Gold-Catalyzed Regio- and Stereoselective Acyloxyalkynylations and Cycloadditions of Alkynes

Presented by:

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From Shanxi, China

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Oral examination: December 14th, 2022

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Gutachter: Prof. Dr. A. Stephen K. Hashmi

Prof. Dr. Milan Kivala

GESAMTFAKULTÄT FÜR MATHEMATIK, INGENIEUR- UND NATURWISSENSCHAFTEN

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Contents

Publications

[1] **Y. Liu**, M. C. Dietl, C. Han, M. Rudolph, F. Rominger, P. Krämer, A. S. K. Hashmi. "Synthesis of Amide Enol 2-Iodobenzoates by the Regio- and Stereoselective Gold-Catalyzed Acyloxyalkynylation of Ynamides with Hypervalent Iodine Reagents" *Org. Lett.* **2022**, *24*, 7101–7106.

[2] **Y. Liu**, C. Han, H, Shi, A. Mackenroth, L. Zhang, M. Rudolph, F. Rominger, A. S. K. Hashmi. "Gold-Catalyzed Regio- and Stereoselective α-Acyloxy-β-Alkynylation of Ynol Ethers" submitted to The Journal of Organic Chemistry, **2022**.

[3] **Y. Liu**, M. C. Dietl, R. Heckershoff, C. Han, M. Rudolph, H. Shi, M. Rudolph, F. Rominger, A. S. K. Hashmi. "Gold-Catalyzed Formal [4+2] Cycloaddition as Access to Spirocyclic Oxindoles from Alkynes and Isatin-Derived Ketimines" manuscript under preparation, **2022**.

[4] C. Han, X. Tian, L. Song, **Y. Liu**, A. S. K. Hashmi. "Tetra-Substituted Furans by a Gold-Catalyzed Tandem C(sp^3)–H Alkynylation/Oxy-Alkynylation Reaction" *Org. Chem. Front.*, **2021**, *8*, 6546–6552.

[5] C. Han, **Y. Liu**, X. Tian, F. Rominger, A. S. K. Hashmi. "Dual Gold/Silver Catalysis: Indolizines from 2-Substituted Pyridine Derivatives via a Tandem C(sp3)–H Alkynylation/Iminoauration" *Org. Lett.* **2021**, *23*, 9480-9484.

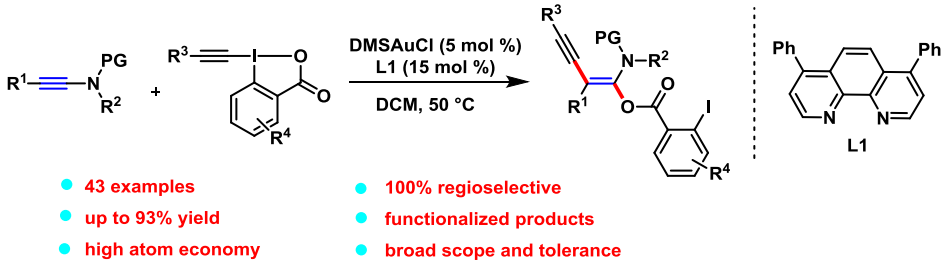
Abbreviations

Ar	Aryl
Bu	Butyl
calcd.	Calculated
CPs	4-Chlorobenzenesulfonyl
Cy	Cyclohexyl
DCM	Dichloromethane
DCE	1,2-Dichloroethane
DMF	N,N'-Dimethyl formamide
DMS	Dimethyl sulfide
DMSO	Dimethyl sulfoxide
EDG	Electro-donating group
EA	Ethyl acetate
EI	Electron ionization
eq.	Equivalent
ESI	Electrospray Ionization
Et	Ethyl
EWG	Electro-withdrawing group
GC	Gas chromatography
H	hour
Hex	Hexyl
HRMS	High resolution mass spectrometry
Hz	Herz
IR	Infrared
Mp	Melting point
m/z	mass per charge
Me	methyl
Mes	Mesityl

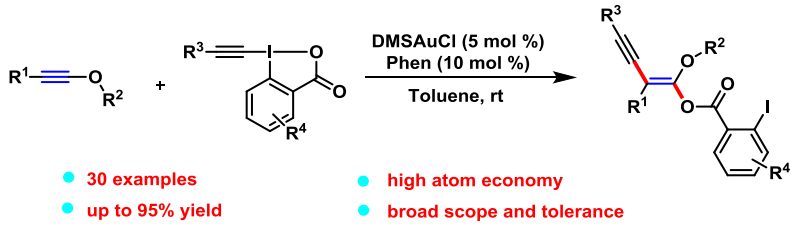
MHz	Megahertz
min	minute
Ms	Mesyl
MS	Mass spectrometry
NBS	*N*-bromo succinimide
NHC	*N*-heterocyclic carben
NIS	*N*-iodo succinimide
NMR	Nuclear magnetic resonance
Ns	4-nitrobenzenesulfonyl
PE	Petroleum ether
Ph	Phenyl
Pr	Propyl
Rt	room temperature
R_f	Ratio of fronts
T	*tert*
Tf	Trifluoromethylsulfonyl
THF	Tetrohedrofuran
TLC	Thin layer chromatography
TMS	Trimethyl silyl
TIPS	Triisopropyl silyl
Ts	4-Toluenesulfonyl

Abstract

In Chapter 2, multi-substituted alkenes are accessible by a gold-catalyzed acyloxyalkynylation of ynamides with ethynylbenziodoxolones (EBXs) in an atom-economic fashion. The EBX reagents act as bifunctional reactants providing both the nucleophilic carboxylate as well as the alkynyl entity. Overall this cascade involves the formation of an alkynyl Au(III) species, stereoselective C(sp)-C(sp^2) bond formation and C-O coupling at the alkynyl position of the ynamides. The introduced method features mild conditions and wide substrate scope. A number of tetrasubstituted amide enol 2-iodobenzoates bearing diverse functionalities were prepared in good to excellent yield. DFT calculations exlain the observed regioselectivity. The synthetic potential of the sequence was further documented by a number of selected follow-up transformations

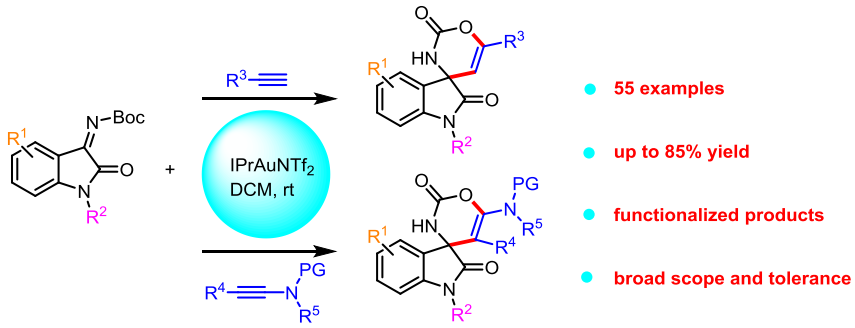


In Chapter 3, Tetrasubstituted alkenes including the ester and ether group, is of great interest in chemistry and material sciences. A variety of tetrasubstituted enol ether 2-iodobenzoate derivatives were prepared in good yields at room temperature through a gold-catalyzed acyloxyalkynylation of ynol ethers with ethynylbenziodoxolones (EBXs), which act as bifunctional reactants in an atom-economic fashion. Furthermore, the mechanism involves an in situ formed alkynyl Au(III) species and a gram-scale reaction was efficiently conducted.



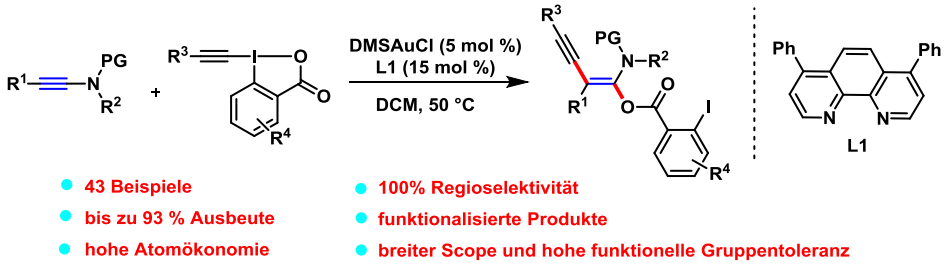
In Chapter 4, an efficient method for the construction of highly functionalized new spirooxindolocarbamates from a gold-catalyzed cycloaddition reaction of terminal alkyne and ynamides with isatin-derived ketimines is described. This protocol features easily accessible starting materials and good functional group compatibility,

enabling the introduction of various functionalized alkyne groups into cyclic carbamates. Gram-scale synthesis and proposed mechanism are also presented.

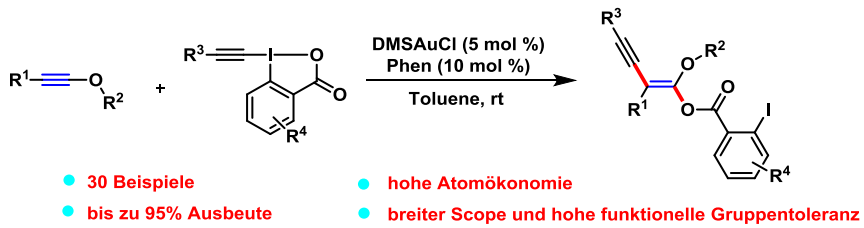


Kurzzusammenfassung

In Kapitel 2 sind mehrfach substituierte Alkene atomökonomisch durch eine Gold-katalysierte Acyloxyalkinylierung von Inamiden mit Ethinylbenziodoxolonen (EBXs) zugänglich. Die EBX-Reagenzien wirken als bifunktionelle Reaktanten, die sowohl das nucleophile Carboxylat als auch die Alkinyleinheit bereitstellen. Insgesamt beinhaltet diese Kaskade die Bildung einer Alkinyl-Au(III)-spezies, stereoselektive C(sp)-C(sp^2)-Bindungsbildung und C-O-Kupplung an der Alkinylposition der Inamide. Die vorgestellte Methode zeichnet sich durch milde Bedingungen und einen breiten Substratbereich aus. Eine Reihe von tetrasubstituierten amid-enol-2-iodbenzoaten mit unterschiedlichen Funktionalitäten wurde in guter bis ausgezeichneter Ausbeute hergestellt. DFT-Rechnungen erklären die beobachtete Regioselektivität. Das Synthesepotential der Sequenz wurde durch eine Reihe ausgewählter Folgetransformationen weiter dokumentiert

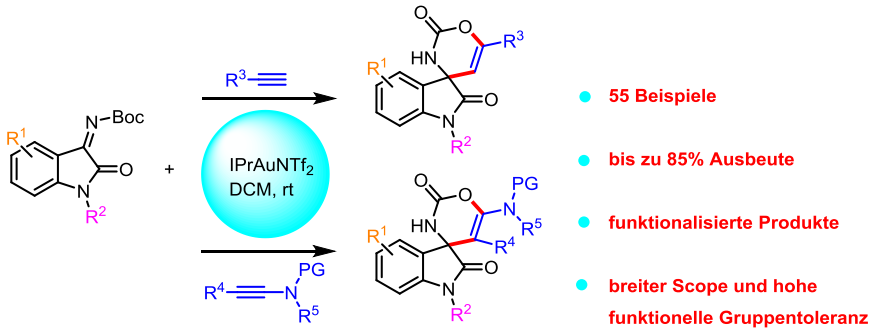


Tetrasubstituierte Alkene, unter anderem die Ester und Ether als funktionelle Gruppen aufweisen, sind von großem chemischen und materialwissenschaftlichem Interesse. Daher wurde in Kapitel 3 eine Vielzahl von tetrasubstituierten Enolether-2-iodbenzoat-derivaten in guten Ausbeuten bei Raumtemperatur durch die Gold-katalysierte Acyloxyalkinylierung von Inolethern mit Ethinylbenziodoxolonen (EBXs), die als bifunktionelle Reaktanten auf atomökonomische Weise wirken, hergestellt. Darüber hinaus umfasst der Mechanismus eine *in situ* gebildete Alkinyl-Au(III)-spezies, und eine Reaktion im Grammmaßstab wurde effizient durchgeführt.



In Kapitel 4 wird eine effiziente Methode zum Aufbau hoch funktionalisierter neuer

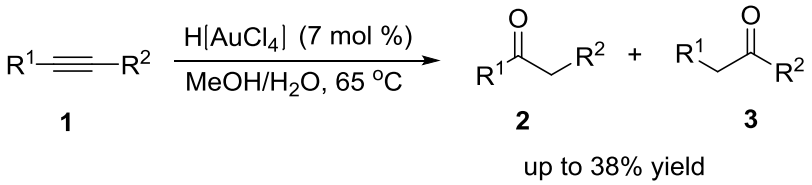
Spirooxindolocarbamate mittels einer Gold-katalysierten Cycloadditionsreaktion von terminalem Alkin und Inamiden mit von Isatin abgeleiteten Ketiminen beschrieben. Dieses Protokoll zeichnet sich durch leicht zugängliche Ausgangsmaterialien und eine gute Kompatibilität mit funktionellen Gruppen aus, was die Einführung verschiedener funktionalisierter Alkingruppen in cyclische Carbamate ermöglicht. Die Synthese im Grammmaßstab und der vorgeschlagene Mechanismus werden ebenfalls vorgestellt. Darüber hinaus wurde die Struktur der Verbindungen auf ihre Antikrebswirkung getestet und sie spielt eine Rolle in verschiedenen Bereichen wie Medizin, Agro und Polymerchemie.



Chapter 1. General Introduction

1.1 Gold Catalysis

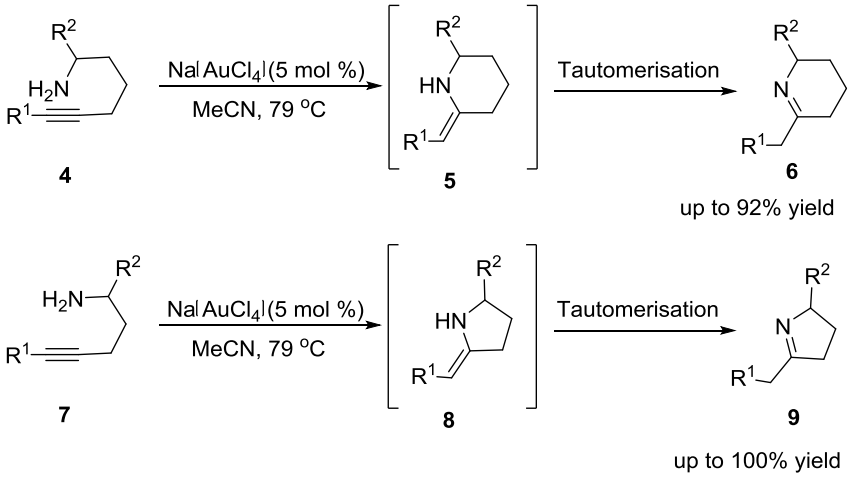
For thousands of years, gold has been considered to be the most valuable metal throughout the world and most civilizations have considered gold as synonym of power, purity, beauty and wealth. Low catalytic activity—also known as "catalytically dead"—was thought to exist in gold, as a result of its highly positive normal potential and as a result, only its organometallic chemistry and stoichiometric coordination were thoroughly studied for a long period. Gold can adopt the oxidation states -1, 0, +1, +2, +3, and +5. So the gold was chemically ignored and misconceived as an inert element. However, until in the 19th century it was extremely common to refer to priceless alkaloid bases as tetrachloroaurates. after their difficult isolation from natural sources.[1] In 1976, the first homogeneous gold-catalyzed reaction was reported by Thomas, who among working with stoichiometric tetrachloroauric acid and alkynes in aqueous methanol, observed major products ketones **2** and **3** (Scheme 1-1).[2]



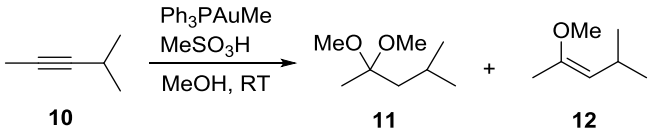
Scheme 1-1 Au(III)-catalyzed with alkynes, arenes and cyclopropanes

But it took until 2000 before a paradigm shift happened.[3] Among the many uses for gold, a catalyst is one of its most popular uses, especially in the field of heterogeneous catalysts has provoked enthusiasm among synthetic chemists. In 1987 and 1991, Utimoto's group[4] successfully achieved intramolecular addition of 5-alkynylamines to make 2,3,4,5-tetrahydropyridines using the gold salts as catalyst, which effectively generate acetals or ketones from unactivated alkynes (Scheme 1-2). Teles[5] later described extremely intermolecular addition of alkynes with alcohols by Au(I) catalyst under benign circumstances (Scheme 1-3). They all demonstrated that for cationic gold(I) species produced outstanding TOFs (turnover frequencies) and TONs

(turnover numbers).



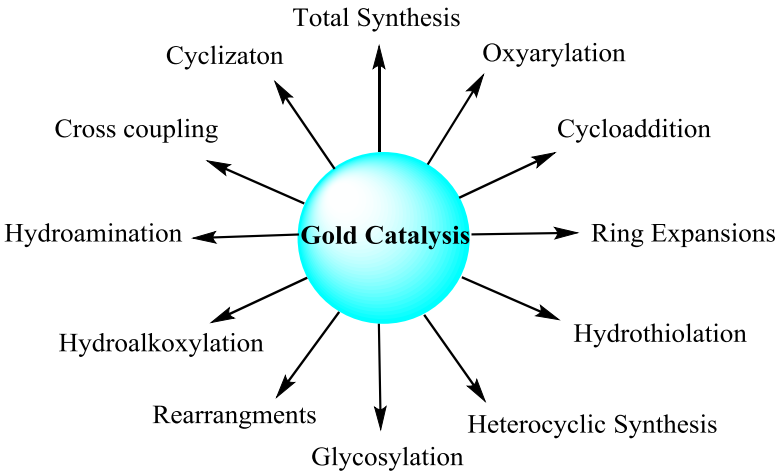
Scheme 1-2 Au(III) catalyzed hydroamination of alkynes



Scheme 1-3 Gold(I) catalyzed alkynes with alcohols

In recent years, due to its high catalytic activity, benign reaction conditions, oxygen tolerance, excellent chemoselectivity, and favorable functional-group compatibility, homogeneous gold-catalysis has received widespread recognition for a wide range of useful synthetic methodologies.[6] Numerous natural products, physiologically active compounds, and pharmaceutical molecules have been synthesized using these techniques.[7] Au(I) and Au(III) are two reactive oxidation states in which homogeneous gold catalysts are typically found. Now, it has been demonstrated that both reactive species carry out a wide range of catalytic processes.[8] Usually, gold(I) is typically a soft *Π*-acid that can selectively activate C-C multiple bonds in mild circumstances. Those tethered or conjugated to strained small ring systems including alkenes, allenes and alkynes that can be actively activated dues to the catalyst's capacity to preferentially activate π-rich systems in the gold(I) catalytic process.[9a]- [9f] However, gold is relatively stable in mild oxidants, possibly because of its high redox potential that have led to the development of numerous flexible oxidative approaches using gold(I) or gold(III) catalysis.

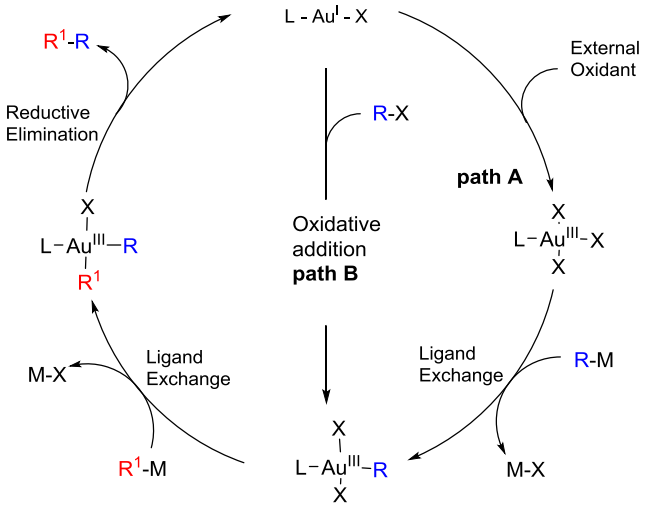
In addition, when powerful oxidants are present, gold can be oxidized from the



oxidation state +1 to +3, and subsequently undergo reductive elimination, which represents another reactivity pattern. Hence, the reactions will cover gold(I)/gold(III) catalytic cycles and the π-Lewis acid Au(I).

1.2 Redox Gold(I)/Gold(III) Catalysis

Traditionally, transition metals have been used to catalyze coupling processes, oxidation of the metal is achieved via an oxidative addition process usually involving M^n/M^{n+2} redox cycles which proceeds through a two-electron oxidation and a reduction. However, gold(I) is highly reluctant to undergo oxidation due to its relatively gold(I)/gold(III) pair has a high redox potential (E^0 = +1.41 V). In order to overcome this potential, two main strategies for Au(I)/Au(III) cycle reactions exsist: the employment of highly electrophilic reagents and powerful exogenous oxidants, for

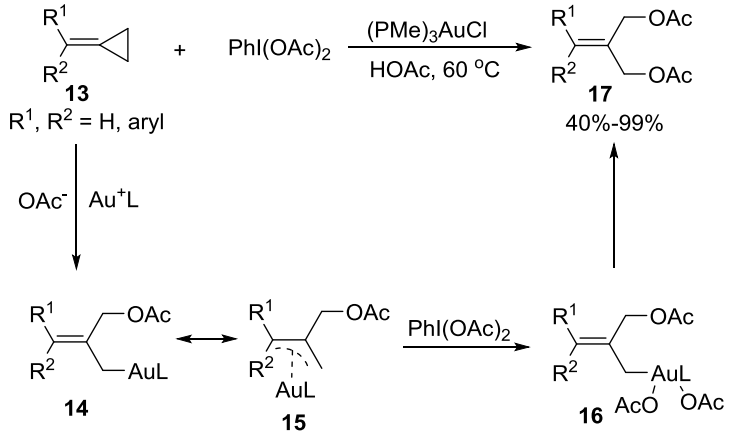


Scheme 1-4 General redox gold catalytic cycle.

example, electrophilic fluorinating reagents[9g]-[9h] or hypervalent iodine reagents.[9i]-[9l] The generalised mechanism for a redox gold-catalysed coupling process firstly has an oxidation of gold(I) to gold(III), then two subsequent transmetalation type events, then, as shown in Scheme 1-4, the new product is produced via reductive elimination, and gold(I) catalyst be reformed simultaneously.

1.2.1 Redox Gold Catalysis with External Oxidants

In Au(I)/Au(III) catalysis, hypervalent iodine reagents for iodine-based oxidants have nearly always been used. The "octet rule" is broken by the iodine atom in the iodine-containing compounds, but valence shell really has more than eight electrons. The PIDA as moderately potent oxidants is the most frequently applied in oxidative gold catalysis. Shi's group used gold(I) catalyst to accelerate the transformation of MCPs diacetoxylated, which involves the redox of gold in 2010.[10] As depicted in Scheme 1-5, AcO-engages in a nucleophilic assault on Au(I)-activated MCP **13** to produce intermediate **14** or allyl-Au(I) species **15**. The acetylated Au(III) species **16** is produced after $PhI(OAc)_2$ oxidizes the intermediates **14** or **15**.

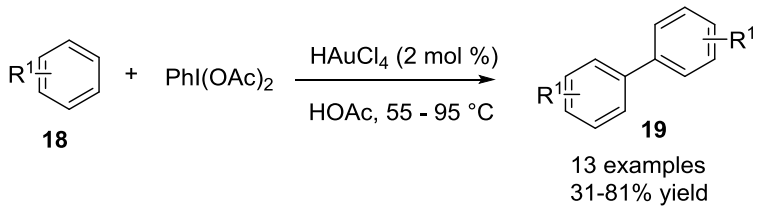


Scheme 1-5 Au(I)-catalyzed MCPs diacetoxylation with $PhI(OAc)_2$

16 is subsequently subjected to reductive elimination, producing the final diacetoxylated product **17**. Due to the potent interaction between $PhI(OAc)_2$ and gold(I)-catalyst, the cyclopropane ring can only be activated at the single bond. A bond is cleaved as a result, and the nucleophilic reagent goes on to functionalize it.

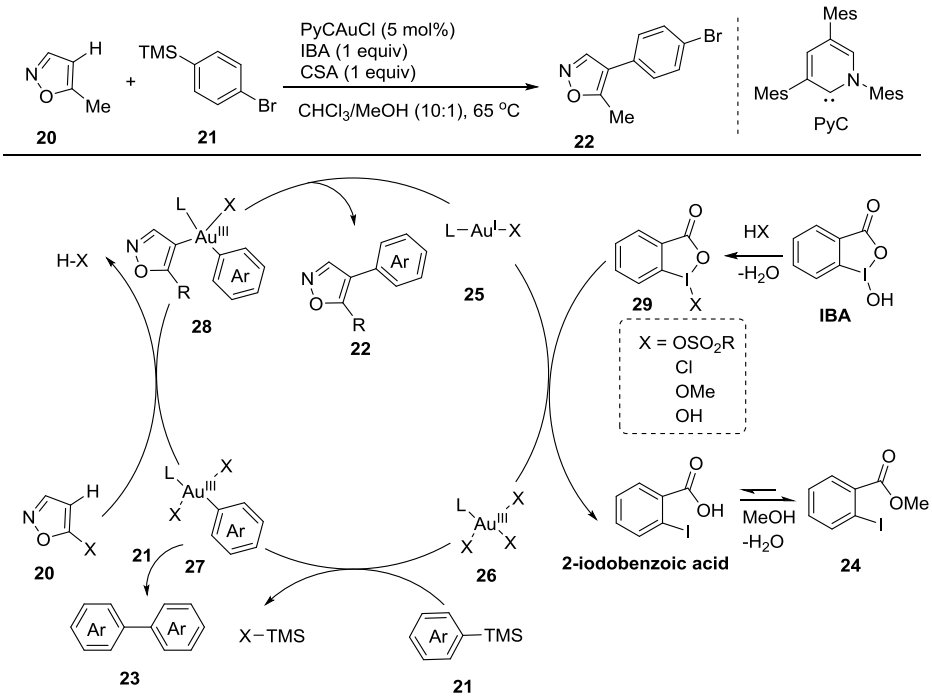
In 2008, a generalized moderate oxidative homo-coupling of arenes that was revealed

by Tse's group, the oxidant was $PhI(OAc)_2$. It doesn't require any substrate or solvent pre-treatment and may be handled easily in the air. Ag salt is not necessary for the reaction process to increase reactivity and it was the first instance of a simple arene oxidative homo-coupling that was successful. (Scheme 1-6).[11]



Scheme 1-6 Gold-catalyzed non-activated arenes coupling

Itami and Segawa achieved the oxidative C-H arylation of heteroarenes using ligand "PyC" coupling with kinds heteroarenes under gold catalysis in 2015. 2-Pyridylidene ligand as a special N-heterocyclic carbene that is able to facilitate C-H arylation of heterocycles compared to traditional ligands including classical N-heterocyclic carbine or triphenylphosphine. In the mechanism the gold(III) species **26** is formed from 25 by the oxidant **29** (which is easily accessible from IBA by exchanging hydroxy group.

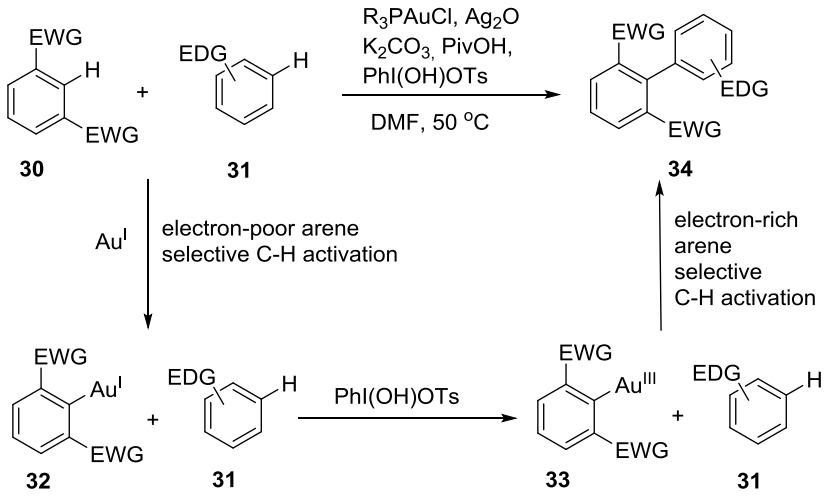


Scheme 1-7 Au(I/III)-catalyzed C–H arylation of heteroarenes

In a chloroform/methanol solution, 2-iodobenzoic acid was smoothly transformed to

24 at 65 °C. Monoarylated gold(III) intermediate **27** is produced via group exchange of arylsilane **21** and gold(III) complex **26**. Diarylated gold(III) species **28** are produced when heteroarene **20** and **27** are electrophilically metalated while simultaneously producing an acid. Finally, the coupling product **22** and the regeneration of gold(I) species **25** are released by the reductive elimination from **28**. The homocoupling byproduct **23** is probably caused by the disproportionation of **27** or by the over-transmetalation of arylsilane **21** with gold(III) species **27** (Scheme 1-7).[12]

In 2013, Larrosa proved that altering the oxidation state of the Au species can totally influence the selectivity of C-H activation of arenes with electron-rich or -poor. An initial reaction with an AuI salt would involve a combination of an electron-deficient **30** and an electron-rich **31** arene that would result in selective C-H activation of **30**.

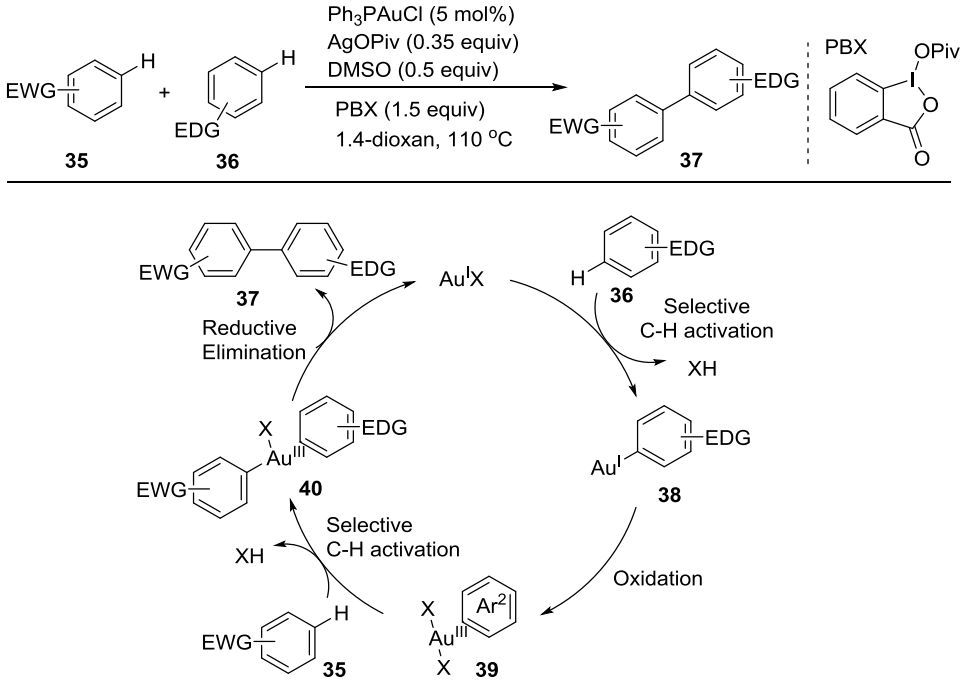


Scheme 1-8 Au-catalyzed C-H activation of arenes cross-coupling

Aryl-AuI species **32** would be transformed into Au^{III} complex **33** by the addition of an oxidant, and following reductive elimination, this compound would selectively activate the C-H bond of electron-rich arene to create biaryl **34** (Scheme 1-8).[13]

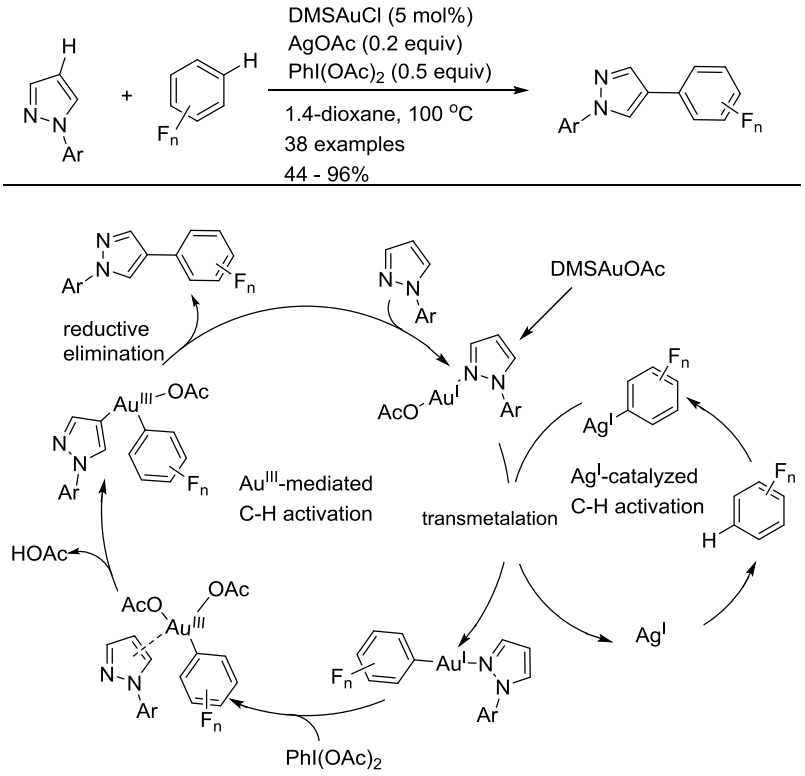
Later, the same authors developed the first approach for an arene oxidative cross-coupling mediated by Au(I/III) through double C-H activation. Au(I) catalysts can well activate C-H bonds for electron-deficient aromatics and heteroaromatics, especially for strongly acidic C-H bonds has good regioselectivity. With scope and regioselectivity suggestive of an electrophilic aromatic substitution, Au(III) species **39** demonstrates a well-known selectivity for C-H activation of electron-rich arenes

(Scheme 1-9).[14]



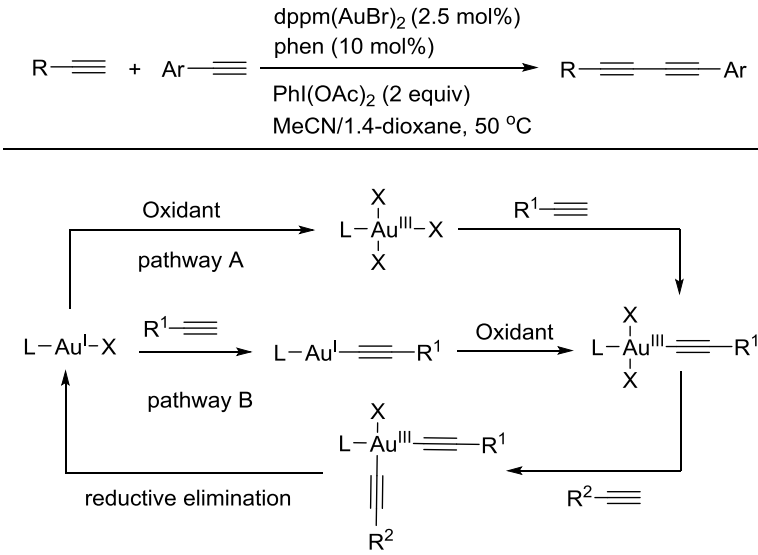
Scheme 1-9 Gold-catalyzed arenes cross-coupling

In 2019, a very efficient and operationally straightforward Au/Ag-catalyzed fluoroarenes with pyrazoles cross-dehydrogenative biaryl coupling was created by S. Li, J. Xie and C. Zhu. With good functional group compatibility, a lot of biheteroaryl compounds were produced in this reaction in yields ranging from modest to good. In Scheme 1-10, a catalytic cross-dehydrogenative biaryl reaction between Au and Ag is proposed. First, a H/D exchange demonstrates that an AgOAc-catalyzed C-H functionalization of the multifluoroarene in the production of Ag-Ar^{Fn}. The silver-catalyzed cycle is subsequently completed by the quick transmetalation between the intermediates Ag-Ar^{Fn} and [AcOAu-pyrazole]. Ar^{Fn}-Au(I) is then further oxidized by PIDA to produce Ar^{Fn}-Au(III), which is then followed by activating the C-H bond of N-phenylpyrazole to produce the Ar^{Fn}-Au(III)-Ar complex. Then, the biaryl products are produced from the tricoordinate diaryl-Au(III) complex through reductive elimination, which also restarts the gold catalytic cycle.[15]



Scheme 1-10 Dual-catalyzed Au/Ag cross-dehydrogenation of biaryl

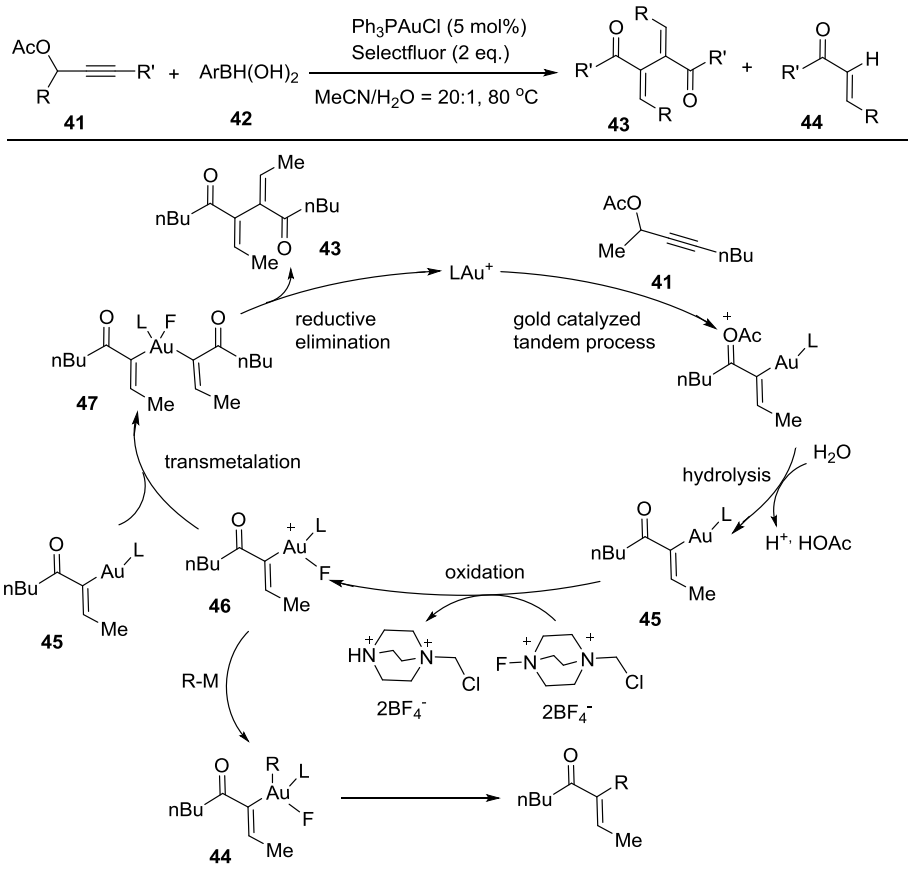
In 2014, the first oxidative cross-coupling of alkynes to asymmetric diynes was accomplished by Shi's group using gold-catalyst. The ligand and $PhI(OAc)_2$ were found to be the two most important ingredients in this transformation, which produced the required conjugated diynes with high selectivity and substrate tolerance in medium yield. Two alternative routes using Au(I) as the precatalyst are suggested



Scheme 1-11 Gold-catalyzed terminal alkynes cross-coupling

(Scheme 1-11). Prior to the creation of gold acetylide (route **A**), in the process of Au(I) salt, or at the course of gold(I) acetylide, oxidation may take place (path **B**).[16]

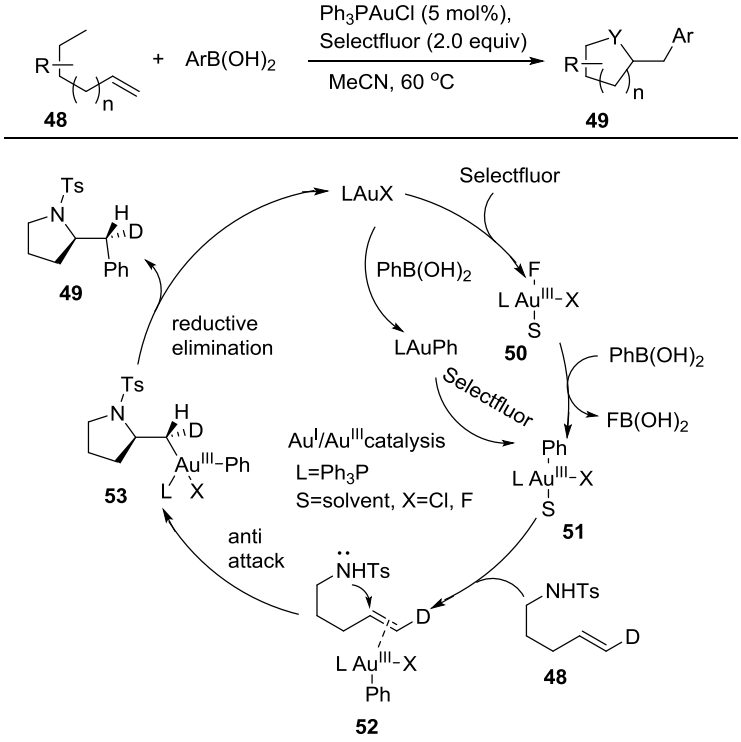
The Selectfluor is one of the electrophilic fluorine reagents that can possible oxidize the state of Au(I) to Au(III). In 2009, Zhang'group published the first instances that gold catalysis with oxidant selectfluor in the reaction.[17] According to Scheme 1-12, when the intermediate **45** from the tandem reactions of propargylic acetate **41** is hydrolyzed, Selectfluor oxidizes it to produce the Au(III) species **46**. The diorganogold(III) intermediate **47** may result from the transmetalation of **45** to **46**. This intermediate may then, by reductive elimination, generate **42** and the gold(I) catalyst.



