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Par

Qing ZHAO

Gold-catalyzed Novel Transformations of Ynamide

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Composition du Jury :

Dr, Grimaud, Laurence	Ecole Normale Supérieure, Paris	Président
Dr, Miesch, Laurence	Université de Strasbourg	Rapporteur
Dr, Hannedouche, Jérôme	Université d'Orsay	Rapporteur
Dr, Harris, Craig	Galderma	Examinateur
Dr, Gagosz, Fabien	Ecole Polytechnique	Directeur de thèse

Table of Content

GENERAL INTRODUCTION 7

ABBREVIATIONS 11

CHAPTER 1. GOLD HOMOGENEOUS CATALYSIS: AN INTRODUCTORY OVERVIEW 17

1. Gold: a fascinating metal 19

2. Gold in organic chemistry: a historical point of view 20

3. Theoretical concerns in homogeneous gold catalysis 23

3.1. Bonding Mode of π-Bonds to Gold 23

3.2. Relativistic Effects 24

4. Homogeneous Gold Catalysts 26

4.3. Gold(III) Complexes 26

4.4. Gold(I) Complexes 27

4.5. Silver effects 31

5. Gold-Catalyzed Homogeneous Reactions 33

5.6. Nucleophilic addition 35

5.7. Cycloisomerizations of 1,*n*-enynes 44

5.8. Gold-catalyzed rearrangement of propargylic carboxylates 49

5.9. Oxidation 51

6. Conclusion and perspective 54

CHAPTER 2. GOLD(I)-CATALYZED REARRANGEMENT OF YNAMIDES *VIA* [1,5]-HYDRIDE SHIFT: AN EXPEDIENT APPROACH TO ALLENAMIDES AND ITS EQUIVALENTS 55

1. Allenamide: a versatile building block 57

2. Synthetic methods of allenamides in literature 58

2.1. Base-triggered isomerization 58

2.2. Transition metal-mediated C-N couplings 60
2.3. Sigmatropic rearrangements 61
2.4. Other approaches 62

3. Reactions involving intramolecular [1, *n*]-Hydride Shift 63
3.1. Hydride donors involving ethers and acetals 63
3.2. Hydride donors involving amines 64
3.3. Hydride donors without heteroatoms 67

4. Origin and objectives of the project 68

5. Results and discussions 69
5.1. Preliminary results and optimization of conditions 69
5.2. Facile synthesis of variously functionalized and poly-substituted allenimides 76
5.3. Extension of the method to the synthesis of allenamide equivalents 80
5.4. Further transformation of allenamide and allenamide equivalents 81

6. Mechanistic scenario 82

7. Conclusion 82

CHAPTER 3. DUAL GOLD CATALYSIS: A UNIQUE APPROACH TO TETRAHYDROQUINOLINE DERIVATIVES BY A FORMAL [4+2] ANNULATION PROCESS 85

1. Introduction 87
1.1. *σ, π*-digold acetylides 87
1.2. Dual gold catalysis 90

2. Origin of our project and preliminary results 99

3. Conditions optimization 102

4. Substrate scope 106

5. Conclusion and perspective 110

EXPERIMENTAL PART 113

PART 1: GOLD(I)-CATALYZED REARRANGEMENT OF YNAMIDES VIA [1,5]-HYDRIDE SHIFT: AN EXPEDIENT APPROACH TO ALLENAMIDES AND ITS EQUIVALEN 115

PART 2 : GOLD(I)-CATALYZED REARRANGEMENT OF YNAMIDES VIA [1,5]-HYDRIDE SHIFT: AN EXPEDIENT APPROACH TO ALLENAMIDES AND ITS EQUIVALENTS 165

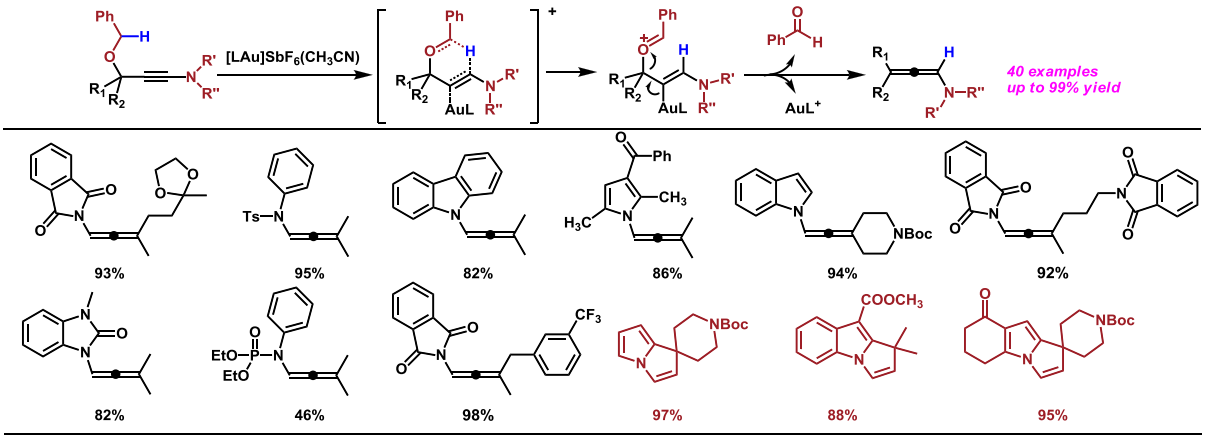
General introduction

Since the pioneering work by Ito, Hayashi, Unimoto and Hashmi in late of last century, homogeneous gold catalysis has witnessed tremendous development by contributions from research groups all over the world. Gold catalysts, possessing unique catalytic reactivity, intrigued a large number of novel approaches to target molecules which cannot be accessed by other methodology. Ynamide, which belongs to a subclass of hetero-substituted alkynes, represents a versatile building block with balanced reactivity and stability and found a series of applications in useful transformations, such as additions, cycloadditions and cycloisomerizations.

As part of our ongoing interest in gold catalysis and ynamide chemistry, in this manuscript, two works involving ynamide in the presence of gold catalyst was presented:

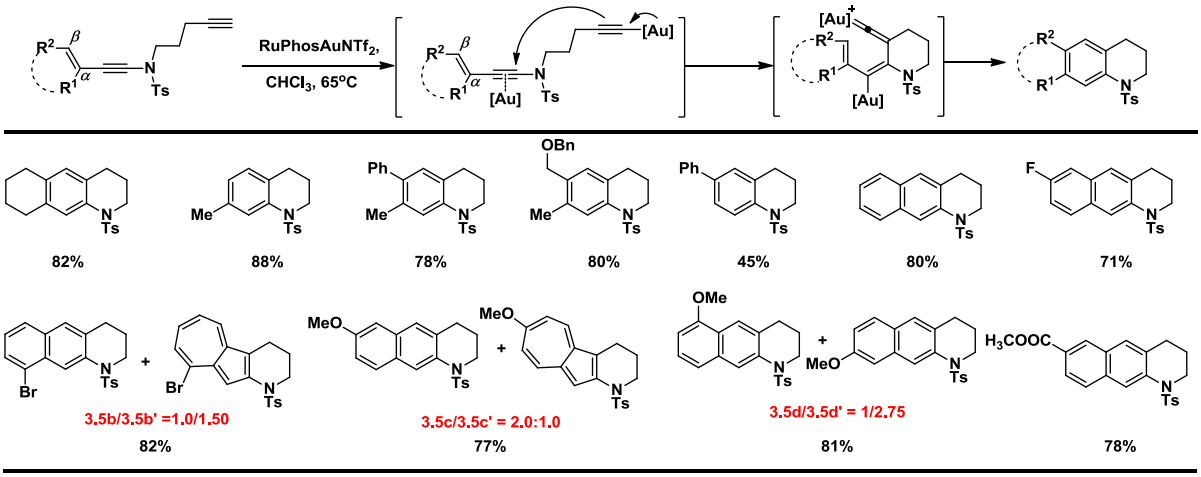
(1). Gold(I)-Catalyzed Rearrangement of Propargyl Ethers of ynamides: A Practical Method for the synthesis of Substituted Allenamides

Allenamides are versatile synthetic building blocks that have seen numerous applications and therefore great efforts have been devoted to the access to such compounds. We have shown that a series of substituted and functionalized allenamides were easily accessible *via* a gold catalysted 1,5-hydride shift/fragmentation sequence using ynamides as the starting material. Our method is rapid and practical. It can be performed under very mild conditions (room temperature) with low catalyst loading (4% gold catalyst) and gave excellent yields (up to 99% yield). Besides the good functionality compatibility in the carbon terminal (R1 and R2), our method also tolerate variuous Nitrogen substituents (R' and R''). Moreover, further transformation using in-situ formed allenamides was achieved. Some interesting spiral and diene compounds were also formed in excellent yield.



(2). Dual gold catalysis: a unique approach to derived-tetrahydroquinolines by a formal [4+2] pathway

Although vast majority of gold catalysis features π-activation of a multiple bond by a single gold complex, recent innovative advance involving two gold centers in one single molecule was disclosed recently by several research groups and also by our group.



The catalytic cycle was initiated by the formation of gold acetylide and coordination of another gold complex to the triple bond of ynamide. After nucleophilic attack of gold acetylide onto ynamide, gold vinylidene was generated. The formed gold vinylidene was then trapped by double bond, giving rise to aromatic rings.

Introduction générale

Suite aux premiers travaux réalisés par Ito, Hayashi, Unimoto et Hashmi à la fin du siècle dernier, de nombreux groupes de recherche à travers le monde ont contribué à l'important développement de la catalyse homogène à l'or. Ce dernier, possédant une activité catalytique unique, donne accès à un bon nombre de nouvelles synthèses de composés, jusque-là inaccessible en utilisant d'autres méthodes.

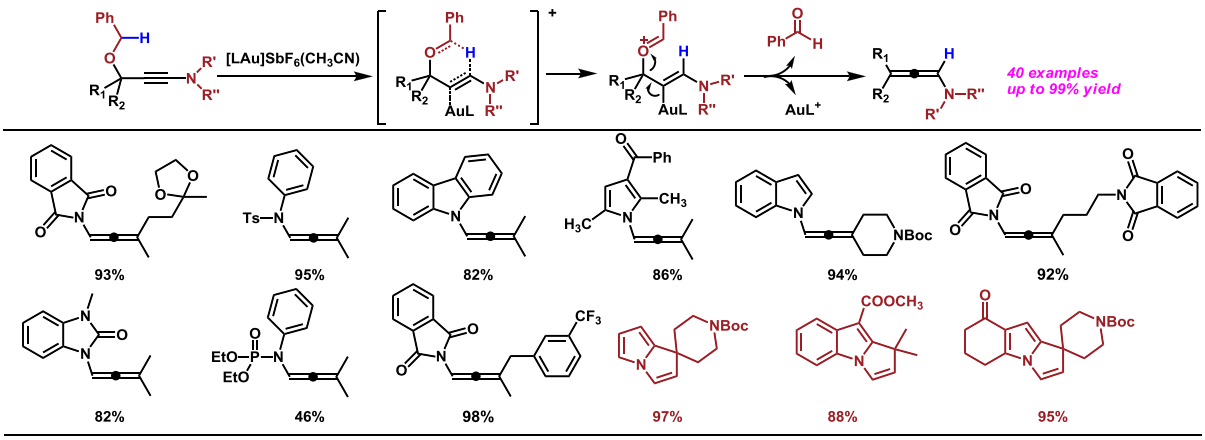
Les ynamides, un sous-groupe d'alcynes hétéro-substitués, sont des intermédiaires de synthèse ayant une réactivité et une stabilité modulable. Ils trouvent leur application dans des réactions telles que les additions, les cycloadditions et les cycloisomérisations.

Dans ce manuscrit sont présentés deux travaux impliquant des réactions d'ynamides en présence d'un catalyseur à l'or.

1) Réarrangement d'éthers de propargyliques d'ynamides catalysé par l'or (I) : Un accès pratique aux allénamides substitués.

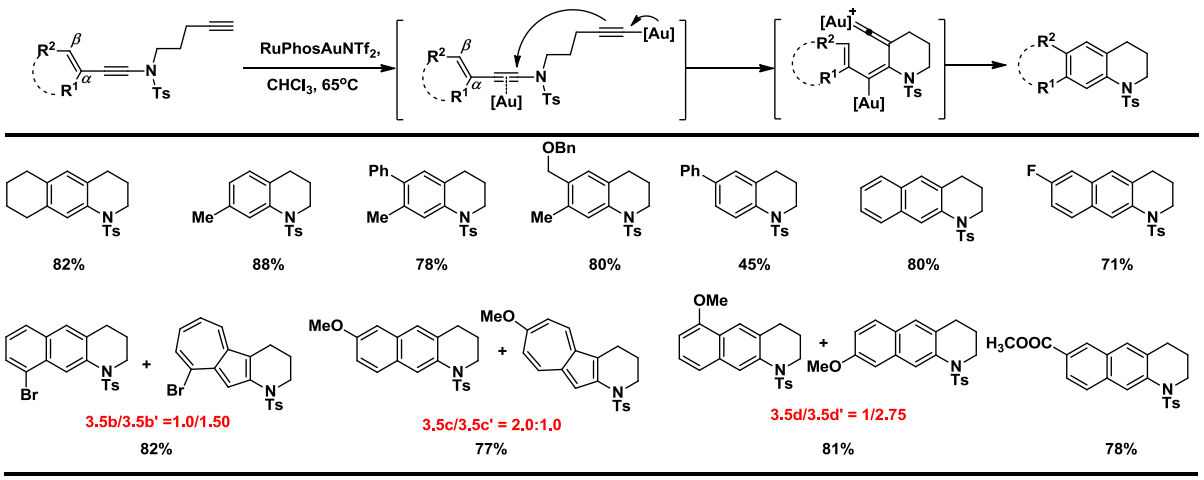
Les allénamides sont des composés qui présentent de nombreuses applications, d'où l'engouement présent pour accéder à ces composés. Nous avons montré que des allénamides substitués et fonctionnalisés sont facilement accessibles par une réaction de transfert d'hydrure [1,5] suivi d'une fragmentation, le tout catalysé par de l'or et en utilisant des ynamides comme substrats.

Notre méthode est rapide et pratique. En effet, la réaction se fait dans des conditions douces (température ambiante) avec une charge catalytique faible (4 mol% de catalyseur à l'or) et donne d'excellents rendements (jusqu'à 99%). En plus d'une bonne compatibilité fonctionnelle sur le carbone terminal (R1 et R2), notre méthode tolère aussi des substituants azotés variés (R' et R''). De plus, d'autres transformations *in-situ* sur les allénamides formés *in-situ* ont été effectuées. Quelques composés spiros et dièns interessants ont été obtenus avec des rendements excellents.



2) Catalyse duale à l'or : Une synthèse originale de dérivés tertahydroquinolines par un mécanisme formel d'addition [4+2]

Bien qu'une vaste majorité de la catalyse à l'or contient une activation du système π d'une liaison multiple par un seul complexe d'or, des innovations récentes mettant en jeu deux atomes d'or sur une seule molécule ont été développées par plusieurs groupes, dont le nôtre.



Le cycle catalytique est initié par la formation de l'acétylénure d'or et par la coordination d'un autre complexe d'or de la liaison triple de l'ynamide. Après une attaque nucléophile de l'acétylenure d'or sur l'ynamine, un vinylidène d'or est formé. Ce dernier est piégé par la double liaison, donnant naissance au cycle aromatique.

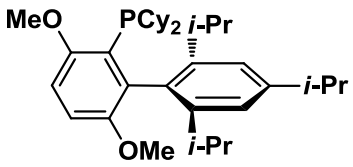
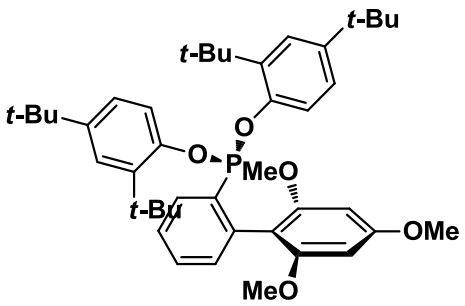
Abbre*via*tions

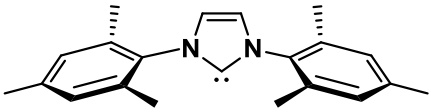
1. Units

°C	Celsius degree
atm	Standard atmosphere
g	Gram
mg	milligram
Kg	Kilogram
Hz	Hertz
MHz	Megahertz
h	Hour
min	Minute
L	Liter
mL	Milliliter
mol	Mole
mmol	Millimole
N	Normal concentration
ppm	Parts per million
t	Tonne
€	Eruo
$Kcal.mol^{-1}$	Kilocalorie per mole
m/z	Mass-to-charge ratio

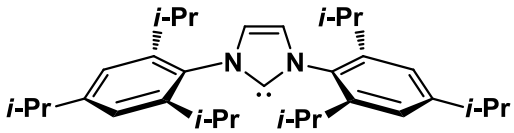
2. Chemical groups and compounds

Ac	Acetyl
Ad	Adamantyl
Ar	Aryl
Bn	Benzyl

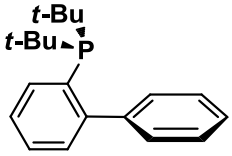
BrettPhos	2-(Dicyclohexylphosphino)3,6-dimethoxy-2’,4’,6’-triisopropyl-1,1’-biphenyl 
Boc	*tert*-Butoxycarbonyl
Bu	Butyl
Bz	Benzoyl
Cbz	Carbobenzyloxy (Benzyloxycarbonyl)
Cp	Cyclopentadienyl
Cy	Cyclohexyl
DCE	1,2-Dichloroethane
DCM	Dichloromethane
DIPA	Diisopropylamine
DMA	Dimethylacetamide
DMAP	*N,N*-Dimethyl-4-aminopyridine
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
Et	Ethyl
GPhos	(r)-bis(2,4-di-tert-butylphenyl) (2',4',6'-trimethoxy-[1,1'-biphenyl]-2-yl)phosphonite 
IMes	N,N’-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene



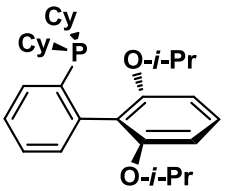
i-Pr	Isopropyl
IPr	N,N’-bis(2,6-diisopropylphenyl)imidazole-2-ylidene



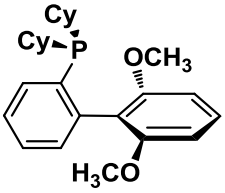
JohnPhos	2-(Di-*tert*-butylphosphino)biphenyl



Me	Methyl
Ms	Mesyl(methanesulfonyl)
n-Bu	*n*-Butyl
NBS	*N*-Bromosuccimide
NHC	*N*-Heterocyclic carbene
PE	Petroleum ether
1,10-Phen	1,10-Phenanthroline
RuPhos	2-Dicyclohexylphosphino-2’,6’-diisopropoxybiphenyl

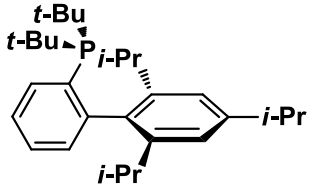


SPhos	2-Dicyclohexylphosphino-2’,6’-dimethoxybiphenyl

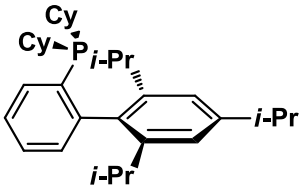


Ts	*p*-Tosyl
TBAF	Tetrabutylammonium fluoride

TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
t-Bu	*tert*-Butyl
*t*BuXPhos	2-Di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl



TMS	Trimethylsilyl
THF	Tetrahydrofuran
Ts	Tosyl(*p*-toluenesulfonyl)
XPhos	2-Dicyclobutylphosphino-2',4',6'-triisopropylbiphenyl



3. Other acronyms and abbre*via*tions

aq.	Aqueous
cat.	Catalytic
conc.	Concentrated
conv.	Conversion
eq.	Equation
equiv	Equivalent
EDG	Electron donating group
HRMS	High resolution mass spectroscopy
IR	Infrared
LG	Leaving group

m-	*Meta*-
MS	Mass spectroscopy
NMR	Nuclear magnetic resonance
Nu	Nucleophile
o-	*Ortho*-
p-	*Para*-
rt	Room temperature
temp.	Temperature
TLC	Thin layer chromatography

Chapter 1. Gold homogeneous catalysis: an introductory overview

1. Gold: a fascinating metal

Gold is intimately related to the evolution of humankind's civilizations, symbolizing authority, richness, nobleness, glory and prestige. This can be best illustrated by the fabrication of a wide range of gold artworks from different civilizations, for instance, the golden funerary mask of Tutankhamun from Egypt, various golden handicrafts from ancient China (**Figure 1-1**), which both created highly-developed civilizations thousands of years ago. Aside from civilized outcomes, the consistent fascination for gold also caused catastrophe to mankind, such as the destruction of the Roman Empire due to Attila's voracity to treasure, the disappearance of the Inca civilization during the 16th century expeditions for pursuing wealth.



Figure 1-1 Gold arts in ancient civilizations

Gold is soft, dense, malleable and ductile with a bright, slightly reddish yellow color in its purest form, different from other pure metals which are generally gray or slivery white. At high temperature, gold can form alloys with diverse metals such as silver, copper, palladium and nickel to modulate its color, hardness, melting point, ductility and other metallurgical properties. Gold is one of the least "reactive" metals that have been ever discovered, it is resistant to oxidative conditions, strong acidic environment and most other chemical reaction conditions. Due to its chemical inertness, gold often naturally occurs in its elemental (native) form in rocks, veins and allu*via*l deposits as nuggets or grains. It also presents in alloys with silver, copper, palladium and etc.

Given all its chemical and physical properties, gold is widely used in jewelry, coinage, arts, and modern industries. Gold jewelry industry still found vast majority application of new produced gold nowadays. Many countries hold gold for economic reasons, for instance, inhibiting inflation, preventing currency depreciation, and as a hedge for various possible economic disruptions. In terms of investment and collector purposes, gold is commonly

minted into bullion coins, such as Chinese Gold Panda, American Gold Eagle, Canadian Gold Maple Leaf, British Gold Sovereign and so on (**Figure 1-2**).



Figure 1-2 A few popular bullion coins in world gold market

Gold has found widespread application in electrical industry, to be specific, manufacturing thin layer coating on electronic connectors in expensive electrical devices, such as computer, audio-visual equipment, and even spacecraft, due to its excellent performance in conductivity, ductility as well as resistance to oxidation and corrosion. Gold also witnesses a range of other applications in modern industries, including gold solder, photography, embroidery in form of gold thread, as color agent in special glasses, as reflector of electromagnetic radiation in high-tech equipment, for heat shielding in automobiles and so forth. Gold has also been employed in medicine, food and drinks in modern times and in chemistry.

According to World Gold Council, there exist 186700 tons of stocks of gold above ground in all, as of 2015.

2. Gold in organic chemistry: a historical point of view

Although transition metal chemistry has seen tremendous development, gold suffered relative ignorance by the synthetic chemist community until the end of the 20th century. There are two reasons behind this neglect. On one hand, native gold has been regarded as chemicals inert for a long time, leading to the prejudice that gold was unsuitable for being used in catalysis. Besides, mechanisms in transition metal chemistry generally involve altering of oxidation states of transition metals, i.e., an oxidative addition/reductive elimination process is involved, however. This is indeed difficult for gold to enter such catalytic cycles. On the other hand, gold was subconsciously considered to be scarce and extremely expensive, leading people to be too reluctant to use it in chemistry. However, other rarest and precious metals such as palladium, platinum, iridium, ruthenium, rhodium and osmium all witnessed broad applications in organic chemistry (**Figure 1-3**). [1]

[1] Source of graph: Wikipedia website. Abundance of elements in earth's crust. https://en.wikipedia.org/wiki/Abundance_of_ elements_in_Earth's_crust.

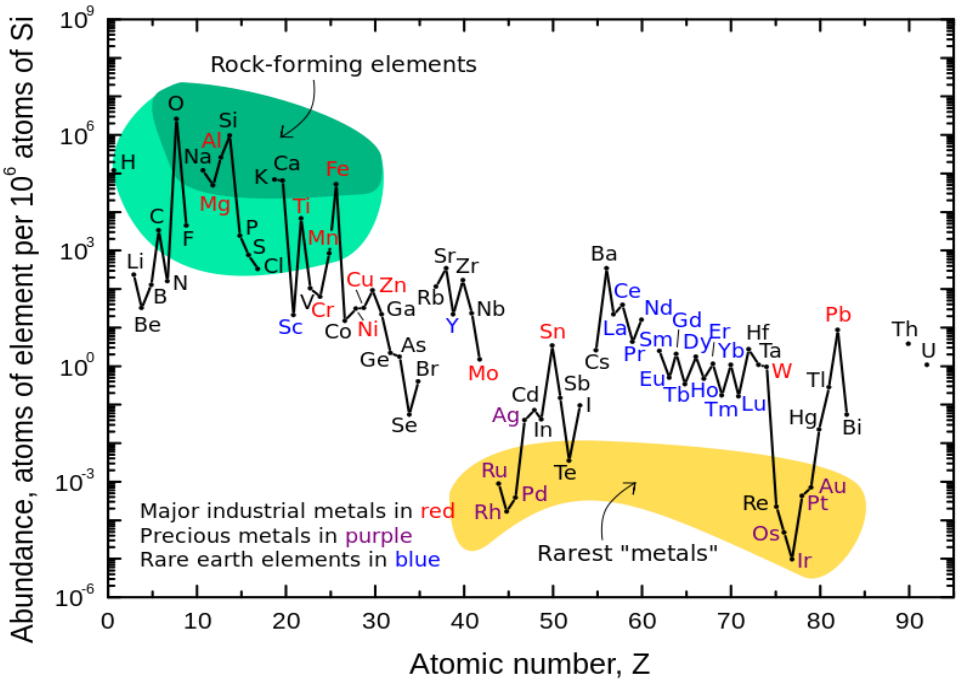


Figure 1-3 Relative atomic abundance of chemical elements in earth's upper crust

The price of gold is comparable to that of platinum although being higher than that of precious metals, implying that organic transformations using gold catalysis would not be much more costly than those employing other metals (**Figure 1-4**).[2]

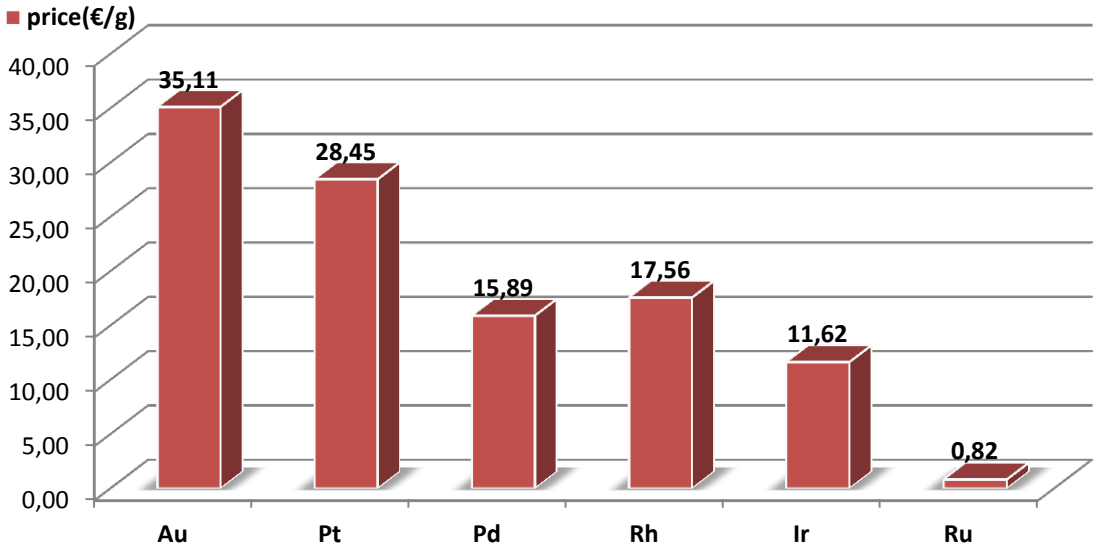
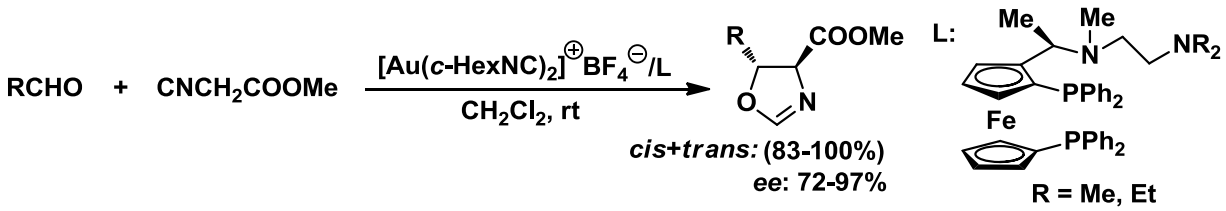


Figure 1-4 Prices of precious metals on May, 10th 2016

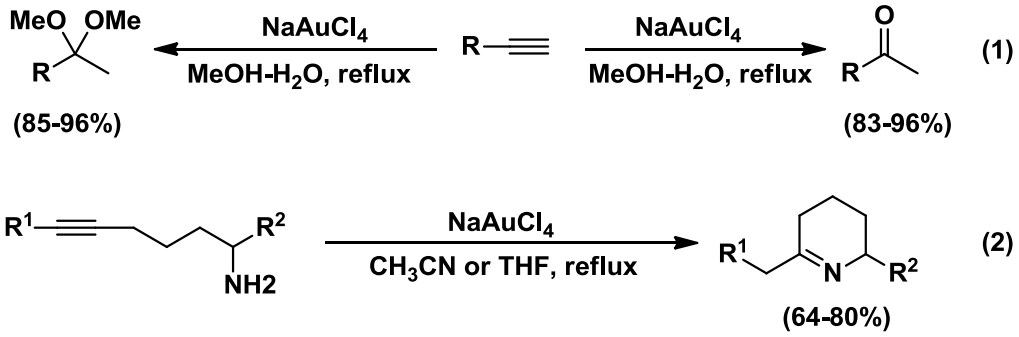
[2] Heraeus Group website. Precious metal prices. Current Heraeus Precious Metal Prices. http://heraeus-trading.com/en/marktinformationen/edelmetallpreise/edelmetallpreise.aspx

In this context, gold's employment in homogeneous catalysis was unexplored until 1986 when Ito, Hayashi et al. disclosed the asymmetric reaction of aldehydes with isocyanoacetates in the presence of gold(I) complexes containing a chiral ferrocenylphosphine, which provided optically active oxazolines (**Scheme 1-1**).[3]



Scheme 1-1 The first application of gold(I) in homogeneous catalysis

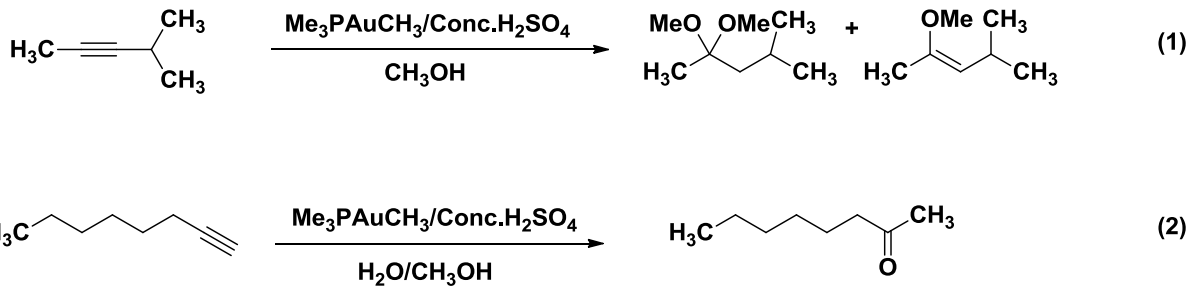
The first investigation of electrophilic gold complexes on the activation of alkynes was implemented in 1991 by Unimoto and Fukuda. It was observed that alkynes reacted with water, alcohols and amines in the presence of Au(III) salts, furnishing ketones, ketals and imines respectively (**Scheme 1-2**).[4]



Scheme 1-2 The first report on activation of alkynes by Au(III)

Afterwards, Teles[5] , Hayashi and Tanaka's[6] pioneering work opened up a real "gold rush" for gold(I)-catalyzed transformations. They employed cationic gold(I) complexes to catalyze the nucleophilic addition of alcohols or water to alkynes to yield ketals or ketones (**Scheme** 1-3). It is worth mentioning that they also observed that ligands (e.g. CO, triphenylphosphite) are of crucial importance in the efficiency of the transformation, what was proposed to be in correlation with the stability of the catalyst.

[3] Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 6405.
[4] (a) Fukuda, Y.; Utimoto, K. *J. Org. Chem.* **1991**, *56*, 3729. (b) Fukuda, Y.; Utimoto, K. *Synthesis,* **1991**, *1991*, 975. (c) Fukuda, Y.; Utimoto, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 2013.
[5] Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1415.
[6] Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem. Int. Ed.* **2002**, *41*, 4563.



Scheme 1-3 The first study upon the activation of alkynes by Au(I)

On the basis of this seminar work, a series of research groups all around the world entered this realm, which finally leads to the flourish of homogeneous gold catalysis. A great number of novel transformations have been developed, which will be discussed in details later (Chapter 1, section 5.).

3. Theoretical concerns in homogeneous gold catalysis

Gold, with symbol ***Au*** from Latin "*aurum*", is a group 11, *d*-block transition metal located in period 6 in the periodic table of elements with an **[Xe]4*f*^{14} 5*d*^{10} 6*s*^{1}** electronic configuration, atomic number as 79, and atomic weight as 197. Its oxidation states range from -1 to +5, with Au(I) and Au(III) dominating their chemical applications.

3.1. Bonding Mode of π-Bonds to Gold

From a mechanistic point of view, gold-catalyzed transformations are generally initiated by the complexation of π-bonds with gold complexes. The bonding situation could be elucidated by use of "Dewar-Chatt-Duncanson model" which qualitatively depicted four couples of orbitals with distinct symmetry to form complexes by orbital overlapping.[7] As an example, herein the coordination of alkynes to transition metals is present (**Figure 1-5**).

The bonding of transition metals and alkynes consists of four components:

(a) Alkyne's p_z orbital overlaps with metal's d_{z^2} orbital to form a σ-symmetric bond with alkyne's electrons delocalized into metallic center, which dominates the bonding of metal and alkyne;

(b) Metal's d_{xz} and alkyne's p^*_z coalesce to give rise to a π-symmetric bond which can be regarded as back-donation from the metallic center into alkyne;

[7] Simonneau, A. "Gold-Catalyzed Cycloisomerization Reactions Through Activation of Alkynes", Springer Thesis, **2014**. DOI: 10.1007/978-3-319-06707-0. And references cited therein.

(c) In the case of alkyne, there exists another p orbital, i.e., p_y which would donate its electrons into metal's d_{yz} orbital to generate another π-symmetric bond;

(d) The fourth component arises from the weak bonding from metal's d_{xy} orbital and alkyne's p_y * orbital.

Afterwards, rehybridization occurs resulting from the preferentially depletion of p bonding orbitals rather than the anti-bonding ones due to metal's back-donation. Dewar-Chatt-Duncanson model is well suitable for gold to explain the elongation of π-bonds as well as the loss of linearity or planarity in alkynes or alkenes. Nonetheless, it is not sufficient to interpret gold's peculiar reactivity reported to date. The unique performance of gold complexes in homogeneous catalysis is closely related to the nature of the metallic center when one considers gold's relativistic effects.

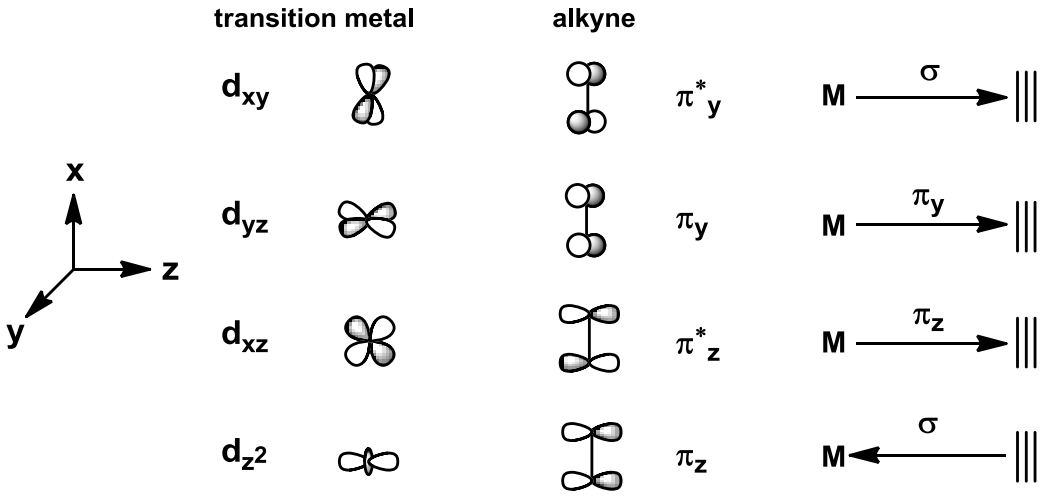


Figure 1-5 Dewar-Chatt-Duncanson model for alkyne-metal bond

3.2. Relativistic Effects

According to the theory of relativity, the high-speed electrons orbiting around gold nucleus result in the increasing of mass as well as the decreasing of atomic radius. This directly leads to the strong contraction of **6*s*** and **6*p*** orbitals, namely making them be closer to nucleus and consequently the expansion of **5*d*** and **4*f*** orbitals which are shielded by the former and thereby subject to weaker nuclear attractions. Besides, this helps rationalize gold's greater ionization energy and makes it the most electronegative transition metal (electronegativity of gold is **2.54**, similar to that of carbon **2.55** according to Pauling's scale). Moreover, the Au-Au interaction ("aurophicility") is rather prominent with the similar intensity as hydrogen bonding.

The electrons in diffuse **5*d*** orbitals are subject to less electron repulsion and therefore are better held around the gold nucleus, leading to gold's low nucleophicility and the reluctance to undergo oxidative addition which consist the key step in redox catalytic cycle ubiquitously in transition metal chemistry. Moreover, this type of diffuse, thus larger, **5*d*** orbitals makes gold complexes outstanding candidates as soft Lewis acids due to their preference to react through their orbitals instead of charges. On the basis of **HSAB** theory[8], gold complexes interact favorably with soft bases, for instance, π-systems in alkynes, allenes and alkynes and are less oxophilic. Therefore, gold complexes can be seen as a type of "**soft π-acids**". On the basis of Pyykko's observations, these relativistic effects are significant for platinum, mercury and reach the summit when it comes to gold (**Figure** 1-6).[9]

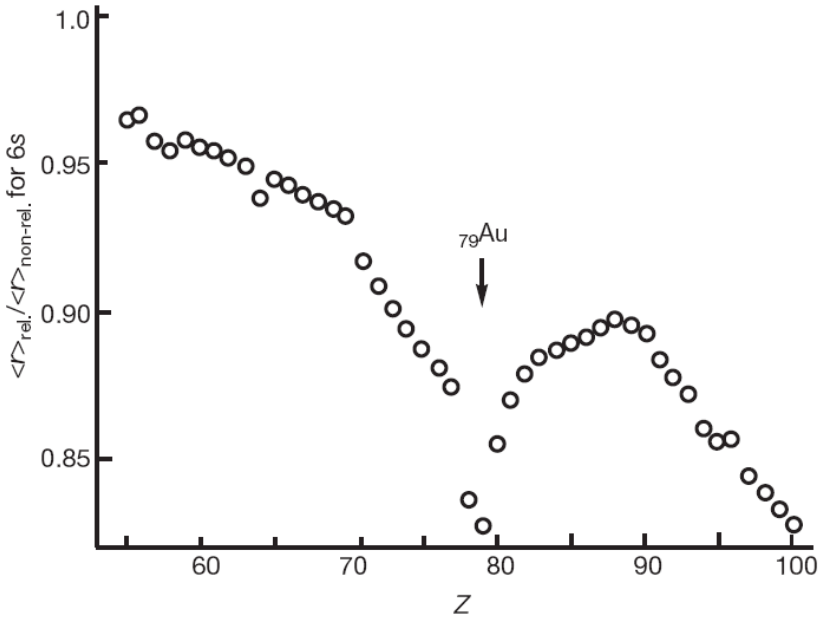


Figure 1-6 Calculated relativistic contraction of the 6s orbital

Under homogeneous conditions, gold complexes would selectively activate π-systems toward nucleophilic attack even in the presence of other functionalities, allowing for the rapid and expedient enhancement of molecular complexity starting from readily available building blocks. This can be attributed to two parameters: the soft Lewis acidity as mentioned above and the back-donation from the gold center to the carbocation generated in intermediates, which must not be neglected as well. The combination of soft Lewis acidity, back-donation and the decreased propensity to undergo β-eliminations collectively contributes to the

[8] (a) Pearson, R. G. *J. Am. Chem. Soc.* **1963**, *85*, 3533. (b) Pearson, R. G. *J. Chem. Educ.* **1968**, *45*, 581. (c) Pearson, R. G. *J. Chem. Educ.* **1968**, *45*, 643.

[9] (a) Pyykko, P.; Desclaux, J. P. *Acc. Chem. Res.* **1979**, *12*, 276. (b) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (c) Pyykkö, P. *Angew. Chem. Int. Ed.* **2002**, *41*, 3573. (d) Pyykkö, P. *Angew. Chem. Int. Ed.* **2004**, *43*, 4412.

excellent selectivity, reactivity, compatibility (with oxygen, moisture, functional groups) and mild reaction conditions in homogeneous gold catalysis.

When it comes to the cases wherein both alkenes and alkynes are present in reaction mixture, the initial nucleophilic attack takes place with preferentially onto alkynes over alkenes. It might be surprising when one considers that both alkenes and alkynes could coordinate to gold complexes and that bonding between alkene and gold is even stronger than alkynes. In fact, it relates to a kinetic outcome which derives from the lower energy of LUMO orbitals in alkynes compared with that of alkenes. This phenomenon was designated as "alkynophicility".

4. Homogeneous Gold Catalysts

Although gold complexes have long been known, its wide application in organic chemistry can be dated back to the end of last century. Since that time, gold complexes have emerged as mild and versatile catalysts or precatalysts for selective activation of multiple bonds such as alkynes, allenes and alkenes toward nucleophilic attack by various nucleophiles. Furthermore, gold catalysts are compatible with air and moisture, allowing some reactions be performed even under "open flask" conditions, thus conferring easier manipulating procedures experimentally.

In general, gold catalysts can be divided into two main types in terms of gold(III) complexes (auric compounds) and gold(I) complexes (aurous compounds), which derived from the two most commonly encountered +1 and +3 oxidation states of gold, albeit ligands and counterions also play vital important role in the efficiency and compatibility of specific transformations. While gold(III) are $\boldsymbol{d}^8$ complexes, preferentially adopting a square planar, tetracoordinated configuration, the gold(I) catalysts, with filled 5*d* orbitals ($\boldsymbol{d}^{10}$ complexes), are commonly encountered as linear, dicoordinated geometry.

4.3. Gold(III) Complexes

Given fact that current blossom of gold catalysis was initiated by the Au(III)-catalyzed transformations, gold(III) have found rather limited applications since then, among which gold(III) salts are mostly involved, e.g. $AuCl_3$, $AuBr_3$, chloroauric acid ($HAuCl_4$) and its sodium, potassium salts derivatives ($NaAuCl_4$, $KAuCl_4$). Reactions catalyzed by these gold(III) salts are largely carried out in polar solvents, such as H_2O, methanol and acetonitrile; in certain cases, these gold(III) salts are employed with silver salts as co-catalysts, such as AgOTf or $AgSbF_6$ to increase reactivity.

Hashmi and co-workers were the first to employ gold(III) complexes bearing pyridine derivatives to catalyze organic transformations and the complexes proved to be more reactive and more stable than gold(III) salts. A series of gold(III) complexes based on N-heterocyclic carbenes, salens, porphirins and so forth have already been developed and found application under homogeneous catalytic conditions (**Figure 1-7**).[10]

It is noteworthy that in certain cases gold(III) complexes are proposed to be *in situ* reduced to their gold(I) counterparts *via* an oxidative homocoupling mechanism, which serve as the real active species to catalyze the corresponding transformations.

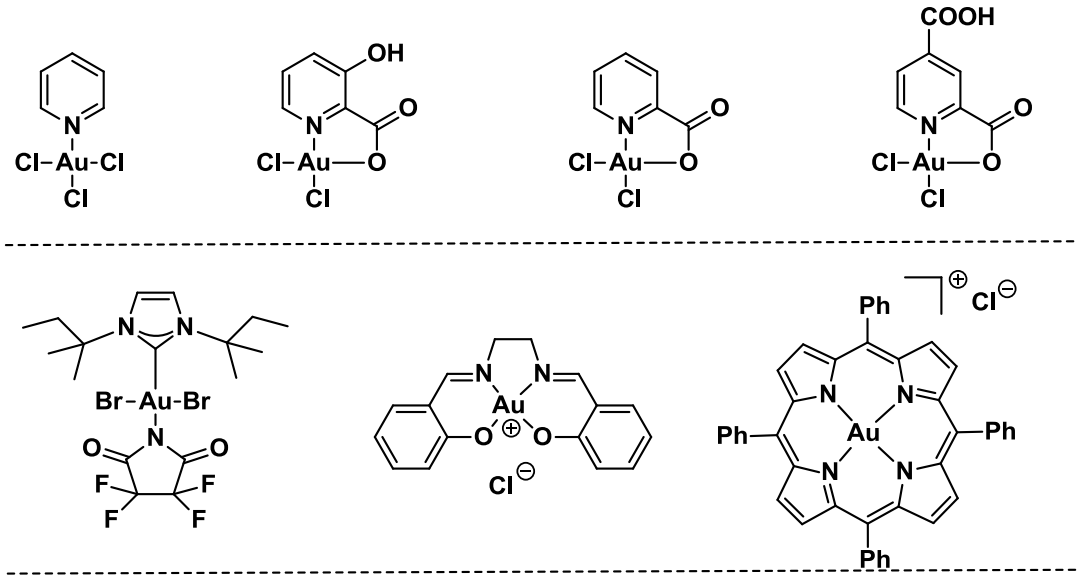


Figure 1-7 Selected examples of gold(III) complexes

4.4. Gold(I) Complexes

Gold(I) complexes have experienced much wider applications in organic transformations compared with their gold (III) counterparts. This can be attributed to their higher stability in reaction medium as well as easier adjustability of electronic and steric properties by switching ligands bound to the metallic center. It has been demonstrated that ligand is of vital importance in adapting catalytic reactivity of gold catalysts, therefore significantly affecting the route a specific transformation could undergo. Gold catalysts based on ligands such as

[10] (a) Hashmi, A. S. K.; Weyrauch, J. P.; Rudolph, M.; Kurpejović, E. *Angew. Chem. Int. Ed.* **2004**, *43*, 6545.(b) Reeds, J. P.; Whitwood, A. C.; Healy, M. P.; Fairlamb, I. J. S. *Chem. Commun.* **2010**, *46*, 2046. (c) Lo, V. K.-Y.; Liu, Y.; Wong, M.-K.; Che, C.-M. *Org. Lett.* **2006**, *8*, 1529. (d) Zhou, C.-Y.; Chan, P. W. H.; Che, C.-M. *Org. Lett.* **2006**, *8*, 325.

phosphines, N-heterocyclic carbenes, phosphites have all been prepared and broadly applied in homogeneous gold catalysis.

A few representative examples[11,12,13] are presented below (**Figure 1-8**).

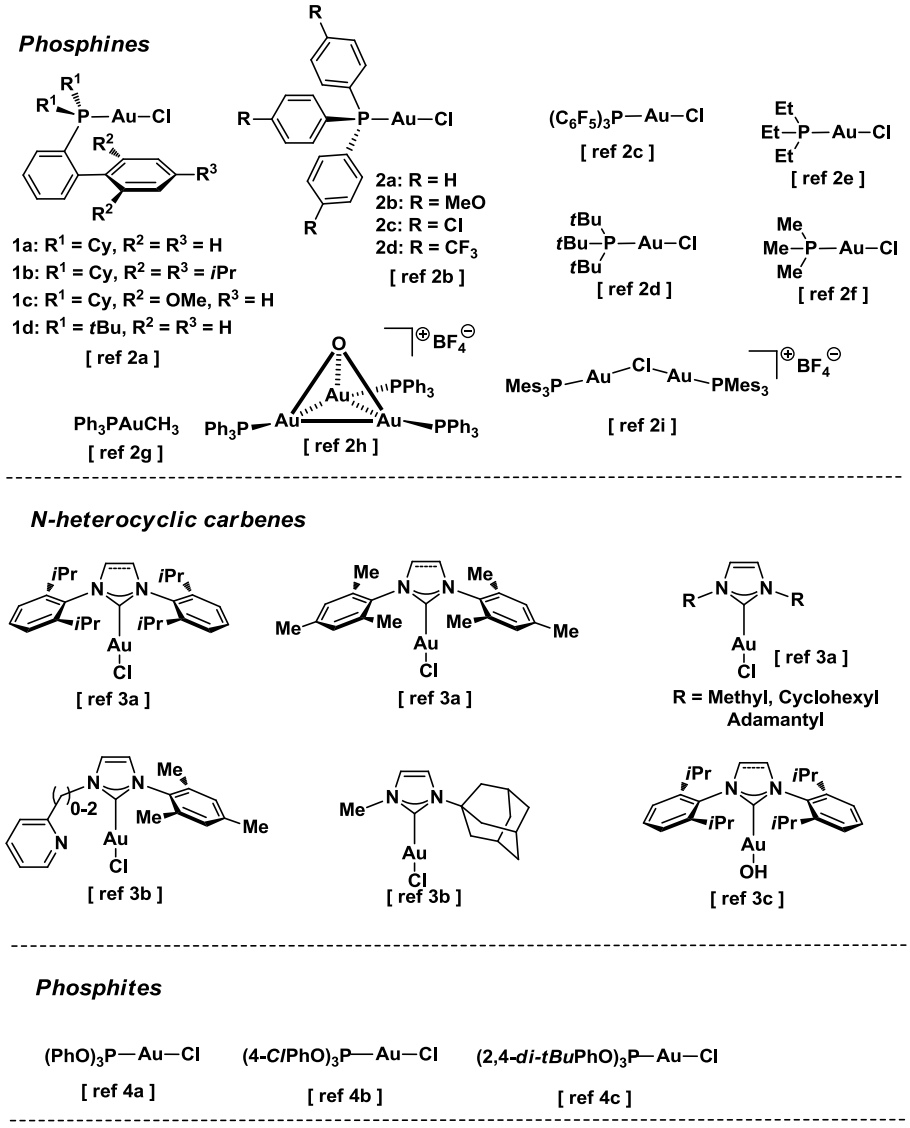


Figure 1-8 Representative examples of gold(I) complexes

[11] (a) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. *J. Am. Chem. Soc.* **2005**, *127*, 6178. (b) Markham, J. P.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 9708. (c) Kang, J.-E.; Shin, S. *Synlett* **2006**, *2006*, 0717. (d) Horino, Y.; Luzung, M. R.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 11364. (e) Barluenga, J.; Fernández-Rodríguez, M. Á.; García-García, P.; Aguilar, E. *J. Am. Chem. Soc.* **2008**, *130*, 2764. (f) Yao, X.; Li, C.-J. *Org. Lett.* **2006**, *8*, 1953. (g) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 1415. (h) Hashmi, A. S. K.; Schäfer, S.; Wölfle, M.; Diez Gil, C.; Fischer, P.; Laguna, A.; Blanco, M. C.; Gimeno, M. C. *Angew. Chem. Int. Ed.* **2007**, *46*, 6184. (i) Hashmi, A. S. K.; Rudolph, M.; Huck, J.; Frey, W.; Bats, J. W.; Hamzić, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 5848.

[12] (a) de Frémont, P.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2005**, *24*, 2411. (b) Pažický, M.; Loos, A.; Ferreira, M. J.; Serra, D.; Vinokurov, N.; Rominger, F.; Jäkel, C.; Hashmi, A. S. K.; Limbach, M. *Organometallics* **2010**, *29*, 4448. (c) Gaillard, S.; Slawin, A. M. Z.; Nolan, S. P. *Chem. Commun.* **2010**, *46*, 2742.

[13] (a) Tarselli, M. A.; Gagné, M. R. *J. Org. Chem.* **2008**, *73*, 2439. (b) Tarselli, M. A.; Liu, A.; Gagné, M. R. *Tetrahedron* **2009**, *65*, 1785. (c) López, S.; Herrero-Gómez, E.; Pérez-Galán, P.; Nieto-Oberhuber, C.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2006**, *45*, 6029.

While gold catalysis has led to the development of a range of novel transformations on the basis of unique reactivity of gold(I) complexes, gold-mediated enantioselective catalysis was constrained to certain cases. Furthermore, extensive and very careful optimization of reaction conditions is generally required, what can be attributed to the linear dicoordinated geometry of gold complexes. This structural arrangement imposed sufficiently long distance between ligand and reactive site, thus curbing the transfer of stereochemical information of chiral ligand to substrate. In general, the success reported to date in enantioselective gold catalysis involves two strategies, that is, the use of chiral ligands, especially axially chiral binaphthyl phosphines and/or the employment of chiral silver salts based on axially binaphthyl phosphonates. Several representative examples commonly involved are listed in **Figure 1-9**. [14]

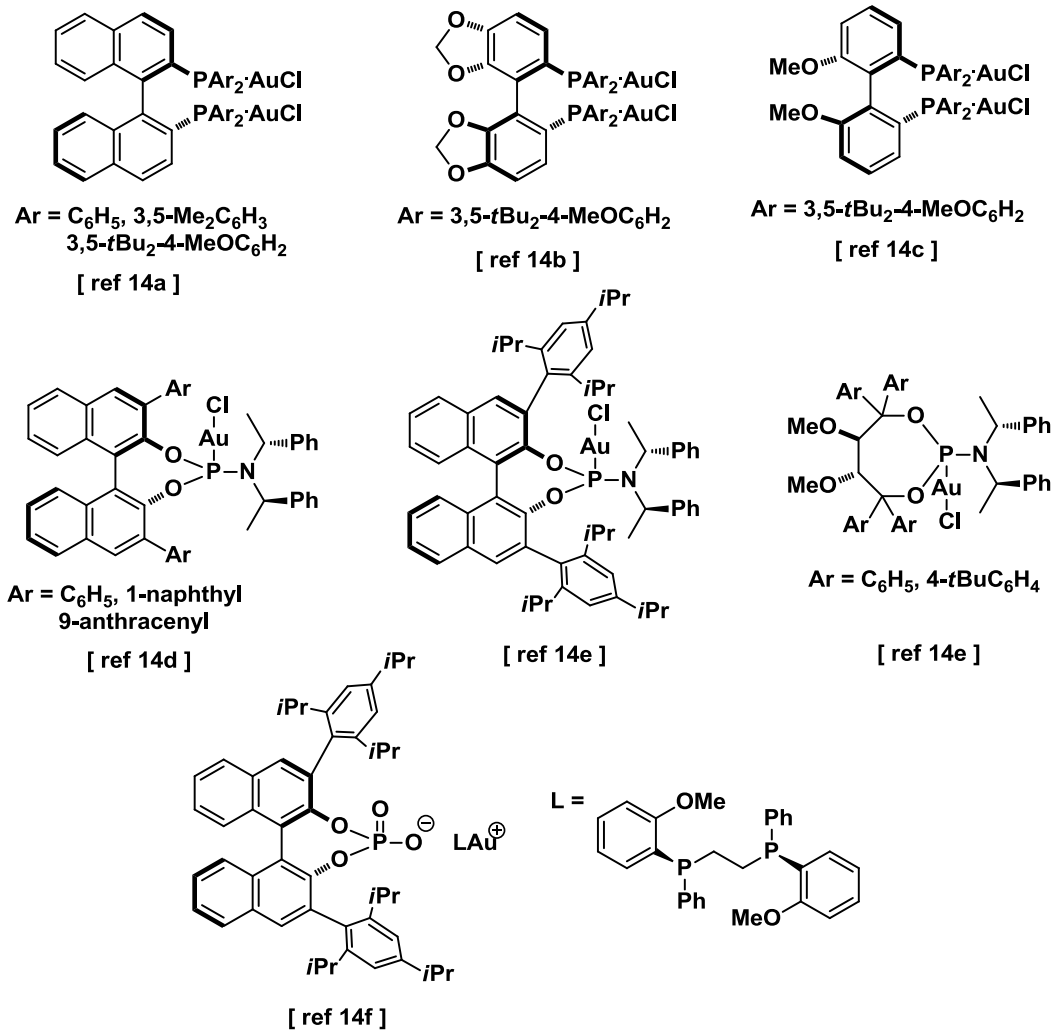


Figure 1-9 Representative complexes employed in enantioselective gold catalysis

[14] (a) Murai, M.; Uenishi, J. i.; Uemura, M. *Org. Lett.* **2010**, *12*, 4788. (b) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002. (c) Zhang, Z.; Bender, C. F.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2007**, *129*, 14148. (d) Alonso, I.; Trillo, B.; López, F.; Montserrat, S.; Ujaque, G.; Castedo, L.; Lledós, A.; Mascareñas, J. L. *J. Am. Chem. Soc.* **2009**, *131*, 13020. (e) Teller, H.; Flügge, S.; Goddard, R.; Fürstner, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 1949. (f) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496.

From an experimental point of view, these gold(I) complexes need to be activated by a prior abstraction of the halides, hydroxides, or methyl groups by using silver salts (**AgOTf**, **$AgSbF_6$**, **$AgBF_4$**, **$AgNTf_2$**, **$AgPF_6$**, **$AgClO_4$**, **AgOTs**, **AgO_2CF_3**), other inorganic salts(**$NaBAr_4$, $KBAr_4$**) or strong Brønsted acids (**HBF_4**, **HOTf**, **$HNTf_2$**, **CF_3COOH**, **$H_3PW_{12}O_{40}$**, **H_2SO_4**) as co-catalysts. This allows the *in situ* generation of real catalytically active species.

More recently, alternative catalytically active complexes were reported through the application of specific ligands, such as bistrifluoromethanesulfonimidate, hexafluoroantimonate, and benzotriazole to allow for the direct formation of air and moisture stable, storable and particularly easy-manipulating gold catalysts, excluding the use of silver salts or strong acids as co-catalysts. The relatively weakly coordinated ligands (e.g. nitriles, alcohol, arenes, etc.) need to be replaced by substrates *via* π-coordination in reaction media, thereafter provoking cationic gold(I) species participate in the catalytic cycle. Several representative gold(I) catalysts [15,16] which fall into this type are listed in

Figure 1-10.

[15] (a) Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133. (b) Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614. (c) Henrion, G.; Chavas, T. E. J.; Le Goff, X.; Gagosz, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 6277. (d) Ochida, A.; Ito, H.; Sawamura, M. *J. Am. Chem. Soc.* **2006**, *128*, 16486. (e) Ricard, L.; Gagosz, F. *Organometallics* **2007**, *26*, 4704.

[16] (a) Amijs, C. H. M.; López-Carrillo, V.; Raducan, M.; Pérez-Galán, P.; Ferrer, C.; Echavarren, A. M. *J. Org. Chem.* **2008**, *73*, 7721. (b) de Frémont, P.; Marion, N.; Nolan, S. P. *J. Organomet. Chem.* **2009**, *694*, 551. (c) de Fremont, P.; Stevens, E. D.; Fructos, M. R.; Mar Diaz-Requejo, M.; Perez, P. J.; Nolan, S. P. *Chem. Commun.* **2006**, 2045.

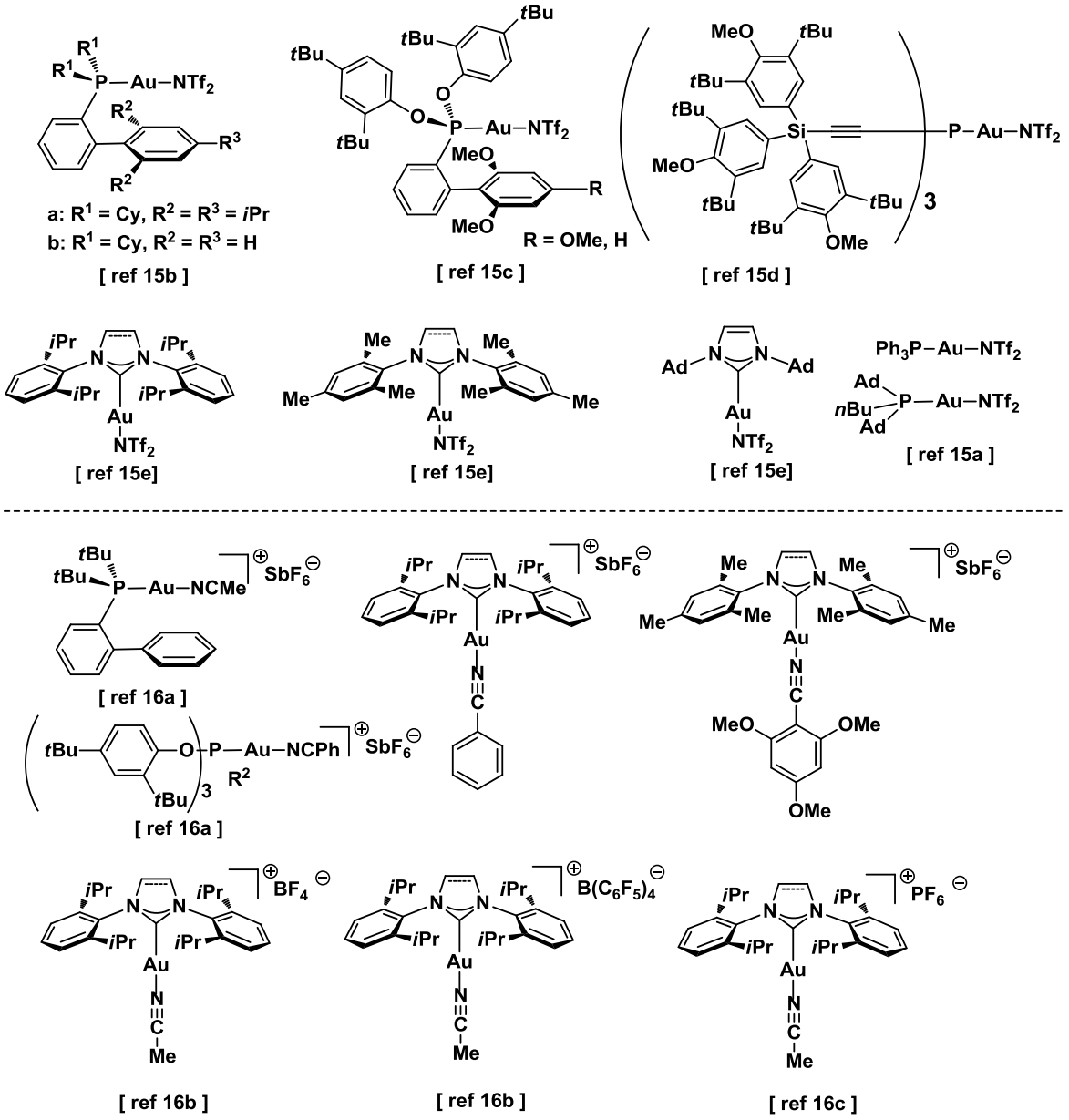
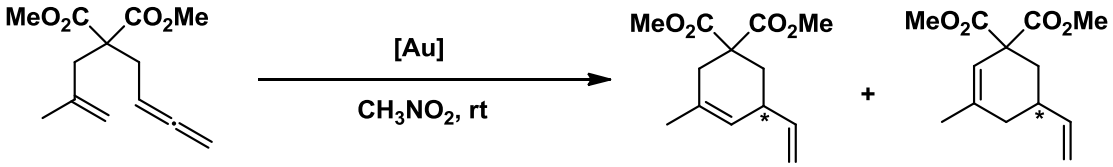


Figure 1-10 Representative examples of preformed catalysts

4.5. Silver effects

As aforementioned, commonly employed gold catalysts were *in situ* generated by treatment of LAuCl with various silver salts to form cationic gold(I) species which are believed to be the catalytically active species although no structural proof for their existence was disclosed so far. In previously reported mechanistic rationale, $[LAu]^+$ has consistently been proposed as the real and exclusive π-philic species with complete ignorance of the function of silver salts. However, in certain early cases it was observed that the presence of silver was of pivotal

importance to obtain the desired experimental results. For instance, in the enantioselective synthesis of vinylcyclohexenes from eneallenes in the presence of gold complexes[17], different enantioselectivities were observed depending on the use of catalysts generated *in situ* or pre-isolated gold catalysts. While the *in situ* generated catalytic system provided sufficiently good enantiomeric excess, the isolated catalyst afforded sluggish reaction and lower enantioselectivity. Intriguingly, re-addition of AgOTf had no influence on the stereochemical outcome, whereas the AgCl which is insoluble in reaction medium slightly improved the stereoselectivity (**Scheme 1-4**).



