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Gold Catalyzed Divergent Scaffold Synthesis from Oxindole Derived 1,6-Enynes

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Declaration/Erklärung

Die vorliegende Arbeit wurde in der Zeit von August 2013 bis August 2018 am Max-Plank-Institut für Molekulare Physiologie Dortmund unter der Anleitung von Prof. Dr. Dr. h.c. Herbert Waldmann durchgeführt.
Hiermit versichere ich an Eides statt, dass ich die vorliegende Arbeit selbstständing und nur mit den angegebenen Hilfsmitteln angefertigt habe.

The work described in this Dissertation was performed from August 2013 to August 2018 at the Max Plank Institute of Molecular Physiology Dortmund under the guidance of Prof. Dr. Dr. h.c. Herbert Waldmann.
I hereby declare that I performed the work independently and did not use any other but the indicated aids.

Dortmund 2018
Yen-Chun Lee

Teile dieser Arbeit wurden bereits in folgenden Publikationen veröffentlicht:

The present work was partly published in the following papers:

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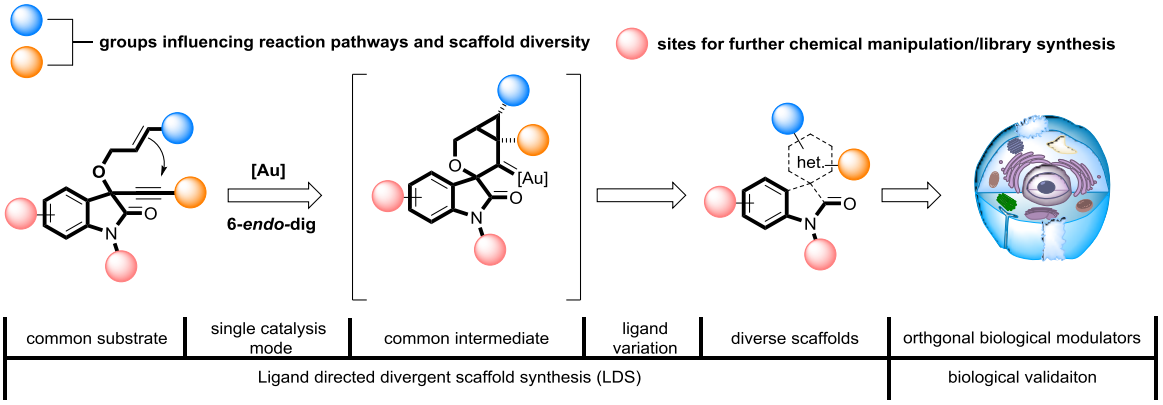
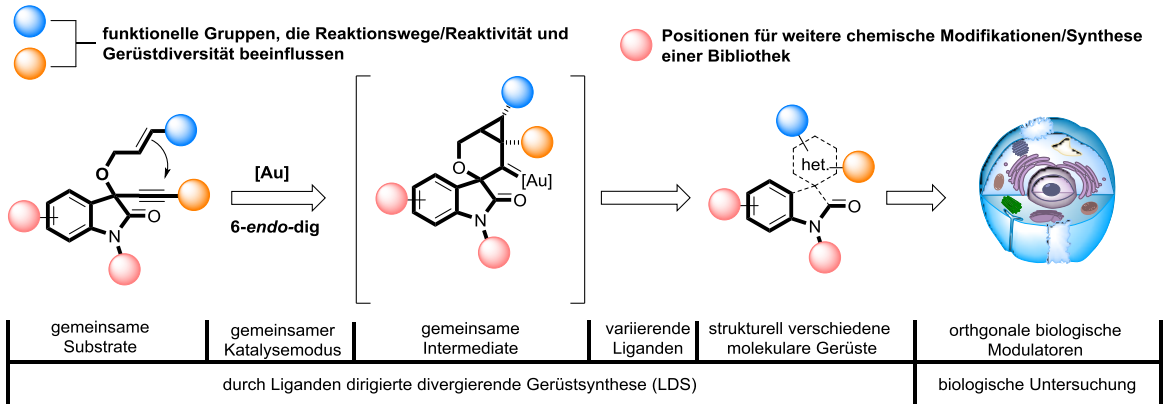
Abstract

In chemical biology and drug discovery, the development of novel methods for efficient synthesis of structurally distinct molecular scaffolds holds an immense importance. Gold catalyzed enyne cycloisomerizations are a powerful tool to access a wide range of complex molecules owing to the tunable nature of gold complexes with ligand and reaction conditions. A number of reactions have disclosed the role of substrates, ligands of gold(I) catalyst and the nucleophiles to afford a variety of products with intriguing molecular frameworks. The development of a ”ligand directed divergent scaffold synthesis” (LDS) approach that aims to create structurally distinct molecular scaffolds by means of a single mode of catalysis on common substrates is presented in this work. In this strategy, when oxindole derived 1,6-enynes were treated with different gold complexes, the fate of the common bicyclic gold carbene intermediates could be steered by ligand variations in gold(I) complexes, and selectively led to three structurally distinct scaffolds, the spirooxindoles, quinolones, and the *df*-oxindoles. Biological investigation of the resulting compound collection in cell-based assays revealed bioactive small molecules based on three different scaffolds displaying orthogonal modulation in the activities of the hedgehog signaling pathway, autophagy and cellular proliferation.



Zusammenfassung

Die Entwicklung neuer Methoden zur effizienten Synthese strukturell verschiedener molekularer Gerüste ist von großer Wichtigkeit in der chemischen Biologie und der Entdeckung neuer Wirkstoffe. Die Gold katalysierte Enin-Cycloisomerisierung ist eine leistungsfähige Methode für den Zugang zu einer Vielzahl komplexer Moleküle, da die Natur der Goldkomplexe durch Änderung der Liganden und Reaktionsbedingungen einstellbar ist. Die genaue Erforschung der Substrate, Liganden des Gold(I)-Katalysators und der Nukleophile führt zu einer Vielfalt an Produkten mit interessanten molekularen Gerüsten. In dieser Arbeit wird die Entwicklung des Ansatzes einer divergierenden Gerüstsynthese, die durch Liganden dirigiert wird (engl. *ligand directed divergent scaffold synthesis*, LDS) präsentiert. Hierbei wird die Synthese strukturell verschiedener molekularer Gerüste durch nur einen Modus der Katalyse für gemeinsame Substrate angestrebt. Wenn die Oxindol-abgeleitete 1,6-Enine in der Gegenwart von Gold-Komplexen reagiert wurden, konnte der Reaktionsverlauf gängiger bicyclische Goldcarbenintermediate durch Variieren der Liganden des Gold(I)-Komplexes gesteuert werden. Als Resultat wurden selektiv zu drei verschiedener Gerüste erhalten: Spirooxindole, Chinolone und *df*-Oxindole. Die biologische Untersuchung der erhaltenen Substanzsammlung in Zell-basierten Experimenten ergab, dass die Moleküle, die auf drei verschiedenen Gerüsten basieren, die Aktivität des Hedgehog Signalwegs, Autophagie und Proliferation selektiv beeinflussen.



1 Introduction

Biologically active small molecules are the crucial elements that underpin research in drug discovery, medicinal chemistry, chemical biology, and allied fields. In ancient time, people managed to apply the extracts of plants or creatures for the treatment of wounds or diseases. For instance, salicylic acid had been utilized to get relief from the pain and fever, and was later acetylated to form the known pain killer, aspirin. With advances in technologies, structures of more complexed natural products (NPs) were elucidated and their intriguing biological activities were also realized. The penicillin antibiotic, isolated from the fungi, acts by inhibition of bacteria cell wall formation. The quinghau su, plant extract, was uncovered by YouYou Tu for the treatment of malaria.[1] The dynemicin A contains the unique bridged enediyne and exhibits the excellent antitumor activity (Figure 1).[2]

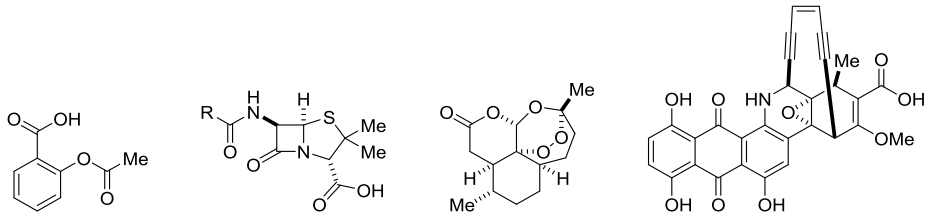


Figure 1. Representative natural products and derivatives.

However, the isolation, structure elucidation, and total synthesis of NPs remain very challenging tasks which often provide only minute amounts of the complex NPs. Moreover, the development of high throughput screening (HTS) has puffed up the demand of small molecules for biological screenings and evaluations[3], which are difficult to achieve *via* NP isolation or total synthesis. Therefore, pharmaceutical industry turned the attention to combinatorial chemistry to generate simple and relatively flat small molecules in a quick manner (around 3,300 compounds per one chemist month).[4] However, these efforts delivered only limited success in drug discovery, *i.e.* two drugs, sorafenib (Nexavar) and ataluren (Translarna), were approved by FDA till 2014.[5] In contrast to NPs, the molecules from combinatorial chemistry are endowed with less structural diversity, less number of chiral centers, and sp^3 atoms, as well as the rigid molecular frameworks.[6]

In order to generate a compound collection with structurally diverse and three-dimensional small molecules in satisfactory quantity, synthetic chemistry community has proposed various approaches. Some library-synthesis designs aim at covering a broad range of chemical space that may interact with various protein targets. Synthesis approaches like diversity-oriented synthesis (DOS)[7], branching cascade approach[8], and complexity to diversity strategy (CtD)[9] broadly fall in this category. On the other side, diverted total synthesis (DTS)[10] and function-oriented synthesis (FOS)[11] try to provide an alternative way to study the biological profiles of NP derivatives and thus remain focused around a particular scaffold.[12]

Structural simplification of NPs can effectively reduce the molecular complexity, molecular weight, and the number of synthetic steps to make good amount of NP-related compounds.[13] Previously mentioned antitumor NP, dynemicin A shows notable biological activities against many cancer cell lines with half-maximal lethal dose (LD_{50}) in the picogram to nanogram per ml range. Wender's group presented a truncated analog of dynemicin A that maintains the biological activities with satisfactory quantity for further studies.[14] Not only the structural simplification but also functional group variation around a NP-scaffold can bequeath biological activity to a small molecule. By replacement of polyene side chain with ethyl ester and the installation of *m*-methoxy group to the phenyl ring, Gademann's group reported a pyridine alkaloid analogue[15], which shares similar neurite outgrowth activity with the parent molecule, farinosone A[16]. Waldmann's group further modified the pyridone core with hydroxyl-*n*-hexyl chain and disclosed that MAP4K4 kinase is the target of this simplified NP analogue.[17] Thus, structural simplification and functional group manipulations on the NP-core scaffolds may reveal the intriguing biological profiles and druggable cellular targets (Figure 2).

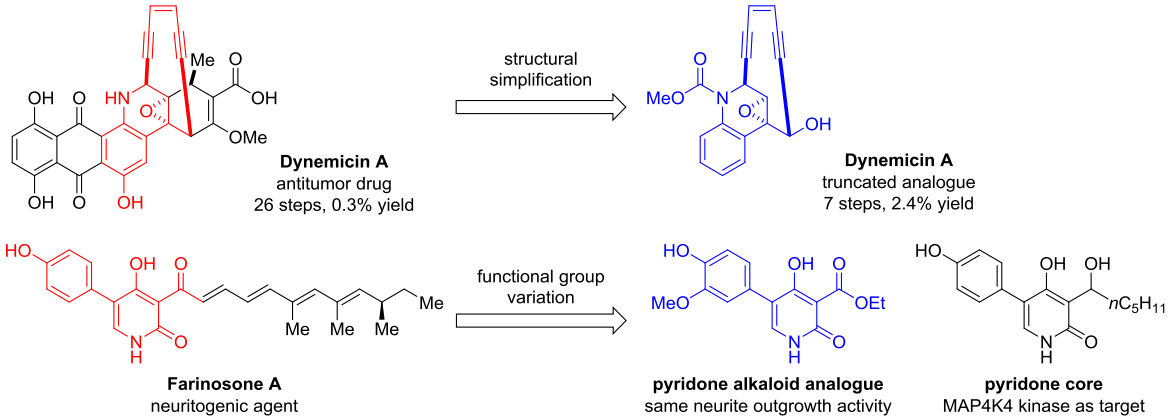


Figure 2. Bioactivity maintenance by structural simplification and functional group variation.

1.1 Biology-oriented synthesis (BIOS)

To rationalize the relationship between small molecules and their corresponding biological targets, the biology-oriented synthesis (BIOS) concept was proposed by Waldmann and co-workers. BIOS accommodates two complementary approaches, *i.e.* protein structure similarity clustering (PSSC) and structural classification of natural product (SCONP) with the extension to non-natural bioactive molecules. Based on this approach, synthetic chemist can identify the scaffolds for similar protein binding sites.[18]

In nature, numerous NPs as secondary metabolites are generated to trigger biological responses for the physiologically important functions of an organism. Being synthesized by protein enzymes, they are inherently biologically relevant chemicals and therefore are suitable starting points to navigate the bio-relevant chemical space (Figure 3a). Importantly, the number of potential ligand-accommodating binding pockets is around 1315 according to the protein data bank (PDB).[19] In such conserved binding sites, the functional diversity of proteins is driven by different peptide sequences or more precisely with the decoration of various amino acid side chains (Figure 3b). Therefore, the protein-ligand interaction is driven by the structural complementarity between a small molecule with suitable functional group decorations and a protein binding site with proper side chains of amino acids (Figure 3c). On the other hand, the nature has also evolved to conserve the molecular scaffolds in NPs, such as alkaloids, terpenoides, and flavonoid, accompanied with the functional group driven structural diversity to interact with the high structural similarity of protein binding site to trigger a biological function, as shown in Figure 3d. The similar binding site subfolds of

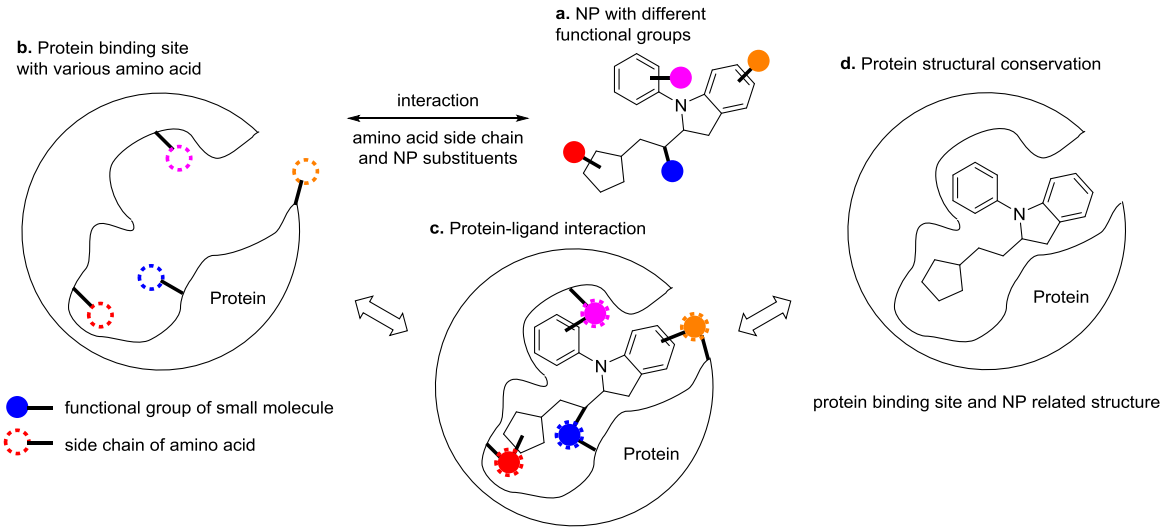


Figure 3. The structural conservation and diversity in protein-ligand interaction.

different protein were grouped and termed as protein structure similarity clustering (PSSC). Identification of a NP inhibitor of one of the proteins in this cluster would thus provide initial compound for optimization as inhibitor for other proteins in the same cluster.

The dictionary of natural product (DNP) as database was explored in a chemiformatic analysis of NPs to identify the corresponding scaffolds by removing the functional group around NPs. Having an essential scaffold was followed by deconstruction of complex NP ring systems to single ring structures in stepwise manner to build up the tree-like diagram, SCONP scaffold tree (Figure 4). This NP tree diagram allows the logical exploration of NP-like chemical space. Within the NP tree, the larger scaffold is called "child" and the smaller scaffold is termed as "parent". While starting from bioactive child scaffold to parent scaffold, the retention of bioactivity can be expected with the decreasing potency, which can be retrieved by the functional group variation.

In a sense, the frequently presented scaffolds in NPs, known as the privileged ring system (PRS), could serve as the guiding segment for the biological relevant chemical space exploration and simplified small molecules with similar and/or unique biological activities can be identified.

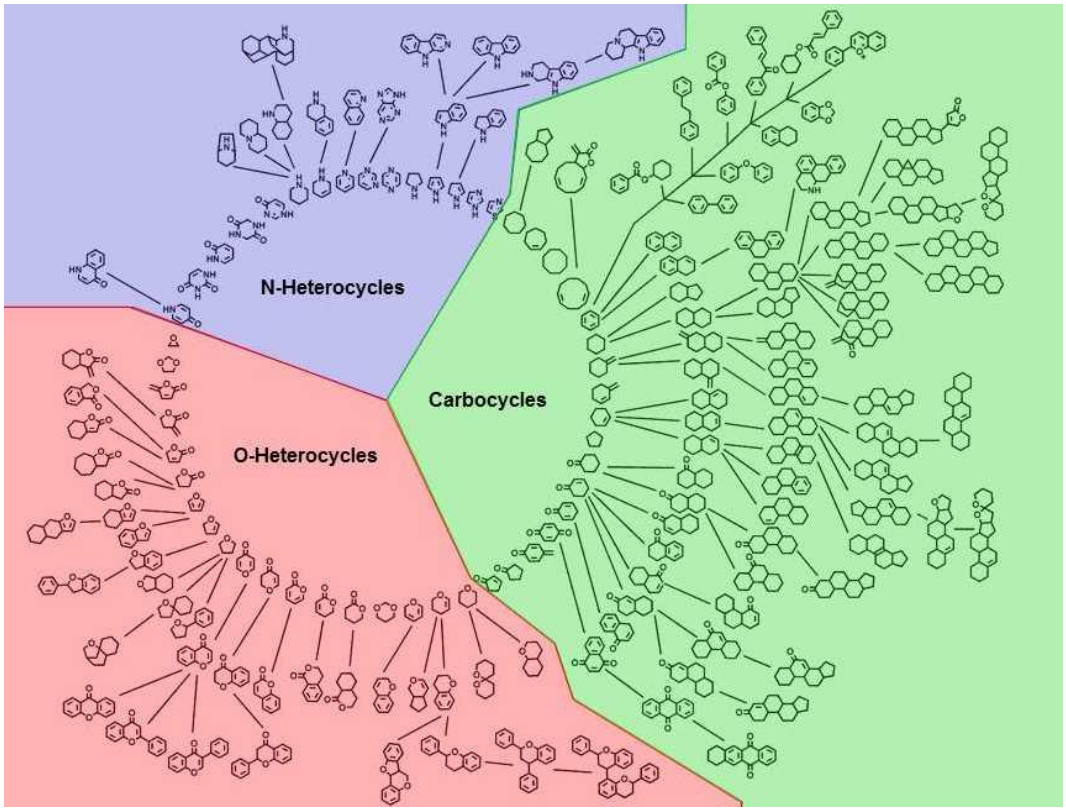


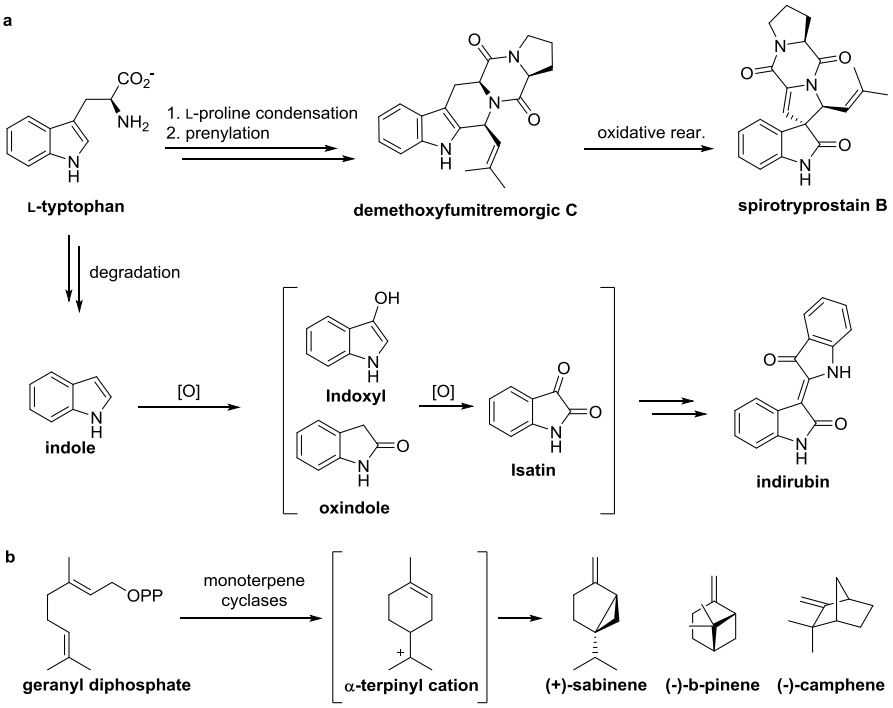
Figure 4. Graphic representation of SCNOP scaffold tree.
Reproduced from ref[20], copy right 2005 National Academy of Sciences.

1.2 Construction of diverse molecular frameworks

For the synthesis of biologically interesting small molecules, both natural and chemical approaches frequently utilize building block endowed with privileged ring system (PRS) and appropriately substituted reaction handles to generate more complicated and diverse molecular frameworks.

1.2.1 Natural approach - divergent-scaffold formation *via* biosynthesis

Generally, nature relies on primary simple building blocks to generate the structural complexity of NPs *via* sequential enzymatic-, degradative cascades, or rearrangement reactions. For instance, the essential amino acid L-tryptophan serves as the fundamental framework to assemble various NPs with distinctive scaffolds, like dimethoxy-fumitremorgic C, spirotryprostain B,[21] indirubin,[22] by multi-step as well as cascade transforamtions (Scheme 1a). Interestingly, structurally diverse terpenoids are generated from a common linear geranyl diphosphate precursor through monoterpene cyclases mediated cyclization reactions (Scheme 1b).[23] This biosynthesis idea has in fact inspired several approaches to synthesize NPs[24] or generate small molecule compound collections using common substrates[8b].

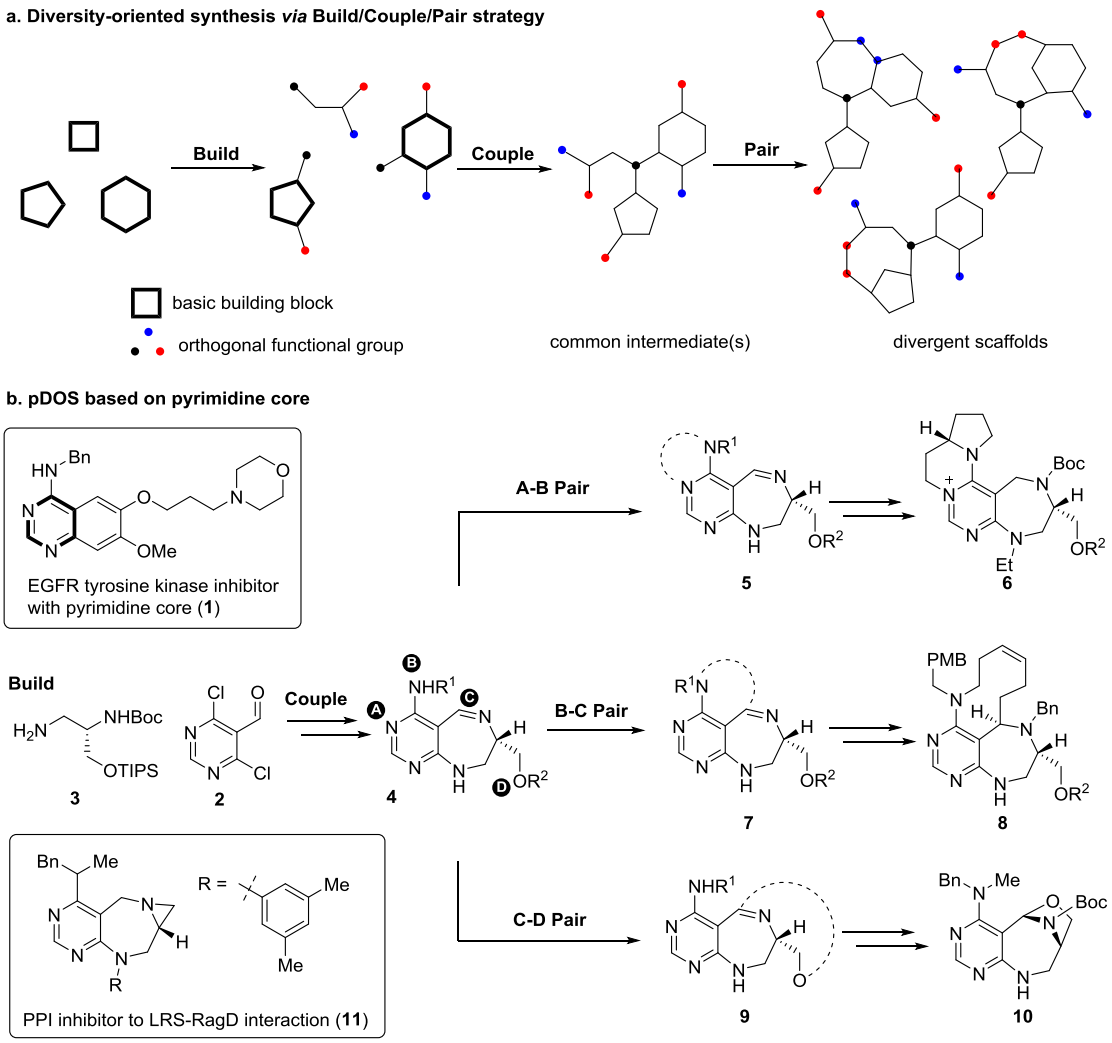


Scheme 1. a) L-Tryptophan derived NPs *via* multi-step biological cascades. b) Geranyl diphosphate derived NPs by monoterpene cyclases.

1.2.2 Chemical approach - diversity-oriented synthesis (DOS)

The diverse enzymatic proteins enable the nature to assemble various molecular frameworks in regio-, stereo-, or chemoselective manner under mild conditions. On the other hand, the chemical approaches may benefit from the tunable reactions that are subject to change with variations in solvents, temperatures, reagents, and additives, as well as catalysts to provide structurally distinct chemotypes. Schreiber *et al.* proposed the diversity-oriented synthesis (DOS) approach to prepare the small molecule compound collections with enriched functional, stereochemistry and scaffold diversity.[7a, 25] The approach makes an extensive use of build/couple/pair strategy. In the build stage, the molecular segments are decorated with chemically orthogonal functionalities, which can be coupled with other segments to get the common intermediates supporting different chemical handles. For the final pairing stage, the diverse molecular frameworks can be formed by connecting the chemical handles orthogonally (Scheme 2a). The DOS approach has been further evolved into other related approaches, such as multidimensional DOS strategy to get higher degree of structurally diverse and complex small molecules[26] and privileged substructure-based DOS (pDOS) as a strategy to construct diverse compound collection with high biological relevance[27].

Based on pDOS, Park *et al.* synthesized a set of pyrimidine-based compound collection that represent one of the medicinally important classes that has been frequently presented in biological active small molecules, such as the EGFR tyrosine kinase inhibitor (**1**). Coupling of the two building segments, pyrimidine (**2**) and amine (**3**), led to the common intermediate **4**, which was ready for further divergent cyclization reactions. For example, A-B pair could lead to the polycyclic compound (**6**), the B-C pair could be cyclized to access the macrocycle **8**, and the closure of C-D points provided the bicyclic compound (**10**). The divergent pairing reactions were achieved within 2.2 steps on average to give 16 distinctive polyheterocycles. Moreover, by utilizing ELISA-based HTS, a tricycle compound (**11**) had been identified as a new class protein-protein interaction (PPI) inhibitor that could perturb the LRS-RagD interaction (Scheme 2b).[28]

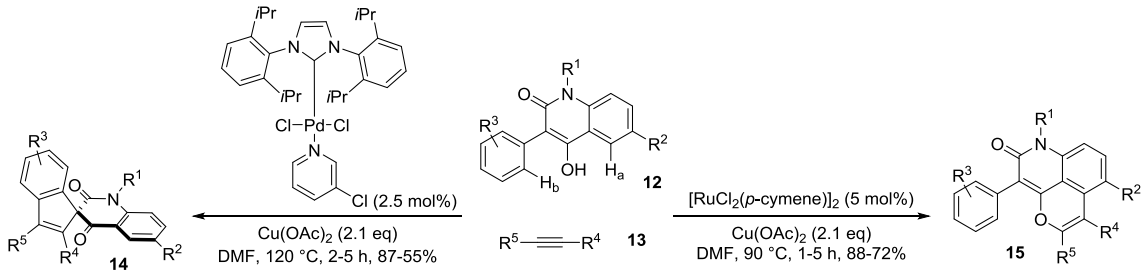


Scheme 2. a) Schematic representation of DOS approach. b) pDOS based approach to generate structurally diversed compound collection.

Basically, DOS and related synthetic approaches can prepare a structurally diverse compound collection within 3-5 steps in a linear manner sharing some common intermediates, which are ideal to perform the initial biological screening. From substrate point of view, the precise selection of chemical handles is crucial to ensure that distinct pairing kind of reactions can work and afford different scaffolds. Besides that, the final divergent pairing steps should be robust enough to provide sufficient amount of final molecules for making a compound collection. Therefore, any new approach that can deliver diverse molecular scaffolds in a single step, under non-tedious and challenging reaction conditions and preferably using common substrates or intermediates would be highly useful and remains is in high demand.

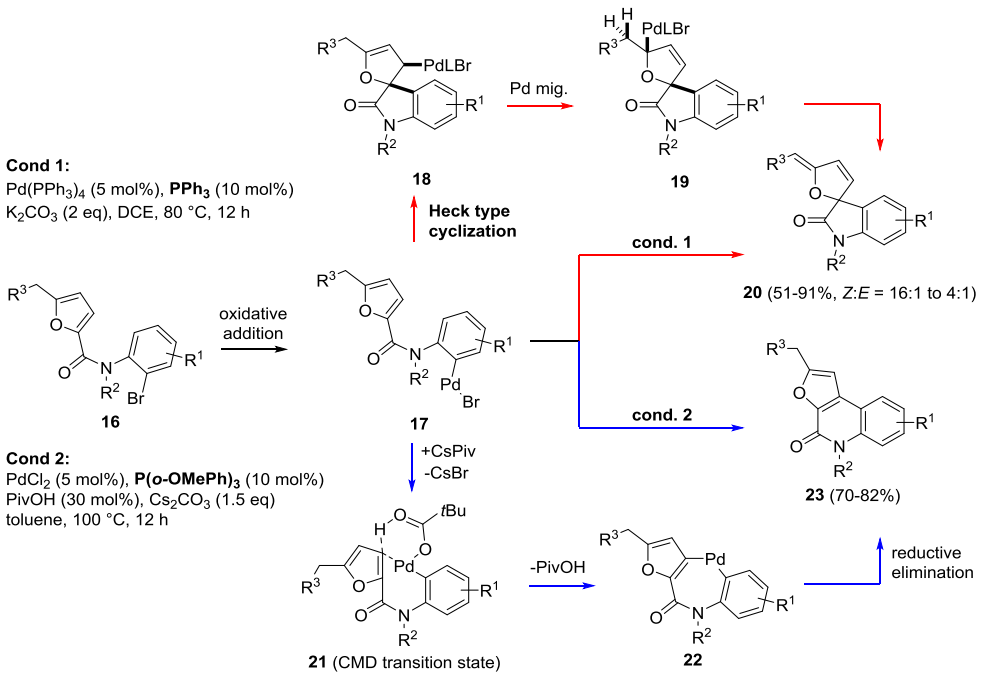
1.3 Transition metal mediated divergent synthesis approaches

Transition metal catalysis is a key scientific discipline in organic synthesis. Due to its robust nature and ability to reduce the potential energy of reactive intermediates, the foreseeable retrosynthetic disconnection, excellent chemo-/regio-/stereoselectivity in chemical transformations, transition metal catalysis is often the first resort for organic synthetic chemists to generate molecular complexity. Furthermore, molecular diversity can also be established by transition metal catalyzed reactions by employing variations in transition metals, ligands, solvents, additives, as well as reaction temperature.[29] Among all these factors, the catalyst-controlled divergent approach has been well-known and developed, since most of the transition metal catalysts have their unique activation and catalysis pattern.[30] Therefore proper selection of transition metal and design of reaction substrate could logically provide divergent scaffolds from the common substrate. For instance, Lam *et al.* applied Pd and Ru catalysts to perform selective C-H functionalizations on quinolone derived substrates (**12**) with acetylenes (**13**) to produce the sprio-quinolones (**14**) and fused-quinolones (**15**), respectively (Scheme 3).[31]



Scheme 3. Catalyst-controlled divergent scaffold synthesis approach by Pd and Ru catalyst.

In recent years, many examples for the ligand-directed divergent synthesis (LDS) approach have been unraveled by using various transition metal catalysts. This is certainly due to many developments in synthesis and commercial availability of different types of ligands.[32] A large proportion of these reports utilized palladium and gold(I) catalyst with proper ligand selections to establish the synthesis of diverse scaffolds. For example, the furanocarboxamides (**16**) could either proceed by Heck type cyclization to give the spirooxindole (**20**) by palladium catalyst with PPh_3 as ligand, or C-H functionalization to generate the fused quinolone (**23**) by palladium catalyst with P(*o*-OMePh)$_3$ as the ligand through concerted metalation-deprotonation (CMD) process, as shown in Scheme 4.[33]



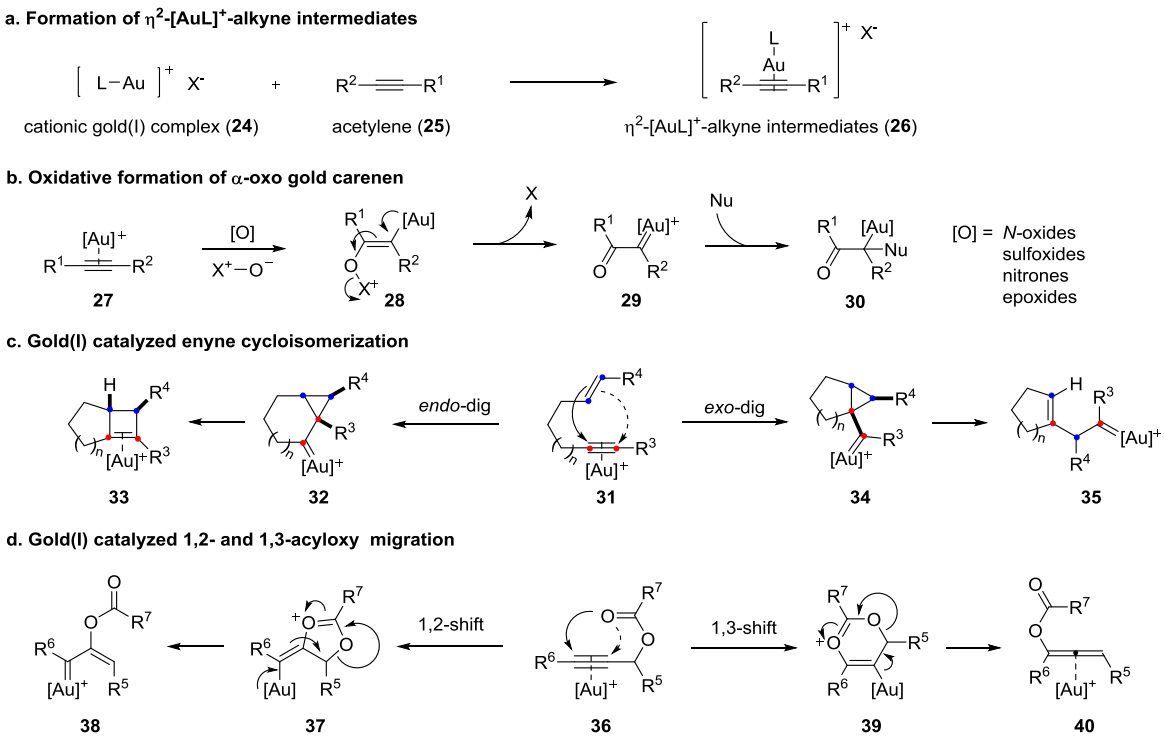
Scheme 4. Ligand-directed divergent scaffold synthesis approach by Pd catalyst.

With distinctive catalytic properties, gold(I) catalyzed transformations behave differently from Pd catalysis and endows with tunable and versatile catalytic nature to support reactions like photoredox reaction[34], cross couplings[35], as well a series of gold(I) catalyzed enyne cycloisomerizations[36], etc. that allow gold(I) catalyzed LDS to cover broader types of reactions and access broader chemical space.

1.3.1 Gold(I) catalyzed transformations

The gold(I) activated alkyne transformations have been extensively investigated among all of the gold catalyzed reactions, and widely applied in the synthesis of NPs and structurally complex molecules.[37] A cationic gold(I) complex (**24**) acts as a unique carbophilic π-acid catalyst to react with acetylene (**25**) and generating linear η^2-$[AuL]^+$-alkyne intermediates (**26**, Scheme 5a).[38] Based on this intermediate (**26**), three types of gold (I) catalyzed reactions were identified and utilized as key transformations to generate structurally complex frameworks, *i.e.* oxidative formation of α-oxo gold carbenes[39], enyne cycloisomerizations[36, 40], and acyloxy migrations[41] (Scheme 5b, 5c, and 5d). Generally, the η^2-$[AuL]^+$-alkynes (**37**, **31**, or **36**) are attacked by various nucleophiles (oxidants, olefin, carbonyl, *etc.*) to deliver *trans*-alkenyl-gold intermediates. When the nucleophile is an oxidant, such as *N*-oxides, sulfoxides, or nitrones, the oxidative α-oxo gold carbene formation reaction takes place to from the *trans*-alkenyl-gold intermediates (**28**).

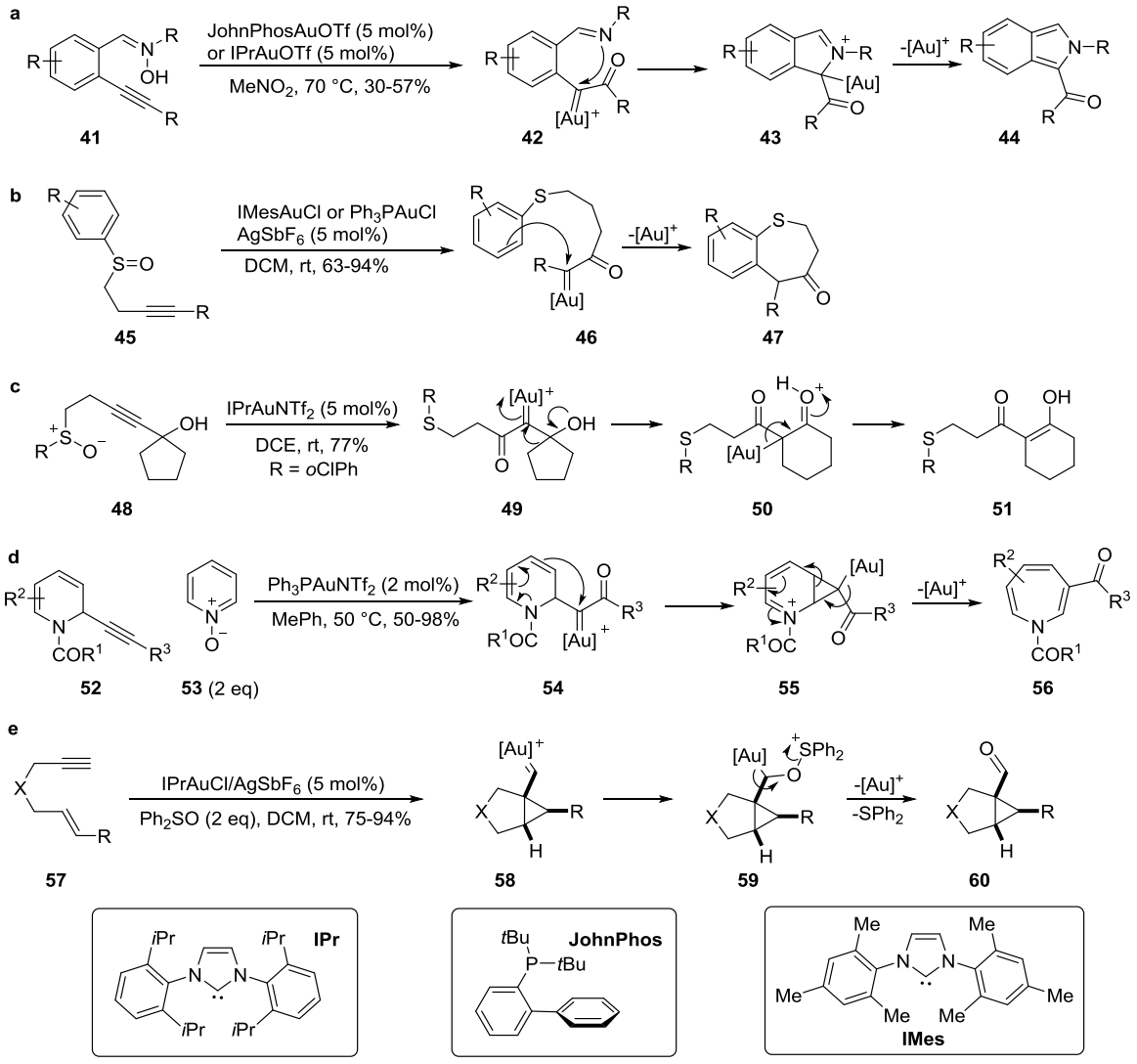
Subsequent elimination of leaving group provides the α-oxo gold carbenes (**29**). However, the experimental and computational results had suggested that the nucleophilic insertion would stabilize the reactive gold carbenes (**29**) leading to the gold(I) carbenoids (**30**, Scheme 5b).[42] An olefin nucleophile can add to the gold(I) activated acetlyenes (**31**) *via* an *endo*-dig or *exo*-dig cyclization mode, generating the endocyclic gold carbenes (**32**) or exocyclic gold carbenes (**34**), respectively. Further skeletal rearrangement of **32** would offer gold(I) activated cyclobutenes (**33**). The exocyclic gold carbenes (**34**) can yield gold carbenes **35** (Scheme 5c).[40] Interestingly, the carbonly function might also act as the nucleophile and add to the gold activated acetylenes (**36**).[43] In particular, the acyloxy group when present in the propargylic position, the carbonyl might follow a 1,2- or 1,3-shift of the acyl group assisted by gold(I) catalyst and *via* a 5-membered ring intermediates (**37**) or 6-membered ring intermediates (**38**) respectively. The 1,2-acyloxy shift will produce the gold carbenes (**38**) and 1,3-acyloxy shift will give the gold(I) activated allenes (**40**) as the reactive intermediates (Scheme 5d).[41] The understanding of these transformations might be helpful for the logically design suitable substrate to discover the divergent reaction pathways.



Scheme 5. a) Formation of η^2-[AuL]$^+$-alkyne intermediates. b) Oxidative formation of α-oxo gold carbene. c) Gold(I) catalyzed enyne cycloisomerization. d) Gold(I) catalyzed 1,2- and 1,3-acyloxy migration.

1.3.2 Oxidative formation of α-oxo gold carbenes

In the presence of internal or external oxidants, such as nitrones, sulfoxides, or *N*-oxides, tandem addition and elimination sequence provides reactive α-oxo gold carbene intermediates, which offer a variety of intriguing transformations. For example, treatment of the nitrone-tethered alkynes (**41**) with *N*-heterocyclic carbenes (NHC), such as IPr, or Johnphos gold(I) catalyst, followed the addition/elimination cascade reaction sequence to yield the α-oxo gold carbene (**42**). This reactive intermediate (**42**) subsequently afforded the isoindole **44** as the product *via* the azomethine ylide intermediate (**43**, Scheme 6a).[44] In 2007, Trost's and Zhang's group independently revealed that the sulfoxide function could behave as an oxygen source to yield the α-oxo gold carbene (**46** or **49**, Scheme 6b or 6c) that followed a Friedel-Crafts reaction (Scheme 6b)[45] or pinacol type ring expansion

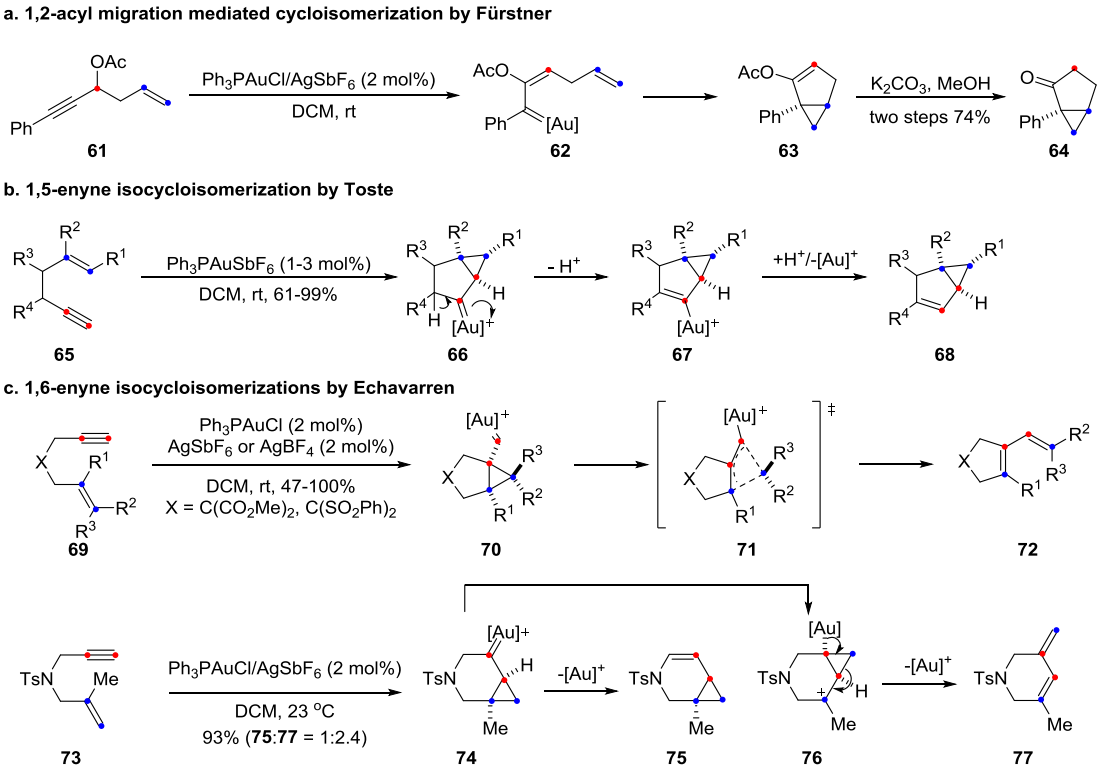


Scheme 6. Gold(I) catalyzed α-oxo gold carbene derived transformations.

reaction (Scheme 6c)[46], respectively. With pinacol type ring expansion method, Chen *et al.* had applied it to build up the azepine scaffold (**56**) by utilizing the pyridine-*N*-oxide (**53**) as an oxidant.[47] The alkynyl-dihydropyridine substrates (**52**) smoothly converted to gold carbene intermediates (**54**). The nitrogen lone pair of intermediates (**54**) triggered the addition to gold carbene moiety to form the cyclopropane intermediates (**55**), which relieved the ring-strain by ring-expansion-deauration to give the corresponding azepine products (**56**, Scheme 6d). It is worthwhile to mention here that Trost's group also revealed that the sulfoxide group can proceed with the oxidation of gold carbene to generate carbonyl decorated products from the enyne cycloisomerization intermediate.[48] The 1,6-enynes (**57**) under gold(I) catalysis followed a 5-*exo*-dig cyclization to give the exocyclic gold carbenes (**58**). The insertion of sulfoxide and elimination of thioether provided the exocyclic aldehydes (**60**) in high yield (Scheme 6e). The application of oxidant to gold activated acetylene could follow different cyclization modes, leading to different skeleton rearrangements, or integrate with cycloisomerizations to install an additional aldehyde functionality. These properties are beneficial to build up the intriguing molecular.

1.3.3 1,6-Enyne cycloisomerizations

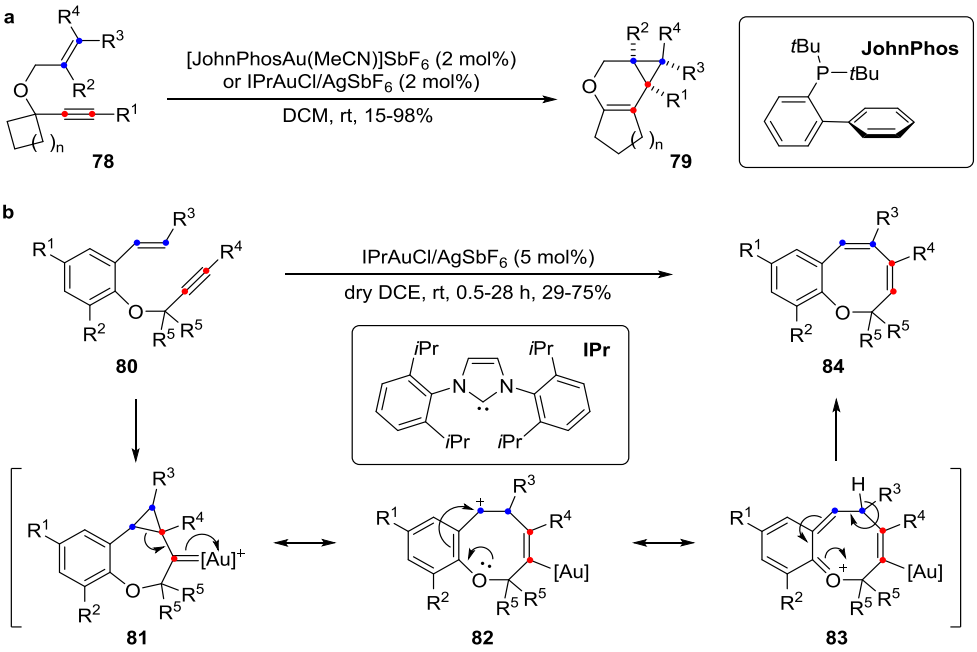
Enyne cycloisomerization reactions present one of the most important and well-investigated chemical transformations in homogeneous gold(I) catalysis. In 2004, Fürstner, Toste, and Echavarren independently reported the gold(I) mediated enyne cyclo-isomerization to form carbo- and heterocyclic molecules (Scheme 7). In case of 1,5-enyne with propargylic ester moiety (**61**), treatment with 2.0 mol% of $Ph_3PAuCl/AgSbF_6$ led to a 1,2-acyl migration to form the gold carbene (**62**) that followed the insertion to olefin and gave the bicyclic[3.1.0] enol acetate (**63**). Under basic reaction conditions, the enol acetate was converted to the ketone **64** (Scheme 7a).[49] Toste and co-workers treated 1,5-enynes (**65**), which lacked the ester moiety, with a gold(I) catalyst (Scheme 7b). A 5-*endo*-dig cyclization of 1,5-enynes (**65**) led to the *endo*-cyclic gold carbenes (**66**). A cascade of deprotonation and protodeauration provided the final bicyclo[3.1.0]hexenes (**68**) in 61-99% yield (Scheme 7b).[50] Echavarren reported that 1,6-enynes with different tethers could follow two different cyclization pathways, 5-*exo*-dig and 6-*endo*-dig cyclization. For instance, the carbon-tethered 1,6-enynes (**69**) gave the single-cleavage products (**72**) *via* 5-*exo*-dig cyclization and the nitrogen tethered 1,6-enyne (**73**) provided the mixture of bicyclic product **75** and single-cleavage product **77** *via* 6-*exo*-dig cyclization (Scheme 7c).[51]



Scheme 7. Gold(I) catalyzed enyne cycloisomerization.

These reports further garnered great attention and highlighted the potential of the gold(I) catalyzed enyne cycloisomerization in organic synthesis. However, usage of further modified enynes as substartes in these reactions had identified a greater synthetic application of gold catalyzed enyne cycloisomerizations. For instance, having a quaternary carbon at the propargylic position would prohibit the deprotonation or 1,2-*H* shift mechanism in oxygen tethered 1,6-enynes (**78**, Scheme 8a). Therefore, a 1,2-alkyl migration dominated the transformation to generate the ring expansion products **79** in 15-98% yield (Scheme 8a).[52] Waldmann, Kumar and coworkers designed the 8-*endo*-dig cyclization in 1,7-enynes (**80**) to construct the benzoxocines (**84**). The inductive effect of phenolic ether moiety was thus cleverly used to achieve desired chemo- and regioselectivity of cyclization reactions. Under gold(I) catalytic reaction conditions, the endocyclic gold carbenes (**81**) were initially formed. Cyclopropane ring opening ensured the formation of benzylic cations (**82**) or oxocarbenium intermediates (**83**), which followed deprotonation and protodeauration to yield benzoxocines (**84**) in 29-75% yield (Scheme 8b).[53]

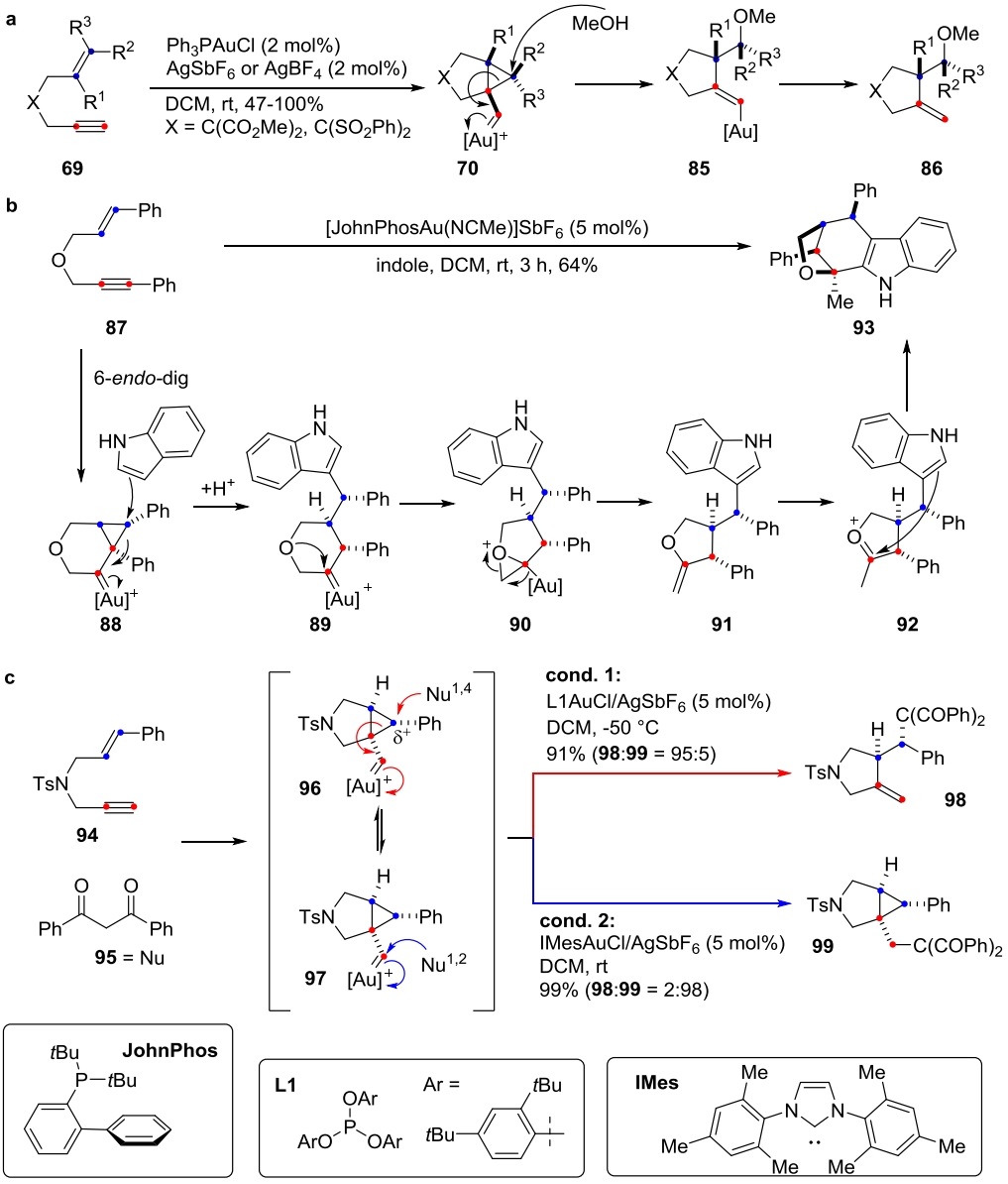
The introduction of nucleophiles to the cycloisomerization reaction intermediates is helpful not only to understand the reaction mechanism but also to enhance the structural diversity of the ensuing products. In the absence of a nucleophile, the carbon-tethered



Scheme 8. Gold(I) catalyzed enyne cycloisomerization.

1,6-enynes (**69**) afforded the dienes (**72**) as the product (Scheme 7c). However, addition of MeOH as nucleophile trapped the intermediates (**70**) by a 1,4-nucleophilic addition and led to the intermediates (**85**). The catalytic cycle was then closed by protodeauration to from the methylenecyclopentanes (**86**, Scheme 9a).[54] Intriguingly, when oxygen-tethered 1,6-enyne (**87**) was exposed to indole as nucleophile under gold (I) catalytic conditions, an endocyclic gold carbene intermediate (**88**) was formed through a more complex mechanistic pathway. The C3-indole addition to cyclopropane led to form the gold carbene (**89**). An internal addition ethereal oxygen to gold carbene formed a highly starained oxinium cation intermediate (**90**). The ring-strain in **90** was released by elimination of cationic gold(I) to generate the vinyl ether (**91**). The keto-enol tautomerization transformed the enol ether to oxocarbenium intermediate (**92**), which served as electrophile for the C2-indole and thus a nucleophilic addition of indole provided the polycycles **93** as the final product (Scheme 9b).[55] Intrestingly, the variation of ligands in gold(I)-complex could further alter the pattern of nucleophilic additions between the nucleophilic 1,2- and 1,4-addition, as shown in Scheme 9c.[55]

In the presence of gold(I) catalyst, the bicyclic gold carbene intermediate (**96**, **97**) was formed from *N*-tethered 1,6-enyne (**94**) *via* 5-*exo*-dig cyclization. The addition of the 1,3-diketone nucleophile (**95**) was modulated by the ligand effect. Thus, the gold(I) catalyst with electron-deficient phosphite ligand (**L1**) presented strong electrophilicity that allowed



Scheme 9. Nucleophiles associated gold(I) catalyzed 1,6-enyne cyclitations.

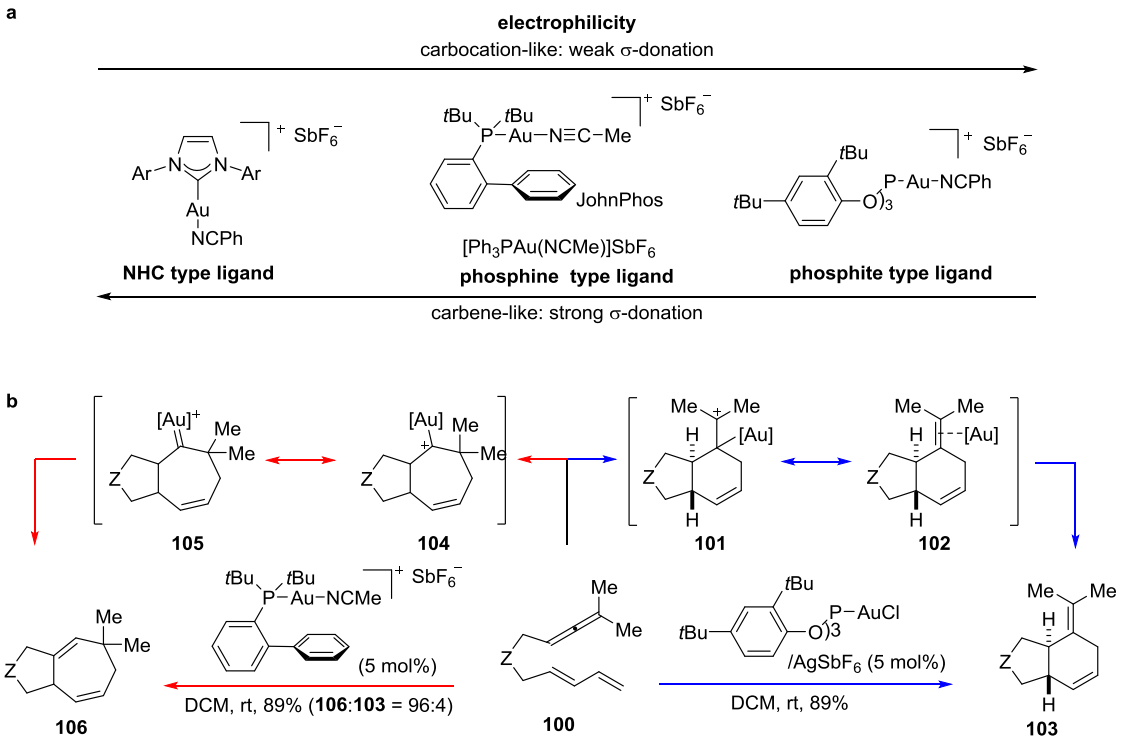
the 1,4-addition to become preferable. Hence, the nucleophilic 1,4-addition and protodeauration sequence took place to give the corresponding pyrrolidine (**98**) with a high selectivity of **98**:**99** = 95:5. In contrast, the electron-rich NHC ligand (**IMes**) enhanced the carbene property of gold carbene intermediate (**97**), which reversed the preference of selectivity in nucleophilic addition form 1,4-addition to 1,2-addition. Hence, the 1,2-addition product (**99**) was obtained in excellent yield and selectivity (Scheme 9c).

In gold(I) catalyzed enyne cycloisomerization, the mode of cyclizations and rearrangements are drastically influenced by several factors, including neighboring groups and heteroatoms in the enyne substrates, the presence of nucleophiles, as well as ligands in the cationic gold(I) complex.

1.3.4 Ligand effects in gold(I) catalyzed divergent reactions

In gold(I) catalyzed reactions, the proper utilization of different ligands can lead to formation of different products in varying selectivity and efficiency. The ligands can influence the reaction pathways owing to steric and/or electronic factors, and these factors cooperatively function to control the selectivity and efficiency of a gold(I) catalyzed reaction.[56] From the electronic factor point of view, the relativistic effect in gold(I) complexes results in the contracted 6s orbital and expanded 5d orbital of gold(I) and influences the electronic nature of the gold complexes, which is attributed to the electronic nature of the ligands used in a gold complex. Therefore, the properties of cationic gold(I) catalyst, gold carbene or carbenoid, can be fine-tuned *via* judicious selection of ligands (Scheme 10).[57] For example, NHC type ligands with strongly σ-donating and weakly π-acidic character will be preferred for the carbene-like reactivity. On the other hand, phosphite as a strong electron-withdrawing ligand may be favored for the carbocationic reaction pathways (Scheme 10a). Besides the ligands effects, gold(I) catalyzed reactions may also depend on the structural properties of the substrates and the reaction conditions employed.[57a]

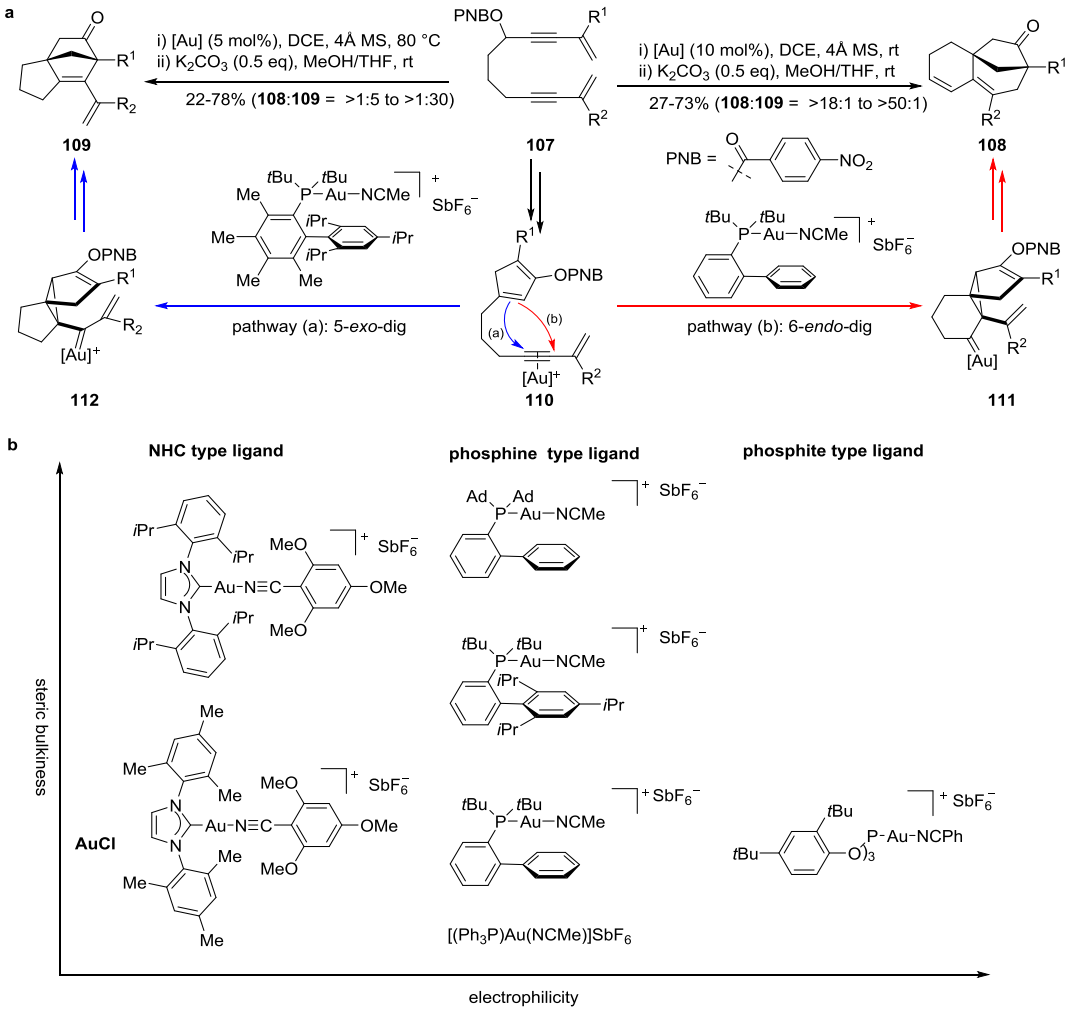
By tuning the ligands, the impact of the electronic nature of gold(I) complexes was observed in gold(I) catalyzed divergent allene diyne cyclization reactions. When utilizing phosphite as the ligand of a gold(I) catalyst, the allene diyne (**100**) underwent the carbocationic reaction pathway throght the carbocationic intermediate (**101**). Subsequently, deauration took place to give the [4+2] cycloaddition product **103** in 89% yield. Using a bulky phosphine ligand, the cyclization mode was altered to [4+3] cycloaddition through gold carbene intermediate (**105**). A subsequent 1,2-*H* shift and protodeauration formed the bicyclic[5.3.0]dienes (**106**) in 89% yield and with excellent selectivity (Scheme 10b).[58] Intriguingly, replacing bulky phosphine, JohnPhos, with PPh_3 led to a drop in the selectivity from **106**:**103** = 96:4 to **106**:**103** = 33:67 and with slight decrease in the reaction yield (**103**+**106**). The steric nature of the ligand also plays an important role in guiding product selectivity. As an example, the diene diynes (**107**) were prepared as substrate. By the treatment of gold(I) complexes with JohnPhos based ligands, the divergent bicyclic compounds were generated as the products (Scheme 11a). In such transformations, the common intermediates (**110**) were generated from the diene diyne substrates (**107**) *via* a gold catalyst assosciated 3-step cascade, 1,3-acyloxy migration to give the allenes, gold(I) assisted Nazarov type cyclization and protodeauration. When utilizing the JohnPhos as



Scheme 10. a) Electrophilicity tendency toward gold(I) catalyst with different ligands.[59] b) Gold(I) catalyzed divergent formal [4+3]/[4+2] cycloaddition with allenediene substrates.

ligand, the 6-*endo*-dig cyclization took place to form the endocyclic gold carbene intermediates (**111**). On the other hand, the highly bulky ligand Me_4tButylXphos modulated the cyclization mode to 5-*exo*-dig cyclization leading to exocyclic gold carbene inter-mediates (**112**) in order to release the steric repulsion between the ligand and the substrate. With the gold carbene intermediates (**111**, **112**) in hand, a sequential rearrangement, deauration, and hydrolysis provided the corresponding bicyclic products **108** and **109** respectively in good to excellent selectivity (Scheme 11a). However, in most of the cases, the steric and electronic nature of the ligand should both be considered to obtain the desired selectivity and yield of the divergent products. Recently, Echavarren *et al.* depicted the electrophilic tendency of the major type of gold(I) catalyst[36] which can be further extended to the commercially available ligands for the assistance of reaction development and optimization (Scheme 11b).