Scheme 1-12 Gold-catalyzed propargylic acetates oxidative coupling

In 2010, Zhang showed how to quickly access a number of substituted N- or O-heterocycles by carboaminations, carbolactonizations of terminal alkenes and carboalkoxylations using gold catalysis oxidative. In this study, $C(sp^3)$-$C(sp^2)$ bonds are converted from $C(sp^3)$-Au bonds by cross-coupling way for the first time, which

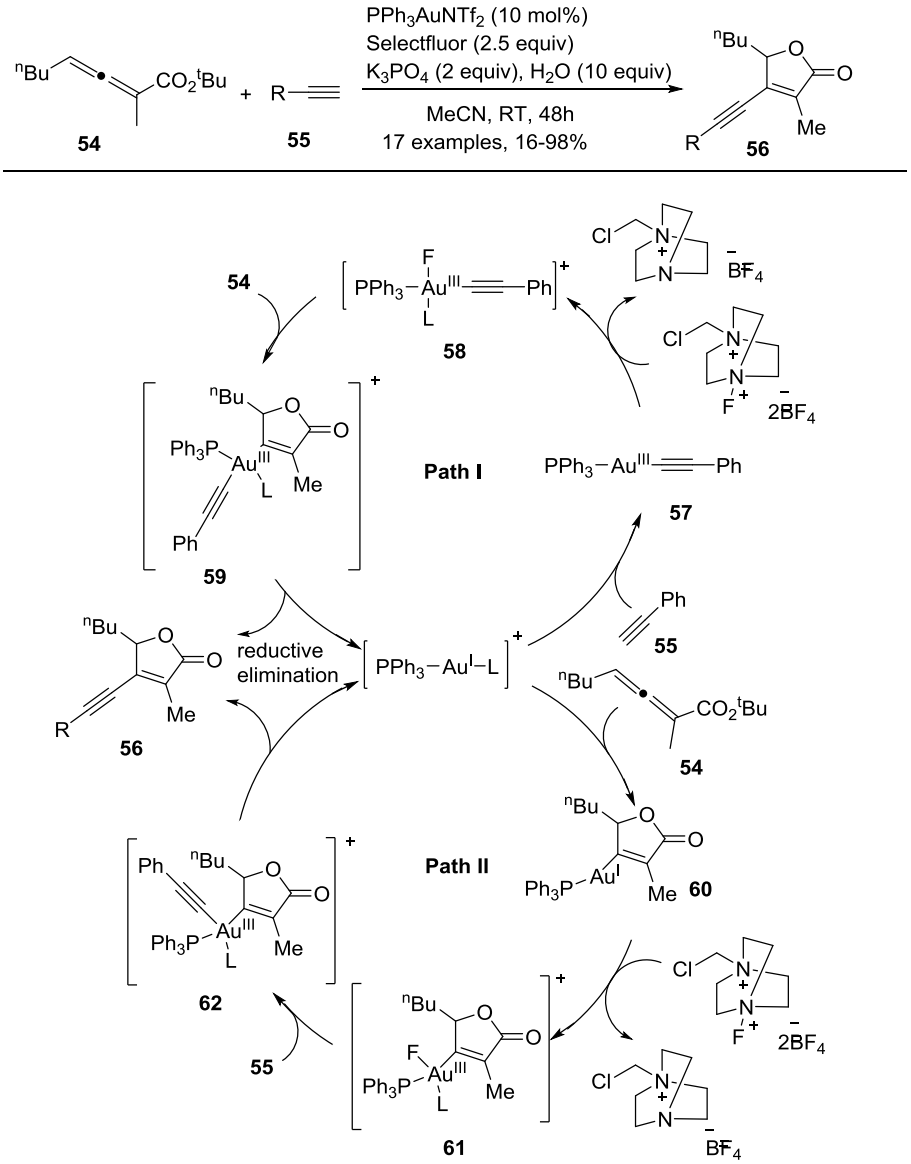
creates new research prospects for the study of gold alkene catalysis. According to the postulated process, Selectfluor could oxidize Ph_3PAuCl to produce Au(III) (**50**), which could then transmetalate with phenylboronic acid with the help of B-F bond. In order to obtain the Au(III) intermediates **53**, the tosylamide attack on the alkene would be activated by the cationic complex **51** that was thus produced. The final step produces the products **49** through a coordinated reductive elimination to form the $C(sp^3)$-Ph bond (Scheme 1-13).[18]



Scheme 1-13 Gold-catalyzed oxidative carboheterofunctionalization of alkenes

In the same year, Gouverneur published cascade cyclization-oxidative cross-coupling for producing β-alkynyl-γ-butenolides from allenoates reaction with terminal alkynes. Selectfluor serves as the external oxidant in a suggested mechanism with an Au^I/Au^{III} redox cycle. This cascade process has two possible routes, both of which involve an Au^I/Au^{III} redox cycle. Alkynylgold(I) intermediate **57** could result from the first deprotonation of the alkyne, then coordination with the cationic gold(I) catalyst in the presence of base. The gold(III) intermediate **58** would be made available by oxidizing the gold core with Selectfluor. The complex **59** would have both alkyne substituents and butenolide as a result of intermediate **58** coordination with allene,

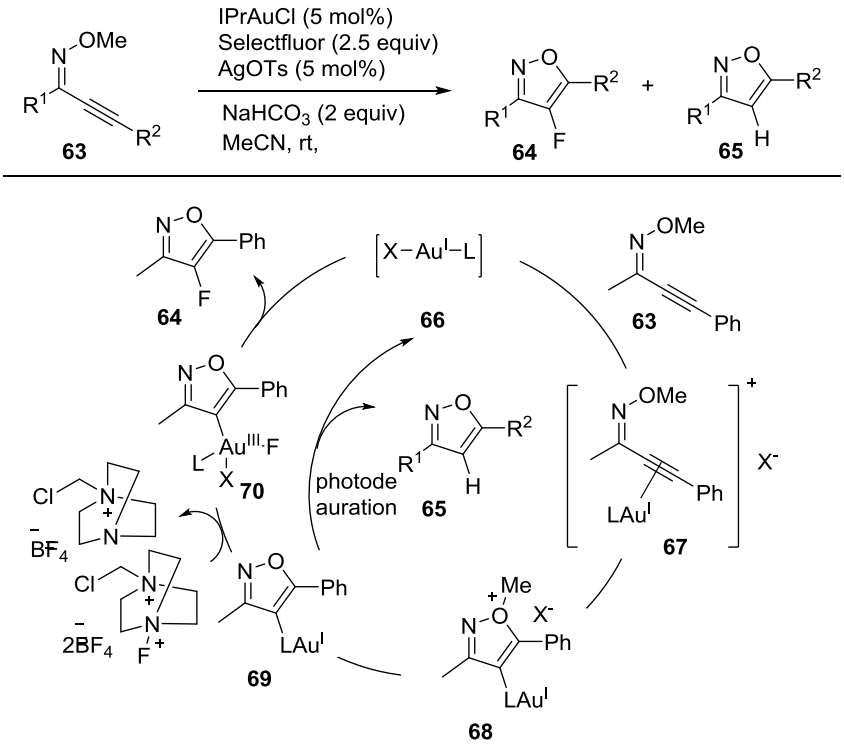
then been attacked by tert-butyl ester. After that, it supplies the products following reductive elimination and reacquire the cationic gold(I) catalyst (Scheme 1-14, Path I). A further possibility is for the allenoate cyclization to take place before the alkyne coordination phase. In this instance, Selectfluor would oxidize the intermediate **60** to the complex **61**. The products were generated from the alkynylation intermediate **62** after reductive elimination (Scheme 1-14, Path II).[19]



Scheme 1-14 Gold-catalyzed oxidative coupling cyclization

After that, in 2014, the Ryu group demonstrated an effective one-pot gold-catalyzed cyclization and fluorination of (*Z*)-2-alkynone *O*-methyl oxime to produce fluoroisoxazole at room temperature. According to possible mechanistic, the complex

68 is produced by first cyclizing the alkyne of *O*-methyl oxime **63** with gold(I) catalyst **66**. Following this, Selectfluor would perform demethylation and oxidation, resulting in the cationic gold(III) intermediate **70** containing isoxazole and fluoride. **70** quickly disintegrates to produce crosscoupled fluoroisoxazole **64** and gold catalyst **66** by reductive elimination. Isoxazole **65** would be produced when protodeauration of **69** was occurring. The exogenous oxidant Selectfluor mediates a redox Au(I)/Au(III) catalytic cycle in this suggested mechanism (Scheme 1-15).[20]

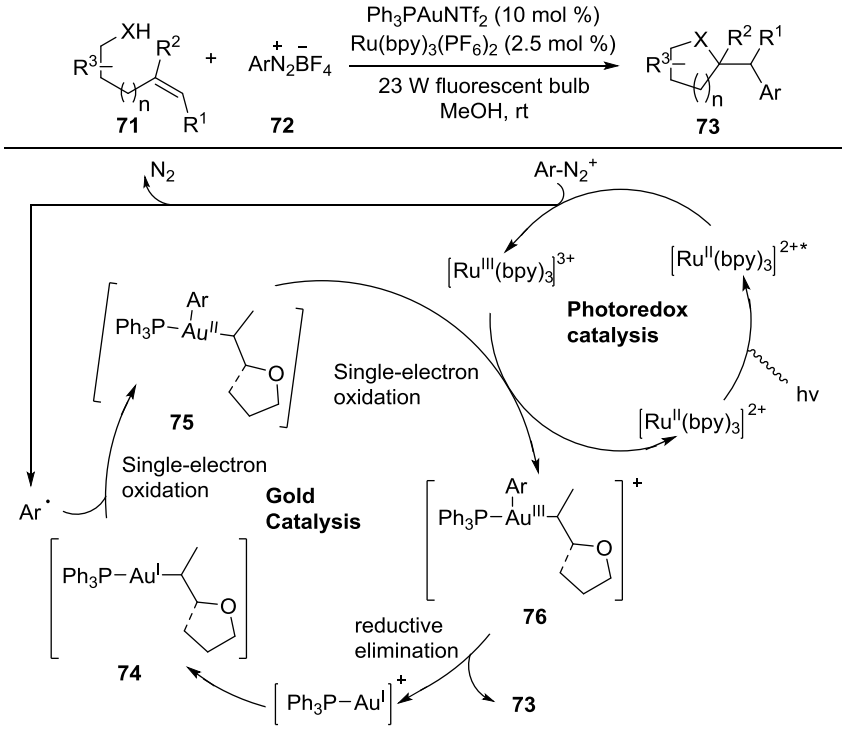


Scheme 1-15 Gold-catalyzed C−F bond oxidative formation

1.2.2 External Oxidant-free Oxidative Gold Catalysis

Compared to the redox gold catalysis with external oxidants, the redox gold catalysis without external oxidants is dominated by using aryldiazonium salts (Ar-N_2X) and ethynylbenzoiodoxolones (EBXs). Aryldiazonium salts are highly electrophilic species that react with concurrent loss of dinitrogen (N_2), a strongly energetically favoured process due to the thermodynamic stability of dinitrogen. In 2013, the Glorius group reported the first example of oxidative gold catalysis without oxidant (Scheme 1-16).[21] They employed an innovative Au and photoredox dual-catalytic

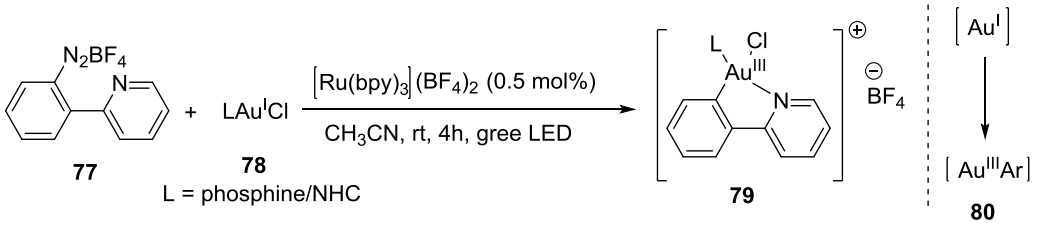
system to oxy- and aminoarylate alkenes intramolecularly using aryldiazonium ions. The plausible mechanism is described in Scheme 1-16. The alkyl gold(I) intermediate **74** is produced firstly through the Au(I) catalyst cyclization with the alkenes. At the same time, this species could interact with the aryl radicals produced by the diazonium salt's photoredox breakdown in order to produce the Au(II) intermediate **75** that contains both coupling partners.



Scheme 1-16 Combination of gold catalysis with ruthenium photoredox catalysis intramolecular alkoxy-and aminoarylation

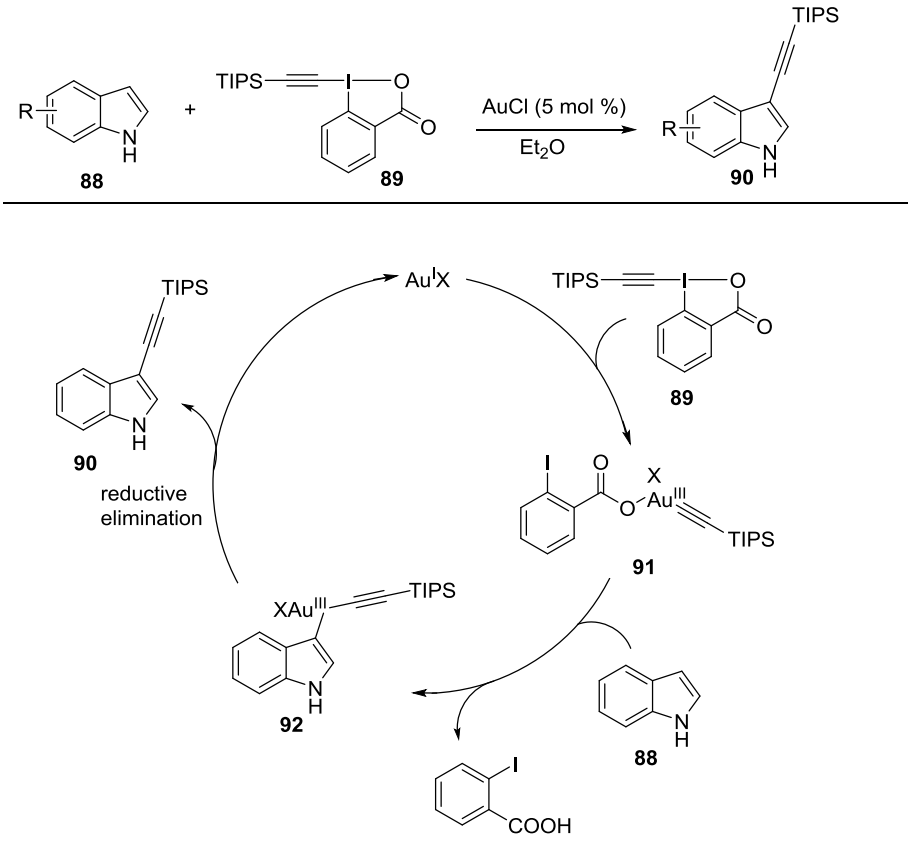
It would be anticipated that Ru^{III} would quickly get an electron from the unstable species, re-producing the Ru^{II} catalyst and the highly electrophilic Au(III) species **76**. At this point, the gold(I) catalyst would be renewed and the product would be produced through reductive elimination.

Then in 2016, the Glorius group reported gold/photoredox-catalyst ligand-supported gold(I) complexes **78** reaction with aryldiazonium salts **77** to synthesis gold(III) species **79** at room temperature. This gave rise to the first experimental proof of the role of Au(I) to Au(III) oxidation in the settings of gold/photoredox catalytic fusion.[22]



Scheme 1-17 ArN_2 X converts gold(I) to gold(III) through photoredox catalysis.

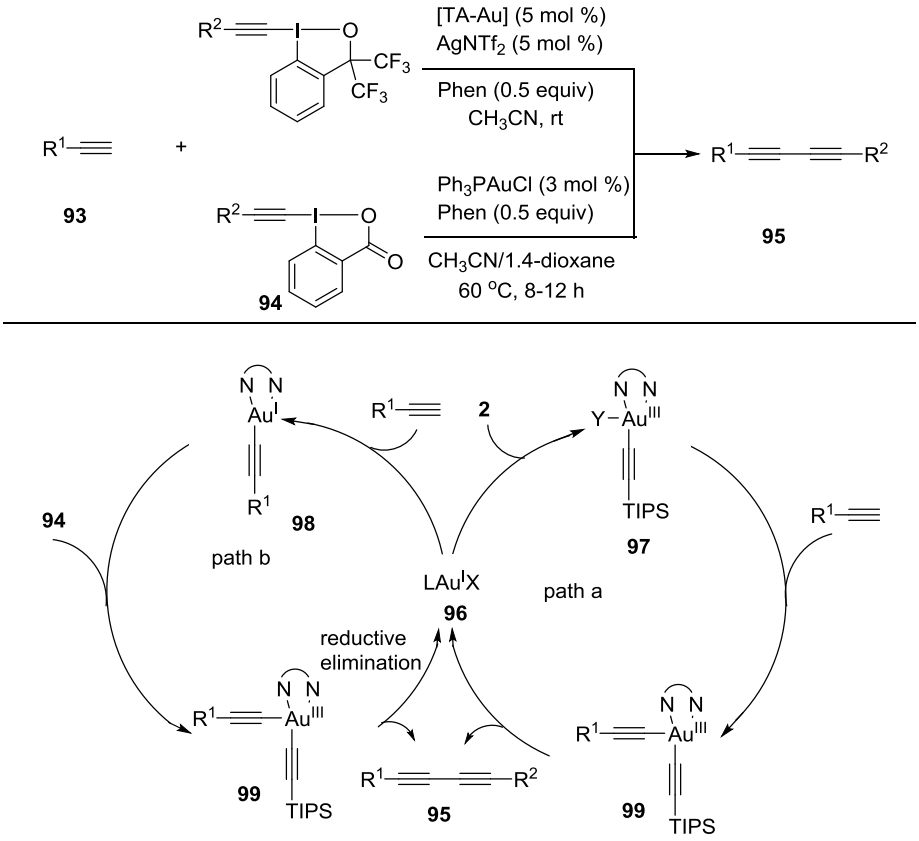
The precise mechanism that photoredox and gold(I)-catalyzed oxyarylation of alkenes was further studied by Yu and colleagues. Contrary to the original mechanism, the results revealed that the oxidation of the gold(I) precatalyst takes place before the cyclization phase. Therefore, the aryl-gold(III) (Au^{III} Ar, **80**) compounds is proved to be actual catalyst that can activate the double bond for nucleophilic attack (Scheme 1-17).[23]



Scheme 1-18 Gold-catalyzed alkynylation reactions

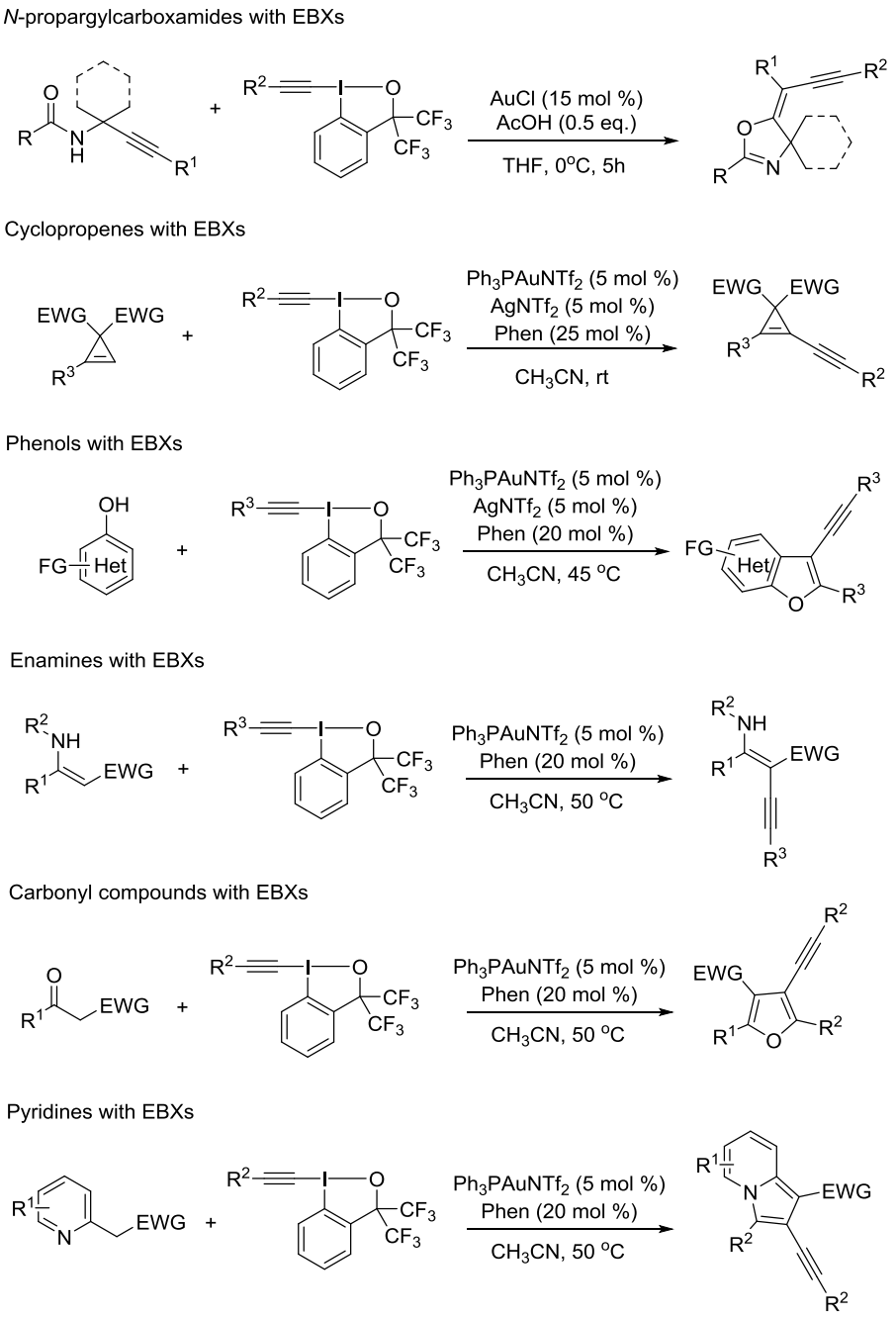
As electrophilic alkyne substitutes, ethynylbenziodoxolone reagents (EBXs) have also been used as reagents that serve as both coupling partners and oxidants. In 2009, by utilizing ethynylbenziodoxolone reagents, Waser and colleagues achieved the first

instance of alkynylation of pyrrole heterocycles with indole under the influence of gold. The gold(I) under the oxidation of **89** to create gold(III)-acetylene intermediate **91**, then indole metalation and reductive elimination (Scheme 1-18).[24]



Scheme 1-19 Gold-catalyzed cross-coupling of terminal alkynes with EBXs

Later, in 2017, the Liu group and the Patil group independently devised a new effective approach that terminal alkynes with alkynyl-EBXs have carbon-carbon coupling reaction to produce unsymmetrical 1,3-butadiynes. Various substrates with polar functional groups like OH, $B(OH)_2$ and NH are compatible under the catalytic system, which doesn't require any external oxidants. Two differently proposed mechanistic pathways were conceived for the reaction. The dialkynylgold(III) species **99** is produced by the terminal alkyne coordination with **97,** which from the direct oxidation of **96**. After that, the complex **99** through reductive elimination to provide the cross-coupling product and gold-catalyst **96** (path a). Another possibility, the oxidation can first take place on in-situ to obtain gold(I)-acetylide **98**, resulting in the formation of the common intermediate **99**. (Path b) (Scheme 1-19).[25]

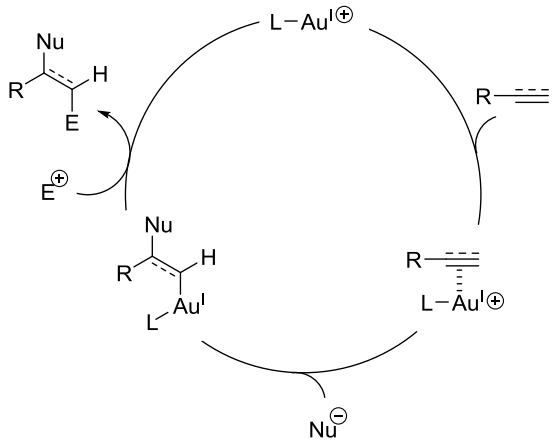


Scheme 1-20 Gold-catalyzed alkynylation of various substrates with EBXs

Recently, the Au(I)/Au(III) catalytic cycles have caught the attention of Hashmi's group and successfully demonstrated alkynyl gold(III) complexes as key to the further alkynylation of various substrates, such as *N*-propargylcarboxamides, cyclopropenes, phenols, acceptor-substituted enamines, acceptor-substituted carbonyl compounds and 2-substituted pyridines. The mechanistic data indicated that alkynyl gold(III) species play a key role in this catalytic cycles. The main features of this work is that the EBXs act as both oxidants and alkyne transfer agents. (Scheme 1-20).[26]

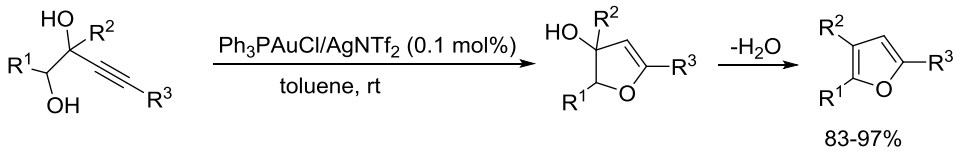
1.3 Redox-Neutral Gold Catalysis

In most gold catalysis cases, there has been a noticeable surge in attention to the Au(I) complexes catalytic. The contracted *s* and *p* orbitals of gold result in a low-lying LUMO, rendering gold a strong Lewis acid. Such catalysts have a special reactivity owing to cationic Au(I) has strong Lewis acidity and the ability to stabilize cationic intermediates, which has been used in the creation of new synthetic techniques. The most efficient catalysts for the homogenous electrophilic activation of alkynes are gold(I) complexes, and a wide range of flexible synthetic techniques have been developed to synthesis C-C bond or carbon-heteroatom bonds. In the majority of isohypsic gold catalysis, a generalized mode of action is that gold(I) serves as a soft Lewis acid activating π-systems towards attack from nucleophiles. The general mechanism includes: gold coordination with C-C triple bond to form π-system; then anti nucleophilic attack onto the gold-activated π-system delivers an organogold complex which reacts with an electrophile, releasing the new organic product and reforming the gold catalyst (Scheme 1-21).[27]



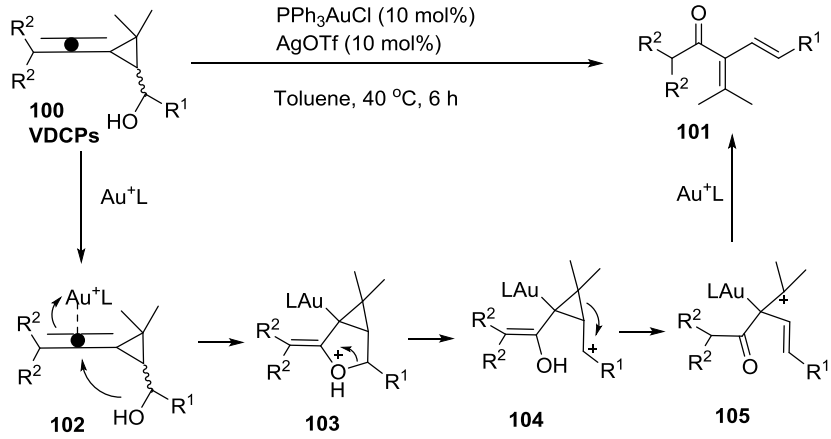
Scheme 1-21 General gold(I) catalytic cycle.

In 2009, in order to access furans, pyrroles, and thiophenes, Marques' team reported gold-catalyzed intramolecular cyclizations and dehydrative of homopropargylic alcohols. The advantages of this proposal are extremely straightforward, easily accessible substrates and functional groups tolerations that to create highly substituted heteroaromatics (Scheme 1-22).[28]



Scheme 1-22 Au(I)-catalyzed cyclization of alkynediols for furans

When shortened the connection of VDCP with alcohol after a year, a different reaction result was founded (Scheme 1-23). In this instance, gold catalysis selectively produced dienone derivatives **101** from a functionalized VDCP **100**.

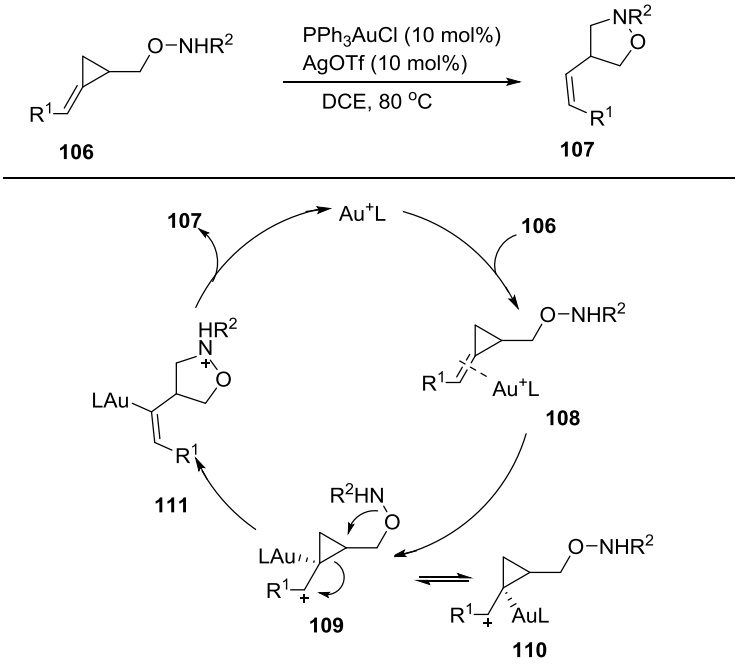


Scheme 1-23 VDCPs intramolecular rearrangement via Au(I) catalysis

The Au(I) catalyst substrates **100** which activated on the allene motif of the VDCP to obtain intermediate **102**. The hydroxy group then engages in an intramolecular nucleophilic assault to produce the five-membered intermediate **103**. Then, the cationic intermediate **104** has been formed through the cleavage of the carbon-oxygen bond. This intermediate then proceeds through the cyclopropane ring opening of and isomerization to produce the ketone intermediate **105**. After cationic gold is removed, the final dienone product **101** is created.[29]

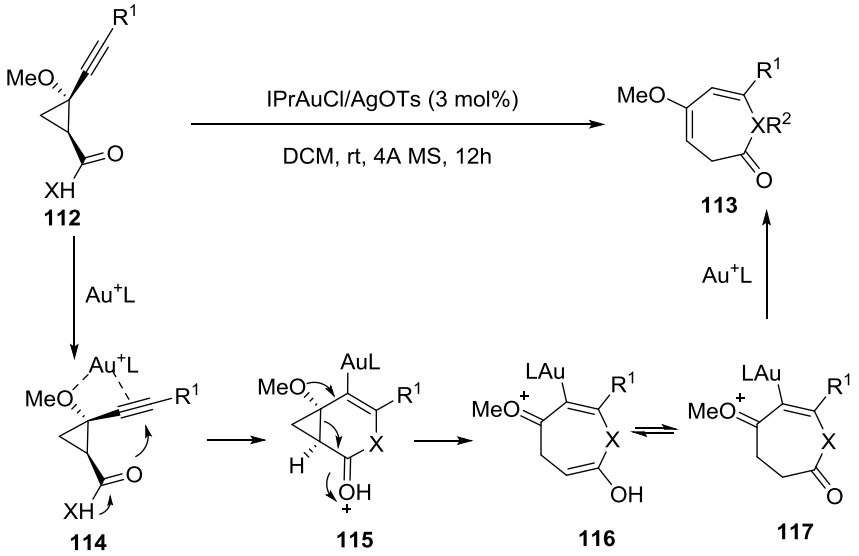
In 2012, Shi's group achieved Au(I)-catalyzed regioselective intramolecular hydroamination of sulfonamide-substituted aryl-MCP substrate for a range of 4-substituted isoxazolidines in excellent yields. As shown in Scheme 1-24, in order to create five-membered N,O- heterocycle **107**, the Au(I) catalyst first reaction with compound **106** to obtain intermediates **108**, then attack by intramolecular oxygen atoms to get intermediate **109** or intermediate **110.** Following the ring-opening of cyclopropane, intermediate **109** passes an intramolecular hydroamination to produce

the matching five-membered heterocyclic intermediate **111**. Last, the final product **107** is created by further protodeauration of intermediate **111**.[30]



Scheme 1-24 Au(I)-catalyzed intramolecular hydroamination

In 2013, Oxepinone and azepinone synthesis from alkynylcyclopropanecarboxylic acid derivatives was described as a regioselective process by Aguilar's group, with

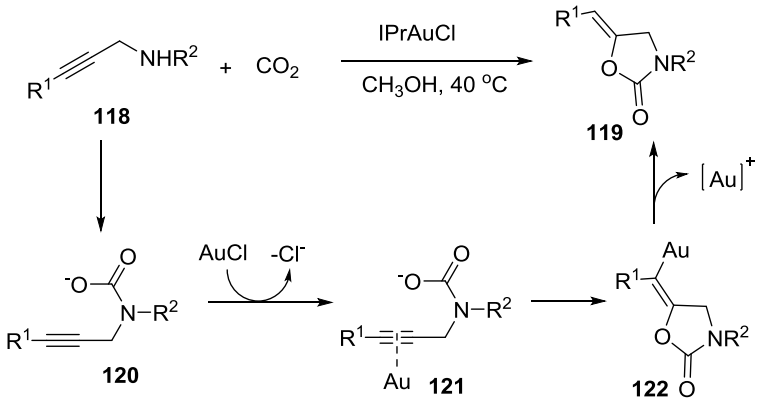


Scheme 1-25 Au(I)-catalyzed intramolecular hydroamination

good to outstanding yields. According to the proposed mechanism shown in Scheme 1-25, the intermediate **114** is formed by gold catalyst coordination with **112**. Then, species **115** was obtained through carboxylic acid regioselective nucleophilic addition

to triple bond. After that, ring-opening reaction of cyclopropane to produce a seven-membered intermediate **116**. Equilibration of the organogold intermediate **116** with another organogold species **117** produces products **113** and regenerates the gold catalyst.[31]

In 2015, According to Yuan and Lin, under atmospheric pressure of CO_2 at 40 °C, carboxylative cyclization of propargylamines **118** can be accomplished with NHC-gold(I) complexes acting as the catalyst to produce oxazolidinone products **119** in 91% yields. One potential mechanism is that the interaction of the alkyne moiety by the cationic species $[Au]^+$ with a propargylic carbamate anion **120**, created by the carboxylation and subsequent deprotonation of propargylamine, results in intermediate **121**. An intermediate **122** is produced by the nucleophilic attack of the carbamate anion on the triple bond; also this intermediate is protonated to produce oxazolidinone **119**. (Scheme 1-26).[32]



Scheme 1-26 Gold-catalyzed carboxylative cyclization of propargylamines.

1.4 Research Objectives

This thesis will further explore Au(I)/Au(III) catalytic cycles by employing EBXs as the oxidant and Au(I) catalyst as the Lewis acid. Taking advantage of gold's distinctive redox characteristic and carbophilic acidity, we will explore 1) regioselective acyloxyalkynylation of ynamides with EBXs 2) regioselective acyloxyalkynylation of ynol ethers with EBXs and 3) gold-catalyzed cycloaddition/[4+2] cascade reaction of terminal alkynes and ynamides with isatin-derived ketimines.

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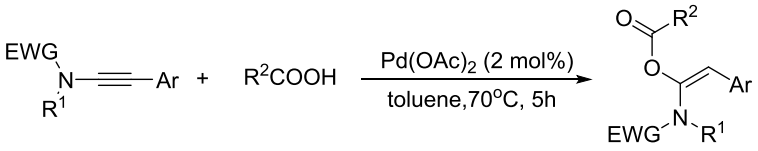
Chapter 2. Synthesis of Amide Enol 2-Iodobenzoates by a Regio- and Stereoselective Gold-Catalyzed Acyloxyalkynylation of Ynamides with Hypervalent Iodine Reagents

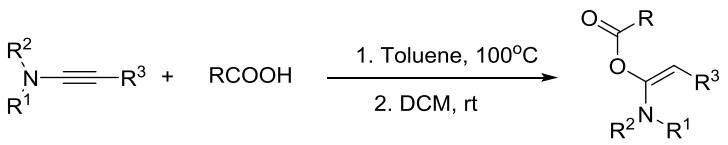
2.1 Introduction

Enol esters as the building blocks have been used as reagents in a wide range of synthetic transformations, such as aldol-type reactions, cycloadditions reaction and heterocycle production in natural compounds.[1] They are employed as substrates and moderate acylation reagents for polymerizations,[3] hydrogenations,[4] cycloadditions,[5] aldol-[6] and Mannich-type conversions,[7] and cross-coupling procedures.[8] In the past decade, one main class of substrates for their synthesis were ynamides,[9] due to the nitrogen atom a lone pair of electrons, that the C-C triple bond can highly regioselective attacked by kinds of nucleophiles.[10] Therefore, ynamides were effectively used to create a variety of skeletons.[11] Allready, a few efficient approaches that hydroacyloxylations of ynamides to generate amide enolates were reported. In 2012, Lam's group achieved the regioselective hydroacyloxylation of ynamides under palladium catalysis.[12]



Scheme 2-1 Palladium-catalyzed hydroacyloxylation of ynamides

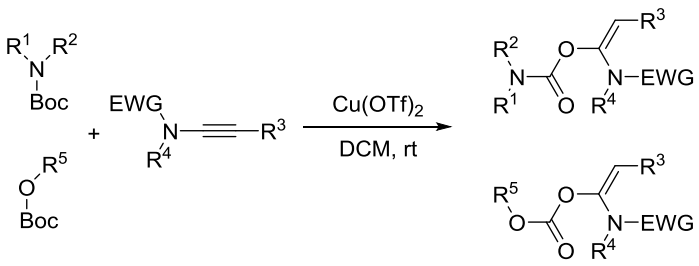
After that, Bi's, Gillaizeau's and Zhao's groups reported a metal-free, acid catalyzed hydroacyloxylation reactions of ynamides to afford amide enol benzoates.[13]



Scheme 2-2 Metal-free hydroacyloxylation of ynamides

Recently, a very regioselective method for obtaining amide enol carbonates was reporated by Wei and co-workers through the Copper-catalyzed nucleophilic reaction

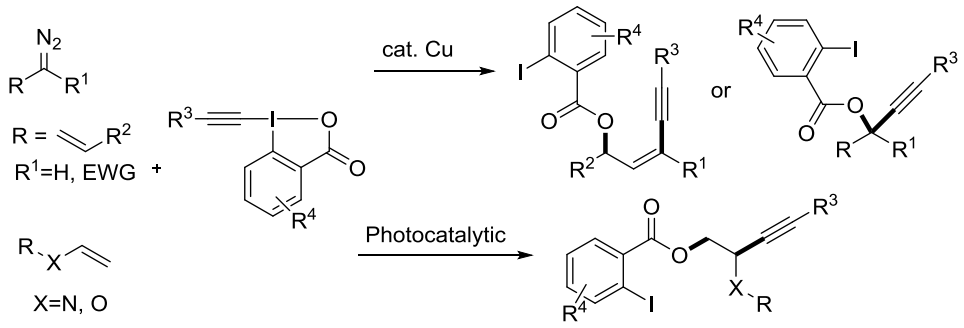
of ynamides.[14]



Scheme 2-3 Copper-catalyzed nucleophilic reaction of ynamides

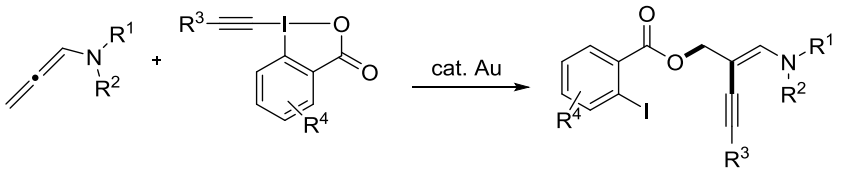
Notably, the lone pair on the ynamide nitrogen atom readily assists the functionalization of the α-position of ynamides. However, a simultaneous difunctionalizations of ynamides with electrophiles and nucleophiles at the α- and β-position, still represents a substantial challenge to the modern organic chemist.