[(R)-3,5-xylyl-binap(AuCl)$_2$] + AgOTf	**72 % *ee*, 16h**
[(R)-3,5-xylyl-binap(AuOTf)$_2$]	**21 % *ee*, >24h**
[(R)-3,5-xylyl-binap(AuOTf)$_2$] + AgOTf	**21 % *ee*, 16h**
[(R)-3,5-xylyl-binap(AuOTf)$_2$] + AgCl	**34% *ee***

Scheme 1-4 Early observations of silver effects

However, the so-called "silver effects" have long been overlooked until a recent report wherein Shi et al.[18] demonstrated that gold catalysts, with or without the presence of silver salts (*in situ* formed and filtered through celite, respectively) presented dramatically different activities through systematically reinvestigation of a series of previously reported transformations. Catalyst using NTf_2^- as the counteranion was an exception.[19]. They observed that while the *in situ* formed gold species gave good to excellent results, the celite-filtered catalysts showed compromised outcomes or even complete loss of reactivity. The addition of silver salts reactivated the catalytic systems, unambiguously indicating the influence of silver salts.

Afterwards, these observations were illustrated by Echavarren et al. through the isolation and X-ray diffraction characterization of a range of chloride-bridged digold(I) complexes (**Figure**

[17] Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem. Int. Ed.* **2007**, *46*, 6670.
[18] 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.
[19] Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.

1-11, **I**).[20] Moreover, this work could also, at least partially, accounted for certain cases wherein excess silver salt was beneficial to the expected outcomes. It was proposed that excess silver salt was used to cleavage the chloride bridge to generate catalytically active cationic gold(I) species. At the same time, Jones and co-workers[21] isolated and determined an Au(I)/Ag(I) complex featuring diphosphine trimetallic chloronium dication incorporating a triangular mixed gold/silver core with silver-arene chelation (**Scheme 1-7**, **II**).

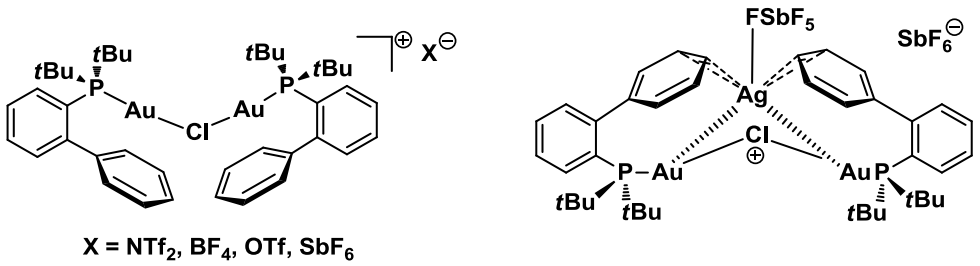


Figure 1-11 Bridged digold complexes

5. Gold-Catalyzed Homogeneous Reactions

Homogeneous gold catalysis[22] has emerged as a fascinating and rapidly growing field of research since the end of last century owing to the high and unique reactivity of cationic gold complexes. It provides an efficient and mild access to a wild variety of important frameworks in biologically active natural products and pharmaceutical important molecules. From a mechanistic point of view, gold complexes behave like the other electrophilic metal complexes, or even Brønsted acids in homogeneous catalysis. The gold-catalyzed reactions proceed *via* pathways which are similar to carbocation-mediated transformations. The special and unique performances of gold complexes arises from the very selective activation of

[20] Homs, A.; Escofet, I.; Echavarren, A. M. *Org. Lett.* **2013**, *15*, 5782.
[21] Zhu, Y.; Day, C. S.; Zhang, L.; Hauser, K. J.; Jones, A. C. *Chem. Eur. J.* **2013**, *19*, 12264.
[22] For reviews on homogeneous gold catalysis, see: (a) Pflasterer, D.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2016**, *45*, 1331. (b) Ranieri, B.; Escofet, I.; Echavarren, A. M. *Organic & Biomolecular Chemistry* **2015**, *13*, 7103.(c) Qian, D.; Zhang, J. *Chem. Soc. Rev.* **2015**, *44*, 677. (d) Jia, M.; Bandini, M. *ACS Catalysis* **2015**, *5*, 1638. (e) Dorel, R.; Echavarren, A. M. *Chem. Rev.* **2015**, *115*, 9028. (f) Debrouwer, W.; Heugebaert, T. S. A.; Roman, B. I.; Stevens, C. V. *Adv. Synth. Catal.* **2015**, *357*, 2975. (g) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev.* **2012**, *41*, 2448. (h) Krause, N.; Winter, C. *Chem. Rev.* **2011**, *111*, 1994. (i) Corma, A.; Leyva-Pérez, A.; Sabater, M. J. *Chem. Rev.* **2011**, *111*, 1657. (j) Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2010**, *49*, 5232. (k) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (l) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (m) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (n) Arcadi, A. *Chem. Rev.* **2008**, *108*, 3266. (o) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (p) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, *46*, 3410. (q) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271. (r) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem. Int. Ed.* **2006**, *45*, 7896.

alkyne, allene and even alkene moieties in complex molecules containing other functional groups, which can be attributed to the relativistic effects as well as the weak, but still remarkable π-back-donation from gold center to carbocation intermediates.

The initial step of gold-catalyzed reactions is always the coordination of the π-systems in alkyne, allene or even alkene to the electrophilic gold(I) or gold(III) complexes, which has been confirmed by the isolation and characterization of a large number of alkyne-, allene-, alkene- and diene-gold complexes. Then the Lewis acidic gold species selectively activate these π-systems toward the addition of various nucleophiles, including heteronucleophiles (e.g. ***O-, N-*** and ***S-***nucleophiles) and carbonucleophiles (**Figure 1-12**). Thereafter, diverse transformations would take place depending on the nature of the generated intermediates. The final step is the formation of products and regeneration of the active cationic gold species. This takes place mainly in three types of pathways: protodeauration, direct Au-elimination, or a trapping by an additional electrophile.

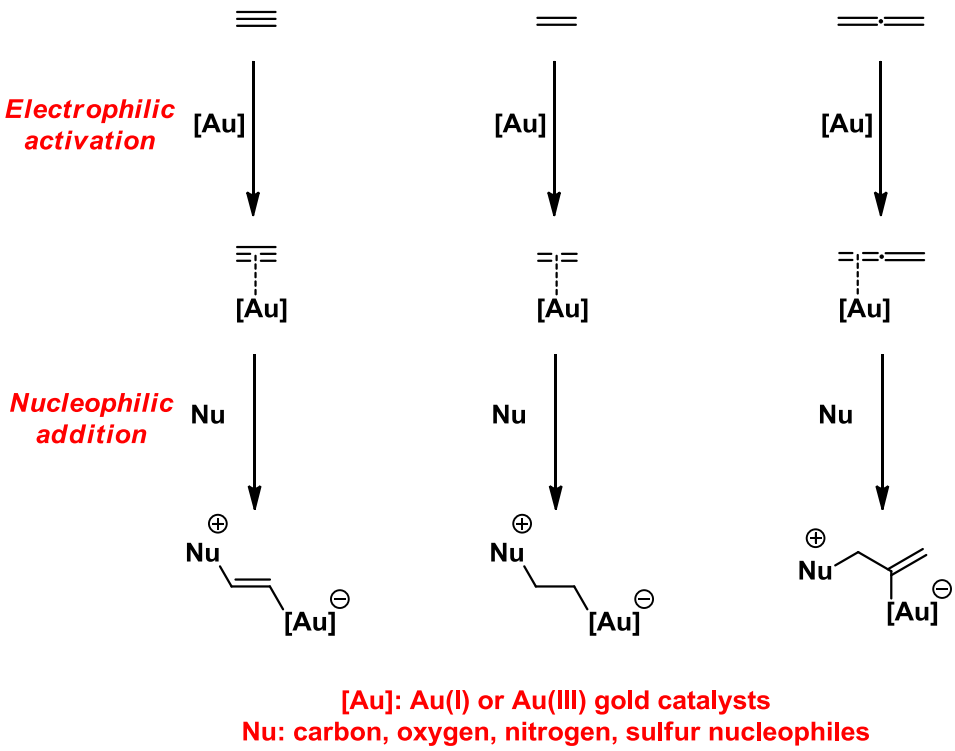


Figure 1-12 General pathways of nucleophilic addition

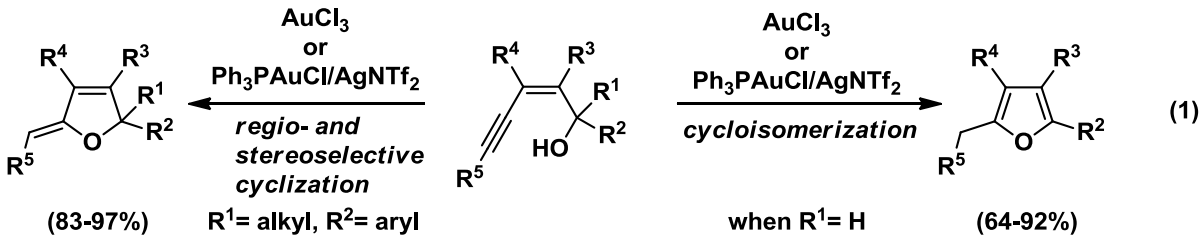
A large number of Au-mediated transformations have been developed during the past decade. The discussions in the following sections have been organized according to mechanistically different reactions that gold-activated π systems can undergo. As presenting a comprehensive review in homogeneous gold catalysis is beyond the scope of this manuscript, several representative examples are listed in each subsection.

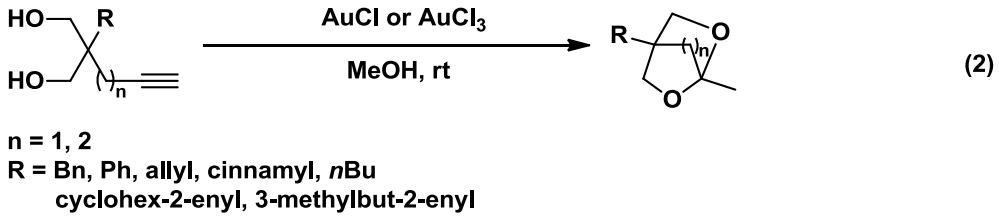
5.6. Nucleophilic addition

5.6.1. Oxygen nucleophiles

Cationic gold complexes possess low oxyphilicity owing to the relativistic effect, thus selective nucleophilic attack onto unsaturated C-C bonds can take place in the presence of ***O***-nucleophiles, such as hydroxyl group, carboxylate, amide, H_2O and so on. With a precursor bearing both ***O***-nucleophile and multiple bonds, gold complexes-mediated transformations would proceed to give oxygen containing heterocycles, such as furans-, pyranes- related derivatives. Given that another internal or external nucleophile exists in the reaction medium, a further transformation could take place with the gold intermediates generated in the first step, therefore rendering further increasing of molecular complexity.

In contrast to intermolecular nucleophilic attack (**Scheme 1-2** and **Scheme 1-3**), a wider range of Au-catalyzed transformations have been exploited intramolecularly by use of alkynol, allenol and their derivatives to provide oxygen containing heterocycles. For instance, Liu and co-workers[23] reported in 2005 a gold-catalyzed efficient and straightforward synthesis of fully substituted furans and dihydrofurans employing (*Z*)-2-en-4-yn-1-ols by cycloisomerizations (**Scheme 1-5**, eq. 1). Almost at the same time, an expedient and interesting access to strained bicyclic ketals was disclosed under homogeneous gold catalysis conditions (**Scheme 1-5**, eq. 2).



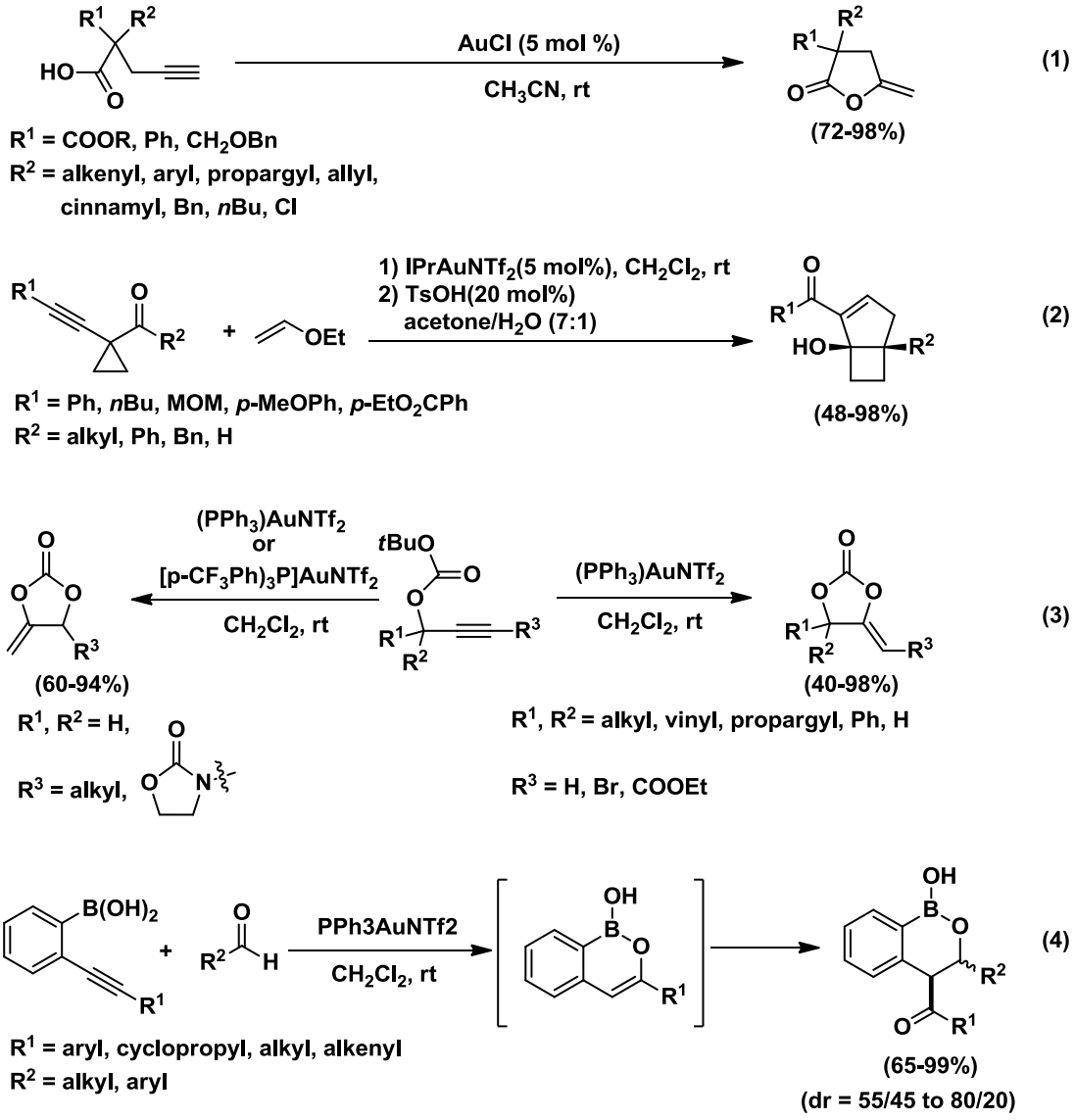


Scheme 1-5 Examples of cycloisomerizations of OH-containing alkynes

Besides free alcohols, other oxygen nucleophiles, such as carboxylic acids, ketones, carbonates, carbamates and boronic acids are all suitable candidates for gold-catalyzed

[23] Liu, Y.; Song, F.; Song, Z.; Liu, M.; Yan, B. *Org. Lett.* **2005**, *7*, 5409.

cycloisomerizations[24]. Several examples are listed in **Scheme 1-6**. Genêt and Michelet et al. reported a mild synthesis of functionalized *γ*-lactones through *exo*-selective cycloisomerizations of acetylenic acids (**Scheme 1-6**, eq. 1). Zhang et al. introduced one-pot, three components reactions to give highly strained [3.2.0]heptanes following a carbonyl nucleophilic addition/1,3-dipolar annulation/1,2-alkyl migration pathway (**Scheme 1-6**, eq. 2). It is noteworthy that when alkynylketones or esters served as nucleophiles the first nucleophilic attack could take place *via* anchimeric assistance of the carbonyl moiety.[25]



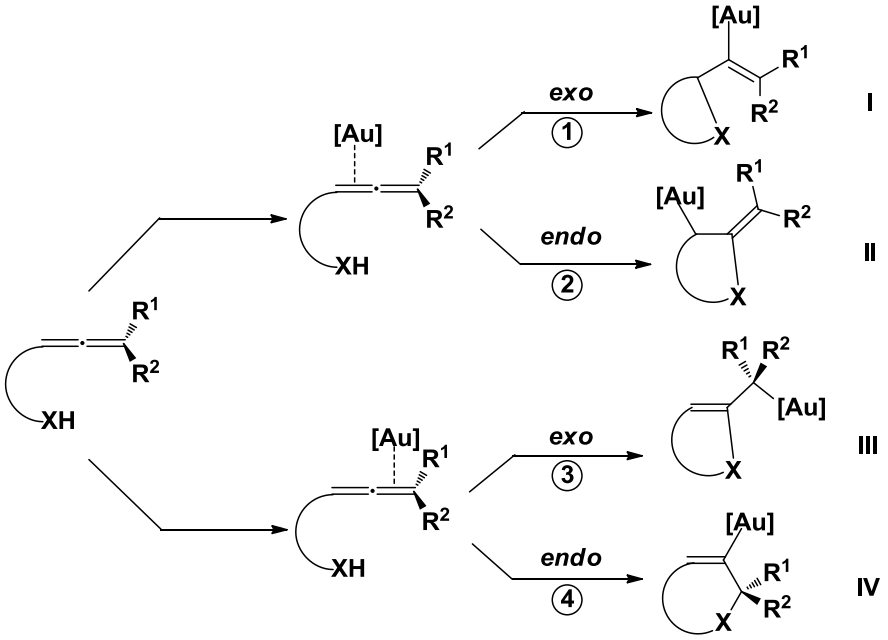
Scheme 1-6 Cycloisomerizations of alkynes bearing various *O*-nucleophiles

[24] (a) Genin, E.; Toullec, P. Y.; Antoniotti, S.; Brancour, C.; Genêt, J.-P.; Michelet, V. *J. Am. Chem. Soc.* **2006**, *128*, 3112. (b) Li, G.; Huang, X.; Zhang, L. *J. Am. Chem. Soc.* **2008**, *130*, 6944. (c) Buzas, A.; Gagosz, F. *Org. Lett.* **2006**, *8*, 515. (d) Buzas, A.; Gagosz, F. *Synlett* **2006**, *2006*, 2727. (e) Körner, C.; Starkov, P.; Sheppard, T. D. *J. Am. Chem. Soc.* **2010**, *132*, 5968.

[25] (a) Tang, J.-M.; Liu, T.-A.; Liu, R.-S. *J. Org. Chem.* **2008**, *73*, 8479. (b) Das, A.; Chang, H.-K.; Yang, C.-H.; Liu, R.-S. *Org. Lett.* **2008**, *10*, 4061. (c) Ghosh, N.; Nayak, S.; Sahoo, A. K. *J. Org. Chem.* **2011**, *76*, 500.

Gagosz and co-workers developed an efficient access to 4-alkylidene-1,3-dioxolan-2-ones by using of propargylic *tert*-butyl carbonates, which are synthetically useful motifs but still lack efficient approach to access so far (**Scheme 1-6**, eq. 3). The same group validated the employment of propargylic *tert*-butyl carbonates in similar transformations. In 2010, Sheppard et al. reported a novel approach to enolate equivalents for efficient aldol condensation *via* a boronic acid addition onto unactivated alkynes in the presence of gold catalysts. With the aldol products in hand, diverse subsequent transformations were investigated to provide a wide range of useful scaffolds (**Scheme 1-6**, eq. 4).

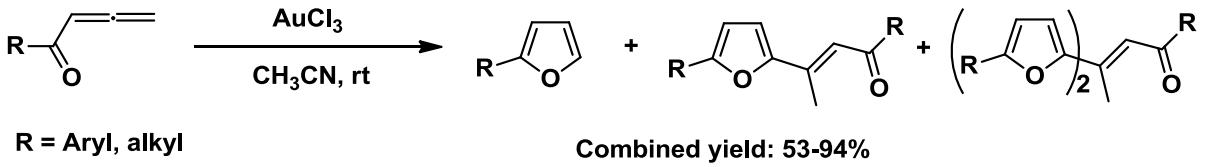
Analogously, the potential of allene derivatives in gold-catalyzed transformations have also been widely investigated. Gold complexes possess the ability to coordinate to both of the allenic double bonds and the regioselectivity in subsequent transformations depends on the nature of the precursor, in particular the length of linker between the allenyl and nucleophilc moieties. Generally, four distinct pathways are available with procedures ① and ④ favored in most cases (**Scheme 1-7**).



Scheme 1-7 General pathway of cyclizations of allene derivatives

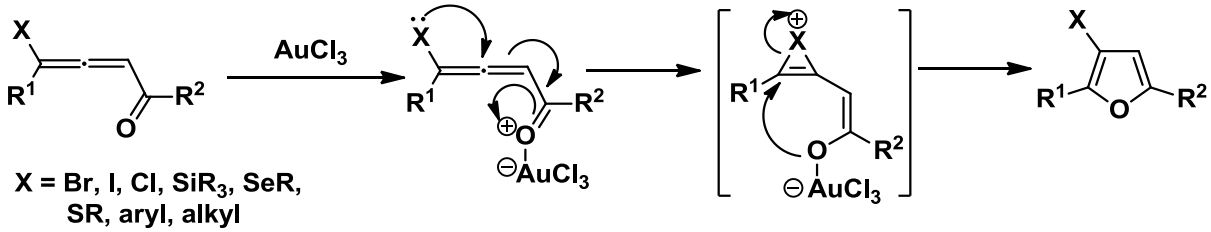
Hashmi et al. accomplished the first gold-catalyzed synthesis of substituted furans employing precursors containing both an allenic and a carbonyl group. The authors also observed some dimerization and trimerization products, which can be attributed to the consecutive Michael addition of the initially produced furans (**Scheme 1-8**).[26]

[26] Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem. Int. Ed.* **2000**, *39*, 2285.



Scheme 1-8 Cycloisomerization to furans from allenic ketones

Afterwards, Gevorgyan and co-workers disclosed an efficient access to a variety of bromo-, iodo-, chloro-, silyl-, seleno-, aryl-, alkyl-, and thio-mutisubstituted furans through an interesting 1,2-group migration mechanism[27] (**Scheme 1-9**). Au(III) salts, which are more oxophilic, were shown to play a crucial important role in the regioselectivity to provide 3-substituted furans whereas the more carbophilic Au(I) alternatively furnished 2-substituted furans *via* a 1,2-hydride shift.

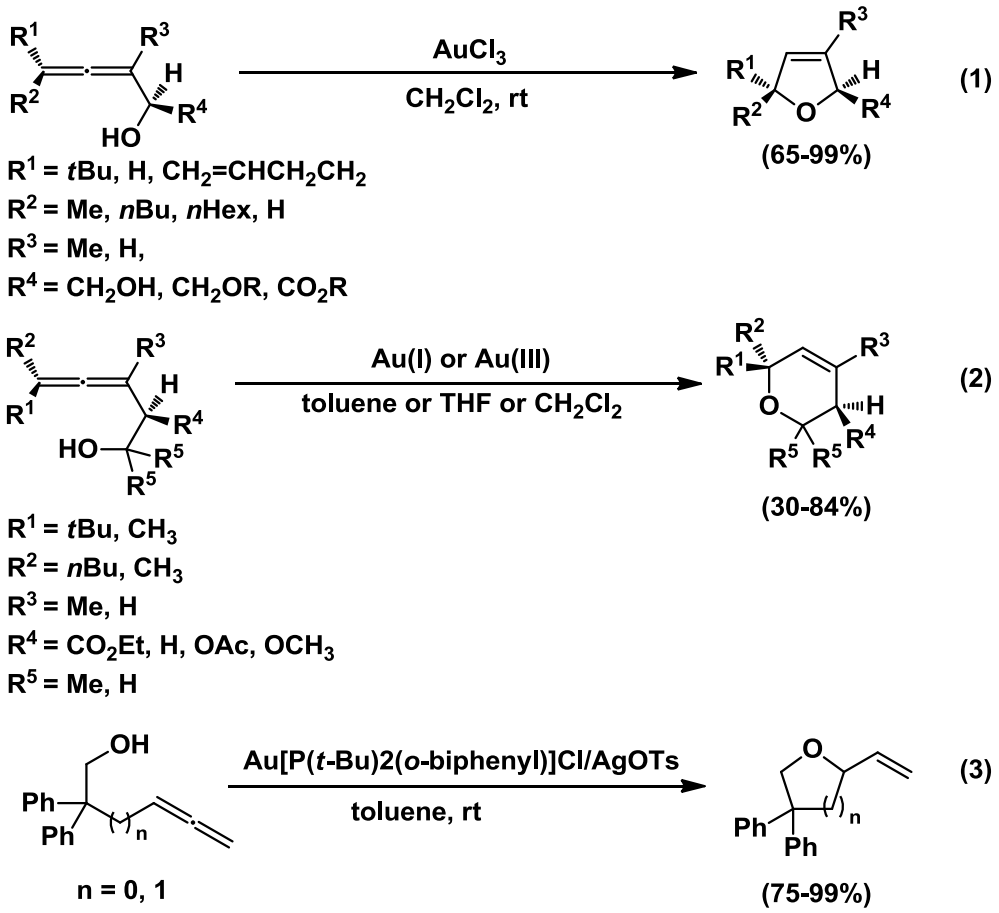


Scheme 1-9 Au(III)-catalyzed 1,2-group migration to substituted furans

Allenol derivatives are also suitable substrates and have found application in the realm of homogeneous catalysis employing gold complexes. In contrast to allenones, allenols could take advantage of the axis chirality of the allenic moiety, in which high levels of axis-to-center chirality transfer was very often observed. Moreover, the regioselectivity can be modulated by adjusting the length and the nature of substituents on the linker between the allenic and nucleophile moieties. For example, *α*- and β- hydroxyallenes underwent 5- and 6-*endo* cycloisomerization respectively to provide intermediate **IV** (**Scheme 1-7**) whereas route ① which gave rise to intermediate **I** (**Scheme 1-7**) *via* a 5- or 6- *exo* pathway was favored for *γ*- and *δ*- hydroxyallenes (**Scheme 1-10**) [28].

[27] (a) Sromek, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, *127*, 10500. (b) Dudnik, A. S.; Sromek, A. W.; Rubina, M.; Kim, J. T.; Kel'i, A. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2008**, *130*, 1440. (c) Xia, Y.; Dudnik, A. S.; Gevorgyan, V.; Li, Y. *J. Am. Chem. Soc.* **2008**, *130*, 6940. (d) Dudnik, A. S.; Xia, Y.; Li, Y.; Gevorgyan, V. *J. Am. Chem. Soc.* **2010**, *132*, 7645.

[28] (a) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537. (b) Gockel, B.; Krause, N. *Org. Lett.* **2006**, *8*, 4485. (c) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066.



Scheme 1-10 Representative examples of Au-catalyzed cycloisomerizations of allenols

A few enantioselective reactions have also been accomplished by several research groups.

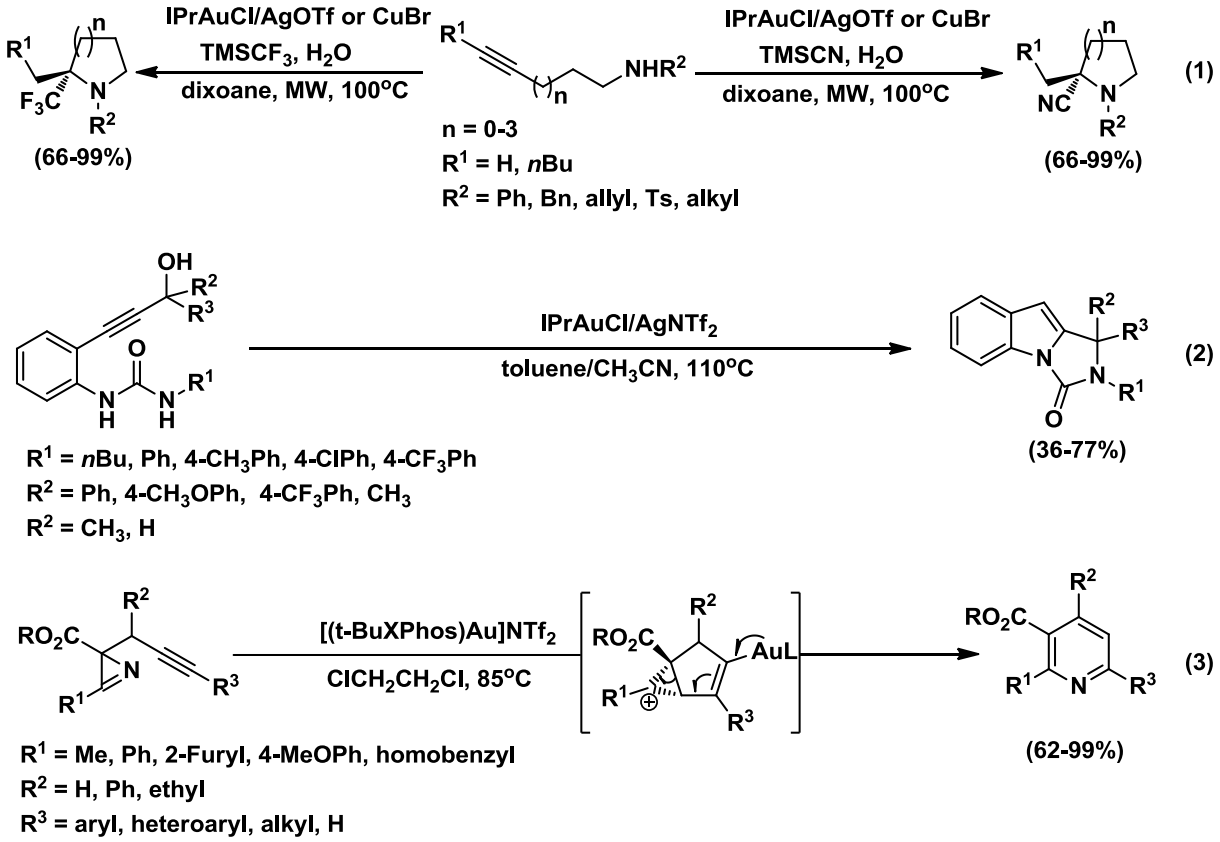
5.6.2. Nitrogen Nucleophiles

In analogous to *O*-nucleophiles, nitrogen-based functionalities have also been employed in a series of cyclizations catalyzed by cationic gold complexes. Free amines, sulfonamides, carbamates, ureas and aziridines can all serve as nucleophiles. These transformations proved to be a very powerful tool for the construction of nitrogen-containing heterocycles.

Generally, the cyclization can proceed by 5-*exo*-dig or 6-*endo*-dig pathways, which depends on the relative position of the alkyne and the *N*-nucleophile. Besides, the electronic properties of the substituents on the alkyne also play an important role in terms of regioselectivity, i.e., alkynes with electron-donating groups are prone to undergo 6-*endo*-dig cyclizations whereas those with electron-withdrawing substituents proceed *via* 5-*exo*-dig pathway. Last but not least, relative steric hindrance in internal alkynes should also be

considered when interpreting the chemical outcomes of the cyclizations. Several examples[29] which fall into this classification are present in **Scheme 1-11**.

Hammond and Xu et al. reported a convenient synthesis of α-CN and/or α-CF_3 nitrogen containing heterocycles using tandem nucleophilic additions in which the *in situ* formed imines or enamines are trapped by a second nucleophile, e.g. TMSCN and/or $TMSCF_3$ (**Scheme 1-11**, eq. 1). The starting materials underwent either *exo*- or *endo*- cyclizations to give, in accordance with Baldwin's rule, 5- and/or 6-membered rings, depending on the nature of the substrates. Hashmi and co-workers discovered the preparation of polycyclic indole scaffolds through a gold catalyzed nucleophilic addition/cyclization sequence (**Scheme 1-11**, eq. 2).



Scheme 1-11 Gold catalyzed transformations of *N*-nuleophiles

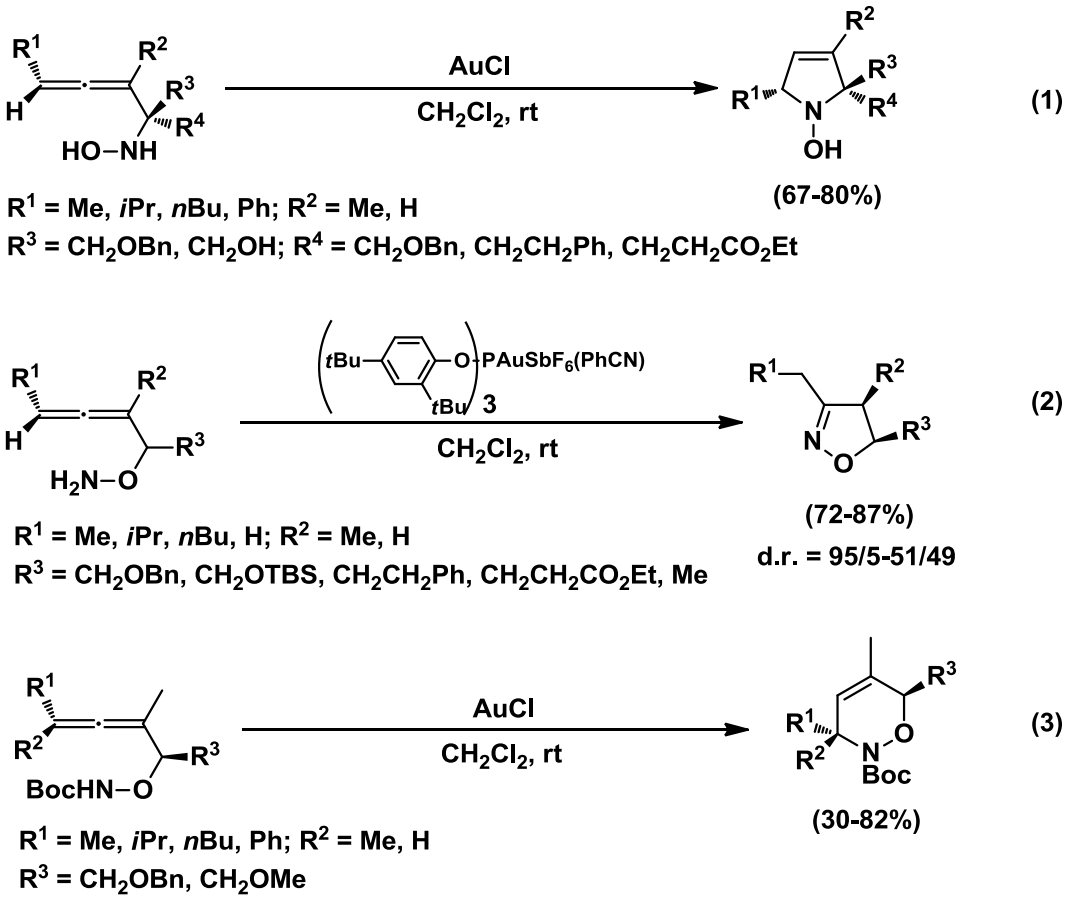
Gagosz and co-workers disclosed an intriguing and unprecedented transformation of 2H-azirines, which can be regarded as the synthetic equivalent of alkenyl nitrenes under gold catalysis conditions, thus allowing the formation of polysubstituted pyridines. In the

[29] (a) Han, J.; Xu, B.; Hammond, G. B. *Org. Lett.* **2011**, *13*, 3450. (b) Wang, T.; Shi, S.; Pflästerer, D.; Rettenmeier, E.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Chem. Eur. J.* **2014**, *20*, 292. (c) Prechter, A.; Henrion, G.; Faudot dit Bel, P.; Gagosz, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 4959.

mechanistic rationale, both a sequential and a concerted ring fragmentation/1,2-migration processes following a nitrogen nucleophilic attack onto gold activated alkynes were proposed to interpret the experimental results (**Scheme 1-11,** eq. 3).

Similar to allenols and allenones, allene derivatives bearing nitrogen nucleophiles have also seen applications in cyclizations. These transformations proceed following the same general mechanism and establish similar regio- and stereoselectivities (**Scheme 1-7**).

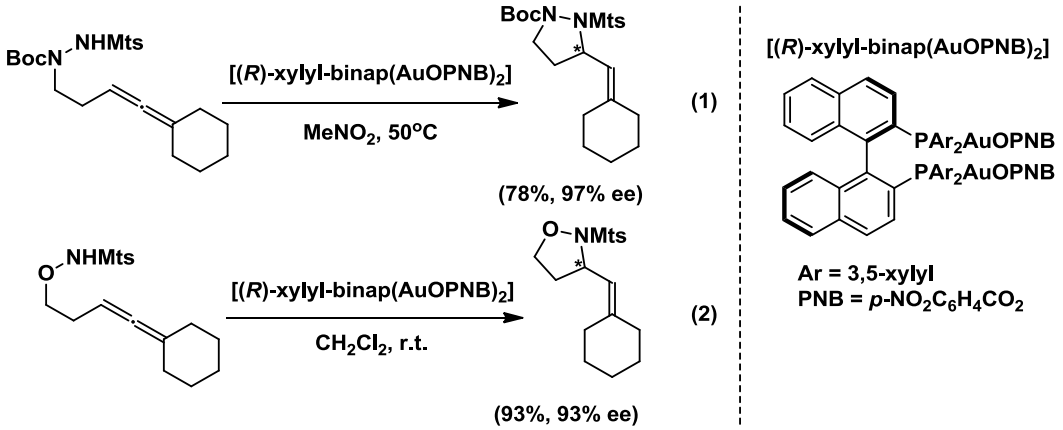
Using allenic precursors containing two vicinal heteroatoms, regio- and stereoselective formations of *N*-hydroxypyrrolines, dihydroisoxazoles, and dihydro-1, 2-oxazines were explored by Krause and co-workers.[30] In such cases, 5-*endo*, 5-*exo* and 6-*endo* cyclizations can selectively occur with high levels of stereoselectivity, by shifting cationic gold complexes or by protecting the nitrogen atoms (**Scheme 1-12**).



Scheme 1-12 Au(I)-catalyzed transformations of allenes containing vicinal nucleophiles

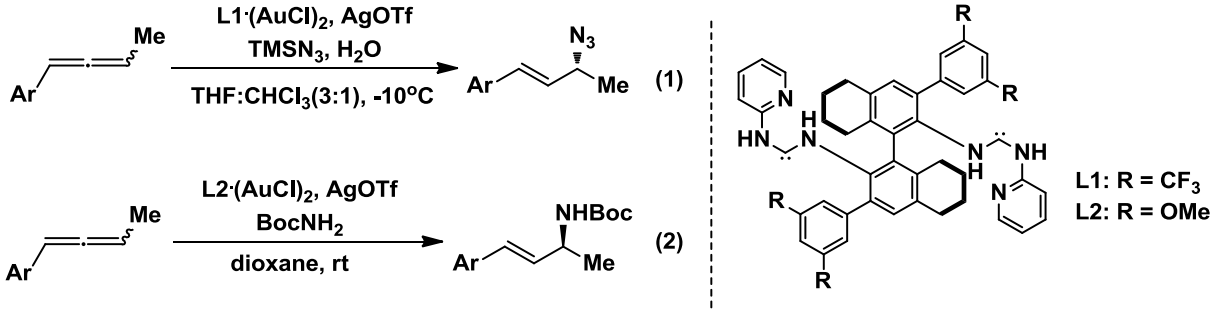
Toste et al. reported the enantioselective hydroamination of allenes for the synthesis of pyrazolidines, isoxazolidines and tetrahydrooxazines using gold catalysts possessing a chiral biarylphosphine ligand. 5- or 6- *exo* Products were exclusively formed (**Scheme 1-13**).

[30] Winter, C.; Krause, N. *Angew. Chem. Int. Ed.* **2009**, *48*, 6339.



Scheme 1-13 Enantioselective hydroaminations of allenes

Gold-catalyzed enantioselective hydroazidation and hydroamination were developed by the same group[31] in an intermolecular manner employing acyclic diaminocarbene (ADC) gold(I) complexes, giving rise to stereodivergent allylic amines precursors (**Scheme 1-14**, eq. 1 and eq. 2).



Scheme 1-14 Gold(I)-mediated intermolecular hydroaminations

5.6.3. Sufur nucleophiles

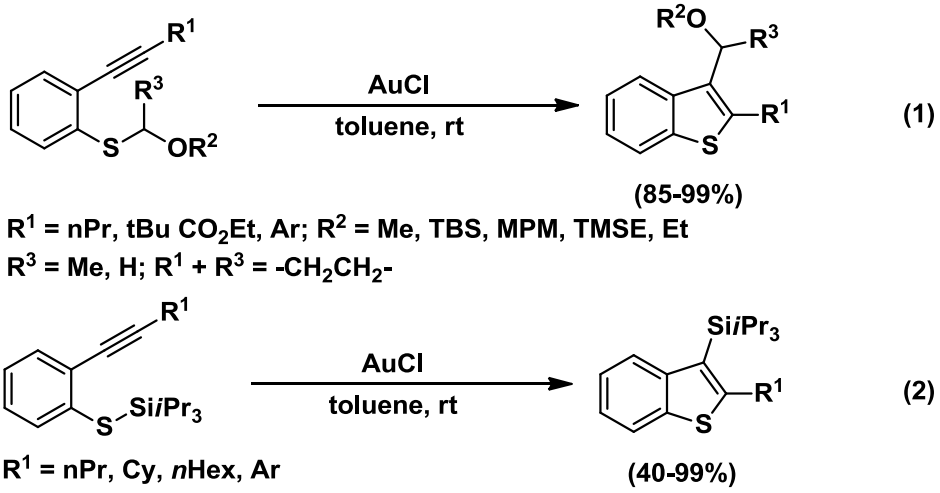
Starting materials with mercapto groups cannot be used in palladium-catalyzed reactions, which can be attributed to catalyst poisoning due to the strong coordinating properties of sulfur. Conversely, gold complexes saw some applications in this area. For example, Nakamura and co-workers[32] provided a convenient and facile access to 2,3-disubstituted benzothiophenes *via* a carbothiolation process, which occurs through the attack of sulfur

[31] (a) LaLonde, R. L.; Wang, Z. J.; Mba, M.; Lackner, A. D.; Toste, F. D. *Angew. Chem. Int. Ed.* **2010**, *49*, 598. (b) Khrakovsky, D. A.; Tao, C.; Johnson, M. W.; Thornbury, R. T.; Shevick, S. L.; Toste, F. D. *Angew. Chem. Int. Ed.* **2016**, ASAP.

[32] (a) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 4473. (b) Nakamura, I.; Sato, T.; Yamamoto, Y. *Angew. Chem. Int. Ed.* **2006**, *45*, 4473.

atom toward gold-activated triple bond followed by a 1,3-migration of the group bound to sulfur (**Scheme 1-15**, eq. 1).

Soon after that, the same group reported a similar transformation in which 3-silylbenzo[b]thiophenes were produced in good to excellent yield through an intramolecular capture of the Au-intermediate after the initial nucleophilic addition of the sulfur functionality (**Scheme 1-15**, eq. 2).



Scheme 1-15 Homogeneous gold catalysis involving sulfur nucleophiles

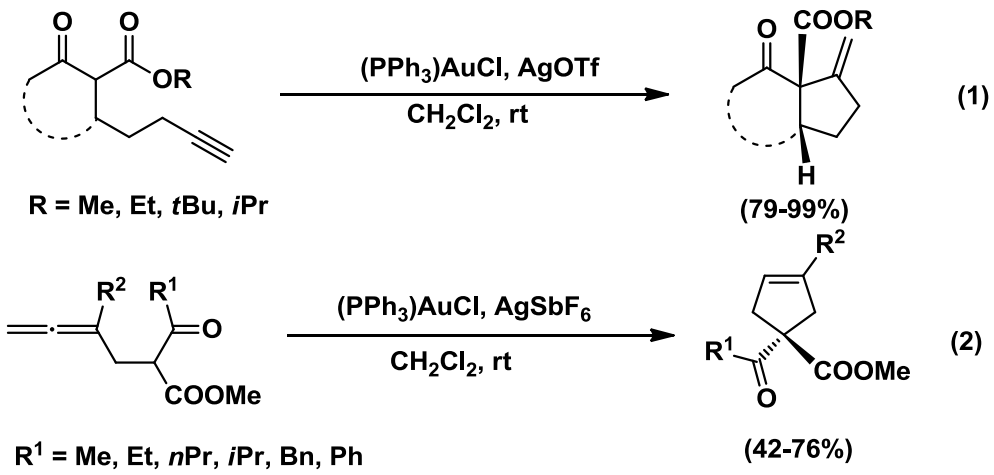
5.6.4. Carbon nucleophiles

The addition of carbon nucleophiles, such as electron rich aromatic rings, 1,3-dicarbonyl compounds and/or alkenes, alkynes to unactivated multiple bonds have also been accomplished under homogeneous gold catalysis conditions, thus allows for the formation of C-C bonds and/or carbocylcles.

Toste et al.[33] developed an Au-catalyzed Conia-ene reaction under neutral and "open flask" conditions by utilizing β-ketoesters, which reacted with alkynes in an intramolecular manner. An excellent diastereoselectivity and yield were achieved, providing an efficient and facile access to quaternary carbon centers (**Scheme 1-16**, eq. 1).

One similar transformation took place with allenes serving as the starting material. In this case, 5-*endo* cycloisomerizations occur exclusively (**Scheme 1-16**, eq. 2).

[33] (a) Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526. (b) Jiang, X.; Ma, X.; Zheng, Z.; Ma, S. *Chem. Eur. J.* **2008**, *14*, 8572.

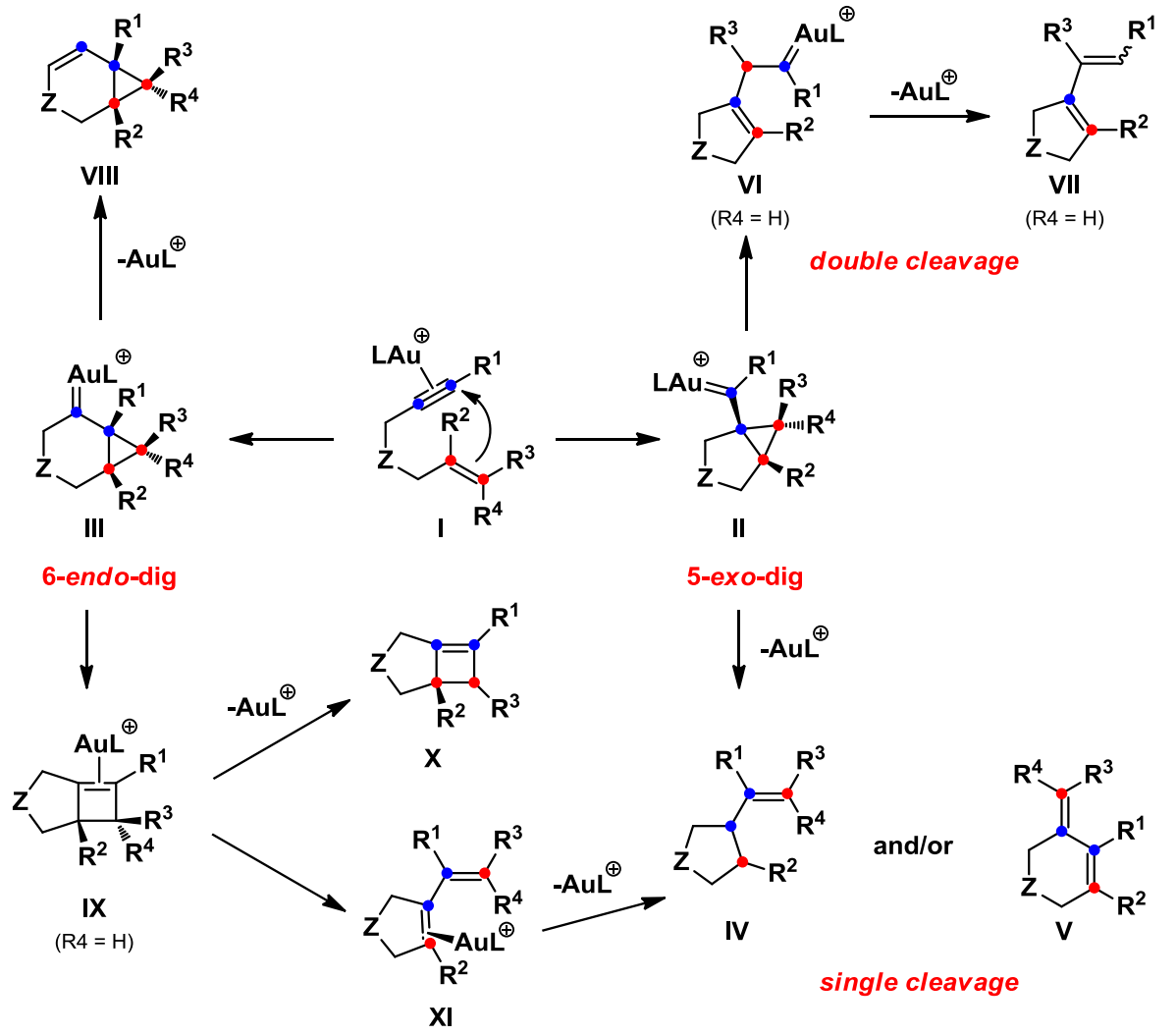


Scheme 1-16 Gold(I)-catalyzed nucleophilic addition of 1,3-dicarbonyl compounds

5.7. Cycloisomerizations of 1,*n*-enynes

Cycloisomerizations involving 1,*n*-enynes have been extensively exploited in the field of homogeneous gold catalysis, in particular the transformations of 1,6-enynes. The mechanistic rationale has been best elucidated on the basis of both experimental and computational contributions. Herein, cycloisomerization of 1,6-enynes has been taken as the example to illustrate general mechanisms (**Scheme 1-17**).[34]

The cycloisomerization of 1,6-enynes begins with the coordination of gold complexes to the alkyne moiety to give rise to complex **I.** This is followed by nucleophilic attack by the alkene motif *via* a 5-*exo*-dig or 6-*endo*-dig pathway to generate intermediates **II** and/or **III** respectively. Then, intermediate **II** could undergo two distinct skeletal rearrangements, namely, single cleavage and double cleavage. The single cleavage skeletal rearrangement takes place *via* a ring opening of the three-membered ring in **II** with concomitant 1,3-migration of the terminal carbon (CR^3R^4) of the alkene to the carbon attached to R^1 of the alkyne. This results in the formation of intermediate **IV**. Compound **V** arises from a 1,3-migration of the internal carbon (CR^2) of the double bond to the carbon (CR^1) attached to R^1 of the alkyne *via* an *endo*-single cleavage of intermediate **II**. Under double cleavage condition, the terminal carbon(CR^3R^4) of the alkene would insert into the alkyne carbons with simutaneous cleavage of the double bond and triple bond, allowing the formation of intermediate **VI**, which finally gives rise to **VII** after protodeauration.



Scheme 1-17 General mechanism for cycloisomerization of 1,6-Enynes[34]

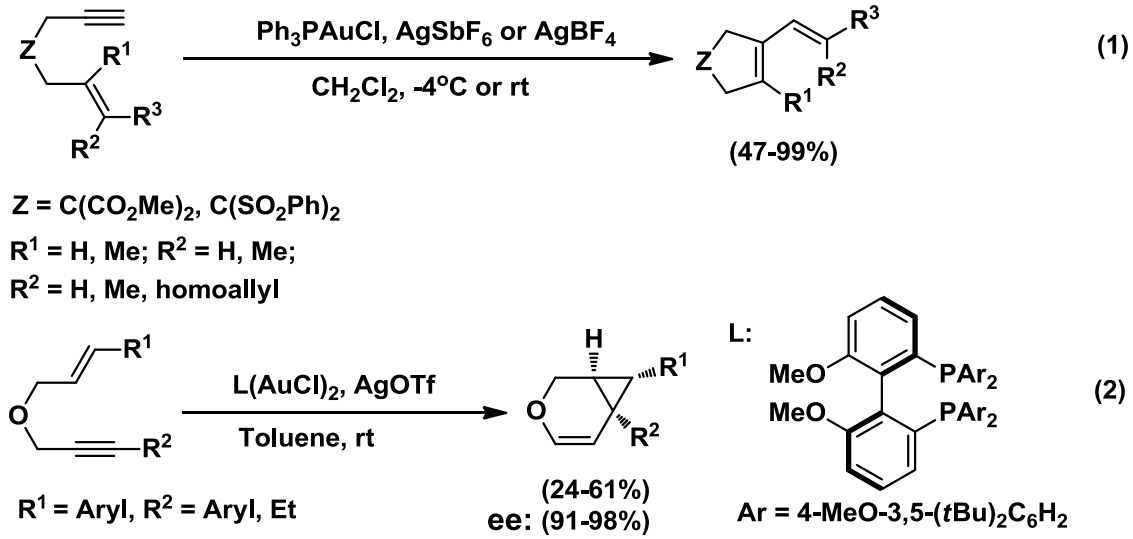
The transformation of 1,6-enynes can alternatively takes place *via* a 6-*endo*-dig pathway, leading to the three-membered ring gold carbene **III** which would gave **VIII** after direct protodeauration. Alternatively, **III** could isomerize into intermediate **IX** *via* a ring expansion en route to **X** following a formal deauration. Intermediate **XI** can also be formed through a ring-opening isomerization, which would give rise to product **IV** after direct deauration.

A few representative examples involving gold-catalyzed cycloisomerization of 1, *n*-enynes are shown in the following paragraphs.

Echavarren and co-workers reported that 1,6-enynes containing a terminal alkynes underwent exclusively 5-*exo*-dig cyclizations followed by single cleavage to give rise to 1,3-dienes in the presence of an *in situ* generated gold(I) catalyst[35] (**Scheme 1-18**, eq. 1).

[34] Dorel, R.; Echavarren, A. M. *Chem. Rev.* **2015**, *115*, 9028.
[35] Nieto-Oberhuber, C.; Muñoz, M. P.; Buñuel, E.; Nevado, C.; Cárdenas, D. J.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2004**, *43*, 2402.

Bicylco[4.1.0]heptane derivatives were enantiomerically produced[36] by a cycloisomerization of 1,6-enynes containing an *O*-linker *via* 6-*endo*-dig pathway in the presence of a chiral dinuclear gold(I) catalyst (**Scheme 1-18**, eq. 2).

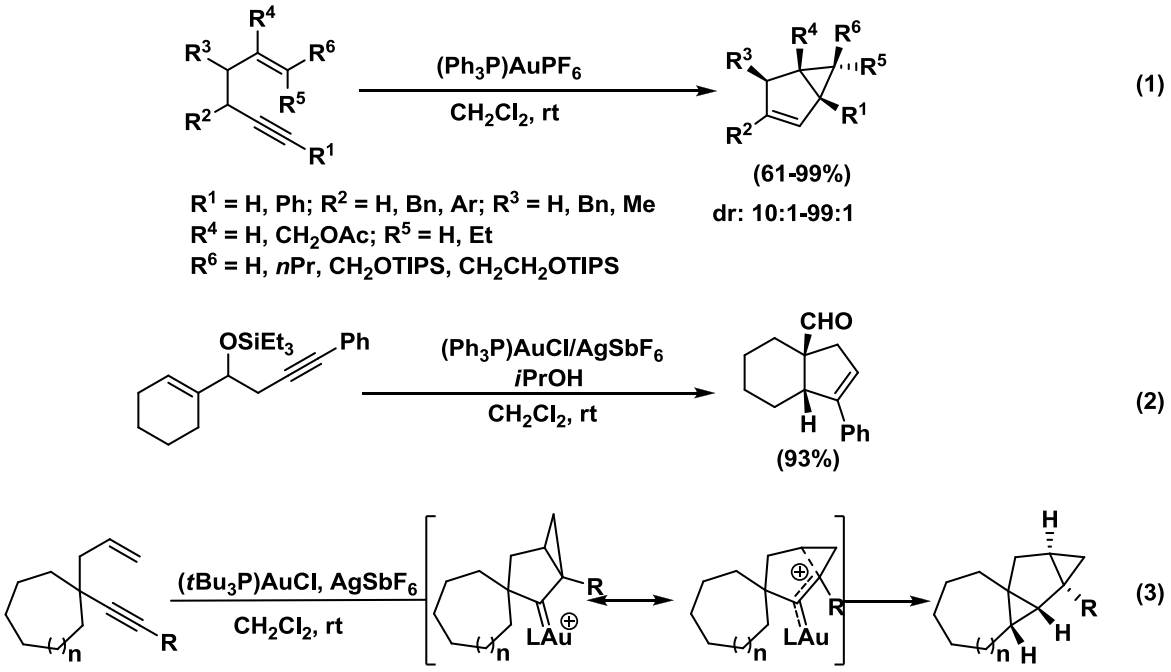


Scheme 1-18 Examples of cycloisomerizations of 1,6-enynes

Formally, 1,5-enynes prefer to undergo *endo*-type cycloisomerization which can be attributed to the favorable formation of bicyclo[3.1.0]hexane scaffolds. The *exo*-type cyclization indeed leads to a more strained intermediate, therefore less stable and favorable. The cycloisomerization of 1,5-enynes catalyzed by gold catalysts proceed through an exclusive 5-*endo*-dig pathway to give rise to bicycle[3.1.0]hexenes bearing a cyclopropane motif with a high stereoselectivity (**Scheme 1-19**, eq. 1).[37] Highly functionalized cyclopentenes were stereoselectively constructed from 3-silyloxy-1,5-enynes following a mechanism involving tandem 6-*endo* cycloisomerization/pinacol rearrangement of the *in situ* formed gold(I) carbocationic species. In this case, counterions played a crucial role with SbF_6^- displaying excellent catalytic activity whereas catalysts with a BF_4^- counterion lead to complete loss of reactivity[38] (**Scheme 1-19**, eq. 2). 1,5-Enynes bearing large and flexible rings at the propargylic position underwent consecutive cycloisomerization/C_{sp3}-H bond insertion instead of 1,2-alkyl shift[38], leading to the formation of tetracyclic products.[39] When the mechanism of C-H bond insertion process was studied, inverse primary kinetic isotope effects were observed. This is different from that of C-H bond insertion of common metal-carbenoid or hydride transfer process toward carbocation species, thus leading to the envision that it is more likely that

[36] Chao, C.-M.; Beltrami, D.; Toullec, P. Y.; Michelet, V. *Chem. Commun.* **2009**, 6988.
[37] Luzung, M. R.; Markham, J. P.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 10858.
[38] Kirsch, S. F.; Binder, J. T.; Crone, B.; Duschek, A.; Haug, T. T.; Liébert, C.; Menz, H. *Angew. Chem. Int. Ed.* **2007**, *46*, 2310.
[39] Horino, Y.; Yamamoto, T.; Ueda, K.; Kuroda, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2809.

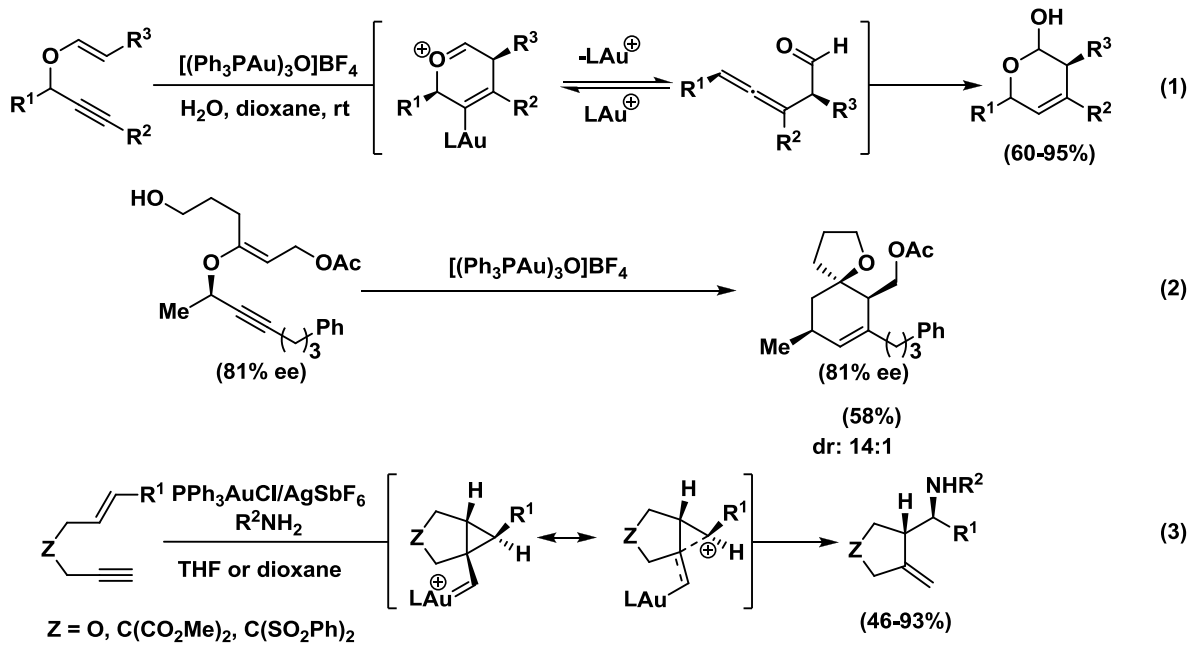
cationic gold(I) intermediate and the hydrogen atom formed a *σ*-complex preceding the final productive hydride transfer (**Scheme 1-19**, eq 3).



Scheme 1-19 Examples of cycloisomerizations of 1,5-enynes

In the presence of an external nucleophile and/or in the case of substrates containing another potential nucleophile, the formed gold(I) intermediate in the cycloisomerization step could be intercepted in a cascade process, therefore leading to a further increase in molecular complexity. Propargyl vinyl ethers react with gold(I) complexes to provide 2-hydroxy-3,6-dihydropyran derivatives stereoselectively in the presence of H_2O, while precursors with an appropriate pendant alcohol allowed for the stereocontrolled construction of bicyclic spiroketal frameworks (**Scheme 1-20**, eq. 1 and eq. 2).[40] Analogously, a tandem cycloisomerization/hydroamination transformation of 1,6-enynes was described for the synthesis of carbo- and heterocyclic derivatives bearing amino functional groups under mild conditions in good to excellent yields (**Scheme** 1-20, eq 3).[41]

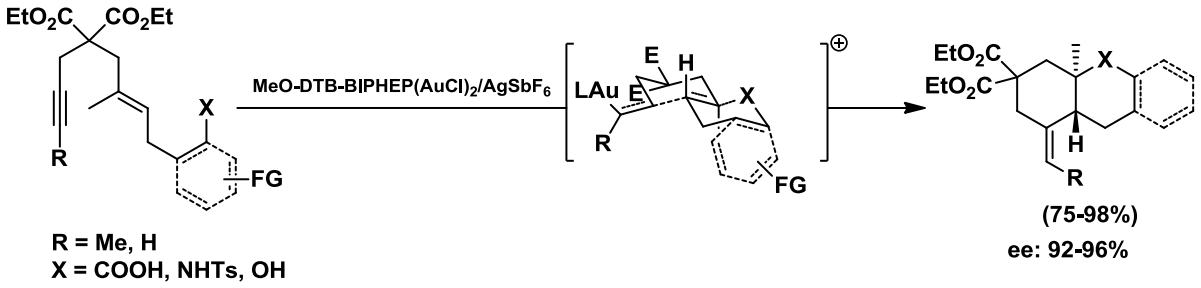
[40] Sherry, B. D.; Maus, L.; Laforteza, B. N.; Toste, F. D. *J. Am. Chem. Soc.* **2006**, *128*, 8132.
[41] Leseurre, L.; Toullec, P. Y.; Genêt, J.-P.; Michelet, V. *Org. Lett.* **2007**, *9*, 4049.



