NANYANG
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GOLD-CATALYZED STRATEGIES FOR CARBOCYCLIC AND N-HETEROCYCLIC SYNTHESIS

TEO WAN TENG

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

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School of Physical and Mathematical Sciences

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DEDICATION

I dedicate this thesis to

My beloved Father
For earning an honest living for me.

My beloved Mother
For constantly giving me unconditional support, care and encouragement to overcome several hurdles in life.

My beloved siblings
Wilson, Barry and Willy, who knowingly and unknowingly, make me to have courage to thrive profusely in every aspect of my life.

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ABSTRACT

The work in this thesis was undertaken in Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences in Nanyang Technological University from August 2010 to August 2014 under the supervision of Assoc. Prof. Philip Wai Hong Chan.

In this thesis the development of several novel gold-catalyzed transformations for the construction of carbocycles and *N*-heterocycles via C–C and C–N bond formation are described. This thesis consists of three parts:

- Part I includes Chapter I, which gives the general introduction of gold catalysis and its application for the construction carbocycles and *N*-heterocycles from readily available alkynols and 1,*n*-diyne esters.
- Part II describes the new strategies that have been employed to access sulfonyl pyrroles, phenolic esters and bicyclo[2.2.1]hept-2-en-7-one derivatives. Chapter II presents gold-mediated tandem aminocyclization/1,3-sulfonyl migration of α-amino propargyl alcohols as a new synthetic tool for the preparation of 3-sulfonyl pyrroles. In Chapter III, a synthetic protocol for synthesizing the phenolic esters from the benzannulation of gold(I)-activated parpargylic alcohol tethered *β*-ketoesters is introduced. This method features its reaction conditions that did not require the exclusion of air or moisture. Chapter IV details a novel synthetic route to bicyclo[2.2.1]hept-2-en-7-one derivatives based on acyloxy migration followed by enyne cycloisomerization of 1,8-diynyl vinyl esters.
- Part III contains experimental data (Chapter V) and references (Chapter VI) pertaining to this thesis.

Publications

(1) "Synthesis of Highly Substituted Indene Derivatives via Brønsted Acid Catalyzed Nazarov Cyclization of Homoallylic Alcohols." Zhang, X.;† **Teo, W. T.**;† Rao, W.; Chan, P. W. H. *Tetrahedron Lett.* **2014**, *55*,3881.

(2) "Gold-Catalyzed Benzannulation of 5-Hydroxy-3-oxoalky-6-ynoate Esters to *o*-Phenolic Esters." **Teo, W. T.**; Rao, W.; Ng, C. J. H.; Koh, S. W. Y. Chan, P. W. H. *Org. Lett.* **2014**, *16*, 1248.

(3) "Gold-Catalyzed Domino Aminocyclization/1,3-Sulfonyl Migration of N-Substituted N-Sulfonyl-aminobut-3-yn-2-ols to 1- Substituted 3-Sulfonyl-1*H*-pyrroles." **Teo, W. T.**; Rao. W.; Koh, M. J.; Chan, P. W. H. *J. Org. Chem.* **2013**, *78*, 7508.

(4) "Efficient Synthesis of Di- and Trisubstituted 2-Aryloxazoles via Ytterbium(III) Triflate Catalyzed Cyclization of Tertiary Propargylic Alcohols with Aryl Amides." Zhang, X.; **Teo, W. T.**; Chan, P. W. H. *J. Organomet. Chem.* **2011**, *696*, 331.

(5) "Brønsted Acid-Catalyzed Cyclization of Propargylic Alcohols with Thioamides. Facile Synthesis of Di- and Trisubstituted Thiazoles." Zhang, X.; **Teo, W. T**.; Sally, Chan, P. W. H. *J. Org. Chem.* **2010**, *75*, 6290.

(6) "Ytterbium(III) Triflate-Catalyzed Tandem Friedel-Crafts Alkylation/Hydroarylation of Propargylic Alcohols with Phenol as an Expedient Route to Indenols." Zhang, X.; **Teo, W. T.**; Chan, P. W. H. *Org. Lett.* **2009**, *11*, 4990.

ABBREVIATIONS

Ac	acetate
Ar	aryl
Bu	butyl
DCE	1,2-dichloroethane
DTBM-SEGPHOS	5,5′-Bis[di(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino]-4,4′-bi-1,3-benzodioxole
DMAP	4-(dimethylamino)pyridine
dr	diastereomeric ratio
ee	enantiomeric excess
Et	ethyl
EDG	electron donating group
EWG	electron withdrawing group
equiv	equivalent
h	hour
HMPA	hexamethylphosphoramide
IPr	1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene
LDA	Lithium diisopropylamide
Me	methyl
m.p	melting point
Ms	methylsulfonyl
NMR	nuclear magnetic resonance
Nu	nucleophile
OTf	trifluoromethanesulfonate
Ph	phenyl

PTSA	*p*-toluenesulfonic acid
r.t.	room temperature
TFA	trifluoroacetic acid
TfOH	trifluoromethanesulfonic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TBS	*tert*-butyldimethylsilyl
TMS	trimethylsilyl
Ts	*p*-methylphenylsulfonyl
α	alpha
β	beta

Chapter I: Alkynol Derivatives in Gold-Catalyzed Synthetic Approaches to Carbocycles and *N*-Heterocycles

1.1 Introduction

The carbocyclic and *N*-heterocyclic motifs are found in a myriad of biologically active natural products as well as important functional materials, selected examples of which are shown in Figure 1.1.[1] They also have widespread applications and utility in many drug discovery programs and the pharmaceutical industry. The past century has seen the establishment of various classical methods for the synthesis of substituted carbocycles and *N*-heterocycles.[2] Typically, a majority of the reported processes for

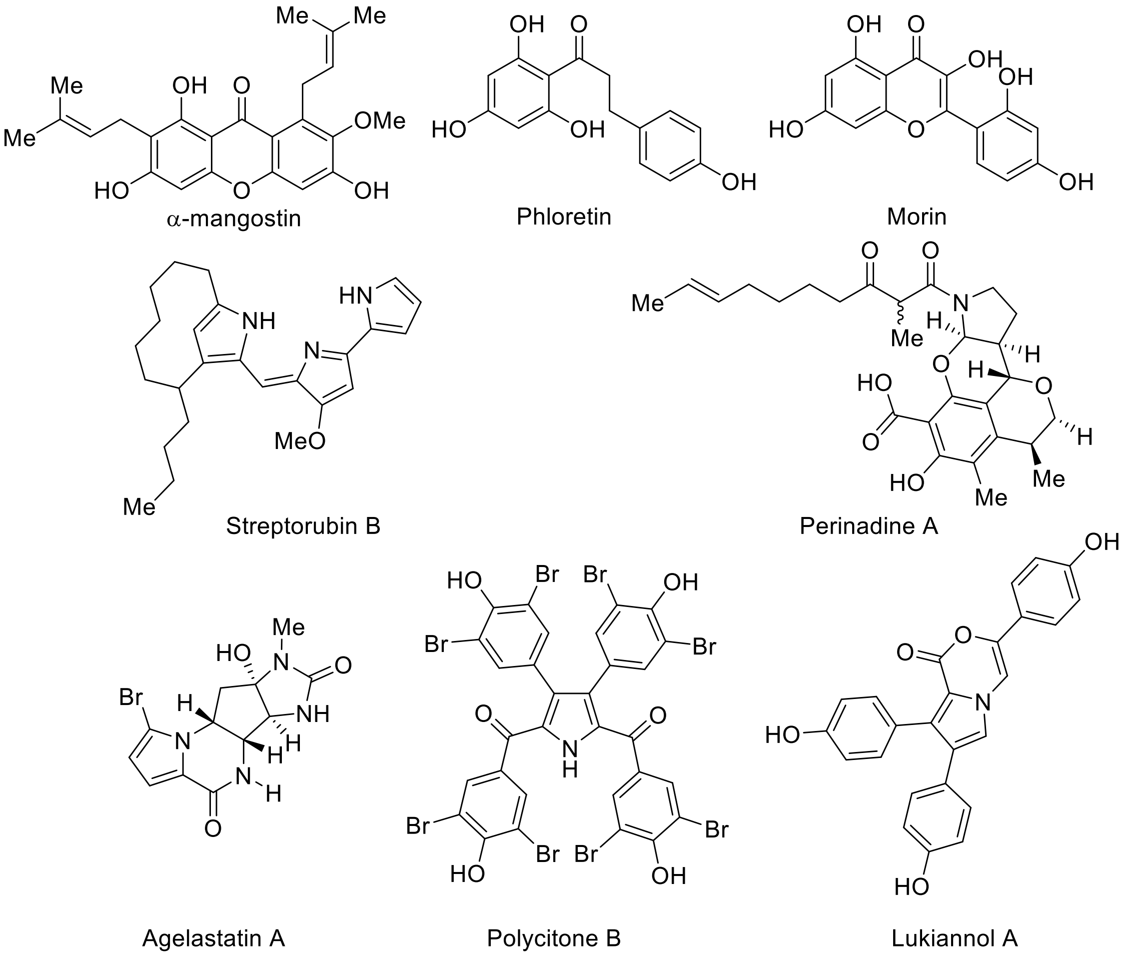
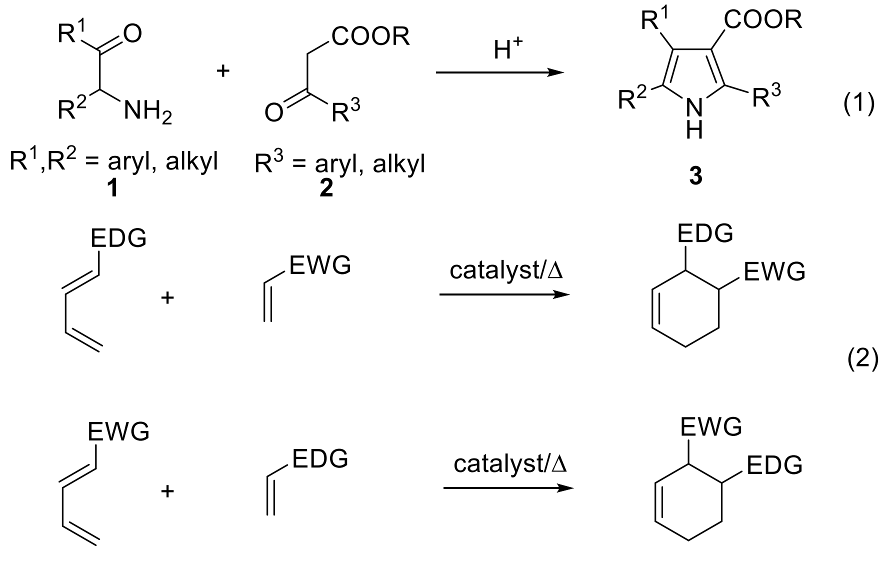


Figure 1.1 Examples of carbocycles and *N*-heterocycles of biological interest.[1]

carbocyclic and *N*-heterocyclic synthesis were shown to suffer from a number of drawbacks. An example is the seminal work reported by Ludwig Knorr in 1884 for pyrrole synthesis, which was achieved by condensation of α-amino-ketones with α-unsubstituted β-ketoesters (Scheme 1.1, eq 1).[3] Although the Knorr reaction has been widely employed for the synthesis of a variety of functionalized pyrroles, the reaction often required a stoichiometric amount of strong acid for it to proceed in high product yields. Another example is the Diels–Alder reaction, which is one of the most powerful and efficient methods for constructing substituted six-membered carbocyclic systems, that has been shown to be best performed with electron-rich dienes and electron-poor dienophiles or vice versa (Scheme 1.1, eq 2).[4] The electronic demand for the substrates in this transformation has restricted the substitution pattern that could be installed on the carbocyclic system. For these reasons, the development of new and efficient methods for the preparation of these class of compounds have and continue to receive significant synthetic interest. Along with this has been the desire to establish novel synthetic protocols that target molecular complexity in an atom and step economical manner from



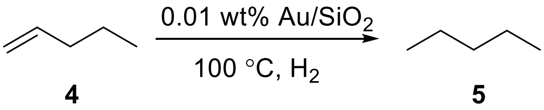
Scheme 1.1 The Knorr pyrrole synthesis and the normal and inverse electron demand Diels–Alder transformations.

low cost and readily available substrates under mild reaction conditions.

One of the most widely employed strategies to access the valuable carbocyclic and *N*-heterocyclic core structures has relied upon the addition of a carbon- or nitrogen-based nucleophile to a transition metal-activated unsaturated C–C bond, resulting in the formation of a new C–C or C–N σ bond, respectively.[5] Included in this has been an increasing number of reported synthetic transformations involving the reactions of alkynol derivatives catalyzed by gold(I) and gold(III) complexes. The focus of this introduction is on recent development in this field of catalytic C–C and C–N bond formation that employs propargylic alcohols and 1,*n*-diyne esters in the presence of gold(I) or gold(III) complex as the catalyst.

1.2 The Reactivity of Gold

Traditionally, the chemical application of gold has been overlooked due to its stability and high monetary value. This changed in 1973 with the discovery of the heterogeneous catalytic ability of gold to hydrogenate olefins by Bond and co-workers (Sheme 1.2).[6] Following this initial finding, gold catalysis has attracted considerable interest in the synthetic community and its significance is reflected by the exponential growth of publications in the last 25 years.[7]



Scheme 1.2 Hydrogenation of pent-1-ene by heterogeneous gold catalysis

Located between platinum (^{78}Pt) and mecury (^{80}Hg), gold (^{79}Au, Z = 79; [Xe]$4f^{14}5d^{10}6s^{1}$) bears a number of chemical similarities with its neighboring elements. With the outer sphere electronic configuration of $5d^{10}6s^{1}$, the most common oxidation states of gold salt are +1 and +3. The rich chemistry of gold that has been developed in the recent years can be attributed to the relativistic effect, which is a result of the contraction of the 6s orbital and the expansion of the 5d orbital.[8] This relativistic effect is present for the elements of the sixth period (mainly Ir, Pt, Au, Hg and Tl) but is most significant for gold, as shown in Figure 1.2.[8g]

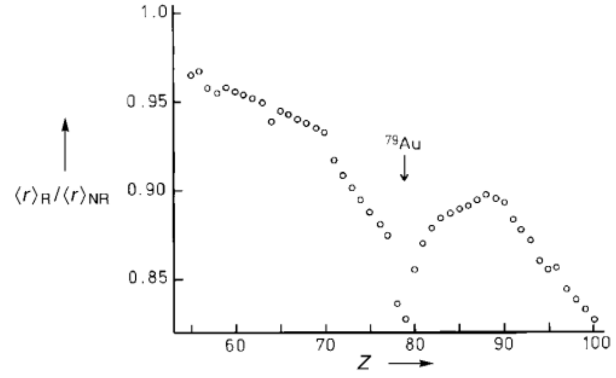
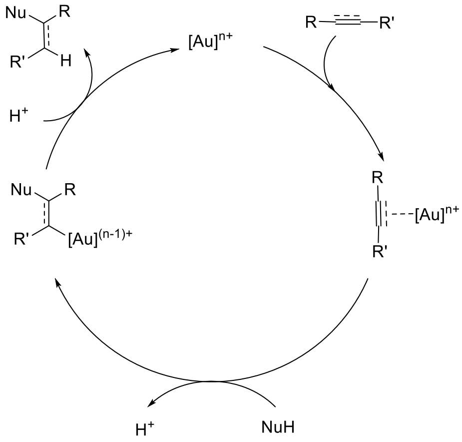


Figure 1.2 The ratio of relativistic to non relativistic contraction of 6s orbitals' radii.[8g]

By virtue of this property, the relativistic effect gives rise to the exceptional π-Lewis acidity in gold complexes towards unsaturated bonds, particularly alkynes (Scheme 1.3). This interaction renders the C≡C bond susceptible to attack by a nucleophile to result in the formation of the corresponding organogold intermediate. Rapid protodeauration of this readily formed organometal complex would then afford the addition product.



Scheme 1.3 General mechanism for the reaction of gold catalyst and unsaturated bond.

In addition to its alkynophilic properties, the contraction of the 6s orbital of gold leads to a shorter metal-ligand (M–L) bond length than that formed for Pt and Hg.[9] Moreover, the electronegativity of the ligand also plays a role in the bond strength of the M–L bond. An example is triphenylphosphine gold chloride (Ph_3PAuCl) where the bonding is more pronounced for a phosphine ligand than the bound chloride (Figure 1.3).

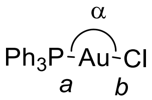
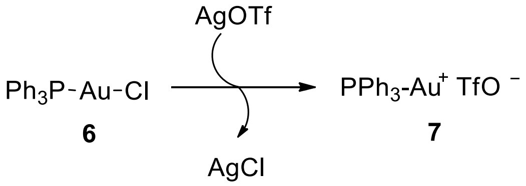


Figure 1.3 Structure of Ph_3PAuCl ($\alpha = 179.6°$, $a = 2.235$ Å, $b = 2.279$ Å)

In general, gold complexes with an oxidation state of +1 exist with a linear geometry, with two coordinating ligands (Scheme 1.4).[8c] In the cases where one of the ligand is distinctly more electronegative, it may be abstracted to form a reactive species of the type LAu^+ with an empty coordination site. In this regard, a silver salt such as AgOTf is often used to replace the more electronegative chlorine by a weakly coordinated triflate counterion through metathesis (Scheme 1.4).[10]



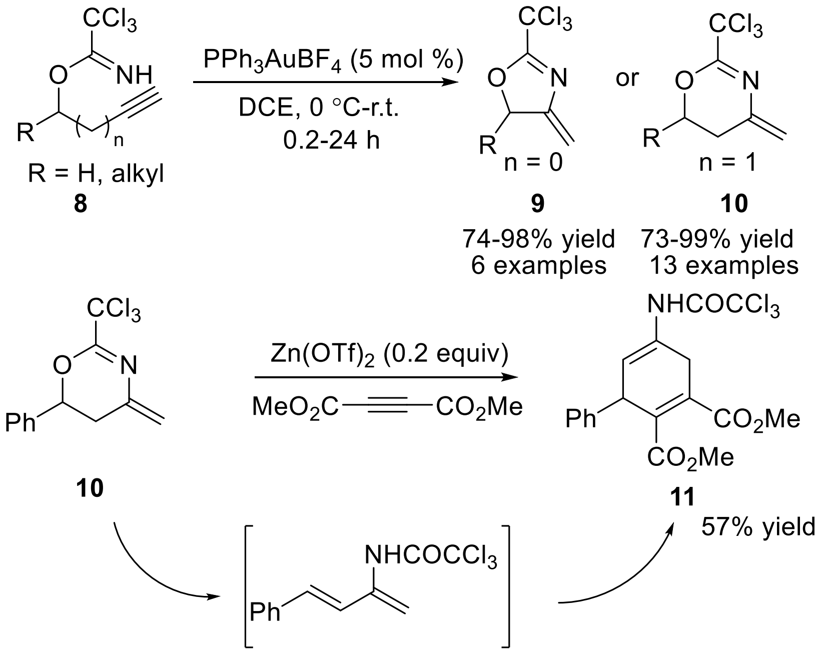
Scheme 1.4 Metathesis between Ph_3PAuCl and AgOTf.

1.3 Gold-Catalyzed Cyclization of Alkynol Derivatives

The synthetic challenge for organic chemistry today is to replace hazardous chemical reagents with more environmentally acceptable analogues.[11] In this regard, alkynols form an attractive synthetic substrate class due to the ease of starting material preparation and water being formed as potentially the only side product. In the past few years, the employment of alkynol derivatives as starting materials in gold-catalyzed methodologies has emerged as an increasingly elegant synthetic tool for the construction of architecturally complex molecules.[12] In most instances, the reaction initially proceeds by gold activation of the alkyne moiety, followed by attack of an external or a tethered nucleophile. Many methods have recently been developed in this area using carbon or a hetereoatom as a nucleophile.

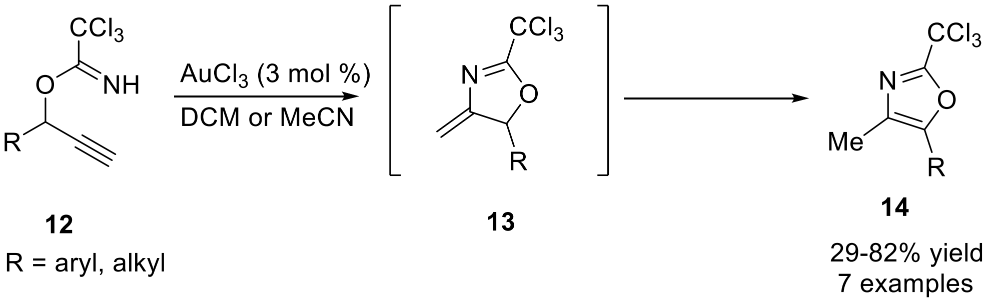
1.3.1 Cyclization Processes Involving Carbon–Nitrogen Bond Formation

Over the past decade, there have been significant advances in gold-mediated carbon-nitrogen bond formation.[7g,7r] Shin and co-workers demonstrated an early example of gold(I)-catalyzed cyclization of alkynol derivatives (Scheme 1.5).[13] In this work, trichloroacetimidates **8**, derived from propargyl and homopropargyl alcohols, were converted to the corresponding dihydrooxazoles **9** and dihydrooxazines **10** via gold-catalyzed 5-*exo*-dig and 6-*exo*-dig cycloisomerization, respectively. The dihydrooxazines **10** were shown to be useful 2-acylamino-1,3-diene precursors that



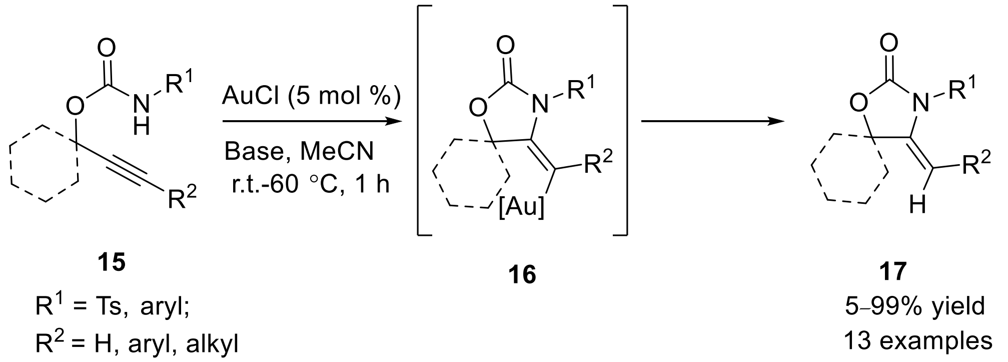
Scheme 1.5 Gold(I)-catalyzed intramolecular hydroamination of trichloroacetimidates.

underwent Diels-Alder cyclization with dimethylacetylenedicarboxylate (DMAD) in the presence of zinc(II) triflate (20 mol%) to afford the cyclohexa-1,4-dienes **11** in 57% yield. At about the same time, Hashmi and co-workers reported a similar transformation that employed trichloroacetimidates **12** to furnish substituted oxazoles **14** with yields ranging between 29–82% in the presence of gold(III) chloride (Scheme 1.6).[14] In this instance, the dihydrooxazole intermediate **13**, generated from intramolecular 5-*exo*-dig hydroamination of **12**, was shown to undergo alkene isomerization to afford the desired oxazole derivatives **14**.



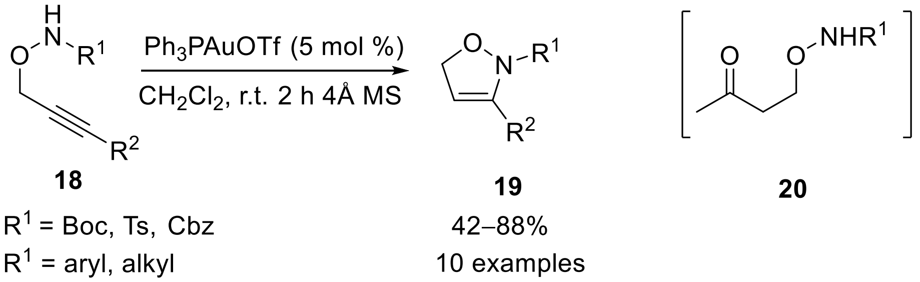
Scheme 1.6 Gold(III)-catalyzed intramolecular hydroamination of trichloroacetimidates.

Subsequently, a similar approach was developed by Schmalz and co-workers who showed that treatment of *O*-propargylic carbamates **15** with an amine or alkoxide base and AuCl catalytic system, the corresponding oxazolidinones **17** were obtained in 5–99% yield (Scheme 1.7).[15] Mechanistic studies suggested that addition of the carbamate moiety with the triple bond occurred in an *anti* 5-*exo*-dig manner to afford vinyl gold complex **16**. This was followed by protodeauration to give the *Z*-configured oxazolidinone **17**, the stereochemistry of which was established by NOE measurements.



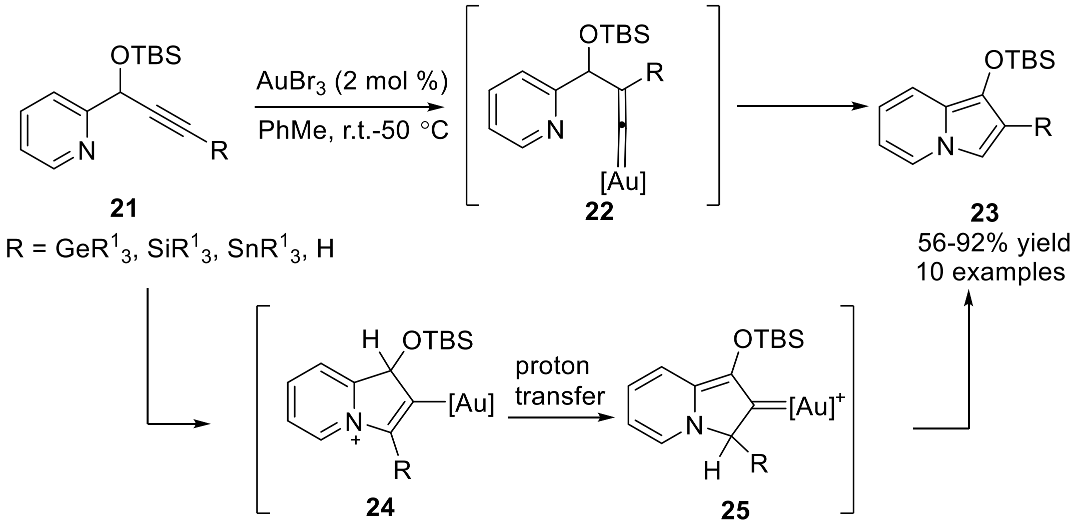
Scheme 1.7 Gold(I)-catalyzed intramolecular hydroamination of *O*-propargylic carbamates

At about the same time, Shin and co-workers demonstrated a similar 5-*endo*-dig process that afforded dihydroisoxazoles **19** from *O*-propargylic hydroxylamines **18** in 42–88% yield (Scheme 1.8).[16] In this reaction, 4Å molecular sieves were required to suppress hydration of the alkyne moiety in **18**, which resulted in the formation of *tert*-butyl 3-oxobutoxycarbamate side product **20**.



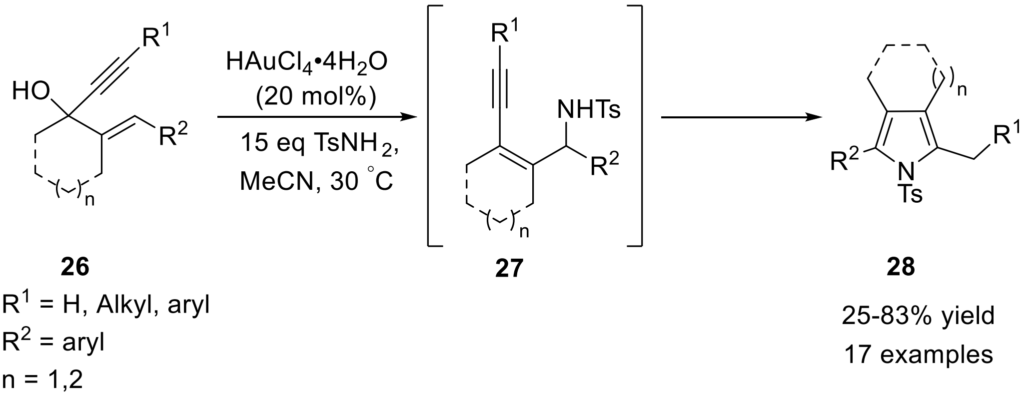
Scheme 1.8 Gold(I)-catalyzed intramolecular hydroamination of *O*-propargylic hydroxylamines.

Gevorgyan and co-workers disclosed an important example of intramolecular AuBr$_3$-catalyzed aminative cycloisomerization of propargylic pyridine derivatives **21** to heterobicyclic targets **23** in 56–92% yield (Scheme 1.9).[17] The mechanism was initially thought to proceed via alkyne-vinylidene **22** until detailed DFT computational and experimental studies were carried out.[18] These latter studies provided a better understanding of the mechanism of this transformation by showing that propargylic pyridine derivative **21** was more likely to undergo gold(III) bromide-mediated 5-*endo*-dig cyclization to yield the vinyl gold intermediate **24**. Subsequent proton transfer was thought to lead to the gold carbenoid **25** followed by 1,2-alkyl migration to the gold carbenoid center and protodeauration to give the desired heterobicyclic product **23**.



Scheme 1.9 Gold(III)-catalyzed tandem 1,2-migration/amination of *o*-propargylic pyridine derivatives

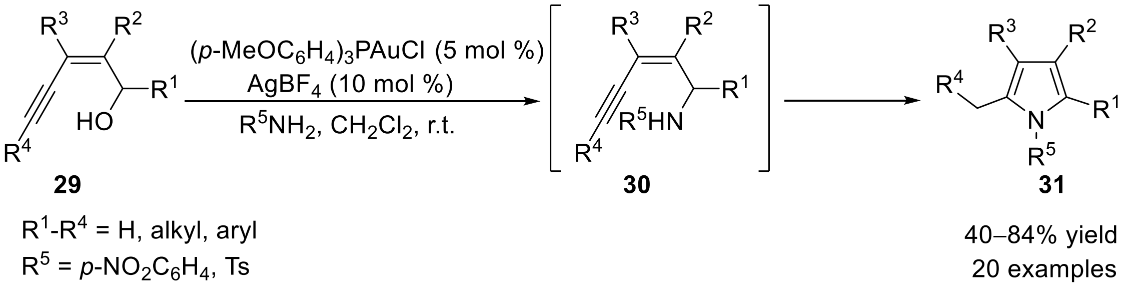
By treating propargylic alcohols as pro-electrophiles, Liang and co-workers demonstrated the formation of highly substituted pyrroles **28** via in situ intermolecular allylic amination of propargylic alcohol **26** with excess tosylamide $TsNH_2$ (Scheme



Scheme 1.10 Gold(III)-catalyzed tandem amination/hydroamination of 1-en-4-yn-3-ols.

1.10).[19] Ensuing hydroamination to intermediate amine-enyne **27** was described to furnish highly substituted pyrroles **28**. Although the desired pyrroles **28** were obtained in modest to good yields of up to 83%, 15 equivalents of $TsNH_2$ and a high catalyst loading of 20 mol % of the $HAuCl_4 \cdot H_2O$ were required. Furthermore, the substrate scope was limited to substrates bearing a cyclohexyl moiety; one acyclic example where $R^1 = R^2 =$ Ph was examined but was found to give the corresponding amine-enyne **27** as the only isolable product under the optimized conditions.

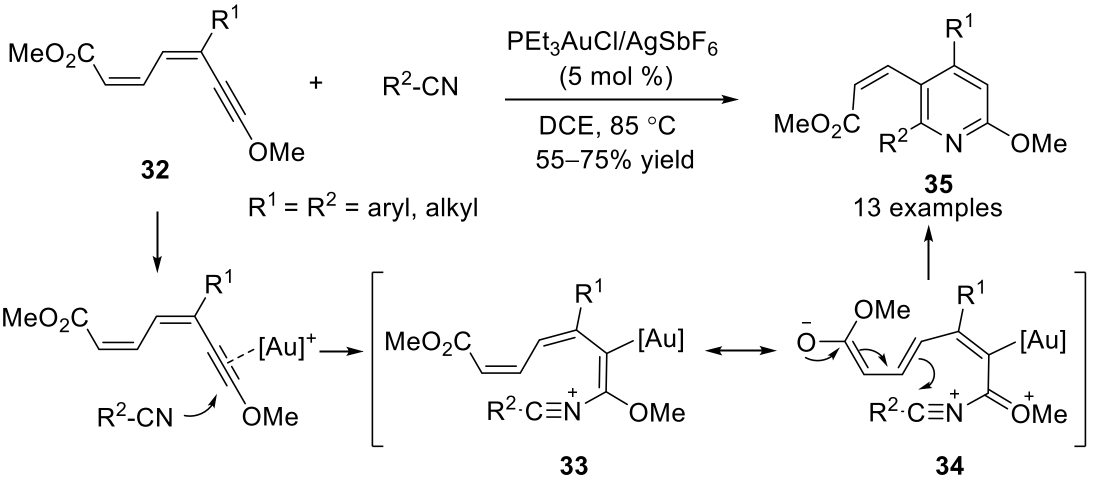
Building on this work, Liu and co-workers demonstrated a similar approach that enhanced the efficiency of the previous protocol by expanding the scope through the use of acyclic enynols **29** (Scheme 1.11).[20] Treatment of (*Z*)-2-en-4-yn-1-ols **26** with *p*-nitroaniline sulfonamide under catalysis by $(p\text{-MeOC}_6H_4)_3PAuCl$ and $AgBF_4$ was shown to lead to direct amination at the carbinol carbon of **29**. This was followed by subsequent cycloisomerization of the resulting enynyl amide intermediate **30** to give the highly substituted pyrrole **31**. This cyclization protocol was shown to be applicable to a range of enynols **29**, with product yields ranging between 40–84% being achieved with a lower nucleophile loading of 4 equivalents of 4-nitroaniline. In both this and the earlier work by Liang and co-workers, it was proposed that excess amines were required so as to act as ligands as well as assisting in stabilizing the surmised cationic complexes formed



Scheme 1.11 Gold(I)-catalyzed amination of (*Z*)-2-en-4-yn-1-ols with 4-nitroaniline sulfonyl amide.

under the reaction conditions.

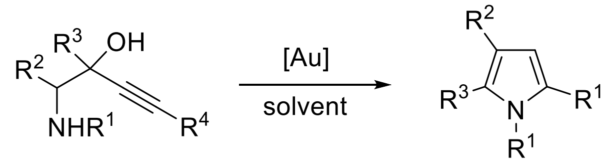
In 2008, Barluenga and Aguilar reported an unusual gold(I)-catalyzed hetero-dehydro-Diels-Alder cyclization employing nitriles as an external *N*-nucleophilic source (Scheme 1.12).[21] In this reaction, treatment of a mixture of dienynol derivatives **32** and nitriles with a catalytic 1:1 mixture of Et_3PAuCl and $AgSbF_6$ in 1,2-dichloroethane led to regioselective isolation of tetra-substituted pyridinyl acrylate **35** in 55–75% yield. This novel transformation was triggered by addition of the nitrile to the activated alkyne, with subsequent cyclization potentially occurring through tautomerization of **33** to **34**. A final protodeauration step then afforded the functionalized pyridine **35**.



Scheme 1.12 Gold(I)-catalyzed hetero-dehydro-Diels-Alder cyclization of dienynol derivatives with nitriles.

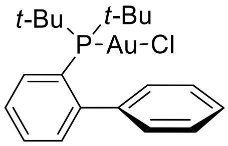
Recently, the research groups of Aponick[22] and Akai[23] independently expanded and improved on the work of Liang and Liu (Table 1.1). In both works, the two groups demonstrated the synthesis of tetra-substituted pyrroles **37** from Au(I)-mediated cycloisomerization of β-aminopropargyl alcohols **36**. The reactions were shown to proceed efficiently at catalyst loadings as low as 0.05 mol % with the corresponding tetra-substituted pyrroles **37** being delivered in excellent yields of up to 99%. In both approaches, the reaction mechanism was thought to involve gold(I)-activated 5-*endo*-dig dehydrative cyclization of *N*-sulfonyl-aminobut-3-yn-2-ols **36**.

Table 1.1 Gold(I)-catalyzed intramolecular cyclization of propargylic alcohols **36**.



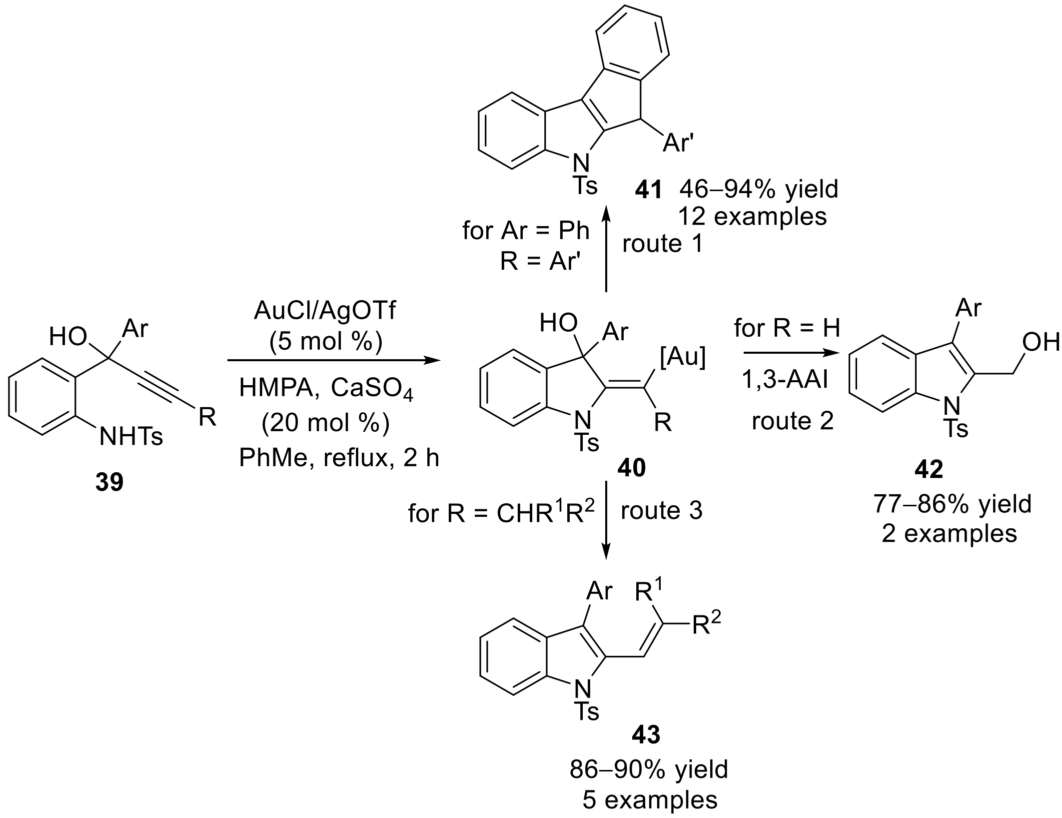
36 **37**

R^1 = Ts, Boc, Bu, Bn
R^2-R^4 = H, alkyl, aryl

Entry	[Au]	Yields (%)	Ref
1	$PPh_3AuCl/AgNTf_2$	85–98 (4 examples)	22
2	 **38** /AgOTf	89–92 (5 examples)	23

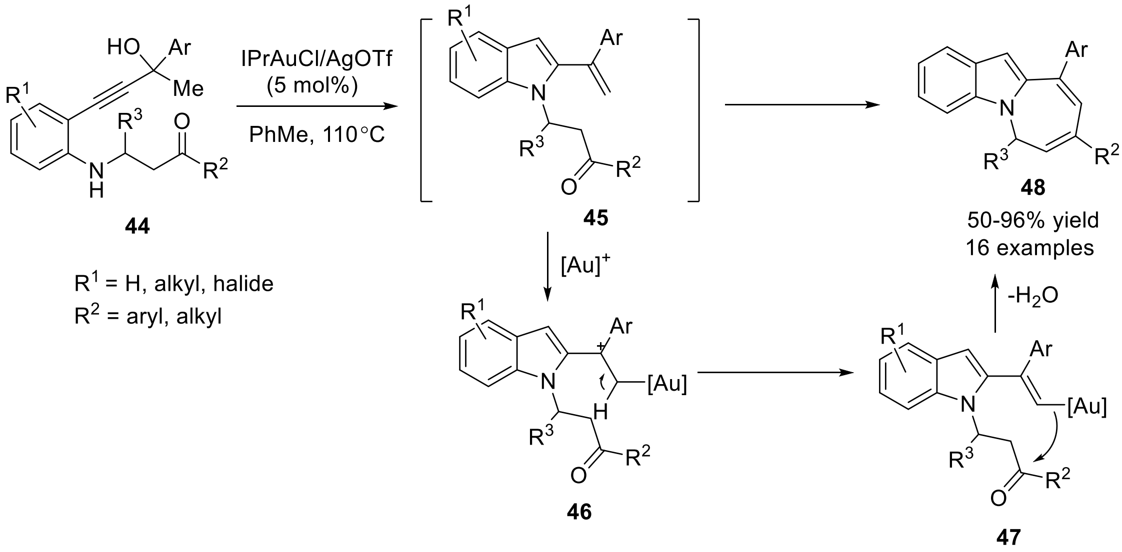
More recently, Chan and co-workers elaborated a pathway to the putative indolic intermediate **40** from amino alkynols **39** (Scheme 1.13).[24] It was proposed that the reaction proceeded by 5-*exo*-dig cyclization to vinyl gold intermediate **40** using a AuCl/AgOTf catalytic combination. Further studies revealed the nature of the vinyl gold intermediate **40** to dictate the course of the reaction, with the pendant R group determining product chemoselectivity. For example, substrates with R = Ar furnished the indole/indene ring-fused products **41** via protodeauration/Friedel-Craft alkylation, whereas for substrates with R = H, the isomerized products **42** via a protodeauration/1,3-allylic alcohol isomerization (1,3-AAI) pathway were obtained (Scheme 1.13, routes 1 and 2). In contrast, in reactions of substrates bearing R = CHR^1R^2, a more facile protodeauration and dehydration step was found to proceed to deliver 2-vinyl-1*H*-indoles **43** (Scheme 1.13, route 3). Interestingly, the addition of hexamethylphosphoramide

(HMPA) in the reaction was shown increase the yield of the respective products. The role of HMPA was believed to moderate the reactivity of the gold catalyst through coordination to the metal center.



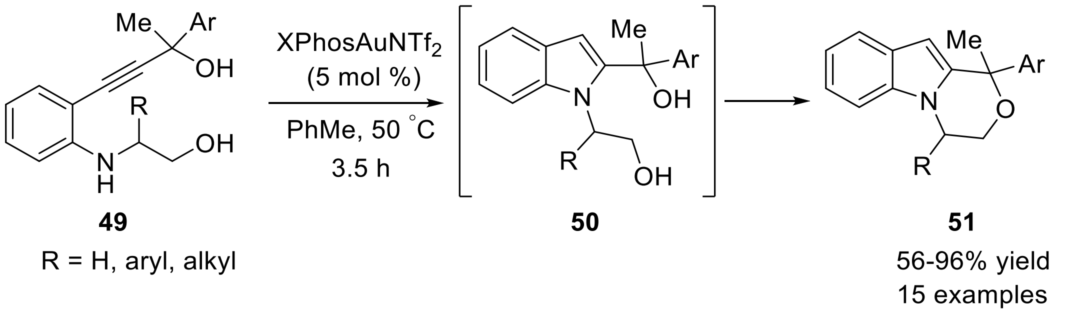
Scheme 1.13 Gold(I)-catalyzed cycloisomerization of 2-tosylamino-phenylprop-1-yn-3-ols **39**.

Following this work, various aniline derivatives of propargylic alcohols were employed as precursors in the synthesis of indole derivatives.[25-28] A recent notable advance in this field was made by Bandini and co-workers who demonstrated that the gold(I)-triggered 5-*endo*-dig hydroamination/dehydration of propargylic alcohol derivatives **44** afforded fused azepino[1,2-*a*]indoles **48** in 50–96% yield (Scheme 1.14).[25] A mechanism involving vinyl gold complex **47**, which was formed following the initial 5-*endo*-dig hydroamination and dehydration steps, was corroborated by deuterium-labelling experiments. Subsequently, the same group disclosed a closely related line of investigation that explored the reactivity of propargylic alcohols **49** (Scheme 1.15).[26] In this study, treatment of the substrate with XPhosAuNTf$_2$ (Xphos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl) was found to give the tricyclic oxazino[4,3-*a*]indoles **51** in 56–96% yield.



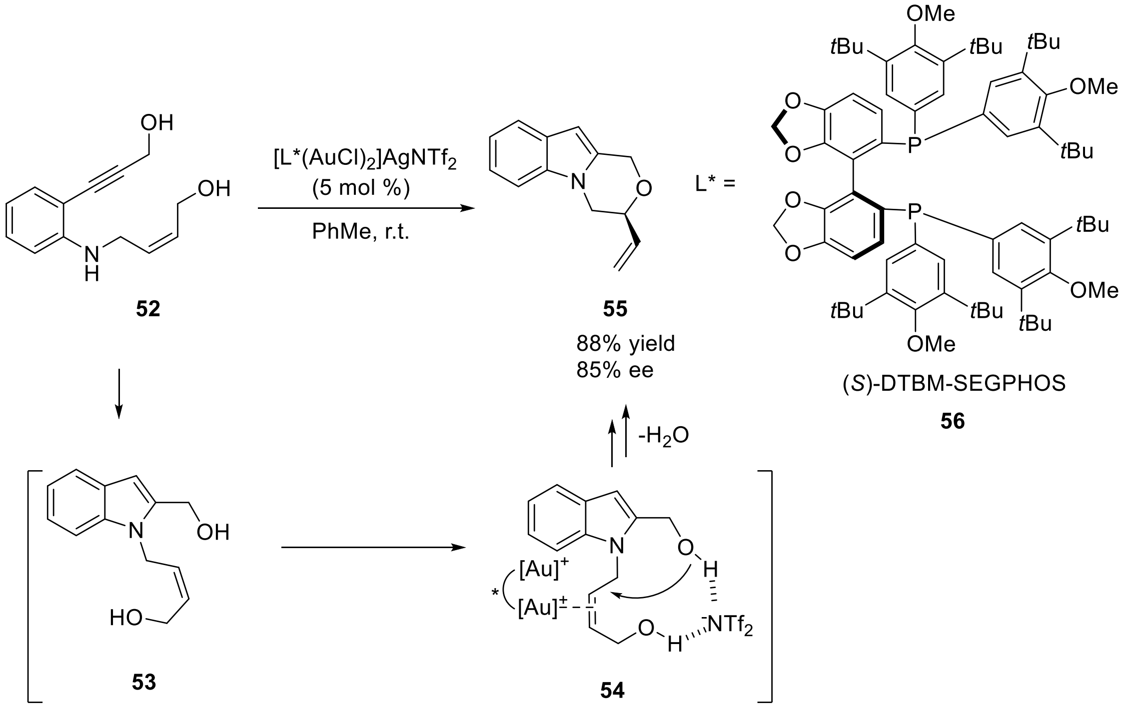
Scheme 1.14 Gold(I)-catalyzed tandem cyclization of **44**.

The reaction protocol was further adopted to afford the targets **55** asymmetrically by employing a bimetallic gold(I) complex and the chiral phosphine ligand **56** (Scheme 1.16).[27] For example, reaction of (*Z*)-4-((2-(3-hydroxyprop-1-yn-1-yl)phenyl)amino)but-2-en-1-ol **52** catalyzed by a 1:1 mixture of [(AuCl)$_2$·**56**] and AgNTf$_2$ in toluene at room temperature led to isolation of (*S*)-3-vinyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indole **55**



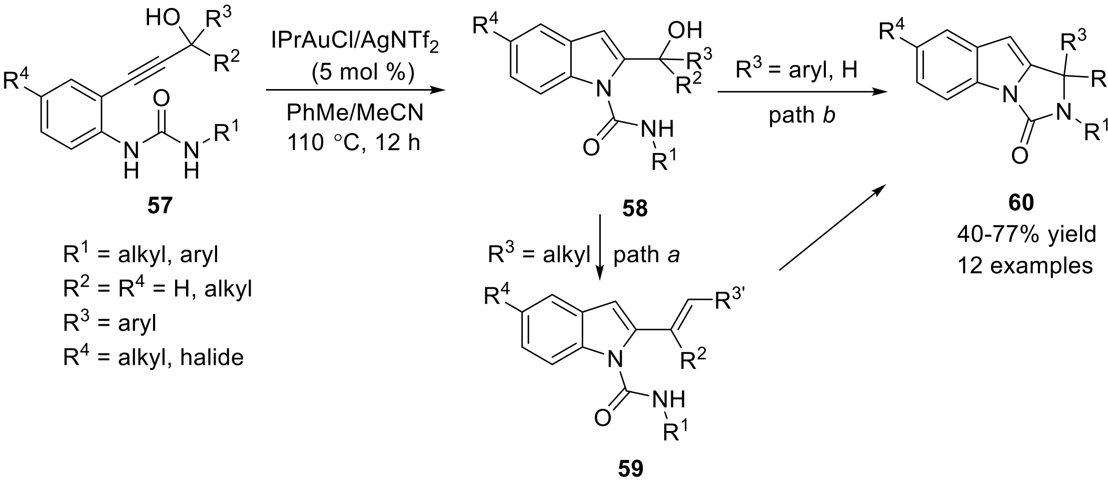
Scheme 1.15 Gold(I)-catalyzed tandem cyclization of **49**.

in 88% yield and with *ee* value of 85%. In this transformation, it was proposed that the initial gold catalyzed hydroaminative protodeauration step led to the formation of indolyl diol intermediate **53**. The indole adduct was then reasoned to undergo alkyloxylation, via intermediate **54**, in the presence of $[(AuCl)_2{\cdot}\mathbf{56}]AgNTf_2$ to give the product.



Scheme 1.16 Gold(I)-catalyzed asymmetric cyclization of **52**.

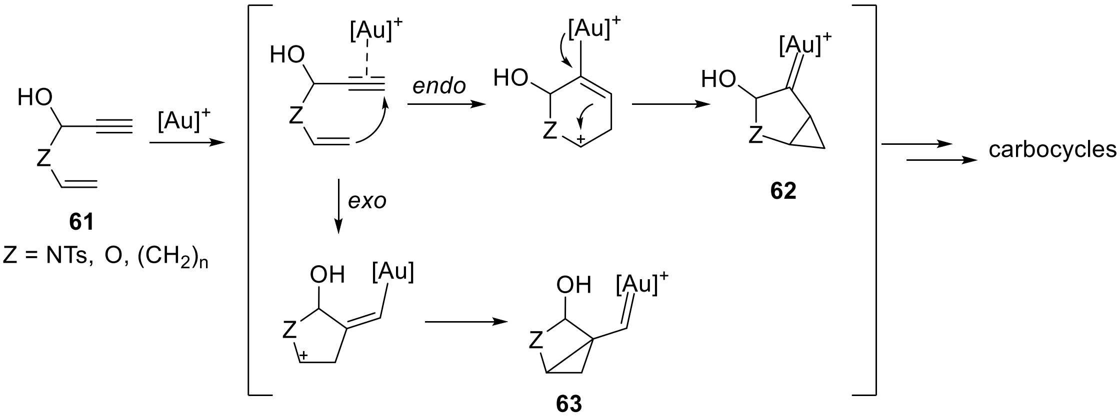
Taking advantage of this methodology, Hashmi and co-workers found that it could be applied to the synthesis of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one derivatives **60** from ureas **57** by gold catalysis (Scheme 1.17).[28] The reaction proceeded efficiently in the presence of IPrAuCl (IPr = 1,3-bis[2,6-bis[(4-tert-butylphenyl)methyl]-4-methylphenyl]imidazol-2-ylidene) in conjunction with $AgNTf_2$ in a mixture of toluene and acetonitrile at 110 °C for 12 h. The reaction was proposed to undergo a cascade 5-*endo*-dig/amination pathway to furnish the 1*H*-imidazo[1,5*a*]indol-3(2*H*)-one derivatives **60** in 40–77% yield. The methodological approach was shown to generally work well for a majority of substrates with the exception of examples where R^1 = 4-$OMeC_6H_4$, R^2 = Ph and $R^3 = R^4$ = H. This was explained by the presence of an electron-rich OMe group increasing the coordinating aptitude of the nitrogen atom in the urea moiety that, in turn, resulted in a decrease in catalyst reactivity.



Scheme 1.17 Gold(I)-catalyzed tandem cyclization of **57**.

1.3.2 Cyclization Processes Involving Carbon-Carbon Bond Formation

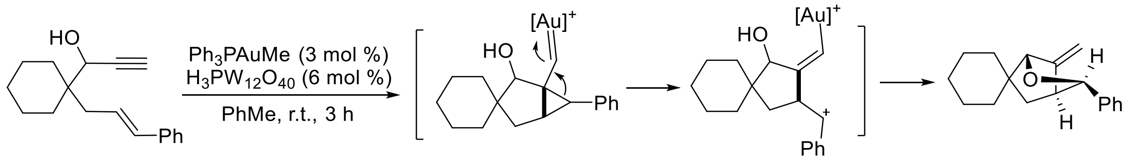
In the development of gold-catalyzed carbocyclization processes involving C–C bond formation from alkynol derivatives, hydroxylated 1,*n*-enynes can be regarded as a useful and elegant precursors (Scheme 1.18).[29] Mechanistically, the approach involves electrophilic activation of the alkyne by the gold salt to trigger possible nucleophilic



Scheme 1.18 A mechanistic outline of hydroxylated 1,*n*-enyne cycloisomerizations under gold catalysis.

attack by the alkene via an *endo* or *exo*-pathway to give metallacyclopropyl carbenoid intermediates **62** or **63**, respectively. These are the key divergent intermediates that may give rise to a variety of target carbocycles.