Although the gold(I) catalyzed LDS approach seems to be robust, the preparation of small molecule collections by this approach is still difficult and challenging due to: 1) A large proportion of substrates are composed by the full carbon backbone with protected heteroatoms. The non-polar nature of the substrates and products renders the purification



Scheme 11. a) Ligand controlled formal [3+2]/[2+2] cycloaddition. b) Relative electrophilicity and steric bulkiness of representative gold(I) catalysts.[36]

and isolation of products relatively difficult. 2) Often, due to the same molecular mass of the products as that of starting material, the structural determination of rearrangement products as well as their regio- and stereoisomers by NMR analyses is also challenging. 3) Generally, the substrates encounter severe restriction on the scope of transformations as not all functionals groups and modifications are tolerated in gold catalysis reactions. 4) In most of the cases, the gold(I) catalyzed LDS approaches provide no more than two distinctive products and the higher order of divergency is still challenging and demanding.

These facts and challenges encouraged us to initiate this gold(I) catalyzed LDS approach to build up a molecule compound collection well represented by scaffold diversity and that can be used in cell based biological screenings to realize the potential of the ensuing products in medicinal and biological research.

2 Design and aim of the project

Gold(I) catalyzed reactions have been reported with versatile transformations by modulating electronic and steric parameters in gold(I) complexes, and therefore gold(I) catalyzed reactions were selected to develop a unified approach to steer common enyne substrates into diverse and distinct molecular scaffolds. In this approach, reactive chemical handles would be an essential segment in substrate to guide different transformations leading to scaffold diversity as well as offering variations on the periphery of distinct scaffolds. The handles could be installed on a privileged ring system that allow the resulting scaffold with potential biological relevance. Moreover, the functional groups of the substrate can participate in further chemical manipulations to build up a compound library (Figure 5a). By treatment with a gold(I) catalyst, the chemical handles can be activated to form the common/divergent intermediate(s), as illustrated in Figure 5b. Subsequently, the isomerization reactions could convert the intermediate(s) to the divergent scaffolds by verifying the ligand properties in a gold(I) catalyst (Figure 5c). If the gold(I) catalyzed transformations were not successful, the chemical handle redesign might be helpful to alter the property of intermediate and provide the desired product-divergency. With the divergent catalytic transformations, a compound library with scaffold divergency could be prepared by verifying the sites for chemical manipulation (Figure 5d). Ultimately, the collection of structurally divergent small molecules could be utilized to explore the biological relevant chemical space and the molecular functions in biological system *via* bioactivity screening.

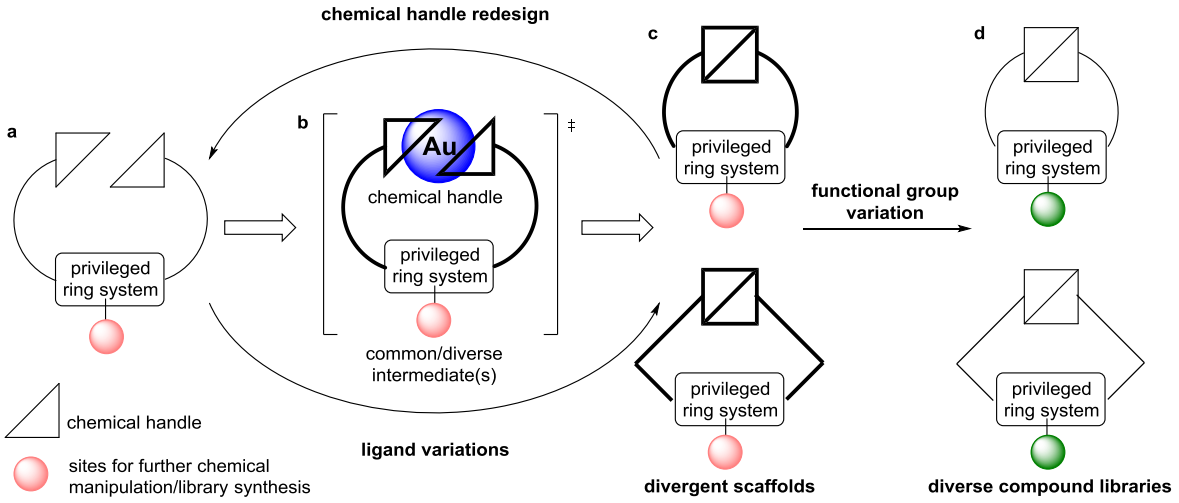


Figure 5. Schematic representation of ligand directed divergent scaffold synthesis (LDS).

Although, the ligand associated gold(I) catalyzed divergent scaffold synthesis should allow to access structurally novel ring systems from a unified substrate class (Figure 6a). To ensure the biological relevance of the products, the substrates are generated based on a privileged ring system (Figure 6b). It was planned to use substrates with different functional groups so that the biological screenings later can display some sort of structure activity relationship (SAR). With these ideas, 1,6-enynes supporting an oxindole as privileged ring were selected as substrates for gold catalyzed divergent scaffold synthesis (Figure 6c). The assembly of substrates was performed in sequential steps, *i.e.* first alkylation of *N*-oxindole, followed by lithium acetylide addition to the ketone moiety of alkylated oxindole, and later allylic ether formation from propargyl alcohol to get the oxindole based 1,6-enyne substrates. Substituents on oxidole nitrogen and phenyl ring could establish diversity in the collections and the substituents on 1,6-enyne could influence the reaction pathway and might also help in generation of functional group variation around different scaffolds. The screenings of small molecule compound collection could be performed at Compound Management and Screening Center (COMAS), Dortmund for the primary screening for HH, Wnt, and Autophagy inhibition to sort out the bioactive molecules (Figure 6d).

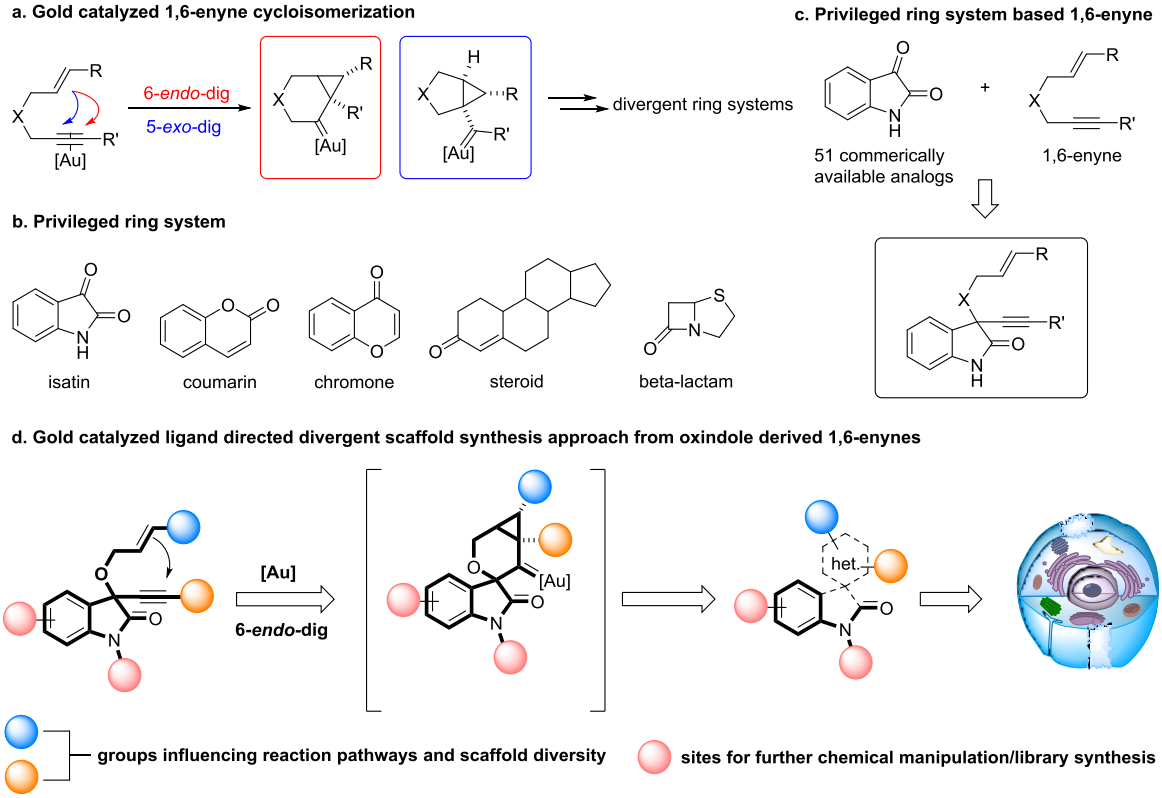
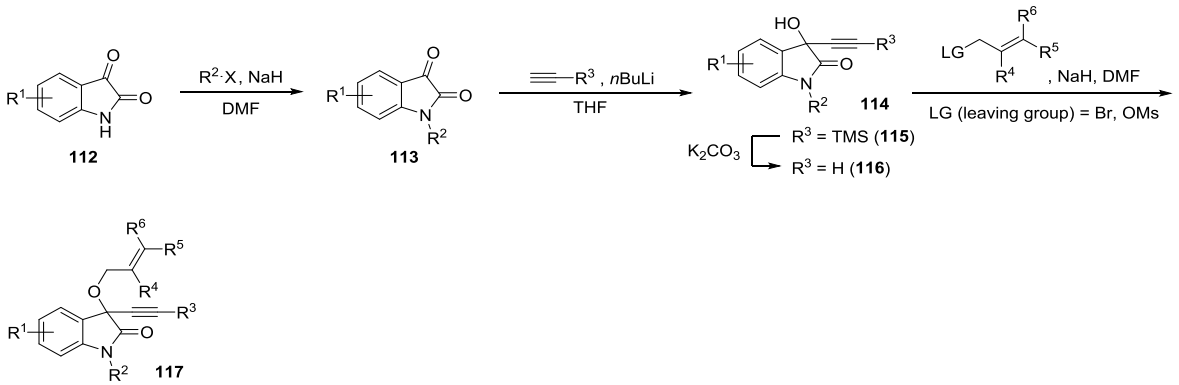


Figure 6. A combination of LDS approach with privileged ring system to generate small molecule collection for biological screening.

3 Results and discussion

The terminal alkynes in *O*-tethered 1,6-enynes predominately react via 5-*exo*-dig cyclizations to give the *exo*-gold carbene intermediates. But alkyl or aryl substituted alkynes prefer 6-*endo*-dig cyclization delivering *endo*-gold carbene intermediates in gold(I) mediated reactions.[60] To develop a unified synthetic route, I chose the oxindole based 1,6-enynes **117** as the substrates for scaffold diversity synthesis planning. A straightforward synthesis of **117** was explored by utilizing isatin **112** as the starting material. After the protection of nitrogen, addition of lithium acetylide to the keto moiety of **113** gave the propargyl alcohol **114**. While the R^3 is TMS group (**115**), the terminal alkyne functionality of **116** could be produced *via* removal of the silyl group with K_2CO_3 in MeOH. The propargyl group with hydrogen, alkyl, or aryl substitutions could then undergo the *O*-allylation to provide the desire substrates **117** (Scheme 12).



Scheme 12. The general synthetic approach of oxindole based 1,6-enyne.

In gold(I) catalyzed enyne cycloisomerizations, the protection of the nitrogen in substrates is important because the substrates bearing nonprotected nitrogen are often considered incompatible for the reactions. The nucleophilicity of nitrogen is stronger than olefin and may either lead to addition of nitrogen to the gold(I) activated acetylene, or the lone pair of the nitrogen can coordinate with the empty orbital of gold(I) catalyst itself resulting in the deactivation of the catalyst. Protection of nitrogen thus with aryl, sulfonyl, and carbonyl groups can be helpful. For instance, Fürstner *et al.* applied the carboxybenzyl (Cbz) as the nitrogen protecting group to complete the synthesis of the antidepressive drug candidate GSK1360707.[65] Encouraged by some reported gold(I) catalyzed transformations of indole derivatives,[66] I believed that the oxindole based 1,6-enyne can also prove interesting substrates of the gold(I) catalyzed reactions to yield structurally different

products. Besides the substrate, the mode of gold(I) catalyzed 1,6-enyne cyclo-isomerizations largely relies on the ligand around the cationic gold(I) complex, so a ligand screen is inevitable in the initial reaction screening process.[61] Therefore, gold(I) catalysts with representative ligand decorations, *i.e.* strong σ-donating NHC ligand, moderate σ-donating JohnPhos ligand, and poor σ-donating phosphite ligand, were selected for uncovering the potential reaction pathways of enyne (**117**) substrates. The other factors, such as solvent[63], counter anion[62] of gold(I) catalyst, and temperature[43c, 64], will also be considered during the condition screening process (Figure 7).

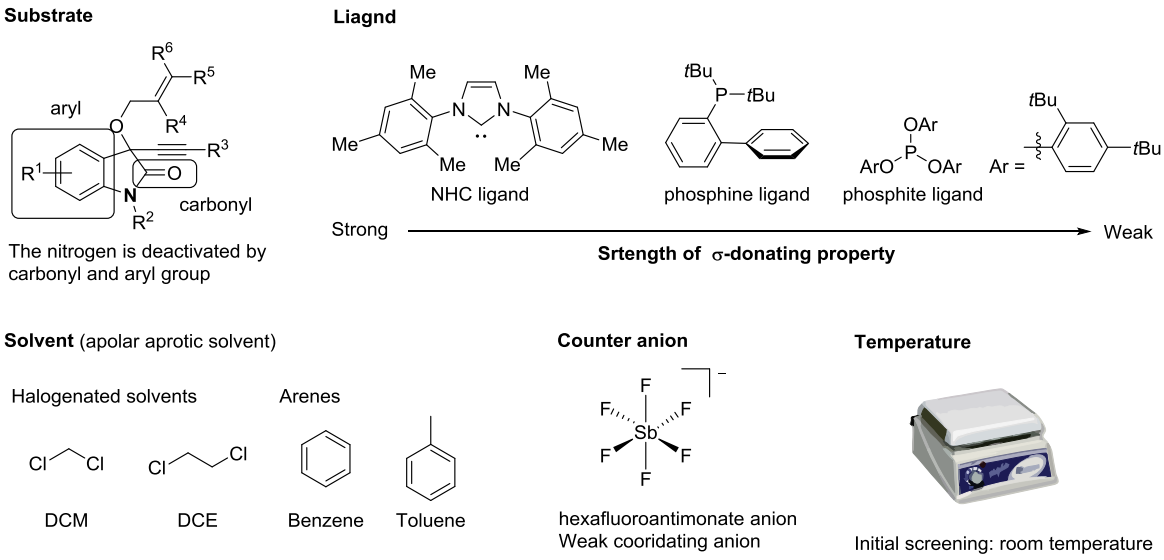
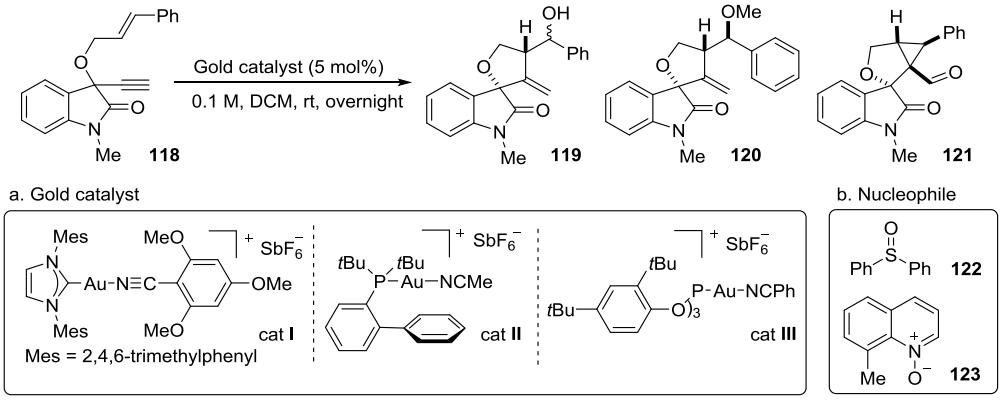


Figure 7. Schematic representation for the initial screening process.

3.1 Gold(I) catalyzed cycloisomerizations of 1,6-enynes with a terminal acetylene

The initial screening for the divergent scaffold synthesis approach began with the terminal alkyne **118** as substrate (Table 1). By treatment of NHC gold(I) catalyst (**I**) or bulky phosphine gold(I) catalyst (**II**) to the 1,6-enyne (**118**) in DCM, the hydroxyl group adducts (**119**) were observed in all reactions along with unidentified side products (Table1, entry 1-2). The selectivity was improved by utilizing the electrophilic phosphite gold(I) catalyst (**III**) and the diastereomeric hydroxyl adducts (**119**) were afforded in 57% with 1:1 diastereomeric ratio (dr) and without generating any side product (entry 3). The hydroxyl group adduct (**119**) might come from the addition of trace amount of moisture to the reactive intermediate. In the presence of 4 Å molecular sieves (MS), no reaction happened, and the starting material remained unrected as the observed from crude NMR elucidation (entry 4). By employing the MeOH as nucleophile in the gold(I) catalyzed reaction, the methoxy adduct (**120**) was formed in a stereoselective manner. The structure was unambiguously determined by single-crystal X-ray analysis (see the experimental section). The less electrophilic gold(I) catalysts, **I** and **II**, gave good yield for **120** in 81% and 72%, respectively (entry 5-6). When most electrophilic gold(I) catalyst (**III**) was applied to the reaction, an excellent yield of 90% was obtained for **120** (entry 7). Inspired by the work from Toste's group[48], the diphenyl sulfoxide (**122**) was used as the oxidative nucleophile to trap the gold carbene intermediate, which might provide the aldehyde (**121**) as the product. The newly generated aldehyde functionality can serve as the reactive handle for various late-stage functional group manipulations, such as reduction, reductive amination, nucleophilic addition, *etc.*, which is beneficial for the further chemical biology studies. The desired aldehyde (**121**) was isolated in relative low yield and along with the hydroxyl group adduct (**119**) by treatment of a series of gold(I) catalysts (entry 8-10). In the presence of 4 Å MS, the conversion of aldehyde (**121**) was drastically improved to 52% yield by phosphite gold(I) catalyst **III** (entry 11). Using another oxidative nucleophile, the 8-methylquinoline *N*-oxide (**123**, entry 12) displayed similar reaction outcome to diphenyl sulfoxide (**122**, entry 8) in the NHC gold(I) (**I**) catalyzed condition. On the other hand, the other gold(I) catalysts (**II** and **V**) did not give any product (entry 13-14).

Table 1. Catalysts and nucleophiles screening of gold(I) catalyzed 5-*exo*-dig cyclization.



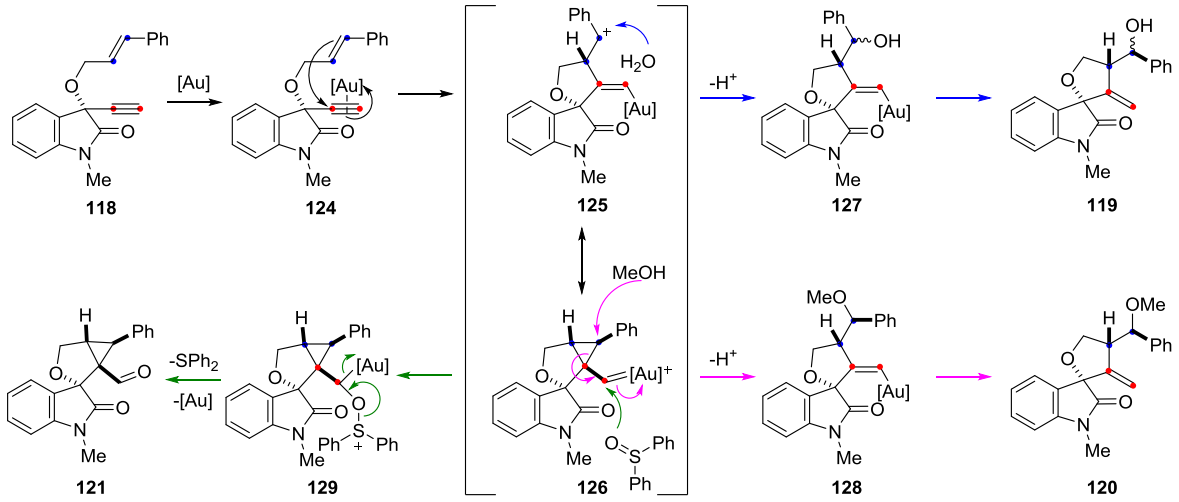
Entry	[Au]	Nu (eq)	Product (Yield)	Note
1	**I**	-	-	observed **119**[a]
2	**II**	-	-	observed **119**[a]
3	**III**	-	**119** (57%)	dr = 1:1
4[b]	**III**	-	-	-[c]
5	**I**	MeOH (20 eq)	**120** (81%)	-
6	**II**	MeOH (20 eq)	**120** (72%)	-
7	**III**	MeOH (20 eq)	**120** (90%)	-
8	**I**	**122** (1.1 eq)	**121** (trace)	observed **119**
9	**II**	**122** (1.1 eq)	**121** (16%)	observed **119**
10	**III**	**122** (1.1 eq)	**121** (21%)	observed **119**
11[b]	**III**	**122** (1.1 eq)	**121** (52%)	-
12[d]	**I**	**123** (1.1 eq)	**121** (trace)	-[a]
13[d]	**II**	**123** (1.1 eq)	-	-[c]
14[d]	**III**	**123** (1.1 eq)	-	-[c]

[a] Non-selective reaction. [b] Addition of 4 Å MS. [c] Starting material recovery. [d] Reaction was operated at 60 °C seal tube.

3.1.2 Reaction mechanism

Taking cognizance of the reported gold(I) catalyzed cycloisomerization reactions, I propose that cationic gold(I) catalyst activates the acetylene first. Nucleophilic addition of olefin concurrently takes place to form the vinyl gold (**125**) or exocyclic gold carbene intermediate (**126**), as shown in Scheme 13.[48, 55] In the presence of trace amounts of moisture, water undergoes nucleophilic addition to the intermediate **125**, which subsequently gives the hydroxylated adduct (**119**) *via* vinyl gold intermediate (**127**). By utilizing excess amount nucleophile, the 1,4-addition of nucleophile dominates the reaction causing the cyclopropane ring-opening in stereospecific manner. The protodeauration of intermediate **128** closed the catalytic cycle to provide the spirooxindole (**120**) as the final product. Interestingly, the 1,2-addition of diphenyl sulfoxide to the gold carbene happened in a different manner and followed the Swern type oxidative elimination of thioether to form the aldehyde (**121**).

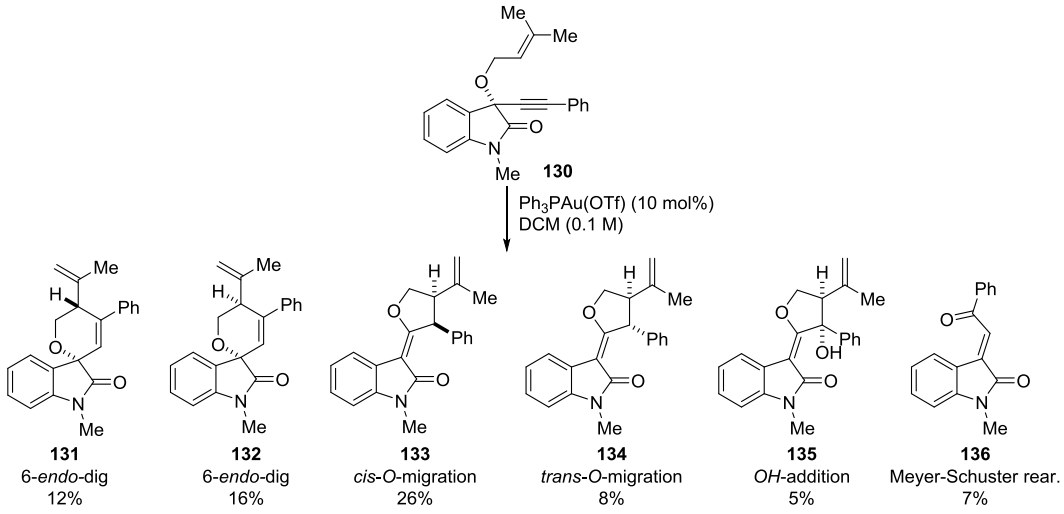
In the terminal alkyne substrate (**118**), the gold(I) catalyzed 5-*exo*-dig cyclization provides the exocyclic gold carbene intermediate (**126**) and the fate of this intermediate can be modulated by different types of nucleophiles to perform 1,2- or 1,4-nucleophilic addition leading to the spirooxindole **121** or **120**, respectively.



Scheme 13. Proposed reaction mechanism of gold(I) catalyzed spirooxindole formation.

3.2 Gold(I) catalyzed cycloisomerizations of oxindole based prenylated 1,6-enynes

The prenylated 1,6-enyne (**130**) was synthesized for the investigation of gold(I) catalyzed cycloisomerization *via* 6-*endo*-dig cyclization. The initial study began with treatment of 5 mol% of $Ph_3PAu(BF_4)$, generated *in situ* by mixing the Ph_3PAuCl and $AgBF_4$ in DCM, to the 1,6-enyne substrate (**130**). In this case, no reaction occurred, and the starting material was fully recovered (Table 2, entry 1). The reactivity of the gold(I) catalyst was improved by replacing the $AgBF_4$ by AgOTf. However, a substantial amount of starting material remained unreacted (entry 2). Complete conversion was observed by applying 10 mol% of *in situ* prepared $Ph_3PAu(BF_4)$ catalyst to the 1,6-enyne (**130**, Scheme 14 and Table 2, entry 3). The spirooxindole (**131**) was isolated in 12% yield accompanied with the *epi*-spirooxindole (**132**) in 16% yield. The major product (**133**) in this reaction was obtained in 26% yield and was found to embody a novel scaffold, *i.e.* (*E*)-3-(dihydrofuran-2 (3H)-ylidene)indolin-2-one (*df*-oxindole) with *iso*-propenyl and phenyl substitution in *cis* configuration. The *trans*-*df*-oxindole (**134**) was also isolated in 8% yield. Among *df*-oxindole products, the *df*-oxindole (**135**) bearing hydroxyl group at benzylic position was the unexpected product from the gold(I) catalyzed enyne cycloisomerization. All the relative configurations of spirooxindoles and *df*-oxindoles were corroborated by single crystal X-ray analysis of representative molecules (see experimental section). The Meyer-Schuster rearrangement product (**136**) was formed in 7% yield and the chemical structure was confirmed by comparing the ^1H NMR with reported reference.[67]



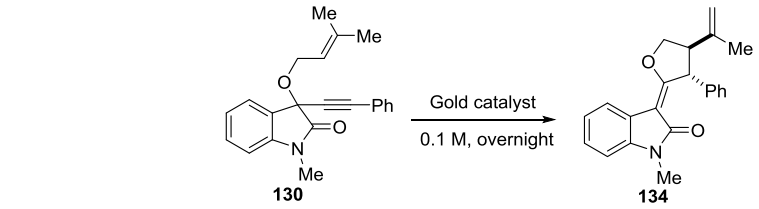
Scheme 14. Proposed reaction mechanism of gold(I) catalyzed spirooxindole formation.

3.2.1 Reaction optimization towards *df*-oxindole scaffold

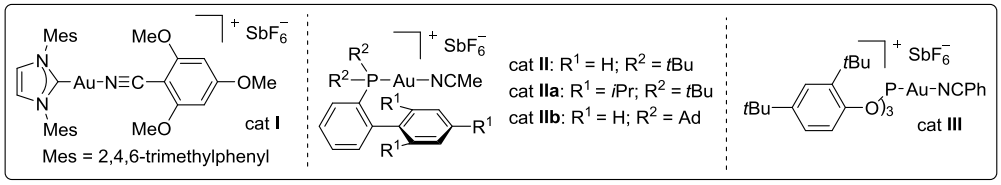
In order to realize the reaction conditions that can offer selective formation of intriguing and novel scaffolds from 1,6-enyne (**130**), further reaction condition screening and optimization was pursued as shown in Table 2. By switching the gold(I) to the higher oxidation state, gold(III) chloride, none of the cycloisomerization products was generated (entry 4). Therefore, further investigation was focused on gold(I) catalysts with different ligands. While the NHC gold(I) catalyst (**I**) provided no product under standard condition, increasing the concentration of substrate to 0.2 M led to the non-selective reaction (entry 5-6). However, the steric bulkiness of phosphine (**II**) drastically enhanced the selectivity towards *df*-oxindole (**134**) that was formed in moderate yield (51%, entry 7). More steric bulkiness on phenyl ring (**IIa**) or the alkyl group (**IIb**) of phosphine ligand didn't further influence the yield of **134** (entry 8-9). The product selectivity was again lost with electrophilic phosphite gold(I) catalyst (**III**), and *df*-oxindole (**134**), starting material (**130**) and spriooxindoles (**131** and **132**) were isolated in 17%, 40%, 13%, and 30% yield, respectively (entry 10).

With the ideal gold(I) catalyst (**II**) in hand that afforded selectively the *df*-oxindole (**134**), the influence of solvents on the reaction was further investigated. With non-polar solvent, toluene, the yield of **134** decreased to 40% (entry 11). While using diethyl ether enhanced the yiled to 38%, tetrahydrofuran (THF) afforded excellent yield of 95% (entry 12-13). With 1,4-dioxane as solvent, the moderate yield of 59% was obtained (entry 14). These results can be rationalized by the tendency of intermediate stabilization by the lone pair of oxygen. The more polar solvents were also examined, but the yield of **134** decreased to 38% in nitromethane ($MeNO_2$) and there was no reaction using acetonitrile as solvent (entry 15-16). When dimethylformamide (DMF) was used as a polar protic solvent, no reaction occurred (entry 17). The reduction of catalyst loading from 5 mol% to 3 mol% also compromised the yield of **134** to 91% (entry 18). Therefore, the optimal condition was settled for 0.1 M of substrate (**130**) with 5 mol% of **II** in THF solvent for an overnight reaction to give *df*-oxindole (**134**) as product.

Table 2. Reaction optimization for the gold(I) catalyzed synthesis of *df*-oxindole.



Gold catalyst

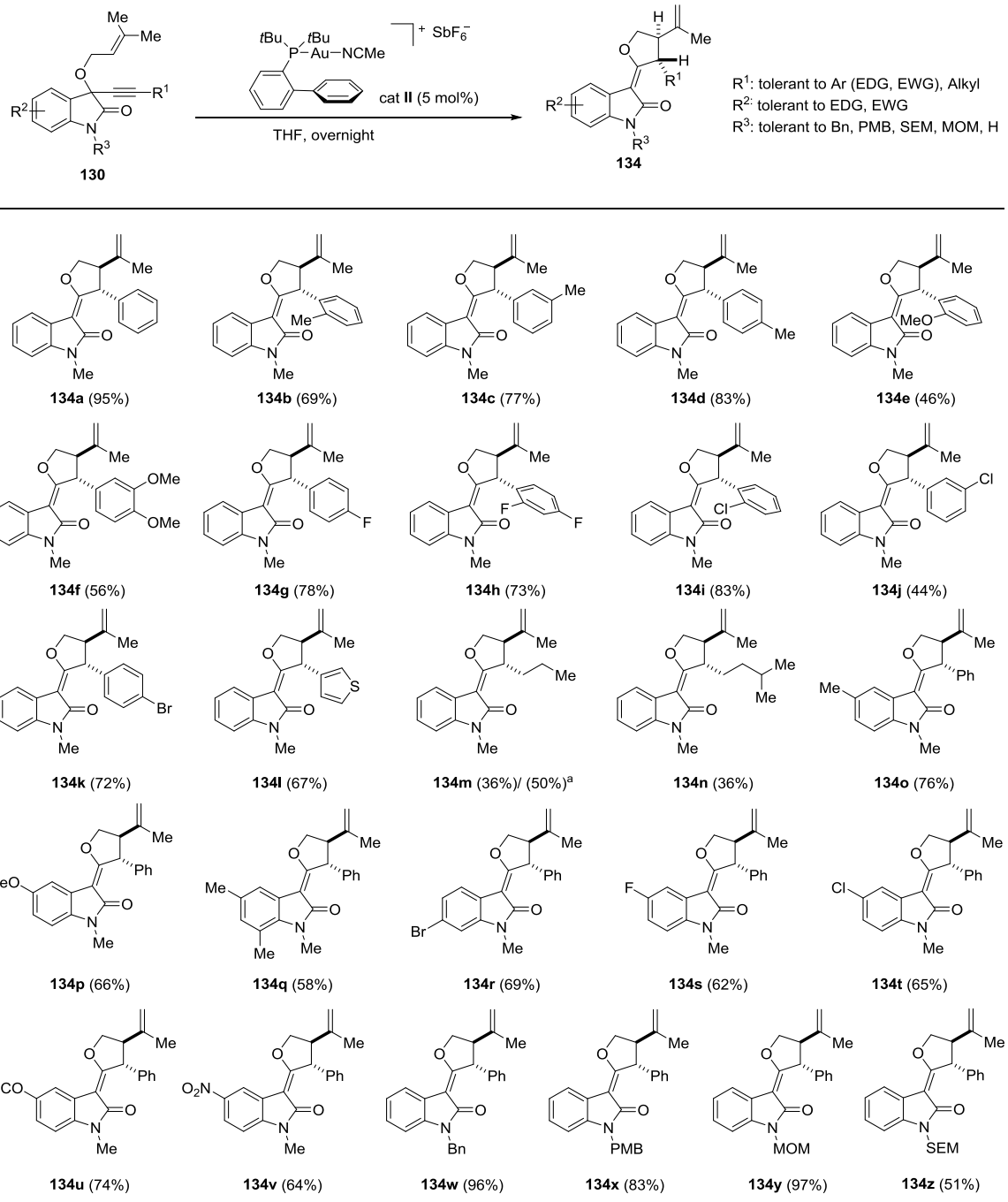


Entry	[Au] (5 mol%)	Solvent	Yield (%)
1	$Ph_3PAu(BF_4)$	DCM	-[a]
2	$Ph_3PAu(OTf)$	DCM	15[b]
3	$Ph_3PAu(OTf)$[c]	DCM	19[d]
4	$AuCl_3$	DCM	-[a]
5	**I**	DCM	-[a]
6	**I**[d]	DCM	-[e]
7	**II**	DCM	51
8	**IIa**	DCM	49
9	**IIb**	DCM	40
10	**III**	DCM	17[f]
11	**II**	toluene	40
12	**II**	diethyl ether	38
13	**II**	**THF**	**95**
14	**II**	1,4-dioxane	59
15	**II**	$MeNO_2$	38
16	**II**	ACN	-[a]
17	**II**	DMF	-[a]
18	**II** [g]	THF	91

[a] Starting material recovery. [b] Incomplete reaction. [c] 10 mol% catalyst loading. [d] The complete compound isolations were shown in Scheme 14. [d] Concentration of SM is 0.2 M. [e] Non-selective reaction. [f] The compound **130** (40%) **131** (13%), and **132** (30%) were isolated. [f] 3 mol% catalyst loading. Ad, adamantly.

3.2.2 Reaction scope

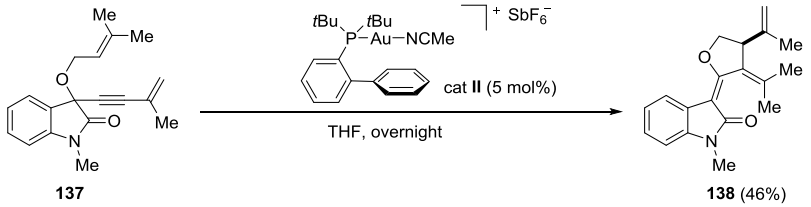
With the optimal reaction conditions in hand, the scope of the gold(I) catalyzed *df*-oxindole formation was studied by varying substitutions on the acetylenic moiety (R^1) as well as on the aryl ring (R^2) and the *N*-protecting group (R^3) on the oxindole based 1,6-enyne (**130**). The results are summarized in Scheme 15. Substitutions on the acetylene (R^1) with differently decorated phenyl ring with mono-methyl substitution on *o*-, *m*-, or *p*-position were well tolerated, giving the products (**134b-d**) in 69-83% yield. An aryl ring with other electron donating groups (EDGs), *i.e. o*-MeO-Ph or *m,p*-diMeO-Ph, could also provide the desired product in 46% (**134e**) or 56% (**134f**) yield. A variety of substrates with electron withdrawing groups (EWGs) on the phenyl ring were prepared to examine the scope of the reaction. The optimal catalytic condition nicely transformed them to the desired products in moderate to good yields (**134g-k**). As a representative example of heterocyclic substitution, the *df*-oxindole (**134g**) bearing thiophene moiety was also synthesized in 67% yield. It's worthy to note that products bearing linear or branched alkyl chains at R^1 position could also be prepared in 36% yield in each case, owing to the incomplete reaction (**134m** and **134n**). Increasing the catalyst loading to 10 mol% improved the yield of **134m** to 50%. Secondly, substitutions on the aryl moiety (R^2) of oxindole were examined. The substrates with Me or OMe substitution at the 5-position of oxindole gave good yield for **134o** and **134p** in 76% or 66%, respectively. However, the dimethyl-substituted analog (**134q**) was obtained in moderate yield (58%). Mono-halogenated oxindole substrates (F-, Cl-, or Br-) followed smooth conversion and the products (**134r-t**) were isolated in 62-69% yields. The oxindoles embodying strong EWG, such as trifluoromethoxyl or nitro group, were also tolerated in this transformation and provided good yields for *df*-oxindoles, **134u** and **134v**. In the end, a series of *N*-protecting groups (R^3), for example benzyl (Bn), *p*-methoxy benzyl (PMB), methoxymethyl (MOM), and 2-(trimethylsilyl)ethoxymethyl (SEM) were installed on to the nitrogen to examine the reactivity of protected and unprotected (NH) substrates in this gold(I) catalyzed reaction. Most of the N-protected substrates provided excellent yields for the desired products (**134w-y**), but the SEM substrate seems to be incompatible with Lewis acidic conditions, affording the product **134z** only isolated in 51% yield. In general, the substitutions on R^1 to R^2 of 1,6-enyne substrates were well tolerated and afforded the desired products in moderate to excellent yields (Scheme 15).



[a] with 10 mol% catalyst loading.

Scheme 15. Reaction scope of gold(I) catalyzed *df*-oxindole formation.

During the exploration of the reaction scope, the *gem*-dimethyl *df*-oxindole (**138**) was generated from 1,6-enyne substrate with *iso*-propenyl moiety (**137**) in 46% yield. In addition to offering an interesting substitution on the *df*-oxindole, this reaction also offers a hint for the mechanistic insights into gold(I) catalyzed *df*-oxindole formation (Scheme 16).

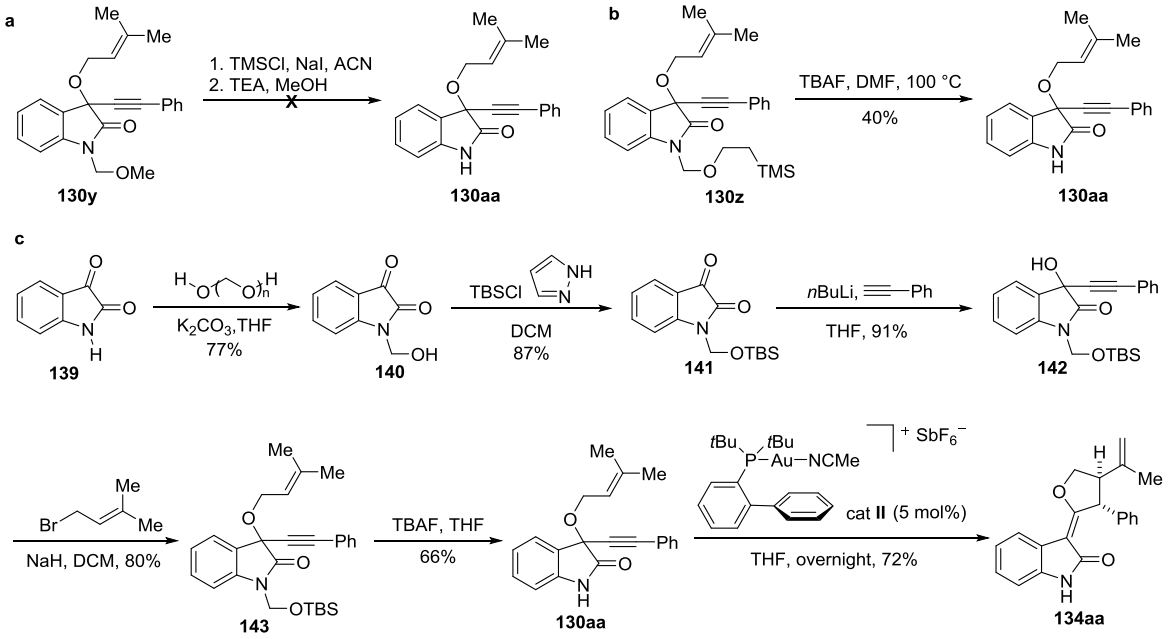


Scheme 16. Gold(I) catalyzed *df*-oxindole **138** formation.

3.2.3 Development of a removable *N*-protecting group for oxindole based 1,6-enyne cycloisomerization reaction

Having a NH group or a removable *N*-protecting group on the oxindole offers opportunities for further chemical manipulations in the compound collection synthesis of *df*-oxindoles. In this regard, the preparation of non-protected oxindole substrates were performed. Considering the substrate synthesis, the nitrogen has to be protected to avoid the over-allylation during the allyl ether formation step. Two factors were to be considered in the protecting group selection, first was the stability of protecting group during the synthesis sequence, and second is the condition for protecting group removal. With the available *N*-protected substrates in hand, the first attempt was the removal of *N*-MOM protection from 1,6-enyne **130y**, however the enyne moiety was sensitive to the acidic condition leading to the decomposition of substrate (Scheme 17a). The second trial was with employing tetra-*n*-butylammonium fluoride (TBAF) assisted SEM cleavage from 1,6-enyne **130z** in DMF as solvent and at 100 °C, and the desired product (**130aa**) was obtained in 40% yield (Scheme 17b). The low yield of the product and the low reproducibility called for a more robust synthetic approach. The silyloxymethyl *N*-protection[68] can be removed under relatively milder fluoride ion deprotection condition than SEM protection. A two-step approach was performed in gram scale synthesis of (tertbutyldimethylsiloxy)methyl protected isatin (**143**). In the presence of potassium carbonate, the isatin (**139**) was treated with paraformaldehyde to form the hemiaminal (**140**), which followed the conventional TBS protection condition to generate the desire substrate with corresponding *N*-protection (**141**). Previously developed 1,6-enyne synthesis approach was applied to form the desired substrate

(**143**) in excellent yield both in the alkynylation step and in the allylation step. The *N*-deprotection could be done by using TBAF to give the enenye **130aa** in 66% yield (Scheme 17c). With the non-protected oxindole based 1,6-enyne (**130aa**), the gold(I) catalyzed synthesis of corresponding *df*-oxindole was performed. In the first attempt, it was proved that the purity of the enyne substrate is crucial for the transformation, *i.e.* trace amounts of TBAF may deactivate the gold(I) catalyst, resulting in recovering of the starting material. Gratefully, after another purification by silica gel column chromatography and removal of moisture by high vacuum, the pure 1,6-enyne (**130aa**) gave the expected product **134aa** in 72% yield under the optimized reacion condition (Scheme 17c).



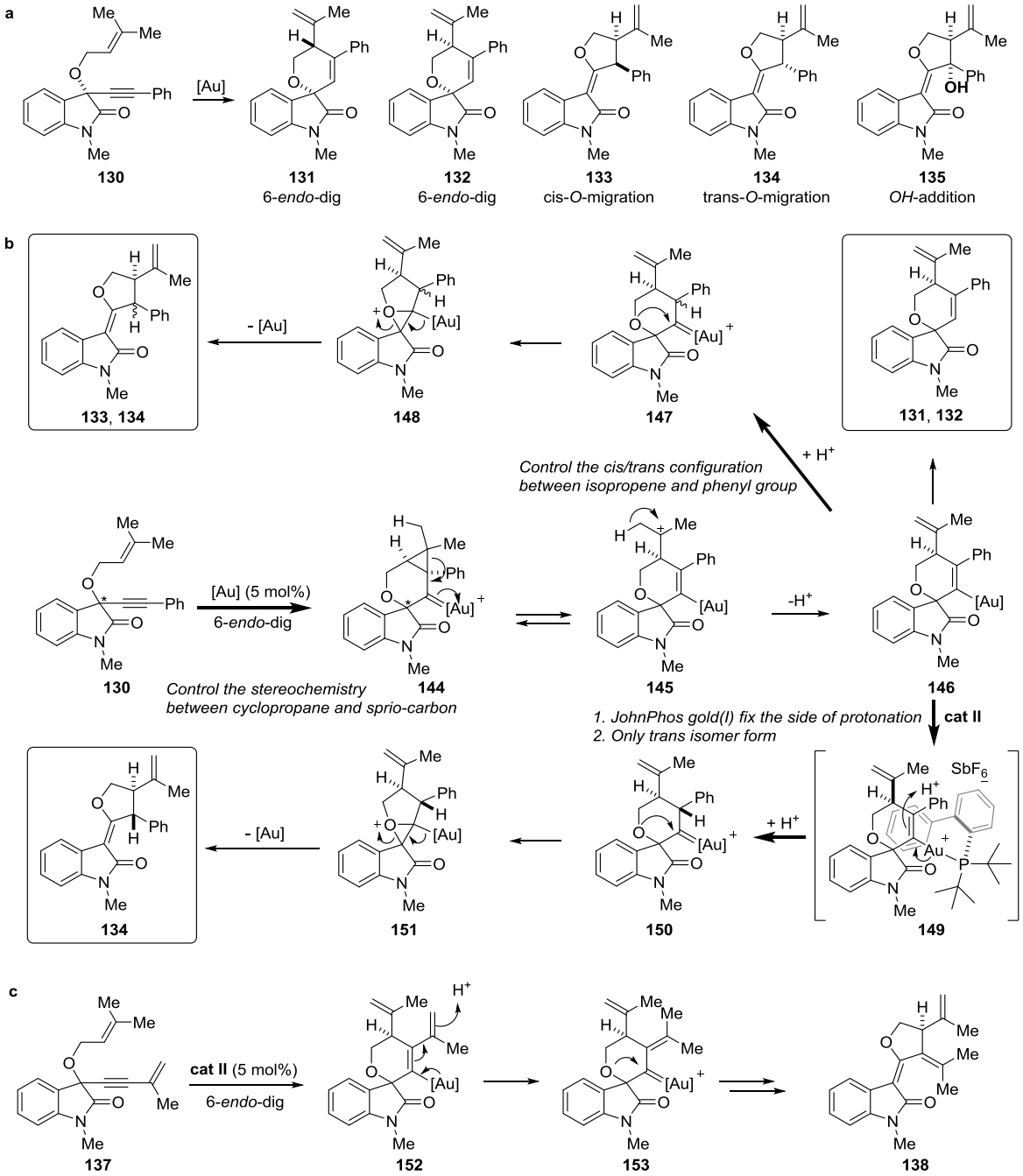
Scheme 17. Synthesis of non-protected oxindole based 1,6-enyne and gold(I) catalyzed non-protected *df*-oxindole formation.

3.2.4 Reaction mechanism

In prenylated 1,6-enyne substrate (**130**), gold(I) catalyzed cycloisomerization provides two diastereomeric spirooxindole (**131**, **132**) as well as *df*-oxindole (**133**, **134**, and **135**), which come from the common 6-*endo*-dig cyclization mode (Scheme 18a). I assume that the formation of spirooxindoles (**131**, **132**) occur by an initial 6-*endo*-dig cyclization of olefin to acetylene, activated by gold(I) catalyst to form cyclopropane gold carbene intermediate (**144**). Spontaneous formation of a stable tertiary carbocation by cyclopropane ring opening facilitates the deprotonation process to yield the *i*-propenyl moiety of sprio-oxindole (**146**), which undergoes protodeauration to yield the diastereomeric spriooxindoles (**131**, **132**). Alternatively, the non-stereoselective protonation of spriooxindole (**146**) results in the formation of gold carbene intermediate (**147**), which is nucleophilically attacked by the spiroether to form a highly strained tetracyclic oxonium ion (**148**). The deauration closes the catalytic cycle with concomitant ring-opening to yield the diastereomeric *df*-oxindoles (**133**, **134**), as shown in Scheme 18b. It is notable that there are two steps determining the stereochemistry of the final product. One is the 6-*endo*-dig cyclization (**130** to **144**), which forms the diastereomeric centers at the cyclopropane ring and the spiro-carbon. Alternatively, the protonation process (**146** to **147**) generates the chiral center at the benzylic position resulting in the *cis*-, *trans*-isomer between two substitutions, *i*-propenyl and phenyl group, on the tetrahydrofuran ring. Increasing the steric bulk of the phosphine ligand can enhance the reaction selectivity, *via* creating stereospecific protonation environment. As presented in Scheme 18b, Johnphos gold(I) catalyst (**II**) catalyzed transformation shares a similar reaction pathway till the vinyl gold intermediate (**146**). At this stage, the steric repulsion between the *i*-propenyl moiety and the ligand of the gold(I) catalyst decisively offers the sterically less hindered face, which consequently blocks the originally more exposed protonation face (**149**). The stereoselective protonation determines the *trans*-orientation of *i*-propenyl and phenyl group, and further sequential cascade forms the *df*-oxindole (**134**).

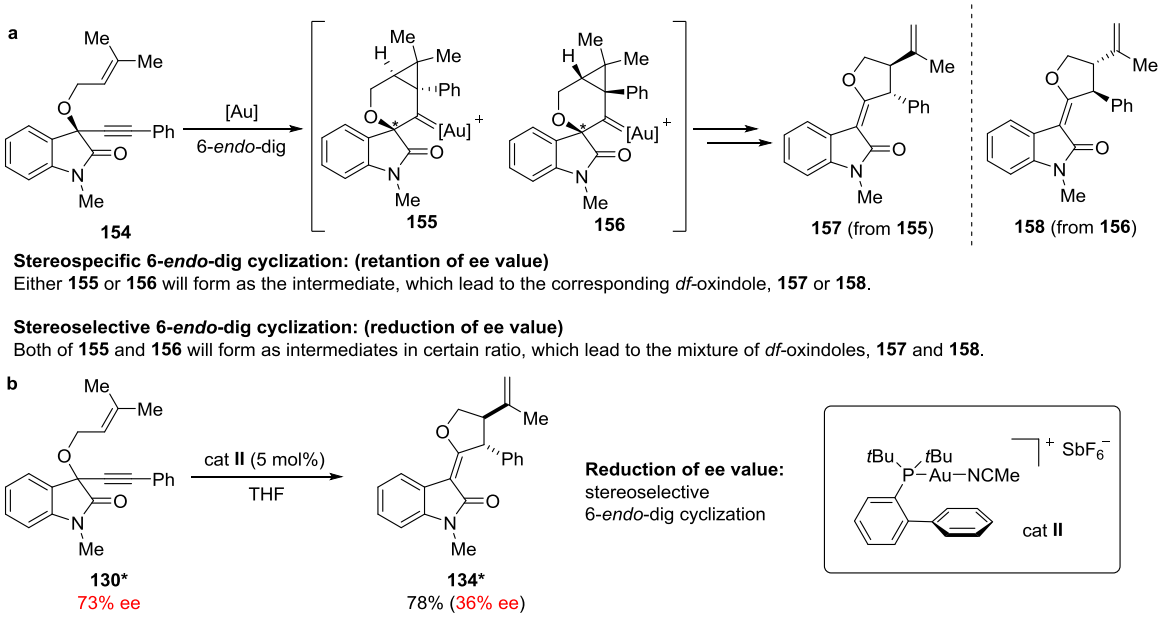
Similary, the 1,6-enyne (**137**) endowed with isopropenylacetylene followed the gold(I) mediated 6-*endo*-dig cyclization to form the conjugated vinyl gold intermediates (**152**). Unlike the protonation of vinyl gold intermediate (**146**) that take place at β-position, the intermediate **152** protonates at the end of the conjugated system, *i.e*. the δ-positon, leading to the unique *df*-oxindole (**138**) by previously described oxygen migration sequence

(Scheme 18c). While formation of most of the products fits in this mechanistic proposal, the formation of *df*-oxindole (**135**) is still unclear and needs further investigation.



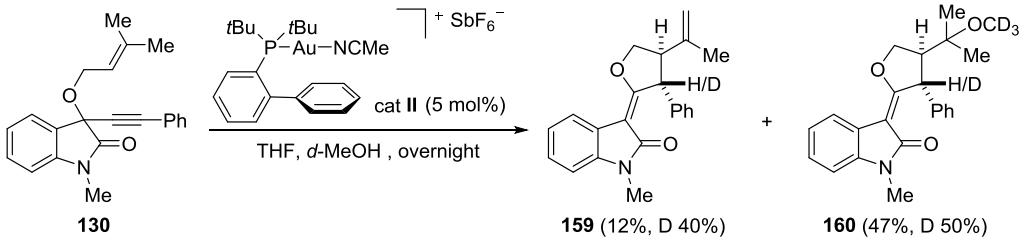
Scheme 18. a) Gold(I) catalyzed cycloisomerization of prenylated 1,6-enyne (**130**). b) Proposed mechanism of gold(I) catalyzed *df*-oxindole and spirooxindole formation. c) Proposed mechanism of gold(I) catalyzed *df*-oxindole formation (**138**).

The bulky phosphine ligand can manipulate the stereochemistry course of the reaction to give the *trans* configuration of *i*-propenyl and phenyl substituents in *df*-oxindoles. Using an enantiopure enyne **154** thus would yield two diastereomeric gold carbene intermediates (**155**, **156**) under the gold(I) catalyzed condition and each of the intermediates will subsequently deliver the corresponding *df*-oxindoles (**157**, **158**). If the 6-*endo*-dig cyclization works in stereospecific manner, gold carbene intermediate (**155** or **156**) will form and give the corresponding product (**157** or **158**) as the enantiopure product, respect-tively. Alternatively, the non-stereospecific 6-*endo*-dig cyclization forms a mixture of gold carbene intermediates (**155** and **156**) which subsequently form a mixture of enantiomeric *df*-oxindoles (**157** and **158**) with reduced ee value (Scheme 19a). To unravel this information, an optically enriched substrate (**130***) was prepared by $Zn(OTf)_2$ catalyzed enantioselective alkylation.[69] After the isolation of desired product (**134***) of a JohnPhos gold(I) catalyzed reaction, chiral high-performance liquid chromatography (HPLC) analysis indicated a decrease of ee value from 73% to 36% ee. This partial racemization stands for the non-stereospecific 6-*endo*-dig cyclization (Scheme 19b).



Scheme 19. a) Hypothesis of the stereoselectivity in gold(I) catalyzed *df*-oxindole formation. b) The experimental result of gold(I) catalyzed chirality transfer reaction.

To confirm the proposed reaction mechanism, the incorporation of CD_3OD, as nucleophile and protonation source, to the gold(I) catalyzed 1,6-enyne transformation successfully provided the deuterated *df*-oxindole (**159**) in 12% yield with 40% of deuteration at benzylic position and the *d*-methoxyl adduct (**160**) in 47% yield with benzylic deuterium in 50% (Scheme 20). The addition of the *d*-methoxyl group hints at the formation of a stable tertiary carbocation or the electrophilic carbon of cyclopropane ring, and the deuteration on benzylic position. These results nicely agree with the proposed reaction mechanism.

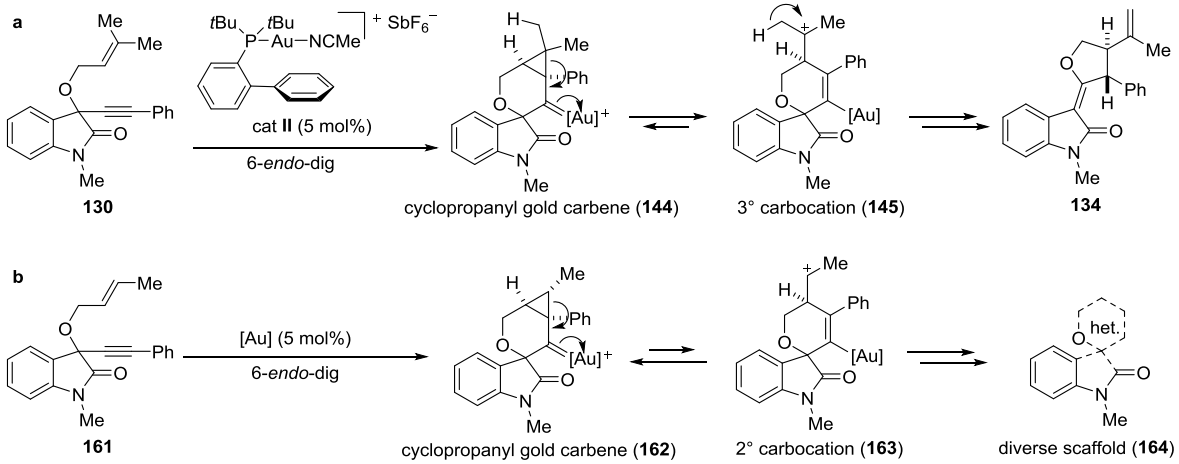


130 **159** (12%, D 40%) **160** (47%, D 50%)

Scheme 20. The deuteration experiment for gold(I) mediated *df*-oxindole formation.

3.3 Gold(I) catalyzed cycloisomerizations of oxindole based crotylated 1,6-enynes

With the successful transformation of 1,6-enyne to *df*-oxindole, I envisaged that the cyclopropanyl gold carbene could be varied to other scaffolds. In the prenylated 1,6-enyne (**130**), the deprotonative cyclopropane ring opening (from **144** to **145**) destabilized the key cyclopropanyl gold carbene intermediate and prohibited its potential to follow other reaction pathways (Scheme 21a). While 1,6-enyne (**130**) leads to **134** through the formation of a tertiary carbocation (**145**), the corresponding gold carbene **162** formed from crotylated 1,6-enyne **161** might offer opportunities to form different scaffolds (**164**) and might be a subject to modulation under the influence of the reaction conditions like ligands, solvent and additives (Scheme 21b). Therefore, further investigations were performed by using enynes **161**.



Scheme 21. Gold(I) catalyzed deprotonative cyclopropane ring opening a) in prenylated 1,6-enyne (**130**) and b) crotylated 1,6-enyne (**161**).

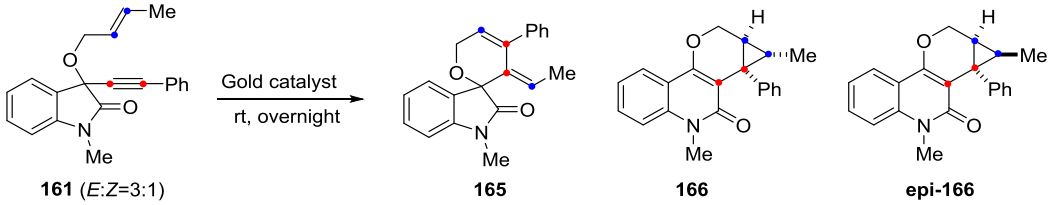
3.3.1 Reaction optimization towards crotylated 1,6-enyne

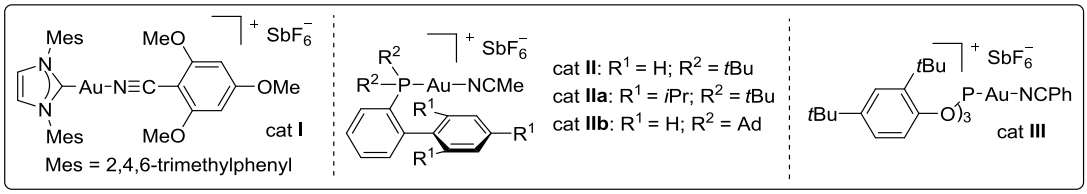
After the 4-step substrate synthesis of crotylated 1,6-enyne (**161**) with the *E*/*Z* isomer in 3 to 1 ratio, the optimization of gold(I) mediated divergent synthesis began with the catalyst screening and is summarized in Table 3. By treatment of *in situ* prepared cationic gold(I) complex $Ph_3PAu(BF_4)$ in DCM, the spirooxindole (**165**) was formed in 33% yield (entry 1). With 5 mol% of $AuCl_3$ as the gold(III) catalyst, the cycloisomerization reaction provided the ring expansion product quinolone (**166**) in 23% yield, which did not improve with doubling the catalyst loading and resulted in complex product mixtures (entry 2-3). When the gold(I) catalyst with NHC as ligand (**I**) was applied for the transformation, the mixture of spirooxindole (**165**) and quinolone (**166**) was isolated as products in 43% and 7 % yield,

respectively (entry 4). Delightfully, the quinolone (**166**) could be selectively generated by utilizing the bulky phosphine as gold(I) ligand (**II**) in good yield. Fine tuning the steric factor of phosphine ligand revealed that the biphenyl ring of phosphine bearing 1,3,5-tri-*iso*-propyl groups (**IIa**) provided the highest yield of 67% as compared to others bulky phosphine ligands (entry 5-7). Interestingly, the epimer of quinolone (*epi*-**166**) was also isolated in the cat **IIa** catalyzed reaction in 20% yield, which would be the product from the *Z*-1,6-enyne (***Z*-161**). Treatment of more electrophilic gold(I) catalyst with phosphite ligand (**III**) selectively gave the spirooxindole as the product in satisfactory yield (entry 8). The *Z*-1,6-enyne (***Z*-161**) seemed to be inert in this catalytic condition, which was in 10% recovery.

In the initial catalyst screening, two structurally distinct scaffolds, spirooxindole (**165**) and quinolone (**166**), were generated in a selective manner by bulky phosphine and electrophilic gold(I) catalysts, (**IIa** and **III**), respectively; and the screening of solvent and catalyst loading were followed up for the further improvements. However, no further improvement was observed during the whole process. For the bulky phosphine gold(I) catalyzed spirooxindole formation (**IIa**), the non-selective result was observed while using toluene as the solvent (entry 9). As the polar solvent, both of ACN and DMF diminished the power of catalysts to give the starting material recovery as the outcome (entry 10, 11) THF, as the optimal solvent for the *df*-oxindole formation, turned out to be incompatible in the condition and leading to the polymerization of THF (entry 12). When decreasing the catalyst loading from 5 mol% to 3 mol%, the yield of spirooxindole also dropped to 27%. On the other hand, by using toluene as solvent, the phosphite gold(I) catalyzed quinolone formation (**III**) could deliver the desired product thought in moderate yield (entry 14). When swiching the solvent to ACN or DMF, stating material was recovered due to the deactivation of catalyst by the polar solvent (entry 15 and 16). The THF was also proven to be not compatible as solvent to the gold(I) catalyzed condition that leading to the polymerization (entry 17). Reducing the catalyst loading to 3 mol% slightly decreased the yield of the quinolone formation (entry 18).

Table 3. Reaction optimization for gold(I) catalyzed divergent scaffold synthesis (I).





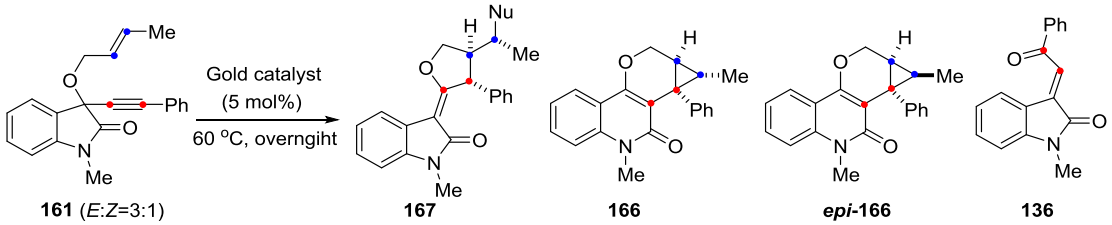
Entry	[Au] (5 mol%)	Solvent	Yield (%)		
			165	**166**	**epi-166**
1	$Ph_3PAu(BF_4)$	DCM	33	-	-
2	$AuCl_3$	DCM	-	23	-
3	$AuCl_3$	DCM		-[a]	
4[b]	**I**	DCM	43	7	-
5	**II**	DCM	-	57	-
6	**IIa**	**DCM**	-	**67**	**20**
7	**IIb**	DCM	-	43	-
8[c]	**III**	**DCM**	**60**	-	-
9	**IIa**	toluene		-[a]	
10	**IIa**	ACN		-[d]	
11	**IIa**	DMF		-[d]	
12	**IIa**	THF		-[e]	
13[d]	**IIa**	DCM	-	27	-
14	**III**	toluene	40	-	-
15	**III**	ACN		-[d]	
16	**III**	DMF		-[d]	
17	**III**	THF		-[e]	
18[f]	**III**	DCM	58	-	-

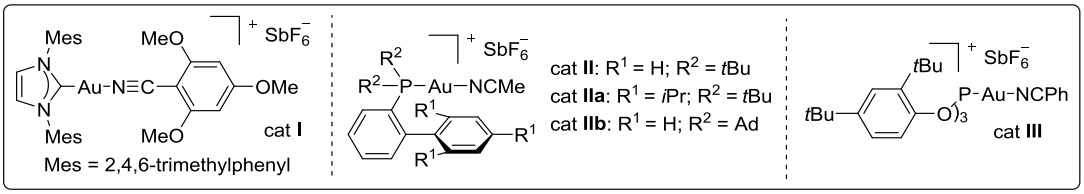
[a] Non-selective reaction. [b] Starting material was in 26% recovery. [c] ***Z*-161** was in 10% recovery. [d] Starting material recovery. [e] THF polymerized. [f] Catalyst loading: 3 mol%.

After identification of the optimal conditions for the formation of spirooxindoles (**165**, Table 3, entry 8) and quinolones (**166**, Table 3, entry 6), I envisioned that the cyclopropane moiety of the gold carbene intermediate could be opened up by nucleophilic addition, allowing the formation of *df*-oxindoles *via O*-migration, as shown in Table 4. In the presence of gold(I) catalyst (**II**), 20 equivalents (eq.) of MeOH were used as the nucleophile to trap the gold carbene intermediate. Since no reaction proceeded at room temperature, the reaction temperature was raised to 60 ^{o}C that also required switching the solvent from DCM to DCE. Indeed, he *df*-oxindole (**167**) was isolated in 62% yield, accompanied by the Mayer-Schuster rearrangement (M.-S. rear.) product (**136**) in 19% yield (entry 1-2). The replacement of catalyst from phosphine gold(I) catalyst (**II**) to NHC gold(I) catalyst (**I**) or phosphite gold(I) catalyst (**III**) didn't provide a better yield of **167** (entry 3, or 4). After tuning the electronic property of the cationic gold(I) catalyst, the role of steric nature of the catalyst on reaction was investigated by tuning the bulky groups on the JohnPhos ligand, such as *t*Bu to Ad or unsubstituted phenyl group to 1,3,5-tri-*iso*-propyl phenyl group. However, none of them gave higher yield than the initial trial (entry 5, 6).

We assumeed that the exccess amount of MeOH influenced the formation of the M.-S. rearrangement product (**136**). Therefore, a series of reactions were set to see the effect of the amount of MeOH on the reaction outcome (entry 7-10). Decreasing the amount of MeOH led to corresponding decrease in the formation of **136**. With only 1.0 eq. of MeOH, no more **136** was formed. At the same time, the quinolone (**166**) started to form when the 3.0 eq or less MeOH was used. With 5 mol% of **II** in the presence of 10 eq. of MeOH, the reaction afforded the *df*-oxindole (**4a**) in 73% yield (entry 7). Lowering the catalyst loading to 3 mol% also decreased the product yield (entries 11). The nucleophiles other than MeOH were also investigated, such as H_2O, AcOH, and indole. In the case of H_2O, a heterogeneous mixture was formed affording a mixture of **166**, ***epi*-166**, and hydroxyl adduct **167OH** in 30%, 15%, and 23% yield, respectively (entry 12). The AcOH nucleophile gave the diasteromeric mixture of acetyl adduct **167OAc** in 56% yield (entry 13). However, the indole molecule failed to serve as carbon nucleophile and did not form the expected adduct (entry 14).[55]

Table 4. Reaction optimization for gold(I) catalyzed divergent scaffold synthesis (II).



