2.41 - 2.35 (virt, m, 1 H), 2.33 - 2.17 (virt, m, 1 H), 1.57 - 1.43 (virt, m, 1 H), 1.40 - 1.33 (virt, m, 1 H), 1.33 - 1.24 (virt, m, 2 H), 1.34 (td, *J*= 7.2, 3.8 Hz, 3H), 0.89* (t, *J* = 7.3 Hz, 3 H), 0.85 (t, *J* = 7.3 Hz, 3 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1/210.3*, 167.0/166.9*, 141.6, 133.5/133.3*, 128.8/128.7* (d), 128.5, 128.4, 127.9, 127.4, 127.2, 126.7, 114.6/114.5*, 106.8/105.8*, 73.7/73.3*, 61.3/61.2*, 30.5/30.3*, 28.8/28.6*, 22.6/22.5*, 14.5/14.4*, 14.0/14.0*.

HRMS (ESI, m/z, $[M+H]^+$): 351.19547 (calculated), 351.19619 (found).

Ethyl 5-hydroxy-2-isopropyl-4,5-diphenylpenta-2,3-dienoate 3.37c



3.37c

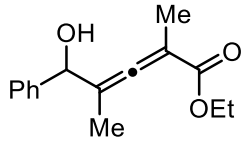
Following the general procedure **3.6.4** using **3.36c** (1.15 g, 5 mmol), TBAF (10.0 mL, 10 mmol, 1 M solution in THF), and benzaldehyde (610.2 mg, 0.63 mL, 5.75 mmol), the allene **3.37c** was obtained (1.3 g, 3.9 mmol, 79 %, *dr* = 48:52).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 - 7.56 (m, 1 H), 7.53 - 7.45 (m, 2 H), 7.40 - 7.27 (m, 7 H), 5.86 (s, 1 H), 5.82 (s, 1 H), 4.36 - 4.16 (m, 2 H), 2.84 (hept, *J* = 6.8 Hz,1 H), 2.71 (hept, *J* = 6.8 Hz,1 H), 1.35 (t, *J* = 7.2 Hz, 3 H), 1.17 (d, *J* = 6.8 Hz, 1.5 H), 1.11 (d, *J* = 6.8 Hz, 1.5 H), 1.04 (d, *J* = 6.8 Hz, 1.5 H), 0.82 (d, *J* = 6.8 Hz, 1.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2/209.3*, 166.6, 141.7/141.6*, 133.4/133.4*, 128.8/128.7*, 128.5/128.3*, 128.2/128.0*, 127.9/127.8*, 127.4/127.3*, 127.0/126.8*, 116.1/115.8*, 113.2/112.4*, 73.7/73.2*, 61.2/61.1*, 28.6/28.4*, 22.3/22.1*, 21.8, 14.4/14.4*

HRMS (ESI, m/z, $[M+H]^+$): 337.17982 (calculated), 337.18051 (found).

Ethyl 5-hydroxy-2,4-dimethyl-5-phenylpenta-2,3-dienoate 3.37d



3.37d

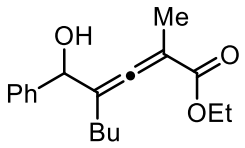
Following the general procedure **3.6.4** using **3.36d** (2.0 g, 14.3 mmol), TBAF (28.6 mL, 28.6 mmol, 1 M solution in THF), and benzaldehyde (1.75 g, 1.81 mL, 16.45 mmol), the allene **3.37d** was obtained (2.95 g, 12 mmol, 84 %, *dr* = 48:52).

^{1}H NMR (400 MHz, $CDCl_3$): δ d = 7.50 - 7.44 (m, 2 H), 7.39 - 7.27 (m, 3H), 5.30* (s, 1 H), 5.18 (s, 1 H), 4.29 - 4.13 (m, 2 H), 3.60 - 2.9 (br. s., 1 H), 1.92* (s, 3 H), 1.91 (s, 3 H), 1.67* (s, 3 H), 1.65 (s, 3 H), 1.36 - 1.29 (m, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 207.3/206.9*, 168.2/168.1*, 141.4/141.3*, 128.4, 128.3, 128.0*/127.7*, 126.9/126.4*, 106.6/106.3*, 97.8/96.9*, 75.1/74.9*, 61.1/61.1*, 15.4/15.3*, 14.4/14.3*, 13.5.

HRMS (ESI, m/z, $[M+H]^+$): 247.13287 (calculated), 247.13313 (found).

Ethyl 4-(hydroxy(phenyl)methyl)-2-methylocta-2,3-dienoate 3.37e



3.37e

Following the general procedure **3.6.4** using **3.36e** (1.82 g, 10 mmol), TBAF (20.0 mL, 20 mmol, 1 M solution in THF), and benzaldehyde (1.22 g, 1.27 mL, 11.5 mmol), the allene **3.37e** was obtained (2.36 g, 8.2 mmol, 82 %, *dr* = 48:52).

The diastereomers were separated by column chromatography (cyclohexane:EtOAc = start from 15:1 to 4:1) obtaining as colorless oils.

Major diastereomer:

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49 - 7.42 (m, 2 H), 7.39 - 7.28 (m, 3 H), 5.17 (s, 1 H), 4.27 - 4.15 (m, 2 H), 1.93 (s, 3 H), 1.96 - 1.89 (m, 2 H), 1.41 - 1.19 (m, 7 H), 0.83 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 207.1, 168.0, 141.6, 128.4, 128.4(d), 127.9, 127.9(d), 126.6, 112.0, 99.2, 74.7, 61.0, 29.7, 27.7, 22.3, 15.4, 14.4, 13.9.

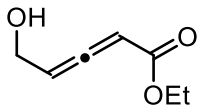
Minor diastereomer:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 - 7.40 (m, 2 H), 7.36 - 7.31 (m, 2 H), 7.30 - 7.27 (m, 1 H), 5.26 (s, 1 H), 4.24 - 4.17 (m, 2 H), 2.03 - 1.91 (m, 2 H), 1.89 (s, 1 H), 1.39 -1.24 (m, 7 H), 0.82 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7, 168.2, 141.7, 128.4, 128.3, 128.1, 127.1, 126.5, 112.0, 99.6, 74.7, 61.0, 29.5, 28.3, 22.2, 15.4, 14.4, 13.9.