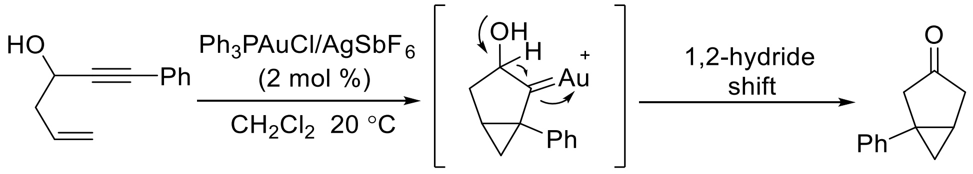
In 2004, Echavarren and co-workers elaborated one of the first examples employing hydroxylated 1,*n*-enynes for carbocyclic synthesis (Scheme 1.19).[30] The work demonstrated the ability of gold in the presence of the additive $H_3PW_{12}O_{40}$, catalyzed the cyclopropanation of 1,6-enynol was shown to give the gold carbenoid species **65**, which then upon ring opening gave the cationic intermediate **66**. Subsequent heterocyclization followed by protodeauration was then thought to give the oxygen-bridged bicyclic adduct **67** as the exclusive product.



64 **65** **66** **67** 100% yield

Scheme 1.19 Gold(I)-catalyzed cycloisomerization of 3-hydroxylated 1,6-enyne **64**.

In the same year, Fürstner and co-workers conducted an experiment on hydroxylated 1,5-enyne **68** under catalysis by Ph_3PAuCl and $AgSbF_6$ at room temperature (Scheme 1.20).[31] It was shown that cycloisomerization of the substrate led to the synthetically valuable bicyclic product **70** in 75% yield. The gold carbenoid species **69** generated by a 6-*endo*-dig cyclization was proposed to be the key intermediate. Prior to this work, the

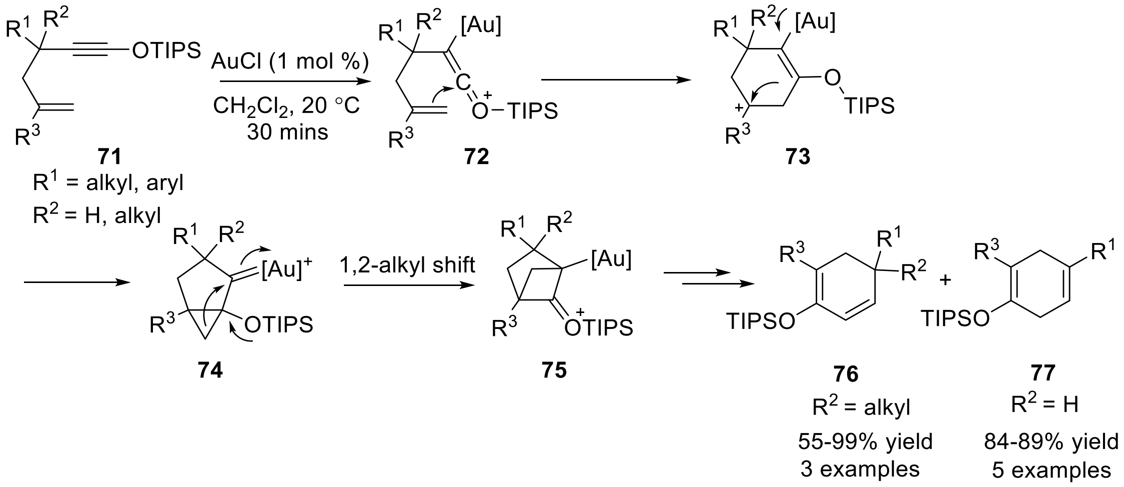


68 **69** **70** 75% yield

Scheme 1.20 Gold(I)-catalyzed cycloisomerization of 3-hydroxylated 1,5-enyne **68.**

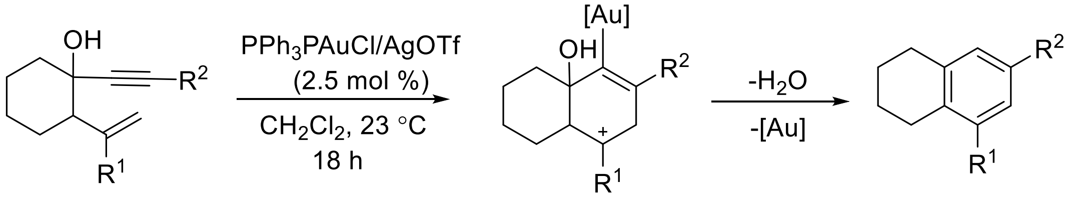
transformation was first accomplished by platinum catalysis in a comparable product yield of 74%.

Subsequently, Zhang and co-workers examined gold-catalyzed cycloisomerization of 1-siloxy-5-en-1-ynes **71** as a mean to provide a better understanding of this class of reaction (Scheme 1.21).[32] The substrate, bearing an alkynyl silyloxy substituent, displayed remarkable efficiency when subjected to AuCl at a catalyst loading as low as 1 mol % and reaction time of 30 minutes to afford 1,2- and 1,3-cyclohexenones (**76** and **77**) in 55–99% and 84–89% yields, respectively. The reaction was thought to proceed via the gold cyclopropyl carbenoid intermediate **74** formed from the reactive alkenone intermediate **72**. Subsequent 1,2-alkyl shift of the gold carbenoid species followed by a series of rearrangement processes would give rise to carbocycles **76** and **77** depending on the substituent at the R^2 position.



Scheme 1.21 Gold(I)-catalyzed cycloisomerization of **71**.

In contrast to these examples, Barriault and co-workers demonstrated that cyclic hydroxylated 1,*n*-enynes such as cyclic 3-hydroxy-1,5-enynes **78** underwent benzannulation in the presence of Ph_3PAuCl in combination with AgOTf to afford substituted tetrahydronaphthalenes **80** in 10–86% yield (Scheme 1.22).[33] This reaction pathway differs from earlier examples as the postulated vinyl gold intermediate **79** which was reasoned to be generated by a 6-*endo*-dig cyclization pathway did not proceed to a gold cyclopropyl carbenoid species as proposed in the previous work. Instead, it underwent dehydration followed by protodeauration to furnish substituted tetrahydronaphthalene products **80**.



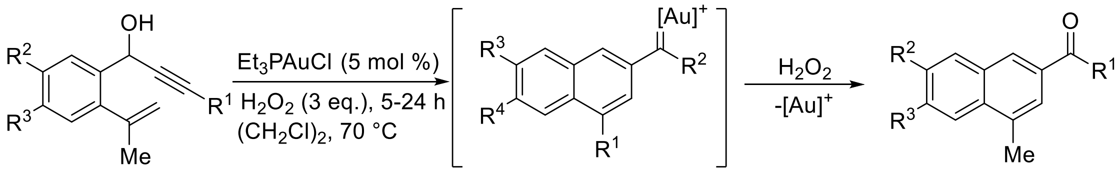
78
R^1 = H, aryl, alkyl, alkoxy
R^2 = H, aryl, alkyl

79

80
10-86% yield
11 examples

Scheme 1.22 Gold(I)-catalyzed cycloisomerization of 3-hydroxylated 1,5-enynes **78**.

The following year, an oxidative benzannulation approach for the synthesis of naphthyl derivatives **83** from 3-hydroxylated 1,6-enynes **81** under catalysis by Et_3PAuCl was reported by Liu and co-workers (Scheme 1.23).[34] The mechanism of this transformation was proposed to involve a gold(I) carbenoid species **82**, which was generated from 6-*exo*-dig dehydrative cyclization of substrate **81**. The gold carbenoid intermediate **82** was then oxidized by the excess amount of hydrogen peroxide and led to the isolation of the desired product.



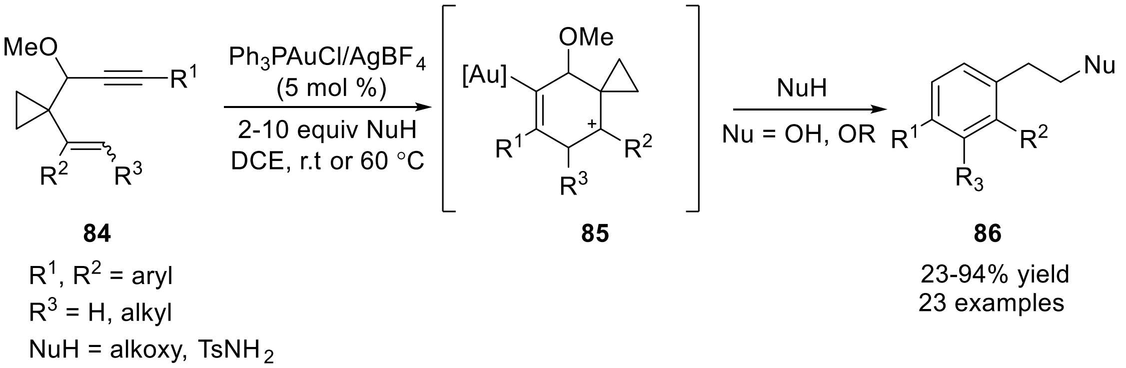
81
R^1 = H, aryl, alkyl
R^2, R^3 = H, aryl, alkyl, alkoxyl, halide

82

83
76-91%
16 examples

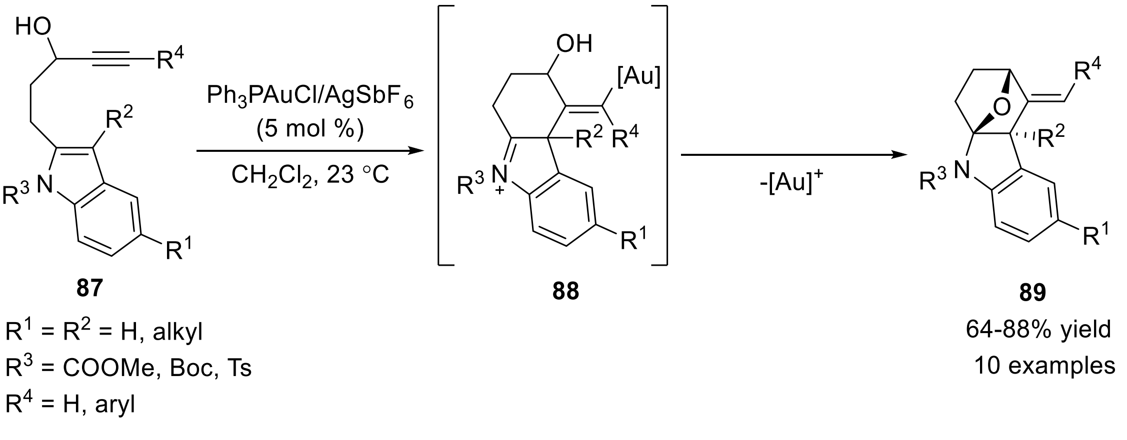
Scheme 1.23 Gold(I)-catalyzed cycloisomerization of 3-hydroxylated 1,5-enynes **81**.

Liu and co-workers demonstrated a further benzannulation procedure involving 3-alkoxy-1,5-enyne derivatives **84** that furnished functionalized benzenes **86** in the presence of $Ph_3PAuCl/AgBF_4$ in yields of up to 94% (Scheme 1.24).[35] It was postulated that the reaction proceeded via 6-*endo*-dig cyclization followed by nucleophilic attack of the resulting vinyl gold intermediate **85** by hydroxyl or alkoxyl nucleophiles to form tri- or tertrasubstituted benzenes.



Scheme 1.24 Gold(I)-catalyzed cycloisomerization of **84**.

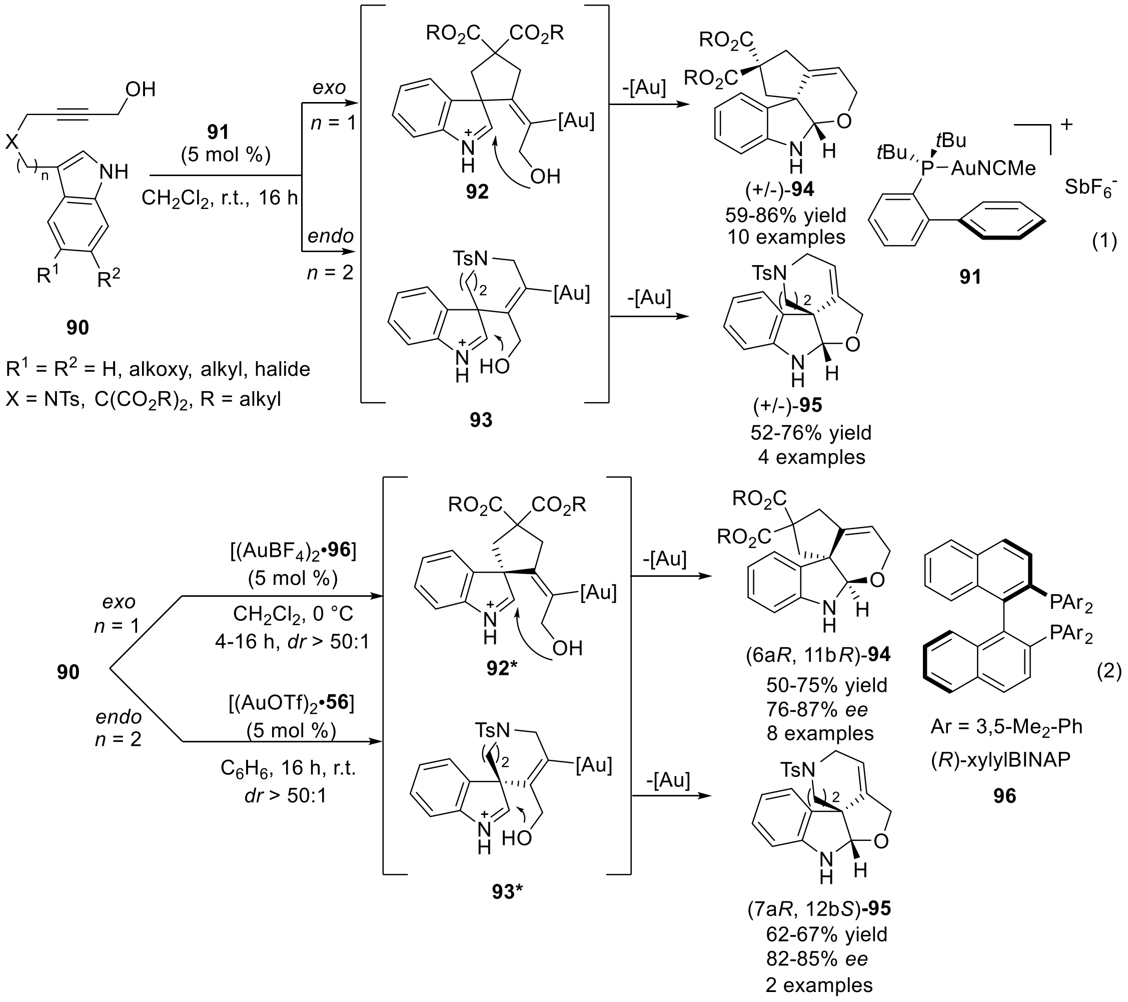
In their works on the cycloisomerization of hydroxylated enynes, Wang and co-workers reported the employment on an indole unit as the internal nucleophilic alkene motif in substrates of the type **87** shown in Scheme 1.25.[36] The imine intermediates **88** generated by $Ph_3PAuCl/AgSbF_6$-mediated Friedel-Crafts cyclization of **87** were subsequently trapped by the hydroxyl group to furnish bioactive 2,3-fused ring indoline



Scheme 1.25 Gold(I)-catalyzed tandem Friedel-Crafts reaction/hydroalkoxylation of **87**.

derivatives **89** in 64–88% yield.

In a similar manner, Bandini and co-workers communicated gold(I)-assisted intramolecular hydroindolination of alkynes **90** to tetracyclic indolines **94** and **95** (Scheme 1.26, eq 1).[37a] In this reaction, JohnPhosAu(NCMe)SbF_6 **91** (JohnPhos = [2-Biphenyl]di-*tert*-butylphosphine) was shown to efficiently catalyze the cyclization of indolyl propargylic alcohols **90** via an *exo*-dig or *endo*-dig pathway to afford the corresponding iminium intermediates **92** and **93**. The chemoselectivity was found to depend on substrate structure; formation of the former resulted when X = $C(CO_2R)_2$ and the latter was afforded when X = NTs. The iminium intermediates were surmised to undergo trapping by the hydroxyl moiety leading to the isolation of tetracyclic indolinyl-



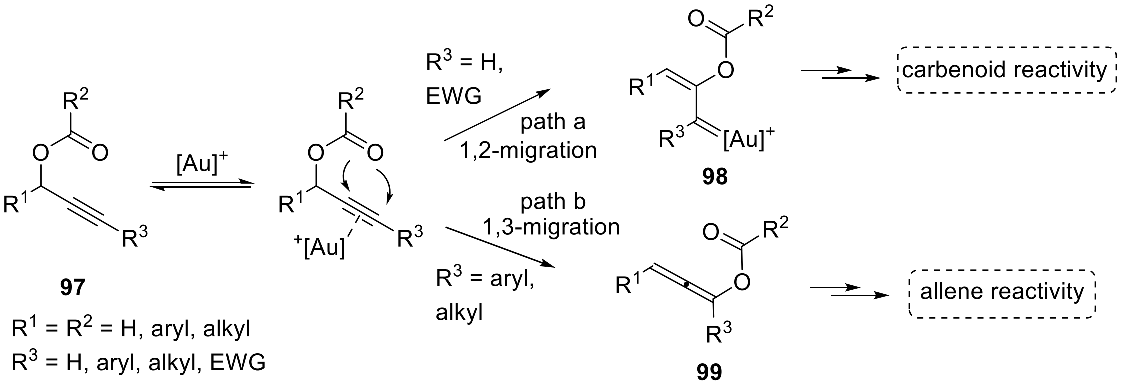
Scheme 1.26 Gold(I)-catalyzed Fridel-Craft/hydroalkoxylation of **90**.

fused products **94** and **95**. It is worth noting that, in contrast with the previous transformation, protection of the indole nitrogen was not necessary for the cycloisomerization. Subsequently, the same group reported an asymmetric adaptation of this methodology by using binuclear gold complex with a chiral *bis*-phsophine ligand, as shown in Scheme 1.26, eq 2.[37b] The asymmetric version of this reaction was proposed to undergo the same mechanistic pathway as its non-enantioselective analogue, resulting the formation of the corresponding chiral indolinyl-fused products (6a*R*, 11b*R*)-**94** and (7a*R*, 12b*S*)-**95** in yields of 50–75% and 62–67%, respectively. Notably, this approach could provide the chiral indolinyl-fused products **94** and **95** with *ee* values of up to 87% and 85%, respectively. The absolute configuration of the products was determined and confirmed by TD-DFT simulation of the electronic circular dichroism spectra of the products.

1.4 1,*n*-Diyne Esters

1.4.1 Typical Reactivity

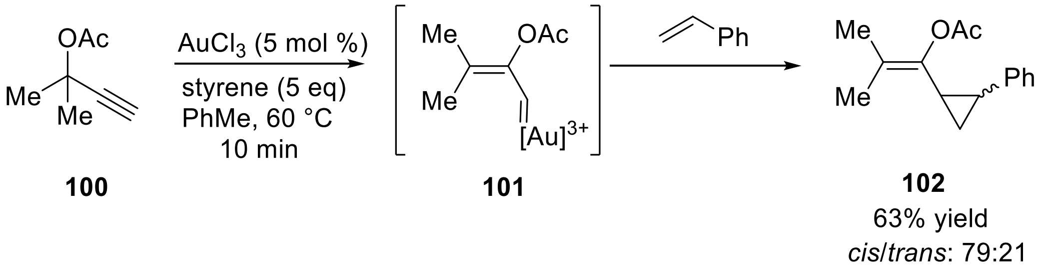
From a mechanistic viewpoint, acyloxy migrations of propargylic esters have been shown to follow two distinct pathways in gold catalysis (Scheme 1.27).[38] It is generally accepted that propargylic esters of terminal alkynes (R^3 = H), or with electron-



Scheme 1.27 Two competing mechanistic pathways for gold-catalyzed reactions of propargylic esters.

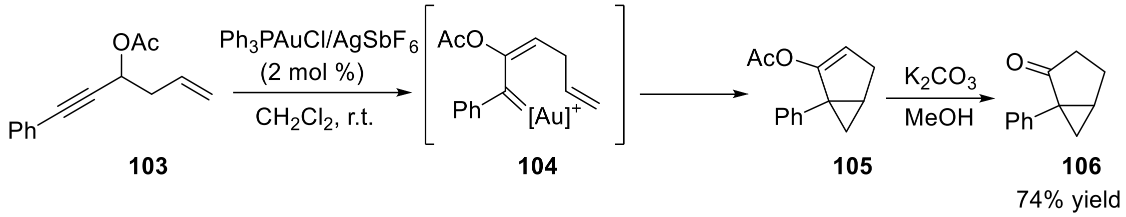
withdrawing groups, typically undergo 1,2-acyloxy migration, to afford gold-carbenoid intermediate **98** (Scheme 1.27, path *a*). Alternatively, internal-alkynyl propargylic esters ($R^3 \neq H$) tend to undergo a 1,3 acyloxy migration pathway and result in the formation of allene intermediates **99** (Scheme 1.27, path *b*). The difference in reactivity and products formed by 1,2- and 1,3-migration of propargylic esters under gold catalysis, combined with the ease of substrate preparation has triggered extensive studies in this intriguing and highly valuable field over the last decade.

The first reported example of gold-catalyzed acyloxy migration of propargylic esters was that described by Ohe and Uemura as part of a wider study examining the reaction of intermolecular cyclopropanation of alkenes by propargylic carboxylates catalyzed by ruthenium complexes (Scheme 1.28).[39] In this work, methylbut-3-yn-2-yl acetate **100** underwent 1,2-acyloxy migration in the presence of gold(III) chloride with toluene as the solvent to form gold carbenoid species **101**. The resulting gold carbenoid intermediate would then undergo cyclopropanation in the presence of an excess amount of styrene to give cyclopropanated adduct **102** in a modest yield of 63% and with a *cis*/*trans* ratio of 79:21.



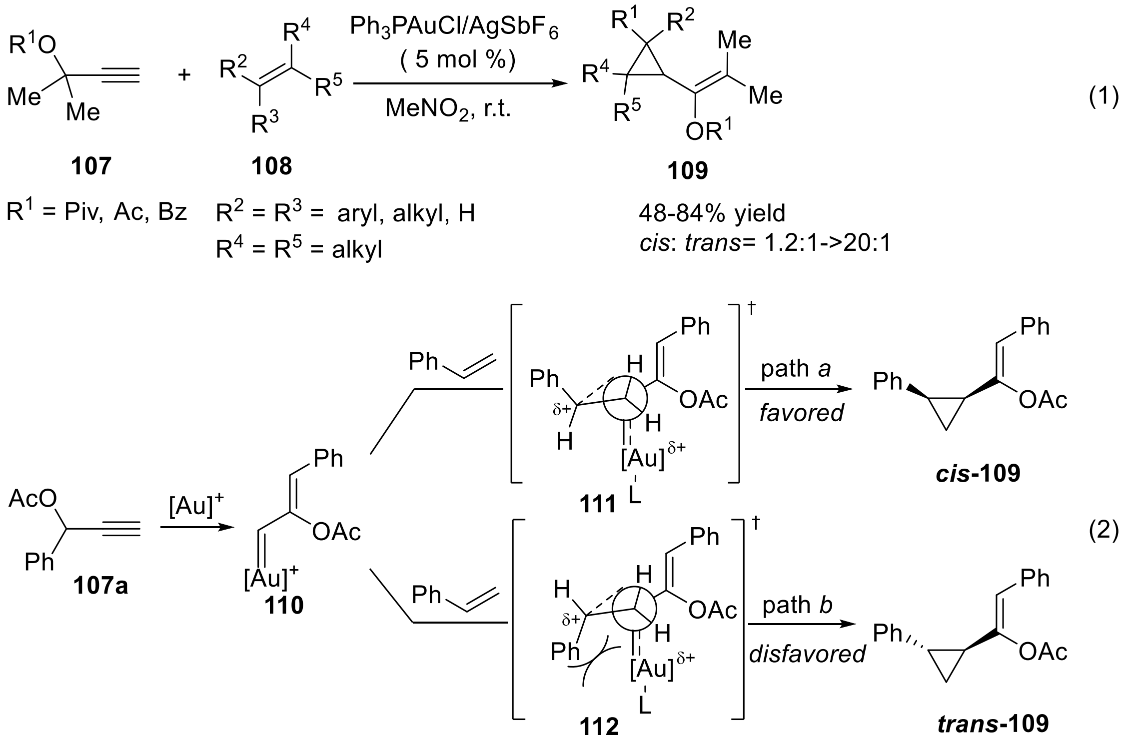
Scheme 1.28 Gold(III)-catalyzed intermolecular alkene cyclopropanation by 2-methylbut-3-yn-2-yl acetate **100**.

In 2004, Fürstner and co-workers revealed one example of intramolecular gold-catalyzed acyloxy migration/cyclopropanation of 1,5-enyne acetate **103** in the course of a study examining platinum-mediated cycloisomerizations of hydroxylated enynes (Scheme 1.29).[31] Under catalysis by 2 mol % of PPh_3AuCl and $AgSbF_6$, 1-phenylhex-5-en-1-yn-3-yl acetate **103** underwent 1,2-acyloxy migration to produce 1-phenylbicyclo[3.1.0]hex-2-en-2-yl acetate **105** via cyclopropanation of the gold carbenoid intermediate **104**. Subsequent deacylation of **105** by potassium carbonate in methanol afforded 1-phenylbicyclo[3.1.0]hexan-2-one **106** in 74% yield.



Scheme 1.29 Gold(I)-catalyzed cycloisomerization of acyloxylated enyne **103**.

Building on this work, Toste and co-workers reported the first intermolecular olefin cyclopropanation of the gold carbenoid intermediate **110** generated in situ by 1,2-migration of propagylic acetates **107** in the presence of Ph_3PAuCl and $AgSbF_6$ as the

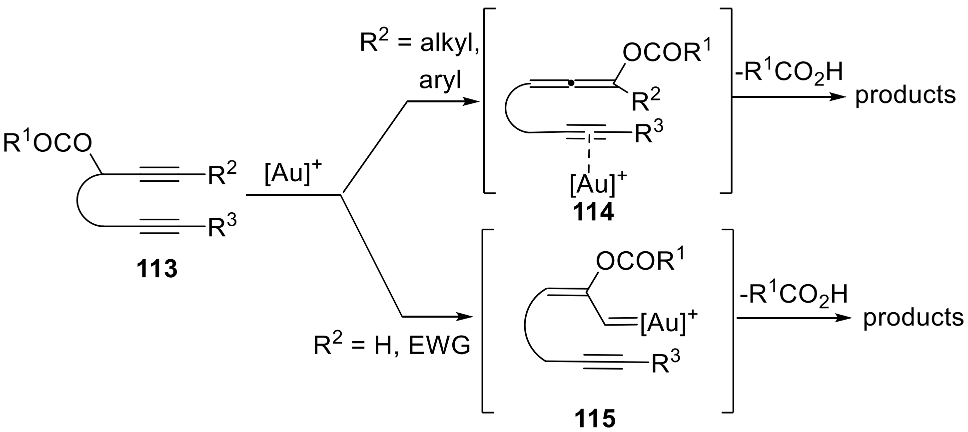


Scheme 1.30 Gold(I)-catalyzed olefin cyclopropanation by propargylic esters **107**.

catalytic system (Scheme 1.30, eq 1).[40] The *cis*-cyclopropanes **109** were obtained chemoselectively in 48–84% yield as the major product. The observed diastereoselectivity was explained by the steric interaction between the olefin substituent and the ligand of the gold catalyst in the two possible transition states (**111** and **112**) during the course of the cyclopropanation process (Scheme 1.30, eq 2). Unfavourable interaction in transition state **112** (Scheme 1.30, eq 2, path *b*) resulted in a preference for the transition state **111** and the selective formation of the *cis*-cyclopropane ***cis*-109** (Scheme 1.30, eq 2, path *a*).

1.4.2 Diyne Substrates

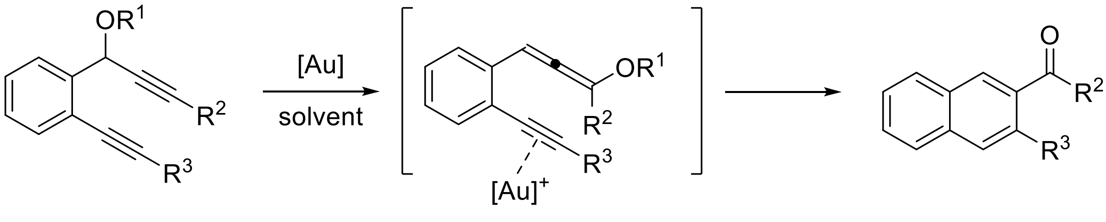
Following these seminal works there has been a handful of studies of examining gold-catalyzed cycloisomerization of 1,*n*-diyne esters (Scheme 1.31).[41-53] By making use of the known mode of cycloisomerization of 1,*n*-diyne esters **113** to undergo 1,2- or 1,3-acyloxy migration to give the corresponding gold carbenoid species **114** and allenic esters **115**, a variety of products were shown to be prepared through further functionalization by the remaining pendant alkyne moiety in these adducts.



Scheme 1.31 Gold-catalyzed reactivities of 1,*n*-diyne esters.

The first example of gold-mediated transformations of 1,*n*-diyne esters was reported by Toste and co-workers investigating the catalytic Myers-Saito cyclization of 1,6-diyne esters to aryl ketones (Table 1.2, entry 1).[41] This methodology showed that *t*-Bu_3PAuCl in combination with $AgSbF_6$ catalyzed the conversion of 1-(2-ethynylphenyl)-3-phenylprop-2-yn-1-yl pivalate **116a** to naphthalen-2-yl(phenyl)methanone **118a** via the allenyl ester **117a** in 71% yield. However, the study also found $AgSbF_6$ with MgO, which acted as a scavenger for the pivalic acid, as the additive were shown to efficiently mediate the reaction in comparable product yield of 84%. At about the same time, Oh and co-workers reported a similar approach for the preparation of aryl ketone **118** using gold(III) salt in combination with PPh_3 in the ratio of 1:1 (Table 1.2, entry 2).[42]

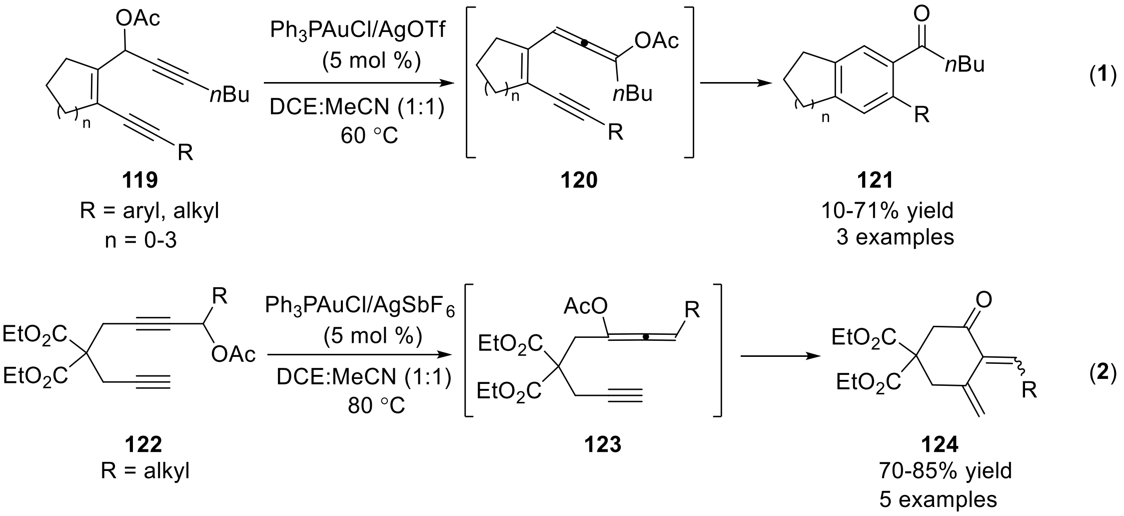
Table 1.2 Gold(I)-catalyzed synthesis of aromatic ketones from 1,6-diyne esters **116**.



116 **117** **118**

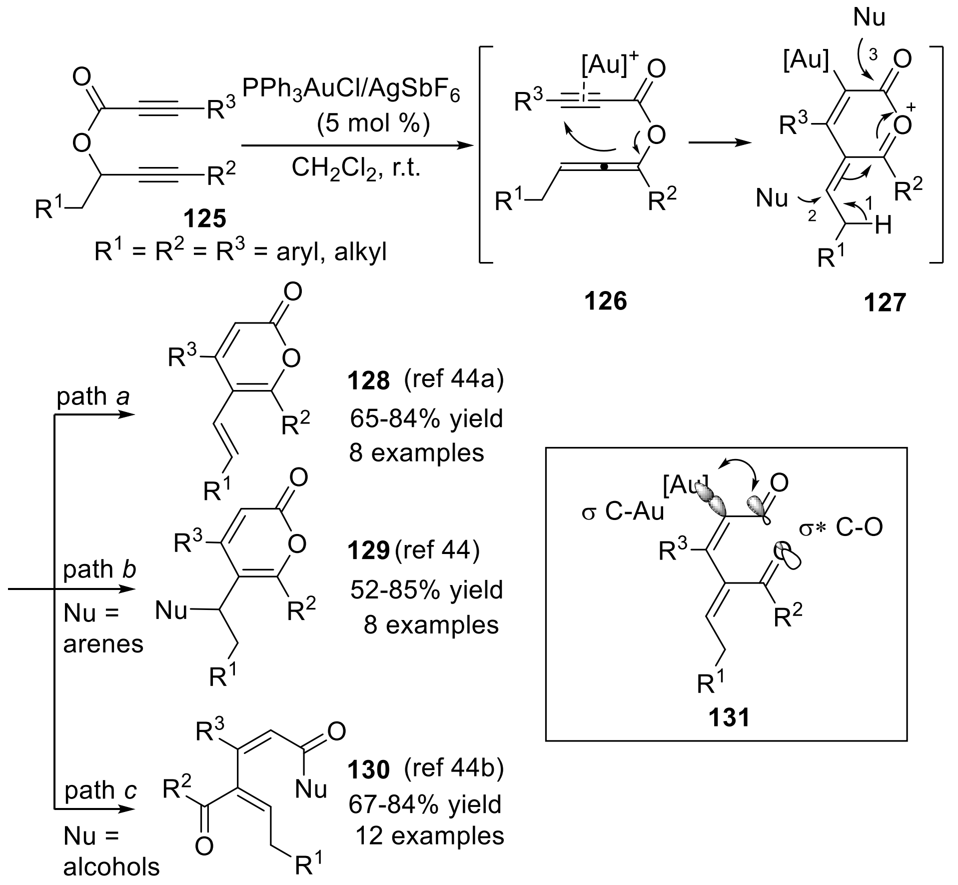
Entry	Substrate	[Au]	Yields (%)	ref
1	R^1 = Piv, R^2 = Ph, R^3 = H (**116a**)	*t*-$Bu_3PAuCl/AgSbF_6$ (5 mol%)	71%	41
2	R^1 = Ac; R^2, R^3= H, aryl, alkyl	$NaAuCl_4/PPh_3$ (3 mol%)	0–91% (10 examples)	42

The outcome of this work by Toste and co-workers showing silver salts to catalyze the cycloisomerization of **116** would appear to nullify the use of gold complexes as catalysts due to the significant lower cost of the former. However, the scope of the silver-catalyzed methodology was found to be limited to substrates bearing a rigid phenyl linker. Following these studies, Oh and co-workers revealed that only gold complexes were able to mediate the efficient cycloisomerization of 1,6-diyne esters with a flexible aliphatic linker (Scheme 1.32).[43] In these reactions, 1,3-acyloxy migration followed by cycloisomerization of 1,6-diyne esters **119** and **122** afforded *ortho*-substituted aryl ketone **121** and α-vinyl cyclohexanone derivatives **124** in yields of 10–71% and 70–85%, respectively. The key intermediates were reasoned to be the yne-allenoates **120** and **123**, respectively.



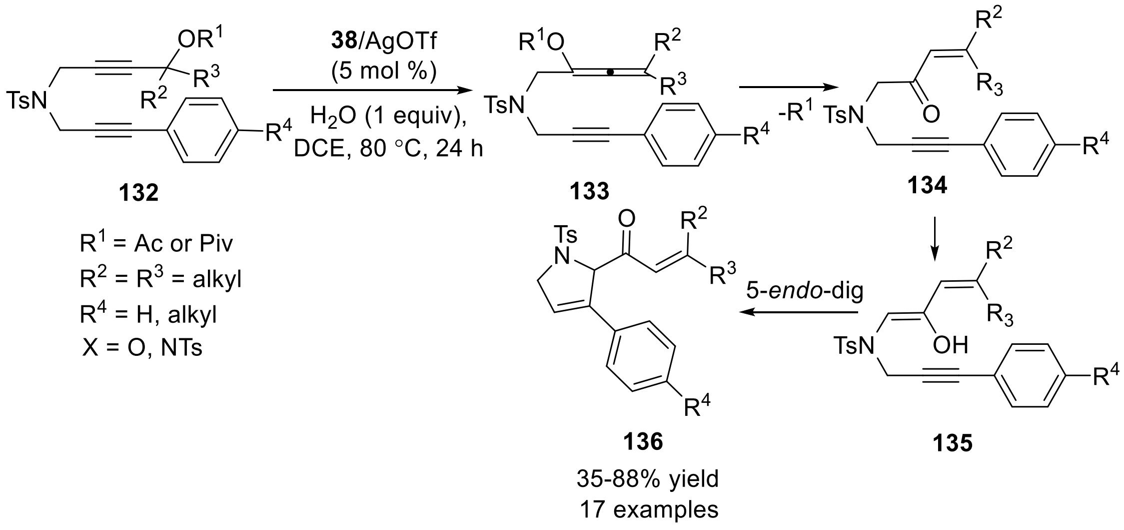
Scheme 1.32 Gold(I)-catalyzed cyclization of diyne propargylic esters **119** and **122**.

In an effort to broaden the synthetic utility of 1,*n*-diyne esters in gold catalysis, Schreiber and co-workers demonstrated the cycloisomerization of readily accessible propargyl propiolates **125** (Scheme 1.33).[44] In this reaction, oxocarbenium **127**, generated by 6-*endo*-dig cyclization of allenyne complex **126**, was deemed to be the key intermediate. In the absence of externa nucleophiles, oxocarbenium **127** was proposed to undergo elimination to afford a vinyl α-pyrone **128**, with yields of 65–84% (Scheme 1.33, path *a*). In the presence of an external arene and alcohol nucleophile, products **129** and **130** were formed in yields of 52–85% and 67–84% respectively (Scheme 1.33, paths *b* and *c*). The chemoselectivity was reasoned to be due to the nature of the nucleophile and the strength of the cleave acyl C–O bond in the oxocarbenium intermediate **127**. This, in turn, was thought to be affected by the delocalization of the C–Au bonding electrons into the C–O antibonding orbital (**131** in Scheme 1.33).



Scheme 1.33 Gold(I)-catalyzed rearrangement of diyne esters **125**.

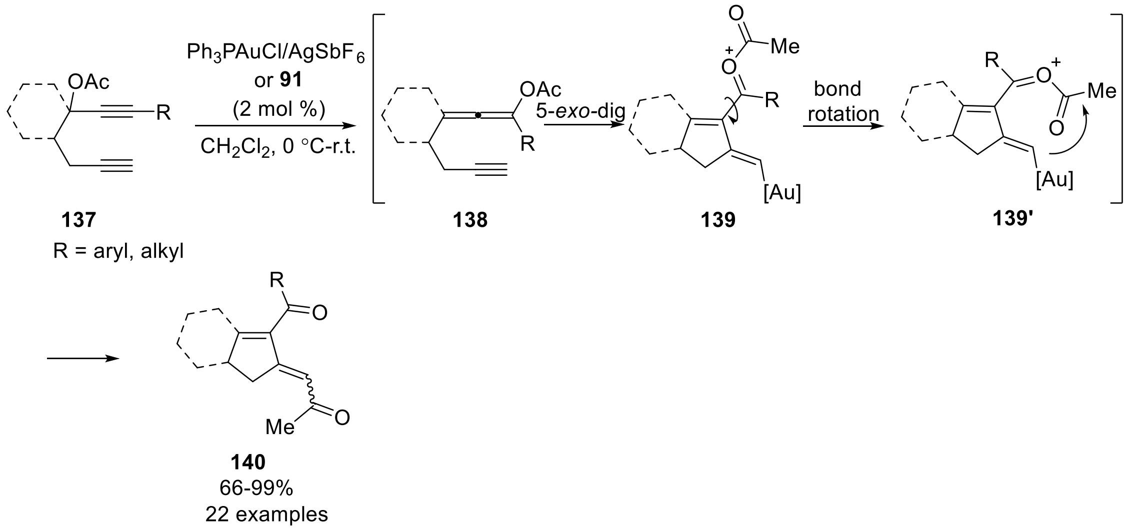
More recently, Shi and co-workers discovered an intriguing gold(I)-catalyzed cyclization of 1,6-diyne esters **132** that produced ketone tethered 2,5-dihydropyrrole



Scheme 1.34 Gold(I)-catalyzed cycloisomerization of 1-hydroacyloxylated 1,6-diynes **132**.

derivatives **136** in 35–88% yield (Scheme 1.34).[45] The mechanism was postulated to initially proceed by 3,3-sigmatropic acyloxy rearrangement of the substrate to give the corresponding allenyne intermediate **133** followed by hydrolysis to yield the conjugated enone **134**. The presence of 1 equivalent of water was required to facilitate the hydrolysis step. Subsequent tautomerization of enone **134** and 5-*endo*-dig cyclization afforded the dihydropyrrole **136**.

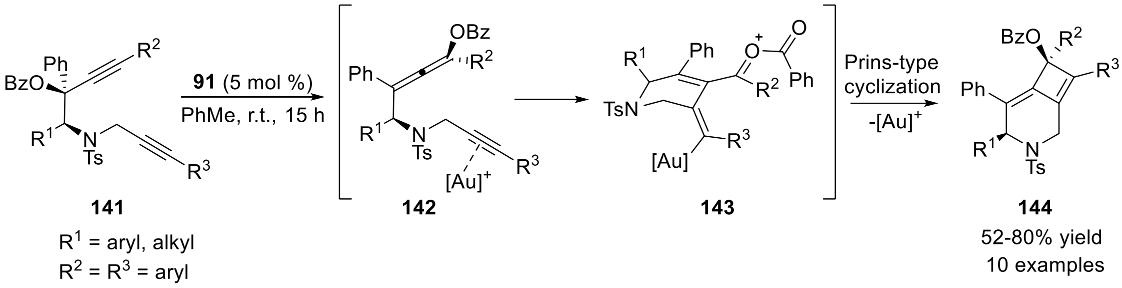
The studies highlighted to this point have, so far, followed a proposed reaction pathway of 1,3-acyloxy migration, cyclization and subsequent acyl elimination to furnish the corresponding cyclic products. Of these steps, it is the acyl elimination process that renders these existing methods deficient in terms of atom-economy. To address this issue, Malacria and co-workers showed the first example of Au(I)-triggered intramolecular 1,5-acyl shift in vinyl gold intermediate **139** (Scheme 1.35).[46] The intermediate **139** with *E* configuration, generated by the 5-*exo*-dig cyclization of **138**, was shown to undergo 1,5-acyl migration to give the corresponding dicarbonyl cycloisomerized products **140** in good yield up to 99%. It is worth noting that the C–C bond rotation process of the acylium



Scheme 1.35 Gold(I)-catalyzed cycloisomerization/1,5-acyl migration of diyne esters **137**.

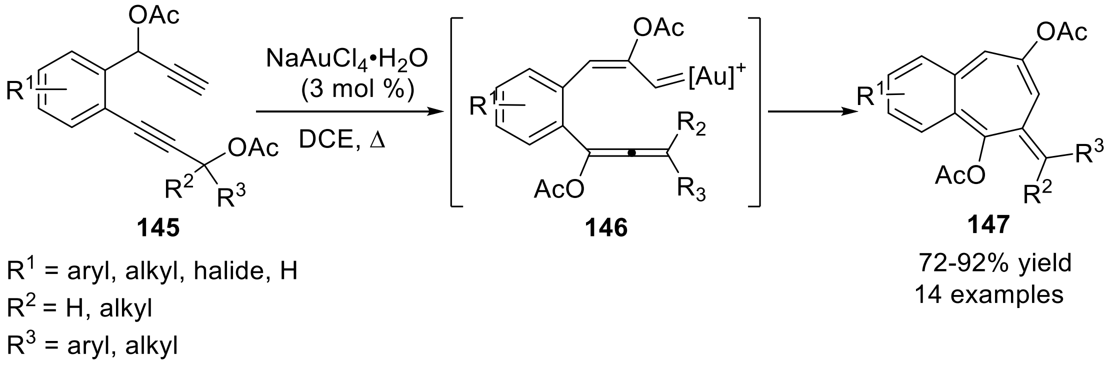
ion, as shown in **139**, was vital to facilitate the migration of the acyl group and this has been confirmed by DFT calculation.

More recently, the trapping of the acylium ion in vinyl gold intermediates was reported by Chan and co-workers in gold(I)-catalyzed cycloisomerization of diyne benzoate **141**, to provide azabicyclo[4.2.0]octa-1(8),5-dines **144** (Scheme 1.36).[47] It was reasoned that the piperidine vinyl gold functionality of intermediate **143** was trapped by the highly electrophilic carbonyl carbon center via a Prins-type cyclization to give corresponding fused bicyclic products in 52–80% yield.



Scheme 1.36 Gold(I)-catalyzed cycloisomerization of monosubstituted 1,7-diyne benzoates **141**.

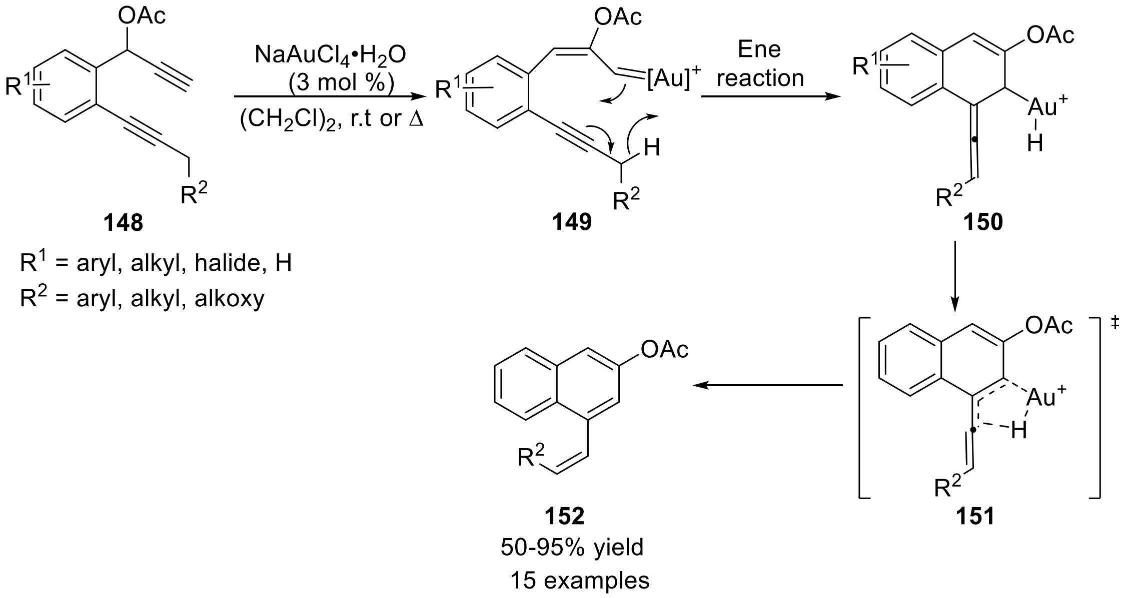
Subsequently, Oh and co-workers branched out by examining the chemistry of substrates **145**, which possesses two propargylic carboxylates, of which one is terminal and the other internal, toward gold-catalyzed cycloisomerization (Scheme 1.37).[48] Mechanistically, the outcome was interesting as the two different propargylic esters in the



Scheme 1.37 Gold(III)-catalyzed sequential activation of proapargylic esters **145**.

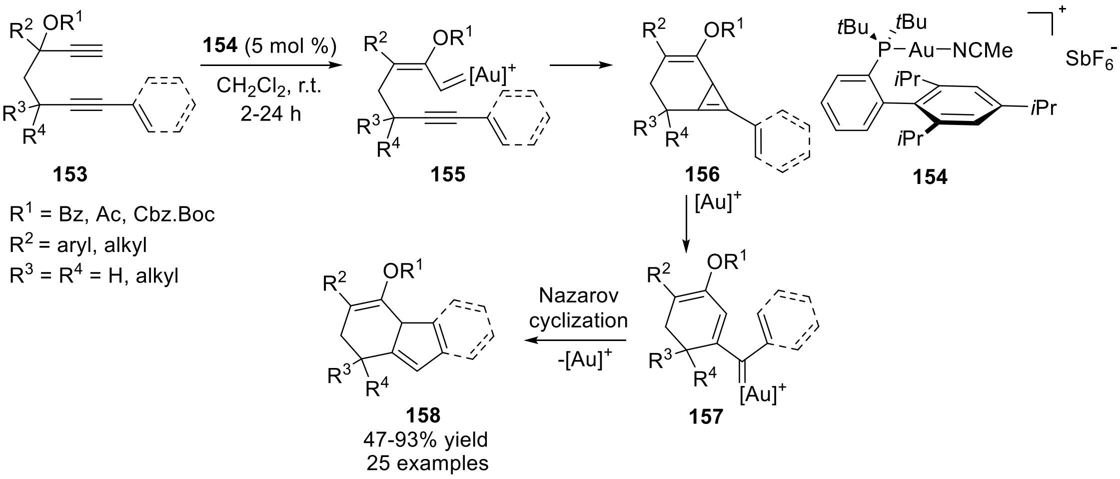
substrate were anticipated to react concomitantly to give a new class of compound, the fused cycloheptadienes **147**. In the work, substrates **145** were subjected to $NaAuCl_4•H_2O$ in 1,2 dichloroethane at reflux. The simultaneous 1,2- and 1,3-acyloxy migrations of both propargylic esters in substrates **145** generated the proposed allenoate gold carbenoid intermediates **146**. The gold carbenoid moiety further reacted with the pendant allenoate in **146** and produced 7-membered fused ring adducts **147** with yields ranging between 72–92%.

In a further modification of this methodology, the same research group demonstrated introduction of a CH_2 group adjacent to the pendant alkyne moiety in substrate **148** would lead to the 2-acetoxynaphthalene targets **152** via an Ene reaction (Scheme 1.38).[49] With an α-hydrogen atom next to the alkyne moiety, the in situ generated gold carbenoid intermediate **149** was surmised to undergo a proposed Ene-type cyclization with the pendant triple bond to afford Au-bound allene intermediate **150**. Deauration of the gold atom from **150** led to the formation of desired 2-acetoxynaphthalene derivatives **152** with yields of 50–95% in a concerted process via a plausible transition state **151**.



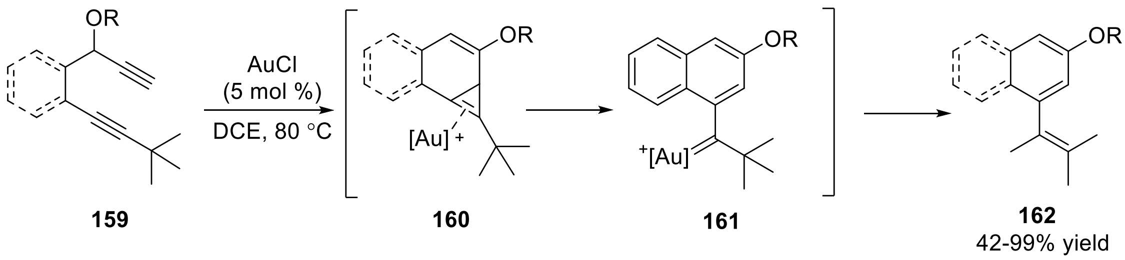
Scheme 1.38 Gold(III)-catalyzed acylocy migration/Ene-type cyclization of **148**.

Recently, Chan and co-workers discovered a conceptually novel transformation which involved trapping of propargylic esters-derived gold carbenoids **155** with a tethered alkyne, resulting in the formation of cyclopropene containing intermediate **156**, as depicted in Scheme 1.39.[50] This approach has allowed elegant access to tricyclic fused ring systems of the targets **158**. In this reaction, cycloreversion of the cyclopropene intermediate **156** would generate a secondary gold carbenoid species **157** and ensuing Nazarov-type cyclization was reported to afford 2,4a-dihydro-1*H*-fluorene derivatives **158**.



Scheme 1.39 Gold(I)-catalyzed cycloisomerization of 1,6-diyne esters **153**.