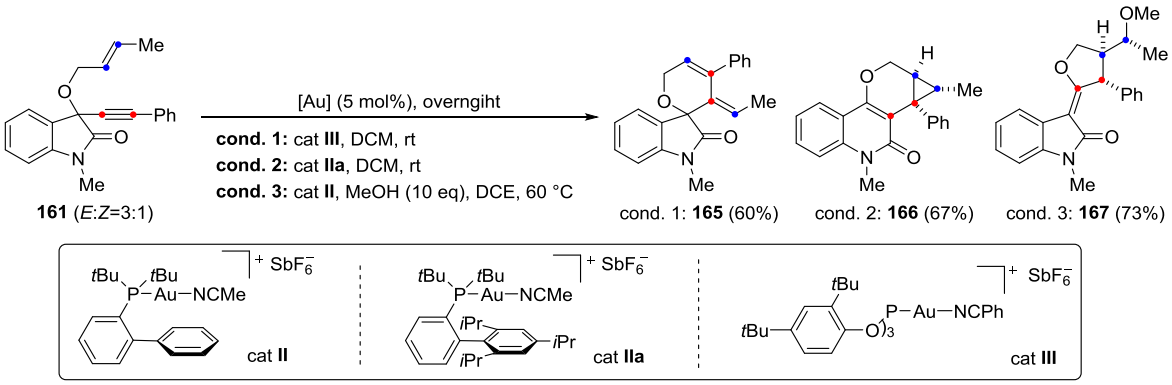


Entry	[Au]	Solvent	Nu (eq)	Yield (%)			
				167	**166**	***epi*-166**	**136**
1[a]	**II**	DCM	MeOH (20.0)	no reaction			
2	**II**	DCE	MeOH (20.0)	62	-	-	19
3	**I**	DCE	MeOH (20.0)	27	-	-	34
4	**III**	DCE	MeOH (20.0)	20	-	-	-
5	**IIa**	DCE	MeOH (20.0)	56	-	-	-
6	**IIb**	DCE	MeOH (20.0)	50	-	-	-
7	**II**	**DCE**	**MeOH (10.0)**	**73**	-	-	**18**
8	**II**	DCE	MeOH (3.0)	56	11	-	7
9	**II**	DCE	MeOH (1.0)	43	32	-	-
10	**II**	DCE	MeOH (0.5)	30	24	-	-
11[c]	**II**	DCE	MeOH (10.0)	64	-	-	-
12	**II**	DCE	H_2O (20.0)	23 (**167OH**)	30	15	-
13	**II**	DCE	AcOH (20.0)	56 (**167OAc**)	20	13	-
14	**II**	DCE	indole (2.0)	-	37	-	23

[a] Reaction was operated at rt. [b] Starting material recovery. [c] Catalyst loading: 3 mol%.

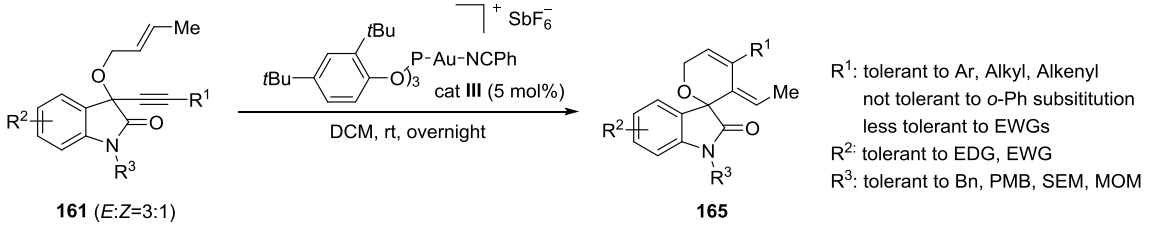
3.3.2 Reaction scope

The extensive reaction screening and optimization identified suitable conditions to selectively form spirooxinodle (**165**), quinolone (**166**), and *df*-oxindole (**167**), in satisfactory yield by merely changing the ligand of the gold(I) catalyst and applying the nucleophile to the reaction (Scheme 22). Based on these optimal conditions, I started to investigate the functional group tolerance for the diverse scaffold generating transformations. As I had already observed that the variation in the allyl moiety alters the scaffold formation, functional group variation was performed at the phenyl ring, aryl ring of the oxindole, and substituents on nitrogen for each scaffold generating gold(I) catalyzed reaction.

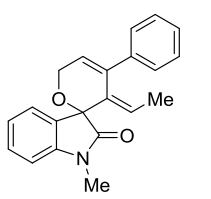


Scheme 22. The optimal conditions for gold(I) catalyzed divergent scaffold synthesis.

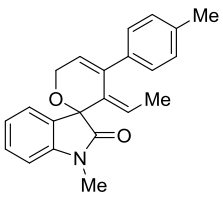
The investigation of the reaction scope began with the cationic gold(I) catalyzed spriooxindole formation (**165**). Substrates with electron rich phenyl ring at the alkynyl position (R^1) provided moderate to good yield (59-66%) of spirooxindoles (**165b-f**, Scheme 23). However, the 1,6-enynes with substituent at *ortho*-position of phenyl ring (**165d**, **165e**) afforded either non-selective reaction reactions or low yield of spirooxindole. A similar phenomenon was observed for 1,6-enynes with *o*-Cl-Ph substitution (**165i**). This might be attributed to inhibition of the coordination of the bulky gold(I) catalyst to acetylene in the *ortho*-substituted enyne While the substrate bearing EWG *p*-F-Ph moiety (**161g**) was tolerable in the reaction, substrate (**161h**) with *m*-Cl-Ph gave a mixture of spirooxindole (**165h**, 31%), and quinolone (**166h,** 19%) along with starting material recovered (**161h**, 12%). The *p*-Br-Ph substitution in **161j** also resulted in low yield (28%, **165j**). As a representative of heterocyclic ring systems, the thiophene substrate (**161k**) was prepared and subjected to the optimal reaction conditions, which provided the desired product **165k** in 45% yield. With further exploring the scope of the reaction, the substrates with *i*-propenyl



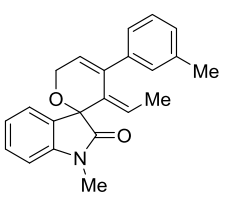
161 (*E*:*Z*=3:1) **165**



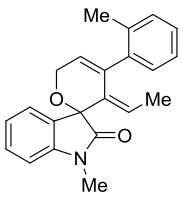
165a (60%)



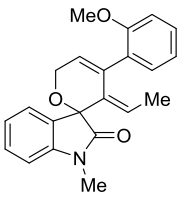
165b (60%)



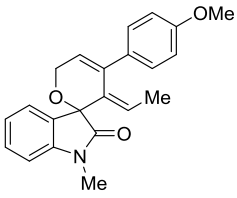
165c (66%)



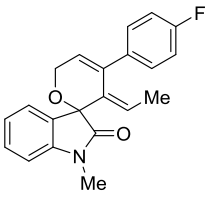
165d messy



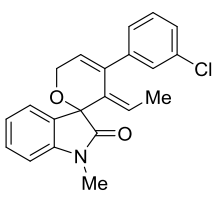
165e (29%)



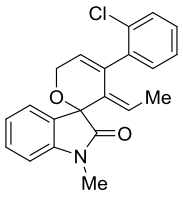
165f (59%)



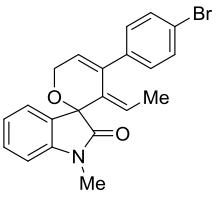
165g (51%)



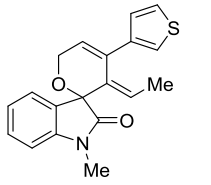
165h (31%)[a]



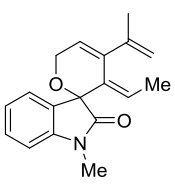
165i messy



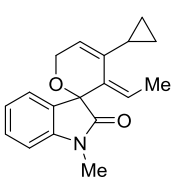
165j (28%)



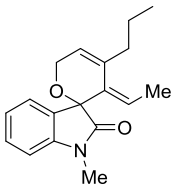
165k (45%)



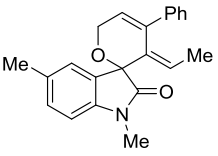
165l (25%)



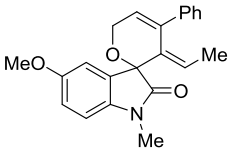
165m (75%)



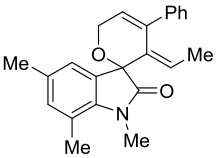
165n (51%)



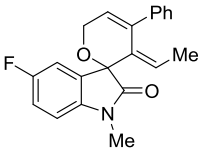
165o (71%)



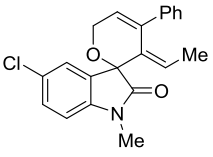
165p (51%)



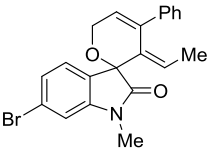
165q (75%)



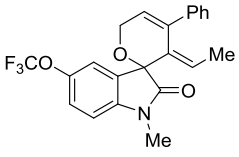
165r (51%)



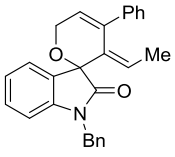
165s (50%)



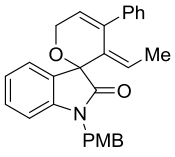
165t (58%)



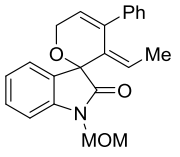
165u (65%)



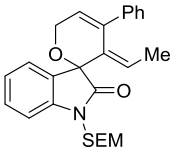
165v (45%)



165w (42%)



165x (29%)



165y (70%)

[a] The starting material (**164h**) was recovered in 12% yield and quinolone (**166h**) was isolated in 19% yield.

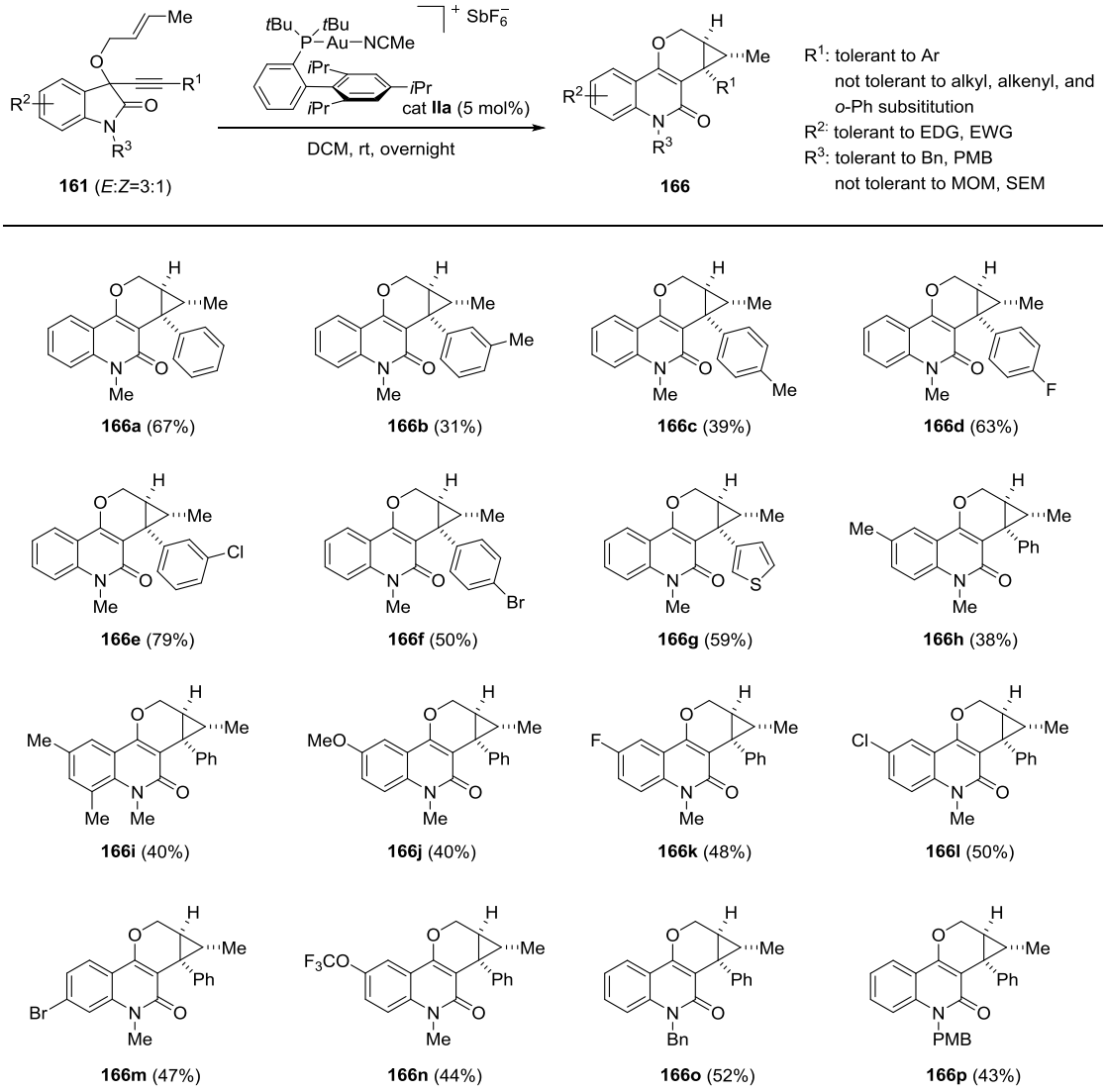
Scheme 23. The reaction scope for gold(I) catalyzed sprioxindole formation.

(**161l**), cyclopropane (**161m**), and *n*-propane (**161n**) groups were smoothly converted into the desired products in 25%, 75%, and 51% yield, respectively. I was pleased to see that the functional groups ranging from EDG to EWG and mono- or di-substituted oxindoles (R^2) were well tolerated in the gold(I) catalyzed reaction conditions to give spirooxindoles in 50-75% yield (**165o-u**). The reactions worked well for differently *N*-protected oxindole enynes to deliver spirooxindoles with four different nitrogen protecting groups (R^3), Bn (**165v**), PMB (**165w**), MOM (**165x**), and SEM (**165y**), in 45%, 42%, 70% and 29%, respectively (Scheme 23).

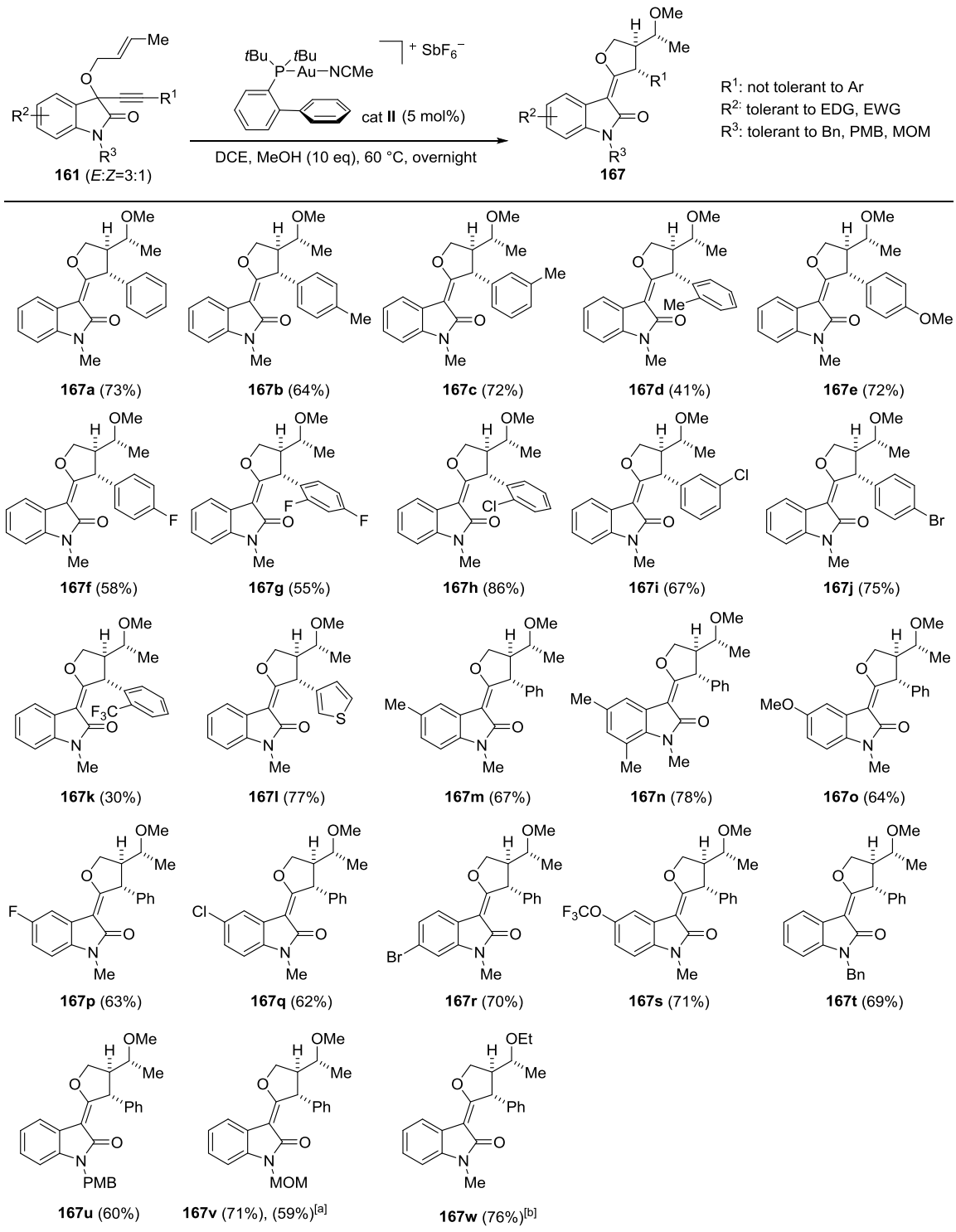
The reaction scope of quinolone (**166**) formation was performed by using bulky phosphine gold(I) catalyst (**IIa**). Based on the same set of substrates, the reaction scope was studied with substitution variation at R^1 to R^3. For R^1 moiety, the phenyl substituted substrates with EDG or EWG at *meta*- or *para*-position gave moderate to good yield for the desired quinolones (**166b-f**). The *ortho*-substituted substrates failed to form the desired products and instead a complex mixture was formed in those reactions. Though the substrate with *i*-propenyl or alkyl group at R^1 led to a complex mixture, the thiophenyl product (**166g**) was isolated in 59% yield. Again, the 1,6-enynes with substitutions at the aryl part of oxindole (R^2) were converted to products (**166h-n**) in moderate yields (38-50%). As expected, the nitrogen with benzyl based protecting groups, such as Bn or PMB, provided the corresponding quinolones (**166o** or **166p**) in 52% or 43% yield, respectively. Whereas, the protecting group endowed with hemiaminal, *i.e.* MOM or SEM, did not give any product. Thus, the functional group tolerance in quinolone synthesis is limited as compared to spirooxindoles (Scheme 24).

With the assistance of alcohols, the scope of *df*-oxindole formation (**167**) was examined. For the two scaffolds discussed above, the substrate with *ortho*-substituted phenyl ring at R^1 position suffered from the nonselective transformation. However, unlike the spirooxindoles and quinolones, all *ortho*-, *meta*-, or *para*-substitutions, decorated with EDG, or EWG, were generally well tolerated in the *df*-oxindole formation in the yields from 30-86% (**167b-k**). However, the strong EWG, trifluoromenthyl group, at *ortho*-position did affect the yield, and the product **167k** was obtained in only 30% yield. The heterocyclic substrate, thiophinyl 1,6-enyne (**161l**), however delivered the corresponding *df*-oxindole (**167**) in 77% yield. The *df*-oxindoles bearing EDG or EWG at R^2 (**166m-s**) were formed in 62-78% yield, and both Bn and PMB protected products (**166t** and **u**) were generated in good yields too. Switching the *N*-protecting group to MOM, the desired *df*-oxindole (**166v**) was isolated in 71% yield. Interestingly, the substrate with SEM protecting group didn't

provide the corresponding *df*-oxindole, but the MOM protected *df*-oxindole (**166v**) was formed in 59% yield (Scheme 25). I proposed that the protecting group replacement happened in a 2-step cascade. Under the gold(I) catalysis conditions, oxygen of SEM protected oxindole (**169**) may coordinate with metal center, which subsequently triggers the elimination reaction giving the iminium (**170**) as the reactive intermediate. The excess amount of MeOH serves as the nucleophile to react with iminium and generate the MOM protected product (**171**, Scheme 26). When lesser nucleophilic EtOH was used, the *df*-oxindole **166w** was formed in 76% yield (Scheme 25).

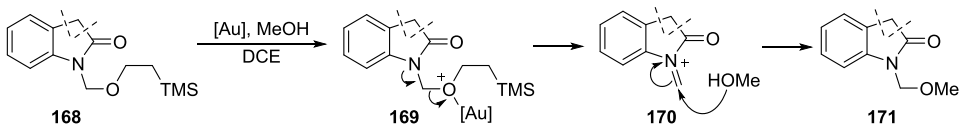


Scheme 24. The reaction scope for gold(I) catalyzed quinolone formation.



[a] from SEM protected 1,6-enyne. [b] EtOH was applied as nucleophile.

Scheme 25. The reaction scope for gold(I) catalyzed *df*-oxindole formation.



Scheme 26. The gold(I) catalyzed protecting group replacement reaction.

3.3.3 Scaffold diversity synthesis with 1,6-enynes supporting differently substituted olefins

It was observed that substituents on the allyl group were critical for accessing divergent rearrangements of 1,6-enyne cycloisomerizations intermediates in gold(I) catalyzed reactions. In this regard, the prenylated 1,6-enynes selectively gave the *df*-oxindoles as products and the crotylated 1,6-enynes generated three distinct scaffolds, spirooxindole, quinolone, and *df*-oxindole. Therefore, I was curious to know how the substitutions on allyl position might affect the reactivity of 1,6-enynes in gold(I) catalyzed cycloisomerization reactions. A series of 1,6-enynes with substituent variations (**172a-g**) were prepared to investigate the gold(I) catalyzed reactions and results are summarized in Table 5 (ligand effect) and 6 (nucleophile effect).

The investigation began with the ligand effect toward the 1,6-enyne with different allyl substitution (Table 5). Since the crotylated 1,6-enyne (**172a**) with *E* to *Z* isomeric ratio in 3:1 could deliver spirooxindole and quinolone by switching the ligand in gold(I) catalyst (Table 5, entry 1-3), I suspected that the reaction mechanism of *E* and *Z* isomer might differ. To investigate this hypothesis, the ethyl substituted *E*- and *Z*-1,6-enyne (**172b** and **172c**) were synthesized and subjected for the catalyst screening. In the *E*-1,6-enyne system (**172b**), the quinolone (**174b**) was selectively generated by the bulky phosphine gold(I) catalyst (**IIa**) and spirooxindole formation could be achieved by applying NHC gold(I) catalyst (**I**) or phosphite gold(I) catalyst (**III**), as shown in entry 4-6. The more electrophilic gold(I) catalyst (**III**) gave spirooxindole (**173b**) in higher yield than the less electrophilic gold(I) catalyst (**I**) from 88% to 79% yield (entry 4-6). Interestingly, the *Z*-1,6-enyne (**172c**) was observed to be selective for the quinolone formation (**174c**) and the highest yield was afforded by the cationic gold(I) catalyst with phosphite ligand (**III**) in 63% yield (entry 7-9). On the basis of these experimental results, I can conclude that the *E*-1,6-enyne plays the major role for the spriooxindole and quinolone scaffold synthesis.

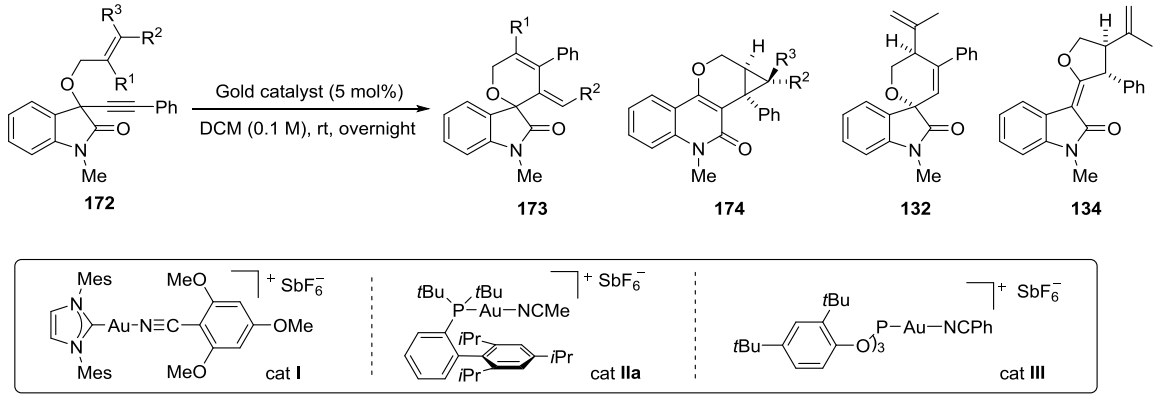
If the sterically demanding functional group, such as phenyl group, was installed at R^2, the NHC gold(I) catalyst (**I**) provided quinolone (**174d**) in 40% yield. For the other gold(I) catalysts (**II** and **III**), only a complex mixture was obtained after the treatment of catalyst to the substrate (entry 10-12). By treatment of bulky phosphine gold(I) catalyst (**IIa**), the allyl propargyl ether (**172e**) was converted to the corresponding quinolone (**174e**) in 56% yield (entry 14). With the same substrate, the cationic gold(I) catalyst with NHC ligand (**I**) or phosphite ligand (**III**) gave only starting material recovery or a complex mixture (entry 13, 15). The gold(I) catalyst **I** could not catalyze the enyne cycloisomerization of the methallyl

substrate (**172f**), but the gold(I) catalyst with phosphine or bulky phosphite ligand (**IIa** and **III**) converted the methallyl 1,6-enyne (**172f**) to spriooxindole (**173f**) albeit in low yield. Changing solvent from DCM to Et_2O could improve the yield from low to moderate (entry 16-19). In case of prenylated 1,6-enynes (**130**), *df*-oxindole (**134**) was selectively generated by utilizing the bulky phosphine gold(I) catalyst (**IIa**), as shown in entry 21. More details for the *df*-oxindole formation of prenylated 1,6-enynes (**130**) were described in section 3.4.

Since addition of a nucleophile to crotylated 1,6-enyne (**172a**) could facilitate the formation of *df*-oxindole (Table 6, entry 1) in the presence of bulky phosphine gold(I) catalyst (**II**), I also examined whether the same strategy could work on enynes with differently substituted olefin (**172b-g**, entry 2-7). The substrates with the substitution on R^2 position, *i.e.* Me, Et, or phenyl, followed the same transformation to give the *df*-oxindoles (**175a**, **175b**, and **175f**) as major product in good yield (entry 1, 2, and 4) along with M.-S. rear. product (**136**) that was formed in low yield. However, the M.-S. rear. product (**136**) was formed as the major product in 56% yield from the *Z*-1,6-enyne (**172c**) and the desired *df*-oxindole (**175c**) was isolated in 20% yield (entry 3). In case of allyl 1,6-enyne (**172d**) as substrate, no *df*-oxindole was observed and the M.-S. rear. product (**136**) was formed in 86% yield (entry 5). The methallyl 1,6-enyne (**172e**) resulted in a non-selective reaction reaction (entry 6). Finally, the prenylated 1,6-enynes (**130**) gave the corresponding methoxyl adduct (**175g**) in good yield with 23% of M.-S. rear. product (**136**). In general, the gold(I) catalyzed *df*-oxindole formation is tolerated by the 1,6-enyne substrates with substitution at R^2 and R^3 position.

The diphenyl sulfoxide (**122**) had been used as an oxidative nucleophile to trap the gold carbene intermediate, giving the carbonyl moiety.[48] However, this reaction did not happen with 1,6-enyne (**172b**, entry 8). A stronger oxidative nucleophile *i.e. N*-oxide (**123**) delivered the ring expansion product (**176b**) bearing the quinolone core in 83% yield (entry 9). In order to compare the nucleophilicity between *N*-oxide (**123**) and MeOH to provide 4-ketoquinolone (**176b**) or *df*-oxindole (**175b**) respectively, I set up the competition reaction under the standard conditions in the presence of MeOH (10 eq) and *N*-oxide (**123**, 1.1 eq). Only quinolone (**176b**) was formed in 70% yield, which indicated that the *N*-oxide (**123**) is a stronger nucleophile than MeOH. Thus, the other 4-ketoquinolone derivative (**176b**) can be generated from oxindole derived 1,6-enyne by treatment of bulky phosphine gold(I) catalyst with *N*-oxide (**123**) as oxidative nucleophile.

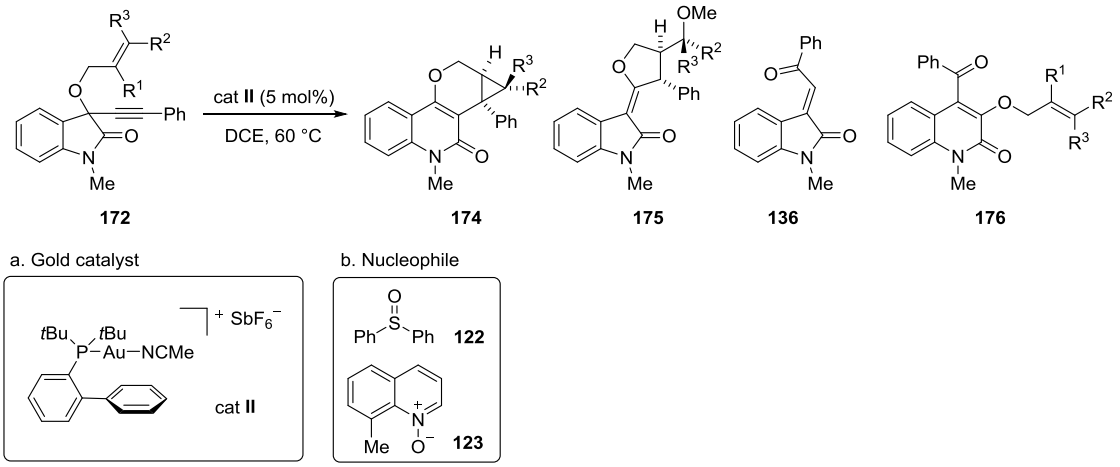
Table 5. Reaction screening of 1,6-enynes with various gold(I) catalysts to establish diversity.



Entry	172	Substitutions			[Au]	Product (Yield %)			
		R^1	R^2	R^3		**173**	**174**	**132**	**134**
1[a,b]	**a**[c]	H	Me	H	**I**	43	7	-	-
2[a]	**a**[c]	H	Me	H	**IIa**	-	67	-	-
3[a]	**a**[c]	H	Me	H	**III**	60	-	-	-
4	**b**	H	Et	H	**I**	79	-	-	-
5	**b**	H	Et	H	**IIa**	-	40	-	-
6	**b**	H	Et	H	**III**	88	-	-	-
7	**c**	H	H	Et	**I**	-	58	-	-
6	**c**	H	H	Et	**IIa**	-	37	-	-
9	**c**	H	H	Et	**III**	-	63	-	-
10	**d**	H	Ph	H	**I**	-	40	-	-
11	**d**	H	Ph	H	**IIa**			-[d]	
12	**d**	H	Ph	H	**III**			-[d]	
13	**e**	H	H	H	**I**			-[e]	
14	**e**	H	H	H	**IIa**	-	56	-	-
15	**e**	H	H	H	**III**			-[d]	
16	**f**	Me	H	H	**I**			-[e]	
17	**f**	Me	H	H	**IIa**	37	-	-	-
18[f]	**f**	Me	H	H	**IIa**	46	-	-	-
19	**f**	Me	H	H	**III**	17	-	-	-
20	**g**[g]	H	Me	Me	**I**			-[e]	
21	**g**[g]	H	Me	Me	**IIa**	-	-	-	51
22[h]	**g**[g]	H	Me	Me	**III**	-	-	33	17

[a] *E*:*Z* = 3:1. [b] (*Z*)-**172a** was in 27% recovery. [c] Crotylated 1,6-enyne (**161a**). [d] Non-selective reaction. [e] Starting material recovery. [f] Solvent is diethylether. [g] Prenylated 1,6-enyne (**130a**). [h] **172g** was in 30% recovery.

Table 6. Reaction screening of gold(I) catalyzed 1,6-enynes with various nucleophiles.

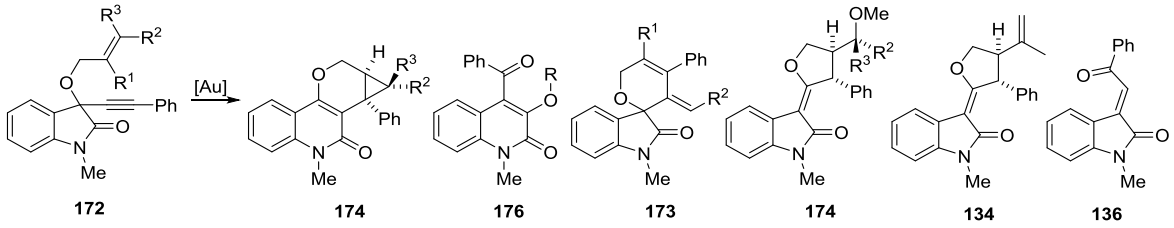


Entry	172	Substitutions			Nu (eq)	Product (Yield %)			
		R^1	R^2	R^3		**174**	**175**	**136**	**176**
1[a]	**a**[b]	H	Me	H	MeOH (10)	-	73	18	-
2	**b**	H	Et	H	MeOH (10)	-	67	15	-
3	**c**	H	H	Et	MeOH (10)	-	20	67	-
4	**d**	H	Ph	H	MeOH (10)	-	56	8	-
5	**e**	H	H	H	MeOH (10)	-	-	86	-
6	**f**	Me	H	H	MeOH (10)	-[c]			
7	**g**[d]	H	Me	Me	MeOH (10)	-	66	23	-
8	**b**	H	Et	H	**122** (2)	60	-	-	-
9	**b**	H	Et	H	**123** (1.1)	-	-	-	83
10	**b**	H	Et	H	MeOH (10)/**123** (1.1)	-	-	-	70

[a] *E*:*Z* = 3:1. [b] Crotylated 1,6-enyne (**161a**). [c] Non-selective reaction. [d] Prenylated 1,6-enyne (**130a**)

3.3.4 Reaction mechanisms

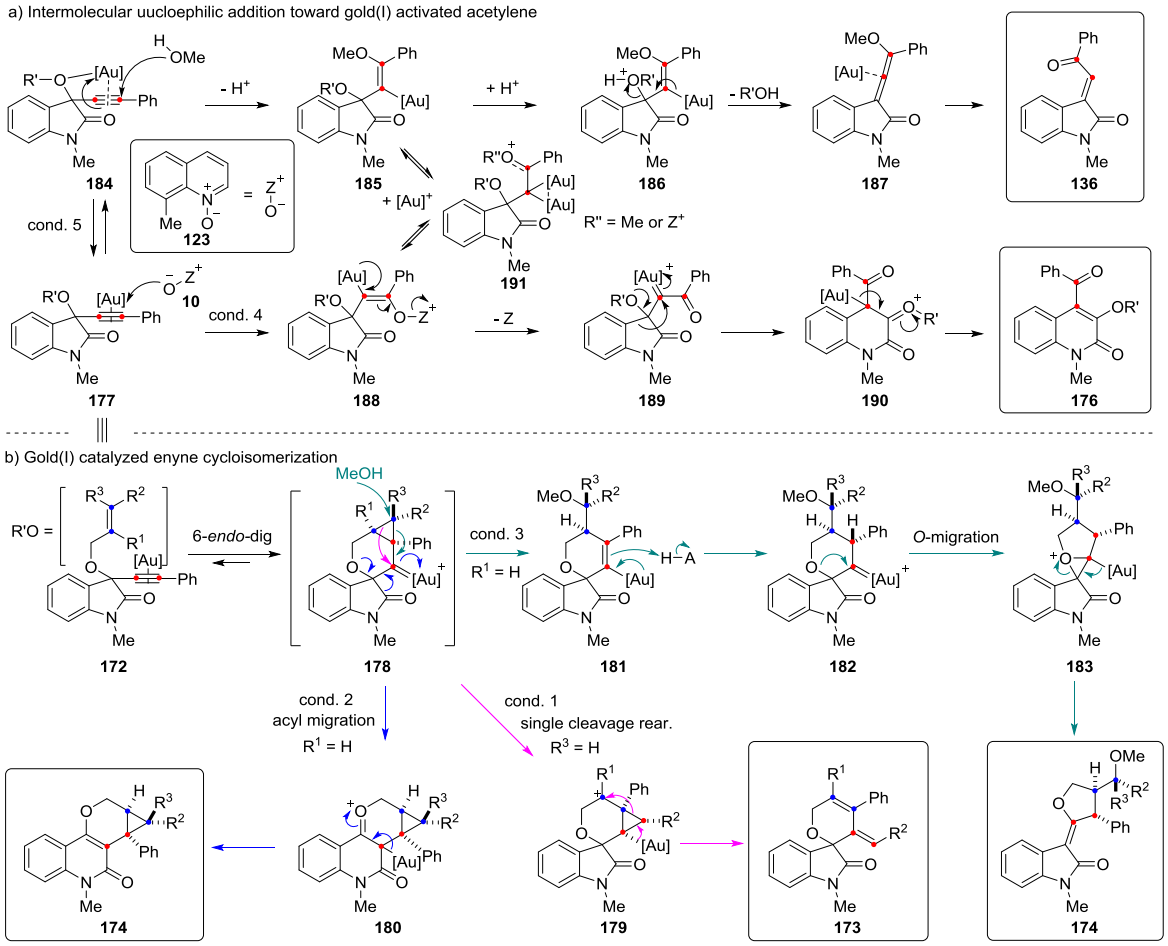
In the presence of gold(I) catalysts and with or without external nucleophiles, such as MeOH and *N*-oxide (**123**), the 1,6-enynes (**172**) can be converted into divergent products with unique quinolone (**174**, **176**), spirooxindole (**173**) and methyleneoxindole (**174**, **134**, and **136**) scaffold (Scheme 27). Since the formation of spirooxindole (**134**) has discussed in the section 3.2.4, I will focus on the formation of quinolone (**174**, **176**), spirooxindole (**173**), *df*-oxindole (**174**), and M.-S. product (**136**).



Scheme 27. Gold(I) catalyzed divergent scaffold formation by allyl-substituents modulation.

I believe that there are two distinctive modes of rearrangements leading to different sets of scaffolds. Addition of external nucleophile to gold(I) activated acetylene leads to the M.-S. product (**136**) and 4-ketoquinolone (**176**), as shown in Scheme 28a. On the other hand, a gold(I) catalyzed enyne cycloisomeritzation *via* 6-*endo*-dig cyclization forms endocyclic gold carbene intermediates (**178**), which led to the formation of quinolones (**174**), spirooxindoles (**173**), or *df*-oxindoles (**174**) as products (Scheme 28b).

For the synthesis of spirooxindole (**173**), the migration of cyclopropane ring in **178** firstly generates the carbocationic intermediates (**179**), which spontaneously rearrange to the final spirooxindoles (**173**), as indicated in Scheme 28b (magenta arrows). In the gold carbene intermediates (**178**), the steric interaction between substrate and bulky gold(I) catalyst is relieved by the pinacol type acyl group migration, which consequently delivers the oxonium intermediates (**180**). The deauration reaction closes the catalytic cycle by forming the quinolones (**174**) as the final product (Scheme 28b, blue arrows).[52] In the prenylated substrate, the cyclopropane opening of bicyclic gold carbene intermediates



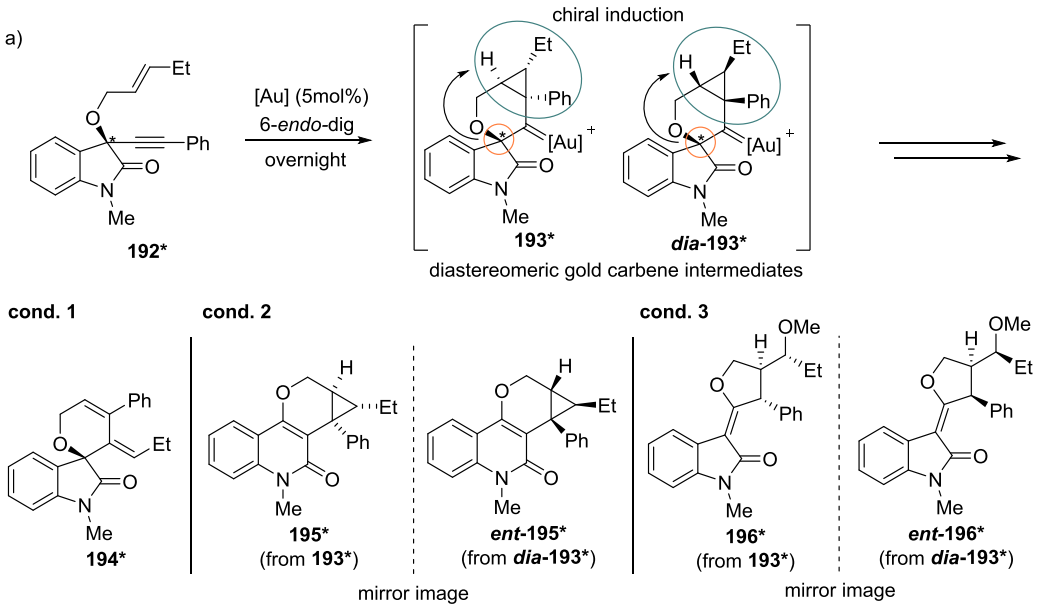
Scheme 28. Proposed reaction mechanism of gold(I) catalyzed divergent scaffold synthesis.

(**178**) undergoes an *O*-migration cascade to form *df*-oxindoles (**174**) as the products (Scheme 17). Alternatively, the nucleophilic 1,4-addition/protonation sequence on **178** finally gives the monocyclic gold carbene intermediates (**182**), which can further undergo the *O*-migration cascade ultimately delivering the *df*-oxindoles (**174**, (Scheme 28b, turquoise arrows).[55] The M.-S. product (**136**) is often observed as the side product or sometime even as the major product from the nucleophilic addition based *df*-oxindole formation. The addition of MeOH to gold(I) activated acetylenes (**184**) form the vinyl gold **185**, which can be stabilized by the *gem*-diaurate intermediate (**191**)[70] and proceed the elimination of alcohol and keto-enol tautomerization giving conjugated ketone (**136**), as depicted in Scheme 28a, cond 5.[71] As the oxidative nucleophile (**123**) is applied, the vinyl gold complex **188** is formed and simultaneously eliminates the 8-methylquinoline (**Z**). Subsequently, the phenyl group migration associated ring expansion and dearuation take place to form the 4-ketoquinolone (**176**, Scheme 28a, cond. 4).

3.3.5 Gold catalyzed cycloisomerization of enantioenriched enynes

In order to explore stereoselective cycloisomerization of enantioenriched enyne substrates that may lead to similar enantioenriched diverse scaffolds, chiral 1,6-enyne (**192***) was employed as the model substrate. The chiral 1,6-enyne (**192***) may result in diastereomeric (dia) gold carbene intermediates (**193*** and ***dia*-193***) via gold(I) mediated 6-*endo*-dig cyclization. While the spirooxindole (**194***) does not generate any new stereogenic center, the enantiomeric ratio for spirooxindole formation should be maintained after the reaction (Scheme 29a, cond. 1). In contrast, the quinolone formation keeps all the stereogenic centers form the cyclopropane ring except the one from the spiro-carbon, and may deliver **195*** from **193*** and the enantiomer (ent) of **195*** from ***dia*-193***. In the stereospecific 6-*endo*-dig cyclization, only one of the gold carbene intermediate will form, which lead to the corresponding quinolone. Under such circumstances, retention of the enantiomeric ratio should be observed. On the other hand, if the cyclization proceeds in stereoselective manner, both gold carbene intermediates (**193***, ***dia*-193***) will be generated, leading to the quinolone **195*** and ***ent*-195*** (Scheme 29a, cond. 2). Since the 1,4-nucleophilic addition and protonation of *df*-oxindole (**196**) are stereospecific, the chiral induction of 6-*endo*-dig cyclization can be determined in the same manner as for the quinolone formation (Scheme 29a, cond. 3).

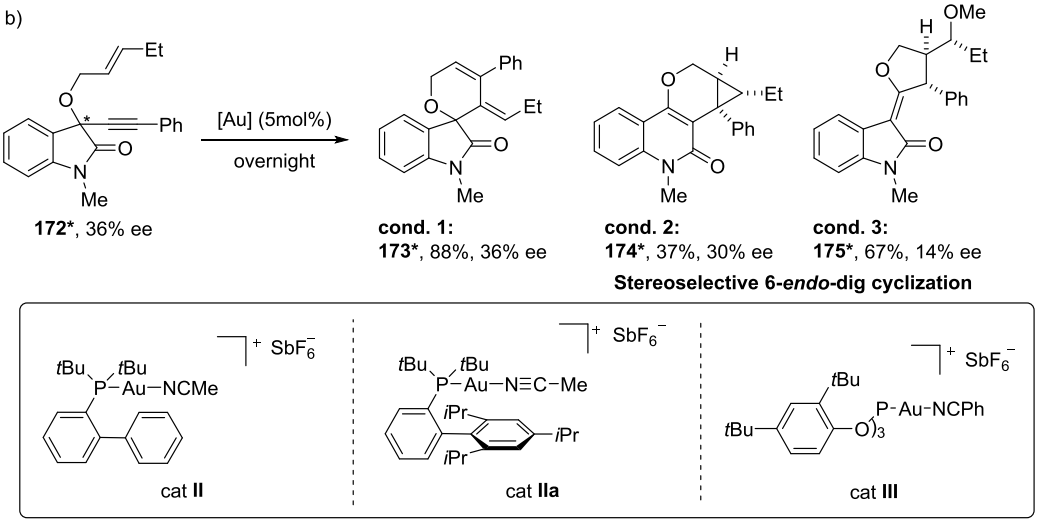
Thus, an optically enriched substrate (**172***, 36% ee) was synthesized to perform the investigation.[69] As expected, the ee value of spirooxindole (**173***) was found to be the same as that of the starting material, *i.e.* 36%. Both quinolone (**174***) and *df*-oxindole (**175***) were formed, and the reduction of ee value from 36% to 30% and 14% respectively was also observed. Therefore, it can be concluded that the 6-*endo*-dig cyclizations in the gold(I) catalyzed quinolone and *df*-oxindole formation was underwent a non-stereospecific cyclization *via* the mixture of **193*** and ***dia*-193*** as the intemedates (Scheme 29b).



Stereospecific 6-*endo*-dig cyclization: (retantion of ee value)
Either **193*** or ***dia*-193*** will selectively form as the intermediate, which lead to the corresponding quinolone, **195*** or ***ent*-195***, as well as *df*-oxindole, **196*** or ***ent*-196***.

Stereoselective 6-*endo*-dig cyclization: (reduction of ee value)
Both of **193*** and ***dia*-193*** will form as intermediates in certain ratio, which lead to the mixture of quinolones, **195*** or ***ent*-195***, or *df*-oxindole, **196*** or ***ent*-196***.

cond. 1: cat **III** (5 mol%), DCM, rt.
cond. 2: cat **IIa** (5 mol%), DCM, rt.
cond. 3: cat **II** (5 mol%), DCE, MeOH (10 eq), 60 °C.



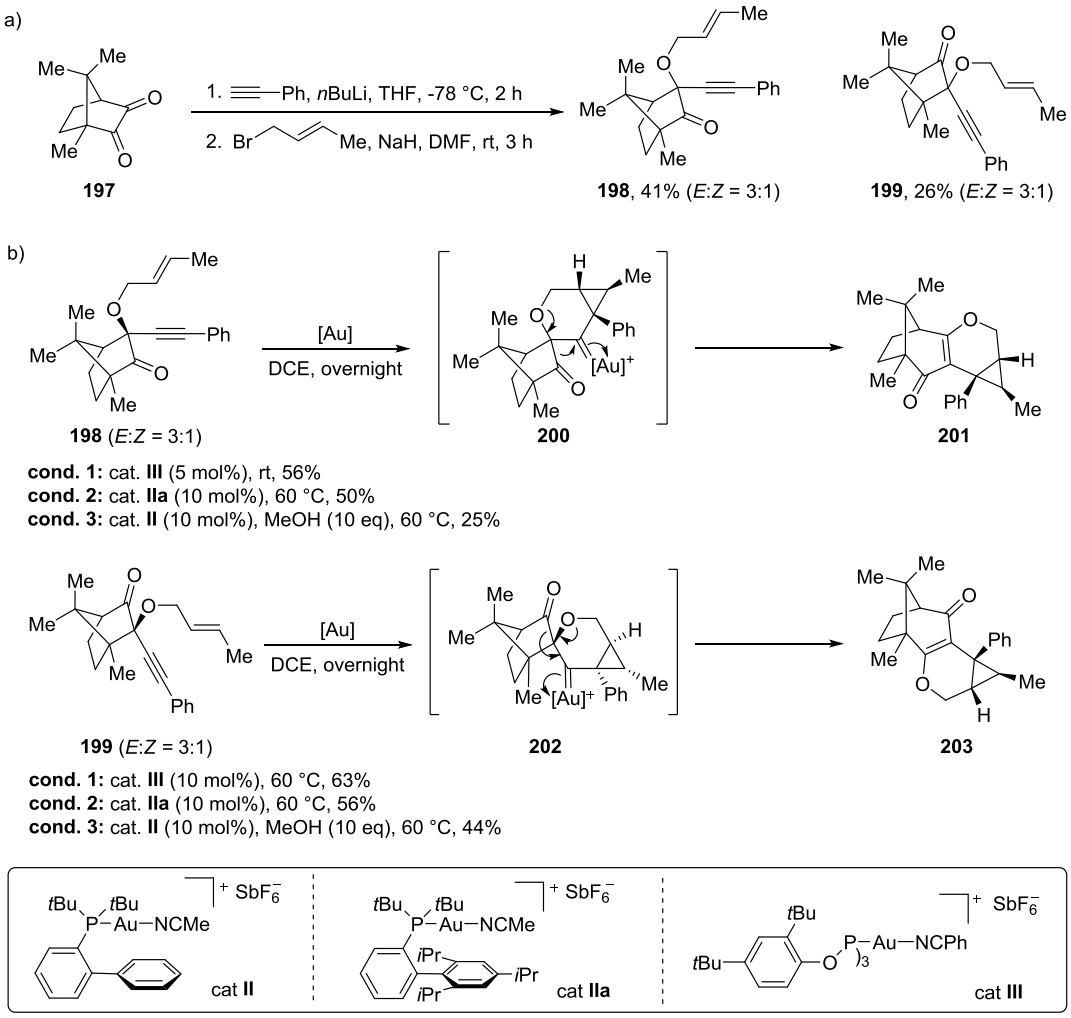
Scheme 29. a) Hypothesis of the stereoselectivity in gold(I) catalyzed divergent scaffold synthesis. b) The experimental results of gold(I) catalyzed chirality induction reactions.

3.4 Gold(I) catalyzed camphorquinone based 1,6-enyne cycloisomerization

Incorporation of the oxindole moiety in the enyne allowed to build scaffold diversity by variation of the ligands around the gold(I) complexes. In order to expand this idea to further intriguing scaffolds, I planned to introduce another natural product based ring-system. Camphor is a terpenoid that has been widely applied in medicinal and industrial applications.

The unique bicyclic [2.2.1] core structure distinguishes itself from the oxindole that I had successfully used in ligand directed scaffold diversity synthesis. Therefore, I selected the camphor derivative, camphorquinone, as starting material to prepare the enyne substrate. A similar preparation sequence, i.e. lithium phenylacetylide addition to ketone (**197**) and *O*-crotylation to the newly generated alcohol, was employed to give the camphor based 1,6-enynes (**198**, **199**, *E*:*Z* = 3:1) in 41% and 26% respectively (Scheme 30a). The strong electrophilic phosphite gold(I) catalyst (**III**), sterically demanding phosphine gold(I) catalyst (**IIa**) and MeOH nucleophile accompanying phosphine gold(I) catalyst (**II**) were chosen as conditions for the initial screening to identify the formation of different scaffolds. Interestingly, the gold(I) catalyzed reactions toward the camphor based 1,6-enynes (**198**, **199**) selectively provided the ring expansion bicyclo[3.2.1]octenones (**201**, **203**) as products, *via* 6-*endo*-dig gold carbene intermediates (**200**, **202**). Treatment of camphor based 1,6-enynes (**198**) with 5 mol% of phosphite gold(I) catalyst (**III**) formed the scaffold **201** in 56% yield, For the other conditions, an increase of catalyst loading and of reaction temperature were mandatory for achieving full conversion, but they afforded **201** in comparatively lower yields (Scheme 30b). The 1,6-enyne substrate (**199**) was found to be inert to the phosphite gold(I) catalyst (**III**) at room temperature presumably due to the steric hindrance. The elevation of reaction temperature and catalyst loading to 10 mol% nicely overcame the energy barrier and desired ring expansion product (**203**) was formed in 63% yield (Scheme 30b). The stereochemistry of bicyclic [3.2.1] products (**201** and **203**) was carefully determined by 2D NMR analysis, COSY, HSQC, HMBC, and NOESY.

From a mechanistic point of view, the bicyclic [3.2.1] system formation (**201**, **203**) shares the similar reaction mechanism to quinolone formation (**166**) *via* the acyl group migration of gold carbene intermediates (**200**, **202**). Intriguingly, the 6-*endo*-dig cyclizations in camphor based 1,6-enynes occur in stereospecific manner to give the enaotiomeric pure diastereomers exclusively, which is different from the stereoselective 6-*endo*-dig cyclization in oxindole based 1,6 enynes.



Scheme 30. a) Synthesis of camphor based 1,6-enynes (**198**, **199**). b) Cationic gold(I) catalyzed of bicyclo[3.2.1]octenone formation (**200**, **201**).

3.5 Biological activity of the small molecule compound collection

In the previous section, the gold(I) catalyzed oxindole based 1,6-enyne cyclo-isomerizations are described to generate divergent products with distinctive core structures, *i.e.* quinolone, spirooxindole, and methyleneoxindole. These core structures cover a broad range of NPs, bioactive molecules, and drugs with intriguing mode of functions in biological systems. For the quinolone scaffold, orixalone D as NP was isolated from the stems of *Orixa japonica*[72], and euodenine A was isolated from the leaves of *Euodia asteridula* and disclosed as an agonist of the human TLR4 receptor with 3.9 μM half maximal effective concentration (EC_{50}), which was further improved to 0.39 μM by the replacement of methyl group to cyclopentantyl group[73]. The spirooxindole with the tetrahydropyran ring frequently present as the bioactive small molecules, *ex.* the inhibitor of human ion channel Nav1.7[74] or the agonist of CB2 receptor[75]. The methylene-oxindole scaffold have been widely investigated for the protein-ligand interaction, dihydrobenzofuran fused methyleneoxindole is the inhibitor of tyrosine kinase[76] and the derivative, sunitinib, is utilizing the receptor tyrosine kinase inhibitory property for the treatment of gastrointestinal stromal tumors and advanced renal cell carcinoma[77] (Figure 8). Therefore, it was investigated whether the scaffold divergency in the compound collection could result in selective bioactivity by utilizing the cell-based screening.

The following cell-based screens and data analysis were performed by Compound Management and Screening Center (COMAS) in Dortmund, and the biological validation experiments were carried out by Dr. Sumersing Patil, a doctoral researcher in Department of Chemical Biology at the Max Plank Institute of Molecular Physiology, Dortmund, Germany.

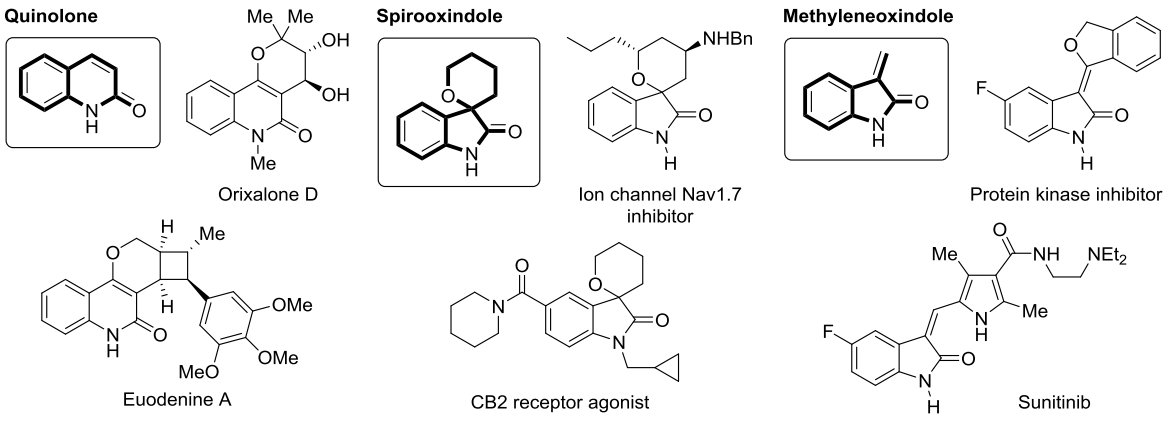


Figure 8. Representative NPs, bioactive and drug molecules with quinolone, spirooxindole or methyleneoxindole scaffold.

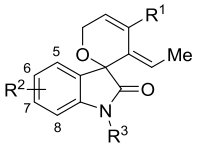
3.5.1 **Cell-based screening of the small molecule compound collection** (performed by COMAS)

The small molecule compound collection was prepared form oxindole based prenylated and crotylated 1,6-enynes (**130**, and **161**), leading to three distinctive molecular frameworks, *df*-oxindole, quinolone, and spirooxindole. In total, *ca.* 60 compounds were tested at COMAS in Dortmund for the cell-based screening of biological activities. The cell-based screening of these compounds revealed inhibition of the Hedgehog (HH) and Wnt signaling pathways, autophagy, and HeLa cell proliferation, as shown in Table 7.

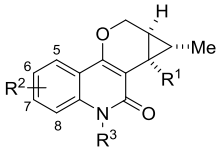
For the primary screening of HH signaling pathway modulators, the osteogenesis assay was performed. C3H/10T1/2 cells were stimulated with SMO agonist, purmorphamine, to activate the HH pathway. As a result, C3H/10T1/2 cells differentiate into osteoblast producing alkaline phosphatase (ALP). To determine the levels of ALP, CDP-star reagent was used, which generated luminescence upon conversion by ALP.[78] In this assay, *df*-oxindoles exhibited selective inhibition of HH signaling pathway. Besides, *df*-oxindoles (**134w**, **134x**) had been identified as the most potent molecules for osteogenesis inhibition with half-maximal inhibitory concentration (IC_{50}) in 2.75 and 3.13 µM, respectively. As another important signaling cascade, Wnt signaling plays a vital role in cell proliferation, migration, polarity, etc. The irregular activation of Wnt has been linked to development various types of cancers.[79] The screening of Wnt signaling was performed by using the HEK293 reporter cell line, which co-transfected with the human Frizzled-1 receptor and the TOPFLASH-driven luciferase reporter gene.[80] The quinolone class of molecules presented the dose-dependent inhibition to the Wnt signaling, for instance the quinolone **166p** displayed the lowest IC_{50} value (4.2 µM) in this class. Screening of autophagy modulators resulted in identification of *df*-oxindole and quinolone compound collections as inhibitors of autophagy with low micromolar concentration. The most potent molecule in the screening is quinolone **166l**, which inhibited autophagy with IC_{50} = 4.8 µM. In order to characterize the cell proliferation, the IncuCyte ZOOM was applied for collecting time-lapse imaging of cell confluency. With the strategy in hand, the small molecule collections were subjected for screening and the spriooxindole **165h** reduced the proliferation of HeLa cells with IC_{50} = 15.4 µM.

Table 7. Initial small molecule biological screening for HH, Wnt, and autophagy.

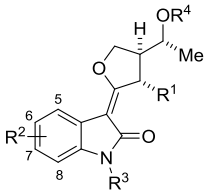
Data are mean values of three independent experiments (n = 3) ± s.d. (standard deviation), n.a. (no activity).



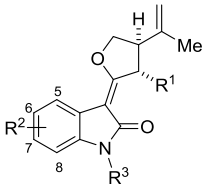
spirooxindole (**165**)



quinolinone (**166**)



df-oxindole (**167**)

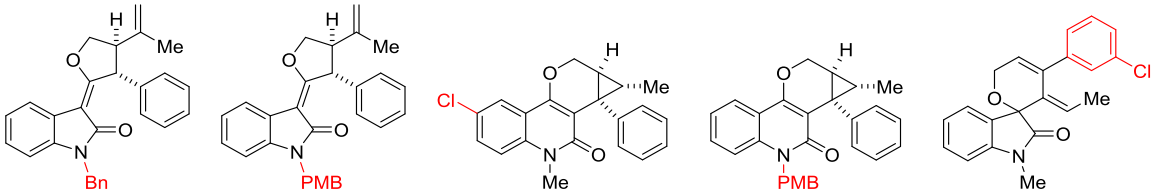


df-oxindole (**134**)

Without specifying
R^2 = H
R^3 = Me
R^1 = Me
R^4 = OMe

Compound	Inhibition of HH signaling IC_{50} [µM]	Inhibition of Wnt signaling IC_{50} [µM]	Inhibition of Autophagy IC_{50} [µM]
165a	n.a	n.a	n.a
165b (R^1 = *p*-MePh)	n.a	n.a	n.a
165g (R^1 = *p*-FPh)	n.a	n.a	n.a
165h (R^1 = *m*-ClPh)	n.a	n.a	n.a
165k (R^1 = 3-thiophene)	n.a	n.a	n.a
165p (R^2 = 6-OMe)	n.a	n.a	n.a
165r (R^2 = 6-F)	n.a	n.a	n.a
165s (R^2 = 6-Cl)	n.a	n.a	n.a
165t (R^2 = 7-Br)	n.a	n.a	n.a
165u (R^2 = 6-OCF_3)	n.a	n.a	n.a
165v (R^3 = Bn)	n.a	n.a	n.a
165w (R^3 = PMB)	n.a	n.a	n.a
166a	n.a	12 (1.32)	n.a
166e (R^1 = *m*-ClPh)	n.a	n.a	5.61 (0.25)
166g (R^1 = 3-thiophene)	n.a	n.a	n.a
166j (R^2 = 6-OMe)	n.a	17 (4.03)	n.a
166k (R^2 = 6-F)	n.a	n.a	n.a
166l (R^2 = 6-Cl)	n.a	n.a	4.81 (0.25)
166m (R^2 = 7-Br)	n.a	n.a	n.a
166n (R^2 = 6-OCF_3)	n.a	8.6 (2.32)	n.a
166o (R^3 = Bn)	9.6 (2.98)	n.a	n.a
166p (R^3 = PMB)	n.a	4.2 (1.35)	n.a
167a	n.a	n.a	n.a
167f (R^1 = *p*-FPh)	n.a	n.a	n.a
167i (R^1 = *m*-ClPh)	n.a	n.a	n.a
167j (R^1 = *p*-BrPh)	6.8 (1.89)	n.a	n.a
167l (R^1 = 3-thiophene)	n.a	n.a	n.a
167n (R^2 = 6,8-diMe)	n.a	n.a	8.33 (0.11)

Compound	Inhibition of HH signaling IC_{50} [μM]	Inhibition of Wnt signaling IC_{50} [μM]	Inhibition of Autophagy IC_{50} [μM]
167o (R^2 = 6-OMe)	6.26 (2.56)	n.a	n.a
167p (R^2 = 6-F)	n.a	n.a	n.a
167q (R^2 = 6-Cl)	n.a	n.a	6.88 (0.36)
167r (R^2 = 7-Br)	n.a	n.a	n.a
167s (R^2 = 6-OCF_3)	n.a	n.a	n.a
167t (R^3 = Bn)	n.a	n.a	n.a
167u (R^3 = PMB)	n.a	n.a	n.a
134a	5.26 (1.25)	n.a	8.92 (0.74)
134c (R^1 = *m*-MePh)	n.a	n.a	n.a
134d (R^1 = *p*-MePh)	n.a	n.a	n.a
134e (R^1 = *o*-OMePh)	6.96 (2.66)	17.03 (6.22)	n.a
134f (R^1 = *m,p*-diOMePh)	n.a	n.a	n.a
134g (R^1 = *p*-FPh)	n.a	n.a	n.a
134l (R^1 = 3-thiophene)	n.a	n.a	n.a
134m (R^1 = *n*-propyl)	n.a	n.a	n.a
134n (R^1 = *i*-pentyl)	n.a	n.a	n.a
134o (R^2 = 6-Me)	n.a	n.a	n.a
134p (R^2 = 6-OMe)	n.a	n.a	n.a
134r (R^2 = 7-Br)	n.a	n.a	n.a
134s (R^2 = 6-F)	6.53 (0.56)	13.65 (3.89)	6.71 (0.79)
134u (R^2 = 6-OCF_3)	n.a	n.a	n.a
134v (R^2 = 6-NO_2)	n.a	n.a	n.a
134t (R^2 = 6-Cl)	n.a	n.a	6.47 (0.60)
134w (R^3 = Bn)	2.75 (0.62)	n.a	n.a
134x (R^3 = PMB)	3.13 (1.02)	n.a	n.a
134y (R^3 = MOM)	9.56 (3.32)	n.a	n.a
134z (R^3 = SEM)	6.33 (0.65)	n.a	n.a
134aa (R^3 = H)	n.a	n.a	n.a



134w, IC_{50} = 2.75 μM hedgehog signaling pathway inhibitor

134x, IC_{50} = 3.31 μM

166l, IC_{50} = 4.8 μM autophagy inhibition

166p, IC_{50} = 4.2 μM Wnt singaling pathway inhibitor

165h, IC_{50} = 15.4 μM reduce the HeLa cells proliferation

Figure 16. The most active compounds in each biological screening.

3.5.2 Hedgehog Signaling Pathway

Among all the biological screening outcomes, the biological mode of action of the synthesized small molecules (**134w** and **134x**) for HH signaling pathway modulation was investigated. After the genetic mutation studies of fruit fly *Drosophila melanogaster* in 1980, hedgehog (HH)-gene had been identified as the key factor to regulate the embryonic development, *i.e.* the mutation of HH in embryonic cell results in the coat of larvae covering with spines. The hedgehog-like phenotype of larvae allowed the gene to be termed as HH-gene.[81] A decade later, three mammalian paralogous genes, Sonic HH, Indian HH, and Desert HH, had also been discovered to share similar biological behaviors with the HH gene from fruit fly.[82] In the development of embryonic cell, they regulate the cell differentiation, proliferation, and tissue polarity. In the absence of HH ligand, their membrane bound receptor Patched (PTCH) localizes in the cilia, and inhibits the trafficking of seven-transmembrane protein smoothened (SMO) to the cilia. In the absence of active SMO in the cilia, GLI is phosphorylated by PKA, CK1 and GSK3 beta. The phosphorylated GLI is proteolytical processed into GLI repressor form (GLI^R), which suppress the expression of HH target genes (Figure 9a). When the HH binding with PTCH, the lysosomal degradation of PTCH takes place and SMO translocate to cilia to initiate the signaling cascade. After the localization of active form of GLI (GLI^A) to the nucleus, it starts to turn on the HH target genes, such as *Patch1*, *Gli1* (Figure 9b).[83]

The dysregulated HH signaling pathway will continuously turn on the HH target gene, resulting as the trigger of various human cancers, such as basal cell carcinoma (BCC), medulloblastoma, etc. When the PTCH losses the original function by the mutation, the SMO constitutively activate the HH target genes as ligand-independent HH activation. Alternatively, the over express of HH ligand will activate PTCH and lead to ligand-dependent HH activation. By targeting the improper activation of HH signaling, two small molecule drugs, vismodegib (GDC0449)[84] and sonidegib (LDE225)[85], were developed as the SMO inhibitor for the treatment of BCC (Scheme 10). However, due to the recently discovered mutation of SMO led to resistance to vismodegib[86] Therefore, small molecule inhibitors of HH signaling that act via different mode of action in demand.