HRMS (ESI, m/z, $[M+H]^+$): 289.17982 (calculated), 289.18013 (found).

Ethyl 5-hydroxypenta-2,3-dienoate 3.40a

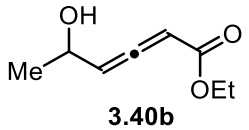


3.40a

Following the general procedure **3.6.2-Method B** using **3.34d** (2.28 g, 20 mmol), 2-Propyn-1-ol (560 mg, 10 mmol), CuI (190 mg, 10 mol%), and Et_3N (1.46 mL, 20 mmol) the allenoate **3.40a** was obtained (1.22 g, 8.5 mmol, 85 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.78 (q, *J* = 6.3 Hz, 1 H), 5.71 - 5.65 (m, 1 H), 4.21 (d, *J* = 3.5 Hz, 2 H), 4.16 (dq, *J* = 1.4, 7.2 Hz, 2 H), 3.50(br. s., 1 H), 1.24 (t, *J* = 7.2 Hz, 3 H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 211.7, 166.2, 96.5, 90.0, 61.3, 59.1, 14.2.
HRMS (ESI, m/z, $[M+H]^+$): 143.07027 (calculated), 143.07065 (found).

Ethyl 5-hydroxyhexa-2,3-dienoate 3.40b

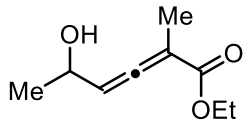


3.40b

Following the general procedure **3.6.2-Method B** using **3.34d** (3.43 g, 30 mmol), but-3-yn-2-ol (1.05 g, 1 mL, 15 mmol), CuI (285 mg, 10 mol%), and Et_3N (2.2 mL, 30 mmol) the allenoate **3.40b** was obtained (1.76 g, 11.2 mmol, 75 %).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.79 - 5.73 (m, 1 H), 5.73 - 5.68 (m, 1 H), 4.53 - 4.44 (m, 1 H), 4.19 (dq, *J* = 1.5, 7.0 Hz, 2 H), 1.36 (t, *J* = 5.9 Hz, 3 H), 1.27 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 211.1/210.9*, 166.0/166.0*, 101.4/101.2*, 90.7/90.3*, 65.5/65.4*, 61.3/61.2*, 23.4/23.2*, 14.3.
HRMS (ESI, m/z, $[M+H]^+$): 157.08592 (calculated), 157.08641 (found).

Ethyl 5-hydroxy-2-methylhexa-2,3-dienoate 3.40c



3.40c

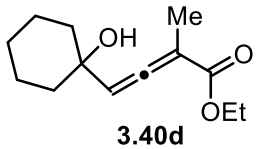
Following the general procedure **3.6.2-Method B** using **3.34a** (3.85 g, 30 mmol), but-3-yn-2-ol (1.05 g, 1 mL, 15 mmol), CuI (285 mg, 10 mol%), and Et_3N (2.2 mL, 30 mmol) the allenoate **3.40c** was obtained (2.05 g, 12 mmol, 80 %).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.63 - 5.57 (dsext, *J* = 1,2, 2,8 Hz 1 H), 4.45 (dquin, *J* = 1.9, 6.2 Hz, 1 H), 4.22 - 4.13 (m, 2 H), 1.88 (dd, *J* = 0.6, 2.9 Hz, 3 H), 1.34 (dd, *J* = 3.1, 6.4 Hz, 3 H), 1.26 (dt, *J* = 1.5, 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 208.7/208.5*, 167.6/167.6*, 99.8, 98.4/98.3*, 65.8, 61.3/61.2*, 23.5/23.4*, 15.2, 14.3.

HRMS (ESI, m/z, $[M+H]^+$): 171.10157 (calculated), 171.10145 (found).

Ethyl 4-(1-hydroxycyclohexyl)-2-methylbuta-2,3-dienoate 3.40d



3.40d

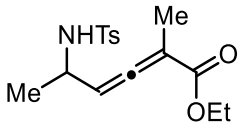
Following the general procedure **3.6.2-Method B** using **3.34a** (1.92 g, 15 mmol), 1-ethynyl-1-cyclohexanol (931 mg, 7.5 mmol) and CuI (143 mg, 10 mol%), and Et_3N (1.1 mL, 15 mmol) the allenoate **3.40d** was obtained (1.1 g, 4.5 mmol, 60 %).

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.59 (q, *J* = 2.8 Hz, 1 H), 4.25 - 4.10 (m, 2 H), 1.89 (d, *J* = 3.0 Hz, 3 H), 1.70 - 1.60 (m, 4 H), 1.47-1.37 (m, 6 H), 1.26 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 208.9, 167.6, 102.7, 98.6, 72.0, 61.1, 38.5, 38.4, 25.6, 22.7, 22.6, 15.1, 14.4.

HRMS (ESI, m/z, $[M+H]^+$): 247.13047 (calculated), 247.13095 (found).

Ethyl 2-methyl-5-((4-methylphenyl)sulfonamido)hexa-2,3-dienoate 3.46a

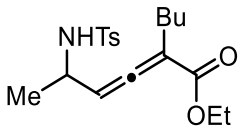


3.46a

Following the general procedure **3.6.2-Method B** using **3.34a (**2.56 g, 20 mmol mmol), N-(but-3-yn-2-yl)-4-methylbenzenesulfonamide[108] (2.23 g, 10 mmol), CuI (190 mg, 10 mol%), and Et_3N (1.47 mL, 20 mmol), **3.46a** was obtained (2.42 g, 7.5 mmol, 75 % yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 2.3, 8.4 Hz, 2 H), 7.30 (d, *J* = 7.3 Hz, 2 H), 5.43 (dq, *J* = 2.0, 5.5 Hz, 0.5 H), 5.37 (dq, *J* = 2.9, 5.5 Hz, 0.5 H), 4.69 (d, *J* = 8.0 Hz, 0.5 H), 4.63 (d, *J* = 8.0 Hz, 0.5 H), 4.21 - 4.12 (m, 2 H), 4.09 - 3.97 (m, 1 H), 2.42 (s, 3 H), 1.81 (d, *J* = 3.1 Hz, 1.5 H), 1.75 (d, *J* = 3.1 Hz, 1.5 H), 1.27 - 1.25 (m, 6 H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 209.0/208.7*, 167.1/167.0*, 143.6/143.6*, 138.0/138.0*, 129.9, 127.2/127.2*, 99.8/99.2*, 97.7/97.3*, 61.3/61.3*, 48.3/47.8*, 22.2/21.9*, 21.6, 14.9/14.9*, 14.3.
HRMS (ESI, m/z, $[M+H]^+$): 324.12715 (calculated), 324.12641 (found).