Because of good leaving group ability and electrophilic nature, ethynyl benziodoxolone reagents (EBXs) have unique reactivities as a commonly used reagent.[15] During the past decade, with the aid of transition metal catalysis, several other effective transformations, including thiols, the alkynylation of aromatic C-H bonds and ketoesters, can be accomplished employing EBXs as excellent electrophilic reagents.[16] Recently, the use of alkynyl iodine(III) agents in gold-catalyzed reactions has garnered the interest of more and more organic chemists involving gold(I)/gold(III) catalytic cycles.[17] Our group also achieved gold-catalyzed C−H alkynylations reactions of cyclopropenes,[18] phenols,[19] N-propargylcarboxamides,[20] acceptor-substituted enamines,[21] acceptor-substituted carbonyl compounds[22] and 2-substituted pyridines[23] triggered by the alkyne moiety of hypervalent iodine(III) reagents. Nevertheless, the EBX reagents suffer from the drawback that techniques frequently only transfer one specific of alkyne and 2-iodobenzoic acid or hexafluoro-2-(2-iodophenyl)propan-2-ol are obtained as stoichiometric byproducts, leading to low atom economy. However, Yoshikai's group achieved a palladium(II)-catalyzed conversion with EBXs to produce multisubstituted furans.[24] Recently, Waser's group reported an oxy-alkynylation of diazo compounds, alkenes with EBXs (Scheme 2-4).[25]



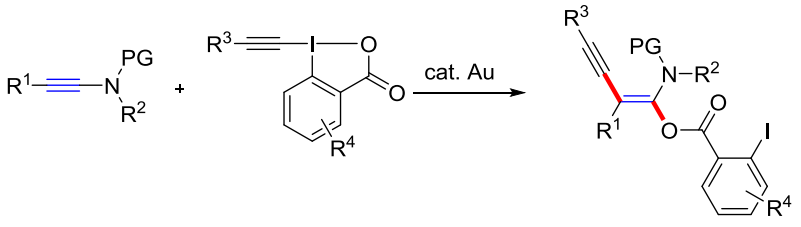
Scheme 2-4 Atom-economical oxy-alkynylation of alkenes with EBXs

In 2019, Patil's group[26] also reported the atom-economic reaction of EBXs with N-allenamides by gold catalysis (Scheme 2-5).



Scheme 2-5 Gold-catalyzed conversion of N-allenamides with EBXs

Despite this breakthrough, there is still need for research on the advancement of the atom-economy of reactions involving EBXs. Until now, no group reported a stereoselective carbon(sp)-carbon(sp^2) bond formation and carbon-oxygen coupling simultaneous at the alkynyl position of ynamides by gold(I)/(III) catalytic systems, a recent focus of our group's activities.[27] Herein, we report a novel highly efficient, atom-economical and diastereoselective gold-catalyzed acyloxyalkynylation of ynamides with EBX reagents for the synthesis of tetra-substituted amide enol 2-iodobenzoates with the substrate scope and functional group tolerance (Scheme 2-6).



Scheme 2-6 Gold-catalyzed reaction of ynamides with EBXs

As this conversion involves a Au(I)/Au(III) catalytic cycle, the reaction is not depending on any additional external oxidants and also exploits the nucleophilic

carboxylate part of EBX reagents.

2.2 Result and Discussion

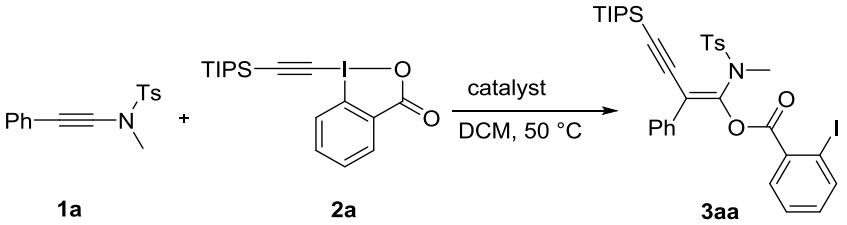
2.2.1 Optimization of the Reaction Conditions

The first step is to optimize the reaction conditions using the ynamide **1a** and the TIPS-EBX **2a** as the starting substrates (Table 1). Different gold catalysts including AuCl, Ph_3PAuCl, IPrAuCl, X-PhosAuCl and Me_3PAuCl in combination with 1,10-phenanthroline as additive were screened to optimize this transformation and to synthesize the product **3aa** in DCM at 50 °C (entries 1−6). Treatment of ynamide **1a** with TIPS-EBX **2a**, DMSAuCl and 1,10-phenanthroline in CH_2Cl_2 at 50 °C afforded the **3aa** in 79% yield (entry 3). Both the gold(I) catalyst and the additional ligand were crucial for the reaction, as omission of each of them resulted in no record of any product **3aa** (entries 7 and 8). Next, a series of other dinitrogen-based ligands, **L1−L7**, was examined (entries 9−15). All of the tested ligands facilitated the reaction and a major improvement was obtained when using 4,7-diphenyl-1, 10-phenanthroline **L1** as ligand which enabled an increase of the yield to 87% (entry 9). Varying the reaction temperature cannot improve the reaction yield (entries 16–19). In summary, the conditions of entry 9 (DMSAuCl (5 mol %), **L1** (15 mol %) in DCM at 50 °C) turned out to be optimal.

2.2.2 Substrate Scope

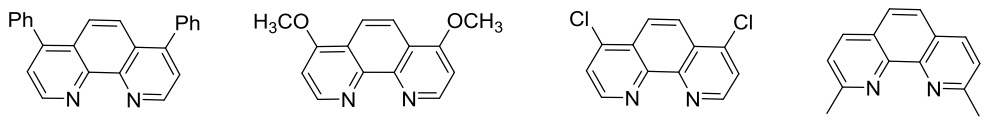
With these optized conditions, the scope with respect to the ynamides was investigated (Scheme 2-7). First, the effect of the substitution pattern of several ynamides **3aa**−**3za** was evaluated, while keeping the EBX reagent constant. Several 2-aryl ynamides **1a**−**1k** were explored using TIPS-EBX (**2a**) as a partner. Various substitution patterns on the β-substituted aryl ring were tolerated, independent from their electronic nature, affording products **3aa**−**3ka** in good to excellent yields (72%−93%). Alkyl substituents at the β-position of ynamides (R^1 = Et, n-hexyl) and electron-withdrawing COOEt substituents were both tolerated (**3la**−**na**). Meanwhile, the product **3oa** also was obtained in 73% yield for the conversion of terminal ynamide **1o**. The single crystal X-ray analysis confirmed the structure of **3aa** (Figure

Table 1 Optimization of the Reaction Conditions[a]



1a 2a 3aa

Entry	Catalyst	Ligand	T (^{o}C)	Yield (%)[b]
1	AuCl	Phen[c]	50	72
2	Ph_3PAuCl	Phen	50	45
3	DMSAuCl	Phen	50	79
4	IPrAuCl	Phen	50	35
5	XPhosAuCl	Phen	50	38
6	Me_3PAuCl	Phen	50	73
7	¬	Phen	50	n.d.[d]
8	DMSAuCl	¬	50	Trace
9	**DMSAuCl**	**L1**	**50**	**87**
10	DMSAuCl	L2	50	79
11	DMSAuCl	L3	50	46
12	DMSAuCl	L4	50	68
13	DMSAuCl	L5	50	62
14	DMSAuCl	L6	50	51
15	DMSAuCl	L7	50	58
16	DMSAuCl	L1	30	56
17	DMSAuCl	L1	40	71
18	DMSAuCl	L1	60	84
19	DMSAuCl	L1	70	81

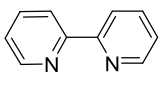


L1

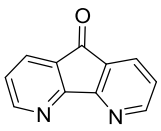
L2

L3

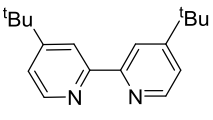
L4



L5



L6



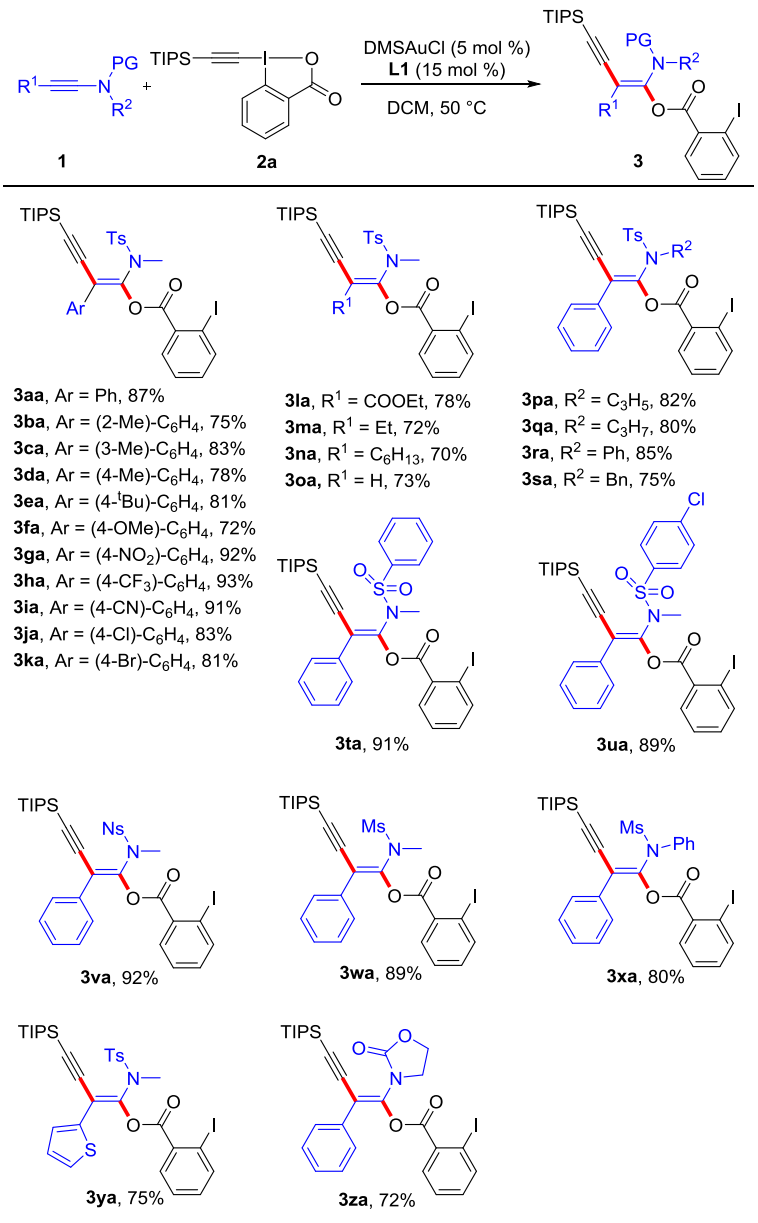
L7

[a]**1a** (0.10 mmol), **2a** (0.12 mmol), Catalyst (5 mol %), Phen (15 mol %) in solvent (1 mL) at 50 ℃.
[b] Isolated yield. [c]Phen: 1,10-phenanthroline. [d]n.d.: not detected.

2-1). Next, the methyl group on the amide moiety was replaced by a cyclopropyl, *n*-propyl, Ph and a Bn substituent. All of the products were isolated in good yield (**3pa**−**3sa**). Subsequently, we screened the nitrogen protecting groups at ynamide moiety. A replacement of the Ts group of substrate **1a**, such as benzenesulfonyl, p-chlorobenzenesulfonyl, the Ns and Ms group, offering the corresponding products in 80−92% yield (**3ta**−**xa**). To our delight, the heterocyclic products **3ya** and **3za** could also be generated in moderate to good yield.

Next, the scope with respect to the EBXs reagents was studied (**2**). Various acyloxyalkynylation products were obtained in high yields (Scheme 2-8, **3ab**−**3as**). Initially, the aromatic ring of the benziodoxolone was varied and electron-donating groups (Me, OMe) or halides (Cl, Br) at different positions of aryl were transformed into the targets **3ab**−**3ai** in 80−85% yield. Furthermore, different silyl groups (**2j** and **2k**) at the alkyne terminus of the EBXs were tested in combination with model ynamide **1a**. The corresponding products **3aj** (88%) and **3ak** (92%) were obtained in high efficiency. To our delight, also electron-deficient aryl substitutions at the alkyne terminus of **2l**−**2r** were tolerated for the oxyalkynylation of **1a**, delivering **3al**−**3ar** in moderate yield (60%−75%). Unfortunately, the alteration of the carboxyl group in **2** to the extremely electron-deficient benzylic alcohol group (possessing two CF_3 groups in *α*-position) delivered none of the expected product (**3as**). But, a gram-scale of **1a** and **2a** gave 82% of **3aa** (Scheme 2-9).

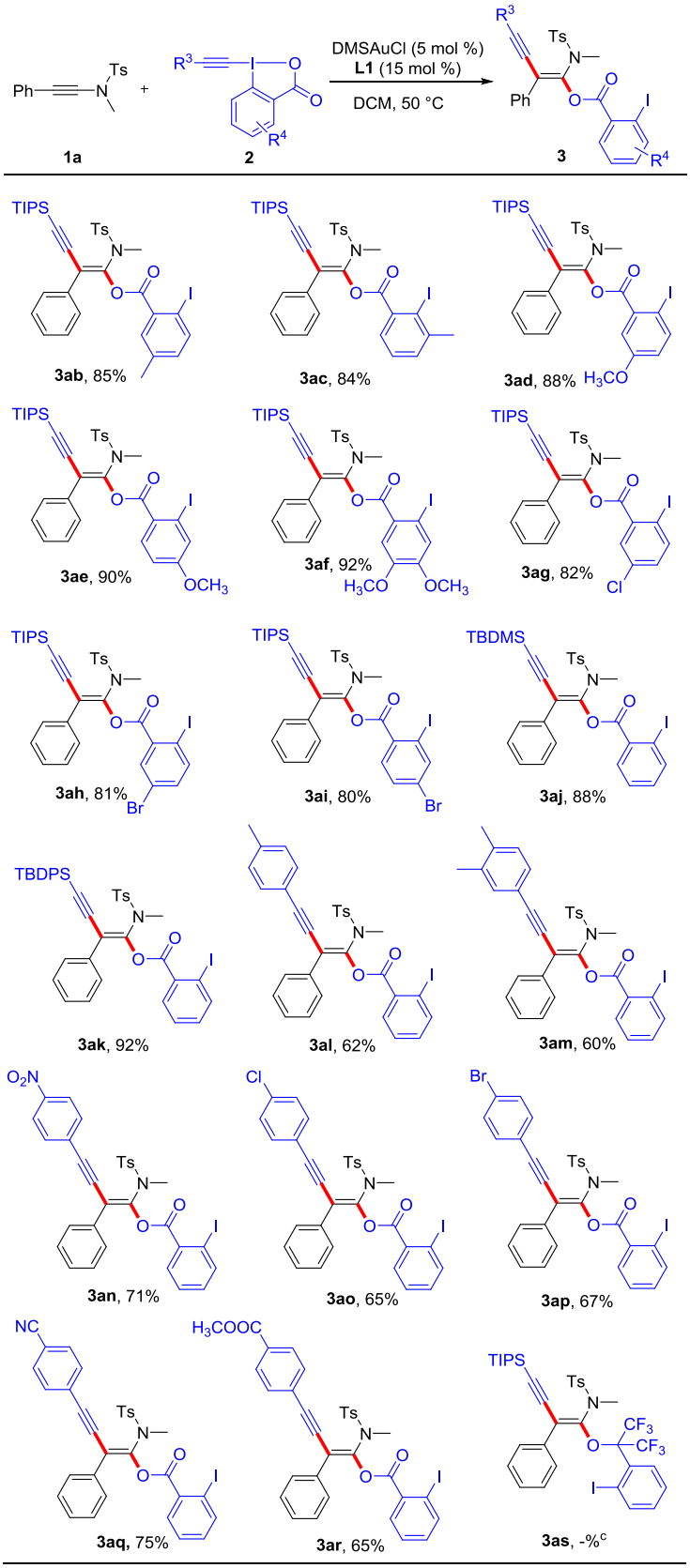
To clarify the mechanism, a number of control experiments were conducted in Scheme 2-10. The crossover products (**3aa** and **3aj'**) were observed via the ESI-HRMS analysis and calculate the ratio by the ^{1}H NMR and HPLC analysis when **2d** combine with **2j** in a crossover experiment; indicating an addition of the carboxylate and the alkyne to the ynamide stepwise. Further control experiments are listed in the experimental section. To assess the thermochemical properties of the obtained products, computational calculations were conducted on the exemplary compound **3al**.[28] Geometry optimizations and subsequent frequency analyses of the



[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.12 mmol), DMSAuCl (5 mol %), Phen (15 mol %) in DCM (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 2-7 Scope with respect to ynamides derivatives[a,b]

two possible stereoisomers **3al**-(*E*) and **3al**-(*Z*) (Figure 2-2) were conducted in ORCA 5.0.1 on the B3LYP/def2-SVP level of theory, for iodine also def2-TZVP was employed. The isomer **3al**-(*E*) depicts a lower enthalpy of 1.53 kcal/mol and free enthalpy of 2.00 kcal/mol respectively compared to **3al**-(*Z*); making **3al**-(*E*) the thermodynamic product of this reaction. The computational results support the experimental findings, in which selectively the (*E*)-isomer was formed.



[a]Reaction conditions: **1a** (0.10 mmol), **2** (0.12 mmol), DMSAuCl (5 mol %), Phen (15 mol %) in DCM (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 2-8 Scope with respect to the hypervalent iodine reagents[a,b]

Based on the DFT calculations and previous reports,[18]-[23] a plausible mechanism was proposed (2-11). First, Au(I) species **A** is formed from the combination of **L1** and DMSAuCl. Subsequently, oxidative addition of Au(I) complex **A** by the EBXs **2** produces an alkynyl Au(III) intermediate **B**. Next, the C–C triple bond of **1** was activated to form π-complex **C**, due to the lone pair of electrons in the nitrogen atom. Then, nucleophilic attack by the carboxylate anion affords Au(III) intermediate **D**. Thereafter, a reductive elimination occurs delivering the desired **3** and Au(I) complexs **A** which completes the catalytic cycle.

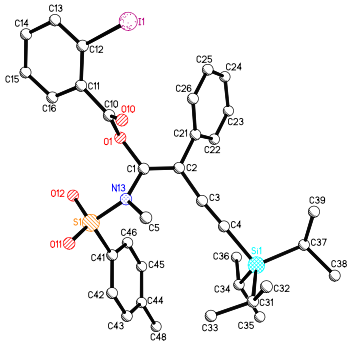
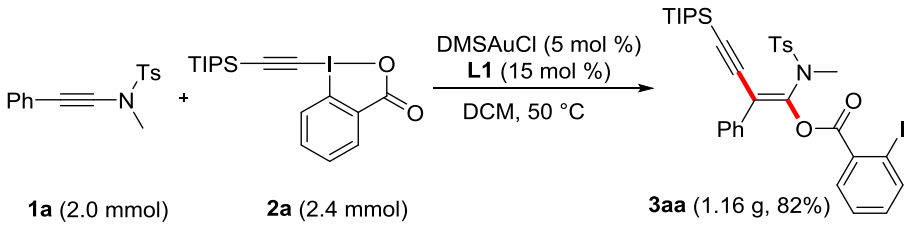
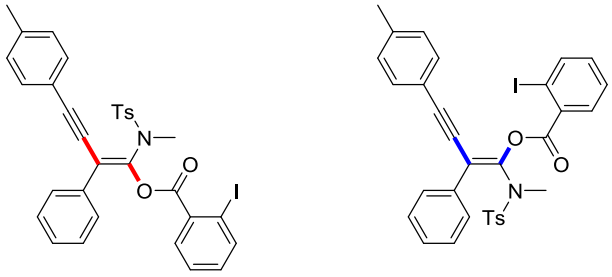


Figure 2-1. Solid state molecular structure of **3aa**



1a (2.0 mmol) **2a** (2.4 mmol) **3aa** (1.16 g, 82%)

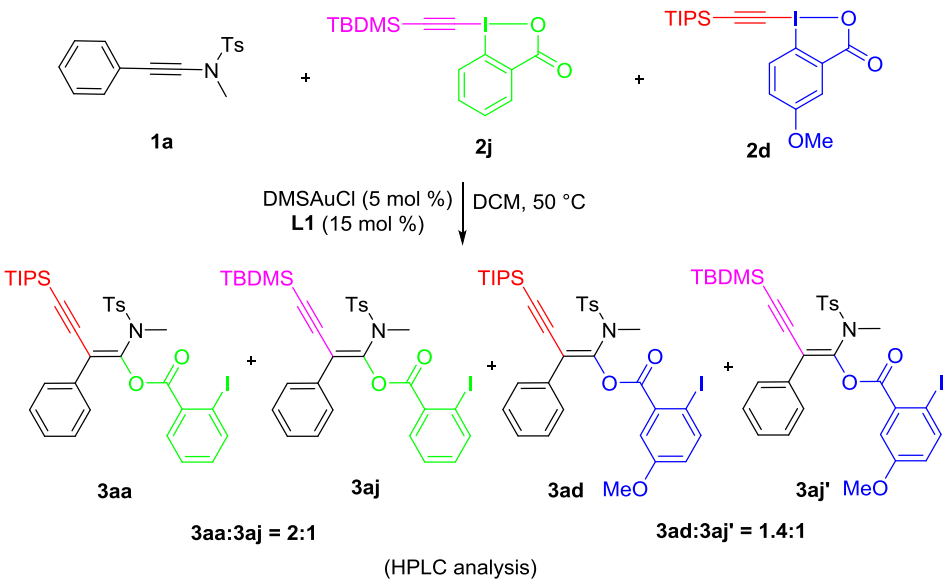
Scheme 2-9 Gram-scale synthesis



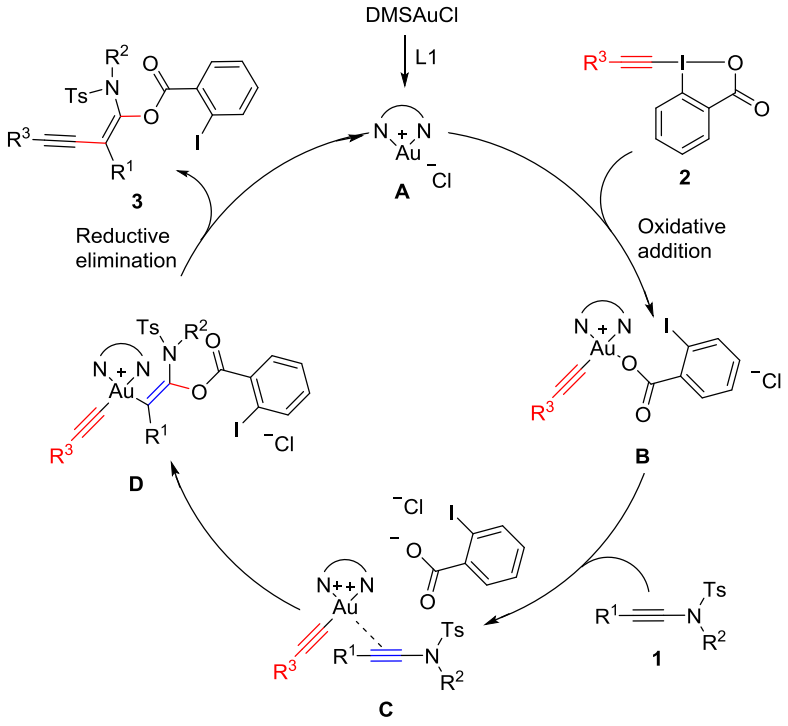
3al-*(E)*
ΔH = 0 (reference)
ΔG = 0 (reference)

3al-*(Z)*
ΔH = 1.53 kcal/mol
ΔG = 2.00 kcal/mol

Figure 2-2. Computational analysis of energies of both possible diastereoisomers **3al**-(E) and **3al**-(Z).



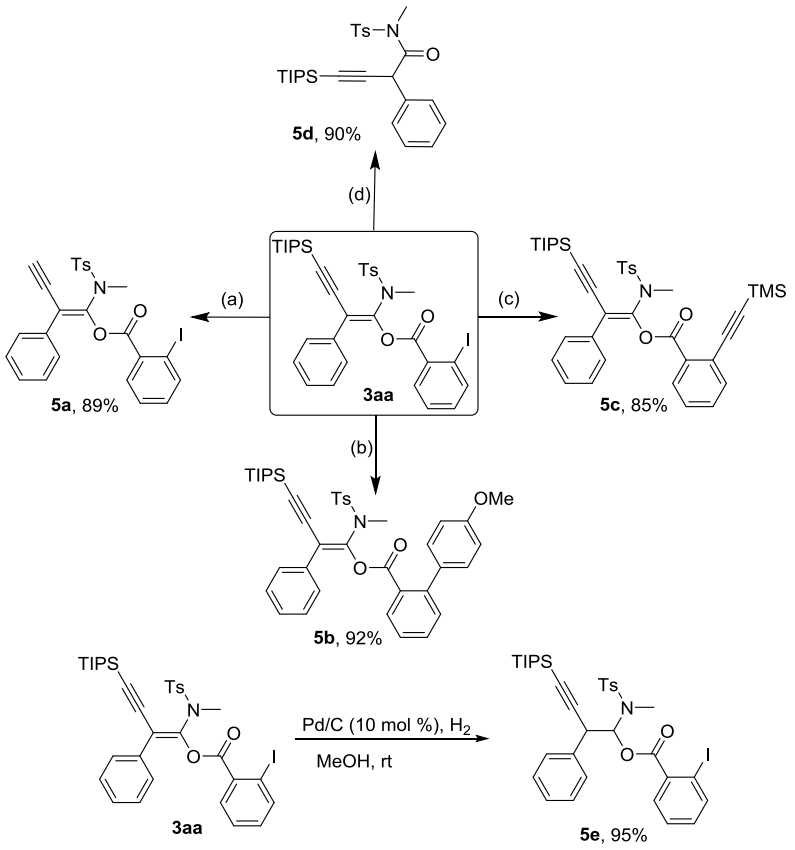
Scheme 2-10. Cross-over experiments.



Scheme 2-11. Proposed reaction mechanism

In order to show the methodology's potential, modifications of the product **3aa** were carried out as shown in Scheme 2-12. The TIPS group on the alkyne motif would be easily removed in the presence of TBAF to produce terminal alkyne **5a** in 89% yield.[29] The product biphenyl **5b** was readily prepared by Suzuki coupling of **3aa** with 4-methoxyphenylboronic acid in 92% yield.[30] Sonogashira cross-coupling of **3aa** with trimethylsilylacetylene provided a 85% yield of **5c**.[31] Furthermore, the

product **5d** could be formed in 90% yield, when **3aa** reaction with 2-phenylethan-1-amine at room temperature,[13c] and the product **5e** was readily prepared in 95% yield by Pd/C hydrogenation of **3aa**.



Scheme 2-12. Product modifications

2.3 Conclusions

In conclusion, we have successfully achieved the first atom-economic, regio- and stereoselective gold-catalyzed acyloxyalkynylation of ynamides with EBX reagents under mild reaction conditions, offering direct access to tetrasubstituted amide enolates in high yields. This efficient transformation tolerates a diverse set of functionalities, thus providing a wide range of amide enol 2-iodobenzoates. Postsynthetic modifications further demonstrate the potential of the new method for generating alkynyl- and alkenyl-functionalized products. Overall, two concomitant functionalizations with a single EBX reagent open up new and efficient synthetic opportunities.

2.4 References

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2.5 Experimental Section

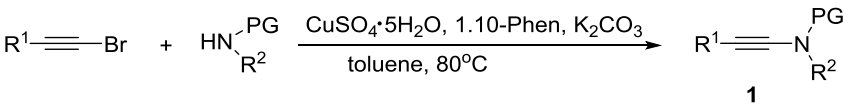
2.5.1 General Remarks

Reactions were performed in oven-dried glassware unless otherwise noted, chemicals were obtained from commercial suppliers (Sigma-Aldrich, ChemPUR and TCI) and used without further purification. Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at 7.26 ppm. Multiplicities were reported using the following abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiple). All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH_2-group), q (quartet, CH_3-group)] were determined by DEPT135 spectra. (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not calibrated. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400

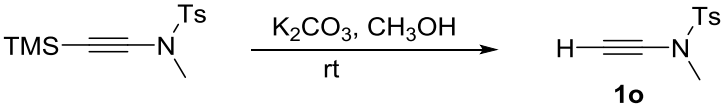
mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

2.5.2 Experiment Procedures

Procedure A: General procedure for the synthesis of ynamides **1**[1,2]

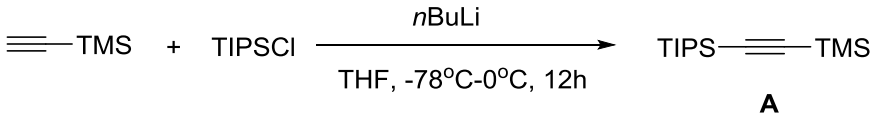


Amide (5.0 mmol), 1-bromo-2-acetylenes (6.0 mmol), $CuSO_4.5H_2O$ (187.0 mg, 0.75 mmol), 1,10- phenanthroline (270.0 mg, 1.5 mmol) and K_2CO_3 (1.38 g, 10.0 mmol), toluene (25 mL) were added under a nitrogen atmosphere. The reaction flask was evacuated under vacuum and flushed with nitrogen three times, then sealed under nitrogen and heated to 80 ºC. The reaction mixture was stirred overnight, then cooled down to room temperature, filtered through a pad of silica gel, the filtrate was evaporated and purified by flash silica gel column chromatrography to give the desired ynamide **1a-1n** and **1p-1z** in high yield.



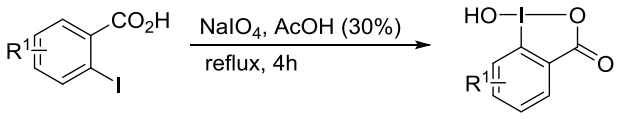
In a 10 ml round-bottom flask equipped with TMS-ynamide (1.0 equiv), CH 3 OH and K_2CO_3 (2.0 equiv) were combined. The reaction mixture was stirred at room temperature under air until TMS-ynamide was fully consumed. The reaction mixture was treated with H_2O at room temperature and aqueous layer was extracted with Et_2O for three times. The combined organic layers were washed with brine, dried over Na_2SO_4 , filtered and evaporated in vacuo. Crude product was purified by flash chromatography to afford the terminal ynamide **1o** in quantitative yield

Procedure B: Synthesis of R-EBX derivatives **2**[3]



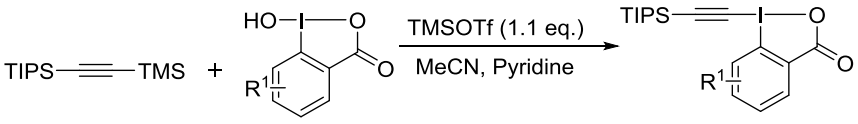
A

n-butyllithium (1.6 M in hexanes, 26.2 mL, 42.3 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (4.2 g, 43 mmol, 1.0 equiv) in THF (66 mL) at -78 °C. The mixture was then stirred for 2 h at -78 °C before chlorotriisopropylsilane (9.2 mL, 43 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (20 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain desired product **A** (11.72 g, 83% yield) as a colorless liquid.



B

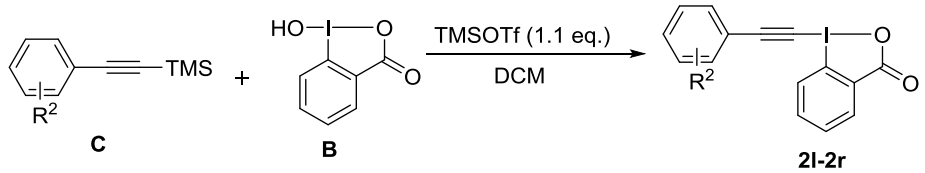
$NaIO_4$ (13.79 g, 64 mmol; 1.0 equiv) and 2-iodobenzoic acids (16.0 g, 64 mmol, 1.0 equiv) were suspended in 30% (v/v) aq. AcOH (125 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (160 mL) and allowed to cool to room temperature, protecting it from light. After 1 h of stirring at rt, the crude product was collected by filtration, washed on the filter with ice water (3 x 30 mL) and acetone (3 x 30 mL), and dried in the dark to give the pure product **B** (27.3 g, 86% yield) as a white solid.



A **B** **2a-2k**

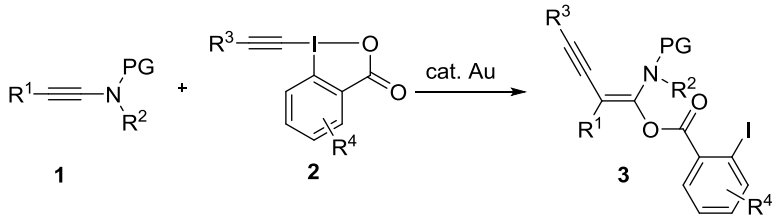
An oven-dried two-neck 250 mL flask equipped with a magnetic stirrer was charged with 2-iodosylbenzoic acids (**B**) (5.28 g, 20.0 mmol, 1.0 equiv) and CH_3CN (70 mL) and the suspension was then cooled to 0 °C. Trimethylsilyltriflate (4.0 mL, 22.0 mmol, 1.1 equiv) was added at one-go into the reaction mixture via syringe which almost immediately produced a clear solution (critical step!). After 20 min,

(trimethylsilyl)(triisopropylsilyl)acetylene (**A**) (5.6 g, 22.0 mmol, 1.1 equiv) was added dropwise via syringe at rt. After 5 min, the solution turned dark yellow. After 30 min, pyridine (2.0 mL, 22.0 mmol, 1.1 equiv) was added via syringe. After 20 min, the reaction mixture was reduced under vacuum until a solid was obtained. The solid was dissolved in CH_2Cl_2 (20 mL), washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The organic layers were then combined, washed with a saturated solution of $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (ca 25 mL) afforded TIPS-EBXs **2a-2k** (87%-95%).



To a suspension of 2-iodosylbenzoic acid B (1.05 mmol) in DCM (10 mL) was added trimethylsilyl triflate (1.1 equiv) at rt. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of terminally substituted 1- (trimethylsilyl) -2-phenylacet ylenes **A** (1.1 equiv) dissolved in DCM (5 mL). The resulting suspension was stirred for 6 h at RT. The mixture was then basified with a saturated solution of $NaHCO_3$ (10 mL). The layers were separated and the organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The products (**2l**-**2r**) obtained thereby was further crystallized using DCM/n-pentane.

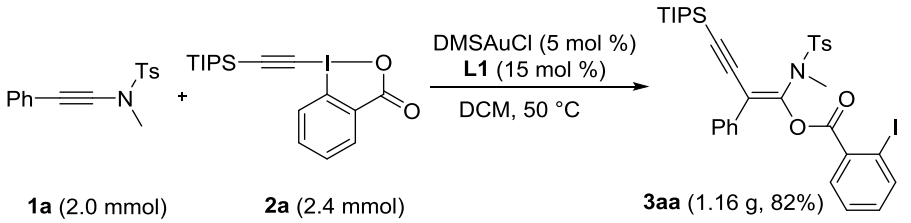
Procedure C: Synthesis of **3**



A mixture of **1** (0.10 mmol, 1.0 equiv) and **2** (0.12 mmol, 1.2 equiv) in 1.0 mL DCM was treated with DMSAuCl (5 mol %), 4,7-diphenyl-1,10-phenanthroline (10 mol %) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed

under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3**.

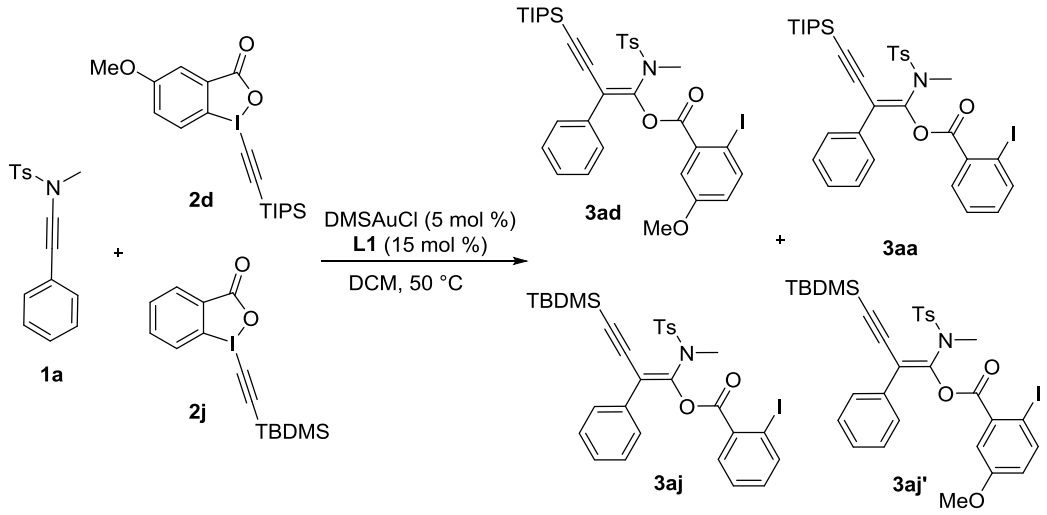
Procedure D: Gram-Scale Synthesis **3aa**



A mixture of **1a** (2.0 mmol, 1.0 equiv) and **2a** (2.4 mmol, 1.2 equiv) in 15 mL DCM was treated with DMSAuCl (5 mol %), 4,7-diphenyl-1,10-phenanthroline (10 mol %) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3aa** in 82% yield (1.16 g).

2.5.3. Mechanistic Experiments

Cross-over experiment



A mixture of **1a** (0.3 mmol, 1.0 equiv), **2d** (0.15 mmol) and **2j** (0.15 mmol) in 2 mL DCM was treated with DMSAuCl (5 mol %), 4,7-diphenyl-1,10-phenanthroline (10 mol %) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **1a** were consumed completely. The reaction mixture was allowed to cool at room temperature, wash the mixture with CH_2Cl_2. Concentrate the residue in vacuo. The crude mixture solution was then measured by ESI-HRMS. HRMS (ESI) $[M+Na]^+$ (m/z) (**3aa**) $C_{34}H_{40}INNaO_4SSi$ calcd for 736.1384, found 736.1402. (**3aj**) $C_{31}H_{34}INNaO_4SSi$ calcd for 694.0914, found 694.0932. (**3ad**)

$C_{35}H_{42}INNaO_5SSi$ calcd for 766.1489, found 766.1520. (**3aj'**) $C_{32}H_{36}INNaO_5SSi$ calcd for 724.1020, found 724.1049. Purify the residue by column chromatography on silica gel (EtOAc : n-Hexane = 1:50) to obtain mixture products **3aa** + **3aj**, **3ad** + **3aj'**. Calculated the ratio (**3aa:3aj** = 2:1, **3ad: 3aj'** = 1.4:1) by the ^{1}H NMR and HPLC analysis

HPLC instrumentation: Eluent: 1:999(2-Propanol:Hexan), Flow rate 1 mL/min; tR = 22.029 min (**3aa**), tR = 24.887 min (**3aj**), tR =36.850 min (**3ad**), tR = 39.030 min (**3aj'**); **3aa:3aj** = 2:1, **3ad: 3aj'** = 1.4:1

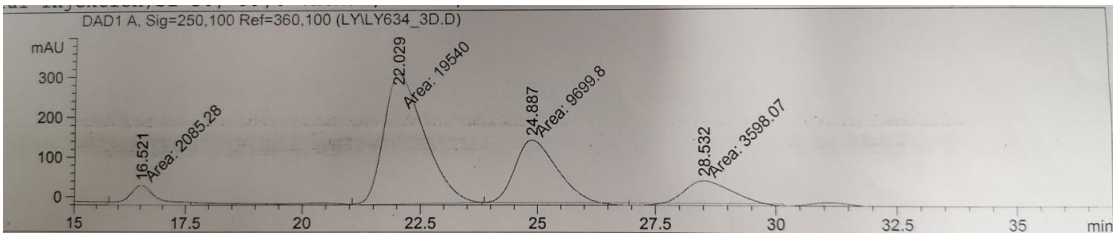
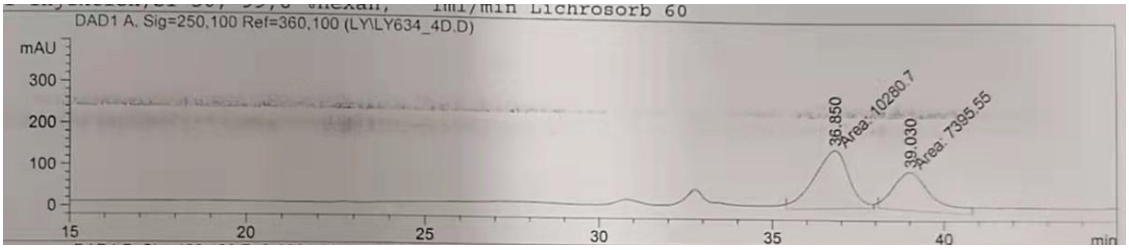
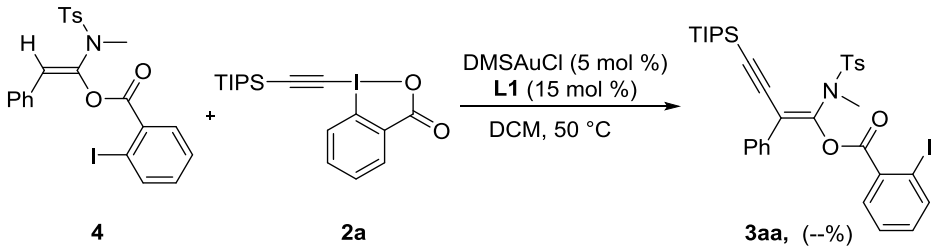


Figure 1: HPLC chromatogram of the mixture((**3aa** and **3aj**)



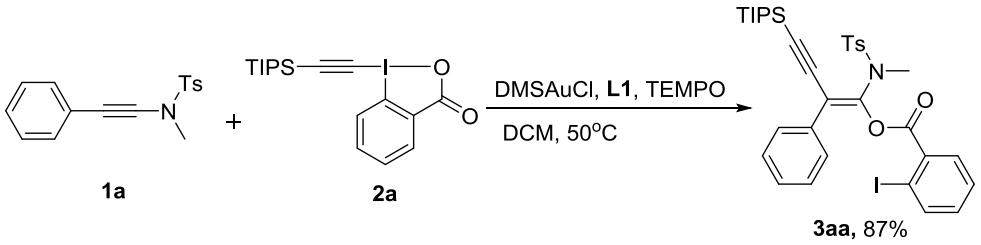
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.850	MM	1.1885	1.02807e4	144.16862	58.1611
2	39.030	MM	1.3072	7395.54785	94.29396	41.8389

Figure 2: HPLC chromatogram of the mixture((**3ad** and **3aj'**)



4 **2a** **3aa,** (--%)

A mixture of **4** (0.1 mmol, 1.0 equiv) and **2a** (0.12 mmol, 1.2 equiv) in 1 mL DCM was treated with DMSAuCl (5 mol %), 4,7-diphenyl-1,10-phenanthroline (10 mol %) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and product **3aa** has not been detected.