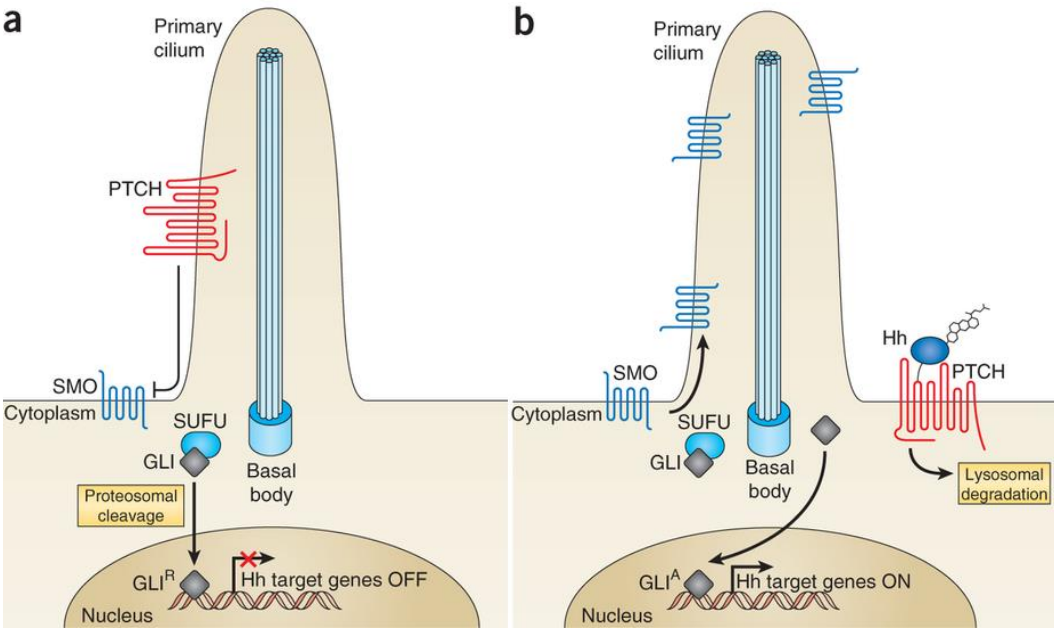


Figure 9. The schematic representation of HH signaling pathway. a) HH signaling pathway without HH ligand. b) HH signaling pathway with HH ligand. Reprinted from ref [83a], copy right 2013 Springer Nature, Inc (license number: 4270991022617).

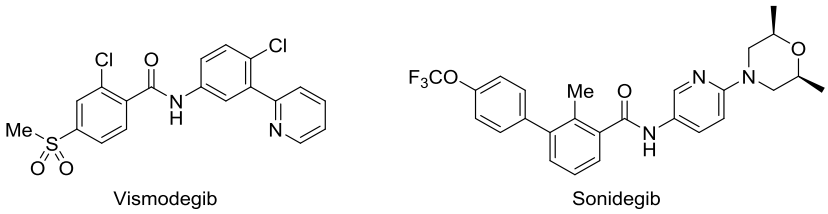


Figure 10. The chemical structure of SMO inhibitors, vismodegib and sonidegib.

3.5.3 **Target Identification for the Hedgehog Signaling Inhibitor** (performed by S. P.)

The *df*-oxindoles (**134w**, **134x**) displayed potent inhibitory activity of the HH signaling pathway in a cell-based osteogenesis assay (Figure 11a). To confirm and determine the HH inhibitory activity of *df*-oxindoles (**134w**, **134x**), orthogonal assays, such as *Gli* reporter gene assay and HH target gene expression by quantitative polymerase chain reaction (qPCR), were performed. In the *Gli* reporter gene assay, the NIH-3T3 cell clones Shh-Light2 cells, which are stably transfected with Gli-luciferase and Renilla luciferase reporter plasmids were used.[87] The Shh-Light2 cells were treated with purmorphamine and various concentrations of compounds. Firefly luciferase was measured as a result of different concentration of **134w** and **134x.** Dose dependent inhibition of firefly luciferase led to IC_{50} values 1.7 µM for **134w** and 0.8 µM for **134x** (Figure 11b). Additionally, *Ptch1* and *Gli1* gene expression were

monitored in C3H/10T1/2 cells as results of compound treatment.[88] First, HH signaling was activated by treatment with purmorphamine followed by compound treatment. Dose-dependent suppression of the *Ptch1* and *Gli1* was observed when different concentration of **134w** and **134x** were applied (Figure 11c, d).

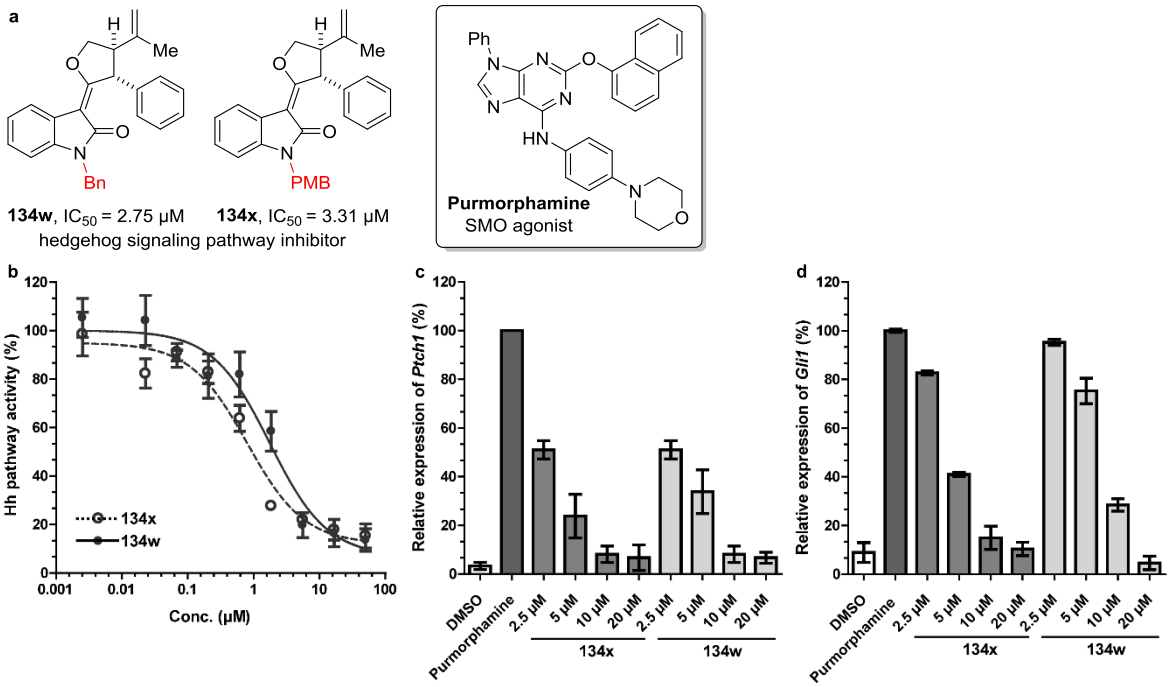


Figure 11. a) The structure of **134w**, **134x**, and Purmorphamine. b) **134w** and **134x** inhibit *Gli*-dependent reporter gene expression. c) **134w** and **134x** inhibit the Hh target gene *Ptch1*. d) **134w** and **134x** inhibit the Hh target gene *Gli1*.

Since SMO frequently serves as the HH signaling pathway inhibition target for small molecules, such as vismodegib and sonidegib, the boron-dipyrromethene (BODIPY)-cyclopamine displacement assay were performed in HEK-293T cells transiently transfected with SMO-expressing construct. The BODIPY-cyclopamine binds to cells expressing SMO thus providing green fluorescence. Vismodegib, a known SMO inhibitor, can replace the BODIPY-cyclopamine from the SMO binding site, which reduce of fluorescence signal. Upon treatment with **134w** and **134x**, the green fluorescence was suppressed certifying the competition between BODIPY-cyclopamine to **134w**, **134x** (Figure 12a). Additionally, the translocation of SMO to primary cilium had been prooved to be vital for triggering the singling cascade.[88] The co-localization experiments were performed to investigate the SMO trafficking to cilium. The SMO agonist, purmorphamine, activates the translocation of SMO to the primary cilium, therefore the co-localization of SMO (red) on

the cilia (green) is observed. In contrast, the SMO antagonist, vismodegib, prohibited the translocation mechanism and the SMO inhibitor **134w** and **134x** share the similar property to vismodegib (Scheme 12b). In this stage, it was concluded that *df*-oxindole **134w** and **134x** are the HH signaling pathway inhibitor by binding to SMO and preventing the SMO trafficking to primary cilia.

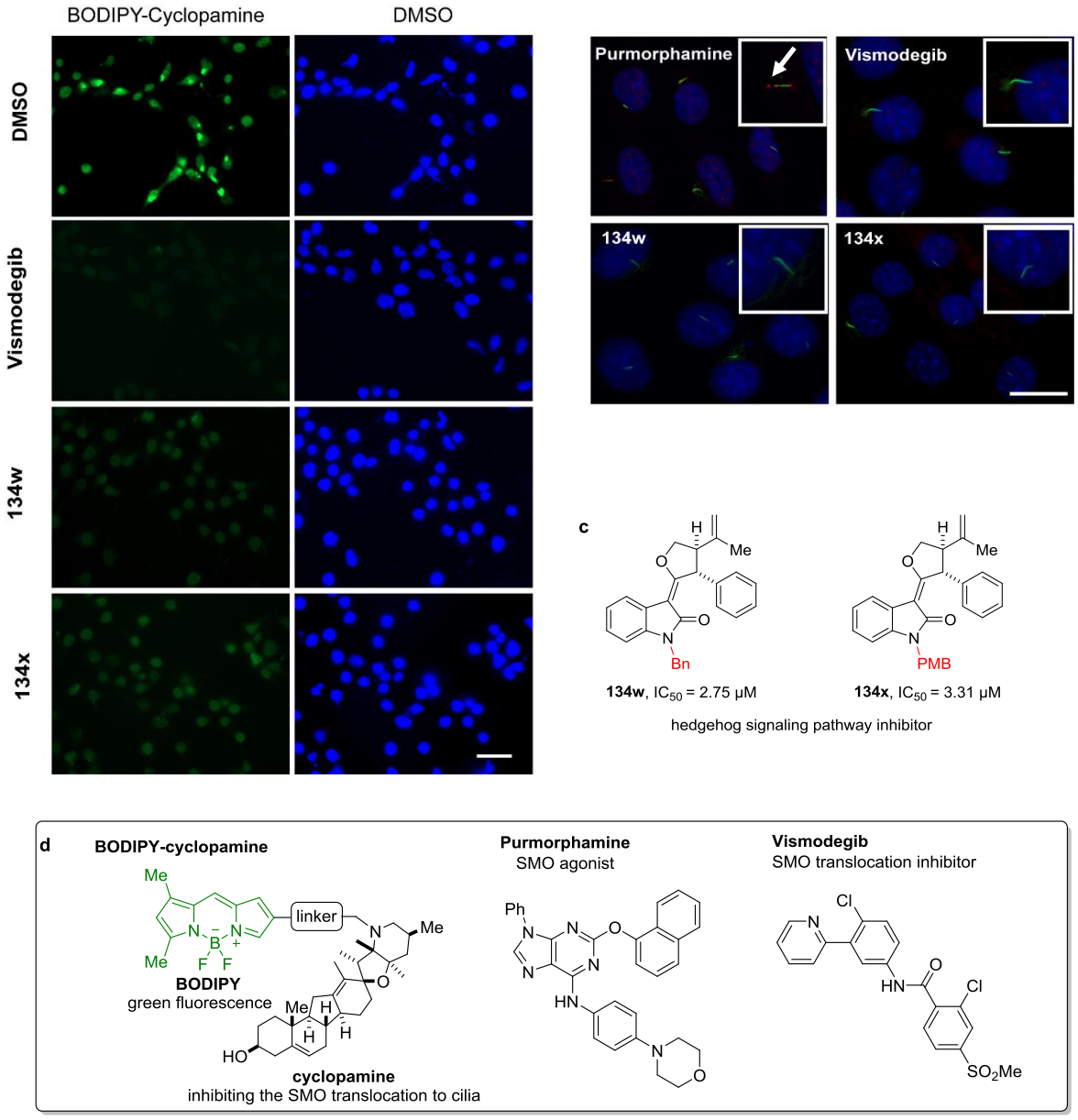
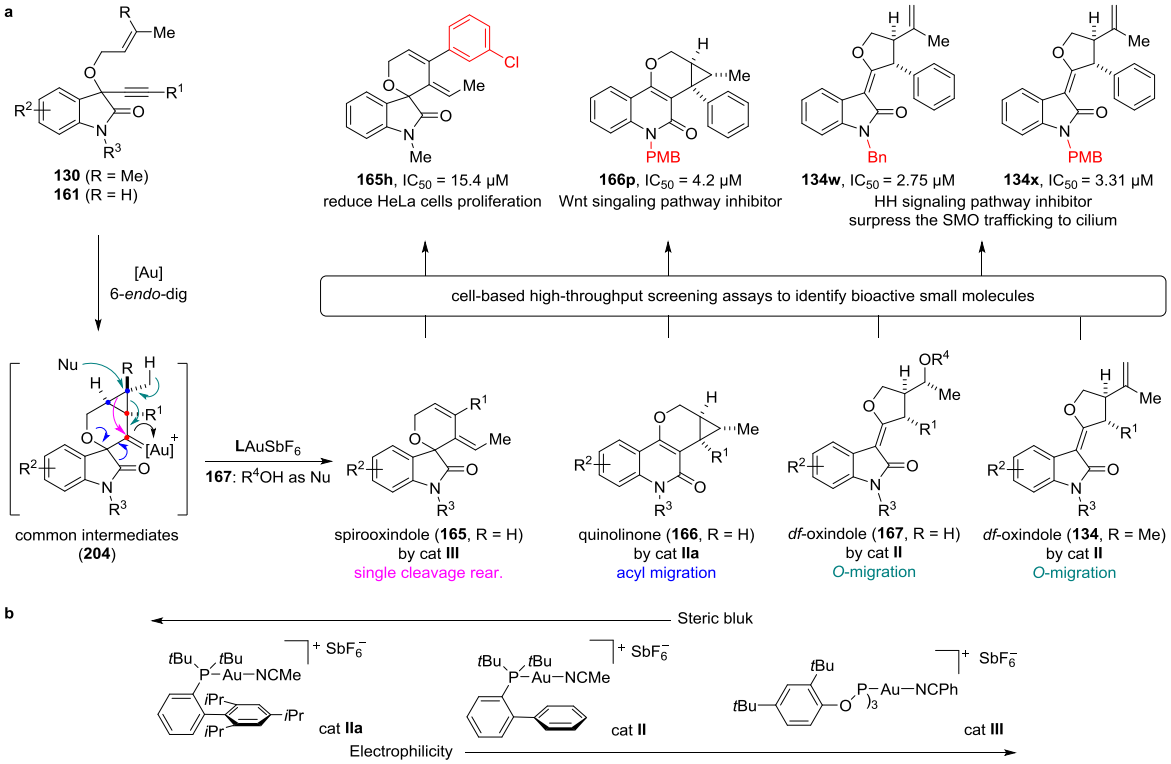


Figure 12. a) The competition experiment of **134w**, **134x** to BODIPY-cyclopamine from SMO. BODIPY-cyclopamine (green), nuclei (blue, staining with 4',6-diamidino-2-phenylindole, DAPI) b) Visualization experiment for SMO trafficking to primary cilium. nuclei (blue, staining with DAPI), Smo (red), cilia (green, acetylated tublin) c) The structure of **134w**, **134x**. d) The structure of BODIPY-cyclopamine, Purmorphamine, and Vismodegib.

4 Summary

The work presented in this thesis focuses on and explores the potential of cationic gold(I) catalyzed oxindole derived 1,6-enyne transformations to build structurally distinct molecular scaffolds, which could be used to build structurally rich compound collections for the exploration of chemical space. The selection of the oxindole fragment was inspired by its prevalence in numerous natural and synthetic bioactive molecules and the enyne segment had been shown to give cycloisomerization products under transition metal catalysis. The oxindole based 1,6-enynes (**130** and **161**) were prepared in up to 4 steps and then subjected to gold(I) catalyzed scaffold transformations. The common gold carbene intermediates (**204**) were generated from the crotylated 1,6-enynes (**161**) and further rearranged into three structurally distinct scaffolds, *i.e.* spirooxindoles (**165**, magenta arrow), quinolones (**166**, blue arrows), and *df*-oxindoles (**134**, turquoise arrow) by single cleavage rearrangement, acyl migration, and *O*-migration, respectively. The steric and electronic factors of ligands in cationic gold(I) catalysts played subtle roles in these transformations to deliver high selectivity and satisfactory yields of desired products which were used for further biological studies. A small compound collection based on different scaffolds generated via gold(I) catalyzed transformations, was subjected to cell-based screening. Interestingly, each compound class could deliver bioorthogonally active small molecule, *i.e.* one of the spirooxindoles (**165**) reduced the proliferation of HeLa cells, a quinolone (**166**) inhibited the Wnt signaling pathway, and one of the *df*-oxindoles (**134**) suppressed the HH signaling pathway. As the representative example, *df*-oxindoles (**134w**, **134x**) were further investigated to find their biological target and mode of function and were found to prevent the translocation of Smo to primary cilia, which ultimately inhibits HH signaling (Scheme 31a). Thus, a ”ligand directed divergent scaffold synthesis” (LDS) approach was successfully developed to access novel and biologically relevant chemical space and to deliver bioactive small molecules.



Scheme 31. a) Gold(I) catalyzed ligand directed divergent scaffold synthesis (LDS). b) The steric and electronic properties of gold(I) catalysts.

5 Experimental section

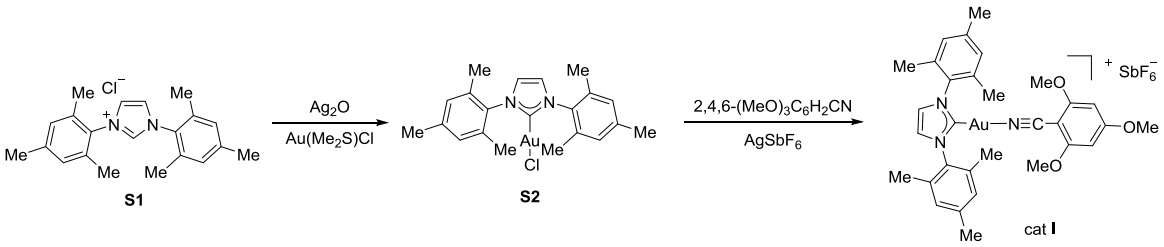
5.1 General information

All commercially obtained chemicals and reagents were used without further purification. Dry dichloromethane (DCM), 1,2-dicholoroethane (DCE), tetrahydrofuran (THF), dimethylformamide (DMF), and diethyl ether (Et_2O) were used the Solvent Purification System M-BRAUN Glovebox Technology SPS-800 or purchased from Arcos Organics. All reactions were performed in flame dried glassware with dry solvent under argon atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminum plates with F-254 indicator. Compounds were visualized by irradiation with UV light. Column chromatography was performed by using silica gel Merck 60 (particle size 0.040-0.063 mm). ^{1}H NMR and ^{13}C NMR were recorded on a *Bruker DPX300* (300 MHz), *Bruker DRX400* (400 MHz), *Bruker DRX500* (500MHz), *Bruker DRX600* (600 MHz) and *Varian INOVA500* (500 MHz) at 300 K using $CDCl_3$ as solvent. chemical shifts of spectra were expressed in parts per million (ppm, δ) and calibrated relative to residual proton and carbon signals in deuterated NMR solvent ($CDCl_3$: δ = 7.26 ppm for ^{1}H NMR and δ = 77.16 ppm for ^{13}C NMR). Multiplicities are indicated as following: (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), and coupling constants (*J*) are represented in Hertz (Hz). High resolution mass spectra (HRMS) were recorded on a LTQ Orbitrap mass spectrometer coupled to an Acceka HPLC-System (HPLC column: Hypersyl GOLD, 50 mm x 1 mm, particle size 1.9 μm, ionization method: electron spray ionization). The enantiomeric excess (ee) was measured by HPLC analysis on the machine *Agilent 1100*. Optical rotations were measured in a *Schmidt + Haensch Polartronic HH8* polarimeter. The substrates of 1-methylisatin [2058-74-4] and 1-benzyl-1*H*-indole-2,3-dione [1217-89-6] were directly purchased from Sigma-Aldrich for later studies. The substrate of 1,6-enynes with the substituent of (*E*)-crotyl group were prepared from crotyl bromide [29576-14-5] with a small amount of inseparable (*Z*)-isomer. Inseparable (*Z*)-isomers were proceeded through the 1,6-enyne synthesizes and following gold catalyzed cycloisomerization reactions. The ratio of (*E,Z*)-isomers in 1,6-enynes were determined by ^{1}H-NMR, and the yield of gold catalyzed cycloisomerizations were calculated on the basis of (*E,Z*)-mixture. The recrystallizations were performed from DCM and petroleum ether.

5.2 Synthesis of gold(I) catalysts

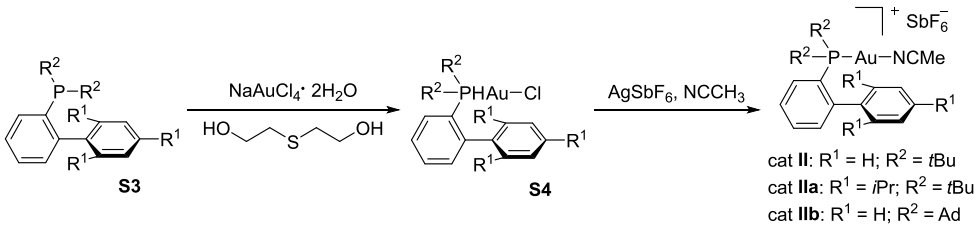
The gold complexes (**I**[55], **II** [866641-66-9][89], **IIa** [1140531-94-7][89], **IIb**[90] and **III**[58, 90]) were either purchased from Sigma-Aldrich or synthesized as following procedures :

5.2.I Synthesis of gold(l) catalyst (I)



To a solution of the 1,3-dimesitylimidazolium chloride (**S1**, 1.0 mmol) in dry DCM was added Ag_2O (0.5 mmol). The suspension became clear after stirring for 3 h at 23 °C. A solution of $Au(Me_2S)Cl$ (1.0 mmol) in dry DCM was added dropwise, the reaction mixture was then stirred for another 4 h, the solution was filtered through Celite®, and the solvent was partially evaporated. Addition of hexane resulted in the precipitation of gold(l) complex (**S2**). A solution of **S2** (0.1 mmol) and 2,4,6-trimethoxybenzonitrile (0.1 mmol) in dry DCM was added over solid $AgSbF_6$ (0.1 mmol) and stirred for 5 min. The mixture was filtered (HPLC Teflon filter) and the solid residue washed with DCM twice. The gold complex precipitated from the filtrate upon addition of Et_2O. Filtration and air-drying furnished a bright white solid (**I**).

5.2.2 Synthesis of gold(l) catalysts (II, IIa, and IIb)

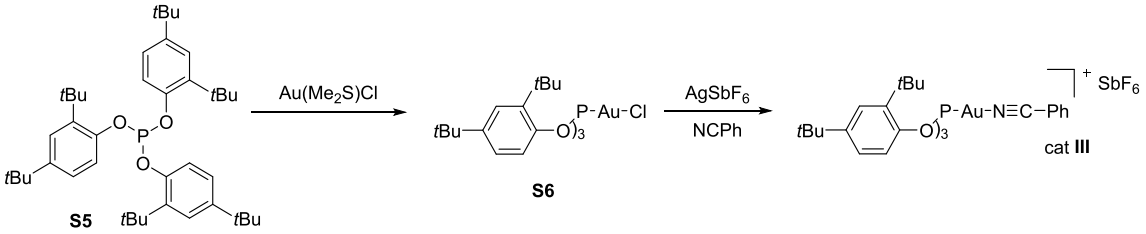


At 0 °C, to the orange solution of sodium tetrachloroaurate dihydrate (1.0 mmol) in water was slowly added 2,2'-thiodiethanol (3.0 mmol) with 45 min stirring. The corresponded phosphine ligand (**S3**, 1.0 mmol) was added to the mixture and a white precipitate was formed during the process. After stirring for 20 min, the solid was filtered off, washed with MeOH, and dried in vacuo to provide the Au(L)Cl (**S4**) .

At 0 °C, to a solution of **S4** (0.5 mmol) in dry DCM was added dry MeCN (1.0 mmol), followed by the addition of $AgSbF_6$ (0.5 mmol). The reaction mixture was stirred at room

temperature overnight, the crude product was filtered through a pad of Celite®, and the solvent was again filtered through a syringe filter to give a clear solution. After the evaporation of solvent, the white solid was obtained as the desired cationic gold(l) complex (**II**, **IIa**, or **IIb**).

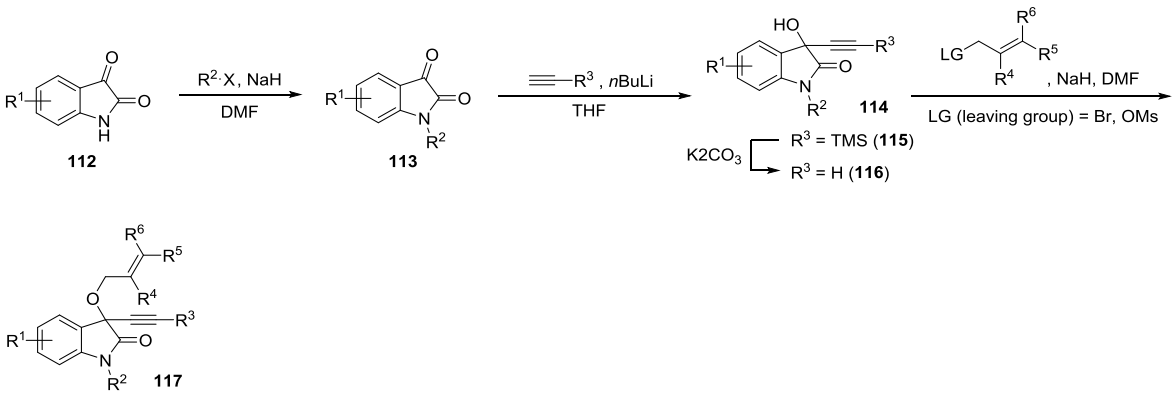
5.2.3 Synthesis of gold(l) catalyst (III)



At 0 °C, to a solution of $Au(Me_2S)Cl$ (1 mmol) in dry DCM was slowly added a solution of tris(2,4-di-tert-butylphenyl) phosphite (**S5**, 1.05 mmol) in dry DCM and the resulting reaction mixture was allowed to warm to room temperature. The reaction was monitored by the consumption of the ligand through TLC. After the reaction was complete, the mixture was filtered through a syringe filter and concentrated to provide the desired Au(l)Cl complex (**S6**).

At 0 °C, to a solution of **S6** (1.00 mmol) and PhCN (1.1 mmol) in dry DCM was added $AgSbF_6$ (1.00 mmol). A white precipitate appeared immediately and the reaction mixture was further stirred at room temperature overnight. The resulting reaction mixture was filtered through a pad of Celite®, and the solvent was again filtered through a syringe filter to give a clear solution. After the evaporation of solvent and drying *in vacuo*, the white solid was obtained as the desired cationic gold(l) complex (**III**).

5.3 Preparation of starting material^



General procedure A (*N*-alkylation)

To a solution of a isatin analog (**112**, 10 mmol) in DMF (30 ml) at 0 °C was added NaH 60% wt (12 mmol) in one portion and the mixture was stirred at the same temperature for 1 h. To the resulting mixture was added dropwise the respective alkyl halide (13 mmol). The mixture was warmed to room temperature and stirred overnight. The reaction was quenched with $NH_4Cl_{(sat)}$ and diluted with EtOAc (100 ml). After extraction, the organic layer was washed with H_2O (300 ml) three times and once with brine, dried over $MgSO_{4(s)}$, filtered, and concentrated under reduced pressure to provide the crude product. The product was purified by flash column chromatography (petroleum ether/EtOAc mixture as eluents,) to afford the desired product (**113**).

General procedure B (lithium acetylide addition)

At -78 °C, to a solution of acetylene (2.4 mmol) in THF (30 ml) was slowly added 2.5 M *n*BuLi in hexanes (2.3 mmol) and the mixture was stirred for 1 h at the same temperature. The *N*-protected isatin analog (**113**, 2 mmol) was then added to the reaction mixture in one portion. Afterwards, the resulting mixture was slowly warmed to room temperature and stirred overnight. The reaction was quenched with $NH_4Cl_{(sat)}$ and extracted with EtOAc (30 ml) three times. The combined organic layers were washed with brine and dried over $MgSO_{4(s)}$. After concentration under reduced pressure, the crude product was purified by flash column chromatography (EtOAc/petroleum ether or DCM/EtOAc mixture as eluents,) to afford the desired product (**114** or **115**).

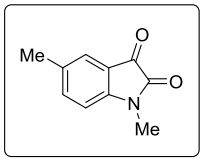
General procedure C (desilylation)

To a soultion of TMS acetylene (2.0 mmol) in MeOH (5 ml) at room temperature was added K_2CO_3 (373 mg, 2.7 mmol) in one portion. The resulting suspension mixture was stirred for 2 h and then quenched with $NH4Cl_{(sat)}$. The mixture was extracted with EtOAc for three times, and the combined organic phases were dried over MgSO4, filtered and concentrated under reduced pressure. The crude product (**116**) was subjected to next step without further purification.

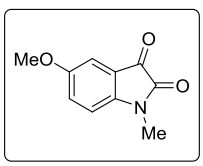
General procedure D (allylation)

To a solution of the propargyl alcohol (**114** or **116**, 0.5 mmol) in DMF (5 ml) at 0 °C was added NaH 60% wt (0.55 mmol) in one portion and the mixture was stirred at same temperature for 1 h. To the resulting mixture was added dropwise the respective allylic halide (0.6 mmol). The mixture was warmed to room temperature and stirred overnight. The reaction was quenched with $NH_4Cl_{(sat)}$ and diluted with EtOAc (50 ml). After extraction, the organic layer was washed with H_2O (50 ml) three times and once with brine, dried over $MgSO_{4(s)}$, filtered, and concentrated under reduced pressure to provide the crude product. The product was purified by flash column chromatography (petroleum ether/EtOAc mixture as eluents,) to afford the desired product (**117**).

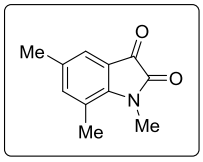
1,5-dimethylindoline-2,3-dione (112a) was prepared according to the general procedure A, by using 5-methylindoline-2,3-dione (150 mg, 0.93 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.30) as eluents, the desired product was obtained in 89% yield (145 mg, 0.83 mmol) as a red solid. The analytical data were identical to literature data.[91] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.40 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 3.23 (s, 3H), 2.34 (s, 3H).



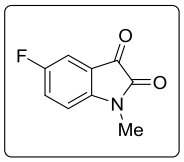
5-methoxy-1-methylindoline-2,3-dione (112b) was prepared according to the general procedure A, by using 5-methoxyindoline-2,3-dione (1074 mg, 6.06 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.23) as eluents, the desired product was obtained in 89% yield (1026 mg, 5.37 mmol) as a black solid. The analytical data were identical to literature data.[92] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 8.5, 2.7 Hz, 1H), 7.09 (d, *J* = 2.7 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 3.78 (s, 3H), 3.19 (s, 3H).



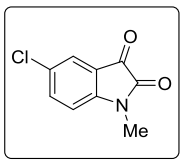
1,5,7-trimethylindoline-2,3-dione (112c) was prepared according to the general procedure A, by using 5,7-dimethylindoline-2,3-dione (1000 mg, 5.71 mmol) and iodomethane. After silica gel column chromatography with EtOAc/DCM = 1/2 (R_f = 0.3) as eluents, the desired product was obtained in 72% yield (781 mg, 4.13 mmol) as a dark red solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.25 (s, 1H), 7.13 (s, 1H), 3.48 (s, 3H), 2.51 (s, 3H), 2.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 184.15, 159.49, 146.92, 142.83, 133.72, 123.83, 121.71, 118.76, 29.78, 20.47, 18.79. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{11}H_{12}O_2N]^+$: 190.0863, found: 190.0869.



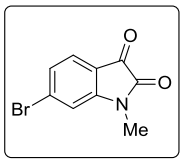
5-fluoro-1-methylindoline-2,3-dione (112d) was prepared according to the general procedure A, by using 5-fluoroindoline-2,3-dione (1001 mg, 6.06 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.3) as eluents, the desired product was obtained in 87% yield (945 mg, 5.27 mmol) as a dark red solid. The analytical data were identical to literature data.[91] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 2H), 6.89 (dd, *J* = 8.5, 3.6 Hz, 1H), 3.26 (s, 3H).



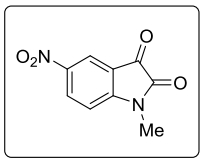
5-chloro-1-methylindoline-2,3-dione (112e) was prepared according to the general procedure A, by using 5-chloroindoline-2,3-dione (1100 mg, 6.06 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.33) as eluents, the desired product was obtained in 96% yield (1142 mg, 5.84 mmol) as a red solid. The analytical data were identical to literature data.[91] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.52 (d, *J* = 2.2 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 3.23 (s, 3H).



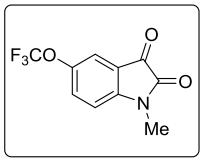
6-bromo-1-methylindoline-2,3-dione (112f) was prepared according to the general procedure A, by using 6-bromoindoline-2,3-dione (1370 mg, 6.06 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.65) as eluents, the desired product was obtained in 80% yield (1162 mg, 4.84 mmol) as an orange solid. The analytical data were identical to literature data.[92] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.30 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.10 (d, *J* = 1.5 Hz, 1H), 3.26 (s, 3H).



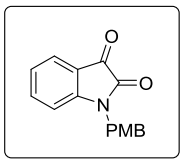
1-methyl-5-nitroindoline-2,3-dione (112g) was prepared according to the general procedure A, by using 5-nitroindoline-2,3-dione (800 mg, 4.16 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.13) as eluents, the desired product was obtained in 99% yield (849 mg, 4.12 mmol) as a brown solid. The analytical data were identical to literature data.[93] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 8.7, 2.3 Hz, 1H), 8.48 (d, *J* = 2.3 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 1H), 3.36 (s, 3H).



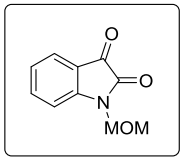
1-methyl-5-(trifluoromethoxy)indoline-2,3-dione (**112h**) was prepared according to the general procedure A, by using 5-(trifluoromethoxy)indoline-2,3-dione (420 mg, 1.82 mmol) and iodomethane. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.35) as eluents, the desired product was obtained in 94% yield (418 mg, 1.71 mmol) as a red solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 – 7.38 (m, 2H), 6.95 (d, *J* = 8.3 Hz, 1H), 3.26 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 182.5, 158.0, 149.9, 145.4, 145.4, 131.3, 120.5 (q, *J* = 258.2 Hz), 118.5, 118.0, 111.2, 26.5. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{10}H_7O_3NF_3]^+$: 246.0373, found: 246.0379.



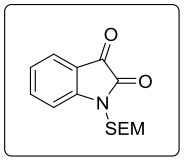
1-(4-methoxybenzyl)indoline-2,3-dione (112i) was prepared according to the general procedure A, by using indoline-2,3-dione (2.000 g, 13.59 mmol) and 4-methoxybenzyl chloride. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.53) as eluents, the desired product was obtained in 95% yield (3.452 g, 12.91 mmol) as an orange solid. The analytical data were identical to literature data.[94] **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.48 (td, *J* = 7.6, 1.3 Hz, 1H), 7.31-7.22 (m, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.89 – 6.85 (m, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 4.87 (s, 2H), 3.79 (s, 3H).



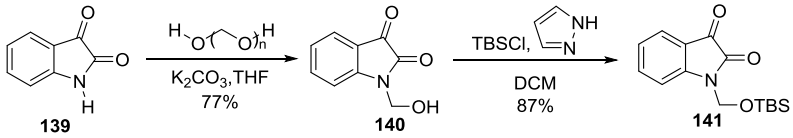
1-(methoxymethyl)indoline-2,3-dione (112j) was prepared according to the general procedure A, by using indoline-2,3-dione (2.000 g, 13.95 mmol) and chloromethyl methyl ether. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.51) as eluents, the desired product was obtained in 64% yield (1.662 g, 8.69 mmol) as an orange solid. The analytical data were identical to the literature data.[95] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.2 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 5.16 (s, 2H), 3.38 (s, 3H).



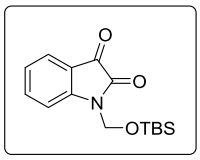
1-((2-(trimethylsilyl)ethoxy)methyl)indoline-2,3-dione (112k) was prepared according to



the general procedure A, by using indoline-2,3-dione (2.000 g, 13.59 mmol) and 2-(trimethylsilyl)ethoxymethyl chloride. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.79) as eluents, the desired product was obtained in 97% yield (3.640 g, 13.12 mmol) as an orange solid. The analytical data were identical to the literature data.[96] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.69 – 7.60 (m, 2H), 7.18 (td, *J* = 7.6, 0.7 Hz, 1H), 7.14 (d, *J* = 8.2 Hz, 1H), 5.18 (s, 2H), 3.60 (dd, *J* = 8.3, 7.8 Hz, 2H), 0.93 (dd, *J* = 8.3, 7.8 Hz, 2H), -0.02 (s, 9H).

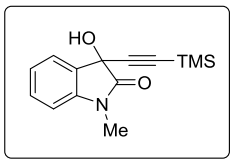


1-(((tert-butyldimethylsilyl)oxy)methyl)indoline-2,3-dione (**141**) was prepared by



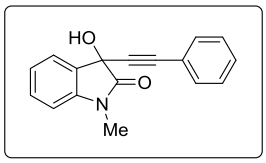
following procedure. A solution of isatin (**139**, 2.5 g, 17.0 mmol) in dry THF (125 ml) was added paraformaldehyde (15.3 g, 0.17 mol) and $K_2CO_{3(s)}$ (2.3 g, 17.0 mmol). The heterogeneous mixture was stirred at room temperature till the indication of full convertion by TLC analysis with EtOAc/petroleum ether = 1/2 (R_f = 0.18) as eluents. The mixture was filtered through a shout pad of celite to remove the insoluable residues. $NH_4Cl_{(sat.)}$ was added to the filtrate and the resulting mixture was extracted with EtOAc for three times, and the combined organic phases were washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product (**140**) was obtained in 77% yield (2.328 g, 13.1 mmol) and subjected to next step without further purification. At 0 °C, to the solution of alcohol (**140**, 2.328 g, 13.1 mmol) in dry DCM (100 ml) was added imidazole (1.047 g, 15.8 mmol) and TBSCl (2.179 g, 14.5 mmol). The resulting mixture was stirred at room temperature for 1 h and quenched with $NH4Cl_{(sat.)}$. The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with DCM/petroleum ether = 2/1 (R_f = 0.45) as eluents and the desired product was obtained in 87% yield (3.323 g, 11.4 mmol) as a pale yellow solid. **mp:** 72 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 – 7.60 (m, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 1H), 5.34 (s, 1H), 0.87 (s, 5H), 0.12 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 183.42, 157.38, 150.50, 138.64, 125.49, 124.21, 117.59, 111.89, 64.75, 25.72, 18.14, -5.14. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{15}H_{22}O_3NSi]^+$: 292.1364, found: 292.1365.

3-hydroxy-1-methyl-3-((trimethylsilyl)ethynyl)indolin-2-one (115) was prepared



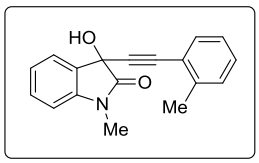
according to the general procedure B, by using 1-methylisatin (1.172 g, 7.27 mmol) and trimethylsilylacetylene. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.32) as eluents, the desired product was obtained in 69% yield (1.307 g, 5.04 mmol) as a pale yellow solid. The analytical data were identical to the literature data.[97] **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 4.08 (s, 1H), 3.18 (s, 3H), 0.13 (s, 9H).

3-hydroxy-1-methyl-3-(phenylethynyl)indolin-2-one (**114a**) was prepared according to the



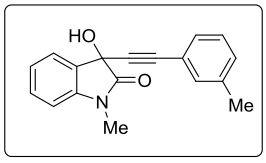
general procedure B, by using 1-methylisatin (**139**, 1.000 g, 6.21 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.32) as eluents, the desired product was obtained in 81% yield (1.326 g, 5.04 mmol) as a pale yellow solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 – 7.21 (m, 3H), 7.16 (td, *J* = 7.6, 0.7 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 3.86 (s, 1H), 3.23 (s, 3H).

3-hydroxy-1-methyl-3-(*o*-tolylethynyl)indolin-2-one (**114b**) was prepared according to the



general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 2-ethynyltoluene. After silica gel column chromatography with EtOAc/DCM = 1/10 (R_f = 0.35) as eluents, the desired product was obtained in 88% yield (454 mg, 1.64 mmol) as a white solid. **mp**: 163 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.24 – 7.19 (m, 1H), 7.19 – 7.14 (m, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 3.63 (s, 1H), 3.25 (s, 3H), 2.39 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.29, 143.08, 141.06, 132.42, 130.45, 129.44, 129.39, 129.02, 125.49, 124.71, 123.83, 121.54, 108.93, 89.61, 85.37, 69.77, 26.70, 20.65. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{16}O_2N]^+$: 278.1176, found: 278.1176.

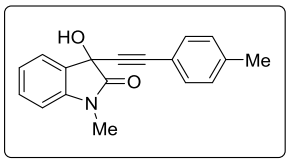
3-hydroxy-1-methyl-3-(*m*-tolylethynyl)indolin-2-one (**114c**) was prepared according to the



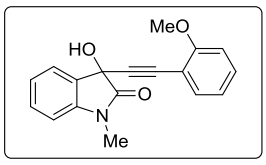
general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 3-ethynyltoluene. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.32) as eluents, the desired product was obtained in 90% yield (466 mg, 1.68 mmol) as a pale yellow solid. **mp**: 161 °C **^{1}H**

NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.28 – 7.21 (m, 2H), 7.20 – 7.08 (m, 3H), 6.85 (d, *J* = 7.6 Hz, 1H), 3.84 (s, 1H), 3.23 (d, *J* = 0.9 Hz, 3H), 2.27 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.10, 143.21, 138.04, 132.78, 130.59, 130.00, 129.25, 129.12, 128.23, 124.85, 123.86, 121.55, 108.96, 86.69, 85.29, 69.69, 26.77, 21.24. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{18}H_{15}O_2NNa]^+$: 300.0995, found: 300.1004.

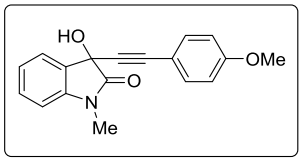
3-hydroxy-1-methyl-3-(*p*-tolylethynyl)indolin-2-one (**114d**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 500 mg, 3.10 mmol) and 4-ethynyltoluene. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.34) as eluents, the desired product was obtained in 88% yield (755 mg, 2.72 mmol) as a yellow solid The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 3.82 (s, 1H), 3.23 (s, 3H), 2.32 (s, 3H).



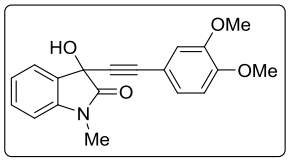
3-hydroxy-3-((2-methoxyphenyl)ethynyl)-1-methylindolin-2-one (**114e**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 2-ethynylanisole. After silica gel column chromatography with EtOAc/DCM = 1/10 (R_f = 0.24) as eluents, the desired product was obtained in 92% yield (503 mg, 1.71 mmol) as a white solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.40 – 7.33 (m, 2H), 7.29 (ddd, *J* = 8.0, 7.6, 1.7 Hz, 1H), 7.15 (td, *J* = 8.0, 0.8 Hz, 1H), 6.90 – 6.81 (m, 3H), 3.85 (s, 3H), 3.24 (s, 3H).



3-hydroxy-3-((4-methoxyphenyl)ethynyl)-1-methylindolin-2-one (**114f**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 4-ethynylanisole. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.33) as eluents, the desired product was obtained in 90% yield (491 mg, 1.67 mmol) as a pale yellow solid. The analytical data were identical to the literature data.[99] **^{1}H NMR** (600 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 7.8 Hz, 1H), 7.39 (td, *J* = 7.8, 1.1 Hz, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.98 – 6.94 (m, 1H), 6.91 – 6.85 (m, 2H), 3.77 (s, 3H), 3.25 (s, 3H).

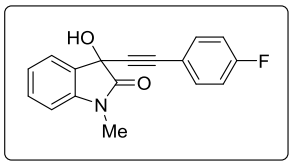


3-((3,4-dimethoxyphenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114g**) was prepared



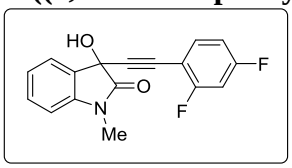
according to the general procedure B, by using 1-methylisatin (**139**, 100 mg, 0.62 mmol) and 3,4-dimethoxyphenyl acetylene. After silica gel column chromatography with EtOAc/DCM = 1/6 (R_f = 0.35) as eluents, the desired product was obtained in 90% yield (180 mg, 0.56 mmol) as a pale yellow solid. **mp**: 160 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7., 0.6 Hz, 1H), 7.28 (td, *J* = 7.6, 1.1 Hz, 1H), 7.09 (td, *J* = 7.6, 0.6 Hz, 1H), 6.96 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.87 (d, *J* = 1.8 Hz, 1H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.63 (d, *J* = 8.3 Hz, 1H), 5.12 (s, 1H), 3.77 (s, 3H), 3.68 (s, 3H), 3.12 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.32, 149.79, 148.32, 142.76, 130.17, 129.39, 125.44, 124.52, 123.61, 114.62, 113.74, 110.71, 108.75, 86.27, 84.24, 69.53, 55.71, 26.49. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{19}H_{17}O_4NNa]^+$: 346.1050, found: 346.1055.

3-((4-fluorophenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114h**) was prepared



according to the general procedure B, by using 1-methylisatin (**139**, 288 mg, 1.79 mmol) and 1-ethynyl-4-fluorobenzene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.32) as eluents, the desired product was obtained in 84% yield (422 mg, 1.50 mmol) as a white solid. **mp**: 159 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.45 – 7.34 (m, 3H), 7.16 (t, *J* = 7.6 Hz, 1H), 6.96 (t, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.80 (s, 1H), 3.24 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.07, 163.01 (d, *J* = 250.6 Hz), 143.17, 134.21 (d, *J* = 8.6 Hz), 130.66, 129.00, 124.83, 123.93, 117.86 (d, *J* = 3.5 Hz), 115.68 (d, *J* = 22.2 Hz), 109.02, 85.46 (d, *J* = 1.5 Hz), 85.39, 69.64, 26.79. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{17}H_{13}O_2NF]^+$: 282.0925, found: 282.0924.

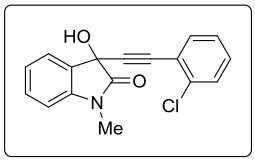
3-((2,4-difluorophenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114i**) was prepared



according to the general procedure B, by using 1-methylisatin (**139**, 329 mg, 2.04 mmol) and 1-ethynyl-2,4-difluorobenzene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.33) as eluents, the desired product was obtained in 90% yield (547 mg, 1.83 mmol) as a white solid. **mp**: 159 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.42 – 7.31 (m, 2H), 7.16 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.78 (t, *J* = 8.7 Hz, 2H), 4.18 (s, 1H), 3.23 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.86, 165.06 (dd, *J* = 21.5, 11.7 Hz), 161.69 (d, *J* = 31.0 Hz), 143.16, 134.97 (dd, *J* = 9.8, 2.5 Hz), 130.75, 128.72, 124.92,

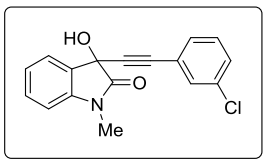
124.01, 111.66 (dd, *J* = 22.0, 3.8 Hz), 109.05, 106.78 (d, *J* = 15.7 Hz), 104.35 (t, *J* = 25.5 Hz), 90.49, 78.93, 69.66, 26.81. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{17}H_{11}O_2NF_2Na]^+$: 322.0650, found: 322.0655.

3-((2-chlorophenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114j**) was prepared



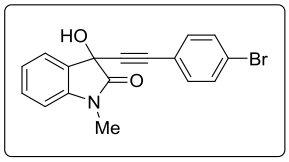
according to the general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 1-chloro-2-ethynylbenzene. After silica gel column chromatography with EtOAc/DCM = 1/10 (R_f = 0.5) as eluents, the desired product was obtained in 93% yield (513 mg, 1.72 mmol) as a red solid. **mp**: 165 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.43 – 7.33 (m, 2H), 7.31 – 7.22 (m, 1H), 7.22 – 7.13 (m, 2H), 6.87 (d, *J* = 7.6 Hz, 1H), 3.47 (s, 1H), 3.25 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.87, 143.19, 136.65, 133.86, 130.65, 130.10, 129.32, 128.90, 126.44, 125.00, 123.92, 121.80, 108.98, 90.75, 83.13, 69.73, 26.79. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{17}H_{12}O_2NClNa]^+$: 320.0449, found: 320.0449.

3-((3-chlorophenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114k**) was prepared



according to the general procedure B, by using 1-methylisatin (**139**, 337 mg, 2.09 mmol) and 3-chloro-1-ethynylbenzene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.38) as eluents, the desired product was obtained in 79% yield (489 mg, 1.64 mmol) as a pale yellow solid. **mp**: 148 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.44 – 7.41 (m, 1H), 7.39 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.17 (td, *J* = 7.6, 0.8 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 3.86 (s, 1H), 3.24 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.88, 143.23, 134.25, 132.06, 130.80, 130.29, 129.61, 129.44, 128.77, 124.89, 123.99, 123.48, 109.08, 86.88, 84.95, 69.62, 26.82. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{17}H_{13}O_2NCl]^+$: 298.0629, found: 298.0634.

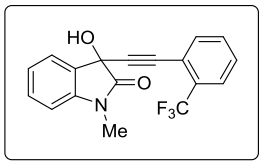
3-((4-bromophenyl)ethynyl)-3-hydroxy-1-methylindolin-2-one (**114l**) was prepared



according to the general procedure B, by using 1-methylisatin (**139**, 300 mg, 1.86 mmol) and 1-bromo-4-ethynylbenzene. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.31) as eluents, the desired product was obtained in 85% yield (543 mg, 1.59 mmol) as a pale yellow solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (300 MHz,

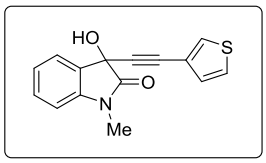
$CDCl_3$) δ 7.63 (d, *J* = 7.4 Hz, 1H), 7.48 – 7.35 (m, 3H), 7.32 – 7.24 (m, 2H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 4.42 (s, 1H), 3.24 (s, 3H).

3-hydroxy-1-methyl-3-((2-(trifluoromethyl)phenyl)ethynyl)indolin-2-one (**114m**) was



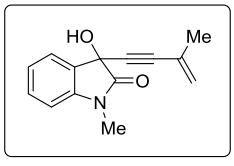
prepared according to the general procedure B, by using 1-methylisatin (**139**, 271 mg, 1.68 mmol) and 1-ethynyl-2-(trifluoromethyl)benzene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.32) as eluents, the desired product was obtained in 78% yield (432 mg, 1.30 mmol) as a pale yellow solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 – 7.54 (m, 3H), 7.49 – 7.34 (m, 3H), 7.17 (td, *J* = 7.6, 0.8 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.71 (s, 1H), 3.24 (s, 3H).

3-hydroxy-1-methyl-3-(thiophen-3-ylethynyl)indolin-2-one (**114n**) was prepared



according to the general procedure B, by using 1-methylisatin (**139**, 292 mg, 1.81 mmol) and 3-ethynylthiophene. After silica gel column chromatography with EtOAc/petroleum ether = 1/10 (R_f = 0.38) as eluents, the desired product was obtained in 87% yield (426 mg, 1.58 mmol) as a brown solid. **mp**: 201 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 2.9 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.22 (dd, *J* = 5.0, 2.9 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.09 (d, *J* = 5.0 Hz, 1H), 6.86 (d, *J* = 7.6 Hz, 1H), 3.58 (s, 1H), 3.24 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.95, 143.24, 130.68, 130.51, 130.10, 128.92, 125.48, 124.87, 123.89, 120.82, 109.00, 85.28, 81.77, 69.71, 26.80. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{15}H_{12}O_2NS]^+$: 270.0583, found: 270.0591.

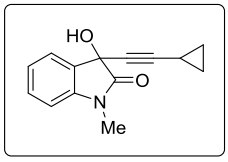
3-hydroxy-1-methyl-3-(3-methylbut-3-en-1-yn-1-yl)indolin-2-one (**114o**) was prepared



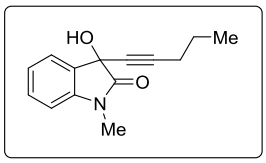
according to the general procedure B, by using 1-methylisatin (**139**, 522 mg, 3.24 mmol) and 2-methyl-1-buten-3-yne. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.32) as eluents, the desired product was obtained in 88% yield (645 mg, 2.84 mmol) as a yellow solid. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 5.31 (s, 1H), 5.22 (s, 1H), 4.67 (s, 1H), 3.18 (s, 3H), 1.81 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.23, 142.88, 130.33, 129.21, 125.66, 124.64, 123.80,

123.74, 108.84, 87.28, 84.55, 69.40, 26.61, 23.00. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{14}H_{14}O_2N]^+$: 228.1019, found: 228.1027.

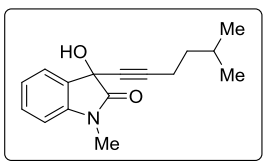
3-(cyclopropylethynyl)-3-hydroxy-1-methylindolin-2-one (**114p**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 522 mg, 3.24 mmol) and cyclopropylacetylene. After silica gel column chromatography with EtOAc/DCM = 1/15 (R_f = 0.33) as eluents, the desired product was obtained in 99% yield (729 mg, 3.21 mmol) as a yellow solid. **mp**: 180 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.6 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 3.73 (s, 1H), 3.19 (s, 3H), 1.33 – 1.15 (m, 1H), 0.86 – 0.59 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.32, 143.03, 130.33, 129.40, 124.55, 123.73, 108.82, 91.00, 72.08, 69.25, 26.66, 8.57, 8.53, -0.31. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{14}H_{14}O_2N]^+$: 228.1019, found: 228.1022.



3-hydroxy-1-methyl-3-(pent-1-yn-1-yl)indolin-2-one (**114q**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 1.000 g, 6.21 mmol) and 1-pentyne. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.26) as eluents, the desired product was obtained in 72% yield (1.021 g, 4.45 mmol) as a brown solid. **mp**: 122 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.35 (td, *J* = 7.6, 1.3 Hz, 1H), 7.13 (td, *J* = 7.6, 0.8 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 3.21 (s, 3H), 2.18 (t, *J* = 7.1 Hz, 2H), 1.51 (qt, *J* = 7.4, 7.1 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.42, 143.12, 130.41, 129.42, 124.58, 123.78, 108.87, 88.03, 77.36, 69.30, 26.69, 21.80, 20.93, 13.57. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{14}H_{16}O_2N]^+$: 230.1176, found: 230.1184.

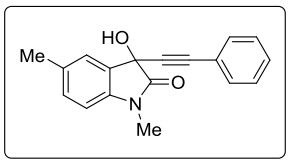


3-hydroxy-1-methyl-3-(5-methylhex-1-yn-1-yl)indolin-2-one (**114r**) was prepared according to the general procedure B, by using 1-methylisatin (**139**, 200 mg, 1.24 mmol) and 5-methyl-1-hexyne. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.44) as eluents, the desired product was obtained in 51% yield (162 mg, 0.63 mmol) as a brown solid. **mp**: 100 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.32 (td, *J* = 7.6, 1.3 Hz, 1H), 7.11 (td, *J* = 7.6, 0.8 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 4.12 (s, 1H), 3.18 (s, 3H), 2.18 (t, *J* = 7.4 Hz, 2H), 1.66 - 1.50 (m, 1H), 1.36 (td, *J* = 7.4, 7.4 Hz, 2H), 0.82 (dd, *J* = 6.6, 0.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.58, 142.96, 130.24, 129.59, 124.51,

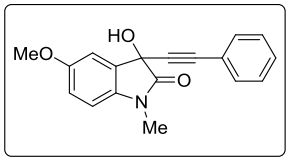


123.71, 108.78, 88.07, 77.36, 69.25, 37.16, 27.32, 26.61, 22.16, 16.95. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{16}H_{19}O_2NNa]^+$: 280.1308, found: 280.1314.

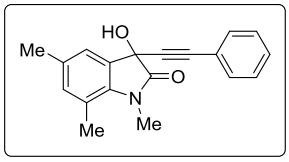
3-hydroxy-1,5-dimethyl-3-(phenylethynyl)indolin-2-one (**114s**) was prepared according to the general procedure B, by using **112a** (88 mg, 0.50 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.29) as eluents, the desired product was obtained in 88% yield (122 mg, 0.44 mmol) as a brown solid. **mp**: 189 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 – 7.40 (m, 3H), 7.37 – 7.22 (m, 3H), 7.17 (dd, *J* = 7.9, 0.8 Hz, 1H), 6.74 (d, *J* = 7.9 Hz, 1H), 3.73 (s, 1H), 3.22 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.96, 140.84, 133.63, 132.21, 130.88, 129.09, 128.92, 128.34, 125.59, 121.82, 108.75, 86.41, 85.80, 69.79, 26.81, 21.20. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{16}O_2N]^+$: 278.1176, found: 278.1177.



3-hydroxy-5-methoxy-1-methyl-3-(phenylethynyl)indolin-2-one (**114t**) was prepared according to the general procedure B, by using **112b** (585 mg, 3.06 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.25) as eluents, the desired product was obtained in 82% yield (734 mg, 2.50 mmol) as a brown solid. **mp**: 157 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.1 Hz, 2H), 7.37 – 7.18 (m, 4H), 6.89 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 1H), 4.41 (s, 1H), 3.82 (s, 3H), 3.19 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.96, 156.92, 136.44, 132.18, 130.21, 129.03, 128.28, 121.78, 115.49, 111.56, 109.52, 86.46, 85.76, 70.00, 56.04, 26.82. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{16}O_3N]^+$: 294.1125, found: 294.1126.

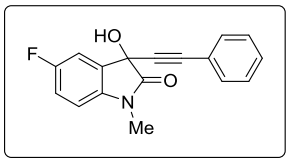


3-hydroxy-1,5,7-trimethyl-3-(phenylethynyl)indolin-2-one (**114u**) was prepared according to the general procedure B, by using **112c** (400 mg, 2.11 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.32) as eluents, the desired product was obtained in 64% yield (393 mg, 1.35 mmol) as a brown solid. **mp**: 172 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.0 Hz, 2H), 7.35 – 7.20 (m, 4H), 6.90 (s, 1H), 3.59 (s, 1H), 3.48 (s, 3H), 2.51 (s, 3H), 2.31 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.64, 138.38, 134.78, 133.49, 132.19, 129.61, 129.03, 128.31, 123.51, 121.90,



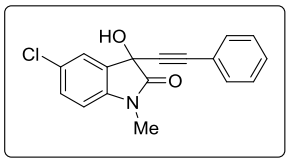
120.36, 86.29, 86.09, 69.30, 30.18, 20.86, 18.89.**HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{19}H_{18}O_2N]^+$: 292.1332, found: 292.1336.

5-fluoro-3-hydroxy-1-methyl-3-(phenylethynyl)indolin-2-one (**114v**) was prepared



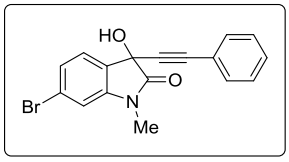
according to the general procedure B, by using **112d** (400 mg, 2.23 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 2/3 (R_f = 0.34) as eluents, the desired product was obtained in 55% yield (345 mg, 1.23mmol) as a brown solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.4 Hz, 2H), 7.39 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.37 – 7.26 (m, 3H), 7.09 (td, *J* = 8.7, 2.0 Hz, 1H), 6.79 (dd, *J* = 8.4, 3.7 Hz, 1H), 4.43 (s, 1H), 3.24 (s, 3H).

5-chloro-3-hydroxy-1-methyl-3-(phenylethynyl)indolin-2-one (**114w**) was prepared



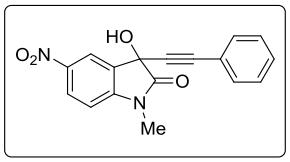
according to the general procedure B, by using **112e** (400 mg, 2.04 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.53) as eluents, the desired product was obtained in 94% yield (574 mg, 1.93 mmol) as a brown solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.59 (d, *J* = 2.0 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.36 – 7.29 (m, 2H), 7.29 – 7.22 (m, 2H), 6.76 (dd, *J* = 8.3, 2.1 Hz, 1H), 4.15 (s, 1H), 3.21 (d, *J* = 1.9 Hz, 3H).

6-bromo-3-hydroxy-1-methyl-3-(phenylethynyl)indolin-2-one (**114x**) was prepared



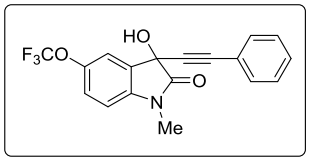
according to the general procedure B, by using **112f** (400 mg, 1.67 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.46) as eluents, the desired product was obtained in % yield (492 mg, 1.44 mmol) as a pale yellow solid. **mp**: 177 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.9 Hz, 2H), 7.44 – 7.38 (m, 4H), 7.34 – 7.23 (m, 9H), 7.00 (d, *J* = 1.6 Hz, 2H), 3.89 (s, 2H), 3.21 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.03, 144.39, 132.16, 129.22, 128.35, 128.05, 126.71, 126.13, 124.28, 121.51, 112.56, 86.78, 85.04, 69.29, 26.88. HRMS (ESI): Calcd for $(M + Na)^+$ $[C_{17}H_{12}O_2NBrNa]^+$: 363.9944, found: 363.9951.

3-hydroxy-1-methyl-5-nitro-3-(phenylethynyl)indolin-2-one (**114y**) was prepared



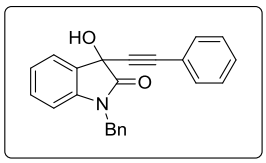
according to the general procedure B, by using **112g** (400 mg, 1.94 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.22) as eluents, the desired product was obtained in 58% yield (346 mg, 1.12 mmol) as a brown solid. **mp**: 176 °C **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 2.3 Hz, 1H), 8.33 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.47 – 7.38 (m, 2H), 7.36 – 7.21 (m, 3H), 6.94 (d, *J* = 8.7 Hz, 1H), 4.50 (s, 1H), 3.29 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.24, 148.57, 144.41, 132.25, 129.89, 129.59, 128.46, 127.46, 121.02, 120.96, 108.79, 87.77, 84.00, 68.98, 27.23. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{17}H_{13}O_4N_2]^+$: 309.0870, found: 309.0868.

3-hydroxy-1-methyl-3-(phenylethynyl)-5-(trifluoromethoxy)indolin-2-one (**114z**) was



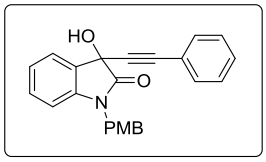
prepared according to the general procedure B, by using **112h** (500 mg, 2.04 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.33) as eluents, the desired product was obtained in 68% yield (485 mg, 1.40 mmol) as a yellow solid. **mp**: 130 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.43 (d, *J* = 7.0 Hz, 2H), 7.33 - 7.24 (m, 4H), 6.84 (d, *J* = 8.5 Hz, 1H), 3.90 (s, 1H), 3.24 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.93, 145.65, 141.80, 132.24, 130.39, 129.38, 128.42, 123.66, 121.39, 120.66 (d, *J* = 257.0 Hz), 118.91, 109.59, 87.18, 84.79, 69.54, 26.96. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{13}O_3NF_3]^+$: 348.0842, found: 348.0848.

1-benzyl-3-hydroxy-3-(phenylethynyl)indolin-2-one (**114aa**) was prepared according to



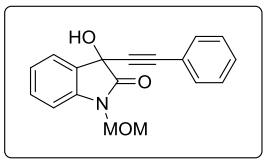
the general procedure B, by using 1-benzyl-1H-indole-2,3-dione (500 mg, 2.11 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.29) as eluents, the desired product was obtained in 71% yield (511 mg, 1.51 mmol) as a white solid. The analytical data were identical to the literature data.[98] **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.0 Hz, 2H), 7.37 – 7.20 (m, 11H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.73 (d, *J* = 7.4 Hz, 1H), 4.94 (s, 2H), 3.58 (s, 1H).

3-hydroxy-1-(4-methoxybenzyl)-3-(phenylethynyl)indolin-2-one (**114ab**) was prepared



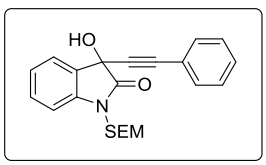
according to the general procedure B, by using **112i** (134 mg, 0.50 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.39) as eluents, the desired product was obtained in 38% yield (70 mg, 0.19 mmol) as a pale yellow solid. **mp**: 228 °C **^{1}H NMR** (500 MHz, DMSO) δ 7.52 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.47 – 7.34 (m, 4H), 7.34 – 7.24 (m, 4H), 7.10 (td, *J* = 7.6, 0.7 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 4.87 (d, *J* = 15.5 Hz, 1H), 4.82 (d, *J* = 15.5 Hz, 1H), 3.71 (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 173.14, 158.65, 141.50, 131.49, 130.27, 129.88, 129.17, 128.73, 128.65, 127.80, 124.22, 123.11, 121.17, 114.07, 109.81, 87.58, 84.41, 68.81, 55.04, 42.25. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{24}H_{20}O_3N]^+$: 370.1438, found: 370.1452.

3-hydroxy-1-(methoxymethyl)-3-(phenylethynyl)indolin-2-one (**114ac**) was prepared



according to the general procedure B, by using **112j** (200 mg, 1.05 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.37) as eluents, the desired product was obtained in 73% yield (224 mg, 0.76 mmol) as a brown solid. **mp**: 158 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.44 – 7.37 (m, 2H), 7.34 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.31 – 7.22 (m, 3H), 7.17 (td, *J* = 7.6, 0.8 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 5.15 (d, *J* = 11.0 Hz, 1H), 5.11 (d, *J* = 11.0 Hz, 1H), 4.22 (s, 1H), 3.33 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.85, 141.36, 132.16, 130.72, 129.18, 128.68, 128.35, 124.99, 124.37, 121.62, 110.51, 86.84, 85.44, 71.97, 69.93, 56.52. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{18}H_{15}O_3NNa]^+$: 316.0944, found: 316.0950.

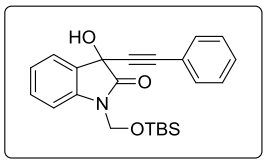
3-hydroxy-3-(phenylethynyl)-1-((2-(trimethylsilyl)ethoxy)methyl)indolin-2-one (**114ad**)



was prepared according to the general procedure B, by using **112k** (100 mg, 0.36 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.44) as eluents, the desired product was obtained in 52% yield (71 mg, 0.19 mmol) as a brown solid. **mp**: 97 °C **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.47 – 7.23 (m, 6H), 7.19 (td, *J* = 7.6, 0.9 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 1H), 5.21 (d, *J* = 11.1 Hz, 1H), 5.15 (d, *J* = 11.1 Hz, 1H), 3.69 – 3.56 (m, 2H), 1.69 (s, 1H), 0.99 – 0.87 (m, 2H), -0.05 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.44, 141.65, 132.19, 130.74, 129.22, 128.56, 128.38,

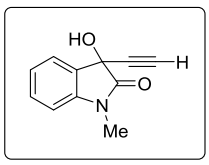
124.93, 124.25, 121.64, 110.64, 86.83, 85.46, 70.04, 69.95, 66.42, 17.85, -1.34. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{25}O_3NSiNa]^+$: 402.1496, found: 402.1508.

1-(((tert-butyldimethylsilyl)oxy)methyl)-3-hydroxy-3-(phenylethynyl)indolin-2-one



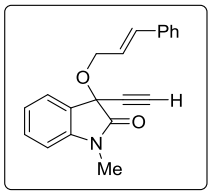
(**114ae**) was prepared according to the general procedure B, by using **141** (102 mg, 0.35 mmol) and phenylacetylene. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.38) as eluents, the desired product was obtained in 91% yield (125 mg, 0.32 mmol) as a yellow oil . **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.5 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.38 (t, *J* = 7.8 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 5.39 (d, *J* = 10.2 Hz, 1H), 5.28 (d, *J* = 10.2 Hz, 1H), 3.70 (s, 1H), 0.86 (s, 9H), 0.12 (d, *J* = 1.3 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.14, 141.64, 132.13, 130.64, 129.13, 128.55, 128.35, 124.82, 124.08, 121.69, 110.77, 86.77, 85.39, 70.02, 65.26, 25.76, 18.08, -5.09, -5.15. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{27}O_3NNaSi]^+$: 416.1652, found: 416.1650.