Ethyl 2-butyl-5-((4-methylphenyl)sulfonamido)hexa-2,3-dienoate 3.46b



3.46b

Following the general procedure **3.6.2-Method B** using **3.34b** (1.7 g, 10 mmol), N-(but-3-yn-2-yl)-4-methylbenzenesulfonamide (1.12 g, 5 mmol), CuI (95 mg, 10 mol%), and Et_3N (0.75 mL, 10 mmol), **3.46b** was obtained (1.39 g, 3.8 mmol, 77 % yield).

Major diastereomer;
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 5.45 (td, *J* = 3.0, 5.8 Hz, 1 H), 4.74 (br. s., 1 H), 4.20 - 4.10 (m, 2 H), 4.02 (sxt, *J* = 6.5 Hz, 1 H), 2.42 (s, 3 H), 2.20 - 2.14 (m, 2 H), 1.37 - 1.28 (m, 4 H), 1.27 - 1.22 (m, 6 H), 0.88 (t, *J* = 6.9 Hz, 3 H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 205.5, 166.8, 143.6, 138.1, 129.8, 127.2, 104.8, 98.7, 61.2, 47.9, 30.3, 28.1, 22.4, 22.0, 21.6, 14.3, 14.0.

[108] H. Song, Y. Liu, Q. Wang, *Org. Lett.* **2013**, 15, 3274-3277.

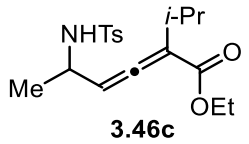
Minor diastereomer;

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 5.51 - 5.48 (m, 1 H), 4.70 (br. s., 1 H), 4.21 - 4.11 (m, 2 H), 4.10 - 4.00 (m, 1 H), 2.43 (s, 3 H), 2.21 - 2.06 (m, 2 H), 1.34 - 1.18 (m, 10 H), 0.91 - 0.83 (m, 3 H)

^{13}C NMR (125 MHz, CDCl3): 208.6, 166.9, 143.6, 138.0, 129.8, 127.2, 104.5, 98.4, 61.2, 48.2, 30.3, 28.2, 22.4, 21.9, 21.6, 14.3, 14.0.

HRMS (ESI, m/z, $[M+H]^+$): 366.17336 (calculated), 366.17480 (found).

Ethyl 2-isopropyl-5-((4-methylphenyl)sulfonamido)hexa-2,3-dienoate 3.46c



3.46c

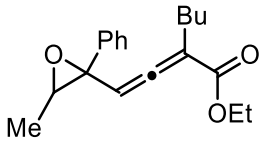
Following the general procedure **3.6.2-Method B** using **3.34c (**1.56 g, 10 mmol), N-(but-3-yn-2-yl)-4-methylbenzenesulfonamide (1.12 g, 5 mmol), CuI (95 mg, 10 mol%), and Et_3N (0.75 mL, 10 mmol), **3.46c** waa obtained (1.5 g, 4.25 mmol, 85 % yield).

^{1}H NMR (500 MHz, $CDCl_3$): δ d = 7.77 (dd, *J* = 1.9, 8.4 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 5.56 (dd, *J* = 2.3, 5.0 Hz, 0.5 H), 5.54 (dd, *J* = 2.3, 5.7 Hz, 0.5 H), 4.70 (d, *J* = 8.0 Hz, 0.5 H), 4.67 (d, *J* = 8.0 Hz, 0.5 H), 4.20 - 4.12 (m, 2 H), 4.09 - 3.96 (m, 1 H), 2.71 - 2.60 (m, 1 H), 2.42 (s, 3 H), 1.42 (s, 3 H), 1.28 - 1.19 (m, 6 H), 1.01 - 0.96 (m, 6 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 207.5/207.5*, 166.5/166.4, 143.6, 138.1/138.1, 129.9, 127.2, 111.4/111.2, 99.9/99.7, 61.1, 48.1/47.9, 27.6/27.5, 27.1, 22.2, 21.9/21.9, 21.6, 14.3.

HRMS (ESI, m/z, $[M+H]^+$): 352.15826 (calculated), 352.15796 (found).

Ethyl 2-(2-(3-methyl-2-phenyloxiran-2-yl)vinylidene)hexanoate (3.48a)

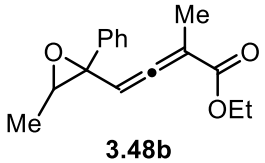


3.48a

Following the general procedure **3.6.2-Method C** using **3.34b (**1.02 g, 6 mmol), propargyl oxirane **3.47** (474.6 mg, 3 mmol), CuI (57.1 mg, 10 mol%), **3.48a** was obtained (585.6 mg, 1.95 mmol, 65 % yield).

^{1}H NMR (500 MHz, C_6D_6): δ 7.40 - 7.35 (m, 2 H), 7.34 - 7.26 (m, 3 H), 5.57 (t, *J* = 2.7 Hz, 4 H), 4.35 - 4.12 (m, 2 H), 3.43 - 3.36 (q, *J* = 5.5 Hz, 1 H), 2.07 (m, 2 H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.19 - 1.12 (m, 4 H), 1.12 - 1.08 (m, 7 H), 1.07 (d, *J* = 5.4 Hz, 3 H), 0.82 - 0.77 (m, 3 H)
^{13}C NMR (125 MHz, C_6D_6): δ 213.0, 166.2, 136.6, 128.5, 128.1, 128.0, 104.6, 100.1, 63.5, 61.7, 61.0, 30.6, 28.7, 22.3, 14.6, 14.5, 14.2.

Ethyl 2-methyl-4-(3-methyl-2-phenyloxiran-2-yl)buta-2,3-dienoate (3.48b)



3.48b

Following the general procedure **3.6.2-Method C** using **3.34a (**128.1 mg, 1 mmol), propargyl oxirane **3.47** (316.4 mg, 2 mmol), CuI (190.4 mg, 10 mol%), **3.48b** was obtained (167.9 mg, 0.65 mmol, 65 % yield).