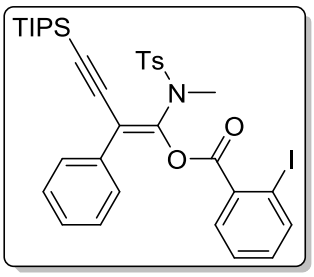


1a **2a** **3aa,** 87%

A mixture of **1a** (0.1 mmol, 1.0 equiv), **2a** (0.12 mmol, 1.2 equiv) and TEMPO (0.2 mmol, 2.0 equiv) in 1 mL DCM was treated with DMSAuCl (5 mol %), 4,7-diphenyl-1,10-phenanthroline (10 mol %) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3aa** in 88% yield.

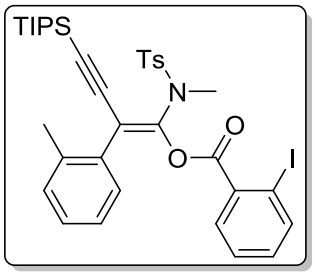
2.5.4 Characterization Data

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3aa)



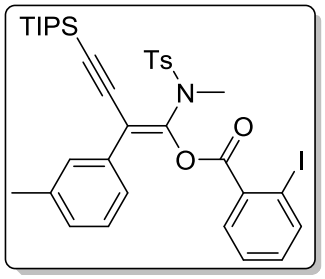
Yield: 62 mg, 87%; white solid; Mp. 101.6-102.3 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 – 7.82 (m, 1H), 7.71 – 7.63 (m, 3H), 7.41 (dd, J = 7.6, 1.4 Hz, 2H), 7.29 – 7.12 (m, 4H), 7.08 – 6.99 (m, 3H), 3.42 (s, 3H), 2.23 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 145.5, 143.6, 141.6, 136.2, 134.4, 133.5, 132.0, 131.7, 129.5, 128.2, 128.1, 127.9, 127.4, 114.7, 101.5, 100.5, 95.2, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2942, 2864, 2144, 1748, 1611, 1582, 1493, 1467, 1444, 1355, 1292, 1267, 1230, 1188, 1160, 1111, 1069, 1032, 1011, 993, 943, 916, 882, 868, 814, 789, 769, 746, 733, 708, 697, 675, 661, 608 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{41}INO_4SSi$ calcd for 714.1565, found 714.1566.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(*o*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ba)



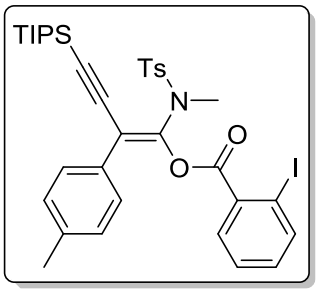
Yield: 54 mg, 75%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.80 (dd, J = 7.9, 0.9 Hz, 1H), 7.68 (d, J = 8.3 Hz, 2H), 7.27 (dd, J = 7.8, 1.7 Hz, 1H), 7.20 – 7.11 (m, 3H), 7.08 (d, J = 3.5 Hz, 3H), 7.06 – 6.97 (m, 3H), 3.43 (s, 3H), 2.34 (s, 3H), 2.27 (s, 3H), 0.95 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.5, 146.3, 143.7, 141.2, 136.4, 136.1, 133.9, 133.1, 132.4, 131.5, 130.1, 129.6, 128.4, 128.2, 127.7, 127.6, 125.7, 115.0, 101.2, 100.5, 94.6, 37.7, 21.5, 19.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2943, 2890, 2865, 2143, 1752, 1631, 1598, 1582, 1562, 1462, 1360, 1303, 1265, 1227, 1160, 1124, 1096, 1067, 1008, 949, 883, 815, 772, 740, 722, 670, 640, 612 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_4SSi$ calcd for 728.1721, found 728.1733.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(*m*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ca)



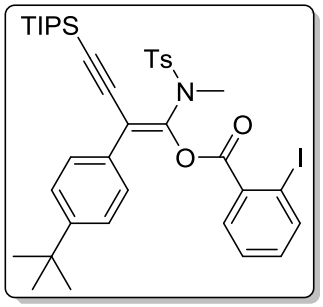
Yield: 60 mg, 83%; white solid; Mp. 97.0-98.0 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85 (d, J = 7.8 Hz, 1H), 7.72 (dd, J = 7.8, 1.6 Hz, 1H), 7.66 (d, J = 8.3 Hz, 2H), 7.30 – 7.19 (m, 3H), 7.06 (ddd, J = 11.6, 6.1, 3.2 Hz, 5H), 6.95 (d, J = 7.5 Hz, 1H), 3.41 (s, 3H), 2.23 (s, 3H), 2.17 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 145.3, 143.6, 141.6, 137.6, 136.2, 134.2, 133.5, 132.0, 131.9, 129.5, 129.0, 128.9, 128.0, 127.9, 127.5, 125.2, 114.8, 101.6, 100.3, 95.1, 37.8, 21.3, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2952, 2864, 2146, 1752, 1600, 1584, 1467, 1430, 1351, 1277, 1229, 1173, 1157, 1114, 1072, 1035, 1010, 965, 907, 885, 851, 813, 783, 760, 739, 707, 684, 665, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_4SSi$ calcd for 728.1721, found 728.1731.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(*p*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3da)



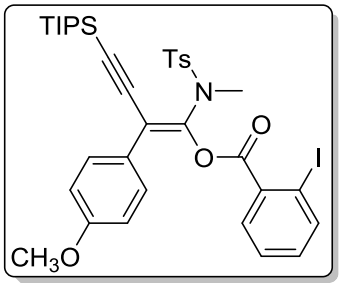
Yield: 56 mg, 78%; white solid; Mp. 115.2-116.2 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88 (dd, J = 7.9, 1.0 Hz, 1H), 7.74 (dd, J = 7.8, 1.6 Hz, 1H), 7.66 (d, J = 8.3 Hz, 2H), 7.30 (ddd, J = 8.8, 6.9, 2.9 Hz, 3H), 7.11 – 6.97 (m, 5H), 3.42 (s, 3H), 2.25 (s, 3H), 2.21 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 145.1, 143.6, 141.6, 138.1, 136.3, 133.5, 132.2, 131.8, 131.5, 129.6, 128.8, 128.1, 128.0, 127.5, 114.8, 101.6, 100.2, 95.2, 37.9, 21.5, 21.2, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2941, 2888, 2863, 2146, 1747, 1619, 1595, 1582, 1511, 1466, 1355, 1316, 1290, 1271, 1231, 1180, 1159, 1124, 1104, 1070, 1032, 1010, 994, 943, 882, 869, 823, 813, 787, 757, 738, 718, 706, 678, 657, 636, 606 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_4SSi$ calcd for 728.1721, found 728.1731.

(*E*)-2-(4-(tert-butyl)phenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ea)



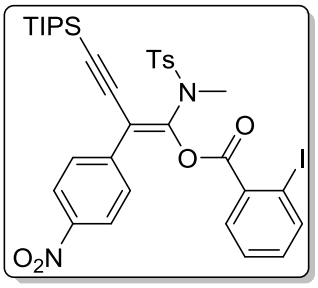
Yield: 62 mg, 81%; white solid; Mp. 116.2-117.6 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 (dd, J = 7.9, 1.0 Hz, 1H), 7.74 – 7.63 (m, 3H), 7.38 (d, J = 8.4 Hz, 2H), 7.27 (td, J = 7.7, 1.1 Hz, 1H), 7.23 – 7.17 (m, 2H), 7.10 – 7.00 (m, 3H), 3.42 (s, 3H), 2.24 (s, 3H), 1.19 (s, 9H), 1.00 (d, J = 1.5 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 151.3, 145.1, 143.6, 141.6, 136.4, 133.4, 132.1, 131.2, 129.5, 128.0, 127.9, 127.5, 125.0, 114.7, 101.6, 100.1, 95.1, 37.9, 34.5, 31.2, 21.5, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2947, 2865, 2146, 1751, 1619, 1583, 1563, 1512, 1494, 1462, 1431, 1406, 1359, 1269, 1226, 1160, 1122, 1094, 1066, 1006, 950, 884, 864, 838, 813, 789, 739, 681, 661, 639, 612 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{38}H_{49}INO_4SSi$ calcd for 770.2191, found 770.2211.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(4-methoxyphenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3fa)



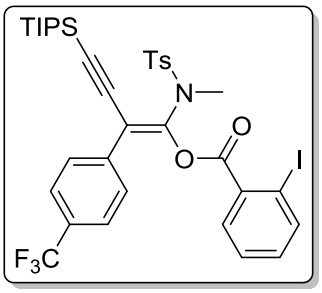
Yield: 53 mg, 72%; white solid; Mp. 76.5-77.3 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, J = 7.9, 1.0 Hz, 1H), 7.75 (dd, J = 7.8, 1.6 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.30 (td, J = 7.7, 1.1 Hz, 1H), 7.08 (ddd, J = 12.8, 9.4, 4.9 Hz, 3H), 6.75 – 6.69 (m, 2H), 3.69 (s, 3H), 3.41 (s, 3H), 2.25 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.3, 159.5, 144.6, 143.6, 141.7, 136.4, 133.5, 132.2, 131.9, 129.7, 129.6, 128.0, 127.6, 126.7, 114.6, 113.6, 101.8, 100.2, 95.3, 55.2, 38.0, 21.6, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2943, 2864, 2146, 1749, 1607, 1582, 1511, 1462, 1356, 1304, 1290, 1251, 1224, 1176, 1158, 1119, 1100, 1065, 1033, 1005, 948, 883, 833, 812, 787, 758, 738, 724, 702, 661, 638, 611 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_5SSi$ calcd for 744.1670, found 744.1695.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(4-nitrophenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ga)



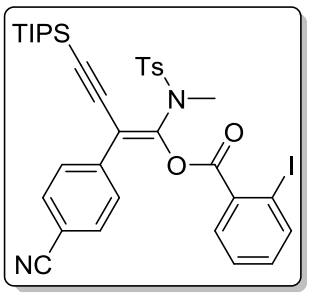
Yield: 69 mg, 92%; white solid; Mp. 132.7-133.2 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.10 – 8.02 (m, 2H), 7.89 (dd, J = 7.9, 0.9 Hz, 1H), 7.73 (dd, J = 7.9, 1.6 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.63 – 7.55 (m, 2H), 7.31 (td, J = 7.7, 1.1 Hz, 1H), 7.15 – 7.03 (m, 3H), 3.42 (s, 3H), 2.26 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.8, 147.3, 144.0, 141.9, 141.4, 135.9, 133.9, 132.1, 131.1, 129.7, 129.2, 128.1, 127.5, 123.5, 112.3, 102.2, 100.2, 95.3, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 3111, 2941, 2862, 2144, 1761, 1623, 1595, 1517, 1462, 1433, 1408, 1356, 1342, 1305, 1265, 1225, 1156, 1113, 1099, 1058, 1030, 994, 949, 919, 882, 869, 849, 810, 788, 760, 737, 702, 690, 656, 638, 606 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{40}IN_2O_6SSi$ calcd for 759.1416, found 759.1436.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(4-(trifluoromethyl)phenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ha)



Yield: 72 mg, 93%; white solid; Mp. 122.5-123.4 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 (d, J = 7.9 Hz, 1H), 7.73 – 7.63 (m, 3H), 7.54 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.29 (dd, J = 11.0, 4.2 Hz, 1H), 7.12 – 7.01 (m, 3H), 3.42 (s, 3H), 2.25 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0, 146.6, 143.9, 141.8, 136.1, 133.7, 132.1, 131.5, 129.7, 128.6, 128.0, 127.5, 125.2, 125.1, 113.2, 101.5, 100.7, 95.2, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2941, 2864, 2136, 1749, 1613, 1582, 1463, 1408, 1355, 1326, 1305, 1264, 1228, 1174, 1156, 1115, 1100, 1065, 1030, 1008, 943, 884, 870, 848, 835, 815, 788, 757, 744, 733, 706, 671, 649, 633, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{40}F_3INO_4SSi$ calcd for 782.1439, found 782.1446.

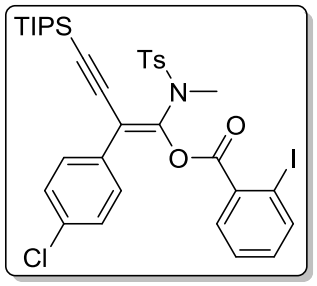
(*E*)-2-(4-cyanophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(triisopropylsilyl) but-1-en-3-yn-1-yl 2-iodobenzoate (3ia)



Yield: 67 mg, 91%; white solid; Mp. 142.5-143.2 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.91 (dd, J = 7.9, 0.8 Hz, 1H), 7.72 (dd, J = 7.8, 1.6 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.56 – 7.47 (m, 4H), 7.32 (td, J = 7.7, 1.0 Hz, 1H), 7.11 (ddd, J = 12.8, 9.4, 4.9 Hz, 3H), 3.41 (s, 3H), 2.27 (s, 3H), 0.99 (d, J = 4.2 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.9, 147.0, 144.0, 141.9, 139.5, 135.9, 133.9, 132.1, 132.0, 131.3, 129.7, 129.0, 128.1, 127.5, 118.5, 112.7, 111.9, 102.0, 100.3, 95.3, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2944, 2864, 2230, 2142, 1758, 1631, 1601, 1582, 1563, 1494, 1460, 1432, 1407, 1355, 1265, 1225, 1158, 1119, 1100, 1057, 1031, 994, 950, 920, 884, 863, 848, 813, 748, 736, 723, 690, 675, 660, 609 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{40}IN_2O_4SSi$ calcd for 739.1517, found 739.1542.

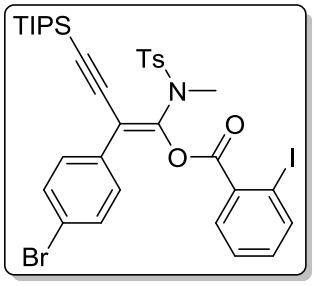
(*E*)-2-(4-chlorophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(triisopropylsilyl) but-1-en-3-yn-1-yl 2-iodobenzoate (3ja)

Yield: 62 mg, 83%; white solid; Mp. 130.4-131.2 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, J = 7.9, 0.9 Hz, 1H), 7.72 (dd, J = 7.8, 1.6 Hz,



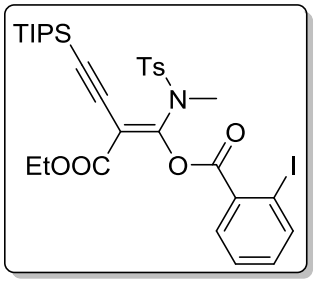
1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.40 – 7.33 (m, 2H), 7.30 (td, *J* = 7.7, 1.1 Hz, 1H), 7.21 – 7.14 (m, 2H), 7.13 – 7.01 (m, 3H), 3.41 (s, 3H), 2.25 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.1, 145.8, 143.8, 141.7, 136.2, 134.1, 133.6, 133.0, 132.1, 131.6, 129.6, 128.4, 128.0, 127.5, 113.6, 101.0, 95.2, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2957, 2942, 2862, 2147, 1916, 1750, 1621, 1595, 1490, 1467, 1400, 1351, 1307, 1293, 1265, 1232, 1181, 1158, 1114, 1100, 1091, 1069, 1032, 1010, 944, 882, 833, 814, 800, 779, 742, 695, 681, 652, 606 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{40}ClINO_4SSi$ calcd for 748.1175, found 748.1194.

(*E*)-2-(4-bromophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(triisopropylsilyl) but-1-en-3-yn-1-yl 2-iodobenzoate (3ka)



Yield: 64 mg, 81%; white solid; Mp. 119.4-119.8 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88 (d, *J* = 7.6 Hz, 1H), 7.69 (dd, *J* = 17.9, 7.5 Hz, 3H), 7.31 (d, *J* = 3.0 Hz, 5H), 7.07 (dd, *J* = 17.7, 7.4 Hz, 3H), 3.40 (s, 3H), 2.25 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0, 145.8, 143.8, 141.7, 136.1, 133.6, 133.5, 132.1, 131.6, 131.4, 129.9, 129.6, 128.0, 127.5, 122.4, 113.6, 101.0, 100.9, 95.3, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2942, 2864, 2143, 1742, 1628, 1582, 1562, 1487, 1462, 1427, 1396, 1348, 1306, 1294, 1267, 1233, 1189, 1159, 1108, 1095, 1069, 1053, 1034, 1010, 995, 948, 882, 869, 831, 815, 791, 782, 743, 721, 705, 673, 651, 627, 608 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{34}H_{40}BrINNaO_4SSi$ calcd for 814.0489, found 814.0503.

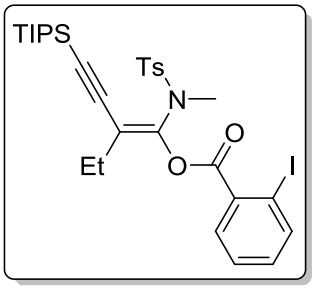
(*Z*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(ethoxycarbonyl)-4-(triisopropylsilyl) but-1-en-3-yn-1-yl 2-iodobenzoate (3la)



Yield: 55 mg, 78%; white solid; Mp. 96.5-97.8 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.04 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.96 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.61 (d, *J* = 8.3 Hz, 2H), 7.38 (td, *J* = 7.7, 1.1 Hz, 1H), 7.14 (td, *J* = 7.7, 1.7 Hz, 1H), 7.02 (d, *J* = 8.1 Hz, 2H), 4.07 (q, *J*

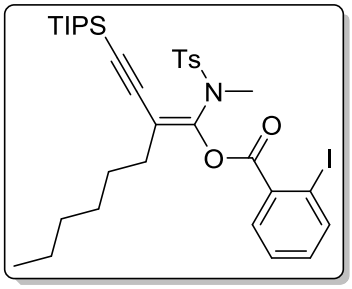
= 7.1 Hz, 2H), 3.38 (s, 3H), 2.26 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.01 (d, *J* = 5.1 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.7, 161.9, 155.0, 144.2, 141.9, 135.8, 133.8, 132.9, 130.8, 129.7, 128.0, 127.5, 104.0, 103.1, 97.2, 95.9, 61.5, 37.9, 21.6, 18.5, 13.9, 11.2. IR (reflection) $\tilde{\nu}$ = 2943, 2864, 2155, 1752, 1717, 1611, 1583, 1563, 1463, 1432, 1367, 1277, 1230, 1162, 1128, 1078, 1063, 1032, 1004, 921, 882, 848, 816, 789, 778, 752, 738, 717, 697, 677, 657, 639, 609 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{31}H_{41}INO_6SSi$ calcd for 710.1463, found 710.1467.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-ethyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ma)



Yield: 48 mg, 72%; white solid; Mp. 78.5-79.4 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.98 – 7.86 (m, 2H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.21 – 7.02 (m, 3H), 3.29 (s, 3H), 2.26 (s, 3H), 2.11 (q, *J* = 7.5 Hz, 2H), 1.05 (t, *J* = 7.5 Hz, 3H), 1.01 – 0.92 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.5, 144.4, 143.5, 141.6, 136.2, 133.5, 132.3, 132.2, 129.5, 128.0, 127.6, 116.3, 101.0, 100.1, 95.0, 37.8, 24.5, 21.5, 18.5, 12.3, 11.2. IR (reflection) $\tilde{\nu}$ = 3064, 3019, 2940, 2862, 2144, 1753, 1612, 1580, 1493, 1460, 1429, 1352, 1322, 1267, 1225, 1180, 1150, 1118, 1101, 1075, 1031, 998, 954, 917, 884, 869, 794, 770, 759, 736, 707, 692, 681, 667, 652, 635 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{30}H_{40}INNaO_4SSi$ calcd for 688.1384, found 688.1385.

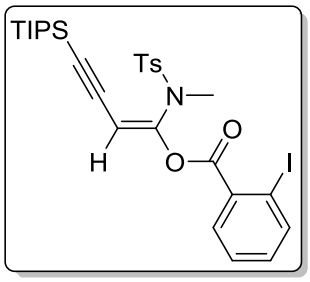
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-((triisopropylsilyl)ethynyl)oct-1-en-1-yl 2-iodobenzoate (3na)



Yield: 50 mg, 70%; white solid; Mp. 66.9-67.7 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.72 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.37 – 7.31 (m, 2H), 7.28 (td, *J* = 7.7, 1.1 Hz, 1H), 7.09 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.06 – 6.98 (m, 4H), 3.42 (s, 3H), 2.52 – 2.40 (m, 2H), 2.25 (s, 3H), 1.46 (dd, *J* = 14.4, 6.7 Hz, 2H), 1.23 – 1.15 (m, 6H), 1.03 – 0.96 (m, 21H), 0.77 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.3, 143.4, 143.1, 141.6, 136.3, 133.4, 132.1, 129.5, 128.1, 127.9, 127.5, 114.8, 101.7, 100.2, 95.2, 37.9, 35.6, 31.6, 31.1, 28.9, 22.5, 21.5,

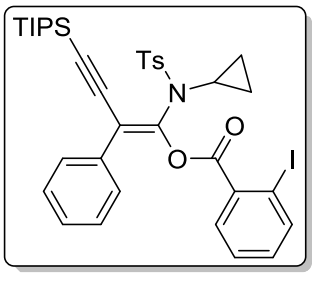
18.6, 14.0, 11.3. IR (reflection) $\tilde{\nu}$ = 2928, 2864, 2145, 1751, 1620, 1582, 1563, 1511, 1463, 1360, 1289, 1225, 1160, 1104, 1067, 1032, 1007, 950, 883, 815, 769, 740, 705, 680, 665, 639, 619 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{49}INO_4SSi$ calcd for 722.2191, found 722.5301.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3oa)



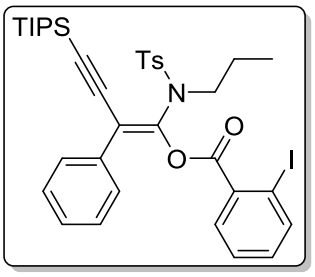
Yield: 46 mg, 73%; white solid; Mp. 89.3-89.7 °C; R_f= 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (td, *J* = 8.1, 1.3 Hz, 2H), 7.72 – 7.66 (m, 2H), 7.36 (td, *J* = 7.7, 1.1 Hz, 1H), 7.16 – 7.09 (m, 3H), 5.51 (s, 1H), 3.32 (s, 3H), 2.29 (s, 3H), 0.97 – 0.90 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ =163.5, 150.2, 143.9, 141.7, 135.7, 133.6, 132.4, 132.3, 129.7, 128.1, 127.7, 101.3, 99.3, 97.92, 95.2, 37.7, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2944, 2865, 2138, 1746, 1646, 1598, 1581, 1463, 1428, 1357, 1327, 1307, 1287, 1264, 1234, 1212, 1152, 1126, 1096, 1069, 1050, 1010, 994, 929, 879, 816, 788, 745, 736, 708, 691, 671, 654, 639, 620 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{37}INO_4SSi$ calcd for 638.1252, found 638.1260.

(*E*)-1-((*N*-cyclopropyl-4-methylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3pa)



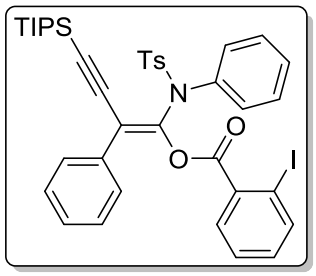
Yield: 60 mg, 82%; white solid; Mp. 138.9-139.6 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 – 7.76 (m, 3H), 7.49 – 7.35 (m, 3H), 7.25 – 7.14 (m, 6H), 7.04 (td, *J* = 7.7, 1.7 Hz, 1H), 2.66 (tt, *J* = 6.9, 3.5 Hz, 1H), 2.33 (s, 3H), 1.28 – 1.10 (m, 2H), 0.99 (s, 21H), 0.79 – 0.73 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.0, 144.0, 143.9, 141.5, 136.0, 135.2, 133.2, 132.9, 131.4, 129.5, 128.4, 128.3, 128.3, 128.2, 127.7, 116.2, 102.6, 98.8, 94.8, 31.0, 21.6, 18.6, 11.3, 8.4. IR (reflection) $\tilde{\nu}$ = 2941, 2862, 2148, 1770, 1621, 1597, 1580, 1494, 1461, 1427, 1353, 1292, 1248, 1221, 1191, 1167, 1096, 1076, 1056, 1037, 1013, 987, 926, 885, 870, 830, 812, 783, 772, 734, 700, 670, 636, 616 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{36}H_{43}INO_4SSi$ calcd for 740.1721, found 740.1741.

(*E*)-1-((4-methyl-*N*-propylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3qa)



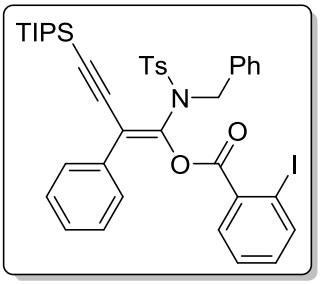
Yield: 59 mg, 80%; white solid; Mp. 90.1-90.7 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (dd, J = 7.9, 1.0 Hz, 1H), 7.78 (d, J = 8.3 Hz, 2H), 7.47 – 7.39 (m, 3H), 7.26 – 7.14 (m, 7H), 7.08 – 7.01 (m, 1H), 3.55 – 3.47 (m, 2H), 2.32 (s, 3H), 1.84 (dd, J = 15.3, 7.5 Hz, 2H), 1.00 – 0.96 (m, 21H), 0.90 (dd, J = 9.3, 5.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.2, 143.5, 142.9, 141.4, 136.8, 135.4, 133.1, 133.0, 131.4, 129.6, 128.2, 128.2, 128.2, 127.9, 127.7, 117.3, 102.3, 100.1, 94.7, 51.9, 22.5, 21.5, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2945, 2864, 2145, 1757, 1612, 1582, 1563, 1494, 1463, 1427, 1357, 1292, 1274, 1241, 1207, 1172, 1116, 1092, 1072, 1009, 972, 920, 883, 812, 768, 744, 728, 697, 682, 665, 642, 614 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{36}H_{45}INO_4SSi$ calcd for 742.1878, found 742.1885.

(*E*)-1-((4-methyl-*N*-phenylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ra)



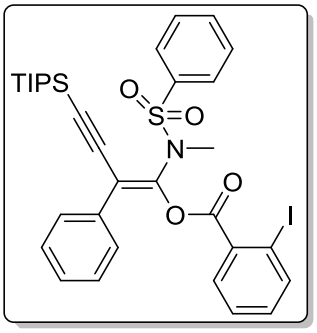
Yield: 66 mg, 85%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.84 (dd, J = 7.9, 1.0 Hz, 1H), 7.64 (d, J = 8.3 Hz, 2H), 7.53 (dd, J = 7.8, 1.6 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.43 – 7.39 (m, 2H), 7.28 (td, J = 7.7, 1.1 Hz, 1H), 7.24 – 7.20 (m, 3H), 7.19 – 7.13 (m, 4H), 7.10 – 7.05 (m, 3H), 2.30 (s, 3H), 1.06 – 0.99 (m, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 161.0, 143.8, 142.5, 141.6, 138.7, 137.1, 135.4, 133.3, 132.6, 132.3, 131.3, 129.3, 129.0, 128.7, 128.3, 128.2, 128.2, 128.2, 127.7, 118.5, 102.8, 100.0, 95.0, 21.6, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2943, 2864, 2142, 1765, 1597, 1492, 1463, 1367, 1262, 1224, 1171, 1095, 1073, 1037, 1010, 987, 942, 883, 814, 774, 738, 696, 670, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{39}H_{43}INO_4SSi$ calcd for 776.1721, found 776.1781.

(*E*)-1-((*N*-benzyl-4-methylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3sa)



Yield: 59 mg, 75%; white solid; Mp. 85.6-86.4 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.81 (dd, J = 7.9, 1.1 Hz, 1H), 7.73 – 7.65 (m, 2H), 7.51 (dd, J = 7.8, 1.7 Hz, 1H), 7.48 – 7.42 (m, 2H), 7.28 – 7.16 (m, 8H), 7.13 – 7.09 (m, 5H), 7.03 (td, J = 7.7, 1.7 Hz, 1H), 4.92 (s, 2H), 2.30 (s, 3H), 0.98 (d, J = 3.1 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.3, 143.6, 143.4, 141.4, 137.1, 135.8, 138.6, 133.0, 133.0, 131.7, 129.5, 129.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 116.1, 102.3, 100.9, 94.7, 53.4, 21.5, 18.6, 11.4. IR (reflection) $\tilde{\nu}$ = 2942, 2864, 2144, 1762, 1597, 1580, 1494, 1459, 1354, 1291, 1264, 1233, 1163, 1092, 1073, 1056, 1013, 993, 921, 897, 883, 814, 785, 771, 737, 707, 696, 681, 664, 642, 617 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{40}H_{45}INO_4SSi$ calcd for 790.1878, found 790.1895.

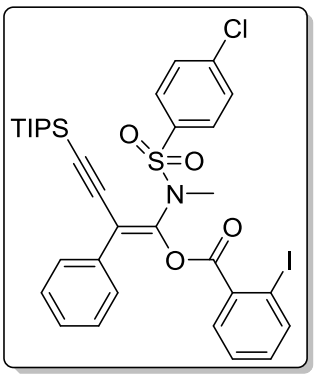
(*E*)-1-(*N*-methylphenylsulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ta)



Yield: 63 mg, 91%; white solid; Mp. 83.1-83.7 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.87 (dd, J = 7.9, 1.0 Hz, 1H), 7.80 (dd, J = 5.2, 3.4 Hz, 2H), 7.68 (dd, J = 7.8, 1.7 Hz, 1H), 7.45 – 7.36 (m, 3H), 7.32 – 7.24 (m, 3H), 7.21 – 7.15 (m, 3H), 7.07 (td, J = 7.7, 1.7 Hz, 1H), 3.43 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.3, 145.2, 141.7, 139.1, 134.4, 133.5, 132.9, 132.0, 131.9, 128.9, 128.3, 128.2, 128.1, 127.9, 127.5, 115.2, 101.4, 100.7, 95.1, 37.8, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 3062, 2943, 2890, 2864, 2145, 1751, 1620, 1582, 1562, 1463, 1447, 1362, 1265, 1226, 1183, 1109, 1069, 1032, 1007, 949, 883, 773, 742, 690, 644, 613 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{39}INO_4SSi$ calcd for 700.1408, found 700.1440.

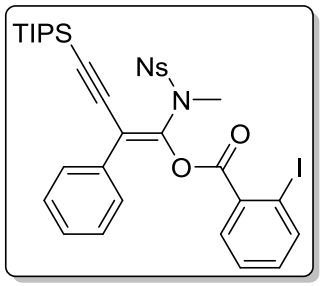
(*E*)-1-((4-chloro-*N*-methylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ua)

Yield: 65 mg, 89%; white solid; Mp. 76.4-76.9 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, J = 7.9, 0.8 Hz, 1H), 7.75 – 7.70 (m, 2H), 7.67 (dd, J = 7.8, 1.6 Hz, 1H), 7.42 (dd, J = 7.8, 1.7 Hz, 2H), 7.29 (td, J = 7.6, 1.0 Hz, 1H),



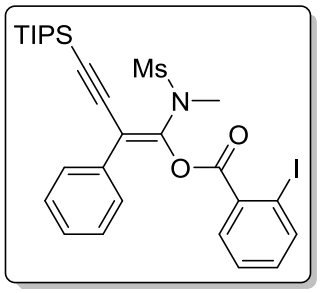
7.25 – 7.16 (m, 5H), 7.09 (td, J = 7.7, 1.6 Hz, 1H), 3.44 (s, 3H), 0.98 (d, J = 4.7 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 145.0, 141.8, 139.5, 137.7, 134.3, 133.6, 131.9, 131.7, 129.3, 128.9, 128.4, 128.2, 128.2, 128.0, 115.3, 101.2, 101.0, 95.2, 38.1, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 3089, 3059, 2943, 2890, 2864, 2143, 1748, 1612, 1583, 1493, 1467, 1444, 1396, 1357, 1274, 1230, 1185, 1161, 1110, 1094, 1067, 1032, 1009, 993, 943, 915, 883, 867, 827, 789, 779, 766, 757, 744, 730, 708, 695, 681, 647, 612 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{38}ClINO_4SSi$ calcd for 734.1019, found 734.1034.

(*E*)-1-((*N*-methyl-4-nitrophenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3va)



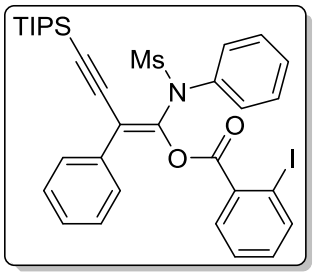
Yield: 68 mg, 92%; white solid; Mp. 133.0-133.7 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.07 – 8.01 (m, 2H), 7.98 – 7.91 (m, 2H), 7.86 (dd, J = 7.9, 0.9 Hz, 1H), 7.64 (dd, J = 7.8, 1.6 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.33 – 7.16 (m, 4H), 7.09 (td, J = 7.7, 1.7 Hz, 1H), 3.51 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.0, 149.9, 144.9, 144.4, 141.9, 133.9, 133.9, 131.8, 131.2, 128.6, 128.6, 128.2, 128.1, 128.0, 124.2, 116.0, 101.6, 101.0, 95.3, 38.4, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 3099, 2937, 2861, 2146, 1761, 1625, 1606, 1581, 1531, 1461, 1429, 1402, 1367, 1348, 1311, 1271, 1225, 1157, 1106, 1088, 1062, 1032, 1000, 973, 950, 927, 883, 854, 789, 772, 751, 739, 705, 695, 681, 671, 644, 619 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{38}IN_2O_6SSi$ calcd for 745.1259, found 745.1262.

(*E*)-1-(*N*-methylmethylsulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3wa)



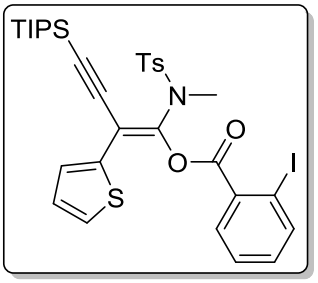
Yield: 57 mg, 89%; white solid; Mp. 96.1-97.3 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, J = 7.9, 1.0 Hz, 1H), 7.80 (dd, J = 7.8, 1.6 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.34 – 7.16 (m, 4H), 7.07 (td, J = 7.7, 1.7 Hz, 1H), 3.48 (s, 3H), 3.05 (s, 3H), 1.04 (d, J = 2.8 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.8, 145.4, 141.4, 134.1, 133.6, 132.5, 132.1, 128.5, 128.3, 128.2, 128.1, 115.2, 101.8, 101.2, 94.7, 39.7, 37.8, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2939, 2862, 2142, 1753, 1612, 1579, 1492, 1460, 1429, 1352, 1323, 1266, 1224, 1179, 1150, 1117, 1100, 1074, 1060, 1030, 998, 954, 917, 883, 869, 793, 770, 759, 736, 706, 692, 681, 666, 651, 635 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{37}INO_4SSi$ calcd for 638.1252, found 638.1262.

(*E*)-2-phenyl-1-(*N*-phenylmethylsulfonamido)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3xa)



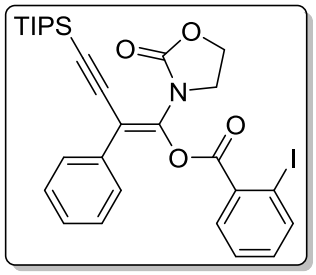
Yield: 56 mg, 80%; white solid; Mp. 89.3-89.7 ^{o}C; R_f = 0.35 (PE/EA = 20/1);^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.83 (dd, J = 7.9, 0.9 Hz, 1H), 7.69 – 7.59 (m, 3H), 7.51 – 7.45 (m, 2H), 7.35 – 7.24 (m, 4H), 7.20 – 7.14 (m, 3H), 7.04 (td, J = 7.7, 1.7 Hz, 1H), 3.25 (s, 3H), 1.04 (d, J = 3.0 Hz, 21H).. ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.7, 142.4, 141.5, 138.1, 134.9, 133.3, 132.8, 131.4, 129.5, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 118.4, 103.4, 99.9, 94.6, 41.1, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 3062, 2943, 2891, 2865, 2140, 1762, 1677, 1595, 1492, 1463, 1447, 1360, 1324, 1260, 1225, 1157, 1097, 1073, 1038, 1012, 989, 964, 920, 883, 772, 738, 696, 680, 613 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{39}INO_4SSi$ calcd for 700.1408, found 700.1455.

(*Z*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-(thiophen-2-yl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ya)



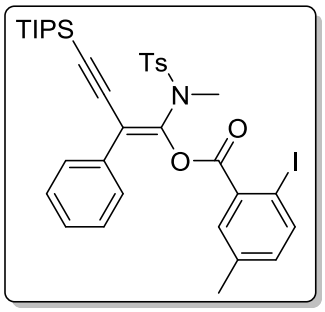
Yield: 54 mg, 75%; yellow liquid; R_f= 0.30 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.16 (dd, J = 7.9, 1.6 Hz, 1H), 7.99 (dd, J = 7.9, 1.0 Hz, 1H), 7.64 (d, J = 8.3 Hz, 2H), 7.42 (td, J = 7.7, 1.1 Hz, 1H), 7.38 (dd, J = 3.7, 1.2 Hz, 1H), 7.21 – 7.14 (m, 2H), 7.01 (d, J = 8.1 Hz, 2H), 6.91 (dd, J = 5.1, 3.8 Hz, 1H), 3.45 (s, 3H), 2.23 (s, 3H), 1.04 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.5, 143.6, 143.5, 142.1, 136.5, 136.1, 133.9, 133.1, 131.1, 129.6, 129.1, 128.1, 127.5, 127.4, 126.6, 109.3, 100.4, 99.3, 95.8, 38.5, 21.5, 18.6, 11.3. IR (reflection) $\tilde{\nu}$ = 2944, 2865, 2153, 1754, 1600, 1582, 1563, 1462, 1429, 1357, 1303, 1264, 1232, 1217, 1160, 1093, 1075, 1060, 1036, 999, 928, 884, 853, 814, 787, 737, 703, 682, 664, 639, 627 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{32}H_{39}INO_4S_2Si$ calcd for 720.1129, found 720.1145.

(*E*)-1-(2-oxooxazolidin-3-yl)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3za)



Yield: 44 mg, 72%; white solid; Mp. 99.8-100.3 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.94 – 7.73 (m, 4H), 7.37 – 7.16 (m, 4H), 7.04 (td, J = 7.8, 1.6 Hz, 1H), 4.56 (t, J = 5.3 Hz, 2H), 4.04 (t, J = 5.3 Hz, 2H), 1.03 (d, J = 3.4 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 165.7, 152.9, 142.7, 141.3, 133.9, 132.8, 131.4, 128.9, 128.6, 127.9, 127.0, 124.2, 107.0, 106.9, 94.3, 92.3, 62.0, 41.5, 18.5, 11.1. IR (reflection) $\tilde{\nu}$ = 3059, 2948, 2868, 2157, 1753, 1728, 1579, 1493, 1462, 1450, 1429, 1387, 1367, 1338, 1284, 1246, 1134, 1099, 1063, 1050, 1015, 1006, 918, 883, 822, 768, 757, 746, 686, 661, 640 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{35}INO_4Si$ calcd for 616.1375, found 616.1392.