3-hydroxy-1-methyl-3-((trimethylsilyl)ethynyl)indolin-2-one (**116**) was prepared



according to the general procedure C, by using **115** (500 mg, 1.93 mmol) as the starting material. Due to the poor solubility and high purity, the crude product was obtained as a brown solid in 94% yield (339 mg, 1.81 mmol) and subjected to next step without further purification. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 7.41 (d, *J* = 7.7 Hz, 1H), 7.37 (td, *J* = 7.7, 1.1 Hz, 1H), 7.10 (td, *J* = 7.7, 1.1 Hz, 1H), 7.05 (s, 1H), 7.03 (d, *J* = 7.7 Hz, 1H), 3.62 (s, 1H), 3.12 (s, 3H). **^{13}C NMR** (126 MHz, DMSO) δ 172.76, 142.58, 130.10, 130.03, 123.94, 123.05, 109.18, 81.95, 76.32, 68.17, 26.24. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{11}H_{10}O_2N]^+$: 188.0706, found: 188.0705.

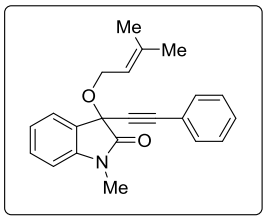
3-(cinnamyloxy)-3-ethynyl-1-methylindolin-2-one (**118**) was prepared according to the



general procedure D, by using **116** (225 mg, 1.20 mmol) and cinnamyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.35) as eluents, the desired product was obtained in 51% yield (186 mg, 0.61 mmol) as a pale yellow solid. **mp**: 99 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.2 Hz, 1H), 7.38 (td, *J* = 7.8, 1.2 Hz, 1H), 7.36 – 7.33 (m, 2H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.15 (td, *J* = 7.6, 0.8 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 15.9 Hz, 1H), 6.30 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.60 (ddd, *J* =

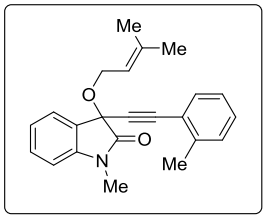
11.6, 6.3, 1.3 Hz, 1H), 4.50 (ddd, *J* = 11.6, 6.3, 1.3 Hz, 1H), 3.17 (s, 3H), 2.71 (s, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.42, 143.31, 136.56, 133.29, 130.86, 128.53, 127.80, 127.18, 126.60, 125.10, 125.02, 123.59, 108.90, 78.43, 76.50, 73.54, 66.77, 26.52. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{20}H_{17}O_2NNa]^+$: 326.1152, found: 326.1152.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130a**) was



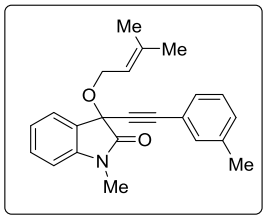
prepared according to the general procedure D, by using **114a** (79 mg, 0.30 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.32) as eluents, the desired product was obtained in 93% yield (92 mg, 0.28 mmol) as a brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 6.3 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.30 - 7.26 (m, 3H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.39 (t, *J* = 7.1 Hz, 1H), 4.42 (dd, *J* = 10.4, 7.1 Hz, 1H), 4.35 (dd, *J* = 10.4, 7.1 Hz, 1H), 3.23 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.08, 143.41, 138.39, 132.26, 130.54, 129.04, 128.32, 128.27, 125.13, 123.56, 121.98, 120.51, 108.76, 87.80, 83.98, 74.26, 62.51, 26.60, 25.97, 18.22. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1645

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(o-tolylethynyl)indolin-2-one (**130b**) was



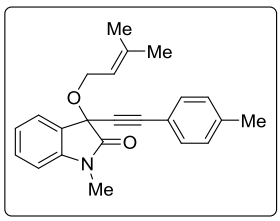
prepared according to the general procedure D, by using **114b** (50 mg, 0.18 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.48) as eluents, the desired product was obtained in 64% yield (40 mg, 0.12 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (ddd, *J* = 7.4, 1.2, 0.5 Hz, 1H), 7.43 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.35 (td, *J* = 7.8, 1.3 Hz, 1H), 7.21 (td, *J* = 7.5, 1.4 Hz, 1H), 7.20 – 7.14 (m, 1H), 7.16 – 7.06 (m, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.45 – 5.34 (m, 1H), 4.51 (dd, *J* = 10.6, 7.2 Hz, 1H), 4.42 (dd, *J* = 10.6, 7.1 Hz, 1H), 3.22 (s, 3H), 2.41 (s, 3H), 1.71 (s, 3H), 1.65 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.09, 143.35, 141.09, 138.29, 132.52, 130.47, 129.51, 129.07, 128.51, 125.57, 125.01, 123.50, 121.72, 120.56, 108.74, 87.75, 86.94, 74.28, 62.54, 26.55, 25.95, 20.82, 18.22. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1621.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(m-tolylethynyl)indolin-2-one (**130c**) was



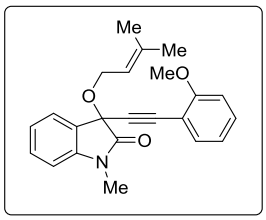
prepared according to the general procedure D, by using **114c** (131 mg, 0.47 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.29) as eluents, the desired product was obtained in 78% yield (127 mg, 0.37 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (dd, *J* = 7.6, 0.6 Hz, 1H), 7.48 (td, *J* = 7.6, 0.5 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.28 – 7.23 (m, 2H), 6.96 (d, *J* = 7.6 Hz, 1H), 5.52 (t, *J* = 7.4 Hz, 1H), 4.57 (dd, *J* = 10.5, 7.4 Hz, 1H), 4.50 (dd, *J* = 10.5, 7.4 Hz, 1H), 3.35 (s, 3H), 2.42 (s, 3H), 1.85 (s, 3H), 1.78 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.12, 143.39, 138.33, 138.02, 132.85, 130.50, 129.93, 129.30, 128.36, 128.22, 125.11, 123.54, 121.76, 120.56, 108.73, 88.06, 83.58, 74.25, 62.50, 26.57, 25.97, 21.25, 18.22. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1623.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(p-tolylethynyl)indolin-2-one (**130d**) was



prepared according to the general procedure D, by using **114d** (100 mg, 0.36 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 90% yield (112 mg, 0.32 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.5 Hz, 1H), 7.40 – 7.30 (m, 3H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 2H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.39 (t, *J* = 6.5 Hz, 1H), 4.42 (dd, *J* = 8.0, 6.5 Hz, 1H), 4.36 (dd, *J* = 8.0, 6.5 Hz, 1H), 3.21 (s, 3H), 2.31 (s, 3H), 1.71 (s, 3H), 1.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.05, 143.30, 139.16, 138.13, 132.06, 130.40, 129.00, 128.28, 124.99, 123.42, 120.52, 118.82, 108.66, 87.95, 83.25, 74.22, 62.37, 26.45, 25.86, 21.53, 18.12. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_2N]^+$: 346.1802, found: 346.1804.

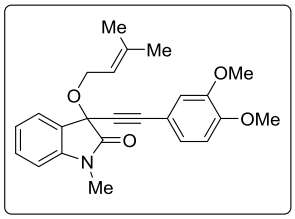
3-((2-methoxyphenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



(**130e**) was prepared according to the general procedure D, by using **114e** (100 mg, 0.34 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.16) as eluents, the desired product was obtained in 61% yield (75 mg, 0.21 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.33 (td, *J* = 7.6, 0.5 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.11 (t, *J* = 7.6

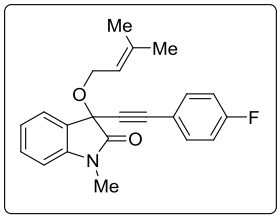
Hz, 1H), 6.90 – 6.78 (m, 3H), 5.41 (t, *J* = 7.3 Hz, 1H), 4.55 (dd, *J* = 10.4, 7.3 Hz, 1H), 4.48 (dd, *J* = 10.4, 7.3 Hz, 1H), 3.83 (s, 3H), 3.21 (s, 3H), 1.72 (s, 3H), 1.67 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.10, 160.79, 143.41, 138.14, 133.99, 130.47, 130.39, 128.61, 125.23, 123.43, 120.74, 120.36, 111.35, 110.86, 108.64, 87.64, 84.76, 74.33, 62.49, 55.87, 26.53, 25.97, 18.20. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{24}O_3NNa]^+$: 384.1570, found: 384.1574.

3-((3,4-dimethoxyphenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-on



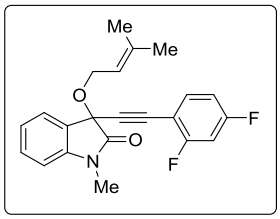
e (**130f**) was prepared according to the general procedure D, by using **114g** (223 mg, 0.69 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/1 (R_f = 0.59) as eluents, the desired product was obtained in 94% yield (256 mg, 0.64 mmol) as a brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.4, 0.6 Hz, 1H), 7.33 (td, *J* = 7.8, 1.1 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.05 (dd, *J* = 8.3, 1.8 Hz, 1H), 6.94 (d, *J* = 1.8 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.37 (t, *J* = 7.2 Hz, 1H), 4.42 – 4.32 (m, 1H), 4.32 – 4.23 (m, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 3.20 (s, 3H), 1.69 (s, 3H), 1.61 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.05, 149.92, 148.42, 143.23, 138.28, 130.41, 128.04, 125.66, 124.95, 123.44, 120.33, 114.66, 113.87, 110.75, 108.68, 87.72, 82.36, 74.22, 62.25, 55.92, 55.85, 26.47, 25.87, 18.10. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{24}H_{25}O_4NNa]^+$: 414.1676, found: 414.1688.

3-((4-fluorophenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



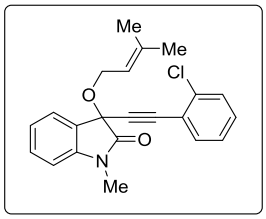
(**130g**) was prepared according to the general procedure D, by using **114h** (100 mg, 0.36 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.37) as eluents, the desired product was obtained in 74% yield (92 mg, 0.26 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.36 (td, *J* = 7.6, 0.8 Hz, 1H), 7.13 (td, *J* = 7.6, 0.8 Hz, 1H), 6.97 (t, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.41 – 5.35 (m, 1H), 4.37 (dd, *J* = 10.5, 7.3 Hz, 1H), 4.31 (dd, *J* = 10.5, 7.1 Hz, 1H), 3.22 (s, 3H), 1.71 (s, 3H), 1.63 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.99, 162.97 (d, *J* = 250.5 Hz), 143.39, 138.45, 134.24 (d, *J* = 8.5 Hz), 130.60, 128.05, 125.07, 123.58, 120.40, 118.03 (d, *J* = 3.5 Hz), 115.66 (d, *J* = 22.1 Hz), 108.80, 86.61, 83.81, 74.23, 62.47, 26.59, 25.95, 18.19. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NFNa]^+$: 372.1370, found: 372.1376.

3-((2,4-difluorophenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



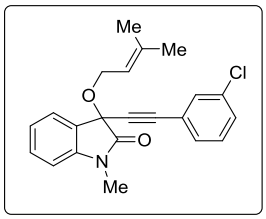
(**130h**) was prepared according to the general procedure D, by using **114i** (50 mg, 0.17 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 98% yield (60 mg, 0.16 mmol) as a pale yellow solid. **mp**: 57 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.47 – 7.39 (m, 1H), 7.35 (td, *J* = 7.8, 1.2 Hz, 1H), 7.12 (td, *J* = 7.6, 0.8 Hz, 1H), 6.86 – 6.75 (m, 3H), 5.43 – 5.33 (m, 1H), 4.45 (dd, *J* = 10.2, 7.6 Hz, 1H), 4.37 (dd, *J* = 10.4, 7.3 Hz, 1H), 3.21 (s, 3H), 1.71 (s, 3H), 1.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.69, 164.43 (dd, *J* = 53.1, 11.8 Hz), 162.41 (dd, *J* = 50.5, 11.8 Hz), 143.38, 138.47, 134.85 (dd, *J* = 9.8, 2.3 Hz), 130.65, 127.89, 125.15, 123.57, 120.36, 111.62 (dd, *J* = 22.0, 3.7 Hz), 108.78, 107.00 (dd, *J* = 15.8, 3.9 Hz), 104.35 (d, *J* = 25.2 Hz), 88.94, 80.26, 74.17, 62.56, 26.55, 25.91, 18.13. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{20}O_2NF_2]^+$: 368.1457, found: 368.1465.

3-((2-chlorophenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



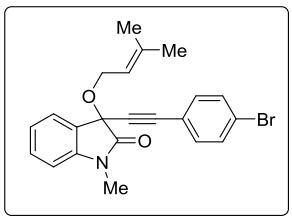
(**130i**) was prepared according to the general procedure D, by using **114j** (50 mg, 0.17 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.37) as eluents, the desired product was obtained in 81% yield (50 mg, 0.14 mmol) as a yellow solid. **mp**: 70 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.60 – 7.54 (m, 1H), 7.48 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.40 – 7.32 (m, 2H), 7.24 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.17 (td, *J* = 7.6, 1.2 Hz, 1H), 7.13 (td, *J* = 7.6, 1.0 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.46 – 5.34 (m, 1H), 4.56 (dd, *J* = 10.6, 7.2 Hz, 1H), 4.47 (dd, *J* = 10.5, 7.2 Hz, 1H), 3.22 (s, 3H), 1.71 (s, 3H), 1.66 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.77, 143.37, 138.43, 136.71, 133.82, 130.59, 130.06, 129.34, 128.14, 126.46, 125.31, 123.54, 121.99, 120.48, 108.76, 88.99, 84.67, 74.19, 62.71, 26.58, 25.96, 18.24. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NClNa]^+$: 388.1075, found: 388.1076.

3-((3-chlorophenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



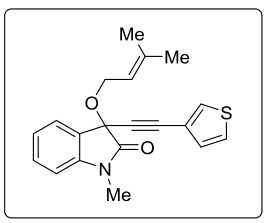
(**130j**) was prepared according to the general procedure D, by using **114k** (50 mg, 0.17 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.33) as eluents, the desired product was obtained in 37% yield (23 mg, 0.06 mmol) as a brown solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.44 (s, 1H), 7.41 – 7.26 (m, 3H), 7.21 (t, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 5.38 (t, *J* = 7.3 Hz, 1H), 4.39 (t, *J* = 10.2, 7.3 Hz, 1H), 4.32 (dd, *J* = 10.2, 7.3 Hz, 1H), 3.23 (s, 3H), 1.72 (s, 3H), 1.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.84, 143.41, 138.55, 134.21, 132.09, 130.70, 130.34, 129.60, 129.36, 127.91, 125.12, 123.66, 123.63, 120.37, 108.84, 86.17, 85.33, 74.18, 62.57, 26.62, 25.96, 18.22. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2N^{37}Cl]^+$: 368.1226, found: 368.1231.

3-((4-bromophenyl)ethynyl)-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)indolin-2-one



(**130k**) was prepared according to the general procedure D, by using **114l** (57 mg, 0.17 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.38) as eluents, the desired product was obtained in 75% yield (51 mg, 0.12 mmol) as a yellow solid. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 1H), 7.31 (d, *J* = 8.6 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 5.45 – 5.32 (m, 1H), 4.37 (dd, *J* = 10.7, 7.1 Hz, 1H), 4.30 (dd, *J* = 10.7, 7.1 Hz, 1H), 3.22 (s, 3H), 1.71 (s, 3H), 1.63 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.83, 143.38, 138.46, 133.62, 131.61, 130.63, 127.87, 125.07, 123.58, 123.42, 120.88, 120.35, 108.80, 86.50, 85.24, 74.22, 62.48, 26.58, 25.92, 18.17. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NBr]^+$: 410.0750, found: 410.0759.

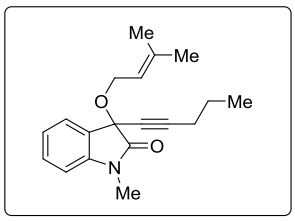
1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(thiophen-3-ylethynyl)indolin-2-one (**130l**)



was prepared according to the general procedure D, by using **114n** (50 mg, 0.19 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.43) as eluents, the desired product was obtained in 83% yield (52 mg, 0.15 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.52 – 7.47 (m, 1H), 7.36 (td, *J* = 7.6, 1.1 Hz, 1H), 7.22 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 – 7.07 (m, 2H),

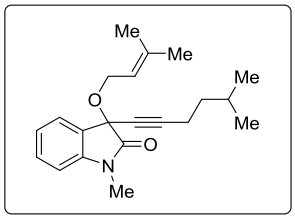
6.83 (d, *J* = 7.6 Hz, 1H), 5.38 (t, *J* = 7.3 Hz, 1H), 4.39 (dd, *J* = 10.4, 7.3 Hz, 1H), 4.32 (dd, *J* = 10.4, 7.3 Hz, 1H), 3.22 (s, 3H), 1.71 (s, 3H), 1.63 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.05, 143.40, 138.39, 130.55, 130.42, 130.20, 128.16, 125.37, 125.13, 123.56, 121.05, 120.49, 108.77, 83.66, 82.95, 74.31, 62.50, 26.60, 25.97, 18.22. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{20}H_{19}O_2NSNa]^+$: 360.1029, found: 360.1045.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(pent-1-yn-1-yl)indolin-2-one (**130m**) was



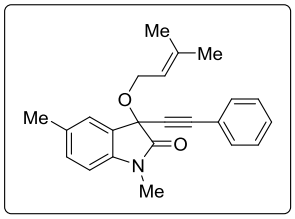
prepared according to the general procedure D, by using **114q** (48 mg, 0.21 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.80) as eluents, the desired product was obtained in 99% yield (61 mg, 0.21 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09 (td, *J* = 7.6, 0.8 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 5.34 (t, *J* = 7.2 Hz, 1H), 4.31 (dd, *J* = 10.5, 7.2 Hz, 1H), 4.25 (dd, *J* = 10.5, 7.2 Hz, 1H), 3.18 (s, 3H), 2.22 (td, *J* = 7.2, 1.9 Hz, 2H), 1.69 (s, 3H), 1.61 (s, 3H),1.53 (qt, *J* = 7.2, 7.2 Hz, 2H), 0.95 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.43, 143.30, 138.01, 130.24, 128.69, 124.84, 123.39, 120.61, 108.59, 89.21, 75.19, 73.90, 62.16, 26.45, 25.92, 21.87, 21.05, 18.13, 13.60. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{19}H_{24}O_2N]^+$: 298.1802, found: 298.1807.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(5-methylhex-1-yn-1-yl)indolin-2-one (**130n**)



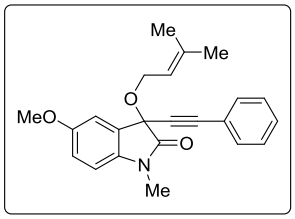
was prepared according to the general procedure D, by using **114r** (64 mg, 0.25 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.8) as eluents, the desired product was obtained in 86% yield (70 mg, 0.22 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.31 (td, *J* = 7.8, 1.2 Hz, 1H), 7.09 (td, *J* = 7.6, 0.8 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.40 – 5.30 (m, 1H), 4.31 (dd, *J* = 10.5, 7.3 Hz, 1H), 4.24 (dd, *J* = 10.5, 7.1 Hz, 1H), 3.18 (s, 3H), 2.24 (td, *J* = 7.4, 1.6 Hz, 2H), 1.69 (s, 3H), 1.67 – 1.61 (m, 1H), 1.61 (s, 3H), 1.41 (td, *J* = 7.4, 7.4 Hz, 2H), 0.86 (d, *J* = 2.3 Hz, 3H), 0.85 (d, *J* = 2.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.42, 143.29, 137.98, 130.23, 128.68, 124.84, 123.38, 120.62, 108.58, 89.47, 74.84, 73.90, 62.15, 37.33, 27.44, 26.45, 25.91, 22.22, 18.13, 17.12. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{27}O_2NNa]^+$: 348.1934, found: 348.1949.

1,5-dimethyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130o**) was



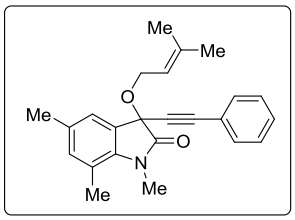
prepared according to the general procedure D, by using **114s** (44 mg, 0.16 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.59) as eluents, the desired product was obtained in 82% yield (45 mg, 0.13 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50 – 7.39 (m, 2H), 7.33 (s, 1H), 7.29 – 7.18 (m, 3H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 1H), 5.36 (t, *J* = 7.2 Hz, 1H), 4.41 (d, *J* = 10.5, 7.2 Hz, 1H), 4.31 (d, *J* = 10.5, 7.2 Hz, 1H), 3.16 (s, 3H), 2.32 (s, 3H), 1.68 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.99, 140.92, 138.34, 133.22, 132.20, 130.74, 128.97, 128.28, 128.13, 125.78, 121.96, 120.51, 108.49, 87.70, 84.06, 74.30, 62.41, 26.56, 25.96, 21.17, 18.19. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1637.

5-methoxy-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one



(**130p**) was prepared according to the general procedure D, by using **114t** (97 mg, 0.33 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.35) as eluents, the desired product was obtained in 74% yield (89 mg, 0.25 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 – 7.37 (m, 2H), 7.31 – 7.19 (m, 3H), 7.14 (d, *J* = 2.5 Hz, 1H), 6.85 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.71 (d, *J* = 8.5 Hz, 1H), 5.37 (t, *J* = 7.5 Hz, 1H), 4.37 (dd, *J* = 10.5, 7.5 Hz, 1H), 4.30 (dd, *J* = 10.5, 7.5 Hz, 1H), 3.77 (s, 3H), 3.16 (s, 3H), 1.68 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.65, 156.56, 138.31, 136.55, 132.07, 129.01, 128.92, 128.18, 121.72, 120.27, 115.10, 111.78, 109.16, 87.63, 83.85, 74.42, 62.32, 55.85, 26.49, 25.82, 18.08. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_3N]^+$: 362.1750, found: 362.1760.

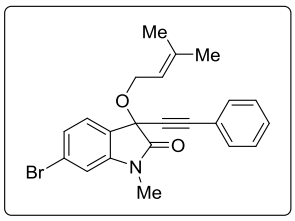
1,5,7-trimethyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130q**)



was prepared according to the general procedure D, by using **114u** (50 mg, 0.17 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.38) as eluents, the desired product was obtained in 73% yield (45 mg, 0.13 mmol) as an orange solid. **mp**: 69 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.42 (m, 2H), 7.34 – 7.24 (m, 3H), 7.21 (s, 1H), 6.88 (s, 1H), 5.45 – 5.34 (m, 1H), 4.42 (dd, *J* = 10.6, 7.3 Hz, 1H), 4.35 (dd, *J* = 10.6, 7.1 Hz, 1H), 3.47 (s, 3H), 2.51 (s, 3H), 2.30 (s, 3H),

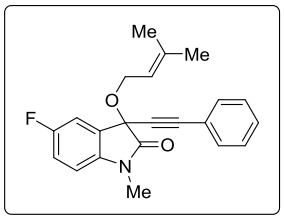
1.72 (s, 3H), 1.66 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.67, 138.50, 138.09, 134.66, 133.06, 132.20, 128.90, 128.26, 123.74, 122.10, 120.69, 120.01, 87.62, 84.42, 73.80, 62.35, 29.91, 25.95, 20.84, 18.91, 18.20. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{24}H_{25}O_2NNa]^+$: 382.1778, found: 382.1791.

6-bromo-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one



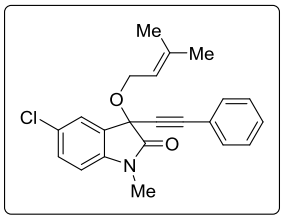
(**130r**) was prepared according to the general procedure D, by using **114x** (117 mg, 0.34 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.91) as eluents, the desired product was obtained in 46% yield (65 mg, 0.16 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45 – 7.38 (m, 2H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.18 (m, 4H), 6.94 (d, *J* = 1.6 Hz, 1H), 5.33 (t, *J* = 7.2 Hz, 1H), 4.39 (dd, *J* = 10.2, 7.2 Hz, 1H), 4.30 (dd, *J* = 10.2, 7.2 Hz, 1H), 3.16 (s, 3H), 1.67 (s, 3H), 1.60 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.81, 144.60, 138.74, 132.20, 129.19, 128.35, 127.13, 126.35, 124.26, 121.63, 120.19, 112.31, 88.18, 83.19, 73.74, 62.54, 29.80, 26.67, 25.96, 18.21. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NBrNa]^+$: 432.0570, found: 432.0571.

5-fluoro-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130s**)



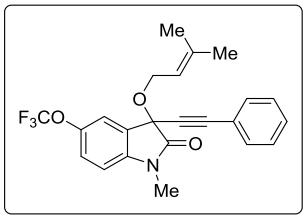
was prepared according to the general procedure D, by using **114v** (40 mg, 0.14 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.45) as eluents, the desired product was obtained in 99% yield (49 mg, 0.14 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56 – 7.36 (m, 2H), 7.33 – 7.17 (m, 4H), 7.02 (td, *J* = 8.6, 2.6 Hz, 1H), 6.72 (dd, *J* = 8.6, 4.0 Hz, 1H), 5.34 (t, *J* = 7.4 Hz, 1H), 4.42 (dd, *J* = 10.3, 7.4 Hz, 1H), 4.34 (dd, *J* = 10.3, 7.4 Hz, 1H), 3.17 (s, 3H), 1.68 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.78, 159.68 (d, *J* = 242.5 Hz), 139.24 (d, *J* = 2.0 Hz), 138.77, 132.22, 129.67 (d, *J* = 7.9 Hz), 129.21, 128.35, 121.60, 120.19, 116.78 (d, *J* = 23.6 Hz), 113.18 (d, *J* = 25.1), 88.29, 83.22, 77.36, 74.12, 62.59, 26.67, 25.94, 18.19. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NFNa]^+$: 372.1370, found: 372.1375.

5-chloro-1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130t**)



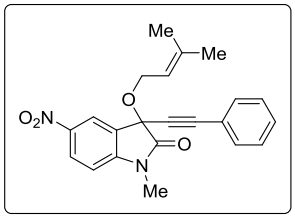
was prepared according to the general procedure D, by using **114w** (37 mg, 0.12 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.49) as eluents, the desired product was obtained in 99% yield (45 mg, 0.12 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 2.1 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.38 – 7.20 (m, 4H), 6.76 (d, *J* = 8.3 Hz, 1H), 5.39 (t, *J* = 7.2 Hz, 1H), 4.48 (dd, *J* = 10.3, 7.3 Hz, 1H), 4.41 (dd, *J* = 10.3, 7.3 Hz, 1H), 3.21 (s, 3H), 1.73 (s, 3H), 1.67 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.60, 141.82, 138.85, 132.23, 130.39, 129.80, 129.25, 128.91, 128.37, 125.55, 121.57, 120.17, 109.75, 88.47, 83.06, 73.92, 62.63, 26.66, 25.96, 18.22. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NClNa]^+$: 388.1075, found: 388.1087.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)-5-(trifluoromethoxy) indolin-2-one (**130u**)



was prepared according to the general procedure D, by using **114z** (102 mg, 0.29 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.57) as eluents, the desired product was obtained in 59% yield (72 mg, 0.17 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54 – 7.36 (m, 3H), 7.34 – 7.14 (m, 4H), 6.80 (d, *J* = 8.5 Hz, 1H), 5.36 (t, *J* = 7.3 Hz, 1H), 4.44 (dd, *J* = 10.1, 7.3 Hz, 1H), 4.36 (dd, *J* = 10.1, 7.3 Hz, 1H), 3.19 (s, 3H), 1.69 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.83, 145.33 (d, *J* = 1.9 Hz), 141.94, 138.96, 132.24, 129.66, 129.30, 128.39, 123.60, 121.51, 120.62 (q, *J* = 257.1 Hz), 120.09, 119.07, 88.55, 82.93, 73.95, 62.67, 29.80, 26.70, 25.94, 18.13. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{20}O_3NF_3Na]^+$: 438.1288, found: 438.11289.

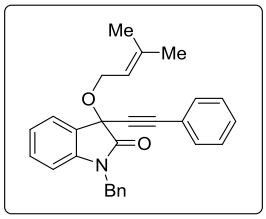
1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-5-nitro-3-(phenylethynyl)indolin-2-one (**130v**)



was prepared according to the general procedure D, by using **114y** (40 mg, 0.13 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.26) as eluents, the desired product was obtained in 90% yield (44 mg, 0.12 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.43 (d, *J* = 2.3 Hz, 1H), 8.33 (dd, *J* = 8.6, 2.3 Hz, 1H), 7.59 – 7.44 (m, 2H), 7.42 – 7.28 (m, 3H), 6.93 (d, *J* = 8.7 Hz, 1H), 5.39 (t, *J* = 7.2 Hz, 1H), 4.59 (dd, *J* = 10.4, 7.5 Hz, 1H), 4.51 (dd, *J* = 10.4, 7.2 Hz, 1H),

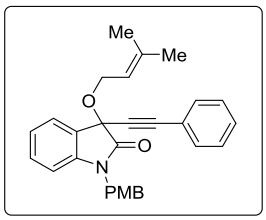
3.29 (s, 3H), 1.74 (s, 3H), 1.70 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.07, 148.73, 144.10, 139.36, 132.28, 129.55, 129.35, 128.48, 127.44, 121.08, 119.88, 108.52, 89.44, 81.97, 73.21, 62.93, 29.80, 26.98, 25.98, 18.26. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_4N_2]^+$: 377.1496, found: 377.1501.

1-benzyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130w**) was



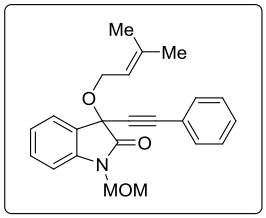
prepared according to the general procedure D, by using **114aa** (47 mg, 0.14 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.69) as eluents, the desired product was obtained in 90% yield (51 mg, 0.13 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.38 – 7.17 (m, 9H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 5.44 (t, *J* = 7.5 Hz, 1H), 4.96 (d, *J* = 15.8 Hz, 1H), 4.90 (d, *J* = 15.8 Hz, 1H), 4.46 (dd, *J* = 10.4, 7.5 Hz, 1H), 4.40 (dd, *J* = 10.4, 7.5 Hz, 1H), 1.74 (s, 3H), 1.68 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.18, 142.41, 138.58, 135.38, 132.23, 130.40, 129.05, 128.94, 128.32, 128.21, 127.82, 127.30, 125.14, 123.59, 121.91, 120.40, 109.79, 87.89, 83.94, 74.30, 62.44, 44.02, 25.96, 18.20. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{28}H_{25}O_2NNa]^+$: 430.1778, found: 430.1792.

1-(4-methoxybenzyl)-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one



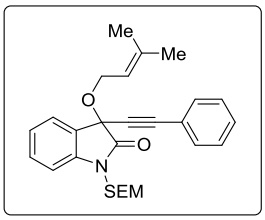
(**130x**) was prepared according to the general procedure D, by using **114ab** (50 mg, 0.14 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.60) as eluents, the desired product was obtained in 90% yield (53 mg, 0.12 mmol) as a transparent oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.41 – 7.19 (m, 6H), 7.10 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 5.44 (t, *J* = 7.6 Hz, 1H), 4.90 (d, *J* = 15.5 Hz, 1H), 4.84 (d, *J* = 15.5 Hz, 1H), 4.44 (dd, *J* = 10.4, 7.6 Hz, 1H), 4.39 (dd, *J* = 10.4, 7.6 Hz, 1H), 3.77 (s, 3H), 1.75 (s, 3H), 1.68 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.12, 159.23, 142.45, 138.52, 132.23, 130.37, 129.03, 128.74, 128.31, 128.22, 127.44, 125.11, 123.52, 121.93, 120.42, 114.31, 109.81, 87.81, 84.00, 74.31, 62.40, 55.33, 43.53, 25.95, 18.20. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{29}H_{27}O_3NNa]^+$: 460.1883, found: 460.1878.

1-(methoxymethyl)-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one

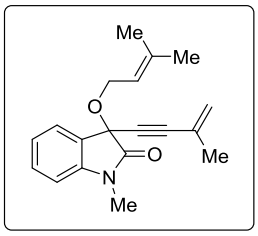


(**130y**) was prepared according to the general procedure D, by using **114ac** (191 mg, 0.65 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.75) as eluents, the desired product was obtained in 89% yield (210 mg, 0.58 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.36 (td, *J* = 7.8, 1.3 Hz, 1H), 7.32 – 7.27 (m, 4H), 7.17 (td, *J* = 7.6, 0.9 Hz, 1H), 7.04 (d, *J* = 7.8 Hz, 1H), 5.41 (t, *J* = 7.7 Hz, 1H), 5.14 (s, 2H), 4.43 (dd, *J* = 10.4, 7.7 Hz, 1H), 4.35 (dd, *J* = 10.5, 7.7 Hz, 1H), 3.37 (s, 3H), 1.72 (s, 3H), 1.65 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.53, 141.53, 138.55, 132.13, 130.59, 129.06, 128.28, 127.72, 125.17, 124.00, 121.74, 120.26, 110.20, 88.07, 83.71, 74.45, 71.73, 62.41, 56.41, 25.88, 18.11. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_3NNa]^+$: 384.1570, found: 384.1585.

3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)-1-((2-(trimethylsilyl)ethoxy)methyl) indolin-2-one (**130z**) was prepared according to the general procedure D, by using **114ad** (57 mg, 0.15 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.63) as eluents, the desired product was obtained in 76% yield (51 mg, 0.11 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.36 (td, *J* = 7.8, 1.2 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.16 (td, *J* = 7.6, 0.9 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 5.45 – 5.32 (m, 1H), 5.19 (d, *J* = 11.1 Hz, 1H), 5.16 (d, *J* = 11.1 Hz, 1H), 4.42 – 4.35 (m, 1H), 4.35 – 4.29 (m, 1H), 3.62 (d, *J* = 7.9 Hz, 1H), 3.60 (d, *J* = 7.8 Hz, 1H), 1.72 (s, 3H), 1.64 (s, 3H), 0.96 – 0.89 (m, 2H), -0.05 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.45, 141.78, 138.57, 132.23, 130.59, 129.07, 128.31, 127.81, 125.17, 123.97, 121.87, 120.33, 110.38, 88.02, 83.83, 74.54, 69.81, 66.30, 62.44, 25.95, 18.19, 17.85, -1.37. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{27}H_{33}O_3NSiNa]^+$: 470.2122, found: 470.2137.

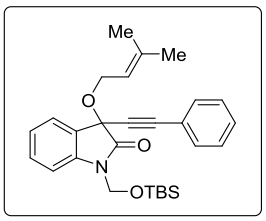


1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(3-methylbut-3-en-1-yn-1-yl)indolin-2-one

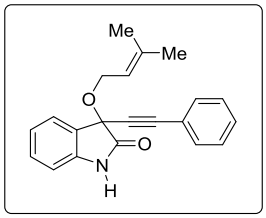


(**137**) was prepared according to the general procedure D, by using **114o** (63 mg, 0.28 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with DCM/petroleum ether = 1/2 (R_f = 0.25) as eluents, the desired product was obtained in 80% yield (145 mg, 0.31 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 (d, J = 7.6 Hz, 1H), 7.34 (td, J = 7.6, 1.0 Hz, 1H), 7.11 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 5.42 – 5.32 (m, 2H), 5.27 (s, 1H), 4.35 (dd, J = 10.4, 7.4 Hz, 1H), 4.27 (dd, J = 10.4, 7.3 Hz, 1H), 3.20 (s, 3H), 1.87 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.06, 143.36, 138.31, 130.47, 128.25, 125.87, 125.07, 123.89, 123.51, 120.50, 108.70, 88.94, 82.82, 74.11, 62.37, 26.55, 25.96, 23.23, 18.18. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{19}H_{21}O_2NNa]^+$: 318.1465, found: 318.1468.

1-(((tert-butyldimethylsilyl)oxy)methyl)-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenyl ethynyl) indolin-2-one (**137**) was prepared according to the general procedure D, by using **114ae** (154 mg, 0.39 mmol) and 3,3-dimethylallyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.32) as eluents, the desired product was obtained in 67% yield (55 mg, 0.19 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.36 (td, *J* = 7.6, 1.3 Hz, 1H), 7.33 – 7.26 (m, 3H), 7.15 (td, *J* = 7.6, 0.8 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 5.42 – 5.36 (m, 2H), 5.28 (d, *J* = 10.1 Hz, 1H), 4.50 – 4.30 (m, 2H), 1.72 (s, 3H), 1.65 (s, 3H), 0.86 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.24, 141.80, 138.56, 132.19, 130.52, 129.04, 128.33, 127.90, 125.09, 123.84, 121.94, 120.39, 110.50, 88.12, 83.74, 74.55, 65.01, 62.43, 26.01, 25.77, 18.22, 18.09, -5.04, -5.16. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{28}H_{36}O_3NSi]^+$: 462.2459, found: 462.2458.



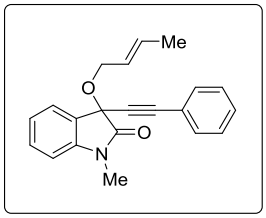
3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (130aa) was prepared by following procedure. TBAF (1.0 M in THF, 0.8 ml, 0.8 mmol) was added to a solution of **130z** (120 mg, 0.27 mmol) in DMF (5 ml). After 1 h stirring at 100 °C, the reaction mixture was cooled, and then diluted with water and ethyl acetate. The aqueous phase was extracted twice with ethyl acetate. The combined organic phases were washed with 1N $HCl_{(aq)}$ and $NaHCO_{3(sat)}$, dried over $MgSO_{4(s)}$ and concentrated to give the crude product. After silica gel



column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.21) as eluents, the desired product was obtained in 40% yield (34 mg, 0.11 mmol) as a brown oil.

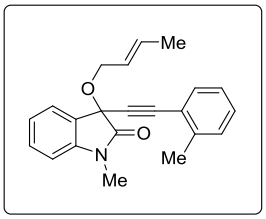
Alternatively, TBAF (1.0 M in THF, 0.1 ml, 0.1 mmol) was added to a solution of **143** (11 mg, 0.02 mmol) in THF (2 ml) at 0 °C. After stirring for 3 h at rt, the reaction mixture was added $NH_4Cl_{(sat)}$, extracted with EtOAc for three times The combined organic phases were washed with H_2O, dried over $MgSO_{4(s)}$ and concentrated under reduce pressure to give the crude product. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.21) as eluents, the desired product was obtained in 66% yield (5 mg, 0.05 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.94 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.35 – 7.24 (m, 4H), 7.11 (td, *J* = 7.6, 0.8 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 5.41 (t, *J* = 7.2 Hz, 1H), 4.37 (dd, *J* = 10.2, 7.2 Hz, 1H), 4.31 (dd, *J* = 10.5, 7.2 Hz, 1H), 1.72 (s, 3H), 1.64 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.49, 140.66, 138.59, 132.25, 130.59, 129.07, 128.57, 128.32, 125.46, 123.55, 121.90, 120.38, 110.88, 87.88, 83.81, 74.78, 62.48, 25.93, 18.19. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1322.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(phenylethynyl)indolin-2-one (**161a**) was prepared



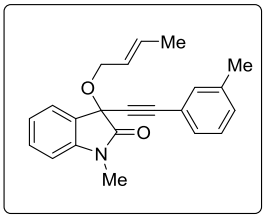
according to the general procedure D, by using **114a** (582 mg, 2.21 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.34) as eluents, the desired product was obtained in 91% yield (640 mg, 2.02 mmol, 82% (*E*)-isomer) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.4 Hz, 1H, *E* and *Z*), 7.46 (dd, *J* = 8.0, 1.6 Hz, 2H, *E* and *Z*), 7.35 (td, *J* = 7.6, 0.8 Hz, 1H, *E* and *Z*), 7.32 – 7.22 (m, 3H, *E* and *Z*), 7.13 (td, *J* = 7.6, 0.8 Hz, 1H, *E* and *Z*), 6.82 (d, *J* = 7.6 Hz, 1H, *E* and *Z*), 5.80 – 5.69 (m, 1H, *E* and *Z*), 5.68 – 5.58 (m, 1H, *E* and *Z*), 4.53 (dd, *J* = 10.7, 6.0 Hz, 1H, *Z*), 4.47 (dd, *J* = 10.7, 6.0 Hz, 1H, *Z*), 4.39 (dd, *J* = 10.7, 6.3 Hz, 4H, *E*), 4.31 (dd, *J* = 10.7, 6.3 Hz, 1H, *E*), 3.21 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 1.68 (dd, *J* = 6.3, 1.0 Hz, 3H, *E*), 1.64 (d, *J* = 5.3 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1319.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(o-tolylethynyl)indolin-2-one (**161b**) was prepared



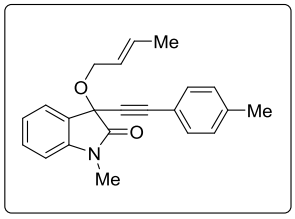
according to the general procedure D, by using **114b** (120 mg, 0.43 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.47) as eluents, the desired product was obtained in 86% yield (124 mg, 0.37 mmol, 79% (*E*)-isomer) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 – 7.52 (m, 1H, *E* and *Z*), 7.42 (dd, *J* = 7.8, 1.2 Hz, 1H, *E* and *Z*), 7.35 (td, *J* = 7.8, 1.2 Hz, 1H, *E* and *Z*), 7.24 – 7.07 (m, 4H, *E* and *Z*), 6.83 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.78 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.59 (m, 1H, *E* and *Z*), 4.62 – 4.59 (m, 1H, *Z*), 4.55 – 4.51 (m, 1H, *Z*), 4.50 – 4.42 (m, 1H, *E*), 4.42 – 4.33 (m, 1H, *E*), 3.22 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 2.42 (s, 3H, *Z*), 2.42 (s, 3H, *E*), 1.69 – 1.66 (m, 3H, *E*), 1.66 – 1.63 (m, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1465.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(m-tolylethynyl)indolin-2-one (**161c**) was prepared



according to the general procedure D, by using **114c** (150 mg, 0.54 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.30) as eluents, the desired product was obtained in 76% yield (137 mg, 0.41 mmol, 84% (*E*)-isomer) as a pale yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.6, 1.3 Hz, 1H, *E* and *Z*), 7.36 (td, *J* = 7.6, 1.3 Hz, 1H, *E* and *Z*), 7.29 (s, 1H, *E* and *Z*), 7.29 – 7.24 (m, 1H, *E* and *Z*), 7.17 (t, *J* = 7.6 Hz, 1H, *E* and *Z*), 7.16 – 7.10 (m, 2H, *E* and *Z*), 6.83 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.76 – 5.70 (m, 1H, *E* and *Z*), 5.68 – 5.59 (m, 1H, *E* and *Z*), 4.55 – 4.50 (m, 1H, *Z*), 4.49 – 4.44 (m, 1H, *Z*), 4.41 – 4.36 (m, 1H, *E*), 4.34 – 4.28 (m, 1H, *E*), 3.23 (s, 3H, *Z*), 3.22 (s, 3H, *E*), 2.29 (s, 3H, *E* and *Z*), 1.68 (dd, *J* = 6.4, 1.3 Hz, 3H, *E*), 1.66 – 1.61 (m, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1480.

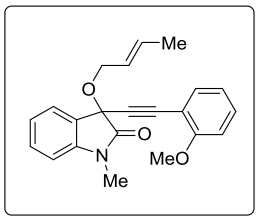
(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(p-tolylethynyl)indolin-2-one (**161c**) was prepared



according to the general procedure D, by using **114d** (180 mg, 0.65 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.30) as eluents, the desired product was obtained in 57% yield (122 mg, 0.37 mmol, 77% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 1H, *E* and *Z*), 7.35 (d, *J* = 8.0 Hz, 3H, *E* and *Z*), 7.12 (t, *J* = 7.6 Hz, 1H, *E* and *Z*), 7.08 (d, *J* = 8.0 Hz, 2H,

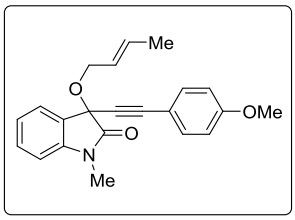
E and *Z*), 6.82 (d, *J* = 7.6 Hz, 1H, *E* and *Z*), 5.77 – 5.68 (m, 1H, *E* and *Z*), 5.68 – 5.58 (m, 1H, *E* and *Z*), 4.52 (dd, *J* = 10.6, 5.8 Hz, 1H, *Z*), 4.47 (dd, *J* = 10.6, 5.8 Hz, 1H, *Z*), 4.38 (dd, *J* = 10.3, 6.6 Hz, 1H, *E*), 4.31 (dd, *J* = 10.3, 6.6 Hz, 1H, *E*), 3.21 (s, 3H, *Z*), 3.20 (s, 3H, *E*), 2.32 (s, 3H, *E* and *Z*), 1.67 (d, *J* = 6.2 Hz, 3H, *E*), 1.64 (d, *J* = 5.7 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1479.

(*E*)-3-(but-2-en-1-yloxy)-3-((2-methoxyphenyl)ethynyl)-1-methylindolin-2-one (**161d**)



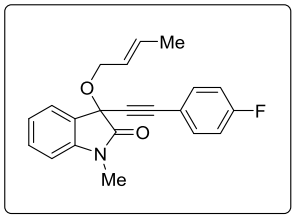
was prepared according to the general procedure D, by using **114e** (120 mg, 0.41 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.37) as eluents, the desired product was obtained in 94% yield (134 mg, 0.39 mmol, 81% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.4 Hz, 1H, *E* and *Z*), 7.40 (dd, *J* = 7.6, 1.3 Hz, 1H, *E* and *Z*), 7.34 (td, *J* = 7.8, 1.3 Hz, 1H, *E* and *Z*), 7.30 – 7.25 (m, 1H, *E* and *Z*), 7.11 (td, *J* = 7.6, 1.3 Hz, 1H, *E* and *Z*), 6.90 – 6.78 (m, 3H, *E* and *Z*), 5.78 – 5.71 (m, 1H, *E* and *Z*), 5.71 – 5.62 (m, 1H, *E* and *Z*), 4.68 – 4.62 (m, 1H, *Z*), 4.62 – 4.56 (m, 1H, *Z*), 4.52 – 4.47 (m, 1H, *E*), 4.46 – 4.40 (m, 1H, *E*), 3.82 (s, 3H, *E* and *Z*), 3.20 (s, 3H, *Z*), 3.20 (s, 3H, *E*), 1.71 – 1.65 (m, 3H, *E* and *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1414.

(*E*)-3-(but-2-en-1-yloxy)-3-((4-methoxyphenyl)ethynyl)-1-methylindolin-2-one (**161e**)



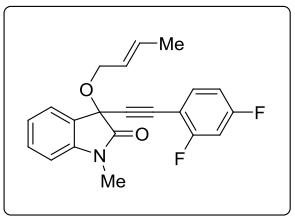
was prepared according to the general procedure D, by using **114f** (150 mg, 0.51 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.20) as eluents, the desired product was obtained in 94% yield (134 mg, 0.39 mmol, 82% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.55 (d, *J* = 6.6 Hz, 1H, *E* and *Z*), 7.36 (td, *J* = 7.8, 1.3 Hz, 1H, *E* and *Z*), 7.18 (t, *J* = 8.0 Hz, 1H, *E* and *Z*), 7.13 (td, *J* = 7.5, 1.0 Hz, 1H, *E* and *Z*), 7.05 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 7.00 – 6.96 (m, 1H, *E* and *Z*), 6.90 – 6.81 (m, 2H, *E* and *Z*), 5.77 – 5.68 (m, 1H, *E* and *Z*), 5.68 – 5. 59 (m, 1H, *E* and *Z*), 4.50 (dd, J = 11.2, 6.5 Hz, 1H, *Z*), 4.44 (dd, *J* = 11.2, 6.5 Hz, 1H, *Z*), 4.36 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 4.28 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.76 (s, 3H, *E* and *Z*), 3.23 (s, 3H, *Z*), 3.22 (s, 3H, *E*), 1.67 (dd, *J* = 6.4, 1.3 Hz, 3H, *E*), 1.63 (d, *J* = 6.3 Hz, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1427.

(*E*)-3-(but-2-en-1-yloxy)-3-((4-fluorophenyl)ethynyl)-1-methylindolin-2-one (**161f**) was



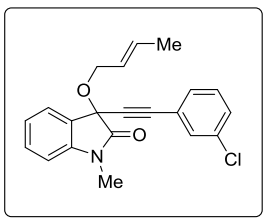
prepared according to the general procedure D, by using **114h** (234 mg, 0.70 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.32) as eluents, the desired product was obtained in 98% yield (234 mg, 0.70 mmol, 78% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 7.51 – 7.39 (m, 2H, *E* and *Z*), 7.37 (td, *J* = 7.5, 0.8 Hz, 1H, *E* and *Z*), 7.14 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 6.98 (t, *J* = 8.7 Hz, 2H, *E* and *Z*), 6.84 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 5.78 – 5.68 (m, 1H, *E* and *Z*), 5.67 – 5.57 (m, 1H, *E* and *Z*), 4.47 (dd, *J* = 11.0, 6.5 Hz, 1H, *Z*), 4.42 (dd, *J* = 10.9, 6.6 Hz, 1H, *Z*), 4.34 (dd, *J* = 10.5, 6.5 Hz, 1H, *E*), 4.26 (dd, *J* = 10.5, 6.4 Hz, 1H, *E*), 3.23 (s, 3H, *Z*), 3.23 (s, 3H, *E*), 1.67 (d, *J* = 6.3 Hz, 3H, *E*), 1.63 (d, *J* = 6.1 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C21H18O2NFNa]^+$: 358.1214, found: 358.1229.

(*E*)-3-(but-2-en-1-yloxy)-3-((2,4-difluorophenyl)ethynyl)-1-methylindolin-2-one (**161g**)



was prepared according to the general procedure D, by using **114i** (215 mg, 0.72 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.32) as eluents, the desired product was obtained in 23% yield (58 mg, 0.16 mmol, 78% (*E*)-isomer) as a light yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.3 Hz, 1H, *E* and *Z*), 7.45 – 7.40 (m, 1H, *E* and *Z*), 7.36 (t, *J* = 7.8 Hz, 1H, *E* and *Z*), 7.13 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 6.86 – 6.75 (m, 3H, *E* and *Z*), 5.76 – 5.67 (m, 1H, *E* and *Z*), 5.67 – 5.59 (m, 1H, *E* and *Z*), 4.54 (dd, *J* = 11.0, 6.4 Hz, 1H, *Z*), 4.47 (dd, *J* = 11.1, 6.4 Hz, 1H, *Z*), 4.40 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 4.32 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 3.22 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 1.67 (d, *J* = 6.3 Hz, 3H, *E*), 1.63 (d, *J* = 6.4 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{18}O_2NF_2]^+$: 354.1300, found: 354.1306.

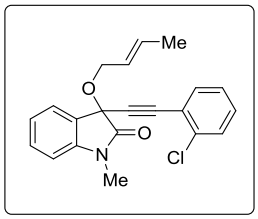
(*E*)-3-(but-2-en-1-yloxy)-3-((3-chlorophenyl)ethynyl)-1-methylindolin-2-one (**161h**) was



prepared according to the general procedure D, by using **114k** (200 mg, 0.67 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.30) as eluents, the desired product was obtained in 94% yield (223 mg, 0.63 mmol, 80% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 6.6 Hz, 1H, *E* and *Z*), 7.45 (s, 1H, *E* and *Z*), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H, *E* and *Z*), 7.34 (d, *J* = 7.7

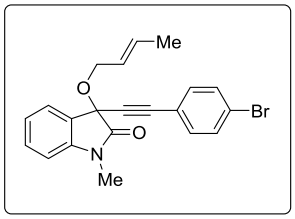
Hz, 1H, *E* and *Z*), 7.30 (d, *J* = 8.1 Hz, 1H, *E* and *Z*), 7.22 (t, *J* = 7.9 Hz, 1H, *E* and *Z*), 7.14 (td, *J* = 7.6, 0.8 Hz, 1H, *E* and *Z*), 6.84 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.77 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.59 (m, 1H, *E* and *Z*), 4.49 (dd, *J* = 11.1, 6.7 Hz, 1H, *Z*), 4.42 (dd, *J* = 11.1, 6.6 Hz, 1H, *Z*), 4.35 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 4.27 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 3.24 (s, 3H, *Z*), 3.23 (s, 3H, *E*), 1.68 (dd, *J* = 6.3, 1.0 Hz, 3H, *E*), 1.63 (d, *J* = 6.2 Hz, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NClNa]^+$: 374.0918, found: 370.0934.

(*E*)-3-(but-2-en-1-yloxy)-3-((2-chlorophenyl)ethynyl)-1-methylindolin-2-one (**161i**) was



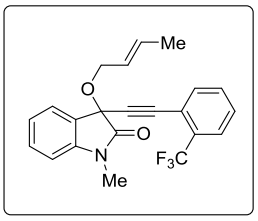
prepared according to the general procedure D, by using **114j** (129 mg, 0.67 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.36) as eluents, the desired product was obtained in 86% yield (131 mg, 0.37 mmol, 78% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.5, 1.3 Hz, 1H, *E* and *Z*), 7.47 (dd, *J* = 7.6, 1.7 Hz, 1H, *E* and *Z*), 7.40 – 7.31 (m, 2H, *E* and *Z*), 7.28 – 7.21 (m, 1H, *E* and *Z*), 7.17 (td, *J* = 7.5, 1.3 Hz, 1H, *E* and *Z*), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H, *E* and *Z*), 6.82 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.79 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.59 (m, 1H, *E* and *Z*), 4.68 – 4.61 (m, 1H, *Z*), 4.60 – 4.54 (m, 1H, *Z*), 4.53 – 4.47 (m, 1H, *E*), 4.44 – 4.38 (m, 1H, *E*), 3.21 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 1.67 (dd, *J* = 6.3, 1.3 Hz, 3H, *E*), 1.66 – 1.62 (m, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NClNa]^+$: 374.0918, found: 375.0919.

(*E*)-3-((4-bromophenyl)ethynyl)-3-(but-2-en-1-yloxy)-1-methylindolin-2-one (**161j**) was



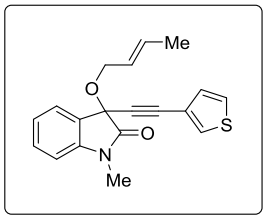
prepared according to the general procedure D, by using **114l** (130 mg, 0.38 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.35) as eluents, the desired product was obtained in 66% yield (100 mg, 0.25 mmol, 76% (*E*)-isomer) as a brown oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 7.42 (d, *J* = 8.6 Hz, 2H, *E* and *Z*), 7.37 (td, *J* = 7.8, 1.2 Hz, 1H, *E* and *Z*), 7.31 (d, *J* = 8.6 Hz, 2H, *E* and *Z*), 7.14 (td, *J* = 7.8, 0.9 Hz, 1H, *E* and *Z*), 6.84 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.76 – 5.67 (m, 1H, *E* and *Z*), 5.67 – 5.57 (m, 1H, *E* and *Z*), 4.45 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.40 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.32 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 4.24 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 3.23 (s, 3H, *Z*), 3.22 (s, 3H, *E*), 1.67 (dd, *J* = 6.4, 1.2 Hz, 3H, *E*), 1.62 (dd, *J* = 6.7, 1.3 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NBrNa]^+$: 418.0413, found: 418.0421.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-((2-(trifluoromethyl)phenyl)ethynyl)indolin-2-one



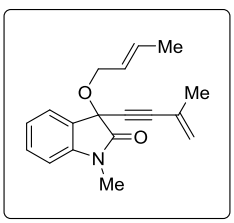
(**161k**) was prepared according to the general procedure D, by using **114m** (200 mg, 0.60 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.33) as eluents, the desired product was obtained in 81% yield (188 mg, 0.49 mmol, 72% (*E*)-isomer) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 – 7.59 (m, 2H, *E* and *Z*), 7.54 (d, *J* = 7.3 Hz, 1H, *E* and *Z*), 7.47 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 7.42 (t, *J* = 7.7 Hz, 1H, *E* and *Z*), 7.39 – 7.33 (m, 1H, *E* and *Z*), 7.13 (t, *J* = 8.0 Hz, 1H, *E* and *Z*), 6.83 (d, *J* = 7.7 Hz, 1H, *E* and *Z*), 5.80 – 5.69 (m, 1H, *E* and *Z*), 5.69 – 5.58 (m, 1H, *E* and *Z*), 4.64 (dd, *J* = 11.1, 6.5 Hz, 1H, *Z*), 4.56 – 4.46 (m, 1H, *E* and *Z*), 4.37 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 3.23 (s, 3H, *Z*), 3.22 (s, 3H, *E*), 1.68 (dd, *J* = 6.3, 1.4 Hz, 3H, *E*), 1.65 (d, *J* = 6.0 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{19}O_2NF_3]^+$: 386.1362, found: 386.1373.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(thiophen-3-ylethynyl)indolin-2-one (**161l**) was



prepared according to the general procedure D, by using **114n** (200 mg, 0.74 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.31) as eluents, the desired product was obtained in 88% yield (211 mg, 0.65 mmol, 83% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.6 Hz, 1H, *E* and *Z*), 7.50 (dd, *J* = 3.0, 0.9 Hz, 1H, *E* nd *Z*), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H, *E* nd *Z*), 7.22 (dd, *J* = 5.0, 3.0 Hz, 1H, *E* nd *Z*), 7.16 – 7.09 (m, 2H, *E* nd *Z*), 6.83 (d, *J* = 7.6 Hz, 1H, *E* nd *Z*), 5.77 – 5.67 (m, 1H, *E* nd *Z*), 5.67 – 5.57 (m, 1H, *E* nd *Z*), 4.48 (dd, *J* = 11.2, 6.3 Hz, 1H, *Z*), 4.42 (dd, *J* = 11.2, 6.3 Hz, 1H, *Z*), 4.35 (dd, *J* = 10.7, 6.3 Hz, 1H, *E*), 4.27 (dd, *J* = 10.7, 6.3 Hz, 1H, *E*), 3.22 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 1.67 (dd, *J* = 6.3, 1.1 Hz, 3H, *E*), 1.63 (dd, *J* = 5.9, 0.5 Hz, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{19}H_{17}O_2NSNa]^+$: 346.0872, found: 346.0882.

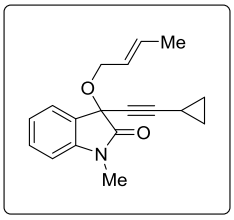
(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(3-methylbut-3-en-1-yn-1-yl)indolin-2-one (**161m**)



was prepared according to the general procedure D, by using **114o** (184 mg, 0.81 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.50) as eluents, the desired product was obtained in 86% yield (197 mg, 0.70 mmol, 79% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.3 Hz, 1H, *E* and *Z*), 7.33 (t, *J* = 7.3 Hz, 1H, *E* and *Z*), 7.10 (t, *J* = 7.3 Hz, 1H, *E* and *Z*), 6.80 (d, *J* =

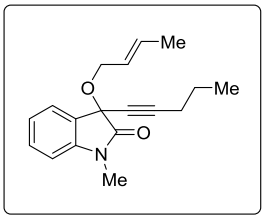
7.3 Hz, 1H, *E* and *Z*), 5.79 – 5.64 (m, 1H, *E* and *Z*), 5.64 – 5.54 (m, 1H, *E* and *Z*), 5.35 (s, 1H, *E* and *Z*), 5.26 (s, 1H, *E* and *Z*), 4.43 (dd, *J* = 11.1, 6.5 Hz, 1H, *Z*), 4.37 (dd, *J* = 11.1, 6.4 Hz, 1H, *Z*), 4.29 (dd, *J* = 10.5, 6.4 Hz, 1H, *E*), 4.21 (dd, *J* = 10.5, 6.6 Hz, 1H, *E*), 3.19 (s, 3H, *Z*), 3.18 (s, 3H, *E*), 1.86 (s, 3H, *E* and *Z*), 1.65 (d, *J* = 6.2 Hz, 3H, *E*), 1.61 (d, *J* = 6.2 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{18}H_{19}O_2NNa]^+$: 304.1308, found: 304.1309.

(*E*)-3-(but-2-en-1-yloxy)-3-(cyclopropylethynyl)-1-methylindolin-2-one (**161n**) was



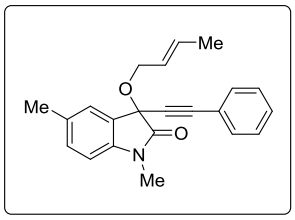
prepared according to the general procedure D, by using **114p** (185 mg, 0.81 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.31) as eluents, the desired product was obtained in 87% yield (200 mg, 0.71 mmol, 78% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 7.32 (t, *J* = 7.6 Hz, 1H, *E* and *Z*), 7.09 (t, *J* = 7.6 Hz, 1H, *E* and *Z*), 6.79 (d, *J* = 7.6 Hz, 1H, *E* and *Z*), 5.76 – 5.62 (m, 1H, *E* and *Z*), 5.62 – 5.51 (m, 1H, *E* and *Z*), 4.36 (dd, *J* = 10.9, 6.5 Hz, 1H, *Z*), 4.31 (dd, *J* = 10.9, 6.9 Hz, 1H, *Z*), 4.22 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 4.15 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 3.19 (s, 3H, *Z*), 3.18 (s, 3H, *E*), 1.66 (d, *J* = 6.2 Hz, 3H, *E*), 1.60 (d, *J* = 6.4 Hz, 3H, *Z*), 1.41 – 1.19 (m, 1H, *E* and *Z*), 0.80 – 0.66 (m, 4H, *E* and *Z*). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{19}O_2N]^+$: 282.1416, found: 282.1418.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(pent-1-yn-1-yl)indolin-2-one (**161o**) was prepared



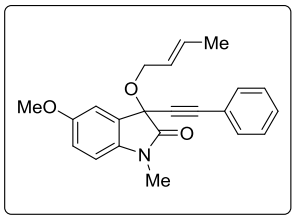
according to the general procedure D, by using **114q** (200 mg, 0.87 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/8 (R_f = 0.33) as eluents, the desired product was obtained in 97% yield (239 mg, 0.84 mmol, 81% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 7.32 (td, *J* = 7.5, 1.3 Hz, 1H, *E* and *Z*), 7.09 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 6.79 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 5.73 – 5.62 (m, 1H, *E* and *Z*), 5.63 – 5.52 (m, 1H, *E* and *Z*), 4.41 (dd, *J* = 11.1, 6.6 Hz, 1H, *Z*), 4.35 (dd, *J* = 11.1, 6.6 Hz, 1H, *Z*), 4.27 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 4.20 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 3.18 (s, 3H, *Z*), 3.18 (s, 3H, *E*), 2.21 (td, *J* = 7.0, 1.5 Hz, 2H, *E* and *Z*), 1.65 (d, *J* = 6.3 Hz, 3H, *E*), 1.60 (d, *J* = 6.2 Hz, 1H, *Z*), 1.57 – 1.46 (m, 2H, *E* and *Z*), 0.95 (t, *J* = 7.3 Hz, 3H, *E* and *Z*). **HRMS** (ESI): Calcd for (M + Na)$^+$ $[C_{18}H_{21}O_2NNa]^+$: 306.1465, found: 346.1472.

(*E*)-3-(but-2-en-1-yloxy)-1,5-dimethyl-3-(phenylethynyl)indolin-2-one (**161p**) was



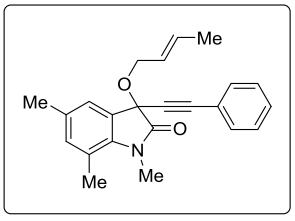
prepared according to the general procedure D, by using **114s** (200 mg, 0.72 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.35) as eluents, the desired product was obtained in 85% yield (204 mg, 0.62 mmol, 80% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.9, 1.7 Hz, 2H, *E* and *Z*), 7.36 (s, 1H, *E* and *Z*), 7.33 – 7.24 (m, 3H, *E* and *Z*), 7.15 (d, *J* = 7.9 Hz, 1H, *E* and *Z*), 6.72 (d, *J* = 7.9 Hz, 1H, *E* and *Z*), 5.79 – 5.68 (m, 1H, *E* and *Z*), 5.68 – 5.57 (m, 1H, *E* and *Z*), 4.53 (dd, *J* = 11.2, 6.0 Hz, 1H, *Z*), 4.48 (dd, *J* = 11.3, 5.9 Hz, 1H, *Z*), 4.39 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 4.32 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.21 (s, 3H, *Z*), 3.20 (s, 3H, *E*), 2.36 (s, 3H, *E* and *Z*), 1.68 (dd, *J* = 6.4, 1.4 Hz, 3H, *E*), 1.65 (d, *J* = 5.8 Hz, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1653.

(*E*)-3-(but-2-en-1-yloxy)-5-methoxy-1-methyl-3-(phenylethynyl)indolin-2-one (**161q**)



was prepared according to the general procedure D, by using **114t** (200 mg, 0.68 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.33) as eluents, the desired product was obtained in 92% yield (218 mg, 0.63 mmol, 83% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 6.6 Hz, 2H, *E* and *Z*), 7.38 – 7.23 (m, 3H, *E* and *Z*), 7.17 (d, *J* = 2.5 Hz, 1H, *E* and *Z*), 6.88 (dd, *J* = 8.5, 2.5 Hz, 1H, *E* and *Z*), 6.74 (d, *J* = 8.5 Hz, 1H, *E* and *Z*), 5.78 – 5.68 (m, 1H), 5.69 – 5.59 (m, 1H), 4.50 (dd, *J* = 11.3, 6.0 Hz, 1H, *Z*), 4.45 (dd, *J* = 11.3, 6.0 Hz, 1H, *Z*), 4.36 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 4.29 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.81 (s, 3H, *E* and *Z*), 3.20 (s, 3H, *Z*), 3.19 (s, 3H, *E*), 1.68 (dd, *J* = 6.3, 1.0 Hz, 3H, *E*), 1.64 (d, *J* = 5.4 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1427.

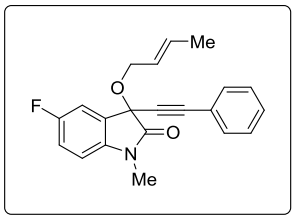
(*E*)-3-(but-2-en-1-yloxy)-1,5,7-trimethyl-3-(phenylethynyl)indolin-2-one (**161r**) was



prepared according to the general procedure D, by using **114u** (200 mg, 0.69 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.38) as eluents, the desired product was obtained in 95% yield (225 mg, 0.65 mmol, 80% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 6.5 Hz, 2H, *E* and *Z*), 7.35 – 7.30 (m, 3H, *E* and *Z*), 7.23 (s, 1H, *E* and *Z*), 6.91 (s, 1H, *E* and *Z*), 5.81 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.60 (m, 1H, *E* and *Z*), 4.53 (dd, *J* = 11.3, 6.1 Hz, 1H,

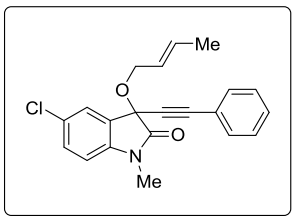
Z), 4.49 (dd, *J* = 11.3, 6.1 Hz, 1H, *Z*), 4.33 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.51 (s, 3H), 3.50 (s, 3H), 2.54 (s, 3H), 2.33 (s, 3H), 1.71 (d, *J* = 6.3 Hz, 3H), 1.68 (d, *J* = 6.1 Hz, 3H). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1632.

(*E*)-3-(but-2-en-1-yloxy)-5-fluoro-1-methyl-3-(phenylethynyl)indolin-2-one (**161s**) was



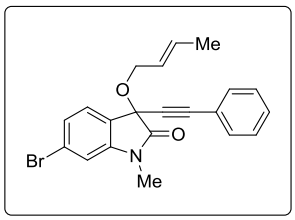
prepared according to the general procedure D, by using **114v** (200 mg, 0.71 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.34) as eluents, the desired product was obtained in 81% yield (194 mg, 0.58 mmol, 77% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 6.6 Hz, 2H, *E* and *Z*), 7.41 – 7.23 (m, 4H, *E* and *Z*), 7.06 (td, *J* = 8.7, 2.6 Hz, 1H, *E* and *Z*), 6.76 (dd, *J* = 8.7, 3.9 Hz, 1H, *E* and *Z*), 5.81 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.56 (m, 1H, *E* and *Z*), 4.55 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.49 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.41 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 4.34 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.21 (s, 3H, *Z*), 3.21 (s, 3H, *E*), 1.69 (dd, *J* = 6.4, 1.1 Hz, 3H, *E*), 1.66 (d, *J* = 6.7 Hz, 1H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NFNa]^+$: 358.1214, found: 358.1228.