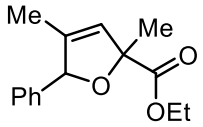
^{1}H NMR (500 MHz, C_6D_6): δ 7.41 - 7.31 (m, 5 H), 5.65 (q, *J* = 3.2 Hz, 1 H), 4.29 - 4.12 (m, 2 H), 3.42 - 3.38 (m, 1 H), 1.67 (d, *J* = 2.9 Hz, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.00 (d, *J* = 5.5 Hz, 3 H)

^{13}C NMR (125 MHz, C_6D_6): δ 213.1, 167.1, 137.0, 128.8, 128.7, 128.7, 128.2, 128.1, 118.2, 99.5, 99.2, 63.9, 62.4, 61.8, 15.0, 14.8, 14.7.

3.6.5 General Procedure for Gold-Catalyzed Cycloisomerization of Hydroxy- and Amino-functionalized Allenes

To a solution of allene (0,3 mmol) in 5 ml of dry toluene was added 10 mol % Ph_3PAuCl and 10 mol% $AgSbF_6$. The mixture was stirred magnetically in a preheated oil bath at 70 °C and the reaction was monitored by TLC. After completion, the mixture was allowed to cool down to room temperature and filtered over celite. The solvent was removed under reduced pressure and the crude product was purified by column chromatography with cyclohexane/EtOAc furnishing the corresponding products.

Ethyl 2,4-dimethyl-5-phenyl-2,5-dihydrofuran-2-carboxylate 3.49a

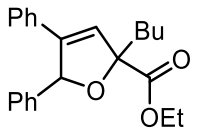


3.49a

Following the general procedure **3.6.5**, using **3.37d** (73.8 mg, 0.3 mmol, *dr* = 48:52), **3.49a** (70.11 mg, 0.28 mmol, 95%, *dr* = 48:52) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, CDCl3): 7.32 - 7.27 (m, 2 H), 7.25 - 7.18 (m, 3 H), 5.62/5.58* (s, 1 H), 5.54 (s, 1 H), 4.22 - 4.09 (m, 2 H), 1.60/1.50* (s, 3 H), 1.47/1.45* (s, 3 H), 1.22 (t, *J* = 7.2 Hz, 3 H).
^{13}C NMR (125 MHz, CDCl3): δ 173.9/173.4*, 141.3/140.1*, 140.0/139.9*, 128.5/128.4*, 128.2/128.1*, 127.4/127.3*, 124.9/124.9*, 91.1/91.0*, 89.8/89.5*, 61.2/61.1*, 25.1/25.0*, 14.3/14.3*, 12.6/12.5*
HRMS (ESI, m/z, [M+H]$^+$): 247.13287 (calculated), 247.13311 (found).

Ethyl 2-methyl-4,5-diphenyl-2,5-dihydrofuran-2-carboxylate 3.49b



3.49b

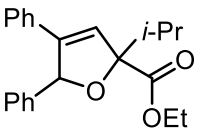
Following the general procedure **3.6.5**, using **3.37b** (105 mg, 0.3 mmol, *dr* = 48:52), **3.49e** (96.6 mg, 0.28 mmol, 92%, *dr* = 48:52) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 - 7.17 (m, 10 H), 6.42* (d, *J* = 22.8, 1 H), 6.42 (d, *J* = 18.8 Hz, 1 H), 6.27* (d, *J* = 42.4 Hz, 1 H), 6.27 (d, *J* = 42.4 Hz, 1 H), 4.32-4.19 (m, 2H), 2.16-1-91 (m, 2H), 1.55-1.25 (m, 4H), 1.34* (t, *J* = 7.2 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 0.94*(t, *J* = 6.8 Hz, 3H), 0.90 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ d = 173.5/173.3*, 143.1*/142.4, 140.3/140.2*, 132.6*/132.3, 128.97*/128.89, 128.87*/128.80, 128.8, 128.78*/128.75, 128.62*/128.53, 127.3*/127.2, 126.5*/125.6, 93.5*/93.3, 89.7*/89.1, 61.7/61.6*, 38.7/38.3*, 26.7*/26.2, 23.3/23.2*, 14.8/14.6*, 14.5/14.3*.

HRMS (ESI, m/z, $[M+H]^+$): 351.19547 (calculated), 351.19621 (found).

Ethyl 2-isopropyl-4,5-diphenyl-2,5-dihydrofuran-2-carboxylate 3.49c



3.49c

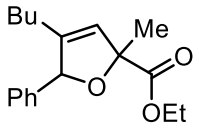
Following the general procedure **3.6.5**, using **3.37c** (100.8 mg, 0.3 mmol, *dr* = 49:51), **3.49c** (91.7 mg, 0.27 mmol, 91%, *dr* = 48:52) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 - 7.17 (m, 10 H), 6.42* (d, *J* = 2.0 Hz, 1 H), 6.40* (d, *J* = 2.5 Hz, 1 H), 6.33 (d, *J* = 2.5 Hz, 2 H), 6.18 (d, *J* = 2.0 Hz, 1 H), 4.35-4.18 (m, 2 H), 3.74 (q, *J* = 7.0 Hz, 1 H), 1.34 (t, *J* = 7.0 Hz, 3 H), 1.29 (t, *J* = 7.0 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H), 1.00* (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5*/173.3, 143.4*/143.0, 140.4/140.0*, 132.8*/132.4, 129.4, 128.9/128.8*, 128.78/128.77*, 128.6/128.5*, 127.3/127.1*, 126.6*/124.7, 96.9/96.4*, 90.4/88.6*, 61.5*/61.4, 36.1/34.4*, 17.9/17.7*, 17.7/17.0*, 14.8/14.6*.

HRMS (ESI, m/z, $[M+H]^+$): 337.17982 (calculated), 337.17955 (found).