Scheme 1-20 Au(I)-catalyzed tandem transformations of 1,2-enynes

The cycloisomerzations of 1,7-, 1,8-, and even higher enynes have also intrigued synthetic chemists, albeit they have not been investigated as wildly as 1,6- and 1,5 analogues.

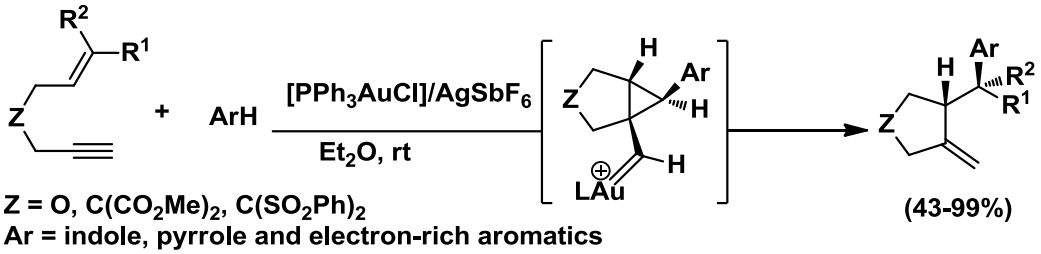
Gold(I)-catalyzed enantioselective polycyclization was also accomplished from polyene, in which the transformation was initiated by the attack of an alkene onto the gold-activated alkyne followed by subsequent tandem trapping by another alkene motif and a terminating nucleophile. The stereochemical outcome of the reaction was in accordance of the "Stork-Eschenmoser hypothesis" (**Scheme 1-21**).[42]



Scheme 1-21 Au(I)-catalyzed polycyclization of polyenes

[42] Sethofer, S. G.; Mayer, T.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8276.

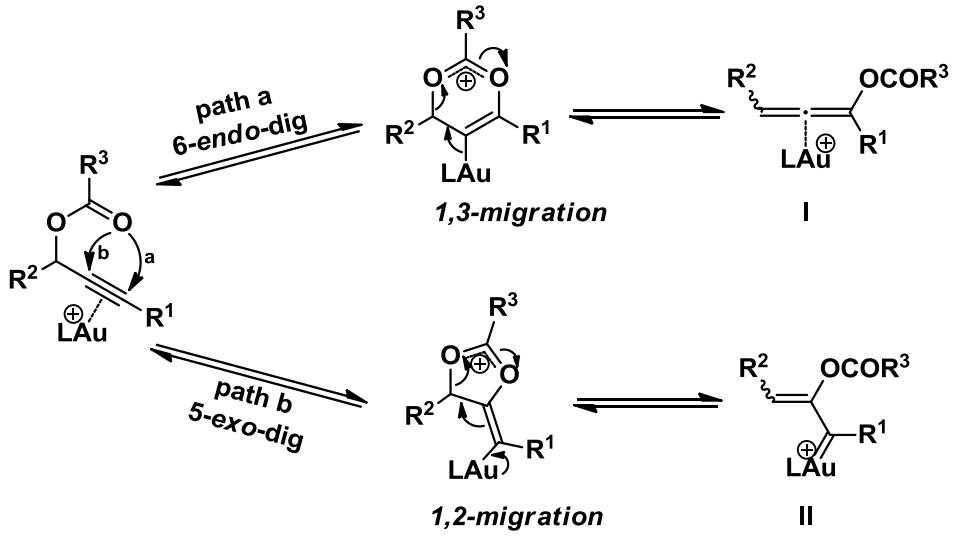
1,6-Enynes react with electron rich aromatic and/or heteoaromatic rings to afford stereocontrolled carbo- and heterocycles under homogeneous gold catalysis conditions following a Friedel-Crafts-type addition and cycloisomerization sequence.[43]



Scheme 1-22 Tandem cycloisomerization and hydroarylation

5.8. Gold-catalyzed rearrangement of propargylic carboxylates

Under homogeneous gold catalysis conditions, propargylic carboxylates could undergo 1,2- or 1,3- acyloxy migrations *via* 5-*exo*-dig (path a) and 6-*endo*-dig (path b) pathwayS, providing access to *α*-acyloxy-*α*,β-unsaturated carbenes **I** and allene-gold intermediate **II** respectively (**Scheme 1-23**).

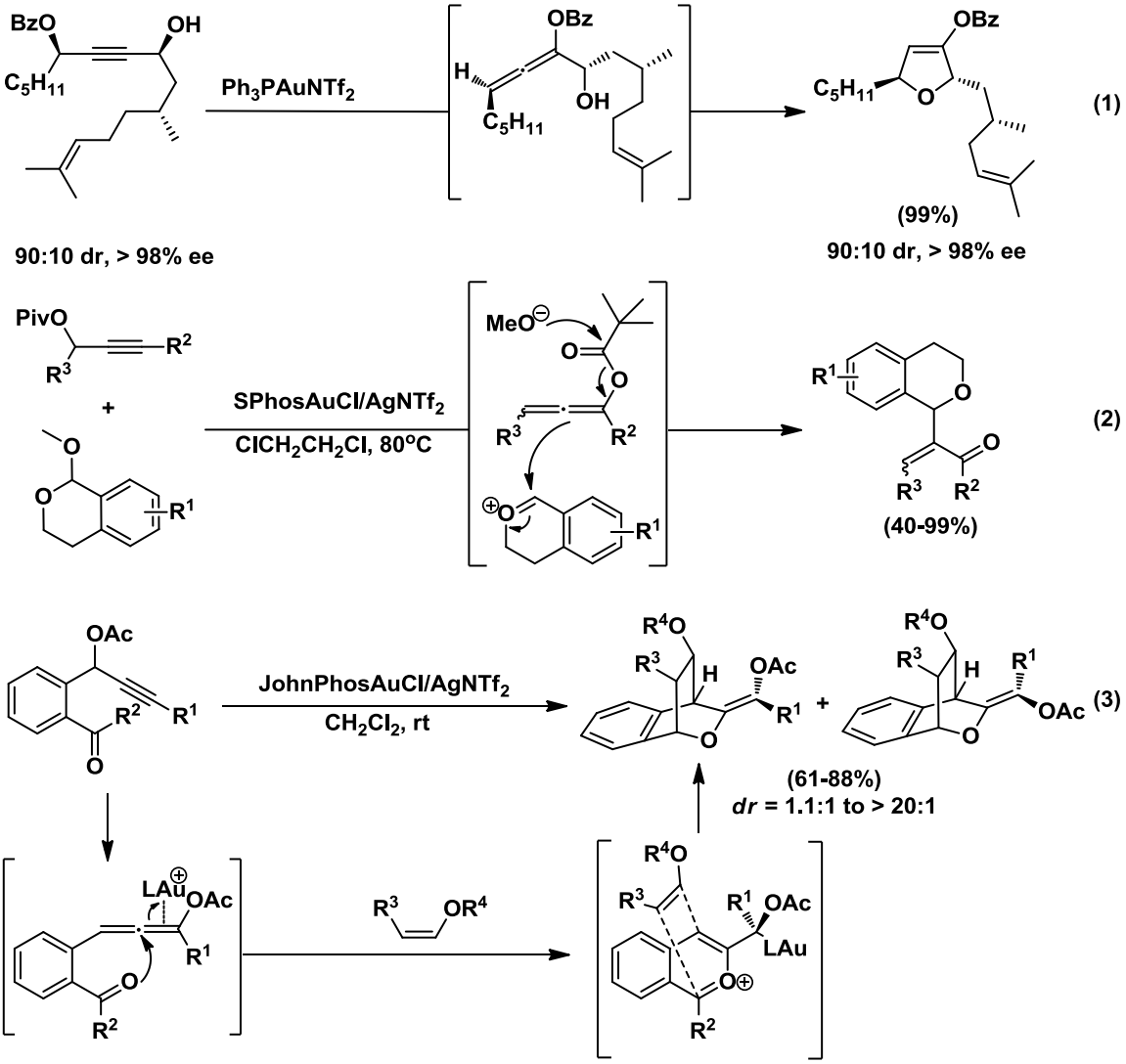


Scheme 1-23

For instance, functionalized 2,5-dihydrofurans were accessed from propargylic benzoates in the presence of $Ph_3PAuNTf_2$ *via* a tandem benzoate migration and nucleophilic addition of hydroxyl group onto an *in situ* formed allene-gold(I) complexe. Notably, the stereochemical information was completely retained after the two-step isomerization process (**Scheme 1-24**, eq. 1).[44] An intermolecular formation of $C(sp^2)—C(sp^3)$ bonds was achieved from *in situ*

[43] Toullec, P. Y.; Genin, E.; Leseurre, L.; Genêt, J.-P.; Michelet, V. *Angew. Chem. Int. Ed.* **2006**, *45*, 7427.
[44] Buzas, A.; Istrate, F.; Gagosz, F. *Org. Lett.* **2006**, *8*, 1957.

generated nucleophilic allenes by gold-catalyzed rearrangement of propargylic esters (**Scheme 1-24**, eq. 2).[45] The same strategy was used for the synthesis of highly functionalized oxacycles from propargylic esters (**Scheme 1-24**, eq. 3).[46]

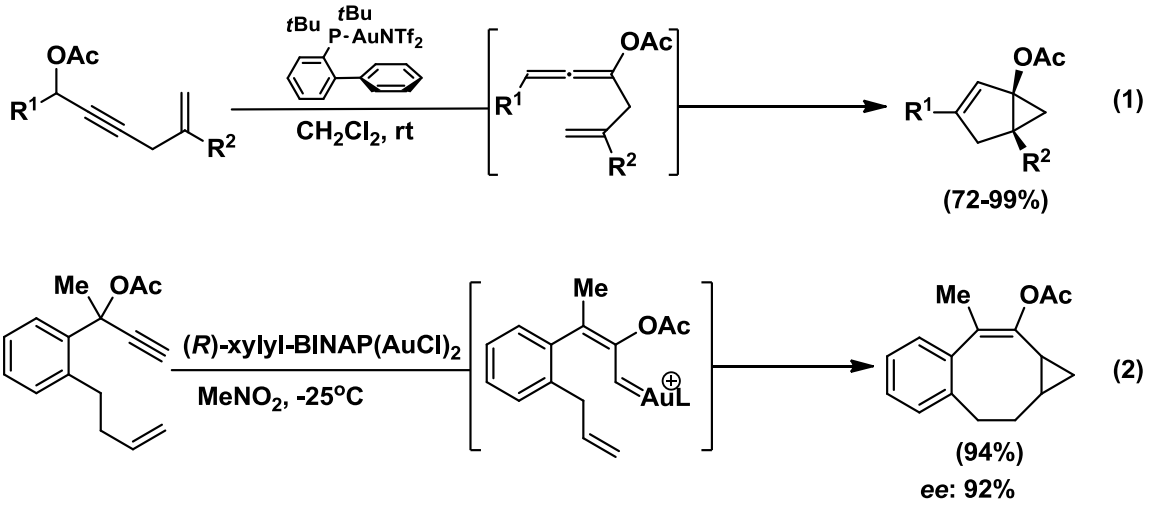


Scheme 1-24 Au(I)-mediated transformations of propargylic carboxylates

1,4-Enynes bearing a propargyl acetate undergo a gold-mediated rearrangement to give rise to allene derivatives. A subsequent electrophilic addition of the pendant alkene moiety allows the synthesis of 5-en-2-yn-1-yl acetates which can be further converted into 2-cycloalken-1-ones.[47] Enantioselective construction of medium rings[48] was accomplished in the presence of chiral binuclear gold(I) complexes from propargylic carboxylates tethered with an alkene

[45] Yu, Y.; Yang, W.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2013**, *52*, 7586.
[46] Teng, T.-M.; Liu, R.-S. *J. Am. Chem. Soc.* **2010**, *132*, 9298.
[47] Buzas, A.; Gagosz, F. *J. Am. Chem. Soc.* **2006**, *128*, 12614.
[48] Watson, I. D. G.; Ritter, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 2056.

moiety. The transformation proceed *via* a 1,2-migration of carboxylate/cyclopropanation cascade (**Scheme 1-25**).

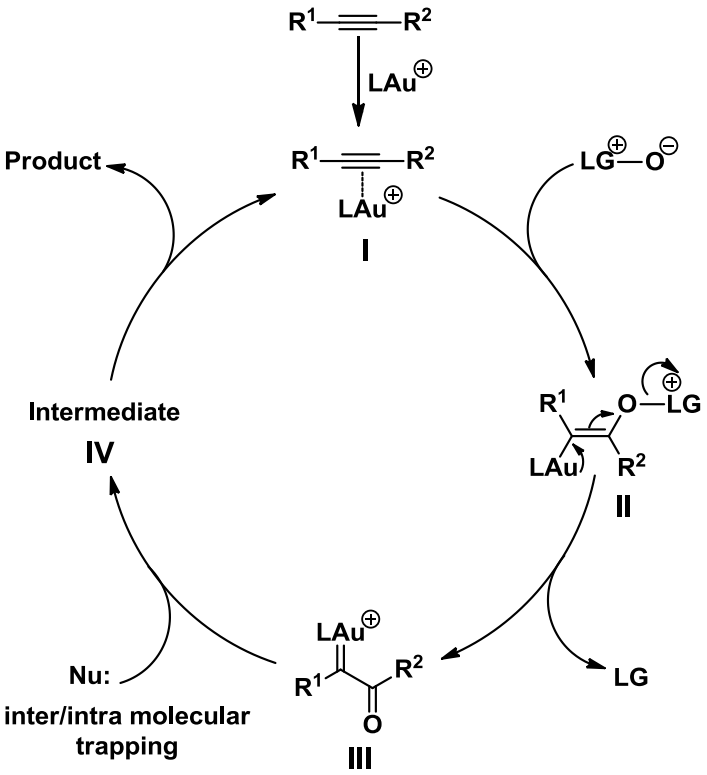


Scheme 1-25

5.9. Oxidation

Mechanistically, gold-mediated oxidations are initiated by the coordination of alkynes to cationic gold complexes (i.g.,**I**). This was followed by the attack of the *O*-nuleophiles containing a potential leaving group en route to formation of intermediate **II**. With the assistance of back-bond-donation of the gold center, **II** formally evolved into gold(I) carbenoid **III** with the concomitant exclusion of the leaving group (i.g., **LG**). Subsequently, various transformations can operate to generate diverse products depending on the nature of the internal and/or external reacting partners and the alkyne precursors. This leads to the generation of a key intermediate **IV,** which gives rise to a variety of products with the regeneration of active gold catalyst (**Scheme 1-26**).

Gold-catalyzed oxidations have been implemented by use of various potential oxidants, including sulfoxides, pyridine *N*-oxides, nitrones, nitroso-and nitrobenzenes and even epoxides. Oxidations involving the use of pyridine *N*-oxides have been largely studied and illustrated by several research groups, e.g., Zhang, Gagosz, Toste, Hashimi, Liu, Davis and Li. Herein several examples which fall into this class of gold-catalyzed oxidations are listed.

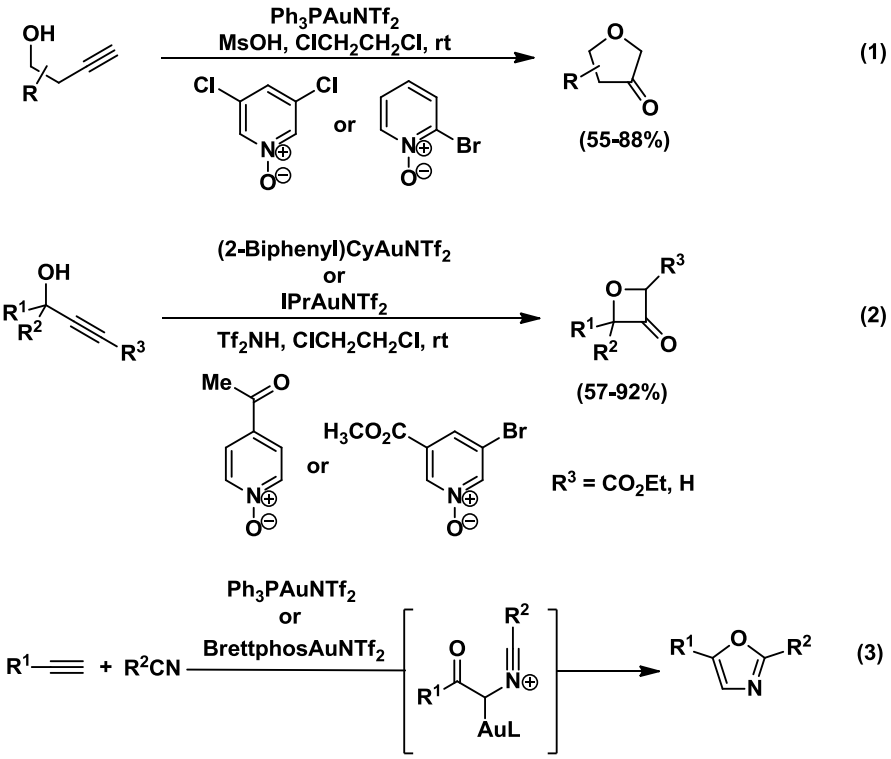


Scheme 1-26 General catalytic cycle of gold-mediated oxidations

Zhang[49] et al. firstly demonstrated the utility of alkynes, in the presence of external oxidant (e.g., pyridine *N*-oxides), as a surrogate of *α*-carbonyl diazo compounds which are hazardous and potentially explosive , leading to the formation of versatile *α*-oxo gold(I) carbenoids. By use of this unprecedented approach to *α*-oxo gold(I) carbenoids, they synthesized oxetan-3-ones and oxetan-3-ones in an expedient, step-economical and economical manner *via* an intramolecular trapping of the carbenoids (**Scheme 1-27**, eq. 1 and eq. 2).

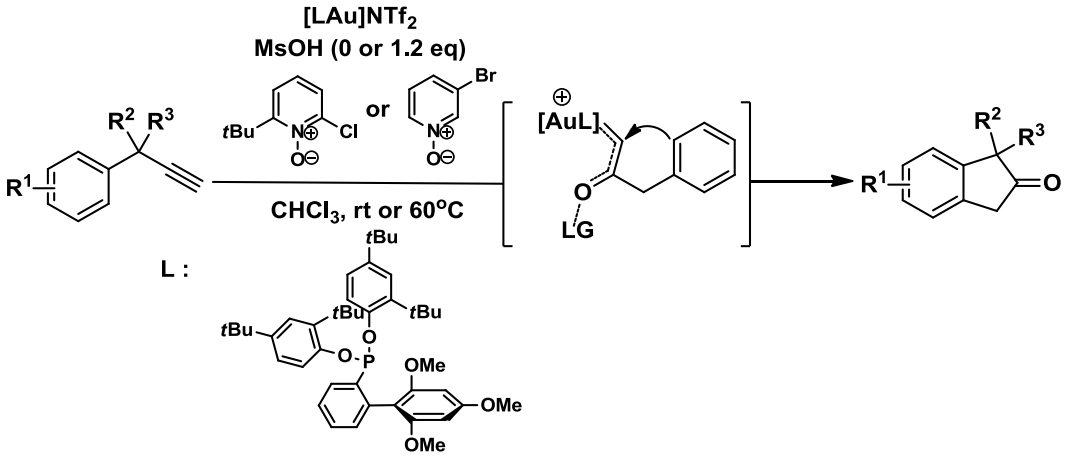
Analogously, the intermolecular trapping[50] of the key carbenoids has also been exemplified with acetonitrile and/or more sophisticated nitriles serving as reacting partners with alkynes, therefore highlighting the synthetic versatility of *α*-oxo gold(I) carbenoids (**Scheme** 1-27, eq. 3).

[49] (a) Ye, L.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 3258. (b) Ye, L.; He, W.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 8550.
[50] (a) He, W.; Li, C.; Zhang, L. *J. Am. Chem. Soc.* **2011**, *133*, 8482. (b) Luo, Y.; Ji, K.; Li, Y.; Zhang, L. *J. Am. Chem. Soc.* **2012**, *134*, 17412. (c) Ji, K.; Zhao, Y.; Zhang, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 6508.



Scheme 1-27 Au(I)-catalyzed oxidations *via in situ* α-oxo gold(I) carbenoids

In 2013, Gagosz and co-workers disclosed a novel gold catalyst/oxidizing agent system for the synthesis of diverse substituted indan-2-ones using propynyl arenes. A new type of a biarylphosphonite gold(I) complex was employed and it proved to be a superior catalyst by comparison with previous reported catalytic systems. Intriguingly, on the basis of their experimental results, it was proposed that the oxidative cyclization proceeded *via* neither intermediate **II** or **III** (**Scheme 1-26**) but at midway between them, allowing the "anti-Baldwin" generation of adducts (**Scheme 1-28**).[51]



Scheme 1-28 Biarylphosphonite gold(I)-catalyzed synthesis of indan-2-ones

[51] (a) Henrion, G.; Chavas, T. E. J.; Le Goff, X.; Gagosz, F. *Angew. Chem. Int. Ed.* **2013**, *52*, 6277.

6. Conclusion and perspective

Homogeneous gold catalysis has emerged as a unique, convenient and efficient tool of significant importance in synthetic organic chemistry. This can be ascribed to gold's relativistic effect and the readily variations of gold complexes. Phosphines, phosphites and N-heterocyclic carbenes are the most common employed ligands in Au(I)-catalyzed transformations. The real catalytically active species are still obscure in most cases, although most mechanistic proposals employed simple $[LAu]^+$ as the solely π-acids.

A vast majority of reports to date have been performed intramolecularly, giving rise to 5- or 6-membered rings and the regioselectivity was closely related to the substituent patterns of the substrates. Progress in enantioselective version of gold catalysis is still very slow due to the general linear, dicoordinated geometry adopted by gold(I) complexes which imposes sufficiently long distance between the ligand and the active reaction sites. Further investigation onto the mechanism of the chiral induction in reported results and developing more general and efficient catalytic systems are still of great importance and must intrigue further progress in the field of gold catalysis.

Chapter 2. Gold(I)-catalyzed rearrangement of ynamides *via* [1,5]-hydride shift: an expedient approach to allenamides and its equivalents

1. Allenamide: a versatile building block

Allenamide, the stabilized derivative of allenamine (**Figure 2-1**) belongs to a subclass of allenes, representing a type of versatile and powerful synthetically important building block.

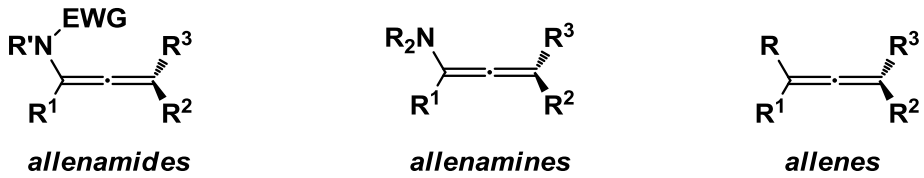
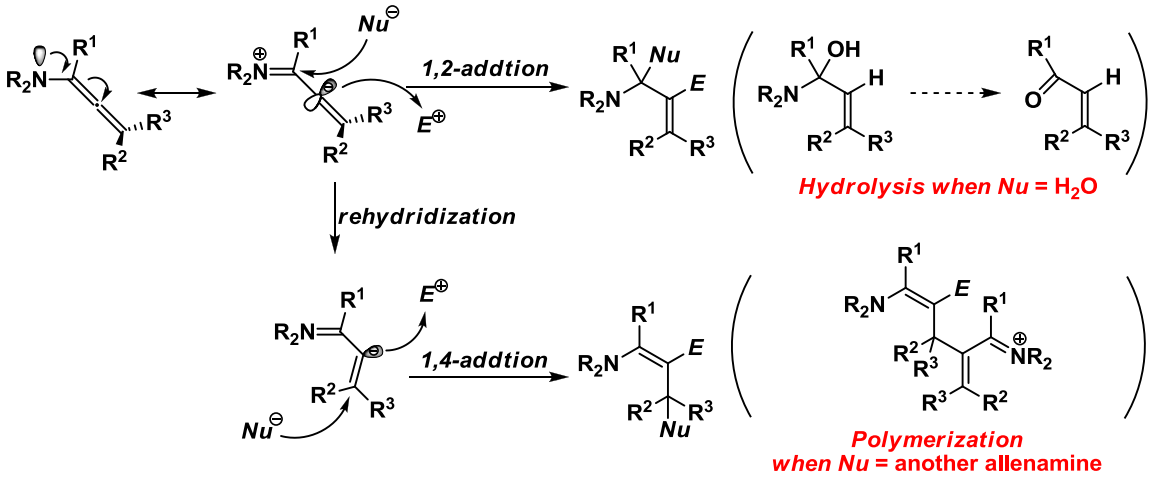


Figure 2-1

Given that the electron-donating nitrogen atom is attached directly to double bonds, delocalization of electrons from nitrogen atom to the allenyl moiety renders allenamines much more electron rich than normal allenes, therefore resulting in extremely high reactivity and regioselectivity (*via* electron bias). By adding electrophiles and nucleophiles sequentially, two consecutive bond formations would occur to allow efficient, expedient and practical construction of sophisticated molecules (**Scheme 2-1**). However, this enhanced reactivity endowed by nitrogen groups in turns imposed limitations to wide exploitation of allenamine chemistry as they activate allenamines toward hydrolysis (sensitive to moisture) and polymerizations which caused serious problems for their preparations, isolations and manipulations.

Allenamide, which is the topic of this chapter, comes to scene as it represents an ideal allenamine equivalent bearing balanced reactivity and stability and found a range of applications as an important synthon.



Scheme 2-1 General reaction pathways of allenamine and allenamide

The increased stability could be ascribed to the electron-withdrawing group bound to nitrogen atom by conjugation and induced effect, which diminishes electron's flow to the allenyl moiety. The nitrogen-containing functionalities could be sulfonamides, amides, carbamates, phosphinamides, ureas, anilines and some hetero-aromatic rings such as imidazoles, benzimidazoles and so on. On the basis of the stable and reactive nature of allenamide, the past 15 years has witnessed broad investigations of allenamide chemistry, including addition reactions, aldol reactions, cyclizations, ring closing metathesis, cycloadditions and deprotonations (**Figure 2-2**).

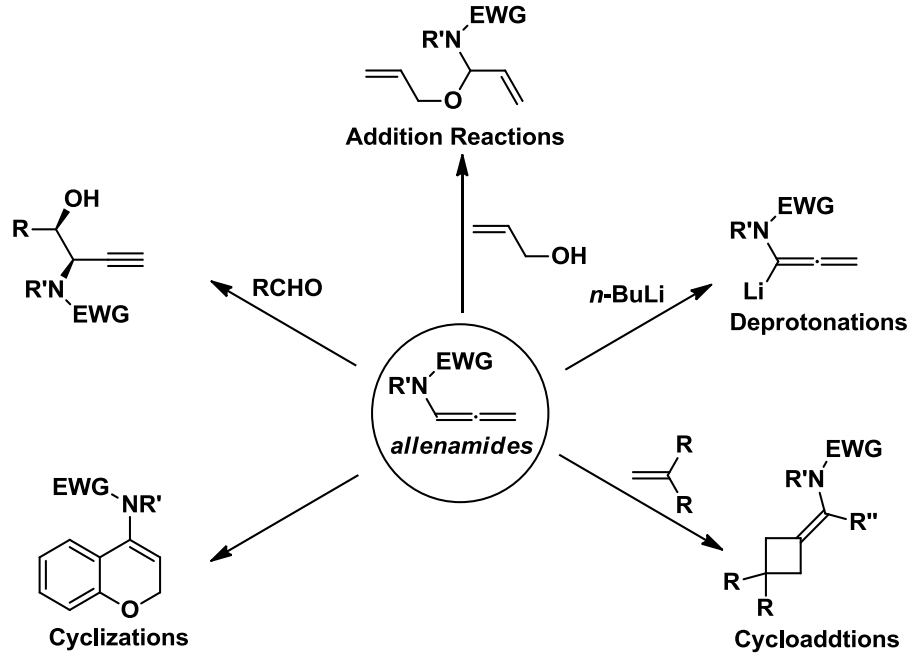


Figure 2-2 Outline of allenamide chemistry

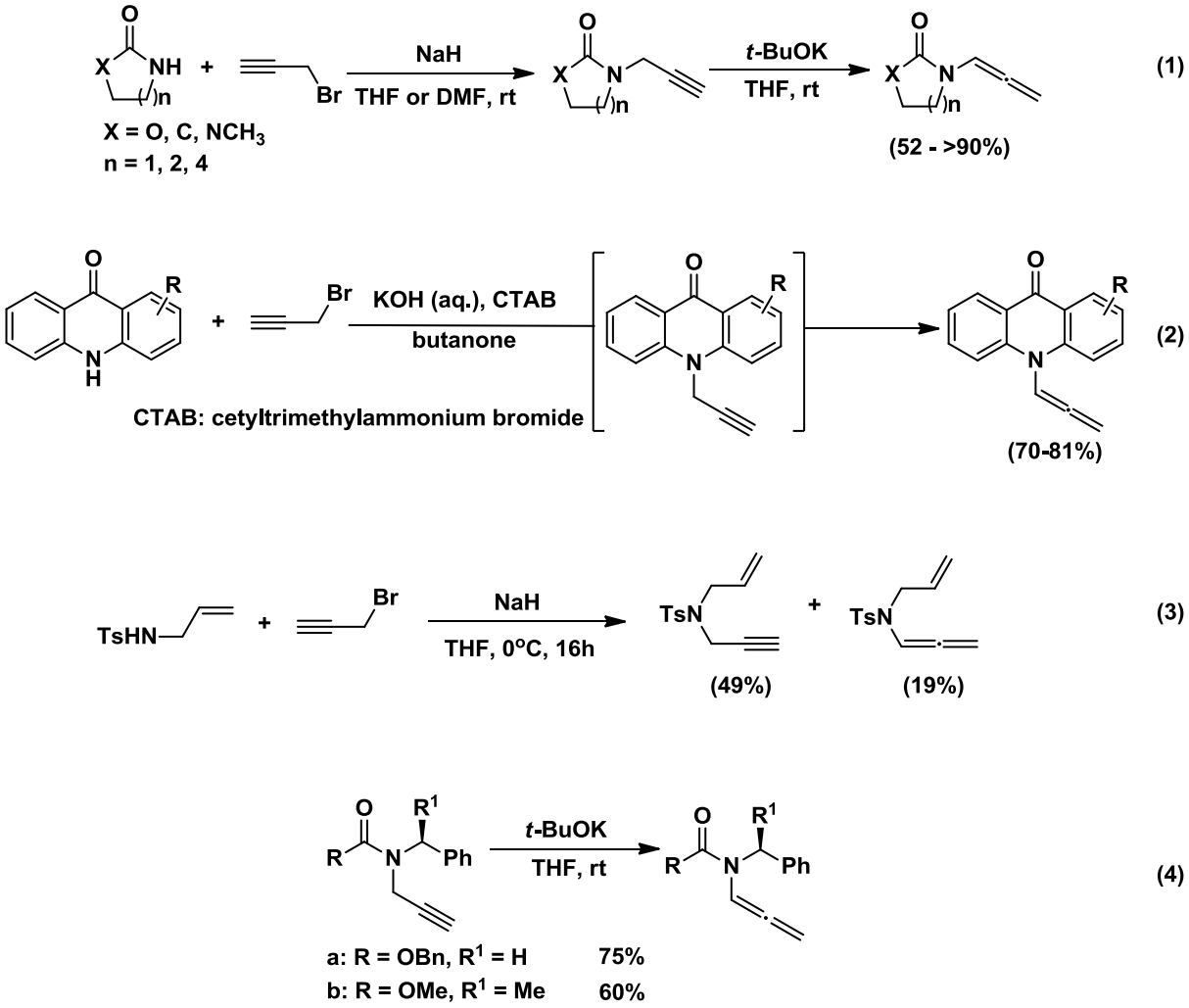
2. Synthetic methods of allenamides in literature

A series of methodologies have been developed to prepare allenamides, which will be discussed in details in the next paragraphs. As providing a comprehensive review is beyond the scope of this manuscript, herein merely personal selected examples will be presented.

2.1. Base-triggered isomerization

Base-triggered isomerization proceeds by prototropic rearrangement of the propargyl amide precursor, thus leading to an atom-economical access to allenamide. For instance, the synthesis of a diverse array of allenamides in the presence of catalytic amount of *t*-BuOK was developed from the corresponding amides following a two-step protocol (**Scheme 2-2,** eq 1).

In this case, both chiral and achiral allenamides were accessible.[52a] This approach was improved to a one-pot procedure by reacting acridones with propargyl bromides in the presence of a phase transfer catalyst (PTC) to furnish allenamides *via in situ* generated propargylated intermediates (**Scheme 2-2**, eq. 2).[52b] In the course to prepare *N*-tosyl-4-azahept-1-en-6-yne, Meijere et al. observed concomitant formation of allenamide as a minor product under basic conditions for 16 hours and extended reaction time resulted in even higher yield of allenamide (**Scheme 2-2**, eq. 3).[52c] In the attempt to get access to chiral ynamides from propargyl amides, Hsung and co-workers discovered that in certain cases, the base-induced isomerization process could be arrested at the allenamides stage without formation of desired ynamides (**Scheme 2-2**, eq. 4).[52d]



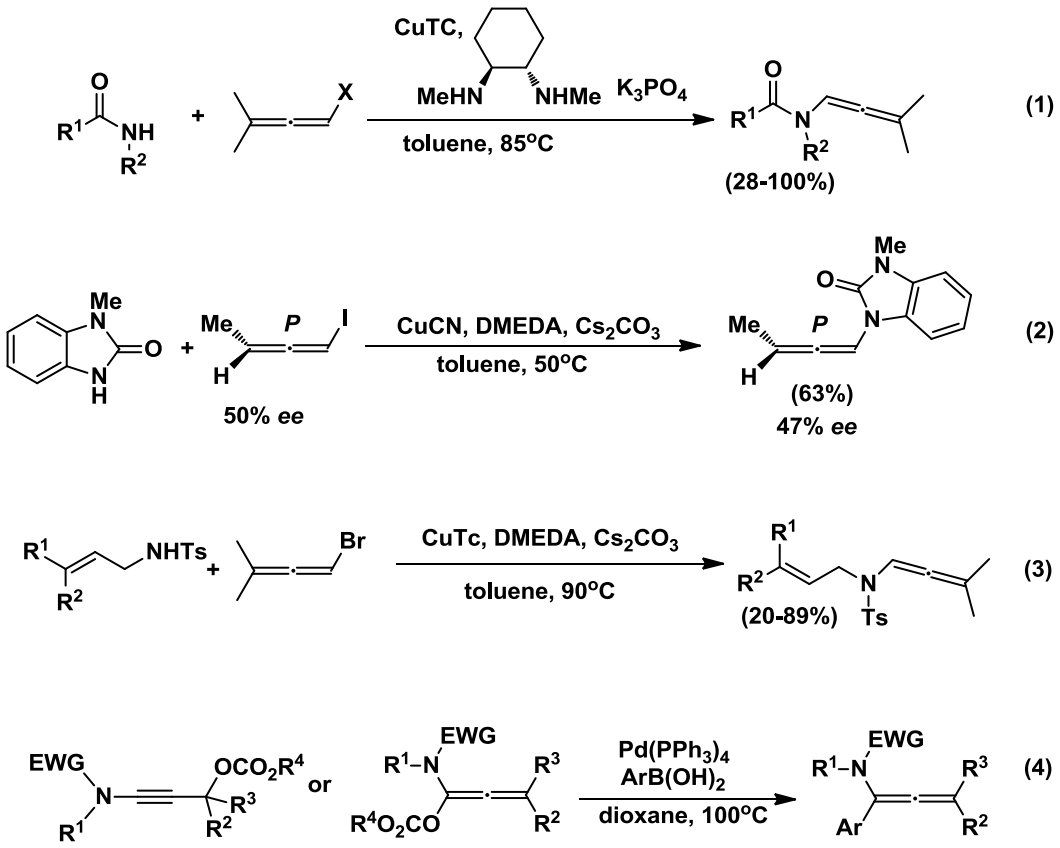
Scheme 2-2 Synthesis of allenamides *via* base-induced isomerization

[52] (a) Wei, L.-L.; Mulder, J. A.; Xiong, H.; Zificsak, C. A.; Douglas, C. J.; Hsung, R. P. *Tetrahedron* **2001**, *57*, 459. (b) Xuárez, L.; Pellón, R. F.; Fascio, M.; Montesano, V.; D'Accorso, N. Heterocycles 2004, 63, 23. (c) van Boxtel, Lonneke J.; Körbe, S.; Noltemeyer, M.; de Meijere, A. *Eur. J. Org. Chem.* **2001**, *2001*, 2283. (d) Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417.

2.2. Transition metal-mediated C-N couplings

Transition metal-catalyzed cross couplings proved to be a facile and convenient synthetic tool for the assembly of C-C and C-X bonds. This strategy could be applied to the preparation of allenamides as well (**Scheme 2-3**).

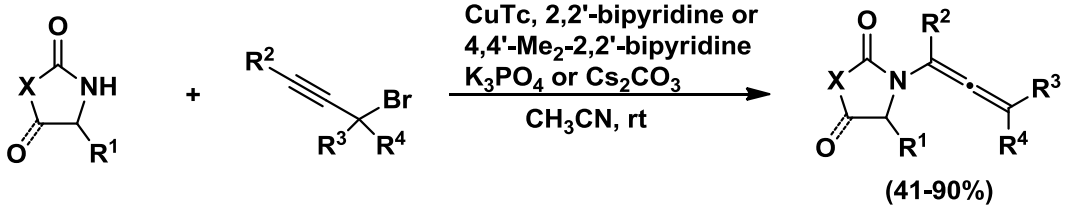
Trost et al. reported that allenyl iodides/bromides reacted with a range of amides, ureas and carbamates in the presence of copper catalysts to provide various allenamides in good to excellent yields (**Scheme 2-3**, eq. 1).[53a] Copper catalysts also promoted the coupling between amides/ureas and enantioenriched allenyl halides to give rise to allenamides. In this course the chirality of starting materials was preserved in high levels throughout the process (**Scheme 2-3**, eq. 2).[53b] *N*-allyl-*N*-allenylsulfonamide was assembled by a similar copper-catalyzed C-N coupling of *N*-allylsulfonamides and bromoallenes in moderate to good yield (**Scheme 2-3**, eq. 3).[53c] Palladium-catalyzed Suzuki-Miyaura coupling is also a feasible strategy to get access to multi-substituted allenamides (**Scheme 2-3**, eq. 4).[53d]



Scheme 2-3 Synthesis of allenamides by copper-catalyzed C-N coupling

[53] (a) Trost, B. M.; Stiles, D. T. *Org. Lett.* **2005**, *7*, 2117. (b) Shen, L.; Hsung, R. P.; Zhang, Y.; Antoline, J. E.; Zhang, X. *Org. Lett.* **2005**, *7*, 3081. (c) Persson, A. K. Å.; Johnston, E. V.; Bäckvall, J.-E. *Org. Lett.* **2009**, *11*, 3814. (d) Cao, J.; Kong, Y.; Deng, Y.; Lai, G.; Cui, Y.; Hu, Z.; Wang, G. *Organic & Biomolecular Chemistry* **2012**, *10*, 9556.

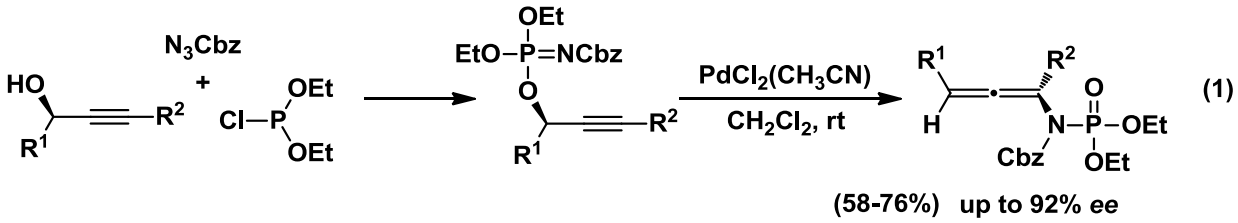
More recently, a straightforward coupling between readily accessible propargyl bromides and oxazolidinones or hydantoins for the synthesis of allenamides were depicted by Evano and co-workers, by which mono-, di- and tri-substituted allenamides were easily accessible under relatively mild conditions in the presence of copper catalysts (**Scheme 2-4**).[54]



Scheme 2-4 Straightforward synthesis of allenamides from propargyl bromides

2.3. Sigmatropic rearrangements

In 2010, Mapp et al. discovered that phosphorimidates, which is readily available from reactions of progargyl alcohols, azides and chlorophosphites, underwent a [3,3]-sigmatropic rearrangement assisted by Pd(II) catalysts to furnish fully protected allenimides. In the case that chiral progargyl alcohols were employed, high levels of chirality transfer were observed. Thus this work represents a practical and convenient entry to chiral allenimides (**Scheme 2-6**).[55a]

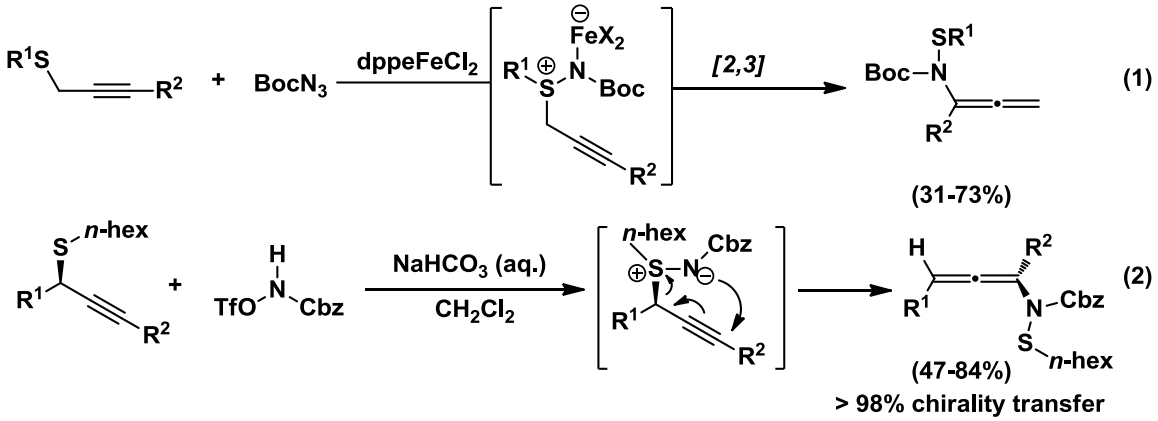


Scheme 2-5 [3,3]-Sigmatropic rearrangement for the synthesis of allenamides

[2,3]-sigmatropic rearrangements also proved to be a facile access to allenamides. For instance, Vranken disclosed an Fe(II)-catalyzed tandem sulfimidation and [2,3]-rearrangement procedure to generate N-allenylsulfenimides, presumably *via* iron-nitrene intermidate (**Scheme 2-6**, eq. 1).[55b] Enantioenriched allenamides were also accessible from chiral progargyl sulfides following consecutive amination/[2,3]-sigmatropic rearrangement pathway (**Scheme 2-6**, eq. 2).[55c]

[54] Demmer, C. S.; Benoit, E.; Evano, G. *Org. Lett.* **2016**, *18*, 1438.

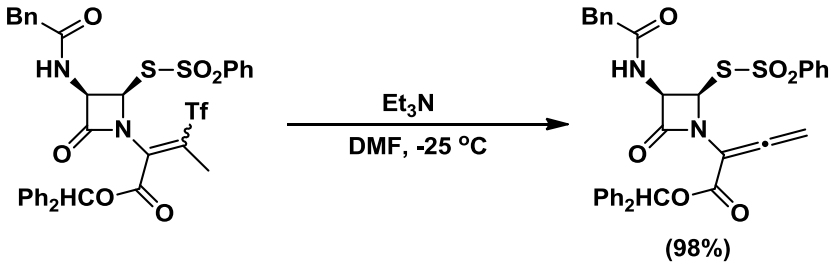
[55] (a) Danowitz, A. M.; Taylor, C. E.; Shrikian, T. M.; Mapp, A. K. *Org. Lett.* **2010**, *12*, 2574. (b) Bacci, J. P.; Greenman, K. L.; Van Vranken, D. L. *J. Org. Chem.* **2003**, *68*, 4955. (c) Armstrong, A.; Emmerson, D. P. G. *Org. Lett.* **2009**, *11*, 1547.



Scheme 2-6 [2,3]-Sigmatropic rearrangement for the synthesis of allenamides

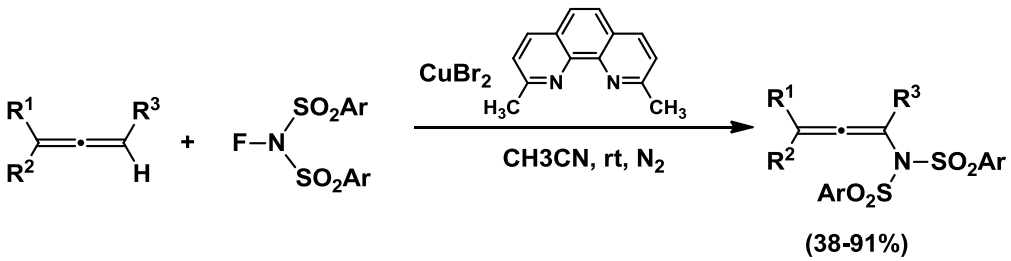
2.4. Other approaches

Besides the methodologies mentioned above, several other approaches are also fruitful for the synthesis of allenamides. For example, lactam derived allenamide was synthesized from the corresponding vinyl triflate *via* Et_3N-assisted *E*2-elimination (**Scheme 2-7**).[56]



Scheme 2-7 Synthesis of allenamide *via E*2 elimination

More recently, a practical radical oxidative amination protocol of allenes with N-arylsulfimide was accomplished, leading to straightforward entry to allenimide regioselectively (**Scheme 2-8**).[57]



Scheme 2-8 Allenamides synthesis by radical amination strategy

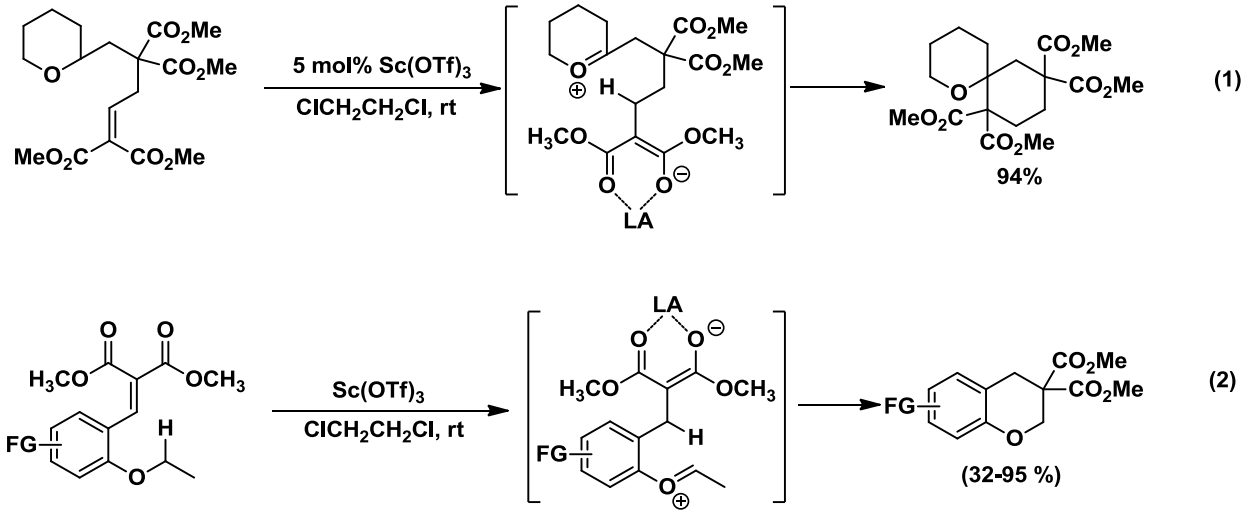
[56] Tanaka, H.; Kameyama, Y.; Sumida, S.; Yamada, T.; Tokumaru, Y.; Shiroi, T.; Sasaoka, M.; Taniguchi, M.; Torii, S. Synlett **1991**, 888.
[57] Zhang, G.; Xiong, T.; Wang, Z.; Xu, G.; Wang, X.; Zhang, Q. *Angew. Chem. Int. Ed.* **2015**, *54*, 12649.

3. Reactions involving intramolecular [1, *n*]-Hydride Shift

Given fact that intramolecular hydride shift represents an attractive strategy for sp^3 C-H bond functionalization, synthetic chemists are becoming increasingly interested in this area and a series of transformations using this strategy was reported recently.

3.1. Hydride donors involving ethers and acetals

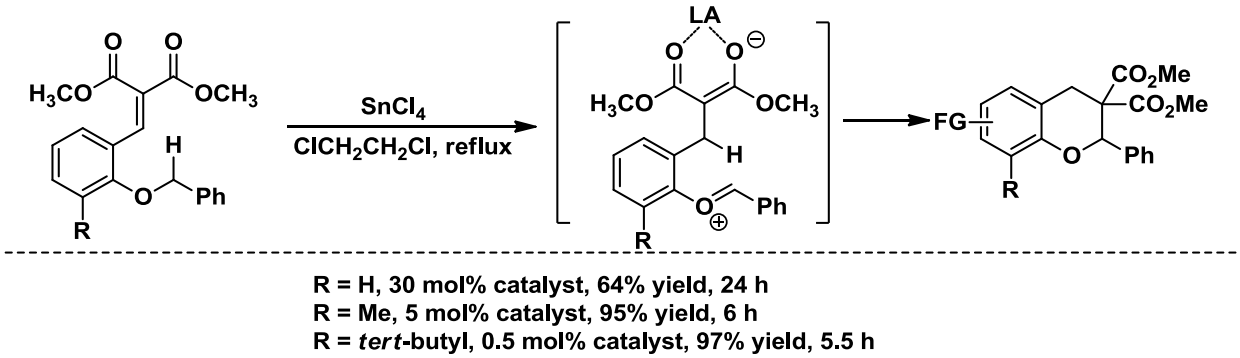
In 2005, sames and co-workers revealed a C (sp^3)-H bond functionalization *via* hydride shift in the presence of Lewis acid, such as $Sc(OTf)_3$, $BF_3{\cdot}Et_2O$ and $PtCl_4$, with an alkylidenemaloate moiety serving as the hydride acceptor. Notably, they observed that tertiary and secondary C-H bonds *α* to ethers or carbamates, as well as tertiary C-H bonds at benzylic positions were all directly functionalized under the reaction conditions (**Scheme 2-9**, eq 1). Later, multi-substituted dihydrobenzopyrans were prepared by the same group from *ortho*-vinylaryl alkyl ethers by [1,5]-hydride transfer-initiated cyclizations (**Scheme 2-9**, eq 2).[58]



Scheme 2-9 [1,5]-hydride transfer with alkylidenemaloates as hydride acceptors

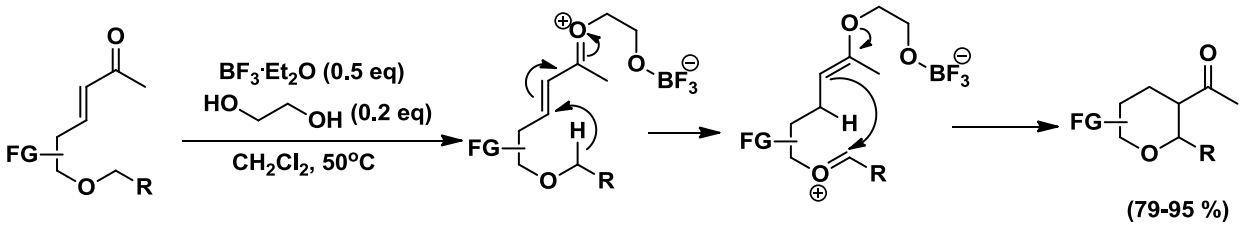
Soon after that, Akiyama et al. found that a sterically hindered substituent *ortho* to the alkoxy groups could dramatically reduce the reaction time and catalyst loading, furnishing the desired products in excellent yield.[59] Thes observations were reasoned on the basis that the *ortho* substituent imposed the favorable conformation required for the hydride transfer process (**Scheme 2-10**).

[58] (a) Pastine, S. J.; McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 12180. (b) McQuaid, K. M.; Long, J. Z.; Sames, D. *Org. Lett.* **2009**, *11*, 2972.
[59] Mori, K.; Kawasaki, T.; Sueoka, S.; Akiyama, T. *Org. Lett.* **2010**, *12*, 1732.



Scheme 2-10 Influence of *ortho* substituent on reaction rate, catalyst loading and yield

In 2009, sames et al. reported a highly reactive catalytic system consisting of boron trifluoride etherate and ethylene glycol, which allowed rapid [1,5]-hydride transfer/cyclization with *α*, β-unsaturated ketones serving as the hydride acceptor. The authors related this success to the *in situ* generated strongly activating alkenyl-oxocarbenium intermediates. In the absence of ethylene glycol, prolonged reaction time was required (**Scheme 2-11**).[60]

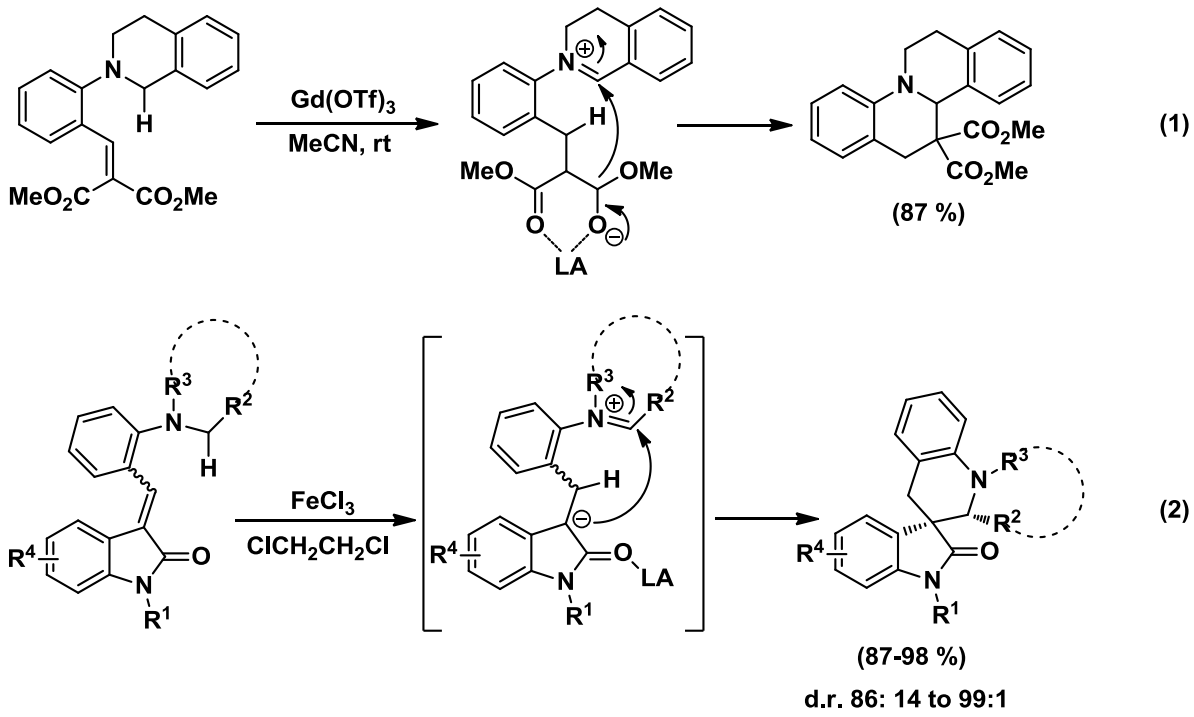


Scheme 2-11 Boron trifluoride etherate/ethylene glycol co-catalytic system

3.2. Hydride donors involving amines

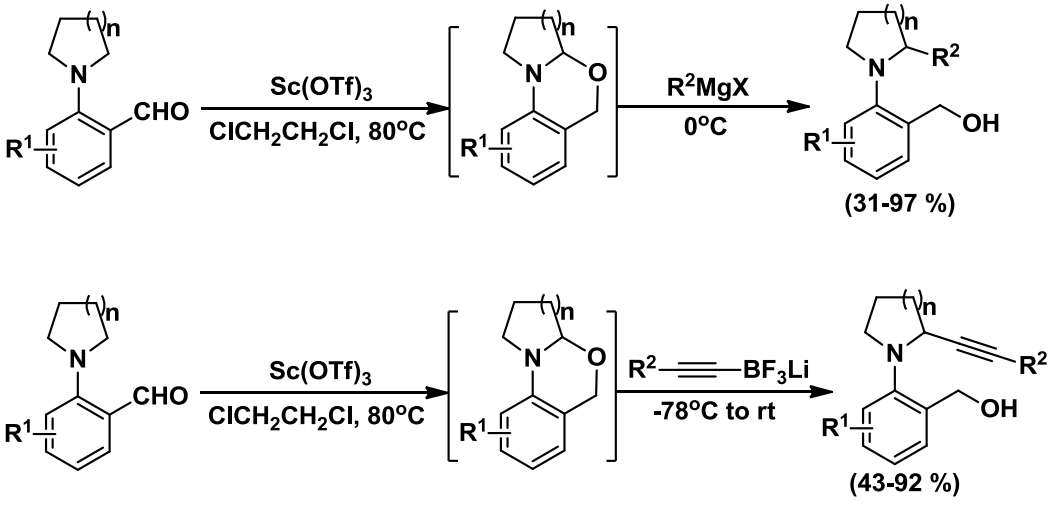
In 2009, Seidel et al. documented the synthesis of tetrahydroquinolines by a tandem [1,5]-hydride shift/cyclization cascade promoted by Lewis acid, i.e. gadolinium(III) triflate. In their studies, C-H bond *α* to pyrrolidine serves as the hydride donor with alkylidenemalonate being the hydride acceptor (**Scheme 2-12**, eq. 1). Yuan and co-workers reported the stereoselective synthesis of spirooxindole tetrahydroquinolines following a tandem hydride shift/ring closure sequence with $FeCl_3$ serving as the catalyst (**Scheme 2-12**, eq. 2).[61]

[60] McQuaid, K. M.; Sames, D. *J. Am. Chem. Soc.* **2009**, *131*, 402.
[61] (a) Murarka, S.; Zhang, C.; Konieczynska, M. D.; Seidel, D. *Org. Lett.* **2009**, *11*, 129. (b) Han, Y.-Y.; Han, W.-Y.; Hou, X.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2012**, *14*, 4054.



Scheme 2-12 Functionalization of C-H bond *α* to amines

In 2012, Maulide group disclosed a one-pot C-H functionalization procedure, in which Grignard reagents or lithium alkynyl trifluoroborates were directly added to position *α* of the amine moiety with the concomitant reduction of the aldehyde. The overall transformation took place *via* the formation of an intermediate aminal. The utility of this methodology was nicely demonstrated by the expedient synthesis of (±)-indolizidine 167B.[62]

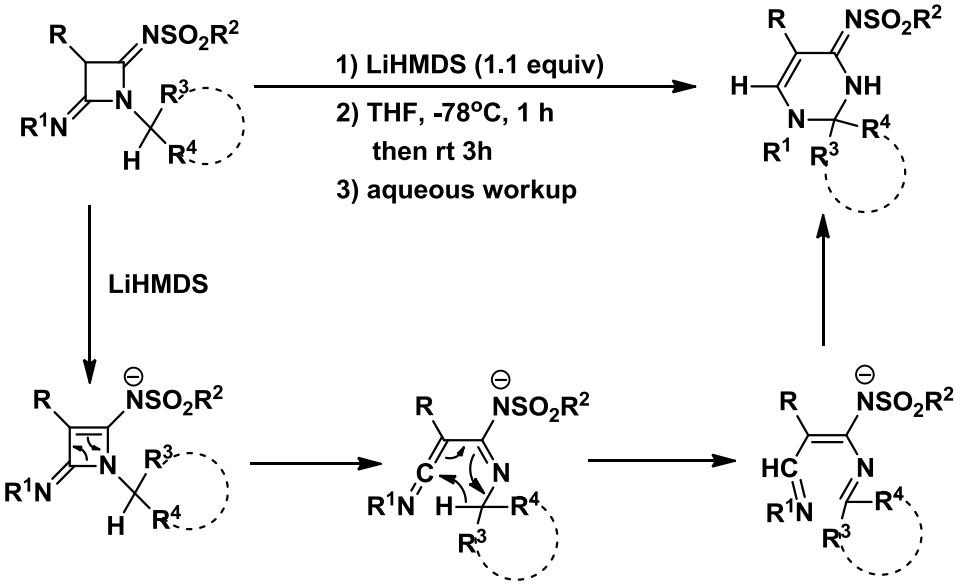


Scheme 2-13 One-pot functionalization of tertiary amines *α* C-H bonds

In 2012, Xi and Zhang documented that 2,3-dihydropyrimidinesulfonamides could be efficiently prepared by a base-assisted ring expansion of 2,4-diiminoazetidines, in which both

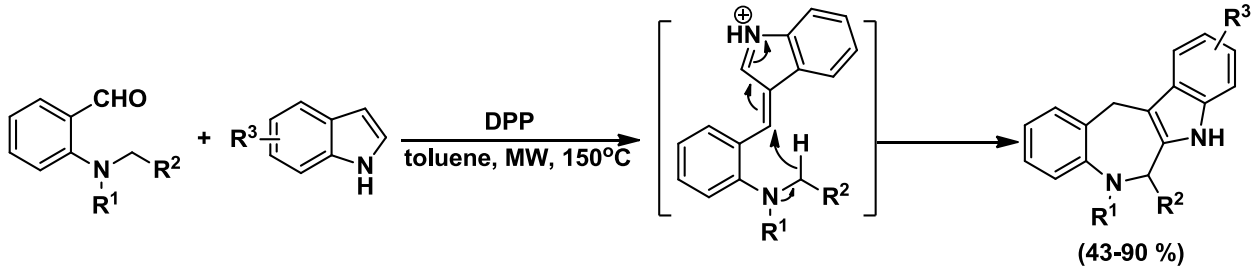
[62] Jurberg, I. D.; Peng, B.; Wöstefeld, E.; Wasserloos, M.; Maulide, N. *Angew. Chem. Int. Ed.* **2012**, *51*, 1950.

the cleavage of a C-N bond and a sp^3 C-H bond occurred. Isotope labeling experiment and intermediates trapping studies validated a mechanism involving a 4 π electrocyclic ring-opening/[1,5]-hydride shift/6π electrocyclic ring-closure cascade (**Scheme 2-14**).[63]



Scheme 2-14 Expedient synthesis of 2,3-dihydropyrimidinesulfonamides

Since most redox neutral cycloisomerizations involving [1,5]-hydride transfer resulted in the formation of six-membered ring products, Seidel et al. sought for an extension of the process to the formation of larger member rings. Treatment of aminobenzaldehyde with nucleophilic compounds such as indoles, pyrroles and hydroazones lead to the generation of seven-membered rings in the presence of diphenylphosphoric acid under microwave irradiation. This represents an unprecedented cascade.[64]

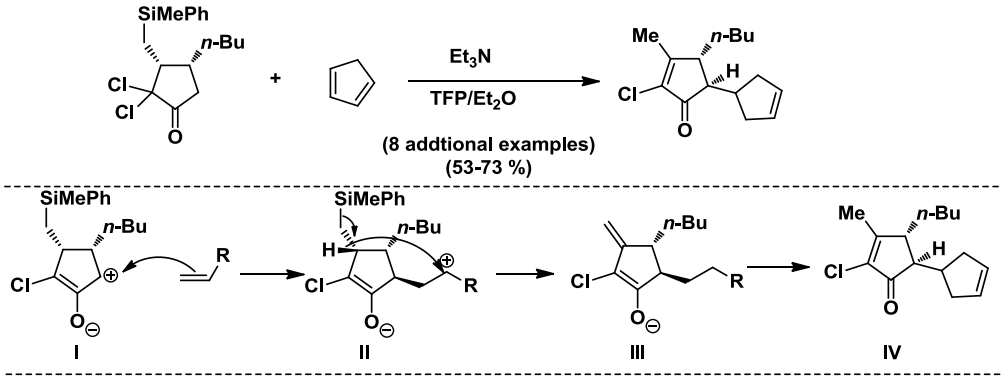


Scheme 2-15 Extension to the preparation of seven-membered rings

[63] Wang, Y.; Chi, Y.; Zhang, W.-X.; Xi, Z. *J. Am. Chem. Soc.* **2012**, *134*, 2926.
[64] Haibach, M. C.; Deb, I.; De, C. K.; Seidel, D. *J. Am. Chem. Soc.* **2011**, *133*, 2100.