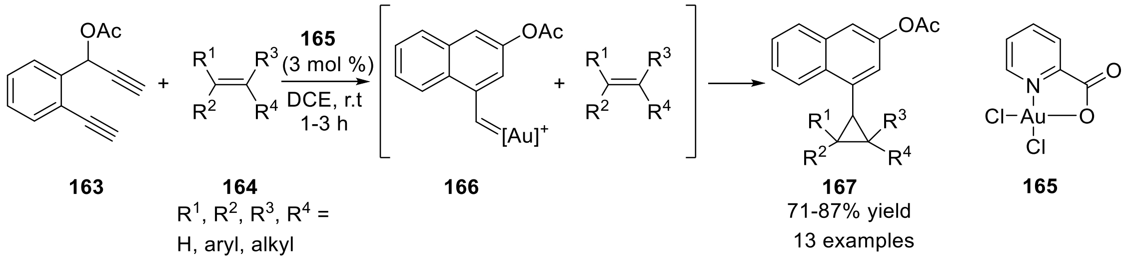
At about the same time, Hashmi reported a related methodology involving the exploitation of 1,6-diyne starting materials **159** (Scheme 1.40).[51] This reaction led to the synthesis of 3-acetoxynaphthalene derivatives **162**, with the reaction pathway surmised to proceed through the formation of the highly reactive cyclopropene intermediate **160**.



Scheme 1.40 Gold(I)-catalyzed cycloisomerization of 1,6-diyne esters **159**.

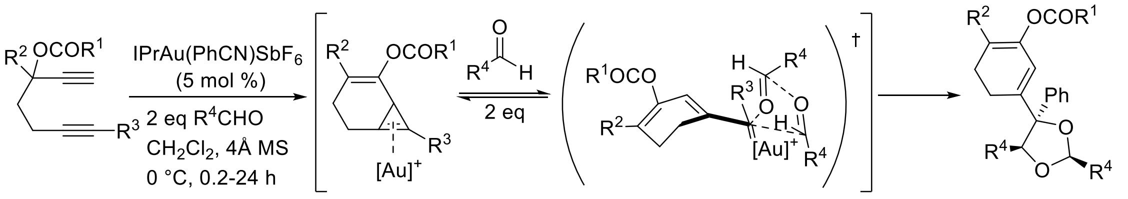
After the gold-mediated ring opening of the cyclopropene unit and 1,2-migration of the methyl group of tertiary butyl moiety, as shown in **161**, the 3-acetoxynaphthalene products were formed.

Following this work, the same research group further extended the methodology by demonstrating the intermolecular approach that involved trapping of a gold carbenoid intermediate, which is analogous to **161**, by various type of external alkenes (Scheme 1.41).[52] In this instance, dichloro(2-pyridinecarboxylato)gold(III) salt was found to efficiently catalyze the cyclopropanation of substituted alkenes **164** with 1-(2-ethynylphenyl)prop-2-yn-1-yl acetate **163** to afford the corresponding arylcyclopropanes **167**. This transformation enables the fast and efficient synthesis of arylcyclopropyl derivatives under mild reaction conditions.



Scheme 1.41 Gold(I)-catalyzed cyclopropanation of alkenes by 1-(2-ethynylphenyl)prop-2-yn-1-yl acetate **164**.

A recent example of this intermolecular approach to achieve the synthesis of 4-(cyclohexa-1,3-dienyl)-1,3-dioxolanes **170** was communicated by Chan and co-workers using alkyl aldehydes as sources of trapping gold carbenoid species resulted from the rearrangement of 1,6-diyne esters **168** (Scheme 1.42).[53] In this reaction, the optimum conditions was found to be IPrAu(PhCN)SbF_6 as the catalyst in dichloromethane at 0 °C and the corresponding products were obtained in 43–84% yield. It was proposed that this [2+2+1] cycloaddition transformation proceeded via the transition state **169**.



168
R^1, R^2, R^3 = aryl, alkyl
R^4 = alkyl

169

170
43-84% yield
29 examples

Scheme 1.42 Gold(I)-catalyzed [2+2+1] cycloaddition of 1,6-diyne esters **168** with alkyl aldehydes.

1.5 Proposed Work

The work of this thesis will focus on developing novel and useful methodologies for the delivery of innovative ring compounds with potential in pharmaceutical and materials applications. It is proposed that this will be accomplished by exploiting the highly reactive and chemoselective nature of environmentally benign gold catalysis and readily accessible alkynol derivatives as starting materials. The developed methods will be designed such that H_2O and AcOH are the only potential by-products, giving a high level of atom economy.

Thus, it is proposed that the aim of this project will be to establish new gold-catalyzed transformations for the synthesis of substituted pyrroles, *o*-phenolic esters and carbon-bridged carbocycles as well as aceanthrylene derivatives. In general, based on the known modes of reactivity in gold catalysis, it may be predicted that activation of internal alkynes present in alkynol precursors by the π-acidic gold species would render the carbons of a triple bond electrophilic in nature. It is envisioned that intramolecular dehydrative aminocyclization followed by 1,3-sulfonyl migration of propargylic alcohol **I** with a pendant nucleophilic sulfonylamino group could lead to the formation of *penta*-substituted pyrroles **I'**. Replacing the nucleophilic component with a β-keto ester group, the *o*-phenolic ester scaffold **II'** can be prepared through dehydrative benzannulation of 5-hydroxy-3-oxoalk-6-ynoates **II**. On the other hand, in can be seen that a synthetic route to carbon-bridged bicyclic carbocycles **III'** can be accessed via a sequential pathway of acyloxy migration and annulation of 1,8-diyne esters **III**.

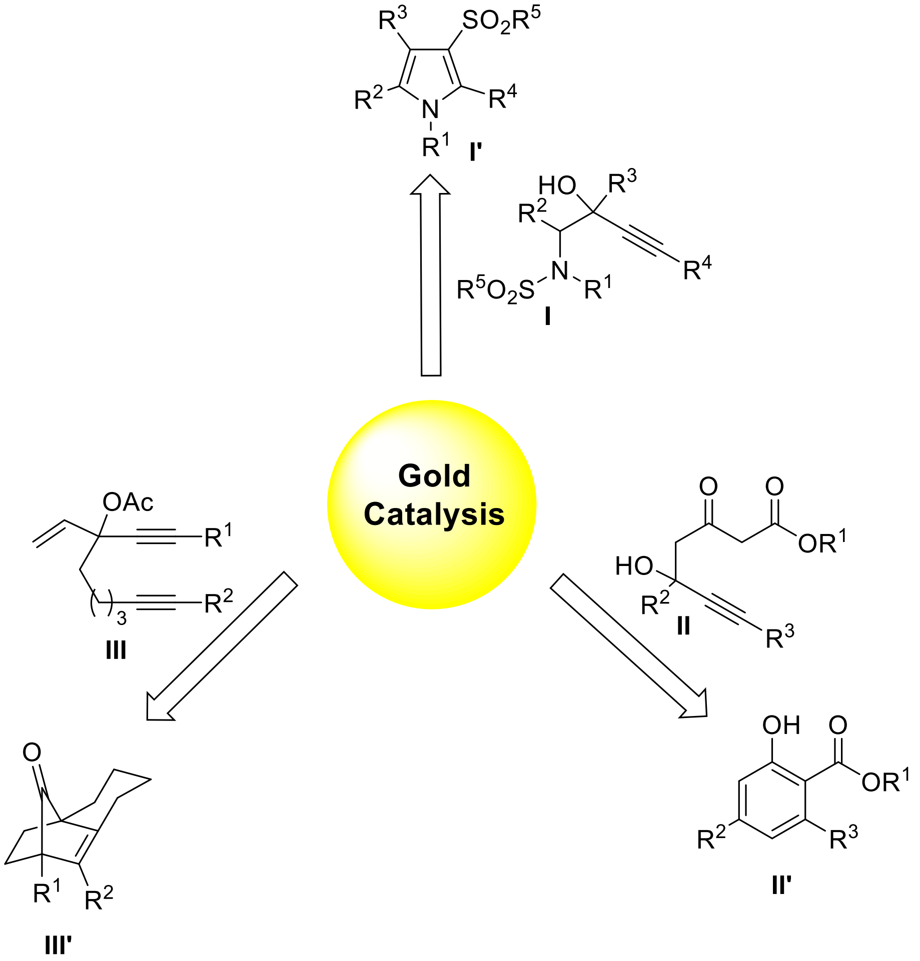
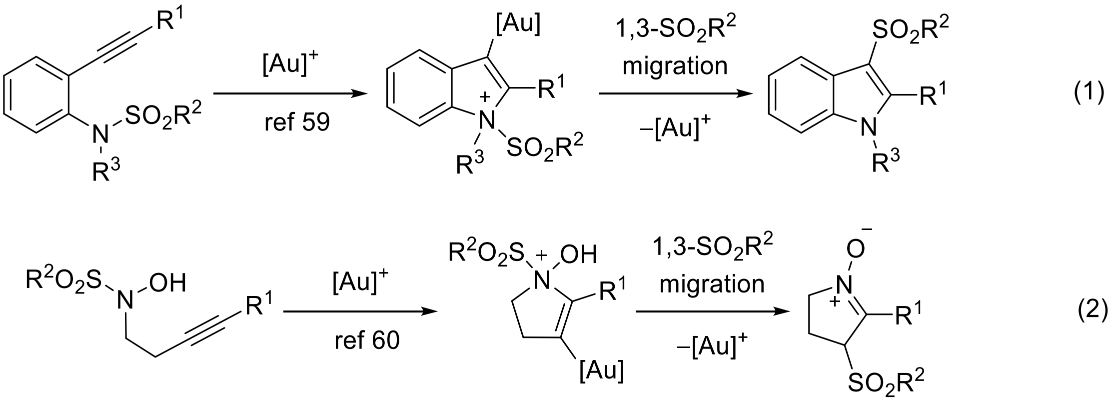


Figure 1.4 Gold-catalyzed synthesis of *N*-heterocycles and carbocycles from alkynol derivatives.

Chapter II: Gold-Catalyzed Tandem Aminocyclization/1,3-Sulfonyl Migration of *N*-Substituted-*N*-sulfonyl-aminobut-3-yn-2-ols to Substituted-3-sulfonyl-1*H*-pyrroles

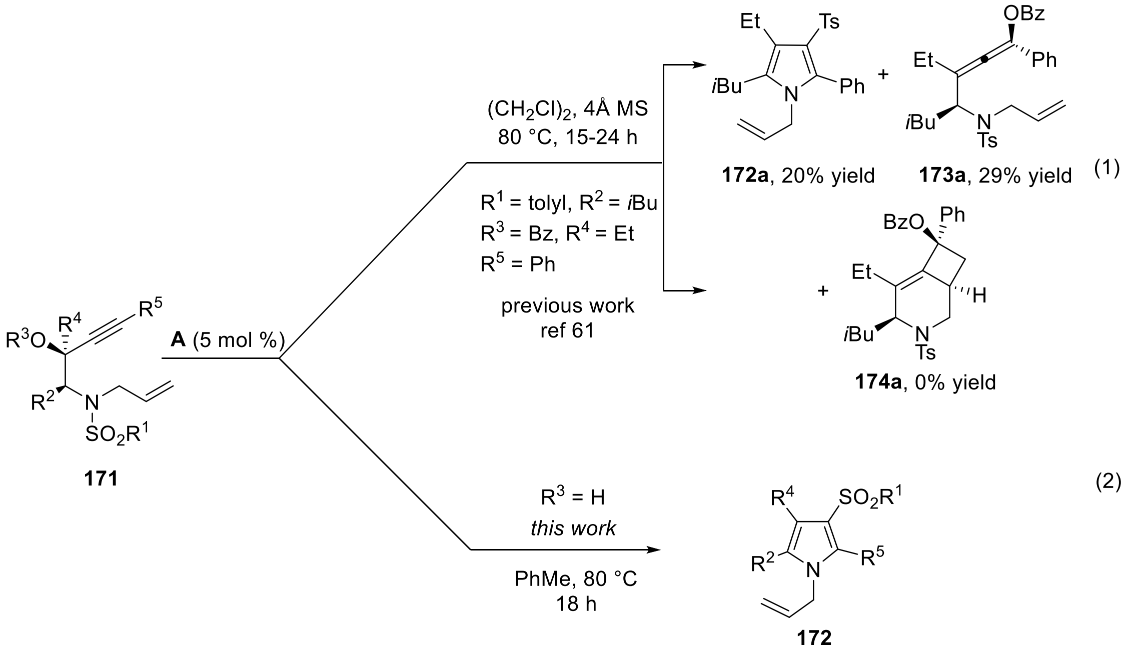
2.1 Introduction

The final step that regenerates the metal complex and release the product in the catalytic cycle of gold-catalyzed organic transformations is often protonolysis of the in situ formed organogold species.[54] Involving replacement of the carbon–gold bond by an allyl/*α*-alkoxy alkyl, iminium, or benzyl functional group, carbodeaurative process to release the Group 11 metal have also come under increasing scrutiny in recent years.[55-58] The incorporation of a heteroatom into the product during an electrophilic deauration step has, by contrast, been less well investigated.[59-62] This approach to regenerate the Lewis acidic gold catalyst has only been reported twice before in gold catalysis, presumably because of the more favorable aforementioned carbodeauration and protodeauration pathways. In this context, a recent noteworthy advance is that by Nakamura and co-workers who showed the deauration step to involve 1,3-sulfonyl migration in gold-catalyzed cycloisomerization of *o*-alkynyl-*N*-sulfonamides to the corresponding 3-sulfonylindole derivatives (Scheme 2.1, eq 1).[59] Following this seminal work, Shin and co-workers reported a similar deaurative 1,3-sulfonyl migration process in the gold-catalyzed [3+2] cycloadditions of *N*-sulfonyl hydroxylamines with a pendant



Scheme 2.1 Gold-catalyzed cycloisomerizations of propargylic substrates involving a 1,3-sulfonyl migration step.

alkyne moiety to 4-sulfonyl-dihydropyrrole-oxide (Scheme 2.1, eq 2).[60] More recently, during the course of an ongoing program examining the utility of gold catalysis in *N*-heterocyclic synthesis,[63] our group found one further example of this type of deaurative process (Scheme 2.2, eq 1).[61] With the NHC-gold(I) complex **A** shown in Figure 2.1 as the catalyst,[64] 3-tosyl *N*-allyl pyrrole **172a** and 1,6-allene **173a** were obtained in 20% and 29% yield, respectively, instead of the anticipated cyclobutane-fused piperidine **174a** from 1,7-enyne benzoate **171**. In a continuation of these investigations, we reasoned that the chemical yield of the potentially useful aromatic *N*-heterocyclic adduct could be enhanced by the use of the corresponding 1,7-enyne alcohol as the substrate in light of the absence of the competitive acyloxy migration process that is instrinsically happened in propargylic ester under gold catalysis.



Scheme 2.2 Gold-catalyzed cycloisomerization of 1,7-Enyne benzoates and alcohols.

In this chapter, we describe the details of this study involving Au(I)-catalyzed tandem aminocyclization/1,3-sulfonyl shift of *N*-substituted-*N*-sulfonyl-aminobut-3-yn-2-ols (Scheme 2.2, eq 2). This process provides a convenient and operationally straightforward route to 1-substituted-3-sulfonyl-1*H*-pyrroles in good to excellent yields for a wide variety of substrates.

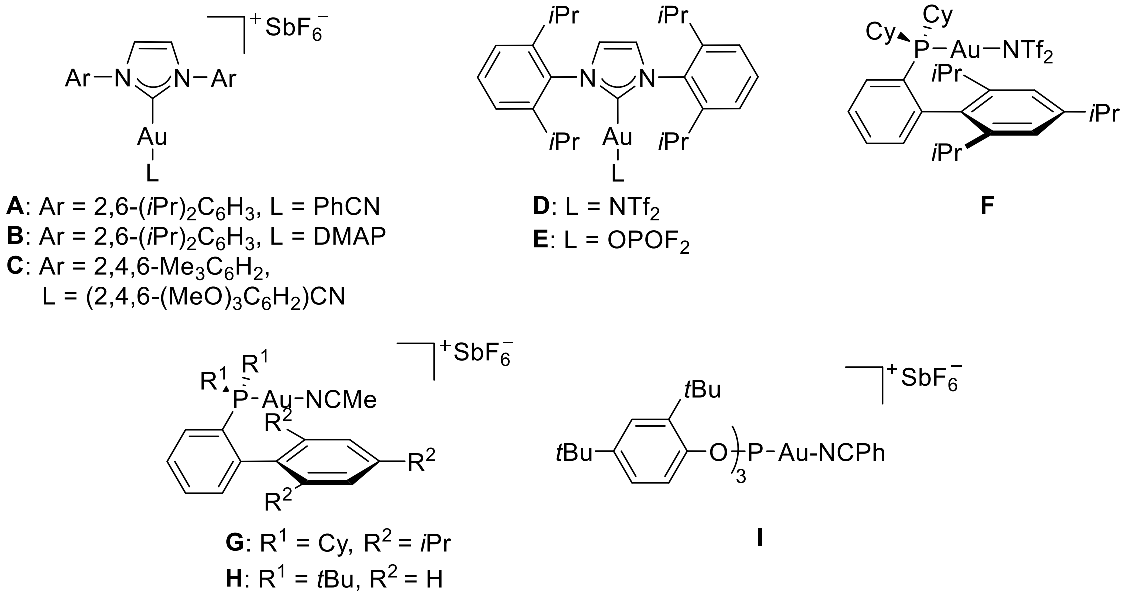
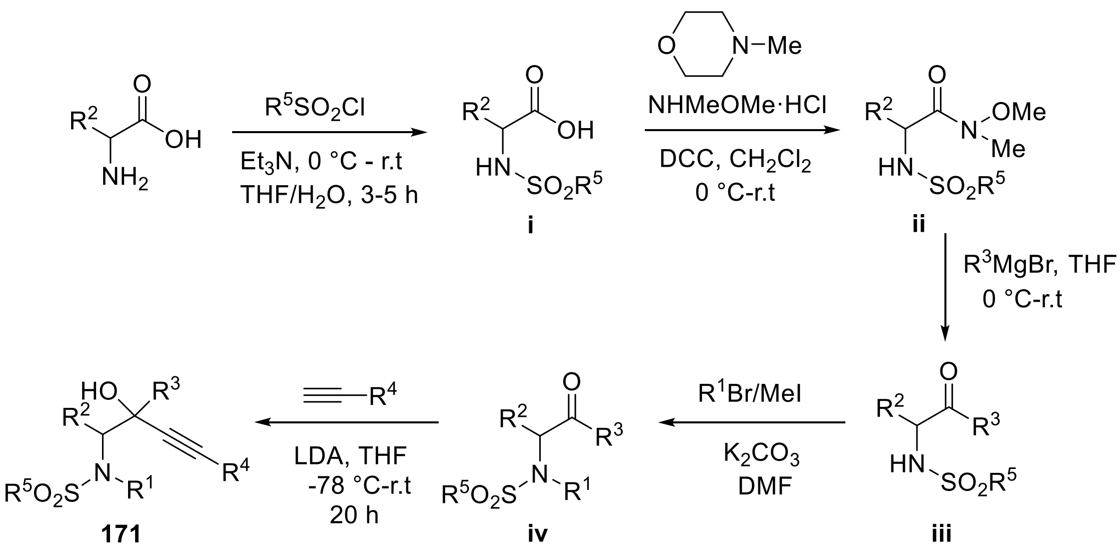


Figure 2.1 Gold(I) complexes examined in this study.[64,66]

2.2 Results and Discussion

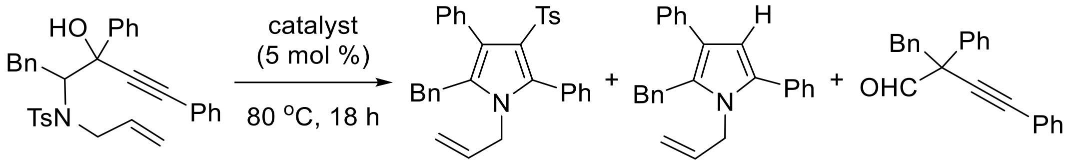
All *N*-substituted-*N*-sulfonyl-aminobut-3-yn-2-ols examined in this work were prepared as shown in Scheme 2.3. It is initially involved tosylation of the corresponding natural amino acid with sulfonyl chloride (3 eq) to give the sulfonylamino acid **i**. Following treatment of **i** with *N*-methylmorpholine (1.2 eq), N,O-dimethylhydroxylamine.HCl (1.2 eq) and *N*,*N*-dicyclohexylcarbodiimide (1.2 eq) furnished the corresponding Weinreb amide intermediate **ii**. The amide **ii** was then treated with alkyl or aryl magnesium bromide (2 eq) to form α-sulfonylamino ketone **iii**. Adding allyl/alkyl bromide or MeI (3 eq) to α-sulfonylamino ketone **iii** in the presence of K_2CO_3 (3 eq) with DMF as solvent produce α-alkylsulfonylamino ketone **iv**. Further reacting the α-alkylsulfonylamino ketone **iv** with LDA-pretreated terminal alkyne afforded the corresponding *N*-substituted-*N*-sulfonyl-aminobut-3-yn-2-ols **171-v**.



Scheme 2.3 Synthesis of *N*-substituted-*N*-sulfonyl-aminobut-3-yn-2-ols.

To test the feasibility of our hypothesis, we choose **171b** as the model substrate to establish the reaction conditions (Table 2.1). This study revealed that treating **171b** with 5 mol % of NHC-gold(I) complex **A** at 80 °C for 18 h gave the best result, affording 1-allyl-2-benzyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole **172b** in 70% yield (entry 1). The structure of the aromatic nitrogen-containing heterocycle was confirmed by X-ray crystal structure analysis (Figure 2.2).[66] Lower product yields were obtained when the reaction was carried out at room temperature or employed THF or 1,2-dichloroethane in place of toluene as the solvent (entries 2, 4 and 5). In the latter two control experiments, the trisubstituted pyrrole **175b** was also furnished in low yields of 10 and 6% (entries 4 and 5), respectively. With 1,2-dichloroethane as the solvent, a similar outcome was found when the reaction was conducted with the NHC-gold(I) complexes **F**–**H**, gold(I) phosphine complexes **F**–**H**, gold(I) phosphite complex **I** shown in Figure 2.1 with $Ph_3PAuNTf_2$ in place of **A** as the catalyst (entries 7–13 and 15). In contrast, for the analogous control experiments with the NHC-gold(I) complex **B** shown in Figure 2.1, $(4\text{-}CF_3Ph)_3PAuCl/AgSbF_6$ or AuCl as the catalyst or MeCN as the reaction solvent were found to be less effective (entries 3, 6, 14 and 16). Subjecting **171b** to these catalysts in

Table 2.1 Optimization of the reaction conditions[a]



171b **172b** **175b** **176b**

entry	catalyst	solvent	yield (%)		
			172b	**175b**	**176b**
1	**A**	PhMe	70	-	-
2[b]	**A**	PhMe	57	-	-
3	**A**	MeCN	-[c]	-	-
4	**A**	THF	62	10	-
5	**A**	$(CH_2Cl)_2$	68	6	-
6	**B**	$(CH_2Cl)_2$	-[d]	-	-
7	**C**	$(CH_2Cl)_2$	36	-	-
8	**D**	$(CH_2Cl)_2$	67	6	-
9	**E**	$(CH_2Cl)_2$	52	7	-
10	**F**	$(CH_2Cl)_2$	50	25	-
11	**G**	$(CH_2Cl)_2$	30	28	-
12	**H**	$(CH_2Cl)_2$	33	15	-
13	**I**	$(CH_2Cl)_2$	49	-	-
14	$(4\text{-}CF_3Ph)_3PAuCl/AgSbF_6$	$(CH_2Cl)_2$	-[e]	-	-
15	$Ph_3PAuNTf_2$	$(CH_2Cl)_2$	38	-	-
16	AuCl	$(CH_2Cl)_2$	-[c]	-	-
17	$AuBr_3$	$(CH_2Cl)_2$	-[d]	-	-
18	$InBr_3$	$(CH_2Cl)_2$	-[c]	-	-
19	$AgSbF_6$	$(CH_2Cl)_2$	-	-	37
20	$AgNTf_2$	$(CH_2Cl)_2$	-	-	10

Table 2.1 (*continued*)

entry	catalyst	solvent	yield (%)		
			172b	**175b**	**176b**
21	TfOH	$(CH_2Cl)_2$	-[c]	-	-
22	Tf_2NH	$(CH_2Cl)_2$	-[c]	-	-

[a] All reactions conducted at the 0.2 mmol scale with 5 mol % of catalyst at 80 °C for 18 h. [b] Reaction carried out at room temperature. [c] Mixture of unknown side products furnished based on ^{1}H NMR analysis of the crude mixture. [d] No reaction based on TLC or ^{1}H NMR analysis of the crude mixture. [e] Recovery of **171b** in 66% yield.

1,2-dichloroethane or NHC-gold(I) complex **A** with MeCN as the solvent led to a variety of unidentifiable decomposition products being detected by ^{1}H NMR measurements of the crude reaction mixtures. Likewise, $AuBr_3$ and $InBr_3$, reported to promote the cycloisomerization of *o*-alkynyl-*N*-sulfonylanilines to 3- and 5-sulfonyl substituted indoles,[59] were found to result in the recovery of **171b** in 89% yield or a mixture of decomposition products, respectively (entries 17 and 18). Control experiments with $AgSbF_6$, $AgNTf_2$ and the Brønsted acids TfOH and Tf_2NH as the catalyst also led to the formation of a mixture of decomposition products as well as provided evidence that the cationic Au(I) complex is the active species (entries 19–22).

To define the scope of present procedure, we next sought to assess its generality for a series of *N*-substituted-*N*-sulfonyl-aminobut-3-yn-2-ols, and the results are summarized in Table 2.2. Overall, the reaction conditions were found to be general and a variety of 3-sulfonyl substituted pyrrole derivatives were afforded in 38–98% yield from the corresponding starting alcohols **171c–171v**. Propargyl alcohols in which the carbinol carbon center is occupied by a pendant phenyl group with an electron-donating (**171c**) or

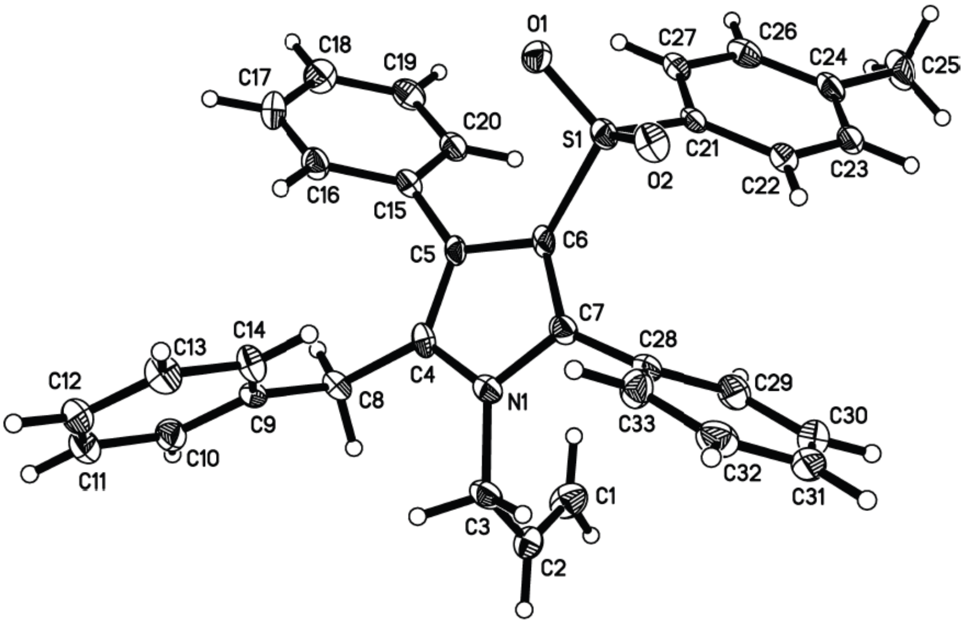
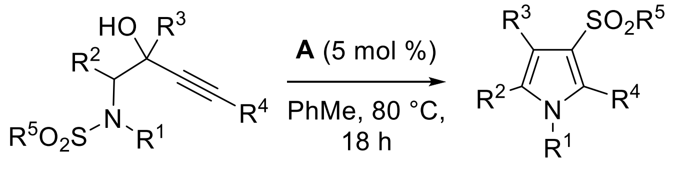


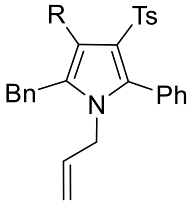
Figure 2.2 ORTEP drawing of **172b** with thermal ellipsoids at 50% probability levels.[66]

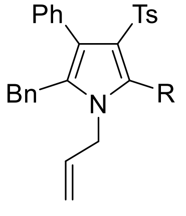
electron-withdrawing (**171d**) substituent at the *para* position, gave the corresponding products **172c** and **172d** in 56 and 41% yield, respectively. Replacing the phenyl substituent at this position with a 2-thiophenyl (**171e**) or Et (**171f**) moiety was found to have no influence on the course of the reaction with **172e** and **172f** afforded in respective yields of 52 and 43%. Likewise, reactions of substrates with the C≡C bond substituted with an aryl, thiophene, alkyl or cycloalkyl group, as in **171g**–**171l**, were found to be well tolerated and afford the corresponding products **172g**–**172l** in 59–93% yield. However, the presence of a terminal alkyne moiety on the substrate (**171m**) was found to give the corresponding pyrrole adduct **172m** in a lower yield of 45%. Increasing the steric demand of the substituent at the amino carbon (**171n** and **171o**) was also found to play a role. In these reactions, cycloisomerization of **171n**, with a pendant Ph group at the amino carbon center, gave **172n** in 74%, whereas the analogous reaction of **171o** containing the more sterically bulky *i*Pr moiety at the same position afforded **172o** in 38% yield. Likewise, increasing the steric demand of the allyl group (**171p–s**) or decreasing the electron-donating ability of the sulfonyl moiety (**171t–v**) on the amino center of the substrate was found to give a similar outcome. Under the standard conditions, the corresponding *N*-methyl (**172p**), *N*-butyl (**172q**), *N*-benzyl (**172r**) and *N*-cinnamyl (**172s**) protected products were obtained in 40–98% yield. For reactions with the *N*-mesyl (**171t**) or *N*-(4-chlorophenylsulfonyl) (**171u**), and *N*-mesyl (**171v**) protected substrates, corresponding 3-tosyl pyrrole adducts **172t–v** were furnished in 67, 54, and 43% yields, respectively.

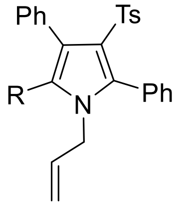
Table 2.2 Dehydrative cycloisomerization of **171c–v** catalyzed by **A**[a]



171 **172**



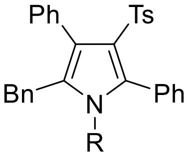


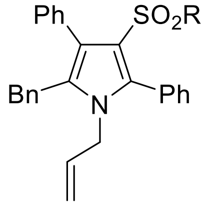


172c: R = pMeC$_6$H$_4$ (56%)
172d: R = pClC$_6$H$_4$ (41%)
172e: R = 2-thiophenyl (52%)
172f: R = Et (43%)

172g: R = pMeC$_6$H$_4$ (61%)
172h: R = pBrC$_6$H$_4$ (59%)
172i: R = 3-thiophenyl (64%)
172j: R = nBu (80%)
172k: R = cC$_3$H$_5$ (77%)
172l: R = 1-cyclohexenyl (93%)
172m:R = H (45%)

172n: R = Ph (74%)
172o: R = iPr (38%)



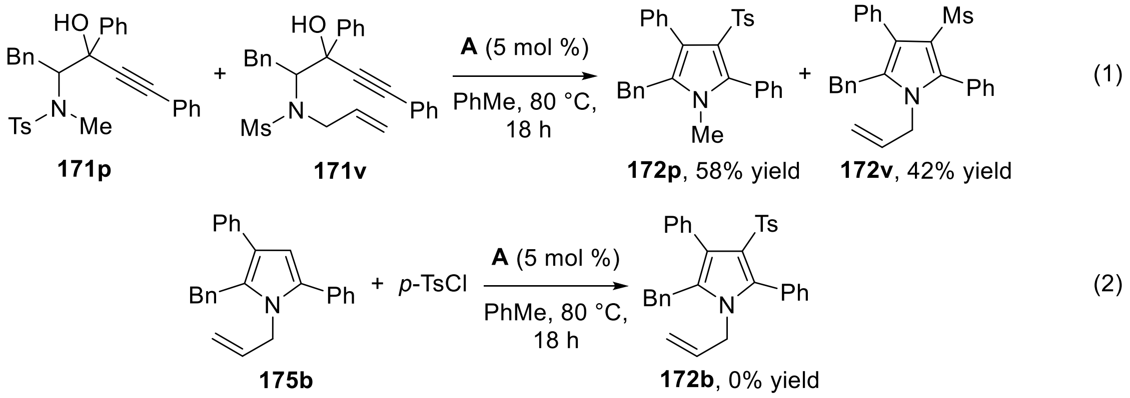


172p: R = Me (98%)
172q: R = nBu (80%)
172r: R = Bn (60%)
172s: R = CH$_2$CH=CHC$_6$H$_5$ (40%)

172t: R = pMeOC$_6$H$_4$ (67%)
172u: R = pClC$_6$H$_4$ (54%)
172v: R = Me (43%)

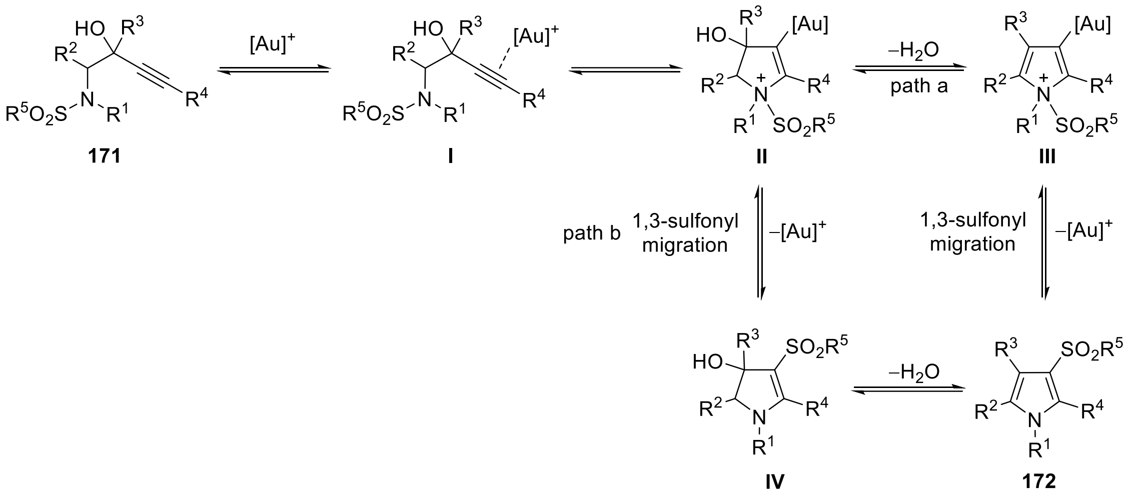
[a] All reaction was conducted at the 0.2 mmol scale with 5 mol % of **A** in toluene at 80 °C for 18 h. Values in parenthesis denote product yields.

To demonstrate that the deaurative 1,3-sulfonyl migration step proceeds in an intramolecular manner, which leads to the formation of the 3-sulfonyl substituted pyrrole adduct, we next examined the crossover experiment of 1 equiv of **171p** with 1 equiv of **171v** in the presence of 5 mol % of **A** in toluene at 80 °C for 18 h (Scheme 2.4, eq 1). Under these conditions, both **172p** and **172v** were afforded as the only products in respective yields of 42 and 58% with analysis of the crude reaction mixture by ^{1}H NMR spectroscopy and mass spectrometry showing no other cyclic products being detected. Our findings that show the near quantitative recovery of starting materials for the reaction of **175b** with *p*TsCl exposed to 5 mol % of **A** under the standard conditions described in Scheme 2.4, eq 2, led us to also posit that an intermolecular deaurative sulfonylation step was unlikely.



Scheme 2.4 Control experiments with **171p, 171v** and **175b** catalyzed by **A**.

Although speculative, the mechanism for the present Au(I)-catalyzed 3-sulfonyl-pyrrole forming reaction is outlined in Scheme 2.4. This could involve activation of the alcoholic substrate through coordination of the metal catalyst with the alkyne moiety of the adduct to give the Au(I)-coordinated intermediate **I**. As a result, this triggers the intramolecular aminocyclization process involving anti addition of the *N*,*N*-disubstituted amino moiety to the C≡C bond to provide the vinyl gold complex **II**. At this juncture, dehydration of this newly formed organogold intermediate might lead to the formation of cationic pyrrole-gold adduct **III** and generation of one molecule of H_2O (Scheme 2.5, path a). Subsequent 1,3-sulfonyl migration of this putative species might then result in deauration and regeneration of the Lewis acidic catalyst and delivery of the product. Alternatively, vinyl gold complex **II** could undergo the deaurative 1,3-sulfonyl migration process first to give 2,3-dihydro-1*H*-pyrrol-3-ol adduct **IV** that upon dehydrative aromatization would provide **172** (Scheme 2.5, path b). The formation of **175b** under certain conditions described in Table 2.1 could be due to a competing pathway in which intermediate **II** or **III** undergoes protodeauration. The premise that the deauration step involves 1,3-sulfonyl migration would also be consistent with the gradual decrease in product yield as the steric and electronic nature of the pendant group at the amino carbon or amine center increases upon going from **171b→171n→171o** and **171p→171b→171r→171s** or a less electron-donating *N*-sulfonyl protecting group upon going from **171b** or **171t → 171u**. It might be anticipated that such a pathway may not be expected to be as efficient because steric interactions between the substituents on the pyrrole ring and the migrating sulfonyl moiety increase as a result of either of these functional groups increasing. In the case of the observed trend when varying the substituent R^1, this could be due to competition between the alkyl and sulfonyl groups on the amine center to migrate as a result of the ability of the former to stabilize a partial positive charge as it increases in steric bulk and π conjugation. Similarly, the lower product yields furnished upon going from substrates containing a *N*-(4-tolylsulfonyl) or *N*-(4-methoxyphenylsulfonyl) to a *N*-(4-chlorophenylsulfonyl) protecting group would be in good agreement with the typically lower migratory aptitudes of less electron-rich moieties. However, the low product yield obtained for the cycloisomerization of *N*-mesyl-protected starting alcohol **171v** could be due to the competitive deprotonation of the mesylate cation to form sulphene during the 1,3-migration process.



Scheme 2.5 Proposed mechanism for Au(I)-catalyzed cycloisomerization of **171**.

2.3 Conclusion

In summary, we have demonstrated a gold(I)-catalyzed synthetic strategy for the construction of 1-substituted 3-sulfonyl-1*H*-pyrroles from *N*-substituted *N*-sulfonyl-amonibut-3-yn-2-ols. The reaction was shown to be applicable to a diverse set of propargylic alcohols and provided a new number of the pyrrole-family of compounds for potential applications in medicinal chemistry. Our studies suggest the nitrogen-containing ring forming process likely involves dehydrative aminocyclization followed by deaurative 1,3-sulfonyl migration.

Chapter III: Gold-Catalyzed Dehydrative Cycloisomerization of 5-Hydroxy-3-oxoalk-6-ynoate Esters to *o*-Phenolic Esters

3.1 Introduction

The phenolic ester structural motif, in particular the *ortho*-substituted family member, is found in a myriad of bioactive natural products and pharmocologically interesting compounds (Figure 3.1).[67] The carbolic acid derivative is also a potentially useful building block in organic synthesis and drug discovery programs. As a consequence, the development of efficient synthetic methods to prepare the aromatic carbocycle with selective control of substitution patterns using readily accessible substrates continues to be actively pursued.[68]

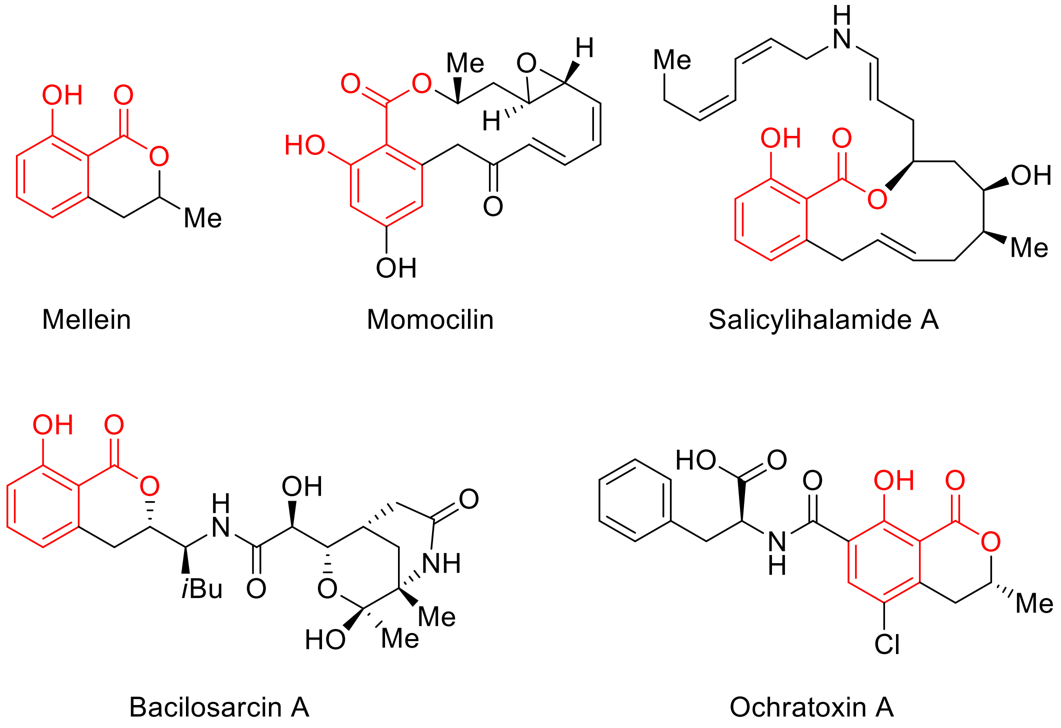
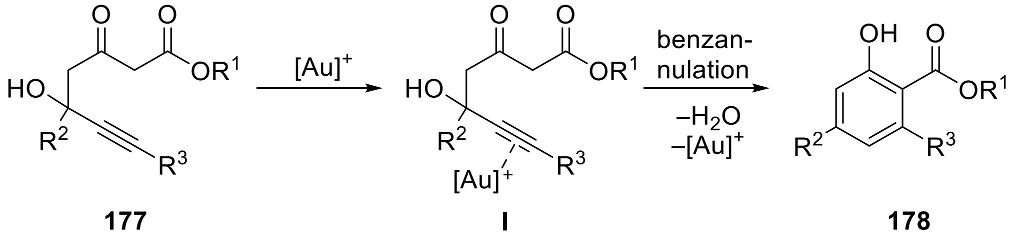


Figure 3.1 Examples of bioactive natural products containing the *o*-phenolic ester motif.

In the previous chapter, we reported an expedient route to 1-substituted 3-sulfonyl-1*H*-pyrroles **172** through domino aminocyclization/1,3-sulfonyl migration of *α*-amino propargylic alcohols 171 involving C–N bond formation catalyzed by gold catalyst. In a continuation of ongoing efforts in this field of gold catalysis,[69] we became interested in exploring the cyclization chemistry catalyzed by gold which involves C–C bond formation. An illustrative example of this is the immense number of elegant approaches to various synthetically useful arenes from gold-catalyzed benzannulation of the corresponding substituted alkyne.[70-72,80] While this has included many impressive works for phenol synthesis,[72] the analogous gold-catalyzed alkyne benzannulations leading to *ortho*-substituted phenolic esters have so far remained unrealized. In this context, we reasoned that the putative Au(I)-activated propargylic alcohol[73] tethered *β*-ketoester **177** that would form in situ might be prone to undergo hydroalkylation involving nucleophilic addition of the *β*-ketoester unit to C≡C bond in the intermediate.[74,75] Protodeauration followed by aromatization would then be expected to provide the *o*-phenolic ester derivative **178** (Scheme 3.1). Herein, we disclose the details of this benzannulation chemistry that delivers an expedient and synthetic route to 2-hydroxybenzoate esters in moderate to excellent yields under conditions that did not require the exclusion of air or moisture.

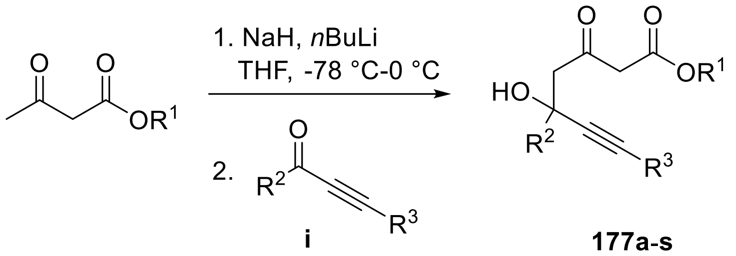


Scheme 3.1 Au(I)-catalyzed cyclization of unsaturated alcohol tethered β-ketoesters to *o*-phenolic esters

3.2 Results and Discussion

Substrates propargylic alcohol tethered *β*-ketoesters **177a-s** were prepared as illustrated in Scheme 3.2. Initially, acetoacetate was treated with the mixture of NaH (1.1

eq) and BuLi (1.2 eq). This was followed by the addition of a THF solution of propargyl ketones **i** to afford the corresponding propargylic alcohol tethered *β*-ketoesters **177a-s**.



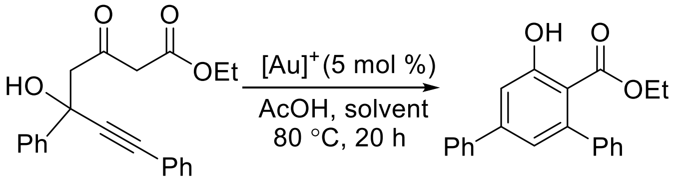
Scheme 3.2 Synthesis of propargylic alcohol tethered *β*-ketoesters **177**.

We began our investigations by examining the gold(I)-catalyzed dehydrative cycloisomerizations of **177a** to establish the reaction conditions (Table 3.1). This study initially revealed that treating the model substrate with 5 mol % of Au(I) phosphine catalyst F in toluene at 80 °C for 20 h gave **178a** in 57% yield (entry 1). The structure of the aromatic carbocycle was confirmed by X-ray crystal structure analysis (Figure 3.2).[76] Lower product yields of 16–52% yield was obtained on replacing **F** with the gold(I) phosphine complexes **G** and **H**, gold(I) phosphite complex **I** and NHC-gold(I) (NHC = *N*-heterocyclic carbene) complexes **A**–**D** as the catalyst (entries 2–8). A similar outcome was observed on changing the solvent from toluene to CH_2Cl_2, MeCN, or THF, with **178a** furnished in 30–45% yield (entries 15–17). On the other hand, either no reaction or a mixture of unidentifiable decomposition products was found in control experiments with toluene as the solvent and AuCl, $AgSbF_6$, $AgNTf_2$, TfOH, *p*TSA or TFA instead of **F** was employed as the catalyst (entries 9–14). Our studies subsequently showed a comparable product yield of 60% was afforded on repeating the Au(I) phosphine complex **F**-catalyzed reaction in $(CH_2Cl)_2$ at 80 °C for 20 h (entry 18). Under these latter conditions, the introduction of 0.1 equiv of AcOH was found to lead an increase in product yield from 60 to 67% (entry 19). The yield of **178a** was further increased from 67 to 74 and 82% on increasing the amount of AcOH from 0.1 to 0.5 to 1 equiv, respectively (entries

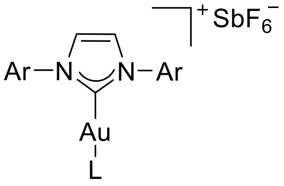
20 and 21). The analogous reactions of **177a** and 1 equiv of AcOH catalyzed by **F** contained in an open round-bottom flask at room temperature and 80 °C afforded, respective, product yields of 13 and 79% (entries 22 and 23). Further control experiments with 10 mol % of di-*tert*-butyl pyridine in place of the Brønsted acid or only 1 equiv of AcOH provided **178a** in 70% yield and a mixture of unidentifiable decomposition products, respectively (entries 24 and 25). On the basis of the above results, the procedure described in entry 23 was deemed to provide the optimum reaction conditions.

Table 3.2 summarizes our efforts to define the scope of the present procedure by examining the reactions of a variety of 5-hydroxy-3-oxoalk-6-ynoate esters. These experiments showed that with the Au(I) complex **F** as the catalyst, the reaction conditions were found to be broad, and a variety of substituted *o*-phenolic esters were afforded in moderate to excellent yields. Starting esters in which the carbinol carbon center bore a phenyl moiety with an electron-donating (**177b**–**177d**) or electron-withdrawing (**177e** and **177f**) at the *meta* or *para* position, were shown to proceed well and give the corresponding products **178b**–**178f** in 58–76% yield. Likewise, substrates containing a 2-naphthalenyl (**177h**), 2-thienyl (**177i**), alkyl (**177j** and **177k**), cyclohexyl (**177l**) or benzyl ethyl ether (**177m**) group at the same position were found to be well tolerated, providing the corresponding *o*-phenolic esters **178h**–**178m** in yields of 52–70%. The presence of a 3-thiophenyl (**177n**), *n*Bu (**177o**) or cyclopropyl (**177p**) substituent on the propargylic carbon center was found to have little influence on the course of the reaction with **178n**–**178p** obtained in 46–62% yield. Reactions of substrates with a pendant Et and *n*Bu moiety on the respective carbinol and propargylic carbon centers, or a benzyl instead of an ethyl ester group or a secondary alcohol, as in **177q**–**177s**, were observed to work well. Under the standard conditions, these Au(I)-catalyzed reactions gave the corresponding *o*-carbolic acid derivatives **178q**–**178s** in 41–62% yield. In our hands, the

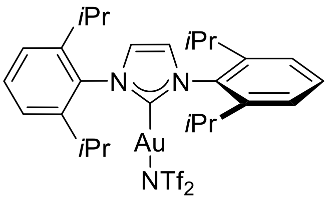
Table 3.1 Optimization of the reaction conditions[a]



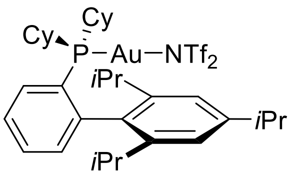
177a **178a**



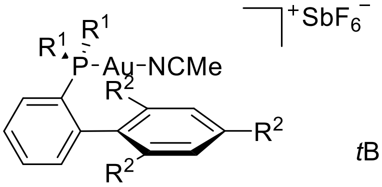
A: Ar = 2,6-(iPr)$_2$C$_6$H$_3$, L = PhCN
B: Ar = 2,6-(iPr)$_2$C$_6$H$_3$, L = DMAP
C: Ar = 2,4,6-Me$_3$C$_6$H$_2$,
L = (2,4,6-(MeO)$_3$C$_6$H$_2$)CN



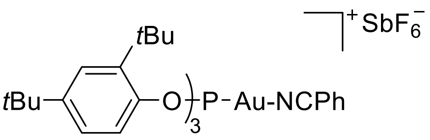
D



F



G: R^1 = Cy, R^2 = iPr
H: R^1 = tBu, R^2 = H



I

entry	catalyst	solvent	AcOH (equiv)	yield (%)[b]
1	**F**	PhMe	-	57
2	**G**	PhMe	-	52
3	**H**	PhMe	-	32
4	**I**	PhMe	-	19
5	**A**	PhMe	-	40

[a]All reactions were conducted at the 0.2 mmol scale with 5 mol % of catalyst at 80 °C for 20 h. [b] Isolated yield. [c] No reaction based on TLC or ^{1}H NMR analysis of the crude mixture.

Table 3.1 (*continued*)

entry	catalyst	solvent	AcOH (equiv)	yield (%)[b]
6	**B**	PhMe	-	16
7	**C**	PhMe	-	46
8	**D**	PhMe	-	29
9	AuCl	PhMe	-	[c]
10	$AgSbF_6$	PhMe	-	[d]
11	$AgNTf_2$	PhMe	-	[d]
12	TfOH	PhMe	-	[d]
13	PTSA	PhMe	-	[d]
14	TFA	PhMe	-	[d]
15[e]	**F**	CH_2Cl_2	-	45
16[e]	**F**	MeCN	-	44
17[e]	**F**	THF	-	30
18[e]	**F**	$(CH_2Cl)_2$	-	60
19	**F**	$(CH_2Cl)_2$	0.1	67
20	**F**	$(CH_2Cl)_2$	0.5	74
21	**F**	$(CH_2Cl)_2$	1.0	82
22[f]	**F**	$(CH_2Cl)_2$	1.0	13

[d] Unknown side products were obtained based on ^1H NMR analysis of the crude mixture. [e] Reaction performed at reflux. [f] Reaction performed in an open round-bottom flask at room temperature.

Table 3.1 (*continued*)

entry	catalyst	solvent	AcOH (equiv)	yield (%)[b]
23[g]	**F**	$(CH_2Cl)_2$	1.0	79
24[h]	**F**	$(CH_2Cl)_2$	1.0	70
25	-	$(CH_2Cl)_2$	1.0	[d]

[g] Reaction performed in an open round-bottom flask with a condenser. [h] Reaction performed in the presence of 10 mol % of di-*tert*-butyl pyridine in place of AcOH.

only exception was the cyclization of **177g** containing a *o*-BrC_6H_4 substituent at the carbinol carbon center, which was found to give **178g** in a low yield of 28%. On the other hand, no other cycloisomerization products arising from possible 5-*exo*-dig cyclization of the substrate was detected by TLC and ^1H NMR analysis of the crude reaction mixtures.