Ethyl 4-butyl-2-methyl-5-phenyl-2,5-dihydrofuran-2-carboxylate 3.49d



3.49d

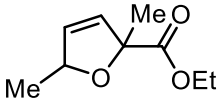
Following the general procedure **3.6.5**, using **3.37e** (86.4 mg, 0.3 mmol, *dr* = 90:10), **3.49d** (82.1 mg, 0.28 mmol, 95%, *dr* = 90:10) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 - 7.25 (m, 3 H), 7.25 - 7.18 (m, 2 H), 5.58 (s, 1H), 4.24 - 4.08 (m, 2H), 1.76 - 1.70 (m, 2 H), 1.61 (s, 3 H), 1.50* (s, 3 H), 1.39 - 1.13 (m, 4 H), 1.22 (t, *J* = 7.1 Hz, 3 H), 0.77 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 174.0/173.5*, 146.2/144.9*, 140.3/140.2*, 128.5/128.4*, 128.3/128.2*, 127.6*/127.5, 123.9/123.8*, 90.6/90.4*, 89.9*/89.6, 61.23*/61.17, 29.5*/29.4, 26.7/26.6*, 25.3*/25.1, 22.43*/22.35, 14.36/14.3*, 13.94*/13.91.

HRMS (ESI, m/z, $[M+H]^+$): 289.17982 (calculated), 289.18021 (found).

Ethyl 2,5-dimethyl-2,5-dihydrofuran-2-carboxylate 3.49e



3.49e

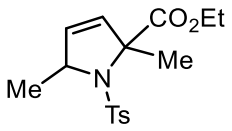
Following the general procedure **3.6.5**, using **3.40c** (51.0 mg, 0.3 mmol, *dr* = 49:51), **3.49e** (42.84 mg, 0.25 mmol, 84%, *dr* = 49:51) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.85 - 5.82 (m, 1 H), 5.81 - 5.77 (m, 1 H), 5.10 - 4.98 (m, 1 H), 4.15 (q, *J* = 7.3 Hz, 2 H), 1.53/1.49* (s, 3 H), 1.30 (d, *J* = 6.5 Hz, 3 H), 1.25 (dt, *J* = 3.8, 7.2 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 173.6/173.6*, 133.3/132.7*, 129.9/129.7*, 90.0/90.0*, 83.0/83.0*, 66.0, 61.2, 25.9/24.7*, 22.4/21.9*, 14.3/14.2*.

HRMS (ESI, m/z, $[M+H]^+$): 171.10157 (calculated), 171.10088 (found).

Ethyl 2,5-dimethyl-1-tosyl-2,5-dihydro-1H-pyrrole-2-carboxylate 3.50a



3.50a

Following the general procedure **3.6.5**, using **3.46a** (96.9 mg, 0.3 mmol, *dr* = 46:54), **3.49e** (42.84 mg, 0.25 mmol, 84%, *dr* = 40:60) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79 (t, *J* = 9.0 Hz, 2 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 5.72 (dd, *J* = 6.1, 1.9 Hz, 1 H), 5.69* (dd, *J* = 6.1, 1.9 Hz, 1 H), 5.52* (t, *J* = 6.0 Hz, 1 H), 5.51 (t, *J* = 6.0 Hz, 1 H), 4.73 (qt, *J* = 6.5, 2.0 Hz, 1 H), 4.59* (qt, *J* = 6.5, 2.0 Hz, 1 H), 4.21 (q, *J* = 7.0, 2 H), 4.18* (q, *J* = 7.0 Hz, 2 H), 2.41 (s, 3 H), 1.82 (s, 3 H), 1.67* (s, 3 H), 1.48* (d, *J* = 6.5 Hz, 3 H), 1.29 (t, *J* = 7.5 Hz, 3 H), 1.29* (t, *J* = 7.5 Hz, 3 H) 1.17 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): 172.2/172.0*, 143.2/143.1*, 139.7/139.2*, 133.2/132.2*, 130.4/129.8*, 129.5/129.5*, 127.6/127.4*, 76.3/75.5*, 63.9/63.5*, 61.9/61.9*,25.2, 23.0, 22.1, 21.7/21.6*, 14.1.

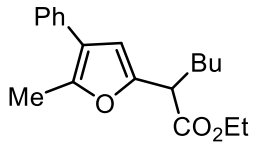
HRMS (ESI, m/z, $[M+H]^+$): 324.12696 (calculated), 324.12682 (found).

3.6.6 General Procedure for the Gold-Catalyzed Cycloisomerization of Epoxy-functionalized Allenes

To a solution of allene (0,3 mmol) in 5 ml of dry DCM was added 10 mol % Ph_3PAuCl and 10 mol% AgOTf. The mixture was stirred magnetically at room temperature and the reaction was monitored by TLC. After completion, filtered over celite, the solvent was removed under reduced

pressure and the crude product was purified by column chromatography with cyclohexane/EtOAc furnishing the corresponding products.

Ethyl 2-(5-methyl-4-phenylfuran-2-yl)hexanoate (2.51a)



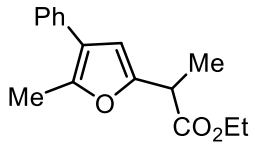
2.51a

Following the general procedure **3.6.6**, using **3.48a** (90 mg, 0.3 mmol), **3.51a** (78.4 mg, 0.26 mmol, 87%) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (500 MHz, C_6D_6): δ 7.30 - 7.26 (m, 2 H), 7.19 (t, *J* = 7.6 Hz, 2 H), 7.11 - 7.06 (m, 1 H), 6.42 (s, 1 H), 4.05 - 3.94 (m, 2 H), 3.76 (t, *J* = 7.6 Hz, 1 H), 2.20 - 2.10 (m, 1 H), 2.15 (s, 3 H), 2.03 - 1.93 (m, 1 H), 1.37 - 1.17 (m, 4 H), 0.94 (t, *J* = 7.1 Hz, 3 H), 0.83 - 0.79 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, C_6D_6): δ 171.8, 151.2, 147.1, 134.7, 128.8, 128.4, 128.2, 128.0, 126.5, 122.3, 108.5, 60.8, 46.0, 31.4, 30.0, 22.8, 14.2, 14.1, 12.9

Ethyl 2-(5-methyl-4-phenylfuran-2-yl)propanoate (2.51b)



3.51b

Following the general procedure **3.6.6**, using **3.48b** (77.5 mg, 0.3 mmol), **3.51b** (69,7 mg, 0.27 mmol, 90%) was obtained as a colorless oil after column chromatography (cyclohexane:EtOAc = 100:5).