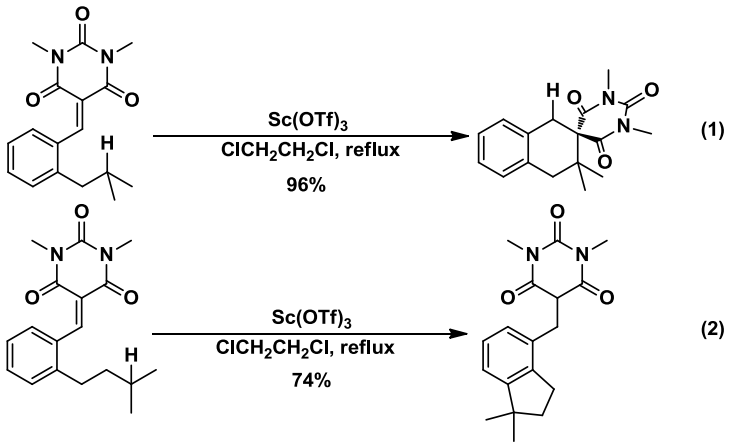
3.3. Hydride donors without heteroatoms

In an attempt to perform [4+3] cycloadditions with dichlorocyclopentanone, Harmata and Schreiner et al. observed an unexpected ene-like reaction between oxyallylic cations and alkenes.[65] On the basis of computational and deuterium labeling experiments, the authors proposed a mechanism involving a [1,5]-hydride transfer as depicted in **Scheme 2-16**. Upon treatment with triethylamine, the starting material undergoes enolization followed by loss of a chloride anion to generate a zwitterionic intermediate **I**. After nucleophilic attack by the alkene, a cationic species II forms, which undergoes desilylation-induced [1,5]-hydride shift to give rise to **III.** Finally, protonation and tautomerization leads to the formation of adduct.



Scheme 2-16 An interrupted [4+3] cycloaddition

Akiyama et al. reported the first example of aliphatic, non-benzylic sp^3 C-H activation involving [1,5]- and [1,6]-hydride shifts. While tertiary C-H bond underwent the transformation smoothly, secondary bonds were unreactive. The use of highly electrophilic benzylidene barbiturate as the hydride acceptor and $Sc(OTf)_3$ as catalyst proved to be the optimal combination (**Scheme 2-17**).



Scheme 2-17 Aliphatic sp^3 C-H activation involving [1,5]- and/or [1,6]-hydride shift

[65] Harmata, M.; Huang, C.; Rooshenas, P.; Schreiner, P. R. *Angew. Chem. Int. Ed.* **2008**, *47*, 8696.

4. Origin and objectives of the project

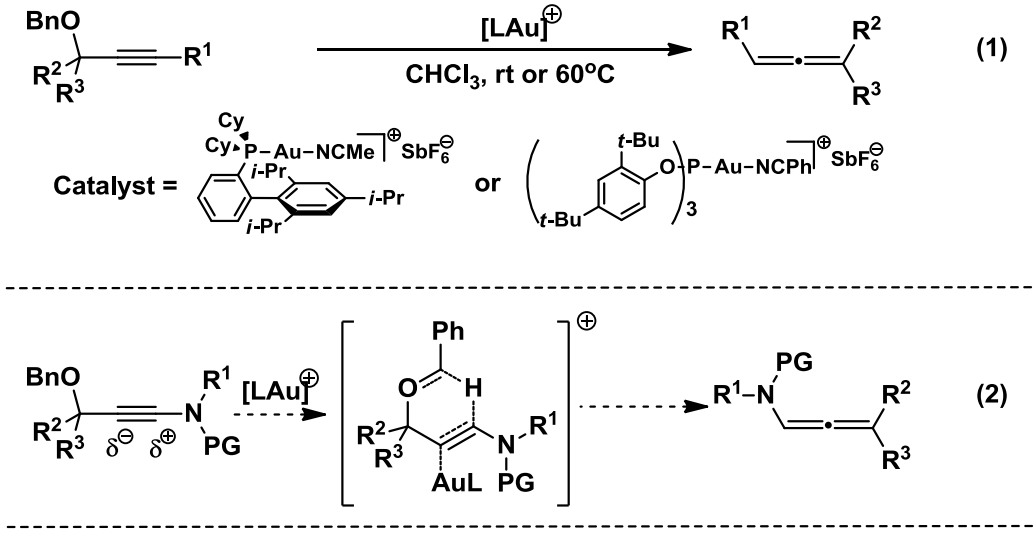
Reviewing the reports so far for the preparation of the allenamides lead to conclusions that the current approaches suffer some limitations: (a) They require harsh conditions, such as highly elevated temperature and strong basic conditions which led to the limited functional group tolerance and substrate scope; (b) They require highly prefunctionalized substrates, for instance, preformed allenyl motif, such as allenyl halides, are necessary in cross coupling reactions; (c) The conditions of preparation make the isolation of the *in situ* generated allenamides different and further tandem transformations frequently take place to form other products. In conclusion, the existing methods are specific to a certain type of allenamides and still there is still a lack of general approach to allenamides.

In light of the profound progress in homogeneous gold catalysis and on the basis of our previous work on gold-catalyzed [1,5] hydride shift, we sought to find a solution to these problems and sought for the development of a gold-catalyzed preparation of allenamide.

5. Results and discussions

5.1. Preliminary results and optimization of conditions

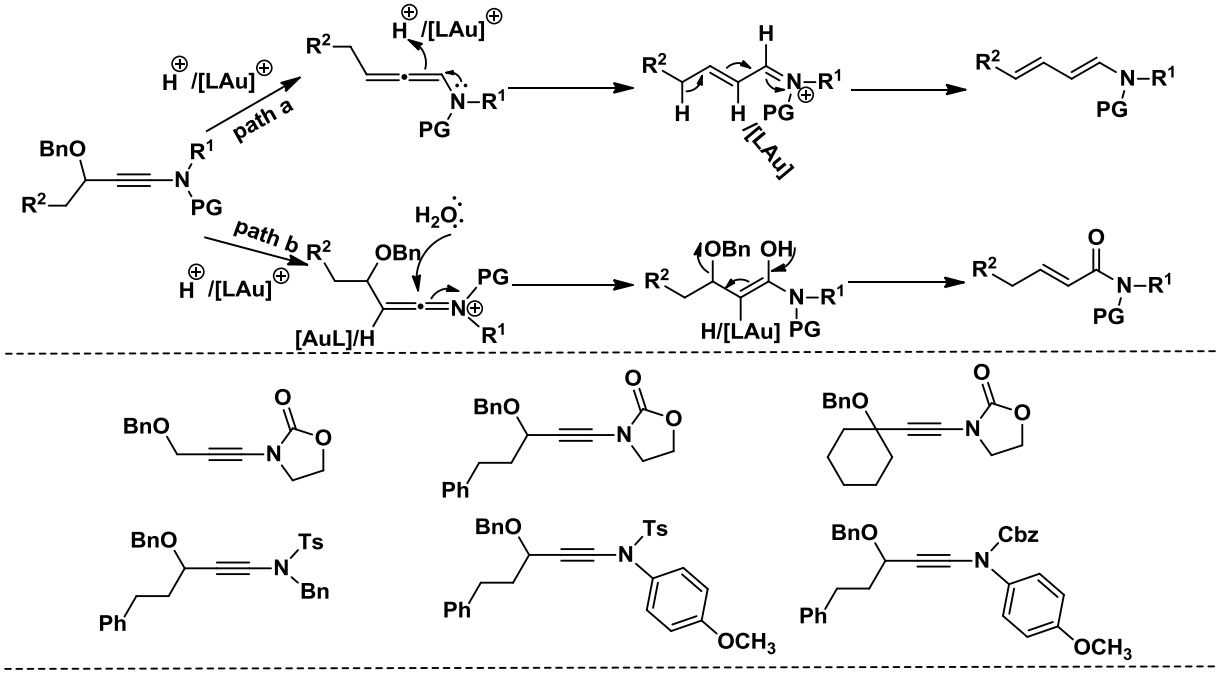
To follow our success in the synthesis of multi-substituted allenes from propargylic benzyl ethers by gold-catalyzed [1,5]-hydride shift, we reasoned that an extension of this methodology to the synthesis of allenamides from ynamide precursors could be . It was postulated that the electron distribution biased by the nitrogen-containing substituent would further favor the hydride transfer to the carbon attaching the nitrogen when compared to the initial transformation we reported(**Scheme 2-18**).



Scheme 2-18 Original idea for synthesis of allenamides by gold-catalyzed [1,5]-hydride shift

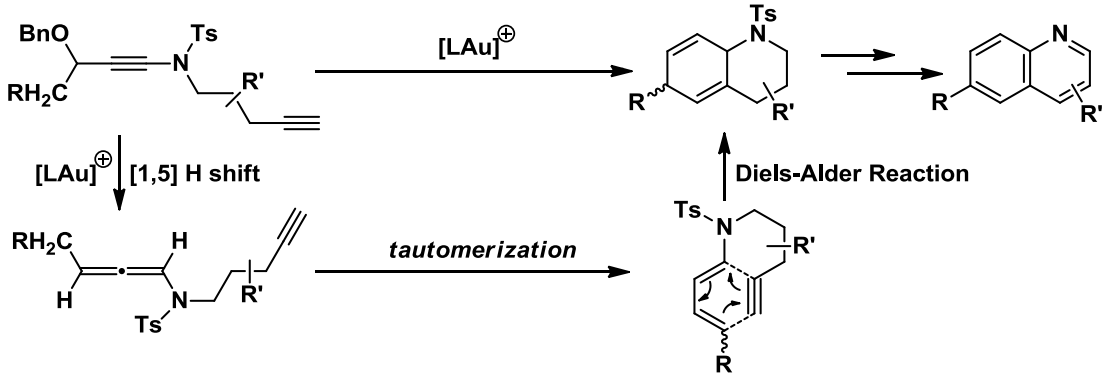
In preliminary explorative studies carried out by Dr. Benoit Bolte, it was found that the gold-catalyzed transformation indeed occurred but only traces amount of allenamides was observed. Dienes were obtained as the result of a gold(I) or Brønsted acid-catalyzed isomerization of the formed allenamide along with amide arising from the easy hydrolysis of ynamide substrate. Switching the stabilizing group on the nitrogen atom from carbamates to sulfonamides did not improve to the yield of allenamides and/or dienes, amides being always formed preferentially as the major products. [66] No allenamide was isolated and characterized. During his preliminary studies, an early conclusion was made that gold-catalyzed [1,5]-H transfer strategy could not be easily applied to the synthesis of allenamides, due to their unstability under "soft Lewis acid" conditions and the vulnerability of ynamide precursor to hydrolysis.

[66] Bolte, B., "Synthesis and reactivity study of allenes by gold-catalyzed hydride transfer", thesis submitted to Ecole Polytechnique for a Ph.D. degree, **2012**.



Scheme 2-19 Dr. Benoit Bolte's preliminary attempts for access to allenamides

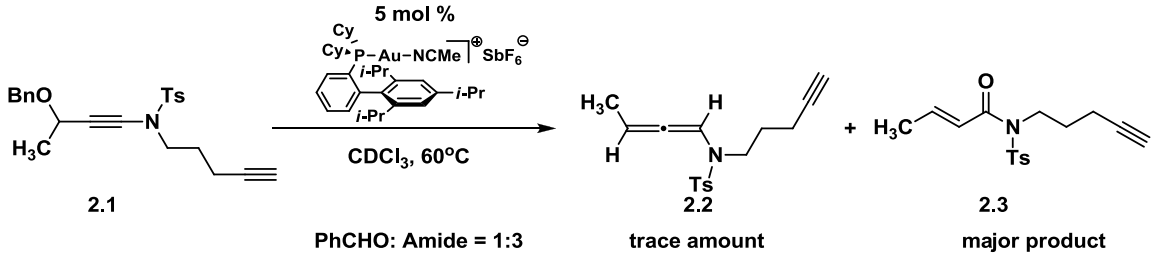
On the basis of these observations, we envisioned a gold-mediated cascade hydride shift/tautomerization/[4+2] cycloaddition processes with an intension to take advantage of the *in situ* generated allenamides to provide quinoline derivatives (**Scheme** 2-20).



Scheme 2-20 Original idea in this project

Ynamide bearing a terminal alkyne **2.1** was chosen as the model substrate to initiate our investigation (**Scheme 2-21**). Treatment of ynamide **2.1** with $XPhosAu(NCCH_3)SbF_6$ in deuterated chloroform ($CDCl_3$) at 60 ℃ for 15 min provided *α*, β-unsaturated amide **2.3** as the major product along with only traces of allenamide **2.2**. No [4+2] cycloaddition product was detected. $CDCl_3$ was used in order to monitor the reaction course and for being able to observe NMR spectroscopy of the formation of reaction intermediate. Surprisingly, benzaldehyde, the side product of [1,5]-H transfer procedure (**Scheme 2-19**, path a) was observed in notable NMR yield. We surmised that the *in situ* generated allenamide

underwent a rapid polymerization in the presence of gold catalyst as shown by the presence of broad multiple peaks as shown NMR spetra. It is noteworthy that in this case 1,3-diene, derived from allenamide isomerization was not observed.

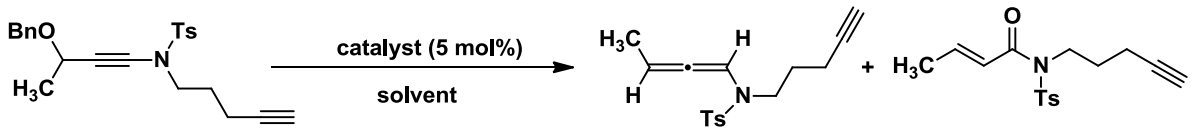


Scheme 2-21 Initial investigation of the synthesis of allenamide

We considered that the adventitious H_2O in the solvent was responsible for the hydrolysis of ynamide and that the elevated temperature presumably promoted the polymerization process in slightly acidic solvent (chloroform would decompose into phosgene along with HCl in the presence of oxygen during prolonged storage, this process being accelerated by light). Consequently, we moved to identify the influence of temperature and moisture on the course of the reaction. Results of this investigation +

+are compiled in **Table 2.1**.

Table 2.1 Optimization of reaction conditions [a]



2.1 2.2 2.3

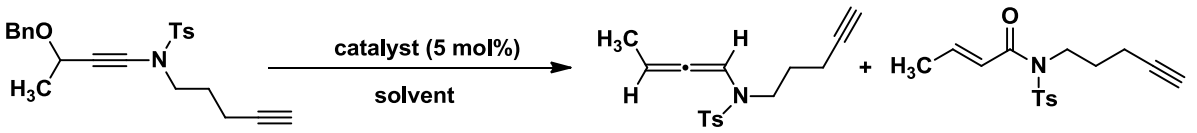
Entry	Catalysts [5 mol%]	Solvent	Temp. [°C]	Time [h]	Conv. [%]	2.2/PhCHO/2.3[b]
1	XPhosAu(CH_3CN)SbF_6	$CDCl_3$	60	0.25	100	trace/1.0/3.5
2	XPhosAu(CH_3CN)SbF_6	" "	rt	0.25	100	1.0/1.0/3.2
3[c]	XPhosAu(CH_3CN)SbF_6	" "	rt	0.25	100	1.0/1.0/3.2
4	RuPhosAu(CH_3CN)SbF_6	" "	60	1.5	74	0.9/1.0/1.3
5	RuPhosAu(CH_3CN)SbF_6	" "	60	3.5	100	0.5/1.0/1.3
6	RuPhosAu(CH_3CN)SbF_6	" "	60	16	100	0.2/1.0/1.3
7	RuPhosAu(CH_3CN)SbF_6	" "	rt	1.5	50	1.0/1.0/1.0
8	RuPhosAu(CH_3CN)SbF_6	" "	rt	4	70	1.0/1.0/1.3
9[d]	RuPhosAu(CH_3CN)SbF_6	" "	rt	7	100	1.0/1.0/1.5

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of the gold catalyst (5 mol %); [b] determined by ^1H NMR analysis; [c] dried $CDCl_3$ and 4A M.S. were used [d] 30% isolated yield

Consistent with our proposal, high temperature was deleterious to the desired product (entries 4, 5 and 6), whereas reactions performed at ambient temperature provided the desired allenamide in comparatively higher amount (compare entries 1 and 2, 5 and 8, **Table 2.1**). While dried solvent did not improve **2.2**/**2.3** ratio, switching the ligand from XPhos to RuPhos led to a notable increase of the desired allenamide (compare entries 3 and 9). Notably, the reaction carried out at ambient temperature in the presence of RuPhosAu(CH_3CN)SbF_6 gave rise to allenamide in 30% isolated yield, which was completely converted into 1,3-diene and (*E*)-but-2-enal in 9:1 ratio after staying in $CDCl_3$ in NMR tube overnight. In contrast with this observation, no 1,3-diene was formed during the gold-catalyzed transformations (entries 1-9), suggesting that polymerization took place in preference to tautomerization for allenamide under homogeneous conditions, in particular at elevated temperature.

Considering the fact that ligands are generally of crucial importance in transition-metal-catalyzed transformations, we turned our attention to the evaluation of the influence of gold catalysts possessing diverse ligands (**Table 2.2**).

Table 2.2 Screening of gold catalysts



2.1 2.2 2.3

Entry	Catalysts [5 mol%]	Solvent	Temp. [°C]	Time [h]	Conv. [%]	2.2/PhCHO/2.3[b]
1	$RuPhosAu(CH_3CN)SbF_6$	$CDCl_3$	rt	14	60	1.0/1.0/1.5
2	Ad_2n-BuPAuNTf$_2$	" "	rt	14	0	--
3	GPhosAuNTf$_2$	" "	rt	14	22	1.0/1.0/3.0
4	IMesAuNTf$_2$	" "	rt	14	5	0/0/1
5	$IMesAu(2,6\text{-}Me_2\text{-}C_6H_3CN)SbF_6$	" "	rt	14	100	0.6/1.0/2.1
6	$IPrAu(PhCN)SbF_6$	" "	rt	14	50	0.7/1.0/0.7
7	*t*BuSPhosAu$(CH_3CN)SbF_6$	" "	rt	2	60	1.0/1.0/4.2
8	$C_6H_5PCy_2PAu(CH_3CN)SbF_6$	" "	rt	20	72	0/0/1.0
9	$(2,4\text{-}t\text{-}Bu_2C_6H_3O)_3$PAuNTf2	" "	rt	20	15	1.0/1.0/3.5
10	BrettPhosAuNTf$_2$	" "	rt	2	15	1.0/1.0/0.3
11	BrettPhosAu$(CH_3CN)SbF_6$	" "	rt	20	25	1.0/1.0/0.5

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^{1}H NMR analysis;

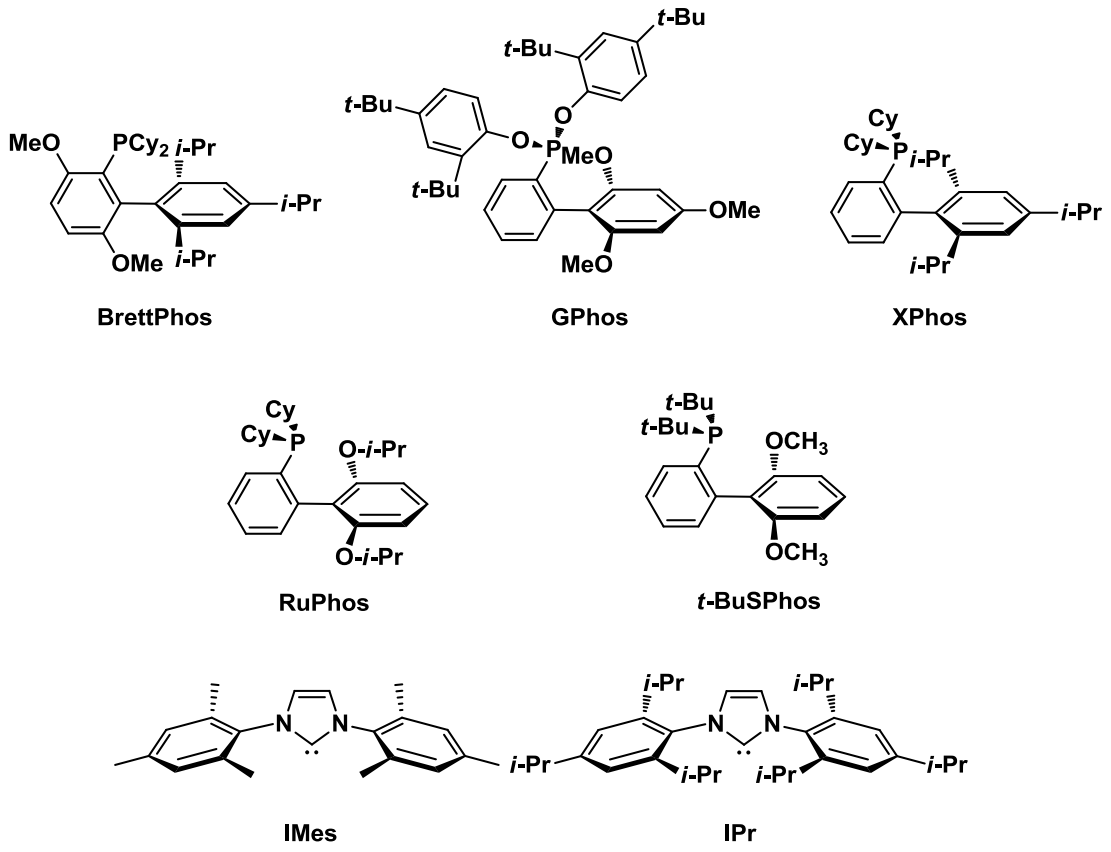


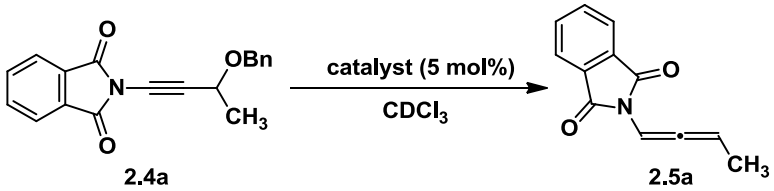
Figure 2-3 Tested ligands **in Table** 2.2

Treatment of the model substrate with gold catalysts possessing phosphines, NHC and phosphites led to low conversion or chemoselectivity. In the course of reactions using NHC derived catalysts, decomposition or polymerization was also observed.

Considering that amide **2.3** was the major product in most cases and that the catalyst screening did not give satisfactory improvement for the desired allenamides, we hypothesized that these experiment results were due to the nature of the nitrogen substituent. The tosylamide still possesses strong electron-donating ability, thus giving the ynamide greater propensity to hydrolysis and the allenamide higher tendency to undergo polymerization in the presence of gold catalyst.

We proposed that altering the nitrogen substituent by introducing more electron withdrawing group would help in stabilizing the ynamide and the *in situ* formed allenamide by inhibiting the nucleophilic attack of H_2O onto ynamide and polymerization and/or decomposition of allenamide respectively. The feasibility of this hypothesis was then investigated by using phthalimide derivatives **2.4a** as model substrate, which was subjected to gold catalysis at diverse temperature and using various catalysts (**Table 2.3**).

Table 2.3 Exploration of phthalimide derived allenamide



2.4a 2.5a

Entry	Catalysts [5 mol%]	Temp. [°C]	Time [h]	Conv. [%]	Yield[b]
1	BrettPhosAu(CH_3CN)SbF_6	rt	1.5	0	0
2	BrettPhosAu(CH_3CN)SbF_6	60	1.5	100	80
3	RuPhosAu(CH_3CN)SbF_6	60	1.5	100	65
4	XPhosAu(CH_3CN)SbF_6	60	1.5	100	92 (86[c])
5	IPrAu(CH_3CN)SbF_6	60	24	5	4

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^1H NMR analysis using 1,2-dichloroethane as internal standard. [c] isolated yield when scaled up to 0.4 mmol of **2.4a**.

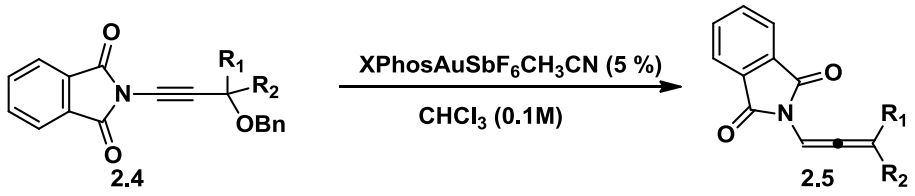
To our delight, it was observed that although no reaction occurred at ambient temperature (entry 1), the use of BrettPhosAu(CH_3CN)SbF_6 as the catalyst allows the formation of the desired allenimide **2.5a** in 80% NMR yield at 60°C in $CDCl_3$ for 1.5 hours. The competitive amide formation was not completely suppressed (less than 20% yield) (entry 2). Considering the higher performance of biphenylphosphine-based catalysts in the transformation of sulfonyl-stabilized ynamide, we firstly focused on this particular ligand. A brief screening of biphenylphosphines indicated that XPhos was superior to RuPhos and BrettPhos for the transformation of phthalimide-derived ynamides. In this case, the allenimide was isolated in 86% yield along with only traces amount of amide (entries 3 and 4). Unexpectedly, IPrAu(CH_3CN)SbF_6 was not catalytically active in this case, yielding only 4% of the desired compound for 24 hours at 60°C (entry 5), although NHC based gold complexes have found wild application in homogeneous gold catalysis. It is noteworthy that an elevated temperature was necessary for the success of this transformation. This tends to prove that this protected allenimide was more stable than analogous allenamide and therefore less prone to undergo polymerization or decomposition.

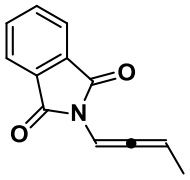
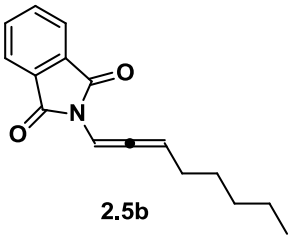
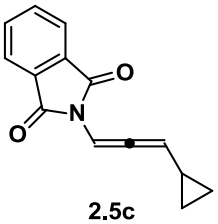
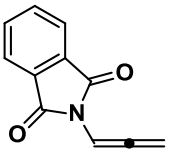
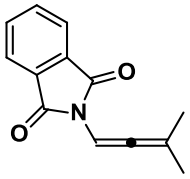
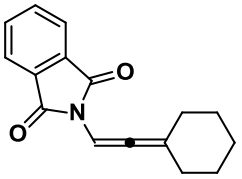
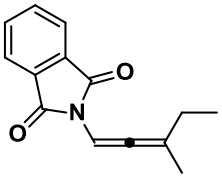
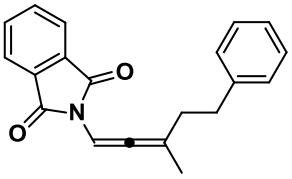
5.2. Facile synthesis of variously functionalized and poly-substituted allenimides

With the most favorable nitrogen substituent and optimized reaction conditions in hand, we next turn our attention to examining the substrate scope in order to demonstrate the applicability and efficiency of this methodology.

We first focused on the possibility to vary the substituent at the propargylic position in order to detect any effect of sterics on the course of reaction and on its efficiency.

Table 2.4 Examination of substituents at proparylic position [a,b]



 **2.5a** 60°C, 1 h 86%	 **2.5b** 60°C, 1 h 78%	 **2.5c** 60°C, 1 h 70%[c]	 **2.5d** 60°C, 4 h 35 %
 **2.5e** R.T. 2 h 93%	 **2.5f** R.T. 2 h 94%[c,d]	 **2.5g** R.T. 2 h 94%	 **2.5h** R.T. 2 h 97%

[a] Reaction Condition: 0.5 mmol of **2.4** dissovled in 5 mL dried chloroform (0.1M) followed by the addition of $XPhosAuSbF_6CH_3CN$ (5 mmol%) and stirred until the complete consumption of starting material; [b] Purification was performed by use of regular silica gel; [c] Isolated using deactivated neutral Al_2O_3; [d] $ClCH_2CH_2Cl$ was used as the solvent

Mono- and di-substituted ynamides possessing various steric demands were found to undergo the gold-catalyzed transformations smoothly in most cases, furnishing the corresponding allenimides **2.5a-c** and **2.5e-h** in good to excellent yields (**Table 2.4**). As anticipated, the tertiary propargylic ethers reacted more readily. Disubstituted allenimides **2.5e-h** were generated in excellent yields at ambient temperature as the result of the Thorpe-Ingold effect. Interestingly, the synthesis of unsubstituted allenimide **2.5d** was also possible with our method albeit in lower yield and after a prolonged reaction time. Moreover, in the

case of allenimide bearing a cylohexanyl group **2.5f**, 1,3-diene formation was observed which might be due to the strained six-membered ring, however, this could be totally suppressed by changing the solvent from $CHCl_3$ to a less acidic chlorinated solvent, such as 1,2-dichloroethane.

It deserves mentioning that allenimide **2.5f** was very sensitive to both slightly acidic and basic conditions, resulting the fact that they could not be isolated using either silica gel or Et_3N-deactivated silica for flash column chromatography. After several attempts, it was finally found that deactivated neutral alumina [Al_2O_3/H_2O=20/1 (v/v)] was suitable for its separation while regular neutral Al_2O_3 also delivered 1,3-dienes.

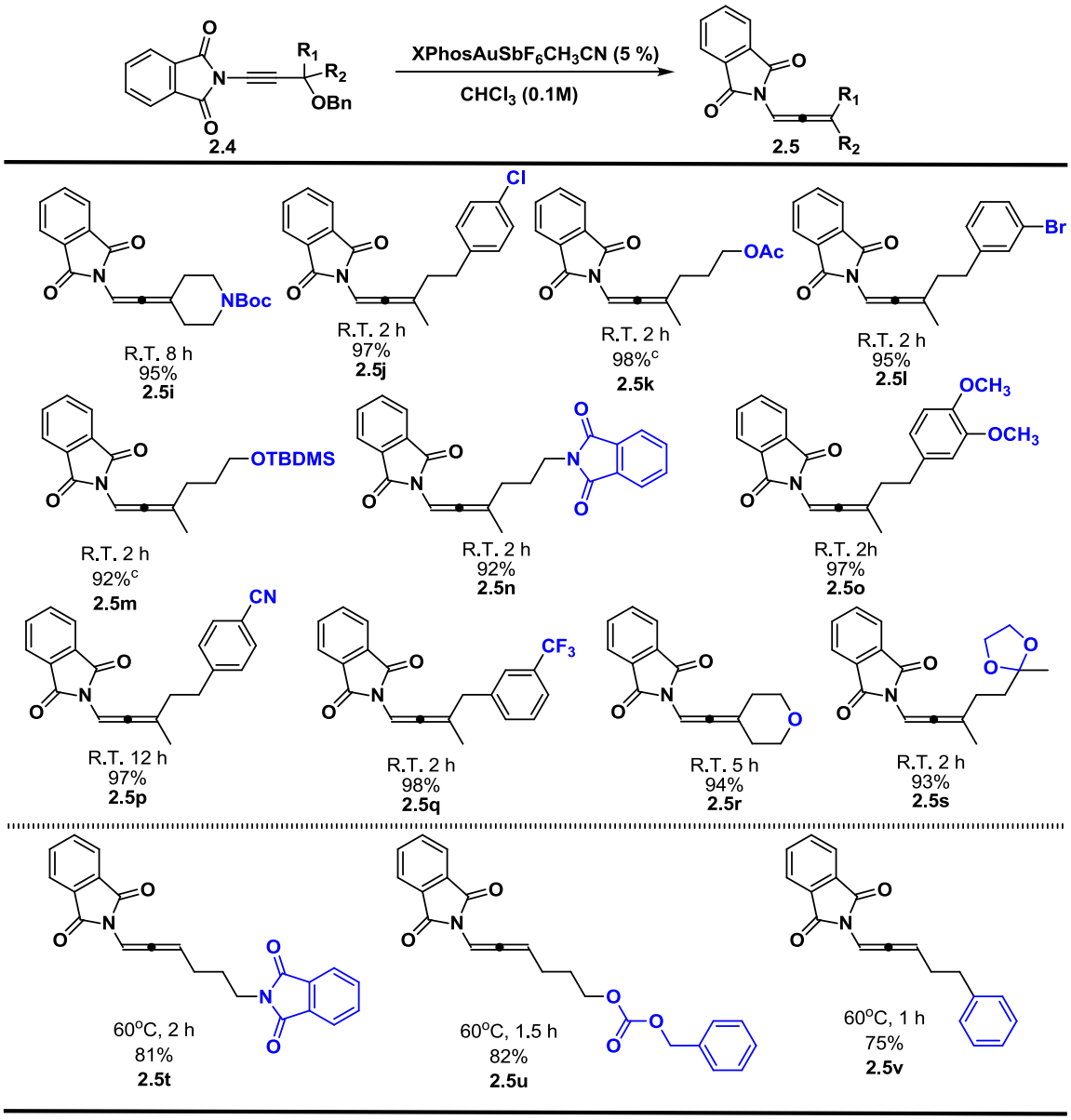
Deactivation procedure was as followed: *a 500 mL beaker was filled with 200 mL of regular neutral Al_2O_3 followed by the slow addition of 10 mL distilled water while stirring vigorously using a glass rod. After addition, the hot Al_2O_3 was transferred into a glass bottle, sealed with a cap and the resulting Al_2O_3 was used for flash column chromatography.*

Given fact that the procedures reported to date are scarcely applicable for the synthesis of allenamides containing functional groups, we next turn our attention to examine the functional group tolereance. To my delight, various mono- and di-substituted ynamides **2.4i-v** bearing a series of functional groups including carbamate, acetate, ether, silyl ether, phthalmide, acetal, carbonate and substituted aromatic rings were tolerated to provide allenimides **2.5i-v** in excellent yields at room temperature within 2 hours.

In the case of **2.4i** and **2.4p**, the ynamides precursors gave rise to the corresponding allenimides in excellent yields, however, these transformations proceeded much slowly and a prolonged reaction time was required to reach completion. We related this phenomenon to the potential coordination properties of cyano group and carbamate, which could competitively coordinate to the gold center during the course of reaction, thus slowing down the reaction. With regard to mono-substituted allenimides bearing functional groups **2.5t-v**, elevated temperature could not be avoided, yet they were consistently compatible with the reaction conditions. To the best of our knowledge, no current methodology to access allenimide and analogues provide such a general functional group tolerance. The present method represents the first general synthesis of functionalized allenimides.

These results demonstrate the practicality and the applicability of our strategy. It is reasonable to expect that this mild and highly efficient preparation of functionalized allenmides will found application in the realm of natural products synthesis and medicinal chemistry.

Table 2.5 Investigation of functionalized allenimides [a,b]



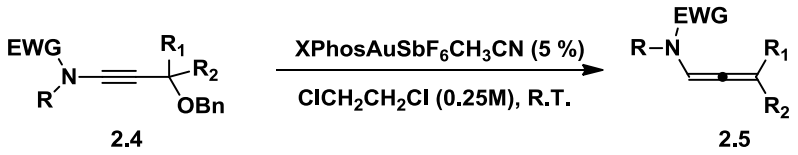
[a] Reaction Condition: 0.5 mmol of 2.4 was dissovled in 5 mL dried chloroform (0.1M) followed by the addition of $XPhosAuSbF_6CH_3CN$ (5 mmol%) and stirred until the complete consumption of starting material; [b] Purification was performed by use of normal silica gel; [c] Isolated using deactivated neutral Al_2O_3;

Having demonstrated the feasibility of the gold-catalyzed strategy for the synthesis of various allenimides, we next sought for a further extension of this approach to the preparation of allenamides, which were found before to have a great propensity to undergo polymerization and/or decomposition in the presence of gold catalysts. After a brief optimization of the reaction conditions, 1,2-dichloroethane proved to be superior solvent in this case when compared to chloroform in which 1,3-dienes were persistently generated along with the desired allenamides. Besides, elevated temperature *must not* be applied in these cases due to the rapid decomposition of the formed. The reaction could be applied to the synthesis of disubstituted allenamides for which the ynamide precursors were disubstituted at the

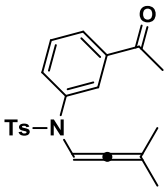
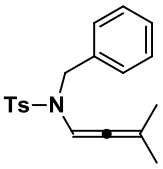
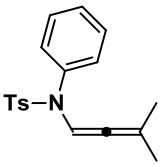
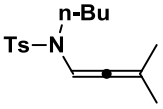
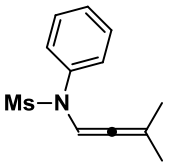
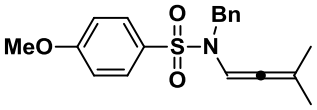
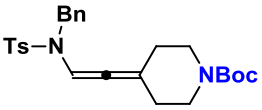
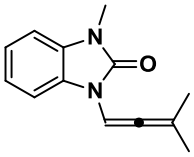
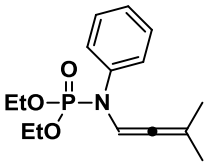
propargylic position. The substrates benefit from the Thorpe-Ingold effect which allowed the transformation to undergo at room temperature. Gratifyingly, a series of sulfonyl-stabilized allenamides bearing diverse substituents **2.5w-ac** were accessible in good to excellent yields by using of XPhosAu(CH_3CN)SbF_6 as the catalyst. Urea and Phosphoramidate derived allenamides **2.5ad** and **2.5ae** could also be obtained by the same method albeit prolonged reaction time and a dilute solution were required. We reasoned that a dilute substrate concentration was beneficial to the overall yield because this could efficiently diminish the degree of the polymerization process. Notably, in the case of **2.5ae**, reaction proceeded with acetone serving as the solvent. An extended reaction time was needed to reach completion and provide acceptable yield of the desired product. It was indeed observed that the formed allenamide **2.5ae** progressively decomposed in chloroform. In the present case the high Lewis base character of acetone should help in disfavoring the polymerization and decomposition process by lowering the π acidity of the electrophilic gold species by complexation.

The required prolonged reaction time, in turns, demonstrated this theory.

Table 2.6 Synthesis of diverse allenamides [a,b]



2.4 → 2.5

				
2.5w R.T. 3 h 88%	**2.5x** R.T. 3 h 85%	**2.5y** R.T. 5 h 95%	**2.5z** R.T. 3 h 91%	**2.5aa** R.T. 2 h 87%
				
2.5ab R.T. 3 h 85%	**2.5ac** R.T. 3 h 89%	**2.5ad** R.T. 20 h 82%[c]	**2.5ae** R.T. 24 h 46%[c,d]	

[a] Reaction Condition: 0.5 mmol of 2.4 was dissovled in 2 mL dried $ClCH_2CH_2Cl$ (0.1M) followed by the addition of XPhosAuSbF6CH3CN (5 mmol%) and stirred until the complete consumption of starting material; [b] Purification was performed by use of deactivated neutral Al_2O_3; [c] Substrate concentration was 0.1M [d] Reaction was carried out in acetone and 10 % catalyst was used.

5.3. Extension of the method to the synthesis of allenamide equivalents

On the basis of our success in synthesizing the allenamides and allenimides, we envisoned that heteroaromatic rings such as pyrroles and indoles, in which the lone electron pair of nitrogen is delocalized into the aromatic ring, could be used as substrate in the hydride transfer process.

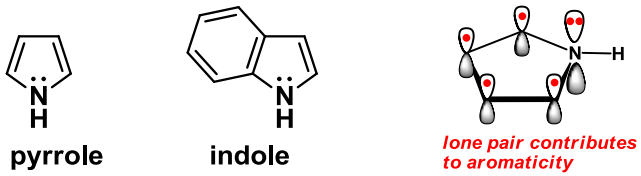
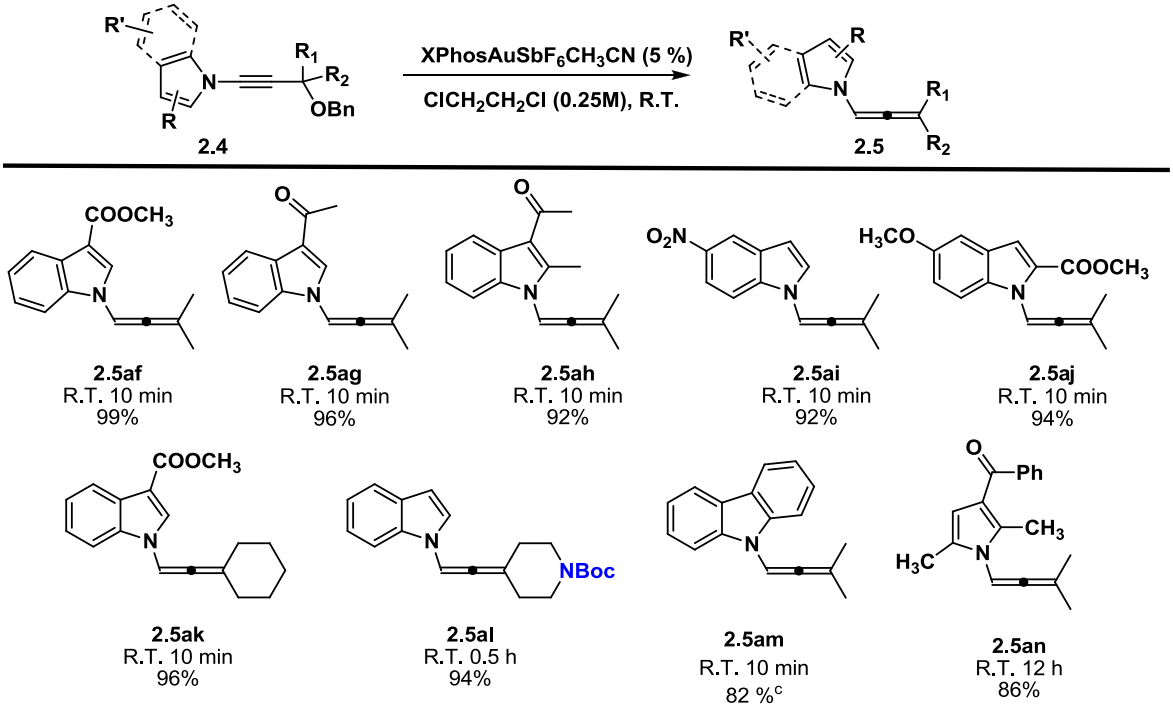


Figure 2-4 Electron distribution of pyrrole and indole

We were pleased to observe that the course of this transformation was even more efficient, furnishing the corresponding allenamide equivalents **2.5af-ak** (**Table 2.7**) containing diverse functionalities in excellent yields in generally less than 10 minutes. The slower process in the case of **2.5al** could also be attributed to the potential coordination of nitrogen atom in carbamate to metallic center, similar to the situation in **2.5l** and **2.5p**. Additionally, carbazole and pyrrole derived ynamines were proved to be suitable substrates in our case, undergoing the transformation smoothly to form **2.5am** and **2.5an** in 82% and 86% yields respectively.

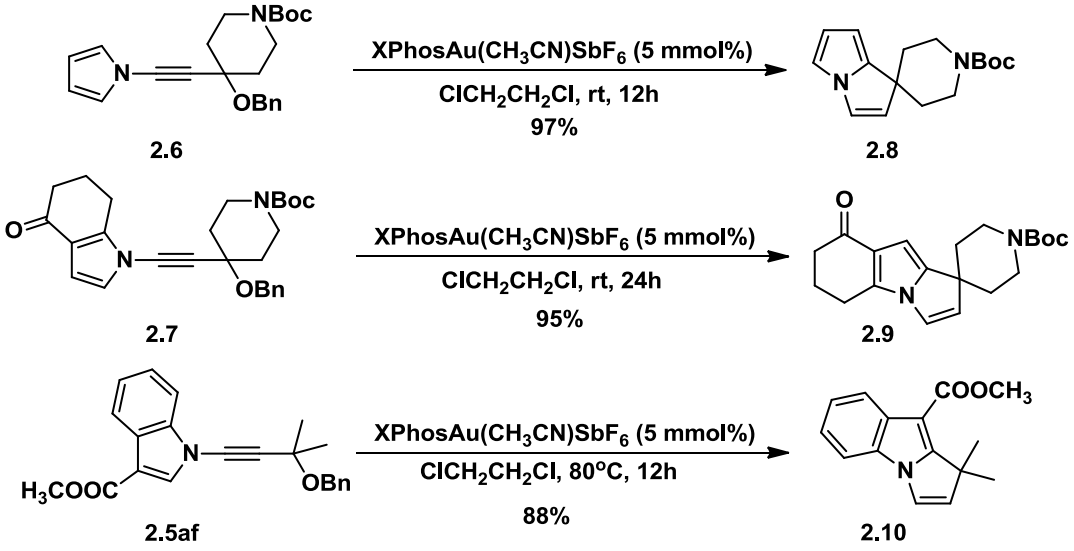
Table 2.7 Synthesis of allenamide equivalents [a,b]



[a] Reaction Condition: 0.5 mmol of 2.4 was dissovled in 2 mL dried $ClCH_2CH_2Cl$ (0.1M) followed by the addition of $XPhosAuSbF_6CH_3CN$ (5 mmol%) and stirred until the complete consumption of starting material; [b] Purification was performed by use of deactivated neutral Al_2O_3; [c] 0.1M concentration of substrate was used.

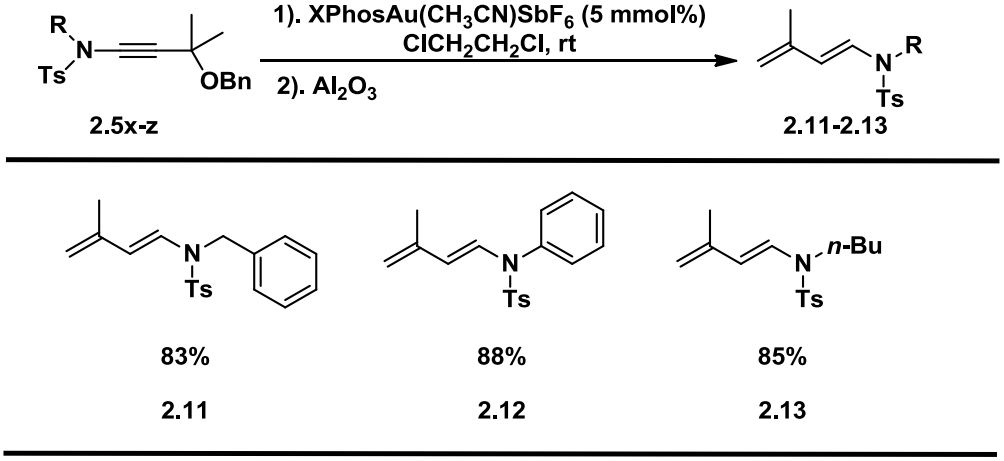
5.4. Further transformation of allenamide and allenamide equivalents

To gain some insights into the synthetic utility and efficiency of the generated allenamine derivatives above, we devised a tandem gold-catalyzed [1,5] hydride shift/Freidel-Craft type reaction process. When N-ethynylpyrroles **2.6** and **2.5af** were treated with XPhosAu(CH_3CN)SbF_6 in 1,2-dichloroethane at room temperature, a slow reaction took place that cleanly provided intriguing spirocyclic compounds **2.8** and **2.9**. A higher temperature was required in the case of the N-ethynylindole **2.5af**, which underwent the same type of transformation at 80°C to afford product **2.10** in 88% yield after 12 hours (**Scheme 2-22**).



Scheme 2-22 Synthesis of allenamide and allenamide equivalents

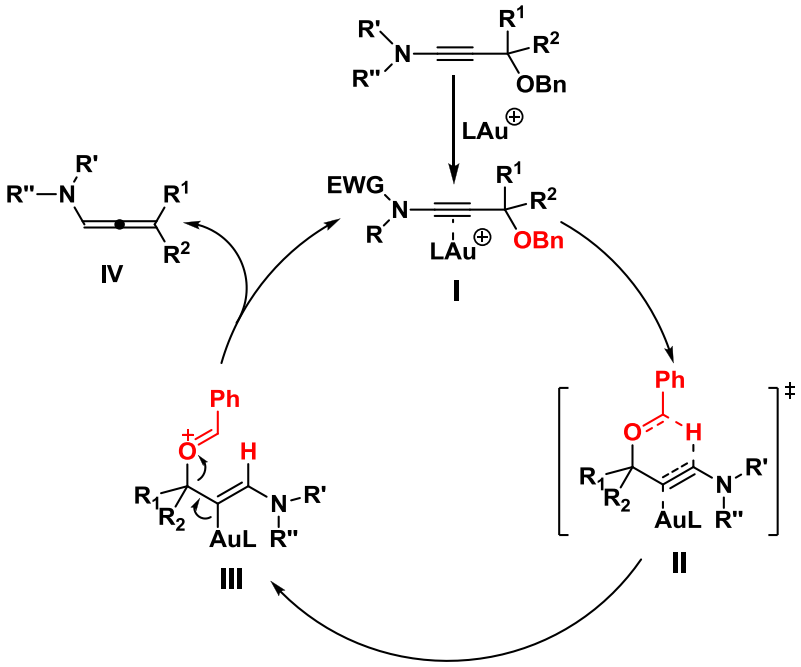
Interestingly, 1,3-dienes **2.11-2.13** were efficiently prepared from starting ynamides 2.5x-z in a one-pot manner at ambient temperature in yields ranging from 83% to 85% *via* gold-catalyzed allenamides formation followed by an isomerization assisted by neutral alumina (**Scheme 2-23**).



Scheme 2-23 Synthesis of 1,3-dienes

6. Mechanistic scenario

From a mechanistic point of view, the gold-catalyzed synthesis of allenamine derivatives was initiated by the coordination of the starting ynamides to the electrophilic cationic gold(I) complex. The hydrogen at the benzylic position then undergoes a gold-assisted [1,5]-hydride transfer to the *α* position next to nitrogen *via* intermediate **II**. This provided a new intermediate intermediate **III** that loses benzaldehyde to afford desired allenamine derivatives **IV**.



Scheme 2-24 Mechanistic proposal for the synthesis of allenamine derivatives from ynamides

7. Conclusion

In summary, we have disclosed a robust and efficient approach toward the synthesis of various allenamine derivatives from readily accessible ynamides in the presence of gold catalysts. This reaction which proceeds *via* a [1,5]-hydride transfer was demonstrated to be quite general and mild since a wide range of sensitive functionalized allenimides, allenamides, and N-allenyl indoles, N-allenyl pyrroles were expediently assembled. This report represents the widest substrate scope tolerance reported so far. In particular, we demonstrated the first facile access to various N-allenyl indoles and pyrroles. In view of the broad application of allenamine derivatives as versatile synthons, there is a great chance that the present method will attract more interest of the synthetic community and promote further development of

the allenamide chemistry. Further investigation of synthetic application of this process is being carried out in our laboratory.

Chapter 3. Dual gold catalysis: a unique approach to tetrahydroquinoline derivatives by a formal [4+2] annulation process

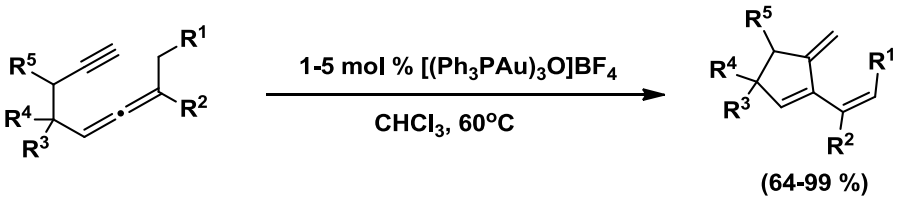
As earlier mentioned and exemplified in this manuscript, the past decade has witnessed significant progress in homogeneous gold catalysis. To be specific, a series of reactions were initiated by the π-coordination of a C-C multiple bond to "a" cationic gold center. This "a" means that only one metal center is involved in the mechanistic scenario, as shown in a number of reported catalytic cycles. This mono activation of alkynes by a gold center is quite common in gold catalysis and other mechanistic possibilities involving several metal centers have been long-standing ignored. However, recent contributions by several research groups revealed a novel reactivity mode in which two gold centers work with the same substrate molecule, one gold complex being σ-coordinated to a terminal alkynyl group and the other gold center being π-coordinated to a different triple bond in the substrate.

This rencent advance in homogeneous gold catalysis is the topic of this chapter. By analogy with vast majority of discoveries, dual gold catalysis has standed as a curiosity of laboratory before being supported by calculations and developed in several new methodologies. Fundamental principles as well as research results from our group in this field will be presented in the following sections.

1. Introduction

1.1. σ, π-digold acetylides

In 2008, Houk, Toste and co-workers reported the synthesis of cross-conjugated trienes by cycloisomerization of 1,5-allenynes catalyzed by trimeric gold catalyst, $[(Ph_3PAu)_3O]BF_4$ (**Scheme 3-1**) [67] .

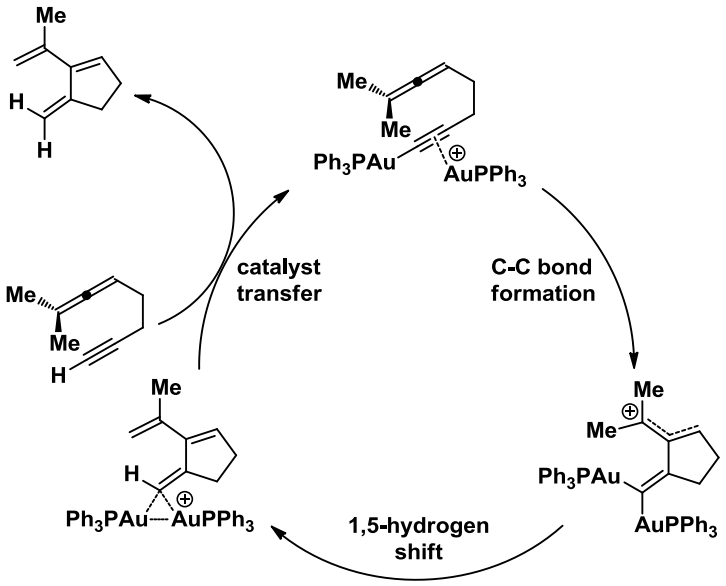


Scheme 3-1 Toste's synthesis of trienes

On the basis of deuterium labeling and crossover experiments, evaluation of primary kinetic effect in combination with computational chemistry, the authors presented a unique mechanism involving a nucleophilic attack of the allene moiety onto a phosphinegold-coordinated phosphinegold acetylide. This was the first proposal of a simultaneous participation of two gold complexes in a gold-catalyzed process (**Scheme 3-2**). It is worth noting that the two gold centers are located in the same alkynyl moiety, which is the more

[67] Cheong, P. H.-Y.; Morganelli, P.; Luzung, M. R.; Houk, K. N.; Toste, F. D. *J. Am. Chem. Soc.* **2008**, *130*, 4517.

thermodynamically stable species according to computational results. Coordination of a cationic gold center a $[LAu]^+$ to gold acetylide has been calculated to be 22 Kcal mol^{-1} more favorable than the coordination to an allene while the energy difference between the coordination to alkyne and an allene is very small.

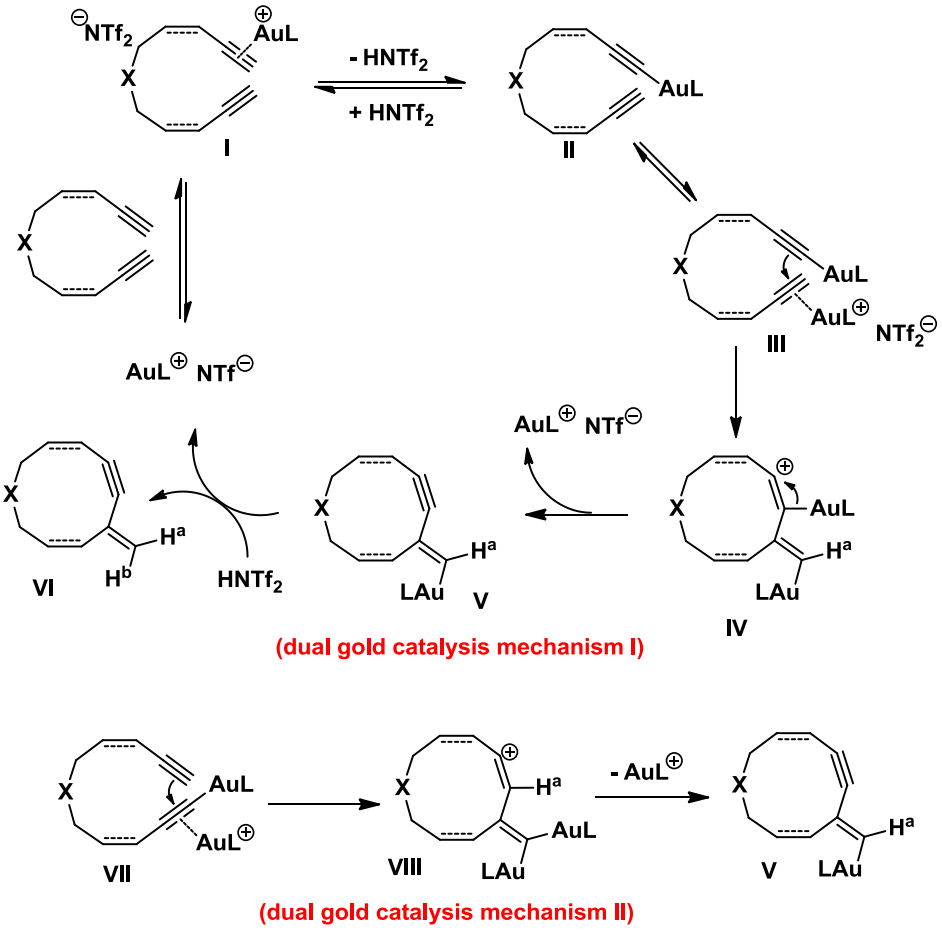


Scheme 3-2 Mechanism proposed by Toste, Houk et al.

In 2009, Gagosz et al. reported[68] an unusual approach to medium-sized alkynes *via* cycloisomerization of 1,9- and 1,10-diynes. In the proposed mechanisms, two different patterns of dual activation modes of the starting material were presented, which are both in agreement with the deuterium labeling experiments (**Scheme 3-3**). In the first present mechanism, a di-coordinated intermediate **III** was proposed. A nucleophilic attack of the gold acetylide onto the gold-activated alkyne furnishes a vinylic cationic intermediate **IV**. It is noteworthy that this activation mode represents the first description of the current hot topic "dual gold catalysis", in which one gold center is σ-bonded to a terminal alkyne and a second gold complex possesses *π*-coordination to a different alkyne.

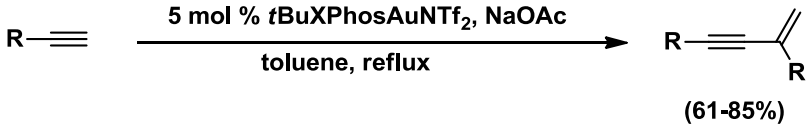
Alternatively, the more thermodynamically stable intermediate **VII** in Toste's work[67] was also considered by the authors. The alkynyl group attacked a cationic gold-coordinated gold acetylide to give rise a gem-diaurated species **VIII**. Subsequent intramolecular hydrogen shift accounts for the stereoisotopic distribution observed during their mechanistic investigations.

[68] Odabachian, Y.; Le Goff, X. F.; Gagosz, F. *Chem. Eur. J.* **2009**, *15*, 8966.



Scheme 3-3 Gagosz's mechanistic proposals for the synthesis of medium-sized alkynes

Analogously, Liming Zhang revealed an intermolecular version of this reaction for the dimerization of alkynes. In this process, a gold acetylide served as the nucleophile that adds onto another gold(I)-activated alkyne (**Scheme 3-4**).[69]

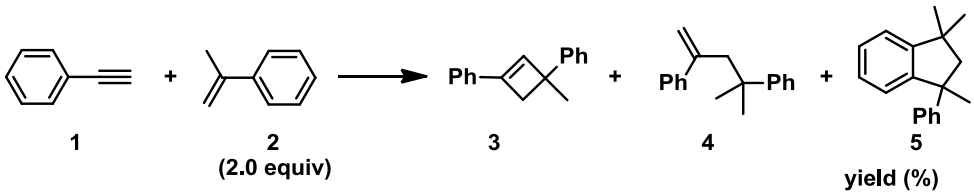


Scheme 3-4

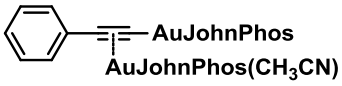
Corma, Garcia and co-workers reported the formation of *σ, π*-digold acetylides bearing sterically hindered biphenylphosphine ligands and tested their synthetic potential.[70] It was found that these diaurated species smoothly catalyzed the intermolecular alkene-alkyne [2+2] cycloadditions to give cyclobutene in higher yield. The transformation was found to be more selective compared to earlier results reported by Echavarren[71]. Although the digold acetylide

[69] Sun, S.; Kroll, J.; Luo, Y.; Zhang, L. *Synlett* **2012**, *2012*, 54.
[70] (a) Grirrane, A.; Garcia, H.; Corma, A.; Álvarez, E. *ACS Catalysis* **2011**, *1*, 1647. (b) Grirrane, A.; Garcia, H.; Corma, A.; Álvarez, E. *Chem. Eur. J.* **2013**, *19*, 12239.
[71] López-Carrillo, V.; Echavarren, A. M. *J. Am. Chem. Soc.* **2010**, *132*, 9292.

species exhibit excellent reactivity and selectivity as the catalyst, it is an inert reaction component, which was proved by control experiment in the absence of alkyne.(**Scheme 3-5**) During the investigation of cycloisomerization of enyenes, Gilbert, Gandon, Fensterbank et al. observed the presence of *σ, π*-digold acetylides *via* electronspray ionization mass spectrometry. They found that gold acetylides showed a high affinity for a second gold center what leads to the formation of digold species. However, both these di-coordinated species seemed to be unlikely involved in the overall cycloisomerization reactions.[72]

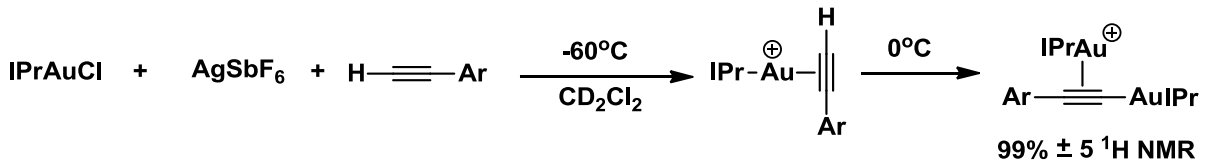


1 2 (2.0 equiv) 3 4 5

	conv. of 1 (%)	conv. of 2 (%)	selectivity of 7 (%)	yield (%) 3	4	5
JohnPhosAuSbF$_6$(CH$_3$CN)	82	96	52	43	33	2
XPhosAuNTf$_2$	88	94	26	23	36	
	89	57	91	81	5	

Scheme 3-5

Widenhoefer and co-workers[73] revealed that (IPr)AuCl/AgSbF$_6$ formed unstable *π*-complexes with terminal arylacetylene at low temperature, which were transformed into *σ, π*-digold acetylide complexes by warming the temperature to 0 ℃ (**Scheme 3-6**).