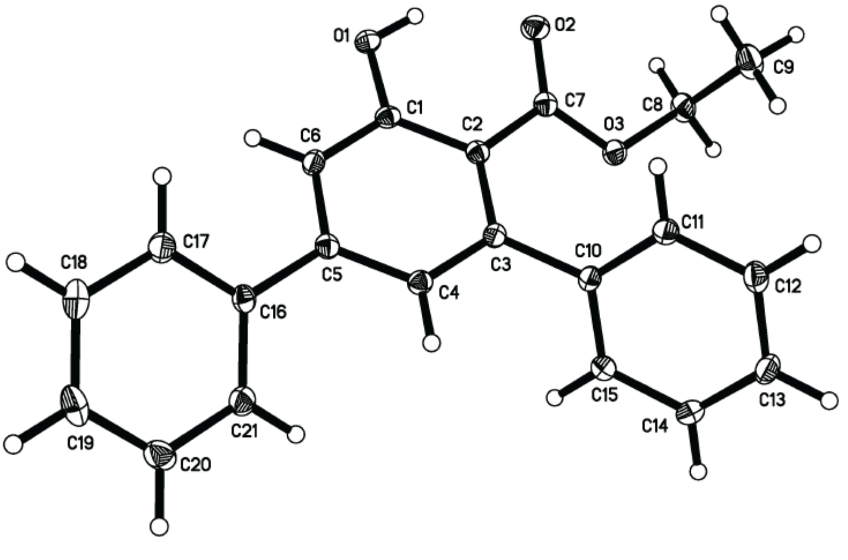
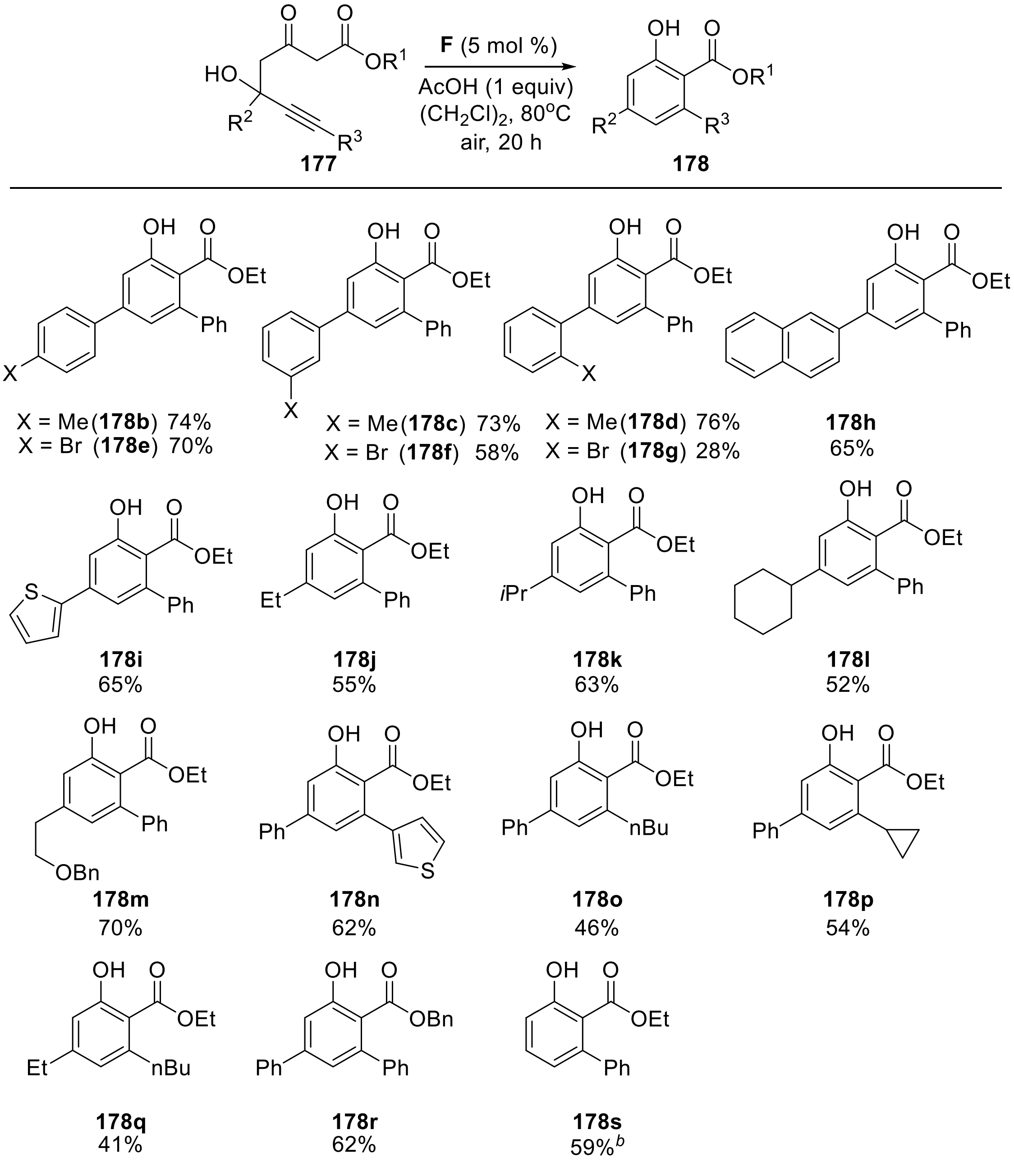


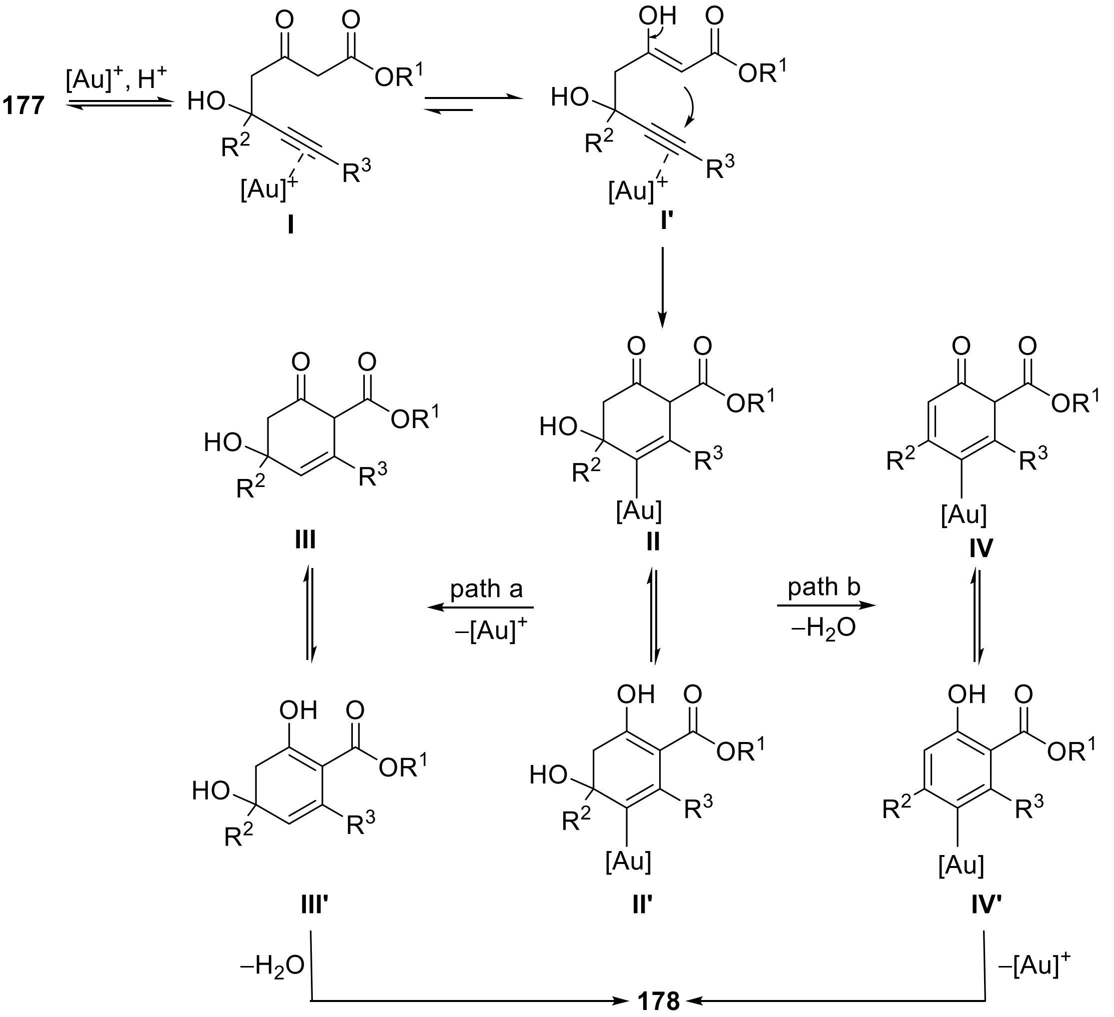
Figure 3.2 ORTEP drawing of **178a** with thermal ellipsoids at 50% probability levels.[76]

Table 3.2 Benzannulation of 5-Hydroxy-3-oxoalk-6-ynoate esters **177b–s** catalyzed by **F**[a]



[a] All reactions were conducted at the 0.2 mmol scale with 5 mol % of **F** and 1 equiv of AcOH in 1,2-dichloroethane at 80 °C in an open-rounded bottom flask with a condenser at 80 °C for 20 h. [b]Value in parentheses denote isolated product yields. [b] Reaction time = 50 min.

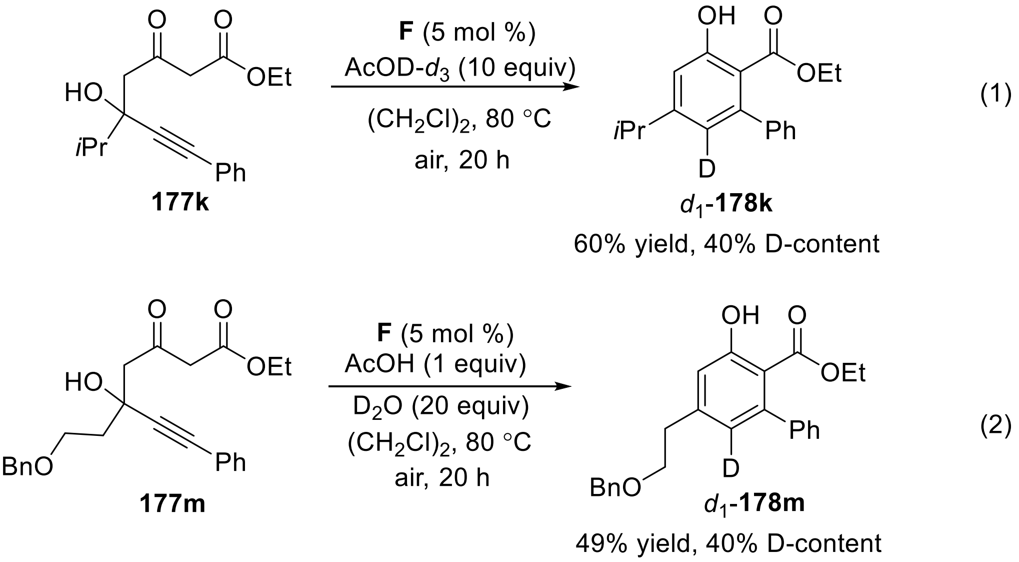
A tentative mechanism for the present Au(I)-catalyzed *o*-phenolic ester transformation is depicted in Scheme 3.3. This could involve activation of the propargylic alcohol by coordination of the Group 11 metal catalyst to the C≡C bond in the substrate. This leads to the resulting Au(I)-coordinated species **I** and its tautomer **I'**, with the equilibrium presumably sitting in favor of the latter due to the acidic conditions, becoming prone to undergoing the hydroalkylation process. Involving *anti* addition of the enol form of the 1,3-dicarbonyl compound moiety to the alkyne bond of the adduct, this gives the vinyl gold intermediate **II** and its enolic isomer **II'**.[77-79] Subsequent protodeauration of this putative organogold species followed by dehydration of the



Scheme 3.3 Proposed mechanism for Au(I)-catalyzed benzannulation of alkynyl tethered *β*-ketoesters.

ensuing cyclohexenone species **III** and its 1,3-diene isomer **III'** might then result in the regeneration of the metal catalyst and provide the phenolic product (Scheme 3.3, path a). Alternatively, dehydration may occur first to give the vinyl gold complex **IV** and its phenolic product **IV'**, which upon protodeauration would provide **178** (Scheme 3.3, path b).

In addition to contributing to the keto–enol tautomerization process, our earlier studies described in Table 3.1, entries 24 and 25 showing the role of AcOH confined to promoting protodeauration and regeneration of the gold(I) catalyst suggests the protodeauration is the rate determining step.[79] Indeed, this was further supported by repeating the Au(I)-catalyzed cyclization of **177k** with AcOD-d_3 and **177m** with D_2O under the respective conditions described in eqs 1 and 2 in Scheme 3.4. These control experiments led to d_1-**178k** and d_1-**178m** being formed in 60% and 49% yield, respectively, and in both cases with 40% deuterium incorporation at the *para*-position of the *o*-phenolic ester. A gold(I)-catalyzed hydroalkylation step would also be consistent with the contrasting reactivities observed for the cyclizations of **177d** and **177g** depicted



Scheme 3.4 Control experiments with 177k and 177m catalyzed by **F**.

in Table 3.2. It may be anticipated that such a pathway might become less efficient as steric interactions between the incoming gold(I) complex and the aryl substituent at the carbinol carbon center significantly increase on going from *o*-MeC_6H_4 in **177d** to *o*-BrC_6H_4 in **177g**.

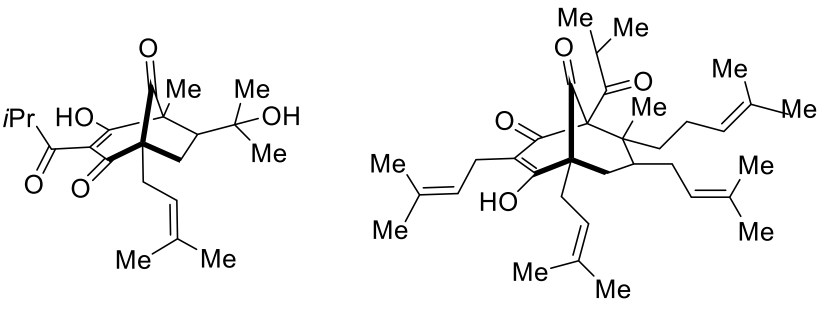
3.3 Conclusion

In summary, we have described an efficient Au(I)-catalyzed synthetic method for the construction of *o*-phenolic esters from 5-hydroxy-3-oxoalk-6-ynone esters. Achieved under conditions that did not require the exclusion of air or moisture, the reaction was shown to be applicable to a diverse set of propargylic alcohol substituted *β*-ketoesters. Acetic acid was needed as an additive in the reaction to facilitate protodeauration step and to assist in regeneration of the gold(I) catalyst.

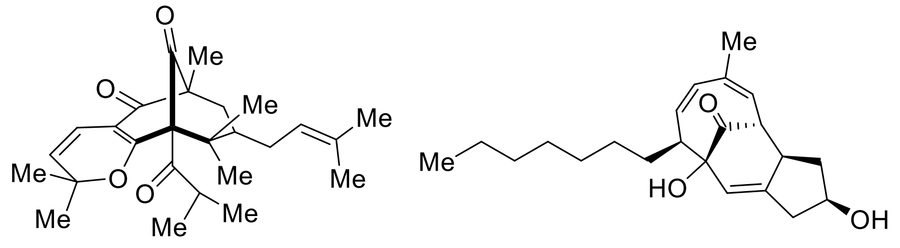
Chapter IV: Gold-Catalyzed Synthesis of Bicyclo[2.2.1]hept-2-en-7-one Derivatives via Carbocyclization Process of 1,8-Diynyl Vinyl Esters

4.1 Introduction

Medium-sized rings bearing a bridgehead ketone are prevalent structures in a myriad of bioactive products and active pharmaceutical ingredients (APIs).[81] Due to the complexity of this framework, the installation of bridgehead ketone segments onto the existing ring system remains a great challenge in the organic synthetic community. For this reason, much effort been made recently to develop new and efficient methodologies to access this scaffold.[82] By virtue of its important utility as well as its omnipresence in many natural products, synthetic approaches to the high value bridgehead ketone scaffold that rely on mild reaction conditions has been actively pursued.[83] For example, Barriault and co-workers demonstrated the construction of these important bridgehead ketone bicyclic frameworks by using gold salt as the catalyst.[83b]



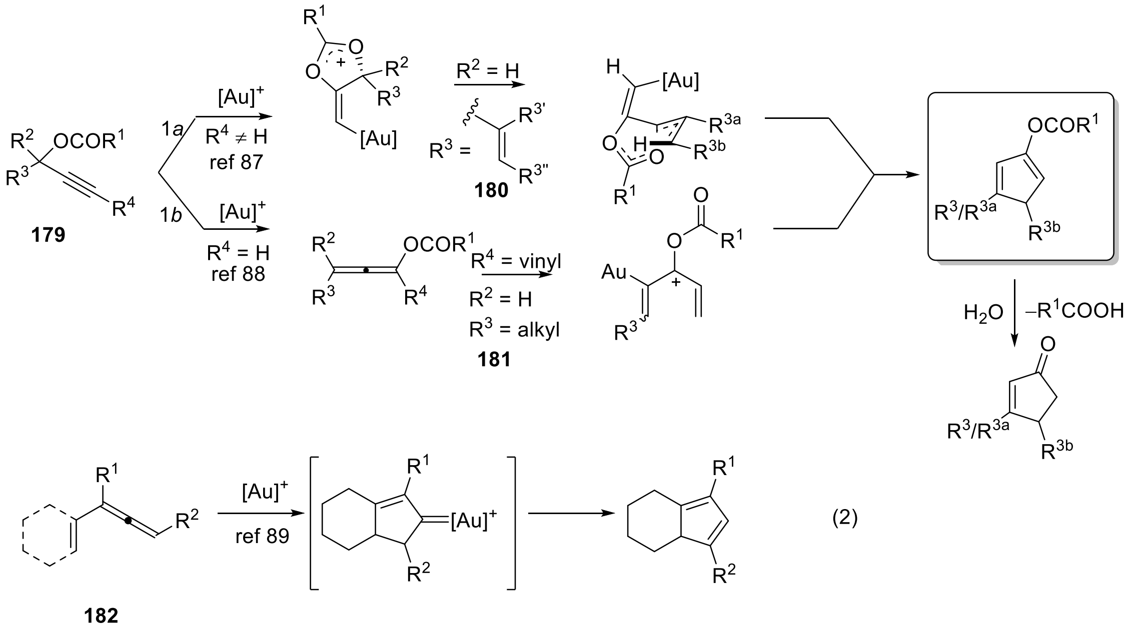
Enaimeone A Hyperforin



Papuaforin A Penostatin F

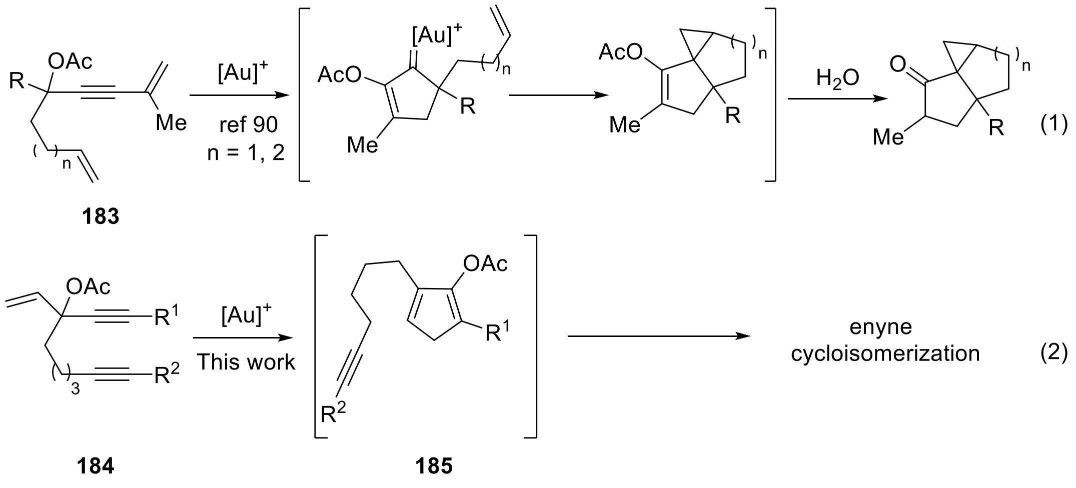
Figure 4.1 Examples of bridged-ketone containing natural products.

As mentioned in Chapter 1, propargylic esters are versatile substrates in gold catalysis and have been converted into a variety of synthetically useful precursors of pharmaceutical interest. The inclusion of a pendant vinyl moiety in the substrate, namely 1,*n*-vinyl propargylic ester, presents an interesting scaffold. 1,*n*-vinyl propargylic esters have recently emerged as valuable alternatives for the construction of cyclopentadiene derivatives,[86-90] which are important building blocks and key intermediates in organic synthesis. After extensive studies with rhodium[84] and platinum[85], gold complexes have emerged lately as powerful catalysts for a myriad of transformations involving propargylic ester substrates. A recent notable advance in this context was demonstrated by Toste and coworkers who reported the gold(I)-catalyzed Rautenstrauch rearrangement[86] of 1,4-enynyl esters **180**, with the vinyl moiety attached at the carbinol carbon, providing an expeditious route to a diverse portfolio of functionalized cyclopentenones (Scheme 4.1, path *a*).[87] Following this seminal work, Zhang and coworkers demonstrated a similar strategy to access cyclopentenones. This work consisted of the Nazarov-type cyclization of 1,3-enynyl esters **181** (Scheme 4.1, path *b*).[88] Subsequently, a variant of this transformation was revealed by Toste's group, where



Scheme 4.1 Gold-Catalyzed carbocylization of vinyl propargylic or vinyl allenic substrates to cyclopentenone or cyclopentadiene derivatives.

functionalized cyclopentadienes were furnished upon treatment of vinyl substrate allene **182** with a gold catalyst (Scheme 4.1, eq 2).[89] More recently, another transformation similar to that by the groups of Toste and Zhang was disclosed by Max Malacria and co-workers, which employed 1,3-enynyl esters **183** with a pendant olefin-containing alkyl chain at the carbinol position. These substrates generated tricyclic ketones under gold catalysis (Scheme 4.2, eq 1).[90] On the basis of these recent examples in the gold-catalyzed cycloisomerisation of 1,*n*-diyne esters,[41-51] and in the context of our ongoing efforts to develop gold-catalyzed tandem reactions,[91] we realized that the chemistry of gold-catalyzed cascade transformation of 1,8-diynyl vinyl esters has thus far remained unexplored. In addition to this and to our knowledge, gold-catalyzed carboannulations of 1,8-diyne esters are not known. Similar to the work of Toste and co-workers, we anticipated that the vinyl propargylic ester fragment in 1,8-diynyl vinyl esters **184** would undergo acyoxy migration followed by annulation, to give rise to cyclopentadiene derivatives **185** with a pendant alkyne chain. The presence of an additional alkyne moiety in **185** may permit a further transformation to occur and generate a new class of carbocycle via a tandem process (Scheme 4.2, eq 2). In doing so, we found that a bicyclic bridgehead ketone was formed upon treating 1,8-diynyl vinyl esters **184** under gold catalysis.



Scheme 4.2 Gold-catalyzed carboannulation of vinyl propargylic esters **183** and **184**.

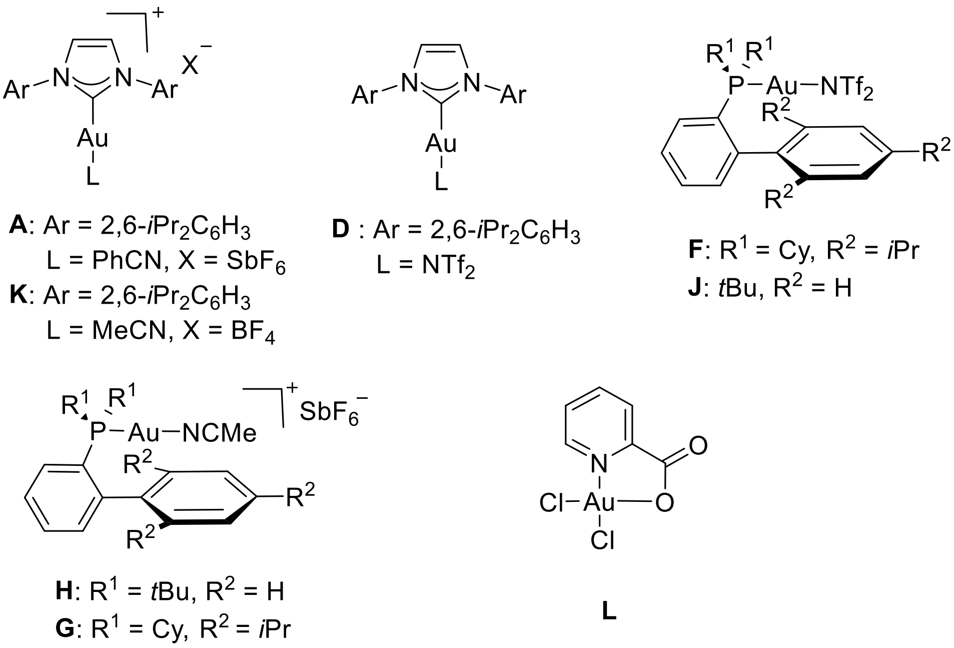
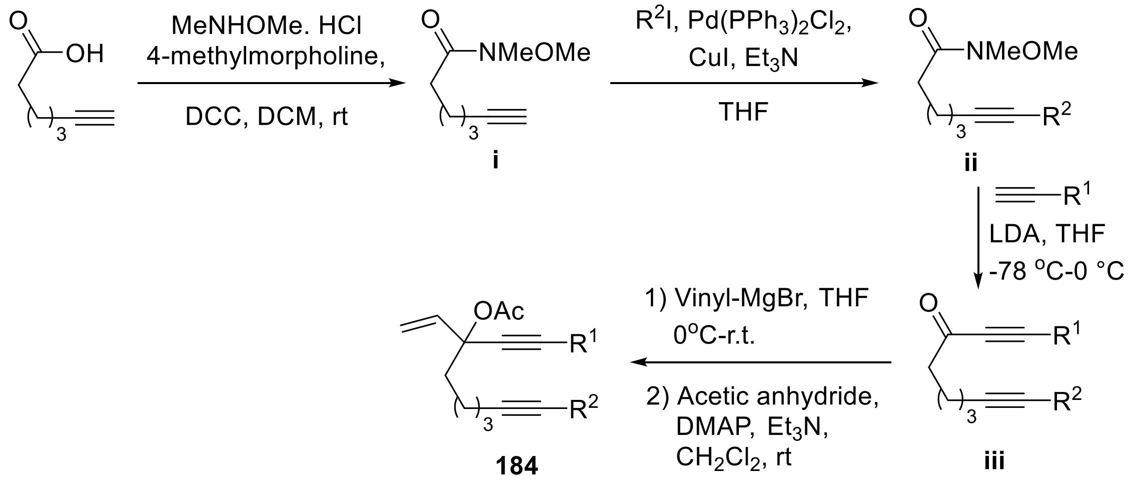


Figure 4.2 Gold complexes examined in this study.

4.2 Results and discussion

All 1,8-diynyl vinyl esters **184** studied in this work were prepared as illustrated in Scheme 4.3. Treatment of hept-6-ynoic acid with *N*-methylmorpholine (1.2 eq), N,O-dimethylhydroxylamine.HCl (1.2 eq) and *N*,*N*-dicyclohexylcarbodiimide (1.2 eq) furnished the corresponding Weinreb amide intermediate **i**. Subsequent Sonogashira coupling of Weinreb amide intermediate **i** with aryl iodide (1.2 eq) gave Weinreb amide intermediate **ii**. Further treatment of **ii** with LDA-pretreated terminal alkyne (2 eq) afforded substituted 1,8-diyn-3-one **iii**. The next step involved the addition of vinyl magnesium bromide to substituted 1,8-diyn-3-one **iii** followed by acetylation of alcohol with acetic anhydride (4 eq), 4-dimethylaminopyridine (0.1 eq) and triethyl amine (5 eq) to furnish the corresponding 1,8-diynyl vinyl esters **184a-n**.

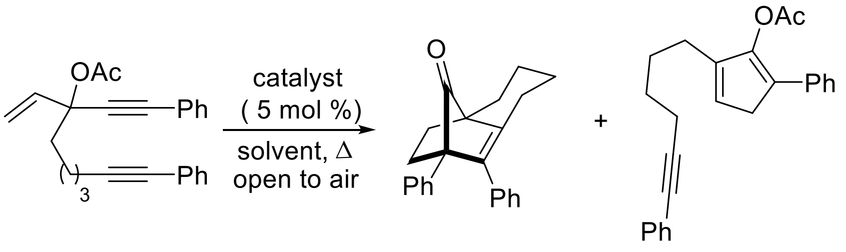
To test the feasibility of our hypothesis, 9-phenyl-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate **184a** was chosen as the model substrate so as to establish the reaction conditions (Table 4.1). The initial study revealed that treatment of **184a** with 5 mol %



Scheme 4.3 Syntheis of 1,8-diynyl vinyl esters **184a-n**.

of Ph_3PAuCl in combination with $AgSbF_6$ in 1,2-dichloroethane at 80 °C for 4 hours afforded 3,4-diphenylbicyclo[2.2.1]hept-2-en-7-one **186a** in 67% yield (entry 1). The structure of the ketone-bridged carbocycle was confirmed by NMR spectroscopy and X-ray crystallography (Figure 4.2). Comparable product yields of 63–65% were obtained on replacing $Ph_3PAuCl/AgSbF_6$ with sterically crowded gold(I) phosphine complexes **H** and **G** (entries 2 and 4). With gold(I) phosphine complex **H** as the catalyst, the analogous reaction at room temperature did not afford the desired product **186a** and instead gave cyclopentadiene **185a** in 84% yield (entry 3). Further examination of gold(I) phosphine complexes **F** and **J** did not afford an improvement in yield over the same reaction time (entries 5–6). Likewise, a survey of NHC-gold(I) complexes **A** and **D**, and gold(III) complex **L** were found to furnish the desired product **167a** in markedly lower yields (6–58%, entries 7, 9 and 10). On the other hand, no formation of the desired product **186a**, or a mixture of unidentifiable decomposition products was observed when the NHC-gold(I) complex **K**, Ph_3PAuCl or silver salt $AgNTf_2$ were employed as the catalyst (entries 8, 11 and 12). Gratifyingly, the analogous reaction with $Ph_3PAuNTf_2$ as the catalyst at ambient temperature was found to increase the yield from 67 to 75% over a 2 hour duration (entry 13). Our studies showed that by changing the solvent from 1,2-dichl-

Table 4.1 Optimization of the reaction conditions^a



184a **186a** **185a**

entry	catalyst	solvent	time	yield^b	
				186a	**185a**
1	Ph$_3$PAuCl/AgSbF$_6$	(CH$_2$Cl)$_2$	4	67	-
2	**H**	(CH$_2$Cl)$_2$	4	65	
3^c	**H**	(CH$_2$Cl)$_2$	2	-	84
4	**G**	(CH$_2$Cl)$_2$	4	63	-
5	**F**	(CH$_2$Cl)$_2$	4	46	-
6	**J**	(CH$_2$Cl)$_2$	4	33	-
7	**A**	(CH$_2$Cl)$_2$	2	58	-
8	**K**	(CH$_2$Cl)$_2$	16	-^{d}	-
9	**D**	(CH$_2$Cl)$_2$	4	24	-
10	**L**	(CH$_2$Cl)$_2$	20	6	-
11	Ph$_3$PAuCl	(CH$_2$Cl)$_2$	22	-^{d}	-
12	AgNTf$_2$	(CH$_2$Cl)$_2$	5	-^{d}	-
13^c	Ph$_3$PAuNTf$_2$	(CH$_2$Cl)$_2$	2	75	-
14	Ph$_3$PAuNTf$_2$	THF	18	6	-
15	Ph$_3$PAuNTf$_2$	MeCN	16	10	-
16	Ph$_3$PAuNTf$_2$	PhMe	3	6	-

Table 4.1 (*continued*)

entry	catalyst	solvent	time	yield[b]	
				186a	**185a**
17	$Ph_3PAuNTf_2$	Me_2CO	16	-[d]	-

[a] All reactions were performed at 0.1 M with 5 mol % of catalyst at reflux temperature. [b] Crude ^{1}H NMR yield with dibromomethane as internal standard. [c] Reaction was carried out at room temperature. [d] Decomposition was detected by TLC and ^{1}H NMR analysis of the crude mixture.

oroethane to THF, MeCN, PhMe, or acetone, the desired bridgehead ketone product **186a** was furnished in less than 10% yield (entries 14–17). Based on the observations above, the procedure described in entry 13 was deemed to provide the optimal reaction conditions.

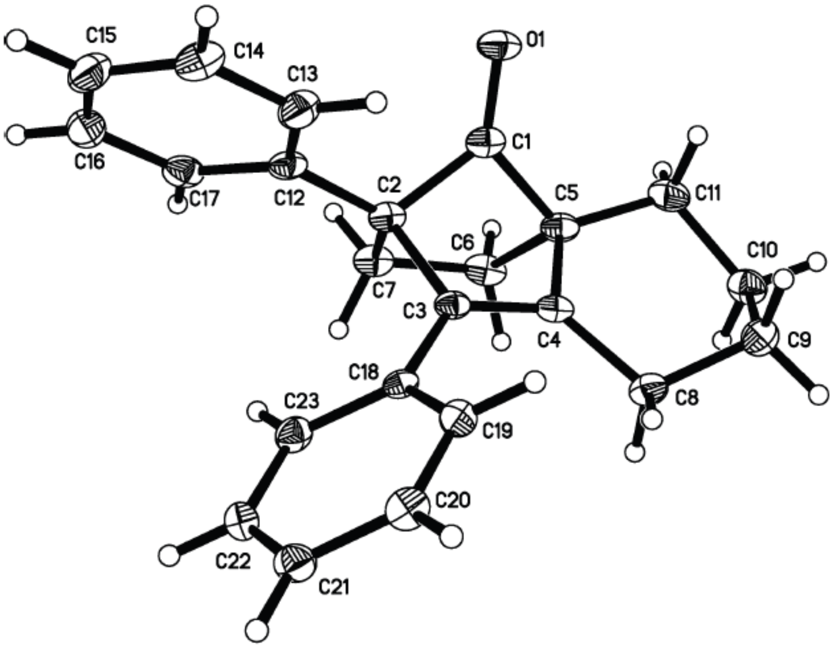
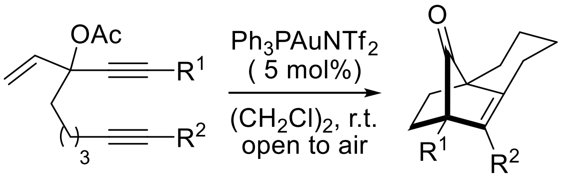


Figure 4.2 ORTEP drawing of **186a** with thermal ellipsoids at 50% probability levels.

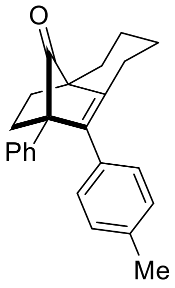
In order to assess the generality of this transformation, a variety of 1,8-diynyl vinyl esters **184b–n** were examined and the results are summarized in Table 4.2. In general, this methodology was found to have a broad scope, with a variety of 3,4-disubstituted bicyclo[2.2.1]hept-2-en-7-one derivatives **186b–n** formed in 35–94% yield from the corresponding 1,8-diynyl vinyl esters. It was found that aryl substituents at R^2 position bearing a *para*-electron-donating group (**184b–c**) or an electron-withdrawing group (**184d–e**) were well-tolerated under the reaction conditions, affording the corresponding 3,4-disubstituted-bicyclo[2.2.1]hept-2-en-7-one adducts **186b–e** in 40–74% yield. Likewise, replacing the aryl substituent at R^2 with a heterocyclic 3-thiophenyl (**184f**) or polyphenyl moiety, as in **184g–h**, was also found to proceed well and furnished **186f**, **186g** and **186h** in 71, 65, and 35% yield, respectively. The lower yield of **186h** may have been due to the instability of substrate **184h**. These conditions also proved amenable toward 1,8-diynyl vinyl ester substrate with electron-donating aryl moiety, hetero-aryl, alkyl and cycloalkyl groups at the R^1 position, as in **184i–m**, giving the corresponding adducts **186i–m** in 47–94% yield. It is noteworthy that starting diyne esters in which R^1 is an alkyl or a cycloalkyl group were more competent when compared to their aromatic counterparts. As an example, the reaction of diyne ester **184k** was completed in a shorter reaction time of 1 hour, giving **186k** in a good yield of 80%.

In order to shed light on the mechanism of the present Au(I)-catalyzed carbocyclization of 1,8-diynyl vinyl esters, several control experiments were conducted (Scheme 4.4). We initially subjected cyclopentadiene **185a**, previously isolated during reaction optimization (Table 4.1, entry 3), to the standard conditions. This exclusively gave the desired bicyclo[2.2.1] product **186a** exclusively in 80% yield (Scheme 4.4, eq 1), which is comparable to that obtained from **184a** (Table 4.1, entry 13). The isolation of **186a** from **185a** suggested that **185a** may be a key intermediate in this transformation.

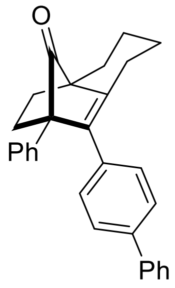
Table 4.2 Carbocyclization of 9-substituted-3-(substituted-ethynyl)non-1-en-8-yn-3-yl acetates **165b–n** catalyzed by $Ph_3PAuNTf_2$[a]



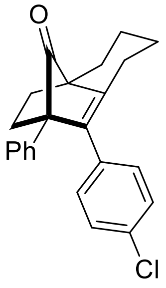
184 **186**



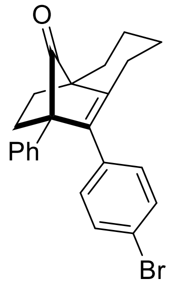
186b
40% (18 h)



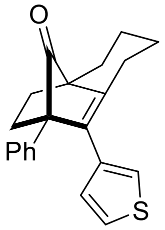
186c
74% (2 h)



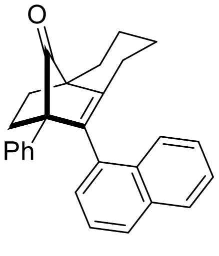
186d
67% (2 h)



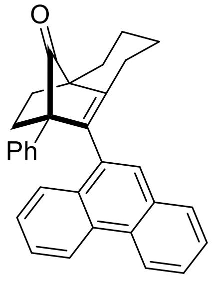
186e
63% (2 h)



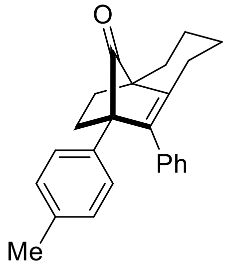
186f
71% (1 h)



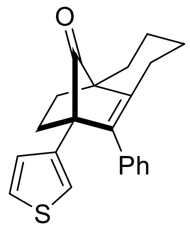
186g
65% (2 h)



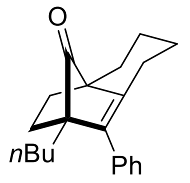
186h
35% (2 h)



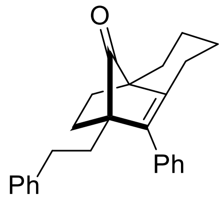
186i
47% (18 h)



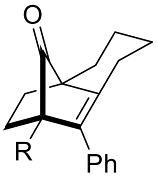
186j
40% (1 h)



186k
80% (0.5 h)



186l
81% (2 h)

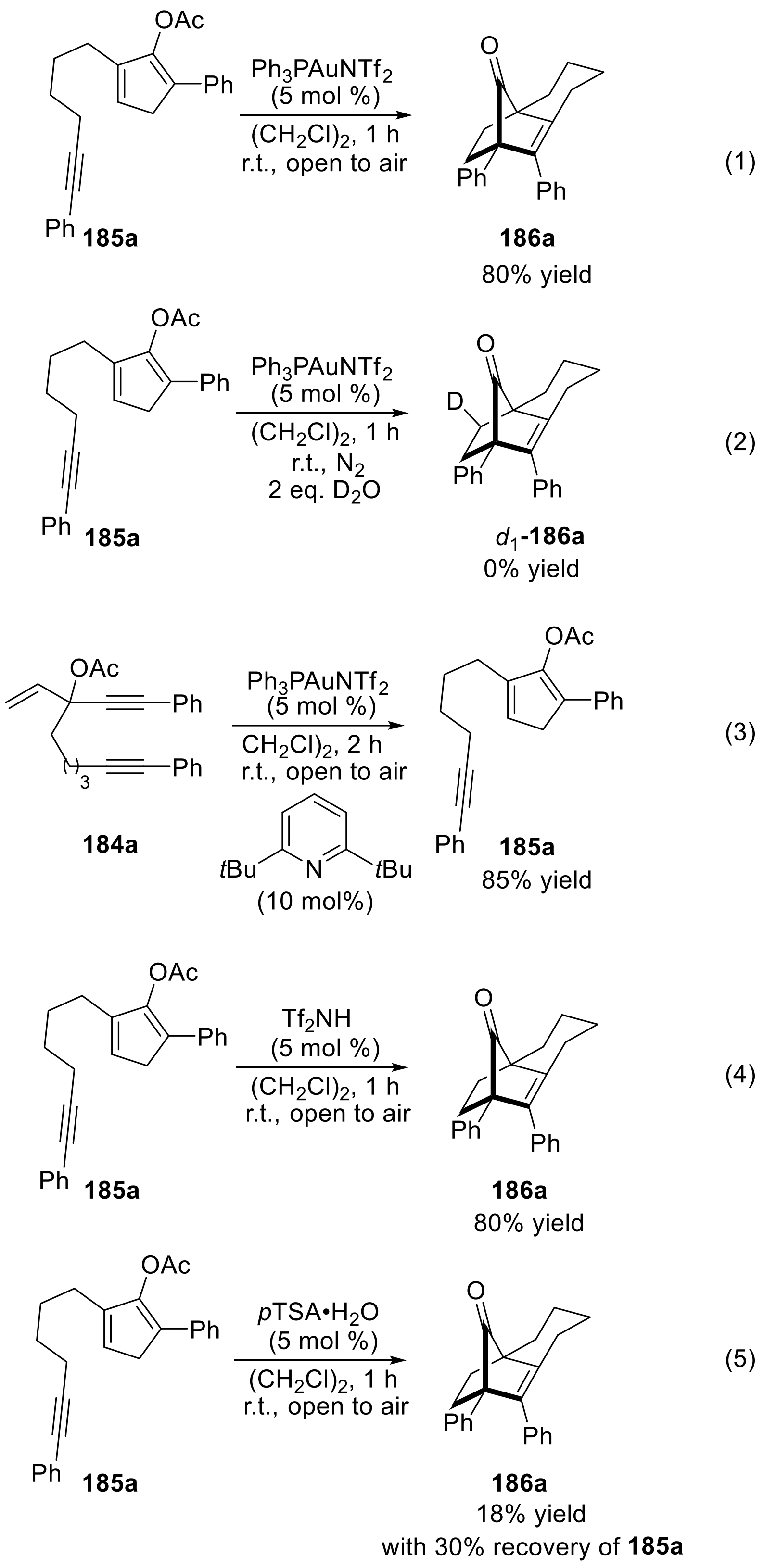


R = cC_6H_{11} (**186m**) 94% (2 h)
R = cC_5H_9 (**186n**) 86% (2 h)

[a] All reactions were performed at the 0.2 mmol scale with 5 mol % of $Ph_3PAuNTf_2$ in 1,2-dichloroethane at room temperature in an open-rounded bottom flask. [b] Value in parentheses denoted the reaction time.

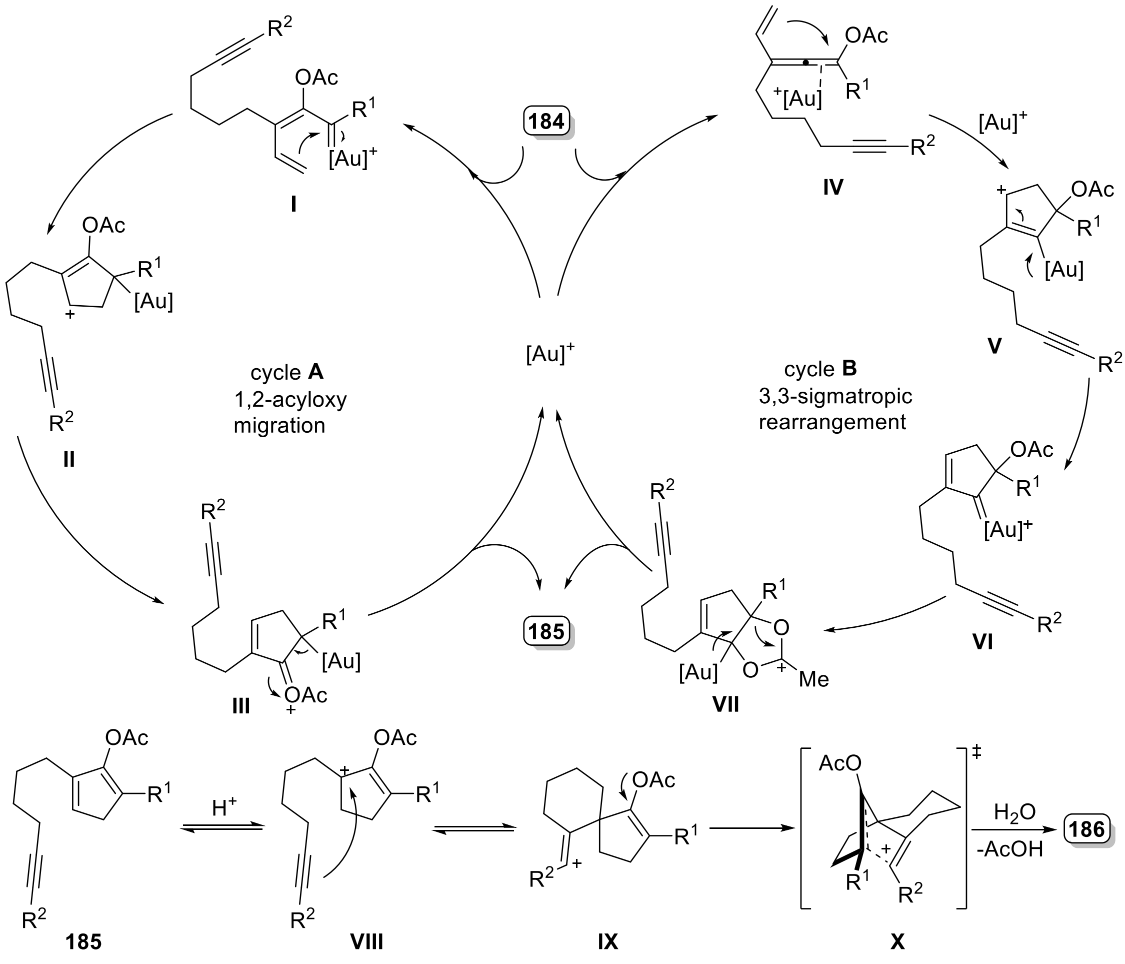
To assess the possible participation of an alkyl sp^3 carbon-gold(I) species in the conversion of **185a** to product **186a**, analogous reaction in the presence of 2 equivalents of D_2O were performed (Scheme 4.4, eq 2). This resulted in no deuterium atom incorporation, which led us to rule out the involvement of an alkyl sp^3C-gold species in this process. Thus, we suspected that a Brønsted acid generated *in situ* by the dissociation of the counter anion in the gold(I) complex could indeed be the active species mediating the transformation of **185a** to **186a**. This was further supported by the exclusive formation of intermediate **185a** when **184a** was treated with 10 mol % of acid scavenger 2,6-di-*tert*-butylpyridine under the standard conditions (Scheme 4.4, eq 3). The Brønsted acid Tf_2NH was found to catalyzed the formation of **186a** from the intermediate **185a** in 80% yield, further validates it is an acid-driven process (Scheme 4.3, eq 4).[92] It is noteworthy that this acid-mediated step is pKa-dependent. This was demonstrated in the reaction of **185a** with 5 mol % of a less acidic *p*-toluenesulfonic acid, which furnished the desired product **186a** in a low 18% yield and recovered **185a** in 30% yield (Scheme 4.4, eq 5).

Based on the studies above, a plausible mechanism for the formation of bicyclo[3.3.0] derivatives **186** is outlined in Scheme 4.5. One potential pathway, c*ycle* **A**, would involve initial gold(I)-catalyzed 1,2-acyloxy migration of 1,8-diynyl vinyl esters **184** to give gold(I)-carbenoid intermediate **I**, with ensuing nucleophilic attack of the proximal vinyl moiety giving the alkyl gold cyclic intermediate **II**. Tautomerization of the carbocation intermediate **II** would give the oxocarbenium **III**, with subsequent deauration furnishing the cyclopentadiene intermediate **185**. Alternatively, 1,8-diynyl vinyl esters **184** may undergo 3,3-sigmatropic rearrangement to afford vinyl allenic ester intermediates **IV**, as shown in *cycle* **B**. Annulation of **IV**, via the nucleophilic attack of the gold(I)-activated allenic moiety by adjacent vinyl group and subsequent tautomerization of **V** would



Scheme 4.4 Control experiments with **184a** and **185a** catalyzed by $Ph_3PAuNTf_2$ or a Brønsted acid.

generate the gold(I)-carbenoid intermediate **VI**. Subsequently, nucleophilic attack by the adjacent acetate group on the electrophilic carbon center of gold(I)-carbenoid intermediate **VI**, may result in the formation of alkyl-gold(I) bicyclic intermediate **VII**. On release of the gold catalyst, this bicyclic intermediate would then deliver cyclopentadiene intermediate **185**. At this juncture, protonation of cyclopentadiene **185** by the Brønsted-acidic counterion, or a Brønsted acid catalyst, may occur at the less-substituted C=C bond and generate the stable cyclic tertiary carbocation species **VIII**. Attack of the pendant alkyne moiety at the cation in **VIII** would afford the spiro-bicyclic vinyl carbocation **IX**. Further cyclization of the vinyl cation and enolate moiety in **IX**,



Scheme 4.5 Proposed mechanism for Au(I)-catalayzed carbocyclization of 1,8-diynyl vinyl esters.

followed by hydrolysis would then afford the desired product **186** via the transition state **X**.

4.3 Conclusion

In conclusion, we have successfully developed a facile and novel synthetic method to prepare substituted bridgehead ketones with bicyclo[2.2.1] framework from a diverse range of 1,8-diynyl vinyl esters with the aid of both gold(I) complex and Brønsted acid as catalysts that did not require the exclusion of air and moisture. It was shown that this methodology tolerates a variety of 1,8-diynyl vinyl esters in general. This tandem process relies on the formation of an intermediate cyclopentadiene motif by the catalysis of a gold(I) complex. Crucially, the Brønsted acid produced in situ by dissociation of the catalyst leads to the formation of the bridgehead ketone targets. Mechanistic studies to determine the formation pathway of cyclopentadiene intermediate, the further expansion of the substrate scope such as investigating substrates fitted with aliphatic subtituent at alkynyl position and exploring the subtrates with longer carbon chain as well as the study of further application of the bridgehead ketone adducts will be carried out in future.

Chapter V: Experimental Section

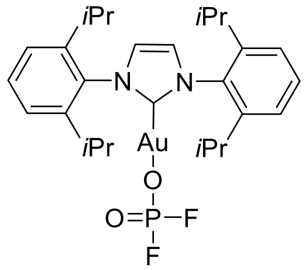
5.1 General Remarks

Unless specified, all metal complexes, reagents and starting materials were purchased directly from commercial sources and used without further purifications. Gold complex **A**, **C**, **K**, **L** were purchased from commercial sources and used as received. Gold complexes **B** and **D–J** were prepared following literature procedures.[64] Analytical TLCs were performed using pre-coated silica gel plate and visualized with ultraviolet radiation at 254 nm or through staining with potassium permanganate solution. Flash chromatography was achieved using silica gel and gradient solvent system

(EtOAc:*n*hexane as eluent). ^{1}H and ^{13}C NMR were recorded at ambient temperatures on a 300 or 400 MHz NMR spectrometer with tetramethylsilane (TMS) as the internal standard. Chemical shifts (ppm) were reported in parts per million (ppm) with coupling constants reported in Hertz (Hz). Multiplicities are given as: s (singlet), br s(broad singlet), d (doublet), t (triplet), dd (doublet of doublets), dt (doublet of triplets) or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H. Infrared spectra were taken on a IR spectrometer. High resolution mass spectra (HRMS) were obtained on a LC/HRMS TOF spectrometer using simultaneous electrospray (ESI).

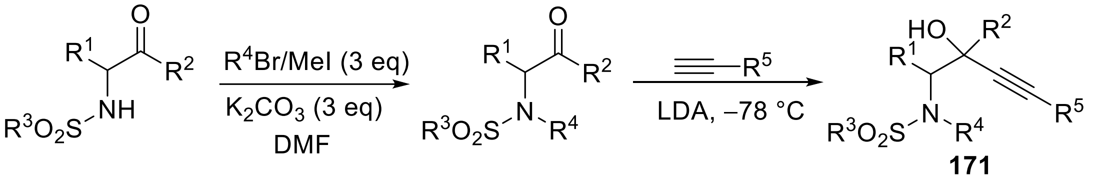
5.2. Gold-Catalyzed Tandem Aminocyclization/1,3-Sulfonyl Migration of *N*-Substituted-*N*- sulfonyl-aminobut-3-yn-2-ols to Substituted-3-sulfonyl-1*H*-pyrroles

Procedure for the Synthesis of Gold(I) Complex E[66]



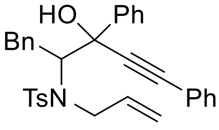
To a solution of IPrAuCl (150 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) was added a solution of $AgPF_6$ (60.7 mg, 0.24 mmol) in CH_2Cl_2 (1 mL) at room temperature. The mixture was stirred for 1 h and the resulting reaction mixture was filtered, washed with CH_2Cl_2 (2 x 4 mL) and concentrated under reduced pressure. Diethyl ether (5 mL) was then slowly added, which resulted in the immediate precipitation of a solid. The precipitate was filtered, washed with diethyl ether (2 x 5 mL) and dried under reduced pressure. This gave the title compound as a light pink, air-stable solid (129.5 mg, 78% yield). m.p. = 199-201 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (d, 14H, J = 6.4 Hz), 1.31 (d, 11H, J = 4.8 Hz), 2.47-2.51 (m, 4H), 7.26-7.31 (m, 6H), 7.50-7.52 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 24.1, 24.3, 28.8, 123.8, 124.4, 131.0, 133.6, 145.5; ^{31}P NMR (161.98 MHz, $CDCl_3$) δ −14.04 (t, $^1J(^{19}F\text{-}^{31}P)$ = 980.0 Hz); HRMS (DART) calcd. for $C_{27}H_{38}N_2OAu$ (M^+-POF_2): 603.2650, found: 603.2632.