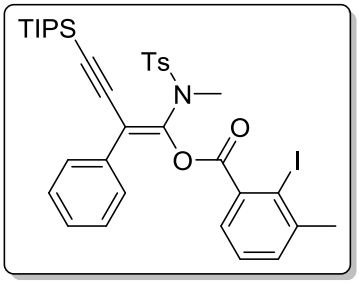
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodo-5-methylbenzoate (3ab)



Yield: 62 mg, 85%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.71 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.46 (d, J = 1.8 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.23 – 7.14 (m, 3H), 7.04 (d, J = 8.0

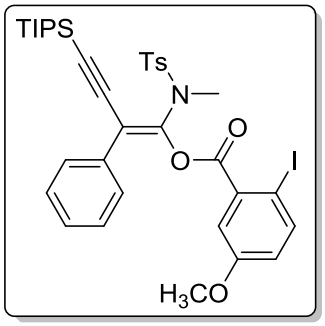
Hz, 2H), 6.90 – 6.85 (m, 1H), 3.42 (s, 3H), 2.24 (s, 3H), 2.20 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4, 145.5, 143.6, 141.3, 138.1, 136.3, 134.5, 134.5, 132.7, 131.6, 129.6, 128.3, 128.2, 128.1, 127.5, 114.8, 101.5, 100.4, 91.1, 37.8, 21.5, 20.7, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2943, 2865, 2143, 1750, 1619, 1598, 1563, 1494, 1465, 1359, 1299, 1263, 1239, 1187, 1160, 1109, 1067, 1007, 951, 919, 902, 884, 815, 768, 731, 698, 670, 642, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_4SSi$ calcd for 728.1721, found 728.1746.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodo-3-methylbenzoate (3ac)



Yield: 61 mg, 84%; white solid; Mp. 78.1-78.9 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.70 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.1 Hz, 2H), 7.36 (d, J = 7.7 Hz, 1H), 7.27 (d, J = 7.4 Hz, 1H), 7.23 – 7.12 (m, 5H), 7.08 (d, J = 8.1 Hz, 2H), 3.41 (s, 3H), 2.41 (s, 3H), 2.27 (s, 3H), 0.97 (d, J = 2.9 Hz, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 164.6, 145.4, 143.8, 143.7, 136.1, 134.5, 134.2, 133.0, 129.6, 128.9, 128.4, 128.2, 128.1, 127.7, 127.6, 115.1, 101.5, 101.4, 100.4, 37.8, 30.0, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2943, 2865, 2142, 1751, 1619, 1599, 1572, 1494, 1461, 1447, 1401, 1359, 1281, 1252, 1236, 1174, 1160, 1084, 1061, 1015, 998, 951, 920, 884, 814, 770, 747, 695, 668, 640, 611 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_4SSi$ calcd for 728.1721, found 728.1758.

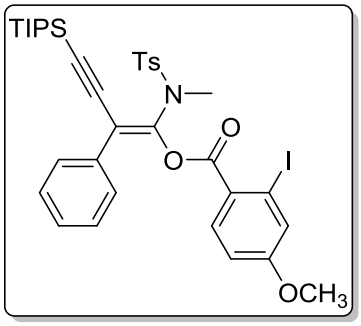
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodo-5-methoxybenzoate (3ad)



Yield: 65 mg, 88%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.69 (dd, J = 8.5, 3.2 Hz, 3H), 7.44 – 7.39 (m, 2H), 7.28 (d, J = 3.1 Hz, 1H), 7.24 – 7.14 (m, 3H), 7.07 (d, J = 8.1 Hz, 2H), 6.67 (dd, J = 8.7, 3.1 Hz, 1H), 3.68 (s, 3H), 3.42 (s, 3H), 2.26 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.3, 159.4, 145.5,

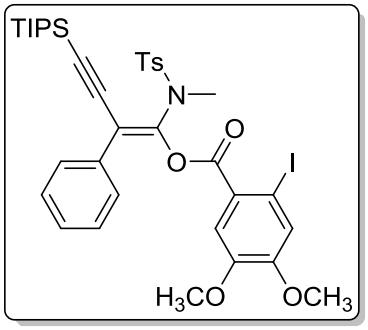
143.8, 141.9, 136.2, 134.5, 132.8, 129.6, 128.3, 128.2, 128.1, 127.5, 120.5, 117.2, 114.7, 101.4, 100.6, 83.3, 55.5, 37.9, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2942, 2864, 2144, 1752, 1620, 1592, 1565, 1467, 1360, 1320, 1289, 1242, 1206, 1177, 1160, 1110, 1071, 1036, 1002, 951, 916, 883, 815, 769, 731, 698, 669, 642, 626 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_5SSi$ calcd for 744.1670, found 744.1685.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodo-4-methoxybenzoate (3ae)



Yield: 67 mg, 90%; white solid; Mp. 105.6-106.2 ^oC; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.72 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 8.3 Hz, 2H), 7.44 – 7.37 (m, 3H), 7.21 – 7.11 (m, 3H), 7.02 (d, J = 8.0 Hz, 2H), 6.76 (dd, J = 8.9, 2.5 Hz, 1H), 3.73 (s, 3H), 3.42 (s, 3H), 2.23 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.7, 162.5, 145.7, 143.5, 136.4, 134.5, 133.7, 129.5, 128.2, 128.1, 128.0, 127.5, 127.4, 123.0, 114.3, 113.4, 101.6, 100.2, 96.8, 55.7, 37.9, 21.5, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2944, 2864, 2137, 1738, 1613, 1590, 1555, 1493, 1461, 1383, 1354, 1310, 1268, 1226, 1176, 1156, 1107, 1067, 1026, 1007, 947, 918, 883, 870, 859, 835, 813, 770, 728, 694, 681, 666, 647, 625 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{43}INO_5SSi$ calcd for 744.1670, found 744.1701.

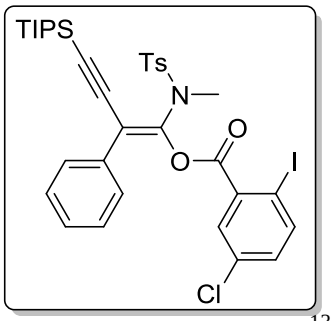
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodo-4,5-dimethoxybenzoate (3af)



Yield: 71 mg, 92%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.67 (d, J = 8.3 Hz, 2H), 7.40 (dd, J = 8.2, 6.8 Hz, 2H), 7.36 (s, 1H), 7.25 (s, 1H), 7.23 – 7.13 (m, 3H), 7.06 (d, J = 8.1 Hz, 2H), 3.81 (s, 3H), 3.73 (s, 3H), 3.43 (s, 3H), 2.25 (s, 3H), 0.98 (d, J = 4.6 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.9, 152.5, 148.5, 145.8, 143.6, 136.2, 134.6, 129.5, 128.2, 128.1, 128.0, 127.4, 123.6, 123.5, 114.7, 113.9, 101.5, 100.5, 85.8, 56.2, 55.9, 38.0, 21.4, 18.5, 11.2. IR

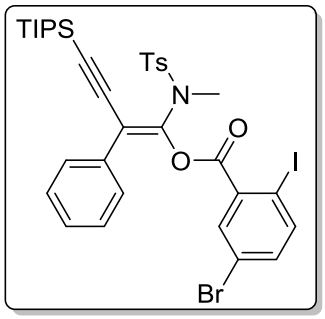
(reflection) $\tilde{\nu}$ = 2943, 2864, 2143, 1743, 1589, 1563, 1508, 1461, 1358, 1342, 1264, 1232, 1202, 1169, 1109, 1064, 1021, 953, 922, 883, 845, 813, 793, 769, 731, 698, 667, 631, 608 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{36}H_{45}INO_6SSi$ calcd for 774.1776, found 774.1797.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 5-chloro-2-iodobenzoate (3ag)



Yield: 61 mg, 82%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.75 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.3 Hz, 2H), 7.55 (d, J = 2.5 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.25 – 7.15 (m, 3H), 7.10 (d, J = 8.1 Hz, 2H), 7.04 (dd, J = 8.4, 2.6 Hz, 1H), 3.42 (s, 3H), 2.26 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.2, 145.2, 143.8, 142.5, 136.3, 134.5, 134.4, 133.5, 133.4, 131.8, 129.7, 128.4, 128.3, 128.2, 127.5, 115.1, 101.3, 100.8, 92.1, 37.8, 21.5, 18.5, 11.2. IR (reflection) $\tilde{\nu}$ = 2943, 2865, 2144, 1754, 1620, 1599, 1553, 1494, 1460, 1360, 1285, 1261, 1216, 1175, 1160, 1108, 1067, 1008, 950, 919, 883, 815, 765, 728, 697, 669, 641, 614 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{40}ClINO_4SSi$ calcd for 748.1175, found 748.1192.

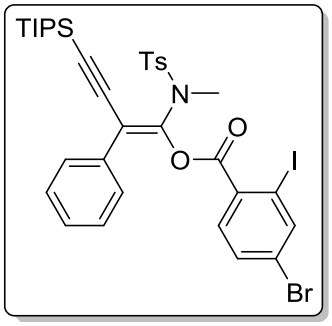
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 5-bromo-2-iodobenzoate (3ah)



Yield: 64 mg, 81%; white solid; Mp. 109.2-109.8 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.04 (d, J = 1.9 Hz, 1H), 7.67 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.4 Hz, 1H), 7.43 – 7.35 (m, 3H), 7.18 (dd, J = 5.3, 1.7 Hz, 3H), 7.07 (d, J = 8.0 Hz, 2H), 3.42 (s, 3H), 2.27 (s, 3H), 0.97 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.6, 145.4, 143.8, 143.7, 136.3, 134.5, 132.9, 131.2, 130.6, 129.6, 128.3, 128.2, 128.1, 127.8, 127.5, 114.6, 101.3, 100.8, 95.8, 38.0, 21.5, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2944, 2865, 2145, 1751, 1620, 1599, 1569, 1545, 1494, 1460, 1359, 1282, 1224, 1160, 1110, 1091, 1071, 1008, 949, 920, 883, 814, 786, 771, 758, 747, 725, 696, 669, 641, 613

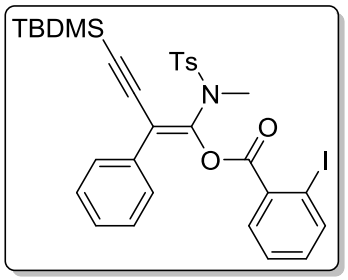
cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{40}BrINO_4SSi$ calcd for 792.0670, found 792.0689.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 4-bromo-2-iodobenzoate (3ai)



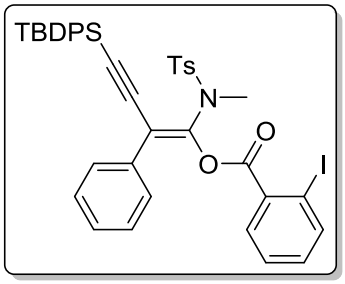
Yield: 63 mg, 80%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.73 – 7.66 (m, 4H), 7.42 – 7.36 (m, 2H), 7.25 – 7.16 (m, 5H), 7.11 (d, J = 8.0 Hz, 2H), 3.42 (s, 3H), 2.27 (s, 3H), 0.99 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.1, 145.2, 143.8, 142.7, 136.5, 136.4, 134.6, 134.4, 133.7, 129.7, 128.4, 128.3, 128.2, 127.5, 122.2, 115.1, 101.3, 100.9, 92.9, 37.8, 21.5, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2943, 2864, 2143, 1754, 1621, 1599, 1571, 1546, 1494, 1459, 1360, 1282, 1216, 1175, 1160, 1138, 1094, 1065, 1006, 949, 920, 883, 815, 765, 747, 726, 697, 669, 640, 612 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{34}H_{40}BrINO_4SSi$ calcd for 792.0670, found 792.0696.

(*E*)-4-(*tert*-butyldimethylsilyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3aj)



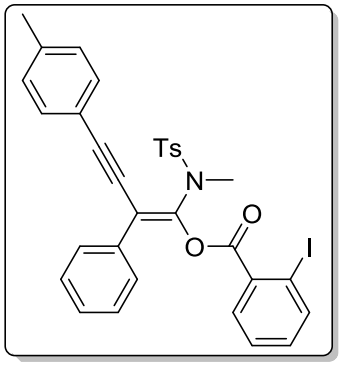
Yield: 59 mg, 88%; white solid; Mp. 121.7-122.5 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.27 (dd, J = 7.9, 0.9 Hz, 1H), 8.19 (dd, J = 7.8, 1.6 Hz, 1H), 8.08 (d, J = 8.3 Hz, 2H), 7.81 – 7.78 (m, 2H), 7.69 (td, J = 7.7, 1.1 Hz, 1H), 7.61 – 7.54 (m, 4H), 7.48 (ddd, J = 9.6, 6.0, 2.1 Hz, 3H), 3.78 (s, 3H), 2.68 (s, 3H), 1.22 (d, J = 3.0 Hz, 9H), 0.36 (s, 6H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 163.4, 145.9, 143.8, 141.6, 136.0, 134.2, 133.5, 132.2, 132.0, 129.7, 128.3, 128.3, 128.2, 128.0, 127.7, 114.4, 101.9, 100.1, 95.1, 37.9, 26.0, 21.6, 16.6. IR (reflection) $\tilde{\nu}$ = 2951, 2853, 2147, 1750, 1619, 1597, 1582, 1494, 1467, 1446, 1422, 1347, 1293, 1273, 1234, 1158, 1123, 1107, 1090, 1072, 1059, 1034, 1011, 948, 920, 870, 827, 812, 776, 739, 699, 688, 675, 657, 639, 605 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{31}H_{35}INO_4SSi$ calcd for 672.1095, found 672.1105.

(*E*)-4-(*tert*-butyldiphenylsilyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3ak)



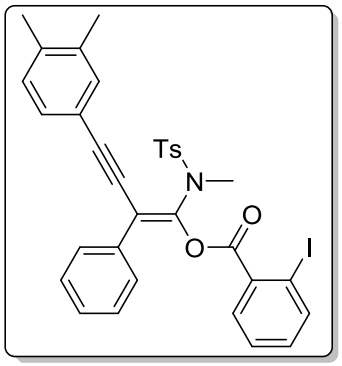
Yield: 73 mg, 92%; white solid; Mp. 109.3-109.8 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, J = 7.9, 0.9 Hz, 1H), 7.74 (dd, J = 7.8, 1.7 Hz, 1H), 7.70 – 7.64 (m, 4H), 7.61 (d, J = 8.3 Hz, 2H), 7.49 (dd, J = 8.0, 1.6 Hz, 2H), 7.37 – 7.25 (m, 7H), 7.24 – 7.15 (m, 3H), 7.09 (td, J = 7.7, 1.7 Hz, 1H), 6.81 – 6.75 (m, 2H), 3.42 (s, 3H), 2.02 (s, 3H), 0.99 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.2, 146.3, 143.8, 141.6, 135.7, 135.6, 134.1, 133.6, 132.7, 131.7, 129.6, 128.4, 128.3, 127.7, 127.4, 114.6, 103.5, 98.8, 95.2, 38.1, 27.0, 21.4, 18.7. IR (reflection) $\tilde{\nu}$ = 3070, 2929, 2856, 2147, 1750, 1617, 1582, 1491, 1464, 1446, 1428, 1358, 1266, 1224, 1158, 1109, 1063, 1032, 1004, 948, 863, 818, 771, 737, 698, 665, 637, 613 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{41}H_{39}INO_4SSi$ calcd for 796.1408, found 796.1435.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(*p*-tolyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3al)



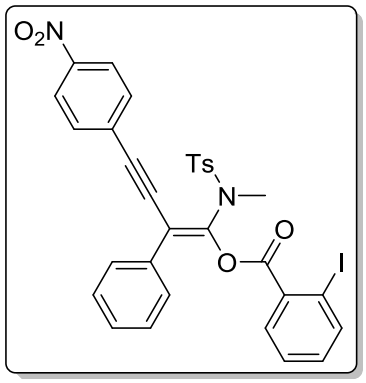
Yield: 40 mg, 62%; white solid; Mp. 91.5-92.2 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (dd, J = 8.0, 1.0 Hz, 1H), 7.88 (dd, J = 7.8, 1.6 Hz, 1H), 7.78 – 7.74 (m, 2H), 7.49 – 7.44 (m, 2H), 7.33 (td, J = 7.7, 1.1 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.22 – 7.19 (m, 1H), 7.13 – 7.08 (m, 1H), 7.04 (d, J = 8.0 Hz, 2H), 7.00 (s, 4H), 3.46 (s, 3H), 2.29 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.9, 144.9, 143.9 141.5, 138.9, 135.9, 134.5, 133.5, 132.5, 132.3, 131.3, 129.7, 128.9, 128.4, 128.3, 128.3, 128.1, 127.8, 119.4, 114.9, 97.3, 94.9, 83.9, 37.9, 29.7, 29.5. IR (reflection) $\tilde{\nu}$ = 3064, 3030, 2924, 2854, 2208, 1748, 1599, 1582, 1563, 1510, 1494, 1446, 1355, 1291, 1266, 1235, 1212, 1158, 1124, 1067, 1004, 946, 865, 814, 772, 737, 698, 666, 638, 610 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{32}H_{27}INO_4S$ calcd for 648.0700, found 648.0706.

(*E*)-4-(3,4-dimethylphenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3am)



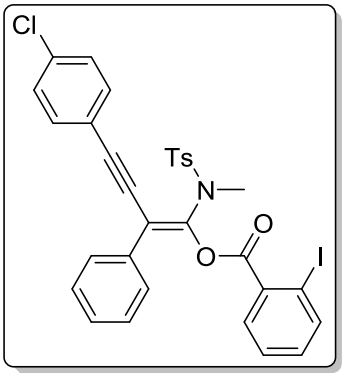
Yield: 39 mg, 60%; white solid; Mp. 130.7-131.5 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.28 (dd, J = 11.7, 4.6 Hz, 2H), 8.15 (d, J = 8.2 Hz, 2H), 7.86 – 7.83 (m, 2H), 7.72 (t, J = 7.6 Hz, 1H), 7.63 (t, J = 7.5 Hz, 2H), 7.60 – 7.58 (m, 1H), 7.51 – 7.47 (m, 1H), 7.44 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 8.7 Hz, 2H), 3.84 (s, 3H), 2.57 (s, 3H), 2.54 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 164.2, 145.2, 144.2, 141.8, 138.0, 136.7, 136.2, 134.8, 133.8, 132.8, 133.7, 133.6, 129.9, 129.7, 129.2, 128.7, 128.6, 128.6, 128.4, 128.1, 119.9, 115.1, 97.8, 95.3, 83.9, 38.3, 21.7, 20.1, 19.8. IR (reflection) $\tilde{\nu}$ = 2924, 2855, 2213, 1747, 1599, 1580, 1495, 1463, 1448, 1426, 1346, 1293, 1264, 1228, 1212, 1176, 1122, 1090, 1077, 1054, 1033, 1012, 948, 878, 815, 778, 744, 705, 666, 638, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{29}INO_4S$ calcd for 662.0856, found 662.0870.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(4-nitrophenyl)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3an)



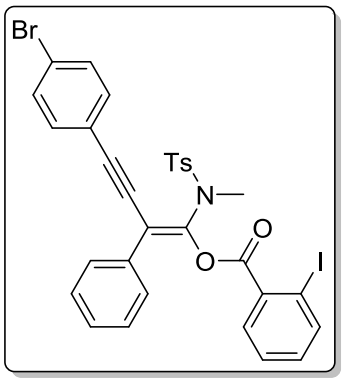
Yield: 48 mg, 71%; white solid; Mp. 184.7-185.1 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.12 – 8.08 (m, 2H), 7.92 (dd, J = 8.0, 1.0 Hz, 1H), 7.80 (dd, J = 7.8, 1.6 Hz, 1H), 7.74 (d, J = 8.3 Hz, 2H), 7.48 – 7.43 (m, 2H), 7.35 – 7.34 (m, 1H), 7.33 (dd, J = 3.0, 1.9 Hz, 1H), 7.32 – 7.31 (m, 1H), 7.30 – 7.28 (m, 1H), 7.28 – 7.26 (m, 1H), 7.26 – 7.21 (m, 1H), 7.13 (td, J = 7.7, 1.7 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 3.44 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 147.2, 146.5, 144.2, 141.7, 135.8, 133.8, 133.6, 132.3, 132.2, 131.8, 129.8, 129.3, 128.8, 128.6, 128.2, 128.2, 127.8, 123.5, 114.4, 95.2, 94.5, 89.8, 38.0, 21.5. IR (reflection) $\tilde{\nu}$ = 2928, 2853, 2203, 1747, 1621, 1588, 1517, 1491, 1465, 1446, 1425, 1361, 1340, 1292, 1214, 1174, 1125, 1107, 1090, 1074, 1032, 1008, 943, 920, 854, 809, 769, 741, 715, 698, 686, 666, 652, 642 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{31}H_{23}IN_2NaO_6S$ calcd for 701.0214, found 701.0216.

(*E*)-4-(4-chlorophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3ao)



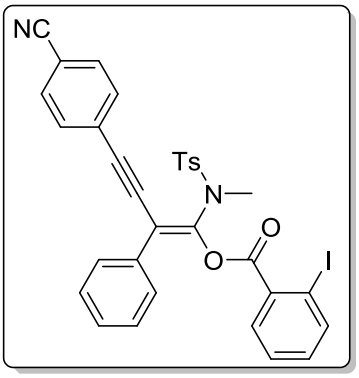
Yield: 45 mg, 65%; white solid; Mp. 120.2-120.7 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.98 (dd, J = 7.9, 0.7 Hz, 1H), 7.92 (dd, J = 7.8, 1.6 Hz, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.52 (dd, J = 5.3, 3.3 Hz, 2H), 7.40 (td, J = 7.7, 0.9 Hz, 1H), 7.34 – 7.31 (m, 2H), 7.29 (dd, J = 4.8, 3.6 Hz, 1H), 7.27 (t, J = 2.0 Hz, 1H), 7.25 (d, J = 2.2 Hz, 1H), 7.18 (td, J = 7.7, 1.6 Hz, 1H), 7.14 – 7.13 (m, 1H), 7.13 – 7.11 (m, 3H), 3.51 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 164.0, 145.8, 144.3, 141.9, 136.2, 135.1, 134.4, 133.9, 132.9, 132.6, 132.5, 130.0, 128.9, 128.8, 128.7, 128.5, 128.4, 128.1, 121.2, 114.9, 95.9, 95.3, 85.8, 38.2, 21.7. IR (reflection) $\tilde{\nu}$ = 2924, 2853, 2210, 1750, 1597, 1490, 1465, 1399, 1358, 1291, 1265, 1212, 1175, 1124, 1072, 1005, 946, 828, 773, 740, 721, 698, 665, 653 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{31}H_{24}ClINO_4S$ calcd for 668.0154, found 668.0173.

(*E*)-4-(4-bromophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3ap)



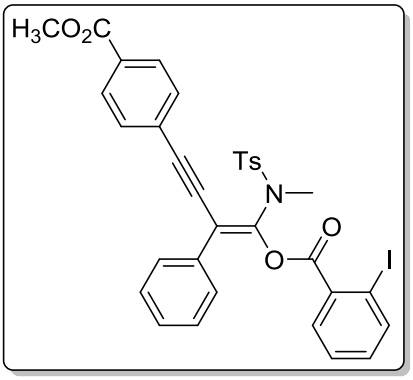
Yield: 47 mg, 67%; white solid; Mp. 98.6-99.4 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (dd, J = 7.9, 0.8 Hz, 1H), 7.86 (dd, J = 7.8, 1.6 Hz, 1H), 7.75 (d, J = 8.3 Hz, 2H), 7.47 – 7.43 (m, 2H), 7.35 (dd, J = 8.6, 1.9 Hz, 3H), 7.27 – 7.21 (m, 3H), 7.12 (td, J = 7.7, 1.6 Hz, 1H), 7.05 (d, J = 8.1 Hz, 2H), 7.01 – 6.97 (m, 2H), 3.44 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.7, 145.5, 144.1, 141.6, 135.8, 134.1, 133.7, 132.8, 132.4, 132.2, 131.4, 129.7, 128.6, 128.5, 128.2, 128.1, 127.8, 123.0, 121.4, 114.6, 95.7, 95.1, 85.7, 37.9, 21.5. IR (reflection) $\tilde{\nu}$ = 2925, 2854, 2209, 1750, 1598, 1582, 1486, 1465, 1394, 1357, 1291, 1266, 1211, 1174, 1124, 1069, 1005, 946, 911, 823, 773, 739, 698, 666, 647 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{31}H_{24}BrINO_4S$ calcd for 711.9649, found 711.9666.

(*E*)-4-(4-cyanophenyl)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3aq)



Yield: 49 mg, 75%; white solid; Mp. 169.9-170.4 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (dd, J = 7.9, 0.6 Hz, 1H), 7.80 (dd, J = 7.8, 1.6 Hz, 1H), 7.73 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H), 7.45 (dd, J = 8.0, 1.5 Hz, 2H), 7.33 (td, J = 7.8, 0.9 Hz, 1H), 7.30 – 7.23 (m, 5H), 7.12 (td, J = 7.7, 1.6 Hz, 1H), 7.05 (d, J = 8.1 Hz, 2H), 3.43 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.5, 146.3, 144.1, 141.7, 135.8, 133.8, 133.6, 132.3, 132.2, 131.9, 131.9, 129.8, 128.8, 128.6, 128.2, 128.1, 127.7, 127.3, 118.3, 114.4, 111.9, 95.2, 94.7, 88.9, 37.9, 21.5. IR (reflection) $\tilde{\nu}$ = 3088, 2925, 2854, 2228, 1736, 1681, 1597, 1579, 1494, 1465, 1446, 1427, 1405, 1357, 1286, 1209, 1187, 1174, 1123, 1075, 1052, 1009, 939, 869, 838, 812, 770, 747, 719, 691, 661, 641 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{32}H_{24}IN_2O_4S$ calcd for 659.0496, found 659.0500.

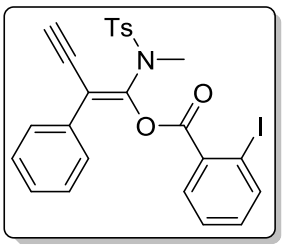
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-4-(4-(methoxycarbonyl)phenyl)-2-phenylbut-1-en-3-yn-1-yl 2-iodobenzoate (3ar)



Yield: 45 mg, 65%; white solid; Mp. 133.6-134.2 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.92 (dd, J = 8.0, 1.0 Hz, 1H), 7.90 – 7.86 (m, 3H), 7.76 (d, J = 8.3 Hz, 2H), 7.48 – 7.43 (m, 2H), 7.34 (td, J = 7.7, 1.1 Hz, 1H), 7.30 – 7.21 (m, 3H), 7.20 – 7.16 (m, 2H), 7.12 (td, J = 7.7, 1.7 Hz, 1H), 7.05 (d, J = 8.0 Hz, 2H), 3.87 (s, 3H), 3.46 (s, 3H), 2.11 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.4, 163.7, 145.9, 144.2, 141.6, 135.7, 134.0, 133.7, 132.4, 132.2, 131.3, 129.8, 129.8, 129.3, 128.7, 128.5, 128.2, 128.2, 127.8, 127.0, 114.4, 95.9, 95.1, 87.3, 52.4, 38.1, 21.5. IR (reflection) $\tilde{\nu}$ = 2926, 2853, 1740, 1720, 1600, 1581, 1494, 1436, 1404, 1356, 1278, 1238, 1213, 1172, 1091, 1010, 941, 858, 806,

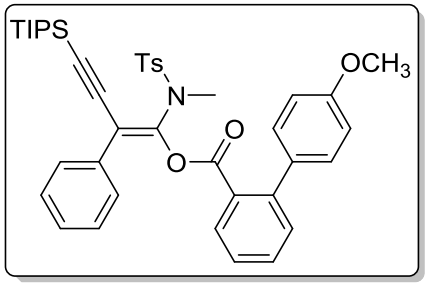
768, 742, 717, 696, 680, 665, 650 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{33}H_{27}INO_6S$ calcd for 692.0598, found 692.0616.

(*Z*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenylbut-1-en-3-yn-1-yl-2-iodobenzoate (5a)



Yield: 49 mg, 89%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.89 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.77 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.39 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.30 (td, *J* = 7.7, 1.1 Hz, 1H), 7.25 – 7.16 (m, 3H), 7.14 (s, 1H), 7.13 – 7.05 (m, 2H), 3.37 (s, 3H), 2.96 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 163.4, 146.7, 144.0, 141.6, 135.3, 133.7, 133.6, 132.3, 131.9, 129.7, 128.5, 128.3, 128.1, 128.0, 127.7, 113.9, 95.1, 84.8, 78.3, 37.9, 21.6. IR (reflection) $\tilde{\nu}$ = 3282, 3064, 2943, 1748, 1598, 1583, 1494, 1464, 1447, 1429, 1354, 1292, 1268, 1223, 1157, 1125, 1091, 1066, 1004, 949, 865, 814, 739, 723, 699, 670, 643, 618 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{21}INO_4S$ calcd for 558.0230, found 558.0244.

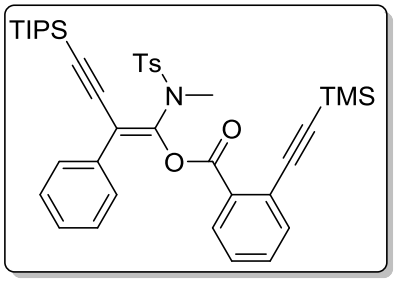
(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 4'-methoxy-[1,1'-biphenyl]-2-carboxylate (5b)



Yield: 64 mg, 92%; yellow liquid; R_f = 0.15 (PE/EA = 10/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.87 (d, *J* = 8.3 Hz, 2H), 7.79 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.57 – 7.53 (m, 2H), 7.51 (td, *J* = 7.6, 1.3 Hz, 1H), 7.37 – 7.31 (m, 4H), 7.28 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.26 (s, 2H), 7.25 (s, 1H), 6.76 – 6.72 (m, 1H), 6.72 – 6.68 (m, 1H), 3.79 (s, 3H), 3.31 (s, 3H), 2.39 (s, 3H), 1.02 (t, J = 4.8 Hz, 21H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 164.9, 159.2, 145.6, 144.1, 144.0, 136.6, 135.3, 132.9, 132.5, 131.4, 131.2, 129.9, 129.8, 129.1, 128.5, 128.4, 128.2, 128.2, 127.1, 115.8, 113.8, 102.0, 100.4, 55.4, 37.7, 21.8, 18.9, 11.6. IR (reflection) $\tilde{\nu}$ = 2941, 2864, 2208, 2144, 1751, 1611, 1582, 1511, 1463, 1446, 1358, 1292, 1245, 1215, 1175, 1090, 1069, 1006, 948, 916, 883, 816, 769,

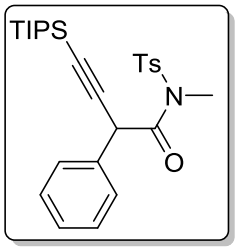
739, 698, 668, 639, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{41}H_{47}NNaO_5SSi$ calcd for 716.2836, found 716.2837.

(*E*)-1-((*N*,4-dimethylphenyl)sulfonamido)-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-((trimethylsilyl)ethynyl)benzoate (5c)



Yield: 58 mg, 85%; white solid; Mp. 80.8-81.3 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.65 (dd, J = 7.9, 0.8 Hz, 1H), 7.62 (d, J = 8.3 Hz, 2H), 7.50 (dd, J = 5.2, 3.3 Hz, 2H), 7.45 (dd, J = 7.8, 0.8 Hz, 1H), 7.38 (td, J = 7.6, 1.2 Hz, 1H), 7.23 – 7.11 (m, 4H), 6.90 (d, J = 8.1 Hz, 2H), 3.44 (s, 3H), 2.17 (s, 3H), 1.04 (s, 21H), 0.16 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.6, 145.8., 143.3, 136.6, 134.5, 134.3, 132.4, 130.9, 129.6, 129.4, 128.3, 128.1, 128.0, 127.9, 127.3, 124.5, 114.3, 102.4, 101.7, 101.1, 99.9, 38.1, 21.4, 18.6, 11.3, 0.3. IR (reflection) $\tilde{\nu}$ = 2944, 2865, 2157, 1746, 1612, 1595, 1567, 1484, 1461, 1446, 1365, 1278, 1250, 1229, 1177, 1124, 1109, 1069, 1044, 1026, 996, 942, 871, 845, 813, 796, 766, 727, 703, 663, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{39}H_{49}NNaO_4SSi_2$ calcd for 706.2813, found 706.2819.

***N*-methyl-2-phenyl-*N*-tosyl-4-(triisopropylsilyl)but-3-ynamide (5d)**



Yield: 43 mg, 90%; white solid; Mp. 83.2-84.1 °C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.72 (d, J = 8.4 Hz, 2H), 7.34 – 7.30 (m, 2H), 7.25 (s, 1H), 7.23 (d, J = 1.5 Hz, 2H), 7.21 (s, 1H), 7.18 (d, J = 1.3 Hz, 1H), 5.29 (s, 1H), 3.28 (s, 3H), 2.36 (s, 3H), 0.98 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 208.9, 168.6, 144.9, 134.4, 129.6, 128.7, 128.0, 127.9, 126.2, 101.1, 85.6, 46.0, 33.7, 21.6, 18.6, 11.2. IR (reflection) $\tilde{\nu}$ = 2942, 2865, 2171, 1923, 1688, 1596, 1495, 1462, 1363, 1306, 1291, 1215, 1187, 1176, 1074, 1042, 1028, 997, 925, 874, 842, 813, 756, 710, 675, 621 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{27}H_{38}NO_3SSi$ calcd for 484.2336, found 484.2341.

2.5.5. DFT Calculations

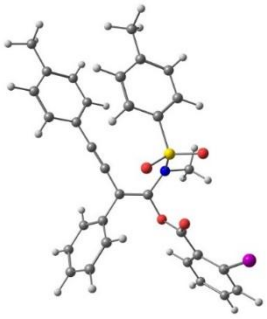
All geometry optimizations, subsequent frequency analyses, and calculations concerning transition states were performed in the gas phase using Orca 5.0.1 on the

bwForCluster Justus 2. The B3LYP functional and the def2-SVP basis set was employed. Furthermore, for Idef2-TZVP basis set was used.

3al-(*E*)

ΔH = -2283,84185427 Eh

ΔG = -2283,94184622 Eh

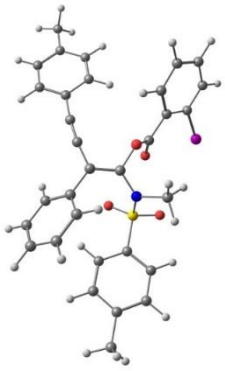


Optimized Structure for **3al**-(*E*)

3al-(*Z*)

ΔH = -2283,83941027 Eh

ΔG = -2283,93896885 Eh

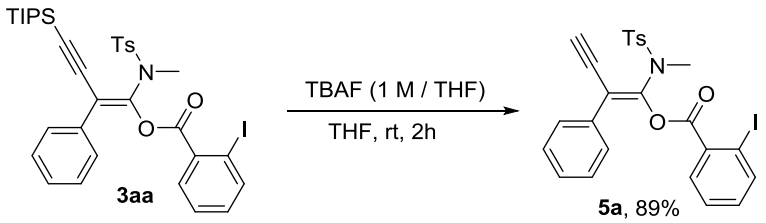


Optimized Structure for **3al**-(*Z*)

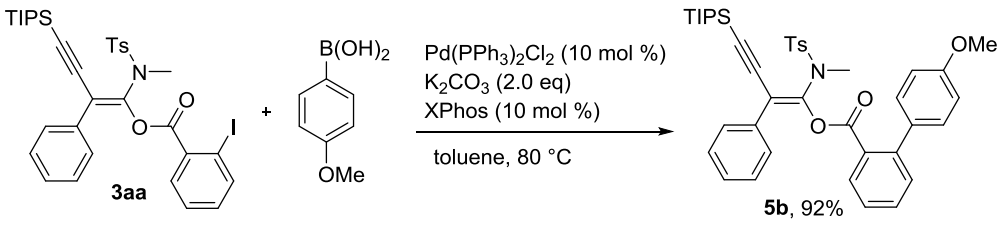
2.5.6. Product modifications

2.5.6.1 Synthesis of terminal alkyne **5a**[3]

The substrate **3aa** (71 mg, 0.1 mmol) was dissolved in THF (2 mL) and TBAF (1.0 M in THF, 15 μL, 1.1 equiv.) was added slowly at 0 °C. The reaction mixture was stirred for 2 h at room temperature. After complete conversion of starting material, reaction mixture was evaporated in vacuo. The crude product, thus obtained, was purified by column chromatography (eluent: pet. ether/EtOAc) to afford the terminal alkyne **5a** as a white solid (89% yield).

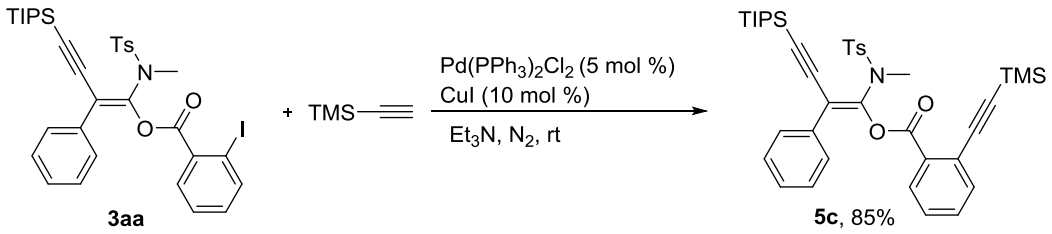


2.5.6.2 Synthesis of biphenyl **5b**[4]



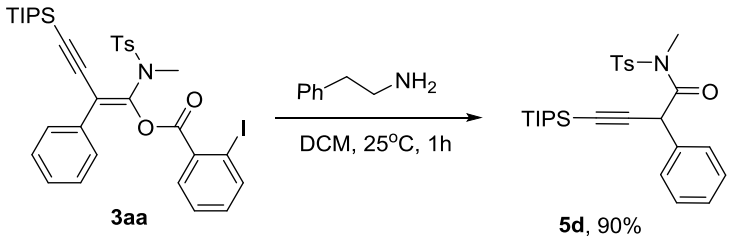
The substrate **3aa** (71 mg, 0.1 mmol), $Pd(PPh_3)_2Cl_2$ (10 mol %), K_2CO_3 (2.0 eq.), XPhos (10 mol %) in 1.5 mL of toluene was heated to 80 °C in an oil bath. Overnight, the reactions were monitored by TLC analysis and the chemical **3aa** were consumed completely. The reaction mixture was filtered through celite and extracted with EtOAc (3 × 5 mL). The organic layer was washed with a saturated solution of water (2 × 5 mL), dried over Na_2SO_4 and the solvent was removed under vacuo. The reaction mixture was purified by flash chromatography on silica gel, to give the desired Sonogashira product **5b** as a white solid (92% yield)

2.5.6.3 Synthesis of **5c**[5].



The substrate **3aa** (71 mg, 0.1 mmol), trimethylsilylacetylene (1.1 eq.), $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (5 mol %) and Et_3N (1 mL) in N_2 atmosphere. After 5 h, the reaction mixture was filtered through celite and extracted with EtOAc (3 × 5 mL). The organic layer was washed with water (2 × 5 mL), dried over Na_2SO_4 and the solvent was removed under vacuo. The reaction mixture was purified by flash chromatography on silica gel, to give the desired Sonogashira product **5c** in 85% yield.

2.5.6.4 Synthesis of biphenyl **5d** [2]



A 2 mL round-bottomed flask was charged with **3aa** (0.2 mmol), DCM (1 mL) and amine (0.2 mmol). The reaction mixture was stirred at room temperature under air until starting material was fully consumed. The reaction mixture was concentrated and purified by silica gel chromatography to afford the amides **5d** in quantitative yields.

2.5.7. Referneces

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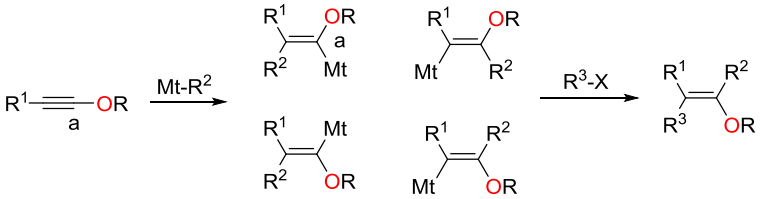
Chapter 3. Gold-Catalyzed Regio- and Stereoselective Acyloxyalkynylation of Ynol Ethers with Ethynylbenziodoxolones

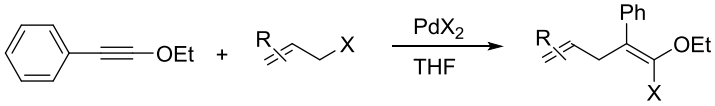
3.1 Introduction

Like ynamides, ynol ethers are also electron-rich alkynes, exhibiting dual electrophilic and nucleophilic properties, induced by the donation of the adjacent lone pair electron of the oxygen atom.[1] Because of the triple bond of alkyne, ynol ethers can also participate in various types of reactions, even with multiple functional groups. Therefore, they may be able to create up to four new bonds one time.[2] Although the ynol ethers are similar to ynamides with regard to their reactivity, little research has been done on it due to its low stability. However, ynol ethers are a special kind of alkyne due to the fact that the oxygen atom is attached to a triple bond. They also have been widely used in organic synthesis, because they possess both nucleophilic and electrophilic properties.[3] Recently, ynol ethers has attracted the interest and attention of chemists.[4] Over the past five decades, many groups[5] achieved the metalated enol ethers by carbometallation and substitution reaction of ynol ethers (Scheme 3-1).