(*E*)-3-(but-2-en-1-yloxy)-5-chloro-1-methyl-3-(phenylethynyl)indolin-2-one (**161t**) was



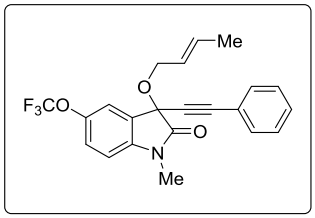
prepared according to the general procedure D, by using **114w** (200 mg, 0.67 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.34) as eluents, the desired product was obtained in 80% yield (190 mg, 0.54 mmol, 77% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 2.1 Hz, 1H, *E* and *Z*), 7.47 (d, *J* = 6.7 Hz, 2H, *E* and *Z*), 7.36 – 7.25 (m, 4H, *E* and *Z*), 6.76 (d, *J* = 8.3 Hz, 1H, *E* and *Z*), 5.80 – 5.67 (m, 1H, *E* and *Z*), 5.67 – 5.55 (m, 1H, *E* and *Z*), 4.57 (dd, *J* = 11.0, 6.8 Hz, 1H, *Z*), 4.51 (dd, *J* = 11.0, 6.8 Hz, 1H, *Z*), 4.43 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 4.35 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 3.21 (d, *J* = 3.6 Hz, 3H, *Z*), 3.20 (s, 3H, *E*), 1.69 (dd, *J* = 6.4, 0.9 Hz, 3H, *E*), 1.67 (d, *J* = 6.7 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NClNa]^+$: 374.0918, found: 374.0932.

(*E*)-6-bromo-3-(but-2-en-1-yloxy)-1-methyl-3-(phenylethynyl)indolin-2-one (**161u**) was



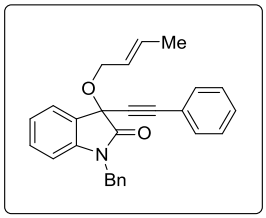
prepared according to the general procedure D, by using **114x** (200 mg, 0.58 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/8 (R_f = 0.37) as eluents, the desired product was obtained in 93% yield (220 mg, 0.56 mmol, 76% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 6.7 Hz, 2H, *E* and *Z*), 7.43 – 7.38 (m, 1H, *E* and *Z*), 7.36 – 7.25 (m, 4H, *E* and *Z*), 6.99 (d, *J* = 1.6 Hz, 1H, *E* and *Z*), 5.79 – 5.67 (m, 1H, *E* and *Z*), 5.66 – 5.56 (m, 1H, *E* and *Z*), 4.53 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.47 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.39 (dd, *J* = 10.7, 6.5 Hz, 1H, *E*), 4.31 (dd, *J* = 10.7, 6.5 Hz, 1H, *E*), 3.21 (s, 3H, *Z*), 3.20 (s, 3H, *E*), 1.68 (dd, *J* = 6.4, 1.2 Hz, 3H, *E*), 1.65 (d, *J* = 6.7 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NBrNa]^+$: 418.0413, found: 418.0430.

(*E*)-3-(but-2-en-1-yloxy)-1-methyl-3-(phenylethynyl)-5-(trifluoromethoxy)indolin-2-one



(**161v**) was prepared according to the general procedure D, by using **114z** (200 mg, 0.58 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.29) as eluents, the desired product was obtained in 80% yield (202 mg, 0.50 mmol, 80% (*E*)-isomer) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 6.7 Hz, 2H, *E* and *Z*), 7.44 (d, *J* = 1.5 Hz, 1H, *E* and *Z*), 7.37 – 7.28 (m, 3H, *E* and *Z*), 7.24 (d, *J* = 8.5 Hz, 1H, *E* and *Z*), 6.82 (d, *J* = 8.5 Hz, 1H, *E* and *Z*), 5.80 – 5.68 (m, 1H, *E* and *Z*), 5.67 – 5.59 (m, 1H, *E* and *Z*), 4.57 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.50 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.43 (dd, *J* = 10.7, 6.5 Hz, 1H, *E*), 4.36 (dd, *J* = 10.7, 6.5 Hz, 1H, *E*), 3.24 (s, 3H, *Z*), 3.23 (s, 3H, *E*), 1.69 (dd, *J* = 6.4, 1.1 Hz, 3H, *E*), 1.65 (d, *J* = 6.7 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{18}O_3NF_3Na]^+$: 424.1131, found: 424.1142.

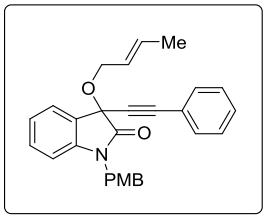
(*E*)-1-benzyl-3-(but-2-en-1-yloxy)-3-(phenylethynyl)indolin-2-one (**161w**) was prepared



according to the general procedure D, by using **114aa** (200 mg, 0.59 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/8 (R_f = 0.33) as eluents, the desired product was obtained in 90% yield (195 mg, 0.60 mmol, 76% (*E*)-isomer) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.1 Hz, 1H, *E* and *Z*), 7.49 (d, *J* = 6.5 Hz, 2H, *E* and *Z*), 7.46 – 7.17 (m, 9H, *E* and *Z*), 7.10 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 6.71 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 5.84 – 5.71 (m, 1H, *E* and *Z*), 5.71 – 5.62 (m, 1H,

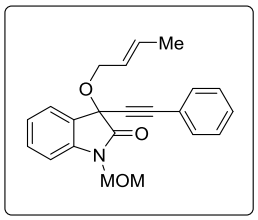
E and *Z*), 4.93 (s, 2H, *E* and *Z*), 4.56 (dd, *J* = 10.5, 5.0 Hz, 1H, *Z*), 4.51 (dd, *J* = 10.5, 5.0 Hz, 1H, *Z*), 4.43 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 4.37 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 1.70 (d, *J* = 6.2 Hz, 3H, *E*), 1.66 (d, *J* = 5.1 Hz, 3H, *Z*).**HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{27}H_{23}O_2NNa]^+$: 416.1621, found: 416.1637.

(*E*)-3-(but-2-en-1-yloxy)-1-(4-methoxybenzyl)-3-(phenylethynyl)indolin-2-one (**161x**)



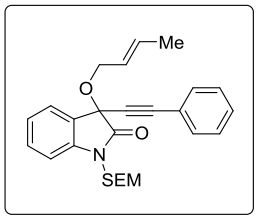
was prepared according to the general procedure D, by using **114ab** (96 mg, 0.26 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.38) as eluents, the desired product was obtained in 87% yield (96 mg, 0.23 mmol, 73% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 7.48 (d, *J* = 6.5 Hz, 2H, *E* and *Z*), 7.36 – 7.19 (m, 6H, *E* and *Z*), 7.09 (t, *J* = 7.5 Hz, 1H, *E* and *Z*), 6.85 (d, *J* = 8.6 Hz, 2H, *E* and *Z*), 6.73 (d, *J* = 7.5 Hz, 1H, *E* and *Z*), 5.80 – 5.70 (m, 1H, *E* and *Z*), 5.70 – 5.60 (m, 1H, *E* and *Z*), 4.87 (s, 2H, *E* and *Z*), 4.52 (dd, *J* = 10.4, 5.5 Hz, 1H, *Z*), 4.48 (dd, *J* = 10.3, 5.5 Hz, 1H, *Z*), 4.39 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 4.34 (dd, *J* = 10.7, 6.4 Hz, 1H, *E*), 3.77 (s, 3H, *E* and *Z*), 1.69 (d, *J* = 6.3 Hz, 3H, *E*), 1.65 (d, *J* = 5.4 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{28}H_{25}O_3NNa]^+$: 446.1727, found: 446.1737.

(*E*)-3-(but-2-en-1-yloxy)-1-(methoxymethyl)-3-(phenylethynyl)indolin-2-one (**161y**) was

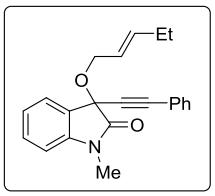


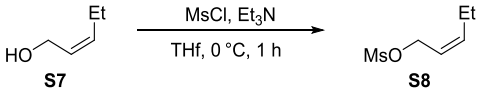
prepared according to the general procedure D, by using **114ac** (150 mg, 0.51 mmol) and crotyl bromide. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.35) as eluents, the desired product was obtained in 51% yield (90 mg, 0.26 mmol, 77% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.4, 1.3 Hz, 1H, *E* and *Z*), 7.46 (dd, *J* = 8.3, 1.5 Hz, 2H, *E* and *Z*), 7.37 (td, *J* = 7.7, 1.3 Hz, 1H, *E* and *Z*), 7.36 – 7.26 (m, 3H, *E* and *Z*), 7.17 (td, *J* = 7.6, 1.0 Hz, 1H, *E* and *Z*), 7.05 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.78 – 5.69 (m, 1H, *E* and *Z*), 5.68 – 5.59 (m, 1H, *E* and *Z*), 5.18 – 5.11 (m, 2H, *E* and *Z*), 4.51 (dd, *J* = 11.1, 6.7 Hz, 1H, *Z*), 4.46 (dd, *J* = 11.1, 6.6 Hz, 1H, *Z*), 4.36 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 4.31 (dd, *J* = 10.6, 6.5 Hz, 1H, *E*), 3.37 (s, 3H, *E*k), 1.68 (d, *J* = 6.4 Hz, 3H, *E*) 1.64 (d, *J* = 6.1 Hz, 3H, *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1424.

(*E*)-3-(but-2-en-1-yloxy)-3-(phenylethynyl)-1-((2-(trimethylsilyl)ethoxy)methyl) indolin-2-one (**161z**) was prepared according to the general procedure D, by using **114ad** (168 mg, 0.44 mmol) and crotyl bromide. After silica gel column chromatography with DCM/petroleum ether = 1/2 (R_f = 0.50) as eluents, the desired product was obtained in 47% yield (90 mg, 0.21 mmol, 82% (*E*)-isomer) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 6.7 Hz, 1H, *E* and *Z*), 7.45 (dd, *J* = 8.3, 1.4 Hz, 2H, *E* and *Z*), 7.36 (td, *J* = 7.8, 1.2 Hz, 1H, *E* and *Z*), 7.34 – 7.26 (m, 3H, *E* and *Z*), 7.16 (td, *J* = 7.5, 1.0 Hz, 1H, *E* and *Z*), 7.07 (d, *J* = 7.8 Hz, 1H, *E* and *Z*), 5.78 – 5.68 (m, 1H, *E* and *Z*), 5.68 – 5.59 (m, 1H, *E* and *Z*), 5.21 – 5.14 (m, 2H, *E* and *Z*), 4.48 (dd, *J* = 11.0, 6.7 Hz, 1H, *Z*), 4.44 (dd, *J* = 11.0, 6.5 Hz, 1H, *Z*), 4.34 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 4.29 (dd, *J* = 10.6, 6.4 Hz, 1H, *E*), 3.64 – 3.57 (m, 2H, *E* and *Z*), 1.68 (d, *J* = 6.4 Hz, 3H, *E*), 1.64 (d, *J* = 6.5 Hz, 3H, *Z*), 0.93 (dd, *J* = 9.2, 7.3 Hz, 2H, *E* and *Z*), -0.05 (s, 9H, *E* and *Z*). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{26}H_{31}O_3NNaSi]^+$: 456.1965, found: 456.1977.



(*E*)-1-methyl-3-(pent-2-en-1-yloxy)-3-(phenylethynyl)indolin-2-one (**172b**) was prepared according to the general procedure, by using **114a** (500 mg, 1.90 mmol) and (*E*)-1-bromo-2-pentene [1576-96-1]. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.58) as eluents, the desired product was obtained in 47% yield (295 mg, 0.89 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.34 (td, *J* = 7.8, 1.3 Hz, 1H), 7.30 – 7.23 (m, 3H), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 5.75 (dt, *J* = 15.4, 6.2 Hz, 1H), 5.61 (dt, *J* = 15.3, 6.4 Hz, 1H), 4.40 (ddd, *J* = 10.7, 6.4, 1.1 Hz, 1H), 4.32 (ddd, *J* = 10.7, 6.4, 1.1 Hz, 1H), 3.18 (s, 3H), 2.09 – 1.95 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.75, 143.18, 136.97, 132.04, 130.45, 128.93, 128.17, 127.91, 124.93, 124.67, 123.37, 121.69, 108.67, 87.69, 83.78, 74.13, 66.75, 26.38, 25.24, 13.07. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1459.

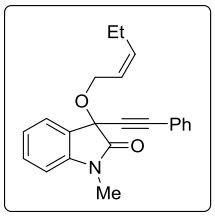




(*Z*)-pent-2-en-1-yl methanesulfonate (**S8**)[100]

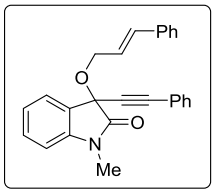
To a solution of *cis*-2-penten-1-ol (**S7**, 0.29 ml, 2.90 mmol) and trimethylamine (0.81 ml, 5.80 mmol) in dry THF (3 ml) was added methanesulfonyl chloride (0.27 mL, 3.48 mmol) at 0 °C. The mixture was stirred for 1 h, and then poured into ether. The organic layer was washed with 1.0% $HCl_{(aq)}$, brine, and $NaHCO_{3(sat.)}$, dried over $MgSO_{4(s)}$ and evaporated to give mesylate (**S8**, 377 mg, 79%) as a light yellow oil. Due to the unstability, the product subjected to the further transformation without purification.

(*Z*)-1-methyl-3-(pent-2-en-1-yloxy)-3-(phenylethynyl)indolin-2-one (**172c**) was prepared



according to the general procedure D, by using **114a** (500 mg, 1.90 mmol) and mesylate **S8**. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 50% yield (313 mg, 0.94 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.4, 0.8 Hz, 1H), 7.48 – 7.41 (m, 2H), 7.33 (td, *J* = 7.8, 1.3 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.61 – 5.53 (m, 2H), 4.53 (dd, *J* = 11.0, 5.5 Hz, 1H), 4.48 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.17 (s, 3H), 2.12 – 2.00 (m, 2H), 0.94 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.63, 143.08, 135.76, 131.91, 130.40, 128.87, 128.11, 127.84, 124.78, 124.65, 123.29, 121.58, 108.62, 87.65, 83.72, 74.08, 61.33, 26.25, 20.83, 14.04. . **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1462.

3-(cinnamyloxy)-1-methyl-3-(phenylethynyl)indolin-2-one (**172d**) was prepared according



to the general procedure D, by using **114a** (200 mg, 0.76 mmol) and cinnamyl bromide [4392-24-9]. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.65) as eluents, the desired product was obtained in 88% yield (320 mg, 1.01 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.4 Hz, 1H), 7.51 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.43 – 7.27 (m, 8H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.61 (d, *J* = 15.9 Hz, 1H), 6.38 (dt, *J* = 15.9, 6.3 Hz, 1H), 4.69 (ddd, *J* = 11.7, 6.3, 0.9 Hz, 1H), 4.59 (ddd, *J* = 11.7, 6.3, 0.8 Hz, 1H), 3.19 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.77, 143.18, 136.52, 133.13, 132.09, 130.61, 129.04, 128.46, 128.23, 127.70, 127.65,

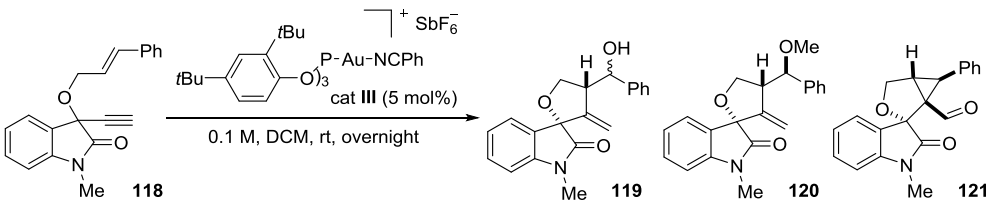
126.52, 125.28, 124.98, 123.47, 121.56, 108.82, 87.92, 83.59, 74.19, 66.68, 26.41. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{26}H_{21}O_2NNa]^+$: 402.1465, found: 402.1458.

3-(allyloxy)-1-methyl-3-(phenylethynyl)indolin-2-one (**172e**) was prepared according to the general procedure D, by using **114a** (200 mg, 0.76 mmol) and allyl bromide [106-95-6]. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.63) as eluents, the desired product was obtained in 84% yield (194 mg, 0.64 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.4 Hz, 1H), 7.50 – 7.43 (m, 2H), 7.36 (td, *J* = 7.8, 1.1 Hz, 1H), 7.33 – 7.24 (m, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.05 – 5.93 (m, 1H), 5.31 (dd, *J* = 17.2, 1.5 Hz, 1H), 5.17 (dd, *J* = 10.4, 1.5 Hz, 1H), 4.49 (dd, *J* = 11.8, 5.8 Hz, 1H), 4.42 (dd, *J* = 11.8, 5.8 Hz, 1H), 3.20 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.68, 143.16, 134.14, 132.07, 130.58, 129.03, 128.23, 127.77, 124.95, 123.46, 121.57, 117.59, 108.77, 87.86, 83.50, 74.15, 66.84, 26.42. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{20}H_{17}O_2NNa]^+$: 326.1152, found: 326.1146.

1-methyl-3-((2-methylallyl)oxy)-3-(phenylethynyl)indolin-2-one (**172f**) was prepared according to the general procedure D, by using **114a** (300 mg, 1.14 mmol) and methallyl bromide [1458-98-6]. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.65) as eluents, the desired product was obtained in 88% yield (320 mg, 1.01 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.3 Hz, 1H), 7.46 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.36 (td, *J* = 7.8, 1.0 Hz, 1H), 7.33 – 7.25 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 5.02 (s, 1H), 4.89 (s, 1H), 4.36 (s, 2H), 3.20 (s, 3H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.70, 143.18, 141.75, 132.08, 130.54, 129.02, 128.25, 128.00, 124.92, 123.46, 121.67, 112.59, 108.73, 87.81, 83.66, 74.24, 69.52, 26.42, 19.81. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1301.

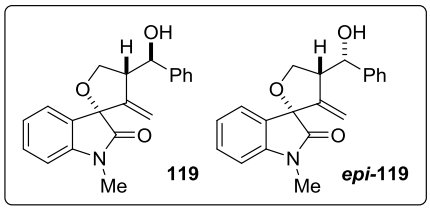
5.4 Synthesis of gold(I) catalyzed cycloisomerization products

5.4.1 Gold(I) catalyzed 5-exo-dig cycloisomerizations



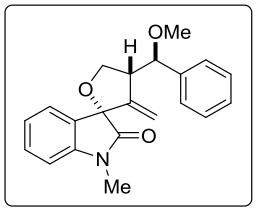
To the solution of 1,6-enyne (**118**, 10 mg, 0.03 mmol) in DCM was added cat **III** (1.9 mg, 1.65 μmol) and the corresponding additive under $Ar_{(g)}$ atmosphere. After stirring for overnight, the reaction mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the desired product.

4-(hydroxy(phenyl)methyl)-1'-methyl-3-methylene-4,5-dihydro-3H-spiro[furan-2,3'-ind



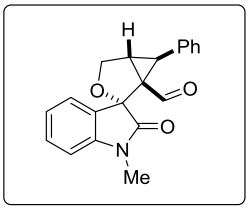
olin]-2'-one (**119**, ***epi*-119**) were prepared according to the general procedure without additive. After silica gel column chromatography with EtOAc/petroleum ether = 1/2 as eluents, the desired products (**119**, ***epi*-119**) were obtained in 57% yield (6 mg, 0.02 mmol, **119**:***epi*-119 =** 1:1) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29 – 7.26 (m, 1H), 7.12 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.05 – 6.99 (m, 3H), 6.99 – 6.94 (m, 3H), 6.75 (d, *J* = 7.8 Hz, 1H), 4.93 (d, *J* = 9.4 Hz, 1H), 4.89 (dd, *J* = 8.8, 6.5 Hz, 1H), 4.58 (dd, *J* = 8.8, 7.2 Hz, 1H), 4.28 (d, *J* = 2.2 Hz, 1H), 3.98 (d, *J* = 2.0 Hz, 1H), 3.50 – 3.42 (m, 1H), 3.14 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.38, 148.68, 144.64, 140.70, 130.05, 129.92, 128.62, 127.29, 126.98, 124.81, 123.11, 111.65, 108.02, 85.88, 83.79, 72.25, 51.53, 26.19. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{20}H_{20}O_3N]^+$: 322.1438, found: 322.1439. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.42 – 7.35 (m, 2H), 7.35 – 7.29 (m, 3H), 7.26 – 7.21 (m, 1H), 7.10 (dd, *J* = 7.5, 1.3 Hz, 1H), 6.99 (td, *J* = 7.6, 1.3 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 4.60 – 4.45 (m, 3H), 4.21 (d, *J* = 2.3 Hz, 1H), 3.89 (d, *J* = 2.3 Hz, 1H), 3.50 – 3.42 (m, 1H), 3.06 (s, 3H**). ^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.39, 148.78, 144.47, 139.29, 130.22, 129.85, 128.84, 128.41, 128.35, 124.67, 123.11, 111.36, 107.96, 85.85, 78.95, 72.90, 50.57, 26.15. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{20}H_{20}O_3N]^+$: 322.1438, found: 322.1439.

4-(methoxy(phenyl)methyl)-1'-methyl-3-methylene-4,5-dihydro-3H-spiro[furan-2,3'-ind



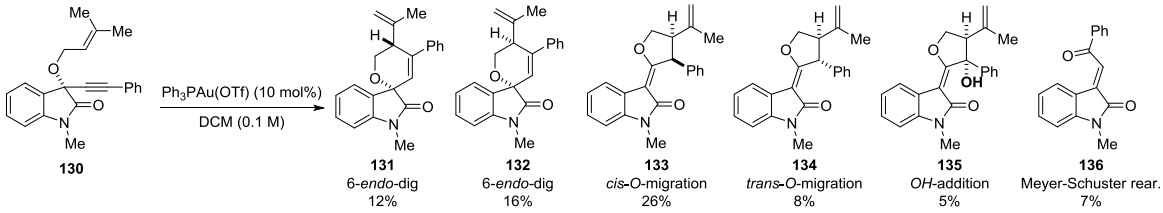
olin-2'-one (**120**) was prepared according to the general procedure with MeOH (27 μL, 0.66 mol) as the additive. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.43) as eluents, the desired product was obtained in 90% yield (10 mg, 0.03 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 191 °C (decomposed) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38 (d, *J* = 6.8 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 2H), 7.32 – 7.25 (m, 3H), 7.14 (dd, *J* = 7.4, 1.0 Hz, 1H), 7.02 (td, *J* = 7.6, 0.7 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.73 (dd, *J* = 9.0, 4.8 Hz, 1H), 4.66 (d, *J* = 10.2 Hz, 1H), 4.49 (dd, *J* = 9.0, 6.9 Hz, 1H), 4.30 (d, *J* = 1.7 Hz, 1H), 3.93 (d, *J* = 1.7 Hz, 1H), 3.34 – 3.24 (m, 1H), 3.24 (s, 3H), 3.17 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.53, 148.55, 144.65, 140.05, 130.33, 130.11, 128.60, 128.17, 128.02, 125.00, 123.43, 112.75, 108.25, 85.98, 84.35, 72.65, 56.72, 52.01, 26.36. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{22}O_3N]^+$: 326.1594, found: 326.1595.

1'-methyl-2'-oxo-6-phenyl-3-oxaspiro[bicyclo[3.1.0]hexane-2,3'-indoline]-1-carb



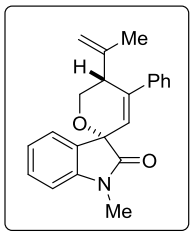
aldehyde (**121**) was prepared according to the general procedure with diphenyl sulfoxide (15 mg, 0.07 mmol) and 4 Å MS (10 mg) as the additive. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.15) as eluents, the desired product was obtained in 52% yield (5.5 mg, 17 μmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 185 °C (decomposed) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.40 – 7.32 (m, 3H), 7.31 (t, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.14 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.8 Hz, 1H), 4.45 (dd, *J* = 8.9, 3.2 Hz, 1H), 4.36 (d, *J* = 8.9 Hz, 1H), 4.11 (d, *J* = 6.3 Hz, 1H), 3.38 (dd, *J* = 6.3, 3.2 Hz, 1H), 3.29 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 195.28, 173.24, 143.70, 133.25, 130.27, 129.16, 128.92, 128.71, 127.52, 123.31, 123.17, 108.85, 80.48, 69.28, 52.66, 33.55, 30.36, 26.75. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{20}H_{18}O_3N]^+$: 320.1281, found: 320.1281.

5.4.2 Gold(I) catalyzed 6-*endo*-dig cycloisomerizations of prenylated 1,6-enyne (130)



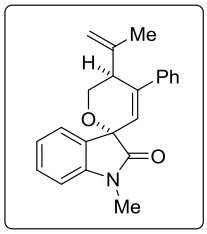
Under $Ar_{(g)}$ atmosphere, a mixture of PPh_3AuCl (12 mg, 25 μmol) and AgOTf (6 mg, 25 μmol) was added dry DCM (1 ml) and stirred at room temperature for 10 min. After cooling to 0 °C, a solution of **130** (150 mg, 0.45 mmol) in dry DCM (1.5 ml) was added to the gold catalyst solution. After gradually warming to room temperature, the resulting mixture was keep stirring till the TLC analysis indicated no starting material remaining. The crude product was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the corresponding products.

1-methyl-4'-phenyl-5'-(prop-1-en-2-yl)-5',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



(**131**) was obtained in 12% yield (18 mg, 0.05 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 124 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 6.9 Hz, 2H), 7.36 – 7.23 (m, 5H), 7.04 (td, *J* = 7.6, 1.0 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.86 (d, *J* = 1.5 Hz, 1H), 5.11 (s, 1H), 4.96 (s, 1H), 4.56 (dd, *J* = 11.5, 5.3 Hz, 1H), 4.19 (dd, *J* = 11.5, 5.3 Hz, 1H), 3.69 (t, *J* = 5.3 Hz, 1H), 3.22 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.13, 143.62, 143.45, 140.90, 139.57, 130.26, 130.14, 128.36, 127.79, 126.10, 124.91, 123.17, 122.61, 115.82, 108.59, 77.75, 65.56, 43.94, 26.41, 20.40. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1474.

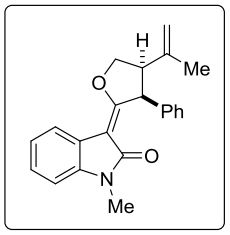
1-methyl-4'-phenyl-5'-(prop-1-en-2-yl)-5',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



(***epi*-132**) was obtained in 16% yield (24 mg, 0.07 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 150 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 7H), 7.08 (t, *J* = 7.1 Hz, 1H), 6.84 (dd, *J* = 8.2, 0.5 Hz, 1H), 5.96 (s, 1H), 5.05 (dd, *J* = 11.4, 3.4 Hz, 1H), 5.03 (s, 1H), 5.01 (s, 1H), 4.05 (dd, *J* = 11.4, 0.9 Hz,

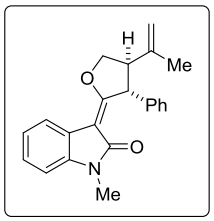
1H), 3.32 (d, *J* = 3.4 Hz, 1H), 3.19 (s, 3H), 1.97 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.92, 144.82, 143.86, 139.78, 139.05, 130.27, 129.61, 128.46, 127.99, 125.91, 125.02, 123.38, 122.20, 114.46, 108.59, 77.73, 65.42, 43.56, 26.31, 22.31. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C22H21O2NNa]^+$: 354.1465, found: 402.1457.

(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one



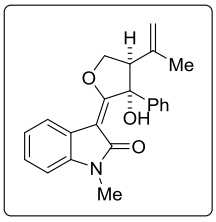
(***epi*-133**) was obtained in 26% yield (39 mg, 0.12 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 188 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.4 Hz, 1H), 7.29 – 7.25 (m, 2H), 7.26 – 7.16 (m, 4H), 7.08 (t, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.31 (d, *J* = 7.8 Hz, 1H), 4.75 (s, 1H), 4.71 (d, *J* = 3.3 Hz, 2H), 4.69 (s, 1H), 4.50 (s, 1H), 3.44 – 3.35 (m, 1H), 3.19 (s, 3H), 1.61 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 173.18, 167.93, 140.54, 138.90, 136.59, 128.66, 128.26, 126.99, 126.18, 122.51, 122.39, 121.50, 113.49, 107.11, 101.23, 72.83, 51.07, 49.15, 25.76, 22.84. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1645.

(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one



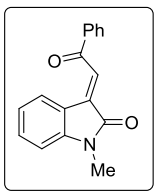
(**134**) was obtained in 8% yield (12 mg, 0.04 mmol) as a brown oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 178 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.13 (m, 6H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.69 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.56 (d, *J* = 9.4 Hz, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 6.1 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.96, 168.05, 144.82, 140.85, 140.70, 129.00, 127.05, 127.03, 126.30, 122.69, 122.56, 121.59, 111.65, 107.23, 101.76, 75.39, 53.84, 53.46, 25.89, 20.77. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1660.

(*E*)-3-(3-hydroxy-3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (**135**) was obtained in 5% yield (8 mg, 0.02 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 205 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.43 – 7.34 (m, 2H), 7.34 – 7.18 (m, 5H), 7.11 (td, *J* = 7.6, 0.9 Hz, 1H), 6.82 (d, *J* = 7.7 Hz, 1H), 4.80 (dd, *J* = 9.2, 7.9 Hz, 1H), 4.74

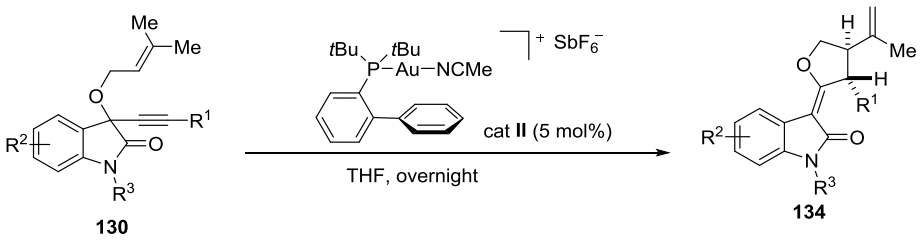


(s, 1H), 4.60 (dd, *J* = 12.2, 9.2 Hz, 1H), 4.47 (s, 1H), 3.61 (dd, *J* = 12.2, 7.9 Hz, 1H), 3.16 (s, 3H), 1.53 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.53, 169.36, 140.65, 139.67, 138.15, 128.11, 128.01, 126.58, 125.65, 122.82, 122.78, 122.38, 114.52, 107.80, 101.71, 85.35, 74.45, 56.12, 26.15, 22.68. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_3N]^+$: 348.1594, found: 348.1594.

(*E*)-1-methyl-3-(2-oxo-2-phenylethylidene)indolin-2-one (**136**)[101] was obtained in 7% yield (8 mg, 0.03 mmol) as a red oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.7 Hz, 1H), 8.11 (d, *J* = 7.5 Hz, 2H), 7.89 (s, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 2H), 7.37 (td, *J* = 7.7, 0.9 Hz, 1H), 7.03 (t, *J* = 7.7 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 3.27 (s, 3H).

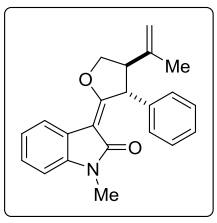


5.4.3 Gold(I) catalyzed *O*-migration reaction of prenylated 1,6-enynes (130)



To a THF (0.6 ml) solution of the 1,6-enyne (**130**, 0.1 mmol) was added a solution of cat **II** (3.9 mg, 5 µmol) in THF (0.4 ml). After warming to room temperature, the reaction mixture was stirred overnight and TLC showed full conversion of the starting material. The reaction mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the desired product.

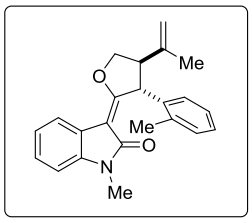
(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one



(**134a**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130a** (49 mg, 0.15 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.26) as eluents, the desired product was obtained in 95% yield (47 mg, 0.14 mmol) as a brown oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 178 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.13 (m, 6H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.69 (dd, *J* = 9.4, 6.1 Hz, 1H),

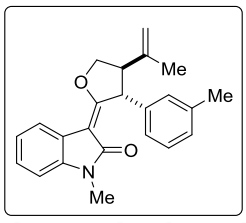
4.56 (d, *J* = 9.4 Hz, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 6.1 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.96, 168.05, 144.82, 140.85, 140.70, 129.00, 127.05, 127.03, 126.30, 122.69, 122.56, 121.59, 111.65, 107.23, 101.76, 75.39, 53.84, 53.46, 25.89, 20.77. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1660.

(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-(o-tolyl)dihydrofuran-2(3H)-ylidene)indolin-2-one



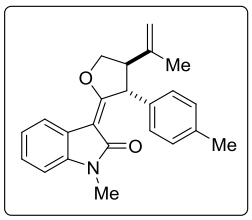
(**134b**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130b** (29 mg, 0.08 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 69% yield (20 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.21 (td, *J* = 7.5, 1.3 Hz, 1H), 7.13 (td, *J* = 7.5, 1.3 Hz, 1H), 7.08 (td, *J* = 7.5, 1.0 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.87 (dd, *J* = 7.5, 1.0 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.31 (s, 1H), 4.88 (s, 1H), 4.83 (t, *J* = 1.5 Hz, 1H), 4.69 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.53 (dd, *J* = 9.4, 0.9 Hz, 1H), 3.17 (s, 3H), 2.87 (d, *J* = 6.0 Hz, 1H), 2.55 (s, 3H), 1.79 (dd, *J* = 1.3, 0.9 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.91, 168.02, 145.08, 140.49, 138.99, 136.19, 130.83, 126.99, 126.13, 126.11, 125.76, 124.92, 122.61, 122.36, 121.47, 112.08, 107.11, 75.37, 52.32, 50.53, 25.77, 20.20, 20.15. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_2N]^+$: 346.1802, found: 346.1801.

(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-(m-tolyl)dihydrofuran-2(3H)-ylidene)indolin-2-on



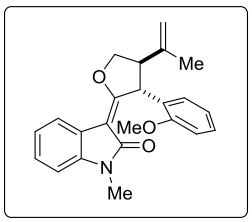
e (**134c**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130c** (18 mg, 0.05 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.25) as eluents, the desired product was obtained in 77% yield (14 mg, 0.04 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.5 Hz, 1H), 7.24 – 7.15 (m, 2H), 7.11 – 7.00 (m, 4H), 6.80 (d, *J* = 7.7 Hz, 1H), 5.12 (s, 1H), 4.83 (s, 1H), 4.81 (s, *J* = 1.2 Hz, 1H), 4.69 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.55 (dd, *J* = 9.4, 0.8 Hz, 1H), 3.18 (s, 3H), 2.96 (d, *J* = 6.0 Hz, 1H), 2.32 (s, 3H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.10, 168.11, 144.91, 140.75, 140.71, 138.62, 128.85, 127.93, 127.67, 126.26, 124.04, 122.77, 122.57, 121.57, 111.58, 107.23, 101.75, 75.35, 53.80, 53.56, 25.92, 21.70, 20.82. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_2N]^+$: 346.1802, found: 346.1815.

(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-(p-tolyl)dihydrofuran-2(3H)-ylidene)indolin-2-one



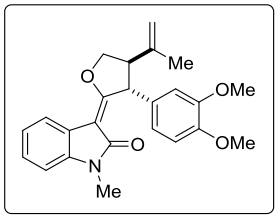
(**134d**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130d** (37 mg, 0.11 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.25) as eluents, the desired product was obtained in 83% yield (31 mg, 0.09 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.19 (td, *J* = 7.6, 1.2 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.10 (s, 1H), 4.81 (s, 1H), 4.80 (s, 1H), 4.69 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.55 (dd, *J* = 9.4, 1.1 Hz, 1H), 3.17 (s, 3H), 2.96 (d, *J* = 6.0 Hz, 1H), 2.29 (s, 3H), 1.79 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.26, 168.06, 144.90, 140.67, 137.85, 136.62, 129.69, 126.89, 126.22, 122.74, 122.52, 121.55, 111.54, 107.20, 101.62, 75.43, 53.54, 53.52, 25.89, 21.18, 20.77. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_2N]^+$: 346.1802, found: 346.1804.

(*E*)-3-(3-(2-methoxyphenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one



(**134e**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130e** (60 mg, 0.17 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.31) as eluents, the desired product was obtained in 46% yield (28 mg, 0.08 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.08 (td, *J* = 7.5, 0.9 Hz, 1H), 6.96 – 6.90 (m, 2H), 6.80 (d, *J* = 7.5 Hz, 2H), 5.36 (s, 1H), 4.83 (s, 1H), 4.80 (s, 1H), 4.62 – 4.54 (m, 2H), 3.93 (s, 3H), 3.17 (s, 3H), 2.92 – 2.83 (m, 1H), 1.87 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.63, 168.06, 157.02, 145.33, 140.64, 128.82, 128.36, 126.56, 126.11, 122.82, 122.46, 121.52, 120.50, 110.96, 110.83, 107.15, 101.90, 75.44, 55.57, 51.73, 49.24, 25.86, 21.24. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_3N]^+$: 362.1751, found: 362.1757.

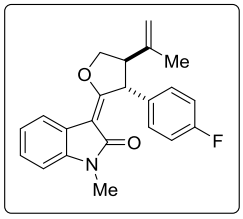
(*E*)-3-(3-(3,4-dimethoxyphenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one



(**134f**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130f** (41 mg, 0.10 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum

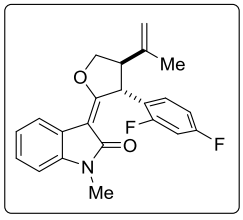
ether = 1/1 (R_f = 0.55) as eluents, the desired product was obtained in 56% yield (23 mg, 0.06 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.83 (s, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.79 – 6.71 (m, 2H), 5.11 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.70 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.55 (d, *J* = 9.4 Hz, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 3.19 (s, 3H), 2.97 (d, *J* = 6.0 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.07, 168.10, 149.38, 148.20, 144.83, 140.67, 133.41, 126.28, 122.71, 122.56, 121.58, 118.65, 111.63, 111.48, 110.83, 107.24, 101.72, 75.48, 56.09, 55.98, 53.56, 53.37, 25.91, 20.80. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{24}H_{26}O_4N]^+$: 392.1856, found: 392.1846.

(*E*)-3-(3-(4-fluorophenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methyl



indolin-2-one (**134g**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130g** (31 mg, 0.09 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 78% yield (24 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.18 (m, 3H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 8.6 Hz, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 5.12 (s, 1H), 4.86 – 4.80 (m, 2H), 4.68 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.57 (dd, *J* = 9.5, 1.0 Hz, 1H), 3.18 (s, 3H), 2.96 (d, *J* = 6.0 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.61, 168.02, 161.86 (d, *J* = 245.4 Hz), 144.58, 140.72, 136.63 (d, *J* = 3.4 Hz), 128.60 (d, *J* = 8.0 Hz), 126.45, 122.62, 122.55, 121.67, 115.85 (d, *J* = 21.5 Hz), 111.84, 107.32, 101.83, 75.36, 53.48, 53.07, 25.91, 20.72. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NF]^+$: 350.1551, found: 350.1554.

(*E*)-3-(3-(2,4-difluorophenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-



methylindolin-2-one (**134h**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130h** (35 mg, 0.10 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.40) as eluents, the desired product was obtained in 73% yield (26 mg, 0.07 mmol) pale yellow solid. **mp**: 151 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.22 (td, *J* = 7.5, 1.2 Hz, 1H), 7.08 (td, *J* = 7.5, 0.9 Hz, 1H), 7.01 (td, *J* = 8.6, 6.4 Hz, 1H), 6.90 – 6.83 (m, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.74 (td, *J* = 8.0, 1.6 Hz, 1H), 5.25 (s, 1H), 4.88 –

4.80 (m, 2H), 4.66 – 4.55 (m, 2H), 3.18 (s, 3H), 2.95 (d, *J* = 4.4 Hz, 1H), 1.84 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 170.33, 167.92, 162.16 (dd, *J* = 236.2, 12.8 Hz), 160.69 (dd, *J* = 249.8, 12.1 Hz), 144.24, 140.82, 128.37 (dd, *J* = 9.6, 5.3 Hz), 126.61, 123.88 (dd, *J* = 15.0, 3.9 Hz), 122.68, 122.37, 121.72, 111.84, 111.27 (dd, *J* = 21.2, 3.7 Hz), 107.38, 104.54 (t, *J* = 25.6 Hz), 102.16, 75.48, 52.21, 47.63 (d, *J* = 2.5 Hz), 25.92, 20.85. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{19}O_2NF_2Na]^+$: 390.1276, found: 350.1289.

(*E*)-3-(3-(2-chlorophenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (**134i**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130i** (30 mg, 0.08 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.33) as eluents, the desired product was obtained in 83% yield (25 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 7.18 (td, *J* = 7.7, 1.7 Hz, 1H), 7.14 – 7.05 (m, 2H), 6.99 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.50 (s, 1H), 4.90 (s, 1H), 4.89 – 4.82 (m, 1H), 4.60 (dd, *J* = 9.3, 5.6 Hz, 1H), 4.56 (dd, *J* = 9.3, 1.2 Hz, 1H), 3.18 (s, 3H), 2.97 (d, *J* = 5.6 Hz, 1H), 1.87 – 1.82 (m, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 171.14, 167.97, 144.58, 140.83, 138.12, 134.27, 130.29, 128.47, 127.05, 126.97, 126.52, 122.61, 122.48, 121.66, 112.26, 107.34, 101.96, 75.39, 51.79, 51.39, 25.92, 20.98. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NCl]^+$: 366.1255, found: 366.1258.

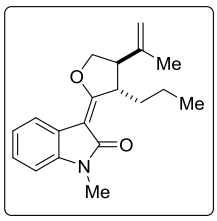
(*E*)-3-(3-(3-chlorophenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (**134j**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130j** (26 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.25) as eluents, the desired product was obtained in 45% yield (12 mg, 0.03 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.29 – 7.18 (m, 4H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.12 (s, 1H), 4.84 (s, 2H), 4.67 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.56 (d, *J* = 9.4 Hz, 1H), 3.18 (s, 3H), 2.96 (d, *J* = 6.1 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.74, 168.02, 144.43, 142.84, 140.81, 134.83, 130.24, 127.38, 127.04, 126.57, 125.43, 122.72, 122.48, 121.71, 112.00,

107.36, 102.12, 75.29, 53.42, 53.39, 25.93, 20.71. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NClNa]^+$: 388.1075, found: 388.1084.

(*E*)-3-(3-(4-bromophenyl)-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (**134k**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130l** (37 mg, 0.09 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.40) as eluents, the desired product was obtained in 72% yield (27 mg, 0.07 mmol) as a pale yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 5.09 (s, 1H), 4.83 (s, 2H), 4.67 (dd, *J* = 9.3, 6.2 Hz, 1H), 4.57 (d, *J* = 9.3 Hz, 1H), 3.18 (s, 3H), 2.95 (d, *J* = 6.2 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.13, 168.02, 144.46, 140.75, 139.96, 132.11, 128.79, 126.53, 122.65, 122.48, 121.71, 121.02, 111.97, 107.37, 101.96, 75.36, 53.37, 53.28, 25.91, 20.67. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{20}O_2NBrNa]^+$: 432.0570, found: 432.0577.

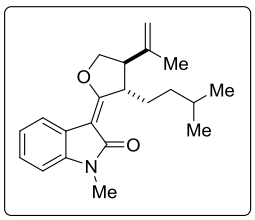
(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-(thiophen-3-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134l**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130l** (35 mg, 0.10 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/6 (R_f = 0.39) as eluents, the desired product was obtained in 67% yield (23 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.15 – 7.04 (m, 3H), 6.85 (d, *J* = 7.6 Hz, 1H), 5.25 (s, 1H), 4.83 (s, 2H), 4.75 (dd, *J* = 9.4, 6.0 Hz, 1H), 4.61 (d, *J* = 9.4 Hz, 1H), 3.24 (s, 3H), 3.06 (d, *J* = 6.0 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.24, 168.74, 144.33, 140.06, 139.64, 127.04, 126.41, 122.64, 122.21, 121.20, 111.86, 107.72, 101.41, 77.36, 76.15, 52.14, 49.22, 26.28, 20.89. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{20}H_{20}O_2NS]^+$: 338.1209, found: 338.1219.

(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-propyldihydrofuran-2(3H)-ylidene)indolin-2-one



(**134m**) was prepared according to the general procedure for the gold catalyzed O-migration reaction with 10 mol% catalyst loading, by using **130m** (18 mg, 0.06 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.29) as eluents, the desired product was obtained in 50% yield (9 mg, 0.03 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 1H), 7.17 (td, *J* = 7.6, 0.9 Hz, 1H), 7.03 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 4.75 (s, 1H), 4.72 (s, 1H), 4.63 (dd, *J* = 9.4, 6.2 Hz, 1H), 4.52 (d, *J* = 9.4 Hz, 1H), 3.85 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.28 (s, 3H), 2.88 (d, *J* = 6.2 Hz, 1H), 1.90 – 1.80 (m, 1H), 1.70 (s, 2H), 1.61 – 1.55 (m, 1H), 1.55 – 1.45 (m, 1H), 1.01 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 176.05, 168.58, 145.38, 140.26, 125.83, 123.03, 122.27, 121.57, 110.98, 107.17, 100.16, 75.90, 48.47, 48.15, 34.61, 25.92, 21.45, 20.60, 13.95. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{19}H_{24}O_2N]^+$: 298.1802, found: 298.1805.

(*E*)-3-(3-isopentyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on



e (**134n**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130n** (35 mg, 0.11 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.31) as eluents, the desired product was obtained in 36% yield (12 mg, 0.04 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1H), 7.09 (td, *J* = 7.6, 0.7 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 5.34 (t, *J* = 7.2 Hz, 1H), 4.31 (dd, *J* = 10.5, 7.2 Hz, 1H), 4.24 (dd, *J* = 10.5, 7.2 Hz, 1H), 3.18 (s, 3H), 2.24 (td, *J* = 7.4, 1.6 Hz, 2H), 1.69 (s, 3H), 1.67 – 1.61 (m, 2H), 1.41 (td, *J* = 7.4 Hz, 2H), 0.85 (dd, *J* = 6.6, 2.3 Hz, 7H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.42, 143.29, 137.98, 130.23, 128.68, 124.84, 123.38, 120.62, 108.58, 89.47, 74.84, 73.90, 62.15, 37.33, 27.44, 26.45, 25.91, 22.22, 18.13, 17.12. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{27}O_2NNa]^+$: 348.1934, found: 348.1945.

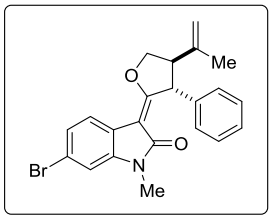
(*E*)-1,5-dimethyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134o**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130o** (24 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.27) as eluents, the desired product was obtained in 76% yield (18 mg, 0.05 mmol) as a brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.35 – 7.23 (m, 5H), 7.03 (dd, *J* = 7.8, 0.8 Hz, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 5.18 (s, 1H), 4.86 (s, 1H), 4.84 (s, 1H), 4.72 (dd, *J* = 9.6, 6.0 Hz, 1H), 4.60 (dd, *J* = 9.5, 1.0 Hz, 1H), 3.18 (s, 3H), 3.00 (d, *J* = 6.0 Hz, 1H), 2.43 (s, 3H), 1.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.64, 168.10, 144.86, 140.89, 138.54, 130.97, 128.99, 127.02, 126.65, 123.33, 122.68, 111.63, 106.97, 101.86, 75.29, 53.76, 53.43, 25.93, 21.42, 20.79. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_2N]^+$: 346.1802, found: 346.1812.

(*E*)-5-methoxy-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134p**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130p** (27 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.27) as eluents, the desired product was obtained in 66% yield (18 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.44 (d, *J* = 2.5 Hz, 1H), 7.37 – 7.16 (m, 5H), 6.76 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 5.15 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.70 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.57 (d, *J* = 9.5 Hz, 1H), 3.86 (s, 3H), 3.14 (s, 3H), 2.98 (d, *J* = 6.0 Hz, 1H), 1.80 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.10, 167.96, 155.49, 144.80, 140.82, 134.85, 129.01, 127.06, 127.02, 123.59, 111.67, 111.35, 109.61, 107.39, 102.12, 75.44, 56.17, 53.81, 53.39, 25.97, 20.77. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_3NNa]^+$: 384.1570, found: 384.1579.

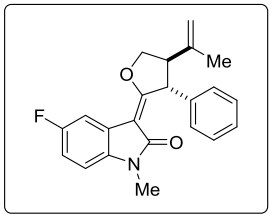
(*E*)-1,5,7-trimethyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134q**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130q** (33 mg, 0.09 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.25) as eluents, the desired product was obtained in 58% yield (19 mg,

0.05 mmol) as a pale yellow solid. **mp**: 183 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.30 (t, *J* = 7.4 Hz, 2H), 7.26 – 7.17 (m, 3H), 6.75 (s, 1H), 5.18 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.68 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.56 (d, *J* = 9.4 Hz, 1H), 3.43 (s, 3H), 2.96 (d, *J* = 6.1 Hz, 1H), 2.52 (s, 3H), 2.35 (s, 3H), 1.80 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.42, 168.67, 144.93, 141.01, 136.37, 130.86, 130.66, 128.97, 127.02, 126.98, 123.31, 121.40, 118.58, 111.60, 101.88, 75.27, 53.89, 53.44, 29.15, 21.08, 20.78, 19.09. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{24}H_{25}O_2NNa]^+$: 382.1778, found: 382.1783.

(*E*)-6-bromo-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134r**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130r** (27 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.54) as eluents, the desired product was obtained in 69% yield (19 mg, 0.05 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.0 Hz, 1H), 7.40 – 7.17 (m, 6H), 6.90 (d, *J* = 1.7 Hz, 1H), 5.08 (s, 1H), 4.79 (s, 2H), 4.68 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.55 (dd, *J* = 9.5, 1.1 Hz, 1H), 3.11 (s, 3H), 2.95 (d, *J* = 6.0 Hz, 1H), 1.77 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.76, 167.84, 144.64, 141.78, 140.50, 129.07, 127.19, 126.99, 124.31, 123.56, 121.55, 119.61, 111.77, 110.62, 101.02, 75.69, 54.00, 53.34, 25.99, 20.76. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NBr]^+$: 410.0750, found: 410.1757.

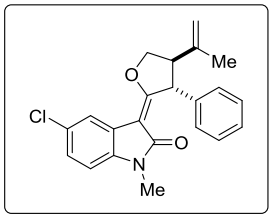


(*E*)-5-fluoro-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134s**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130s** (31 mg, 0.09 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.33) as eluents, the desired product was obtained in 62% yield (19 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.39 – 7.28 (m, 2H), 7.28 – 7.19 (m, 3H), 6.89 (td, *J* = 8.9, 2.6 Hz, 1H), 6.68 (dd, *J* = 8.9, 4.2 Hz, 1H), 5.14 (s, 1H), 4.83 (s, 2H), 4.72 (dd, *J* = 9.5, 6.1 Hz, 1H), 4.60 (dd, *J* = 9.5, 1.0 Hz, 1H), 3.16 (s, 3H), 2.99 (d, *J* = 6.1 Hz, 1H), 1.81 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.01, 167.86, 158.99 (d, *J* = 236.7 Hz), 144.62, 140.51, 136.69, 129.07, 127.17, 126.98, 123.64 (d, *J* = 10.0 Hz), 112.22 (d, *J* = 24.0 Hz), 111.75, 101.68, 110.13 (d, *J* = 26.0 Hz), 107.31 (d, *J* = 8.5

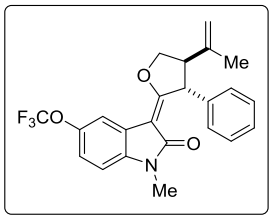


Hz), 75.73, 53.94, 53.33, 26.03, 20.76. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NF]^+$: 350.1551, found: 350.1558.

(*E*)-5-chloro-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134t**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130t** (31 mg, 0.08 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.29) as eluents, the desired product was obtained in 65% yield (20 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 2.1 Hz, 1H), 7.38 – 7.29 (m, 2H), 7.28 – 7.21 (m, 3H), 7.17 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 5.14 (s, 1H), 4.84 (s, 2H), 4.74 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.62 (dd, *J* = 9.5, 1.1 Hz, 1H), 3.16 (s, 3H), 3.00 (d, *J* = 6.0 Hz, 1H), 1.82 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.24, 167.67, 144.59, 140.44, 139.07, 129.08, 127.20, 126.98, 126.92, 125.84, 123.99, 122.56, 111.79, 107.99, 101.05, 75.80, 54.02, 53.31, 26.01, 20.76. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{21}O_2NCl]^+$: 366.1255, found: 366.1267.



(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-5-(trifluorom ethoxy)indolin-2-one (**134u**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130u** (28 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.38) as eluents, the desired product was obtained in 74% yield (21 mg, 0.05 mmol) as a brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.66 (d, *J* = 1.5 Hz, 1H), 7.39 – 7.28 (m, 2H), 7.28 – 7.17 (m, 3H), 7.06 (dd, *J* = 8.4, 1.3 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.14 (s, 1H), 4.84 (s, 2H), 4.75 (dd, *J* = 9.6, 6.1 Hz, 1H), 4.62 (dd, *J* = 9.6, 1.1 Hz, 1H), 3.17 (s, 3H), 3.00 (d, *J* = 5.9 Hz, 1H), 1.81 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.57, 167.89, 144.55, 144.27, 140.42, 139.12, 129.10, 127.23, 127.00, 124.68 (d, *J* = 317.8 Hz), 123.58, 119.13, 116.20, 111.83, 107.28, 101.21, 75.94, 54.07, 53.30, 26.04, 20.77. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{21}O_3NF_3]^+$: 416.1468, found: 416.1460.



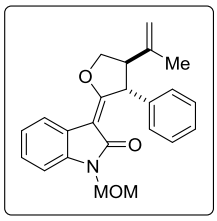
(*E*)-1-methyl-5-nitro-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134v**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130v** (28 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.18) as eluents, the desired product was obtained in 64% yield (18 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 (d, *J* = 2.3 Hz, 1H), 8.20 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.43 – 7.31 (m, 2H), 7.31 - 7.18 (m, 3H), 6.86 (d, *J* = 8.6 Hz, 1H), 5.15 (s, 1H), 4.98 – 4.78 (m, 3H), 4.74 (dd, *J* = 9.6, 1.0 Hz, 1H), 3.26 (s, 3H), 3.06 (d, *J* = 5.8 Hz, 1H), 1.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.30, 168.02, 145.37, 144.31, 142.88, 139.93, 129.19, 127.42, 126.96, 123.20, 122.86, 117.89, 112.00, 106.54, 100.04, 76.56, 54.48, 53.16, 26.32, 20.73. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{20}O_4N_2]^+$: 377.1496, found: 377.1503.

(*E*)-1-benzyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134w**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130w** (25 mg, 0.06 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.61) as eluents, the desired product was obtained in 96% yield (24 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.2, 1.1 Hz, 1H), 7.37 – 7.16 (m, 10H), 7.14 – 7.00 (m, 2H), 6.71 (d, *J* = 7.2 Hz, 1H), 5.20 (s, 1H), 5.00 (d, *J* = 15.9 Hz, 1H), 4.87 (s, 1H), 4.86 (s, 1H), 4.80 (d, *J* = 15.9 Hz, 1H), 4.73 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.61 (dd, *J* = 9.5, 1.2 Hz, 1H), 3.02 (d, *J* = 6.0 Hz, 1H), 1.85 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.87, 168.26, 144.68, 140.73, 139.67, 136.75, 129.02, 128.70, 128.41, 127.36, 127.31, 127.11, 127.05, 126.28, 122.84, 122.69, 121.88, 111.79, 108.44, 101.64, 75.62, 54.09, 53.55, 43.59, 20.84. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{28}H_{26}O_2N]^+$: 408.1958, found: 408.1958.

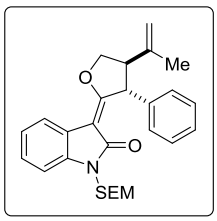
(*E*)-1-(4-methoxybenzyl)-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134x**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130x** (33 mg, 0.08 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f

= 0.30) as eluents, the desired product was obtained in 83% yield (27 mg, 0.06 mmol) as a brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.43 – 7.20 (m, 5H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.13 – 6.98 (m, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 6.71 (d, *J* = 7.5 Hz, 1H), 5.20 (s, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.87 (s, 1H), 4.85 (s, 1H), 4.77 – 4.67 (m, 2H), 4.59 (dd, *J* = 9.5, 1.0 Hz, 1H), 3.75 (s, 3H), 3.01 (d, *J* = 5.8 Hz, 1H), 1.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.24, 167.95, 158.84, 144.73, 140.83, 139.82, 129.03, 128.99, 128.68, 127.03, 127.01, 126.20, 122.84, 122.61, 121.59, 114.04, 111.72, 108.25, 101.63, 75.42, 55.33, 53.91, 53.51, 42.89, 20.85. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{29}H_{28}O_3N]^+$: 438.2064, found: 438.2065.

(*E*)-1-(methoxymethyl)-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134y**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130y** (39 mg, 0.11 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.37) as eluents, the desired product was obtained in 97% yield (38 mg, 0.10 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 6.9 Hz, 1H), 7.35 – 7.17 (m, 6H), 7.11 (td, *J* = 7.7, 0.9 Hz, 1H), 7.01 (d, *J* = 7.7 Hz, 1H), 5.15 (d, *J* = 10.9 Hz, 1H), 5.14 (s, 1H), 5.04 (d, *J* = 10.9 Hz, 1H), 4.85 (s, 1H), 4.84 (s, 1H), 4.71 (dd, *J* = 9.5, 5.7 Hz, 1H), 4.59 (dd, *J* = 9.5, 1.2 Hz, 1H), 3.25 (s, 3H), 3.00 (d, *J* = 5.7 Hz, 1H), 1.82 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.76, 168.38, 144.69, 140.66, 139.08, 129.00, 128.38, 127.08, 126.99, 126.47, 122.72, 122.25, 111.75, 108.64, 101.50, 75.58, 71.13, 56.16, 54.04, 53.51, 20.78. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_3NNa]^+$: 384.1570, found: 384.1584.

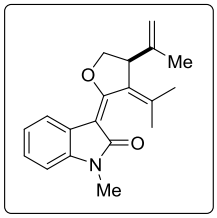


(*E*)-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)-1-((2-(trimethylsilyl)ethoxy)methyl)indolin-2-one (**134z**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **130z** (22 mg, 0.05 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/10 (R_f = 0.42) as eluents, the desired product was obtained in 51% yield (11 mg, 0.03 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.6 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.33 (d, *J* = 8.9 Hz, 2H), 7.29 (d, *J* = 5.9 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 5.24 (d, *J* = 11.0 Hz, 1H), 5.23 (s, 1H), 5.16 (d, *J* =

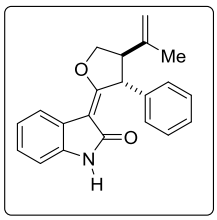


11.0 Hz, 1H), 4.92 (s, 1H), 4.91 (d, *J* = 1.1 Hz, 1H), 4.78 (dd, *J* = 9.4, 6.2 Hz, 1H), 4.66 (d, *J* = 9.4 Hz, 1H), 3.60 – 3.48 (m, 2H), 3.08 (d, *J* = 6.2 Hz, 1H), 1.89 (s, 3H), 0.92 (dd, *J* = 8.2, 8.0 Hz, 2H), -0.03 (s, 9H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.57, 168.23, 144.76, 140.68, 139.27, 128.99, 127.07, 127.02, 126.43, 122.73, 122.65, 122.11, 111.73, 108.81, 101.57, 75.54, 69.14, 65.74, 53.93, 53.48, 20.76, 17.93, -1.35. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{27}H_{33}O_3NSiNa]^+$: 470.2122, found: 470.2137.

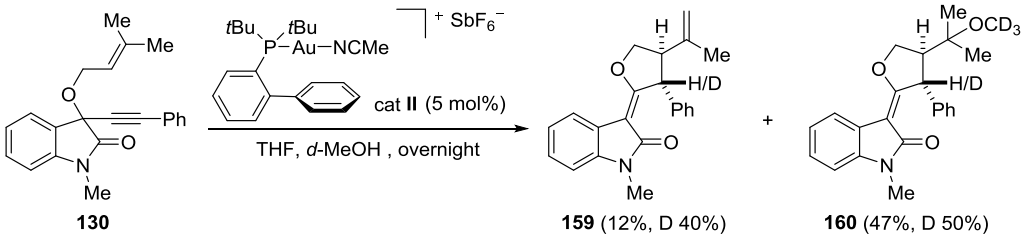
(*E*)-1-methyl-3-(4-(prop-1-en-2-yl)-3-(propan-2-ylidene)dihydrofuran-2(3H)-ylidene)indolin-2-one (**138**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **137** (22 mg, 0.07 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 46% yield (10 mg, 0.03 mmol) as a yellow solid. **mp**: 147 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 4.83 (s, 1H), 4.76 (s, 1H), 4.46 – 4.36 (m, 2H), 3.66 (d, *J* = 6.0 Hz, 1H), 3.28 (s, 3H), 2.01 (s, 3H), 1.99 (s, 3H), 1.71 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 166.39, 165.35, 148.00, 143.07, 140.21, 127.86, 125.77, 124.22, 122.78, 121.16, 113.01, 106.90, 102.99, 73.62, 49.52, 26.07, 24.84, 23.76, 20.28. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{19}H_{22}O_2N]^+$: 296.1645, found: 296.1649.



(*E*)-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one (**134aa**) was prepared according to the general procedure for the gold catalyzed O-migration reaction, by using **133aa** (33 mg, 0.01 mmol) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.23) as eluents, the desired product was obtained in 95% yield (31 mg, 0.10 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.28 – 7.18 (m, 3H), 7.12 (td, *J* = 7.6, 1.0 Hz, 1H), 7.04 (td, *J* = 7.6, 0.6 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 5.12 (s, 1H), 4.84 (s, 1H), 4.83 (s, 1H), 4.71 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.58 (dd, *J* = 9.5, 1.0 Hz, 1H), 3.00 (d, *J* = 6.0 Hz, 1H), 1.81 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.78, 169.50, 144.73, 140.69, 137.85, 128.93, 127.13, 127.09, 126.33, 123.59, 122.87, 121.65, 111.80, 108.96, 101.88, 75.65, 53.87, 53.44, 20.71. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1312.

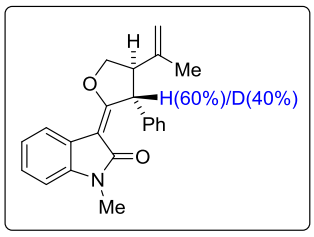


5.4.4 Gold catalyzed *O*-migration reaction with deuterated CD_3OD as nucleophile



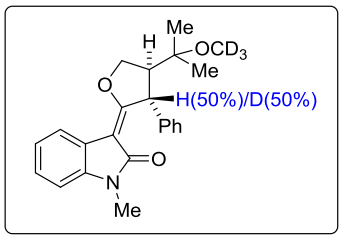
At 0 °C, to a THF (0.4 ml) solution of **130** (0.08 mmol) and *d*-MeOH (53 µL, 0.75 mmol) was added a solution of cat **II** (3 mg, 4 µmol) in THF (0.4 mL). The reaction mixture was stirred at room temperature overnight. Afterwards, the reaction mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether = 1:4 as eluents) to obtain compounds **159** in 12% yield **(**3 mg, 0.01 mmol, *D*-40%**)** as a yellow oil and **160** in 47% yield (13 mg, 0.04 mmol, *D*-50%**)** as a yellow oil.

(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one



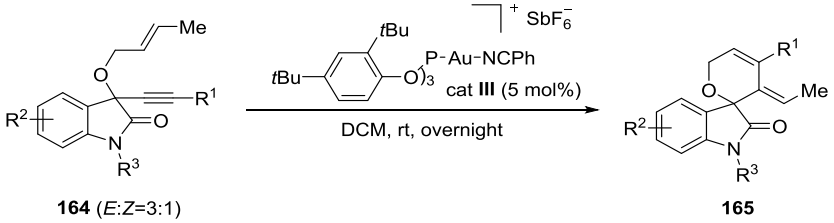
(**159**) **^{1}H NMR** (300 MHz, cdcl$_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.13 (m, 6H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 0:6H), 4.83 (s, 1H), 4.81 (s, 1H), 4.69 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.56 (d, *J* = 9.4 Hz, 1H), 3.17 (s, 3H), 2.98 (d, *J* = 6.1 Hz, 1H), 1.80 (s, 3H).

(*E*)-3-((4-(2-(methoxy-d3)propan-2-yl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methyli



ndolin-2-one (**160**) **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.5 Hz, 1H), 7.34 – 7.12 (m, 6H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 7.5 Hz, 1H), 5.10 (s, 0.5H), 4.73 (dd, *J* = 9.9, 1.7 Hz, 1H), 4.64 (dd, *J* = 9.9, 6.8 Hz, 1H), 3.15 (s, 3H), 2.51 (d, *J* = 6.8 Hz, 1H), 1.26 (s, 3H), 1.09 (s, 3H).

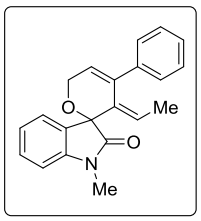
5.4.5 Gold(I) catalyzed single cleavage rearrangement of crotylated 1,6-enyne (161)



164 (*E*:*Z*=3:1) **165**

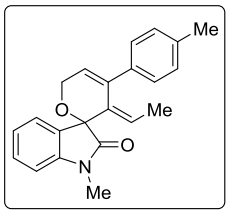
At 0 °C, to a DCM (0.6 ml) solution of 1,6-enyne (0.1 mmol) was added a solution of cat **III** (5.9 mg, 5 µmol) in DCM (0.4 ml). After warming to room temperature, the reaction mixture was stirred overnight and then passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the desired product.

(*E*)-3'-ethylidene-1-methyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



(**165a**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161a** (30 mg, 0.09 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.20) as eluents, the desired product was obtained in 60% yield (18 mg, 0.06 mmol) as a yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 131.0 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.6 Hz, 1H), 7.40 (td, *J* = 7.6, 1.1 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.33 – 7.28 (m, 1H), 7.25 (dd, *J* = 8.1, 1.3 Hz, 2H), 7.09 (td, *J* = 7.6, 1.1 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.11 (s, 1H), 5.49 (q, *J* = 7.3Hz, 1H), 4.87 (dd, *J* = 17.8, 2.9 Hz, 1H), 4.65 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.30 (s, 3H), 1.19 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.34, 143.80, 141.86, 136.54, 130.84, 129.76, 129.40, 128.48, 128.39, 127.23, 127.17, 125.95, 124.84, 122.96, 108.73, 79.61, 63.77, 26.35, 16.34. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1321.

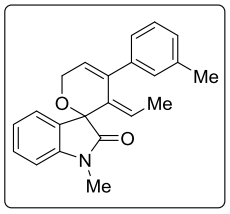
(*E*)-3'-ethylidene-1-methyl-4'-(p-tolyl)-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



(**165b**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161c** (40 mg, 0.12 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.35) as eluents, the desired product was obtained in 60% yield (24 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H),

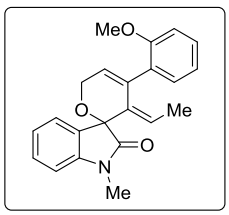
7.12 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.04 (s, 1H), 5.44 (q, *J* = 7.3 Hz, 1H), 4.80 (dd, *J* = 17.7, 3.0 Hz, 1H), 4.59 (dd, *J* = 17.7, 3.0 Hz, 1H), 3.26 (s, 3H), 2.35 (s, 3H), 1.16 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.45, 143.84, 139.01, 136.96, 136.57, 131.02, 129.75, 129.56, 129.21, 127.91, 127.15, 125.91, 124.87, 122.99, 108.76, 79.74, 63.86, 26.42, 21.29, 16.45. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1480.

(*E*)-3'-ethylidene-1-methyl-4'-(m-tolyl)-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



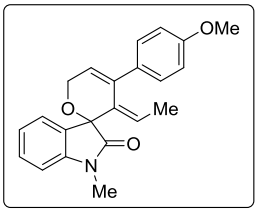
(**165c**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161c** (41 mg, 0.12 mmol, 84% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.43) as eluents, the desired product was obtained in 66% yield (27 mg, 0.08 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.5 Hz, 1H), 7.35 (td, *J* = 7.5, 1.2 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.04 (td, *J* = 7.5, 0.9 Hz, 1H), 7.02 (s, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.07 – 6.01 (m, 1H), 5.43 (q, *J* = 7.3 Hz, 1H), 4.81 (dd, *J* = 17.8, 3.0 Hz, 1H), 4.59 (dd, *J* = 17.8, 3.2 Hz, 1H), 3.26 (s, 3H), 2.33 (s, 3H), 1.14 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.40, 143.86, 141.86, 138.11, 136.66, 130.87, 129.78, 129.47, 128.39, 128.17, 127.97, 127.91, 125.98, 124.92, 124.46, 123.01, 108.77, 79.67, 63.83, 26.42, 21.55, 16.43. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1455. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1455.