General Procedure for the Preparation of 171a-t:


171

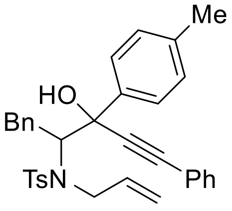
To a round-bottom flask containing 4-methyl-*N*-(1,2-disubstituted)benzenesulfonamide[61] (3.0 mmol) was added K_2CO_3 (9.0 mmol) followed by dimethylformamide (10 mL). The corresponding allyl/alkyl bromide or MeI (9.0 mmol) was then added and the reaction mixture was allowed to stir for 12-48 h at room temperature. On completion, H_2O (10 mL) and diethyl ether (10 mL) was sequentially added to the reaction mixture. The aqueous layer was extracted with ether (3 x 20 mL) and the organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was then purified by flash column chromatography on silica gel (eluent: *n*hexane:EtOAc = 6:1) to afford the α-allylsulfonylamino ketone product, which was used directly for the next step. To a solution of ethynylbenzene (3.0 mmol) in THF (15 mL) was added Lithium diisopropylamide (LDA, 2.0 M in THF, 1.5 mL, 3.0 mmol) at −78 °C. The resulting solution was stirred for 1 h at −78 °C. The α-allylsulfonylamino ketone (1 mmol) in THF (2 mL) was subsequently added dropwise to the reaction mixture at −78 °C. The resulting reaction mixture was slowly warmed up to room temperature and stirred for 16 h. On completion, the reaction mixture was quenched by addition of saturated NH_4Cl (10 mL) and extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane:EtOAc = 7:1) to afford the title compound. The title compound was obtained as one diastereomer.

N-Allyl-*N*-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-4methylbenzenesulfonamide (171b)



Yield 86%; Colorless solid; m.p. = 155-157 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 2.85 (d, 1H, *J* = 14.1 Hz), 2.98 (d, 1H, *J* = 11.1 Hz), 3.61 (s, 1H), 4.31 (d, 1H, *J* = 6.0 Hz), 4.37 (d, 1H, *J* = 13.2 Hz), 4.89 (d, 1H, *J* = 9.2 Hz), 5.05 (d, 1H, *J* = 10.1 Hz), 5.16 (d, 1H, *J* = 17 Hz), 5.79-5.83 (m, 1H), 6.83 (d, 2H, *J* = 6.6 Hz), 6.94 (d, 2H, *J* = 7.7 Hz), 7.10-7.15 (m, 5H), 7.36-7.39 (m, 4H), 7.45 (t, 2H, *J* = 7.5 Hz), 7.53-7.55 (m, 2H), 7.89 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 34.3, 46.8, 69.6, 75.3, 89.0, 89.3, 117.3, 122.1, 126.3, 126.8, 127.9, 128.5, 128.55, 128.58, 129.0, 129.2, 131.7, 135.9, 136.9, 138.0, 142.9, 143.1; IR (NaCl, neat) *v*: 3412, 3021, 1599, 1325 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{31}NO_3SNa$ (M$^+$+Na): 544.1922, found: 544.1926.

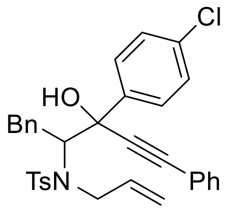
N-Allyl-*N*-(3-hydroxy-1,5-diphenyl-3-(*p*-tolyl)pent-4-yn-2-yl)-4-methylbenzenesulfonamide (171c)



Yield 75%; Yellow solid; m.p. = 56-58 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 2.40 (s, 3H), 2.83 (d, 1H, *J* = 14.5 Hz), 2.96 (d, 1H, *J* = 11.6 Hz), 3.52 (s, 1H), 4.30 (d, 1H, *J* = 6.0 Hz), 4.37 (d, 1H, *J* = 13.6 Hz), 4.89 (d, 1H, *J* = 9.4 Hz), 5.04 (d, 1H, *J* = 10.1 Hz), 5.15 (d, 1H, *J* = 17.1 Hz), 5.79-5.82 (m, 1H), 6.85 (d, 2H, *J* = 6.9 Hz), 6.94 (d, 2H, *J* = 7.9 Hz), 7.09-7.16 (m, 4H), 7.25 (d, 3H, *J* = 7.8 Hz), 7.35-7.38 (m, 3H), 7.51-7.54

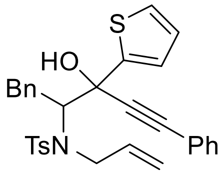
(m, 2H), 7.77 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.2, 21.5, 34.4, 46.8, 69.6, 75.2, 89.2, 117.3, 122.2, 126.3, 126.7, 127.9, 128.5, 128.6, 129.0, 129.16, 129.24, 131.7, 136.0, 137.0, 138.1, 138.2, 140.3, 142.9; IR (NaCl, neat) *v*: 3460, 3019, 1599, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{33}NO_3SNa$ (M^++Na): 558.2079, found: 558.2076.

N-Allyl-N-(3-(4-chlorophenyl)-3-hydroxy-1,5-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171d)



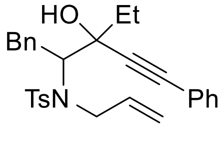
Yield 65%; Yellow solid; m.p. = 127-129 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.33 (s, 3H), 2.84 (d, 1H, *J* = 14.0), 2.97 (d, 1H, *J* = 11.1 Hz), 3.64 (s, 1H), 4.26 (d, 1H, *J* = 4.6 Hz), 4.34 (d, 1H, *J* = 12.9 Hz), 4.84 (d, 1H, *J* = 8.6 Hz), 5.06 (d, 1H, *J* = 10.0 Hz), 5.16 (d, 1H, *J* = 17.1 Hz), 5.70-5.90 (m, 1H), 6.85 (d, 2H, *J* = 6.4 Hz), 6.96 (d, 2H, *J* = 7.3 Hz), 7.08-7.17 (m, 5H), 7.38-7.40 (m, 5H), 7.51-7.53 (m, 2H), 7.80 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 34.4, 46.8, 69.4, 75.0, 88.6, 89.5, 117.5, 121.9, 126.4, 127.9, 128.4, 128.5, 128.6, 129.16, 129.2, 131.7, 134.3, 135.7, 136.7, 137.7, 141.7, 143.1; IR (NaCl, neat) *v*: 3480, 3019, 1597, 1489 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{30}ClNO_3S$ (M^++Na): 578.1533, found: 578.1538.

N-Allyl-*N*-(3-hydroxy-1,5-diphenyl-3-(thiophen-2-yl)pent-4-yn-2-yl)-4-methylbenzenesulfonamide (171e)



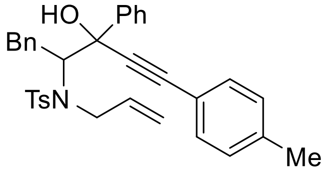
Yield 72%; Yellow solid; m.p. = 129-131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.33 (s, 3H), 2.96-3.04 (m, 2H), 3.78 (s, 1H), 4.30-4.36 (m, 2H), 4.91 (d, 1H, *J* = 7.6 Hz), 5.08 (d, 1H, *J* = 10.1 Hz), 5.18 d, 1H, *J* = 17.2 Hz), 5.70-5.86 (m, 1H), 6.91-6.97 (m, 4H), 7.03 (dd, 1H, *J* = 5.1, 3.6 Hz), 7.09-7.17 (m, 5H), 7.34-7.39 (m, 4H), 7.43 (dd, 1H, *J* = 3.5, 1.0 Hz), 7.52-7.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 34.9, 46.8, 69.7, 72.7, 88.1, 88.6, 117.4, 121.9, 126.2, 126.3, 126.4, 127.0, 127.9, 128.5, 128.6, 129.16, 129.21, 131.7, 136.0, 136.8, 137.9, 143.0, 148.3; IR (NaCl, neat) *v*: 3429, 3019, 1599, 1493, 1090 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{29}NO_3S_2Na$ (M^++Na): 550.1487, found: 550.1469.

N-Allyl-*N*-(3-ethyl-3-hydroxy-1,5-diphenylpent-4-yn-2-yl)-4 methylbenzenesulfonamide (171f)



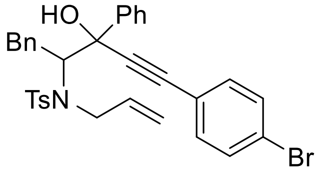
Yield 85%; Pale yellow solid; m.p. = 83-85 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21 (t, 3H, *J* = 7.3 Hz), 1.84-2.01 (m, 2H), 2.33 (s, 3H), 2.63 (s, 1H), 3.02 (dd, 1H, *J* = 14.4, 10.3 Hz), 3.32 (d, 1H, *J* = 12.6 Hz), 4.12 (dd, 1H, *J* = 16.1, 6.1 Hz), 4.22 (dd, 1H, *J* = 16.2, 5.0 Hz), 4.59 (d, 1H, *J* = 6.8 Hz), 3.57 (d, 1H, *J* = 10.1 Hz), 5.17 (d, 1H, *J* = 17.2 Hz), 5.79-5.85 (m, 1H), 6.46 (d, 2H, *J* = 7.6 Hz), 7.09-7.15 (m, 4H), 7.18-7.21 (m, 3H), 7.30-7.33 (m, 3H), 7.42-7.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 8.5, 21.5, 34.0, 35.4, 47.0, 67.2, 74.8, 86.8, 90.3, 117.5, 122.4, 126.4, 127.8, 128.4, 128.6, 129.2, 129.4, 131.7, 136.1, 137.0, 138.75, 142.8; IR (NaCl, neat) *v*: 3524, 3019, 1599 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{32}NO_3S$ (M$^+$+H): 474.2103, found: 474.2123.

N-Allyl-N-(3-hydroxy-1,3-diphenyl-5-(p-tolyl)pent-4-yn-2-yl)-4-methylbenzenesulfonamide (171g)



Yield 76%; Yellow solid; m.p. = 116-118 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H), 2.38 (s, 3H), 2.84 (d, 1H, *J* = 13.7 Hz), 2.97 (d, 1H, *J* = 11.4 Hz), 3.58 (s, 1H), 4.31-4.36 (m, 2H), 4.89 (d, 1H, *J* = 8.5 Hz), 5.05 (d, 1H, *J* = 9.8 Hz), 5.16 (d, 1H, *J* = 16.9 Hz),5.65-5.81 (m, 1H), 6.83 (d, 2H, *J* = 5.4 Hz), 6.94 (d, 2H, *J* = 7.4 Hz), 7.10-7.19 (m, 7H), 7.37-7.46 (m, 5H), 7.89 (d, 2H, *J* = 7.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 21.6, 34.4, 46.7, 69.6, 75.4, 88.3, 89.5, 117.3, 119.1, 126.3, 126.9, 127.9, 128.4, 128.5, 129.16, 129.19, 129.3, 131.6, 136.0, 137.0, 138.0, 139.2, 142.9, 143.2; IR (NaCl, neat) *v*: 3443, 3019, 1599, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{34}NO_3S$ (M$^+$+H): 536.2259, found: 536.2249.

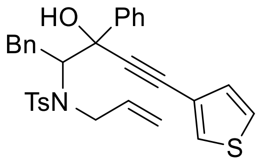
N-Allyl-N-(5-(4-bromophenyl)-3-hydroxy-1,3-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171h)



Yield 72%; Yellow solid; m.p. = 64-66 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.31 (s, 3H), 2.84 (d, 1H, *J* = 14.0 Hz), 2.94 (d, 1H, *J* = 10.8 Hz), 3.65 (s, 1H), 4.25-4.36 (m, 2H), 4.88

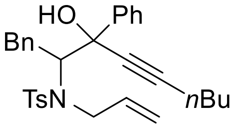
(d, 1H, *J* = 8.6 Hz), 5.04 (d, 1H, *J* = 10.0 Hz), 5.14 (d, 1H, *J* = 16.8 Hz), 5.76-5.80 (m, 1H), 6.82 (d, 2H, *J* = 6.5 Hz), 6.93 (d, 2H, *J* = 7.5 Hz), 7.08-7.17 (m, 5H), 7.37-7.40 (m, 3H), 7.42-7.52 (m, 4H), 7.86 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 34.3, 46.7, 69.5, 75.5, 88.0, 90.2, 117.3, 121.0, 123.3, 126.3, 126.7, 127.9, 128.4, 128.6, 129.1, 129.2, 131.5, 131.8, 133.1, 135.9, 136.9, 142.9, 143.0; IR (NaCl, neat) *v*: 3447, 3019, 1599, 1487, 754 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{30}BrNO_3SNa$ (M^++Na): 622.1027, found: 622.1012.

N-Allyl-N-(3-hydroxy-1,3-diphenyl-5-(thiophen-3-yl)pent-4-yn-2-yl)-4-methylbenzenesulfonamide (171i)



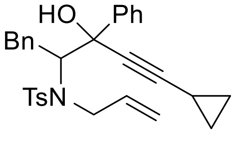
Yield 90%; Yellow solid; m.p. = 154-156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H), 2.82, (d, 1H, *J* = 14.1 Hz), 2.95 (d, 1H, *J* = 11.2 Hz), 3.59 (s, 1H), 4.27 (d, 1H, *J* = 6.2 Hz), 4.36 (d, 1H, *J* = 14.1 Hz), 4.89 (d, 1H, *J* = 8.9 Hz), 5.06 (d, 1H, *J* = 9.9 Hz), 5.16 (d, 1H, *J* = 17.0 Hz), 5.82-5.83 (m, 1H), 6.83 (d, 2H, *J* = 6.5 Hz), 6.94 (d, 2H, *J* = 7.7 Hz), 7.08-7.15 (m, 5H), 7.19 (dd, 1H, *J* = 5.0, 0.7 Hz), 7.32 (dd, 1H, *J* = 4.9, 3.0 Hz), 7.36-7.39 (m, 1H), 7.45 (t, 2H, *J* = 7.5 Hz), 7.55 (d, 1H, *J* = 2.0 Hz), 7.87 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 34.3, 46.7, 69.5, 75.4, 84.6, 88.4, 117.2, 121.1, 125.8, 126.3, 126.8, 127.9, 128.4, 128.5, 129.2, 129.5, 129.7, 136.0, 136.9, 137.9, 142.9, 143.0; IR (NaCl, neat) *v*: 3414, 3022, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{30}NO_3S_2$ (M^++H): 528.1667, found: 528.1668.

N-Allyl-N-(3-hydroxy-1,3-diphenylnon-4-yn-2-yl)-4-methylbenzenesulfonamide (171j)



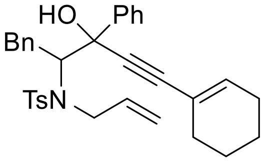
Yield 94%; Yellow solid; m.p. = 55-57 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.44-1.53 (m, 2H), 1.57-1.64 (m, 2H), 2.31 (s, 3H), 2.38 (t, 2H, *J* = 7.0 Hz), 2.75 (d, 1H, *J* = 14.3 Hz), 2.87 (d, 1H, *J* = 11.2 Hz), 3.41 (s, 1H), 4.20-4.29 (m, 2H), 4.77 (d, 1H, *J* = 9.2 Hz), 5.04 (d, 1H, *J* = 10.0 Hz), 5.15 (d, 1H, *J* = 17.1 Hz), 5.75-5.77 (m, 1H), 6.80 (d, 2H, *J* = 6.7 Hz), 6.92 (d, 2H, *J* = 7.8 Hz), 7.06-7.14 (m, 5H), 7.34-7.36 (m, 1H), 7.41 (t, 2H, *J* = 7.4 Hz), 7.81 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.6, 18.6, 21.4, 22.2, 30.6, 34.4, 46.6, 69.3, 75.0, 80.2, 90.2, 116.8, 126.2, 126.8, 127.9, 128.2, 128.3, 128.4, 129.07, 129.14, 136.1, 137.2, 138.2, 142.8, 143.6; IR (NaCl, neat) *v*: 3410, 3019, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{36}NO_3S$ (M^++H): 502.2416, found: 502.2421.

N-Allyl-N-(5-cyclopropyl-3-hydroxy-1,3-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171k)



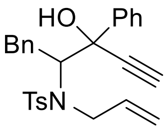
Yield 86%; Colorless solid; m.p. = 105-107 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.77-0.81 (m, 2H), 0.83-0.88 (m, 2H), 1.39-1.43 (m, 1H), 2.31 (s, 3H), 2.71 (d, 1H, *J* = 14.0 Hz), 2.85 (d, 1H, *J* = 11.2 Hz), 3.36 (s, 1H), 4.22-4.31 (m, 2H), 4.76 (d, 1H, *J* = 9.2 Hz), 5.05 (d, 1H, *J* = 9.6 Hz), 5.18 (d, 1H, *J* = 17.2 Hz), 5.65-5.75 (m, 1H), 6.81 (d, 2H, *J* = 6.8 Hz), 6.93 (d, 2H, *J* = 7.8 Hz), 7.05-7.16 (m, 5H), 7.32-7.36 (m, 1H), 7.39-7.43 (m, 2H), 7.79 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): -0.4, 8.26, 8.28, 21.5, 34.3, 46.6, 69.4, 74.9, 75.2, 93.1, 116.9, 126.2, 126.8, 127.9, 128.2, 128.3, 128.4, 129.1, 129.2, 136.2, 137.0, 138.1, 142.8, 143.5; IR (NaCl, neat) *v*: 3480, 3026, 1599, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{32}NO_3S$ (M$^+$+H): 486.2103, found: 486.2102.

N-Allyl-*N*-((2S,3S)-5-(cyclohex-1-en-1-yl)-3-hydroxy-1,3-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171l)



Yield 80%; Yellow solid; m.p. = 117-119 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.61-1.70 (m, 4H), 2.13-2.15 (m, 2H), 2.20-2.22 (m, 2H), 2.32 (s, 3H), 2.75 (d, 1H, *J* = 14.4 Hz), 2.88 (d, 1H, *J* = 10.9 Hz), 3.41 (s, 1H), 4.26-4.28 (m, 2H), 4.82 (d, 1H, *J* = 9.0 Hz), 5.05 (d, 1H, *J* = 10.0 Hz), 5.17 (d, 1H, *J* = 17.2 Hz), 5.75-5.77 (m, 1H), 6.22-6.24 (m, 1H), 6.82 (d, 2H, *J* = 7.0 Hz), 6.94 (d, 2H, *J* = 7.9 Hz), 7.08-7.14 (m, 5H), 7.36 (t, 1H, *J* = 7.2 Hz), 7.42 (t, 2H, *J* = 7.8 Hz), 7.82 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 22.2, 25.7, 29.0, 34.4, 46.7, 69.5, 75.2, 86.2, 91.2, 117.1, 120.0, 126.2, 126.9, 127.9, 128.3, 128.4, 129.1, 129.2, 136.1, 137.2, 138.1, 142.8, 143.4; IR (NaCl, neat) *v*: 3400, 3019, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{36}NO_3S$ (M$^+$+H): 526.2416, found: 526.2421.

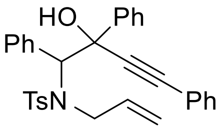
N-Allyl-*N*-(3-hydroxy-1,3-diphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171m)



Yield 73%; Colourless oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 2.78 (d, 1H, *J* =

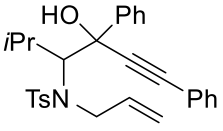
14.4 Hz), 2.91-2.98 (m, 2H), 3.61 (s, 1H), 4.27-4.29 (m, 2H), 4.80 (d, 1H, *J* = 9.6 Hz), 5.06 (d, 1H, *J* = 10 Hz), 5.19 (d, 1H, *J* = 17.2 Hz), 5.71-5.74 (m, 1H), 6.80 (d, 2H, *J* = 6.4 Hz), 6.93 (d, 2H, *J* = 8.0 Hz), 7.05-7.15 (m, 5H), 7.35-7.46(m, 3H), 7.83 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 34.2, 46.6, 74.9,77.8, 83.7, 117.4, 126.3, 126.7, 127.9, 128.4, 128.5, 129.1, 135.7, 136.9, 137.9, 142.6, 142.9; IR (NaCl, neat) *ν*: 3300, 3026, 1599, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{28}NO_3S$ (M$^+$+H): 446.1790, found: 446.1784.

N-Allyl-N-(2-hydroxy-1,2,4-triphenylbut-3-yn-1-yl)-4-methylbenzenesulfonamide (171n)



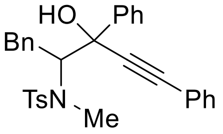
Yield 76%; Colorless solid; m.p. = 117-119 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.29 (s, 3H), 3.99 (dd, 1H, *J* = 16.7, 5.9 Hz), 4.29 (dd, 1H, *J* = 16.7, 6.4 Hz), 5.07 (dd, 1H, *J* = 10.2, 1.2 Hz), 5.19 (dd, 1H, *J* = 1.4 Hz), (s, 1H), 5.79-5.90 (m, 1H), 7.00 (d, 2H, *J* = 8.1 Hz), 7.15-7.24 (m, 5H), 7.33-7.35 (m, 3H), 7.40-7.44 (m, 4H), 7.52-7.60(m, 5H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.4, 49.4, 70.4, 88.1, 91.2, 117.4, 122.4, 126.5, 127.8, 127.9, 127.96, 128.02, 128.4, 128.7, 129.1, 130.8, 131.9, 135.2, 136.4, 137.4, 142.4, 143.0; IR (NaCl, neat) *ν*: 3019, 1599, 1327 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{29}NO_3SNa$ (M$^+$+Na): 530.1766, found: 530.1776.

N-Allyl-N-((3S,4S)-4-hydroxy-2-methyl-4,6-diphenylhex-5-yn-3-yl)-4-methylbenzenesulfonamide (171o)



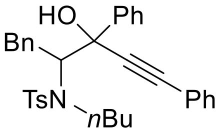
Yield 74%; Yellow solid; m.p. = 101-103 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.50 (d, 3H, *J* = 6.6 Hz), 0.82 (d, 3H, *J* = 6.6 Hz), 2.26-2.28 (m, 1H), 2.41 (s, 3H), 3.03 (s, 1H), 4.25 (dd, 1H, *J* = 16.4, 5.6 Hz), 4.38 (d, 1H, *J* = 7.6 Hz), 4.44 (d, 1H, *J* = 9.8 Hz), 5.09 (dd, 1H, *J* = 10.1, 1.1 Hz), 5.24 (dd, 1H, *J* = 17.1, 1.1 Hz), 6.00-6.08 (m, 1H), 7.28 (d, 1H, *J* = 8 Hz), 7.32-7.43 (m, 6H), 7.48-7.51 (m, 2H), 7.82-7.88 (m, 4H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 21.6, 22.0, 29.7, 47.5, 72.5, 74.3, 88.8, 89.9, 117.8, 122.2, 127.0, 128.3, 128.4, 128.5, 128.6, 129.0, 129.3, 131.6, 135.8, 137.8, 143.3, 144.6; IR (NaCl, neat) *v*: 3501, 3019, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{31}NO_3SNa$ (M$^+$+Na): 496.1922, found: 496.1925.

N-(3-Hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-N,4-dimethylbenzenesulfonamide (171p)



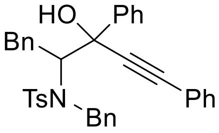
Yield 99%; Yellow solid; m.p. = 129-131 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.31 (s, 3H), 2.82-2.97 (m, 2H), 3.04 (s, 3H), 3.52 (s, 1H), 4.83 (dd, 1H, *J* = 11.0, 3.3 Hz), 6.85 (d, 2H, *J* = 7.2 Hz), 6.93 (d, 2H, *J* = 8.2 Hz), 7.00 (d, 2H, *J* = 8.3 Hz), 7.07-7.15 (m, 3H), 7.35-7.40 (m, 4H), 7.43-7.47 (m, 2H), 7.52-7.55 (m, 2H), 7.90 (d, 2H, *J* = 7.2 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 29.7, 33.6, 68.8, 75.3, 89.2, 122.2, 126.4, 126.9, 127.6, 128.5, 128.58, 128.61, 129.0, 129.3, 131.7, 135.7, 138.0, 142.70, 132.74; IR (NaCl, neat) *v*: 3410, 3019, 1599, 1327 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{30}NO_3S$ (M^++H): 496.1946, found: 496.1952.

_N_-butyl-_N_-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171q)



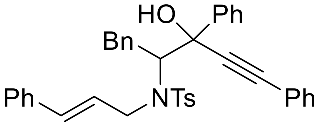
Yield 89%; White solid; m.p. = 184-186 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.84 (t, 3H, *J* = 7.2 Hz), 1.18-.122 (m, 2H), 1.85-1.94 (m, 2H), 2.32 (s, 3H), 2.81 (d, 1H, *J* = 14.3 Hz), 2.90 (d, 1H, *J* = 10.2 Hz), 3.42-3.57 (m, 2H), 3.94 (s, 1H), 4.73 (d, 1H, *J* = 8.2 Hz), 6.69 (d, 2H, *J* = 7.1 Hz), 7.01 (t, 2H, *J* = 7.4 Hz), 7.07-7.16 (m, 3H), 7.34-7.44 (m, 6H), 7.53-7.56 (m, 2H), 7.87 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.7, 20.7, 21.5, 32.8, 34.3, 44.5, 75.2, 88.7, 89.0, 122.2, 126.2, 126.9, 127.5, 128.4, 128.46, 128.52, 128.91, 128.94, 129.3, 131.6, 136.6, 137.8, 142.9, 143.3; IR (NaCl, neat) *v*: 3444, 3053, 1599, 1448 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{35}NO_3S$ (M^++H): 538.2418, found: 538.2418.

_N_-Benzyl-_N_-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171r)



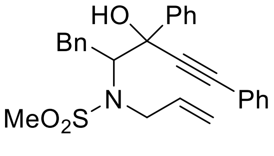
Yield 80%; Yellow solid; m.p. = 165-167 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.28 (s, 3H), 2.84 (d, 1H, *J* = 13.8 Hz), 2.94 (d, 1H, *J* = 9.32 Hz), 3.59-3.73 (m, 1H), 4.92-5.00 (m, 2H), 6.64-6.66 (m, 2H), 6.83-6.86 (m, 2H), 7.04-7.19 (m, 8H), 7.30-7.45 (m, 10H), 7.89-7.91 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.4, 34.9, 48.2, 69.5, 75.3, 88.8, 89.9, 122.1, 126.2, 126.8, 127.3, 127.6, 128.1, 128.2, 128.5, 128.6, 128.9, 129.1, 129.4, 131.7, 137.3, 137.7, 142.6, 143.5; IR (NaCl, neat) *v*: 3419, 3019, 1599, 1447 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{33}NO_3SNa$ (M^++Na): 594.2079, found: 594.2099.

N-Cinnamyl-N-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-4-methylbenzenesulfonamide (171s)



Yield 49%; Yellow solid; m.p. = 79-81 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.23 (s, 3H), 2.92 (d, 1H, *J* = 14.1 Hz), 3.04 (d, 1H, *J* = 11.2 Hz), 3.56 (s, 1H), 4.46 (dd, 1H, *J* = 16.1, 5.4 Hz), 4.56 (dd, 1H, *J* = 16.3, 6.9 Hz), 5.03 (d, 1H, *J* = 9.3 Hz), 5.82-5.89 (m, 1H), 6.37 (d, 1H, *J* = 15,9 Hz), 6.85-6.92 (m, 3H), 7.03-7.09 (m, 4H), 7.13-7.25 (m, 7H), 7.34-7.40 (m, 4H), 7.46 (t, 2H, *J* = 7.4 Hz), 7.53 (d, 2H, *J* = 6.2 Hz), 7.92 (d, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.4, 34.6, 46.2, 69.3, 75.5, 89.2, 89.5, 122.1, 126.3, 126.4, 126.7, 126.8, 127.7, 128.0, 128.5, 128.57, 128.61, 129.05, 129.12, 129.4, 131.7, 132.2, 136.4, 137.5, 138.0, 142.9, 143.1; IR (NaCl, neat) *v*: 3400, 3019, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{39}H_{36}NO_3S$ (M^++H): 598.2416, found: 598.2406.

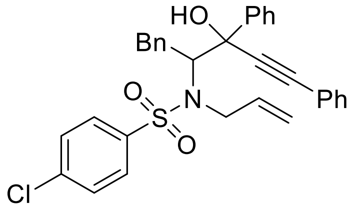
N-Allyl-N-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)methanesulfonamide (171t)



Yield 75%; Brown solid; m.p. = 100-102 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.23 (s, 3H), 2.94 (d, 1H, *J* = 14.2 Hz), 3.04 (d, 1H, *J* = 11.4 Hz), 3.27 (s, 1H), 4.21-4.30 (m, 2H), 4.73 (d, 1H, *J* = 9.9 Hz), 5.21 (d, 1H, *J* = 9.6 Hz), 5.33 (d, 1H, *J* = 17.2), 6.12-6.15 (m, 1H), 7.06 (d, 2H, *J* = 7.2 Hz), 7.15-7.18 (m, 1H), 7.22-7.25 (m, 2H), 7.35-7.39 (m, 4H), 7.45

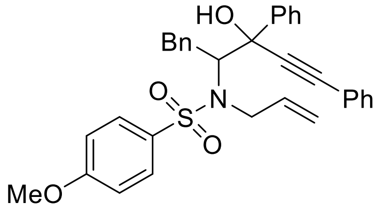
(t, 2H, J = 7.5 Hz), 7.53-7.56 (m, 2H), 7.85 (d, 2H, J = 7.4 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 34.4, 41.0, 46.9, 69.3, 75.6, 89.1, 118.7, 122.0, 126.7, 126.9, 128.55, 128.59, 128.6, 129.1, 129.3, 131.7, 135.5, 138.0, 143.3; IR (NaCl, neat) v: 3458, 3019, 1599, 1449 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{27}NO_3S$ (M$^+$+Na): 468.1609, found: 468.1618.

N-Allyl-4-chloro-N-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)benzenesulfonamide (171u)



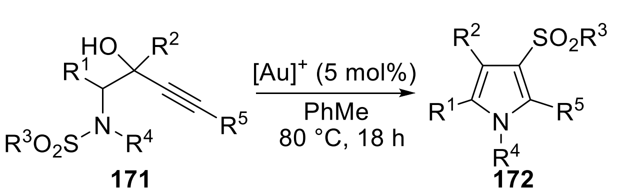
Yield 76%; Pale yellow solid; m.p. = 137-139 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.89 (d, 1H, J = 14.2 Hz), 2.97 (d, 1H, J = 11.0 Hz), 3.55 (s, 1H), 4.27-4.38 (m, 2H), 4.90 (d, 1H, J = 9.5 Hz), 5.03 (d, 1H, J = 10.1 Hz), 5.16 (d, 1H, J = 17.1 Hz), 5.73-5.77 (m, 1H), 6.85 (d, 2H, J = 7.1 Hz), 7.04 (s, 4H), 7.10-7.20 (m, 3H), 7.33-7.39 (m, 4H), 7.45 (t, 2H, J = 7.5 Hz), 7.50-7.53 (m, 2H), 7.90 (d, 2H, J = 7.5 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 34.4, 46.9, 69.9, 75.4, 89.0, 89.4, 117.7, 122.0, 125.4, 126.6, 126.8, 128.7, 129.1, 129.25, 129.32, 131.7, 135.6, 138.1, 138.4, 138.9, 143.2, 150.9; IR (NaCl, neat) v: 3019, 1585, 1329 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{28}ClNO_3SNa$ (M$^+$+Na): 564.1376, found: 564.1369.

_N_-allyl-_N_-(3-hydroxy-1,3,5-triphenylpent-4-yn-2-yl)-4-methoxybenzenesulfonamide (171v)



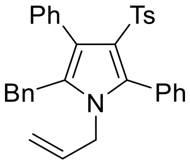
Yield 92%; Pale yellow solid; m.p. = 122-124 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.85 (d, 1H, *J* = 14.4 Hz), 2.96-3.02 (m, 1H), 3.68 (s, 1H), 3.77 (s, 3H), 4.23-4.39 (m, 2H), 4.90 (d, 1H, *J* = 9.6 Hz), 5.04 (d, 1H, *J* = 10.0 Hz), 5.15 (d, 1H, *J* = 17.2 Hz), 5.81-5.83 (m, 1H), 6.60 (d, 2H, *J* = 8.6 Hz), 6.84 (d, 2H, *J* = 6 Hz), 7.11-7.14 (m, 5H), 7.35-7.39 (m, 4H), 7.45 (t, 2H, *J* = 7.5 Hz), 7.52-7.54 (m, 2H), 7.90 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 34.3, 46.7, 55.5, 69.6, 75.4, 89.0, 89.3, 113.7, 117.2, 122.1, 126.4, 126.8, 128.47, 128.54, 128.6, 129.2, 130.0, 131.5, 131.7, 136.0, 138.0, 143.1, 162.5; IR (NaCl, neat) *v*: 3057, 1597, 1490 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{31}NO_4SNa$ (M$^+$+Na): 560.1872, found: 560.1871.

General Experimental Procedure for NHC-Gold(I) Complex A-Catalyzed Cycloisomerization of 171b-s:



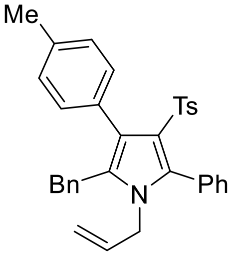
A two neck round-bottom flask containing 1,7-enyne alcohol 1**71** (0.19 mmol) and NHC-gold(I) complex **A** (0.01 mmol) was purged twice with argon gas before toluene (2 mL) was added. The resulting reaction mixture was then stirred at 80 °C for 18 h. On completion, the reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane:EtOAc = 6:1) to afford the product **172**.

Allyl-2-benzyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172b)



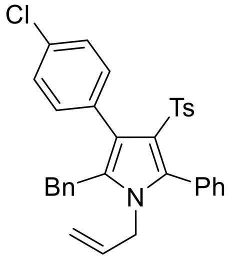
Colorless solid; m.p. = 118-119 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 3.78 (s, 2H), 4.00-4.01 (m, 2H), 4.66 (dd, 1H, *J* = 17.1, 0.9 Hz), 5.04 (dd, 1H, *J* = 10.4, 0.92 Hz), 5.51-5.59 (m, 1H), 6.98-7.00 (m, 4H), 7.14-7.18 (m, 3H), 7.22-7.30 (m, 7H), 7.33-7.43 (m, 5H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 30.3, 47.0, 116.6, 120.4,123.7, 126.4, 127.1, 127.6, 127.75, 127.80, 128.68, 128.72, 129.0, 129.6, 130.6, 131.3, 131.5, 133.4, 133.6, 136.7, 138.8, 141.0, 142.3; IR (NaCl, neat) *v*: 3019, 1599, 1493, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{29}NO_2S$ (M$^+$+Na): 526.1817, found: 526.1835.

Allyl-2-benzyl-5-phenyl-3-(*p*-tolyl)-4-tosyl-1*H*-pyrrole (172c)



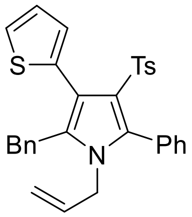
Brown solid; m.p. 128-130 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 2.36 (s, 3H), 3.78 (s, 2H), 3.98-3.99 (m, 2H), 4.65 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.02 (dd, 1H, *J* = 10.4, 0.9 Hz), 5.51-5.57 (m, 1H), 6.97-7.01 (m, 4H), 7.10 (d, 2H, *J* = 7.9 Hz), 7.15-7.18 (m, 4H), 7.21-7.25 (m, 3H), 7.31-7.42 (m, 5H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.4, 21.5, 30.3, 47.0, 116.5, 120.4, 123.7, 126.4, 127.2, 127.8, 127.8, 128.3, 128.7, 128.7, 129.0, 129.6, 130.6, 131.3, 133.4, 136.7, 136.8, 138.9, 141.2, 142.3; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1495 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{32}NO_2S$ (M$^+$+H): 518.2154, found: 518.2171.

Allyl-2-benzyl-3-(4-chlorophenyl)-5-phenyl-4-tosyl-1*H*-pyrrole (172d)



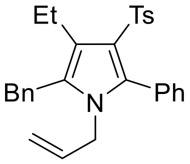
Grey solid; m.p. 155-157 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.33 (s, 3H), 3.77 (s, 2H), 4.00-4.01 (m, 2H), 4.65 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.04 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.51-5.60 (m, 1H), 6.95 (d, 2H, *J* = 7.1 Hz), 7.02 (d, 2H, *J* = 8.1 Hz), 7.15-7.28 (m, 9H), 7.31-7.33 (m, 2H), 7.37-7.43 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 30.2, 47.0, 116.7, 120.4, 122.3, 126.6, 127.1, 127.7, 127.79, 127.81, 128.7, 128.8, 129.1, 129.7, 130.3, 131.3, 132.2, 132.8, 133.3, 137.1, 138.5, 140.9, 142.6; IR (NaCl, neat) *v*: 3019, 2399, 1597, 1489 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{29}ClNO_2S$ (M$^+$+H): 538.1639, found: 538.1619.

Allyl-2-benzyl-5-phenyl-3-(thiophen-2-yl)-4-tosyl-1*H*-pyrrole (172e)



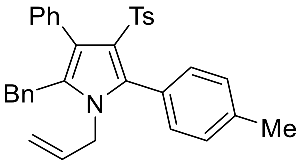
Brown solid; m.p. 133-135 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.34 (s, 3H), 3.88 (s, 2H), 3.99-4.00 (m, 2H), 4.67 (dd, 1H, *J* = 17.0, 0.5 Hz), 5.03 (dd, 1H, *J* = 15.0, 0.6 Hz), 5.48-5.58 (m, 1H), 7.00-7.06 (m, 6H), 7.15-7.19 (m, 1H), 7.15-7.29 (m, 5H), 7.32-7.34 (m, 2H), 7.34-7.44 (m, 3H); ^{13}C NMR ($CDCl_3$,100 MHz): 21.5, 30.5, 47.1, 11.5.1, 116.8, 126.2, 126.5, 126.7, 127.2, 127.8, 127.9, 128.7, 128.9, 129.1, 130.1, 130.3, 131.2, 131.9, 133.1, 133.3, 137.3, 138.4, 140.7, 142.5, 143.1; IR (NaCl, neat) *v*: 3019, 2399, 1597, 1472 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{28}NO_2S_2$ (M^++H): 510.1561, found: 510.1571.

Allyl-2-benzyl-3-ethyl-5-phenyl-4-tosyl-1*H*-pyrrole (172f)



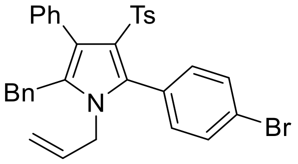
Brown solid; m.p. 135-137 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.15 (t, 3H, *J* = 7.4 Hz), 2.35 (s, 3H), 2.83 (q, 2H, *J* = 7.6 Hz), 3.92-3.95 (m, 4H), 4.59 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.00 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.48-5.55 (m, 1H), 7.05 (d, 2H, *J* = 7.2 Hz), 7.11 (d, 2H, *J* = 8.1 Hz), 7.14-7.18 (m, 2H), 7.20 (d, 1H, *J* = 7.3 Hz), 7.28-7.32 (m, 4H), 7.36 (d, 1H, *J* = 7.4 Hz), 7.44 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 16.8, 18.1, 21.5, 29.8, 46.8, 116.3, 123.8, 126.5, 126.7, 127.6, 127.8, 128.4, 128.7, 128.8, 129.0, 129.4, 130.5, 131.4, 133.6, 136.7, 138.8, 142.3; IR (NaCl, neat) *v*: 3019, 2438, 1599, 1495 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{30}NO_2S$ (M^++H): 456.1997, found: 456.2005.

Allyl-2-benzyl-3-phenyl-5-(p-tolyl)-4-tosyl-1*H*-pyrrole (172g)



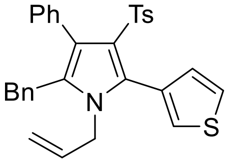
Dark Brown solid; m.p. 67 °C-70 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 2.40 (s, 3H), 3.77 (s, 2H), 4.00-4.01 (m, 2H), 4.67 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.04 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.53-5.60 (m, 1H), 6.97-7.00 (m, 4H), 7.15-7.19 (m, 3H), 7.21-7.29 (m, 11H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.49, 21.51, 30.3, 46.9, 116.5, 120.3, 123.6, 126.4, 127.12, 127.14, 127.5, 127.6, 127.8, 128.5, 128.67, 128.70, 129.5, 131.1, 131.6, 133.5, 133.6, 137.0, 138.83, 138.84, 141.1, 142.3; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1493, 1389 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{32}NO_2S$ (M^++H): 518.2154, found: 518.2153.

Allyl-2-benzyl-5-(4-bromophenyl)-3-phenyl-4-tosyl-1*H*-pyrrole (2h)



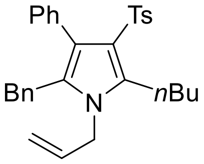
Brown solid; m.p. 129-131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H), 3.77 (s, 2H), 4.00-4.01 (m, 2H), 4.65 (dd, 1H, *J* = 17.1, 0.6 Hz), 5.05 (dd, 1H, *J* = 10.4, 0.7 Hz), 5.50-5.60 (m, 1H), 6.96-7.01 (m, 4H), 7.13-7.18 (m, 3H), 7.22-7.25 (m, 6H), 7.27-7.29 (m, 3H), 7.52 (d, 2H, *J* = 1.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 30.3, 47.0, 116.7, 120.8, 123.6, 123.8, 126.5, 127.1, 127.3, 127.6, 127.8, 128.7, 128.8, 129.6, 130.1, 131.1, 131.5, 132.9, 133.2, 133.3, 135.3, 138.6, 140.7, 142.6; IR (NaCl, neat) *v*: 3019, 2399, 1597, 1493 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{29}BrNO_2S$ (M^++H): 582.1102, found: 582.1113.

Allyl-2-benzyl-3-phenyl-5-(thiophen-3-yl)-4-tosyl-1*H*-pyrrole (172i)



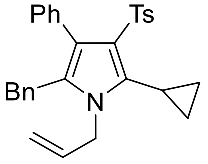
Brown solid; m.p. 83-85 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H), 3.77 (s, 2H), 4.04-4.05 (m, 2H), 4.68 (dd, 1H, *J* = 17.1, 0.9 Hz), 5.05 (dd, 1H, *J* = 10.4, 0.9 Hz), 5.55-5.63 (m, 1H), 6.97-7.02 (m, 4H), 7.07 (dd, 1H, *J* = 4.6, 1.5 Hz), 7.16-7.23 (m, 5H), 7.26-7.34 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 30.3, 47.1, 116.5, 121.1, 124.0, 124.6, 126.5, 127.0, 127.2, 127.6, 127.9, 128.7, 128.8, 129.7, 130.0, 130.2, 131.5, 133.5, 133.6, 138.6, 140.9, 132.4; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1495 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{28}NO_2S_2$ (M$^+$+H): 510.1561; found: 510.1566.

Allyl-2-benzyl-5-butyl-3-phenyl-4-tosyl-1*H*-pyrrole (172j)



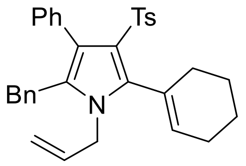
Dark yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.95 (t, 3H, *J* = 7.3 Hz), 1.41-1.50 (m, 2H), 1.59-1.66 (m, 2H), 2.33 (s, 3H), 2.99-3.03 (m, 2H), 3.67 (s, 2H), 4.23-4.24 (m, 2H), 4.74 (d, 1H, *J* = 17.1 Hz), 5.10 (d, 1H, *J* = 11.0 Hz), 5.65-5.70 (m, 1H), 6.93 (d, 2H, *J* = 7.1 Hz), 7.02-7.07 (m, 4H), 7.15-7.25 (m, 6H), 7.29 (d, 2H, *J* = 8.2 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.9, 21.5, 23.0, 24.8, 30.2, 33.1, 46.2, 116.4, 117.5, 123.3, 126.4, 126.9, 127.4, 127.7, 128.6, 128.8, 128.9, 131.6, 133.2, 133.6, 138.3, 138.9, 141.3, 142.2; IR (NaCl, neat) *v*: 3019, 2399, 1601, 1408 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{34}NO_2S$ (M$^+$+H): 484.2310, found: 484.2318.

Allyl-2-benzyl-5-cyclopropyl-3-phenyl-4-tosyl-1*H*-pyrrole (172k)



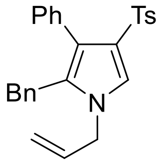
Dark green solid; m.p. 107-109 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.89-0.91 (m, 2H), 1.05-1.10 (m, 2H), 1.69-1.76 (m, 1H), 2.32 (s, 3H), 3.68 (s, 2H), 4.46-4.48 (m, 2H), 4.72 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.11 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.71-5.79 (m, 1H), 6.93 (d, 2H, *J* = 7.1 Hz), 7.02 (d, 2H, 8.0 Hz), 7.07-7.10 (m, 2H), 7.14-7.25 (m, 6H), 7.36 (d, 2H, *J* = 8.3 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 6.7, 8.2, 21.5, 30.1, 46.7, 116.1, 120.3, 123.5, 126.4, 126.9, 127.0, 127.4, 127.7, 128.6, 128.7, 128.8, 131.4, 133.5, 133.8, 137.4, 138.9, 141.2, 142.3; IR (NaCl, neat) *v*: 3019, 2399, 1601, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{30}NO_2S$ (M$^+$+H): 468.1997, found: 468.2007.

Allyl-2-benzyl-5-(cyclohex-1-en-1-yl)-3-phenyl-4-tosyl-1*H*-pyrrole (172l)



Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.60-1.81 (m,4H), 2.02-2.27 (m, 3H), 2.33 (s, 3H), 2.57-2.61 (m, 1H), 3.71 (d, 2H, *J* = 8.6 Hz), 4.09 (d, 1H, *J* = 16.2 Hz), 4.25 (d, 1H, *J* = 12.7 Hz), 4.79 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.08 (dd, 1H, *J* = 10.3, 0.8 Hz), 5.64-5.71 (m, 2H), 6.93 (d, 2H, *J* = 7.2 Hz), 7.05 (d, 2H, *J* = 8.0 Hz), 7.15-7.16 (m, 3H), 7.20-7.25 (m, 5H), 7.33 (d, 2H, 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 21.7, 22.7, 25.6, 30.3, 30.9, 46.8, 116.5, 118.2, 123.2, 126.4, 127.0, 127.1, 127.5, 127.8, 128.6, 128.7, 129.7, 131.5, 132.2, 133.6, 134.1, 139.0, 139.5, 141.4, 142.2; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1495 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{34}NO_2S$ (M$^+$+H): 508.2310, found: 508.2312.

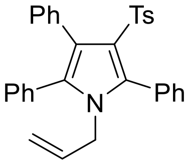
Allyl-2-benzyl-3-phenyl-4-tosyl-1*H*-pyrrole (172m)



Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.33 (s, 3H), 3.78 (s, 2H), 4.21 (d, 2H), 5.01 (dd, 1H, *J* = 17, 0.8 Hz), 5.20 (dd, 1H, *J* = 10.3, 0.8 Hz), 5.68-5.80 (m, 1H), 6.94 (d, 2H, *J* = 7.2 Hz), 7.05 (d, 2H, *J* = 8.2 Hz), 7.13-7.18 (m, 3H), 7.21-7.36 (m, 7H), 7.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 30.1, 50.2, 118.7, 122.8, 123.0, 125.5, 126.5, 127.2, 127.27, 127.32, 127.8, 128.7, 129.0, 129.8, 131.1, 132.5, 132.8, 138.4, 140.0, 142.8; IR

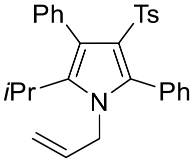
(NaCl, neat) *v*: 3019, 2399, 1746, 1599 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{26}NO_2S$ (M$^+$+H): 428.1684, found: 428.1689.

Allyl-2,3,5-triphenyl-4-tosyl-1*H*-pyrrole (172n)



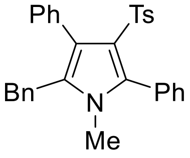
Yellow solid; m.p. 136-138 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.29 (s, 3H), 4.21-4.22 (m, 2H), 4.54 (dd, 1H, *J* = 17.1, 0.9 Hz), 4.93 (dd, 1H, *J* = 10.3, 0.9 Hz), 5.41-5.49 (m, 1H), 6.96 (d, 2H, *J* = 8.1 Hz), 7.12-7.17 (m, 9H), 7.18-7.20 (m, 3H), 7.43-7.46 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 27.5, 117.0, 121.2, 123.2, 126.7, 127.1, 127.2, 127.8, 127.97, 128.04, 128.7, 129.0, 130.8, 130.9, 131.2, 131.5, 131.9, 133.1, 133.3, 133.4, 136.9, 140.8, 142.4; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1464 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{28}NO_2S$ (M$^+$+H): 490.1841, found: 490.1847.

Allyl-2-isopropyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172o)



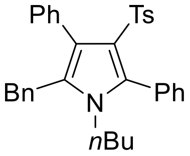
Yellow solid; m.p. 114-116 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.98 (s, 3H), 0.99 (s, 3H), 2.32 (s, 3H), 2.88 (sep, 1H, *J* = 7.1 Hz), 4.25-4.27 (m, 2H), 4.75 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.13 (dd, 1H, *J* = 10.5, 0.9 Hz), 6.99 (d, 2H, *J* = 8.0 Hz), 7.07 (d, 2H, *J* = 8.3 Hz), 7.13-7.16 (m, 2H), 7.24-7.31 (m, 3H), 7.36-7.45 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.5, 22.6, 26.4, 46.6, 116.5, 120.8, 124.3, 127.0, 127.3, 127.7, 128.7, 128.9, 131.2, 131.3, 132.3, 134.0, 134.3, 135.4, 136.1, 141.0, 142.2; IR (NaCl, neat) *v*: 3017, 2399, 1605, 1472 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{30}NO_2S$ (M$^+$+H): 456.1997, found: 456.1996.

2-Benzyl-1-methyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172p)



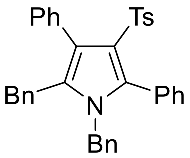
Dark green solid; m.p. 183-185 °C ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.30 (s, 3H), 3.05 (s, 3H), 3.81 (s, 2H), 6.97-7.00 (m, 4H), 7.13-7.18 (m, 3H), b7.22-7.30 (m, 7H), 7.34-7.36 (m, 2H), 7.41-7.44 (m, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 30.6, 32.1, 120.0, 123.1, 126.4, 127.1, 127.2, 127.6, 127.9, 128.0, 128.72, 128.74, 129.0, 129.8, 130.8, 131.3, 131.5, 133.7, 136.7, 138.5, 141.1, 142.3; IR (NaCl, neat) *v*: 3019, 1597, 1493, 1454 cm^{-1}; HRMS (ESI) calcd. for $C_{31}H_{28}NO_2S$ (M$^+$+H): 478.1841, found: 478.1855.

2-benzyl-1-butyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172q)



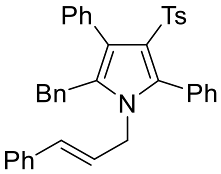
Brown solid; m.p. 167-169 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.55 (t, 3H, *J* = 7.2 Hz), 0.87 (sextet, 2H, *J* = 7.2 Hz), 1.09-1.17 (m, 2H), 2.31 (s, 3H), 3.39-3.43 (m, 2H), 3.81 (s, 2H), 6.97-7.02 (m, 4H), 7.12-7.18 (m, 3H), 7.21-7.30 (m, 7H), 7.34-7.37 (m, 2H), 7.40-7.43 (m, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.3, 19.8, 21.5, 30.6, 32.6, 44.7, 120.2, 123.3, 126.4, 127.08, 127.14, 127.5, 127.8, 127.9, 128.6, 128.7, 128.8, 129.3, 131.0, 131.4, 131.6, 133.8, 136.4, 138.9, 141.1, 142.2; IR (NaCl, neat) *v*: 3055, 2303, 1599 cm^{-1}; HRMS (ESI) calcd. for $C_{34}H_{34}NO_2S$ (M$^+$+H): 520.2310, found: 520.2301.

1,2-Dibenzyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172r)



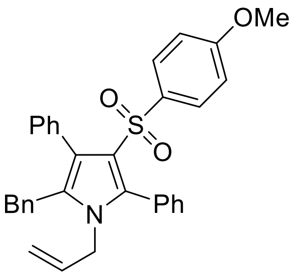
Colorless solid; m.p. 194-196 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.33 (s, 3H), 3.59 (s, 2H), 4.62 (s, 2H), 6.71 (d, 2H, *J* = 6.6 Hz), 6.92 (d, 2H, *J* = 7.2 Hz), 7.01 (d, 2H, *J* = 8.0 Hz), 7.15-7.36 (m, 18H), ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 30.5, 48.1, 120.6, 124.1, 125.6, 126.5, 127.18, 127.21, 127.4, 127.6, 127.79, 127.81, 128.7, 128.8, 129.0, 129.9, 130.4, 131.3, 131.5, 133.5, 137.1, 137.4, 138.7, 141.0, 142.4; IR (NaCl, neat) *v*: 3019, 2399, 1524, 1393 cm^{-1}; HRMS (ESI) calcd. for $C_{37}H_{32}NO_2S$ (M$^+$+H): 554.2154, found: 554.2145.