Scheme 3-1 Carbometallation of ynol ethers

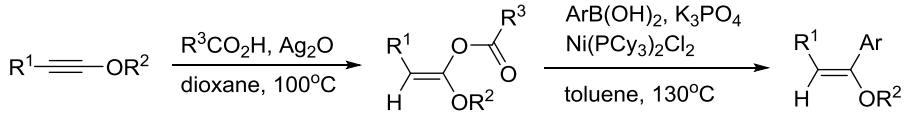
In 2011, Zhu's group achieved Pd-catalyzed regioselective haloallylation of aromatic ynol ethers to obtain (1*E*)-a-chloroenol ethers under mild conditions. This protocol represents the first example of a halopalladation reaction featuring the β-addition pathway and could be applied to the synthesis of multi-substituted enol ethers and



Scheme 3-2 Pa-catalyzed haloallylation of ynol ethers

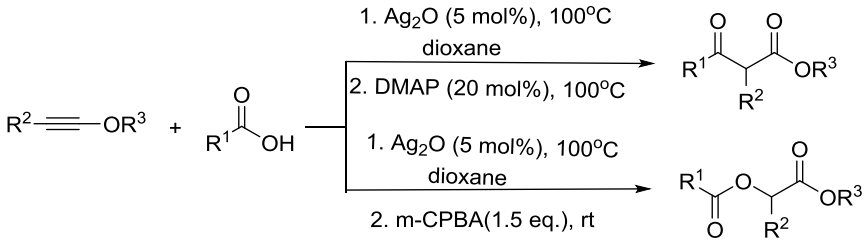
α-allylated carbonyl compounds (Scheme 3-2).[6]

After that, the same group in 2014 described regioselective addition reaction of ynol ethers with carboxylic acids by silver catalysis delivering (*Z*)-α-alkoxy enol esters in good yields. Meaningful, a practical way that boronic acids selectively attack the ester group of enol esters by Ni-catalyzed to obtain enol ethers was accomplished (Scheme 3-3).[7]



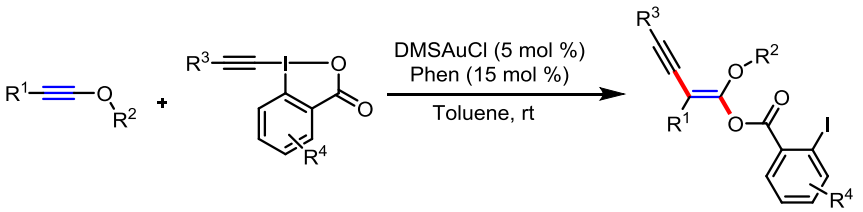
Scheme 3-3 Silver-catalyzed carboxylic acids with ynol ethers

In 2018 and 2019, Cui and co-workers achieved achieved ynol ethers with carboxylic acids by Ag_2O-catalyzed for accessing α-acyloxy enol esters in excellent yields. Interestingly, when m-CPBA instead of DMAP was added to the reaction, an intramolecular in situ Baeyer−Villiger reaction cascade with the generated α-alkoxy enol delivered carbonyloxy esters directly (Scheme 3-4).[8]



Scheme 3-4 Carboxylic acids and ynol ethers for β-keto esters, α-carbonyloxy esters

Recently, gold-catalyzed reactions with EBX agents have caught the attention of chemists.[9] Among them, the transformations involving gold(I)/gold(III) catalytic cycles are very important and we successfully demonstrated alkynyl gold(III) complexes as key to the further alkynylation of various substrates.[10] Encouraged by the above results, we describe the successful atom-economic gold-catalyzed regio-



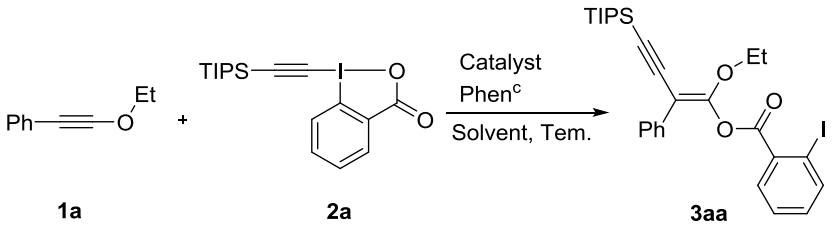
Scheme 3-5 Gold-catalyzed acyloxyalkynylation of ynol ethers with EBXs

and stereoselective β-alkynylation/α-acyloxylation of ynol ethers with EBX reagents, affording β-alkynylated enol ether 2-iodobenzoates as products under mild conditions in excellent yield (Scheme 3-5).

3.2 Result and Discussion

3.2.1 Optimization of the Reaction Conditions

Table 1 Optimization of the reaction conditions[a]



1a **2a** **3aa**

Entry	Catalyst	Solvent	T (^{o}C)	Yield (%)[b]
1	DMSAuCl	DCM	50	75
2	IPrAuCl	DCM	50	56
3	Cy_3AuCl	DCM	50	62
4	$Ph_3PAuNTf_2$	DCM	50	49
5	JohnphosAuCl	DCM	50	33
6	Ph_3PAuCl	DCM	50	68
7[d]		DCM	50	n.d.[f]
8[e]	DMSAuCl	DCM	50	trace
9	DMSAuCl	CH_3CN	50	55
10	DMSAuCl	Toluene	50	78
11	DMSAuCl	CH_3OH	50	trace
12	DMSAuCl	Et_2O	50	73
13	DMSAuCl	THF	50	36
14	**DMSAuCl**	**Toluene**	**rt**	**87**
15	DMSAuCl	Toluene	40	81
16	DMSAuCl	Toluene	60	77
17	DMSAuCl	Toluene	70	80
18	DMSAuCl	Toluene	80	79

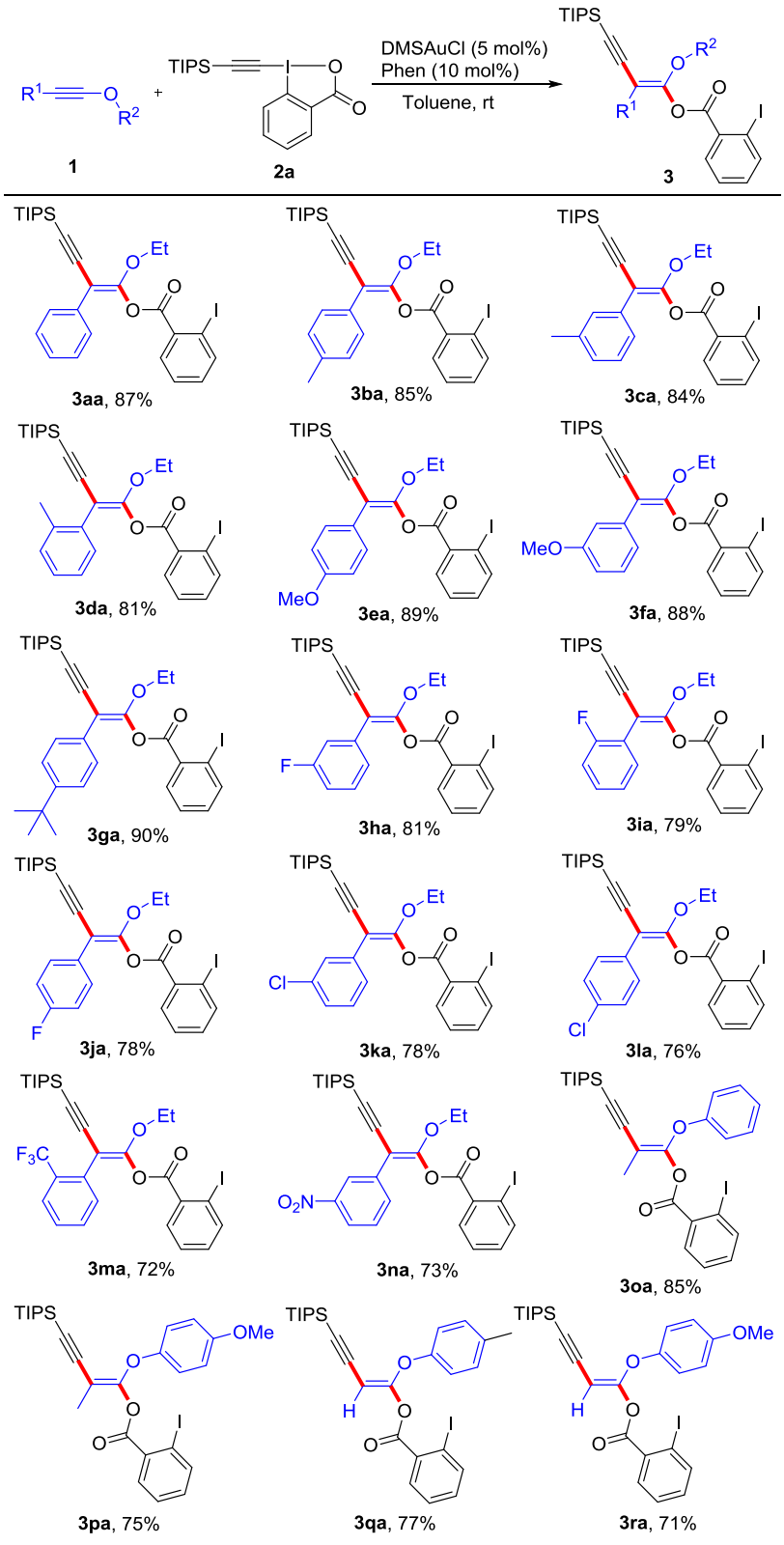
[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), catalyst (5 mol %), Phen (5 mol %) in solvent (1.0 mL) at rt. [b]Isolated yield. [c]Phen: 1,10-phenanthroline. [d]without DMSAuCl. [e]without Phen. [f]n.d.: not detected.

At the beginning, the (ethoxyethynyl)benzene **1a** and and TIPS-EBX **2a** were selected

as model substrates were selected to optimize conditions (Table 1). To improve the reactivity of (ethoxyethynyl)benzene **1a**, an examination to determine the most suitable reaction parameters began with an analysis of gold catalysts. Several gold catalysts were evaluated (entries 1−6). Although most of the gold catalysts met with lower yields, to our delight, the desired enol ether 2-iodobenzoates **3aa** could be afforded in 75% yield when DMSAuCl served as a catalyst (entry 1). Furthermore, in the absence of DMSAuCl or Phen, no transfer acyloxy- alkynylation product **3aa** was observed (entries 7 and 8). After that, solvents effects were investigated and toluene turned out to be most suitable to deliver 3aa in 78% yield (entries 9−13). Encouraged by this result, we then examined different reaction temperatures, such as room temperature, 40^{o}C, 60^{o}C, 70^{o}C and 80^{o}C (entries 14−18), and the target product **3aa** was obtained in 87% yield at the room temperature (entry 14).

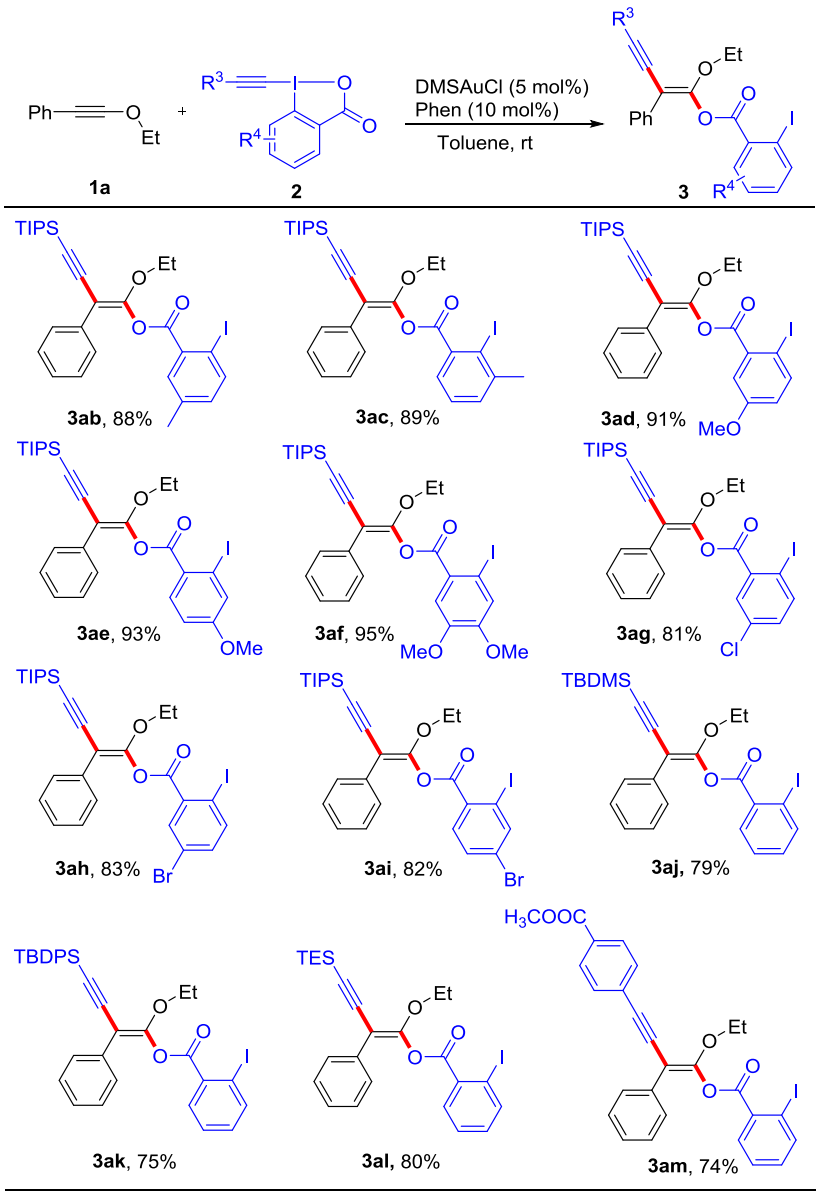
3.2.2 Substrate Scope

With the optimal conditions determined, we first explored the scope of alkyne ether substituents, while keeping the EBX-TIPS reagent constant (Scheme 3-6). In general, diverse substitution patterns including electron-rich, electronically neutral, and electron-poor units on the aromatic ring were tolerated. Substrates **1a**−**1m** all delivered the corresponding products **3aa**−**3ma** in 72% yield to 90% yield. Notably, the steric environment of the R^1 group has no dis-cernible impact on the reaction, as shown by the comparison of **3ba**, **3ca** and **3da**; **3ea** and **3fa**; **3ha**, **3ha** and **3ia**; as well as **3ja** and **3ka**. Concerning electronic effects, electron-donating groups, if placed at the same position of the aryl moiety, showed better efficiency than electron-withdrawing group. These were better than for electron-withdrawing group on the aryl (**3ba**, **3ea**, **3ga** vs **3ja**, **3la**; **3ca**, **3fa** vs **3ha**, **3ka** and **3na**). Furthermore, variations of the alkoxy moiety of the ynol ethers or changing the alkyne terminus to an alkyl substituent or a terminal alkyne were all possible and ethyl group on the R^2 was replaced by aryl. Alkyl-substituted (**1n** and **1o**) and terminal-substituted ynol ethers (**1p** and **1q**) the corresponding functionalized products were obtained in 71−85% yield (**3oa**−**3ra**).



[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.12 mmol), DMSAuCl (5 mol %), Phen (5 mol %) in Toluene (1.0 mL) at rt. [b]Isolated yield.

Scheme 3-6 Scope with respect to ynole ether derivatives[a,b]

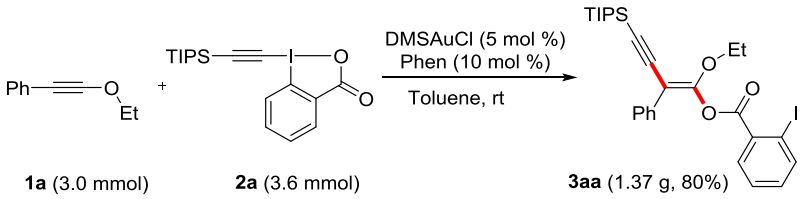


[a]Reaction conditions: **1a** (0.10 mmol), **2** (0.12 mmol), DMSAuCl (5 mol %), Phen (5 mol %) in Toluene (1.0 mL) at rt. [b]Isolated yield.

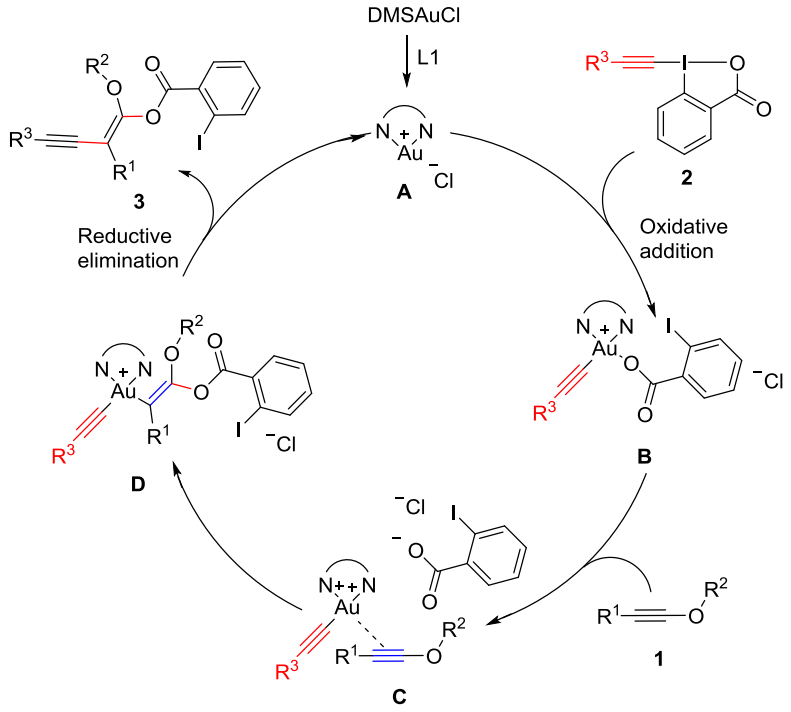
Scheme 3-7 Scope with respect to the hypervalent iodine reagents[a,b]

Next, we further explored the scope by changing the R-EBX reagents **2** with (ethoxyethynyl)benzene **1a** as a reaction partner (Scheme 3-7). Substituents on the core benzene ring of EBXs have little effect on the reactivity, so both electron-donating groups (Me or OMe) and halides (Cl or Br) could be transformed into the products **3ab**−**3ai** in 79−95% yield. Furthermore, the replacement of TIPS with different silicon groups (**2j**, **2k** and **2l**) on the alkyne terminus of the EBXs were tested and worked efficiently in this transformation giving products **3aj**−**3al** in

75%−80% yield. To our delight, also an electron-withdrawing (COOMe) aryl substitution at the alkyne terminus of **2m** was tolerated, delivering **3am** in moderate yield (74%). Additionally, a gram-scale reaction between **1a** and **2a** was carried out, and the product **3aa** was obtained in 80% yield (Scheme 3-8).



Scheme 3-8 Gram-scale synthesis



Scheme 3-9 Proposed reaction mechanism

Based on previous literature reports, we propose a plausible catalytic cycle for this reaction as shown in Scheme 3-9. First, DMSAuCl is chelated by 1,10-phenanthroline to form Au(I) species **A**, which then oxidative addition with EBXs reagent **2** to afford the alkynyl Au(III) complex **B**. Subse-quently, the carbon-carbon triple bond of **1** is coordinated under formation of Π-complex **C**. This activates the alkyne towards the nucleophilic attack of the carboxylate anion to form Au(III) intermediate **D**. Finally, reductive elimination leads to the release of product **3** under release of Au(I) species **A**, which completes the catalytic cycle.

3.3 Conclusions

In conclusion, we achieved an effective protocol for the regio- and stereoselective acyloxyalkynylation of ynol ethers with ethynylbenziodoxolones to form enol ether 2-iodobenzoates in an atom-economic fashion via an Au(I)/Au(III) redox cycle. This protocol efficiently enables access to a series of tetra-substituted amide enolates under mild conditions. This ap-proach might be used for the synthesis of various ethers and ester derivatives with relevance for medicine development. The wide substrate range, high efficiency, and superior func-tional group tolerance should contribute to this developement.

3.4 References

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3.5 Experimental Section

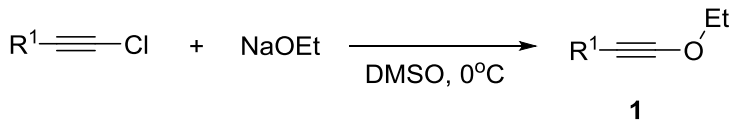
3.5.1 General Remarks

Reactions were performed in oven-dried glassware unless otherwise noted, chemicals were obtained from commercial suppliers (Sigma-Aldrich, ChemPUR and TCI) and used without further purification. Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at 7.26 ppm. Multiplicities were reported using the following abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiple). All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH_2-group), q (quartet, CH_3-group)] were determined by DEPT135 spectra. (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not calibrated. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400

mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

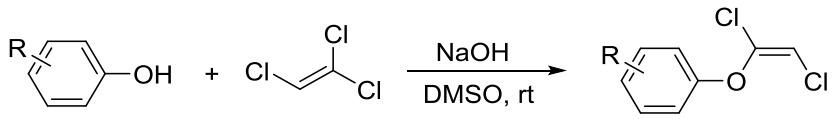
3.5.2 Experiment Procedures

Procedure A: General procedure for the synthesis of ynol ethers **1**[1,2]



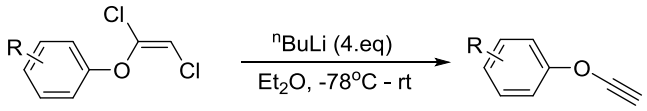
1

A dry reaction tube was charged with sodium alkoxide (20 mmol). The tube was sealed, evacuated, and backfilled with nitrogen. Then, a solution of chlorinated alkyne (5 mmol) in dry DMSO (5 mL) was added dropwise at 0 °C and the progress of the reaction was monitored by TLC. Upon completion, water was added at 0 °C to quench the reaction. The mixture was then extracted with ether (3 × 25 mL) and the combined organic layer was dried over $MgSO_4$, filtered and concentrated in vacuum. The residue was purified by flash chromatography on silica gel to afford the alkynyl ether **1a-1n** in high yield.

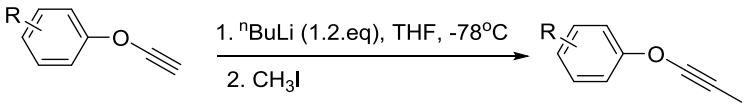


A round bottom flask was charged with a solution of the 1.0 eq of the phenol derivative in DMSO. To this solution 1.0 eq NaOH (pounded) was added and the resulting mixture was stirred at room temperature for 2 hours. Afterwards 1.0 eq 1,1,2-trichloroethylene was slowly added and the resulting mixture was stirred for the given amount of time (monitor by TLC). After completion the reaction was quenched with water. The phases were separated and aqueous phase was extracted with DCM. The combined organic layers were washed with brine, dried over magnesium sulphate

and concentrated under reduced pressure. The crude product was subjected to flash column chromatography.

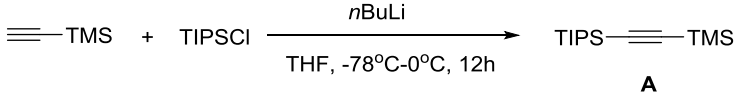


A flame dried Schlenk tube under an inert gas atmosphere was charged with a solution of the 1,2-dichlorovinyl ether derivative (1.0 eq) in dry diethyl ether and cooled to –78 °C. At this temperature the given amount of n-BuLi was dropwise added. The resulting solution was stirred at maintained temperature for 1 h before it was allowed to warm to –40 °C in the cause of 1 h. The mixture was stirred at this temperature for another 2 h before being quenched with water. The phases were separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were washed with a saturated ammonium chloride solution and brine, dried over magnesium sulphate and concentrated under reduced pressure to get the products **1q** and **1r**.



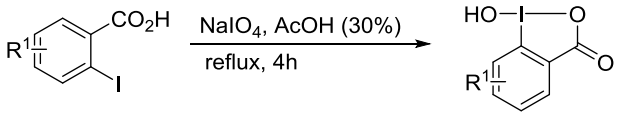
A flame dried Schlenk flask under inert gas atmosphere was charged with a solution of the ethynyl aryl ether derivative (1.0 eq) in dry THF (0.4 M) and cooled to -78°C. At this temperature n-Buli (1.2 eq, 1.6 M in hexane) was added. The resulting solution was allowed to warm to room temperature over 2 hours and then cooled to -78°C. Methyl iodide (2.0 eq) was added dropwise and the reaction mixture was allowed to warm to room temperature in the cause of 1 h. After being stirred overnight, the reaction was quenched by addition of a saturated ammonium chloride solution (2 mL). Water (10 ml) was added, and the aqueous layer was extracted with diethyl ether (2 x 10 ml). The combined organic layers were then dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. The crude product was adsorbed on Celite® and then purified by flash column chromatography (**1o** and **1p**)

Procedure B: Synthesis of R-EBX derivatives **2**[3]



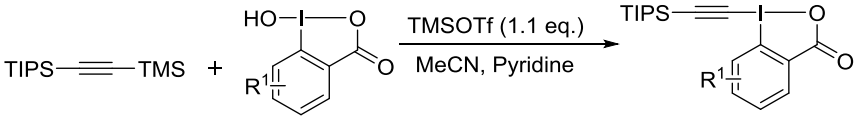
A

n-butyllithium (1.6 M in hexanes, 26.2 mL, 42.3 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (4.2 g, 43 mmol, 1.0 equiv) in THF (66 mL) at -78 °C. The mixture was then stirred for 2 h at -78 °C before chlorotriisopropylsilane (9.2 mL, 43 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (20 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain desired product **A** (11.72 g, 83% yield) as a colorless liquid.



B

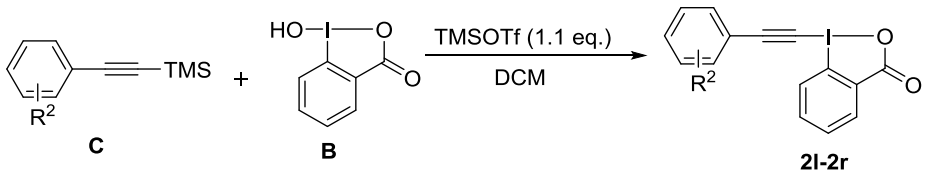
$NaIO_4$ (13.79 g, 64 mmol; 1.0 equiv) and 2-iodobenzoic acids (16.0 g, 64 mmol, 1.0 equiv) were suspended in 30% (v/v) aq. AcOH (125 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (160 mL) and allowed to cool to room temperature, protecting it from light. After 1 h of stirring at rt, the crude product was collected by filtration, washed on the filter with ice water (3 x 30 mL) and acetone (3 x 30 mL), and dried in the dark to give the pure product **B** (27.3 g, 86% yield) as a white solid.



A **B** **2a-2k**

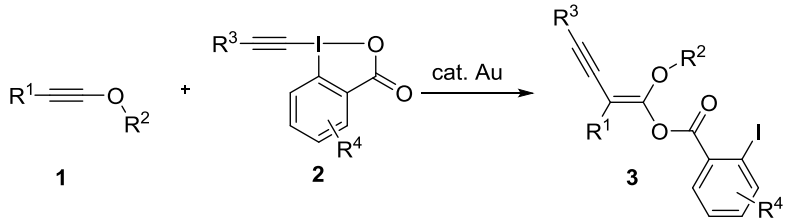
An oven-dried two-neck 250 mL flask equipped with a magnetic stirrer was charged with 2-iodosylbenzoic acids (**B**) (5.28 g, 20.0 mmol, 1.0 equiv) and CH_3CN (70 mL) and the suspension was then cooled to 0 °C. Trimethylsilyltriflate (4.0 mL, 22.0 mmol, 1.1 equiv) was added at one-go into the reaction mixture via syringe which almost immediately produced a clear solution (critical step!). After 20 min, (trimethylsilyl)(triisopropylsilyl)acetylene (**A**) (5.6 g, 22.0 mmol, 1.1 equiv) was added dropwise via syringe at rt. After 5 min, the solution turned dark yellow. After 30 min, pyridine (2.0 mL, 22.0 mmol, 1.1 equiv) was added via syringe. After 20 min,

the reaction mixture was reduced under vacuum until a solid was obtained. The solid was dissolved in CH_2Cl_2 (20 mL), washed with 1 M HCl (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The organic layers were then combined, washed with a saturated solution of $NaHCO_3$ (2 x 20 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (ca 25 mL) afforded TIPS-EBXs **2a-2k** (87%-95%).



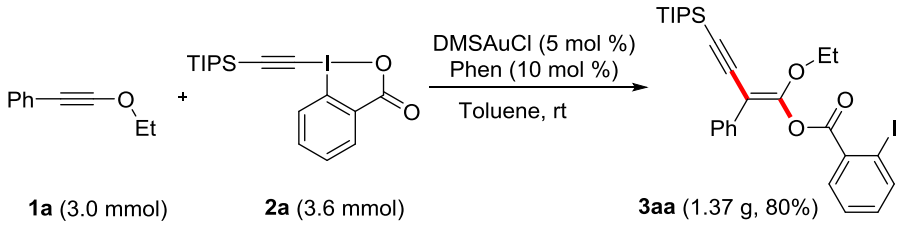
To a suspension of 2-iodosylbenzoic acid B (1.05 mmol) in DCM (10 mL) was added trimethylsilyl triflate (1.1 equiv) at rt. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of terminally substituted 1- (trimethylsilyl) -2-phenylacet ylenes **A** (1.1 equiv) dissolved in DCM (5 mL). The resulting suspension was stirred for 6 h at RT. The mixture was then basified with a saturated solution of $NaHCO_3$ (10 mL). The layers were separated and the organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The products (**2m**) obtained thereby was further crystallized using DCM/n-pentane.

Procedure C: Synthesis of **3**



A mixture of **1** (0.10 mmol, 1.0 equiv) and **2** (0.12 mmol, 1.2 equiv) in 1.0 mL toluene was treated with DMSAuCl (5 mol %), 1,10-phenanthroline (5 mol %) at rt. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3**.

Procedure D: Gram-Scale Synthesis **3aa**

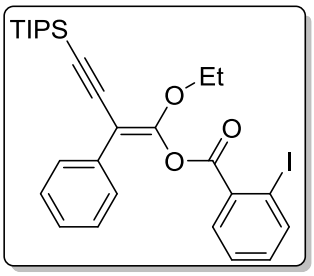


1a (3.0 mmol) **2a** (3.6 mmol) **3aa** (1.37 g, 80%)

A mixture of **1a** (3.0 mmol, 1.0 equiv) and **2a** (3.6 mmol, 1.2 equiv) in 10 mL toluene was treated with DMSAuCl (5 mol %), 1,10-phenanthroline (5 mol %) at rt. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3aa** in 80% yield (1.37 g).

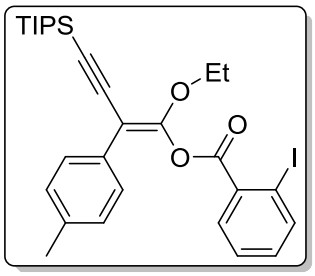
3.5.3 Characterization Data

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3aa)



Yield: 50 mg, 87%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.9 Hz, 1H), 7.62 (dd, J = 7.8, 1.5 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.27 (dd, J = 11.1, 4.2 Hz, 1H), 7.17 (t, J = 7.4 Hz, 2H), 7.09 (ddd, J = 9.4, 5.2, 1.4 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.9, 156.7, 141.8, 135.1, 133.6, 132.6, 131.5, 128.3, 128.1, 128.0, 127.0, 102.7, 96.1, 95.5, 94.9, 68.3, 18.6, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2865, 2142, 1916, 1755, 1712, 1631, 1582, 1494, 1463, 1386, 1366, 1289, 1246, 1205, 1099, 1072, 1042, 1003, 918, 882, 766, 738, 694, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{36}IO_3Si$ calcd for 575.1472, found 575.1484.

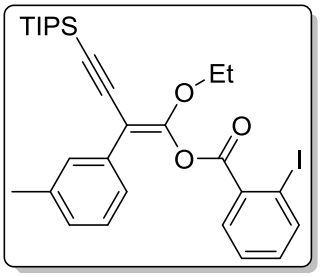
(*E*)-1-ethoxy-2-(*p*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3ba)



Yield: 50 mg, 85%; white solid; Mp. 91.3-92.5 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.94 (dd, J = 7.9, 0.9 Hz, 1H), 7.67 (dd, J = 7.8, 1.6 Hz, 1H), 7.32 (dd, J = 7.6, 1.1 Hz, 1H), 7.30 – 7.28 (m, 2H), 7.13 – 7.09 (m,

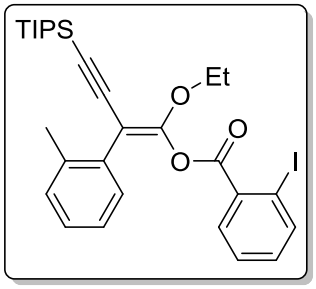
1H), 6.99 (d, J = 8.0 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 2.21 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.0, 155.4, 140.8, 135.7, 132.5, 130.9, 130.6, 128.2, 127.8, 127.0, 126.9, 101.7, 95.2, 94.3, 93.9, 67.3, 20.1, 17.7, 14.1, 10.4. IR (reflection) $\tilde{\nu}$ = 2940, 2864, 2140, 1916, 1748, 1712, 1642, 1581, 1511, 1465, 1367, 1260, 1219, 1127, 1097, 1070, 1042, 1011, 919, 883, 825, 804, 761, 739, 685 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_3Si$ calcd for 589.1629, found 589.1647.

(*E*)-1-ethoxy-2-(*m*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3ca)



Yield: 49 mg, 84%; white solid; Mp. 65.2-66.8 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.91 (dd, J = 7.9, 1.0 Hz, 1H), 7.62 (dd, J = 7.8, 1.7 Hz, 1H), 7.27 (td, J = 7.7, 1.1 Hz, 1H), 7.23 (s, 1H), 7.20 (d, J = 7.8 Hz, 1H), 7.08 (dd, J = 7.6, 1.4 Hz, 1H), 7.04 (d, J = 7.9 Hz, 1H), 6.89 (d, J = 7.5 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.16 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.0, 156.6, 141.8, 137.6, 134.9, 133.5, 132.7, 131.5, 129.1, 128.0, 127.9, 127.8, 125.3, 102.8, 96.2, 95.5, 94.9, 68.3, 21.4, 18.7, 15.1, 11.5. IR (reflection) $\tilde{\nu}$ = 2961, 2938, 2889, 2862, 2139, 1764, 1638, 1581, 1562, 1463, 1430, 1368, 1259, 1212, 1187, 1165, 1125, 1099, 1059, 1045, 996, 883, 851, 833, 791, 734, 696, 674, 655, 635 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_3Si$ calcd for 589.1629, found 589.1641.

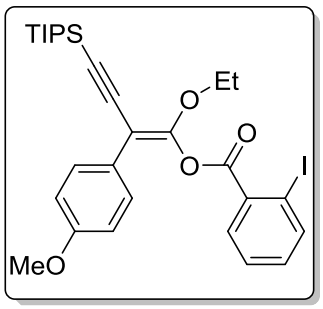
(*E*)-1-ethoxy-2-(*o*-tolyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3da)



Yield: 47 mg, 81%; white solid; Mp. 48.6-49.5 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.80 (dd, J = 7.9, 0.9 Hz, 1H), 7.16 – 7.12 (m, 2H), 7.08 – 7.03 (m, 3H), 7.03 – 6.98 (m, 2H), 4.34 (q, J = 7.1 Hz, 2H), 2.34 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H), 1.00 (s, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.2, 156.7, 141.2, 137.3, 134.1, 133.2, 133.1, 130.9, 130.1,

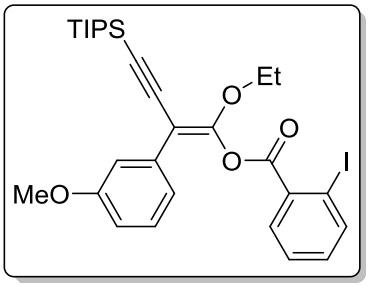
129.7, 127.7, 127.6, 125.5, 101.8, 95.5, 94.6, 94.3, 67.9, 19.7, 18.6, 15.0, 11.3. IR (reflection) $\tilde{\nu}$ = 2943, 2892, 2866, 2185, 2140, 1922, 1808, 1747, 1640, 1582, 1463, 1385, 1368, 1342, 1288, 1248, 1192, 1092, 999, 883, 740, 679 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_3Si$ calcd for 589.1629, found 589.1652.

(*E*)-1-ethoxy-2-(4-methoxyphenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodob enzoate (3ea)



Yield: 53 mg, 89%; white solid; Mp. 74.3-75.7 ^oC; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.9 Hz, 1H), 7.66 (dd, J = 7.8, 1.5 Hz, 1H), 7.36 – 7.26 (m, 3H), 7.09 (td, J = 7.8, 1.7 Hz, 1H), 6.72 (dd, J = 9.3, 2.5 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 3.68 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.0, 157.5, 155.1, 140.8, 132.5, 131.6, 130.5, 128.4, 126.9, 126.3, 112.5, 101.9, 94.9, 94.3, 93.9, 67.3, 54.2, 17.7, 14.1, 10.4. IR (reflection) $\tilde{\nu}$ = 2941, 2891, 2865, 2139, 1913, 1751, 1637, 1607, 1579, 1510, 1462, 1367, 1289, 1248, 1216, 1175, 1126, 1097, 1062, 1030, 1003, 919, 883, 835, 759, 736, 679 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_4Si$ calcd for 605.1578, found 605.1597.

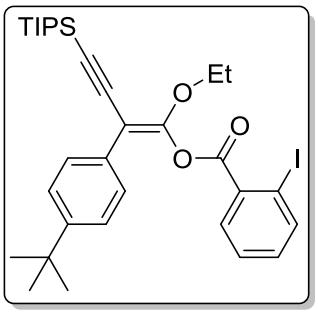
(*E*)-1-ethoxy-2-(3-methoxyphenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodob enzoate (3fa)



Yield: 53 mg, 88%; white solid; Mp. 59.6-60.5 ^oC; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.93 (d, J = 7.9 Hz, 1H), 7.67 (dd, J = 7.8, 1.5 Hz, 1H), 7.30 (t, J = 7.6 Hz, 1H), 7.11 (dd, J = 7.5, 1.5 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 7.01 – 6.95 (m, 2H), 6.69 – 6.62 (m, 1H), 4.33 (q, J = 7.1 Hz, 2H), 3.61 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.8, 159.3, 156.7, 141.9, 136.3, 133.6, 132.4, 131.7, 129.0, 128.0, 120.6, 113.6, 113.1, 102.6, 96.0, 95.5, 95.0, 68.2, 55.1, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2960, 2939, 2863, 2140, 1918, 1763, 1638, 1605, 1579, 1484, 1462, 1431, 1367, 1263, 1225, 1202, 1123, 1095, 1057, 1032, 998, 920, 882, 782, 735,

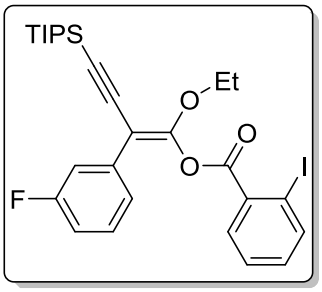
712, 695, 673, 657, 637 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_4Si$ calcd for 605.1578, found 605.1590.

(*E*)-2-(4-(tert-butyl)phenyl)-1-ethoxy-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3ga)



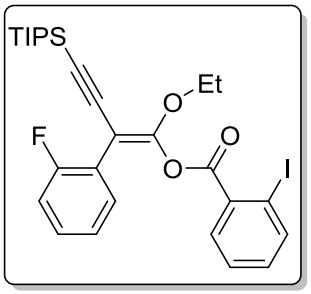
Yield: 56 mg, 90%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (700 MHz, $CDCl_3$) δ = 7.92 (d, J = 7.9 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.36 – 7.32 (m, 2H), 7.27 (t, J = 7.6 Hz, 1H), 7.18 (d, J = 8.3 Hz, 2H), 7.08 (td, J = 7.7, 1.6 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H), 1.19 (s, 9H), 1.05 (s, 21H). ^{13}C NMR (175 MHz, $CDCl_3$) δ = 162.0, 155.5, 148.8, 140.7, 132.5, 131.7, 130.7, 130.5, 126.9, 126.8, 124.0, 101.7, 95.1, 94.3, 93.8, 67.2, 33.4, 30.2, 17.7, 14.0, 10.4. IR (reflection) $\tilde{\nu}$ = 2960, 2865, 2142, 1917, 1758, 1713, 1631, 1582, 1561, 1512, 1463, 1430, 1390, 1365, 1247, 1207, 1096, 1064, 1041, 1004, 920, 883, 836, 787, 738, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{32}H_{44}IO_4Si$ calcd for 631.2098, found 631.2113.