^{1}H NMR (500 MHz, C_6D_6): δ 7.31 - 7.28 (m, 4 H), 7.20 - 7.15 (m, 1H), 6.24 (s, 1 H), 4.12 (q, *J* = 7.0 Hz, 2 H), 3.71 (q, *J* = 7.1 Hz, 1 H), 2.35 (s, 3 H), 1.46 (d, *J* = 7.3 Hz, 3 H), 1.20 (t, *J* = 7.0 Hz, 3 H).

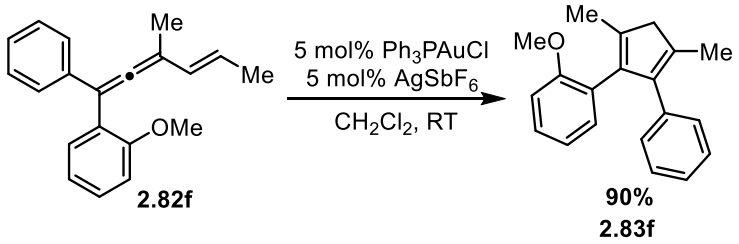
^{13}C NMR (125 MHz, C_6D_6): δ 173.0, 151.3, 147.1, 134.4, 128.7, 127.6, 126.4, 121.7, 107.6, 61.3, 39.7, 27.1, 16.1, 14.4, 13.3.

CHAPTER 4

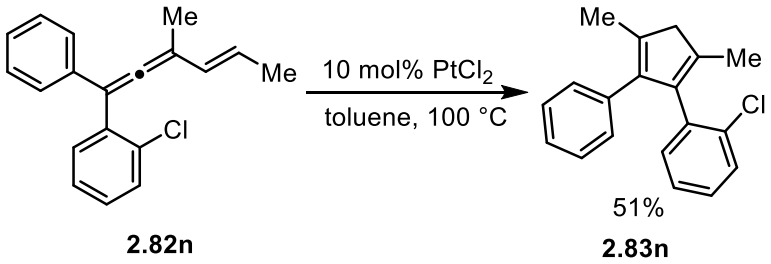
Summary

A particular attractive approach toward the synthesis of densely functionalized hetero- and carbocyclic products involves the incorporation of rearrangement steps into transition-metal-catalyzed cycloisomerization cascade reactions. In this context, the diverse reactivity of gold- and platinum-catalyzed transformations has attracted much interest for the development of cascade reaction patterns. The activation of allenes with a homogeneous catalyst sets the stage for a cyclization by intramolecular attack of various nucleophiles, affording highly useful carbo- or heterocyclic products. Among various methods for the synthesis of these heterocycles, the gold- or platinum-catalyzed transformations of allenes play an important role in synthetic organic chemistry. The thesis entitled '**Novel Strategies for the Synthesis and Cycloisomerization Reactions of Functionalized Allenes**' describes new routes to functionalized carbo- and heterocyclic products by formation of C-O, C-N, and C-C bonds with transition metal catalysis in high yields and selectivities. A brief introduction to allenes and cyclopentadienes and their application in organic synthesis is presented in Chapter 1.

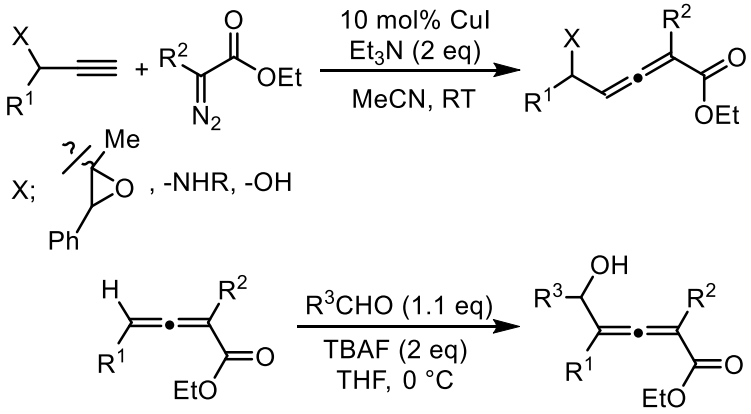
Chapter 2 deals with metal-catalyzed [1,2]-migratory cycloisomerization cascade reactions of 1,1-disubstituted vinylallenes which provides a regioselective access to highly substituted cyclopentadiene derivatives. We achieved 8-90 % yield of highly functionalized cyclopentadienes **2.83** using a $Ph_3PAuCl/AgSbF_6$ catalytic system. The method provides a selective 1,2-aryl migration profile where the migrating aryl group contains a strongly electron-donating methoxy substituent. The effect of substituents provides an interesting input to further studies of the nature of the gold-carbenoid species and their reactivities in [1,2]-migration sequences. The effect of the methoxy substituent on the gold-catalyzed cycloisomerization reaction can be explained by the importance of the aryl rings for the stabilization of the gold-carbenoid intermediates by resonance delocalization in accordance with the reports by Fürstner[61] and Widenhoefer[57]. Furthermore, the gold-catalyzed method tolerates a variety of substituents on the alkenyl and the allenyl moieties which serves for the synthesis of differently substituted cyclopentadiene derivatives.



After having determined the importance of electron-rich aryl groups on the [1,2]-migration aptitude in gold-catalyzed reactions, the cycloisomerization reaction was extended to platinum catalysts. We have found that, vinylallenes, whether or not bearing a methoxyphenyl group, are suitable substrates. The Pt(II)-catalyzed cyclization has a wider substrate scope and showed no dependence on the electronic properties of the migrating group.

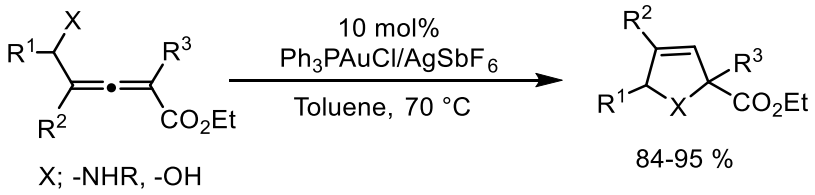


Chapter 3 deals with Cu(I)-catalyzed cross-coupling reactions of alkynes**,** propargyl alcohols, propargyl amines and propargyl epoxides with diazo compounds. The desired di- and trifunctionalized allenes were obtained in good yields. The tetrasubstituted hydroxyallenoates were obtained by aldol reaction of allenoates with aldehydes in the presence of TBAF in good yields.