2-Benzyl-1-cinnamyl-3,5-diphenyl-4-tosyl-1*H*-pyrrole (172s)



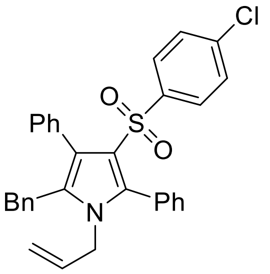
Reddish brown solid; m.p. 153-155 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.32 (s, 3H), 3.84 (s, 2H), 4.18 (d, 2H), 5.69-5.74 (m, 1H), 5.82 (d, 1H, *J* = 15.9 Hz), 7.01 (t, 4H, *J* = 8.8 Hz), 7.12-7.19 (m, 5H), 7.23-7.35 (m, 10H), 7.35-7.44 (m, 5H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.5, 30.5, 46.8, 124.4, 126.4, 126.5, 127.2, 127.6, 127.8, 128.0, 128.6, 128.8, 129.0, 129.6, 130.7, 131.5, 131.6, 132.1, 133.6, 136.0, 136.9, 138.7, 141.0, 142.3; IR (NaCl, neat) *v*: 3019, 2399, 1599, 1391 cm^{-1}; HRMS (ESI) calcd. for $C_{39}H_{34}NO_2S$ (M$^+$+H): 580.2310, found: 580.2328.

Allyl-2-benzyl-4-(methylsulfonyl)-3,5-diphenyl-1*H*-pyrrole (172t)



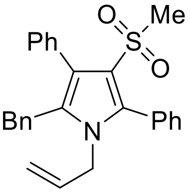
Reddish brown solid; m.p. 80-82 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 2.64 (s, 3H), 3.89 (s, 2H), 4.07-4.08 (m, 2H), 4.73 (d, 1H, *J* = 17.1 Hz), 5.10 (d, 1H, *J* = 10.4 Hz), 5.57-5.67 (m, 1H), 7.05 (d, 2H, *J* = 7.2 Hz); 7.20-7.38 (m, 6H); 7.40-7.41 (m, 5H), 7.49 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 30.4, 45.2, 47.0, 116.6, 119.9, 123.0, 126.6, 127.6, 127.8, 128.0, 128.1, 128.8, 129.2, 129.7, 130.4, 131.1, 131.3, 133.4, 133.5, 136.6, 138.7; IR (NaCl, neat) *v*: 3019, 2399, 1605, 1493 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{26}NO_2S$ (M^++H): 428.1684, found: 428.1699.

Allyl-2-benzyl-4-((4-chlorophenyl)sulfonyl)-3,5-diphenyl-1*H*-pyrrole (172u)



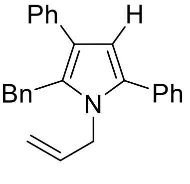
Yellow solid; m.p. 132-134 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 3.79 (s, 2H), 4.01-4.03 (m, 2H), 4.66 (dd, 1H, *J* = 17.1, 0.8 Hz), 5.05 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.52-5.60 (m, 1H), 6.98 (d, 2H, *J* = 7.2 Hz), 7.16-7.19 (m, 4H), 7.22-7.25 (m, 5H), 7.29-7.35 (m, 5H), 7.39-7.45 (m, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 30.3, 47.0, 116.7, 126.5, 127.4, 127.7, 127.8, 127.9, 128.3, 128.6, 128.7, 129.2, 129.9, 130.3, 131.2, 131.5, 133.2, 137.2, 138.2, 138.6, 142.2; IR (NaCl, neat) *v*: 3019, 2399, 1584, 1476 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{26}ClNO_2SNa$ (M^++Na): 546.1270, found: 546.1280.

Allyl-2-benzyl-4-((4-methoxyphenyl)sulfonyl)-3,5-diphenyl-1*H*-pyrrole (172v)



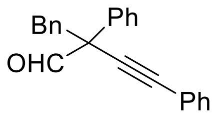
Yellow solid; m.p. 57-59 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.78 (s, 3H), 3.99-4.01 (m, 2H), 4.66 (dd, 1H, *J* = 17.1, 0.7 Hz), 5.03 (dd, 1H, *J* = 10.4, 0.8 Hz), 5.51-5.60 (m, 1H), 6.65-6.67 (m, 2H), 6.98 (d, 2H), 7.16-7.22 (m, 3H), 7.24-7.27 (m, 7H), 7.27-7.34 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 30.3, 46.9, 55.5, 113.2, 116.5, 120.8, 123.5, 126.4, 127.1, 127.6, 127.75, 127.78, 128.7, 128.9, 129.2, 129.5, 130.6, 131.3, 131.5, 133.4, 133.6, 135.8, 136.6, 138.8, 162.2; IR (NaCl, neat) *v*: 3053, 2304, 1495 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{30}NO_3S$ (M^++H): 520.1946, found: 520.1948.

Allyl-2-benzyl-3,5-diphenyl-1*H*-pyrrole (175b)



Dark yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.17 (s, 2H), 4.31-4.33 (m, 2H), 4.83 (dd, 1H, *J* = 17.1, 1.2 Hz), 5.13 (dd, 1H, *J* = 10.4, 1.2 Hz), 5.80-5.87 (m, 1H), 6.47 (s, 1H), 7.15-7.21 (m, 5H), 7.29-7.34 (m, 5H), 7.36-7.47 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz): 30.8, 46.7, 108.8, 115.9, 124.0, 125.5, 126.2, 127.0, 127.75, 127.82, 129.9, 128.4, 128.5, 128.7, 128.8, 133.5, 134.5, 135.0, 137.0, 140.1; IR (NaCl, neat) *v*: 3017, 1603,1493 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{24}N$ (M^++H): 530.1909, found: 350.1920.

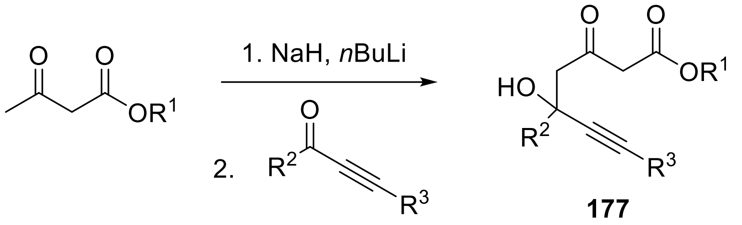
2-Benzyl-2,4-diphenylbut-3-ynal (176b)



Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 3.26 (d, 1H, *J* = 13.2 Hz), 3.54 (d, 1H, *J* = 13.2 Hz), 6.99-7.01 (m, 2H), 7.13-7.15 (m, 3H), 7.29-7.44 (m, 10H); ^{13}C NMR (CDCl$_3$, 100 MHz): 42.3, 59.5, 85.4, 91.5, 122.5, 126.6, 127.6, 128.2, 128.4, 128.65, 128.67, 128.71, 128.8, 130.7, 131.7, 135.4, 136.2; IR (NaCl, neat) *ν*: 3028, 1728 cm^{-1}; HRMS (DART) calcd. for $C_{23}H_{19}O$ (M$^+$+H): 311.1436, found: 311.1431.

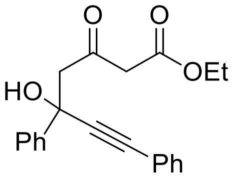
5.3 Gold-Catalyzed Benzannulation of 5-Hydroxy-3-oxoalk-6-ynoate Esters to *o*-Phenolic Esters

General Procedure for the Preparation of 5-Hydroxy-3-oxoalk-6-ynoate (177a–s)



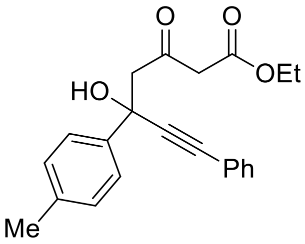
To a flame-dried round-bottomed flask containing NaH (60% in mineral oil, 11 mmol, 1.1 equiv) suspension in THF was added alkyl acetoacetate (10 mmol, 1 equiv) dropwise via syringe at 0 °C under a nitrogen atmosphere. A strong gas evolution was observed, which ceased after 15 mins. The resulting mixture was then cooled to −78 °C before adding *n*BuLi (1.6 M in hexane, 11 mmol) dropwise over 10 mins. After 30 mins, a THF solution of propargyl ketone, which was prepared following literature procedures,[93] was added dropwise to the reaction mixture at the same temperature. The reaction was monitored by TLC analysis (*n*hexane/EtOAc = 6:1). Upon completion, the reaction was quenched at 0 °C with sat. NH_4Cl solution (10 mL), diluted with 40 mL of EtOAc and allowed to warm to room temperature. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel (*n*hexanane/EtOAc = 20:1 to 8:1) to afford the product **177** as a mixture of the keto and enol tautomers. The labile product was kept frozen until use or used immediately for the next step.

Ethyl 5-hydroxy-3-oxo-5,7-diphenylhept-6-ynoate (177a)



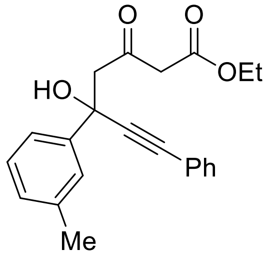
Yield 78%; Yellowish brown oil; keto/enol ratio = 9.8:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 1.17 (t, 3H, *J* = 7.1 Hz), 3.06 (d, 1H, *J* = 16.1 Hz), 3.24 (d, 1H, *J* = 16.1 Hz), 3.53 (s, 2H), 4.10 (q, 2H, *J* = 7.1 Hz), 4.66 (s, 1H), 7.25-7.29 (m, 4H), 7.32-7.36 (m, 2H), 7.41-7.43 (m, 2H), 7.66-7.68 (m, 2H); enol isomer: δ 1.22 (t, 3H, *J* = 7.3 Hz), 2.73 (d, 1H, *J* = 13.9 Hz), 2.89 (d, 1H, *J* = 13.9 Hz), 3.53 (s, 2H), 4.10 (q, 2H, *J* = 7.1 Hz), 4.66 (s, 1H), 7.25-7.29 (m, 4H), 7.32-7.36 (m, 2H), 7.41-7.43 (m, 2H), 7.66-7.68 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz), keto isomer: 14.1, 50.5, 56.3, 61.5, 70.6, 86.2, 90.2, 122.2, 125.3, 128.1, 128.4, 128.5, 128.8, 131.8, 143.2, 166.8, 202.4; enol isomer: 14.3, 50.7, 56.3, 60.4, 72.3, 86.2, 93.0, 122.2, 125.5, 128.1, 128.4, 128.5, 128.8, 131.8, 143.2, 166.8, 202.4; IR (NaCl, neat) *v*: 3483, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for C$_{21}$H$_{19}$O$_3$: 319.1334, found: 319.1341.

Ethyl 5-hydroxy-3-oxo-7-phenyl-5-(p-tolyl)hept-6-ynoate (177b)



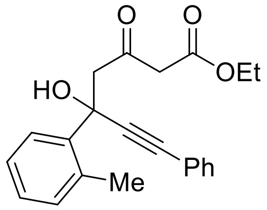
Yield 80%; Yellow oil; keto/enol ratio = 9.1:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.35 (s, 3H), 3.10 (d, 1H, *J* = 16.4 Hz), 3.28 (d, 1H, *J* = 16.4 Hz), 3.56 (s, 2H), 4.16 (q, 2H, *J* = 7.2 Hz), 4.45 (s, 1H), 7.19 (d, 2H), 7.29-7.31 (m, 3H), 7.43-7.46 (m, 2H), 7.56-7.58 (m, 2H); enol isomer: δ 1.28 (t, 3H, *J* = 7.2 Hz), 2.35 (s, 3H), 2.73 (d, 1H, *J* = 14 Hz), 2.92 (d, 1H, *J* = 14 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 4.45 (s, 1H), 5.15 (s, 1H), 7.19 (d, 2H), 7.29-7.31 (m, 3H), 7.43-7.46 (m, 2H), 7.56-7.58 (m, 2H), 12.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 21.1, 50.6, 56.2, 61.6, 70.5, 86.0, 90.2, 122.2, 125.2, 128.3, 128.7, 129.2, 131.9, 137.9, 140.2, 166.7, 202.6; enol isomer: 14.1, 21.1, 56.2, 61.6, 70.5, 86.0, 93.0, 122.2, 125.3, 128.3, 128.7, 129.1, 131.9, 137.9, 140.2, 166.7, 202.6; IR (NaCl, neat) *v*: 3470, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{22}H_{21}O_3$: 333.1491, found: 333.1480.

Ethyl 5-hydroxy-3-oxo-7-phenyl-5-(m-tolyl)hept-6-ynoate (177c)



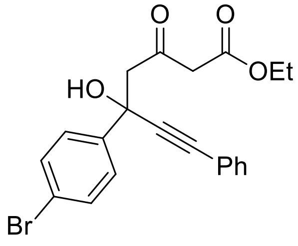
Yield 70%; Yellow oil; keto/enol ratio = 8.9:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.35 (s, 3H), 3.10 (d, 1H, *J* = 16.3 Hz), 3.30 (d, 1H, *J* = 16.3 Hz), 3.56 (s, 2H), 4.16 (q, 2H, *J* = 7.2 Hz), 4.48 (s, 1H), 7.13 (d, 1H, *J* = 7.5 Hz), 7.24-7.32 (m, 4H), 7.44-7.50 (m, 4H); enol isomer: δ 1.28 (t, 3H, *J* = 7.0 Hz), 2.35 (s, 3H), 2.73 (d, 1H, *J* = 14.0 Hz); 2.92 (d, 1H, *J* = 14 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 4.48 (s, 1H), 5.16 (s, 1H), 7.13 (d, 1H, *J* = 7.5 Hz), 7.24-7.32 (m, 4H), 7.44-7.50 (m, 4H); 12.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 21.6, 50.6, 56.2, 61.6, 70.6, 86.0, 90.2, 122.3, 122.4, 125.8, 128.3, 128.4, 128.7, 128.9, 131.9, 138.2, 143.0, 166.6, 202.6; enol isomer: 14.1, 21.6, 50.6, 56.2, 61.6, 70.6, 86.0, 93.0, 122.3, 122.4, 125.8, 128.3, 128.4, 128.7, 128.9, 131.9, 138.2, 143.0, 166.6, 202.6; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{22}H_{21}O_3$: 333.1467, found: 333.1460.

Ethyl 5-hydroxy-3-oxo-7-phenyl-5-(*o*-tolyl)hept-6-ynoate (177d)



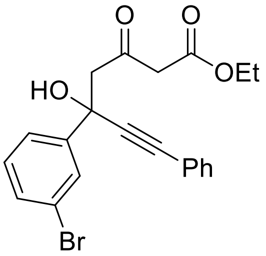
Yield 57%; Yellow oil; keto/enol ratio = 6:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.67 (s, 3H), 3.18 (d, 1H, *J* = 16.4 Hz), 3.43 (d, 1H, *J* = 15.0 Hz), 3.58 (s, 2H), 4.16 (q, 2H, *J* = 7.2 Hz), 4.51 (s, 1H), 7.19-7.22 (m, 3H), 7.26-7.30 (m, 3H), 7.40-7.42 (m, 2H), 7.72-7.74 (m, 1H); enol isomer: δ 1.28 (t, 3H, *J* = 6.0 Hz), 2.67 (s, 3H), 3.18 (d, 1H, *J* = 16.4 Hz), 3.43 (d, 1H, *J* = 15.0 Hz), 5.18 (s, 1H), 7.19-7.22 (m, 3H), 7.26-7.30 (m, 3H), 7.40-7.42 (m, 2H), 7.72-7.74 (m, 1H), 12.4 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz), keto isomer: 14.1, 21.4, 50.7, 53.1, 61.6, 70.3, 86.1, 90.2, 122.3, 125.5, 126.0, 128.1, 128.3, 128.7, 131.7, 132.5, 135.5, 139.9, 166.7, 202.6; enol isomer: 14.1, 21.4, 50.1, 61.4, 70.3, 86.1, 90.2, 122.3, 125.5, 126.0, 128.1, 128.3, 128.7, 131.7, 132.5, 135.5, 139.9, 166.7, 202.6; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for C$_{22}$H$_{21}$O$_3$: 333.1467, found: 333.1465.

Ethyl 5-(4-bromophenyl)-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177e)



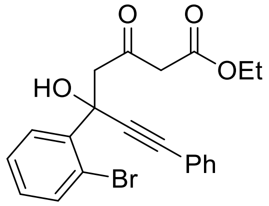
Yield 78%; Pale orange oil; keto/enol ratio = 6:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer, Rotamer A: 1.27 (t, 3H, *J* = 7.2 Hz), 3.07 (d, 1H, *J* = 16.5 Hz), 3.30 (d, 1H, *J* = 16.5 Hz), 3.56 (s, 2H), 4.17 (q, 2H, *J* = 7.2 Hz), 4.49 (d, 1H, *J* = 3.4 Hz), 7.28-7.36 (m, 4H), 7.39-7.52 (m, 4H), 7.55-7.60 (m, 1H), 7.68-7.72 (m, 1H); Rotamer B: 1.27 (t, 3H, *J* = 7.2 Hz), 3.11 (d, 1H, *J* = 16.4 Hz), 3.32 (d, 1H, *J* = 16.4 Hz), 3.57 (s, 2H), 4.17 (q, 2H, *J* = 7.2 Hz), 4.57 (d, 1H, *J* = 3.6 Hz), .28-7.36 (m, 4H), 7.39-7.52 (m, 4H), 7.55-7.60 (m, 1H), 7.68-7.72 (m, 1H); enol isomer, Rotamer C: 1.29 (t, 3H, *J* = 7.2 Hz), 2.72 (d, 1H, *J* = 16.4 Hz), 2.89 (d, 1H, *J* = 17.0 Hz), 4.17 (q, 2H, *J* = 7.2 Hz), 4.49 (d, 1H, *J* = 3.4 Hz), 7.28-7.36 (m, 4H), 7.39-7.52 (m, 4H), 7.55-7.60 (m, 1H), 7.68-7.72 (m, 1H), 12.4 (s, 1H); Rotamer D: 1.29 (t, 3H, *J* = 7.2 Hz), 2.75 (d, 1H, *J* = 11.3 Hz), 2.93 (d, 1H, *J* = 17.0 Hz), 3.57 (s, 2H), 4.17 (q, 2H, *J* = 7.2 Hz), 4.57 (d, 1H, *J* = 3.6 Hz), .28-7.36 (m, 4H), 7.39-7.52 (m, 4H), 7.55-7.60 (m, 1H), 7.68-7.72 (m, 1H), 12.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer, Rotamer A: 14.0, 50.6, 55.9, 61.6, 70.3, 86.1, 89.5, 121.9, 125.2, 127.2, 128.3, 128.7, 128.8, 131.6, 142.2, 166.5, 202.4; Rotamer B: 14.1, 50.6, 56.2, 61.7, 70.6, 86.3, 89.5, 122.2, 125.2, 127.3, 128.4, 128.5, 128.9131.8, 143.0, 166.6, 202.6; IR (NaCl, neat) *ν*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{21}H_{18}O_3{}^{79}Br$: 397.0439, found: 397.0446.

Ethyl 5-(3-bromophenyl)-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177f)



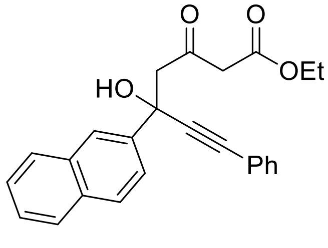
Yield 75%; Pale orange oil; keto/enol ratio = 6:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 1.24 (t, 3H, *J* = 7.2 Hz), 3.07 (d, 1H, *J* = 16.6 Hz), 3.31 (d, 1H, *J* = 16.6 Hz), 3.56 (s, 2H), 4.18 (q, 2H, *J* = 7.1 Hz), 4.61 (s, 1H), 7.27-7.34 (m, 3H), 7.43-7.46 (m, 4H), 7.61-7.63 (m, 1H), 7.85 (t, 1H, *J* = 1.8 Hz); enol isomer: δ 1.29 (t, 3H, *J* = 7.2 Hz), 2.72 (d, 1H, *J* = 14.0 Hz), 2.89 (d, 1H, *J* = 14 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 4.61 (s, 1H), 5.14 (s, 1H), 7.27-7.34 (m, 3H), 7.43-7.46 (m, 4H), 7.61-7.63 (m, 1H), 7.85 (t, 1H, *J* = 1.8 Hz), 12.43 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 50.6, 55.9, 61.7, 70.1, 86.4, 89.3, 121.9, 122.6, 124.0, 128.3, 128.5, 128.9, 130.1, 131.2, 131.9, 145.3, 166.5, 202.4; enol isomer: 14.1, 55.9, 60.6, 70.1, 86.4, 89.3, 121.9, 133.6, 124.2, 128.3, 128.5, 128.9, 130.1, 131.2, 131.9, 145.3, 166.5, 202.4; IR (NaCl, neat) *v*: 3483, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{21}H_{18}O_3{}^{79}Br$: 397.0439, found: 397.0448.

Ethyl 5-(2-bromophenyl)-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177g)



Yield 50%; Pale yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.25 (t, 3H, *J* = 7.1 Hz), 3.58 (s, 2H), 3.95 (d, 1H, *J* = 16.6 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 4.74 (s, 1H), 7.18 (td, 1H, *J* = 7.6, 1.7 Hz), 7.27-7.32 (m, 3H), 7.34-7.47 (m, 3H), 7.63 (dd, 1H, *J* = 7.9, 1.2 Hz), 7.96 (dd, 1H, *J* = 8.0, 1.6 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 14.1, 50.7, 51.7, 61.6, 70.0, 86.2, 88.8, 120.5, 122.3, 127.6, 127.7, 128.2, 128.6, 129.5, 131.7, 135.0, 140.4, 166.5, 202.6; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{21}H_{18}O_3{}^{79}Br$: 397.0439, found: 397.0441.

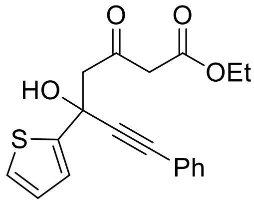
Ethyl 5-hydroxy-5-(naphthalen-2-yl)-3-oxo-7-phenylhept-6-ynoate (177h)



Yield 80%; Brown oil; keto/enol ratio = 7.1:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 1.25 (t, 3H, *J* = 7.2 Hz), 3.22 (d, 1H, *J* = 16.4 Hz), 3.43 (d, 1H, *J* = 16.4 Hz), 3.60 (s, 2H), 4.18 (q, 2H, *J* = 7.2 Hz), 4.65 (s, 1H), 7.30-7.36 (m, 3H), 7.46-7.53 (m, 5H), 7.76-7.91 (m, 3H), 8.19 (s, 1H); enol isomer: 1.30 (t, 3H, *J* = 7.2 Hz), 2.87 (d, 1H, *J* = 14.0 Hz), 3.04 (d, 1H, *J* = 14.0 Hz), 4.18 (q, 2H, *J* = 7.2 Hz), 4.65 (s, 1H), 5.20 (s, 1H), 7.30-7.36 (m, 3H), 7.46-7.53 (m, 5H), 7.76-7.91 (m, 3H), 8.19 (s, 1H), 12.5 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz), keto isomer: 14.1, 50.6, 55.9, 61.6, 70.8, 86.3, 90.0, 122.2, 123.3, 124.1, 126.4, 127.6, 128.3, 128.4, 128.5, 128.8, 131.9, 133.0, 133.1, 140., 166.6, 202.5;

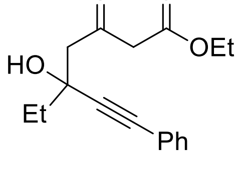
enol isomer: 14.2, 55.9, 61.6, 70.8, 86.3, 90.0, 122.2, 123.3, 124.1, 126.4, 127.6, 128.3, 128.4, 128.5, 128.8, 131.9, 133.0, 133.1, 140., 166.6, 202.5; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{25}H_{21}O_3$: 369.1491, found: 369.1483.

Ethyl 5-hydroxy-3-oxo-7-phenyl-5-(thiophen-2-yl)hept-6-ynoate (177i)



Yield 81%; Yellow oil; keto/enol ratio = 8.2:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 1.24 (t, 3H, *J* = 7.2 Hz), 3.29 (d, 1H, *J* = 16.5 Hz), 3.43 (d, 1H, *J* = 16.5 Hz), 3.57 (s, 2H), 4.18 (q, 2H, *J* = 7.1 Hz), 4.64 (s, 1H), 6.97 (dd, 1H, *J* = 5.0, 4.0 Hz), 7.23 (dd, 1H, *J* = 3.6, 1.2 Hz), 7.26-7.32 (m, 4H), 7.44-7.47 (m, 2H); enol isomer: 1.28 (t, 3H, *J* = 7.12 Hz), 2.88 (d, 1H, *J* = 14.0 Hz), 3.08 (d, 1H, *J* = 14.0 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 4.64 (s, 1H), 5.17 (s, 1H), 6.97 (dd, 1H, *J* = 5.0, 4.0 Hz), 7.23 (dd, 1H, *J* = 3.6, 1.2 Hz), 7.26-7.32 (m, 4H), 7.44-7.47 (m, 2H), 12.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 50.5, 56.2, 61.7, 68.4, 85.6, 89.3, 121.9, 124.4, 125.6, 126.8, 128.3, 128.9, 131.9, 147.7, 166.5, 202.1; enol isomer: 14.1, 56.2, 60.4, 68.4, 85.6, 89.3, 121.9, 124.4, 125.6, 126.8, 128.3, 128.9, 131.9, 147.7, 166.5, 202.1; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{19}H_{19}O_4S$: 343.0970, found: 343.0984.

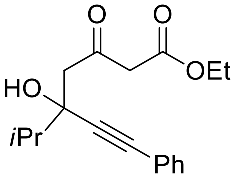
Ethyl 5-ethyl-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177j)



Yield 68%; Yellow oil; keto/enol ratio = 6.1:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 1.12 (t, 3H, *J* = 7.4 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.73-1.90 (m, 2H), 2.83 (d, 1H, *J* =

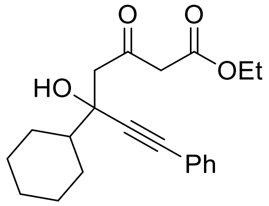
16.4 Hz), 3.14 (d, 1H, *J* = 16.3 Hz), 3.58 (s, 2H), 3.99 (s, 1H), 4.18 (q, 2H, *J* = 7.1 Hz), 7.27-7.30 (m, 3H), 7.39-7.41 (m, 2H); enol isomer: δ 1.12 (t, 3H, *J* = 7.4 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.73-1.90 (m, 2H), 2.63 (d, 1H, *J* = 6.6 Hz), 3.14 (d, 1H, *J* = 16.3 Hz), 3.99 (s, 1H), 4.18 (q, 2H, *J* = 7.1 Hz), 5.17 (s, 1H), 7.27-7.30 (m, 3H), 7.39-7.41 (m, 2H), 12.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 8.5, 14.1, 35.2, 50.7, 52.5, 61.6, 69.5, 84.6, 90.2, 122.4, 128.2, 128.5, 131.8, 166.7, 203.1; enol isomer: 8.5, 14.1, 35.2, 52.5, 61.6, 69.5, 84.6, 92.7, 122.4, 128.2, 128.5, 131.8, 166.7, 203.1; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{17}H_{19}O_3$: 271.1334, found: 271.1325.

Ethyl 5-hydroxy-5-isopropyl-3-oxo-7-phenylhept-6-ynoate (177k)



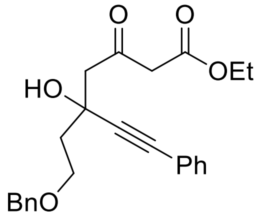
Yield 71%; Yellow oil; keto/enol ratio cannot be determined; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.07 (d, 3H, *J* = 6.8 Hz), 1.12 (d, 3H, *J* = 6.8 Hz), 1.24 (t, 3H, *J* = 7.2 Hz), 1.93-1.99 (m, 1H), 2.81 (d, 1H, *J* = 16.2 Hz), 3.14 (d, 1H, *J* = 16.1 Hz), 3.60 (s, 2H), 4.09 (s, 1H), 4.17 (q, 2H, *J* = 7.2 Hz), 7.28-7.30 (m, 3H), 7.39-7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 17.1, 17.7, 38.2, 44.5, 50.5, 50.8, 60.3, 61.5, 72.4, 74.1, 85.3, 89.4, 122.5, 128.2, 128.4, 131.8, 166.8, 203.6; enol isomer: 14.1, 17.1, 17.7, 44.5, 50.5, 60.3, 72.4, 74.1, 85.3, 92.8, 122.5, 128.2, 128.4, 131.8, 166.8, 203.6; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{18}H_{21}O_3$: 285.1491, found: 285.1483.

Ethyl 5-cyclohexyl-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177l)



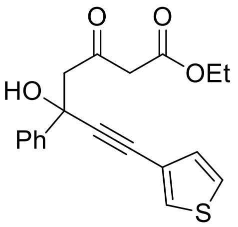
Yield 74%; Colourless oil; keto/enol ratio = 7.1:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 1.20-1.27 (m, 8H), 1.62-1.68 (m, 2H), 1.82-1.91 (m, 3H), 2.03 (bs, 1H), 2.82 (d, 1H, *J* = 16.2 Hz), 3.15 (d, 1H, *J* = 16.1 Hz), 3.59 (s, 2H), 4.00 (s, 1H), 4.18 (q, 2H, *J* = 6.9 Hz), 7.26-7.31 (m, 3H), 7.40-7.42 (m, 2H); enol isomer: δ 1.20-1.27 (m, 8H), 1.62-1.68 (m, 2H), 1.82-1.91 (m, 3H), 2.03 (bs, 1H), 2.82 (d, 1H, *J* = 16.2 Hz), 3.15 (d, 1H, *J* = 16.1 Hz), 4.00 (s, 1H), 4.18 (q, 2H, *J* = 6.9 Hz), 7.26-7.31 (m, 3H), 7.40-7.42 (m, 2H), 12.4 (s, 1H), 12.34 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 14.1, 26.1, 26.3, 27.0, 27.6, 47.9, 50.5, 50.9, 61.6, 71.9, 85.3, 89.9, 122.5, 128.2, 128.4, 131.8, 166.7, 203.7; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{21}H_{25}O_3$: 325.1804, found: 325.1797.

Ethyl 5-(2-(benzyloxy)ethyl)-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (1m)



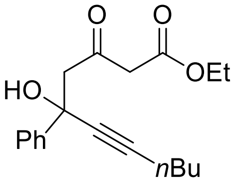
Yield 83%;Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.23 (t, 3H, *J* = 7.2 Hz), 2.02-2.09 (m, 1H), 2.17-2.24 (m, 1H), 2.99 (d, 1H, *J* = 15.1 Hz), 3.08 (d, 1H, *J* = 15.1 Hz), 3.64 (s, 2H), 3.77-3.82 (m, 1H), 4.00-4.05 (m, 1H), 4.15 (q, 2H, *J* = 7.2 Hz), 4.54 (s, 2H), 4.67 (s, 1H), 7.29-7.39 (m, 10H); ^{13}C NMR (CDCl$_3$, 100 MHz): 14.1, 40.6, 50.7, 54.1, 61.3, 67.7, 69.1, 73.6, 85.3, 89.9, 122.3, 127.8, 127.9, 128.3, 128.5, 128.6, 131.8, 137.6, 167.1, 201.8; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{24}H_{25}O_4$: 377.1753, found: 377.1752.

Ethyl 5-hydroxy-3-oxo-5-phenyl-7-(thiophen-3-yl)hept-6-ynoate (177n)



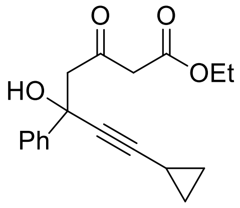
Yield 69%; Brown oil; keto/enol ratio = 6.5:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 1.24 (t, 3H, *J* = 7.2 Hz), 3.10 (d, 1H, *J* = 16.4 Hz), 3.30 (d, 1H, *J* = 16.3 Hz), 3.55 (s, 2H), 4.17 (q, 2H, *J* = 7.2 Hz), 4.52 (s, 1H), 7.11 (dd, 1H, *J* = 5, 1.1 Hz), 7.23-7.25 (m, 1H), 7.31-7.40 (m, 3H), 7.47 (dd, 1H, *J* = 3, 1.1 Hz), 7.66-7.69 (m, 2H); enol isomer: δ 1.24 (t, 3H, *J* = 7.2 Hz), 2.74 (d, 1H, *J* = 14.0 Hz), 2.91 (d, 1H, *J* = 14 Hz), 4.09 (q, 2H, *J* = 7.2 Hz), 4.52 (s, 1H), 5.13 (s, 1H), 7.11 (dd, 1H, *J* = 5, 1.1 Hz), 7.23-7.25 (m, 1H), 7.31-7.40 (m, 3H), 7.47 (dd, 1H, *J* = 3, 1.1 Hz), 7.66-7.69 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz), keto isomer: 14.1, 50.6, 56.1, 61.6, 70.7, 81.3, 89.6, 121.2, 125.2, 125.4, 128.1, 128.5, 129.5, 129.9, 143.0, 166.6, 202.6; enol isomer: 20.7, 54.1, 58.8, 70.7, 84.5, 93.0, 121.2, 125.2, 125.4, 128.1, 128.5, 129.5, 129.9, 143.0, 166.6, 202.6; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) $[M - OH]^+$ calcd. for $C_{19}H_{17}O_3S$: 325.0898, found: 325.0899.

Ethyl 5-hydroxy-3-oxo-5-phenylundec-6-ynoate (177o)



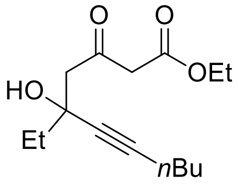
Yield 50%; Yellow oil; keto/enol ratio = 6.7:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 0.91 (t, 3H, *J* = 7.2 Hz), 1.27 (t, 3H, *J* = 7.2 Hz), 1.36-1.45 (m, 2H), 1.48-1.53 (m, 2H), 2.24 (t, 2H, *J* = 7.0 Hz), 3.00 (d, 1H, *J* = 16.1 Hz), 3.15 (d, 1H, *J* = 16.1 Hz), 3.52 (s, 2H), 4.03 (q, 2H, *J* = 7.2 Hz), 4.26 (s, 1H), 7.28-7.37 (m, 3H), 7.61-7.63 (m, 2H); enol isomer: δ 0.91 (t, 3H, *J* = 7.2 Hz), 1.27 (t, 3H, *J* = 7.2 Hz), 1.36-1.45 (m, 2H), 1.48-1.53 (m, 2H), 2.24 (t, 2H, *J* = 7.0 Hz), 2.60 (d, 1H, *J* = 14.0 Hz), 2.82 (d, 1H, *J* = 14.0 Hz), 4.03 (q, 2H, *J* = 7.2 Hz), 4.26 (s, 1H), 5.13 (s, 1H), 7.28-7.37 (m, 3H), 7.61-7.63 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz), keto isomer: 16.7, 17.2, 21.5, 25.1, 33.8, 53.7, 59.6, 64.6, 73.4, 84.6, 90.2, 128.4, 131.0, 131.4, 146.9, 169.9, 205.6; enol isomer: 16.7, 17.4, 21.5, 25.0, 33.8, 53.9, 59.6, 63.4, 64.6, 73.4, 128.5, 131.0, 131.3, 146.9, 169.9, 205.6; IR (NaCl, neat) *v*: 3483, 1732, 1713 cm^{-1}; HRMS (ESI) $[M - OH]^+$ calcd. for $C_{19}H_{23}O_3$: 299.1647, found: 299.1641.

Ethyl 7-cyclopropyl-5-hydroxy-3-oxo-5-phenylhept-6-ynoate (177p)



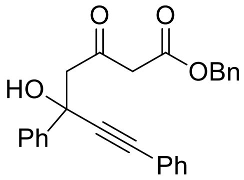
Yield 65%; Yellow oil; keto/enol ratio = 10:1; ^{1}H NMR ($CDCl_3$, 400 MHz), keto isomer: δ 0.70-0.72 (m, 2H), 0.76-0.78 (m, 2H), 1.24-1.28 (m, 3H), 2.98 (d, 1H, *J* = 16.0 Hz), 3.12 (dd,, 1H, *J* = 16.0, 1.6 Hz), 3.51 (s, 2H), 4.17 (qd, 2H, *J* = 7.1, 1.1 Hz), 4.24 (s, 1H), 7.27-7.36 (m, 3H), 7.58-7.60 (m, 2H); enol isomer: δ 0.70-0.72 (m, 2H), 0.76-0.78 (m, 2H), 1.24-1.28 (m, 3H), 2.58 (d, 1H, *J* = 13.9 Hz), 2.79 (d, 1H, *J* = 13.9 Hz), 4.17 (qd, 2H, *J* = 7.1, 1.1 Hz), 4.24 (s, 1H), 7.27-7.36 (m, 3H), 7.58-7.60 (m, 2H), 12.3 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz), keto isomer: -0.5, 8.3, 8.4, 14.1, 50.6, 56.4, 61.5, 70.2, 76.3, 90.2, 125.2, 127.9, 128.3, 143.6, 166.7, 202.5; enol isomer: -0.5, 8.3, 8.4, 14.1, 56.4, 60.3, 70.2, 76.3, 92.8, 125.3, 127.9, 128.2, 143.6, 166.7, 202.5; IR (NaCl, neat) *v*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) $[M - OH]^+$ calcd. for $C_{18}H_{19}O_3$: 283.1334, found: 283.1335.

Ethyl 5-ethyl-5-hydroxy-3-oxoundec-6-ynoate (177q)



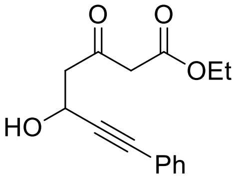
Yield 68%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 0.85 (t, 3H, *J* = 7.1 Hz), 0.98 (t, 3H, *J* = 7.4 Hz), 1.21-1.26 (m, 4H), 1.29-1.47 (m, 4H), 1.58-1.70 (m, 2H), 2.13 (t, 2H, *J* = 6.8 Hz), 2.68 (d, 1H, *J* = 16.1 Hz), 2.94 (d, 1H, *J* = 16.1 Hz), 3.51 (s, 2H), 4.15 (q, 2H, *J* = 7.2 Hz); ^{13}C NMR (CDCl$_3$, 75 MHz): 8.4, 13.5, 14.0, 18.2, 21.8, 30.6, 35.3, 50.6, 52.7, 61.4, 69.1, 81.2, 85.3, 166.8, 203.1; IR (NaCl, neat) *ν*: 3483, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{15}H_{23}O_3$: 251.1647, found: 251.1639.

Benzyl 5-hydroxy-3-oxo-5,7-diphenylhept-6-ynoate (177r)



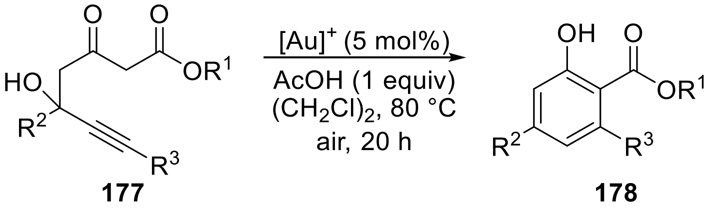
Yield 80%; Yellow oil; keto/enol ratio = 6:1; ^{1}H NMR (CDCl$_3$, 400 MHz), keto isomer: δ 3.08 (d, 1H, *J* = 16.4 Hz), 3.27 (d, 1H, *J* = 16.4 Hz), 3.62 (s, 2H), 5.15 (s, 2H), 7.27-7.38 (m, 11H), 7.40-7.44 (m, 2H), 7.66 (d, 2H, *J* = 7.5 Hz); enol isomer: 2.75 (d, 1H, *J* = 14.0 Hz), 2.94 (d, 1H, *J* = 14.0 Hz), 4.67 (s, 1H), 5.15 (s, 2H), .27-7.38 (m, 11H), 7.40-7.44 (m, 2H), 8.08 (d, 2H, *J* = 7.1 Hz), 12.3 (s, 1H); 50.6, 56.2, 67.4, 70.6, 86.2, 89.9, 122.1, 125.3, 127.0, 128.1, 128.3, 128.4, 128.5, 128.67, 128.74, 131.9, 135.1, 143.0, 166.5, 202.3; IR (NaCl, neat) *ν*: 3443, 1732, 1713 cm^{-1}; HRMS (ESI) [M - OH]$^+$ calcd. for $C_{26}H_{21}O_3$: 381.1491, found: 381.1496.

Ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (177s)



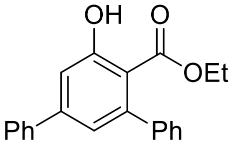
Yield 83%; Reddish brown oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.28 (t, 3H, *J* = 7.2 Hz), 3.00-3.18 (m, 2H), 3.53 (s, 2H), 4.21 (q, 2H, *J* = 7.2 Hz), 5.03-5.08 (m, 1H), 7.26-7.31 (m, 3H), 7.40-7.43 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 14.1, 49.8, 49.9, 58.7, 61.6, 85.3, 88.0, 122.2, 128.3, 128.6, 131.7, 166.7, 201.5; IR (NaCl, neat) *v*: 3443, 1732, 1712 cm^{-1}; HRMS (ESI) calcd. for $C_{15}H_{15}O_3$ (M-OH): 243.1021, found: 243.1019.

General Procedure for Gold Complex A Catalyzed Benzannulation of 5-Hydroxy-3-oxoalk-6-ynoate (1) to *o*-Phenolic Esters (178a–s)



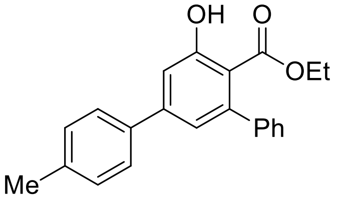
A two-neck round-bottomed flask was charged with 5-Hydroxy-3-oxoalk-6-ynoate **177** (0.2 mmol) and gold complex **A** (0.01 mmol) followed by the addition of 1,2-dichloroethane (2ml). The resulting mixture was then stirred at 80 °C for 20 h under open-to-air conditions. On completion, the reaction mixture was concentrated under reduced pressure and purified by flash column chromatography on silica gel (eluent: hexane/ethyl acetate 20/1) to afford product **178**.

Ethyl 5'-hydroxy-[1,1':3',1''-terphenyl]-4'-carboxylate (178a)



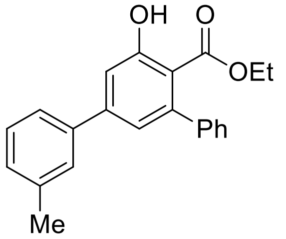
White solid; m.p: 79-81°C; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 0.76 (t, 3H, *J* = 7.2 Hz), 3.99 (q, 2H, *J* = 7.2 Hz), 7.04 (d, 1H, *J* = 1.8 Hz), 7.23-7.45 (m, 9H), 7.62 (dd, 2H, *J* = 8.1, 1.2 Hz), 10.99 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 13.0, 61.0, 110.9, 114.8, 121.5, 126.8, 127.2, 127.6, 128.3, 128.5, 128.9, 139.4, 143.2, 145.5, 146.2, 162.1, 170.9; IR (NaCl, neat) *v*: 3443, 1661 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{19}O_3$: 319.1334, found: 319.1340.

Ethyl 5'-hydroxy-4-methyl-[1,1':3',1''-terphenyl]-4'-carboxylate (178b)



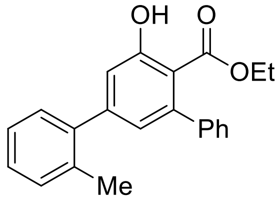
White solid; m.p:121-123°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.76 (t, 3H, *J* = 7.2 Hz), 2.39 (s, 3H), 4.00 (q, 2H, *J* = 7.2 Hz), 7.04 (d, 1H, *J* = 1.8 Hz), 7.23-7.29 (m, 5H), 7.34-7.37 (m, 3H), 7.53 (d, 2H, *J* = 8.2 Hz), 11.0 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 21.2, 61.0, 114.4, 121.3, 126.8, 127.1, 127.6, 128.2, 129.6, 136.4, 138.5, 143.2, 145.4, 146.2, 162.0, 171.0; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{22}H_{21}O_3$: 333.1491, found: 333.1489.

Ethyl 5'-hydroxy-3-methyl-[1,1':3',1''-terphenyl]-4'-carboxylate (178c)



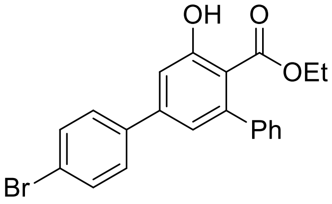
Pale yellow solid; m.p: 45–47°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.76 (t, 3H, *J* = 7.2 Hz), 2.40 (s, 3H), 4.00 (q, 2H, *J* = 7.2 Hz), 7.04 (d, 1H, *J* = 1.8 Hz), 7.19 (d, 1H, *J* = 7.7 Hz), 7.24-7.38 (m, 7H), 7.43 (d, 2H, *J* = 7.2 Hz), 11.0 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 13.0, 21.5, 61.0, 114.7, 121.5, 124.3, 126.8, 127.6, 128.0, 128.2, 128.8, 129.2, 138.5, 146.4, 162.0, 170.9; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{22}H_{21}O_3$: 333.1491, found: 333.1493.

Ethyl 5'-hydroxy-2-methyl-[1,1':3',1''-terphenyl]-4'-carboxylate (178d)



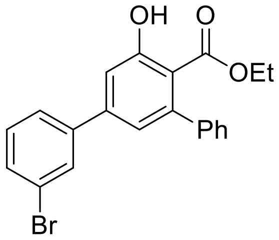
Yellow solid; m.p: 60-62 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.77 (t, 3H, *J* = 7.2 Hz), 2.32 (s, 3H), 4.01 (q, 2H, *J* = 7.2 Hz), 6.79 (d, 1H, *J* = 1.7 Hz), 6.99 (d, 1H, *J* = 1.7 Hz), 7.22-7.28 (m, 6H), 7.31-7.34 (m, 3H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 20.4, 61.1, 110.7, 117.2, 123.9, 125.9, 126.8, 127.6, 128.0, 128.3, 129.4, 130.5, 135.2, 140.4, 143.0, 144.7, 147.6, 161.4, 171.0; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{22}H_{21}O_3$: 333.1491, found: 333.1490.

Ethyl 4-bromo-5'-hydroxy-[1,1':3',1''-terphenyl]-4'-carboxylate (178e)



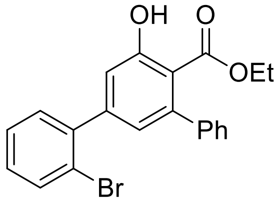
White solid; m.p: 81-83°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.76 (td, 3H, *J* = 7.2, 1.2 Hz), 4.00 (q, 2H, *J* = 7.2 Hz), 7.00 (d, 1H, *J* = 1.8 Hz), 7.20 (d, 1H, *J* = 1. 8 Hz), 7.25-7.29 (m, 2H), 7.34-7.36 (m, 3H), 7.37-7.48 (m, 2H), 7.49-7.62 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 61.1, 111.2, 114.6, 121.2, 122.9, 127.0, 127.7, 128.2, 128.8, 132.0, 138.3, 142.9, 144.9, 145.7, 162.1, 170.8; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{17}{}^{79}BrO_3$: 397.0439, found: 397.0435.

Ethyl 3-bromo-5'-hydroxy-[1,1':3',1''-terphenyl]-4'-carboxylate (178f)



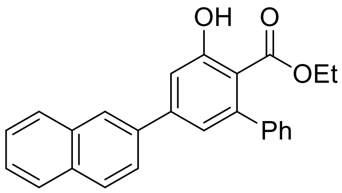
Light orange solid; m.p: 99-101°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.77 (t, 3H, *J* = 7.2 Hz), 4.00 (q, 2H, J = 7.2 Hz), 6.99 (d, 1H, *J* = 1.8 Hz), 7.20 (d, 1H, *J* = 1.8 Hz), 7.25-7.32 (m, 3H), 7.34-7.37 (m, 3H), 7.49-7.55 (m, 2H), 7.76 (t, 1H, *J* = 1.8 Hz), 11.0 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 61.1, 111.4, 114.8, 121.3, 123.0, 125.9, 127.0, 127.7, 128.2, 130.3, 130.4, 131.3, 141.5, 142.9, 144.6, 145.7, 162.0, 170.8; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) calcd. for $C_{21}H_{17}{}^{79}BrO_3$: 397.0439, found: 397.0428.

Ethyl 2-bromo-5'-hydroxy-[1,1':3',1''-terphenyl]-4'-carboxylate (178g)



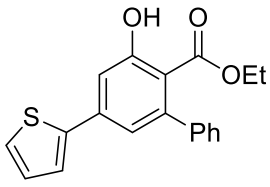
Orange solid; m.p: 65-67°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.78 (t, 3H, *J* = 7.2 Hz), 4.00 (q, 2H, *J* = 7.2 Hz), 6.88 (d, 1H, *J* = 1.7 Hz), 7.06 (d, 1H, *J* = 1.7 Hz), 7.20-7.23 (m, 1H), 7.27-7.35 (m, 10H), 7.66 (d, 1H, *J* = 7.9 Hz), 10.9 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 61.1, 111.3, 117.4, 122.0, 124.0, 126.9, 127.5, 127.6, 128.3, 129.4, 130.9, 133.3, 141.1, 142.8, 144.6, 146.2, 161.2, 170.9; IR (NaCl, neat) *v*: 3408, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{21}H_{17}{}^{79}BrO_3$: 397.0439, found: 397.0427.

Ethyl 3-hydroxy-5-(naphthalen-2-yl)-[1,1'-biphenyl]-2-carboxylate (178h)



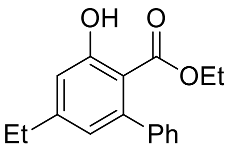
White solid; m.p:126-128°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.77 (t, 3H, *J* = 7.2 Hz), 4.01 (q, 2H, *J* = 7.2 Hz), 7.18 (d, 1H, *J* = 1.9 Hz), 7.23-7.33 (m, 2H), 7.35-7.39 (m, 4H), 7.40-7.51 (m, 2H), 7.75 (dd, 1H, *J* = 7.5 Hz), 7.83-7.90 (m, 3H), 8.09 (d, 1H, *J* = 1.3 Hz), 11.05 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 61.1, 111.0, 115.0, 121.7, 125.1, 126.47, 126.53, 126.9, 127.7, 128.3, 128.4, 128.7, 133.2, 133.5, 136.6, 143.2, 145.6, 146.1, 162.1, 171.0; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for 369.1491, found: 369.1488.

Ethyl 3-hydroxy-5-(thiophen-2-yl)-[1,1'-biphenyl]-2-carboxylate (178i)



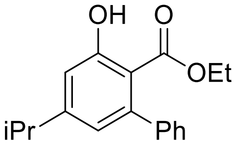
Orange solid; m.p:117-119°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.79 (t, 3H, *J* = 7.2 Hz), 4.02 (q, 2H, *J* = 7.2 Hz), 7.08 (d, 1H, *J* = 1.9 Hz), 7.12 (dd, 1H, *J* = 5.0, 3.7 Hz), 7.29-7.31 (m, 3H), 7.37-7.42 (m, 4H), 7.45 (dd, 1H, J = 4.0, 1.0 Hz), 11.1 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 61.0, 110.8, 113.1, 120.1, 125.0, 126.7, 126.9, 127.6, 128.2, 128.3, 139.1, 142.6, 142.9, 145.8, 162.2, 170.7; IR (NaCl, neat) *v*: 3408, 1661 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{19}H_{16}O_3S$: 325.0898, found: 325.0903.

Ethyl 5-ethyl-3-hydroxy-[1,1'-biphenyl]-2-carboxylate (178j)



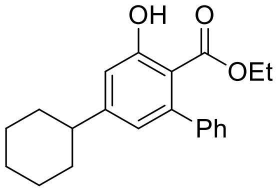
Yellow solid; m.p: 52-54°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.74 (t, 3H, *J* = 7.2 Hz), 1.24 (t, 3H, *J* = 8.0 Hz), 2.63 (q, 2H, *J* = 8 Hz), 3.96 (q, 2H, *J* = 7.2 Hz), 6.64 (d, 1H, *J* = 1.7 Hz), 6.84 (d, 1H, *J* = 1.7 Hz), 7.21-7.23 (m, 2H), 7.31-7.35 (m, 3H), 10.9 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 14.8, 28.9, 60.8, 109.7, 115.6, 122.7, 126.6, 127.5, 128.2, 143.3, 145.0, 150.9, 161.9, 171.0; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{17}H_{19}O_3$: 271.1334, found: 271.1339.

Ethyl 3-hydroxy-5-isopropyl-[1,1'-biphenyl]-2-carboxylate (178k)



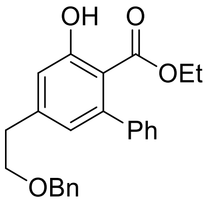
Yellow solid; m.p:120-122°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.74 (t, 3H, *J* = 7.2 Hz), 1.24 (s, 3H), 1.26 (s, 3H), 2.84-2.91 (m, 1H), 3.96 (q, 2H, *J* = 7.2 Hz), 6.66 (d, 1H, *J* = 1.7 Hz), 6.87 (d, 1H, *J* = 1.7 Hz), 7.21-7.25 (m, 2H), 7.31-7.36 (m, 3H), 10.9 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 23.4, 34.3, 60.8, 109.8, 114.2, 121.4, 126.6, 127.5, 128.2, 143.4, 145.0, 155.5, 161.9, 171.0; IR (NaCl, neat) *v*: 3019, 1663 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{18}H_{21}O_3$: 285.1491, found: 285.1490.