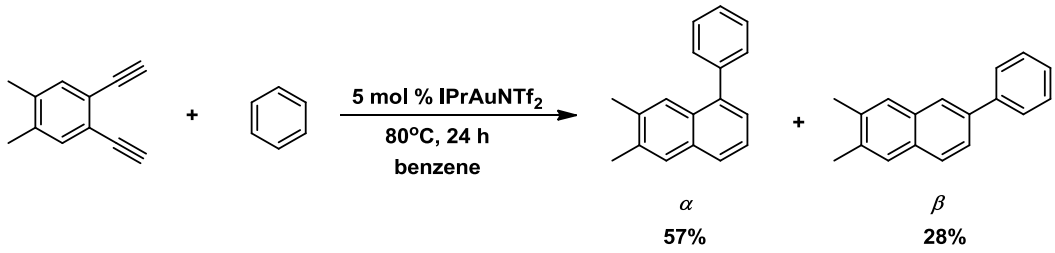
Scheme 3-6 formation of *σ, π*-digold acetylides

1.2. Dual gold catalysis

In 2012, in the course of their investigation of transformations involving terminal 1,2-dialkynylarenes, Hashmi and co-workers observed an unexpected intermolecular hydroarylation leading to the formation of naphthalenes. In addition to the formation of *α*-naphthalene derivative *via* a reasonable initial Markovnikov addition, the formation of β-

[72] Simonneau, A.; Jaroschik, F.; Lesage, D.; Karanik, M.; Guillot, R.; Malacria, M.; Tabet, J.-C.; Goddard, J.-P.; Fensterbank, L.; Gandon, V.; Gimbert, Y. *Chem. Sci.* **2011**, *2*, 2417.
[73] Brown, T. J.; Widenhoefer, R. A. *Organometallics* **2011**, *30*, 6003.

naphthalene was also observed in significant amount (**Scheme 3-7**). this was the starting point of the development in the field of dual gold catalysis.



Scheme 3-7 Unexpected formation of β-naphthalene

On the basis of mechanistic investigations, a gold acetylide was proposed to be formed and involved in the reaction course. So the corresponding gold acetylide of the model substrate was separately prepared and warmed at 80°C for 24 hours but no conversion was observed. However, the addition of catalytic amount of the active catalyst (i.e. $IPrAuNTf_2$) led to almost exclusive formation of the β-product. Based on these experiments and additional kinetic studies (**Figure 3-1**), the authors proposed that during the course of the reaction, two different reaction pathways compete. At the beginning of the reaction, a single gold activation of one alkyne moiety leads to the generation of the *α*-isomer, slowly the *π*-coordinated alkyne was converted into a gold acetylide, which cooperates with another cationic gold(I) species to give rise to the β-isomer selectively. This proposal was confirmed by studying the additive effects of additives among which triethylamine and aluminum oxide were shown to favor the formation of β-isomer (98:2) with high selectivity. It was also found that an equilibrium between the gold acetylide and the active gold(I) catalyst were required for efficient transformation and a high β-selectivity.

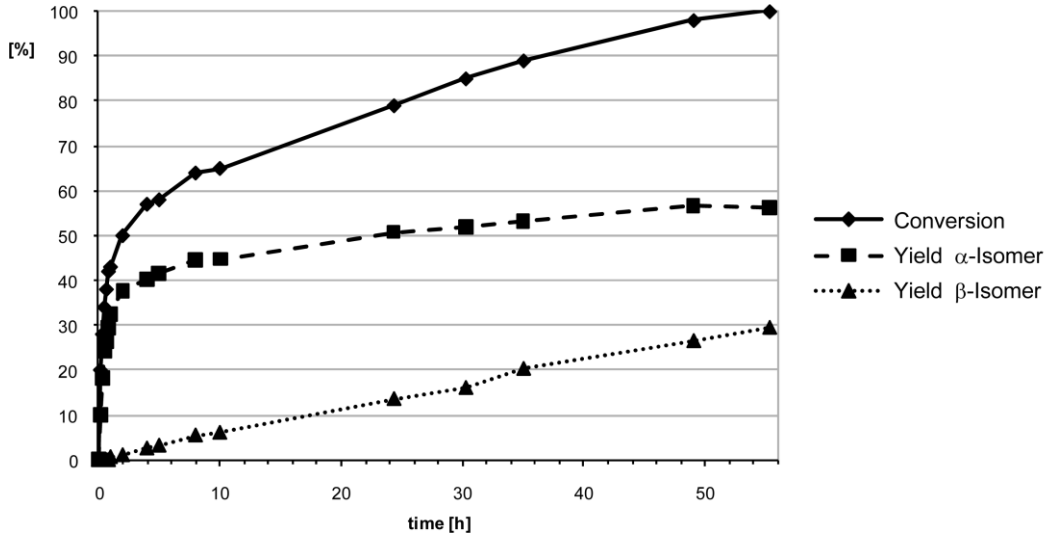
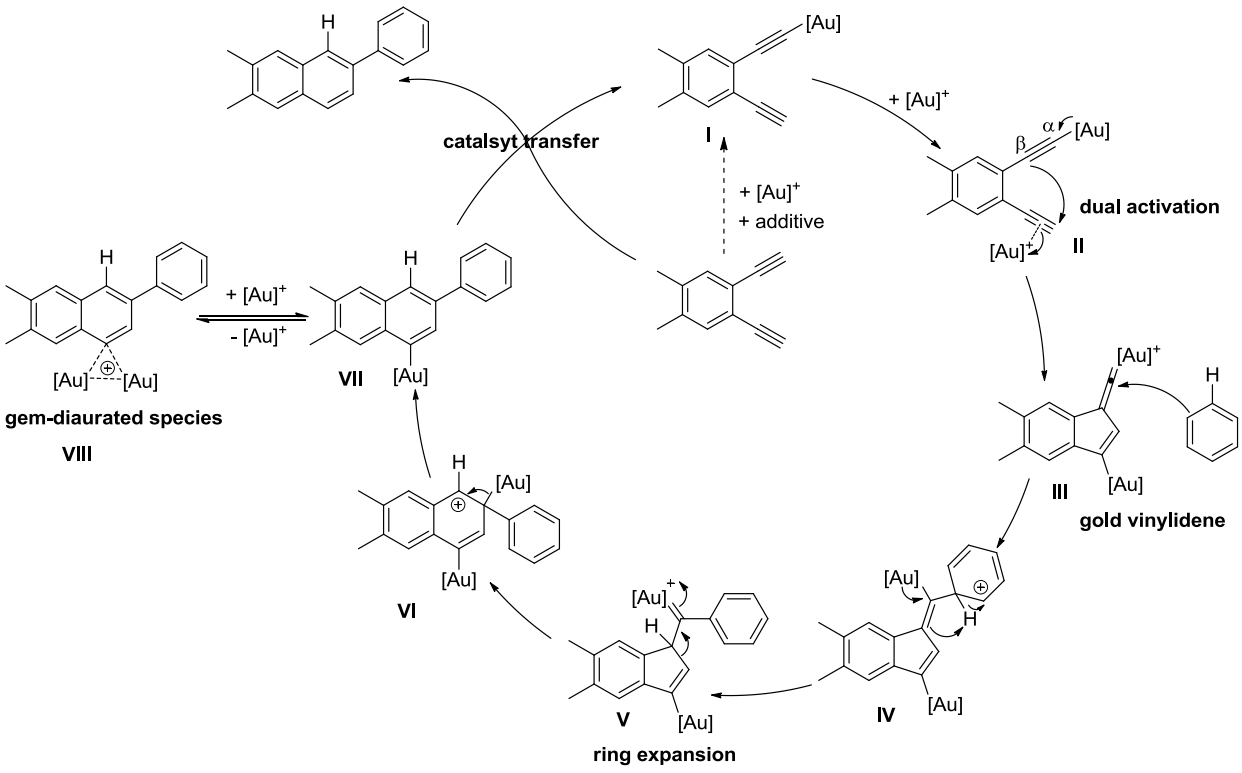


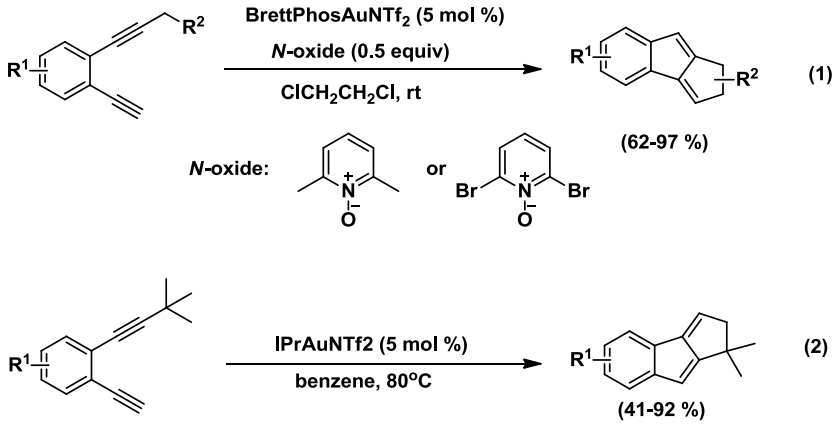
Figure 3-1 Conversion and yields of *α*-isomer and β-isomer against reaction time

With regard to the catalyst transfer that completes the catalytic cycle, the protodeauration of the naphthyl gold(I) intermediate by another alkyne substrate molecule was unavoided to maintain high β-selectivity. This catalyst transfer process was also invoked by Toste [67]. This type of process allows the formation of the final product and regenerates the earlier active gold acetylide species which enter the next catalytic cycle to give rise to β-isomer. If naphthyl gold(I) species was protodeaurated by an external proton source (e.g. residual water in solvent), cationic gold species, LAu^+ is then generated which lead to the formation of *α*-isomer.

On the basis of extensive mechanistic studies, the following mechanism was proposed. In the presence of basic additive, the starting material was converted into gold acetylide **I**. Coordination of a second gold complex to the other triple bond triggered the nucleophilic attack at the β-position, which furnishes gold vinylidene as a key intermediate (**III**). Subsequently, eletrophilic attack by benzene gives rise to intermediate **IV**, which underwent an intramolecular [1,3]-hydrogen shift to provide carbenoid species **V**. Afterwards, a ring expansion provided intermediate **VI**, which undergoes deauration to give rise to napthyl gold (I) intermediate **VII** and gem-diaurated species **VIII** was supposed to be in an equilibrium in the reaction course. Finally, a catalyst transfer from **VII** to another substrate molecule completes catalyic cycle and regenerates the active species gold acetylide **I**.



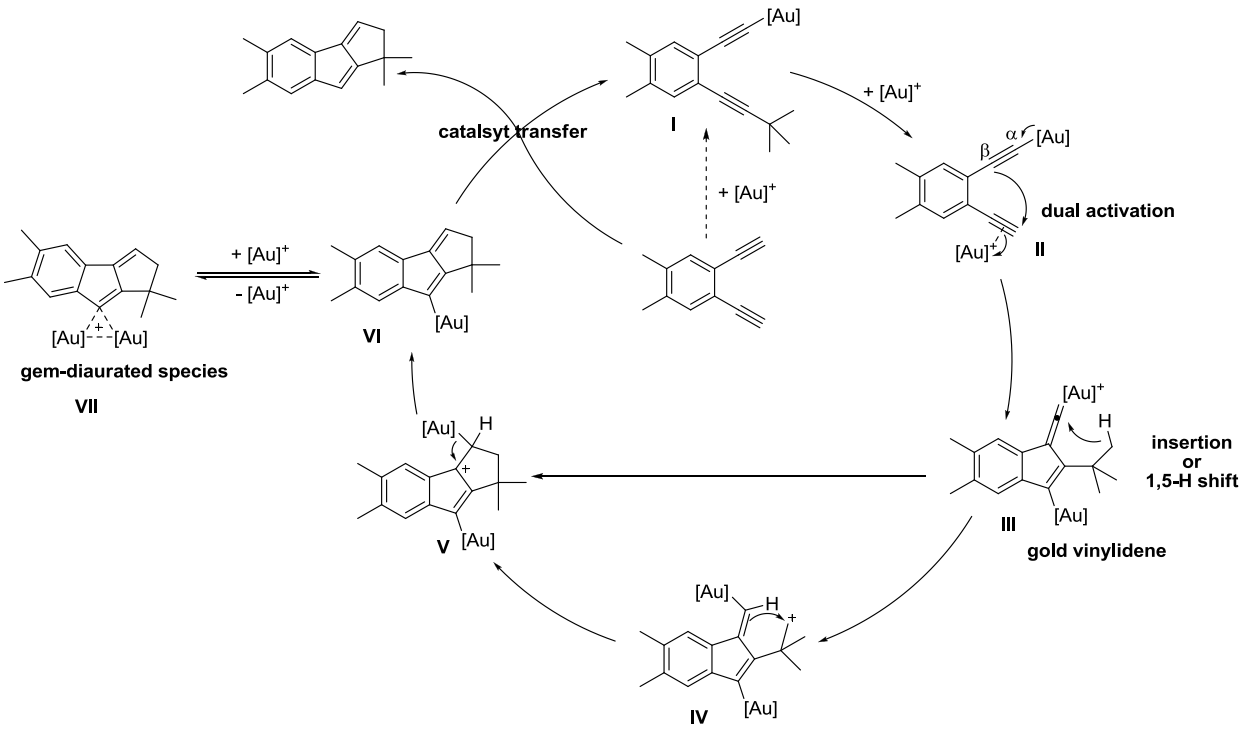
The formation of gold vinylidene **III** as a crucial intermediate herein was later proved by the same group (**Scheme 3-8**, eq 1)[74] and by a parallel work of Liming Zhang (**Scheme 3-8**, eq 2)[75]. The generated gold vinylidene was trapped by insertion into C(sp^3)-H bond. While NHC ligand gave the best results in Hashmi's work, Zhang and co-workers achieved the same success using BrettPhos as the ligand and in the presence of pyridine N-oxide as a weak basic additive.



Scheme 3-8 C(sp^3)-H bond activation involving gold vinylidene

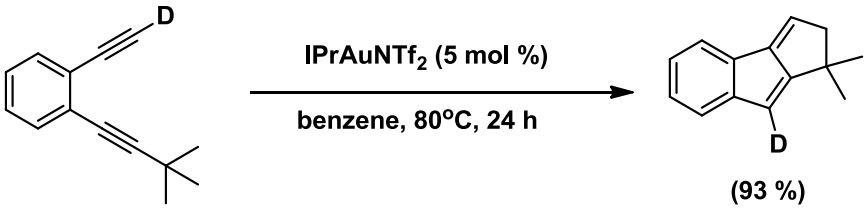
They proposed a very similar mechanism for this transformation. (2-ethynylphenyl)alkynes was converted to gold acetylide **I** with $IPrAuNTf_2$ in the absence of basic additives. Subsequently, a second gold complex coordinated to the other triple bond, thus activating this C≡C bond for an electrophilic attack by gold acetylide at the β position, which gave rise to gold vinylidene **III**. Although in the original publication, Hashmi et al. proposed a stepwise 1,5-hydrogen shift for the ring closure process (*via* intermediate **IV**) to give rise cationic vinyl species **V**, in a later review[76] they amended it and described a concerted C-H insertion procedure (**Scheme 3-9**).

[74] Hashmi, A. S. K.; Braun, I.; Nösel, P.; Schädlich, J.; Wieteck, M.; Rudolph, M.; Rominger, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 4456.
[75] Ye, L.; Wang, Y.; Aue, D. H.; Zhang, L. *J. Am. Chem. Soc.* **2012**, *134*, 31.
[76] Hashmi, A. S. K. *Acc. Chem. Res.* **2014**, *47*, 864.



Scheme 3-9 Hashmi's proposal involving C-H activation to benzofulvenes

This modification was based on a new discovery of stereospecific addition to alkenes by potential gold vinylidene intermediates.[77] Intermediate **V** underwent deauration to furnish the vinyl gold (I) species **VI**, which gave rise to a gem-diaurated species after coordination with $[Au]^+$. Species **VI** and **VII** are in a side equilibrium. Catalytic cycle was completed by a catalyst transfer, which was validated by deuterium labeling experiments: 93 % of deuterium atom at terminal position of alkyne was transferred into the gold position of intermediate **VI** (**Scheme** 3-10).

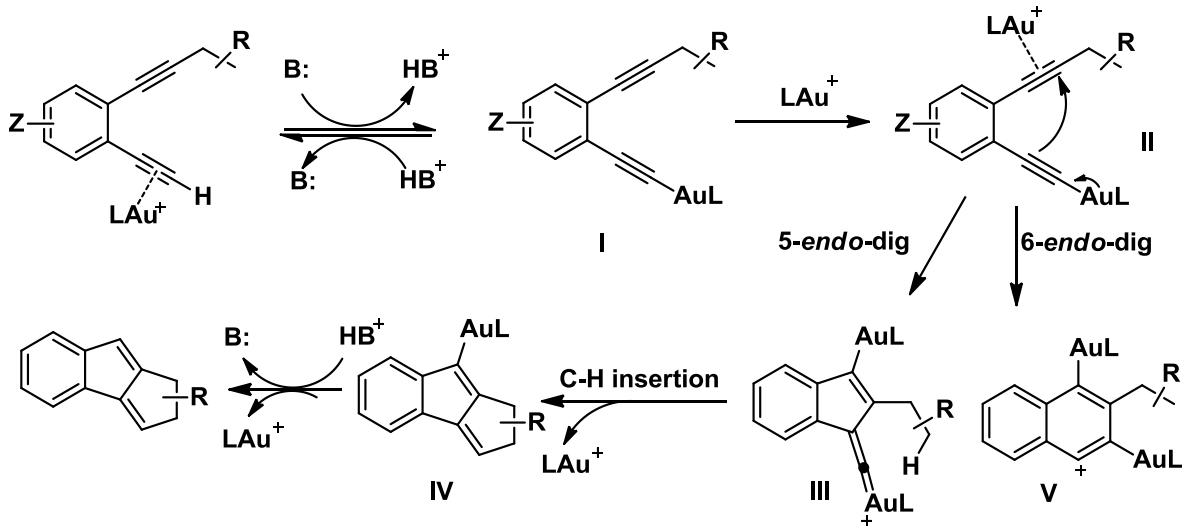


Scheme 3-10

Zhang et al. introduced an interesting bifurcation mechanism on the basis of computational studies (**Scheme** 3-11). Zhang's proposal is different from two points from the parallel work of Hashmi: (a) during the first step, gold acetylide is proposed to be formed with the assistance of weak base, i.e. pyridine N-oxide in this case; (b) in the last step, catalyst transfer was not

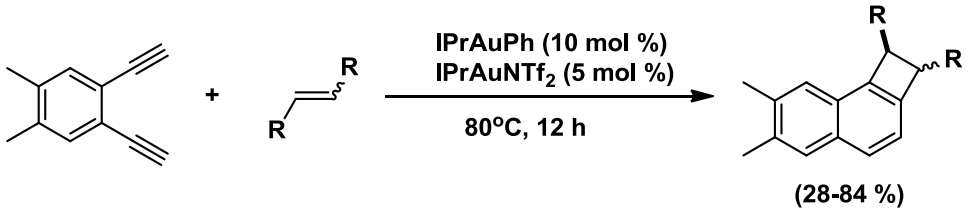
[77] Hashmi, A. S. K.; Wieteck, M.; Braun, I.; Rudolph, M.; Rominger, F. *Angew. Chem. Int. Ed.* **2012**, *51*, 10633.

considered whereas a direct protodeauration was invoked. However, their wording was very careful "the alkyne terminal hydrogen might become labile in the course of the reaction" although their deuterium labeling experiments clearly indicated that the proton replacing the gold atom in intermediate IV was not from the terminal position of an alkyne.



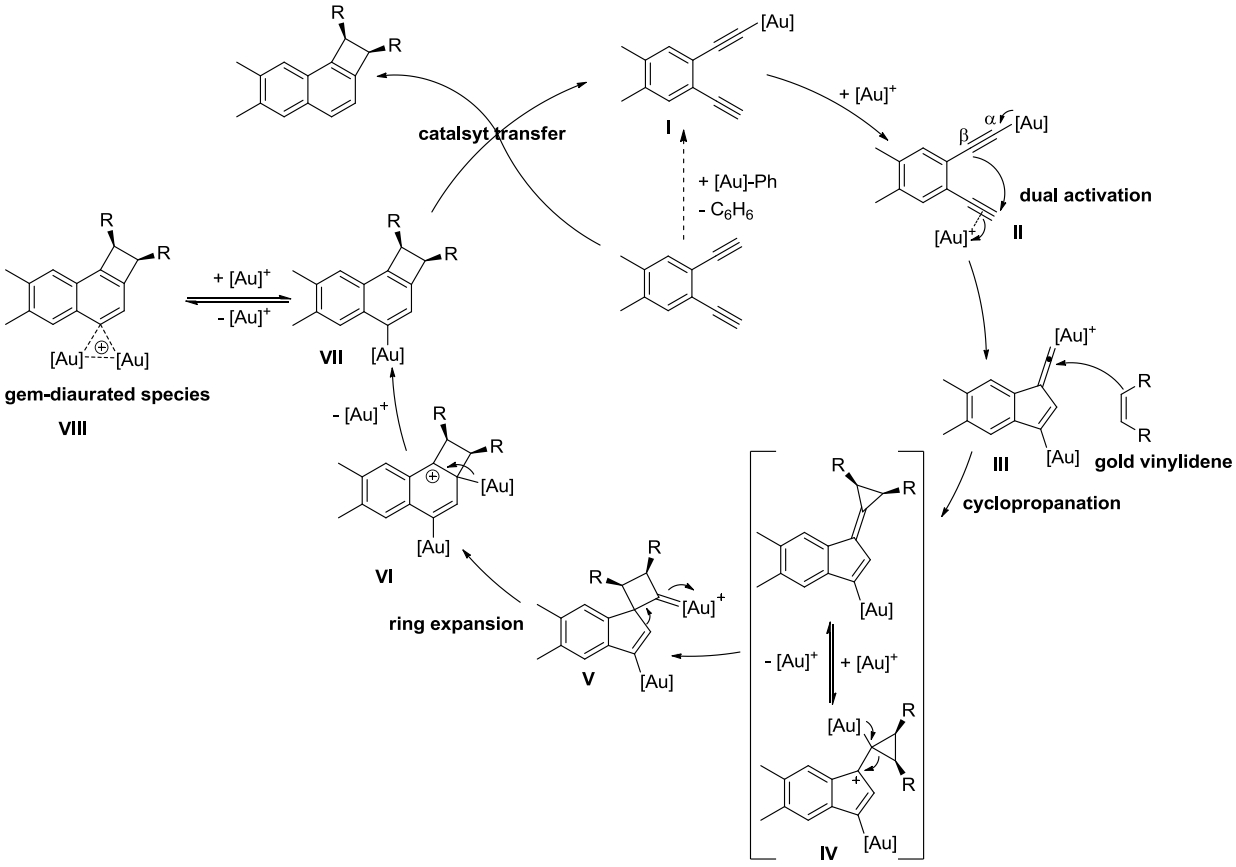
Scheme 3-11 Zhang's proposal involving C-H activation to benzofulvenes

Another transformation involving the intermedicy of gold vinylidene was reported in 2012, still by Hashmi group. Benzocyclobutenes were synthesized by an intermolecular reaction of diynes with alkenes. A high stereospecificity was observed: (*Z*)-olefin gave rise to cis product while trans product was obtained from (*E*)-olefin.



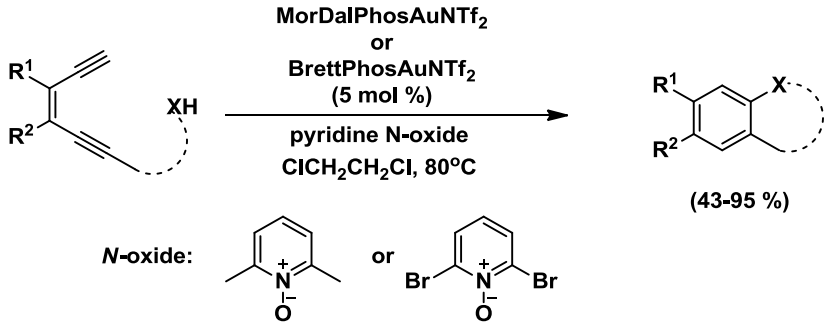
Scheme 3-12 Intermolecular approach to benzocyclobutene *via* dual gold catalysis

This stereospecificity unambiguously demonstrated a concerted pathway. This led the authors to modify the initial mechanism for the C(sp^3)-H activation to be concerted C-H insertion pathway. The generated gold vinylidene **III** reacted with an external alkene *via* a concerted, thus stereospecific, cyclopropanation mechanism, furnishing methylenecyclopropane **IV.** Afterwards, **IV** underwent a tandem ring expansion to give rise to the naphthyl framework of the final product. The other elementary steps are the same as previously mentioned for dual gold catalysis processes (**Scheme 3-13**).



Scheme 3-13 Cyclopropanation pathway *via* gold vinylidene

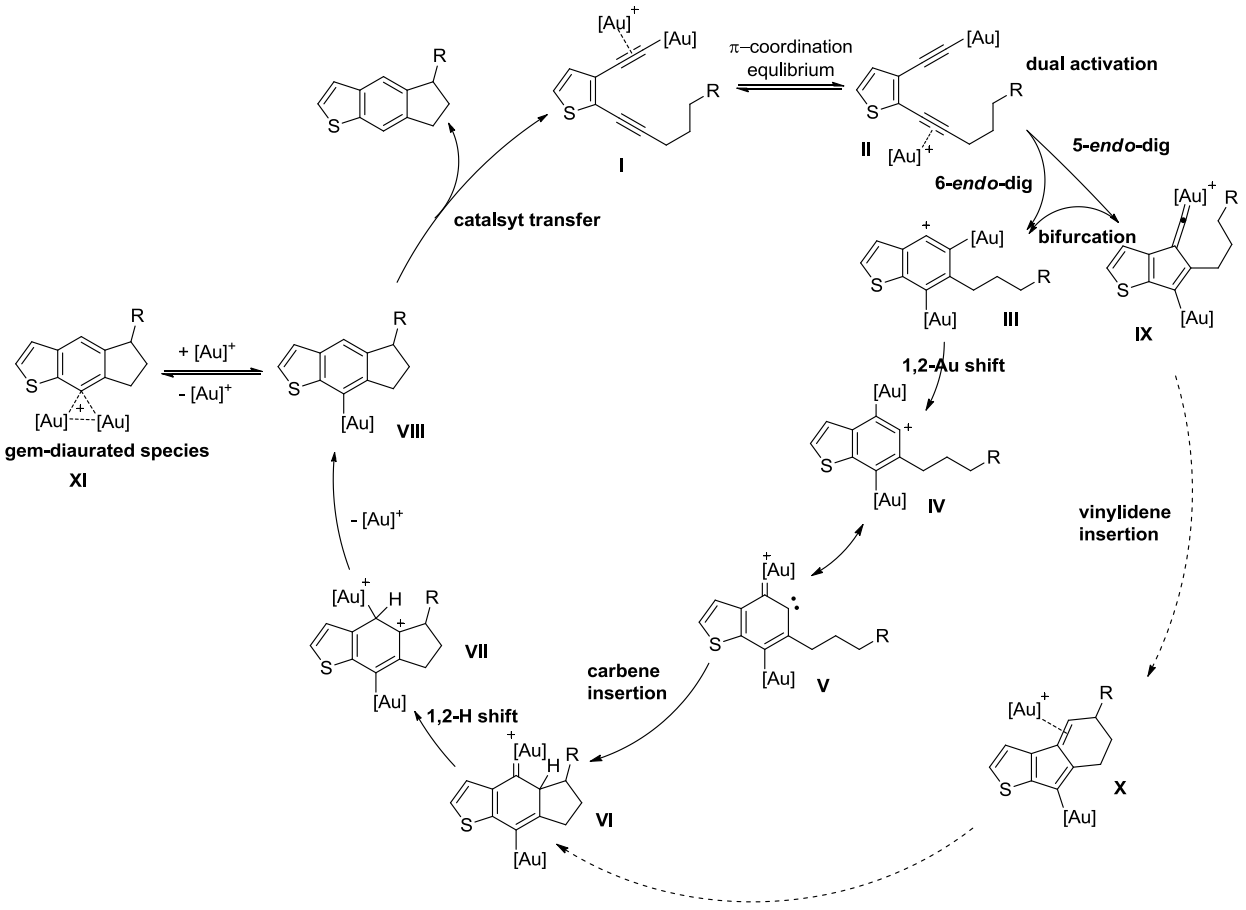
As mentioned earlier[75], Zhang's computational results on the synthesis of benzofulvene revealed an alternative 6-endo-dig pathway which could lead to the formation of naphthyl products (**Scheme 3-11**, species **V**). In 2013, when they switched the substrate backbone to double bond instead of a phenyl ring, they were able to put in evidence for this divergence in their mechanism. Substituted indanes, heterocycle-fused benzenes and phenol derivatives are accessible from *cis*-enediynes *via* dual gold catalysis (**Scheme 3-14**). [78]



Scheme 3-14 Cycloisomerization of *cis*-enediynes

[78] Wang, Y.; Yepremyan, A.; Ghorai, S.; Todd, R.; Aue, D. H.; Zhang, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 7795.

Gold aryne was considered to be the transition state. The cyclization process proved to be a concerted C(sp^3)-H insertion to a relatively stable carbene-like intermediate. Almost at the same time, Hashmi et al. implemented the same type of 6-endo-dig cyclization with a thiophene motif in the backbone.[79] A series of indanothiophenes and fluorenothiophenes were produced by the same strategy.



Scheme 3-15 Hashmi's proposal for 6-endo-dig cycloisomerization

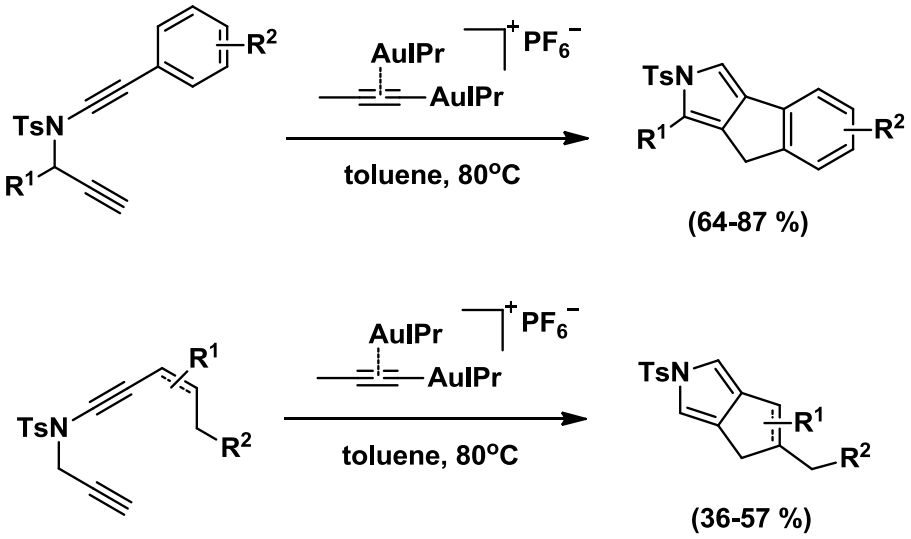
After the generation of gold acetylide, a second $[Au]^+$ preferentially coordinated to the same triple bond rather than the other one energetically. So in the mechanistic proposal, equilibrium between species **I** and **II** was envisioned. Di-gold coordinated species **II** would undergo a 5-*endo*-dig or a 6-*endo*-dig cyclization to provide gold vinylidene **IX** and species **III** respectively. Analogous to Zhang's calculation results[75], a transition state connecting species **III** and **IX** was also located. It was assumed that the two cyclization products equilibrate and that the final product depends on the possible subsequent transformations. On the basis of their computational results, it was found that the formation of 6-endo-dig cyclization product III was favorable by 10 $Kcalmol^{-1}$. III was converted into a carbene-like intermediate **V** *via* a

[79] Hansmann, M. M.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem. Int. Ed.* **2013**, *52*, 2593.

1,2-hydrogen shift with gold-aryne being the transition state. Subsequent carbene insertion followed by a 1,2-H shift and deauration give rise to species **VIII**. The latter undergoes catalyst transfer with another molecule of substrate to furnish the final product.

The selective 6-*endo*-dig pathway raised a significant question now: what determines the reaction pathway of the dual-activated starting material? A number of calculations[80] revealed that these two distinct pathways have a good correlation with the aromaticity of the 6-endo-dig cyclization mode,i.e. it is preferred when the corresponding cyclization product was sufficiently stable, otherwise, 5-endo-dig mode occurs.

In 2015, this type of dual-activated reaction mode of 1,2-diynes was extended to ynamide substrate.[81] Multisubstituted pyrroles were accessed through the cycloisomerization of *N*-propargylynamides. Interestingly, the commonly encountered nuleophilic attack at the *α*-position of ynamide was not observed. Instead the β-position was found to be the active site. Besides alkyne C-H bond activation, aryl C(sp^2)-H bond activation was also successfully demonstrated.

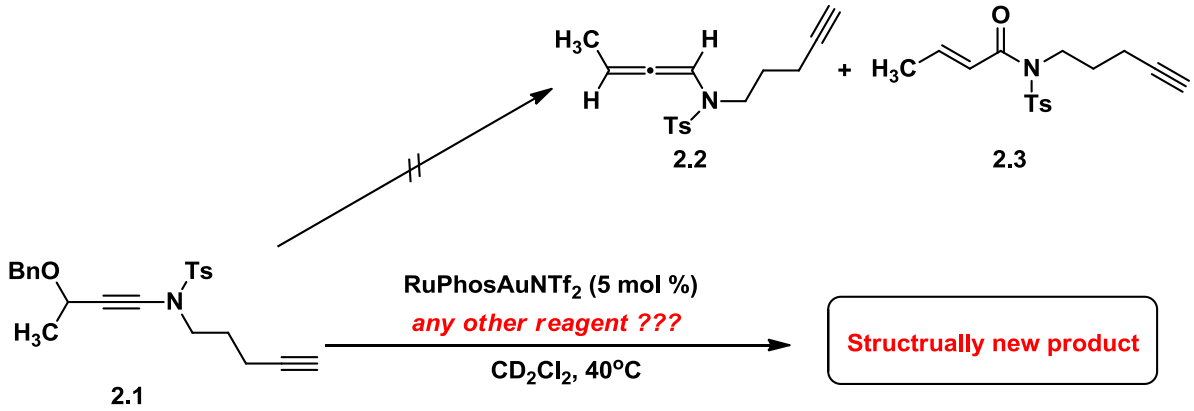


Scheme 3-16 Synthesis of multisubstituted pyrroles *via* dual gold catalysis

[80] Hansmann, M. M.; Tšupova, S.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Chem. Eur. J.* **2014**, *20*, 2215.
[81] Tokimizu, Y.; Wieteck, M.; Rudolph, M.; Oishi, S.; Fujii, N.; Hashmi, A. S. K.; Ohno, H. *Org. Lett.* **2015**, *17*, 604.

2. Origin of our project and preliminary results

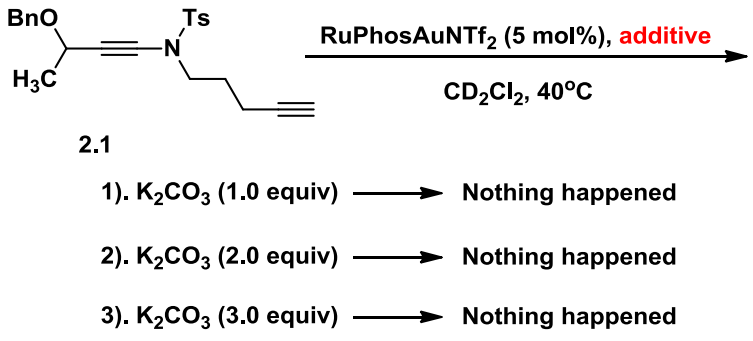
In the course of our studies to access allenamides, we examined the ligand effects of gold catalyst. This was performed with an intension to improve the yield of the desired product (**Table 2.2, Chapter 2**). To our great surprise, when RuPhosAuNTf$_2$ was employed as catalyst, it was found that a completely different compound was obtained (**Scheme 3-17**). This appears to be rather surprising since all the other catalytic systems gave rise to a mixture of the allenamide and the 1,3-diene in different ratios from model substrate **2.1**.



Scheme 3-17 New product in the desired allenamide reaction

This was the first time we observed a product other than allenamide **2.2** or 1,3-diene **2.3**. Surprisingly and somewhat disappointing, this reaction result ***could not*** be reproduced although different solvents (d^8-toluene, $CDCl_3$ and CD_2Cl_2) and a new batch of starting material were employed (ynamide was unstable even at -30 °C. ^{1}H NMR analysis indicated somewhat decomposition of **2.1** before we redo this reaction).

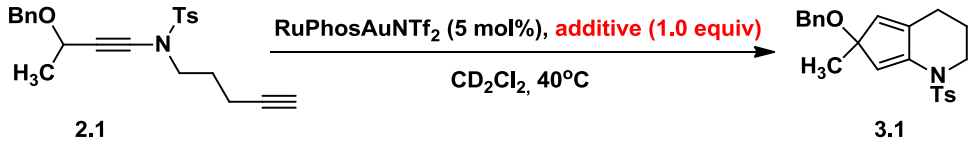
Since the deuterated dichloromethane used for the reaction was dried over K_2CO_3 and supposing that some might have been introduced into the reaction medium, we carried out the reaction in the presence of K_2CO_3 as a basic additive. However no expected conversion was observed even with different amounts of potassium carbonate (**Scheme 3-18**).



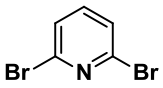
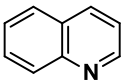
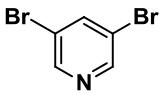
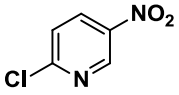
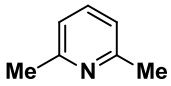
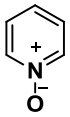
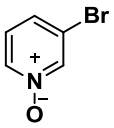
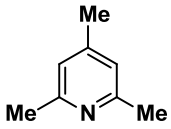
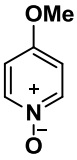
Scheme 3-18 Use of potassium carbonate as an additive

Although this preliminary test of basic additive didn't provide the desired product, the potential influence of basic additives in combination with our knowledge of dual gold catalysis indeed triggered us to further investigate different bases. Thus, a series of pyridines, quinoline, pyridine *N*-oxide were explored (**Table 3.1**).

Table 3.1 Examination of different additives



2.1 3.1

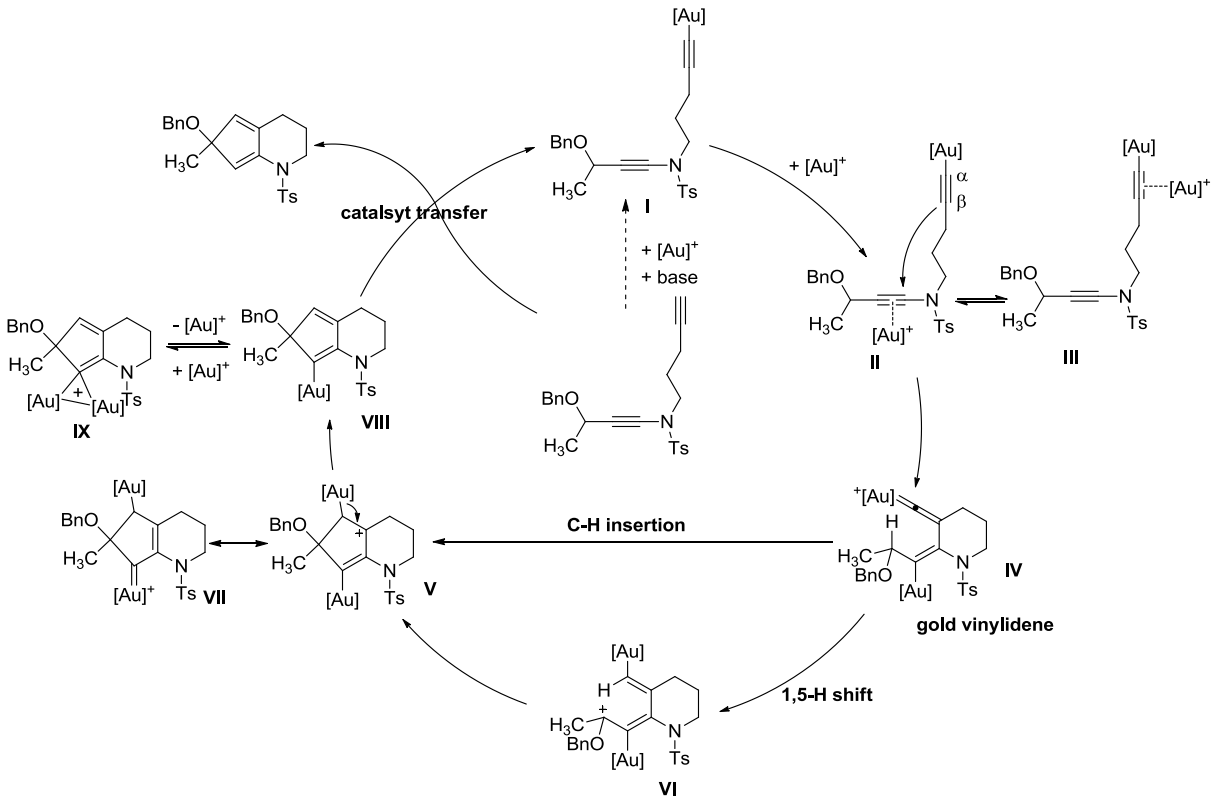
Entry	Additive	Yield [%][b]	Entry	Additive	Yield [%][b]
1		– [c]	6		– [c]
2		38 (43[d])	7		– [c]
3		63 (70[d])	8		– [c]
4		64 (70[d])	9		– [c]
5		– [c]	10		– [c]

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL CD_2Cl_2 (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^1H NMR analysis; [c] complex reaction mixture, NMR yield was not determined; [d] $SPhosAuNTf_2$ was employed.

To our delight, bases such as 3,5-dibromopyridine, lutidine and pyridine all reproduced the reaction in **Scheme 3-17**, giving rise to the same product in modest to good yields using $RuPhosAuNTf_2$ as the catalyst (entries 2, 3, 4). Simple investigation of other Buchwald's biphenyl ligands indicated that $SPhosAuNTf_2$ performed slightly better than $RuPhosAuNTf_2$, providing the new compound in 70 % NMR yield (entry 4).

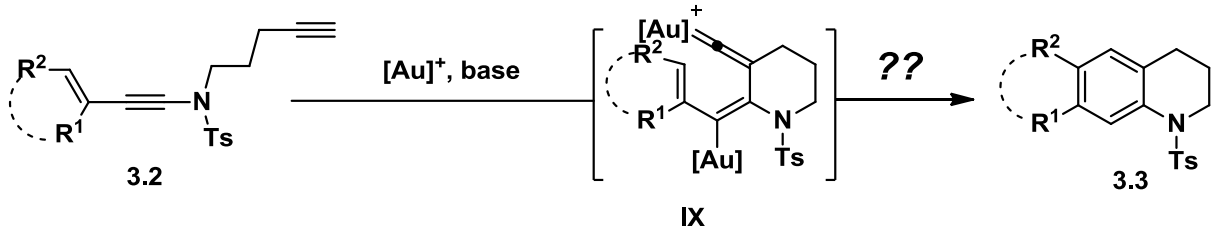
Fully ^1H NMR spectroscopy analysis allowed the characterization of the separated product which was assighned as **3.1**. A tentative mechanism for this transformation was envisioned based on the involvement of dual gold catalysis (**Scheme 3-19**). With the assistance of basic additive, starting material could react with a cationic $[Au]^+$ species to furnish the gold

acetylide **I**. A second gold complex would then activate the C≡C of the ynamide toward the nuleophilic attack at the β-postion of the gold acetylide, affording the gold vinylidene intermediate **IV.** This highly reactive species could allow ring-closure *via* C-H insertion to furnish species **V**. Alternatively, it is also likely that intermediate **V** would be accessed *via* species **VI** following 1,5-hydrogen shift, followed by electrocyclization by the vinyl gold moiety. Subsequently, **V** undergoes deauration to provide vinyl gold(I) intermediate **VIII** which is in equilibrium with digold species **IX**. The desired product would be observed after a catalyst transfer. Alternatively, **VIII** could also undergo a direct protodeauration to give product with the regeneration of $[LAu]^+$.



Scheme 3-19 Tentative mechanism for the formation of compound **3.1**

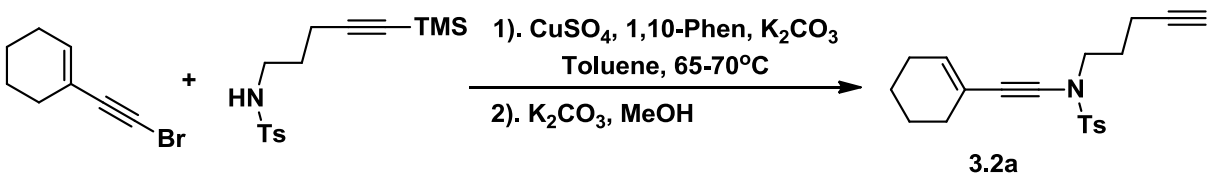
The mechanistic proposal is very similar to the previous proposal by Hashmi an Zhang, however, this mode of reaction has not been reported so far. On the basis of the above mechanistic proposal for the formation of **3.1**, we envisioned that the replacement of the C-H single bond at the *γ*-position of ynamide with a C=C double bond would lead to the formation of intermediate **IX,** which could evolve into aromatic product **3.3** after cyclization. This formal unprecedented [4+2] strategy would represent a facile approach to tetrahydroquinolines (**Scheme 3-20**).



Scheme 3-20 Designed [4+2] strategy for access to tetrahydroquinolines

3. Conditions optimization

To confirm the viability of our synthetic design, model substrate **3.2a** was synthesized using Hsung's C-N coupling methodology (**Scheme 3-21**).



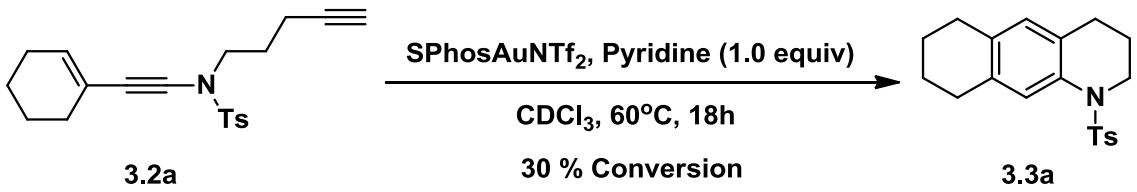
Scheme 3-21 Synthesis of starting material ynamide **3.2a**

It is noteworthy that:

(a) To get **3.2a** with a high purity, the use of TMS-protected sulfonamide is unavoided. Indeed under the coupling conditions, C-C coupling of the alkynyl bromide with the terminal alkyne leads to the formation of a by-product in non-neglegible amount;

(b) To deprotect TMS group at the terminal position of alkyne, basic conditions (catalytic amount of K_2CO_3 in methanol) proved to be much better than the use of TBAF (the following aqueous workup caused hydrolysis of ynamide) due to the sensitivity of ynamide.

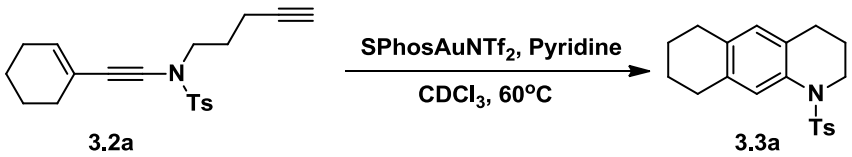
Ene-diyne **3.2a** was subjected to the typical conditions developed in earlier stage of our studies. Gratifyingly, the expected tetrahydroquinoline product was formed although the conversion was low even after a prolonged time (18 hours) (**Scheme 3-22**).



Scheme 3-22

Considering that pyridine possesses the property to coordinate to gold center, thereby deactivating the gold catalyst, we then examined the influence of the quantity of pyridine (**Table 3.2**). We were surprised to find that contrary to the previous observation, pyridine was deleterious to this transformation. The less pyridine employed, the better conversion and yield were. Without pyridine, 1-tosyl-1,2,3,4,6,7,8,9-octahydrobenzo[g]quinolone **3.3a** was obtained in 51 % NMR yield (entry 4, **Table 3.2**).

Table 3.2 Influence of the quantity of pyridine on the reactivity



3.2a 3.3a

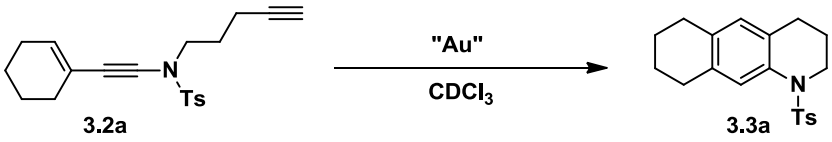
Entry	Base	Amount (equiv)	Time [h]	Conv. [%]	Yield [%][b]
1		0.5	12	50	25
2		1.0	12	32	12
3		1.5	12	29	8
4		none	12	83	51

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^1H NMR analysis with 1,2-dichloroethane as internal standard.

Encouraged by this preliminary observation, we next concentrated on optimizing the reaction conditions. At the outset, various gold catalysts were investigated. As shown in **Table 3.3**, catalysts based on phosphine, phosphite, phosphonite and N-heterocyclic carbene ligands were screened. Among all the examined catalysts, $RuPhosAuNTf_2$ proved to be optimal in catalyzing the cyclization of **3.2a**, furnishing tetrahydroquinoline derivative **3.3a** in 82 % isolated yield (entry 1). Temperature was also found to be a crucial parameter. While the reaction with $RuPhosAuNTf_2$ as the catalyst provided 100 % conversion after 10 hours at 65 °C, no product was observed at room temperature even after 15 hours (entry 1 vs entry 2). It seems that the efficiency of desired transformation was related to steric bulk of the ligand used. For instance, the more sterically hindered $RuPhosAuNTf_2$ was more efficient than $SPhosAuNTf_2$ (entry 1 vs entry 3). Catalysts which are stronger π-acidic species proved to be

deleterious to this reaction (entries 7 and 8). N-heterocyclic carbene-based catalyst was also efficient, furnishing **3.3a** in 76 % yield.

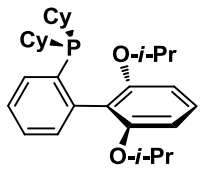
Table 3.3 Examination of influence of catalysts



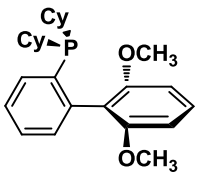
3.2a 3.3a

Entry	Catalysts [5 mol%]	Temp. [°C]	Time [h]	Conv. [%]	Yield [%][b]
1	$RuPhosAuNTf_2$	65	10	100	86 (82[c])
2	$RuPhosAuNTf_2$	RT	15	0	0
3	$SPhosAuNTf_2$	65	15	83	51
4	$XPhosAuNTf_2$	65	15	37	11
5	t-$BuXPhosAuNTf_2$	65	15	29	0
6	$Ph_3PAuNTf_2$	65	15	52	25
7	$(2,5\text{-}t\text{-}Bu_2C_6H_3O)_3PAuNTf_2$	65	15	44	7
8	$GPhosAuNTf_2$	65	15	47	5
9	$IPrAuNTf_2$	65	15	100	76
10	$JohnPhosAuNTf_2$	65	15	51	27

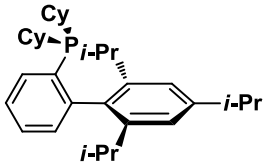
[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^1H NMR analysis with 1,2-dichloroethane as internal standard; [c] isolated yield.



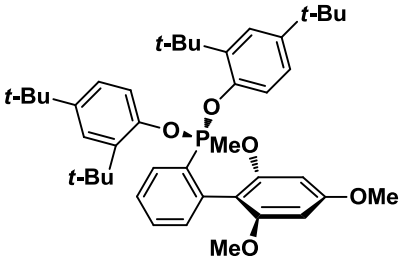
RuPhos



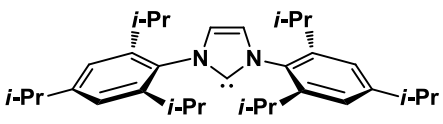
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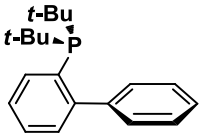
XPhos



GPhos



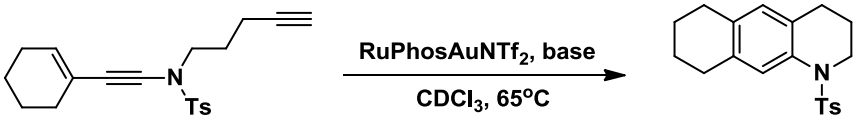
IPr



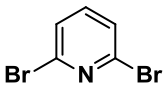
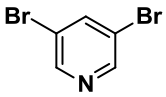
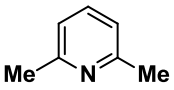
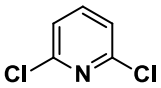
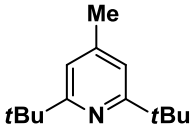
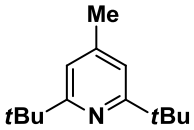
JohnPhos

After having determined the most efficient gold catalyst for this designed [4+2] annulation reaction, we moved to examine the base effect. It is of significant interest considering that base (pyridine or lutidine) was indispensable for the C(sp^3)-H activation while pyridine was detrimental for this [4+2] annulation reaction.

Table 3.4 Base screening



3.2a 3.3a

Entry	Base	Amount	Time [h]	Conv. [%]	Yield [%][b]
1		0.5 equiv	10	100	83
2		0.5 equiv	10	100	91 (86[c])
3		0.5 equiv	10	32	18
4		0.5 equiv	10	100	81
5		0.5 equiv	10	100	85
6		1.0 equiv	10	100	85
7		0.5 equiv	10	58	32
8	none	0	10	100	86

[a] Reaction Conditions: 0.05 mmol of starting material was dissolved in 0.5 mL $CDCl_3$ (0.1 M) in NMR tube followed by addition of gold catalyst (5 mol %); [b] determined by ^1H NMR analysis with 1,2-dichloroethane as internal standard; [c] isolated yield

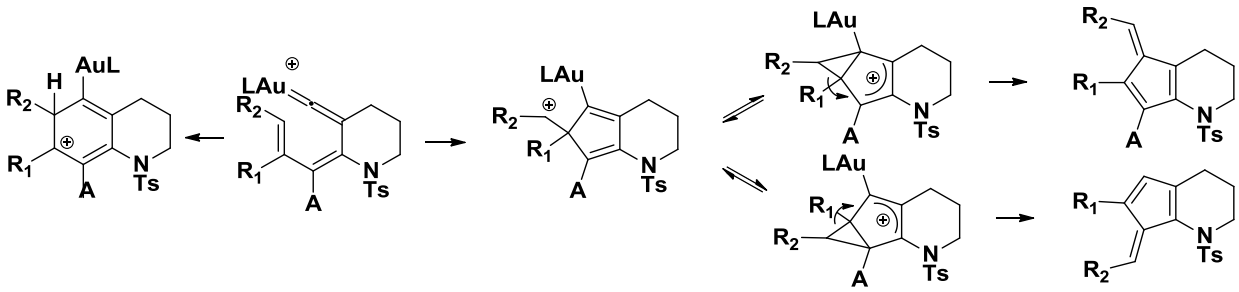
Pyridines possessing different electronic and steric properties were investigated. Pyridines with electron withdrawing substituents, such as 2,6-dibromopyridine, 2,6-dichoropyridine and 3,5-dibromopyridine all provided expected product **3.3a** in good yield (entries 1, 2 and 4. Pyridines containing sterically encumbered substituents which inhibit coordination to metal center, such as 2,6-di-*tert*-butyl-4-methylpyridine also gave rise to **3.3a** in good yield and the amount of base used was found to be no influence for this transformation (entries 5 and 6).

Pyridine and lutidine was indeed detrimental to this model reaction, giving rise to 3.3a in 18 % and 32 % yields respectively (entries 3 and 7).

4. Substrate scope

With the optimal conditions in hand for the model reaction, we next turn our attention to the substrate scope examination. Initially, substrates with different substituent patterns at the *α* and β positions of the alkene moiety were examined.

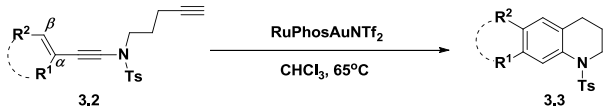
It was found that alkyl, aryl groups were all well tolerated under the catalytic conditions, furnishing the corresponding tetrahydroquinolines in modest to good yields (**Table 3.5**). Notably, an ether functional group was compatible too, giving rise to tetrahydroquinoline in 80 % yield (entry 4). When a substrate unsubstituted at the *α* position was used, transformation proved to be sluggish and a 45 % yield of the desired product was obtained for 60 hours (entry 3). We attributed this lower yield and prolonged reaction time to the cabocation-stabilizing effect of the phenyl group and the absence of stabilizing group at the *α* position, which might change reactive site from β to *α* position (**Scheme 3-23**). This prolonged reaction time led to more side reactions and thus lower reaction yield.

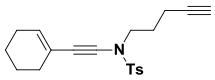
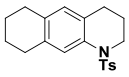
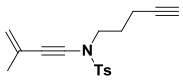
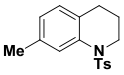
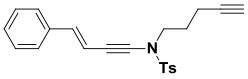
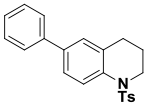
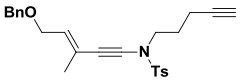
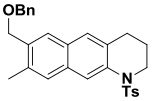
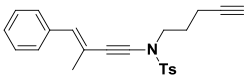
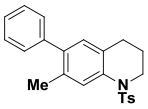
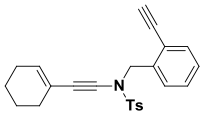
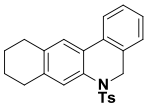
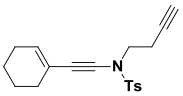
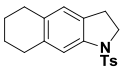
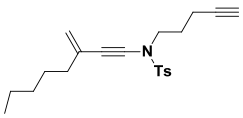
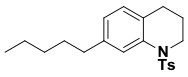
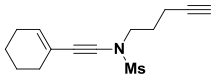
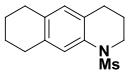
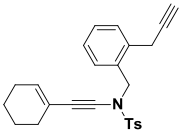
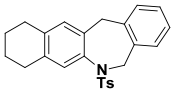


Scheme 3-23 Mechanistic explanation for the lower yield of **3.2e**

Moreover, the N-stabilizing group could be changed into Ms from Ts and a even more reaction yield (83 %)could be obtained (**Table 3.5**, entry 9). Beseids six-membered ring, five and seven-membered ring could also be accessible using the typical conditions, furnishing the corresponding dihydroindole and azepine (**Table 3.5**, entries 7 and 10).

Table 3.5 Substrate scope examination **I** [a]



Entry	Substrate	Time [h]	Product	Yield [%][b]
1		10		82
2		10		88
3		60		45
4		12		80
5		12		72
6		18		62[c] (40[d])
7		24		56[e]
8		12		72
9		12		83
10		24		81

[a] Reaction Conditions: 0.2 mmol of starting material was dissolved in 2 mL $CHCl_3$ (0.1 M) in vial followed by addition of gold catalyst (5 mol %);
[b] isolated yield
[c] 0.5 equiv. of 3,5-dibromopyridine was added;
[d] yield without base present, reaction time was 40 h
[e] reaction was performed at 80 °C in $ClCH_2CH_2Cl$

Meantime, we also explored the reactivity of the double bonds in aromatic and heteroaromatic rings under the optimized reaction conditions. We were pleased to find that

this new type of substrate also underwent the cyclization smoothly, providing the tetrahydrobenzo[*g*]quinolines in moderate to good yields (**Table 3.6**). It was found that aromatic rings with both EWG and EDG substituents underwent the transformations smoothly. In tha case of substrates substituted at the meta position, two regioisomers were observed (**Table 3.6**, entries 3 and 11). When it comes to heteroaromatic rings, such as thiophene and furan, the cyclization process occurred in the presence of basic additives, i.e. 3,5-dibromopyridine and a prolonged reaction time (50 hours) was found to be necessary (**Table 3.6**, entries 14 and 15). Interestingly, in the case of aromatic rings possessing an *ortho*-halide or para-methoxy group, azulenes, which are dark blue color, were also generated along with the desired tetrahydrobenzo[*g*]quinolines (**Table 3.6**, entries 2, 4, 9 and 10).

We attributed the formation of azulene to the cyclization at the *ipso*-carbon, which is elctron rich when an electron-donating group was present in the *ortho*- or *para*-position.

Inspired by this initial discovery, we were deeply intrigued by the wide application of azulene in modern organic electronics. We envisioned that by blocking both ortho positions of the substrate, the cyclization at the ortho position could be inhibited and then azulene could be formed as the major product. To validate this hypothesis, we synthesized two substrates, which were substituted at both ortho-positions (entries 12 and 13) and we were very pleased to find that the corresponding azulenes were indeed formed as the major product. Although azulenes have been known for more than one century, their organic synthesis method was quite limited and generally suffered from long synthetic route, low yield and poor generality. This result demonstrated a facile and expedient approach to azulenes.