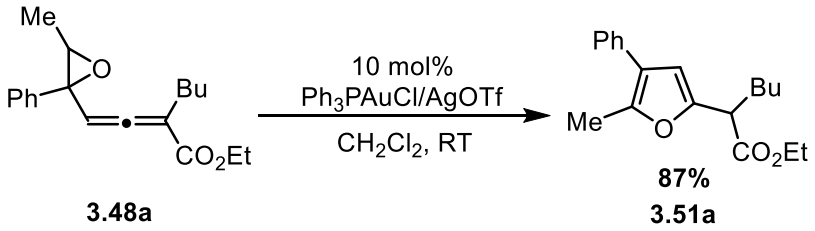


The synthesized allene derivatives were subjected to gold-catalyzed cycloisomerization reactions to afford synthetically valuable heterocycles depending on the substituents on the

nucleophilic moiety. When hydroxy-functionalized allenoates were subjected to cycloisomerization reaction under $Ph_3PAuCl/AgSbF_6$ catalysis, the corresponding 2,5-dihydrofuran carboxylate derivatives were obtained in excellent yields. In order to understand the stereochemical outcome of the process, the reaction was conducted with diastereomerically enriched allene **3.37b (***dr***=** 90:10). A complete axis-to-center chirality transfer was observed and the product **3.49d** was obtained diasteroselectively (*dr***=** 90:10). When the procedure was applied to disubstituted ($R^2 = R^3 = H$) allene derivatives, the reaction resulted in complex product mixtures. The trisubstituted ($R^2 = H$, R^3 = Me) amino-functionalized allene was subjected to $Ph_3PAuCl/AgSbF_6$ catalyzed cycloisomerization reaction, and the desired dihydropyrrole was obtained in 93 % yield.



Although several methods have been reported for the gold-catalyzed cyclization of functionalized allenes, epoxy-functionalized allenes have not been explored so far. We investigated the gold-catalyzed cycloisomerization reaction of epoxy-functionalized allene **3.48a**. To our delight, the $Ph_3PAuCl/AgSbF_6$ catalyzed reaction resulted in the formation of furan **3.51a** in 87 % yield.



In conclusion, we have developed new approaches for the synthesis of highly substituted cyclopentadienes derivatives which are very useful synthetic intermediates in organic and organometallic chemistry. In addition to this, the developed method for the synthesis and cyclization reactions of difunctionalized allenes afford new routes to functionalized heterocyclic products which are found in bioactive natural compounds.

Zusammenfassung

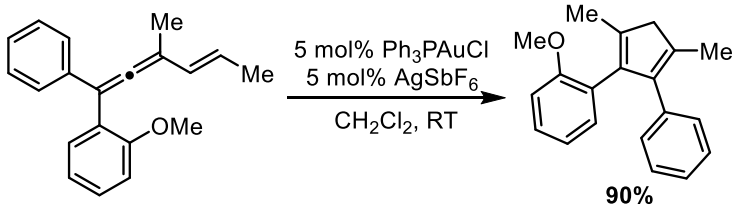
Ein besonders attraktiver, synthetischer Zugang zu hoch funktionalisierten hetero- und carbozyklischen Verbindungen ist die Integrierung von Umlagerungsschritten in übergangsmetallkatalysierten Zykloisomerisierungskaskadenreaktionen. In diesem Zusammenhang hat die vielfältige Reaktivität von Gold- und Platinkatalysatoren ein hohes Interesse in der Entwicklung von Kaskadenreaktionen erhalten. Die Aktivierung von Allenen mit homogenen Katalysatoren schaffte die Voraussetzung für die Zyklisierung, bei der durch intramolekulare Angriffe verschiedenster Nukleophile wertvolle carbo- und heterozyklische Verbindungen entstehen.

Neben den bisherigen Synthesemethoden dieser Heterozyklen spielen gold- und platinkatalysierte Reaktionen von Allenen eine wichtige Rolle in der synthetischen, organischen Chemie. Die Arbeit mit dem Titel '**Novel Strategies for the Synthesis and Cycloisomerization Reactions of Functionalized Allene**' beschreibt neue Wege, wie funktionalisierte carbo- und heterozyklische Verbindungen durch die Bildung neuer C-O, C-N und C-C Bindungen mit Hilfe von Übergangsmetallkatalysatoren in hohen Ausbeuten und Selektivitäten dargestellt werden können. Eine kurze Einführung zu Allenen und Cyclopentadienen sowie ihre Anwendungen in der organischen Synthese wird in Kapitel 1 dargestellt.

Kapitel 2 handelt von metallkatalysierten, [1,2]-umlagernden Zykloisomerisierungs-kaskadenreaktionen von 1,1-disubstituierten Vinylallenen, welche einen regioselektiven Zugang zu hoch substituierten Cyclopentadienderivaten bieten. Wir erhielten 8-90 % Ausbeute an hoch funktionalisierten Cyclopentadienen **2.83** unter Verwendung des $Ph_3PAuCl/AgSbF_6$ Katalysatorsystems. Diese Methode ermöglichte eine selektive 1,2-Arylumlagerung, wenn die delokalisierte Arylgruppe einen stark elektronschiebenden Methoxysubstituenten aufwies.

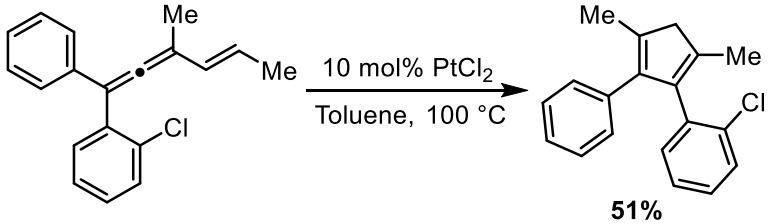
Dieser Substituenteneffekt leistet einen nützlichen Beitrag zum weiteren Verständnis der Natur von Goldcarbenoidspezies und ihrer Reaktivität in [1,2]-Umlagerungen. Der Effekt des Methoxysubstituenten auf die goldkatalysierte Zykloisomerisierungsreaktion kann auf das Streben des Arylrings das Goldcarbenoidintermetidat durch Rensonanzdelokalisierung zu stabilisieren zurückgeführt werden. Dies stimmt mit Berichten von Fürstner[61] und Widenhoefer[57] überein.