Ethyl 5-cyclohexyl-3-hydroxy-[1,1'-biphenyl]-2-carboxylate (178l)



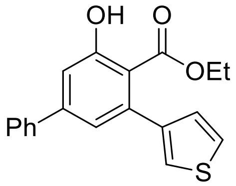
Orange oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.74 (t, 3H, *J* = 7.2 Hz), 1.34-1.43 (m, 5H), 1.72-1.76 (m, 1H), 1.81-1.89 (m, 5H), 3.96 (q, 2H, *J* = 7.2 Hz), 6.65 (d, 1H, *J* = 1.6 Hz), 6.85 (d, 1H, *J* = 1.6 Hz), 7.21-7.23 (m, 2H), 7.32-7.34 (m, 3H), 10.9 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 13.0, 26.0, 26.7, 33.8, 44.7, 60.8, 109.8, 114.6, 121.9, 126.6, 127.5, 128.2, 143.4, 144.9, 154.6, 161.9, 171.0; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{25}O_3$: 325.1804, found: 325.1807.

Ethyl 5-(2-(benzyloxy)ethyl)-3-hydroxy-[1,1'-biphenyl]-2-carboxylate (178m)



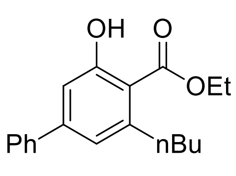
Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.74 (t, 3H, J = 7.2 Hz), 2.90 (t, 2H, J = 7.2 Hz), 3.71 (t, 2H, J = 6.8 Hz), 3.96 (q, 2H, J = 6.8 Hz), 4.51 (s, 2H), 6.67 (d, 1H, J = 1.7 Hz), 6.88 (d, 1H, J = 1.7 Hz), 7.19-7.21 (m, 2H), 7.25-7.33 (m, 8H), 10.9 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 36.3, 60.9, 70.2, 110.2, 116.8, 123.6, 126.7, 127.5, 127.6, 127.7, 128.2, 128.4, 138.2, 143.2, 145.0, 161.8, 171.0; IR (NaCl, neat) v: 3443, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{24}H_{25}O_4$: 377.1753, found: 377.1746.

Ethyl 3-hydroxy-5-(thiophen-3-yl)-[1,1'-biphenyl]-4-carboxylate (178n)



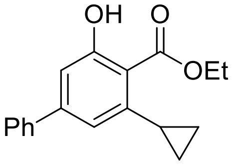
Yellow solid; m.p: 88-90°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.94 (t, 3H, J = 7.2 Hz); 4.09 (q, 2H, J = 7.2 Hz), 7.03 (dd, 1H, J = 4.9, 1.2 Hz), 7.09 (d, 1H, J = 1.8 Hz), 7.16 (dd, 1H, J = 3.0, 1.2 Hz), 7.24 (d, 1H, J = 1.9 Hz), 7.28 (dd, 1H, J = 5.4, 3.0 Hz), 7.38-7.46 (m, 3H), 7.61-7.63 (m, 2H), 11.0 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.2, 61.2, 111.1, 115.1, 121.4, 121.7, 124.1, 127.2, 128.5, 128.9, 129.1, 139.3, 140.0, 143.1, 146.4, 162.1, 170.9; IR (NaCl, neat) v: 3412, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{19}H_{16}O_3S$: 325.0898, found: 325.0894.

Ethyl 3-butyl-5-hydroxy-[1,1'-biphenyl]-4-carboxylate (178o)



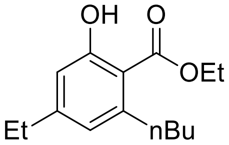
Yellow solid; m.p: 88-90°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.94 (t, 3H, J = 7.2 Hz), 1.38-1.46 (m, 5H), 1.55-1.63 (m, 2H), 2.96-3.00 (m, 2H), 4.46 (q, 2H, *J* = 7.2 Hz), 6.97 (d, 1H, *J* = 1.8 Hz), 7.08 (d, 1H, *J* = 1.8 Hz), 7.36-7.46 (m, 3H), 7.60-7.62 (m, 2H), 11.4 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 14.08, 14.12, 23.0, 34.5, 36.8, 61.7, 110.7, 113.8, 121.5, 127.2, 128.3, 128.8, 139.7, 146.6, 163.1, 171.6; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{19}H_{23}O_3$: 299.1647, found: 299.1648.

Ethyl 3-cyclopropyl-5-hydroxy-[1,1'-biphenyl]-4-carboxylate (178p)



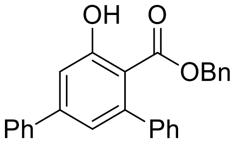
White solid; m.p: 73-75°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.71-0.96 (m, 2H), 0.93-0.97 (m, 2H), 1.44 (t, 3H, *J* = 7.2 Hz), 2.44-2.51 (m, 1H), 4.47 (t, 2H, *J* = 7.2 Hz), 6.93 (d, 1H, *J* = 1.3 Hz), 7.08 (d, 1H, *J* = 1.8 Hz), 7.35-7.46 (m, 3H), 7.57-7.59 (m, 2H), 11.3 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 8.2, 14.2, 17.0, 61.6, 112.6, 114.0, 118.4, 127.2, 128.3, 128.8, 139.9, 146.2, 146.6, 162.7, 171.7; IR (NaCl, neat) *v*: 3410, 1612 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{18}H_{19}O_3$: 283.1334, found: 283.1338.

Ethyl 2-butyl-4-ethyl-6-hydroxybenzoate (178q)



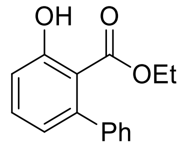
Colourless oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.93 (t, 3H, *J* = 7.2 Hz), 1.22 (t, 3H, *J* = 7.6 Hz), 1.35 (m, 5H), 1.51-1.57 (m, 2H), 2.57 (q, 2H, *J* = 7.6 Hz), 2.86-2.90 (m, 2H), 4.42 (q, 2H, *J* = 7.2 Hz), 6.56 (d, 1H, *J* = 1.2 Hz), 6.68 (d, 1H, *J* = 1.6 Hz), 11.3 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): 14.06, 14.11, 14.7, 23.0, 28.8, 34.5, 36.6, 61.4, 109.4, 114.6, 122.7, 146.0, 151.3, 163.0, 171.7; IR (NaCl, neat) *v*: 3410, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{15}H_{23}O_3$: 251.1647, found: 251.1647.

Benzyl 5'-hydroxy-[1,1':3',1''-terphenyl]-4'-carboxylate (178r)



Orange solid; m.p: 98-100°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 5.01 (s, 2H), 6.79-6.81 (m, 2H), 7.02 (d, 1H, J = 1.9 Hz), 7.02-7.26 (m, 9H), 7.37-7.45 (m, 3H), 7.60-7.62 (m, 2H), 10.9 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 67.1, 110.7, 114.8, 121.9, 127.0, 127.2, 127.8, 128.1, 128.19, 128.24, 128.3, 128.5, 128.9, 162.1, 170.8; IR (NaCl, neat) ν: 3418, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{26}H_{21}O_3$: 381.1491, found: 381.1496.

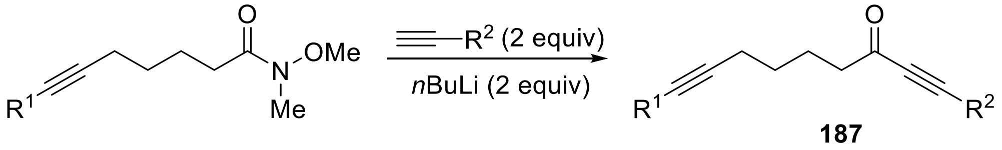
Ethyl 3-hydroxy-[1,1'-biphenyl]-2-carboxylate (178s)



Yellow solid; m.p: 54-56°C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.75 (t, 3H, J = 7.2 Hz), 3.98 (q, 2H, J = 7.2 Hz), 6.79 (dd, 1H, J = 7.5, 1.2 Hz), 7.00 (dd, 1H, J = 8.0, 1.2 Hz), 7.21-7.23 (m, 2H), 7.31-7.41 (m, 4H), 10.8 (s, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.0, 61.0, 112.3, 116.7, 122.5, 126.8, 127.6, 128.2, 133.6, 143.0, 145.0, 161.5, 171.0; IR (NaCl, neat) ν: 3379, 1661 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{15}H_{15}O_3$: 243.1021, found: 243.1012.

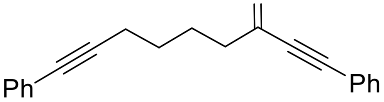
5.4 Gold-Catalyzed Synthesis of bicyclo[2.2.1]hept-2-en-7-one Derivatives via Carbocyclization Process of 1,8-Diynyl Vinyl Esters

General Experimental Procedure for the Preparation of Ketones 187



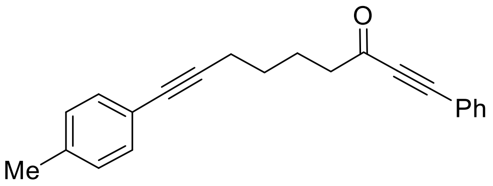
To a flame-dried 50 mL round-bottom-flask charged with alkyl or aryl acetylene (9 mmol, 2 equiv) in THF (18 mL) was added *n*BuLi (1.6 M in Hexane, 2 equiv) dropwise over 10 minutes at -78 °C under nitrogen atmosphere. The reaction mixture was allowed to stir at the same temperature for 1 hr. A solution (5 mL) of weinreb amide in THF (4.5 mmol, 1 equiv), which was prepared following the literature procedure,[48] was added dropwise subsequently to the resulting mixture at the same temperature. The mixture was then allowed to stir for overnight at room temperature. Upon completion, the mixture was quenched by satutrated aqueous NH_4Cl solution (10 mL) and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). After this, the organic layers were combined, dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was then purified by flash column chromatography on silica gel (eluent: *n*hexane:EtOAc = 10:1) to give the ketone **187a-n** which was used for next step.

1,9-diphenylnona-1,8-diyn-3-one (187a)



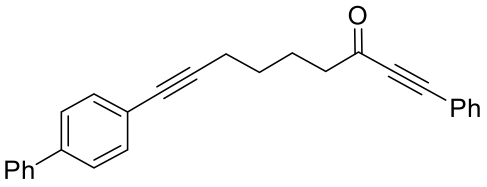
Yield 70%; Brown oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.63-1.70 (m, 2H), 1.88-1.96 (m, 2H), 2.45 (t, 2H, *J* = 7.0 Hz), 2.71 (t, 2H, *J* = 7.4 Hz), 7.23-7.25 (m, 3H), 7.30-7.32 (m, 2H), 7.34-7.41 (m, 3H), 7.52-7.55 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.2, 23.4, 28.0, 45.0, 81.2, 87.8, 89.6, 90.9, 120.0, 123.9, 127.6, 128.2, 128.7, 130.7, 131.6, 133.1, 187.7; IR (NaCl, neat) *v*: 2203, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{21}H_{19}O$: 287.1436, found: 287.1433.

1-phenyl-9-(p-tolyl)nona-1,8-diyn-3-one (187b)



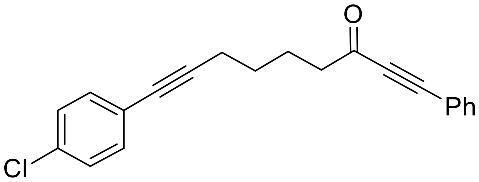
Yield 74%; Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.62-1.69 (m, 2H), 1.87-1.95 (m, 2H), 2.29 (s, 3H), 2.43 (t, 2H, *J* = 7.2 Hz), 2.70 (t, 2H, *J* = 7.2 Hz), 7.04 (d, 2H, *J* = 8.0 Hz), 7.26-7.34 (m, 4H), 7.39-7.43 (m, 1H), 7.52-7.54 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.3, 21.4, 23.5, 28.0, 45.0, 81.3, 87.9, 88.8, 90.8, 120.0, 120.9, 128.7, 129.0, 130.7, 131.5, 133.1, 137.5, 187.5; IR (NaCl, neat) *v*: 2201, 1666 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{22}H_{21}O$: 301.1592, found: 301.1587.

9-([1,1'-biphenyl]-4-yl)-1-phenylnona-1,8-diyn-3-one (187c)



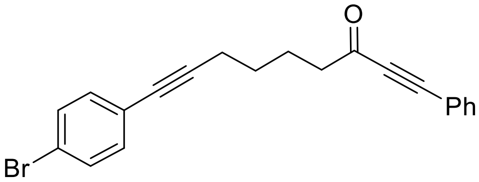
Yield 80%; Yellow oil; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.66-1.73 (m, 2H), 1.91-1.98 (m, 2H), 2.48 (t, 2H, *J* = 6.9 Hz), 2.73 (t, 2H, *J* = 7.3 Hz), 7.30-7.34 (m, 3H), 7.39-7.50 (m, 7H), 7.53-7.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.3, 23.5, 28.0, 45.0, 81.1, 87.8, 90.3, 90.9, 120.0, 122.9, 126.9, 127.0, 127.5, 128.7, 128.9, 130.7, 132.0, 133.1, 140.3, 140.5, 187.8; IR (NaCl, neat) *v*: 2201, 1667 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. For $C_{27}H_{23}O$: 363.1749, found: 363.1743.

9-(4-chlorophenyl)-1-phenylnona-1,8-diyn-3-one (187d)



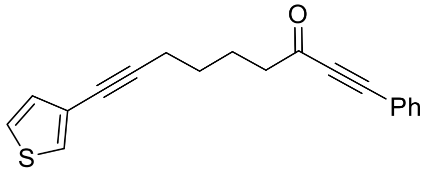
Yield 80%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.72 (m, 2H), 1.89-1.96 (m, 2H), 2.46 (t, 2H, *J* = 6.8 Hz), 2.73 (t, 2H, *J* = 7.2 Hz), 7.20-7.23 (m, 2H), 7.28-7.30 (m, 2H), 7.33-7.37 (m, 2H), 7.42-7.45 (m, 1H), 7.53-7.55 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.2, 23.4, 27.8, 45.0, 80.1, 87.8, 90.6, 90.9, 119.9, 122.4, 128.5, 128.6, 130.7, 132.8, 133.1, 133.5, 187.7; IR (NaCl, neat) *v*: 2201, 1666 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{18}{}^{35}ClO$: 321.1046, found: 321.1045.

9-(4-bromophenyl)-1-phenylnona-1,8-diyn-3-one (187e)



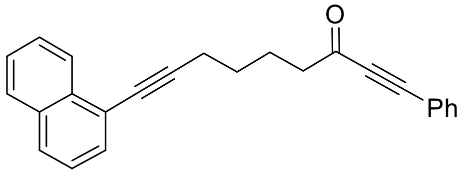
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.63-1.71 (m, 2H), 1.88-1.95 (m, 2H), 2.44 (t, 2H, *J* = 6.8 Hz), 2.72 (t, 2H, *J* = 7.2 Hz), 7.21-7.24 (m, 2H), 7.32-7.38 (m, 4H), 7.41-7.45 (m, 1H), 7.52-7.54 9m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 23.4, 27.8, 45.0, 80.2, 87.8, 90.87, 90.91, 119.9, 121.7, 122.9, 128.7, 130.8, 131.4, 133.1, 187.6; IR (NaCl, neat) *v*: 2203, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{18}{}^{81}BrO$: 367.0521, found: 367.0522.

1-phenyl-9-(thiophen-3-yl)nona-1,8-diyn-3-one (187f)



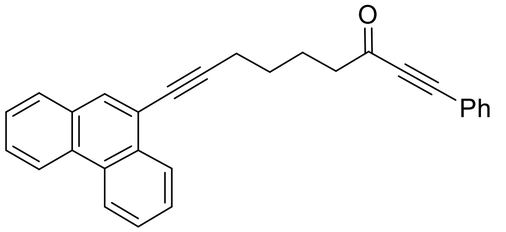
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.71 (m, 2H), 1.88-1.96 (m, 2H), 2.44 (t, 2H, *J* = 7.2 Hz); 2.72 (t, 2H, *J* = 7.2 Hz), 7.05 (dd, 1H, *J* = 5.0, 1.1 Hz); 7.20 (dd, 1H, *J* = 5.0, 3.0 Hz), 7.32-7.37 (m, 3H), 7.42-7.46 (m, 1H), 7.54-7.56 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.2, 23.4, 27.9, 45.0, 76.2, 87.8, 89.0, 90.9, 120.0, 122.8, 125.0, 127.7, 128.6, 130.0, 130.7, 133.1, 187.7; IR (NaCl, neat) *v*: 2201, 1651 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{19}H_{17}OS$: 293.1000, found: 293.0997.

9-(naphthalen-1-yl)-1-phenylnona-1,8-diyn-3-one (187g)



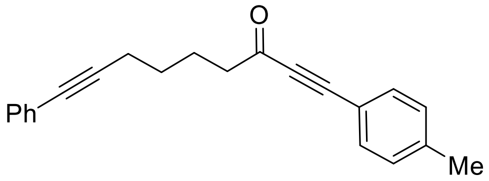
Yield 84%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.78-1.85 (m, 2H), 2.02-2.09 (m, 2H), 2.66 (t, 2H, *J* = 7.2 Hz), 2.80 (t, 2H, *J* = 7.2 Hz), 7.33 (t, 2H, *J* = 7.5 Hz), 7.40-7.45 (m, 2H), 7.52-7.64 (m, 4H), 7.71 (d, 1H, *J* = 7.2 Hz), 7.81 (d, 1H, *J* = 8.2 Hz), 7.87 (d, 1H, *J* = 8.0 Hz), 8.46 (d, 1H, *J* = 8.2 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.6, 23.6, 28.2, 45.1, 79.3, 87.9, 90.9, 94.8, 120.0, 121.7, 125.3, 126.3, 126.4, 126.7, 128.1, 128.3, 128.7, 130.2, 130.8, 133.1, 133.3, 133.6, 187.7; IR (NaCl, neat) *v*: 2201, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{25}H_{21}O$: 337.1592, found: 337.1584.

9-(phenanthren-9-yl)-1-phenylnona-1,8-diyn-3-one (187h)



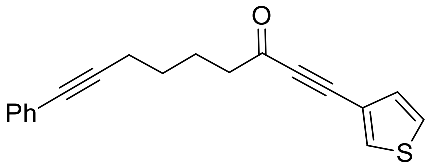
Yield 85%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.74-1.84 (m, 2H), 1.97-2.07 (m, 2H), 2.63 (t, 2H, J = 6.9 Hz), 2.76 (t, 2H, J = 7.2 Hz), 7.21-7.37 (m, 3H), 7.47-7.63 (m, 6H), 7.76 (d, 1H, J = 7.6 Hz), 7.91 (s, 1H), 8.43-8.46 (m, 1H), 8.57-8.64 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.6, 23.6, 28.2, 45.1, 79.4, 87.8, 91.0, 94.3, 119.9, 120.3, 122.6, 122.7, 126.9, 126.95, 127.01, 127.1, 128.4, 128.6, 130.0, 130.1, 130.7, 131.37, 131.39, 131.5, 133.1, 187.7; IR (NaCl, neat) *v*: 2201, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{29}H_{23}O$: 387.1749, found: 387.1750.

9-phenyl-1-(p-tolyl)nona-1,8-diyn-3-one (187i)



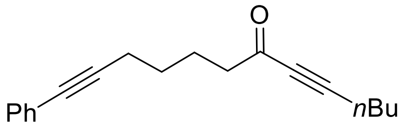
Yield 45%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.65-1.72 (m, 2H), 1.90-1.97 (m, 2H), 2.37 (s, 3H), 2.47 (t, 2H, J = 7.2 Hz), 2.72 (t, 2H, J = 7.6 Hz), 7.15 (d, 2H, J = 7.9 Hz), 7.24-7.27 (m, 3H), 7.34-7.39 (m, 2H), 7.44-7.46 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.2, 21.7, 23.5, 28.0, 45.0, 81.1, 87.7, 89.5, 91.6, 116.9, 123.9, 127.6, 128.2, 129.4, 131.6, 133.1, 141.4, 187.8; IR (NaCl, neat) *v*: 2197, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{22}H_{21}O$: 301.1592, found: 301.1591.

9-phenyl-1-(thiophen-3-yl)nona-1,8-diyn-3-one (187j)



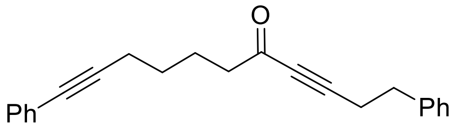
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.62-1.70 (m, 2H), 1.87-1.94 (m, 2H), 2.44 (t, 2H, *J* = 6.9 Hz), 2.69 (t, 2H, *J* = 7.3 Hz), 7.17 (dd, 1H, *J* = 5.0, 1.0 Hz), 7.23-7.29 (m, 4H), 7.37-7.39 (m, 2H), 7.69 (dd, 1H, *J* = 3.0, 1.0 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.2, 23.4, 28.0, 44.9, 81.2, 86.2, 88.1, 89.6, 119.2, 123.9, 126.3, 127.7, 128.3, 130.3, 131.6, 133.9, 187.6; IR (NaCl, neat) *v*: 2199, 1651 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{19}H_{17}OS$: 293.1000, found: 293.0992.

1-phenyltrideca-1,8-diyn-7-one (187k)



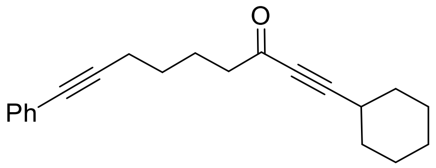
Yield 76%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.90 (t, 3H, *J* = 7.2 Hz), 1.35-1.44 (m, 2H), 1.49-1.56 (m, 2H), 1.58-1.65 (m, 2H), 1.79-1.87 (m, 2H), 2.32 (t, 2H, *J* = 6.8 Hz), 2.41 (t, 2H, *J* = 6.8 Hz), 2.57 (t, 2H, *J* = 7.2 Hz), 7.23-7.27 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.5, 18.6, 19.2, 21.9, 23.3, 27.9, 29.7, 44.9, 80.9, 81.1, 89.5, 94.4, 123.9, 127.6, 128.2, 131.5, 187.8; IR (NaCl, neat) *v*: 2208, 1655 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{19}H_{23}O$: 267.1749, found: 267.1754.

1,11-diphenylundeca-3,10-diyn-5-one (187l)



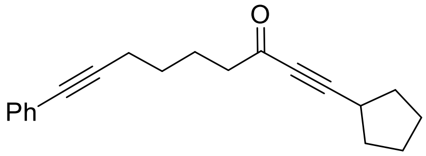
Yield 84%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.55-1.65 (m, 2H), 1.74-1.84 (m, 2H), 2.40 (t, 2H, *J* = 7.0 Hz), 2.54 (t, 2H, *J* = 7.2 Hz), 2.63 (t, 2H, *J* = 7.3 Hz), 2.86 (t, 2H, *J* = 7.4 Hz), 7.17-7.32 (m, 7H), 7.37-7.40 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.2, 21.1, 23.3, 28.0, 34.0, 45.0, 81.1, 81.4, 89.6, 93.3, 123.9, 126.7, 127.6, 128.2, 128.4, 128.6, 131.6, 139.7, 187.8; IR (NaCl, neat) *v*: 2208, 1668 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{23}O$: 315.1749, found: 315.1734.

1-cyclohexyl-9-phenylnona-1,8-diyn-3-one (187m)



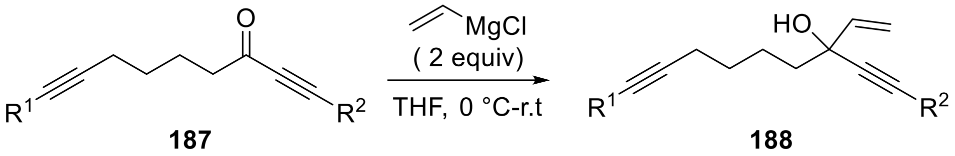
Yield 72%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.26-1.34 (m, 4H), 1.44-1.51 (m, 3H), 1.60-1.71 (m, 4H), 1.79-1.89 (m, 3H), 2.44 (t, 2H, *J* = 7.0 Hz), 2.50-2.55 (m, 1H), 2.59 (t, 2H, *J* = 7.3 Hz), 7.26-7.28 (m, 3H), 7.37-7.40 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.2, 23.5, 24.7, 25.6, 28.0, 29.1, 31.6, 45.0, 80.7, 81.1, 89.5, 98.1, 123.9, 127.6, 128.2, 131.5, 188.2; IR (NaCl, neat) *v*: 2205, 1667 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{25}O$: 293.1905, found: 293.1906.

1-cyclopentyl-9-phenylnona-1,8-diyn-3-one (187n)



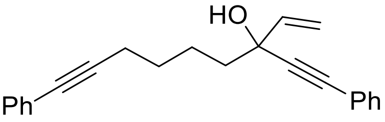
Yield 75%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.50-1.70 (m, 8H), 1.76-1.84 (m, 2H), 1.86-1.93 (m, 2H), 2.39 (t, 2H, *J* = 7.0 Hz), 2.53 (t, 2H, *J* = 7.3 Hz), 2.69-2.74 (m, 1H), 7.21-7.25 (m, 3H), 7.36-7.38 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.1, 23.3, 25.1, 27.9, 30.0, 33.2, 44.9, 80.3, 81.0, 89.5, 98.2, 123.9, 127.5, 128.1, 131.4, 187.5; IR (NaCl, neat) *v*: 2205, 1661 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{20}H_{23}O$: 279.3900, found: 279.3902.

General Experimental Procedure for the Preparation of alcohols 188



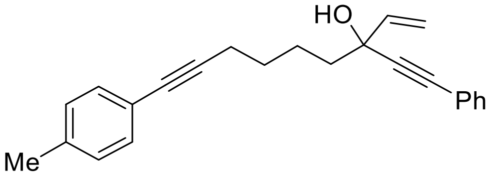
To a stirred solution contained ketones **187** (3 mmol, 1 equiv) in THF (15 mL) was added vinyl magnesium chloride solution (1.6 M in THF, 2 equiv) dropwise at 0 ˚C under nitrogen atmosphere. The solution of mixture was then allowed to warm to room temperature and stir for 5-10 hours. Upon completion, the reaction was quenched by the addition of saturated aqueous NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (2 x 20 mL) and the combined organic laters were dried over $MgSO_4$, and concentrated under reduced pressure. The mixture was then purified by flash column chromatography (*n*hexanane/EtOAc = 20:1 to 10:1) to yield the title compound (**188a–n**) as yellow oil.

9-phenyl-3-(phenylethynyl)non-1-en-8-yn-3-ol (188a)



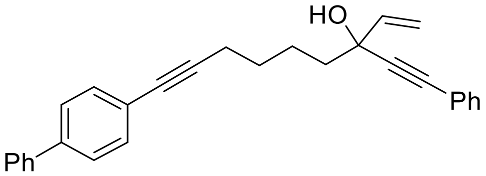
Yield 84%; Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.64-1.89 (m, 6H), 2.33 (s, 1H), 2.43 (t, 2H, *J* = 6.7 Hz), 5.21 (dd, 1H, *J* = 10.4, 1.2 Hz), 5.61 (dd, 1H, *J* = 17.0, 1.2 Hz), 5.98 (dd, 1H, J = 16.8, 10.4 Hz), 7.21-7.29 (m, 6H), 7.35 (m, 2H), 7.41-7.43 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 23.9, 28.7, 41.9, 72.1, 81.0, 86.2, 89.9, 90.1, 114.8, 122.6, 124.1, 127.5, 128.2, 128.3, 128.5, 131.6, 131.8, 141.2; IR (NaCl, neat) *ν*: 3416, 2201 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{23}H_{23}O$: 315.1749, found: 315.1763.

3-(phenylethynyl)-9-(p-tolyl)non-1-en-8-yn-3-ol (188b)



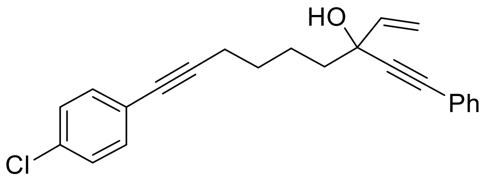
Yield 85%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.65-1.88 (m, 6H), 2.29 (s, 3H), 2.37-2.44 (m, 2H), 5.20 (dd, 1H, *J* = 10.2, 1.1 Hz), 5.60 (dd, 1H, *J* = 17.1, 1.1 Hz), 5.98 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.02 (d, 2H, *J* = 7.9 Hz), 7.20-7.27 (m, 5H), 7.40-7.43 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.4, 21.4, 23.9, 28.8, 42.0, 72.1, 81.0, 86.2, 89.3, 90.0, 114.8, 121.0, 122.6, 128.3, 128.4, 129.0, 131.5, 131.8, 137.4, 141.3; IR (NaCl, neat) *v*: 3406, 2200 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{24}H_{25}O$: 329.1905, found: 329.1912.

9-([1,1'-biphenyl]-4-yl)-3-(phenylethynyl)non-1-en-8-yn-3-ol (188c)



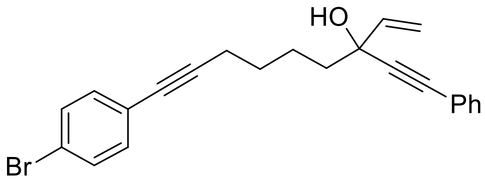
Yield 90%; Yellow oil; ^{1}HNMR (CDCl$_3$, 300 MHz): δ 1.69-1.85 (m, 6H), 2.22 (s, 1H), 2.46 (t, 2H, *J* = 6.7 Hz), 5.22 (dd, 1H, *J* = 10.2, 1.2 Hz), 5.62 (dd, 1H, *J* = 17.1, 1.0 Hz), 6.00 (dd, 1H, *J* = 17.0, 10.5 Hz), 7.22-7.35 (m, 4H), 7.39-7.47 (m, 8H), 7.54-7.57 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.5, 23.8, 28.7, 42.0, 72.1, 80.8, 86.2, 89.9, 90.8, 114.8, 122.6, 123.0, 126.9, 127.0, 127.5, 128.3, 128.6, 128.8, 131.8, 132.0, 140.2, 140.6, 141.2 IR (NaCl, neat) *v*: 3583, 2225 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{29}H_{27}O$: 391.2062, found: 391.2077.

9-(4-chlorophenyl)-3-(phenylethynyl)non-1-en-8-yn-3-ol (188d)



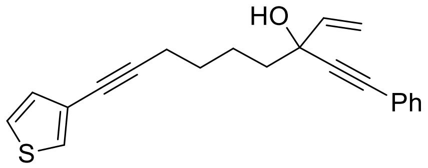
Yield 87%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.65-1.90 (m, 6H), 2.20 (s, 1H), 2.43 (t, 2H, *J* = 6.4 Hz), 5.22 (dd, 1H, *J* = 10.2, 0.9 Hz), 5.61 (dd, 1H, *J* = 17.0, 1.0 Hz), 5.99 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.17-7.20 (m, 2H), 7.23-7.34 (m, 5H), 7.40-7.43 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.3, 23.8, 28.6, 41.9, 72.1, 79.9, 86.2, 89.8, 91.1, 114.8, 122.5, 128.3, 128.5, 131.7, 132.8, 133.4, 141.2; IR (NaCl, neat) *v*: 3564, 2228 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{22}{}^{35}ClO$: 349.1359, found: 349.1362.

9-(4-bromophenyl)-3-(phenylethynyl)non-1-en-8-yn-3-ol (188e)



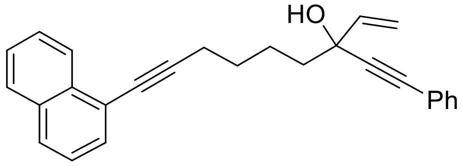
Yield 83%; Brown oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.88 (m, 6H), 2.28 (s, 1H), 2.42 (t, 2H, *J* = 6.5 Hz), 5.22 (dd, 1H, *J* = 10.2, 1.0 Hz), 5.62 (dd, 1H, *J* = 17.0, 1.0 Hz), 5.99 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.19-7.21 (m, 2H), 7.25-7.35 (m, 5H), 7.40-7.43 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.4, 23.8, 28.5, 41.8, 72.1, 80.0, 86.2, 89.8, 91.4, 114.8, 121.6, 122.5, 123.0, 128.3, 128.5, 131.4, 131.7, 133.0, 141.2; IR (NaCl, neat) *v*: 3404, 2230 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{22}{}^{79}BrO$: 393.0854, found: 393.0844.

3-(phenylethynyl)-9-(thiophen-3-yl)non-1-en-8-yn-3-ol (188f)



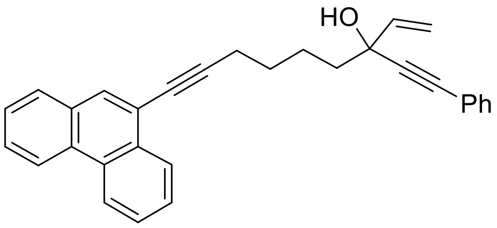
Yield 88%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.62-1.91 (m, 6H), 2.31 (s, 1H), 2.42 (t, 2H, *J* = 6.9 Hz), 5.21 (dd, 1H, *J* = 10.2, 1.2 Hz), 5.61 (dd, 1H, *J* = 17.2, 1.2 Hz), 5.99 (dd, 1H, *J* = 17.0, 10.0 Hz), 7.03 (dd, 1H, *J* = 5.0, 1.0 Hz), 7.18 (dd, 1H, *J* = 5.0, 3.0 Hz), 7.24-7.30 (m, 4H), 7.41-7.43 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.4, 23.9, 28.7, 41.9, 72.1, 76.0, 86.2, 89.6, 89.9, 114.8, 122.6, 123.0, 125.0, 127.6, 128.3, 128.5, 130.0, 131.8, 141.2; IR (NaCl, neat) *v*: 3385, 2228 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{21}OS$: 321.1313, found: 321.1322.

9-(naphthalen-1-yl)-3-(phenylethynyl)non-1-en-8-yn-3-ol (188g)



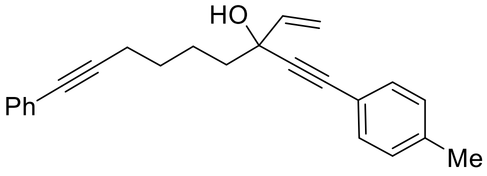
Yield 91%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.73-1.85 (m, 6H), 2.42 (s, 1H), 2.58 (t, 2H, *J* = 6.7 Hz), 7.16-7.19 (m, 2H), 7.21-7.25 (m, 1H), 7.30-7.34(m, 1H), 7.30-7.50 (m, 4H), 7.58 (d, 1H, *J* = 7.0 Hz), 7.72 (d, 1H, *J* = 8.2 Hz), 7.78 (d, 1H, *J* = 7.6 Hz), 8.34 (d, 1H, *J* = 8.1 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.8, 24.0, 29.0, 42.0, 72.1, 79.0, 86.3, 90.0, 95.2, 114.9, 121.8, 122.6, 125.3, 126.3, 126.4, 126.6, 128.0, 128.25, 128.32, 128.5, 130.2, 131.8, 133.3, 133.6, 141.3, IR (NaCl, neat) *v*: 3406, 2224 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{27}H_{25}O$: 365.1905, found: 365.1893.

9-(phenanthren-9-yl)-3-(phenylethynyl)non-1-en-8-yn-3-ol (188h)



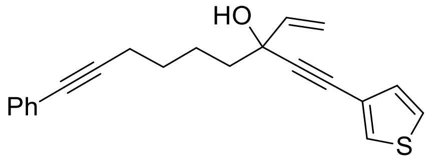
Yield 90%; Yellow oil; ^{1}HNMR ($CDCl_3$, 400 MHz): δ 1.72-1.98 (m, 6H), 2.23 (s, 1H), 2.63 (t, 2H, *J* = 6.5 Hz), 7.14-7.16 (m, 2H), 7.21-7.25 (m, 1H), 7.37-7.39 (m, 2H), 7.52-7.65 (m, 4H), 7.74-7.76 (m, 1H), 7.90 (s, 1H), 8.44-8.46 (m, 1H), 8.60-8.65 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.8, 24.0, 28.9, 42.0, 72.1, 79.1, 86.2, 89.9, 94.8, 114.9, 120.4, 122.5, 122.6, 122.7, 126.8, 126.89, 126.94, 127.1, 128.3, 128.4, 128.41, 130.0, 130.1, 131.3, 131.4, 131.5, 131.7, 141.2; IR (NaCl, neat) *v*: 3407, 2224 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{31}H_{27}O$: 415.2062, found: 415.2065.

9-phenyl-3-(p-tolylethynyl)non-1-en-8-yn-3-ol (188i)



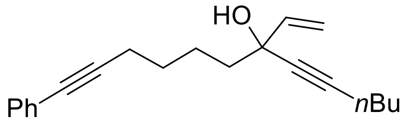
Yield 86%; Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.64-1.91 (m, 6H), 2.22-2.23 (m, 1H), 2.32 (s, 3h), 2.44 (t, 2H, *J* = 6.6 Hz), 5.20 (dd, 1H, *J* = 10.6, 1.2 Hz), 5.61 (dd, 1H, *J* = 17.0, 1.0 Hz), 5.98 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.06 (d, 2H, *J* = 7.9 Hz), 7.22-7.24 (m, 3H), 7.30-7.35 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 21.5, 23.9, 28.7, 42.0, 72.1, 80.9, 86.3, 89.2, 90.1, 114.7, 119.5, 124.0, 127.5, 128.2, 129.1, 131.6, 131.7, 138.5, 141.3; IR (NaCl, neat) *v*: 3406, 2200 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{24}H_{25}O$: 329.1905, found: 329.1909.

9-phenyl-3-(thiophen-3-ylethynyl)non-1-en-8-yn-3-ol (188j)



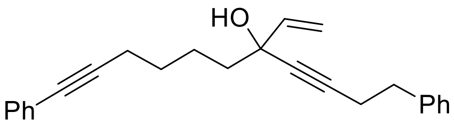
Yield 89%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.63-1.89 (m, 6H), 2.24 (s, 1H), 2.44 (t, 2H, *J* = 6.4 Hz), 5.21 (dd, 1H, *J* = 10.2, 0.9 Hz), 5.59 (dd, 1H, *J* = 17.1, 0.9 Hz), 5.98 (dd, 1H, *J* = 17.1, 10.2 Hz), 7.08 (dd, 1H, *J* = 5.0, 1.0 Hz), 7.20-7.26 (m, 4H), 7.35-7.41 (m, 3H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.4, 23.8, 28.7, 41.9, 72.1, 80.9, 81.3, 89.5, 90.1, 114.8, 121.6, 124.0, 125.3, 127.5, 128.2, 129.0, 129.9, 131.6, 141.2; IR (NaCl, neat) *v*: 3412, 2228 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{21}OS$: 321.1313, found: 321.1321.

1-phenyl-7-vinyltrideca-1,8-diyn-7-ol (188k)



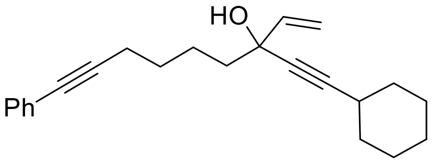
Yield 82%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 7.3 Hz), 1.36-1.42 (m, 2H), 1.45-1.53 (m, 2H), 1.59-1.77 (m, 6H), 2.05 (s, 1H), 2.22 (t, 2H, *J* = 7.0 Hz), 2.42 (t, 2H, *J* = 6.5 Hz), 5.14 (dd, 1H, *J* = 10.0 Hz), 5.90 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.25-7.27 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.6, 18.4, 19.4, 22.0, 23.9, 28.8, 30.8, 42.0, 71.7, 80.8, 81.0, 86.8, 90.1, 114.2, 124.1, 127.5, 128.2, 131.5, 141.8; IR (NaCl, neat) *v*: 3422, 2236 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{27}O$: 295.2062, found: 295.2071.

1,11-diphenyl-5-vinylundeca-3,10-diyn-5-ol (188l)



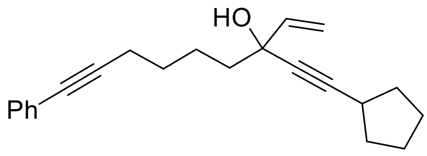
Yield 86%; Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.51-1.74 (m, 6H), 1.97 (s, 1H), 2.40 (t, 2H, *J* = 6.8 Hz), 2.53 (t, 2H, *J* = 7.4 Hz), 2.82 (t, 2H, *J* = 7.4 Hz), 5.11 (dd, 1H, *J* = 10.4, 1.0 Hz), 5.43 (dd, 1H, *J* = 17.1, 1.1 Hz), 5.87 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.17-7.31 (m, 8H), 7.37-7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.4, 20.9, 23.8, 28.8, 35.0, 42.0, 71.7, 80.8, 81.9, 85.9, 90.2, 114.3, 124.1, 126.3, 127.5, 128.2, 128.4, 128.5, 131.5, 140.5, 141.5; IR (NaCl, neat) *v*: 3418, 2236 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{25}H_{27}O$: 343.2062, found: 343.2078.

3-(cyclohexylethynyl)-9-phenylnon-1-en-8-yn-3-ol (188m)



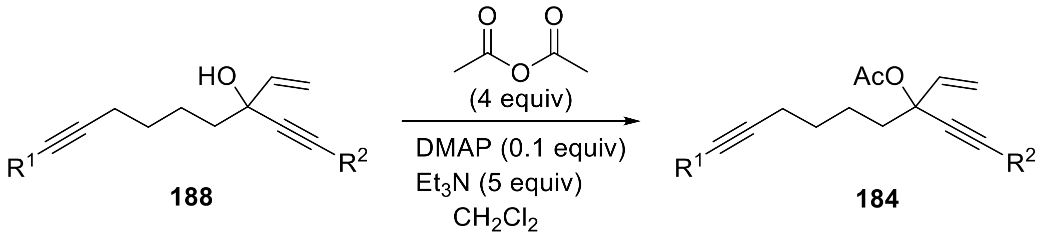
Yield 85%; Yellow oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.26-1.29 (m, 4H), 1.38-1.48 (m, 4H), 1.64-1.78 (m, 8H), 1.99 (s, 1H), 2.38-2.44 (m, 3H), 5.13 (dd, 1H, *J* = 10.2, 1.3 Hz), 5.52 (dd, 1H, *J* = 17.0, 1.4 Hz), 5.90 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.24-7.28 (m, 3H), 7.36-7.40 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.4, 23.9, 24.8, 25.8, 28.8, 29.0, 32.7, 42.1, 71.7, 80.8, 80.9, 90.1, 91.0, 114.2, 124.1, 127.5, 128.1, 131.5, 141.8; IR (NaCl, neat) *v*: 3426, 2234 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{23}H_{29}O$: 321.2218, found: 321.2229.

3-(cyclopentylethynyl)-9-phenylnon-1-en-8-yn-3-ol (188n)



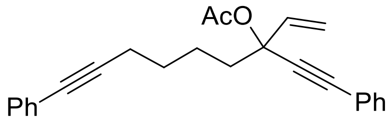
Yield 85%; Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.49-1.77 (m, 12H), 1.85-1.92 (m, 2H), 2.04 (brs, 1H), 2.41 (t, 2H, *J* = 6.5 Hz), 2.60-2.67 (m, 1H), 5.13 (dd, 1H, *J* = 10.2, 1.4 Hz), 5.50 (dd, 1H, *J* = 17.0, 1.3 Hz), 5.90 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.24-7.29 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 23.9, 24.9, 28.8, 30.1, 33.9, 42.0, 71.7, 80.4, 80.8, 90.1, 91.2, 114.2, 124.1, 127.5, 128.2, 131.6, 141.8; IR (NaCl, neat) *v*: 3420, 2234 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{22}H_{27}O$: 307.4519, found: 307.4520.

General Experimental Procedure for the Preparation of 1,8-diynyl vinyl esters 184



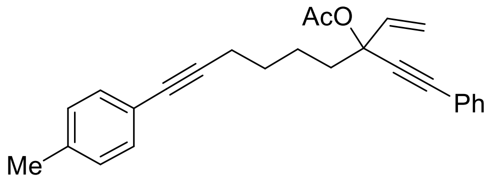
To a solution of alcohol **188** (1 mmol, 1 equiv) and DMAP (0.1 mmol, 0.1 equiv) in CH_2Cl_2 was sequentially added Et_3N (0.698 mL, 5 mmol) and acetic anhydride (0.377 mL, 4 mmol) The reaction mixture was stirred at room temperature for 2 hours. Upon completion (monitored by TLC analysis), the reaction mixture was quenched by adding saturated aqeous $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (2 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated under reduced pressure and purified by flash column chromatography on neutral Al_2O_3 (eluent: *n*hexane: EtOAc = 100:0 to 100:5) to afford ester **184** as yellow oil. The column chromatography must be performed at a fast pace to avoid decomposition.

9-phenyl-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184a)



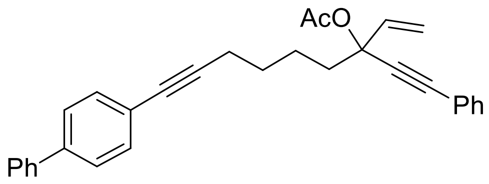
Yield 72%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.65-1.78 (m, 4H), 1.90-1.96 (m, 1H), 2.05 (s, 3H), 2.10-2.18 (m, 1H), 2.45 (t, 2H, *J* = 6.4 Hz), 5.32 (d, 1H, *J* = 10.4 Hz), 5.99 (dd, 1H, *J* = 13.6, 10.4 Hz), 7.22-7.29 (m, 6H), 7.35-7.37 (m, 2H), 7.43-7.46 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.9, 23.4, 28.5, 40.5, 78.4, 81.0, 86.5, 87.8, 89.9, 116.6, 122.5, 124.0, 127.5, 128.2, 128.5, 131.6, 131.9, 137.9, 168.9; IR (NaCl, neat) *v*: 2232, 1748 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{25}H_{25}O_2$: 357.1855, found: 357.1848.

3-(phenylethynyl)-9-(p-tolyl)non-1-en-8-yn-3-yl acetate (184b)



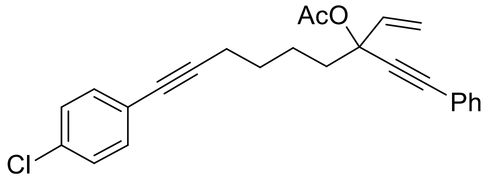
Yield 65%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.62-1.83 (m, 4H), 1.85-1.97 (m, 1H), 2.06 (s, 3H), 2.05-2.19 (m, 1H), 2.32 (s, 3H), 2.44 (t, 2H, *J* = 6.5 Hz), 5.32 (d, 1H, *J* = 10.4 Hz), 5.65 (d, 1H, *J* = 17.2 Hz), 5.99 (dd, 1H, *J* = 10.0, 17.0 Hz), 7.05 (d, 2H, *J* = 7.90 Hz), 7.24-7.30 (m, 5H), 7.44-7.46 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.4, 21.9, 23.4, 28.6, 40.5, 78.3, 81.0, 86.5, 87.8, 89.1, 116.6, 120.9, 122.5, 128.2, 128.5, 128.9, 131.4, 132.0, 137.5, 137.9, 168.9; IR (NaCl, neat) *v*: 2232, 1744 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{26}H_{27}O_2$: 371.2011, found: 371.2013.

9-([1,1'-biphenyl]-4-yl)-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184c)



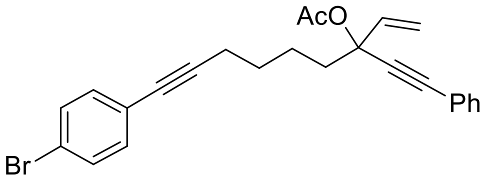
Yield 73%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.66-1.81 (m, 4H), 1.91-1.98 (m, 1H), 2.01 (s, 3H), 2.10-2.17 (m, 1H), 2.48 (t, 2H, *J* = 6.6 Hz), 5.33 (d, 1H, *J* = 10.0 Hz), 5.66 (d, 1H, *J* = 17.2 Hz), 6.00 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.21-7.30 (m, 3H), 7.32-7.35 (m, 1H), 7.41-7.48 (m, 8H), 7.55-7.57 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.4, 21.9, 23.4, 28.5, 40.5, 78.4, 80.9, 86.5, 87.8, 90.6, 116.7, 122.5, 123.0, 126.9, 127.0, 127.5, 128.2, 128.5, 128.9, 132.0, 137.9, 140.3, 140.5, 168.9; IR (NaCl, neat) *v*: 2232, 1746 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{31}H_{29}O_2$: 433.2168, found: 433.2180.

9-(4-chlorophenyl)-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184d)



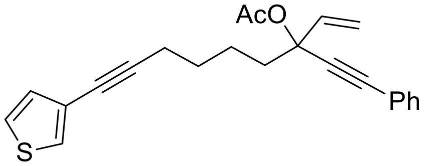
Yield 76%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.65-1.77 (m, 4H), 1.88-1.98 (m, 1H), 2.06 (s, 3H), 2.08-2.17 (m, 1H), 2.44 (t, 2H, *J* = 6.5 Hz), 5.32 (d, 1H, *J* = 10.2 Hz), 5.65 (d, 1H, *J* = 17.1 Hz), 6.02 (dd, 1H, *J* = 17.0, 10.5 Hz), 7.18-7.31 (m, 7H), 7.42-7.45 (m, 2H); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.3, 21.8, 23.4, 28.4, 40.4, 78.3, 80.0, 86.5, 87.8, 91.0, 116.7, 122.4, 122.5, 128.2, 128.47, 128.54, 131.9, 132.7, 133.4, 137.9, 168.8; IR (NaCl, neat) *v*: 2232, 1746 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{25}H_{24}{}^{35}ClO_2$: 391.1465, found: 391.1465.

9-(4-bromophenyl)-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184e)



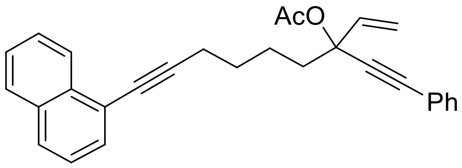
Yield 50%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.74 (m, 4H), 1.93-1.95 (m, 1H), 2.06 (s, 3H), 2.07-2.13 (m, 1H), 2.43 (t, 2H, *J* = 6.6 Hz), 5.32 (d, 1H, *J* = 10.0 Hz), 5.65 (d, 1H, *J* = 17.2 Hz), 5.99 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.19-7.21 (m, 2H), 7.23-7.27 (m, 2H), 7.28-7.31 (m, 1H), 7.33-7.36 (m, 2H), 7.43-7.45 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.9, 23.4, 28.3, 40.4, 78.3, 80.0, 86.5, 87.8, 91.2, 116.7, 121.6, 122.4, 122.9, 128.2, 128.6, 131.4, 131.9, 133.0, 137.9, 168.9; IR (NaCl, neat) *v*: 2232, 1744 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for C$_{25}$H$_{24}$^{81}BrO$_2$: 437.0939, found: 437.0947.

3-(phenylethynyl)-9-(thiophen-3-yl)non-1-en-8-yn-3-yl acetate (184f)



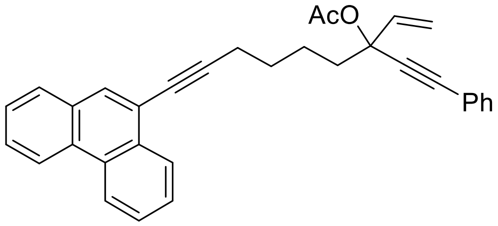
Yield 50%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.75 (m, 4H), 1.89-1.96 (m, 1H), 2.05 (s, 3H), 2.07-2.16 (m, 1H), 2.43 (t, 2H, *J* = 6.6 Hz), 5.32 (dd, 1H, *J* = 10.4, 0.4 Hz), 5.65 (dd, 1H, *J* = 17.2, 0.4 Hz), 5.98 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.02 (dd, 1H, *J* = 5.0, 1.1 Hz), 7.19 (dd, 1H, *J* = 5.0, 3.0 Hz), 7.24-7.29 (m, 4H), 7.43-7.46 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.9, 23.4, 28.5, 40.5, 76.0, 78.3, 86.5, 87.8, 89.4, 116.7, 122.5, 122.9, 125.0, 127.6, 128.2, 128.6, 130.0, 131.9, 137.9, 168.9; IR (NaCl, neat) *v*: 2232, 1748 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for C$_{23}$H$_{23}$O$_2$S: 363.1419, found: 363.1439.

9-(naphthalen-1-yl)-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184g)



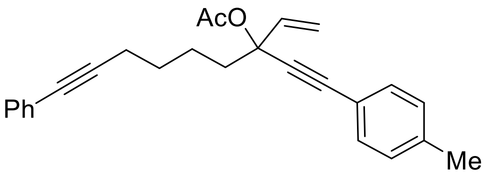
Yield 75%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.74-1.84 (m, 4H), 1.97-2.00 (m, 1H), 2.02 (s, 3H), 2.14-2.20 (m, 1H), 2.60 (t, 2H, *J* = 6.5 Hz), 5.32 (d, 1H, *J* = 10.4 Hz), 5.66 (d, 1H, *J* = 16.8 Hz), 6.00 (dd, 1H, J = 17.0, 10.0 Hz), 7.14-7.25 (m, 3H), 7.33 (dd, 1H, *J* = 8.0, 7.4 Hz), 7.39-7.51 (m, 4H), 7.57-7.59 (m, 1H), 7.74 (d, 1H, *J* = 8.2 Hz), 7.79 (d, 1H, *J* = 7.5 Hz), 8.42 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (CDCl$_3$, 100 MHz): 1.7, 21.9, 23.6, 28.7, 40.6, 78.4, 79.1, 86.6, 87.9, 95.0, 116.7, 121.7, 122.5, 125.3, 126.29, 126.32, 126.6, 128.0, 128.2, 128.3, 128.5, 130.1, 132.0, 133.3, 133.5, 138.0, 168.9; IR (NaCl, neat) *v*: 2228, 1746 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{29}H_{27}O_2$: 407.2011, found: 407.2015.