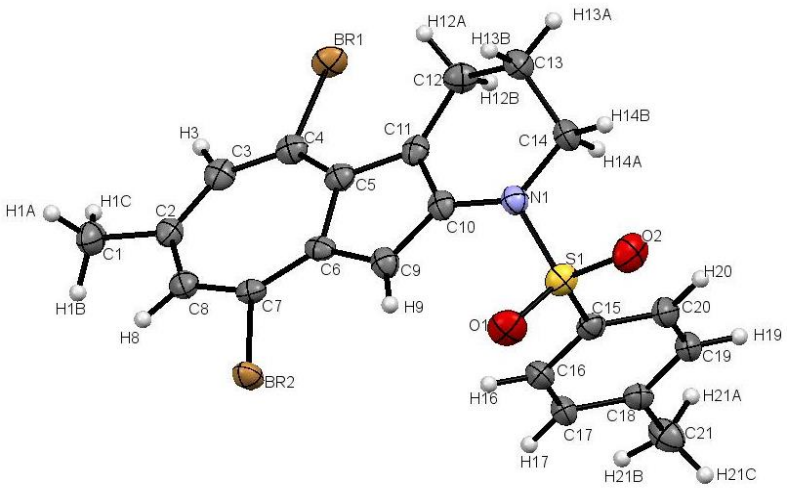
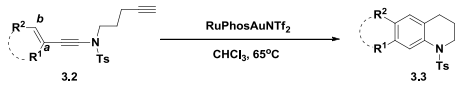
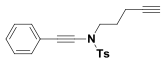
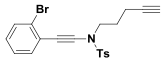
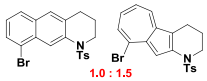
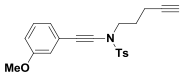
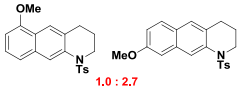
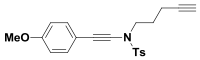
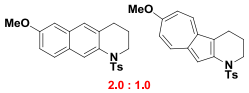
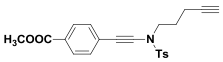
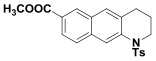
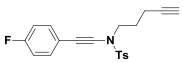
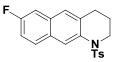
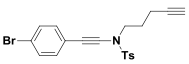
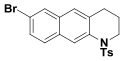
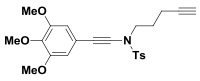
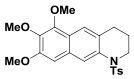
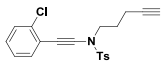
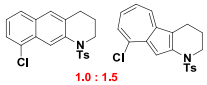
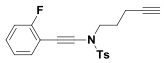
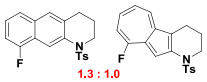
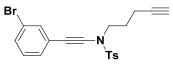
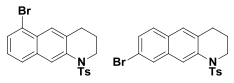
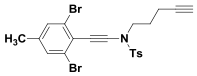
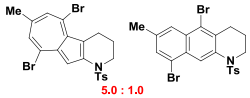
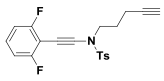
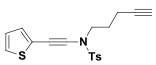
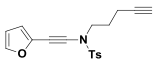


Figure 3-2 X-ray structure of azulene

Table 3.6 Substrate scope examination **II** [a]

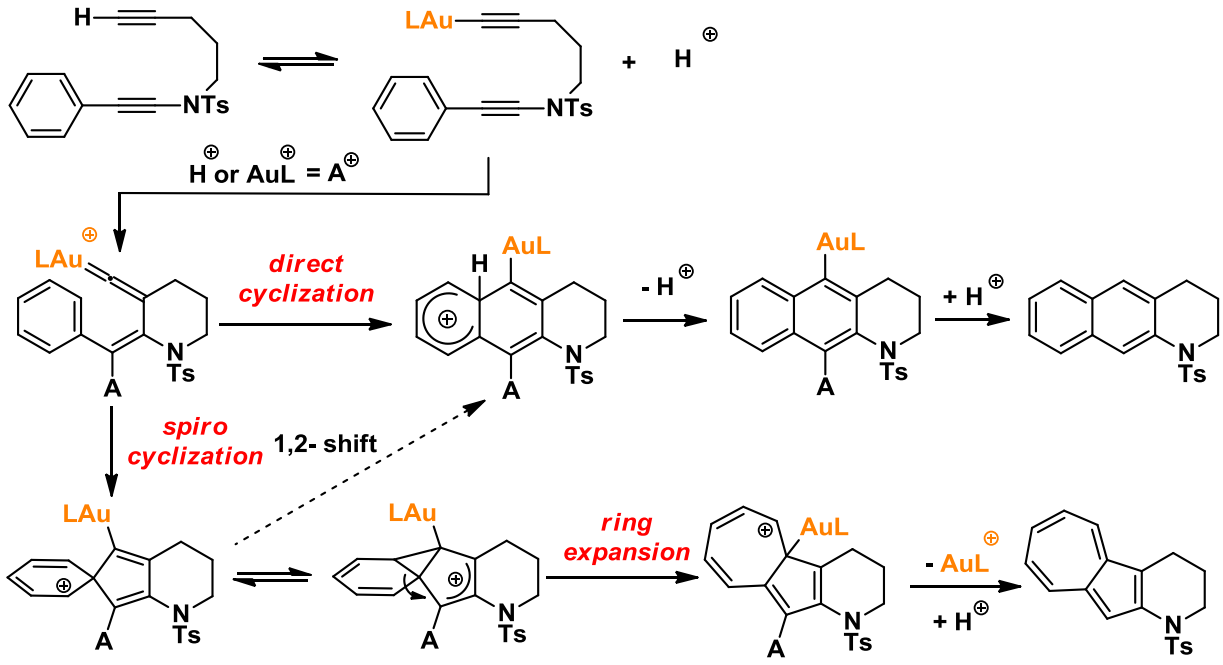


Entry	Substrate	Time [h]	Product	Yield [%][b]
1		18		80
2		18	 1.0 : 1.5	83
3		18	 1.0 : 2.7	81
4		18	 2.0 : 1.0	77
5		18		78
6		18		71
7		18		72
8		4		78
9		36	 1.0 : 1.5	77
10		36	 1.3 : 1.0	62
11		24	 1.0 : 1.7	66
12		50	 5.0 : 1.0	71[c]
13		50		72[c]
14		50		60[c]
15		50		62[c]

[a] Reaction Conditions: 0.2 mmol of starting material was dissolved in 2 mL $CHCl_3$ (0.1 M) in vial followed by addition of gold catalyst (5 mol %);
[b] isolated yield
[c] 0.5 equiv. of 3,5-dibromopyridine was added;

5. Mechanistic Proposal

To explain the formation the cyclization product and the formation of azulenes, we propsed a mechanism as followed. The transformation was initialted by the formation of gold acetylide, which might be accelerated by the presence of basic additives. This is why base, such as 3,5-dibromopyridine is necessary. Afterwards, a 6-exo-dig cyclization gives rise to the six-memberd ring in conjunction of the formation of gold vinylidene as the key intermediate. From gold vinylidene, two diverse reaction pathways are possible. A direct cyclization at the ortho-position of the aromatic ring provided the tetrahydrobenzo[g]quinoline product after deprotonation and protodeauration. Alternatively, a spiro cycliztion process worked, furnishing a spiro compound as the key intermediate. Following the ring expansion of the aromatic ring and deauration process, the formation of azulene was observed.



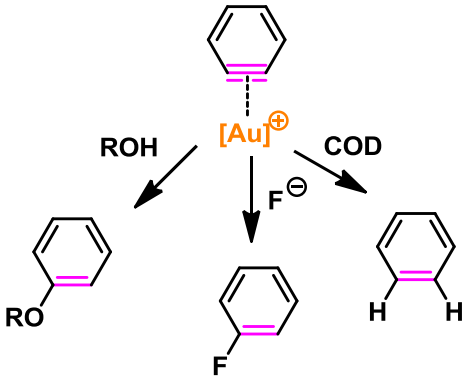
Scheme 3-24 Mechanistic proposal

6. Conclusion and perspective

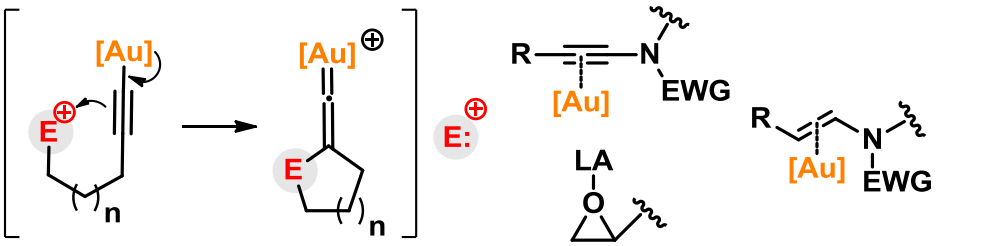
We have demonstrated a facile synthesis of tetrahydroquinolines and 1,2,3,4-tetrahydrobenzo[g]quinolines from ynamides *via* 6-exo-dig cyclization process. The formation of gold vinylidene was proposed as the key intermediate, which is trapped by the double in alkenes or aromatic rings. The demonstrated a novel application of gold vinylidene chemistry. Moreover, a very interesting and facile synthesis of azulene was also discoved. Although azulenes have been known for more than one century, their organic synthesis method was quite limited and generally suffered from long synthetic route, low yield and poor generality. This result demonstrated a facile and expedient approach to azulenes.

Besides this initial discoveries, a number of further application of this novel chemistry could be envisioned, such as:

- ❑ Trapping benzyne-gold intermediate with other reagent (ROH, F-, reduction with cyclooctane…)



- ❑ Attemps to generate vinylidene and trap them with other sources of electrophiles: activated epoxide, enamides....



LA: Lewis acid EWG: electron withdrawing group

- ❑ Selective synthesis of azulenes (colored), use of dibromoazulenes as bricks for e-conductors by linking them with acetylene (LED applications)

Experimental part

Part 1: Gold(I)-Catalyzed Rearrangement of Ynamides via [1,5]-Hydride Shift: An Expedient Approach to Allenamides and Its Equivalen

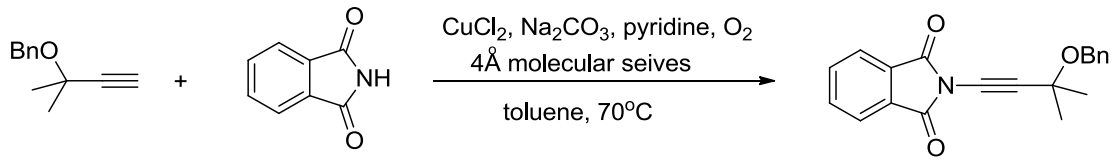
1. General Information

All commercial available reagents were purchased from chemical suppliers (Sigma-Aldrich, Alfa-Aesar, TCI Europe and Fluochem) and were used as delivered without further purification unless otherwise noted. Dried solvents employed in experimental parts were obtained from solvent purification system MB-SPS 800. Reactions carried out under inert atmosphere were performed under an atmosphere of nitrogen and the reaction vessels are vacuumed and then refilled with nitrogen for three times before reagents were added. Flame-dried reaction flask was used if noted. Thin layer chromatography was performed on TLC Silica gel 60 F_{254} plates (25 aluminum sheets, purchased from Merck KGaA), which was visualized by using UV-light (254 nm), aq. $KMnO_4$ solution ($KMnO_4$, 6 g; K_2CO_3, 40 g; 5% aqeous NaOH, 10 mL; H_2O, 600 mL) or *p*-anisaldehyde stain (*p*-anisaldehyde, 12 g; Conc. H_2SO_4, 5 mL; ethanol, 500 mL). Concentration under reduced pressure was carried out by rotary evaporation at 40°C or room temperature in water bath. Flash column chromatrography was carried out on silica gel 60 (0.04-0.063 mm, purchased from VWR chemicals*)* or Al_2O_3 90 neutral (acitivity stage I for chromatography, 0.063-0.200 mm, 70-230 mesh ASTM, purchased from Merck KGaA) using a forced flow of eluents at 1–4 bar pressure and technical-grade solvents were used.

NMR spectra were recorded at room temperature in the given solvent on a Bruker Avance DPX 400 instrument operating at the indicated frequency for the specified nucleus given in mega Hertz (MHz). Chemical shifts δ are given in parts per million (ppm) using tetramethylsilane (TMS) as the standard reference sample for ^{1}H-NMR and ^{13}C-NMR spectra and are calibrated in relation to the deuterated solvent ($CDCl_3$: 7.26 / 77.16 ppm; CD_2Cl_2: 5.32 / 53.80 ppm; d_6-acetone: 2.05 / 29.84 ppm). Coupling constants *J* are given in Hertz (Hz). Signal multiplicities are depicted using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sex = sextuplet, sept = septuplet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, tt = triplet of triplet, dq = doublet of quartet, ddd = doublet of doublet of doublet, ddt = doublet of doublet of triplet, bs = broad singlet. High-resolution mass spectrometry by eletron impact (EI) was performed on a JMC GCmate II mass spectrometer and fragment signals were given in mass per charge number (*m/z*). IUPAC names of compounds described in the experimental section were directly generated using ChemBioDraw.

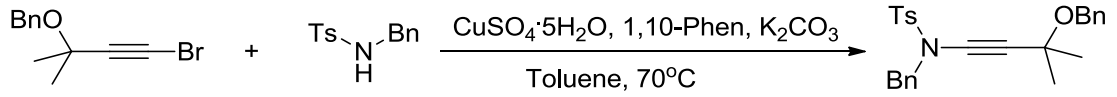
2. General Procedures

General procedure 1: synthesis of phthalimide-derived ynimides[82,83]



In a 500 mL flame dried one-neck round-bottom flask equipped with a magnetic stir bar, $CuCl_2$ (2.0 mmol, 0.27 g), phthalimide (50 mmol, 7.36 g), Na_2CO_3 (20.0 mmol, 2.1 g), and 4Å molecular sieves (6.0 g) were combined together. A solution of pyridine (20.0 mmol, 1.6 mL) in 90 mL dry toluene was added to the reaction flask. Afterwards, the reaction flask was stoppered. Then the flask was evacuated and refilled with oxygen gas for three times. Next, one large balloon filled with oxygen gas was connected to the reaction vessel via a short needle. The flask was then placed in a preheated oil-bath at 70 ºC. The reaction mixture was stirred at this temperature for 2 hours and then a solution of (((2-methylbut-3-yn-2-yl)oxy)methyl)benzene (10.0 mmol, 1.74 g) in 10 mL dry toluene was added to the flask over 4 hours by use of a syringe pump. After the addition of this solution, the reaction mixture was allowed to stir at the same temperature for another 30 hours and then the resulting slurry was cooled to room temperature. The crude reaction mixture was filtered warm through celite and the filtrate was concentrated under reduced pressure. To the resulting residual was added 50 mL Et_2O and the solid which was not dissolved was filtered. The filtrate was concentrated under vacuum again. Then, the resulting reaction mixture was purified by flash chromatography on silica gel to yield the ynimide as dense oil (78 % yield).

General procedure 2: synthesis of sulfonyl-derived ynamides[84]

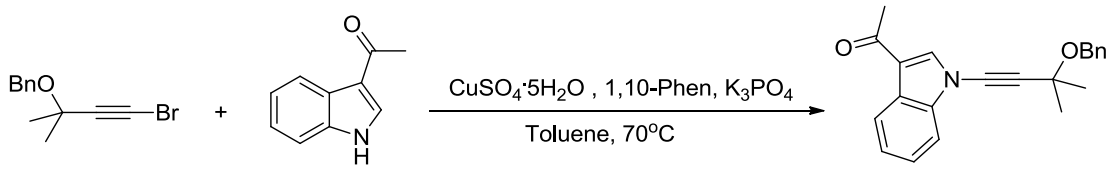


In a flame dried schlenk tube, *N*-benzyltoluenesulfonamide (1.31 g, 5.0 mmol), K_2CO_3 (1.38 g, 10.0 mmol), $CuSO_4{\cdot}5H_2O$ (250 mg, 1.0 mmol), and 1,10-phenanthroline (360.4 mg, 2.0 mmol) was combined together. Afterwards, the schlenk tube was vacuumed and refilled with nitrogen for 3 times and then the alkyne bromide (1.52 g, 6.0 mmol) in 5 mL of toluene was added via a syringe.

[82] J. S. Alford, H. M. L. Davies, *Org. Lett*. **2012**, *14*, 6020-6023.
[83] T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833-835.
[84] Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151-1154.

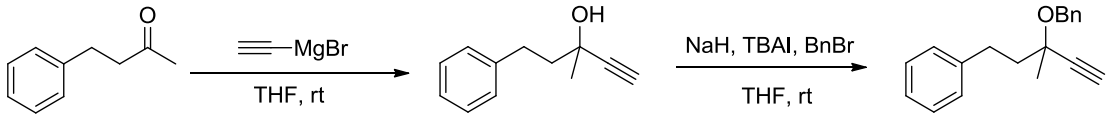
The resulting reaction mixture was heated in an oil bath at 70 °C for 24 h until the complete consumption of the starting material. Then, the reaction mixture was cooled to room temperature and diluted with 100 mL of EtOAc followed by the addition of 50 mL distilled water. The resulting two-phase mixture was separated and the water phase was washed with 50 mL of EtOAc for three times. The collected organic phase was dried over MgSO4 and then was concentrated under reduced pressure. The resulting crude residue was purified using flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine) to give ynamide as clear oil (83 % yield).

General procedure 3: synthesis of N-alkynyl indoles, pyrroles and ureas[3]



In a flame dried schlenk tube, 1-(1*H*-indol-3-yl)ethanone (0.796 g, 5.0 mmol), K_3PO_4 (2.12 g, 10.0 mmol), $CuSO_4{\cdot}5H_2O$ (250 mg, 1.0 mmol), and 1,10-phenanthroline (360.4 mg, 2.0 mmol) was combined together. Afterwards, the schlenk tube was vacuumed and refilled with nitrogen for 3 times and then the alkyne bromide (1.52 g, 6.0 mmol) in 5 mL of toluene was added via a syringe. The resulting reaction mixture was heated in an oil bath at 70 °C for 24 h until the complete consumption of the starting material. Then, the reaction mixture was cooled to room temperature and diluted with 100 mL of EtOAc followed by the addition of 50 mL distilled water. The resulting two-phase mixture was separated and the water phase was washed with 50 mL of EtOAc for three times. The collected organic phase was dried over MgSO4 and then was concentrated under reduced pressure. The resulting crude residue was purified using flash chromatography on silica gel to give ynamide as clear oil (80 % yield).

General procedure 4: synthesis of propargyl benzyl ethers

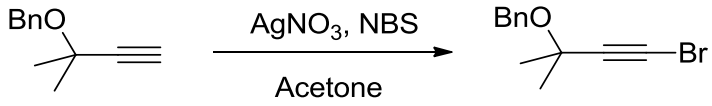


Step 1: To a solution of 4-phenylbutan-2-one (1.482 g, 10.0 mmol) in 40 mL anhydrous THF was added ethynylmagnesium bromide (0.5 M solution in THF, 24 mL, 12 mmol) at 0°C and the resulting reaction mixture was stirred at 0 °C for 10 min and then warmed to room temperature for 2 h. Upon complete consumption of the starting material, the resulting solution was quenched with a saturated solution of NH_4Cl (40 mL). The two-phase mixture was separated and the water phase was extracted with Et_2O (3×100 mL). The collected organic phase was dried over anhydrous $MgSO_4$

and then evaporated under reduced pressure. The resulting residual was used in the next step without any further purification.

Step 2: To a solution of 3-methyl-5-phenylpent-1-yn-3-ol obtained in last step in 40 mL anhydrous THF was added NaH (0.48 g, 12 mmol) portionwise at 0°C. After stirring for 1 hour at 0°C, benzyl bromide (2.05 g, 12 mmol) and tetrabutylammonium iodide (369 mg, 1 mmol) was added to the reaction. The reaction was then stirred at room temperature overnight. After the complete consumption of the alcohol indicated by TLC monitoring, the reaction mixture was quenched with a saturated solution of NH_4Cl (40 mL), extracted with ethyl acetate (3 x 100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel afforded the pure propargyl benzyl ether (85% for 2 steps).

General procedure 5: preparation of alkynyl bromide



To a stirred solution of (((2-methylbut-3-yn-2-yl)oxy)methyl)benzene (1.74 g, 10 mmol) in 30 mL of acetone was added N-bromosuccinimide (1.96 g, 11 mmol) and $AgNO_3$ (170 mg, 1 mmol). The resulting reaction mixture was stirred untill complete consumption of starting material monitored by TLC and was filtered through a celite column. The filtrate was concentrated under reduced pressure. The resulting residue was diluted with saturated K_2CO_3 and extracted with ether (100 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and then concentrated under reduced pressure. Purification by flash column chromatography on silica gel with petroleum ether/ethyl acetate as the eluent provided (((4-bromo-2-methylbut-3-yn-2-yl)oxy)methyl)benzene as colorless oil (98 % yield).

General Procedure 6: Gold catalysis procedure I

To a stirred solution of 0.20 mmol of starting material in chloroform (2 mL) was added $XPhosAu(CH_3CN)SbF_6$ and the solution was stirred at indicated temperature until TLC showed complete consumption of starting material. The reaction mixture was purified by flash chromatography directly without any other workup procedure.

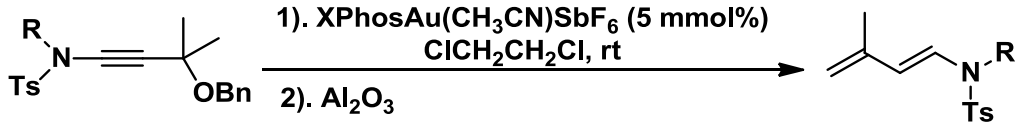
General Procedure 7: Gold catalysis procedure II

To a stirred solution of 0.50 mmol of starting material in 1,2-dichloroethane (2 mL) was added XPhosAu(CH_3CN)SbF_6 and the solution was stirred at ambient temperature until TLC showed complete consumption of starting material. The reaction mixture was purified by flash chromatography on deactivated neutral Al_2O_3 directly without any other workup procedure.

Note 1: *The reaction mixture must not be concentrated after reaction was completed. As soon as starting material was completely consumed, the reaction mixture was submitted to column chromatography.*

Note 2: *Deactivation procedure was as followed: a 500 mL beaker was filled with 200 mL normal neutral Al_2O_3 followed by the slow addition of 10 mL distilled water while stirring vigorously using a glass rod. After addition, the hot Al_2O_3 was transferred into a glass bottle, sealed with a cap and then kept for overnight.*

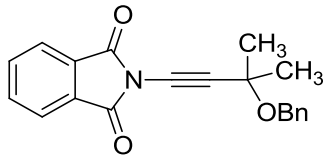
General Procedure 8:



To a stirred solution of 0.50 mmol of starting material in 1,2-dichloroethane (2 mL) was added XPhosAu(CH_3CN)SbF_6 and the solution was stirred at ambient temperature until TLC showed complete consumption of starting material. Afterwards, newly ordered neutral Al_2O_3 was added and the resulting slurry was stirred for 2 hours at room temperature followed by flash chromatography.

3. Preparation of Starting Materials

2-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)isoindoline-1,3-dione



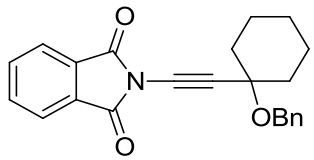
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 65 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.43 – 7.39 (m, 2H), 7.36 – 7.30 (m, 2H), 7.29 – 7.22 (m, 1H), 4.73 (s, 2H), 1.68 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 138.96, 135.16, 131.14, 128.28, 127.88, 127.35, 124.23, 81.66, 71.11, 68.37, 66.81, 29.04.

HRMS (EI): *m/z* 319.1213 (M^+), calculated for $[C_{20}H_{17}NO_3]^+$: 319.1208.

2-((1-(benzyloxy)cyclohexyl)ethynyl)isoindoline-1,3-dione



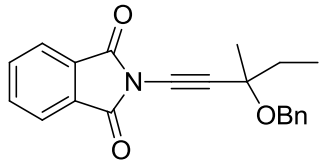
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 56 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.1, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.2, 3.1 Hz, 2H), 7.34 (d, *J* = 7.3 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.17 (t, *J* = 7.1 Hz, 1H), 4.64 (s, 2H), 2.04 (m, 2H), 1.86 – 1.42 (m, 7H), 1.38 – 1.20 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.11, 139.18, 135.08, 131.23, 128.24, 127.88, 127.25, 124.21, 80.97, 74.63, 69.90, 65.83, 37.36, 25.47, 22.87.

HRMS (EI): *m/z* 359.1537 (M^+), calculated for $[C_{23}H_{21}NO_3]^+$: 359.1521.

2-(3-(benzyloxy)-3-methylpent-1-yn-1-yl)isoindoline-1,3-dione



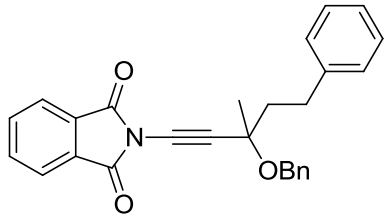
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 68 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.88 (m, 2H), 7.85 – 7.75 (m, 2H), 7.45 – 7.37 (d, *J* = 7.2 Hz, 2H), 7.38 – 7.29 (tt, *J* = 7.3, 1.7 Hz, 2H), 7.25 (ddd, *J* = 7.3, 4.2, 1.3 Hz, 1H), 4.76 (d, *J* = 11.1 Hz, 1H), 4.69 (d, *J* = 11.1 Hz, 1H), 2.02 – 1.83 (m, 2H), 1.62 (s, 3H), 1.14 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 139.16, 135.07, 131.22, 128.22, 127.73, 127.23, 124.21, 80.95, 74.75, 69.30, 66.53, 34.65, 25.99, 8.79.

HRMS (EI): *m/z* 333.1368 (M^+), calculated for $C_{21}H_{19}NO_3$: 333.1365.

2-(3-(benzyloxy)-3-methyl-5-phenylpent-1-yn-1-yl)isoindoline-1,3-dione



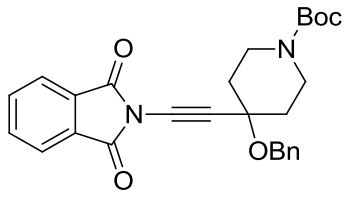
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 51 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.76 – 7.69 (m, 2H), 7.34 (dd, *J* = 7.9, 0.9 Hz, 2H), 7.29 – 7.23 (tt, *J* = 7.3, 1.3 Hz 2H), 7.22 – 7.16 (m, 5H), 7.10 (m, 1H), 4.73 (d, *J* = 11.1 Hz, 1H), 4.64 (d, *J* = 11.1 Hz, 1H), 3.00 – 2.80 (m, 2H), 2.26 – 2.01 (m, 2H), 1.61 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.04, 142.23, 139.04, 135.11, 131.23, 128.54, 128.35, 128.26, 127.70, 127.30, 125.72, 124.26, 80.75, 74.12, 69.74, 66.67, 43.98, 30.93, 26.57.

HRMS (EI): *m/z* 409.1697 (M^+), calculated for $C_{27}H_{23}NO_3$: 409.1678.

Tert-butyl4-(benzyloxy)-4-((1,3-dioxoisoindolin-2-yl)ethynyl)piperidine-1-carboxylate



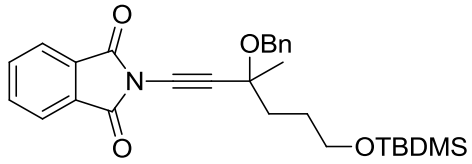
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 44 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.32 (d, *J* = 7.1 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.15 (m, 1H), 4.67 (s, 2H), 3.80 – 3.64 (m, 2H), 3.37 – 3.27 (m, 2H), 2.09 – 1.97 (m, 2H), 1.84 (m, 2H), 1.39 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.90, 154.66, 138.53, 135.24, 131.12, 128.32, 127.88, 127.49, 124.32, 79.59, 79.22, 73.01, 70.98, 66.13, 36.66 (br), 28.44.

HRMS (EI): *m/z* 460.1995 (M^+), calculated for $C_{27}H_{28}N_2O_5$: 460.1998.

2-(3-(benzyloxy)-6-((tert-butyldimethylsilyl)oxy)-3-methylhex-1-yn-1-yl)isoindoline-1,3-dione



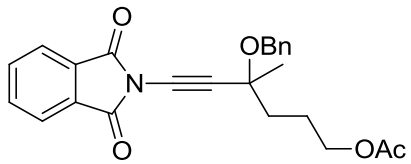
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 40 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.33 (d, *J* = 7.1 Hz, 2H), 7.29 – 7.23 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.13 (m, 1H), 4.69 (d, *J* = 11.1 Hz, 1H), 4.62 (d, *J* = 11.1 Hz, 1H), 3.72 – 3.55 (m, 2H), 1.95 – 1.71 (m, 4H), 1.57 (s, 2H), 0.85 (s, 9H), 0.01 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.01, 139.09, 135.08, 131.19, 128.22, 127.73, 127.24, 124.21, 80.98, 74.08, 69.33, 66.49, 63.26, 38.18, 27.88, 26.56, 26.00, 18.37, -5.24.

HRMS (EI): *m/z* 477.2340 (M^+), calculated for $C_{28}H_{35}NO_4Si$: 477.2335.

4-(benzyloxy)-6-(1,3-dioxoisoindolin-2-yl)-4-methylhex-5-yn-1-yl acetate



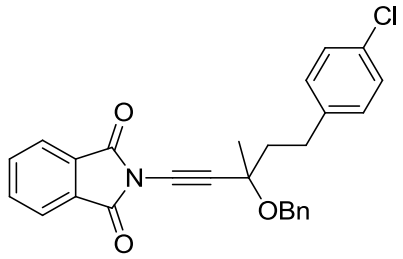
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 38 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.29 – 7.23 (m, 1H), 4.78 (d, *J* = 11.1 Hz, 1H), 4.68 (d, *J* = 11.1 Hz, 1H), 4.17 (t, *J* = 6.1 Hz, 1H), 2.07 (s, 3H), 2.03 – 1.89 (m, 4H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.06, 164.92, 138.82, 135.09, 131.08, 128.19, 127.65, 127.26, 124.18, 80.38, 73.74, 69.62, 66.53, 64.44, 38.45, 26.41, 23.79, 20.91.

HRMS (EI): *m/z* 405.1572 (M^+), calculated for $C_{24}H_{23}NO_5$: 405.1576.

2-(3-(benzyloxy)-5-(4-chlorophenyl)-3-methylpent-1-yn-1-yl)isoindoline-1,3-dione



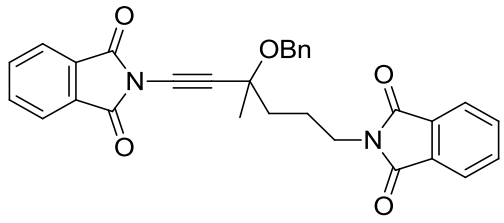
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 62 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.32 (d, *J* = 7.0 Hz, 2H), 7.29 – 7.22 (m, 2H), 7.21 – 7.08 (m, 5H), 4.72 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.1 Hz, 1H), 2.95 – 2.78 (m, 2H), 2.17 – 1.90 (m, 2H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.01, 140.72, 138.95, 135.15, 131.43, 131.21, 129.92, 128.41, 128.27, 127.69, 127.34, 124.28, 80.56, 74.04, 69.91, 66.72, 44.01, 30.37, 26.56.

HRMS (EI): the experiment was carried out twice but no signal for $C_{27}H_{22}ClNO_3$ was found.

2,2'-(3-(benzyloxy)-3-methylhex-1-yne-1,6-diyl)bis(isoindoline-1,3-dione)



This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 33 % (yellowish solid).

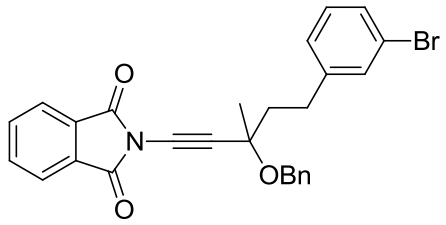
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.62 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.30 (d, *J* = 7.1 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.16 (t, *J*

= 7.2 Hz, 1H), 4.67 (d, *J* = 11.1 Hz, 1H), 4.57 (d, *J* = 11.1 Hz, 1H), 3.72 (t, *J* = 6.9 Hz, 2H), 2.06 – 1.79 (m, 4H), 1.54 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.28, 164.89, 138.86, 135.12, 133.79, 132.15, 131.12, 128.23, 127.74, 127.28, 124.20, 123.12, 80.40, 73.82, 69.75, 66.61, 39.23, 38.06, 26.51, 23.86.

HRMS (EI): *m/z* 477.1465 $[M\text{-}CH_3]^+$, calculated for $[C_{30}H_{24}N_2O_5\text{-}CH_3]^{+:}$ 477.1450.

2-(3-(benzyloxy)-5-(3-bromophenyl)-3-methylpent-1-yn-1-yl)isoindoline-1,3-dione



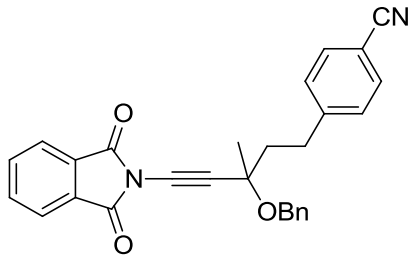
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 70 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.31 (d, *J* = 7.0 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.14 (m, 2H), 7.10 (d, *J* = 7.6 Hz, 1H), 7.05 (t, *J* = 7.7 Hz, 1H), 4.71 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.1 Hz, 1H), 2.93 – 2.81 (m, 2H), 2.16 – 1.96 (m, 2H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 144.64, 138.93, 135.18, 131.60, 131.18, 129.94, 128.87, 128.31, 127.71, 127.38, 127.28, 124.31, 122.40, 80.49, 73.98, 69.94, 66.73, 43.88, 30.68, 26.58.

HRMS (EI): the experiment was carried out twice but no signal for $C_{27}H_{22}BrNO_3$ was found.

4-(3-(benzyloxy)-5-(1,3-dioxoisoindolin-2-yl)-3-methylpent-4-yn-1-yl)benzonitrile



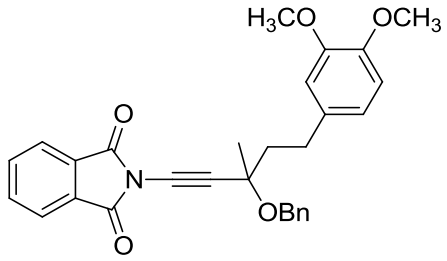
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 59 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.21 (m, 6H), 7.16 (t, *J* = 7.0 Hz, 1H), 4.70 (d, *J* = 11.1 Hz, 1H), 4.58 (d, *J* = 11.1 Hz, 1H), 3.00 – 2.95 (m, 2H), 2.20 – 1.95 (m, 2H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.00, 148.09, 138.80, 135.25, 132.16, 131.15, 129.43, 128.29, 127.69, 127.42, 124.32, 119.12, 109.62, 80.30, 73.98, 70.17, 66.79, 43.68, 31.30, 26.55.

HRMS (EI): *m/z* 434.1636 (M^+), calculated for $C_{28}H_{22}N_2O_3$: 434.1630.

2-(3-(benzyloxy)-5-(3,4-dimethoxyphenyl)-3-methylpent-1-yn-1-yl)isoindoline-1,3-dione



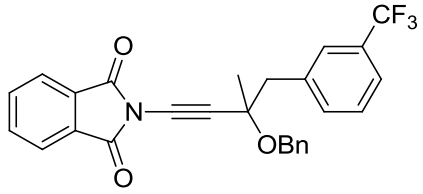
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 45% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.34 (d, *J* = 7.1 Hz, 2H), 7.27 (t, *J* = 7.4 Hz, 2H), 7.18 (m, 1H), 6.79 – 6.65 (m, 3H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.63 (d, *J* = 11.1 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.94 – 2.77 (m, 2H), 2.10 (m, 2H), 1.61 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.03, 148.90, 147.15, 139.02, 135.12, 134.93, 131.21, 128.26, 127.73, 127.32, 124.25, 120.26, 111.99, 111.37, 80.74, 74.14, 69.76, 66.70, 55.95, 55.85, 44.26, 30.55, 26.55.

HRMS (EI): *m/z* 469.1890 (M^+), calculated for $C_{29}H_{27}NO_5$: 469.1889.

2-(3-(benzyloxy)-3-methyl-4-(3-(trifluoromethyl)phenyl)but-1-yn-1-yl)isoindoline-1,3-dione



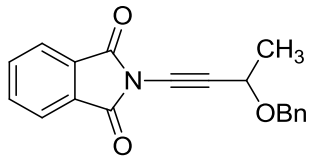
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 28 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.60 (d, *J* = 10.5 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.14 (m, 4H), 4.71 (d, *J* = 11.1 Hz, 1H), 4.61 (d, *J* = 11.2 Hz, 1H), 3.21 (d, *J* = 13.3 Hz, 1H), 3.09 (d, *J* = 13.3 Hz, 1H), 1.54 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.87, 138.72, 137.34, 135.14, 134.54, 131.15, 130.05 (q, *J* = 31.9 Hz), 128.62 (q, *J* = 270.6 Hz), 128.23, 127.86 (q, *J* = 3.7 Hz), 127.55, 127.31, 124.27, 123.52 (q, *J* = 3.6 Hz), 79.82, 74.30, 71.15, 66.74, 47.79, 26.30.

HRMS (EI): *m/z* 463.1399 (M^+), calculated for $C_{27}H_{20}F_3NO_3$: 463.1395.

2-(3-(benzyloxy)but-1-yn-1-yl)isoindoline-1,3-dione



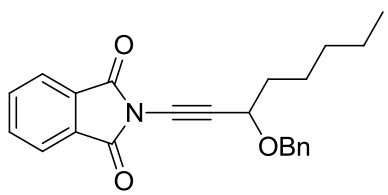
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 66 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.32 (d, *J* = 7.1 Hz, 2H), 7.26 (t, *J* = 7.3 Hz, 2H), 7.22 – 7.16 (m, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.43 (q, *J* = 6.6 Hz, 1H), 1.50 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.09, 137.82, 135.21, 131.11, 128.40, 128.19, 127.71, 124.32, 79.41, 70.60, 68.95, 64.60, 22.05.

HRMS (EI): *m/z* 319.1065 $[M\text{-}CH_3]^+$, calculated for $[C_{20}H_{18}NO_3\text{-}CH_3]^+$: 305.1052.

2-(3-(benzyloxy)oct-1-yn-1-yl)isoindoline-1,3-dione



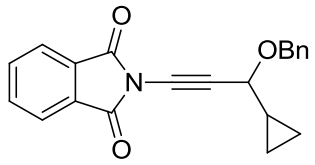
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 42 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.43 – 7.40 (m, 2H), 7.38 – 7.32 (m, 2H), 7.31 – 7.26 (m, 1H), 4.87 (d, *J* = 11.8 Hz, 1H), 4.60 (d, *J* = 11.8 Hz, 1H), 4.38 (t, *J* = 6.6 Hz, 1H), 1.96 – 1.79 (m, 2H), 1.61 – 1.47 (m, 2H), 1.41 – 1.25 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.11, 137.98, 135.12, 131.19, 128.34, 128.13, 127.62, 124.27, 78.87, 70.58, 69.45, 68.88, 35.56, 31.47, 24.98, 22.53, 14.00.

HRMS (EI): *m/z* 361.1686 (M^+), calculated for $C_{23}H_{13}NO_3$: 361.1678.

2-(3-(benzyloxy)-3-cyclopropylprop-1-yn-1-yl)isoindoline-1,3-dione



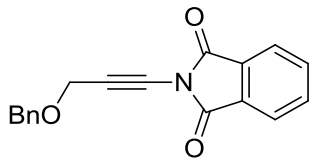
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 22 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.43 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.26 (m, 1H), 4.87 (d, *J* = 11.8 Hz, 1H), 4.64 (d, *J* = 11.8 Hz, 1H), 4.22 (d, *J* = 6.5 Hz, 1H), 1.42 – 1.32 (m, 1H), 0.68 – 0.57 (m, 3H), 0.54 – 0.45 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.27, 138.06, 135.45, 131.32, 128.61, 128.45, 127.92, 124.53, 76.95, 72.24, 70.51, 69.88, 15.21, 3.54, 2.43.

HRMS (EI): *m/z* 331.1205 (M^+), calculated for $C_{21}H_{17}NO_3$: 331.1208.

2-(3-(benzyloxy)prop-1-yn-1-yl)isoindoline-1,3-dione



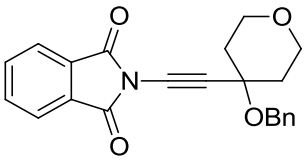
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 54 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.81 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.37 – 7.33 (m, 2H), 7.32 – 7.26 (m, 1H), 4.67 (s, 2H), 4.47 (s, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 137.24, 135.23, 131.01, 128.40, 128.20, 127.84, 124.34, 75.94, 71.47, 69.90, 57.31.

HRMS (EI): *m/z* 291.0890 (M^+), calculated for $C_{18}H_{13}NO_3$: 291.0895.

2-((4-(benzyloxy)tetrahydro-2H-pyran-4-yl)ethynyl)isoindoline-1,3-dione



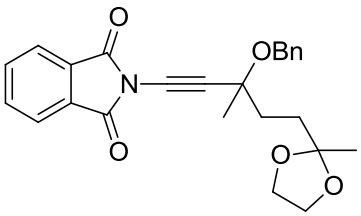
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 29 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.82 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.37 – 7.32 (m, 2H), 7.27 (m, 1H), 4.76 (s, 2H), 3.96 (dt, *J* = 11.7, 4.4 Hz, 2H), 3.77 (ddd, *J* = 11.9, 9.2, 2.8 Hz, 2H), 2.24 – 2.11 (m, 2H), 2.10 – 1.94 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.94, 138.58, 135.19, 131.18, 128.32, 127.90, 127.47, 124.32, 79.51, 72.17, 70.87, 65.87, 64.68, 37.73.

HRMS (EI): *m/z* 361.1322 (M^+), calculated for $C_{22}H_{19}NO_4$: 361.1314.

2-(3-(benzyloxy)-3-methyl-5-(2-methyl-1,3-dioxolan-2-yl)pent-1-yn-1-yl)isoindoline-1,3-dione



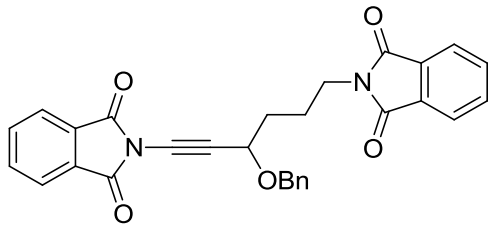
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 22 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.35 – 7.28 (m, 2H), 7.27 – 7.22 (m, 2H), 7.20 – 7.14 (m, 1H), 4.68 (d, *J* = 11.1 Hz, 1H), 4.60 (d, *J* = 11.1 Hz, 1H), 3.95 – 3.84 (m, 4H), 1.98 – 1.86 (m, 4H), 1.55 (s, 3H), 1.30 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.97, 139.07, 135.06, 131.22, 128.19, 127.67, 127.21, 124.20, 109.90, 80.79, 73.95, 69.51, 66.54, 64.60, 36.30, 33.57, 26.55, 23.94.

HRMS (EI): The experiment was carried out twice but no signal for $C_{18}H_{19}NO_4$ was found.

2,2'-(3-(benzyloxy)hex-1-yne-1,6-diyl)bis(isoindoline-1,3-dione)



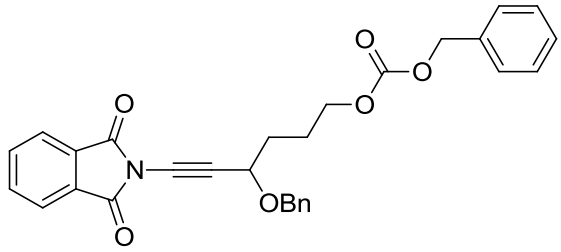
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 36 % (yellowish solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.87 – 7.79 (m, 4H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.42 – 7.38 (m, 2H), 7.36 – 7.31 (m, 2H), 7.30 – 7.25 (m, 1H), 4.85 (d, *J* = 11.7 Hz, 1H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.43 (t, *J* = 5.8 Hz, 1H), 3.80 – 3.70 (m, 2H), 2.01 – 1.88 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.30, 164.97, 137.72, 135.13, 133.80, 132.17, 131.16, 128.36, 128.16, 127.67, 124.29, 123.17, 78.14, 70.68, 69.90, 68.22, 37.63, 32.88, 24.60.

HRMS (EI): *m/z* 478.1525 (M^+), calculated for $C_{29}H_{22}N_2O_5$: 478.1529.

Benzyl (4-(benzyloxy)-6-(1,3-dioxoisoindolin-2-yl)hex-5-yn-1-yl) carbonate



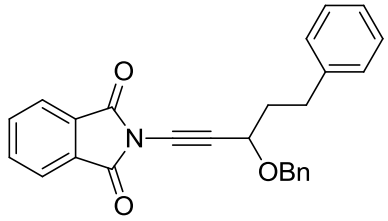
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 26 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.35 – 7.19 (m, 9H), 5.08 (s, 2H), 4.80 (t, *J* = 9.9 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.35 (t, *J* = 5.8 Hz, 1H), 4.16 – 4.12 (m, 2H), 2.00 – 1.76 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.00, 155.14, 137.71, 135.34, 135.17, 131.15, 128.55, 128.43, 128.38, 128.29, 128.12, 127.72, 124.32, 78.12, 70.68, 69.90, 69.49, 68.17, 67.81, 31.89, 24.65.

HRMS (EI): *m/z* 483.1678 (M^+), calculated for $C_{29}H_{25}NO_6$: 483.1682.

2-(3-(benzyloxy)-5-phenylpent-1-yn-1-yl)isoindoline-1,3-dione



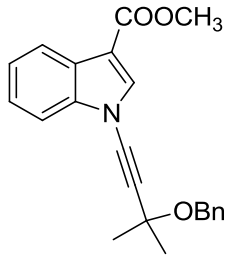
This compound was prepared using general procedure 1 and was purified by flash chromatography on silica gel. Yield: 48 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.37 – 7.32 (m, 2H), 7.31 – 7.25 (m, 2H), 7.25 – 7.16 (m, 3H), 7.15 – 7.07 (m, 3H), 4.81 (d, *J* = 11.6 Hz, 1H), 4.50 (d, *J* = 11.6 Hz, 1H), 4.31 (t, *J* = 6.5 Hz, 1H), 2.91 – 2.72 (m, 2H), 2.24 – 2.01 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.07, 141.38, 137.87, 135.16, 131.18, 128.58, 128.38, 128.18, 127.69, 125.88, 124.31, 78.56, 70.73, 69.83, 68.11, 37.25, 31.47.

HRMS (EI): *m/z* 395.1525 (M^+), calculated for $C_{26}H_{21}NO_3$: 395.1521.

Methyl 1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-1H-indole-3-carboxylate



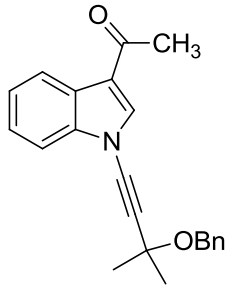
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 68 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 1H), 7.81 (s, 1H), 7.45 – 7.41 (m, 1H), 7.34 – 7.22 (m, 6H), 7.21 – 7.15 (m, 1H), 4.64 (s, 2H), 3.84 (s, 3H), 1.63 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.28, 138.79, 138.43, 134.93, 128.37, 127.62, 127.47, 125.39, 124.55, 123.70, 121.98, 111.29, 110.88, 74.75, 73.97, 71.01, 66.76, 51.36, 29.20.

HRMS (EI): *m/z* 347.1514 (M^+), calculated for $C_{22}H_{21}NO_3$: 347.1521.

1-(1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-1H-indol-3-yl)ethanone



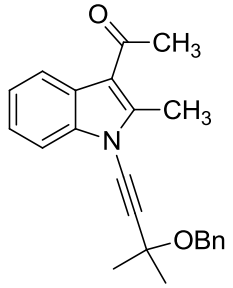
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 62 % (yellowish solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.27 (m, 1H), 7.71 (s, 1H), 7.44 – 7.40 (m, 1H), 7.34 – 7.26 (m, 4H), 7.27 – 7.22 (m, 2H), 7.21 – 7.16 (m, 1H), 4.65 (s, 2H), 2.45 (s, 3H), 1.64 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.77, 138.82, 138.59, 135.23, 128.37, 127.57, 127.47, 125.08, 124.98, 124.21, 122.96, 119.76, 111.05, 74.72, 74.10, 71.01, 66.76, 29.21, 27.68.

HRMS (EI): *m/z* 331.1573 (M^+), calculated for $C_{22}H_{21}NO_2$: 331.1572.

1-(1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-2-methyl-1H-indol-3-yl)ethanone



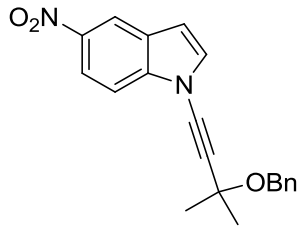
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 44 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 5.8, 3.2 Hz, 1H), 7.40 (dd, *J* = 6.1, 3.1 Hz, 1H), 7.30 (d, *J* = 7.3 Hz, 2H), 7.26 – 7.21 (m, 4H), 7.20 – 7.14 (m, 1H), 4.65 (s, 2H), 2.72 (s, 3H), 2.57 (s, 3H), 1.66 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.25, 145.31, 138.73, 137.22, 128.39, 127.63, 127.51, 125.88, 123.83, 123.68, 121.24, 116.37, 111.06, 78.58, 73.01, 71.23, 66.83, 31.53, 29.31, 13.57.

HRMS (EI): *m/z* 345.1719 (M^+), calculated for $C_{23}H_{23}NO_2$: 345.1729.

1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-5-nitro-1H-indole



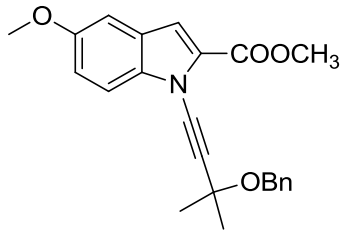
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 50 % (yellow s olid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 – 8.33 (m, 1H), 8.03 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.36 (d, *J* = 3.3 Hz, 1H), 7.33 (d, *J* = 7.4, 2H), 7.28 – 7.24 (m, 2H), 7.18 (m, 1H), 6.59 (dd, *J* = 3.3, 0.9 Hz, 1H), 4.67 (s, 2H), 1.66 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.62, 138.80, 137.06, 134.23, 132.46, 128.36, 127.54, 127.44, 121.34, 117.36, 107.80, 105.60, 74.42, 74.37, 71.04, 66.75, 29.23.

HRMS (EI): *m/z* 334.1321 (M^+), calculated for $C_{20}H_{18}N_2O_3$: 334.1317.

Methyl 1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-5-methoxy-1H-indole-2-carboxylate



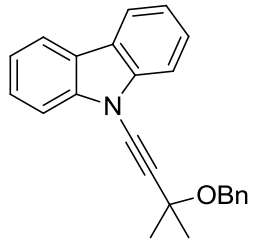
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 48 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.9 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.26 – 7.20 (m, 2H), 7.18 – 7.13 (m, 2H), 7.00 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.96 (d, *J* = 2.3 Hz, 1H), 4.71 (s, 2H), 3.84 (s, 3H), 3.76 (s, 3H), 1.65 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.51, 156.37, 139.24, 135.68, 129.47, 128.28, 127.80, 127.31, 126.38, 117.56, 112.83, 112.62, 103.37, 74.97, 74.75, 71.33, 66.77, 55.76, 51.88, 29.30.

HRMS (EI): *m/z* 377.1627 (M^+), calculated for $C_{23}H_{23}NO_4$: 377.1627.

9-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-9H-carbazole



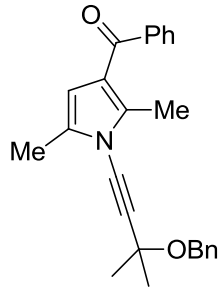
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 29 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.7 Hz, 2H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.59 – 7.55 (m, 2H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.42 – 7.36 (m, 4H), 7.31 (t, *J* = 7.3 Hz, 1H), 4.87 (s, 2H), 1.86 (s, 6H)**.**

^{13}C NMR (101 MHz, $CDCl_3$) δ 140.55, 139.15, 128.33, 127.73, 127.36, 126.71, 123.50, 121.99, 120.36, 111.06, 74.48, 71.49, 66.72, 29.66.

HRMS (EI): *m/z* 339.1619 (M^+), calculated for $C_{24}H_{21}NO$: 339.1623.

(1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-2,5-dimethyl-1H-pyrrol-3-yl)(phenyl)methanone



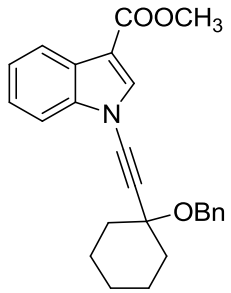
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 32 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.66 (m, 2H), 7.45 – 7.41 (m, 1H), 7.36 (ddt, *J* = 8.2, 6.6, 1.2 Hz, 2H), 7.27 (m, 4H), 7.19 (ddd, *J* = 8.6, 4.7, 2.0 Hz, 1H), 6.02 (d, *J* = 1.0 Hz, 1H), 4.61 (s, 2H), 2.48 (s, 3H), 2.20 (d, *J* = 0.4 Hz, 3H), 1.60 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.72, 140.12, 139.09, 138.79, 131.41, 130.32, 128.98, 128.35, 128.06, 127.58, 127.47, 120.43, 109.77, 77.49, 74.11, 71.12, 66.77, 29.21, 12.65, 12.12.

HRMS (EI): *m/z* 371.1881 (M^+), calculated for $C_{25}H_{25}NO_2$: 371.1885.

Methyl 1-((1-(benzyloxy)cyclohexyl)ethynyl)-1H-indole-3-carboxylate



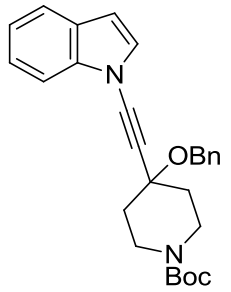
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 52 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 1H), 7.80 (s, 1H), 7.43 (dd, *J* = 6.9, 1.5 Hz, 1H), 7.34 – 7.21 (m, 6H), 7.19 – 7.14 (m, 1H), 4.65 (s, 2H), 3.83 (s, 3H), 2.05 (m, 2H), 1.83 – 1.66 (m, 4H), 1.63 – 1.46 (m, 3H), 1.31 (m, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.31, 139.03, 138.50, 135.03, 128.36, 127.64, 127.42, 125.41, 124.57, 123.70, 122.00, 111.34, 110.80, 76.32, 74.46, 73.20, 65.75, 51.38, 37.53, 25.45, 22.96.

HRMS (EI): *m/z* 387.1830 (M^+), calculated for $C_{25}H_{25}NO_3$: 387.1834.

Tert-butyl 4-((1H-indol-1-yl)ethynyl)-4-(benzyloxy)piperidine-1-carboxylate



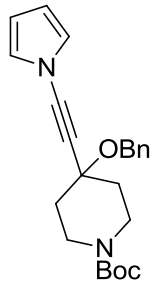
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 38 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.41 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.32 (dd, *J* = 7.9, 1.0 Hz, 2H), 7.29 – 7.12 (m, 5H), 7.10 (d, *J* = 3.4 Hz, 1H), 6.50 (dd, *J* = 3.4, 0.8 Hz, 1H), 4.69 (m, 2H), 3.72 (s, 2H), 3.42 – 3.30 (m, 2H), 2.12 – 1.98 (m, 2H), 1.98 – 1.86 (m, 2H), 1.40 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.71, 138.66, 138.15, 128.77, 128.37, 127.81, 127.67, 127.51, 123.70, 122.11, 121.29, 110.98, 105.62, 79.67, 78.82, 72.93, 70.19, 65.88, 40.64 (br), 36.97 (br), 28.44.

HRMS (EI): *m/z* 330.1740 $[M\text{-Boc}]^+$, calculated for $[C_{27}H_{30}N_2O_3 – Boc]^+$: 330.1732.

Tert-butyl 4-((1H-pyrrol-1-yl)ethynyl)-4-(benzyloxy)piperidine-1-carboxylate



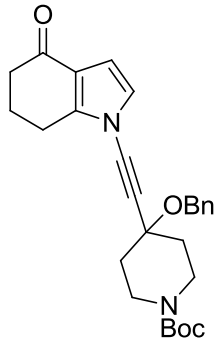
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 47 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.28 (m, 5H), δ 6.88 (d, *J* = 2.1 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 6.23 (d, *J* = 2.1 Hz, 1H), 6.22 (d, *J* = 2.2 Hz, 1H), 4.72 (s, 2H), 3.78 (m, 2H), 3.50 – 3.33 (m, 2H), 2.04 (m, 2H), 1.93 (m, 2H), 1.49 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.71, 138.68, 128.37, 127.64, 127.51, 124.70, 110.60, 80.91, 79.64, 72.56, 65.93, 65.84, 40.58 (br), 36.76 (br), 28.48.

HRMS (EI): *m/z* 280.1580 $[M\text{-}Boc]^+$, calculated for $[C_{23}H_{28}N_2O_3 - Boc]^+$: 280.1576.

Tert-butyl 4-(benzyloxy)-4-((4-oxo-4,5,6,7-tetrahydro-1H-indol-1-yl)ethynyl)piperidine-1-carboxylate



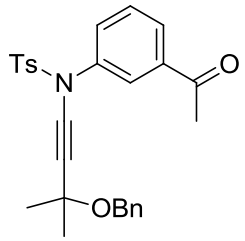
This compound was prepared using general procedure 3 and was purified by flash chromatography on silica gel. Yield: 44 % (yellowish solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.25 (m, 5H), 6.75 (d, *J* = 3.3 Hz, 1H), 6.56 (d, *J* = 3.3 Hz, 1H), 4.69 (s, 2H), 3.74 (br, 2H), 3.52 – 3.31 (m, 2H), 2.80 (t, *J* = 6.2 Hz, 2H), 2.57 – 2.45 (m, 2H), 2.18 (m, 2H), 2.03 (m, 2H), 1.95 (m, 2H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.56, 154.63, 147.01, 138.31, 128.41, 127.64, 127.52, 124.79, 121.62, 107.32, 79.81, 77.43, 72.53, 70.56, 65.98, 40.34, 37.59, 36.63, 28.42, 23.18, 21.82.

HRMS (EI): *m/z* 348.1834 $[M\text{-Boc}]^+$, calculated for $[C_{27}H_{32}N_2O_4 - Boc]^+$: 348.1838.

N-(3-acetylphenyl)-N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-4-methylbenzenesulfonamide



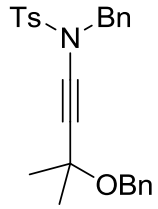
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 60 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.78 (dt, *J* = 6.7, 1.9 Hz 1H), 7.78 – 7.73 (m, 1H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.30 (m, 2H), 7.25 – 7.15 (m, 5H), 7.12 (d, *J* = 8.1 Hz, 2H), 4.47 (s, 2H), 2.44 (s, 3H), 2.29 (s, 3H), 1.48 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.66, 145.37, 139.52, 138.98, 138.08, 132.62, 130.25, 129.60, 129.43, 128.30, 128.23, 127.73, 127.51, 127.34, 125.71, 78.04, 73.57, 71.12, 66.52, 28.93, 26.59, 21.66.

HRMS (EI): *m/z* 461.1659 (M^+), calculated for $C_{27}H_{27}NO_4S$: 461.1661.

N-benzyl-N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-4-methylbenzenesulfonamide

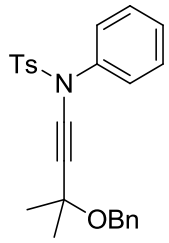


This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 68 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.3 Hz, 2H), 7.25 – 7.13 (m, 10H), 7.09 (d, *J* = 7.2 Hz, 2H), 4.41 (s, 2H), 4.21 (s, 2H), 2.31 (s, 3H), 1.33 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.61, 139.12, 134.56, 134.41, 129.63, 129.01, 128.46, 128.33, 128.18, 127.77, 127.59, 127.20, 78.18, 73.70, 70.98, 66.23, 55.43, 28.85, 21.59. **HRMS (EI)**: *m/z* 433.1710 (M^+), calculated for $C_{26}H_{27}NO_3S$: 433.1712.

N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-4-methyl-N-phenylbenzenesulfonamide



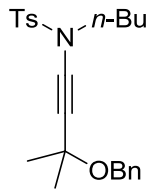
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 59 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.45 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.15 (m, 10H), 7.14 – 7.10 (d, *J* = 8.3 Hz, 2H), 4.47 (s, 2H), 2.31 (s, 3H), 1.47 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.86, 139.16, 138.98, 133.07, 129.37, 129.01, 128.26, 128.21, 128.04, 127.50, 127.22, 126.01, 78.64, 72.84, 71.14, 66.47, 28.96, 21.57.

HRMS (EI): *m/z* 404.1311 $[M\text{-}CH_3]^+$, calculated for $[C_{25}H_{25}NO_3S\text{-}CH_3]^+$: 404.1320.

N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-N-butyl-4-methylbenzenesulfonamide



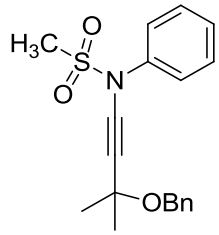
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 60 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.28 – 7.13 (m, 7H), 4.44 (s, 2H), 3.23 (t, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 1.57 – 1.48 (qn, *J* = 7.2 Hz, 2H), 1.45 (s, 6H), 1.26 (sex, *J* = 7.5 Hz, 2H), 0.82 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.48, 139.20, 134.60, 129.62, 128.21, 127.66, 127.56, 127.22, 78.13, 72.80, 71.12, 66.35, 51.02, 29.91, 29.06, 21.55, 19.42, 13.53.

HRMS (EI): *m/z* 384.1641 $[M\text{-}CH3]^+$, calculated for $[C_{23}H_{29}NO_3S]^+$: 384.1633.

N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-N-phenylmethanesulfonamide



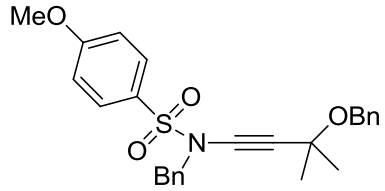
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 52 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.37 (m, 2H), 7.36 – 7.22 (m, 7H), 7.17 (tt, *J* = 7.5, 1.5 Hz, 1H), 4.59 (s, 2H), 2.93 (s, 3H), 1.52 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 139.26, 138.68, 129.42, 128.28, 128.17, 127.46, 127.28, 125.28, 77.78, 73.49, 71.19, 66.62, 36.52, 29.03.

HRMS (EI): *m/z* 328.0996 $[M\text{-}CH_3]^+$, calculated for $[C_{19}H_{21}NO_3S\text{-}CH_3]^+$: 328.1007.

N-benzyl-N-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-4-methoxybenzenesulfonamide



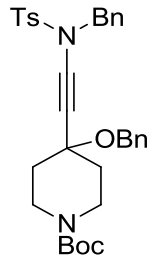
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 44 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 9.0 Hz, 2H), 7.38 – 7.21 (m, 10H), 6.93 (d, *J* = 9.0 Hz, 2H), 4.53 (s, 2H), 4.35 (s, 2H), 3.83 (s, 3H), 1.46 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 163.69, 139.16, 134.48, 129.97, 129.02, 128.49, 128.34, 128.21, 127.59, 127.23, 114.21, 78.39, 73.69, 71.02, 66.23, 55.67, 55.40, 28.89.

HRMS (EI): *m/z* 449.1656 (M^+), calculated for $C_{26}H_{27}NO_4S$: 449.1661.

Tert-butyl 4-((N-benzyl-4-methylphenylsulfonamido)ethynyl)-4-(benzyloxy)piperidine-1-carboxylate



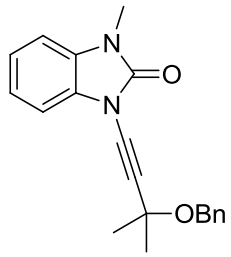
This compound was prepared using general procedure 2 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 44 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.39 – 7.25 (m, 10H), 7.23 (d, *J* = 7.9 Hz, 2H), 4.53 (s, 2H), 4.37 (s, 2H), 3.69 (d, *J* = 10.1 Hz, 2H), 2.97 (t, *J* = 10.2 Hz, 1H), 2.42 (s, 3H), 1.82 – 1.74 (m, 2H), 1.72 – 1.62 (m, 2H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.61, 144.88, 138.75, 134.46, 134.24, 129.81, 128.98, 128.58, 128.52, 128.25, 127.70, 127.60, 127.37, 80.80, 79.50, 77.39, 73.02, 71.27, 65.50, 55.30, 40.64, 36.68, 28.46, 21.62.

HRMS (EI): *m/z* 574.2511 (M^+), calculated for $C_{33}H_{38}N_2O_5$: 574.2501.

1-(3-(benzyloxy)-3-methylbut-1-yn-1-yl)-3-methyl-1H-benzo[d]imidazol-2(3H)-one



This compound was prepared using general procedure 3 and was purified by flash chromatography on Et_3N-deactivated silica gel (eluent contains 5 % triethylamine). Yield: 41 % (white solid).

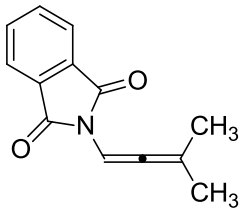
^{1}H NMR (400 MHz, Acetone) δ 7.25 (d, *J* = 7.3 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 2H), 7.09 (t, *J* = 7.3 Hz, 1H), 7.05 – 6.95 (m, 4H), 4.60 (s, 2H), 3.23 (s, 3H), 1.52 (s, 6H).

^{13}C NMR (101 MHz, Acetone) δ 153.53, 140.36, 130.97, 128.95, 128.92, 128.41, 127.96, 124.36, 122.80, 109.97, 109.21, 77.74, 72.31, 71.77, 67.11, 29.56, 27.75.

HRMS (EI): *m/z* 320.1531 (M^+), calculated for $C_{20}H_{20}N_2O_2$: 320.1525.

4. Catalysis and Products

2-(3-methylbuta-1,2-dien-1-yl)isoindoline-1,3-dione



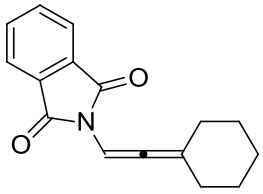
This compound was obtained following general procedure 6 at room temperature and was purified using flash column chromatography on silica gel. Reaction time: 2 h. Yield : 93% of white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.54 – 6.49 (sept, *J* = 2.6 Hz, 1H), 1.86 (d, *J* = 2.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.22, 166.11, 134.04, 132.12, 123.21, 106.12, 85.57, 21.22.

HRMS (EI): *m/z* 213.0784 (M^+), calculated for $C_{13}H_{11}NO_2$: 213.0790.