(*E*)-1-ethoxy-2-(3-fluorophenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3ha)



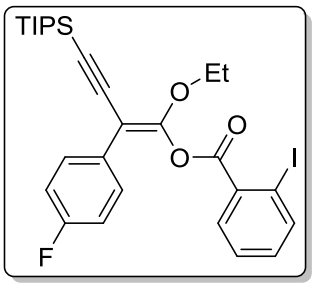
Yield: 48 mg, 81%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.95 (d, J = 7.9 Hz, 1H), 7.68 (dd, J = 7.8, 1.6 Hz, 1H), 7.32 (td, J = 7.8, 0.9 Hz, 1H), 7.21 – 7.09 (m, 4H), 6.79 (ddd, J = 8.4, 2.5, 1.4 Hz, 1H), 4.33 (q, J = 7.0 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.05 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.7, 157.0, 141.9, 133.7, 131.5, 129.5, 129.4, 128.1, 124.0, 123.9, 115.4, 115.2, 113.9, 113.7, 102.1, 96.1, 95.0, 68.3, 18.7, 15.0, 11.4. IR (reflection) $\tilde{\nu}$ = 2944, 2892, 2866, 2143, 1916, 1745, 1713, 1611, 1584, 1487, 1463, 1443, 1386, 1366, 1289, 1247, 1213, 1102, 1041, 999, 882, 738, 679 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}FIO_3Si$ calcd for 593.1378, found 593.1395.

(*E*)-1-ethoxy-2-(2-fluorophenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3ia)



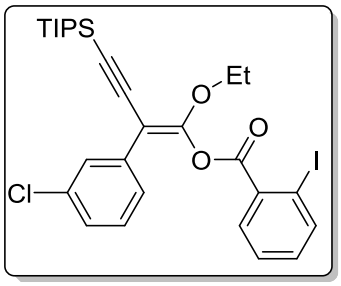
Yield: 46 mg, 79%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 (dd, J = 7.9, 0.9 Hz, 1H), 7.51 (dd, J = 7.8, 1.6 Hz, 1H), 7.35 (td, J = 7.6, 1.8 Hz, 1H), 7.23 (td, J = 7.7, 1.0 Hz, 1H), 7.12 – 7.06 (m, 1H), 7.04 (td, J = 7.7, 1.7 Hz, 1H), 6.97 (td, J = 7.6, 1.1 Hz, 1H), 6.89 (ddd, J = 9.6, 8.3, 1.0 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.02 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.4, 160.7, 158.3, 157.6, 141.7, 133.5, 132.4, 131.4, 129.1, 127.9, 123.9, 122.9, 115.7, 115.5, 101.9, 95.2, 94.9, 89.0, 68.4, 18.6, 15.0, 11.4. IR (reflection) $\tilde{\nu}$ = 2943, 2892, 2865, 2143, 1926, 1762, 1713, 1637, 1582, 1491, 1463, 1367, 1249, 1094, 1002, 882, 757, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}FIO_3Si$ calcd for 593.1378, found 593.1396.

(*E*)-1-ethoxy-2-(4-fluorophenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodoben zoate (3ja)



Yield: 46 mg, 78%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.94 (d, J = 7.9 Hz, 1H), 7.63 (dd, J = 7.8, 1.5 Hz, 1H), 7.33 (ddd, J = 16.5, 8.3, 3.1 Hz, 3H), 7.10 (td, J = 7.7, 1.6 Hz, 1H), 6.86 (dd, J = 12.1, 5.3 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.03 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.4, 162.8, 156.6, 141.9, 133.7, 132.4, 131.5, 130.0, 129.9, 128.0, 115.2, 114.9, 102.5, 95.8, 95.0, 68.3, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2943, 2865, 2142, 1919, 1756, 1712, 1633, 1603, 1583, 1508, 1464, 1387, 1367, 1235, 1160, 1093, 1038, 1015, 1002, 919, 882, 838, 738, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}FIO_3Si$ calcd for 593.1378, found 593.1392.

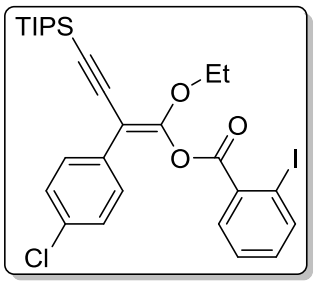
(*E*)-2-(3-chlorophenyl)-1-ethoxy-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodoben zoate (3ka)



Yield: 47 mg, 78%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.95 (d, J = 7.9 Hz, 1H), 7.68 (dd, J = 7.8, 1.5 Hz, 1H), 7.43 (s, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.15 – 7.07 (m, 3H),

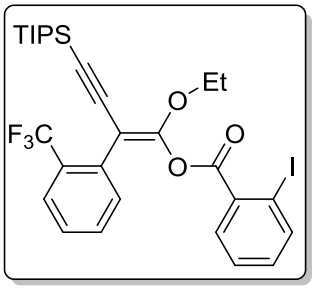
4.34 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.05 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.7, 156.0, 140.9, 135.9, 132.9, 132.7, 131.3, 130.5, 128.3, 127.4, 127.1, 126.0, 125.3, 100.9, 95.1, 93.9, 93.7, 67.3, 17.6, 14.0, 10.3. IR (reflection) $\tilde{\nu}$ = 3067, 2943, 2891, 2866, 2143, 1915, 1745, 1713, 1628, 1593, 1464, 1426, 1387, 1367, 1290, 1244, 1089, 1039, 1016, 998, 921, 882, 790, 738, 678 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}ClIO_3Si$ calcd for 609.1083, found 609.1101.

(*E*)-2-(4-chlorophenyl)-1-ethoxy-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3la)



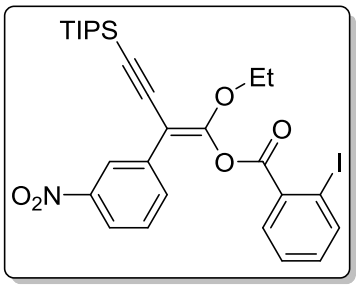
Yield: 46 mg, 76%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.98 – 7.92 (m, 1H), 7.66 (dd, J = 7.8, 1.5 Hz, 1H), 7.31 (dd, J = 11.0, 4.7 Hz, 3H), 7.17 – 7.08 (m, 3H), 4.33 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.02 (d, J = 7.2 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.7, 155.7, 140.9, 132.7, 132.6, 131.7, 131.2, 130.5, 128.5, 127.3, 127.0, 101.2, 94.9, 94.0, 93.9, 67.3, 17.6, 14.0, 10.3. IR (reflection) $\tilde{\nu}$ = 2943, 2891, 2866, 2143, 1917, 1744, 1712, 1631, 1583, 1491, 1463, 1389, 1366, 1247, 1207, 1175, 1092, 1038, 1015, 920, 883, 833, 739, 675 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}ClIO_3Si$ calcd for 609.1083, found 609.1096.

(*E*)-1-ethoxy-2-(2-(trifluoromethyl)phenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ma)



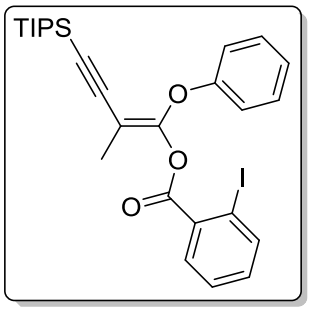
Yield: 46 mg, 72%; white solid; Mp. 52.5-53.4 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 7.8 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.30 – 7.23 (m, 1H), 7.17 – 7.11 (m, 2H), 7.05 – 6.97 (m, 1H), 4.39 (dd, J = 6.0, 2.6 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H), 0.98 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.6, 155.8, 140.6, 132.6, 132.4, 131.2, 130.9, 130.1, 126.9, 126.8, 125.1, 125.0, 121.1, 100.3, 95.7, 93.7, 91.5, 67.4, 28.7, 17.5, 14.0, 10.3. IR (reflection) $\tilde{\nu}$ = 2941, 2892, 2864, 2149, 1758, 1657, 1603, 1580, 1462, 1429, 1384, 1367, 1312, 1267, 1245, 1196, 1168, 1128, 1094, 1059, 1024, 1001, 880, 789, 766, 731, 671 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{35}F_3IO_3Si$ calcd for 643.1346, found 643.1369.

(*E*)-1-ethoxy-2-(3-nitrophenyl)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3na)



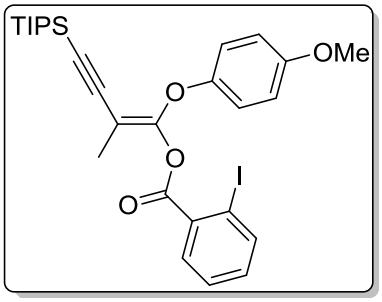
Yield: 45 mg, 73%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (700 MHz, $CDCl_3$) δ = 8.34 (t, J = 1.8 Hz, 1H), 7.95 (dd, J = 13.3, 4.7 Hz, 2H), 7.82 (dd, J = 7.8, 1.4 Hz, 1H), 7.78 – 7.75 (m, 1H), 7.39 – 7.34 (m, 2H), 7.14 (td, J = 7.8, 1.5 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H), 1.06 (d, J = 2.4 Hz, 21H). ^{13}C NMR (175 MHz, $CDCl_3$) δ = 161.2, 156.6, 147.0, 141.1, 136.0, 133.2, 133.1, 130.7, 130.5, 128.1, 127.2, 122.0, 120.7, 100.4, 95.9, 94.2, 92.6, 67.3, 17.6 14.0, 10.3. IR (reflection) $\tilde{\nu}$ = 3084, 2943, 2891, 2865, 2144, 1916, 1747, 1627, 1582, 1532, 1464, 1431, 1386, 1349, 1287, 1246, 1208, 1123, 1095, 1040, 996, 882, 807, 739, 679 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{28}H_{34}F_3INNaO_5Si$ calcd for 642.1143, found 642.1146.

(*E*)-2-methyl-1-phenoxy-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3oa)



Yield: 47 mg, 85%; yellow liquid; R_f= 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.93 (dd, J = 7.9, 1.0 Hz, 1H), 7.67 (dd, J = 7.8, 1.7 Hz, 1H), 7.29 (td, J = 7.7, 1.1 Hz, 1H), 7.24 – 7.17 (m, 2H), 7.12 – 7.05 (m, 3H), 7.01 – 6.93 (m, 1H), 1.81 (s, 3H), 0.90 (d, J = 1.5 Hz, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.3, 155.3, 151.4, 141.9, 133.6, 132.5, 131.7, 129.4, 128.0, 123.4, 116.9, 102.5, 96.2, 95.8, 94.9, 18.5, 16.2, 11.1. IR (reflection) $\tilde{\nu}$ = 2942, 2890, 2864, 2149, 1764, 1667, 1592, 1490, 1463, 1431, 1383, 1289, 1237, 1202, 1169, 1125, 1094, 1064, 1033, 1008, 919, 883, 737, 677, 639 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{27}H_{33}INaO_3SSi$ calcd for 583.1135, found 583.1138.

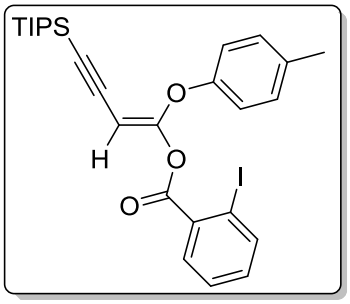
(*E*)-1-(4-methoxyphenoxy)-2-methyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodobenzoate (3pa)



Yield: 44 mg, 75%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.93 (dd, J = 7.9, 1.0 Hz, 1H), 7.65 (dd, J = 7.8, 1.7 Hz, 1H), 7.29 (td, J = 7.7, 1.1 Hz, 1H), 7.09 (td, J = 7.7, 1.7 Hz, 1H), 7.06 –

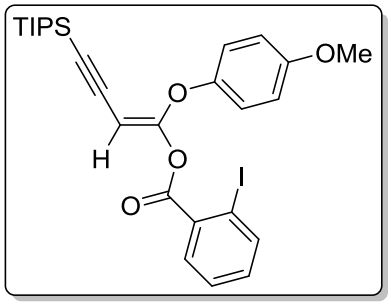
6.99 (m, 2H), 6.77 – 6.70 (m, 2H), 3.68 (s, 3H), 1.79 (s, 3H), 0.93 (d, J = 1.7 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.3, 155.8, 152.1, 149.0, 141.8, 133.6, 132.5, 131.6, 127.9, 118.4, 114.4, 102.8, 95.4, 94.9, 94.7, 55.6, 18.5, 16.2, 11.1. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2864, 2147, 1763, 1666, 1582, 1504, 1463, 1383, 1289, 1237, 1197, 1170, 1125, 1093, 1064, 1034, 1007, 919, 882, 828, 796, 737, 676 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{28}H_{35}INaO_4Si$ calcd for 613.1241, found 613.1247.

(*E*)-1-(*p*-tolyloxy)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3qa)



Yield: 44 mg, 77%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.82 (dd, J = 7.9, 1.0 Hz, 1H), 7.78 (d, J = 8.3 Hz, 2H), 7.47 – 7.39 (m, 3H), 7.26 – 7.14 (m, 7H), 7.08 – 7.01 (m, 1H), 3.55 – 3.47 (m, 2H), 2.32 (s, 3H), 1.84 (dd, J = 15.3, 7.5 Hz, 2H), 1.00 – 0.96 (m, 21H), 0.90 (dd, J = 9.3, 5.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.2, 143.5, 142.9, 141.4, 136.8, 135.4, 133.1, 133.0, 131.4, 129.6, 128.2, 128.2, 128.2, 127.9, 127.7, 117.3, 102.3, 100.1, 94.7, 51.9, 22.5, 21.5, 18.5, 11.3. IR (reflection) $\tilde{\nu}$ = 2958, 2943, 2921, 2866, 2184, 2143, 1932, 1733, 1695, 1581, 1508, 1465, 1430, 1384, 1261, 1199, 1166, 1119, 1016, 883, 806, 736, 678 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{27}H_{33}INaO_3Si$ calcd for 583.1135, found 583.1143.

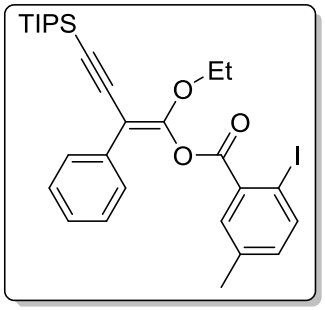
(*E*)-1-(4-methoxyphenoxy)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3ra)



Yield: 42 mg, 71%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.01 (dd, J = 7.9, 0.9 Hz, 1H), 7.70 (dd, J = 7.8, 1.7 Hz, 1H), 7.37 (td, J = 7.7, 1.1 Hz, 1H), 7.18 (td, J = 7.7, 1.6 Hz, 1H), 7.16 – 7.13 (m, 2H), 6.84 – 6.80 (m, 2H), 5.19 (s, 1H), 3.76 (s, 3H), 1.00 (d, J = 4.7 Hz, 21H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 163.0, 157.3, 156.5, 148.6, 142.2, 134.0, 132.6, 132.0, 128.3, 119.5, 114.7, 98.7, 97.5, 95.3, 83.9, 55.9, 18.8, 11.5. IR (reflection) $\tilde{\nu}$ = 2943, 2891, 2865, 2183, 2141, 1932, 1764, 1730, 1656, 1582, 1505, 1464, 1385, 1331, 1235, 1196, 1122, 1064, 1034, 1007, 882, 840,

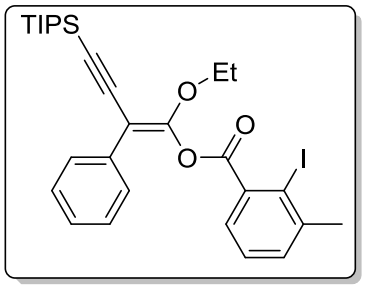
779, 736, 672 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{27}H_{34}INaO_4Si$ calcd for 599.1085, found 599.1090.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodo-5-methylbenzoate (3ab)



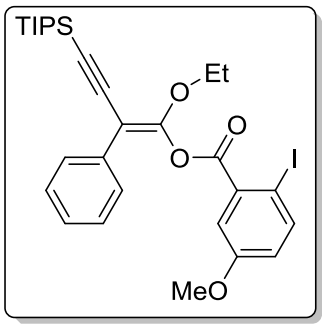
Yield: 51 mg, 88%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.77 (d, J = 8.1 Hz, 1H), 7.41 (t, J = 1.6 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.18 (dd, J = 10.3, 4.6 Hz, 2H), 7.13 – 7.07 (m, 1H), 6.93 – 6.88 (m, 1H), 4.34 (q, J = 7.1 Hz, 2H), 2.20 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.2, 156.8, 141.5, 138.2, 135.1, 134.6, 132.5, 132.3, 128.4, 128.1, 127.0, 102.7, 95.9, 95.5, 90.7, 68.3, 20.7, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2865, 2141, 1916, 1757, 1712, 1631, 1563, 1494, 1465, 1386, 1366, 1296, 1258, 1179, 1097, 1072, 1015, 882, 796, 769, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_3Si$ calcd for 589.1629, found 589.1640.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodo-3-methylbenzoate (3ac)



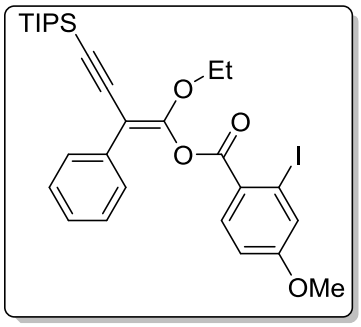
Yield: 52 mg, 89%; white solid; Mp. 70.5-71.2 ^oC; R_f = 0.35 (PE/EA = 20/1); ^1H NMR (400 MHz, $CDCl_3$) δ = 7.41 (dd, J = 5.2, 3.4 Hz, 2H), 7.26 (dd, J = 7.2, 1.7 Hz, 1H), 7.21 – 7.15 (m, 3H), 7.12 (dd, J = 10.0, 4.6 Hz, 2H), 4.36 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 164.4, 156.7, 144.0, 135.3, 135.1, 132.9, 128.4, 128.1, 127.9, 127.7, 127.0, 102.8 100.8, 96.2, 95.4, 68.3, 29.9, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2943, 2893, 2865, 2144, 1916, 1751, 1714, 1637, 1569, 1494, 1461, 1447, 1399, 1368, 1278, 1258, 1240, 1217, 1178, 1122, 1087, 1040, 1016, 998, 919, 883, 807, 769, 744, 701, 680 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_3Si$ calcd for 589.1629, found 589.1645.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodo-5-methoxybenzoate (3ad)



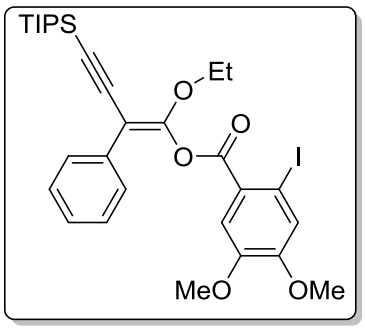
Yield: 54 mg, 91%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (700 MHz, $CDCl_3$) δ = 7.76 (d, J = 8.7 Hz, 1H), 7.40 (d, J = 1.1 Hz, 1H), 7.39 (s, 1H), 7.19 (dd, J = 8.4, 7.0 Hz, 2H), 7.11 (d, J = 7.4 Hz, 1H), 7.09 (d, J = 3.1 Hz, 1H), 6.69 (dd, J = 8.7, 3.0 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 3.66 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.04 (d, J = 2.8 Hz, 21H). ^{13}C NMR (175 MHz, $CDCl_3$) δ = 161.8, 158.4, 155.6, 141.2, 134.1, 132.4, 127.3, 127.1, 126.0, 119.3, 115.7, 101.6, 95.0, 94.6, 82.1, 72.7, 67.4, 54.5, 17.7, 14.1, 10.4. IR (reflection) $\tilde{\nu}$ = 3061, 2942, 2891, 2865, 2142, 1916, 1756, 1711, 1632, 1590, 1565, 1493, 1466, 1389, 1366, 1317, 1288, 1234, 1196, 1177, 1121, 1072, 1042, 1000, 916, 883, 821, 769, 695, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_4Si$ calcd for 605.1578, found 605.1590.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodo-4-methoxybenzoate (3ae)



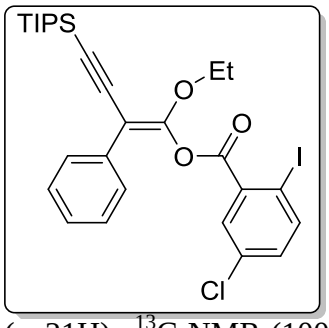
Yield: 56 mg, 93%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (700 MHz, $CDCl_3$) δ = 7.72 (d, J = 8.8 Hz, 1H), 7.46 (d, J = 2.4 Hz, 1H), 7.40 (d, J = 7.3 Hz, 2H), 7.15 (t, J = 7.7 Hz, 2H), 7.07 (t, J = 7.4 Hz, 1H), 6.79 (dd, J = 8.8, 2.4 Hz, 1H), 4.30 (q, J = 7.1 Hz, 2H), 3.74 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (175 MHz, $CDCl_3$) δ = 161.7, 161.0, 155.8, 134.0, 132.4, 132.3, 127.1, 126.6, 125.8, 122.4, 112.6, 101.8, 95.8, 94.6, 94.2, 66.9, 54.7, 17.7, 14.0, 10.4. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2865, 2142, 1917, 1752, 1712, 1630, 1591, 1558, 1491, 1462, 1386, 1366, 1309, 1234, 1210, 1180, 1100, 1027, 998, 918, 883, 767, 694, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{29}H_{38}IO_4Si$ calcd for 605.1578, found 605.1597.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-2-iodo-4,5-dimethoxybenzoate (3af)



Yield: 60 mg, 95%; white solide; Mp. 68.3-69.5 ^{o}C; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (700 MHz, $CDCl_3$) δ = 7.40 (d, J = 1.2 Hz, 1H), 7.39 (d, J = 0.8 Hz, 1H), 7.31 (s, 1H), 7.19 – 7.17 (m, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.10 – 7.08 (m, 1H), 4.35 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 3.71 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H), 1.04 (d, J = 2.9 Hz, 21H). ^{13}C NMR (175 MHz, $CDCl_3$) δ = 161.2, 155.9, 151.6, 147.5, 134.2, 127.2, 127.0, 125.8, 122.9, 122.7, 113.1, 101.7, 94.6, 94.5, 84.9, 67.2, 55.3, 54.9, 17.6, 14.1, 10.3. IR (reflection) $\tilde{\nu}$ = 2942, 2864, 2140, 1917, 1753, 1717, 1646, 1589, 1559, 1509, 1461, 1442, 1367, 1340, 1263, 1240, 1213, 1195, 1168, 1131, 1071, 1020, 959, 921, 882, 846, 776, 748, 694, 661, 609 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{30}H_{40}IO_5Si$ calcd for 635.1684, found 635.1702.

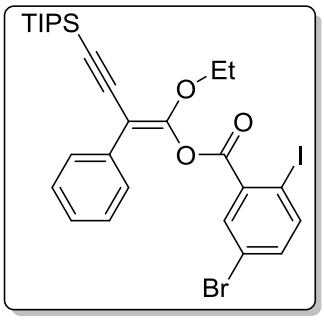
(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-5-chloro-2-iodoben zoate (3ag)



Yield: 49 mg, 81%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 – 7.81 (m, 1H), 7.51 (d, J = 2.5 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.19 (d, J = 7.3 Hz, 2H), 7.15 – 7.10 (m, 1H), 7.07 (dd, J = 8.5, 2.5 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.04 (s, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.0, 156.4, 142.6, 135.0, 134.6, 134.2, 133.5, 131.4, 128.3, 128.2, 127.2, 102.4, 96.4, 95.9, 91.9, 68.6, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2943, 2891, 2865, 2142, 1916, 1758, 1714, 1633, 1552, 1494, 1460, 1383, 1283, 1237, 1200, 1104, 1072, 1006, 918, 882, 819, 767, 695, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}ClIO_3Si$ calcd for 609.1083, found 609.1095.

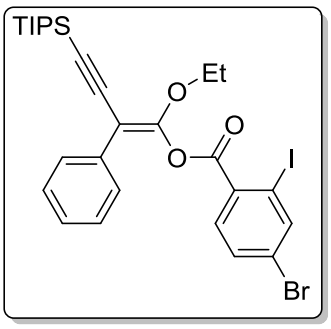
(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-5-bromo-2-iodoben zoate (3ah)

Yield: 54 mg, 83%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.11 (d, J = 1.8 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.45 – 7.43 (m, 1H), 7.38 – 7.34 (m, 2H), 7.18 – 7.15 (m, 2H), 7.12 (dd, J = 5.0, 3.7 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.04 (d, J = 1.4 Hz, 21H). ^{13}C NMR (100 MHz,



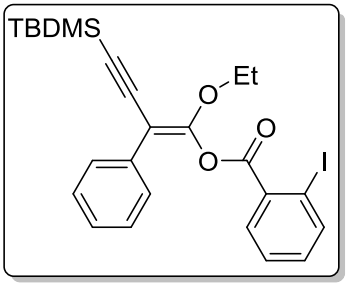
$CDCl_3$) δ = 162.3, 156.5, 144.1, 135.0, 132.3, 131.3, 128.3, 128.2, 128.1, 127.9, 127.1, 102.5, 96.3, 95.8, 95.6, 68.5, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2865, 2142, 1916, 1755, 1713, 1632, 1569, 1544, 1494, 1461, 1386, 1364, 1242, 1204, 1097, 1024, 1006, 919, 882, 829, 764, 694, 675 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}BrIO_3Si$ calcd for 653.0578, found 653.0593.

(*E*)-1-ethoxy-2-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-yl-4-bromo-2-iodobenzoate (3ai)



Yield: 53 mg, 82%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.74 (d, J = 8.4 Hz, 1H), 7.64 (d, J = 2.4 Hz, 1H), 7.38 (t, J = 1.6 Hz, 1H), 7.36 (d, J = 1.0 Hz, 1H), 7.22 – 7.18 (m, 3H), 7.15 – 7.12 (m, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.04 (d, J = 1.4 Hz, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.9, 156.5, 142.9, 136.5, 135.0, 134.5, 134.2, 128.3, 128.2, 127.2, 122.2, 102.4, 96.4, 95.9, 92.7, 68.6, 18.7, 15.1, 11.4. IR (reflection) $\tilde{\nu}$ = 2942, 2891, 2865, 2142, 1916, 1757, 1713, 1633, 1546, 1494, 1460, 1368, 1279, 1236, 1200, 1095, 1004, 918, 882, 818, 767, 695, 676 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{28}H_{35}BrIO_3Si$ calcd for 653.0578, found 653.0593.

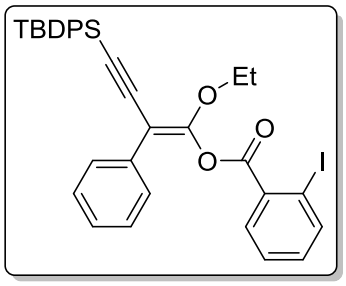
(*E*)-4-(tert-butyldimethylsilyl)-1-ethoxy-2-phenylbut-1-en-3-yn-1-yl-2-iodobenzoate (3aj)



Yield: 42 mg, 79%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.84 (dd, J = 7.9, 0.9 Hz, 1H), 7.50 (dd, J = 7.8, 1.7 Hz, 1H), 7.29 (dd, J = 5.3, 3.4 Hz, 2H), 7.19 (td, J = 7.7, 1.1 Hz, 1H), 7.13 – 7.05 (m, 2H), 7.04 – 7.01 (m, 1H), 6.99 (dd, J = 7.5, 1.6 Hz, 1H), 4.25 (q, J = 7.1 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H), 0.83 (d, J = 1.5 Hz, 9H), 0.00 (d, J = 1.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.9, 156.8, 141.8, 134.8, 133.5, 132.6, 131.5, 128.3, 128.1, 127.9, 127.1, 101.5, 97.4, 95.8, 94.8, 68.5, 26.1,

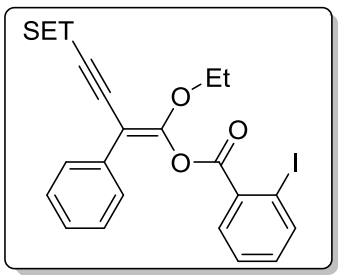
16.7, 15.1, 4.5. IR (reflection) $\tilde{\nu}$ = 3064, 2955, 2929, 2884, 2857, 2176, 2143, 1917, 1756, 1713, 1583, 1494, 1465, 1449, 1391, 1364, 1251, 1175, 1123, 1091, 1016, 940, 826, 811, 778, 741, 694 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{30}IO_3SSi$ calcd for 533.1003, found 533.1015.

(*E*)-4-(tert-butyldiphenylsilyl)-1-ethoxy-2-phenylbut-1-en-3-yn-1-yl-2-iodobenzoate (3ak)



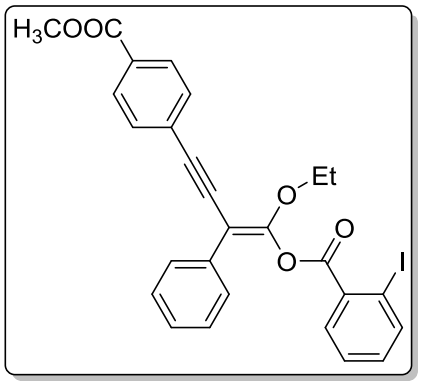
Yield: 49 mg, 75%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.94 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.80 – 7.75 (m, 4H), 7.63 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.46 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.32 – 7.27 (m, 7H), 7.22 – 7.18 (m, 2H), 7.14 – 7.07 (m, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.8, 157.2, 141.9, 135.7, 134.7, 133.7, 133.6, 132.4, 131.6, 129.4, 128.4, 128.3, 128.0, 127.6, 127.2, 105.2, 95.4, 95.0, 94.0, 68.1, 27.2, 18.8, 15.1. IR (reflection) $\tilde{\nu}$ = 3069, 2957, 2929, 2893, 2856, 2144, 1919, 1759, 1629, 1581, 1470, 1445, 1428, 1390, 1248, 1209, 1110, 1062, 1043, 1026, 1002, 859, 820, 763, 737, 697 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{35}H_{34}IO_3Si$ calcd for 657.1316, found 657.1324.

(*E*)-1-ethoxy-2-phenyl-4-(triethylsilyl)but-1-en-3-yn-1-yl 2-iodobenzoate (3al)



Yield: 42 mg, 80%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.93 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.59 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.28 (td, *J* = 7.7, 1.1 Hz, 1H), 7.21 – 7.15 (m, 3H), 7.13 – 7.06 (m, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.9 Hz, 9H), 0.58 (q, *J* = 7.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 163.0, 156.9, 141.8, 134.9, 133.5, 132.6, 131.5, 128.3, 128.2, 127.9, 127.1, 102.0, 96.7, 95.9, 94.9, 68.6, 15.1, 7.5, 4.5. IR (reflection) $\tilde{\nu}$ = 3060, 2955, 2910, 2875, 2142, 1916, 1798, 1757, 1712, 1632, 1599, 1582, 1562, 1494, 1463, 1430, 1391, 1366, 1247, 1205, 1174, 1120, 1073, 1043, 1005, 974, 915, 860, 768, 739, 697 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{30}IO_3Si$ calcd for 533.1003, found 533.1011.

(*E*)-1-ethoxy-4-(4-(methoxycarbonyl)phenyl)-2-phenylbut-1-en-3-yn-1-yl-2-iodobenzoate (3am)



Yield: 40 mg, 74%; yellow liquid; R_f = 0.35 (PE/EA = 20/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 8.03 (dd, *J* = 7.9, 0.9 Hz, 1H), 8.02 – 7.98 (m, 2H), 7.95 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.91 – 7.88 (m, 2H), 7.64 – 7.60 (m, 2H), 7.48 – 7.41 (m, 4H), 7.20 (td, *J* = 7.7, 1.7 Hz, 1H), 4.28 (qq, *J* = 10.8, 7.1 Hz, 2H), 3.92 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ = 167.2, 166.7, 164.9, 141.8, 135.9, 134.5, 133.4, 132.3, 131.6, 130.5, 129.8, 129.7, 128.9, 128.3, 126.9, 126.7, 94.6, 87.9, 87.6, 78.3, 63.4, 52.6, 14.2. IR (reflection) $\tilde{\nu}$ = 2961, 2917, 2849, 2238, 1724, 1605, 1582, 1561, 1434, 1405, 1276, 1177, 1091, 1016, 965, 859, 805, 769, 752, 695, 640, 610 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{27}H_{22}IO_4$ calcd for 553.0506, found 553.0515.

3.5.4. Referneces

1. Zhu, X.; Yuan, H.; Sun, Q.; Zhou, B,; Han, X,; Zhang, Z.; Lu, X.; Ye, L. *Green Chem.*, **2018**, *20*, 4287–4291.

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Chapter 4. Gold-Catalyzed Formal [4+2] Cycloaddition as Access to Spirocyclic Oxindoles from Alkynes and Isatin-Derived Ketimines

4.1 Introduction

Spirocyclic frameworks are ubiquitous in natural products which since a long time has inspired chemists to construct carbo-cyclic and heterocyclic precursors with rational and valuable strategies.[1] Spirocycles as class of scaffold has been found in drug discovery as a result of inherent three-dimensionality.[2] In various spirocyclic frameworks, spirooxindoles, containing a nitrogen heterocycle, represent a very important structural motif that is often found in natural products owing to the excellent bioactivity profil.[3] As shown in Figure 4-1, for example strychnofoline - antimitotic activity.[4] Spirotryprostatin A - anticancer activity,[5] and other spiro-compounds have antimalarial.[6] Many researchers have developed effective methods to construct spirooxindole scaffolds which have importance and potential biological activities.

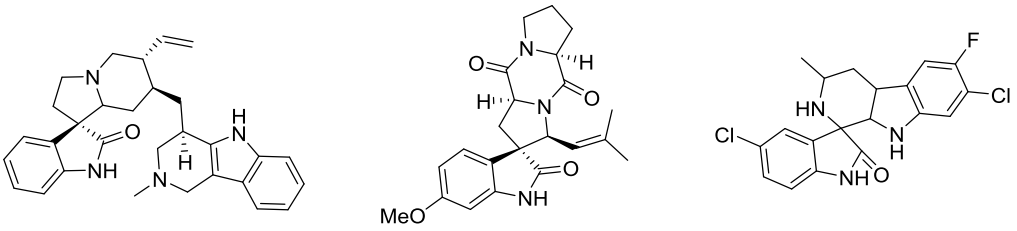
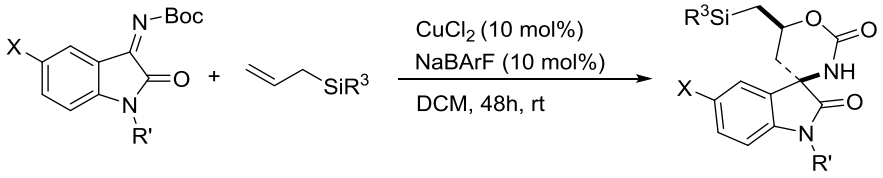


Figure 4-1 Biologically active of spiro-compounds

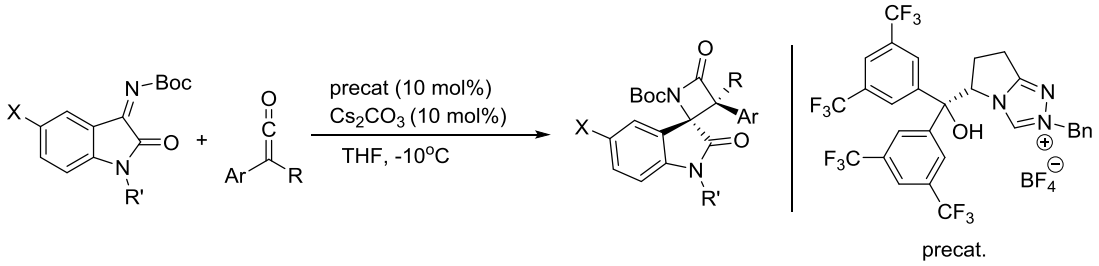
In 2013, Franz's group developed a Lewis acid-catalyzed novel technique using allylsilanes and N-Boc-iminooxindoles to access spirocarbamate oxindoles by trapping a transient β-silyl carbocations intramolecularly under mild conditions. Fluoride-promoted elimination can be used to transform the spirocarbamate to produce novel silylated furoindoline derivatives (Scheme 4-1).[7]

After that, Ye's group in 2014 reported isatin-derived ketimines to undergo a Staudinger reaction with ketenes by a bifunctional N-heterocyclic carbene catalyst



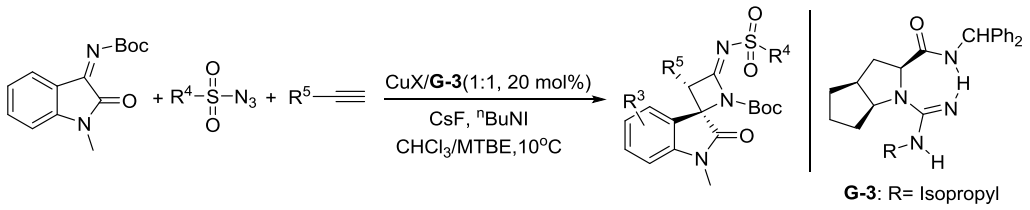
Scheme 4-1 Lewis acid-catalyzed cyclization of N-Boc-iminooxindoles

that delivered the nitrogen-containing spiroheterocycle oxindolo-β-lactams with enantio-and diastereo-selectivity in good yield (Scheme 4-2).[8]



Scheme 4-2 Carbene-catalyzed of ketimines to spiroheterocycle compounds

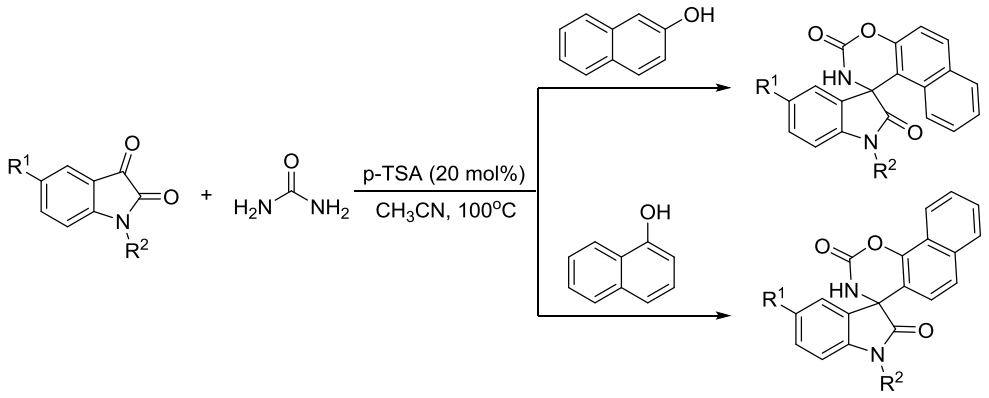
In 2018, Liu's group constructed various spiro oxindoles with high enantioselectivity and excellent yields by using chiral copper-catalyst to induce an cycloaddition of azide-alkyne at low temperature (Scheme 4-3).[9]



Scheme 4-3 Copper-catalyzed asymmetric azide-alkyne cycloaddition

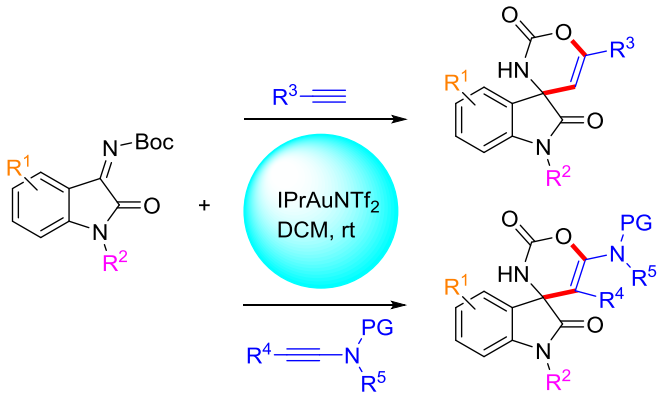
Then, in 2020 the Basavoju group realized a one-pot multi-component approach to synthesize a series of new spirooxindolocarbamates via the reaction of spirooxindoles and carbamates in CH_3CN at 100 C with 20 mol% of p-TSA. The products have antibacterial, antifungal and antioxidant activities (Scheme 4-4).[10]

Although numerous efficient syntheses for constructing diverse biological activities spirocyclohexane oxindoles have become an attractive highly desirable objective and been developed, the development of efficient and highly selective protocols for the preparation of six-membered spiro N/O-heterocycle oxindole derivatives is desirable.[11]



Scheme 4-4 Synthesis of spirooxindolocarbamates

However, terminal alkynes or ynamides have not been investigated with the Boc group of isatin-derived ketimines for synthesis of spirocyclic oxindoles. Herein, we present the discovery of a new gold-catalyzed synthesis of six-membered spirocarbamate oxindole derivatives through a cycloaddition/[4+2] cascade reaction of terminal alkynes, ynamides with isatin-derived ketimines under mild conditions (Scheme 4-5).