(*E*)-3'-ethylidene-4'-(2-methoxyphenyl)-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165e**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161e** (31 mg, 0.09 mmol, 81% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.15) as eluents, the desired product was obtained in 29% yield (9 mg, 0.03 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.5 Hz, 1H), 7.34 (td, *J* = 7.7, 1.3 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.06 (td, *J* = 7.5, 1.0 Hz, 1H), 6.93 (td, *J* = 7.5, 1.0 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 8.2 Hz, 1H), 5.94 (s, 1H), 5.26 (q, *J* = 7.4 Hz, 1H), 4.80 (dd, *J* = 17.9, 2.6 Hz, 1H), 4.59 (dd, *J* = 17.9, 2.8 Hz, 1H), 3.65 (s, 3H), 3.25 (s, 3H), 1.06 (d, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.58, 157.02,

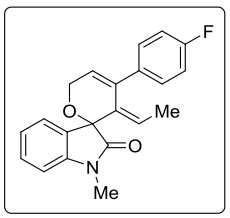


143.83, 130.17, 129.62, 129.55, 128.72, 128.48, 125.56, 124.42, 122.60, 120.83, 108.57, 93.35, 63.49, 55.41, 26.41, 14.48. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{20}O_3N]^+$: 348.1594, found: 348.1595.

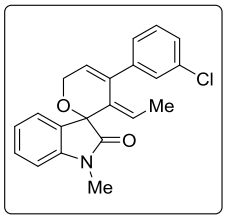
(*E*)-3'-ethylidene-4'-(4-methoxyphenyl)-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165f**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161f** (51 mg, 0.15 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.27) as eluents, the desired product was obtained in 59% yield (30 mg, 0.09 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.5 Hz, 1H), 7.34 (td, *J* = 7.8, 1.0 Hz, 1H), 7.22 (t, *J* = 7.9 Hz, 1H), 7.04 (td, *J* = 7.5, 1.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.85 – 6.77 (m, 2H), 6.77 – 6.73 (m, 1H), 6.10 – 6.04 (m, 1H), 5.43 (q, *J* = 7.3 Hz, 1H), 4.81 (dd, *J* = 17.8, 3.0 Hz, 1H), 4.59 (dd, *J* = 17.8, 3.2 Hz, 1H), 3.77 (s, 3H), 3.25 (s, 3H), 1.18 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.35, 159.82, 143.84, 143.36, 136.44, 130.79, 129.79, 129.50, 129.42, 128.40, 126.09, 124.88, 122.99, 119.91, 113.06, 112.56, 108.76, 79.62, 63.76, 55.37, 26.39, 16.34. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1407.



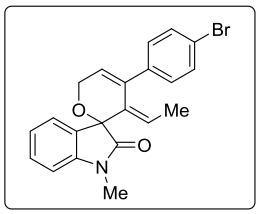
(*E*)-3'-ethylidene-4'-(4-fluorophenyl)-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165g**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161g** (49 mg, 0.15 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.18) as eluents, the desired product was obtained in 51% yield (25 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 1H), 7.17 (dd, *J* = 8.7, 5.5 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.00 (t, *J* = 8.7 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.03 (s, 1H), 5.42 (q, *J* = 7.5 Hz, 1H), 4.81 (dd, *J* = 17.8, 3.0 Hz, 1H), 4.59 (dd, *J* = 17.8, 3.0 Hz, 1H), 3.25 (s, 3H), 1.14 (d, *J* = 7.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.34, 162.26 (d, *J* = 246.1 Hz), 143.91, 137.96, 135.56, 130.94, 129.90, 129.35, 128.85 (d, *J* = 7.8 Hz), 128.60, 126.16, 124.91, 123.05, 115.44 (d, *J* = 21.4 Hz), 108.81, 79.61, 63.79, 26.41, 16.40. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NFNa]^+$: 358.1214, found: 358.1223.



(*E*)-4'-(3-chlorophenyl)-3'-ethylidene-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165h**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161i** (48 mg, 0.14 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.19) as eluents, the desired product was obtained in 31% yield (15 mg, 0.04 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.25 – 7.23 (m, 2H), 7.20 (s, 1H), 7.11 – 7.08 (m, 1H), 7.07 (td, *J* = 7.6, 0.9 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.08 (s, 1H), 5.44 (q, *J* = 7.3 Hz, 1H), 4.83 (dd, *J* = 18.0, 2.9 Hz, 1H), 4.60 (dd, *J* = 18.0, 3.0 Hz, 1H), 3.25 (s, 3H), 1.16 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.23, 143.94, 143.73, 135.26, 134.46, 130.48, 129.98, 129.84, 129.46, 129.17, 127.36, 126.42, 125.55, 124.97, 123.11, 108.84, 79.47, 63.79, 26.43, 16.59.**HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NClNa]^+$: 374.0918, found: 374.0929.



(*E*)-4'-(4-bromophenyl)-3'-ethylidene-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165j**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161k** (44 mg, 0.11 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.25) as eluents, the desired product was obtained in 28% yield (12 mg, 0.03 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.5 Hz, 2H), 7.40 – 7.31 (m, 2H), 7.13 – 7.02 (m, 3H), 6.91 (d, *J* = 7.8 Hz, 1H), 6.11 – 6.03 (m, 1H), 5.43 (q, *J* = 7.2 Hz, 1H), 4.80 (dd, *J* = 17.9, 2.9 Hz, 1H), 4.59 (dd, *J* = 17.9, 3.1 Hz, 1H), 3.26 (s, 3H), 1.16 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.98, 143.95, 140.98, 135.76, 131.98, 130.74, 130.25, 129.59, 129.30, 129.16, 126.67, 125.15, 123.56, 121.52, 109.26, 79.98, 77.65, 77.40, 77.14, 64.04, 26.78, 16.84. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NBrNa]^+$: 418.0413, found: 418.0418.



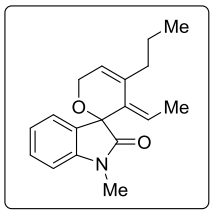
(*E*)-3'-ethylidene-1-methyl-4'-(thiophen-2-yl)-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165k**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161m** (44 mg, 0.14 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.33) as eluents, the desired product was obtained in 45% yield (20 mg, 0.06 mmol) as a dark brown oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.46 – 7.30 (m, 2H), 7.26 – 7.22 (m, 1H), 7.10 – 6.98 (m, 2H), 6.93 (d, *J* = 5.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.12 (s, 1H), 5.43 (q, *J* = 7.2 Hz, 1H), 4.79 (dd, *J* = 17.7, 3.0 Hz, 1H), 4.56 (dd, *J* = 17.7, 3.0 Hz, 1H), 3.25 (s, 3H), 1.24 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174 .38, 143.78, 142.66, 131.55, 131.10, 129.82, 129.42, 127.80, 127.50, 126.09, 125.52, 124.86, 123.04, 121.07, 108.78, 79.63, 63.71, 26.42, 15.89. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{19}H_{17}O_2NSNa]^+$: 346.0872, found: 346.0884.

(*E*)-3'-ethylidene-1-methyl-4'-(prop-1-en-2-yl)-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165l**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161n** (51 mg, 0.18 mmol, 79% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.43) as eluents, the desired product was obtained in 25% yield (13 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 2H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 8.2 Hz, 1H), 6.10 – 6.03 (m, 1H), 5.38 (q, *J* = 7.1 Hz, 1H), 4.93 (s, 2H), 4.67 (dd, *J* = 17.0, 3.3 Hz, 1H), 4.45 (dd, *J* = 17.0, 3.5 Hz, 1H), 3.21 (s, 3H), 1.88 (s, 3H), 1.70 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.81, 145.12, 143.72, 138.42, 130.27, 129.71, 129.68, 126.26, 125.56, 124.91, 122.91, 113.81, 108.67, 79.95, 63.52, 26.37, 21.37, 15.70. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{20}O_2N]^+$: 282.1489, found: 282.1499.

(*E*)-4'-cyclopropyl-3'-ethylidene-1-methyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165m**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161o** (51 mg, 0.18 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.30) as eluents, the desired product was obtained in 75% yield (38 mg, 0.14 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.31 (td, *J* = 7.7, 1.2 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.03 (td, *J*

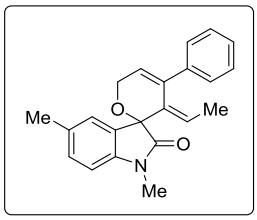
= 7.7, 0.9 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 5.78 (s, 1H), 5.27 (q, *J* = 7.5 Hz, 1H), 4.65 (d, *J* = 17.6 Hz, 1H), 4.39 (d, *J* = 17.6 Hz, 1H), 3.19 (s, 3H), 2.01 (d, *J* = 7.5 Hz, 3H), 1.76 – 1.67 (m, 1H), 0.84 – 0.71 (m, 2H), 0.67 – 0.56 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.62, 143.89, 135.65, 132.08, 129.98, 129.68, 124.80, 124.16, 123.74, 122.88, 108.57, 79.98, 63.20, 26.26, 17.06, 15.46, 8.30, 7.54. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{20}O_2N]^+$: 282.1489, found: 282.1496.

(*E*)-3'-ethylidene-1-methyl-4'-propyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



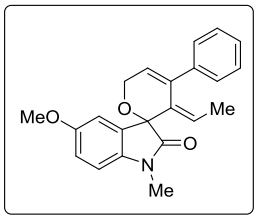
(**165n**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161p** (50 mg, 0.18 mmol, 81% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.35) as eluents, the desired product was obtained in 48% yield (24 mg, 0.08 mmol) as a yellow solid. **mp**: 96 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 4H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.83 (s, 1H), 5.82 (s, 1H), 5.21 (q, *J* = 7.5 Hz, 1H), 4.66 (d, *J* = 17.8 Hz, 1H), 4.40 (d, *J* = 17.8 Hz, 1H), 3.20 (s, 3H), 2.45 (tq, *J* = 15.5, 7.6 Hz, 3H), 1.82 (d, *J* = 7.5 Hz, 3H), 1.55 – 1.45 (m, 2H), 0.97 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.70, 143.88, 135.03, 131.56, 130.02, 129.66, 125.27, 124.95, 123.30, 122.83, 108.57, 80.19, 63.17, 38.30, 26.29, 22.23, 15.45, 14.06. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{22}O_2N]^+$: 284.1645, found: 284.1635.

(*E*)-3'-ethylidene-1,5-dimethyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one

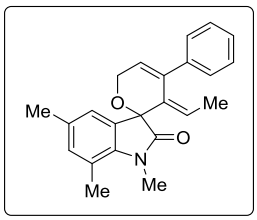


(**165o**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161q** (28 mg, 0.08 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.43) as eluents, the desired product was obtained in 71% yield (20 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.35 – 7.26 (m, 3H), 7.24 – 7.19 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 6.06 (s, 1H), 5.41 (q, *J* = 7.3 Hz, 1H), 4.82 (dd, *J* = 17.7, 2.9 Hz, 1H), 4.60 (dd, *J* = 17.7, 3.0 Hz, 1H), 3.23 (s, 3H), 2.31 (s, 3H), 1.13 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.45, 142.05, 141.52, 136.55, 132.60, 130.98, 130.02, 129.57, 128.51, 128.49, 127.37, 127.16, 125.99, 125.69, 108.49, 79.85, 63.77, 26.42, 21.31, 16.38. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{22}O_2N]^+$: 332.1645, found: 332.1637.

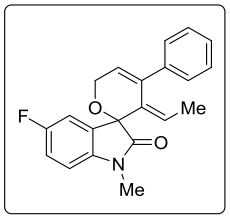
(*E*)-3'-ethylidene-5-methoxy-1-methyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165p**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161r** (45 mg, 0.13 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.35) as eluents, the desired product was obtained in 51% yield (23 mg, 0.07 mmol) as a dark red oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42 – 7.27 (m, 3H), 7.25 – 7.16 (m, 2H), 7.03 (d, *J* = 2.5 Hz, 1H), 6.88 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 6.06 (s, 1H), 5.44 (q, *J* = 7.4 Hz, 1H), 4.82 (dd, *J* = 17.8, 3.1 Hz, 1H), 4.60 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.74 (s, 3H), 3.23 (s, 3H), 1.13 (d, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.17, 156.23, 141.87, 137.26, 136.55, 130.77, 130.60, 128.52, 128.38, 127.30, 127.21, 126.23, 113.87, 112.41, 109.08, 79.93, 63.78, 55.99, 26.50, 16.42. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1426.



(*E*)-3'-ethylidene-1,5,7-trimethyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165q**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161s** (40 mg, 0.12 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.30) as eluents, the desired product was obtained in 75% yield (30 mg, 0.09 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.16 (m, 5H), 7.04 (s, 1H), 6.89 (s, 1H), 6.06 (s, 1H), 5.35 (q, *J* = 7.2 Hz, 1H), 4.83 (dd, *J* = 17.5, 2.9 Hz, 1H), 4.57 (dd, *J* = 17.5, 3.2 Hz, 1H), 3.50 (s, 3H), 2.55 (s, 3H), 2.25 (s, 3H), 1.12 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.37, 142.10, 139.12, 136.47, 134.02, 132.47, 131.31, 130.43, 128.62, 128.47, 127.37, 127.09, 126.03, 123.64, 119.97, 79.15, 63.59, 29.76, 20.95, 19.16, 16.38. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1607.

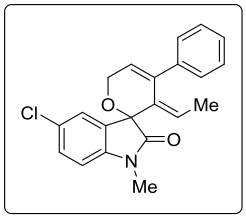


(*E*)-3'-ethylidene-5-fluoro-1-methyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165r**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161t** (41 mg, 0.12 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.35) as eluents, the desired product was obtained in 51% yield (21 mg, 0.06 mmol) as an orange oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 – 7.20 (m, 3H), 7.18 – 7.09 (m, 3H), 7.02 (td,

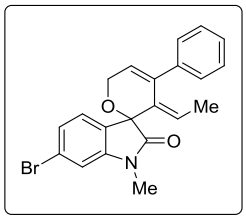


J = 8.7, 2.6 Hz, 1H), 6.78 (dd, *J* = 8.7, 4.1 Hz, 1H), 6.03 (s, 1H), 5.41 (q, *J* = 7.3 Hz, 1H), 4.78 (dd, *J* = 17.9, 3.0 Hz, 1H), 4.55 (dd, *J* = 17.9, 3.0 Hz, 1H), 3.21 (s, 3H), 1.10 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.14, 159.38 (d, *J* = 241.3 Hz), 141.61, 139.75, 136.49, 130.86 (d, *J* = 7.7 Hz), 130.43, 128.60, 128.28, 127.36, 127.23, 126.53, 115.94 (d, *J* = 23.5 Hz), 113.04 (d, *J* = 25.3 Hz), 109.27 (d, *J* = 8.0 Hz), 79.69, 63.84, 26.58, 16.45. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NFNa]^+$: 358.1214, found: 358.1225.

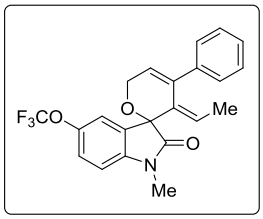
(*E*)-5-chloro-3'-ethylidene-1-methyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165s**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161u** (40 mg, 0.11 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.34) as eluents, the desired product was obtained in 50% yield (20 mg, 0.06 mmol) as an orange oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 5H), 7.21 (d, *J* = 1.8 Hz, 1H), 7.19 (s, 1H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.07 (d, *J* = 1.1 Hz, 1H), 5.42 (q, *J* = 7.3 Hz, 1H), 4.82 (dd, *J* = 17.8, 3.1 Hz, 1H), 4.59 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.24 (s, 3H), 1.14 (d, *J* = 7.3 Hz, 3H).**^{13}C NMR** (75 MHz, $CDCl_3$) δ 174.00, 142.40, 141.65, 136.42, 131.03, 130.38, 129.69, 128.60, 128.41, 128.33, 127.35, 127.29, 126.58, 125.27, 109.73, 79.58, 63.83, 26.54, 16.44. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NCl]^+$: 352.1099, found: 352.1107.



(*E*)-6-bromo-3'-ethylidene-1-methyl-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**165t**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161v** (43 mg, 0.11 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/8 (R_f = 0.28) as eluents, the desired product was obtained in 58% yield (25 mg, 0.06 mmol) as an orange oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.22 (m, 4H), 7.21 – 7.16 (m, 3H), 7.05 (d, *J* = 1.7 Hz, 1H), 6.08 – 6.03 (m, 1H), 5.42 (q, *J* = 7.1 Hz, 1H), 4.80 (dd, *J* = 17.8, 3.1 Hz, 1H), 4.57 (dd, *J* = 17.8, 3.1 Hz, 1H), 3.24 (s, 3H), 1.14 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.18, 145.20, 141.64, 136.52, 130.51, 128.60, 128.39, 128.36, 127.36, 127.21, 126.34, 126.15, 125.78, 123.57, 112.35, 79.33, 63.86, 26.54, 16.43. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NBr]^+$: 396.0594, found: 396.0600.

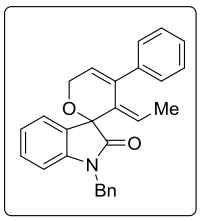


(*E*)-3'-ethylidene-1-methyl-4'-phenyl-5-(trifluoromethoxy)-3',6'-dihydrospiro



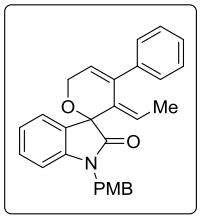
[indoline-3,2'-pyran]-2-one (**165u**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161w** (49 mg, 0.12 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.20) as eluents, the desired product was obtained in 65% yield (32 mg, 0.08 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 – 7.27 (m, 4H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.18 (d, *J* = 6.8 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 1H), 6.09 (s, 1H), 5.43 (q, *J* = 7.2 Hz, 1H), 4.82 (dd, *J* = 17.7, 2.8 Hz, 1H), 4.58 (dd, *J* = 17.7, 3.0 Hz, 1H), 3.27 (s, 3H), 1.15 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.26, 144.95, 142.52, 141.54, 136.64, 130.95, 130.50, 128.63, 128.39, 127.42, 127.21, 126.59, 122.92, 120.67 (d, *J* = 256.9 Hz), 119.08, 109.17, 79.59, 63.86, 26.60, 16.38. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{19}O_3NF_3]^+$: 402.1312, found: 402.1323.

(*E*)-1-benzyl-3'-ethylidene-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



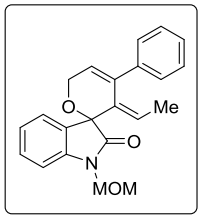
(**165v**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161x** (42 mg, 0.11 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/8 (R_f = 0.31) as eluents, the desired product was obtained in 45% yield (19 mg, 0.05 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 6.8 Hz, 1H), 7.38 – 7.30 (m, 6H), 7.30 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 7.01 (td, *J* = 7.6, 0.8 Hz, 1H), 6.76 (d, *J* = 7.6 Hz, 1H), 6.10 (s, 1H), 5.48 (q, *J* = 7.1 Hz, 1H), 5.05 (d, *J* = 15.8 Hz, 1H), 4.89 (d, *J* = 15.8 Hz, 1H), 4.86 (dd, *J* = 17.7, 3.0 Hz, 1H), 4.63 (dd, *J* = 17.7, 3.1 Hz, 1H), 1.16 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.59, 142.95, 141.90, 136.64, 135.82, 131.13, 129.68, 129.60, 128.96, 128.58, 128.55, 127.75, 127.35, 127.31, 127.25, 126.06, 124.97, 123.04, 109.83, 79.75, 63.85, 43.87, 16.48. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{27}H_{24}O_2N]^+$: 394.1802, found: 394.1810.

(*E*)-3'-ethylidene-1-(4-methoxybenzyl)-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran



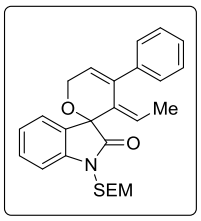
]-2-one (**165w**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161y** (24 mg, 0.06 mmol, 73% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.35) as eluents, the desired product was obtained in 42% yield (10 mg, 0.02 mmol) as a yellow oil. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.35 – 7.19 (m, 8H), 7.00 (td, *J* = 7.6, 0.9 Hz, 1H), 6.90 – 6.83 (m, 2H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.09 (td, *J* = 3.1, 1.4 Hz, 1H), 5.47 (q, *J* = 7.0 Hz, 1H), 4.98 (d, *J* = 15.4 Hz, 1H), 4.85 (dd, *J* = 17.7, 3.2 Hz, 1H), 4.83 (d, *J* = 15.4 Hz, 1H), 4.62 (dd, *J* = 17.7, 3.2 Hz, 1H), 3.78 (s, 3H), 1.15 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.52, 159.22, 142.96, 141.91, 136.65, 131.09, 129.65, 129.59, 128.76, 128.56, 127.87, 127.31, 127.25, 126.02, 124.92, 122.98, 114.36, 109.86, 79.72, 63.86, 55.42, 43.36, 16.51. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{28}H_{25}O_3NNa]^+$: 446.1727, found: 446.1734.

(*E*)-3'-ethylidene-1-(methoxymethyl)-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-



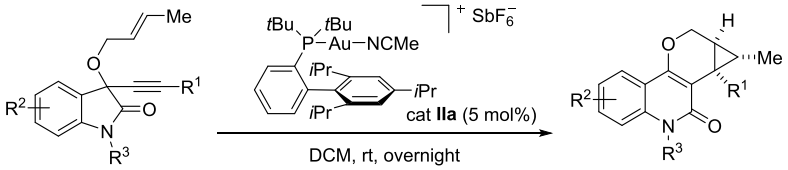
2-one (**165x**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161z** (31 mg, 0.09 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.33) as eluents, the desired product was obtained in 29% yield (9 mg, 0.03 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.8 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.24 – 7.17 (m, 2H), 7.09 (t, *J* = 8.6 Hz, 2H), 6.09 (s, 1H), 5.43 (q, *J* = 7.3 Hz, 1H), 5.23 (d, *J* = 10.9 Hz, 1H), 5.14 (d, *J* = 10.9 Hz, 1H), 4.82 (dd, *J* = 17.7, 3.0 Hz, 1H), 4.61 (dd, *J* = 17.7, 3.1 Hz, 1H), 3.38 (s, 3H), 1.14 (d, *J* = 7.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 142.36, 142.08, 130.21, 128.82, 127.53, 126.55, 125.43, 123.81, 110.51, 71.87, 64.08, 56.72, 16.72. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1405.

(*E*)-3'-ethylidene-4'-phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-3',6'-dihydrospiro



[indoline -3,2'-pyran]-2-one (**165y**) was prepared according to the general procedure for the gold catalyzed *C*-migration reaction, by using **161aa** (33 mg, 0.08 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/10 (R_f = 0.33) as eluents, the desired product was obtained in 70% yield (23 mg, 0.05 mmol) as a pale yellow solid. **mp**: 117 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.8, 1.2 Hz, 1H), 7.34 – 7.26 (m, 3H), 7.23 – 7.18 (m, 2H), 7.12 (d, *J* = 7.8 Hz, 1H), 7.09 (td, *J* = 7.6, 0.9 Hz, 1H), 6.13 – 6.04 (m, 1H), 5.41 (q, *J* = 7.3 Hz, 1H), 5.28 (d, *J* = 11.1 Hz, 1H), 5.13 (d, *J* = 11.1 Hz, 1H), 4.82 (dd, *J* = 17.7, 3.0 Hz, 1H), 4.61 (dd, *J* = 17.7, 3.1 Hz, 1H), 3.66 – 3.57 (m, 2H), 1.13 (d, *J* = 7.3 Hz, 2H), 1.01 – 0.91 (m, 2H), -0.02 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.86, 142.32, 141.89, 136.41, 131.09, 129.93, 129.08, 128.61, 128.55, 127.29, 127.24, 126.26, 125.16, 123.45, 110.37, 109.73, 79.98, 69.62, 66.17, 63.83, 17.96, 16.45, -1.32. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{26}H_{31}O_3NNaSi]^+$: 456.1965, found: 456.1953.

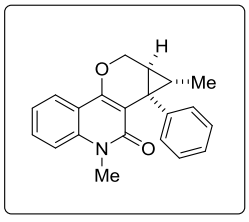
5.4.6 Gold(I) catalyzed acyl-migration reaction of crotylated 1,6-enyne (161)



164 (*E*:*Z*=3:1) **166**

At 0 °C, to a DCM (0.5 ml) solution of 1,6-enyne (0.1 mmol) was added a solution of cat **IIa** (4.5 mg, 5 μmol) in DCM (0.5 ml). After warming to room temperature, the reaction mixture was stirred overnight. After TLC showed full conversion of the starting material, the mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as the eluent) to obtain the desired product.

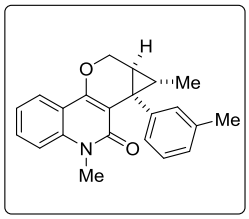
1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H



)-one (**166a**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161a** (30 mg, 0.09 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether =

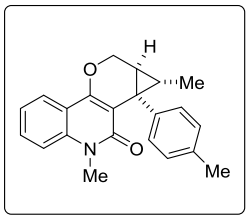
1/5 (R_f = 0.24) as eluents, the desired product was obtained in 67% yield (20 mg, 0.06 mmol) as a brown oil. The recrystallization was performed from DCM and petroleum ether. **mp** 196.8-197.3 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.51 – 7.45 (m, 1H), 7.27 (t, *J* = 7.8 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.21 – 7.15 (m, 2H), 5.05 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.93 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.57 (s, 3H), 1.61 – 1.54 (m, 1H), 1.30 – 1.23 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.29, 158.12, 140.01, 138.71, 132.63, 130.44, 127.53, 126.50, 123.53, 121.50, 116.44, 115.72, 113.80, 71.77, 31.49, 29.26, 26.70, 26.50, 16.50. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1320.

1,3-dimethyl-1a-(m-tolyl)-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(



1H)-one (**166b**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161c** (45 mg, 0.14 mmol, 84% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/5 (R_f = 0.30) as eluents, the desired product was obtained in 31% yield (14 mg, 0.04 mmol) as a yellow solid. **mp**: 135 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.55 – 7.47 (m, 1H), 7.42 (s, 1H), 7.28 – 7.16 (m, 3H), 7.02 (d, *J* = 7.7 Hz, 1H), 5.08 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.95 (dd, *J* = 11.9, 6.0 Hz, 1H), 3.60 (s, 3H), 2.33 (s, 3H), 1.63 – 1.53 (m, 1H), 1.30 – 1.26 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.33, 158.15, 139.97, 138.79, 137.05, 133.10, 130.45, 129.97, 127.36, 127.31, 123.58, 121.52, 116.55, 115.97, 113.84, 71.88, 60.53, 31.57, 29.35, 26.62, 21.59, 16.56. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1636.

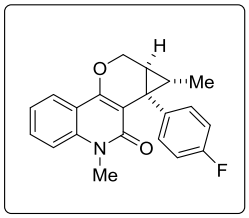
1,3-dimethyl-1a-(p-tolyl)-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1



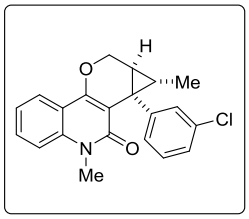
H)-one (**166c**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161d** (33 mg, 0.10 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/5 (R_f = 0.30) as eluents, the desired product was obtained in 39% yield (13 mg, 0.04 mmol) as a pale orange solid. **mp**: 177 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.1 Hz, 2H), 7.52 – 7.45 (m, 1H), 7.24 (d, *J* = 7.9 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 7.07 (d, *J* = 8.1 Hz, 2H), 5.04 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.92 (dd, *J* = 11.9, 6.0 Hz, 1H), 3.57 (s, 3H), 2.29 (s, 3H), 1.59 – 1.50 (m, 1H), 1.30 – 1.22 (m, 4H). **^{13}C NMR** (126

MHz, $CDCl_3$) δ 162.63, 158.29, 139.01, 137.26, 136.31, 132.75, 130.68, 128.59, 123.82, 121.77, 116.79, 116.19, 114.08, 72.06, 31.79, 29.58, 26.83, 26.59, 21.53, 16.75. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1645, found: 354.1454.

1a-(4-fluorophenyl)-1,3-dimethyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**166d**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161g** (29 mg, 0.09 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/7 (R_f = 0.25) as eluents, the desired product was obtained in 63% yield (18 mg, 0.05 mmol) as a pale orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.67 – 7.59 (m, 2H), 7.54 – 7.45 (m, 1H), 7.28 – 7.15 (m, 2H), 6.94 (t, *J* = 8.8 Hz, 2H), 5.04 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.93 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.58 (s, 3H), 1.58 – 1.48 (m, 1H), 1.23 (s, 4H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.35, 161.68 (d, *J* = 245.0 Hz), 158.15, 138.78, 135.64 (d, *J* = 3.2 Hz), 134.19 (d, *J* = 8.0 Hz), 130.60, 123.62, 121.65, 116.45, 115.50, 114.39 (d, *J* = 21.2 Hz), 113.92, 71.67, 31.55, 29.34, 26.61, 26.03, 16.46. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{18}O_2NFNa]^+$: 358.1214, found: 358.1223.



1a-(3-chlorophenyl)-1,3-dimethyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**166e**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161i** (27 mg, 0.08 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.25) as eluents, the desired product was obtained in 52% yield (16 mg, 0.05 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.56 (t, *J* = 1.5 Hz, 1H), 7.54 – 7.47 (m, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 2H), 7.18 – 7.13 (m, 1H), 5.03 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.94 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.58 (s, 3H), 1.62 – 1.50 (m, 1H), 1.25 (s, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.25, 158.26, 142.13, 138.85, 133.26, 132.41, 131.20, 130.69, 128.64, 126.84, 123.66, 121.67, 116.40, 115.03, 113.92, 71.42, 31.57, 29.35, 26.61, 26.50, 16.52. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NCl]^+$: 352.1099, found: 352.1113.



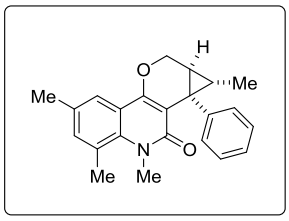
1a-(4-bromophenyl)-1,3-dimethyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**166f**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161k** (30 mg, 0.08 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/5 (R_f = 0.25) as eluents, the desired product was obtained in 50% yield (15 mg, 0.04 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.53 – 7.48 (m, 1H), 7.38 (d, *J* = 8.5 Hz, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.17 (m, 1H), 5.03 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.94 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.58 (s, 3H), 1.56 – 1.46 (m, 1H), 1.24 (s, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.55, 158.44, 139.34, 139.03, 134.66, 130.98, 130.92, 123.88, 121.93, 120.93, 116.65, 115.33, 114.19, 71.72, 31.73, 29.59, 26.81, 26.48, 16.73. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NNBr]^+$: 396.0594, found: 396.0588.

1,3-dimethyl-1a-(thiophen-3-yl)-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**166g**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161m** (51 mg, 0.16 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.16) as eluents, the desired product was obtained in 59% yield (30 mg, 0.09 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 2.9 Hz, 1H), 7.35 (d, *J* = 4.9 Hz, 1H), 7.29 – 7.10 (m, 4H), 5.04 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.88 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.61 (s, 3H), 1.63 (t, *J* = 6.7 Hz, 1H), 1.20 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.40, 158.21, 140.10, 138.69, 131.47, 130.52, 125.63, 123.51, 123.42, 121.61, 116.47, 115.22, 113.89, 71.97, 31.90, 29.34, 26.14, 21.87, 15.85. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{19}H_{18}O_2NS]^+$: 324.1053, found: 324.1062.

1,3,6-trimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**166h**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161q** (32 mg, 0.10 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/4 (R_f = 0.28) as eluents, the desired product was obtained in 38%

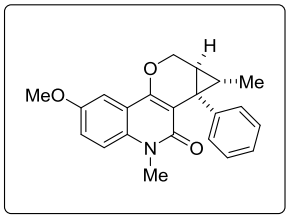
yield (12 mg, 0.04 mmol) as a pale orange solid. **mp**: 215 °C (decomposed) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.67 (d, *J* = 7.0 Hz, 2H), 7.30 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.28 – 7.23 (m, 2H), 7.17 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 8.6 Hz, 1H), 5.05 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.91 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.55 (s, 3H), 2.41 (s, 3H), 1.61 – 1.51 (m, 1H), 1.26 (s, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.23, 158.05, 140.14, 136.85, 132.67, 131.67, 131.09, 127.56, 126.51, 123.29, 116.35, 115.82, 113.83, 71.87, 31.51, 29.31, 26.79, 26.57, 20.88, 16.54. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_2N]^+$: 332.1645, found: 332.1637.

1,3,4,6-tetramethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]



quinolin-2(1H)-one (**166i**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161s** (40 mg, 0.12 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography EtOAc/petroleum ether = 1/4 (R_f = 0.20) as eluents, the desired product was obtained in 40% yield (16 mg, 0.05 mmol) as an orange solid. **mp**: 153 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.9 Hz, 2H), 7.58 (s, 1H), 7.30 – 7.19 (m, 2H), 7.19 – 7.14 (m, 1H), 7.08 (s, 1H), 5.05 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.89 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.65 (s, 3H), 2.54 (s, 3H), 2.35 (s, 3H), 1.61 – 1.50 (m, 1H), 1.23 (s, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.13, 158.16, 139.88, 135.85, 132.41, 131.32, 127.51, 126.39, 124.74, 120.93, 118.41, 109.99, 71.82, 71.48, 36.33, 31.17, 26.58, 25.74, 23.43, 20.50, 16.31. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1623.

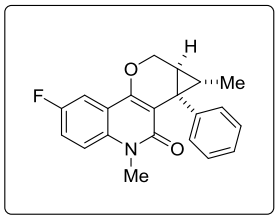
6-methoxy-1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]



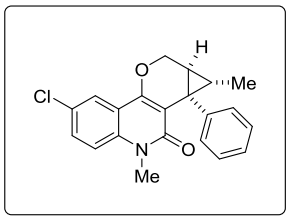
quinolin-2(1H)-one (**166j**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161r** (52 mg, 0.15 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.29) as eluents, the desired product was obtained in 40% yield (21 mg, 0.06 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 2.9 Hz, 1H), 7.31 – 7.22 (m, 3H), 7.22 – 7.12 (m, 2H), 7.11 (dd, *J* = 9.1, 2.9 Hz, 1H), 5.06 (dd, *J* = 11.9, 7.9 Hz, 1H), 3.92 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.87 (s, 3H), 3.56 (s, 3H), 1.63 – 1.51 (m, 1H), 1.26 (s, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.14, 157.94, 154.84, 140.30, 133.70, 132.93, 127.83, 126.80, 119.74, 117.32,

116.55, 115.57, 105.38, 72.21, 56.10, 31.81, 29.68, 27.15, 26.85, 16.78. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_3N]^+$: 348.1594, found: 348.1605.

6-fluoro-1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano [3,2-c]quinolin-2(1H)-one (**166k**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161t** (44 mg, 0.13 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.14) as eluents, the desired product was obtained in 48% yield (21 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.2 Hz, 2H), 7.57 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.31 – 7.07 (m, 5H), 5.01 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.91 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.52 (s, 3H), 1.59 – 1.49 (m, 1H), 1.22 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.96, 159.43, 156.72 (d, *J* = 73.4 Hz), 139.73, 135.26, 132.66, 127.61, 126.65, 118.13 (d, *J* = 23.9 Hz), 117.42 (d, *J* = 8.4 Hz), 116.71, 115.43 (d, *J* = 8.0 Hz), 109.08 (d, *J* = 24.1 Hz), 71.81, 31.61, 29.56, 26.75, 26.52, 16.50. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NF]^+$: 336.1394, found: 336.1404.



6-chloro-1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano [3,2-c]quinolin-2(1H)-one (**166l**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161u** (44 mg, 0.13 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.17) as eluents, the desired product was obtained in 50% yield (22 mg, 0.06 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 2.4 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 2H), 7.43 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.33 – 7.23 (m, 2H), 7.23 – 7.12 (m, 2H), 5.05 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.96 (dd, *J* = 11.9, 5.8 Hz, 1H), 3.55 (s, 3H), 1.65 – 1.51 (m, 1H), 1.27 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.99, 157.03, 139.67, 137.21, 132.65, 130.41, 127.62, 127.31, 126.68, 123.09, 117.56, 116.66, 115.32, 71.79, 31.62, 29.47, 26.71, 26.50, 16.49. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NCl]^+$: 352.1099, found: 352.1112.



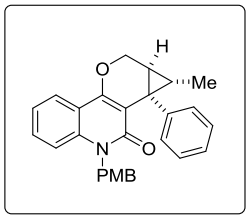
5-bromo-1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano [3,2-c]quinolin-2(1H)-one (**166m**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161v** (51 mg, 0.13 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.30) as eluents, the desired product was obtained in 47% yield (24 mg, 0.06 mmol) as a red oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.5 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.36 (s, 1H), 7.34 – 7.19 (m, 4H), 7.17 (d, *J* = 7.2 Hz, 1H), 5.01 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.91 (dd, *J* = 11.9, 5.9 Hz, 1H), 3.50 (s, 3H), 1.53 (t, *J* = 6.4 Hz, 1H), 1.22 (s, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.11, 157.70, 139.70, 139.59, 132.63, 127.61, 126.66, 124.99, 124.84, 124.75, 116.79, 115.95, 115.31, 71.74, 31.54, 29.41, 26.64, 26.46, 16.49. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{19}O_2NBr]^+$: 396.0594, found: 396.0602.

1,3-dimethyl-1a-phenyl-6-(trifluoromethoxy)-1a,3,9,9a-tetrahydrocyclopropa [4,5]pyrano[3,2-c]quinolin-2(1*H*)-one (**166n**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161w** (34 mg, 0.08 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.24) as eluents, the desired product was obtained in 44% yield (15 mg, 0.04 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.34 (dd, *J* = 9.1, 2.0 Hz, 1H), 7.32 – 7.16 (m, 5H), 5.05 (dd, *J* = 11.9, 7.8 Hz, 1H), 3.97 (dd, *J* = 11.9, 5.8 Hz, 1H), 3.57 (s, 3H), 1.26 (s, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.04, 157.10, 143.65, 139.63, 137.25, 132.67, 127.64, 126.73, 123.58, 120.73 (d, *J* = 257.0 Hz), 117.24, 116.85, 115.89, 115.25, 71.75, 31.71, 29.58, 26.79, 26.60, 16.49. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{19}O_3NF_3]^+$: 402.1312, found: 402.1323.

3-benzyl-1-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c] quinolin-2(1*H*)-one (**166o**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161x** (46 mg, 0.12 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.40) as eluents, the desired product was obtained in 52%

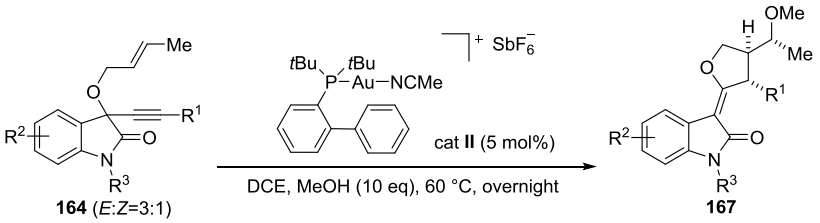
yield (24 mg, 0.06 mmol) as a brown oil. **^{1}H NMR** (500 MHz, DMSO) δ 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 2H), 7.47 – 7.42 (m, 1H), 7.32 – 7.12 (m, 9H), 7.05 (d, *J* = 7.3 Hz, 2H), 5.47 (bs, 1H), 5.27 (bs, 1H), 5.14 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.99 (dd, *J* = 12.0, 6.1 Hz, 1H), 1.66 – 1.59 (m, 1H), 1.33 – 1.26 (m, 1H), 1.14 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.65, 158.66, 140.22, 138.47, 137.22, 132.90, 130.72, 129.00, 127.82, 127.30, 126.80, 123.92, 121.88, 116.94, 115.84, 114.99, 72.17, 45.97, 31.83, 27.11, 26.61, 16.79. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{27}H_{24}O_2N]^+$: 394.1802, found: 394.1809.

3-(4-methoxybenzyl)-1-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]



pyrano[3,2-c]quinolin-2(1*H*)-one (**166p**) was prepared according to the general procedure for the gold catalyzed carbonyl-migration reaction, by using **161y** (23 mg, 0.05 mmol, 73% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.28) as eluents, the desired product was obtained in 43% yield (10 mg, 0.02 mmol) as a red oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 7.9 Hz, 1H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.34 (m, 1H), 7.28 – 7.25 (m, 2H), 7.20 – 7.12 (m, 3H), 6.99 (d, *J* = 8.2 Hz, 2H), 6.74 (d, *J* = 8.2 Hz, 2H), 5.49 (bs, 1H), 5.19 (bs, 1H), 5.09 (dd, *J* = 11.9, 8.0 Hz, 1H), 3.96 (dd, *J* = 11.9, 6.1 Hz, 1H), 3.72 (s, 3H), 1.62 – 1.58 (m, 1H), 1.34 – 1.27 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.63, 158.94, 158.62, 140.23, 138.46, 132.90, 130.66, 129.32, 128.15, 127.81, 126.77, 123.89, 121.82, 116.94, 115.88, 114.97, 114.43, 72.20, 55.60, 45.40, 31.81, 27.12, 26.60, 16.79. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{28}H_{25}O_3NNa]^+$: 446.1727, found: 446.1734.

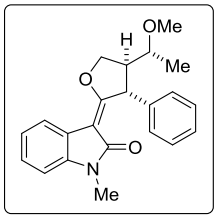
5.4.7 Gold(I) catalyzed *O*-migration reaction of crotylated 1,6-enyne (161)



To a DCE (0.5 ml) solution of 1,6-enyne (**161**, 0.5 mmol) and MeOH (41 µL, 1 mmol) in a pressure tube equipped with a stirring bar was added a solution of cat **II** (3.9 mg, 5 µmol) in DCE (0.5 mL) and the mixture was stirred at 60 °C overnight until TLC showed full conversion of the starting material. After cooling to room temperature, the reaction mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was

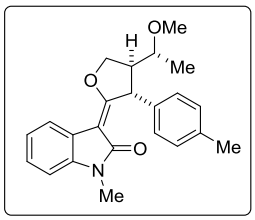
concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the desired product.

(*E*)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one



(**167a**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161a** (30 mg, 0.09 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.20) as eluents, the desired product was obtained in 73% yield (24 mg, 0.07 mmol) as a yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp:** 127.9-129.6 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.35 – 7.23 (m, 5H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.18 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.06 (td, *J* = 7.6, 0.9 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 5.06 (s, 1H), 4.73 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.60 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.36 – 3.26 (m, 4H), 3.17 (s, 3H), 2.44 (t, *J* = 6.5 Hz, 1H), 1.28 (d, *J* = 6.1 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.58, 168.06, 141.13, 140.61, 128.96, 127.08, 126.92, 126.16, 122.81, 122.53, 121.55, 107.17, 101.20, 76.98, 73.23, 56.74, 52.93, 51.21, 25.88, 16.63.**HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{24}O_3N]^+$: 350.1751, found: 350.1763.

(*E*)-3-(4-(1-methoxyethyl)-3-(p-tolyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on



e (**167b**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161d** (33 mg, 0.10 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.30) as eluents, the desired product was obtained in 64% yield (23 mg, 0.06 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 5.02 (s, 1H), 4.72 (d, *J* = 9.5 Hz, 1H), 4.60 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.33 (s, 3H), 3.32 – 3.28 (m, 1H), 3.17 (s, 3H), 2.42 (t, *J* = 6.3 Hz, 1H), 2.29 (s, 3H), 1.28 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.85, 168.07, 140.59, 138.11, 136.47, 129.66, 126.94, 126.09, 122.86, 122.49, 121.52, 107.14, 101.09, 73.25, 56.72, 53.04, 50.88, 25.90, 21.18, 16.66. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_3NNa]^+$: 386.1727, found: 386.1726.

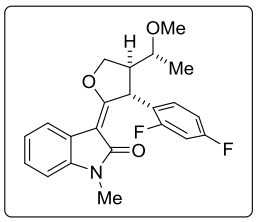
(*E*)-3-(4-(1-methoxyethyl)-3-(m-tolyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (**167c**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161c** (51 mg, 0.15 mmol, 84% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.30) as eluents, the desired product was obtained in 72% yield (40 mg, 0.11 mmol) as a pale yellow solid. **mp**: 136 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.24 – 7.13 (m, 2H), 7.12 – 6.98 (m, 5H), 6.80 (d, *J* = 7.7 Hz, 1H), 5.04 (s, 1H), 4.73 (d, *J* = 9.5 Hz, 1H), 4.59 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.34 (d, *J* = 2.4 Hz, 3H), 3.32 – 3.27 (m, 1H), 3.18 (s, 3H), 2.42 (t, *J* = 6.5 Hz, 1H), 2.32 (s, 3H), 1.29 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.94, 168.36, 141.26, 140.87, 138.81, 129.07, 128.06, 127.92, 126.38, 124.39, 123.13, 122.80, 121.80, 107.43, 101.45, 77.24, 73.42, 57.00, 53.31, 51.44, 26.16, 21.96, 16.92. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_3NNa]^+$: 386.1727, found: 386.1721.

(*E*)-3-(4-(1-methoxyethyl)-3-(o-tolyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (**167d**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161b** (33 mg, 0.10 mmol, 79% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.33) as eluents, the desired product was obtained in 41% yield (15 mg, 0.04 mmol) as a yellow solid. **mp**: 184 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.12 (td, *J* = 7.5, 1.3 Hz, 1H), 7.07 (td, *J* = 7.5, 1.0 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.23 (s, 1H), 4.72 (dd, *J* = 9.4, 1.1 Hz, 1H), 4.59 (dd, *J* = 9.4, 6.2 Hz, 1H), 3.39 – 3.32 (m, 1H), 3.33 (s, 3H), 3.17 (s, 3H), 2.61 (s, 3H), 2.29 (t, *J* = 6.2 Hz, 1H), 1.27 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.70, 168.10, 140.33, 138.97, 135.99, 130.83, 126.93, 126.13, 125.92, 125.32, 122.74, 122.30, 121.43, 109.99, 107.04, 72.86, 56.73, 51.25, 47.92, 25.80, 20.25, 16.34. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_3NNa]^+$: 386.1727, found: 386.1723.

(*E*)-3-(4-(1-methoxyethyl)-3-(4-methoxyphenyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167e) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161f** (47 mg, 0.12 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.15) as eluents, the desired product was obtained in 72% yield (34 mg, 0.09 mmol) as a pale yellow solid. **mp**: 130 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.4 Hz, 1H), 7.25 – 7.16 (m, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.88 – 6.71 (m, 5H), 5.04 (s, 1H), 4.71 (d, *J* = 9.5 Hz, 1H), 4.59 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.77 (s, 3H), 3.33 (s, 3H), 3.33 – 3.26 (m, 1H), 3.18 (s, 3H), 2.44 (t, *J* = 6.3 Hz, 1H), 1.28 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.70, 168.10, 140.33, 138.97, 135.99, 130.83, 126.93, 126.13, 125.92, 125.32, 122.74, 122.30, 121.43, 109.99, 107.04, 77.26, 72.86, 56.73, 51.25, 47.92, 25.80, 20.25, 16.34. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_4NNa]^+$: 402.1676, found: 402.1671.

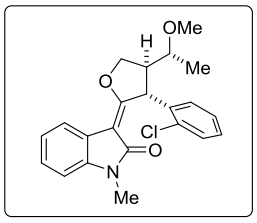
(*E*)-3-(3-(4-fluorophenyl)-4-(1-methoxyethyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167f) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161g** (36 mg, 0.11 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.14) as eluents, the desired product was obtained in 58% yield (23 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.14 (m, 3H), 7.06 (td, *J* = 7.6, 0.8 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.03 (s, 1H), 4.72 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.59 (dd, *J* = 9.5, 6.4 Hz, 1H), 3.37 – 3.30 (m, 4H), 3.18 (s, 3H), 2.42 (t, *J* = 6.4 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.25, 168.03, 161.77 (d, *J* = 245.1 Hz), 140.63, 136.96, 128.63 (d, *J* = 8.0 Hz), 126.30, 122.67, 122.57, 121.63, 115.81 (d, *J* = 21.4 Hz), 107.25, 101.25, 76.91, 73.21, 56.73, 52.91, 50.42, 25.90, 16.53. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NF]^+$: 368.1657, found: 368.1669.

(*E*)-3-(3-(2,4-difluorophenyl)-4-(1-methoxyethyl)dihydrofuran-2(3H)-ylidene)-1-methyli



ndolin-2-one (167g) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161h** (30 mg, 0.08 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.25) as eluents, the desired product was obtained in 55% yield (18 mg, 0.05 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 7.06 – 6.97 (m, 1H), 6.89 – 6.81 (m, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.73 (t, *J* = 8.3 Hz, 1H), 5.13 (s, 1H), 4.78 (dd, *J* = 9.4, 1.7 Hz, 1H), 4.54 (dd, *J* = 9.4, 6.3 Hz, 1H), 3.33 (s, 3H), 3.34 – 3.27 (m, 1H), 3.17 (s, 3H), 2.37 (t, *J* = 6.3 Hz, 1H), 1.30 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.34, 168.19, 162.38 (d, *J* = 248.2 Hz), 159.82 (d, *J* = 12.0 Hz), 140.97, 126.67, 128.85 (dd, *J* = 9.5, 5.4 Hz), 124.44 (dd, *J* = 14.6, 3.9 Hz), 122.90, 122.77, 121.93, 111.54 (dd, *J* = 21.2, 3.7 Hz), 107.55, 104.68 (t, *J* = 25.6 Hz), 101.67, 77.02, 73.55, 57.04, 52.41, 45.52, 26.16, 16.97. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{22}O_3NF_2]^+$: 386.1562, found: 386.1562.

(*E*)-3-(3-(2-chlorophenyl)-4-(1-methoxyethyl)dihydrofuran-2(3H)-ylidene)-1-methyl



indolin-2-one (167h) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161j** (32 mg, 0.09 mmol, 78% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.38) as eluents, the desired product was obtained in 86% yield (30 mg, 0.08 mmol) as a red oil. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 7.7 Hz, 1H), 7.45 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.21 (td, *J* = 7.7, 1.4 Hz, 1H), 7.17 (td, *J* = 7.7, 1.7 Hz, 1H), 7.15 – 7.05 (m, 2H), 7.00 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 5.40 (s, 1H), 4.81 (dd, *J* = 9.4, 1.5 Hz, 1H), 4.50 (dd, *J* = 9.4, 6.2 Hz, 1H), 3.47 (qd, *J* = 6.2, 6.2 Hz, 1H), 3.34 (s, 2H), 3.18 (s, 3H), 2.35 (t, *J* = 6.2 Hz, 1H), 1.35 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.83, 167.93, 138.28, 133.76, 130.09, 128.24, 127.10, 126.96, 126.13, 122.51, 122.44, 121.47, 107.09, 77.15, 72.46, 56.86, 51.47, 49.52, 25.79, 16.96. ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.83, 167.93, 140.53, 138.28, 133.76, 130.09, 128.24, 127.10, 126.96, 126.13, 122.51, 122.44, 121.47, 108.22, 107.09, 77.15, 72.46, 56.86, 51.47, 49.52, 25.79, 16.96. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NCl]^+$: 384.1361, found: 384.1366.

(*E*)-3-(3-(3-chlorophenyl)-4-(1-methoxyethyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167i) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161i** (34 mg, 0.10 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.15) as eluents, the desired product was obtained in 67% yield (25 mg, 0.07 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.25 – 7.12 (m, 5H), 7.07 (td, *J* = 7.6, 0.9 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 5.03 (s, 1H), 4.71 (dd, *J* = 9.6, 1.6 Hz, 1H), 4.58 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.33 (s, 4H), 3.18 (s, 3H), 2.43 (t, *J* = 6.5 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.40, 168.01, 143.18, 140.70, 134.75, 130.18, 127.24, 127.05, 126.39, 125.49, 122.66, 122.59, 121.66, 107.29, 101.48, 76.86, 73.09, 56.75, 52.79, 50.81, 25.91, 16.49. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NCl]^+$: 384.1361, found: 384.1378.

(*E*)-3-(3-(4-bromophenyl)-4-(1-methoxyethyl)dihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (167j) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161k** (41 mg, 0.10 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.17) as eluents, the desired product was obtained in 75% yield (33 mg, 0.08 mmol) as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.20 (td, *J* = 7.5, 0.9 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.80 (d, *J* = 7.5 Hz, 1H), 4.99 (s, 1H), 4.71 (dd, *J* = 9.6, 1.5 Hz, 1H), 4.57 (dd, *J* = 9.5, 6.5 Hz, 1H), 3.36 – 3.30 (m, 4H), 3.17 (s, 3H), 2.41 (t, *J* = 6.5 Hz, 1H), 1.26 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.77, 167.99, 140.66, 140.30, 132.06, 128.85, 126.37, 122.60, 121.65, 120.85, 107.28, 101.35, 76.88, 73.20, 56.74, 52.76, 50.63, 25.91, 16.49. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NBr]^+$: 428.0856, found: 428.0865.

(*E*)-3-(4-(1-methoxyethyl)-3-(2-(trifluoromethyl)phenyl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167k) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161l** (40 mg, 0.10 mmol, 72% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.38) as eluents, the desired product was obtained in 30% yield (13 mg, 0.03 mmol) as a pale yellow solid. **mp**: 146 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.4 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.20 (td, *J* = 7.7, 1.1 Hz, 1H), 7.12 – 7.04 (m, 2H), 6.80 (d, *J* = 7.4 Hz, 1H), 5.46 (s, 1H), 4.82 (d, *J* = 9.4 Hz, 1H), 4.49 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.53 (p, *J* = 6.0 Hz, 1H), 3.28 (s, 3H), 3.17 (s, 3H), 2.38 – 2.33 (m, 1H), 1.22 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.26, 168.11, 140.77, 132.32, 128.08 (d, *J* = 30.0 Hz), 127.49, 127.27 (d, *J* = 6.3 Hz), 127.21, 126.26, 122.83, 122.68, 121.60, 107.21, 100.92, 77.82, 71.82, 57.33, 52.12, 49.59, 25.96, 16.90. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{22}O_3NF_3Na]^+$: 440.1444, found: 440.1444.

(*E*)-3-(4-(1-methoxyethyl)-3-(thiophen-3-yl)dihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167l) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161m** (44 mg, 0.14 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.10) as eluents, the desired product was obtained in 77% yield (37 mg, 0.10 mmol) as a red oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.24 (m, 1H), 7.18 (td, *J* = 7.5, 1.2 Hz, 1H), 7.13 – 6.99 (m, 3H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.16 (s, 1H), 4.73 (dd, *J* = 9.4, 1.1 Hz, 1H), 4.60 (dd, *J* = 9.4, 6.3 Hz, 1H), 3.31 (s, 3H), 3.29 – 3.23 (m, 1H), 3.21 (s, 3H), 2.50 (t, *J* = 6.3 Hz, 1H), 1.25 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.29, 168.14, 140.51, 140.13, 127.08, 126.19, 126.16, 122.79, 122.52, 121.57, 120.95, 107.17, 100.93, 76.72, 73.50, 56.73, 51.74, 46.38, 25.91, 16.65. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{20}H_{22}O_3NS]^+$: 356.1315, found: 356.1326.

(*E*)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1,5-dimethylindolin-2-one (167m) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161q** (42 mg, 0.13 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.20) as eluents, the desired product was obtained in 67% yield (31 mg, 0.09 mmol) as a pale yellow solid. **mp**: 173 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.33 – 7.23 (m, 4H), 7.21 (t, *J* = 7.1 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 5.07 (s, 1H), 4.74 (d, *J* = 9.5 Hz, 1H), 4.60 (dd, *J* = 9.5, 6.8 Hz, 1H), 3.34 (s, 3H), 3.35 – 3.27 (m, 1H), 3.15 (s, 2H), 2.44 (t, *J* = 6.8 Hz, 1H), 2.40 (s, 3H), 1.29 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.19, 168.09, 141.18, 138.47, 130.91, 128.93, 127.06, 126.88, 126.51, 123.29, 122.80, 106.89, 101.32, 76.99, 73.10, 56.73, 52.93, 51.14, 25.90, 21.39, 16.63. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{23}O_2NNa]^+$: 368.1621, found: 368.1607.

(*E*)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1,5,7-trimethylindolin-2-one (167n) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161s** (40 mg, 0.12 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.18) as eluents, the desired product was obtained in 78% yield (34 mg, 0.09 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.34 – 7.15 (m, 5H), 6.74 (s, 1H), 5.09 (s, 1H), 4.73 (dd, *J* = 9.5, 1.3 Hz, 1H), 4.58 (dd, *J* = 9.5, 6.4 Hz, 1H), 3.43 (s, 3H), 3.34 (s, 3H), 3.30 (dd, *J* = 7.3, 6.3 Hz, 1H), 2.52 (s, 3H), 2.42 (dd, *J* = 7.3, 6.4 Hz, 1H), 2.34 (s, 3H), 1.29 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.96, 168.64, 141.24, 136.27, 130.78, 130.51, 128.91, 127.04, 126.83, 123.38, 121.33, 118.47, 101.30, 77.00, 73.04, 56.72, 52.89, 51.23, 29.12, 21.06, 19.08, 16.63. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{24}H_{28}O_3N]^+$: 378.2064, found: 378.2075.

(*E*)-5-methoxy-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167o) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161r** (47 mg, 0.14 mmol, 83% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.22) as eluents, the desired product was obtained in 64% yield (33 mg, 0.09 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 2.5 Hz, 1H), 7.43 – 7.41 (m, 1H), 7.33 – 7.23 (m, 4H), 7.23 – 7.18 (m, 1H), 6.75 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 5.06 (s, 1H), 4.73 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.60 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.86 (s, 3H), 3.34 (s, 3H), 3.31 (dd, *J* = 7.4, 6.1 Hz, 1H), 3.14 (s, 3H), 2.44 (dd, *J* = 7.4, 6.3 Hz, 1H), 1.28 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.65, 167.94, 155.49, 141.12, 134.78, 128.95, 127.06, 126.91, 123.69, 111.37, 109.52, 107.31, 101.58, 76.95, 73.27, 56.73, 56.18, 52.89, 51.18, 25.96, 16.62. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{26}O_4N]^+$: 380.1856, found: 380.1867.

(*E*)-5-fluoro-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167p) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161t** (39 mg, 0.12 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.30) as eluents, the desired product was obtained in 63% yield (27 mg, 0.07 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.35 – 7.16 (m, 5H), 6.92 – 6.82 (m, 1H), 6.67 (dd, *J* = 8.6, 4.2 Hz, 1H), 5.04 (s, 1H), 4.75 (dd, *J* = 9.6, 1.6 Hz, 1H), 4.63 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.34 (s, 4H), 3.15 (s, 3H), 2.50 – 2.41 (m, 1H), 1.27 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.69, 167.87, 159.01 (d, *J* = 236.5 Hz), 140.91, 136.63, 129.02, 127.05, 127.03, 123.83 (d, *J* = 9.9 Hz), 112.04 (d, *J* = 24.0 Hz), 110.10 (d, *J* = 26.1 Hz), 107.20 (d, *J* = 8.6 Hz), 101.08, 76.99, 73.56, 56.76, 52.83, 51.44, 26.01, 16.58. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{24}O_3N]^+$: 350.1751, found: 350.1757.

(*E*)-5-chloro-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167q) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161u** (37 mg, 0.11 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.28) as eluents, the desired product was obtained in 62% yield (25 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 2.0 Hz, 1H), 7.34 – 7.16 (m, 5H), 7.14 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 5.03 (s, 1H), 4.76 (dd, *J* = 9.6, 1.5 Hz, 1H), 4.64 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.36 – 3.29 (m, 4H), 3.15 (s, 3H), 2.46 (t, *J* = 6.4 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.19, 167.94, 141.10, 139.26, 129.29, 127.30, 127.15, 125.93, 124.43, 122.80, 108.15, 100.69, 77.26, 77.17, 73.89, 57.04, 53.05, 51.79, 26.25, 16.82. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NCl]^+$: 384.1361, found: 384.1379.

(*E*)-6-bromo-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one (167r) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161v** (42 mg, 0.11 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.33) as eluents, the desired product was obtained in 70% yield (32 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.19 (m, 6H), 7.17 (d, *J* = 7.9 Hz, 1H), 6.92 (s, 1H), 5.01 (s, 1H), 4.73 (d, *J* = 9.5 Hz, 1H), 4.68 – 4.57 (m, 1H), 3.33 (s, 4H), 3.14 (s, 3H), 2.45 (s, 1H), 1.27 (d, *J* = 5.7 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.70, 168.08, 141.97, 141.14, 129.28, 127.35, 127.31, 124.51, 123.79, 121.98, 119.68, 110.79, 100.67, 77.24, 73.78, 57.02, 53.10, 51.76, 26.23, 16.85. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{23}O_3NBr]^+$: 428.0856, found: 428.0866.

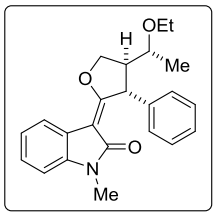
(*E*)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methyl-5-(trifluoro methoxy)indolin-2-one (**167s**) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161w** (35 mg, 0.09 mmol, 80% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.11) as eluents, the desired product was obtained in 71% yield (27 mg, 0.06 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.35 – 7.29 (m, 2H), 7.28 – 7.15 (m, 3H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 5.04 (s, 1H), 4.77 (dd, *J* = 9.6, 1.6 Hz, 1H), 4.65 (dd, *J* = 9.6, 6.5 Hz, 1H), 3.34 (s, 4H), 3.16 (s, 3H), 2.46 (t, *J* = 6.5 Hz, 1H), 1.27 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.27, 167.88, 144.29, 140.82, 139.03, 129.05, 127.06, 123.76, 120.91 (d, *J* = 255.9 Hz), 118.92, 116.15, 107.17, 100.61, 76.97, 73.80, 56.77, 52.80, 51.60, 32.77, 26.04, 16.57. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{23}O_4NF_3]^+$: 434.1574, found: 434.1573.

(*E*)-1-benzyl-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene) indolin-2-one (**167t**) was prepared according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161x** (39 mg, 0.10 mmol, 76% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.29) as eluents, the desired product was obtained in 69% yield (29 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 6.4 Hz, 1H), 7.37 – 7.13 (m, 11H), 7.12 – 7.05 (m, 1H), 7.05 – 7.00 (m, 1H), 6.68 (d, *J* = 7.4 Hz, 1H), 5.10 (s, 1H), 5.01 (d, *J* = 15.8 Hz, 1H), 4.81 – 4.74 (m, 2H), 4.63 (dd, *J* = 9.5, 6.6 Hz, 1H), 3.36 (s, 4H), 2.47 (t, *J* = 6.6 Hz, 1H), 1.31 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.95, 167.98, 141.13, 139.75, 137.01, 128.95, 128.65, 127.33, 127.27, 127.10, 126.92, 126.09, 122.96, 122.60, 121.62, 108.20, 101.07, 76.91, 73.35, 56.74, 53.03, 51.30, 43.43, 16.72. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{26}H_{28}O_3N]^+$: 426.2064, found: 426.2076.

(*E*)-1-(4-methoxybenzyl)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)indolin-2-one (167u) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161y** (25 mg, 0.06 mmol, 73% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.28) as eluents, the desired product was obtained in 60% yield (16 mg, 0.04 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.25 (m, 4H), 7.25 – 7.20 (m, 1H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.07 (td, *J* = 7.5, 1.2 Hz, 1H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.09 (s, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.75 (dd, *J* = 9.6, 1.5 Hz, 1H), 4.70 (d, *J* = 15.6 Hz, 1H), 4.61 (dd, *J* = 9.6, 6.6 Hz, 1H), 3.74 (s, 3H), 3.36 (s, 4H), 2.46 (t, *J* = 6.6 Hz, 1H), 1.31 (d, *J* = 6.1 Hz, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.09, 168.20, 159.15, 141.40, 140.04, 129.42, 129.21, 128.95, 127.37, 127.17, 126.33, 123.23, 122.85, 121.82, 114.34, 108.46, 101.40, 77.16, 73.57, 57.00, 55.62, 53.30, 51.52, 43.14, 16.99. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{29}H_{30}O_4N]^+$: 456.2169, found: 456.2179.

(*E*)-3-(4-(1-methoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-(methoxymethyl) indolin -2-one (**167v**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161z** (27 mg, 0.08 mmol, 77% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.20) as eluents, the desired product was obtained in 71% yield (21 mg, 0.06 mmol) as a yellow solid. **mp**: 107 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.33 – 7.16 (m, 6H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 5.15 (d, *J* = 10.9 Hz, 1H), 5.05 (s, 1H), 5.03 (d, *J* = 10.9 Hz, 1H), 4.75 (dd, *J* = 9.5, 1.5 Hz, 1H), 4.62 (dd, *J* = 9.5, 6.7 Hz, 1H), 3.34 (s, 3H), 3.41 – 3.29 (m, 1H), 3.24 (s, 3H), 2.46 (t, *J* = 6.7 Hz, 1H), 1.29 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.45, 168.35, 140.96, 138.97, 128.95, 127.05, 126.95, 126.32, 122.84, 122.67, 122.21, 108.57, 100.87, 76.92, 73.43, 71.10, 56.74, 56.13, 52.92, 51.41, 16.64. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_4NNa]^+$: 402.1676, found: 402.1669.

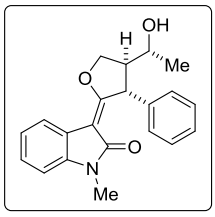
(*E*)-3-(-4-(-1-ethoxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-one



(**167w**) was prepared from according to the general procedure for the gold catalyzed *O*-migration reaction with MeOH as nucleophile, by using **161a** (30 mg, 0.09 mmol, 82% (*E*)-isomer) as the starting material. After the purification done by silica gel column chromatography with Et_2O/petroleum ether = 1/2 (R_f = 0.25) as eluents, the desired product was obtained in 76% yield (26 mg, 0.07 mmol) as a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.21 (d, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.06 (s, 1H), 4.74 (d, *J* = 9.5 Hz, 1H), 4.59 (dd, *J* = 9.4, 6.5 Hz, 1H), 3.66 – 3.57 (m, 1H), 3.43 – 3.32 (m, 2H), 3.17 (s, 3H), 2.43 (t, *J* = 6.5 Hz, 1H), 1.29 (d, *J* = 6.1 Hz, 3H), 1.15 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.70, 168.07, 141.01, 140.54, 128.95, 127.06, 126.91, 126.12, 122.78, 122.48, 121.55, 107.17, 101.16, 75.23, 73.31, 64.51, 52.98, 51.23, 25.89, 17.47, 15.55. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{26}O_3N]^+$:364.1907, found:364.1902.

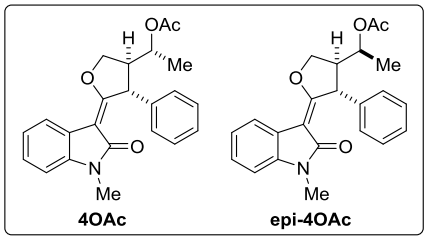
5.4.8 Compounds isolated from the condition screening

(*E*)-3-(-4-(-1-hydroxyethyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on



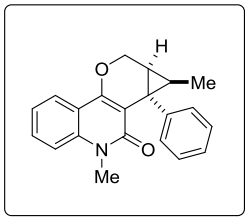
e (**167OH**) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.5 Hz, 1H), 7.34 – 7.23 (m, 4H), 7.23 – 7.14 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.5 Hz, 1H), 5.07 (s, 1H), 4.81 (d, *J* = 9.6 Hz, 1H), 4.62 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.89 (qd, *J* = 6.3 Hz, 6.3 Hz, 1H), 3.12 (s, 3H), 2.40 (dd, *J* = 6.3 Hz, 1H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.25 (s, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.52, 168.14, 140.97, 140.49, 129.00, 127.04, 127.00, 126.20, 122.70, 122.53, 121.66, 107.26, 101.20, 72.92, 68.34, 54.15, 51.51, 25.88, 21.70. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{22}O_3N]^+$: 336.1594, found: 336.1589.