9-(phenanthren-9-yl)-3-(phenylethynyl)non-1-en-8-yn-3-yl acetate (184h)



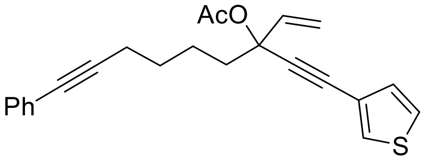
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.79-1.84 (m, 4H), 1.96-1.99 (m, 1H), 2.00 (s, 3H), 2.15-2.21 (m, 1H), 2.63 (t, 2H, *J* = 6.4 Hz), 5.32 (d, 1H, *J* = 10.4 Hz), 5.67 (d, 1H, *J* = 17.2 Hz), 6.00 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.11-7.15 (m, 2H), 7.17-7.19 (m, 1H), 7.40-7.42 (m, 2H), 7.50-7.54 (m, 1H), 7.56-7.62 (m, 3H), 7.73 (d, 1H, *J* = 7.9 Hz), 7.90 (s, 1H), 8.43-8.46 (m, 1H), 8.57-8.62 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.8, 21.9, 23.6, 28.8, 40.6, 78.4, 79.3, 86.6, 87.9, 94.7, 116.8, 120.4, 122.4, 122.6, 122.8, 126.9, 127.0, 127.05, 127.14, 128.2, 128.4, 128.5, 130.0, 130.1, 131.3, 131.4, 131.6, 132.0, 138.0, 168.9; IR (NaCl, neat) *v*: 2228, 1732 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{33}H_{29}O_2$: 457.2168, found: 457.2175.

9-phenyl-3-(p-tolylethynyl)non-1-en-8-yn-3-yl acetate (184i)



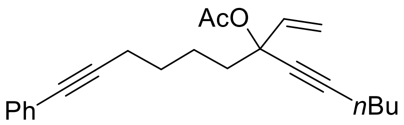
Yield 47%; Yellow oil, ; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.64-1.73 (m, 4H), 1.76-1.81 (m, 1H), 1.90-1.97 (m, 1H), 2.05 (s, 3H), 2.07 (s, 1H), 2.09-2.15 (m, 1H), 2.3 (s, 3H), 2.34 (s, 1H), 2.45 (t, 3H, *J* = 6.9 Hz), 5.35 (d, 1H, *J* = 10.4 Hz), 5.68 (d, 1H, *J* = 17.2 Hz), 6.02 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.07-7.13 (m, 2H), 7.25-7.29 (m, 3H), 7.35-7.42 (m, 4H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.5, 21.9, 23.4, 28.5, 40.5, 63.1, 80.9, 85.8, 88.0, 89.9, 116.6, 119.4, 124.0, 127.5, 128.9, 129.1, 131.5, 131.8, 138.0. 138.6, 168.9; IR (NaCl, neat) *v*: 2230, 1744 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. For $C_{26}H_{27}O_2$: 371.2011, found: 371.2020.

9-phenyl-3-(thiophen-3-ylethynyl)non-1-en-8-yn-3-yl acetate (184j)



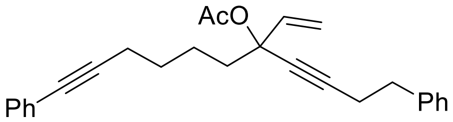
Yield 61%; Yellow oil; ^{1}H NMR (CDCl$_3$, 300 MHz): δ 1.62-1.76 (m, 4H), 1.93-1.96 (m, 1H), 2.05 (s, 3H), 2.07-2.11 (m, 1H), 2.45 (t, 2H, *J* = 6.5 Hz), 5.31 (dd, 1H, *J* = 10.4, 0.9 Hz), 5.63 (dd, 1H, *J* = 17.1, 0.6 Hz), 5.98 (dd, 1H, *J* = 17.0, 10.2 Hz), 7.10 (dd, 1H, *J* = 5.0, 1.1 Hz), 7.19 (dd, 1H, *J* = 5.0, 3.0 Hz), 7.23-7.27 (m, 3H), 7.35-7.38 (m, 2H), 7.44 (dd, 1H, *J* = 3.0, 1.1 Hz); ^{13}C NMR (CDCl$_3$, 75 MHz): 19.3, 21.8, 23.4, 28.5, 40.5, 78.4, 81.0, 82.9, 86.1, 89.9, 116.6, 121.4, 124.0, 125.2, 127.6, 128.2, 129.4, 130.1, 131.5, 137.9, 168.9; IR (NaCl, neat) *v*: 2232, 1738 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{23}O_2S$: 363.1419, found: 363.1408.

1-phenyl-7-vinyltrideca-1,8-diyn-7-yl acetate (184k)



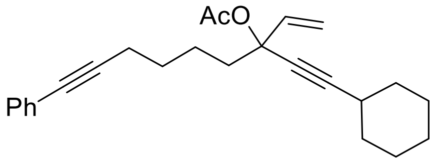
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.88 (t, 3H, *J* = 7.2 Hz), 1.36-1.43 (m, 2H), 1.47-1.54 (m, 2H), 1.60-1.67 (m, 4H), 1.78-1.85 (m, 1H), 1.99-2.05 (m, 4H), 2.25 (t, 2H, *J* = 7.0 Hz), 2.42 (t, 2H, *J* = 6.6 Hz), 5.24 (dd, 1H, *J* = 8.8, 1.0 Hz), 5.55 (dd, 1H, *J* = 17.1, 1.0 Hz), 5.91 (dd, 1H, *J* = 17.1, 10.3 Hz), 7.25-7.28 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.6, 18.5, 19.3, 21.9, 22.0, 23.4, 28.6, 30.7, 40.6, 78.4, 80.9, 88.7, 90.0, 116.1, 124.0, 127.5, 128.2, 131.5, 138.4, 168.9; IR (NaCl, neat) *v*: 2243, 1732 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{29}O_2$: 337.2168, found: 337.2155.

1,11-diphenyl-5-vinylundeca-3,10-diyn-5-yl acetate (184l)



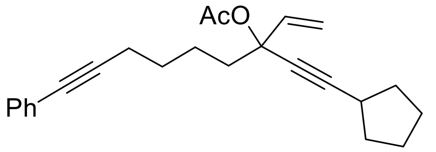
Yield 76%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.49-1.63 (m, 4H), 1.73-1.80 (m, 1H), 1.93-1.99 (m, 1H), 2.00 (s, 3H), 2.39 (t, 2H, *J* = 6.7 Hz), 2.55 (t, 2H, *J* = 7.4 Hz), 2.82 (t, 2H, *J* = 7.4 Hz), 5.21 (d, 1H, *J* = 10.4 Hz), 5.45 (d, 1H, *J* = 17.2 Hz), 5.87 (dd, 1H, *J* = 17.2, 10.4 Hz), 7.17-7.21 (m, 3H), 7.22-7.29 (m, 5H), 7.36-7.39 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.0, 21.9, 23.3, 28.6, 34.9, 40.6, 78.3, 80.9, 87.7, 90.0, 116.2, 124.1, 126.3, 127.6, 128.2, 128.3, 128.6, 131.5, 138.3, 140.6, 168.9; IR (NaCl, neat) *v*: 2245, 1748 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{27}H_{29}O_2$: 385.2168, found: 385.2152.

3-(cyclohexylethynyl)-9-phenylnon-1-en-8-yn-3-yl acetate (184m)



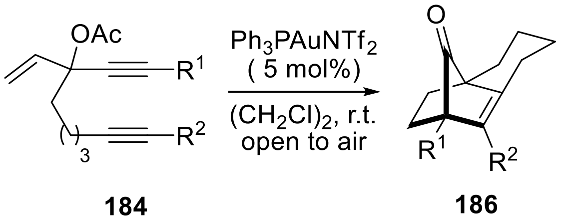
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.25-1.31 (m, 3H), 1.44-1.49 (m, 3H), 1.59-1.66 (m, 6H), 1.75-1.83 (m, 3H), 1.99-2.06 (m, 4H), 2.41-2.46 (m, 3H), 5.24 (dd, 1H, *J* = 10.3 Hz), 5.56 (dd, 1H, *J* = 17.1, 0.9 Hz), 5.92 (dd, 1H, *J* = 17.0, 10.3 Hz), 7.25-7.28 (m, 3H), 7.37-7.39 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 22.0, 23.4, 24.7, 25.9, 28.6, 29.0, 32.5, 40.6, 78.5, 80.8, 90.0, 92.8, 116.2, 124.0, 127.5, 128.2, 131.5, 138.5, 168.9; IR (NaCl, neat) *v*: 2240, 1744 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{25}H_{31}O_2$: 363.2324, found: 363.2338.

3-(cyclopentylethynyl)-9-phenylnon-1-en-8-yn-3-yl acetate (184n)



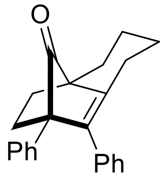
Yield 70%; Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.48-1.69 (m, 10H), 1.76-1.89 (m, 3H), 1.97-2.03 (m, 4H), 2.41 (t, 2H, *J* = 6.5 Hz), 2.64-2.68 (m, 1H), 5.23 (dd, 1H, *J* = 10.3, 1.0 Hz), 5.54 (dd, 1H, *J* = 17.0, 1.0 Hz), 5.91 (dd, 1H, *J* = 18.7, 10.3 Hz), 7.24-7.26 (m, 3H), 7.35-7.38 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 19.3, 21.9, 23.4, 24.9, 28.6, 30.2, 33.8, 40.6, 77.0, 78.5, 80.9, 90.0, 93.0, 116.1, 124.1, 127.5, 128.2, 131.5, 138.5, 168.8; IR (NaCl, neat) *v*: 2240, 1746 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{24}H_{25}O_2$: 349.2101, found: 349.2102.

General Experimental Procedure for Phosphine Gold(I)-Catalyzed Carbocyclization of 184a-n:



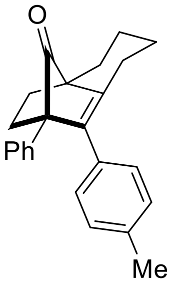
A 10 mL round-bottomed flask was charged with 1,8-diynyl vinyl ester **184** (0.2 mmol) and $Ph_3PAuNTf_2$ (0.01 mmol) followed by the addition of 1,2-dichloroethane (2mL). The resulting mixture was then stirred at room temperature under open-to-air conditions. On completion, The solvent of the mixture was removed under reduced pressure and purified by flash column chromatography on silica gel (eluent: *n*hexane: EtOAc 10:1) to afford product **186**.

1,2-diphenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186a)



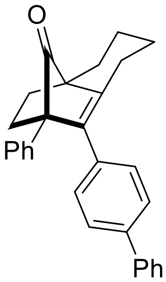
White solid; m.p: 170-172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.39-1.56 (m, 2H), 1.70-1.74 (m, 1H), 1.74-1.92 (m, 4H), 2.06-2.24 (m, 3H), 2.57-2.64 (m, 1H), 2.85-2.90 (m, 1H), 6.90 (m, 2H), 7.04-7.15 (m, 6H), 7.19-7.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.5, 23.9, 24.0, 24.1, 28.0, 29.3, 52.4, 60.7, 126.6, 126.6, 127.7, 127.9, 128.6, 129.3, 134.7, 135.8, 139.9, 140.6, 205.7; IR (NaCl, neat) *v*: 1172 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{23}H_{23}O$: 315.1702, found: 315.1702.

2-phenyl-1-(p-tolyl)-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186b)



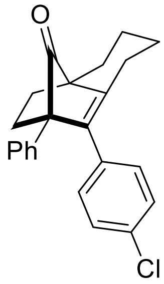
White solid; m.p: 176-178 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.42-1.53 (m, 2H), 1.70-1.73 (m, 1H), 1.79-1.89 (m, 4H), 2.05-2.12 (m, 2H), 2.20 (s, 3H), 2.22-2.60 (m, 1H), 2.85-2.89 (m, 1H), 6.80 (d, 2H, *J* = 8.4 Hz), 6.90 (d, 2H, *J* = 8.4 Hz), 7.13-7.16 (m, 3H), 7.21-7.25 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 21.2, 22.5, 23.9, 24.0, 24.1, 28.0, 29.3, 52.3, 60.6, 126.6, 127.9, 128.4, 128.5, 129.3, 131.7, 135.9, 136.2, 139.8, 140.1, 205.8. IR (NaCl, neat) *v*: 1773 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{24}H_{25}O$: 329.1905, found: 329.1909.

1-([1,1'-biphenyl]-4-yl)-2-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186c)



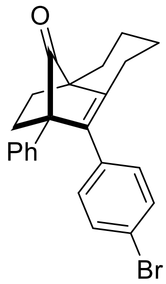
Yellow solid; m.p: 154-156 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.48-1.52 (m, 2H), 1.72-1.83 (m, 1H), 1.85-1.92 (m, 4H), 2.08-2.15 (m, 2H), 2.15-2.24 (m, 1H), 2.63-2.67 (m, 1H), 2.94 (m, 1H), 6.99 (d, 2H, *J* = 8.4 Hz) 7.13-7.20 (m, 3H), 7.22-7.30 (m, 4H), 7.32-7.38 (m, 4H), 7.47-7.49 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.5, 23.9, 24.0, 24.2, 28.0, 29.4, 52.4, 60.7, 76.7, 77.0, 77.4, 126.4, 126.7, 126.8, 127.2, 128.0, 128.7, 129.0, 129.3, 133.7, 135.8, 139.1, 139.5, 140.6, 140.9, 205.7; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{29}H_{27}O$: 391.2062, found: 391.2057.

1-(4-chlorophenyl)-2-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186d)



White solid; m.p: 174-176 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.45-1.57 (m, 2H), 1.74-1.78 (m, 1H), 1.85-1.91 (m, 4H), 1.93-2.23 (m, 3H), 2.61-2.63 (m, 1H), 2.83-2.87 (m, 1H), 6.86-6.88 (m, 2H), 7.08-7.11 (m, 2H), 7.16-7.21 (m, 3H), 7.25-7.28 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.4, 23.8, 23.9, 24.1, 28.0, 29.3, 52.4, 60.5, 76.7, 77.0, 77.4, 126.8, 128.0, 128.1, 129.2, 129.8, 132.4, 133.1, 135.5, 138.8, 141.3, 205.4; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{23}H_{22}{}^{35}ClO$: 349.1359, found: 349.1361.

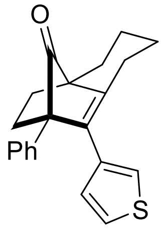
1-(4-bromophenyl)-2-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186e)



White solid; m.p: 188-190 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.42-1.54 (m, 2H), 1.71-

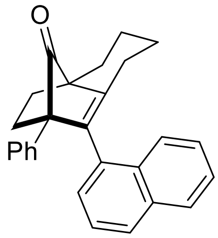
1.74 (m, 1H), 1.81-1.92 (m, 4H), 2.02-2.20 (m, 3H), 2.57-2.60 (m, 1H), 2.81 (m, 1H), 6.78 (d, 2H, *J* = 8.4 Hz), 7.12-7.18 (m, 3H), 7.20-7.25 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.4, 23.8, 23.9, 24.1, 28.0, 29.3, 52.5, 60.5, 76.7, 77.0, 77.4, 120.6, 126.8, 128.1, 129.2, 130.2, 131.0, 133.5, 135.5, 138.8, 141.4, 205.4; IR (NaCl, neat) *v*: 1773 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{23}H_{22}{}^{81}BrO$: 395.0834, found: 395.0821.

2-phenyl-1-(thiophen-3-yl)-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186f)



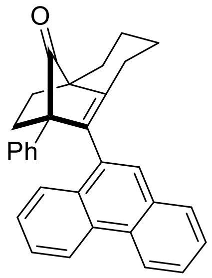
White solid; m.p 170-172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.42-1.53 (m, 2H), 1.70-1.74 (m, 1H), 1.80-1.89 (m, 4H), 1.95-2.06 (m, 1H), 2.08-2.09 (m, 1H), 2.51-2.53 (m, 1H), 2.88-2.93 (m, 1H), 6.63 (dd, 2H, *J* = 3.0, 1.6 Hz), 7.04 (dd, 1H, *J* = 4.0, 3.0 Hz), 7.21-7.29 (m, 3H), 7.30-7.32 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 22.3, 23.9, 24.0, 25.0, 27.5, 29.7, 52.2, 60.2, 76.7, 77.3, 122.8, 124.1, 127.0, 127.8, 128.1, 129.3, 134.5, 134.9, 136.2, 140.1, 205.9; IR (NaCl, neat) *v*: 1776 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for C321.1313, found: 321.1319.

1-(naphthalen-1-yl)-2-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186g)



White solid; m.p: 132-134 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.50-1.78 (m, 3H), 1.80-1.81 (m, 3H), 1.91-2.01 (m, 5H), 2.10-2.27 (m, 3H), 2.30-2.32 (m, 3H), 6.95-7.10 (m, 4H), 7.10-7.23 (m, 5H), 7.41-7.46 (m, 3H), 7.47-7.48 (m, 1H), 7.55-7.73 (m, 1H), 7.94-7.96 (m, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.6, 23.7, 24.1, 25.0, 28.9, 29.1, 52.8, 61.7, 76.7, 77.1, 77.4, 124.8, 124.9, 125.4, 125.4, 125.6, 125.6, 126.0, 126.2, 126.5, 126.6, 127.3, 127.6, 127.7, 128.3, 128.3, 128.6, 129.0, 131.0, 133.1, 133.5, 135.7, 137.4, 142.0, 143.2; IR (NaCl, neat) *v*: 1773 cm^{-1}; HRMS (ESI) calcd. for $C_{27}H_{25}O$: 365.1905, found: 365.1901.

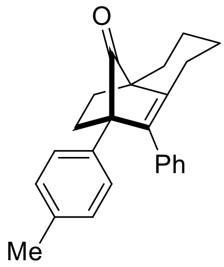
1-(phenanthren-9-yl)-2-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186h)



Pale yellow solid; m.p: 179-181 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.40-1.60 (m, 4H), 1.74-1.84 (m, 1H), 1.93-2.02 (m, 3H), 2.24-2.29 (m, 2H), 2.38-2.50 (m, 1H), 2.68-2.75 (m, 1H), 6.91-7.01 (m, 3H), 7.18-7.20 (m, 2H), 7.28-7.30 (m, 1H), 7.47-7.61 (m, 4H), 7.67-7.69 (m, 1H), 8.02-8.04 (m, 1H), 8.55-8.61 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz):

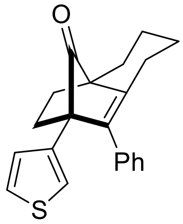
22.5, 23.7, 24.1, 25.0, 29.1, 29.3, 52.8, 61.6, 122.4, 122.8, 126.1, 126.3, 126.4, 126.5, 126.6, 127.6, 127.7, 128.4, 128.5, 129.0, 129.3, 129.8, 130.2, 131.1, 131.9, 135.7, 137.4, 143.7, 205.3; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{31}H_{27}O$: 415.2096, found: 415.2080.

1-phenyl-2-(p-tolyl)-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186i)



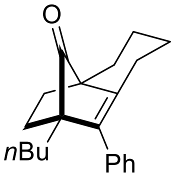
White solid; m.p: 158-160 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.42-1.54 (m, 3H), 1.72-1.74 (m, 1H), 1.81-1.89 (m, 3H), 2.04-2.23 (m, 3H), 2.24 (s, 3H), 2.58-2.60 (m, 1H), 2.86-2.90 (m, 1H), 6.92-6.95 (m, 2H), 7.02-7.11 (m, 4H), 7.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 21.1, 22.5, 23.9, 24.0, 24.0, 28.0, 29.3, 52.3, 60.4, 76.7, 77.0, 77.3, 126.5, 127.7, 128.6, 128.7, 129.1, 132.6, 134.8, 136.1, 140.0, 140.6, 206.1; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) $[M + H]^+$ calcd. for $C_{24}H_{25}O$: 329.1905, found: 329.1910.

1-phenyl-2-(thiophen-3-yl)-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186j)



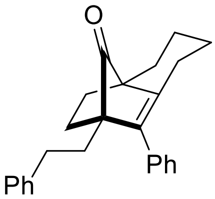
White solid; m.p: 170-172 °C; ^1H NMR ($CDCl_3$, 400 MHz): δ ^1H NMR ($CDCl_3$, 400 MHz): δ 1.40-1.54 (m, 2H), 1.70-1.80 (m, 1H), 1.81-1.89 (m, 4H), 2.05-2.12 (m, 2H), 2.20-2.50 (m, 1H), 2.80-2.84 (m, 1H), 6.79 (dd, 1H, *J* = 5.0, 1.6 Hz), 6.91-6.94 (m, 2H), 7.11-7.26 (m, 5H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.4, 23.7, 24.0, 29.1, 29.9, 30.9, 52.0, 57.5, 122.6, 124.8, 126.8, 127.8, 128.4, 128.5, 134.5, 137.1, 139.3, 140.3, 205.7; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{21}OS$: 321.1313, found: 321.1305.

2-butyl-1-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186k)



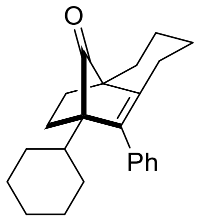
Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.71 (t, 3H, *J* = 7.2 Hz), 1.01-1.26 (m, 2H), 1.27-1.44 (m, 5H), 1.57-1.76 9m, 7H), 1.93-1.97 (m, 2H), 1.99-2.09 (m, 1H), 2.62-2.66 (m, 1H), 7.13-7.15 (m, 2H), 7.23-7.27 (m, 1H), 7.30-7.34 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 13.8, 22.5, 23.4, 23.57, 23.62, 26.4, 26.8, 29.0, 29.5, 51.1, 55.3, 126.9, 128.2, 131.5, 135.7, 139.4, 140.4; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{21}H_{27}O$: 295.2062, found: 295.2056.

2-phenethyl-1-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186l)



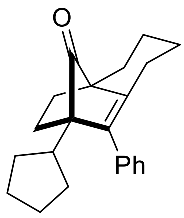
Yellow oil; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.26-1.42 (m, 3H), 1.63-1.79 (m, 4H), 1.84-1.93 (m, 1H), 1.94-2.06 (m, 5H), 2.25 (dt, 1H, *J* = 13.0, 4.5 Hz), 2.60 (dt, 1H, *J* = 13.0, 5.4 Hz), 2.69-2.74 (m, 1H), 6.88 (d, 2H, *J* = 7.2 Hz), 7.08-7.10 (m, 1H), 7.14-7.20 (m, 2H), 7.21-7.30 (m, 2H), 7.34-7.36 (m, 1H), 7.37-7.38 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.5, 23.6, 24.0, 29.1, 29.7, 30.0, 31.1, 51.3, 55.3, 76.8, 77.1, 77.4, 125.5, 127.1, 128.2, 128.2, 128.4, 135.6, 138.8, 140.7, 143.1, 208.8; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{25}H_{27}O$: 343.2010, found: 343.2011.

2-cyclohexyl-1-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186m)



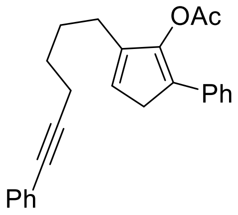
White solid; m.p: 120-122 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 0.91-1.05 (m, 1H), 1.07-1.10 (m, 2H), 1.24-1.38 (m, 3H), 1.41-1.79 (m, 12H), 1.80-1.88 (m, 2H), 1.90-1.96 (m, 2H), 2.18-2.19 (m, 1H), 2.57-2.61 (m, 1H), 7.14-7.16 (m, 2H), 7.24-7.30 (m, 1H), 7.32-7.34 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.5, 23.4, 23.5, 24.0, 26.5, 26.9, 27.4, 27.8, 27.9, 28.7, 36.1, 51.1, 58.4, 76.7, 77.0, 77.3, 126.8, 128.1, 128.3, 136.7, 139.7, 140.7, 208.8; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{23}H_{29}O$: 321.2218, found: 321.2203.

2-cyclopentyl-1-phenyl-3,4,5,6,7,8-hexahydro-2H-2,4a-methanonaphthalen-9-one (186n)



White solid; m.p: 118-120 °C; ^{1}H NMR (CDCl$_3$, 400 MHz): δ 1.23-1.47 (m, 6H), 1.49-1.75 (m, 9H), 1.80-2.13 (m, 4H), 2.24-2.33 (m, 1H), 2.56-2.60 (m, 1H), 7.13-7.15 (m, 2H), 7.22-7.26 (m, 1H), 7.30-7.33 (m, 2H); ^{13}C NMR (CDCl$_3$, 100 MHz): 22.5, 23.5, 23.5, 24.0, 26.1, 26.2, 28.3, 28.5, 28.7, 28.9, 37.1, 51.2, 58.6, 126.8, 128.1, 128.4, 136.4, 140.3, 140.4, 208.1; IR (NaCl, neat) *v*: 1775 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. for $C_{22}H_{27}O$: 307.2020, found: 307.2014.

2-phenyl-5-(6-phenylhex-5-yn-1-yl)cyclopenta-1,4-dien-1-yl acetate (185a)



Yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.65-1.69 (m, 2H), 1.70-1.77 (m, 2H), 2.22-2.26 (m, 2H), 2.27 (s, 3H), 2.44 (t, 2H, *J* = 7.2 Hz), 3.33 (d, 2H, *J* = 1.6 Hz), 6.11 (t, 1H, *J* = 1.6 Hz), 7.15-7.19 (m, 1H), 7.21-7.32 (m, 5H), 7.38-7.40 (m, 2H), 7.44-7.47 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): 19.4, 20.9, 26.4, 27.0, 28.5, 38.2, 81.0, 90.2, 124.1, 125.3, 126.2, 126.7, 127.6, 128.3, 128.5, 128.6, 131.6, 134.4, 143.8, 148.0, 168.9; IR (NaCl, neat) *v*: 2130, 1765 cm^{-1}; HRMS (ESI) [M + H]$^+$ calcd. For $C_{25}H_{25}O_2$: 357.1810, found: 357.1809.

Chapter VI: References

1. (a) Fei, X.; Jo, M.; Lee, B.; Han, S.-B.; Lee, K.; Jung, J. K.; Seo, S.-Y.; Kwak, Y.-S. *Bioorg. Med. Lett.* **2014**, *24*, 2062. (b) Young, I. S.; Thornton, P. D.; Thompson, A. *Nat. Prod. Rep.* **2010**, *27*, 1801. (c) Gupton, J. T. *Top. Heterocycl. Chem.* **2006**, *2*, 53. (d) Fürstner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3582. (e) Whiting, D. A. *Nat. Prod. Rep.* **2001**, *18*, 583. (f) Rudi, A.; Evan, T.; Aknin, M.; Kashman, Y. *J. Nat. Prod.* **2000**, *63*, 832. (g) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry II*; Katritzky A. R.; Rees C. W.; Scriven E. F. V., Eds.; Elsevier: Oxford, 1996, pp 119. (h) Donnelly D. M. X.; Meegan, M. J. *Comprehensive Heterocyclic Chemistry*; Katritzky A. R.; Rees C. W.; Eds.; Pergamon, Oxford, 1984, vol. 4, pp 657.

2. Selected examples, see: (a) Tehrani, K. A.; Kimpe, N. D. *Curr. Org. Chem.* **2009**, *13*, 854. (b) Mitchinson, A.; Nadin, A. *J. Chem, Soc., Perkin Trans. 1*, **1999**, 2553. (c) Kametani, T.; Fukumoto, K. *Heterocycles* **1975**, *3*, 931.

3. Knorr, L. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 1635.

4. Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167.

5. For selective reviews, see: (a) Yamamoto, Y.; *Chem. Soc. Rev.* **2014**, *43*, 1575. (b) Candeias, N. R.; Branco, L. C.; Gois, P. M. P.; Afonso, C. A. M.; Trindade, A. F. *Chem. Rev.* **2009**, *109*, 2703. (c)Yamamoto, Y.; Nakamura, I. *Chem. Rev.* **2004**, *104*, 2127. (d) Montgomery, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 3890.

6. Bond, G. C.; Sermon, P. A.; Webb, G.; Buchanan, D. A.; Wells, P. B. *J. Chem. Soc. Chem. Commun.* **1973**, 444.

7. For selected reviews on gold catalysis, see: (a) Hashmi, A. S. K. *Acc. Chem. Res.* **2014**, *47*, 864. (b) López, F.; Mascareñas, J. L. *Beilstein J. Org. Chem.* **2013**, *9*, 2250. (c)

Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. (d) Garayalde, D.; Nevado, C. *ACS Catal.* **2012**, *2*, 1462. (e) Rudolph, M.; Hashmi, A. S. K. *Chem. Commun.* **2011**, *47*, 6536. (f) Bandini, M. *Chem. Soc. Rev.* **2011**, *40*, 1358. (g) Shapiro, N. D.; Toste, F. D. *Synlett* **2010**, 675. (h) Hashmi, A. S. K. *Pure Appl. Chem.* **2010**, *82*, 657. (i) Hashmi, A. S. K.; Rudolph, M.; *Chem. Soc. Rev.* **2008**, *37*, 1766. (j) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (k) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (l) Yamamoto, Y.; Lipshutz, B. H. *Chem. Rev.* **2008**, *108*, 2793. (m) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (n) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Commun.* **2007**, 333. (o) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (p) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. (q) Echavarren, A. M.; Nevado, C.; *Chem. Soc. Rev.* **2004**, *33*, 431. (r) Hashmi, A. S. K. *Gold Bull.* **2003**, *36*, 3.

8. (a) Leyva-Pérez, A.; Corma, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 614; (b) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (c) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (d) Pyykkö, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 4412. (e) Schwerdtfeger, P. *Heteroat. Chem.* **2002**, *13*, 578. (f) Bartlett, N. *Gold Bull.* **1998**, *31*, 22. (g) Pyykkö, P.; Desclaux, J. P. *Acc. Chem. Res.* **1979**, *12*, 276.

9. (a) Schwerdtfeger, P.; Hermann, H, L.; Schmidbaur, H. *Inorg. Chem.* **2003**, *42*, 1334. (b) Bayler, A.; Schier, A.; Bowmaker, G. A.; Schmidbaur, H. *J. Am. Chem. Soc.* **1996**, *118*, 7006.

10. (a) Wang, D.; Cai, R.; Sharma, S.; Jirak, J.; Thummanapelli, S. K.; Akhmedov, N. G.; Zhang, H.; Liu, X.; Petersen, J. L.; Shi, X. *J. Am. Chem. Soc.* **2012**, *134*, 9012. (b) Patrick, S. R.; Boogaerts, I. I. F.; Gaillard, S.; lawin, A. M. Z.; Nolan, S. P. *Beilstein J. Org. Chem.* **2011**, *7*, 892.

11. Mukaiyama, T. *Challenges in Synthetic Organic Chemistry*, translation edited by Baldwin, J. E.; New York: Oxford University Press, 1990.

12. (a) Alcaide, B.; Almendros, P. *Acc. Chem. Res.* **2014**, *47*, 939. (b) Rodríguez, F.; Fañanás, F. J. *Synlett* **2013**, 1757.

13. Kang, J.-E.; Kim, H.-B.; Lee, J.-W.; Shin, S. *Org. Lett.* **2006**, *8*, 3537.

14. Hashmi, A. S. K.; Rudolph, M.; Schymura, S.; Visus, J.; Frey, W. *Eur. J. Org. Chem.* **2006**, 4905.

15. Ritter, S.; Horino, Y.; Lex, J.; Schmalz, H.-G. *Synlett* **2006**, 3309.

16. Yeom, H.-S.; Lee, E.-S.; Shin, S. *Synlett* **2007**, 2292.

17. (a) Seregin, I. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2006**, *128*, 12050. (b) Seregin, I. V.; Schammel, A. W.; Gevorgyan, V. *Tetrahedron* **2008**, *64*, 6876.

18. Xia, Y.; Dudnik, A. S.; Li, Y.; Gevorgyan, V. *Org. Lett.* **2010**, *12*, 5538.

19. Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Liang, Y.-M. *Adv. Synth. Catal.* **2008**, *350*, 243.

20. Lu, Y.; Fu, X.; Chen. H.; Du, X.; Jia, X.; Liu, Y. *Adv. Synth. Catal.* **2009**, *351*, 129.

21. Barluenga, J.; Fernández-Rodríguez, M. Á.; García-García, P.; Aguilar, E. *J. Am. Chem. Soc.* **2008**, *130*, 2764.

22. Aponick, A.; Li, C.-Y.; Malinge, J.; Marques, E. F. *Org. Lett.* **2009**, *11*, 4624.

23. Egi, M.; Azechi, K.; Akai, S. *Org. Lett.* **2009**, *11*, 5002.

24. Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4619.

25. Cera, G.; Piscitelli, S.; Chiarucci, M.; Fabrizi, G.; Goggiamani, A.; Ramón, R. S.; Nolan, S. P.; Bandini, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9891.

26. Chiarucci, M.; Matteucci, E.; Cera, G.; Fabrizi, G.; Bandini, M. *Chem.-Asian J.* **2013**, *8*, 1776.

27. Chiarucci, M.; Mocci, R.; Syntrivanis, L.-D.; Cera, G.; Mazzanti, A. l.; Bandini, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 10850.

28. Wang, T.; Shi, S.; Pflästerer, D.; Rettenmeier, E.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Chem.-Eur. J.* **2014**, *20*, 292.

29. For selected reviews, see references 7k, 7n, 7o and 7q, and (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2008**, *47*, 6754. (b) Ma, S.; Yu, S.; Gu, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 200.

30. Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem.; Int. Ed.* **2004**, *43*, 2402.

31. Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. *J. Am. Chem. Soc.* **2004**, *126*, 8654.

32. Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2004**, *126*, 11806.

33. Grisé. C. M.; Barriault, L. *Org. Lett.* **2006**, *8*, 5905.

34. Taduri, B. P.; Sohel, S. M. A.; Cheng, H.-M.; Lin, G.-Y.; Liu, R.-S. *Chem. Commun.* **2007**, 2530.

35. Li, G.; Liu, Y. *J. Org. Chem.* **2010**, *75*, 2903.

36. Liu, Y.; Xu, W.; Wang, X. *Org. Lett.* **2010**, *12*, 1448.

37. (a) Cera, G.; Crispino, P.; Monari, M.; Bandini, M. *Chem. Commun.* **2011**, *47*, 7803. (b) Cera, G.; Chiarucci, M.; Mazzanti, A.; Mancinelli, M.; Bandini, M. *Org. Lett.* **2012**, *14*, 1350.

38. (a) Shiroodi, R. K.; Gevorgyan, V. *Chem. Soc. Rev.* **2013**, *42*, 4991. (b) Wang, S.; Zhang, G.; Zhang, L. *Synlett* **2010**, 692. (c) Marion, N.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2750. (d) Marco-Contelles, J.; Soriano, E. *Chem.-Eur. J.* **2007**, *13*, 1350.

39. (a) Miki, K.; Ohe, K.; Uemura, S. *J. Org. Chem.* **2003**, *68*, 8505. (b) Miki, K.; Ohe, K.; Uemura, S. *Tetrahedron Lett.* **2003**, *44*, 2019.

40. Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002.

41. Zhao, J.; Hughes, C. O.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 7436.

42. Oh, C. H.; Kim, A.; Park, W.; Park, D. I.; Kim, N. *Synlett* **2006**, 2781.

43. Oh, C. H.; Kim, A. *New J. Chem.* **2007**, *31*, 1719.

44. (a) Luo, T.; Schreiber, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 8250. (b) Luo, T.; Schreiber, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 5667.

45. Zhang, D.-H.; Yao, L.-F.; Wei, Y.; Shi, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 2583.

46. Lebœuf, D.; Simonneau, A.; Aubert, C.; Malacria, M.; Gandon, V.; Fensterbank, L. *Angew. Chem., Int. Ed.* **2011**, *50*, 6868.

47. Rao, W.; Koh, M. J.; Kothandaraman, P.; Chan, P. W. H. *J. Am. Chem. Soc.* **2012**, *134*, 10811.

48. Oh, C. H.; Kim, J. H.; Oh, B. K.; Park, J. R.; Lee, J. H. *Chem.-Eur. J.* **2013**, *19*, 2592.

49. Oh, C. H.; Kim, J. H.; Piao, L.; Yu, J.; Kim, S. Y. *Chem.–Eur. J.* **2013**, *19*, 10501.

50. Rao, W.; Koh, M. J.; Li, D.; Hirao, H.; Chan, P. W. H. *J. Am. Chem. Soc.* **2013**, *135*, 7926.

51. Lauterbach, T.; Gatzweiler, S.; Nösel, P.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Adv. Synth. Catal.* **2013**, *355*, 2481.

52. Lauterbach. T.; Ganschow, M.; Hussong, M. W.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Adv. Synth. Catal.* **2014**, *356*, 680.

53. Rao, W.; Chan, P. W. H. *Chem. Eur. J.* **2014**, *20*, 713.

54. For selected examples of studies probing the mechanisms of gold-catalyzed organic reactions, see: (a) Hansmann, M. M.; Rominger, F.; Hashmi, A. S. K. *Chem. Sci.* **2013**, *4*, 1552. (b) Klatt, G.; Xu, R.; Pernpointner, M.; Molinari, L.; Hung, T. Q.; Rominger, F.; Hashmi, A. S. K.; Köppel, H. *Chem.-Eur. J.* **2013**, *19*, 3954. (c) Hansmann, M. M.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 2593. (d) Gómez-Suárez, A.; Dupuy, S.; Slawin, A. M. Z.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2013**, *52*, 938.(e) Wang, W.; Hammond, G. B.; Xu, B. *J. Am. Chem. Soc.* **2012**, *134*, 5697. (f) Dupuy, S.; Crawford, L.; Bühl, M.; Slawin, A. M. Z.; Nolan, S. P. *Adv. Synth. Catal.* **2012**, *354*, 2380. (g) López-Carrillo, V.; Huguet, N.; Mosquera, Á.; Echavarren, A. M. *Chem.-Eur. J.* **2011**, *17*, 10972. (h) Pérez-Galán, P.; Herrero-Gómez, E.; Hog, D. T.; Martin, N. J. A.; Maseras, F.; Echavarren, A. M. *Chem. Sci.* **2011**, *2*, 141. (i) Egorova, O. A.; Seo, H.; Kim, Y.; Moon, D.; Rhee, Y. M.; Ahn, K. H. *Angew. Chem., Int. Ed.* **2011**, *50*, 11446. (j) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2010**, *49*, 5232. (k) Wang, Z. J.; Benitez, D.; Tkatchouk, E.; Goddard III, W. A.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 13064. (l) Echavarren, A. M. *Nature Chem.* **2009**, *1*, 431. (m) Mauleón, P.;

Krinsky, J. L.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 4513. (n) Liu, L.-P.; Xu, B.; Mashuta, M. S.; Hammond, G. B. *J. Am. Chem. Soc.* **2008**, *130*, 17642.

55. For an illustrative review on carbodeauration process, see: a) Adcock, H. V.; Davies, P. W. *Synthesis* **2012**, 3401.

56. (a) Park, S. R.; Kim, C.; Kim, D.-G.; Thrimurtulu, N.; Yeom, H.-S.; Jun, J.; Shin, S.; Rhee, Y. H. *Org. Lett.* **2013**, *15*, 1166. (b) Hashmi, A. S. K.; Lothschütz, C.; Döpp, R.; Ackermann, M.; Becker, J. D. B.; Rudolph, M.; Scholz, C.; Rominger, F. *Adv. Synth. Catal.* **2012**, *354*, 133. (c) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2006**, *45*, 4473.

57. Zhang, L. *J. Am. Chem. Soc.* **2005**, *127*, 16804.

58. Dubé P.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 12062.

59. (a) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Chem.-Asian. J.* **2008**, *3*, 285. (b) Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 2284.

60. Yeon, H.-S.; So, E.; Shin, S. *Chem.-Eur. J.* **2011**, *17*, 1764.

61. Rao, W.; Susanti, D.; Chan, P. W. H. *J. Am. Chem. Soc.* **2011**, *133*, 15248.

62. For the only other examples of a heteroatom- or transmetalation-triggered deaurative processes in gold catalysis, see: (a) Chen, Y.; Chen, M.; Liu, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 6181. (b) Hopkinson, M. N.; Giuffredi, G. T.; Gee, A. D.; Gouverneur, V. *Synlett* **2010**, 2737. (c) Schuler, M.; Silva, F.; Bobbio, C.; Tessier, A.; Gouverneur, V. *Angew. Chem., Int. Ed.* **2008**, *47*, 7927. (d) Nakamura, I.; Sato, T.; Terada, M.; Yamamoto, Y. *Org. Lett.* **2007**, *9*, 4081.

63. For selected examples, see ref 61, and: (a) Rao, W.; Sally; Koh, M. J.; Chan, P. W. H. *J. Org. Chem.* **2013**, *78*, 3183. (b) Rao. W.; Koh, M. J.; Kothandaraman, P.; Chan, P.

W. H. *J. Am. Chem. Soc.* **2012**, *134*, 10811. (c) Kothandaraman, P.; Huang, C.; Susanti, D.; Rao, W.; Chan, P. W. H. *Chem.-Eur. J.* **2011**, *17*, 10081. (d) Kothandaraman, P.; Mothe, S. R.; Toh, S. S. M.; Chan, P. W. H. *J. Org. Chem.* **2011**, *76*, 7633. (e) Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem. Int. Ed.* **2010**, *49*, 4619.

64. (a) Barabé, F.; Levesque, P.; Korobkov, L.; Barriault, L. *Org. Lett.* **2011**, *13*, 5580. (b) López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292. (c) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721. (d) Richard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704.

65. For selected examples of sulfonyl group migrations mediated by other Lewis and Brønsted acids or a base, see: (a) Yu, X.; Xin, X.; Wan, B.; Li, X. *J. Org. Chem.* **2013**, *78*, 4895. (b) Prasad, B.; Adepu, R.; Sandra, S.; Rambabu, D.; Krishna, G. R.; Reddy, C. M.; Deora, G. S.; Misra, P., Pal, M. *Chem. Commun.* **2012**, *48*, 10434. (c) Xin, X.; Wang, D.; Li, X.; Wan, B. *Angew. Chem. Int. Ed.* **2012**, *51*, 1693. (d) Lee, Y. T.; Chung, Y. K. *J. Org. Chem.* **2008**, *73*, 4698. (e) Weatherhead-Kloster, R. A.; Corey, E. J. *Org. Lett.* **2006**, *8*, 171. (f) Matsumoto, S.; Kishimoto, T.; Ogura, K. *Chem. Lett.* **2002**, 134.

66. CCDC 918205 (**E**), 918206 (**171b**) and 918207 (**172b**) contain the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

67. (a) Butler, M. S. *Nat. Prod. Rep.* **2008**, *25*, 475. (b) Yet, L. *Chem. Rev.* **2003**, *103*, 4283. (c) Rappoport, Z. *The Chemistry of Phenols*; Wiley-VCH: Weinheim, 2003. (d) Fiegel, H.; Voges, H. W.; Hamamoto, T.; Umemura, S.; Iwata, T.; Miki, H.; Fujita, Y.; Buysch, H. J.; Garbe, D.; Paulus, W. *Phenol Derivatives in Ullmann's Encyclopedia of Industrial Chemistry*; Wiley-VCH: New York, 2002. (e) Höller, U.; König, G. M.;

Wright, A. D. *J. Nat. Prod.* **1999**, *62*, 114. (f) Tyman, J. H. P. *Synthetic and Natural Phenols*; Elsevier: New York, 1996.

68. Selected recent examples: (a) Liu, W.; Ackermann, L. *Org. Lett.* **2013**, *15*, 3484. (b) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. *Org. Lett.* **2013**, *15*, 3366. (c) Shan, G.; Han, X. Lin, Y.; Yu, S.; Rao, Y. *Org. Biomol. Chem.* **2013**, *11*, 2318. (d) Yang, F.; Ackermann, L. *Org. Lett.* **2013**, *15*, 718. (e) Lee, D.-H.; Kwon, K.-H, Yi, C. S. *J. Am. Chem. Soc.* **2012**, *134*, 7325. (f) Thirunavukkarasu, V. S.; Ackermann, L. *Org. Lett.* **2012**, *14*, 6206. (g) Thirunavukkarasu, V. S.; Hubrich, J.; Ackermann, L. *Org. Lett.* **2012**, *14*, 4210. (h) Yang, Y.; Lin, Y.; Rao, Y. *Org. Lett.* **2012**, *14*, 2874.

69. For examples, see: refs 24, 47, 50 and 63.

70. Review on gold-catalyzed benzannnulations: Patil, N. T.; Yamamoto, Y. *Arkivoc* **2007**, 6.

71. For selected examples on gold-catalyzed benzannulation, see ref. 30, and: (a) Hashmi, A. S. K.; Yang, W.; Rominger, F. *Chem.-Eur. J.* **2012**, *18*, 6576. (b) Gudla, V.; Balamurugan, R. *J. Org. Chem.* **2011**, *76*, 9919. (c) Liu, L.-P.; Hammond, G. B. *Org. Lett.* **2010**, *12*, 4640. (d) Balamurugan, R.; Gudla ,V. *Org. Lett.* **2009**, *11*, 3116. (e) Gorin, D. J.; Watson, I. D. G.; Toste, D. *J. Am. Chem. Soc.* **2008**, *130*, 3736. (f) Dudnik, A. S., Schwier, T.; Gevorgyan, V. *Org. Lett.* **2008**, *10*, 1465. (g) Sato, K.; Asao, N.; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 9877. (h) Asao, N., Sato, K.; Menggenbateer; Yamamoto, Y. *J. Org. Chem.* **2005**, *70*, 3682. (i) Asao, N.; Nogami, T.; Lee, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2003**, *125*, 10921. (j) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12650.

72. For gold-catalyzed phenol syntheses: (a) Hashmi, A. S. K.; Häffner, T.; Rudolph, M.; Rominger, F. *Chem.-Eur. J.* **2011**, *17*, 8195. (b) Chen, Y.; Yan, W.; Akhmedov, N. G.; Shi, X. *Org. Lett.* **2010**, *12*, 344. (c) Hashmi, A. S. K.; Rudolph, M.; Bats, J. W.; Frey,

W.; Rominger, F.; Oeser, T. *Chem.-Eur. J.* **2008**, *14*, 6672. (d) Hashmi, A. S. K.l Salathé, R.; Frey, W. *Chem.-Eur. J.* **2006**, *12*, 6996. (e) Hashmi, A. S. K.; Weyrauch, J. P.; Kurpejović, E.; Frost, T. M.; Miehlich, B.; Frey, W.; Bats, J. W. *Chem.-Eur. J.* **2006**, *12*, 5806. (f) Hashmi, A. S. K.; Haufe, P.; Schmid, C.; Nass, A. R.; Frey, W. *Chem.-Eur. J.* **2006**, *12*, 5376. (g) Hashmi, A. S. K.; Frost, T. M.; Bats, J. W. *J. Am. Chem. Soc.* **2000**, *122*, 11553.

73. Reviews on gold-catalyzed reactions of unsaturated alcohols: (a) Cera, G.; Chiarucci, M.; Bandini, M. *Pure Appl. Chem.* **2012**, *84*, 1673. (b) Bandini, M.; Cera, G.; Chiarucci, M. *Synthesis* **2012**, 504. (c) Biannic, B.; Aponick, A. *Eur. J. Org. Chem.* **2011**, 6605. (d) Emer, E.; Sinisi, R.; Capdevila, M. G.; Petruzziello, D.; De Vincentiis, F.; Cozzi, P. G. *Eur. J. Org. Chem.* **2011**, 647. (e) Bandini, M.; Tragni, M. *Org. Biomol. Chem.* **2009**, *7*, 1501. (f) Muzart, J. *Tetrahedron* **2008**, *64*, 5815.

74. Review on hydroalkylation reactions, see: (a) Dénés, F.; Pérez-Luna, A.; Chemla, F. *Chem. Rev.* **2010**, *110*, 2366.

75. For selected examples on gold-catalyzed hydroalkylation reaction, see: (a) Guérinot, A.; Fang, W.; Sircoglou, M.; Bour, C.; Bezzenine-Lafollée, Gandon, V. *Angew. Chem. Int. Ed.* **2013**, *52*, 5848. (b) Persich, P.; Llaveria, J.; Lhermet, R.; de Haro, T.; Stade, R.; Kondoh, A.; Fürstner, A. *Chem.-Eur. J.* **2013**, *19*, 13047. (c) Boutier, A.; Kammerer-Pentier, C.; Krause, N.; Prestat, G.; Poli, G. *Chem.-Eur. J.* **2012**, *18*, 3840. (d) Xiao, Y.-P.; Liu, X.-Y.; Che, C.-M. *Angew. Chem., Int. Ed.* **2011**, *50*, 4937. (e) Jurberg, I. D.; Odabachuan, Y.; Gagosz, F. *J. Am. Chem. Soc.* **2010**, *132*, 3543. (f) Nguyen, R.-V.; Yao, X.-Q.; Bohle, S.; Li, C.-J. *Org. Lett.* **2005**, *7*, 673.

76. CCDC 967743 (**178a**) contains the supplementary crystallographic data. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

77. For review on vinyl gold intermediates, see ref 54j.

78. For selected examples, see: (a) Döpp, R.; Lothschütz, C.; Wurm, T.; Pernpointner, M.; Keller, S.; Rominger, F.; Hashmi, A. S. K. *Organometallics* **2011**, *30*, 5894. (b) Egorova, O. A.; Seo, H.; Chatterjee, A.; Ahn, K. H. *Org. Lett.* **2010**, *12*, 401. (c) Hashmi, A. S. K.; Schuster, A. M.; Rominger, F. *Angew. Chem., Int. Ed.* **2009**, 48, 8247. (d) Liu, L.-P.; Hammond, G. B. *Chem.-Asian, J.* **2009**, *4*, 1230. (e) Weber, D.; Tarselli, M. A.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 5733.

79. See refs 54e and: Hashmi, A. S. K.; Pernpointner, M.; Hansmann, M. M. *Faraday Discuss.* **2011**, *152*, 179.

80. Reviews on transition metal-catalyzed benzannulations: (a) Rubin, M.; Sromek, A. W.; Gevorgyan, V. *Synlett* **2003**, 2265. (b) Saito, S.; Yamamoto, Y. *Chem. Rev.* **2000**, *100*, 2901.

81. Ciochina, R.; Grossman, R. B. *Chem. Rev.* **2006**, *106*, 3963.

82. For reviews on the novel synthesis of bridge-containing organic compounds, see: (a) Barabé, F.; Levesque, P.; Sow, B.; Bellavance, G.; Bétournay, G.; Barriault, L. *Pure Appl. Chem.* **2013**, *85*, 1161. (b) Zhao, W. *Chem. Rev.* **2010**, *110*, 1706. (c) Poulin, J.; Grisé-Bard, C. M.; Barriault, L. *Chem. Soc. Rev.* **2009**, *38*, 3092.

83. For selected examples, see: (a) Sow, B.; Bellavance, G.; Barabé, F.; Barriault, L. *Beilstein J. Org. Chem.* **2011**, *7*, 1007. (b) Barabé, F.; Bétournay, G.; Bellavance, G.; Barriault, L. *Org. Lett.* **2009**, *11*, 4236. (c) Lavigne, R. M. A.; Riou, M.; Girardin, M.; Morency, L.; Barriault, L. *Org. Lett.* **2005**, *7*, 5921. (d) Barriault, L.; Ang, P. J. A.; Lavigne, M. A. *Org. Lett.* **2004**, *6*, 1317. (e) Armstrong, A.; Critchley, T. J.; Gourdel-Martin, M.-E.; Kelsey, R. D.; Mortlock, A. A. *J. Chem. Soc., Perkin Trans. 1*, **2002**,

1344. (f) Armstrong, A.; Critchley, T. J.; Mortlock, A. A. *Synlett* **1998**, 553. (g) Sgarbi, P. W. M.; Clive, D. L. J. *Chem. Comm.* **1997**, 333.

84. Shu, X.-Z.; Shu, D.; Schienebeck, C. M.; Tang, W. *Chem. Soc. Rev.* **2012**, *41*, 7698.

85. For selected examples, see: (a) Lu, L.; Liu, X.-Y.; Shu, X.-Z.; Yang, K.; Ji, K.-G.; Liang, Y.-M. *J. Org. Chem.* **2009**, *74*, 474. (b) Harrak, Y.; Blaszykowski, C.; Bernard, M.; Cariou, K.; Mainetti, E.; Mouriès, V.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2004**, *126*, 8656. (c) Mainetti, E.; Mouriès, V.; Fensterbank, L.; Malacria, M.; Marco-Contelles, J. *Angew. Chem., Int. Ed.* **2002**, *41*, 2132.

86. Rautenstrauch, V. *J. Org. Chem.* **1984**, *49*, 950.

87. Shi, X.; Gorin, D. J.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 5802.

88. Zhang, L.; Wang, S. *J. Am. Chem. Soc.* **2006**, *128*, 1442.

89. Lee, J. H.; Toste, F. D. *Angew. Chem., Int. Ed.* **2007**, *46*, 912.

90. Lemière, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2009**, *131*, 2993. For an analogous reaction catalyzed by platinum, see: Funami, H.; Kusama, H.; Iwasawa, N. *Angew. Chem., Int. Ed.* **2007**, *46*, 909.

91. See references 50, 63 and: Rao, W.; Chan, P. W. H. *Chem-Eur. J.* **2014**, *20*, 713.

92. For examples on Brønsted acid-catalyzed cycloisomerization of enynes, see: (a) Jin, T.; Uchiyama, J.; Himuro, M.; Yamamoto, Y. *Tetrahedron Lett.* **2011**, *52*, 2069. (b) Jin, T.; Himuro, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **2010**, *132*, 5590.

93. (a) Yuan, H.; Shen, Y.; Yu, S.; Shan, L.; Sun, Q.; Zhang, W. *Synth. Commun.* **2013**, *43*, 2817. (b) Xu, B.-H.; Kehr, G.; Fröhlich, R.; Wibbeling, B.; Schirmer, B.; Grimme, S.; Erker, G. *Angew. Chem. Int. Ed.* **2011**, *50*, 7183.