Darüber hinaus toleriert die goldkatalysierte Variante eine Vielzahl von Substituenten an den Alkenyl- und Allenylresten, welche vorteilhaft für die Synthese unterschiedlich substituierter Cyclopentadienderivate sind.



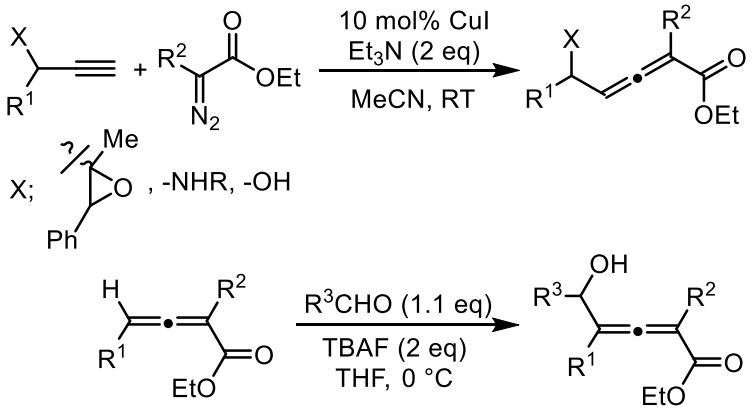
2.82f **2.83f**

Nachdem die Bedeutung der Methoxygruppe auf die goldkatalysierte [1,2]-Umlagerung bekannt war, wurden die Untersuchungen zu Zykloisomerisierungsreaktionen auf Platinkatalysatoren ausgeweitet. Wir stellten fest, dass Vinylallene unabhängig davon, ob sie eine Methoxyphenylgruppe tragen oder nicht, geeignete Substrate darstellten. Zudem ermöglichte die Pt(II)-katalysierte Variante die Umsetzung einer weitaus größeren Menge an Vinylallenen und zeigte keine Abhängigkeit von den elektronischen Eigenschaften der umlagernden Gruppe.

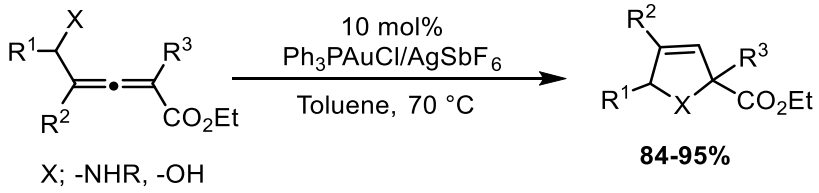


2.82n **2.83n**

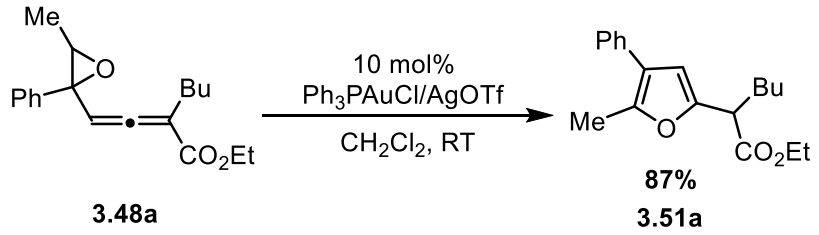
Kapitel 3 befasst sich mit Cu(I)-katalysierten Kreuz-Kupplungsreaktionen von Alkinen, Propargylalkoholen, Propargylaminen und Propargylepoxiden mit Diazoverbindungen. Die gewünschten di- und trifunktionalisierten Allene konnten in guten Ausbeuten erhalten werden. Die tetrasubstituierten Hydroxyallenoate wurden in einer Aldol-Reaktion von Allenoaten mit Aldehyden in Anwesenheit von TBAF und mit guten Ausbeuten erzeugt. Die dargestellten Allenderivate wurden in der goldkatalysierten Zykloisomerisierung eingesetzt, um synthetisch wertvolle Heterozyklen mit verschiedenen Substituenten an den nukleophilen Resten zu erhalten.



Wurden hydroxyfunktionalisierte Allenoate unter Verwendung des $Ph_3PAuCl/AgSbF_6$ Katalysatorsystems in der Zykloisomerisierungsreaktion umgesetzt, so konnten die entsprechenden 2,5-Dihydrofurancarboxylate in exzellenten Ausbeuten erhalten werden. Um das stereochemische Ergebnis dieser Reaktion zu verstehen, wurde die Umsetzung mit dem Diastereomerenangereicherten Allen **3.37b** durchgeführt. Hierbei wurde ein vollständiger Achse-zu-Zentrum Chiralitätstransfer beobachtet und das Produkt **3.49d** konnte mit einer hohen Diastereomerenselektivität (*dr* = 90:10) isoliert werden. Wurde die Methode auf disubstituierte Allenderivate ($R^2 = R^3 = H$) angewandt, führte die Reaktion zu komplexen Produktgemischen. Das trisubstituierte (R^2 = H, R^3 = Me) aminofunktionalisierte Allen lieferte hingegen in der $Ph_3PAuCl/AgSbF_6$-katalysierten Zykloisomerisierung das gewünschte Dihydropyrrol mit einer Ausbeute von 93%.



Obwohl mehrere Methoden für die goldkatalysierte Zyklisierung von funktionalisierten Allenen bekannt sind, blieben epoxyfunktionalisierte Allene bislang unerforscht. Wir haben die goldkatalysierte Zykloisomerisierungsreaktion der epoxyfunktionalisierten Allene **3.48a** daher näher untersucht. Erfreulicherweise ergab die $Ph_3PAuCl/AgSbF_6$-katalysierte Reaktion die Bildung von **3.51a** mit einer Ausbeute von 87%.



Zusammenfassend haben wir einen neuen Zugang zur Synthese hoch substituierter Cyclopentadienderivaten entwickelt, die sehr nützliche synthetische Intermediate in der organischen und metallorganischen Chemie darstellen. Zusätzlich ergeben sich durch die hier aufgezeigten Methoden zur Synthese und Zyklisierung von Allenen neue Synthesewege zu funktionalisierten heterozyklischen Verbindungen, deren Strukturen in bioaktiven Naturstoffen vorkommen.

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(Surname, first name)

Matrikel-Nr.
(Enrolment number)

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