2-(2-cyclohexylidenevinyl)isoindoline-1,3-dione



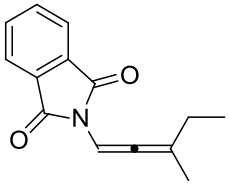
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 2 h. Yield : 94% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.62 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.52 – 6.39 (m, 1H), 2.29 – 2.20 (m, 2H), 2.19 – 2.09 (m, 2H), 1.71 – 1.48 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.91, 166.12, 134.00, 132.17, 123.18, 112.87, 85.39, 32.19, 26.91, 25.96.

HRMS (EI): *m/z* 253.1113 (M^+), calculated for $C_{16}H_{15}NO_2$: 253.1103.

2-(3-methylpenta-1,2-dienyl)isoindoline-1,3-dione



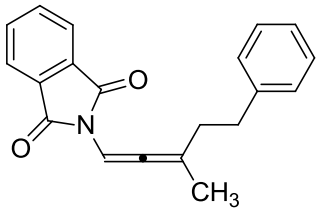
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 94% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.68 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.61 (q, *J* = 2.7 Hz, 1H), 2.10 (m, 2H), 1.84 (d, *J* = 2.7 Hz, 2H), 1.07 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.24 , 166.09 , 134.02 , 132.14 , 123.18 , 112.15 , 87.43 , 27.76 , 19.80 , 11.84 .

HRMS (EI): *m/z* 227.0941 (M^+), calculated for $C_{14}H_{13}NO_2$: 227.0946.

2-(3-methyl-5-phenylpenta-1,2-dien-1-yl)isoindoline-1,3-dione



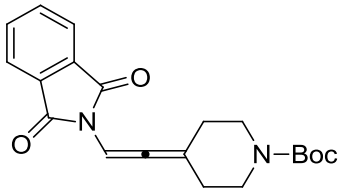
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 97% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.60 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.21 – 7.07 (m, 4H), 7.05 – 6.93 (m, 1H), 6.53 – 6.50 (sex, *J* = 2.6 Hz, 1H), 2.83 – 2.68 (m, 2H), 2.42 – 2.23 (m, 2H), 1.81 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.90, 166.04, 141.84, 134.08, 132.16, 128.40, 128.23, 125.72, 123.24, 110.07, 87.59, 36.21, 33.60, 20.14.

HRMS (EI): *m/z* 303.1266 (M^+), calculated for $C_{20}H_{17}NO_2$: 303.1259.

Tert-butyl 4-(2-(1,3-dioxoisoindolin-2-yl)vinylidene)piperidine-1-carboxylate



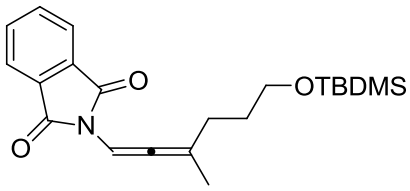
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 8 h. Yield : 95% (yellowish solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.63 (s, 1H), 3.66 (dd, *J* = 11.8, 6.0 Hz, 2H), 3.44 (m, 2H), 2.37 – 2.22 (m, 4H), 1.46 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.72, 165.88, 154.67, 134.13, 132.08, 123.26, 109.07, 86.67, 79.64, 44.28 (br), 31.50, 28.42.

HRMS (EI): *m/z* 354.1567 (M^+), calculated for $C_{20}H_{22}N_2O_4$: 354.1580.

2-(6-((tert-butyldimethylsilyl)oxy)-3-methylhexa-1,2-dien-1-yl)isoindoline-1,3-dione



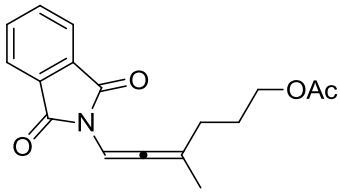
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 92% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.61 (sex, *J* = 2.6 Hz, 1H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.16 (m, 2H), 1.87 (d, *J* = 2.6 Hz, 3H), 1.78 – 1.71 (m, 2H), 0.87 (s, 9H), 0.03 (d, *J* = 1.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.46, 166.08, 134.04, 132.22, 123.23, 110.41, 87.21, 62.67, 31.02, 30.50, 25.96, 20.09, 18.34, -5.31, -5.33.

HRMS (EI): *m/z* 371.1915 (M^+), calculated for $C_{21}H_{29}NO_3Si$: 371.1917.

6-(1,3-dioxoisoindolin-2-yl)-4-methylhexa-4,5-dien-1-yl acetate



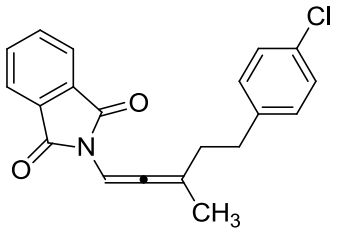
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 98% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 5.4, 2.9 Hz, 2H), 7.63 (dd, *J* = 5.3, 3.0 Hz, 2H), 6.57 (sex, *J* = 2.6 Hz, 1H), 4.03 (t, *J* = 6.6 Hz, 2H), 2.15 – 2.04 (m, 2H), 1.95 (s, 3H), 1.86 – 1.74 (m, 5H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.35, 171.04, 165.99, 134.10, 132.08, 123.24, 109.63, 87.62, 63.94, 30.90, 26.36, 20.91, 20.05.

HRMS (EI): *m/z* 299.1161 (M^+), calculated for $C_{17}H_{17}NO_4$: 299.1158.

2-(5-(4-chlorophenyl)-3-methylpenta-1,2-dien-1-yl)isoindoline-1,3-dione



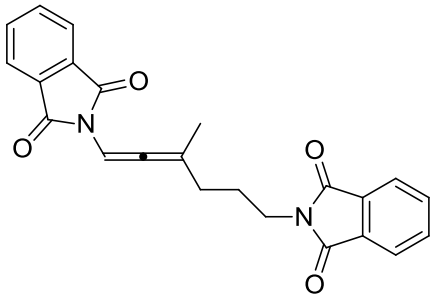
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 97% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.18 – 7.08 (m, 4H), 6.62 – 6.57 (sex, *J* = 2.6 Hz, 1H), 2.89 – 2.72 (m, 2H), 2.50 – 2.29 (m, 2H), 1.88 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.99, 165.99, 140.19, 134.12, 132.08, 131.41, 129.75, 128.26, 123.26, 109.73, 87.75, 35.82, 32.83, 20.11.

HRMS (EI): *m/z* 337.0864 (M^+), calculated for $C_{20}H_{16}ClNO_2$: 337.0870.

2,2'-(3-methylhexa-1,2-diene-1,6-diyl)bis(isoindoline-1,3-dione)



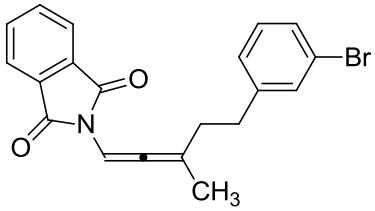
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 93% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.80 (m, 4H), 7.72 – 7.64 (m, 4H), 6.66 (sex, *J* = 2.7 Hz, 1H), 3.85 – 3.62 (m, 2H), 2.32 – 2.03 (m, 2H), 1.92 (qn, *J* = 7.4 Hz, 2H), 1.88 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.22, 168.29, 165.98, 134.00, 133.76, 132.17, 123.22, 123.11, 109.56, 87.79, 37.60, 31.84, 26.25, 20.06.

HRMS (EI): *m/z* 386.1276 (M^+), calculated for $C_{23}H_{18}N_2O_4$: 386.1267.

2-(5-(3-bromophenyl)-3-methylpenta-1,2-dien-1-yl)isoindoline-1,3-dione



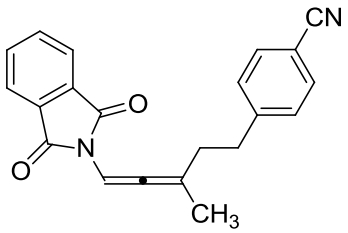
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 95% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.34 (s, 1H), 7.21 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.17 – 7.04 (m, 2H), 6.64 – 6.59 (sex, *J* = 2.7 Hz, 1H), 2.88 – 2.75 (m, 2H), 2.48 – 2.31 (m, 2H), 1.89 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.92, 165.98, 144.17, 134.09, 132.13, 131.47, 129.76, 128.82, 127.07, 123.27, 122.29, 109.69, 87.81, 35.75, 33.16, 20.13.

HRMS (EI): *m/z* 381.0361 (M^+), calculated for $C_{20}H_{16}BrNO_2$: 381.0364.

4-(5-(1,3-dioxoisoindolin-2-yl)-3-methylpenta-3,4-dien-1-yl)benzonitrile



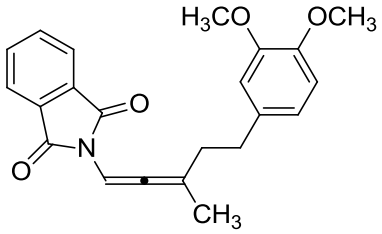
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 12 h. Yield : 97% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.39 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.50 (sex, *J* = 2.7 Hz, 1H), 2.90 – 2.76 (m, 2H), 2.42 – 2.29 (m, 2H), 1.80 (d, *J* = 2.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.02, 165.87, 147.42, 134.25, 131.97, 129.21, 123.26, 118.89, 109.59, 109.36, 88.02, 35.17, 33.51, 20.07.

HRMS (EI): *m/z* 328.1214 (M^+), calculated for $C_{21}H_{16}N_2O_2$: 328.1212.

2-(5-(3,4-dimethoxyphenyl)-3-methylpenta-1,2-dien-1-yl)isoindoline-1,3-dione



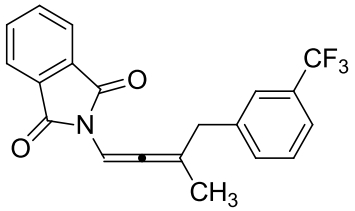
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 97% (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.75 – 6.69 (m, 3H), 6.61 (sex, *J* = 2.6 Hz, 1H), 3.85 (s, 3H), 3.76 (s, 3H), 2.83 – 2.72 (m, 2H), 2.46 – 2.34 (m, 2H), 1.89 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.91, 166.01, 148.72, 147.10, 134.46, 134.06, 132.12, 123.21, 120.12, 111.83, 111.12, 110.07, 87.56, 55.81, 55.78, 36.27, 33.18, 20.13.

HRMS (EI): *m/z* 363.1466 (M^+), calculated for $C_{22}H_{21}NO_4$: 363.1471.

2-(3-methyl-4-(3-(trifluoromethyl)phenyl)buta-1,2-dien-1-yl)isoindoline-1,3-dione



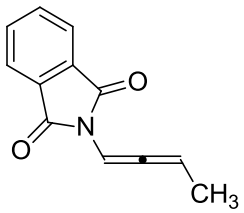
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 98% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.57 (s, 1H), 7.51 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 1H), 6.67 – 6.62 (sex, *J* = 2.6 Hz, 1H), 3.52 (d, *J* = 2.2 Hz, 2H), 1.83 (d, *J* = 2.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.73, 165.85, 139.55, 134.13, 132.52, 132.08, 130.55 (q, *J* = 31.9 Hz), 128.67, 126.02 (q, *J* = 3.7 Hz), 124.16 (q, *J* = 270.6 Hz), 123.30, 123.25 (q, *J* = 3.7 Hz), 108.94, 87.31, 41.47, 19.31.

HRMS (EI): *m/z* 357.0975 (M^+), calculated for $C_{20}H_{14}F_3NO_2$: 357.0977.

2-(buta-1,2-dien-1-yl)isoindoline-1,3-dione



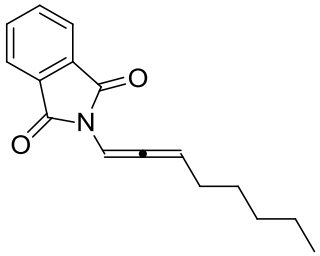
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on silica gel. Reaction time: 1 h. Yield : 86% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.60 (dq, *J* = 5.9, 2.9 Hz, 1H), 5.78 – 5.69 (m, 1H), 1.78 (dd, *J* = 7.2, 2.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.65, 165.88, 134.15, 132.05, 123.33, 96.36, 87.41, 15.18.

HRMS (EI): *m/z* 199.0638 (M^+), calculated for $[C_{12}H_9NO_2]^+$: 199.0633.

2-(octa-1,2-dienyl)isoindoline-1,3-dione



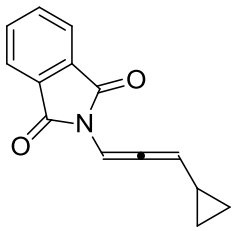
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 1 h. Yield : 78% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.74 – 6.70 (dt, *J* = 6.2, 2.8 Hz, 1H), 5.84 (q, *J* = 6.6 Hz, 1H), 2.18 (ddd, *J* = 14.8, 6.9, 2.9 Hz, 2H), 1.52 (dd, *J* = 14.9, 7.4 Hz, 2H), 1.40 – 1.28 (m, 4H), 0.93 – 0.86 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.70, 165.89, 134.12, 132.10, 123.33, 101.64, 88.02, 31.35, 29.52, 28.16, 22.44, 14.01.

HRMS (EI): *m/z* 255.1262 (M^+), calculated for $C_{16}H_{17}NO_2$: 255.1259.

2-(3-cyclopropylpropa-1,2-dienyl)isoindoline-1,3-dione



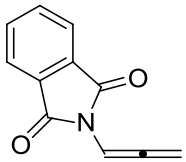
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 1 h. Yield : 60% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.78 (d, *J* = 6.2 Hz, 1H), 5.71 (dd, *J* = 7.5, 6.4 Hz, 1H), 1.46 – 1.36 (m, 1H), 0.80 (dd, *J* = 8.1, 2.4 Hz, 2H), 0.60 – 0.56 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 197.82, 165.83, 134.17, 132.08, 123.36, 105.63, 89.14, 10.10, 7.14, 6.90.

HRMS (EI): *m/z* 255.0792 (M^+), calculated for $C_{14}H_{11}NO_2$: 255.0790.

2-(propa-1,2-dienyl)isoindoline-1,3-dione



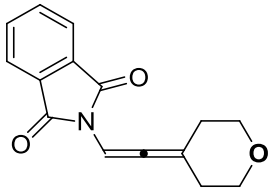
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on silica gel. Reaction time: 4 h. Yield : 35% (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.66 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.75 (t, *J* = 6.7 Hz, 1H), 5.41 (d, *J* = 6.7 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 204.45, 165.72, 134.37, 132.06, 123.56, 88.33, 85.51.

HRMS (EI): *m/z* 185.0475 (M^+), calculated for $C_{11}H_7NO_2$: 185.0477.

2-(2-(2H-pyran-4(3H,5H,6H)-ylidene)vinyl)isoindoline-1,3-dione



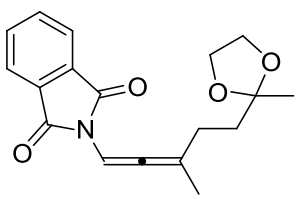
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 5 h. Yield : 94% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.4, 3.0 Hz, 2H), 6.61 – 6.56 (m, 1H), 3.81 – 3.70 (m, 4H), 2.37 – 2.25 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.39, 165.94, 134.15, 132.07, 123.28, 108.31, 86.66, 68.09, 32.31.

HRMS (EI): *m/z* 255.0904 (M^+), calculated for $C_{15}H_{13}NO_3$: 255.0895.

2-(3-methyl-5-(2-methyl-1,3-dioxolan-2-yl)penta-1,2-dienyl)isoindoline-1,3-dione



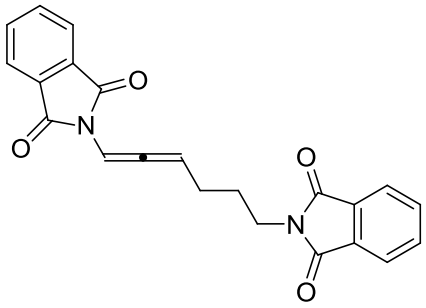
This compound was obtained following general procedure 6 at room temperature and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 93% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.3, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.0 Hz, 2H), 6.63 (m, 1H), 4.00 – 3.89 (m, 4H), 2.30 – 2.10 (m, 2H), 1.97 – 1.79 (m, 5H), 1.34 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.17, 165.98, 134.03, 132.12, 123.20, 110.36, 109.69, 87.50, 64.63, 36.65, 29.06, 23.84, 20.18.

HRMS (EI): *m/z* 313.1295 (M^+), calculated for $C_{18}H_{19}NO_4$: 313.1314.

2,2'-(hexa-1,2-diene-1,6-diyl)diisoindoline-1,3-dione



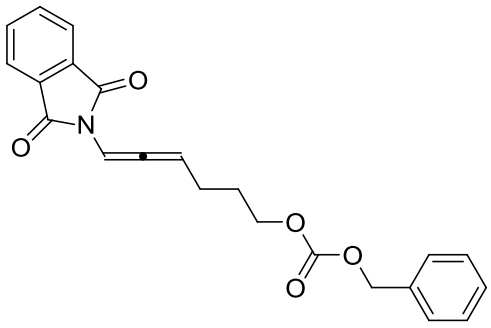
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on silica gel. Reaction time: 2 h. Yield : 81% (yellowish solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.73 (m, 4H), 7.69 – 7.61 (m, 4H), 6.71 (dt, *J* = 6.1, 3.0 Hz, 1H), 5.82 (q, *J* = 6.4 Hz, 1H), 3.74 – 3.69 (m, 2H), 2.20 (m, 2H), 1.91 – 1.82 (qn, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.78, 168.33, 165.77, 134.14, 133.82, 132.17, 132.08, 123.36, 123.16, 100.39, 88.87, 37.47, 27.20, 26.77.

HRMS (EI): *m/z* 372.1108 (M^+), calculated for $C_{22}H_{16}N_2O_4$: 372.1110.

Benzyl 6-(1,3-dioxoisoindolin-2-yl)hexa-4,5-dienyl carbonate



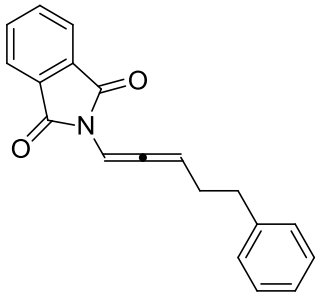
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on silica gel. Reaction time: 1.5 h. Yield : 82% (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.42 – 7.30 (m, 5H), 6.77 (dt, *J* = 6.1, 3.0 Hz, 1H), 5.86 (q, *J* = 6.4 Hz, 1H), 5.14 (s, 2H), 4.25 (t, *J* = 6.5 Hz, 2H), 2.38 – 2.19 (m, 2H), 1.93 (qn, *J* = 6.8 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.86, 165.76, 155.15, 135.31, 134.21, 132.01, 128.55, 128.45, 128.28, 123.39, 100.33, 88.82, 69.48, 67.42, 27.34, 25.61.

HRMS (EI): *m/z* 377.1265 (M^+), calculated for $C_{22}H_{19}NO_5$: 377.1263.

2-(5-phenylpenta-1,2-dienyl)isoindoline-1,3-dione



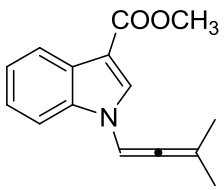
This compound was obtained following general procedure 6 at 60 °C and was purified using column chromatography on silica gel. Reaction time: 1 h. Yield : 75 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.66 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.23 – 7.14 (m, 4H), 7.08 (t, *J* = 6.9 Hz, 1H), 6.66 (dt, *J* = 5.9, 2.8 Hz, 1H), 5.82 (q, *J* = 6.4 Hz, 1H), 2.82 – 2.76 (m, 2H), 2.44 (ddd, *J* = 15.8, 6.8, 2.9 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.02, 165.81, 141.47, 134.20, 132.06, 128.52, 128.31, 125.89, 123.37, 100.78, 88.59, 34.60, 31.10.

HRMS (EI): *m/z* 289.1105 (M^+), calculated for $C_{19}H_{15}NO_2$: 289.1103.

Methyl 1-(3-methylbuta-1,2-dienyl)-1H-indole-3-carboxylate



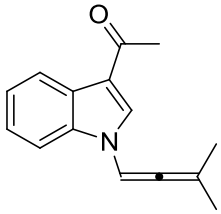
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 99 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.05 (m, 1H), 7.77 (s, 1H), 7.44 – 7.38 (m, 1H), 7.21 – 7.15 (m, 2H), 6.81 (qn, *J* = 2.5 Hz, 1H), 3.81 (s, 3H), 1.82 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.95, 165.27, 135.87, 132.07, 127.12, 123.23, 122.33, 121.78, 110.51, 109.49, 108.64, 94.03, 51.06, 21.70.

HRMS (EI): *m/z* 241.1096 (M^+), calculated for $C_{15}H_{15}NO_2$: 241.1103.

1-(1-(3-methylbuta-1,2-dienyl)-1H-indol-3-yl)ethanone



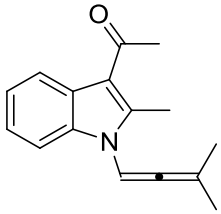
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 96 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.33 (m, 1H), 7.78 (s, 1H), 7.56 – 7.49 (m, 1H), 7.35 – 7.28 (m, 2H), 6.94 (qn, *J* = 2.5 Hz, 1H), 2.55 (s, 3H), 1.96 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.08, 193.06, 136.15, 132.49, 126.81, 123.68, 122.94, 122.65, 118.20, 110.43, 109.60, 94.05, 27.75, 21.73.

HRMS (EI): *m/z* 225.1152 (M^+), calculated for $C_{15}H_{15}NO$: 225.1154.

1-(2-methyl-1-(3-methylbuta-1,2-dienyl)-1H-indol-3-yl)ethanone



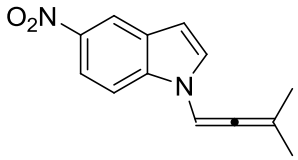
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 92 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 1H), 7.46 – 7.40 (m, 1H), 7.20 – 7.10 (m, 2H), 6.60 (qn, *J* = 2.5 Hz, 1H), 2.68 (s, 3H), 2.56 (s, 3H), 1.82 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.19, 194.66, 144.11, 135.89, 126.68, 122.31, 120.68, 115.23, 110.85, 106.33, 90.93, 31.71, 21.29, 13.27.

HRMS (EI): *m/z* 239.1308 (M^+), calculated for $C_{16}H_{17}NO$: 239.1310.

1-(3-methylbuta-1,2-dienyl)-5-nitro-1H-indole



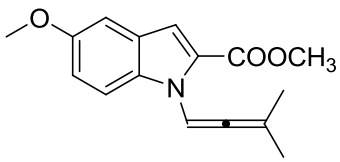
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 92 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 1.7 Hz, 1H), 8.02 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.43 (d, *J* = 3.2 Hz, 1H), 6.97 (qn, *J* = 2.5 Hz, 1H), 6.66 (d, *J* = 3.2 Hz, 1H), 1.98 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.77, 143.25, 133.99, 133.73, 131.68, 120.75, 115.46, 109.72, 107.34, 103.86, 94.26, 21.79.

HRMS (EI): *m/z* 228.0898 (M^+), calculated for $C_{13}H_{12}N_2O_2$: 228.0899.

Methyl 5-methoxy-1-(3-methylbuta-1,2-dienyl)-1H-indole-2-carboxylate



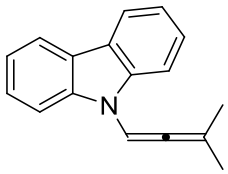
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 94 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (qn, *J* = 2.6 Hz, 1H), 7.65 (d, *J* = 9.2 Hz, 1H), 7.27 (s, 1H), 7.06 (d, *J* = 2.4 Hz, 1H), 7.00 (dd, *J* = 9.1, 2.5 Hz, 1H), 3.91 (s, 3H), 3.85 (s, 3H), 1.94 (d, *J* = 2.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 195.09, 162.23, 155.03, 133.75, 127.29, 127.15, 116.60, 113.51, 111.59, 106.06, 102.81, 94.37, 55.66, 51.70, 21.92.

HRMS (EI): *m/z* 271.1202 (M^+), calculated for $C_{16}H_{17}NO_3$: 271.1208.

9-(3-methylbuta-1,2-dienyl)-9H-carbazole



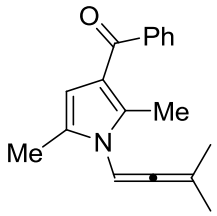
This compound was obtained following general procedure 7 (substate concentration 0.1 M) at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 82 % (colorless oil).

^{1}H NMR (400 MHz, Acetone) δ 8.14 (ddd, *J* = 7.8, 1.1, 0.8 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.48 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 2H), 7.41 (qn, *J* = 2.6 Hz, 1H), 7.27 (ddd, *J* = 7.9, 7.3, 0.9 Hz, 2H), 1.99 (d, *J* = 2.6 Hz, 6H).

^{13}C NMR (101 MHz, Acetone) δ 195.68, 140.35, 127.01, 124.56, 120.99, 120.92, 111.13, 107.79, 93.27, 22.42.

HRMS (EI): *m/z* 233.1205 (M^+), calculated for $C_{17}H_{15}N$: 233.1204.

(2,5-dimethyl-1-(3-methylbuta-1,2-dienyl)-1H-pyrrol-3-yl)(phenyl)methanone



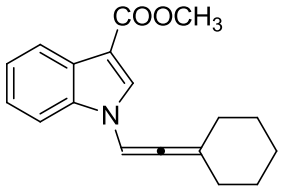
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 12 h. Yield : 86 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.66 (m, 2H), 7.37 (tt, *J* = 7.2, 2.6 Hz, 1H), 7.34 – 7.29 (m, 2H), 6.38 (qn, *J* = 2.4 Hz, 1H), 6.00 (d, *J* = 0.8 Hz, 1H), 2.47 (s, 3H), 2.12 (s, 3H), 1.75 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.14, 192.15, 140.95, 136.36, 130.88, 129.01, 127.88, 127.80, 119.65, 110.48, 105.44, 91.84, 21.12, 13.04, 12.71.

HRMS (EI): *m/z* 265.1471 (M^+), calculated for $C_{18}H_{19}NO$: 265.1467.

Methyl 1-(2-cyclohexylidenevinyl)-1H-indole-3-carboxylate



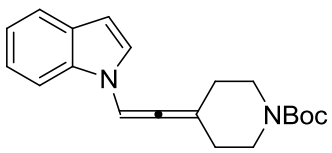
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 10 min. Yield : 96 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (ddd, *J* = 6.1, 3.2, 0.6 Hz, 1H), 7.89 (s, 1H), 7.58 (dd, *J* = 6.2, 3.1, 1H), 7.33 – 7.27 (m, 2H), 6.96 – 6.93 (qn, *J* = 1.8 Hz,1H), 3.93 (s, 3H), 2.42 – 2.26 (m, 4H), 1.80 – 1.68 (m, 4H), 1.67 – 1.59 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.64, 165.30, 135.89, 132.08, 127.13, 123.12, 122.30, 121.77, 116.25, 110.65, 108.53, 93.78, 51.05, 32.52, 27.15, 25.82.

HRMS (EI): Experiment was carried out twice but no signal was found for $C_{18}H_{19}NO_2$.

Tert-butyl 4-(2-(1H-indol-1-yl)vinylidene)piperidine-1-carboxylate



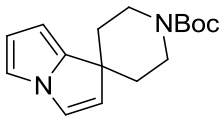
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 30 min. Yield : 94 % (colorless oil).

^{1}H NMR (400 MHz, Acetone) δ 7.68 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.21 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.09 (ddd, *J* = 8.0, 7.2, 0.9 Hz, 1H), 6.58 (dd, *J* = 3.3, 0.6 Hz, 1H), 3.67 – 3.57 (m, 4H), 2.50 – 2.30 (m, 4H), 1.47 (s, 9H).

^{13}C NMR (101 MHz, Acetone) δ 191.68, 154.95, 136.31, 130.52, 126.94, 123.01, 121.70, 121.03, 112.24, 111.22, 104.37, 96.57, 79.76, 45.00 (br), 32.86, 28.56.

HRMS (EI): *m/z* 324.1839 (M^+), calculated for $C_{20}H_{24}N_2O_2$: 324.1838.

Tert-butyl spiro[piperidine-4,1'-pyrrolizine]-1-carboxylate



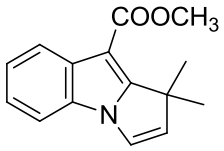
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on silica gel. Reaction time: 12 h. Yield : 97 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.89 (d, *J* = 4.0 Hz, 1H), 6.73 (d, *J* = 2.1 Hz, 1H), 6.24 (t, *J* = 2.6 Hz, 1H), 6.10 (d, *J* = 3.2 Hz, 1H), 5.73 (d, *J* = 3.7 Hz, 1H), 3.82 (m, 2H), 3.45 (ddd, *J* = 13.4, 10.3, 3.0 Hz, 2H), 1.75 (ddd, *J* = 15.4, 10.4, 4.0 Hz, 2H), 1.50 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.95, 142.04, 126.53, 125.95, 111.18, 111.03, 102.39, 79.56, 46.57, 40.65, 33.76, 28.49.

HRMS (EI): *m/z* 274.1683 (M^+), calculated for $C_{16}H_{22}N_2O_2$: 274.1681.

Methyl 1,1-dimethyl-1H-pyrrolo[1,2-a]indole-9-carboxylate



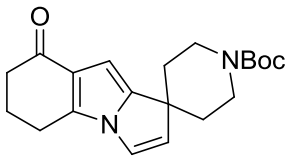
This compound was obtained following general procedure 7 at 80 °C and was purified using column chromatography on silica gel. Reaction time: 12 h. Yield : 88 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.09 (m, 1H), 7.31 (ddd, *J* = 4.8, 2.8, 0.6 Hz, 1H), 7.18 – 7.15 (m, 2H), 7.01 (d, *J* = 4.1 Hz, 1H), 5.77 (d, *J* = 4.1 Hz, 1H), 3.87 (s, 3H), 1.53 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.49, 157.75, 130.27, 129.92, 129.53, 122.40, 122.10, 121.99, 121.80, 109.50, 101.48, 50.71, 46.55, 22.53.

HRMS (EI): *m/z* 241.1107 (M^+), calculated for $C_{15}H_{15}NO_2$: 241.1103.

Tert-butyl-8'-oxo-5',6',7',8'-tetrahydrospiro[piperidine-4,1'-pyrrolo[1,2-a]indole]-1-carboxylate



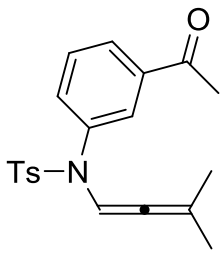
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on silica gel. Reaction time: 24 h. Yield : 95 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, *J* = 4.1 Hz, 1H), 6.47 (s, 1H), 5.86 (d, *J* = 4.2 Hz, 1H), 3.82 (s, 2H), 3.35 (t, *J* = 11.2 Hz, 2H), 2.80 (t, *J* = 6.2 Hz, 2H), 2.49 – 2.43 (m, 2H), 2.18 – 2.11 (m, 2H), 1.80 – 1.68 (m, 2H), 1.46 (m, 11H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.27, 154.83, 142.16, 135.22, 129.10, 123.79, 123.47, 99.54, 46.40, 40.43, 37.79, 33.65, 28.44, 23.71, 21.44.

HRMS (EI): *m/z* 342.1947 (M^+), calculated for $C_{20}H_{26}N_2O_3$: 342.1943.

N-(3-acetylphenyl)-4-methyl-N-(3-methylbuta-1,2-dienyl)benze-nesulfonamide



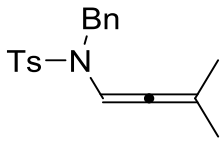
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 88 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.45 – 7.43 (m, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 8.1 Hz, 2H), 7.16 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1H), 6.73 (qn, *J* = 2.5 Hz, 1H), 2.41 (s, 3H), 2.36 (s, 3H), 1.40 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 196.81 , 192.69 , 143.98 , 138.63 , 137.62 , 135.26 , 134.02 , 129.50 , 129.24 , 128.93 , 127.85 , 127.64 , 109.15 , 99.58 , 26.49 , 21.57 , 21.11 .

HRMS (EI): *m/z* 355.1260 (M^+), calculated for $C_{20}H_{21}NO_3S$: 355.1242.

N-benzyl-4-methyl-N-(3-methylbuta-1,2-dienyl)benzenesulfonamide



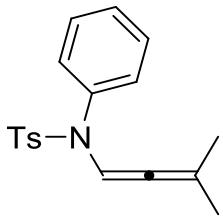
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 85 % (colorless oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.48 – 7.36 (m, 5H), 6.75 (qn, *J* = 2.5 Hz, 1H), 4.40 (s, 2H), 2.61 (s, 3H), 1.55 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.53 , 143.55 , 136.57 , 135.38 , 129.60 , 128.18 , 127.51 , 127.26 , 127.07 , 108.91 , 97.01 , 50.21 , 21.56 .

HRMS (EI): *m/z* 327.1300 (M^+), calculated for $C_{19}H_{21}NO_2S$: 327.1293.

4-methyl-N-(3-methylbuta-1,2-dienyl)-N-phenylbenzenesulfonamide



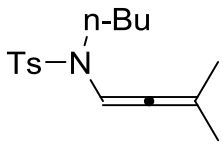
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 5 h. Yield : 95 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.3 Hz, 2H), 7.18 (m, 5H), 6.97 – 6.85 (m, 2H), 6.73 (qn, *J* = 2.4 Hz, 1H), 2.35 (s, 3H), 1.39 (d, *J* = 2.3 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.85 , 143.56 , 138.12 , 135.74 , 129.35 , 129.29 , 128.57 , 128.17 , 127.67 , 108.56 , 99.86 , 21.57 , 21.11 .

HRMS (EI): *m/z* 313.1131 (M^+), calculated for $C_{18}H_{19}NO_2S$: 313.1136.

N-butyl-4-methyl-N-(3-methylbuta-1,2-dienyl)benzenesulfonamide



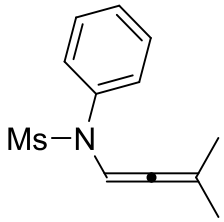
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 91 % (yellowish oil).

^{1}H NMR (400 MHz, Methylene Chloride-d_2) δ 7.57 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.42 (qn, *J* = 2.5 Hz, 1H), 2.97 – 2.88 (m, 2H), 2.33 (s, 3H), 1.60 (d, *J* = 2.5 Hz, 6H), 1.45 – 1.31 (m, 2H), 1.29 – 1.06 (m, 2H), 0.79 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, Methylene Chloride-d_2) δ 193.03 , 143.87 , 136.07 , 129.83 , 127.45 , 108.60 , 97.54 , 46.73 , 30.08 , 21.76 , 21.57 , 20.26 , 13.74 .

HRMS (EI): *m/z* 293.1452 (M^+), calculated for $C_{16}H_{23}NO_2S$: 293.1449.

N-(3-methylbuta-1,2-dienyl)-N-phenylmethanesulfonamide



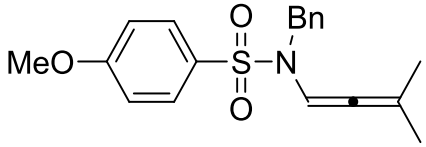
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 87 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.22 (m, 5H), 6.60 (qn, *J* = 2.4 Hz, 1H), 2.92 (s, 3H), 1.52 (d, *J* = 2.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.60 , 138.17 , 129.04 , 128.90 , 128.34 , 108.95 , 99.39 , 38.03 , 21.12 .

HRMS (EI): *m/z* 237.0828 (M^+), calculated for $C_{12}H_{15}NO_2S$: 237.0823.

N-benzyl-4-methoxy-N-(3-methylbuta-1,2-dienyl)benzenesulfonamide



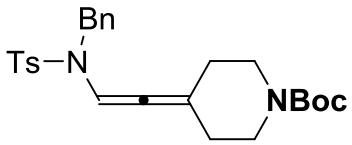
This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 85 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 9.0 Hz, 2H), 7.39 – 7.16 (m, 5H), 7.01 (d, *J* = 9.0 Hz, 2H), 6.59 (p, *J* = 2.5 Hz, 1H), 4.24 (s, 2H), 3.88 (s, 3H), 1.40 (d, *J* = 2.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 193.57 , 163.01 , 136.62 , 129.99 , 129.34 , 128.19 , 127.51 , 127.07 , 114.18 , 108.89 , 97.05 , 55.65 , 50.20 , 21.57 .

HRMS (EI): *m/z* 343.1247 (M^+), calculated for $C_{19}H_{21}NO_3S$: 343.1242.

tert-butyl 4-(2-(N-benzyl-4-methylphenylsulfonamido)vinylidene)piperidine-1-carboxylate

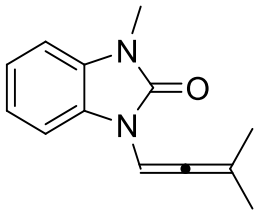


This compound was obtained following general procedure 7 at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 3 h. Yield : 89 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.30 – 7.17 (m, 5H), 6.72 (t, *J* = 2.0 Hz, 1H), 4.29 (s, 2H), 3.29 (ddd, *J* = 12.0, 6.7, 4.3 Hz, 2H), 3.11 (ddd, *J* = 12.9, 7.3, 4.2 Hz, 2H), 2.44 (s, 3H), 1.94 – 1.78 (m, 2H), 1.72 (m, 2H), 1.42 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.86 , 154.47 , 143.70 , 136.17 , 135.47 , 129.68 , 128.30 , 127.22 , 127.19 , 127.05 , 111.54 , 98.08 , 79.69 , 50.27 , 43.88 , 31.68 , 28.39 , 21.54 . **HRMS (EI)**: *m/z* 468.2076 (M^+), calculated for $C_{26}H_{32}N_2O_4S$: 468.2083.

1-methyl-3-(3-methylbuta-1,2-dienyl)-1H-benzo[d]imidazol-2(3H)-one



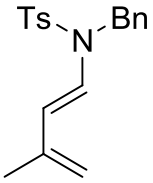
This compound was obtained following general procedure 7 (substrate concentration 0.1 M)at room temperature and was purified using column chromatography on water-deactivated neutral Al_2O_3. Reaction time: 20 h. Yield : 82 % (yellowish oil).

^{1}H NMR (400 MHz, Acetone-d_6) δ 7.18 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.99 – 6.89 (m, 3H), 6.85 (p, *J* = 2.7 Hz, 1H), 3.23 (s, 3H), 1.78 (d, *J* = 2.7 Hz, 6H).

^{13}C NMR (101 MHz, Acetone-d_6) δ 193.75 , 153.15 , 131.38 , 128.54 , 122.69 , 122.23 , 110.06 , 108.84 , 108.40 , 91.46 , 27.24 , 22.31 .

HRMS (EI): *m/z* 214.1104 (M^+), calculated for $C_{13}H_{14}N_2O$: 214.1106.

(*E*)-N-benzyl-4-methyl-N-(3-methylbuta-1,3-dienyl)benzenesulfonamide



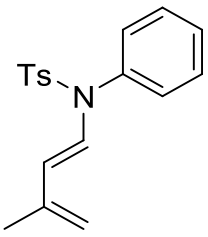
This compound was obtained following general procedure 8 and was obtained as colorless oil (83 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.21 (m, 7H), 6.95 (d, *J* = 14.4 Hz, 1H), 5.49 (d, *J* = 14.5 Hz, 1H), 4.79 – 4.63 (m, 2H), 4.56 (s, 2H), 2.43 (s, 3H), 1.82 (d, *J* = 1.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.92 , 140.05 , 136.05 , 135.47 , 129.86 , 128.59 , 127.43 , 126.89 , 126.85 , 126.70 , 115.27 , 113.98 , 49.40 , 21.52 , 18.78 .

HRMS (EI): *m/z* 327.1292 (M^+), calculated for $C_{19}H_{21}NO_2S$: 327.1293.

(*E*)-4-methyl-N-(3-methylbuta-1,3-dienyl)-N-phenylbenzenesulfonamide



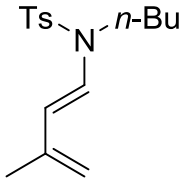
This compound was obtained following general procedure 8 and was obtained as colorless oil (88 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.3 Hz, 2H), 7.34 – 7.26 (m, 3H), 7.19 (d, *J* = 8.2 Hz, 2H), 7.14 (d, *J* = 14.2 Hz, 1H), 6.92 – 6.87 (m, 2H), 5.03 (d, *J* = 14.3 Hz, 1H), 4.70 – 4.47 (m, 2H), 2.35 (s, 3H), 1.81 (d, *J* = 1.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.99 , 140.00 , 136.26 , 135.81 , 130.30 , 129.61 , 129.47 , 129.45 , 129.08 , 127.48 , 115.06 , 113.83 , 21.55 , 18.92 .

HRMS (EI): *m/z* 313.1146 (M^+), calculated for $C_{18}H_{19}NO_2S$: 313.1136.

(*E*)-N-butyl-4-methyl-N-(3-methylbuta-1,3-dienyl)benzenesulfonamide



This compound was obtained following general procedure 8 and was obtained as colorless oil (85 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.3 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 6.78 (d, *J* = 14.5 Hz, 1H), 5.48 (d, *J* = 14.5 Hz, 1H), 4.74 (s, 1H), 3.28 – 3.22 (m, 1H), 2.33 (s, 2H), 1.79 (s, 2H), 1.57 – 1.44 (m, 1H), 1.37 – 1.21 (m, 1H), 0.84 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.68 , 140.36 , 136.21 , 129.78 , 126.76 , 126.74 , 113.87 , 113.60 , 45.26 , 29.14 , 21.50 , 19.97 , 18.89 , 13.64 .

HRMS (EI): *m/z* 293.1453 (M^+), calculated for $C_{16}H_{23}NO_2S$: 293.1449.

Part 2 : Gold(I)-Catalyzed Rearrangement of Ynamides via [1,5]-Hydride Shift: An Expedient Approach to Allenamides and Its Equivalents

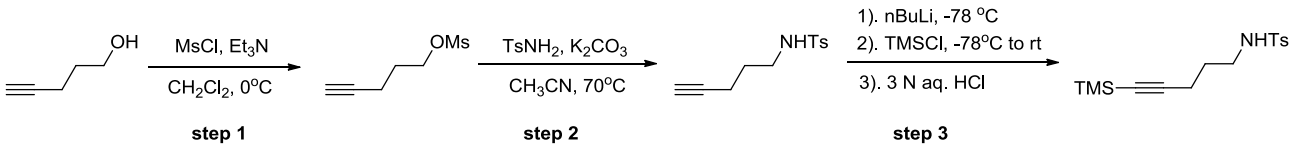
1. General Information

All commercial available reagents were purchased from chemical suppliers (Sigma-Aldrich, Alfa-Aesar, TCI Europe and Fluochem) and were used as delivered without further purification unless otherwise noted. Dried solvents employed in the experimental parts were obtained from solvent purification system MB-SPS 800. Reactions carried out under inert atmosphere were performed under an atmosphere of nitrogen and the reaction vessels are vacuumed and then refilled with nitrogen for three times before reagents were added. Flame-dried reaction flask was used if noted. Thin layer chromatography was performed on TLC Silica gel 60 F_{254} plates (25 aluminum sheets, purchased from Merck KGaA), which was visualized by using UV-light (254 nm), aq. $KMnO_4$ solution ($KMnO_4$, 6 g; K_2CO_3, 40 g; 5% aqueous NaOH, 10 mL; H_2O, 600 mL) or *p*-anisaldehyde stain (*p*-anisaldehyde, 12 g; Conc. H_2SO_4, 5 mL; ethanol, 500 mL). Concentration under reduced pressure was carried out by rotary evaporation at 40°C or room temperature in water bath. Flash column chromatography was carried out on silica gel 60 (0.04-0.063 mm, purchased from VWR chemicals*)* or Al_2O_3 90 neutral (acitivity stage I for chromatography, 0.063-0.200 mm, 70-230 mesh ASTM, purchased from Merck KGaA) using a forced flow of eluents at 1–4 bar pressure and technical-grade solvents were used.

NMR spectra were recorded at room temperature in the given deuterated solvent on a Bruker Avance DPX 400 instrument operating at the indicated frequency given in mega Hertz (MHz) for the specified nucleus. Chemical shifts δ are given in parts per million (ppm) using tetramethylsilane (TMS) as the standard reference sample for ^{1}H-NMR and ^{13}C-NMR spectra and are calibrated in relation to the deuterated solvent ($CDCl_3$: 7.26 / 77.16 ppm; CD_2Cl_2: 5.32 / 53.80 ppm; d_6-acetone: 2.05 / 29.84 ppm). Coupling constants *J* are given in Hertz (Hz). Signal multiplicities are depicted using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sex = sextuplet, sept = septuplet, m = multiplet, dd = doublet of doublet, dt = doublet of triplet, tt = triplet of triplet, dq = doublet of quartet, ddd = doublet of doublet of doublet, ddt = doublet of doublet of triplet, bs = broad singlet. High-resolution mass spectrometry by electron impact (EI) was performed on a JEOL JMCGCmate II mass spectrometer and fragment signals were given in mass per charge number (*m/z*). IUPAC names of compounds described in the experimental section were directly generated using ChemBioDraw.

2. General Procedures

General procedure 1: Synthesis of 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide

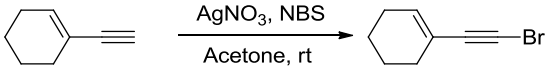


step 1: To a stirred solution of 4-pentyn-1-ol (0.84 g, 10 mmol) in DCM (40 mL) at 0 ^{0}C were added triethylamine (1.52 g, 15 mmol) and then methanesulfonyl chloride (1.72 g, 15 mmol) was added dropwise at this temperature. After complete consumption of the starting material monitored by TLC (1 hour), the crude mixture was poured into water and DCM was added and the organic layer was washed with 2 N aq. HCl solution, brine, dried over Na_2SO_4 and then concentrated under reduced pressure to afford the desired product as yellowish oil, which was used in the next step without further purification.

step 2: To a stirred solution of the obtained pent-4-yn-1-yl methanesulfonate in CH_3CN (40 mL) at room temperature was added $TsNH_2$ (2.05g, 12 mmol) and K_2CO_3 (2.76 g, 20 mmol). The resulted mixture was heated at 70 ℃ until TLC showed complete consumption of the starting material (24 hours). Then, H_2O and EtOAc were added and the reaction mixture was separated. The water phase was extracted with EtOAc for three times and the combined organic phase was dried over anhydrous $MgSO_4$, filtered and then concentrated under reduced pressure. Flash column purification on silica gel afforded the desired 4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide (1.7 g, 72 % yield).

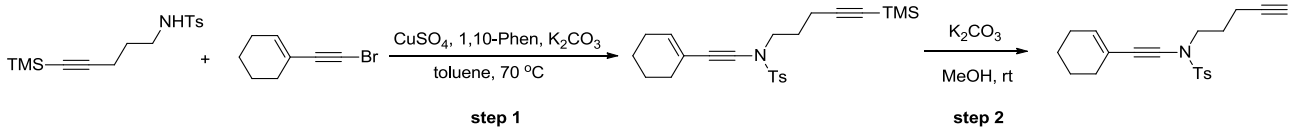
step 3: This reaction was carried out under inert atmosphere and flame-dried glassware was used. To a stirred solution of 4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide (1.7 g, 7.2 mmol) in dry THF (28 mL) was added 2.5 M *n*-BuLi (6.4 mL) at -78 ℃. The mixture was stirred at -78 ℃ for 1 hour. Afterwards, TMSCl (2.0 g, 18 mmol) were added at -78 ℃, and then the mixture was warmed to room temperature for 1h (TLC indicated the complete consumption of the starting material). To the solution was added 3 M aq. HCl solution and then stirred for 6 hours, then the organic phase was separated, dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The residue was purified through flash chromatography to provide the desired 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide (1.0 g, 45 % yield).

General procedure 2: Synthesis of alkynyl bromide



To a stirred solution of 1-ethynylcyclohex-1-ene (1.06 g, 10 mmol) in 30 mL of acetone was added N-bromosuccinimide (1.96 g, 11 mmol) and $AgNO_3$ (170 mg, 1 mmol). The resulting reaction mixture was stirred untill complete consumption of starting material monitored by TLC and was filtered through a celite column. The filtrate was concentrated under reduced pressure. The resulting residue was diluted with saturated K_2CO_3 and extracted with ether (100 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and then concentrated under reduced pressure. Purification by flash column chromatography on silica gel with petroleum ether/ethyl acetate as the eluent provided 1-(bromoethynyl)cyclohex-1-ene as colorless oil (1.76 g, 95 % yield).

General procedure 3: Synthesis of N-(cyclohex-1-en-1-ylethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide[85]



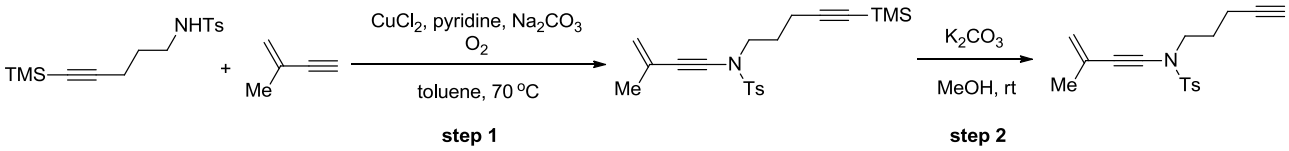
step 1: In a flame-dried schlenk tube, *N*-benzyltoluenesulfonamide (1.55 g, 5.0 mmol), K_2CO_3 (1.38 g, 10.0 mmol), $CuSO_4{\cdot}5H_2O$ (250 mg, 1.0 mmol), and 1,10-phenanthroline (360.4 mg, 2.0 mmol) was combined. Afterwards, the schlenk tube was vacuumed and refilled with nitrogen for 3 times and then the 1-(bromoethynyl)cyclohex-1-ene (1.11 g, 6.0 mmol) in 5 mL of toluene was added via a syringe. The resulting reaction mixture was heated in a pre-heated oil bath at 70 °C for 24 h until the complete consumption of the starting material. Then, the reaction mixture was cooled to room temperature and diluted with 20 mL of EtOAc and the resulting mixture was filtered through celite. The filtrate was concentrated and the residual was used in the next step without further purification.

step 2: A schlenk tube containing K_2CO_3 (345 mg, 2.5 mmol) was vacuumed and refilled with nitrogen for 3 times and then N-(cyclohex-1-en-1-ylethynyl)-4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide obtained in last step in 25 mL of dry methanol was added. The resulting reaction mixture was stirred at room temperature for 4 hours until the complete consumption of the starting material indicated by TLC monitoring

[85] Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151-1154

and then was concentrated under reduced pressure. The resulted residual was purified by flash column chromatography on silica gel using petroleum ether/EtOAc (containing 5 % triethylamine) as the eluent to provide the desired N-(cyclohex-1-en-1-ylethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide.

General procedure 4: Synthesis of 4-methyl-N-(3-methylbut-3-en-1-yn-1-yl)-N-(pent-4-yn-1-yl)benzenesulfonamide[86]

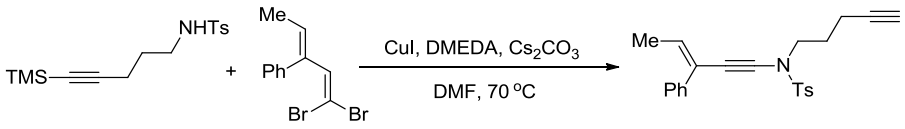


step 1: To a 500 mL round-bottom flask equipped with a stir-bar, $CuCl_2$ (135 mg, 1.0 mmol), 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide (3.1 g, 10.0 mmol) and sodium carbonate (1.06 g, 10.0 mmol) were added. The reaction flask was purged with oxygen gas for 0.5 hour. A solution of pyridine (0.79 g, 10.0 mmol) in 25 mL dry toluene was added to the reaction flask via a syringe. Two large balloons filled with oxygen gas were connected to the reaction flask via needles. The flask was placed in a pre-heated oil-bath at 70 °C. A solution of 2-methylbut-1-en-3-yne (0.33 g, 5 mmol) in 25.0 ml dry toluene was added to the flask over 5 hours via a syringe pump. The resulted reaction mixture was allowed to stir at 70 °C for another 36 hours and then cooled to room temperature. Afterwards, EtOAc (50 mL) was added and the mixture was filtered using a celite column. The resulted solution was concentrated under reduced pressure and was used in the next step without further purification.

step 2: A schlenk tube containing K_2CO_3 (345 mg, 2.5 mmol) was vacuumed and refilled with nitrogen for 3 times and then 4-methyl-N-(3-methylbut-3-en-1-yn-1-yl)-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide obtained in last step in 25 mL of dry methanol was added. The resulting reaction mixture was stirred at room temperature for 4 hours until the complete consumption of the starting material indicated by TLC monitoring and then was concentrated under reduced pressure. The resulted residual was purified by flash column chromatography on silica gel using petroleum ether/EtOAc (containing 5 % triethylamine) as the eluent to provide the desired N-4-methyl-N-(3-methylbut-3-en-1-yn-1-yl)-N-(pent-4-yn-1-yl)benzenesulfonamide (44 % yield).

[86] T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833-835.

General procedure 5: Synthesis of (*E*)-4-methyl-N-(pent-4-yn-1-yl)-N-(3-phenylpent-3-en-1-yn-1-yl)benzenesulfonamide[87]



To a schlenk tube was added 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide (0.62 g, 2.0 mmol), (*Z*)-(1,1-dibromopenta-1,3-dien-3-yl)benzene (0.91 g, 3.0 mmol), Cs_2CO_3 (2.60 g, 8.0 mmol), and copper(I) iodide (76 mg, 0.4 mmol). The tube was fitted with a rubber septum, evacuated under high vacuum and backfilled with nitrogen for 3 times. Dry and degassed DMF (4 mL) and N,N'- dimethylethylenediamine (60 µL, 0.6 mmol) were next added and the resulted suspension was heated at 70 °C for 24 h. When the reaction mixture was cooled to rt, the crude reaction mixture was diluted with water, extracted with diethyl ether and the combined organic layers were washed with brine, dried over MgSO4, filtered and concentrated. The crude residue was purified by flash chromatography on silica gel using petroleum ether/EtOAc (containing 5 % triethylamine) as the eluent to provide the desired (*E*)-4-methyl-N-(pent-4-yn-1-yl)-N-(3-phenylpent-3-en-1-yn-1-yl)benzenesulfonamide (yellowish oil, 62 % yield).

Note: *In this procedure, TMS was removed in the course of the reaction and no further deprotection step was needed.*

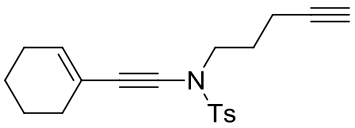
General procedure 6: Gold catalysis

To a stirred solution of 0.20 mmol of ynamide starting material in chloroform (2 mL) was added RuPhosAuNTf$_2$ (5 mmol%) at room temperature and the solution was stirred at preheated 70 °C oil bath until TLC showed complete consumption of starting material. Then the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography on silica gel using petroleum ether/EtOAc as the eluent.

[87] A. Coste, G. Karthikeyan, F. Couty, G. Evano, *Angew. Chem. Int. Ed.* **2009**, *48*, 4381-4385.

3. Preparation of Starting Materials

N-(cyclohex-1-en-1-ylethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)cyclohex-1-ene using general procedure 3. Yield: 65 % (yellowish oil).

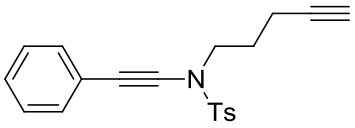
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.2 Hz, 2H), 5.99 (dq, *J* = 4.0, 1.7 Hz, 1H), 3.41 (t, *J* = 6.9 Hz, 2H), 2.44 (s, 3H), 2.23 (td, *J* = 7.0, 2.7 Hz, 2H), 2.07 (m, 4H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.85 (qn, *J* = 7.0 Hz, 2H), 1.68 – 1.49 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.60, 134.46, 134.08, 129.78, 127.75, 119.93, 82.92, 79.58, 72.45, 69.34, 50.48, 29.53, 26.96, 25.72, 22.41, 21.75, 21.59, 15.66.

HRMS (EI): *m/z* 341.1451 (M^+), calculated for $[C_{20}H_{23}NO_2S]^+$: 341.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2938, 2862, 2228, 2120, 1599, 1437, 1368, 1170, 1096

4-methyl-N-(pent-4-yn-1-yl)-N-(phenylethynyl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and (bromoethynyl)benzene using general procedure 3. Yield: 72 % (yellowish oil).

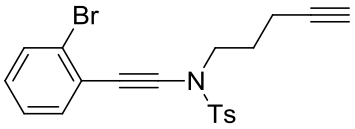
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.34 (m, 4H), 7.32 – 7.28 (m, 3H), 3.53 (t, *J* = 6.9 Hz, 2H), 2.46 (s, 3H), 2.30 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.94 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.84, 134.46, 131.43, 129.92, 128.37, 127.94, 127.78, 122.80, 82.81, 82.19, 70.88, 69.50, 50.53, 27.05, 21.77, 15.68.

HRMS (EI): *m/z* 341.1128 (M^+), calculated for $[C_{20}H_{19}NO_2S]^+$: 337.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3065, 2929, 2595, 2239, 1599, 1494, 1443, 1367, 1171, 1095

N-((2-bromophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-bromo-2-(bromoethynyl)benzene using general procedure 3. Yield: 70 % (yellowish oil).

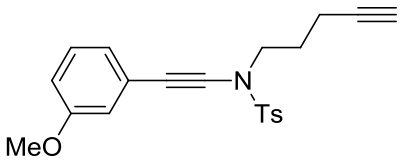
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.5 Hz, 2H), 7.54 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.39 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.24 (td, *J* = 7.6, 1.3 Hz, 1H), 7.11 (td, *J* = 7.8, 1.7 Hz, 1H), 3.57 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.30 (td, *J* = 6.9, 2.7 Hz, 2H), 2.06 – 1.92 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.91, 134.30, 132.46, 132.22, 129.88, 128.69, 127.65, 127.00, 125.00, 124.50, 86.52, 82.69, 70.12, 69.51, 50.41, 26.80, 21.64, 15.54.

HRMS (EI): *m/z* 260.0063 $[M\text{-}Ts]^+$, calculated for $[C_{20}H_{18}BrNO_2S\text{-}Ts]^+$: 260.0075.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3068, 2940, 2877, 2260, 2238, 1599, 1434, 1369, 1171

N-((3-methoxyphenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)-3-methoxybenzene using general procedure 3. Yield: 75 % (yellowish solid).

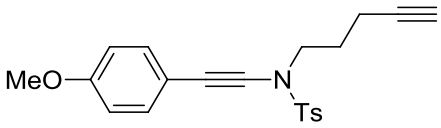
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.24 – 7.16 (m, 1H), 6.96 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.89 (dd, *J* = 2.7, 1.5 Hz, 1H), 6.84 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 3.80 (s, 3H), 3.53 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.29 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.93 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.41, 144.87, 134.52, 129.95, 129.44, 127.82, 123.96, 123.87, 116.38, 114.37, 82.84, 82.08, 70.91, 69.51, 55.41, 50.55, 27.11, 21.80, 15.71.

HRMS (EI): *m/z* 367.1254 $[M]^+$, calculated for $[C_{21}H_{21}NO_3S]^+$: 367.1242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3007, 2941, 2838, 2240, 1576, 1465, 1368, 1187, 1096

N-((4-methoxyphenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)-4-methoxybenzene using general procedure 3. Yield: 68 % (yellowish oil).

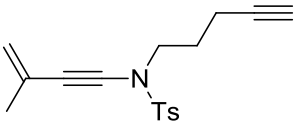
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 3.50 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.92 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.59, 144.70, 134.45, 133.45, 129.83, 127.74, 114.64, 113.98, 82.86, 80.66, 70.47, 69.42, 55.36, 50.56, 26.99, 21.72, 15.65.

HRMS (EI): *m/z* 367.1251 $[M]^+$, calculated for $[C_{21}H_{21}NO_3S]^+$: 367.1242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3043, 2958, 2938, 2840, 2242, 1606, 1512, 1366, 1248, 1171, 1095

4-methyl-N-(3-methylbut-3-en-1-yn-1-yl)-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 2-methylbut-1-en-3-yne using general procedure 4. Yield: 46 % (yellowish oil).

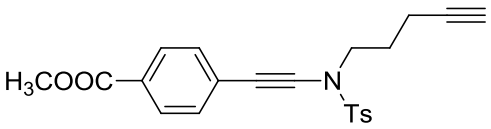
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 5.16 – 5.12 (m, 1H), 5.12 – 5.09 (m, 1H), 3.44 (t, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 2.24 (td, *J* = 7.0, 2.7 Hz, 2H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.91 – 1.79 (m, 5H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.78, 134.36, 129.83, 127.70, 126.07, 119.71, 82.76, 81.54, 72.44, 69.41, 50.36, 26.98, 23.55, 21.71, 15.59.

HRMS (EI): *m/z* 301.1123 $[M]^+$, calculated for $[C_{17}H_{19}NO_2S]^+$: 301.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3099, 2978, 2955, 2877, 2230, 1599, 1364, 1171, 1095, 1021

methyl 4-((4-methyl-N-(pent-4-yn-1-yl)phenylsulfonamido)ethynyl)benzoate



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and methyl 4-(bromoethynyl)benzoate using general procedure 3. Yield: 55 % (yellowish solid).

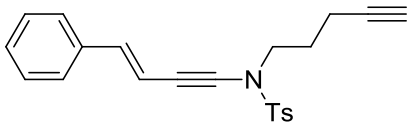
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.3 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.44 – 7.34 (m, 4H), 3.90 (s, 3H), 3.55 (t, *J* = 6.9 Hz, 2H), 2.44 (s, 3H), 2.29 (td, *J* = 7.0, 2.6 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.93 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.64, 145.09, 134.45, 130.66, 130.03, 129.57, 128.88, 127.83, 127.76, 85.52, 82.67, 70.97, 69.62, 52.30, 50.50, 27.14, 21.79, 15.67.

HRMS (EI): *m/z* 395.1182 $[M]^+$, calculated for $[C_{22}H_{21}NO_4S]^+$: 395.1191.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2954, 2251, 2234, 1718, 1606, 1438, 1369, 1288, 1172, 1109

(*E*)-4-methyl-N-(pent-4-yn-1-yl)-N-(4-phenylbut-3-en-1-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and (*E*)-(4-bromobut-1-en-3-yn-1-yl)benzene using general procedure 3. Yield: 48 % (yellowish oil).

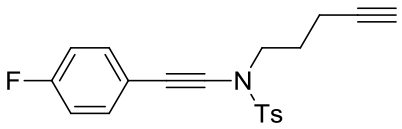
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.41 – 7.25 (m, 7H), 6.84 (d, *J* = 16.2 Hz, 1H), 6.24 (d, *J* = 16.2 Hz, 1H), 3.50 (t, *J* = 6.9 Hz, 2H), 2.46 (s, 3H), 2.28 (td, *J* = 7.0, 2.6 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.92 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.86, 139.77, 136.46, 134.56, 129.97, 128.82, 128.50, 127.75, 126.17, 107.56, 84.21, 82.83, 70.65, 69.50, 50.58, 27.05, 21.81, 15.70.

HRMS (EI): *m/z* 363.1300 $[M]^+$, calculated for $[C_{22}H_{21}NO_2S]^+$: 363.1293.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3033, 2939, 2263, 2221, 1599, 1449, 1367, 1171, 1095

N-((4-fluorophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



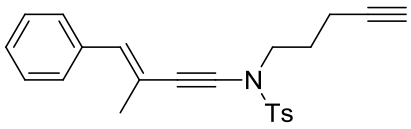
This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)-4-fluorobenzene using general procedure 3. Yield: 72 % (white solid).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.31 (m, 4H), 6.98 (t, *J* = 8.7 Hz, 2H), 3.52 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.29 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.92 (p, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.38 (d, *J* = 249.2 Hz), 144.90, 134.47, 133.54 (d, *J* = 8.3 Hz), 129.94, 127.75, 118.82 (d, *J* = 3.5 Hz), 115.63 (d, *J* = 22.0 Hz), 82.77, 81.80 (d, *J* = 1.5 Hz), 69.79, 69.51, 50.52, 27.06, 21.76, 15.67.

HRMS (EI): *m/z* 355.1050 $[M]^+$, calculated for $[C_{20}H_{18}FNO_2S]^+$: 355.1042.