1-(-5-((*E*)-1-methyl-2-oxoindolin-3-ylidene)-4-phenyltetrahydrofuran-3-yl)ethyl



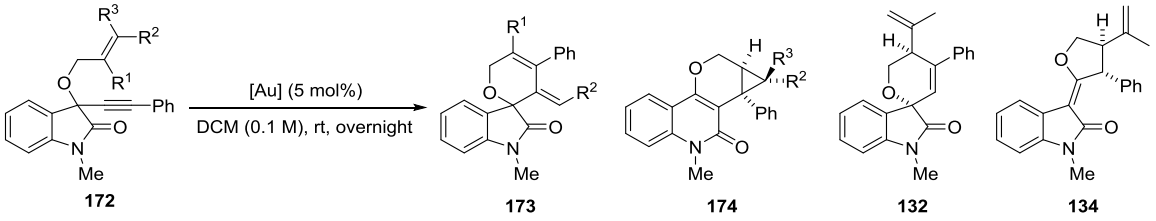
acetate (**167OAc**/***epi*-167OAc = 4/3**) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.3 Hz, 1H, 4OAc), 7.77 (d, *J* = 7.2 Hz, 1H, epi-4OAc), 7.35 – 7.18 (m, 6H, 4OAc and epi-4OAc), 7.10 - 7.05 (m, 1H, 4OAc and epi-4OAc), 6.82 (d, *J* = 7.7 Hz, 1H, 4OAc), 6.79 (d, *J* = 7.7 Hz, 1H, epi-4OAc), 5.19 - 5.18 (m, 1H, 4OAc and epi-4OAc), 5.04 (qd, *J* = 6.3, 6.3

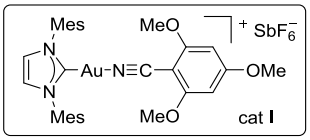
Hz, 1H, 4OAc), 4.76 (dd, *J* = 8.7, 8.7 Hz, 1H, epi-4OAc), 4.69 - 4.55 (m, 2H, 4OAc and epi-4OAc), 3.20 (s, 3H, 4OAc), 3.18 (s, 3H, epi-4OAc), 3.00 – 2.93 (m, 1H, epi-4OAc), 2.67 (t, *J* = 6.3 Hz, 1H, 4OAc), 2.04 (s, 3H, 4OAc), 1.91 (s, 3H, epi-4OAc), 1.34 - 1.27 (m, 3H, 4OAc and epi-4OAc). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{24}O_4N]^+$: 378.1700, found: 378.1700.

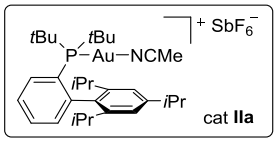
1,3-dimethyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (***epi*-166**) 

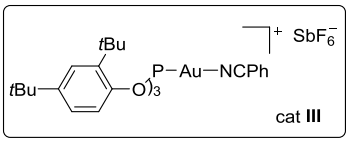
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.19 – 7.14 (m, 3H), 7.08 (t, *J* = 7.3 Hz, 1H), 4.87 (dd, *J* = 12.3, 8.5 Hz, 1H), 4.02 (dd, *J* = 12.3, 5.3 Hz, 1H), 3.51 (s, 3H), 2.14 (dq, *J* = 8.1, 6.4 Hz, 1H), 1.58 – 1.51 (m, 1H), 1.02 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.26, 158.39, 144.56, 139.18, 130.65, 128.92, 128.09, 126.20, 123.64, 121.60, 116.10, 113.99, 109.62, 65.15, 29.40, 25.93, 22.60, 21.62, 8.96. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{21}H_{20}O_2N]^+$: 318.1489, found: 318.1489.

5.4.9 Gold(I) catalyzed cycloisomerizations to 1,6-enyens with different olefins (172)





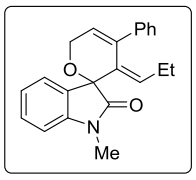




At 0 °C, to a mixture of 1,6-enyne (**172**, 0.1 mmol) and corresponding gold catalyst (5 µmol) was added dry DCM (1.0 ml)* under $Ar_{(g)}$ atmosphere. After warming to room temperature, the reaction mixture was stirred overnight and then passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents,) to obtain the desired product.

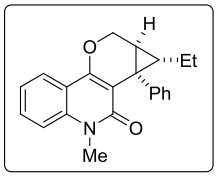
*In the formation of **173f**, dry Et_2O was applied as the solvent.

(*E*)-1-methyl-4'-phenyl-3'-propylidene-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



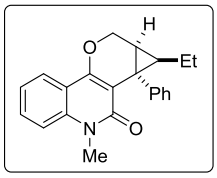
(**2b**) was prepared according to the general procedure, by using **172b** (39 mg, 0.12 mmol) and cat **III** (7 mg, 5.88 µmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.25) as eluents, the desired product was obtained in 88% yield (34 mg, 0.11 mmol) as an orange solid. **mp**: 104 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 1H), 7.34 – 7.25 (m, 3H), 7.21 (d, *J* = 7.5 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.04 (s, 1H), 5.28 (t, *J* = 7.3 Hz, 1H), 4.82 (d, *J* = 17.4 Hz, 1H), 4.60 (d, *J* = 17.4 Hz, 1H), 3.27 (s, 3H), 1.54 – 1.39 (m, 2H), 0.68 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 174.29, 143.88, 142.17, 136.68, 133.60, 129.81, 129.36, 129.30, 128.46, 128.42, 127.25, 127.18, 124.91, 123.00, 108.81, 79.53, 63.84, 26.45, 23.48, 13.58. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1461.

1-ethyl-3-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]



quinolin-2(1H)-one (**174b**) was prepared according to the general procedure, by using **172b** (40 mg, 0.12 mmol) and cat **IIa** (4 mg, 4.83 μmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.28) as eluents, the desi1red product was obtained in 40% yield (16 mg, 0.05 mmol) as a yellow solid. **mp**: 186 °C **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.29 – 7.23 (m, 3H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 5.08 (dd, *J* = 11.8, 7.9 Hz, 1H), 3.93 (dd, *J* = 11.8, 6.1 Hz, 1H), 3.59 (s, 3H), 2.04 – 1.97 (m, 1H), 1.59 (dd, *J* = 12.4, 6.1 Hz, 1H), 1.21 – 1.13 (m, 1H), 1.07 (t, *J* = 7.1 Hz, 3H), 1.06 – 0.95 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.37, 158.11, 140.46, 138.75, 132.49, 130.50, 127.59, 126.55, 123.59, 121.57, 116.50, 115.73, 113.88, 71.97, 39.44, 29.33, 27.12, 25.31, 24.54, 14.09. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1462.

1-ethyl-3-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]



quinolin-2(1H)-one (**174c**) was prepared according to the general procedure, by using **172c** (30 mg, 0.09 mmol) and cat **III** (5 mg, 4.53 μmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.25) as eluents, the desired product was obtained in 63% yield (19 mg, 0.06 mmol) as an orange solid. **mp**: 190 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.55 (t, *J* = 8.6 Hz, 1H), 7.43 (d, *J* = 7.1 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.17 (t, *J* = 7.3 Hz, 1H), 4.96 (dd, *J* = 12.3, 8.5 Hz, 1H), 4.08 (dd, *J* = 12.3, 5.5 Hz, 1H), 3.58 (s, 3H), 2.05 (dd, *J* = 15.3, 7.3 Hz, 1H), 1.71 – 1.61 (m, 1H), 1.59 – 1.48 (m, 1H), 1.35 (td, *J* = 14.5, 7.3 Hz, 1H), 1.08 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.09, 158.03, 144.68, 139.12, 130.59, 129.22, 127.99, 126.15, 123.62, 121.51, 116.01, 113.91, 109.97, 65.39, 30.63, 29.36, 25.99, 21.36, 17.79, 13.73. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1454.

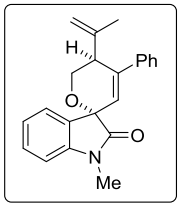
3-methyl-1,1a-diphenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**174d**) was prepared according to the general procedure, by using **172d** (30 mg, 0.08 mmol) and cat **I** (4 mg, 4.0 µmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.35) as eluents, the desired product was obtained in 40% yield (12 mg, 0.03 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.53 (t, *J* = 8.0 Hz, 1H), 7.31 – 7.26 (m, 3H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.20 – 7.13 (m, 3H), 7.08 – 7.04 (m, 3H), 6.99 – 6.94 (m, 2H), 5.15 (dd, *J* = 11.9, 7.4 Hz, 1H), 4.14 (dd, *J* = 11.9, 5.4 Hz, 1H), 3.59 (s, 3H), 2.51 (d, *J* = 5.6 Hz, 1H), 2.50 – 2.45 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 162.09, 158.12, 138.89, 138.47, 137.61, 132.79, 130.71, 128.27, 127.90, 127.14, 126.49, 126.30, 123.59, 121.66, 116.30, 115.39, 113.93, 70.90, 41.77, 30.43, 29.37, 25.72. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{26}H_{22}O_2N]^+$: 380.1645, found: 380.1643.

3-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c]quinolin-2(1H)-one (**174e**) was prepared according to the general procedure, by using **172e** (9 mg, 0.03 mmol) and cat **IIa** (1.3 mg, 1.5 µmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.18) as eluents, the desired product was obtained in 56% yield (5 mg, 0.02 mmol) as an orange soild. **mp**: 153 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 7.3 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 1H), 7.28 – 7.21 (m, 3H), 7.16 (t, *J* = 7.3 Hz, 1H), 4.96 (dd, *J* = 11.8, 7.2 Hz, 1H), 3.99 (dd, *J* = 11.8, 5.2 Hz, 1H), 3.60 (s, 3H), 2.07 (dd, *J* = 8.0, 5.2 Hz, 1H), 1.67 – 1.59 (m, 1H), 0.96 (t, *J* = 5.2 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.28, 158.00, 143.43, 138.90, 130.62, 128.41, 128.13, 126.20, 123.57, 121.63, 116.18, 113.94, 113.59, 70.57, 29.31, 22.74, 21.56, 20.40. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{20}H_{17}O_2NNa]^+$: 326.1152, found: 326.1145.

1,5'-dimethyl-3'-methylene-4'-phenyl-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**173f**) was prepared according to the general procedure, by using **172f** (50 mg, 0.16 mmol), cat **IIa** (7 mg, 7.9 µmol), and dry Et_2O (1.6 ml) as the solvent. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.50) as eluents, the desired product was obtained in 46% yield (23 mg, 0.07 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp**: 95 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 4H),

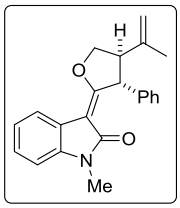
7.29 (t, *J* = 7.5 Hz, 1H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 4.82 (d, *J* = 17.1 Hz, 1H), 4.52 (s, 1H), 4.48 (s, 1H), 4.41 (d, *J* = 17.1 Hz, 1H), 3.22 (s, 3H), 1.61 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 174.11, 144.23, 140.53, 137.94, 132.54, 131.76, 130.15, 130.09, 129.46, 128.35, 127.09, 125.00, 123.22, 112.48, 108.65, 78.76, 66.39, 26.29, 16.58. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{21}H_{19}O_2NNa]^+$: 340.1308, found: 340.1308.

1-methyl-4'-phenyl-5'-(prop-1-en-2-yl)-5',6'-dihydrospiro[indoline-3,2'-pyran]-2-one



(**132**) was prepared according to the general procedure, by using **130** (30 mg, 0.09 mmol) and cat **III** (5 mg, 5.4 μmol). After silica gel column chromatography with toluene/DCM as eluents, in gradient manner,* the desired product was obtained in 33% yield (10 mg, 0.03 mmol) as a pale yellow oil. The recrystallization was performed from DCM and petroleum ether. **mp**: 150 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 – 7.22 (m, 8H), 7.08 (t, *J* = 7.1 Hz, 1H), 6.84 (dd, *J* = 8.2, 0.5 Hz, 1H), 5.96 (s, 1H), 5.05 (dd, *J* = 11.4, 3.4 Hz, 1H), 5.03 (s, 1H), 5.01 (s, 1H), 4.05 (dd, *J* = 11.4, 0.9 Hz, 1H), 3.32 (d, *J* = 3.4 Hz, 1H), 3.19 (s, 3H), 1.97 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 175.92, 144.82, 143.86, 139.78, 139.05, 130.27, 129.61, 128.46, 127.99, 125.91, 125.02, 123.38, 122.20, 114.46, 108.59, 77.73, 65.42, 43.56, 26.31, 22.31. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_2NNa]^+$: 354.1465, found: 354.1475. *In the solvent of EtOAc/ petroleum ether, the compound **132** and **134** present the same R_f value.

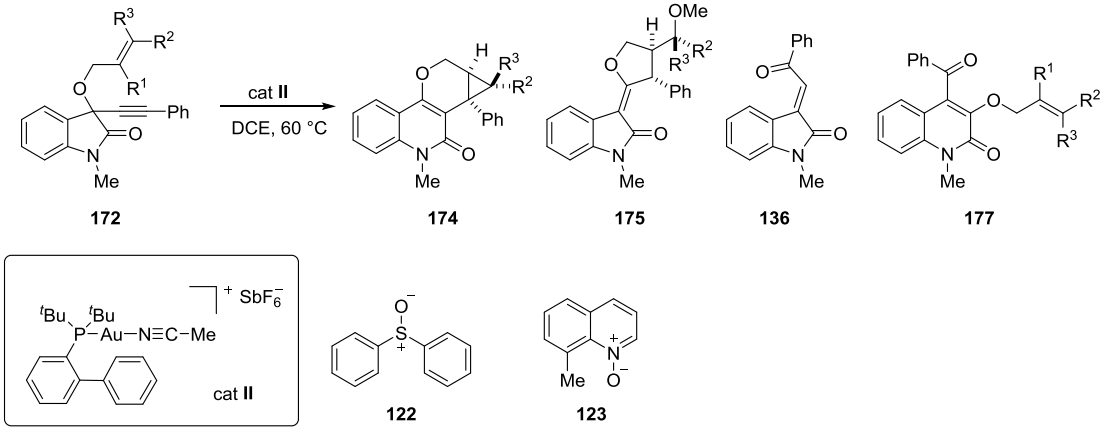
(*E*)-1-methyl-3-(3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene)indolin-2-one



(**134**) [101] was prepared according to the general procedure, by using **130** (50 mg, 0.15 mmol) and cat **IIa** (6 mg, 7.5 μmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.26) as eluents, the desired product was obtained in 51% yield (25 mg, 0.08 mmol) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.4 Hz, 1H), 7.36 – 7.13 (m, 6H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 5.15 (s, 1H), 4.83 (s, 1H), 4.81 (s, 1H), 4.69 (dd, *J* = 9.4, 6.1 Hz, 1H), 4.56 (d, *J* = 9.4 Hz, 1H), 3.16 (s, 3H), 2.97 (d, *J* = 6.1 Hz, 1H), 1.80 (s, 3H).

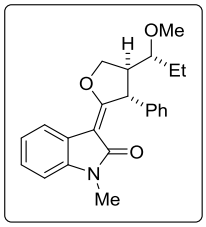
5.4.10 Gold(I) catalyzed cycloisomerizations with allyl moiety and nucleophile variations

To a mixture of 1,6-enyne (**172**, 0.15 mmol), gold(I) catalyst (**II**), and corresponding nucleophile, *i.e.* dry MeOH (61 µL, 1.51 mmol), or *N*-oxide **10** [4053-38-7] (27 mg, 0.17 mmol), in a pressure tube with a stirring bar was added dry DCE (1.5 mL). The mixture was stirred at 60 °C overnight until TLC showed full conversion of the starting material. After cooling to room temperature, the reaction mixture was passed through a short pad of silica gel (Et_2O as the eluent). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography (EtOAc/petroleum ether as eluents) to obtain the desired product.



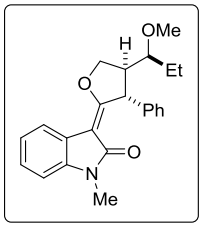
172 **174** **175** **136** **177** **122** **123**

(*E*)-3-(4-(1-methoxypropyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on



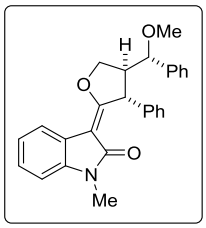
e (**175b**) was prepared according to the general procedure, by using **172b** (40 mg, 0.12 mmol) and MeOH (48 µL, 1.21 mmol) as the nucleophile. After silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.33) as eluents, the desired product was obtained in 50% yield (22 mg, 0.06 mmol) as an orange solid. **mp**: 108 °C ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.0 Hz, 1H), 7.35 – 7.15 (m, 6H), 7.06 (td, *J* = 7.7, 0.8 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 5.04 (s, 1H), 4.70 (dd, *J* = 9.5, 1.4 Hz, 1H), 4.61 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.35 (s, 3H), 3.17 (s, 3H), 3.16 – 3.13 (m, 1H), 2.54 (t, *J* = 6.8 Hz, 1H), 1.78 – 1.61 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 172.69, 168.07, 141.05, 140.53, 128.99, 127.06, 126.95, 126.14, 122.75, 122.50, 121.57, 107.19, 101.10, 82.10, 73.22, 57.90, 51.34, 49.69, 25.90, 23.26, 8.94. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_3NNa]^+$: 386.1727, found: 386.1725.

(*E*)-3-(4-(1-methoxypropyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on



e (**175c**) was prepared according to the general procedure, by using **172c** (49 mg, 0.15 mmol) and MeOH (64 µL, 1.48 mmol) as the nucleophile. After silica gel column chromatography with EtOAc/petroleum ether = 1/7 (R_f = 0.27) as eluents, the desired product was obtained in 20% yield (11 mg, 0.03 mmol) as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.1 Hz, 1H), 7.34 – 7.15 (m, 6H), 7.06 (td, *J* = 7.7, 0.7 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 5.11 (s, 1H), 4.63 (dd, *J* = 9.7, 6.4 Hz, 1H), 4.56 (dd, *J* = 9.7, 1.1 Hz, 1H), 3.36 (s, 3H), 3.17 (s, 4H), 2.64 (t, *J* = 6.4 Hz, 1H), 1.60 – 1.43 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.85, 168.03, 141.41, 140.57, 128.97, 127.11, 126.87, 126.14, 122.79, 122.44, 121.53, 107.20, 101.15, 83.12, 73.57, 58.13, 50.44, 49.27, 25.90, 23.22, 9.83. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{23}H_{26}O_3N]^+$: 364.1907, found: 364.1904.

(*E*)-3-(4-(methoxy(phenyl)methyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methyl



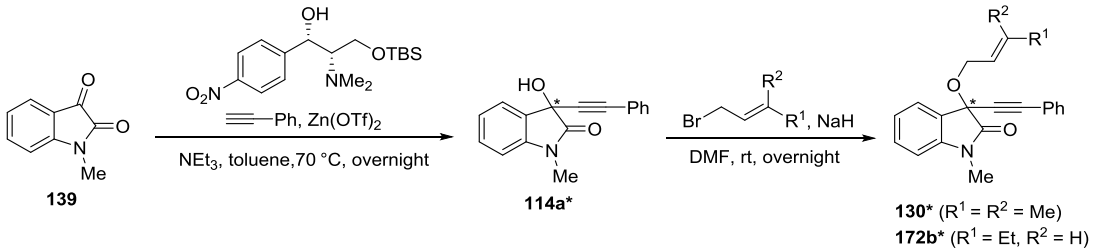
indolin-2-one (**175d**) was prepared according to the general procedure, by using **172d** (18 mg, 0.05 mmol) and MeOH (19 µL, 0.47 mmol) as the nucleophile. After silica gel column chromatography with EtOAc/petroleum ether = 1/3 (R_f = 0.27) as eluents, the desired product was obtained in 56% yield (11 mg, 0.03 mmol) as a brown solid. **mp**: 143 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 1H), 7.44 (t, *J* = 7.3 Hz, 2H), 7.41 – 7.35 (m, 1H), 7.33 (d, *J* = 7.0 Hz, 2H), 7.23 – 7.12 (m, 4H), 7.08 (td, *J* = 7.6, 0.8 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 2H), 6.80 (d, *J* = 7.7 Hz, 1H), 4.95 (dd, *J* = 9.6, 1.0 Hz, 1H), 4.82 (s, 1H), 4.61 (dd, *J* = 9.6, 5.9 Hz, 1H), 3.99 (d, *J* = 9.6 Hz, 1H), 3.19 (s, 3H), 3.15 (s, 3H), 2.68 (dd, *J* = 9.6, 5.9 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.01, 167.79, 140.69, 140.65, 139.23, 129.07, 128.81, 128.71, 128.57, 128.49, 128.20, 127.75, 126.81, 126.25, 122.70, 122.55, 121.55, 107.18, 101.57, 83.93, 73.49, 57.04, 54.11, 50.93, 25.94. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{27}H_{26}O_3N]^+$: 412.1907, found: 412.1905.

(*E*)-3-(4-(2-methoxypropan-2-yl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methyl indolin-2-one (**175g**) was prepared according to the general procedure, by using **130** (50 mg, 0.15 mmol) and MeOH (61 µL, 1.51 mmol) as the nucleophile. After silica gel column chromatography with EtOAc/petroleum ether = 1/5 (R_f = 0.18) as eluents, the desired product was obtained in 66% yield (36 mg, 0.10 mmol) as an orange solid. **mp**: 201 °C **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.0 Hz, 1H), 7.31 – 7.15 (m, 6H), 7.05 (td, *J* = 7.6, 0.8 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 5.11 (s, 1H), 4.73 (dd, *J* = 9.9, 1.6 Hz, 1H), 4.64 (dd, *J* = 9.9, 6.9 Hz, 1H), 3.18 (s, 3H), 3.16 (s, 3H), 2.53 (d, *J* = 6.9 Hz, 1H), 1.27 (s, 3H), 1.10 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.43, 167.99, 141.88, 140.47, 128.95, 126.99, 126.81, 126.05, 122.82, 122.38, 121.52, 107.18, 100.64, 75.48, 73.25, 55.74, 50.56, 49.42, 25.88, 22.05, 21.39. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{23}H_{25}O_3NNa]^+$: 386.1727, found: 386.1724.

(*E*)-4-benzoyl-1-methyl-3-(pent-2-en-1-yloxy)quinolin-2(1H)-one (**176**) was prepared according to the general procedure, by using **172b** (15 mg, 0.05 mmol) and *N*-oxide **10** (8 mg, 0.17 mmol), as the nucleophile. After silica gel column chromatography with EtOAc/petroleum ether = 1/4 (R_f = 0.37) as eluents, the desired product was obtained in 70% yield (11 mg, 0.03 mmol) as a brown oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.53 – 7.43 (m, 3H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 5.61 (dt, *J* = 15.3, 6.6 Hz, 1H), 5.36 (dt, *J* = 15.3, 6.6 Hz, 1H), 4.62 (dd, *J* = 6.6, 0.4 Hz, 2H), 3.82 (s, 3H), 1.92 (qd, *J* = 7.3, 6.6 Hz, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.58, 159.11, 143.57, 138.00, 137.35, 136.72, 134.68, 134.34, 129.72, 129.34, 128.95, 126.06, 124.15, 123.06, 118.52, 114.53, 73.56, 30.13, 25.28, 13.16. **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{21}O_3NNa]^+$: 370.1414, found: 370.1415.

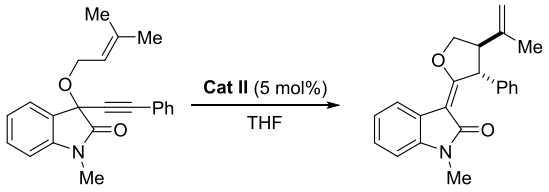
5.5 Investigations toward gold(I) catalyzed chirality transfer experiments

5.5.1 Preparation of optically enriched 1,6- enyne substrates 130* and 172b*



To a solution of $Zn(OTf)_2$ (451 mg, 1.24 mmol) and chiral ligand (483 mg, 1.37 mmol) in phenyl acetylene (2.04 ml, 18.62 mmol) was added trientylamine (0.26 ml, 1.86 mmol) under N_2 atmosphere at room temperature. After the resulting mixture was stirred for 2h, the 1-methylisatin (**139**, 1000 mg, 6.21 mmol) was introduced to the reaction mixture in one portion. After stirring for overnight at 70 °C, the mixture was diluted with DCM and washed with 0.5M $HCl_{(aq)}$ for three times. The organic phase was washed with brine, water, and dried over $MgSO_{4\,(s)}$. After removal of solvent, the crude product was purified by silica gel column chromatography with EtOAc/petroleum ether = 1/2 (R_f = 0.34) as eluents, to obtain the desire product in 93% yield (**114a***, 1519 mg, 5.77 mmol) as pale yellow solid.[69] The allylation step was employed the general procedure D for the preparation of starting material (Section 5.3) to obtain the corresponding optically enrich 1,6-enynes (**130*** or **172b***).

5.5.2 Chirality transfer reaction with oxindole based prenylated 1,6-enyne (130*)



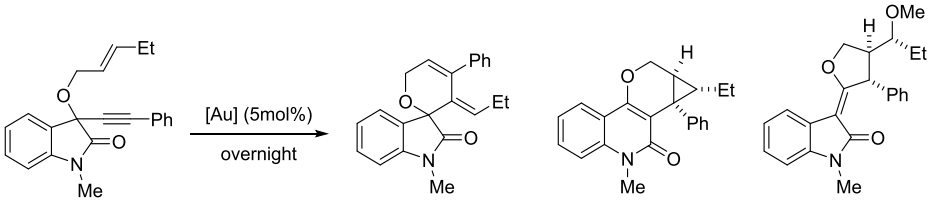
The transformations toward compound **134*** were performed according to the synthesis of **134**. The enantiomeric excess values were determined by the HPLC analysis.

1-methyl-3-((3-methylbut-2-en-1-yl)oxy)-3-(phenylethynyl)indolin-2-one (**130***) yield: 93%; major enantiomer: t_R = 42.0 min; minor enantiomer: t_R = 45.7 min; ee: 73%
(eluents: *i*hexane/ethanol = 90/10, flow rate: 0.5 ml/min, column: chiralpak IC)

(E)-1-methyl-3-((3R,4R)-3-phenyl-4-(prop-1-en-2-yl)dihydrofuran-2(3H)-ylidene) indolin-2-one (**134***) yield: 73%; major enantiomer: t_R = 24.0 min; minor enantiomer: t_R =

34.0 min; ee: 36% (eluents: *i*hexane/*i*propanol = 97/3, flow rate: 0.5 ml/min, column: chiralpak IC)

5.5.3 Chirality transfer reaction with oxindole based crotylated 1,6-enyne (172b*)



172b*, 36% ee **173b***, 88%, 36% ee[a] **174b***, 37%, 30% ee[b] **175b***, 67%, 14% ee[c]

[a]cat **III** (5 mol%), DCM, rt. [b]cat **IIa** (5 mol%), DCM, rt. [c]cat **II** (5 mol%), DCE, MeOH (10 eq), 60 °C.

The transformations toward compounds (**2b***, **3b***, and **4b***) were performed according to the synthesis of **2b**, **3b**, and **4b**. The enantiomeric excess values were determined by the HPLC analysis.

(*E*)-1-methyl-3-(pent-2-en-1-yloxy)-3-(phenylethynyl)indolin-2-one (172b*) yield: 88%; major enantiomer: t_R = 15.6 min; minor enantiomer: t_R = 18.7 min; ee: 36% (eluents: *i*hexane/ethanol = 95/5, flow rate: 0.5 ml/min, column: chiralpak IA)

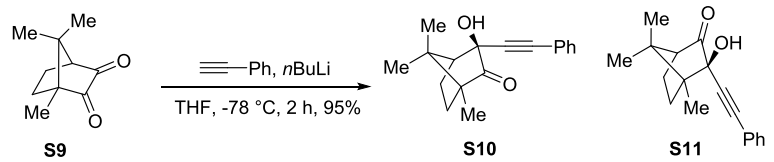
(*E*)-1-methyl-4'-phenyl-3'-propylidene-3',6'-dihydrospiro[indoline-3,2'-pyran]-2-one (**173b***) yield: 37%; major enantiomer: t_R = 18.5 min; minor enantiomer: t_R = 22.7 min; ee: 36% (eluents: *i*hexane/ethanol = 95/5, flow rate: 0.5 ml/min, column: chiralpak IA)

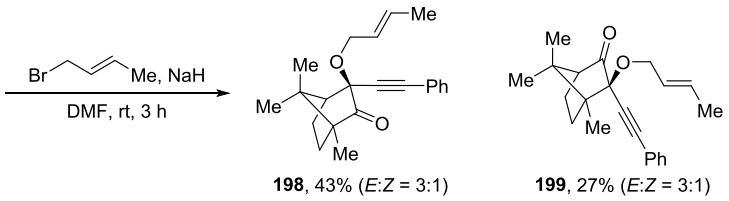
1-ethyl-3-methyl-1a-phenyl-1a,3,9,9a-tetrahydrocyclopropa[4,5]pyrano[3,2-c] quinolin -2(1H)-one (**174b***) yield: 67%; major enantiomer: t_R = 21.9 min; minor enantiomer: t_R = 20.1 min; ee: 29.85% (eluents: *i*hexane/ethanol = 95/5, flow rate: 0.5 ml/min, column: chiralpak IA)

(*E*)-3-(4-(1-methoxypropyl)-3-phenyldihydrofuran-2(3H)-ylidene)-1-methylindolin-2-on e (**175b***) major enantiomer: t_R = 18.2 min; minor enantiomer: t_R = 15.2 min; ee: 14% (eluents: *i*hexane/ethanol = 95/5, flow rate: 0.5 ml/min, column: chiralpak IA)

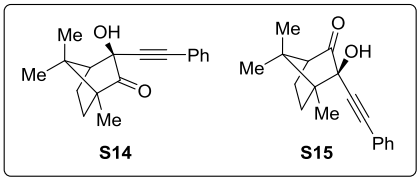
5.6 Formation of bicyclic [3.2.1] system by gold(I) catalyzed acyl group migration

5.6.1 Preparation of camphorquinon derived 1,6-enyne substrate (198 and 199)





Synthesis of propargyl alcohol (S10 and S11) At -78 °C, to a solution of phenyl acetylene

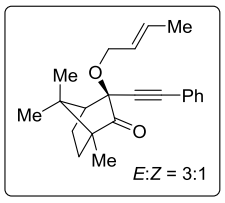


(0.25 ml, 2.26 mmol) in THF (9 ml) was slowly added 2.5 M *n*BuLi in hexanes (0.87 ml, 2.17 mmol) and the mixture was stirred for 1 h at the same temperature. To the reaction mixture was added the THF solution (9ml) of camphorquinon [10334-26-6] (**S9**, 300 mg, 1.80 mmol) in dropwise manner. After stirring for 2 h at same temperature, the reaction was quenched with $NH_4Cl_{(sat)}$ and extracted with EtOAc (30 ml) for three times. The combined organic layers were washed with brine and dried over $MgSO_{4(s)}$. After concentration under reduced pressure, the crude product was purified by flash column chromatography with EtOAc/petroleum ether = 1/10 (R_f = 0.52) as eluents, the desired products were obtained in 95% yield (461 g, 1.72 mmol, **S10**:**S11** = 1:1 by ^{1}H NMR) as a pale yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.45 – 7.39 (m, 4H), 7.37 – 7.26 (m, 6H), 3.06 (s, 1H), 2.99 (s, 1H), 2.34 (d, *J* = 5.2 Hz, 1H), 2.30 – 2.22 (m, 2H), 2.22 – 2.15 (m, 1H), 2.03 – 1.91 (m, 2H), 1.85 – 1.75 (m, 1H), 1.75 – 1.57 (m, 3H), 1.12 (s, 3H), 1.12 (s, 3H), 1.08 (s, 3H), 1.02 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{18}H_{21}O_2N]^+$: 269.1536, found: 269.1534.

Synthesis of camphorquinon derived 1,6-enyne substrate (198 and 199)

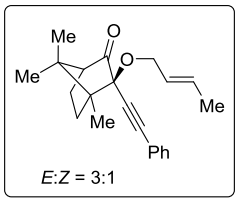
To a solution of the mixture of propargyl alcohol **S10** and **S11** (406 mg, 1.51 mmol) in DMF (15 ml) at 0 °C was added NaH 60% wt (79 mg, 1.97 mmol) in one portion and the mixture was stirred at same temperature for 1 h. To the resulting mixture was added dropwise the respective crotyl bromide (0.20 ml, 1.97 mmol). The mixture was warmed to room temperature and stirred overnight. The reaction was quenched with $NH_4Cl_{(sat)}$ and the mixture was diluted with EtOAc (60 ml). After extraction, the organic layer was washed with H_2O (150 ml) three times and once with brine, dried over $MgSO_{4(s)}$, filtered, and concentrated under reduced pressure to provide the crude product. The product was purified by flash column chromatography with the combination of petroleum ether/DCM (R_f = 0.3 in *n*-pentane) as gradient eluent to separate **199** 26% yield (first fraction, *E*:*Z* = 3:1, 132 mg, 0.41 mmol) as a pale yellow oil and **198** in 41% yield (second fraction, *E*:*Z* = 6:1, 208 mg, 0.62 mmol) as a pale yellow oil.

(3S)-3-(((*E*)-but-2-en-1-yl)oxy)-1,7,7-trimethyl-3-(phenylethynyl)bicyclo[2.2.1]heptan



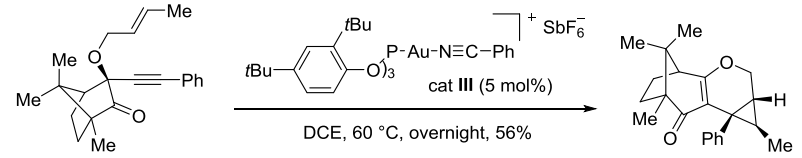
-2-one (198) According to the major (*E*)-isomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 – 7.41 (m, 2H), 7.31 (dt, *J* = 3.0, 2.0 Hz, 3H), 5.77 – 5.65 (m, 1H), 5.62 – 5.54 (m, 1H), 4.36 (dd, *J* = 11.3, 6.1 Hz, 1H), 4.30 (dd, *J* = 11.3, 6.3 Hz, 1H), 2.28 (d, *J* = 4.6 Hz, 1H), 2.17 (ddd, *J* = 13.2, 8.9, 4.0 Hz, 1H), 2.01 – 1.90 (m, 1H), 1.68 (dd, *J* = 6.5, 1.2 Hz, 3H), 1.67 – 1.56 (m, 2H), 1.08 (s, 3H), 1.00 (s, 3H), 0.97 (s, 3H). **HRMS** (ESI): Calcd for $(M + H)^+$ $[C22H26O2Na]^+$: 345.1825, found: 345.1818.

(3S)-3-(((*E*)-but-2-en-1-yl)oxy)-4,7,7-trimethyl-3-(phenylethynyl)bicyclo[2.2.1]heptan

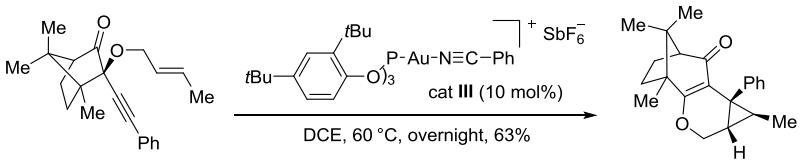


-2-one (199) According to the major (*E*)-isomer: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 – 7.41 (m, 2H), 7.36 – 7.27 (m, 3H), 5.73 – 5.63 (m, 1H), 5.60 – 5.50 (m, 1H), 4.48 – 4.36 (m, 2H), 2.34 – 2.24 (m, 2H), 1.98 – 1.88 (m, 1H), 1.79 – 1.70 (m, 1H), 1.69 (dd, *J* = 6.4, 1.3 Hz, 3H), 1.61 – 1.52 (m, 1H), 1.14 (s, 3H), 1.10 (s, 3H), 0.98 (s, 3H). **HRMS** (ESI): Calcd for $(M + Na)^+$ $[C_{22}H_{26}O_2Na]^+$: 345.1825, found: 345.1818.

5.6.2 Gold(I) catalyzed bicyclic [3.2.1] system formation (201 and 203)



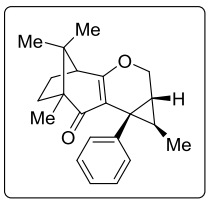
198 (*E*:*Z* = 3:1) **201**



199 (*E*:*Z* = 3:1) **203**

At 0 °C, to a mixture of 1,6-enyne (16 mg, 0.05 mmol) and gold catalyst (**III**) with corresponding catalyst loading in a pressure tube equipped with a stirring bar was added dry DCE (0.5 ml) under $Ar_{(g)}$ atmosphere. At 60 °C, the reaction mixture was stirred overnight and then passed through a short pad of silica gel (Et_2O as eluents,). The resulting solution was concentrated under reduced pressure, followed by silica gel column chromatography to obtain the desired product.

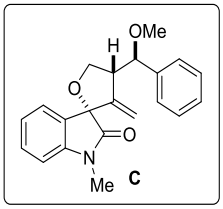
(1R,1aR,4S,7S,8bS)-1,7,9,9-tetramethyl-8b-phenyl-1,1a,2,4,5,6,7,8b-octahydro-8H-4,7-methanocyclohepta[b]cyclopropa[d]pyran-8-one (201) was prepared according to the general procedure, by using **198** and gold catalyst **III** (5 mol%, 3 mg, 2.48 μmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/20 (R_f = 0.32) as eluents, the desired product was obtained in 56% yield (9 mg, 0.03 mmol) as a white solid. **mp**: 131 °C **optical rotation**: $[\alpha]_D^{20}$ = 34.8 (*c* 1.00, DCM) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.3 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 4.90 (dd, *J* = 12.0, 8.0 Hz, 1H), 3.69 (dd, *J* = 12.0, 5.7 Hz, 1H), 2.36 (d, *J* = 6.3 Hz, 1H), 2.18 – 2.09 (m, 1H), 1.75 (ddd, *J* = 13.8, 10.2, 3.6 Hz, 1H), 1.59 – 1.52 (m, 1H), 1.39 (ddd, *J* = 13.0, 9.5, 3.6 Hz, 1H), 1.25 (dt, *J* = 8.0, 5.7 Hz, 1H), 1.13 (d, *J* = 6.3 Hz, 3H), 0.94 (s, 3H), 0.91 – 0.85 (m, 1H), 0.83 (s, 3H), 0.66 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 201.47, 175.34, 140.37, 132.20, 127.53, 126.12, 115.42, 72.84, 57.68, 52.74, 46.64, 33.88, 31.42, 27.33, 25.36, 24.65, 23.65, 18.46, 16.37, 13.71. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{27}O_2]^+$: 323.2006, found: 323.2004.

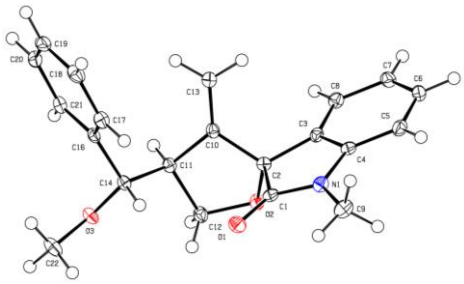


(1S,1aS,4S,7S,8bR)-1,4,9,9-tetramethyl-8b-phenyl-1,1a,2,4,5,6,7,8b-octahydro-8H-4,7-methanocyclohepta[b]cyclopropa[d]pyran-8-one (203) was prepared according to the general procedure, by using **199** and cat **III** (10 mol%, 6 mg, 4.96 μmol). After silica gel column chromatography with EtOAc/petroleum ether = 1/10 (R_f = 0.35) as eluents, the desired product was obtained in 63% yield (10 mg, 0.03 mmol) as a white solid. **mp**: 147 °C **optical rotation**: $[\alpha]_D^{20}$ = -14.3 (*c* 1.00, DCM) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.3 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 4.97 (dd, *J* = 12.0, 8.2 Hz, 1H), 3.54 (dd, *J* = 12.0, 6.4 Hz, 1H), 2.30 (d, *J* = 7.4 Hz, 1H), 2.14 – 2.05 (m, 1H), 1.83 (ddd, *J* = 13.1, 10.1, 5.0 Hz, 1H), 1.54 (ddd, *J* = 13.1, 9.5, 3.6 Hz, 1H), 1.38 (ddd, *J* = 14.1, 9.5, 5.0 Hz, 1H), 1.32 – 1.27 (m, 1H), 1.12 (s, 3H), 1.11 (d, *J* = 6.3 Hz, 3H), 0.90 – 0.85 (m, 1H), 0.79 (s, 3H), 0.63 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 200.48, 177.85, 140.13, 132.20, 127.53, 126.23, 116.35, 74.26, 61.37, 51.60, 46.90, 36.16, 31.09, 25.69, 25.13, 24.42, 23.15, 18.26, 16.23, 12.63. **HRMS** (ESI): Calcd for $(M + H)^+$ $[C_{22}H_{27}O_2]^+$: 323.2006, found: 323.2002.

5.7 X-ray crystallographic analysis (performed by C.G., L.K, K. L., and C.S.)

5.7.1 Crystal data and structure refinement for 120

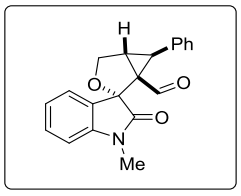


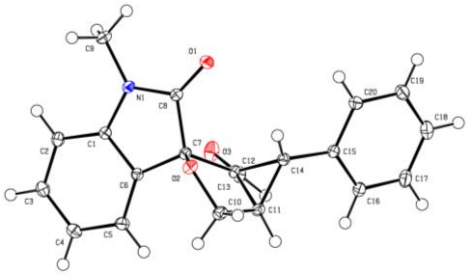


Identification code	CCDC# 1577276
Empirical formula	$C_{21}H_{21}NO_3$
Formula weight	335.39
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	12.2227(15)
b/Å	11.6138(11)
c/Å	13.0593(16)
α/°	90
β/°	111.996(4)
γ/°	90
Volume/Å^3	1718.9(3)
Z	4
ρ_{calc}g/cm^3	1.296
μ/mm^{-1}	0.087
F(000)	712.0
Crystal size/mm^3	0.63 × 0.47 × 0.37
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.86 to 55.998
Index ranges	$-16 \leq h \leq 16$, $-14 \leq k \leq 15$, $-17 \leq l \leq 17$
Reflections collected	24344
Independent reflections	4149 [R_{int} = 0.0364, R_{sigma} = 0.0254]

Data/restraints/parameters	4149/0/237
Goodness-of-fit on F^2	1.069
Final R indexes [I>=2σ (I)]	R_1 = 0.0399, wR_2 = 0.0933
Final R indexes [all data]	R_1 = 0.0498, wR_2 = 0.0980
Largest diff. peak/hole / e $Å^{-3}$	0.41/-0.21

5.7.2 Crystal data and structure refinement for 121

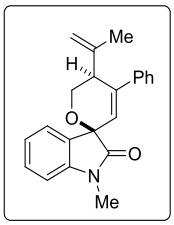


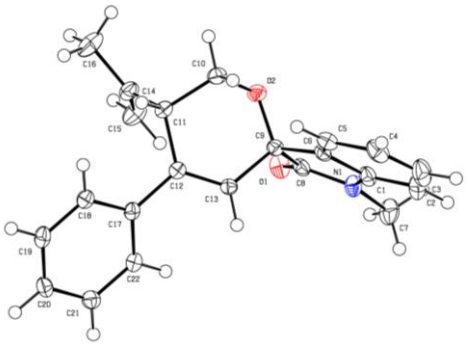


Identification code	CCDC# 1577691
Empirical formula	$C_{20}H_{17}NO_3$
Formula weight	319.35
Temperature/K	100.0
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.3530(8)
b/Å	12.2650(9)
c/Å	12.1885(9)
α/°	90
β/°	98.562(3)
γ/°	90
Volume/$Å^3$	1530.4(2)
Z	4
ρ_{calc}g/cm^3	1.386
μ/mm^{-1}	0.093
F(000)	672.0
Crystal size/mm^3	0.399 × 0.295 × 0.19

Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.504 to 82.346
Index ranges	$-19 \leq h \leq 19$, $-22 \leq k \leq 22$, $-22 \leq l \leq 22$
Reflections collected	131617
Independent reflections	10178 [R_{int} = 0.0413, R_{sigma} = 0.0191]
Data/restraints/parameters	10178/0/218
Goodness-of-fit on F^2	1.080
Final R indexes [I>=2σ (I)]	R_1 = 0.0433, wR_2 = 0.1186
Final R indexes [all data]	R_1 = 0.0525, wR_2 = 0.1242
Largest diff. peak/hole / e $Å^{-3}$	0.73/-0.28

5.7.3 Crystal data and structure refinement for 131

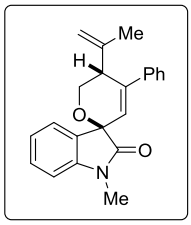


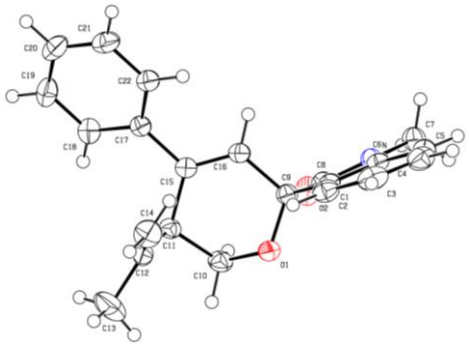


Identification code	CCDC# 1577690
Empirical formula	$C_{22}H_{22}NO_2$
Formula weight	332.40
Temperature/K	100.0
Crystal system	orthorhombic
Space group	Pbca
a/Å	8.5705(3)
b/Å	15.3132(6)
c/Å	26.7732(11)
α/°	90
β/°	90
γ/°	90
Volume/$Å^3$	3513.8(2)

Z	8
ρ_{calc}g/cm^3	1.257
μ/mm^{-1}	0.631
F(000)	1416.0
Crystal size/mm^3	0.426 × 0.217 × 0.147
Radiation	CuKα (λ = 1.54178)
2Θ range for data collection/°	6.602 to 149.344
Index ranges	-10 ≤ h ≤ 10, -15 ≤ k ≤ 19, -33 ≤ l ≤ 33
Reflections collected	46513
Independent reflections	3590 [R_{int} = 0.0281, R_{sigma} = 0.0127]
Data/restraints/parameters	3590/0/229
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0454, wR_2 = 0.1268
Final R indexes [all data]	R_1 = 0.0474, wR_2 = 0.1287
Largest diff. peak/hole / e Å^{-3}	0.59/-0.68

5.7.4 Crystal data and structure refinement for 132

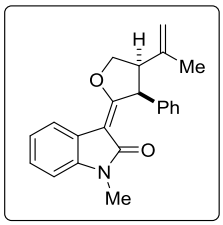


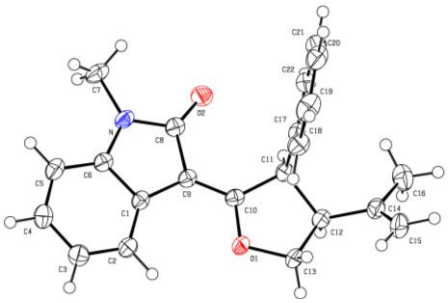


Identification code	CCDC# 1577715
Empirical formula	$C_{22}H_{21}NO_2$
Formula weight	331.40
Temperature/K	173(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	13.2924(7)
b/Å	10.9029(5)

c/Å	12.0252(6)
α/°	90
β/°	94.289(5)
γ/°	90
Volume/Å^3	1737.88(15)
Z	4
ρ_{calc}g/cm^3	1.267
μ/mm^{-1}	0.081
F(000)	704.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.838 to 51.996
Index ranges	-9 ≤ h ≤ 16, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14
Reflections collected	11976
Independent reflections	3411 [R_{int} = 0.0209, R_{sigma} = 0.0202]
Data/restraints/parameters	3411/0/228
Goodness-of-fit on F^2	1.035
Final R indexes [I>=2σ (I)]	R_1 = 0.0372, wR_2 = 0.0919
Final R indexes [all data]	R_1 = 0.0452, wR_2 = 0.0975
Largest diff. peak/hole / e Å^{-3}	0.20/-0.19

5.7.5 Crystal data and structure refinement for 133

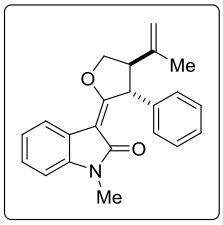


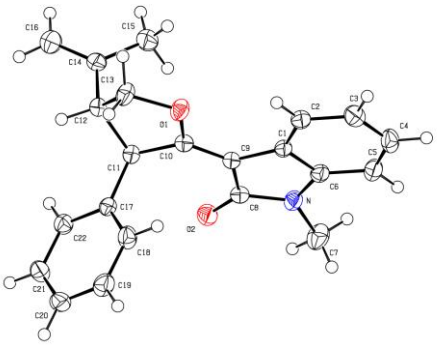


Identification code	CCDC# 1577705
Empirical formula	$C_{22}H_{21}NO_2$
Formula weight	331.40

Temperature/K	173.15
Crystal system	triclinic
Space group	P-1
a/Å	7.4182(5)
b/Å	9.4457(7)
c/Å	12.4918(8)
α/°	82.200(6)
β/°	86.582(5)
γ/°	81.408(6)
Volume/Å^3	856.78(10)
Z	2
ρ_{calc}g/cm^3	1.285
μ/mm^{-1}	0.082
F(000)	352.0
Crystal size/mm^3	0.3 × 0.19 × 0.116
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.398 to 51.99
Index ranges	$-9 \leq h \leq 9$, $-11 \leq k \leq 11$, $-15 \leq l \leq 15$
Reflections collected	11871
Independent reflections	3381 [R_{int} = 0.0363, R_{sigma} = 0.0344]
Data/restraints/parameters	3381/0/228
Goodness-of-fit on F^2	1.043
Final R indexes [I>=2σ (I)]	R_1 = 0.0399, wR_2 = 0.0982
Final R indexes [all data]	R_1 = 0.0517, wR_2 = 0.1061
Largest diff. peak/hole / e Å^{-3}	0.23/-0.22

5.7.6 Crystal data and structure refinement for 134

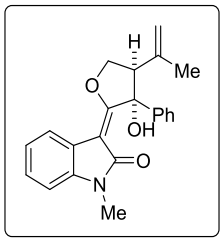


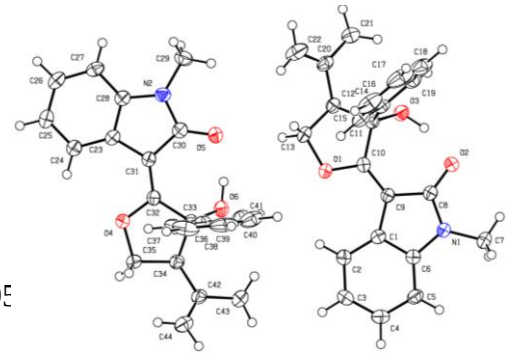


Identification code	CCDC# 1448645
Empirical formula	$C_{22}H_{21}NO_2$
Formula weight	331.40
Temperature/K	173(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	10.5511(7)
b/Å	9.3096(5)
c/Å	17.9883(10)
α/°	90
β/°	90.151(6)
γ/°	90
Volume/Å^3	1766.93(19)
Z	4
ρ_{calc}g/cm^3	1.246
μ/mm^{-1}	0.079
F(000)	704.0
Crystal size/mm^3	0.3 × 0.25 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.528 to 53.996
Index ranges	$-13 \leq h \leq 12$, $-11 \leq k \leq 11$, $-22 \leq l \leq 22$
Reflections collected	16629
Independent reflections	3819 [R_{int} = 0.0392, R_{sigma} = 0.0338]
Data/restraints/parameters	3819/0/228

Goodness-of-fit on F^2	1.036
Final R indexes [I>=2σ (I)]	R_1 = 0.0436, wR_2 = 0.0994
Final R indexes [all data]	R_1 = 0.0599, wR_2 = 0.1088
Largest diff. peak/hole / e $Å^{-3}$	0.21/-0.24

5.7.7 Crystal data and structure refinement for 135

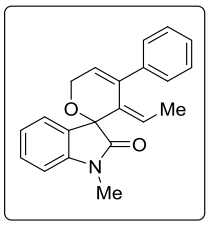


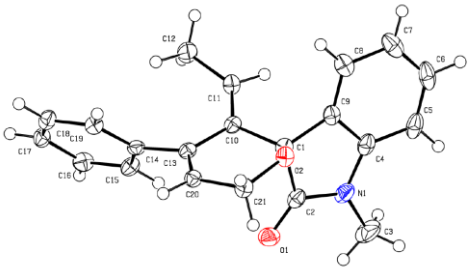


Identification code	CCDC# 157769[illegible]
Empirical formula	$C_{22}H_{21}NO_3$
Formula weight	347.40
Temperature/K	173.15
Crystal system	triclinic
Space group	P-1
a/Å	8.5820(5)
b/Å	12.8508(6)
c/Å	16.8775(8)
α/°	94.396(4)
β/°	104.686(4)
γ/°	99.416(4)
Volume/$Å^3$	1762.60(16)
Z	4
ρ_{calc}g/cm^3	1.309
μ/mm^{-1}	0.087
F(000)	736.0
Crystal size/mm^3	0.35 × 0.2 × 0.18

Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.338 to 54
Index ranges	$-10 \leq h \leq 10$, $-16 \leq k \leq 16$, $-21 \leq l \leq 21$
Reflections collected	27169
Independent reflections	7686 [R_{int} = 0.0451, R_{sigma} = 0.0393]
Data/restraints/parameters	7686/2/481
Goodness-of-fit on F^2	1.016
Final R indexes [I>=2σ (I)]	R_1 = 0.0429, wR_2 = 0.0988
Final R indexes [all data]	R_1 = 0.0639, wR_2 = 0.1099
Largest diff. peak/hole / e $Å^{-3}$	0.23/-0.27

5.7.8 Crystal data and structure refinement for 165

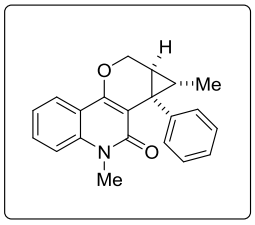


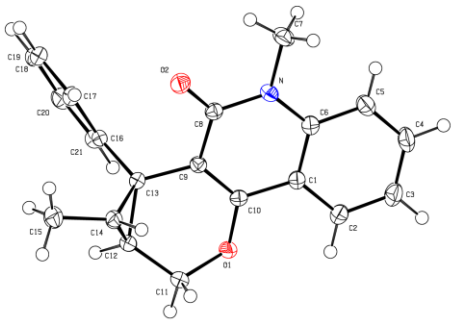


Identification code	CCDC# 1448677
Chemical formula	$C_{21}H_{19}NO_2$
Formula weight	317.37 g/mol
Temperature	100(2) K
Wavelength	1.54178 Å
Crystal size	0.042 x 0.227 x 0.279 mm
Crystal system	monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 12.8527(5) Å α = 90°
	b = 9.9453(4) Å β = 114.4410(10)°
	c = 13.9172(5) Å γ = 90°
Volume	1619.54(11) $Å^3$

Z	4
Density (calculated)	1.302 g/cm^3
Absorption coefficient	0.662 mm^{-1}
F(000)	672
Diffractometer	Bruker APEX-II CCD
Theta range for data collection	3.78 to 65.31°
Index ranges	-15<=h<=15, -11<=k<=11, -16<=l<=16
Reflections collected	13387
Independent reflections	2757 [R(int) = 0.0417]
Coverage of independent reflections	99.5%
Absorption correction	none
Max. and min. transmission	0.9730 and 0.8370
Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick 2008)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014 (Sheldrick 2014)
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	2757 / 0 / 219
Goodness-of-fit on F^2	1.025
Final R indices	2323 data; I>2σ(I) R1 = 0.0481, wR2 = 0.1171 all data R1 = 0.0585, wR2 = 0.1243
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0686P)^2+0.8411P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.258 and -0.290 $eÅ^{-3}$
R.M.S. deviation from mean	0.055 $eÅ^{-3}$

5.7.9 Crystal data and structure refinement for 166

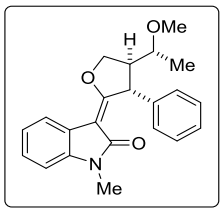


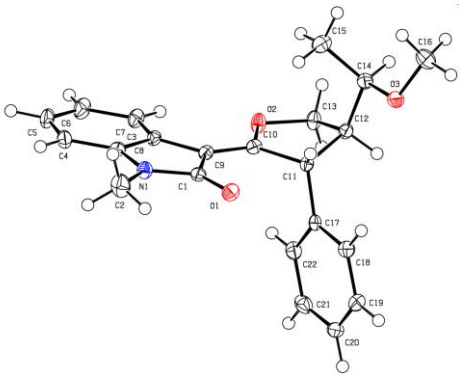


Identification code	CCDC# 1448646
Empirical formula	$C_{21}H_{19}NO_2$
Formula weight	317.37
Temperature/K	173(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	13.3456(6)
b/Å	7.5048(3)
c/Å	16.0725(7)
α/°	90
β/°	99.871(4)
γ/°	90
Volume/Å^3	1585.93(11)
Z	4
ρ_{calc}g/cm^3	1.329
μ/mm^{-1}	0.085
F(000)	672.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	5.146 to 58.228
Index ranges	$-16 \leq h \leq 18$, $-10 \leq k \leq 10$, $-21 \leq l \leq 21$
Reflections collected	21487
Independent reflections	3879 [R_{int} = 0.0357, R_{sigma} = 0.0290]
Data/restraints/parameters	3879/0/219

Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0444, wR_2 = 0.1023
Final R indexes [all data]	R_1 = 0.0576, wR_2 = 0.1093
Largest diff. peak/hole / e $Å^{-3}$	0.28/-0.25

5.7.10 Crystal data and structure refinement for 167

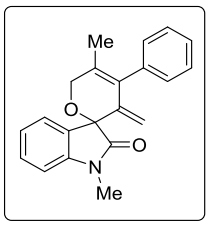


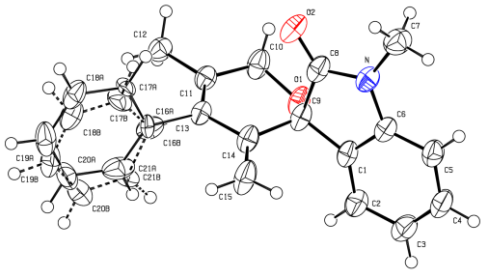


Identification code	CCDC# 144865
Empirical formula	$C_{22}H_{23}NO_3$
Formula weight	349.41
Temperature/K	100.03
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	14.9063(10)
b/Å	7.2965(4)
c/Å	17.0837(11)
α/°	90
β/°	102.332(2)
γ/°	90
Volume/$Å^3$	1815.2(2)
Z	4
ρ_{calc}g/cm^3	1.279
μ/mm^{-1}	0.085
F(000)	744.0
Crystal size/mm^3	0.603 × 0.388 × 0.378
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	4.882 to 55.796
Index ranges	$-19 \leq h \leq 19$, $-9 \leq k \leq 9$, $-22 \leq l \leq 22$
Reflections collected	35891
Independent reflections	4339 [R_{int} = 0.0490, R_{sigma} = 0.0314]
Data/restraints/parameters	4339/0/238
Goodness-of-fit on F^2	1.076
Final R indexes [I>=2σ (I)]	R_1 = 0.0466, wR_2 = 0.1015
Final R indexes [all data]	R_1 = 0.0646, wR_2 = 0.1102
Largest diff. peak/hole / e $Å^{-3}$	0.35/-0.27

5.7.11 Crystal data and structure refinement for 173f





Identification code	CCDC #1448387
Empirical formula	$C_{21}H_{19}NO_2$
Formula weight	317.37
Temperature/K	173(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.5601(10)
b/Å	7.5169(5)
c/Å	18.7897(15)
α/°	90
β/°	108.189(9)
γ/°	90
Volume/$Å^3$	1685.4(2)
Z	4

ρ_{calc}g/cm^3	1.251
μ/mm^{-1}	0.080
F(000)	672.0
Crystal size/mm^3	? × ? × ?
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.564 to 51.994
Index ranges	$-15 \leq h \leq 15$, $-9 \leq k \leq 9$, $-23 \leq l \leq 23$
Reflections collected	19281
Independent reflections	3298 [R_{int} = 0.0500, R_{sigma} = 0.0401]
Data/restraints/parameters	3298/0/294
Goodness-of-fit on F^2	1.013
Final R indexes [I>=2σ (I)]	R_1 = 0.0431, wR_2 = 0.0986
Final R indexes [all data]	R_1 = 0.0743, wR_2 = 0.1151
Largest diff. peak/hole / e Å^{-3}	0.16/-0.18

6 References

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7 Appendix

7.1 List of abbreviations

Ac	acetyl
ACN	acetonitrile
Ad	adamantyl
Ar	aryl
BCC	basal cell carcinoma
BIOS	biology-oriented synthesis
Bn	benzyl
BODIPY	borondipyrromethene
Calcd	calculated
Cat.	catalyst
CB2	cannabinoid receptor type 2
Cbz	carboxybenzyl
COMAS	Compound Management and Screening Center
cond.	condition
COX	cyclooxygenase
CtD	complexity to diversity synthesis
DAPI	4’-6-diamidino-2-phenylindole
DCE	1,2-dichloroethane
DCM	dichloromethane
df-oxindole	(*E*)-3-(dihydrofuran-2(3H)-ylidene) indolin-2-one
dia	diastereomer
DMSO	dimethylsulfoxide
DMF	dimethylformamide
DNP	dictionary of natural product
DOS	diversity-oriented synthesis
dr	diastereomeric ratio
DTS	diverted total synthesis
EC_{50}	half maximal effective concentration
EDG	electron-donating group
ee	enantiomeric excess
ent	enantiomer
eq	equivalent

ESI	electrospray ionization
Et	ethyl
EWG	electron-withdrawing group
FDA	Food and Drug Administration
FOS	function-oriented synthesis
HH	hedgehog
HPLC	high-performance liquid chromatography
HRMS	high resolution mass spectrometry
HTS	high throughput screening
Hz	Hertz
IC_{50}	half-maximal inhibitory concentration
IMes	1,3-Bis(2,4,6-trimethylphenyl)-1,3-dihydro-2H-imidazol-2-ylidene
*i*Pr	*iso*-propyl
IPr	1,3-bis(diisopropylphenyl)-imidazol-2-ylidene
J	coupling constants
L	ligand
LD_{50}	half-maximal lethal dose
LDS	ligand directed divergent scaffold synthesis
LG	leaving group
M.-S. rear.	Meyer-Schuster rearrangement
Me	methyl
Mes	2,4,6-trimethylphenyl
MOM	methoxymethyl
mp	melting point
n.a.	no activity
MS	molecular sieves
*n*Bu	normal butyl
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
NP	natural product
Nu	nucleophile
PDB	protein data bank
Ph	phenyl

PMB	*para*-methoxy benzyl
ppm, δ	parts per million
PRPP	5-phosphoribosyl-1-pyrophosphate
PRS	privileged ring system
PTCH	Patched
*p*Tol	*para*-tolyl
qPCR	quantitative polymerase chain reaction
R_f	retardation factor
rt	room temperature
SAR	structure activity relationship
SCNOP	structural classification of natural product
s.d.	standard deviation
SEM	2-(trimethylsilyl)ethoxymethyl
SM	stating material
SMO	smoothened
TBAF	tetra-*n*-butylammonium fluoride
TBS	*tert*-butyl dimethylsilyl
*t*Bu	*tert*-butyl
TEA	trimethylamine
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	trimethylsilyl
TOM	(triisopropylsiloxy)methyl
Ts	*para*-tosyl

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7.3 Eidesstattliche Versicherung (Affidavit)

Lee,Yen-Chun **148528**

Name, Vorname (Surname, first name) | Matrikel-Nr. (Enrollment bunmer)

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(Title of the thesis):

Gold Catalyzed Divergent Scaffold Synthesis from Oxindole Derived 1,6-Enynes

Ich versichere hiermit an Eides statt, dass ich die vorliegende Dissertation mit dem Titel selbstständig und ohne unzulässige fremde Hilfe angefertigt habe. Ich habe keine anderen als die angegebenen Quellen und Hilfsmittel benutzt sowie wörtliche und sinngemäße Zitate kenntlich gemacht. Die Arbeit hat in gegenwärtiger oder in einer anderen Fassung weder der TU Dortmund noch einer anderen Hochschule im Zusammenhang mit einer staatlichen oder akademischen Prüfung vorgelegen.

I hereby swear that I have completed the present dissertation independently and without inadmissible external support. I have not used any sources or tools other than those indicated and have identified literal and analogous quotations. The thesis in its current version or another version has not been presented to the TU Dortmund University or another university in connection with a state or academic examination.

Cambridge (USA), Jan 16th, 2018 | 

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7.3 Curriculum vitae

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PERSONAL INFORMATION

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EDUCATION

Max Planck Institute of Molecular Physiology (Dortmund, Germany)

Department of Chemical Biology, PhD student

Technical University of Dortmund (Dortmund, Germany)

Department of Chemistry and Chemical Biology, PhD student 2013~2018

Advisor: Prof. Herbert Waldmann and Dr. Kamal Kumar Second thesis advisor: Prof. Alois Fürstner

Field: Chemical Biology, Synthetic Methodology, Transition Metal Catalysis

Topic: Gold catalyzed cycloisomerization of 1.6-enynes to build a structural divergent compound collection

Massachusetts Institute of Technology (Cambridge, United States)

Department of Chemistry, visiting student 2017-2018

Advisor: Prof. Bradley L. Pentelute Field: Peptide Chemistry, Combinatorial Library

Topic: Label-free quantitative solution-phase peptide libraries screening

National Tsing Hua University (Hsinchu, Taiwan)

Department of Chemistry, Master of Science (GPA: 3.9/4.0; Thesis: 92/100) 2008~2010

Advisor: Prof. Minoru Isobe Field: Organic Chemistry, Target Oriented Synthesis

Topic: Synthetic studies toward the Zanamivir (Relenza®)

Department of Chemistry, Bachelor of Science (GPA: 3.5/4.0) 2004~2008

Advisor: Prof. Chun-Chen Liao Field: Organic Chemistry, Synthetic Methodology

Topic: The investigation of Diels-Alder reaction toward masked *o*-benzyoquinone with $Pb(OAc)_4$ assisted derivatizations

National Chung Hsing University (Taichung, Taiwan)

High school chemistry gifted student training program. 2002~2004

Advisor: Prof. Ru-Jen Cheng Field: Inorganic Chemistry, Host-Guest Chemistry

Topic: Determining the equilibrium constant of different ligands to Fe-porphyrin complex on the bases of Beer's rule via computational method.

PUBLICATION

Journal:

1. **Y.-C. Lee**, K. Kumar*, Gold(I) catalyzed enyne cycloisomerization – a roadmap to privileged heterocyclic scaffolds, *Isr. J. Chem.* DOI: 10.1002/ijch.201700067
2. **Y.-C. Lee**, K. Kumar, H. Waldmann*, Ligand-directed divergent synthesis of carbo- and heterocyclic ring systems, *Angew. Chem. Int. Ed.* DOI: 10.1002/anie.201710247.
3. H.-R. Wu, **Y.-C. Lee***, The synthetic approach and logic of design behind the small molecule compound library synthesis, *Chemistry* (The Chinese Chemical Society, Taipei) **2017**, *75*, 267.
4. P.-K. Tsou, **Y.-C. Lee**, T. Lankau, M. Isobe, C.-H. Yu*, Substituent effects in the Nicholas epimerization of glycosides, *J. Phys. Org. Chem.* DOI: 10.1002/poc.3780.
5. **Y.-C. Lee**, S. Patil, C. Golz, C. Strohmann, S. Ziegler, K. Kumar*, H. Waldmann*, A ligand-directed divergent catalytic approach to establish structural and functional scaffold diversity, *Nat. Commun.* **2017**, *8*, 14043.
6. Y.-Y. Ke, H.-Y. Shiao, Y. C. Hsu, C.-Y. Chu, W.-C. Wang, **Y.-C. Lee**, W.-H. Lin, C.-H. Chen, J. T. A. Hsu, C.-W. Chang, C.-W. Lin, T.-K. Yeh, Y.-S. Chao, M. S. Coumar and H.-P. Hsieh*, 3D-QSAR-Assisted Drug Design: Identification of a Potent Quinazoline-Based Aurora Kinase Inhibitor, *ChemMedChem* **2013**, *8* (1), 1546-1550.
7. J.-Y. Yeh, M. S. Coumar, H.-Y. Shiao, T.-J. Lin, **Y.-C. Lee**, H.-C. Hung, S. Ko, F.-M. Kuo, M.-Y. Fang, Y.-L. Huang, J. T. A. Hsu, T.-K. Yeh, S.-R. Shih, Y.-S. Chao, J.-T. Horng, and H.-P. Hsieh*, Identification of an Orally Bioavailable Quinoline Derivative through Activity- and Property-Guided Lead Optimization, *ChemMedChem* **2012**, *7* (9), 1546-1550.
8. Y.-P. Wang, **Y.-C. Lee**, Y.-J. Hong, T.-R. Yew*, A novel method for soluble hydrophilic anthracene derivative self-assembled on APTES in air, *Organic Electronics* **2012**, *13* (11), 2417-2421.

HONOR

Sep, 2015 2015 MOE Technologies Incubation Scholarship from Taiwan

Jul, 2014 Scholarship from MPI Dortmund

Jul, 2013 Scholarship form IMPRS-CMB