(*E*)-4-methyl-N-(3-methyl-4-phenylbut-3-en-1-yn-1-yl)-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and (*Z*)-(1,1-dibromopenta-1,3-dien-3-yl)benzene using general procedure 5. Yield: 62 % (yellowish oil).

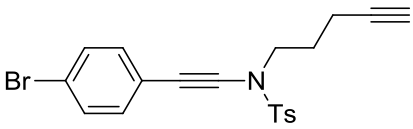
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.5 Hz, 2H), 7.21 – 7.13 (m, 3H), 6.63 (s, 1H), 3.42 (t, *J* = 6.9 Hz, 2H), 2.38 (s, 3H), 2.21 (td, *J* = 7.0, 2.7 Hz, 2H), 1.97 (d, *J* = 1.6 Hz, 3H), 1.91 (t, *J* = 2.7 Hz, 1H), 1.84 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.81, 136.94, 134.54, 134.36, 129.91, 128.98, 128.37, 127.81, 127.12, 119.29, 82.87, 81.53, 74.84, 69.47, 50.53, 27.11, 21.80, 19.47, 15.72.

HRMS (EI): *m/z* 377.1436 $[M]^+$, calculated for $[C_{23}H_{23}NO_2S]^+$: 377.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3065, 3026, 2955, 2877, 2252, 2223, 1598, 1494, 1442, 1367, 1171

N-((4-bromophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-bromo-4-(bromoethynyl)benzene using general procedure 3. Yield: 77 % (yellowish solid).

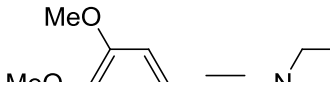
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 3.53 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.92 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.98, 134.47, 132.79, 131.62, 129.98, 127.76, 122.00, 121.85, 83.37, 82.73, 70.07, 69.57, 50.51, 27.11, 21.79, 15.68.

HRMS (EI): *m/z* 415.0244 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2939, 2877, 2239, 1598, 1489, 1368, 1171, 1117, 1095

4-methyl-N-(pent-4-yn-1-yl)-N-((3,4,5-trimethoxyphenyl)ethynyl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 5-(bromoethynyl)-1,2,3-trimethoxybenzene using general procedure 3. Yield: 80 % (white solid).

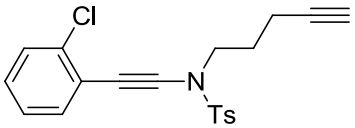
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.58 (s, 2H), 3.82 (s, 9H), 3.50 (t, *J* = 6.9 Hz, 2H), 2.43 (s, 3H), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.91 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.05, 144.80, 138.64, 134.46, 129.87, 127.72, 117.75, 108.90, 82.77, 81.17, 70.79, 69.44, 60.97, 56.20, 50.47, 27.04, 21.70, 15.63.

HRMS (EI): *m/z* 427.1469 $[M]^+$, calculated for $[C_{23}H_{25}NO_5S]^+$: 427.1453.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2941, 2844, 2258, 1599, 1578, 1465, 1411, 1372, 1236, 1132, 1095

N-((2-chlorophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)-2-chlorobenzene using general procedure 3. Yield: 65 % (yellowish oil).

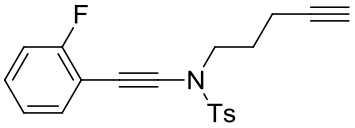
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.43 – 7.33 (m, 4H), 7.22 – 7.15 (m, 2H), 3.57 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.30 (td, *J* = 7.0, 2.7 Hz, 2H), 2.05 – 1.94 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.98, 135.21, 134.56, 132.60, 129.99, 129.27, 128.67, 127.88, 126.54, 123.03, 87.23, 82.81, 69.53, 68.51, 50.57, 26.97, 21.81, 15.71.

HRMS (EI): This experiment was carried out twice but no corresponding signal was observed.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3068, 2939, 2877, 2239, 2121, 1599, 1438, 1369, 1171, 1095

N-((2-fluorophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)-2-fluorobenzene using general procedure 3. Yield: 66 % (yellowish oil).

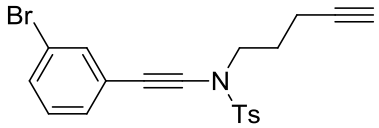
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.42 – 7.33 (m, 3H), 7.25 (tdd, *J* = 7.5, 5.3, 2.6 Hz, 1H), 7.11 – 7.01 (m, 2H), 3.55 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.29 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.94 (qn, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.55 (d, *J* = 250.5 Hz), 144.95, 134.42, 133.10 (d, *J* = 1.3 Hz), 129.96, 129.53 (d, *J* = 7.8 Hz), 127.84, 124.00 (d, *J* = 3.7 Hz), 115.48 (d, *J* = 20.8 Hz), 111.50 (d, *J* = 15.7 Hz), 86.95 (d, *J* = 3.0 Hz), 82.77, 69.51, 64.71, 50.51, 26.95, 21.78, 15.67.

HRMS (EI): This experiment was carried out twice but no corresponding signal was observed.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3067, 2940, 2248, 1600, 1496, 1454, 1369, 1171, 1095

N-((3-bromophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-bromo-3-(bromoethynyl)benzene using general procedure 3. Yield: 60 % (yellowish oil).

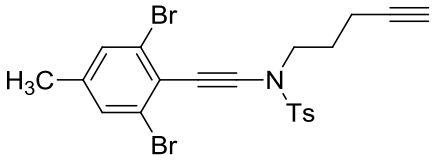
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 2H), 7.49 (t, *J* = 1.8 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.37 (d, *J* = 8.3 Hz, 2H), 7.28 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.16 (t, *J* = 7.9 Hz, 1H), 3.53 (t, *J* = 6.9 Hz, 2H), 2.46 (s, 3H), 2.29 (td, *J* = 6.9, 2.5 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.92 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.06, 134.48, 133.94, 130.97, 130.04, 129.85, 129.81, 127.79, 124.95, 122.20, 83.64, 82.72, 69.79, 69.62, 50.52, 27.13, 21.83, 15.70.

HRMS (EI): *m/z* 415.0259 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3068, 2940, 2877, 2595, 2238, 1597, 1556, 1368, 1187, 1092

N-((2,6-dibromo-4-methylphenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1,3-dibromo-2-(bromoethynyl)-5-methylbenzene using general procedure 3. Yield: 78 % (white solid).

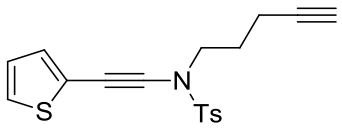
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.33 (s, 2H), 3.59 (t, *J* = 6.9 Hz, 2H), 2.44 (s, 3H), 2.32 – 2.27 (m, 5H), 2.04 (qn, *J* = 6.9 Hz, 2H), 1.98 (t, *J* = 2.6 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.01, 139.72, 134.64, 132.00, 130.01, 127.92, 124.77, 124.14, 90.09, 82.90, 70.33, 69.53, 50.76, 26.92, 21.83, 20.90, 15.76.

HRMS (EI): *m/z* 506.9508 $[M]^+$, calculated for $[C_{21}H_{19}Br_2NO_2S]^+$: 506.9503.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2926, 2876, 2261, 2239, 2121, 1599, 1369, 1188, 1171, 1095

4-methyl-N-(pent-4-yn-1-yl)-N-(thiophen-2-ylethynyl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 2-(bromoethynyl)thiophene using general procedure 3. Yield: 56 % (yellowish oil).

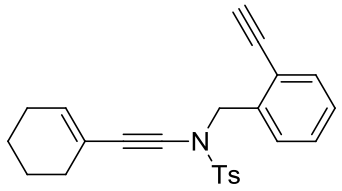
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.27 (dd, *J* = 5.2, 1.1 Hz, 1H), 7.18 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.98 (dd, *J* = 5.2, 3.6 Hz, 1H), 3.53 (t, *J* = 7.0 Hz, 2H), 2.47 (s, 3H), 2.28 (td, *J* = 7.0, 2.7 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.92 (p, *J* = 7.0 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.95, 134.47, 133.19, 129.98, 127.95, 127.82, 127.12, 122.83, 85.70, 82.77, 69.53, 64.27, 50.70, 27.02, 21.83, 15.71.

HRMS (EI): *m/z* 343.0713 $[M]^+$, calculated for $[C_{18}H_{17}NO_2S_2]^+$: 343.0701.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3112, 2940, 2876, 2264, 2248, 2229, 1599, 1433, 1371, 1171, 1096

N-(cyclohex-1-en-1-ylethynyl)-N-(2-ethynylbenzyl)-4-methylbenzenesulfonamide



This compound was prepared from 4-methyl-N-(2-((trimethylsilyl)ethynyl)benzyl)benzenesulfonamide and 1-(bromoethynyl)cyclohex-1-ene using general procedure 3. Yield: 65 % (white solid).

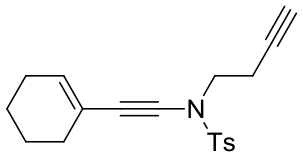
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.3 Hz, 2H), 7.47 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.42 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.30 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.25 (dt, *J* = 7.6, 1.5 Hz, 1H), 5.87 (tt, *J* = 3.8, 1.8 Hz, 1H), 4.73 (s, 2H), 3.26 (s, 1H), 2.45 (s, 3H), 2.11 – 1.99 (m, 2H), 1.98 – 1.95 (m, 2H), 1.62 – 1.45 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.62, 137.09, 134.59, 133.42, 132.82, 129.76, 129.09, 128.62, 127.88, 121.65, 119.87, 82.63, 80.93, 80.20, 72.67, 53.65, 29.23, 25.62, 22.35, 21.76, 21.56. (**1 sp^2 carbon missed probably because of peaks overlap at ppm 127.88)**

HRMS (EI): *m/z* 389.1436 $[M]^+$, calculated for $[C_{24}H_{23}NO_2S]^+$: 389.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3305, 3031, 2933, 2862, 2261, 2230, 1600, 1450, 1367, 1187, 1170, 1091

N-(but-3-yn-1-yl)-N-(cyclohex-1-en-1-ylethynyl)-4-methylbenzenesulfonamide



This compound was prepared from 4-methyl-N-(4-(trimethylsilyl)but-3-yn-1-yl)benzenesulfonamide and 1-(bromoethynyl)cyclohex-1-ene using general procedure 3. Yield: 70 % (yellowish oil).

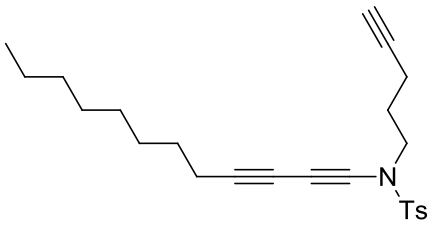
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 6.01 (dq, *J* = 4.0, 1.8 Hz, 1H), 3.53 – 3.46 (m, 2H), 2.55 – 2.48 (m, 2H), 2.45 (s, 3H), 2.10 – 2.05 (m, 4H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.65 – 1.52 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.78, 134.59, 134.56, 129.86, 127.79, 119.86, 79.95, 79.08, 72.86, 70.58, 50.25, 29.54, 25.77, 22.43, 21.80, 21.60, 18.45.

HRMS (EI): *m/z* 327.1300 $[M]^+$, calculated for $[C_{19}H_{21}NO_2S]^+$: 327.1293.

IR ($CDCl_3$): *v* (cm^{-1}) 3692, 3309, 3031, 2932, 2862, 2338, 2254, 1728, 1683, 1599, 1368, 1169, 1092

N-(dodeca-1,3-diyn-1-yl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



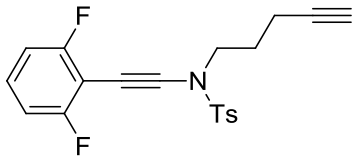
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 3.42 (t, *J* = 7.0 Hz, 2H), 2.44 (s, 3H), 2.29 (t, *J* = 7.1 Hz, 2H), 2.21 (td, *J* = 6.9, 2.7 Hz, 2H), 1.97 (t, *J* = 2.8 Hz, 1H), 1.85 (qn, *J* = 7.0 Hz, 2H), 1.55 – 1.47 (m, 2H), 1.41 – 1.34 (m, 2H), 1.30 – 1.20 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.07, 134.46, 130.04, 127.68, 84.35, 82.59, 69.55, 66.99, 64.35, 58.80, 50.41, 31.92, 29.25, 29.16, 28.98, 28.38, 26.84, 22.75, 21.78, 19.68, 15.60, 14.22.

HRMS (EI): *m/z* 397.2089 $[M]^+$, calculated for $[C_{24}H_{31}NO_2S]^+$: 397.2075.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2930, 2858, 2263, 2249, 2164, 1600, 1460, 1372, 1187, 1172, 1094

N-((2,6-difluorophenyl)ethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 2-(bromoethynyl)-1,3-difluorobenzene using general procedure 3. Yield: 66 % (yellowish solid).

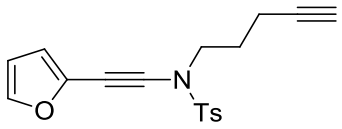
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.21 (tt, *J* = 8.4, 6.3 Hz, 1H), 6.88 (dd, *J* = 8.5, 7.0 Hz, 2H), 3.56 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.29 (td, *J* = 6.9, 2.6 Hz, 2H), 1.99 (t, *J* = 2.7 Hz, 1H), 1.94 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.89 (d, *J* = 252.7), 162.83 (d, *J* = 252.7), 145.06, 134.34, 129.99, 129.11 (t, *J* = 9.9 Hz), 127.93, 111.22 (d, *J* = 24.1 Hz), 111.22 (d, *J* = 12.9 Hz), 102.08 (t, *J* = 19.8 Hz), 91.34 (t, *J* = 2.9 Hz), 82.72, 69.54, 58.85, 50.49, 26.90, 21.82, 15.68.

HRMS (EI): *m/z* 373.0954 $[M]^+$, calculated for $[C_{20}H_{17}F_2NO_2S]^+$: 373.0948.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3050, 2939, 2878, 2246, 1623, 1582, 1469, 1371, 1241, 1172, 1095

N-(furan-2-ylethynyl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 2-(bromoethynyl)furan using general procedure 3. Yield: 45 % (yellowish oil).

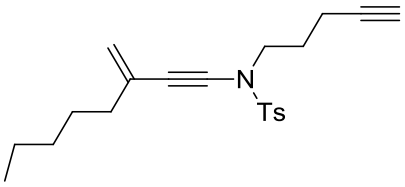
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.2 Hz, 2H), 7.39 – 7.34 (m, 3H), 6.61 (d, *J* = 2.7 Hz, 1H), 6.44 – 6.35 (m, 1H), 3.52 (t, *J* = 6.9 Hz, 2H), 2.45 (s, 3H), 2.25 (t, *J* = 6.9 Hz, 2H), 1.97 (s, 1H), 1.90 (qn, *J* = 6.9 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 145.04, 144.14, 136.70, 134.51, 130.01, 127.75, 117.39, 111.22, 86.17, 82.67, 69.54, 61.76, 50.61, 26.90, 21.79, 15.65.

HRMS (EI): *m/z* 327.0933 $[M]^+$, calculated for $[C_{18}H_{17}NO_3S]^+$: 327.0929.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3068, 2940, 2878, 2230, 1599, 1492, 1367, 1172, 1094

4-methyl-N-(3-methyleneoct-1-yn-1-yl)-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-bromo-3-methyleneoct-1-yne using general procedure 3. Yield: 58 % (colorless oil).

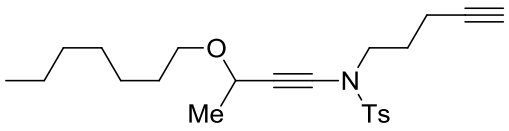
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 5.17 – 5.15 (m, 1H), 5.12 (q, *J* = 1.4 Hz, 1H), 3.46 (t, *J* = 6.9 Hz, 2H), 2.44 (s, 3H), 2.25 (td, *J* = 7.0, 2.6 Hz, 2H), 2.12 (dd, *J* = 8.2, 6.9 Hz, 2H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.87 (qn, *J* = 6.9 Hz, 1H), 1.47 (tdd, *J* = 8.7, 7.3, 6.2 Hz, 2H), 1.35 – 1.23 (m, 4H), 0.89 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.77, 134.48, 131.19, 129.87, 127.79, 119.06, 82.82, 82.02, 71.76, 69.43, 50.44, 37.44, 31.21, 27.90, 27.05, 22.62, 21.79, 15.67, 14.19.

HRMS (EI): *m/z* 357.1771 $[M]^+$, calculated for $[C_{21}H_{27}NO_2S]^+$: 357.1762.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2958, 2931, 2859, 2263, 2228, 1599, 1447, 1366, 1170, 1095

N-(3-(heptyloxy)but-1-yn-1-yl)-4-methyl-N-(pent-4-yn-1-yl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(5-(trimethylsilyl)pent-4-yn-1-yl)benzenesulfonamide and 1-((4-bromobut-3-yn-2-yl)oxy)heptane using general procedure 3. Yield: 64 % (colorless oil).

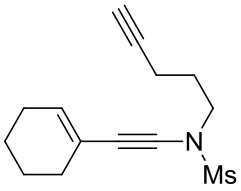
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.25 (q, *J* = 6.6 Hz, 1H), 3.56 (dt, *J* = 9.0, 6.8 Hz, 1H), 3.50 – 3.35 (m, 2H), 3.28 (dt, *J* = 9.0, 6.7 Hz, 1H), 2.44 (s, 3H), 2.24 (td, *J* = 7.0, 2.7 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.86 (qn, *J* = 6.9 Hz, 2H), 1.53 (qn, *J* = 6.9 Hz, 2H), 1.41 (d, *J* = 6.6 Hz, 3H), 1.34 – 1.22 (m, 8H), 0.96 – 0.80 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.77, 134.53, 129.84, 127.81, 82.79, 77.82, 71.35, 69.43, 68.83, 65.50, 50.30, 31.96, 29.82, 29.30, 27.03, 26.35, 22.75, 22.33, 21.77, 15.66, 14.23.

HRMS (EI): This experiment was carried out twice but no corresponding signal was observed.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2956, 2931, 2858, 2246, 1599, 1366, 1171, 1096

N-(cyclohex-1-en-1-ylethynyl)-N-(pent-4-yn-1-yl)methanesulfonamide



This compound was prepared from N-(5-(trimethylsilyl)pent-4-yn-1-yl)methanesulfonamide and 1-(bromoethynyl)cyclohex-1-ene using general procedure 3. Yield: 66 % (colorless oil).

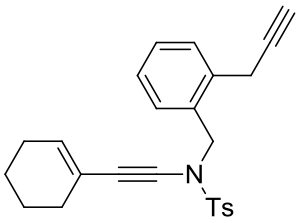
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.07 (tt, *J* = 3.6, 1.6 Hz, 1H), 3.57 (t, *J* = 6.9 Hz, 2H), 3.08 (s, 3H), 2.32 (td, *J* = 7.0, 2.7 Hz, 2H), 2.14 – 2.07 (m, 4H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.95 (qn, *J* = 7.0 Hz, 2H), 1.66 – 1.54 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.84, 119.82, 82.76, 78.84, 72.89, 69.61, 50.40, 37.97, 29.64, 27.24, 25.79, 22.44, 21.60, 15.66.

HRMS (EI): *m/z* 265.1149 $[M]^+$, calculated for $[C_{14}H_{19}NO_2S]^+$: 265.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3027, 2940, 2862, 2260, 2254, 1724, 1682, 1436, 1358, 1164

N-(cyclohex-1-en-1-ylethynyl)-4-methyl-N-(2-(prop-2-yn-1-yl)benzyl)benzenesulfonamide



This compound was prepared from 4-methyl-N-(2-(prop-2-yn-1-yl)benzyl)benzenesulfonamide and 1-(bromoethynyl)cyclohex-1-ene using general procedure 3. Yield: 40 % (yellowish oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.30 (td, *J* = 7.3, 1.9 Hz, 1H), 7.25 – 7.15 (m, 2H), 5.81 (dq, *J* = 4.1, 2.0 Hz, 1H), 4.49 (s, 2H), 3.66 (d, *J* = 2.7 Hz, 2H), 2.45 (s, 3H), 2.19 (t, *J* = 2.7 Hz, 1H), 2.01 – 1.97 (m, 2H), 1.95 – 1.87 (m, 2H), 1.57 – 1.45 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.77, 135.42, 133.90, 133.38, 131.77, 130.89, 129.80, 129.00, 128.95, 127.86, 127.05, 119.67, 81.33, 79.86, 73.10, 71.28, 53.02, 29.15, 25.57, 22.29, 21.76, 21.51. (**1 sp^3 carbon missed probably because of peaks overlap at ppm 71.28)**

HRMS (EI): *m/z* 403.1604 $[M]^+$, calculated for $[C_{25}H_{25}NO_2S]^+$: 403.1606.

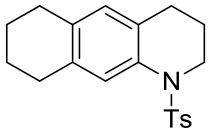
IR ($CDCl_3$): *v* (cm^{-1}) 3308, 3030, 2932, 2837, 2268, 2229, 1631, 1599, 1456, 1368, 1187, 1090

4. Catalysis and Products

All the gold-catalyzed reactions were carried out following the general procedure 6:

To a stirred solution of 0.20 mmol of ynamide starting material in chloroform (2 mL) was added RuPhosAuNTf$_2$ (5 mmol%) at room temperature and the solution was stirred at preheated 70 ℃ oil bath until TLC indicated complete consumption of starting material. Then the reaction mixture was concentrated under reduced pressure and then purified by flash column chromatography on silica gel using petroleum ether/EtOAc as the eluent.

1-tosyl-1,2,3,4,6,7,8,9-octahydrobenzo[g]quinoline



Yield: 82 % (yellowish oil); Reaction time: 10 h.

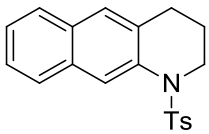
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.3 Hz, 2H), 7.49 (s, 1H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.70 (s, 1H), 3.82 – 3.69 (m, 2H), 2.77 (br, 2H), 2.68 (br, 2H), 2.38 (s, 3H), 2.35 (t, *J* = 6.8 Hz, 2H), 1.78 (qn, *J* = 3.2 Hz, 4H), 1.64 – 1.52 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.39, 137.06, 135.47, 134.28, 134.08, 129.60, 129.33, 127.86, 127.23, 125.31, 46.56, 29.37, 28.90, 26.17, 23.33, 23.30, 21.77, 21.63.

HRMS (EI): *m/z* 341.1440 $[M]^+$, calculated for $[C_{20}H_{23}NO_2S]^+$: 341.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3011, 2937, 2861, 2841, 2262, 2251, 1599, 1496, 1353, 1163, 1093

1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline



Yield: 80 % (white solid); Reaction time: 18 h.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.91 – 7.80 (m, 1H), 7.74 – 7.65 (m, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.46 (s, 1H), 7.42 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 3.95 – 3.82 (m, 2H), 2.49 (t, *J* = 6.5 Hz, 2H), 2.34 (s, 3H), 1.77 (qn, *J* = 6.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.61, 136.62, 134.86, 132.52, 131.04, 131.01, 129.62, 128.02, 127.10, 126.85, 126.80, 125.69, 122.74, 46.83, 27.32, 22.67, 21.57. (**1 sp^2 carbon missed probably because peaks overlap.)**

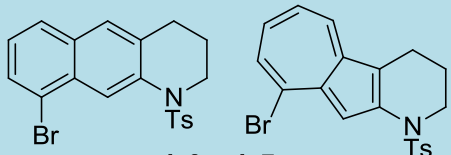
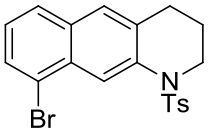
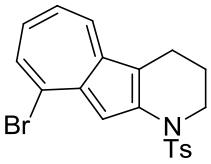
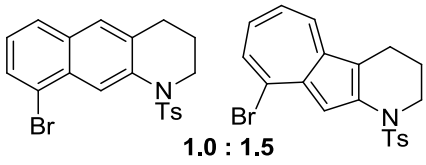
HRMS (EI): *m/z* 337.1120 $[M]^+$, calculated for $[C_{20}H_{19}NO_2S]^+$: 337.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3059, 2957, 2896, 2251, 1635, 1599, 1501, 1464, 1352, 1261, 1163, 1002

9-bromo-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

9-bromo-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine

Overall Yield: 83 % (deep bule solid); Reaction time: 18 h.

 **1.0 : 1.5**	
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.67 (d, *J* = 7.4 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.43 (s, 1H), 7.18 – 7.15 (m, 3H), 3.97 – 3.92 (m, 2H), 2.64 (t, *J* = 6.5 Hz, 2H), 2.33 (s, 3H), 1.85 (qn, *J* = 6.4 Hz, 2H).
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.83 (d, *J* = 10.2 Hz, 1H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 10.4 Hz, 1H), 7.23 – 7.13 (m, 3H), 7.07 (t, *J* = 9.6 Hz, 1H), 3.91 – 3.86 (m, 2H), 2.91 (t, *J* = 6.4 Hz, 2H), 2.31 (s, 3H), 1.99 (qn, *J* = 6.1 Hz, 2H).
 **1.0 : 1.5**	**^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.25, 144.26, 143.80, 136.52, 136.46, 136.40, 135.31, 133.61, 131.55, 131.31, 131.14, 131.06, 130.78, 129.78, 129.64, 129.62, 129.59, 128.85, 127.63, 127.32, 126.99, 126.72, 125.64, 122.46, 122.35, 120.18, 115.89, 109.82, 47.10, 46.82, 27.28, 22.57, 21.81, 21.56, 20.90. **(1 sp^3 carbon missed probably because peaks overlap at ppm 21.56)**

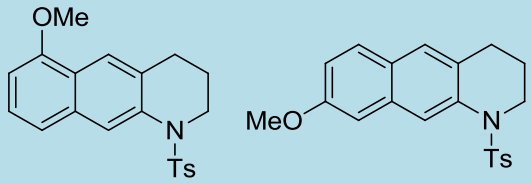
HRMS (EI) (mixture of products): *m/z* 415.0255 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242.

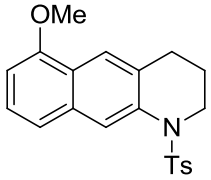
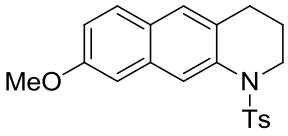
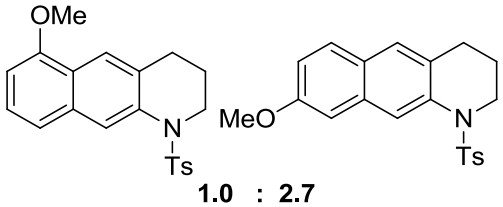
IR (mixture of products) ($CDCl_3$): *v* (cm^{-1}) 3691, 3147, 3033, 2956, 2933, 2891, 2251, 1918, 1598, 1558, 1481, 1461, 1444, 1357, 1285, 1166, 1099, 1006

6-methoxy-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

8-methoxy-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline

Overall Yield: 81 % (colorless oil); Reaction time: 18 h.

<table>
<tr><td colspan="2">

1.0 : 2.7</td></tr>
<tr><td>
</td><td>^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.87 (s, 1H), 7.48 – 7.41 (m, 3H), 7.33 (t, J = 7.9 Hz, 1H), 7.14 – 7.10 (m, 2H), 6.74 (dd, J = 7.6, 0.9 Hz, 1H), 3.97 (s, 3H), 3.90 – 3.86 (m, 2H), 2.50 (t, J = 6.4 Hz, 2H), 2.33 (s, 3H), 1.77 – 1.71 (m, 2H).</td></tr>
<tr><td>
</td><td>^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.57 (d, J = 8.9 Hz, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.36 (s, 1H), 7.13 (m, 3H), 7.07 (dd, J = 8.9, 2.5 Hz, 1H), 3.91 (s, 3H), 3.89 – 3.86 (m, 2H), 2.45 (t, J = 6.6 Hz, 2H), 2.33 (s, 3H), 1.78 – 1.71 (m, 2H).</td></tr>
<tr><td>

1.0 : 2.7</td><td>^{13}C NMR (100 MHz, $CDCl_3$) δ 157.54, 154.76, 143.56, 136.62, 136.55, 135.40, 135.36, 133.64, 133.61, 130.11, 129.59, 128.34, 128.29, 127.08, 127.06, 126.70, 126.58, 125.80, 123.05, 122.30, 121.69, 121.29, 120.42, 118.79, 105.68, 103.48, 55.50, 55.37, 46.89, 27.48, 27.07, 22.58, 21.57, 21.55. (2 sp^2 carbons and 2 sp^3 carbons missed probably because peaks overlap.)</td></tr>
</table>

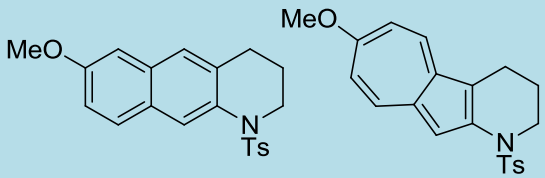
HRMS (EI) (mixture of products): *m/z* 367.1223 $[M]^+$, calculated for $[C_{21}H_{21}NO_3S]^+$: 367.1242.

IR ($CDCl_3$) **(mixture of products)**: *v* (cm^{-1}) 3691, 3064, 3007, 2957, 2844, 2256, 1634, 1609, 1502, 1465, 1362, 1247, 1165

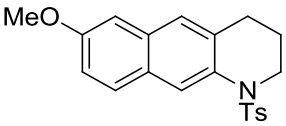
7-methoxy-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

7-methoxy-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine

Overall Yield: 77 % (colorless oil); Reaction time: 18 h.



2.0 : 1.0

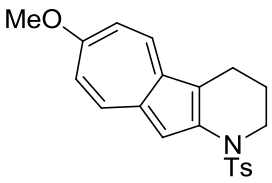


^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.74 (d, *J* = 9.1 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.34 (s, 1H), 7.13 (d, *J* = 8.1 Hz, 2H), 7.10 (dd, *J* = 6.5, 2.6 Hz, 1H), 6.99 (d, *J* = 2.6 Hz, 1H), 3.90 (s, 3H), 3.88 – 3.83 (m, 2H), 2.47 – 2.41 (m, 2H), 2.35 (s, 3H), 1.74 (qn, *J* = 6.4 Hz, 2H).

^{13}**C NMR** (100 MHz, $CDCl_3$) δ 157.77, 143.54, 136.74, 132.90, 132.33, 131.80, 129.71, 129.63, 128.04, 127.20, 125.66, 123.31, 118.67, 104.82, 55.43, 46.80, 27.29, 22.71, 21.66.

HRMS (EI): *m/z* 367.1241 $[M]^+$, calculated for $[C_{21}H_{21}NO_3S]^+$: 367.1242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3007, 2958, 2254, 1608, 1506, 1352, 1256, 1212, 1163, 1092



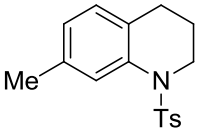
^{1}**H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 10.7 Hz, 1H), 7.80 (d, *J* = 10.9 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.54 (s, 1H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.78 (td, *J* = 10.7, 2.7 Hz, 2H), 3.90 (s, 3H), 3.89 – 3.84 (m, 2H), 2.92 (t, *J* = 6.4 Hz, 2H), 2.33 (s, 3H), 1.99 – 1.90 (m, 2H).

^{13}**C NMR** (100MHz, $CDCl_3$) δ 164.86, 143.86, 141.01, 135.85, 135.07, 133.11, 130.66, 129.76, 129.58, 127.05, 115.31, 110.80, 110.41, 107.28, 56.03, 47.24, 21.99, 21.67, 21.01.

HRMS (EI): *m/z* 367.1249 $[M]^+$, calculated for $[C_{21}H_{21}NO_3S]^+$: 367.1242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3005, 2958, 2930, 2855, 2260, 1583, 1481, 1408, 1359, 1197, 1162, 1091

7-methyl-1-tosyl-1,2,3,4-tetrahydroquinoline



Yield: 88 % (colorless oil); Reaction time: 10 h.

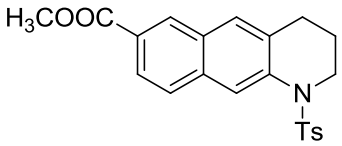
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.88 (s, 2H), 3.80 – 3.74 (m, 2H), 2.38 (t, *J* = 6.6 Hz, 2H), 2.37 (s, 3H), 2.34 (s, 3H), 1.59 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.51, 136.92, 136.75, 136.22, 129.61, 128.91, 127.71, 127.19, 126.00, 125.59, 46.63, 26.24, 21.66, 21.64, 21.41.

HRMS (EI): *m/z* 301.1133 $[M]^+$, calculated for $[C_{17}H_{19}NO_2S]^+$: 301.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3030, 2954, 2927, 2870, 2259, 1599, 1505, 1343, 1165, 1093

Methyl 1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline-7-carboxylate



Yield: 78 % (white solid); Reaction time: 18 h.

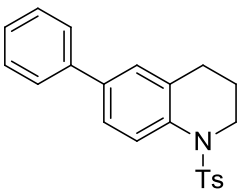
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.27 (s, 1H), 7.99 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 1H), 7.55 (s, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.3 Hz, 2H), 3.96 (s, 3H), 3.94 – 3.86 (m, 2H), 2.62 – 2.52 (m, 2H), 2.35 (s, 3H), 1.80 (qn, *J* = 6.3 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.36, 143.91, 137.21, 136.53, 134.73, 131.54, 130.09, 129.83, 129.77, 128.46, 128.19, 127.14, 127.11, 125.13, 121.75, 52.32, 46.97, 27.55, 22.56, 21.64.

HRMS (EI): *m/z* 391.1175 $[M]^+$, calculated for $[C_{22}H_{21}NO_4S]^+$: 395.1191.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 3032, 2954, 2256, 1716, 1635, 1599, 1464, 1354, 1231, 1163, 1092

6-phenyl-1-tosyl-1,2,3,4-tetrahydroquinoline



Yield: 45 % (white solid); Reaction time: 60 h.

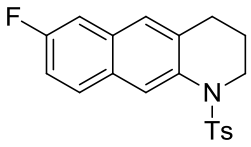
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.6 Hz, 1H), 7.59 – 7.56 (m, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.46 – 7.40 (m, 3H), 7.36 – 7.30 (m, 1H), 7.25 (s, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 3.98 – 3.73 (m, 2H), 2.53 (t, *J* = 6.7 Hz, 2H), 2.38 (s, 3H), 1.67 (qn, *J* = 6.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.69, 140.38, 137.64, 136.90, 136.36, 130.77, 129.75, 128.90, 127.70, 127.36, 127.25, 126.93, 125.28, 125.18, 46.74, 27.00, 21.68. **(1 sp^3 carbon missed probably because peaks overlap at ppm 21.68)**

HRMS (EI): *m/z* 363.1285 $[M]^+$, calculated for $[C_{22}H_{21}NO_2S]^+$: 363.1293.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3065, 3033, 2957, 2928, 2254, 1600, 1483, 1343, 1164, 1092

7-fluoro-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline



Yield: 71 % (white solid); Reaction time: 18 h.

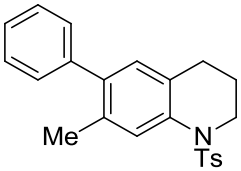
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.81 (dd, *J* = 9.0, 5.6 Hz, 1H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.39 (s, 1H), 7.29 (dd, *J* = 9.9, 2.5 Hz, 1H), 7.21 (td, *J* = 8.8, 2.6 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 3.94 – 3.82 (m, 2H), 2.52 – 2.44 (m, 2H), 2.35 (s, 3H), 1.76 (qn, *J* = 6.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.70 (d, *J* = 245.7 Hz), 143.73, 136.61, 134.33 (d, *J* = 2.8 Hz), 132.34, 131.69 (d, *J* = 9.3 Hz), 130.48 (d, *J* = 9.0 Hz), 129.70, 129.55, 127.14, 126.20 (d, *J* = 5.5 Hz), 122.99, 116.23 (d, *J* = 25.5 Hz), 109.85 (d, *J* = 20.6 Hz), 46.77, 27.33, 22.59, 21.63.

HRMS (EI): *m/z* 355.1053 $[M]^+$, calculated for $[C_{20}H_{18}FNO_2S]^+$: 355.1042.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3073, 3002, 2954, 2849, 2259, 2205, 1722, 1601, 1582, 1440, 1295, 1217, 1108

7-methyl-6-phenyl-1-tosyl-1,2,3,4-tetrahydroquinoline



Yield: 72 % (colorless oil); Reaction time: 12 h.

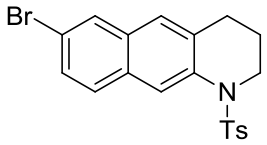
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.35 – 7.28 (m, 3H), 7.23 (d, *J* = 8.1 Hz, 2H), 6.89 (s, 1H), 3.83 – 3.78 (m, 2H), 2.47 (t, *J* = 6.7 Hz, 2H), 2.40 (s, 3H), 2.27 (s, 3H), 1.64 (qn, *J* = 6.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.62, 141.38, 138.79, 137.11, 135.98, 133.69, 130.44, 129.73, 129.28, 128.20, 127.68, 127.30, 126.92, 126.33, 46.68, 26.27, 21.69 (d, *J* = 2.2 Hz), 20.62.

HRMS (EI): *m/z* 377.1445 $[M]^+$, calculated for $[C_{23}H_{23}NO_2S]^+$: 377.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3544, 3308, 3064, 3029, 2932, 2887, 2260, 1703, 1599, 1486, 1404, 1351, 1164, 1092

7-bromo-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline



Yield: 72 % (yellowish oil); Reaction time: 18 h.

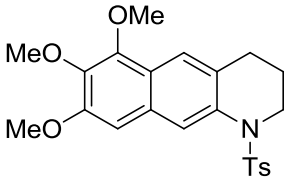
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.83 (d, *J* = 2.2 Hz, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.48 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.35 (s, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 3.93 – 3.80 (m, 2H), 2.57 – 2.46 (t, *J* = 6.4 Hz, 2H), 2.35 (s, 3H), 1.77 (qn, *J* = 6.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.82, 136.50, 135.33, 132.18, 132.00, 130.96, 129.73, 129.13, 128.85, 127.11, 126.00, 122.57, 119.56, 46.84, 27.44, 22.54, 21.65. (**1 sp^2 carbon missed probably because peaks overlap**)

HRMS (EI): *m/z* 415.0231 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2959, 2873, 2255, 1590, 1494, 1353, 1165, 1092, 1063

6,7,8-trimethoxy-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline



Yield: 78 % (white solid); Reaction time: 4 h.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.63 (s, 1H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 6.96 (s, 1H), 4.02 (s, 3H), 3.97 (s, 3H), 3.95 (s, 3H), 3.88 – 3.82 (m, 2H), 2.50 – 2.43 (m, 2H), 2.35 (s, 3H), 1.72 (qn, *J* = 6.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.02, 147.18, 143.56, 140.66, 136.68, 134.90, 129.90, 129.63, 128.61, 127.11, 121.97, 121.73, 120.88, 61.48, 61.25, 55.98, 46.89, 27.29, 22.62, 21.61.

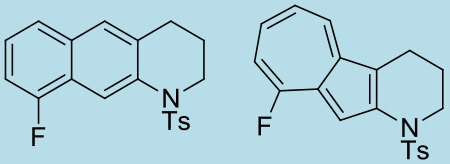
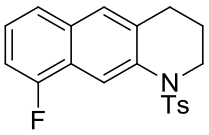
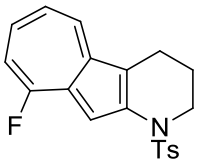
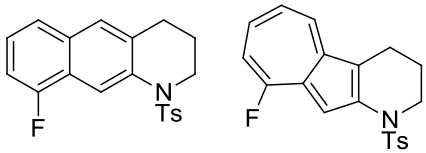
HRMS (EI): *m/z* 427.1459 $[M]^+$, calculated for $[C_{23}H_{25}NO_5S]^+$: 427.1453.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3003, 2940, 2852, 2255, 1601, 1496, 1465, 1400, 1343, 1257, 1164, 1104

9-fluoro-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

9-fluoro-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine

Overall Yield: 62 % (deep blue dense oil); Reaction time: 36 h.

 **1.3 : 1.0**	
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (s, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.36 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.22 – 7.14 (m, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 7.00 – 6.90 (m, 1H), 3.81 – 3.77 (m, 2H), 2.50 – 2.36 (m, 2H), 2.23 (s, 3H), 1.70 (qn, *J* = 6.4 Hz, 2H).
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 10.0 Hz, 1H), 7.70 (s, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.28-7.23 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.00 – 6.92 (m, 2H), 3.81 – 3.76 (m, 2H), 2.81 (t, *J* = 6.4 Hz, 2H), 2.21 (s, 3H), 1.87 (qn, *J* = 6.4 Hz, 2H).
 **1.3 : 1.0**	**^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.70 (d, *J* = 254.7 Hz), 158.56 (d, *J* = 252.5 Hz), 144.14, 143.76, 143.25 (d, *J* = 2.5 Hz), 136.44, 135.47, 135.37 (d, *J* = 1.5 Hz), 134.14 (d, *J* = 18.9 Hz), 132.22 (d, *J* = 4.6 Hz), 131.89, 131.66 (d, *J* = 15.8 Hz), 130.42 (d, *J* = 2.0 Hz), 129.75, 129.63, 127.11, 126.92, 126.79 (d, *J* = 3.0 Hz), 125.24 (d, *J* = 8.2 Hz), 124.95 (d, *J* = 21.6 Hz), 122.75 (d, *J* = 16.0 Hz), 122.55 (d, *J* = 4.1 Hz), 121.06 (d, *J* = 3.8 Hz), 115.03 (d, *J* = 1.9 Hz), 114.77 (d, *J* = 5.2 Hz), 112.93 (d, *J* = 33.3 Hz), 109.13 (d, *J* = 19.5 Hz), 101.64 (d, *J* = 3.3 Hz), 47.14, 46.76, 27.38, 22.55, 21.76, 21.51, 20.83. (**1 sp^3 carbon missed probably because peaks overlap**)

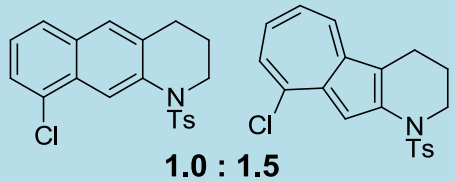
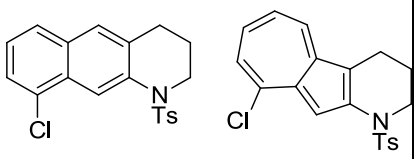
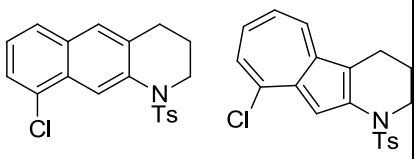
HRMS (EI) (mixture of products): *m/z* 355.1037 $[M]^+$, calculated for $[C_{20}H_{18}FNO_2S]^+$: 355.1042.

IR ($CDCl_3$) **(mixture of products)**: *v* (cm^{-1}) 3691, 3065, 2955, 2891, 2263, 2254, 1598, 1481, 1461, 1355, 1167

9-chloro-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

9-chloro-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine

Overall Yield: 77 % (deep blue dense oil); Reaction time: 36 h.

<table>
<tr><td colspan="2">
1.0 : 1.5</td></tr>
<tr><td></td><td>^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.79 (d, J = 8.4 Hz, 3H), 7.70 (d, J = 8.1 Hz, 3H), 7.48 (t, J = 8.2 Hz, 4H), 7.42 – 7.33 (m, 2H), 7.24 (d, J = 10.7 Hz, 2H), 7.20 – 7.04 (m, 8H), 6.98 (t, J = 9.7 Hz, 2H), 3.87 – 3.79 (m, 5H), 2.83 (t, J = 6.4 Hz, 3H), 2.52 (t, J = 6.5 Hz, 3H), 2.24 (s, 5H), 2.22 (s, 5H), 1.89 (p, J = 6.1 Hz, 4H), 1.75 (p, J = 6.5 Hz, 3H).</td></tr>
<tr><td></td><td>^{13}C NMR (100 MHz, $CDCl_3$) δ 144.91, 144.27, 143.82, 138.90, 136.51, 136.24, 135.46, 134.70, 133.89, 131.64, 131.62, 131.24, 131.19, 129.99, 129.85, 129.83, 129.68, 127.52, 127.35, 127.04, 125.98, 125.90, 125.68, 125.27, 122.28, 117.91, 115.64, 106.88, 47.16, 46.85, 27.38, 22.64, 21.88, 21.60, 20.91. (1 sp^3 carbon missed probably because peaks overlap at ppm 21.68)</td></tr>
</table>

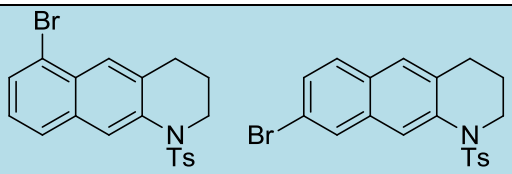
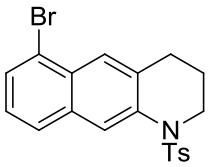
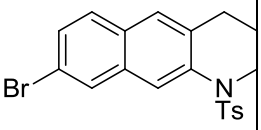
HRMS (EI) (mixture of products): *m/z* 371.0741 $[M]^+$, calculated for $[C_{20}H_{18}ClNO_2S]^+$: 371.0747.

IR (mixture of products) ($CDCl_3$): *v* (cm^{-1}) 3691, 3151, 3033, 2955, 2930, 2892, 2251, 1598, 1560, 1482, 1461, 1444, 1356, 1166, 1091

6-bromo-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline and

8-bromo-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline

Overall Yield: 66 % (colorless oil); Reaction time: 24 h.

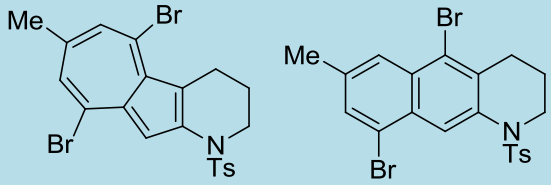
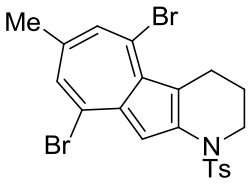
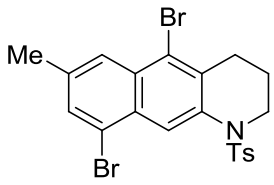
 **1.0 : 1.7**	
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.84 (s, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.68 (dd, *J* = 7.4, 1.1 Hz, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.26 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 3.95 – 3.84 (m, 2H), 2.69 – 2.51 (m, 2H), 2.35 (s, 3H), 1.79 (qn, *J* = 6.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.88, 136.60, 135.93, 133.79, 132.40, 129.79, 129.59, 129.49, 128.14, 127.19, 126.44, 126.17, 122.62, 121.73, 46.96, 27.76, 22.59, 21.65. **HRMS (EI)**: *m/z* 415.0242 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242. **IR** ($CDCl_3$): *v* (cm^{-1}) 3691, 3061, 2959, 2929, 2254, 1598, 1493, 1357, 1261, 1164, 1092
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.97 (d, *J* = 1.9 Hz, 1H), 7.53 (d, *J* = 8.6 Hz, 1H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.45 (dd, *J* = 8.7, 1.9 Hz, 1H), 7.42 (s, 1H), 7.16 (d, *J* = 8.3 Hz, 2H), 3.93 – 3.86 (m, 2H), 2.53 (t, *J* = 6.4 Hz, 2H), 2.35 (s, 3), 1.79 (qn, *J* = 6.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.82, 136.69, 136.01, 133.70, 131.28, 129.91, 129.74, 129.30, 129.01, 128.52, 127.17, 127.01, 121.22, 119.74, 46.91, 27.52, 22.60, 21.63. **HRMS (EI)**: *m/z* 415.0255 $[M]^+$, calculated for $[C_{20}H_{18}BrNO_2S]^+$: 415.0242. **IR** ($CDCl_3$): *v* (cm^{-1}) 3691, 3052, 2958, 2929, 2258, 1631, 1598, 1493, 1353, 1164, 1092

5,9-dibromo-7-methyl-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine and

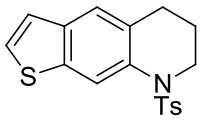
5,9-dibromo-7-methyl-1-tosyl-1,2,3,4-tetrahydrobenzo[g]quinoline

Overall Yield: 71 % (deep blue solid); Reaction time: 50 h.

0.5 equivalent of 3,5-dibromopyridine was added to the reaction before heating it up.

 **5.0 : 1.0**	
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.79 (d, *J* = 8.3 Hz, 2H), 7.49 (s, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 3.91 – 3.83 (m, 2H), 3.47 (t, *J* = 6.5 Hz, 2H), 2.51 (s, 3H), 2.35 (s, 3H), 1.93 (qn, *J* = 6.4 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.87, 144.37, 140.04, 135.46, 134.46, 131.85, 131.11, 130.17, 129.89, 129.87, 129.77, 127.22, 119.21, 113.34, 46.44, 27.10, 26.90, 22.55, 21.70. **HRMS (EI)**: *m/z* 506.9506$[M]^+$, calculated for $[C_{21}H_{19}Br_2NO_2S]^+$: 506.9503. **IR** ($CDCl_3$): *v* ($cm^{-1}$) 3691, 3158, 2958, 2928, 2862, 2261, 2253, 1600, 1562, 1481, 1461, 1363, 1165, 1090
	**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.95 (s, 1H), 7.63 (s, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 3.94 – 3.90 (m, 2H), 2.80 (t, *J* = 6.8 Hz, 2H), 2.50 (s, 3H), 2.36 (s, 3H), 1.85 (qn, *J* = 6.8 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.01, 137.15, 136.85, 136.08, 132.69, 130.94, 130.81, 129.53, 127.87, 127.49, 125.95, 124.26, 122.54, 120.82, 46.15, 29.53, 22.29, 21.78. **(1 sp^3 carbon missed probably because peaks overlap with one signal of 5,9-dibromo-7-methyl-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine at ppm 27.09)**

8-tosyl-5,6,7,8-tetrahydrothieno[3,2-g]quinoline



Yield: 60 % (yellowish dense oil); Reaction time: 50 h. 0.5 equivalent of 3,5-dibromopyridine was added to the reaction before heating it up.

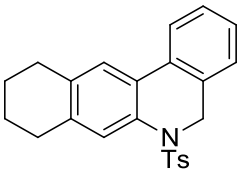
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.46 – 7.42 (m, 3H), 7.40 (d, *J* = 5.5 Hz, 1H), 7.20 (dd, *J* = 5.5, 0.8 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 3.90 – 3.74 (m, 2H), 2.40 (t, *J* = 6.6 Hz, 2H), 2.36 (s, 3H), 1.70 (qn, *J* = 6.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.63, 138.23, 137.19, 136.60, 133.83, 129.66, 129.12, 127.17, 127.11, 122.99, 122.78, 119.26, 46.75, 27.07, 22.59, 21.65.

HRMS (EI): *m/z* 343.0690$[M]^+$, calculated for $[C_{18}H_{17}NO_2S_2]^+$: 343.0701.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3152, 2956, 2928, 2854, 2264, 2255, 1600, 1454, 1352, 1164, 1092

6-tosyl-5,6,8,9,10,11-hexahydrobenzo[b]phenanthridine



Yield: 62 % (white solid); Reaction time: 18 h. 0.5 equivalent of 3,5-dibromopyridine was added to the reaction before heating it up.Without 3,5-dibromopyridine present in the reaction, the reaction time was extended to 40 h and give the same product in 45 % yield.

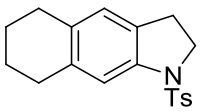
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.25 (s, 1H), 7.22 – 7.14 (m, 1H), 7.09 – 7.04 (m, 2H), 7.02 (m, 1H), 6.98 (d, *J* = 8.3 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 2.87 (br, 2H), 2.80 (br, 2H), 2.14 (s, 3H), 1.84 (m, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 142.77, 137.97, 136.60, 134.87, 133.43, 131.36, 131.15, 128.43, 128.29, 127.89, 127.48, 127.24, 127.19, 126.03, 124.20, 122.69, 50.13, 29.47, 29.42, 23.23, 23.10, 21.36.

HRMS (EI): *m/z* 389.1442$[M]^+$, calculated for $[C_{24}H_{23}NO_2S]^+$: 389.1449.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3066, 2932, 2861, 2840, 2257, 1600, 1487, 1451, 1437, 1351, 1164, 1090

1-tosyl-2,3,5,6,7,8-hexahydro-1H-benzo[f]indole



Yield: 56 % (colorless oil); Reaction time: 24 h; Temperature: 80℃ in 1,2-dichloroethane.

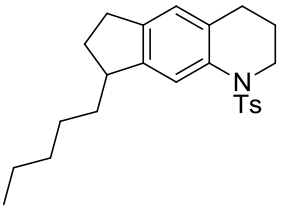
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.3 Hz, 2H), 7.34 (s, 1H), 7.23 (d, *J* = 8.2 Hz, 2H), 6.77 (s, 1H), 3.86 (t, *J* = 8.3 Hz, 2H), 2.84 – 2.75 (m, 4H), 2.69 – 2.62 (m, 2H), 2.37 (s, 3H), 1.76 (qd, *J* = 4.0, 1.6 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.94, 139.79, 136.71, 134.32, 132.66, 129.74, 129.28, 127.45, 125.59, 115.40, 50.28, 30.00, 29.31, 27.74, 23.37, 23.34, 21.67.

HRMS (EI): *m/z* 327.1293 $[M]^+$, calculated for $[C_{19}H_{21}NO_2S]^+$: 327.1293.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3308, 2932, 2860, 2263, 2249, 1599, 1484, 1353, 1247, 1165, 1094

8-pentyl-1-tosyl-2,3,4,6,7,8-hexahydro-1H-cyclopenta[g]quinoline



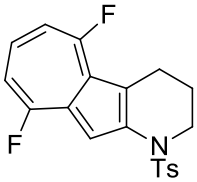
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.83 (s, 1H), 3.86 – 3.67 (m, 2H), 3.19 – 3.01 (m, 1H), 2.89 – 2.67 (m, 2H), 2.44 – 2.22 (m, 4H), 2.38 (s, 3H), 1.91 – 1.75 (m, 1H), 1.73 – 1.51 (m, 3H), 1.41 – 1.22 (m, 6H), 1.02 – 0.85 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 146.56, 143.38, 141.22, 137.12, 135.03, 129.60, 129.08, 127.31, 124.57, 120.82, 46.62, 44.94, 35.20, 32.56, 32.28, 31.08, 27.42, 26.65, 22.85, 21.98, 21.68, 14.30.

HRMS (EI): *m/z* 397.2066 $[M]^+$, calculated for $[C_{24}H_{31}NO_2S]^+$: 397.2075.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3153, 2957, 2928, 2855, 2261, 2254, 1601, 1483, 1342, 1262, 1162, 1093

5,9-difluoro-1-tosyl-1,2,3,4-tetrahydroazuleno[2,1-b]pyridine



Overall Yield: 72 % (red solid); Reaction time: 50 h.

0.5 equivalent of 3,5-dibromopyridine was added to the reaction before heating it up.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.26 (ddt, *J* = 11.0, 6.9, 4.3 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 2H), 7.01 – 6.78 (m, 2H), 3.94 – 3.75 (m, 2H), 3.17 (t, *J* = 6.1 Hz, 2H), 2.32 (s, 3H), 1.92 (qn, *J* = 6.7 Hz, 2H).

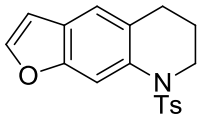
^{13}C NMR (100 MHz, $CDCl_3$) δ 163.64 (dd, *J* = 253.8, 2.2 Hz), 162.04 (dd, *J* = 253.3, 2.3 Hz), 144.24, 142.59 (t, *J* = 2.2 Hz), 135.62, 130.89 (t, *J* = 15.8 Hz), 129.85, 127.04, 124.57 (dd, *J* = 23.6, 20.6 Hz), 120.93 (dd, *J* = 20.4, 17.6 Hz), 115.09 (dd, *J* = 4.1, 1.6 Hz), 111.36 (dd, *J* = 34.8,

3.5 Hz), 110.74 (dd, *J* = 33.7, 4.0 Hz), 103.90 (d, *J* = 4.5 Hz), 46.84, 23.76 (d, *J* = 9.4 Hz), 22.08 (d, *J* = 2.3 Hz), 21.61.

HRMS (EI): *m/z* 373.0957 $[M]^+$, calculated for $[C_{20}H_{17}F_2NO_2S]^+$: 373.0948.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3153, 2955, 2928, 2852, 2260, 2255, 1596, 1482, 1460, 1365, 1217, 1166

8-tosyl-5,6,7,8-tetrahydrofuro[3,2-g]quinoline



Yield: 62 % (yellowish solid); Reaction time: 50 h. 0.5 equivalent of 3,5-dibromopyridine was added to the reaction before heating it up.

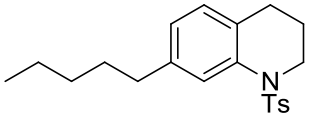
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.60 (d, *J* = 2.2 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.18 (s, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.71 – 6.59 (m, 1H), 3.88 – 3.71 (m, 2H), 2.38 (t, *J* = 6.7 Hz, 2H), 2.36 (s, 3H), 1.69 (qn, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.71, 145.89, 143.57, 136.67, 133.59, 129.62, 127.43, 127.17, 125.04, 119.96, 108.93, 105.99, 46.61, 26.97, 22.73, 21.63.

HRMS (EI): *m/z* 327.0931 $[M]^+$, calculated for $[C_{18}H_{17}NO_3S]^+$: 327.0929.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3067, 3032, 2954, 2852, 2256, 1599, 1537, 1461, 1344, 1164, 1128, 1092

7-pentyl-1-tosyl-1,2,3,4-tetrahydroquinoline



Yield: 72 % (colorless oil); Reaction time: 10 h.

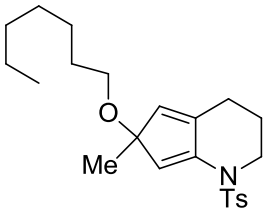
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.48 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.91 – 6.86 (m, 2H), 3.85 – 3.73 (m, 2H), 2.63 – 2.54 (m, 2H), 2.41 (t, *J* = 6.7 Hz, 2H), 2.37 (s, 3H), 1.68 – 1.57 (m, 4H), 1.38 – 1.27 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.50, 141.45, 137.00, 136.76, 129.61, 128.95, 127.71, 127.29, 125.26, 124.80, 46.74, 35.79, 31.59, 31.30, 26.40, 22.71, 21.70, 21.67, 14.23.

HRMS (EI): *m/z* 357.1764 $[M]^+$, calculated for $[C_{21}H_{27}NO_2S]^+$: 357.1762.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 2958, 2931, 2859, 2254, 1599, 1500, 1422, 1342, 1164, 1092

6-(heptyloxy)-6-methyl-1-tosyl-2,3,4,6-tetrahydro-1H-cyclopenta[b]pyridine



Yield: 95 % (colorless oil); Reaction time: 24 h.

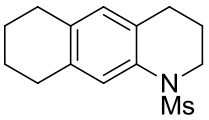
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 5.73 (d, *J* = 2.4 Hz, 1H), 5.64 (q, *J* = 2.1 Hz, 1H), 3.70 (ddd, *J* = 12.2, 7.2, 3.5 Hz, 1H), 3.63 (ddd, *J* = 12.2, 7.2, 3.5 Hz, 1H), 3.02 (m, 2H), 2.40 (s, 2H), 2.34 (t, *J* = 5.8 Hz, 2H), 1.84 – 1.71 (m, 2H), 1.39 (qn, *J* = 7.0 Hz, 2H), 1.34 (s, 3H), 1.30 – 1.17 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 144.08, 135.92, 135.71, 135.17, 134.90, 129.57, 127.61, 116.98, 85.97, 64.34, 46.63, 32.02, 30.89, 29.39, 26.20, 23.83, 23.21, 23.01, 22.79, 21.70, 14.27.

HRMS (EI): *m/z* 403.2176$[M]^+$, calculated for $[C_{23}H_{33}NO_3S]^+$: 403.2181.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3392, 2931, 2859, 2258, 1706, 1600, 1409, 1334, 1162, 1079

1-(methylsulfonyl)-1,2,3,4,6,7,8,9-octahydrobenzo[g]quinoline



Yield: 83 % (white solid); Reaction time: 12 h.

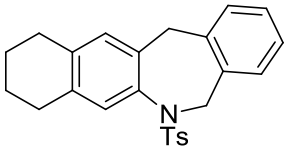
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 6.83 (s, 1H), 3.84 – 3.71 (m, 2H), 2.88 (s, 3H), 2.78 (t, *J* = 6.8 Hz, 2H), 2.74 (br, 2H), 2.69 (br, 2H), 2.02 – 1.92 (m, 2H), 1.77 (qn, *J* = 3.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.93, 134.35, 133.82, 130.02, 126.44, 123.22, 46.67, 38.53, 29.40, 28.82, 26.71, 23.29, 23.25, 22.42.

HRMS (EI): *m/z* 265.1125 $[M]^+$, calculated for $[C_{14}H_{19}NO_2S]^+$: 265.1136.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3013, 2937, 2861, 2842, 2264, 2254, 1602, 1501, 1420, 1339, 1155, 1087

6-tosyl-2,3,4,6,7,12-hexahydro-1H-benzo[e]naphtho[2,3-b]azepine



Yield: 81 % (white solid); Reaction time: 24 h.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 – 7.06 (m, 3H), 7.04 – 7.00 (m, 2H), 6.88 (s, 1H), 4.99 (s, 2H), 3.59 (s, 2H), 2.75 – 2.68 (m, 4H), 2.41 (s, 3H), 1.75 (qn, *J* = 3.3 Hz, 4H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 143.28, 138.23, 137.54, 137.24, 136.63, 136.54, 135.30, 134.31, 129.77, 129.62, 129.59, 129.39, 128.02, 127.22, 127.17, 126.65, 52.59, 38.76, 29.15, 29.10, 23.11, 23.04, 21.66.

HRMS (EI): *m/z* 403.1602 $[M]^+$, calculated for $[C_{25}H_{25}NO_2S]^+$: 403.1606.

IR ($CDCl_3$): *v* (cm^{-1}) 3691, 3065, 3020, 2933, 2861, 2258, 2249, 1599, 1496, 1438, 1344, 1162, 1095

université PARIS-SACLAY | ÉCOLE DOCTORALE INTERFACES Approches Interdisciplinaires : Fondements, Applications et Innovation

Titre : Nouvelles Transformations d'ynamides catalysées par l'or

Mots clés : or, allénamides, Vinylidène d'or, Catalyse duale à l'or

Résumé : Ce dernier, possédant une activité catalytique unique, donne accès à un bon nombre de nouvelles synthèses de composés, jusque-là inaccessible en utilisant d'autres méthodes.
Les ynamides, un sous-groupe d'alcynes hétéro-substitués, sont des intermédiaires de synthèse ayant une réactivité et une stabilité modulable. Ils trouvent leur application dans des réactions telles que les additions, les cycloadditions et les cycloisomérisations.
Dans ce manuscrit sont présentés deux travaux impliquant des réactions d'ynamides en présence d'un catalyseur à l'or.

(1) Réarrangement d'éthers de propargyliques d'ynamides catalysé par l'or (I) : Un accès pratique aux allénamides substitués.

(2) Catalyse duale à l'or : Une synthèse originale de dérivés tertahydroquinolines par un mécanisme formel d'addition [4+2]

Title : Gold-Catalyzed Novel Transformations of Ynamides

Keywords : Gold, Allenamide, Gold vinylidene, dual gold catalysis

Abstract :
Gold catalysts, possessing unique catalytic reactivity, intrigued a large number of novel approaches to target molecules which cannot be accessed by other methodology. Ynamide, which belongs to a subclass of hetero-substituted alkynes, represents a versatile building block with balanced reactivity and stability and found a series of applications in useful transformations, such as additions, cycloadditions and cycloisomerizations.
As part of our ongoing interest in gold catalysis and ynamide chemistry, in this manuscript, two works involving ynamide in the presence of gold catalyst was presented:

(1). Gold(I)-Catalyzed Rearrangement of Propargyl Ethers of ynamides: A Practical Method for the synthesis of Substituted Allenamides

(2). Dual gold catalysis: a unique approach to derived-tetrahydroquinolines by a formal [4+2] pathway