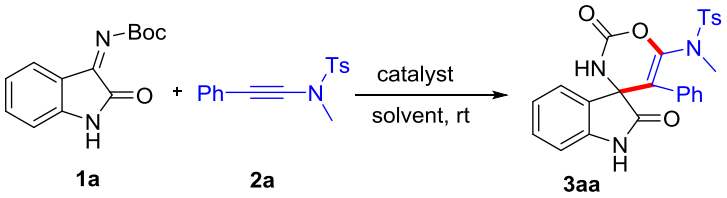
Scheme 4-5 Gold-catalyzed synthesis of spirocyclic oxindoles

4.2 Result and Discussion

4.2.1 Optimization of the Reaction Conditions

We initiated our studies by choosing *tert*-butyl (Z)-(2-oxoindolin-3-ylidene)carbamate **1a** and N,4-dimethyl-N-(phenylethynyl)benzenesulfonamide **2a** as strating substrates to evaluate the approach's viability and to improve the reaction conditions (Table 1). After extensive investigation, we were delighted that the desired spiro compound **3aa**

Table 1 Optimization of the reaction conditions[a]



Entry	Catalyst	Additive	Solvent	Yield (%)[b]
1	IPrAuCl	$AgNTf_2$	DCE	72
2	DMSAuCl	$AgNTf_2$	DCE	56
3	Ph_3PAuCl	$AgNTf_2$	DCE	62
4	SPhosAuCl	$AgNTf_2$	DCE	49
5	XPhosAuCl	$AgNTf_2$	DCE	57
6	thtAuCl	$AgNTf_2$	DCE	42
7[d]	$HAuBr_4$	$AgNTf_2$	DCE	29
8[e]	Cy_3PAuCl	$AgNTf_2$	DCE	58
9	$IPrAuNTf_2$		DCE	75
10	$IPrAuNTf_2$		DCM	88
11	$IPrAuNTf_2$		EtOAc	32
12	$IPrAuNTf_2$		Toluene	53
13	$IPrAuNTf_2$		THF	37
14	$IPrAuNTf_2$		Et_2O	Trace
15	$IPrAuNTf_2$		CH_3CN	26
16	$IPrAuNTf_2$ (1 mol %)		DCM	88
17	**$IPrAuNTf_2$ (0.1 mol %)**		**DCM**	**88 (89)**[c]
18	$Sc(OTf)_3$		DCM	72
19	pTsOH		DCM	33
20	$Zn(OTf)_2$		DCM	78
21	$In(OTf)_3$		DCM	71
22	$ZnCl_2$		DCM	67
23	CF_3COOH		DCM	Trace
24	$SnCl_4$		DCM	30

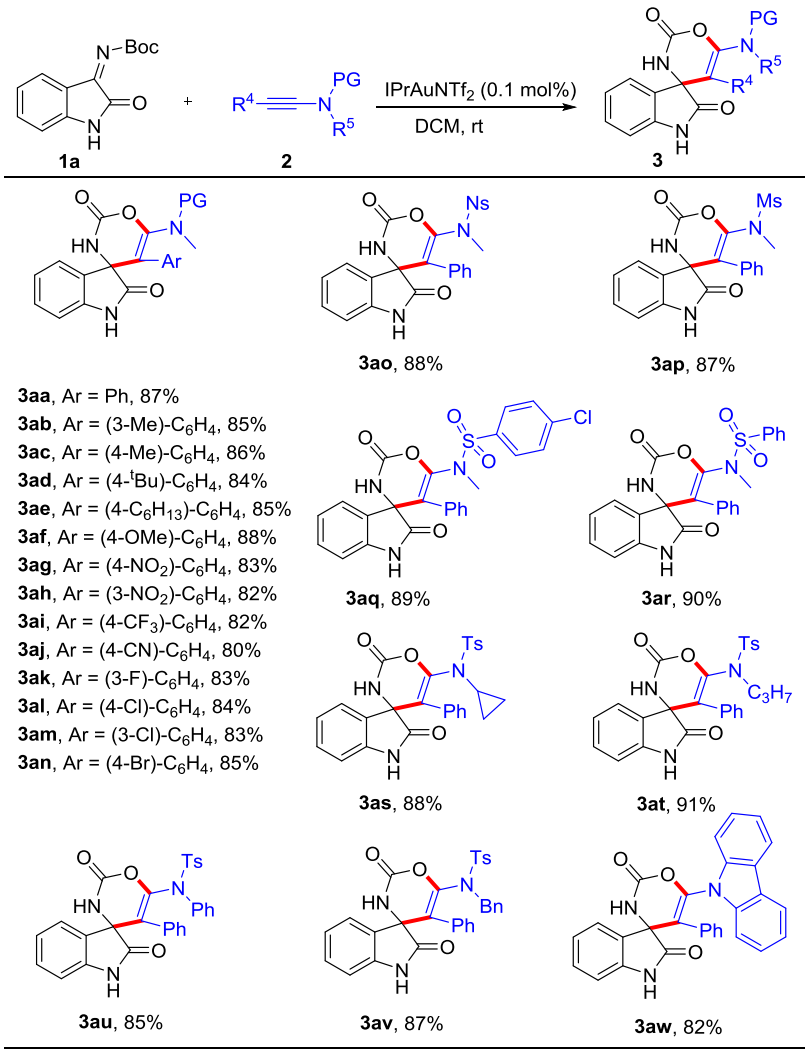
[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.12 mmol), catalyst (0.1 mol %), additive (5 mol %) in solvent (1.0 mL) at rt. [b]Isolated yield. [c]NMR yield with CH_2Br_2 as an internal standard.

was offered in 70% yield with IPrAuCl/$AgNTf_2$ as the catalytic species in DCE under

open-flask conditions at room temperature (entry 1). With those promising results in hand, we opt to screen all kinds of commercially available gold(I) and gold(III) complexes, including DMSAuCl, Ph_3PAuCl, SPhosAuCl, XPhosAuCl, thtAuCl, $HAuBr_4$, and Cy_3PAuCl (entries 2−8) but the yield of product was less efficient than IPrAuCl. Preactivated $IPrAuNTf_2$ was also tested in DCE, affording **3aa** in 75% yield (entry 9). Further investigation of different solvents, covering DCM, EtOAc, Toluene, THF, Et_2O, and CH_3CN, were carried out by using $IPrAuNTf_2$ as the best catalyst. As a result, DCM improved the yield and produced the desired **3aa** in 88% (entries 10−15). Interestingly, the maximum yield (88%) of **3aa** also was obtained with $IPrAuNTf_2$ (1 mol %) or $IPrAuNTf_2$ (0.1 mol %) in DCM at room temperature (entries 16 and 17). Several acids, including $Sc(OTf)_3$, pTsOH, $Zn(OTf)_2$, $In(OTf)_3$, $ZnCl_2$, CF_3COOH and $SnCl_4$, were evaluated, but all resulted in lower yields (entries 18−24).

Since entry 17 provided the best outcome in terms of chemical yield and selectivity we turned our focus to prove the versatility of the developed protocol. Under theoptimized condition *tert*-butyl (Z)-(2-oxoindolin-3-ylidene)carbamate **1a** and structurally diverse ynamides **2** (Scheme 4-6) were reacted. A wide range of aryl-substituted ynamides bearing aryl motifs at the alkyne terminal position (R^4) with either electron-donating groups (Me, OMe, ^tBu and C_6H_{13}) or electron-withdrawing groups (F, Cl, Br, CN, NO_2 and CF_3) all reacted well to obtain the products **3aa**−**3an** in good to excellent yields. Next, the nitrogen substituent and the protecting group of the ynamides were investigated. It was found that substituents with different aryl sulfonyl groups (PG) including nosyl (**2o**), mesyl (**2p**), *para*-chlorobenzene sulfonyl groups (**2q**) and benzene sulfonyl groups (**2r**) on nitrogen of the ynamides all proceeded smoothly to give **3ao**−**3ar** in 87−90% yield.

4.2.2 Substrate Scope

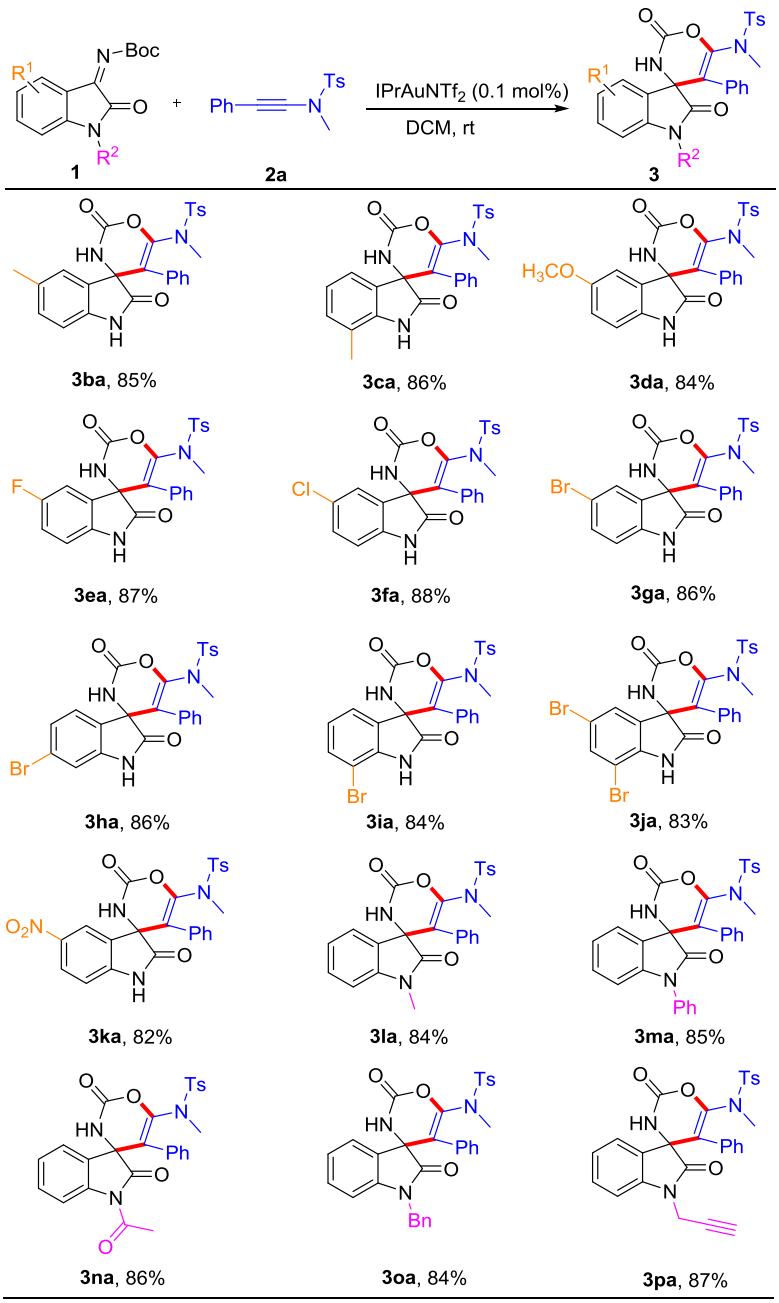


[a]Reaction conditions: **1a** (0.10 mmol), **2** (0.12 mmol), $IPrAuNTf_2$ (0.1 mol %), in DCM (1.0 mL) at rt. [b]Isolated yield.

Scheme 4-6 Scope with respect to ynamides derivatives[a,b]

A series of N-cyclopropyl, alkyl-, aryl- and benzyl-substituted ynamides also afforded the desired products (**3as**–**3av**) with high yields. Further good results, a carbazole-derived ynamide, in addition to these sulfonamide-substituted ynamides, also performed well to provide the desired product **3aw** in 50% yield.

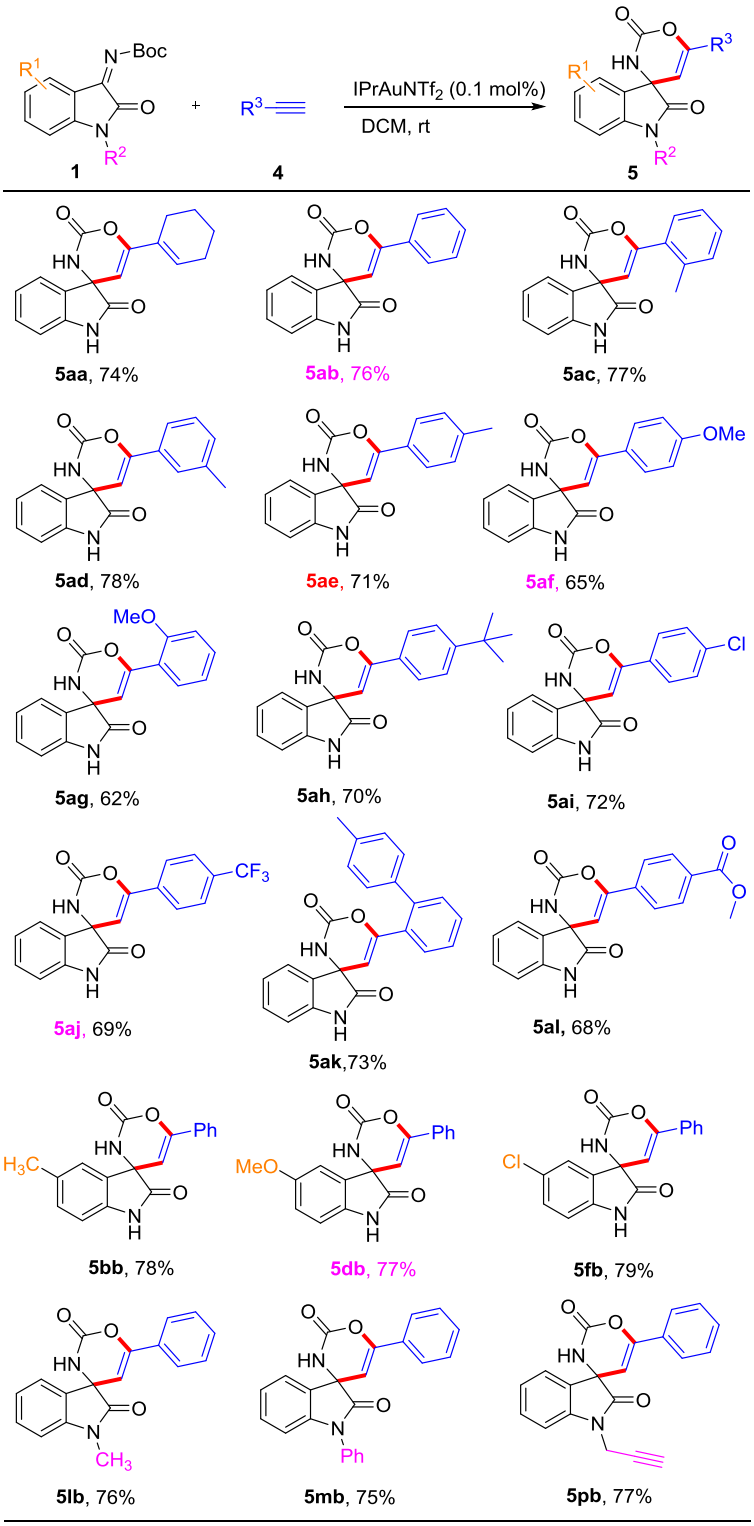
Next, we were particularly interested in extending the N,4-dimethyl-N-(phenylethynyl)benzenesulfonamide **2a** to differently substituted isatin-derived ketimines derivatives **1** (Scheme 4-7). We were pleased to observe that a number of ketimines with either electron-donating or electron-withdrawing groups on the aromatic ring had little impact on the results and that these substrates were all



[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.12 mmol), $IPrAuNTf_2$ (0.1 mol %), in DCM (1.0 mL) at rt. [b]Isolated yield.

Scheme 4-7 Scope with respect to ketimines[a,b]

efficiently transformed into spirocarbamate oxindole products **3ba**−**3ka** in high yields. We also tested isatin-derived ketimines with different N-protecting groups as methyl, phenyl, aldehyde group, benzyl, and alkynyl at the N-1 of the oxindole (**3la**−**3pa**), delivering the appropriate products in high yields.



[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.12 mmol), $IPrAuNTf_2$ (0.1 mol %), in DCM (1.0 mL) at rt. [b]Isolated yield.

Scheme 4-8 Scope with respect to terminal alkynes and ketimines[a,b]

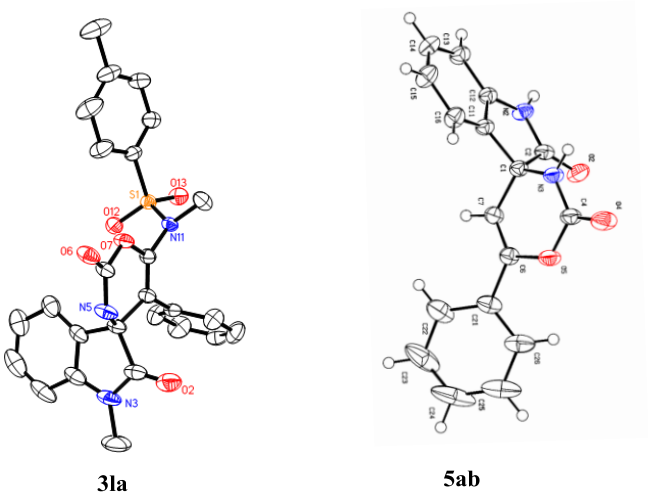
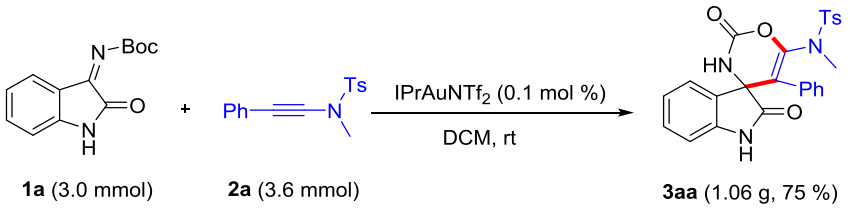


Figure 4-2 Solid state molecular structure of **3la** and **5ab**.

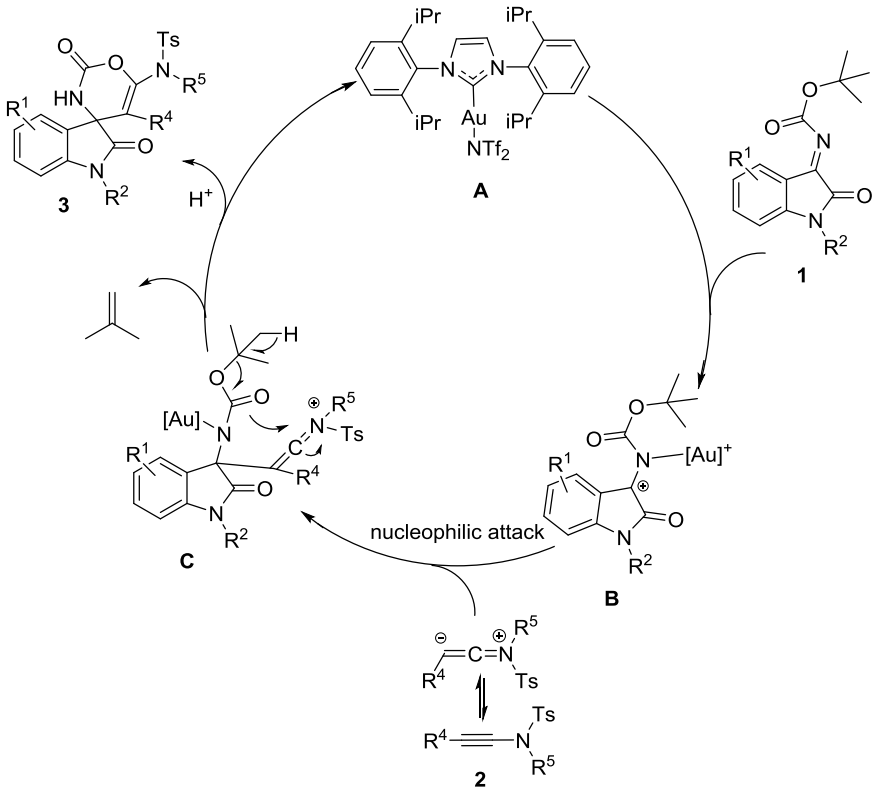
To demonstrate the generality of this cyclization under the optimized conditions, we also selected ketimines derivatives **1** and terminal alkynes **4** as the model substrates to explore the efficiency of this transformation. As shown in Scheme 4-8, all of these terminal alkynes with different groups could smoothly convert to the expected products **5aa**-**5al** in moderate yields. On the other hand, various ketimines bearing different substituents on the aromatic ring or N-1 of the oxindole, such as -CH_3, −OCH_3, −Cl, -Ph and –$CH_2C{\equiv}C$, reacted with phenylacetylene to get the products **5bb**-**5pb**. Specimens suited for single crystal X-ray analysis were obtained for **5ab** and **3la** by slow evaporation of concentrated racemic solutions of the compounds in DCM (Figure 4-2). Additional, a gram-scale experiment of substrates **1a** with **2a** was combined, and product **3aa** was achieved in 75% yield (Scheme 4-9).



Scheme 4-9 Gram-scale synthesis

Based on previous reports,[7] a plausible mechanism to form spirocarbamate oxindoles is proposed, as shown in Scheme 4-10. Initially, the intermediate **B** is formed from the gold(I) catalyst **A** complexation of iminooxindole. In a subsequent step the C-N double bond of intermediate **B** can easily be attacked by nucleophile **2** generating

intermediate **C**, duo to the strong electrophilicity of the imine. Finally, oxygen from the Boc group of intermediate **C** attacks the alkynamide to form a ring, while removing 2-methylpropene leads to the formation of spirocarbamate **3** and Au(I) species **A**, which accomplish the catalytic cycle.



Scheme 4-10 Proposed mechanism

4.3 Conclusions

In summary, we discovered a novel protocol to produce spirocarbamates by the gold-catalyzed cyclization of alkynes with isatin-derived ketimines under mild conditions. The easily available starting materials of N-Boc-iminooxindoles and varius alkynes can precisely be assembled in a modular approach. Gram-scale synthesis and proposed mechanism are also addresed. Importantly, spirocarbamates are versatile and preeminent structural units, which are most commonly present in several biologically active natural products with impact on medicinal chemistry.

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4.5 Experimental Section

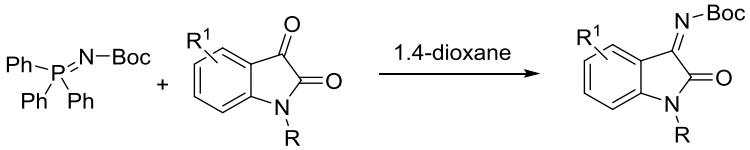
4.5.1 General Remarks

Reactions were performed in oven-dried glassware unless otherwise noted, chemicals were obtained from commercial suppliers (Sigma-Aldrich, ChemPUR and TCI) and used without further purification. Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. ^{1}H NMR spectra were recorded in $CDCl_3$ and referenced to residual $CHCl_3$ at 7.26 ppm. Multiplicities were reported using the following abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiple). All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH_2-group), q (quartet, CH_3-group)] were determined by DEPT135 spectra. (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not calibrated. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400

mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

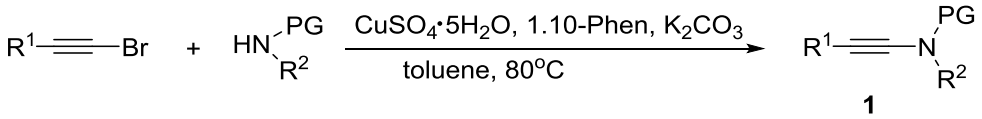
4.5.2 Experiment Procedures

Procedure A: General procedure for the synthesis of N-alkoxycarbonyl Ketimines[1]



In an oven–dried Schlenk flask under argon atmosphere, isatin (10 mmol) and compound A (11 mmol) were placed. After an injection of anhydrous 1,4-dioxane (10 mL), the mixture was heated under reflux until complete disappearance of the starting materials. Then the reaction was cooled to room temperature. After an evaporation of the volatile organic solvents, the crude residue was purified by flash chromatography (silica gel, hexane/ethyl acetate) and afforded the products **1**

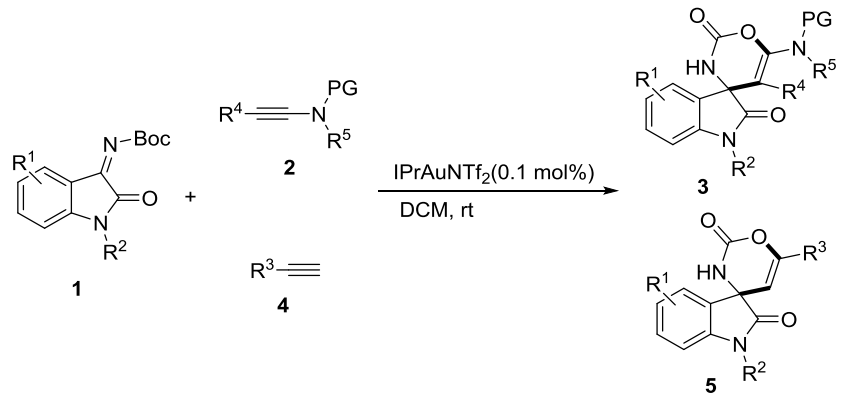
Procedure B: General procedure for the synthesis of ynamides **2**[2,3]



1

Amide (5.0 mmol), 1-bromo-2-acetylenes (6.0 mmol), $CuSO_4{\cdot}5H_2O$ (187.0 mg, 0.75 mmol), 1,10- phenanthroline (270.0 mg, 1.5 mmol) and K_2CO_3 (1.38 g, 10.0 mmol), toluene (25 mL) were added under a nitrogen atmosphere. The reaction flask was evacuated under vacuum and flushed with nitrogen three times, then sealed under nitrogen and heated to 80 ºC. The reaction mixture was stirred overnight, then cooled down to room temperature, filtered through a pad of silica gel, the filtrate was evaporated and purified by flash silica gel column chromatrography to give the desired ynamide **2** in high yield.

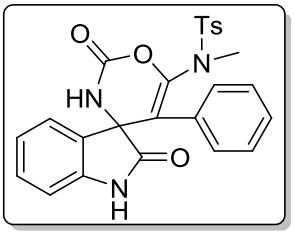
Procedure C: Synthesis of **3** and **5**



A mixture of **1** (0.10 mmol, 1.0 equiv) and **2** or **4** (0.12 mmol, 1.2 equiv) in 1.0 mL DCM was treated with IPrAuCl (0.1 mol %) at rt. The reactions were monitored by TLC analysis and the chemical **1** were consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3**and **5**

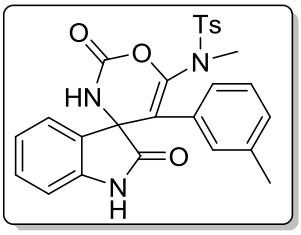
4.5.3 Characterization Data

***N*-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*,4-di methylbenzenesulfonamide (3aa)**



Yield: 41 mg, 87%; yellow solid; Mp. 173.1-174.7 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (600 MHz, DMSO) δ = 10.49 (s, 1H), 8.84 (s, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.47 (d, J = 7.4 Hz, 1H), 7.36 (d, J = 8.1 Hz, 2H), 7.21 (dt, J = 15.5, 4.3 Hz, 2H), 7.14 (t, J = 7.5 Hz, 2H), 7.06 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 7.1 Hz, 2H), 6.65 (d, J = 7.8 Hz, 1H), 2.76 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ = 175.6, 149.1, 144.9, 142.6, 142.2, 135.4, 131.7, 131.1, 130.4, 130.1, 128.8, 128.5, 128.4, 125.9, 123.2, 113.6, 110.8, 65.8, 36.6, 21.8. IR (reflection) $\tilde{\nu}$ = 3312, 2925, 1735, 1620, 1472, 1348, 1188, 1055, 1006, 906, 876, 814, 752, 700, 680, 659, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{21}N_3NaO_5S$ calcd for 498.1094, found 498.1103.

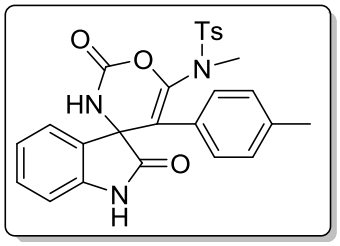
***N*-(2,2'-dioxo-5'-(*m*-tolyl)-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*,4-dimethylbenzenesulfonamide (3ab)**



Yield: 41 mg, 85%; yellow solid; Mp. 134.6-135.4 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (600 MHz, DMSO) δ = 10.48 (s, 1H), 8.81 (s, 1H), 7.51 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 7.4 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H), 7.22 (td, J = 7.7, 1.1 Hz,

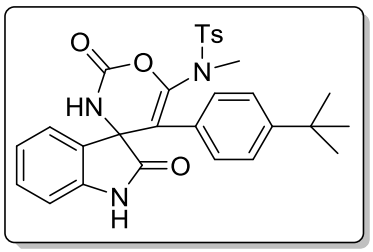
1H), 7.07 (td, *J* = 7.5, 0.5 Hz, 1H), 7.01 (dd, *J* = 4.6, 1.7 Hz, 2H), 6.66 (d, *J* = 7.7 Hz, 1H), 6.63 (s, 1H), 6.61 – 6.58 (m, 1H), 2.75 (s, 3H), 2.39 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ = 175.6, 149.1, 144.8, 142.5, 142.2, 137.4, 135.4, 131.5, 131.0, 130.6, 130.4, 130.2, 129.4, 128.4, 128.3, 127.2, 125.9, 123.2, 113.5, 110.7, 65.8, 36.6, 21.8, 21.6. IR (reflection) $\tilde{\nu}$ = 3309, 2923, 1717, 1617, 1469, 1356, 1295, 1266, 1216, 1169, 1114, 1084, 1036, 920, 800, 747, 703, 668, 619 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_5S$ calcd for 512.1251, found 512.1260.

_N_-(2,2'-dioxo-5'-(*p*-tolyl)-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ac)



Yield: 42 mg, 86%; yellow solid; Mp. 138.3-139.8 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.47 (s, 1H), 8.81 (s, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.23 (td, *J* = 7.7, 1.1 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 7.7 Hz, 1H), 2.76 (s, 3H), 2.40 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.8, 144.5, 142.2, 141.9, 137.8, 135.2, 130.8, 130.0, 129.6, 129.6, 128.8, 128.3, 128.1, 125.6, 122.9, 113.1, 110.5, 65.5, 36.4, 21.5, 21.1. IR (reflection) $\tilde{\nu}$ = 3309, 2921, 1719, 1616, 1510, 1469, 1355, 1295, 1266, 1186, 1170, 1113, 1083, 1054, 1034, 1000, 909, 889, 817, 793, 748, 718, 704, 666, 637, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{26}H_{23}N_3NaO_5S$ calcd for 512.1250, found 512.1254.

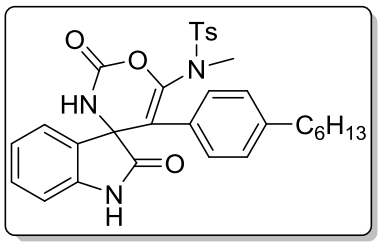
_N_-(5'-(4-(tert-butyl)phenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ad)



Yield: 44 mg, 84%; yellow solid; Mp. 155.2-156.5 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (600 MHz, DMSO) δ = 10.50 (s, 1H), 8.85 (s, 1H), 7.49 – 7.45 (m, 3H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.24 (td, *J* = 7.7, 0.6 Hz, 1H), 7.16 – 7.14 (m, 2H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.74 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 7.7 Hz, 1H), 2.77 (s, 3H), 2.36 (s, 3H), 1.20 (s, 9H). ^{13}C NMR (150 MHz, DMSO) δ = 175.4, 151.0, 149.1, 144.7, 142.5, 142.2, 135.4, 131.1, 130.5, 130.3, 129.7, 128.7, 128.4,

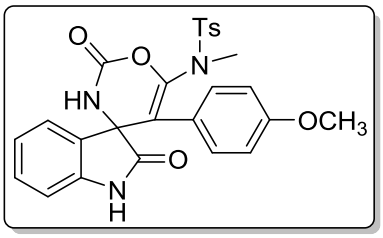
125.8, 125.2, 123.3, 113.4, 110.8, 65.7, 36.6, 34.9, 31.7, 21.8. IR (reflection) $\tilde{\nu}$ = 3294, 2963, 1734, 1619, 1470, 1355, 1301, 1266, 1187, 1170, 1109, 1083, 1051, 1000, 910, 837, 814, 749, 704, 665, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{29}H_{29}N_3NaO_5S$ calcd for 554.1720, found 554.1730.

_N_-(5'-(4-hexylphenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ae)



Yield: 47 mg, 85%; yellow solid; Mp. 112.9-113.6 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (300 MHz, DMSO) δ = 10.48 (s, 1H), 8.83 (s, 1H), 7.51 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 7.6 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.22 (t, J = 7.5 Hz, 1H), 7.07 (t, J = 7.5 Hz, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 7.9 Hz, 2H), 6.67 (d, J = 7.6 Hz, 1H), 2.77 (s, 3H), 2.38 (s, 3H), 1.49 (s, 2H), 1.25 (s, 8H), 0.84 (t, J = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.8, 148.4, 143.9, 142.1, 141.7, 141.5, 134.7, 130.2, 129.5, 129.1, 128.0, 127.6, 127.5, 125.1, 122.4, 112.7, 109.9, 65.0, 35.8, 34.7, 31.0, 30.6, 28.3, 21.9, 20.9, 13.8. IR (reflection) $\tilde{\nu}$ = 2947, 2865, 2146, 1751, 1619, 1583, 1563, 1512, 1494, 1462, 1431, 1406, 1359, 1269, 1226, 1160, 1122, 1094, 1066, 1006, 950, 884, 864, 838, 813, 789, 739, 681, 661, 639, 612 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{31}H_{33}N_3NaO_5S$ calcd for 582.2033, found 582.2044.

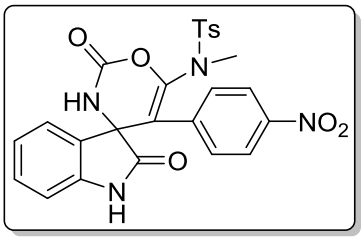
_N_-(5'-(4-methoxyphenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3af)



Yield: 44 mg, 88%; yellow solid; Mp. 149.5-150.7 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (300 MHz, DMSO) δ = 10.46 (s, 1H), 8.79 (s, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 7.3 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.23 (t, J = 7.4 Hz, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.74 (d, J = 8.9 Hz, 2H), 6.69 (dd, J = 8.3, 4.4 Hz, 3H), 3.67 (s, 3H), 2.77 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.8, 158.8, 148.3, 144.0, 141.8, 141.4, 134.8, 130.5, 130.2, 129.6, 129.5, 127.6, 125.1, 122.6, 122.5, 113.1, 112.4, 110.0, 65.1, 54.9, 35.8, 20.9. IR (reflection) $\tilde{\nu}$ =

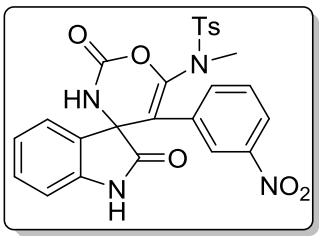
3313, 2936, 1735, 1609, 1513, 1470, 1349, 1290, 1249, 1173, 1112, 1084, 1035, 999, 908, 834, 815, 751, 660, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_6S$ calcd for 528.1200, found 528.1209.

***N*,4-dimethyl-*N*-(5'-(4-nitrophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1, 3]oxazin]-6'-yl)benzenesulfonamide (3ag)**



Yield: 41 mg, 83%; yellow solid; Mp. 143.5-145.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (300 MHz, DMSO) δ = 10.64 (s, 1H), 8.97 (s, 1H), 8.03 (d, J = 8.7 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 7.2 Hz, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.24 (t, J = 7.5 Hz, 1H), 7.10 (dd, J = 20.8, 8.0 Hz, 3H), 6.71 (d, J = 7.7 Hz, 1H), 2.89 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.1, 148.5, 147.5, 144.8, 142.9, 141.9, 139.0, 134.8, 131.2, 130.2, 129.1, 128.1, 125.8, 123.3, 111.8, 110.8, 65.1, 36.2, 21.5. IR (reflection) $\tilde{\nu}$ = 1716, 1613, 1595, 1520, 1467, 1345, 1292, 1170, 1084, 1032, 996, 928, 891, 853, 813, 798, 752, 727, 702, 667, 631, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{21}N_4NaO_7S$ calcd for 521.1125, found 521.1859.

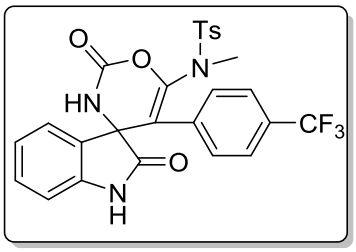
***N*,4-dimethyl-*N*-(5'-(3-nitrophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1, 3]oxazin]-6'-yl)benzenesulfonamide (3ah)**



Yield: 42 mg, 82%; yellow solid; Mp. 216.8-217.9 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (300 MHz, DMSO) δ = 10.65 (s, 1H), 8.98 (s, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.64 (s, 1H), 7.62 (s, 2H), 7.56 (d, J = 7.4 Hz, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.38 (d, J = 8.1 Hz, 3H), 7.23 (t, J = 7.6 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 6.69 (d, J = 7.7 Hz, 1H), 2.90 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.7, 147.9, 146.8, 144.3, 142.6, 141.3, 136.4, 134.3, 132.9, 130.6, 129.7, 129.5, 128.6, 127.6, 125.3, 123.9, 123.0, 122.7, 110.9, 110.2, 64.8, 35.7, 20.91. IR (reflection) $\tilde{\nu}$ = 3384, 3075, 2957, 1711, 1659, 1613, 1530, 1465, 1370, 1348, 1315, 1261, 1212, 1192, 1174, 1120, 1103, 1084, 1033, 1008, 939, 920, 896, 875, 845, 815, 805, 794, 750, 729,

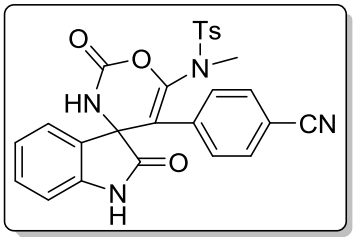
704, 678, 660, 619 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}N_4NaO_7S$ calcd for 543.0945, found 543.0950.

_N_-(2,2'-dioxo-5'-(4-(trifluoromethyl)phenyl)-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ai)



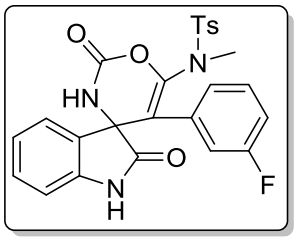
Yield: 44 mg, 82%; yellow solid; Mp. 124.2-125.7 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.59 (s, 1H), 8.95 (s, 1H), 7.54 (t, J = 10.3 Hz, 5H), 7.35 (d, J = 8.2 Hz, 2H), 7.24 (t, J = 7.7 Hz, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.05 (d, J = 7.4 Hz, 2H), 6.70 (d, J = 7.7 Hz, 1H), 2.85 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.1, 148.6, 144.7, 142.7, 141.8, 136.1, 134.9, 131.0, 130.7, 130.1, 129.4, 128.1, 125.7, 125.2, 125.1, 123.2, 112.3, 110.7, 65.3, 36.2, 21.4. IR (reflection) $\tilde{\nu}$ = 1714, 1685, 1614, 1469, 1408, 1364, 1322, 1166, 1117, 1085, 1066, 1019, 998, 933, 889, 840, 813, 796, 747, 719, 701, 667, 634, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{20}F_3N_3NaO_5S$ calcd for 566.0968, found 566.7127.

_N_-(5'-(4-cyanophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3aj)



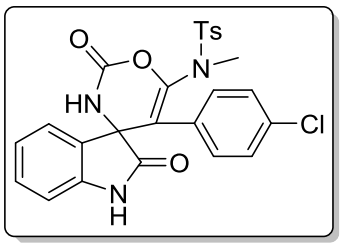
Yield: 40 mg, 80%; yellow solid; Mp. 138.6-139.9 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.58 (s, 1H), 8.91 (s, 1H), 7.65 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 7.02 (d, J = 7.9 Hz, 2H), 6.70 (d, J = 7.7 Hz, 1H), 2.85 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 179.9, 153.3, 149.5, 147.5, 146.6, 141.7, 139.6, 136.8, 135.8, 135.6, 134.9, 133.9, 132.8, 130.5, 127.9, 123.5, 116.9, 116.1, 115.5, 69.9, 40.9, 26.2. IR (reflection) $\tilde{\nu}$ = 2229, 1714, 1612, 1468, 1360, 1293, 1188, 1168, 1084, 1032, 997, 931, 889, 839, 814, 796, 747, 704, 667, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{20}N_4NaO_5S$ calcd for 523.1047, found 523.0919.

_N_-(5'-(3-fluorophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ak)



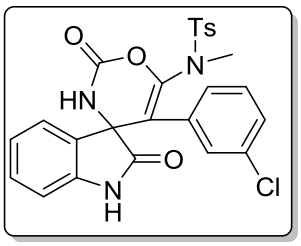
Yield: 41 mg, 83%; yellow solid; Mp. 193.2-194.4 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (300 MHz, DMSO) δ = 10.57 (s, 1H), 8.89 (s, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.27 – 7.18 (m, 2H), 7.09 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 2.9 Hz, 1H), 6.70 (dd, J = 7.6, 3.4 Hz, 2H), 6.58 (d, J = 9.8 Hz, 1H), 2.82 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.7, 162.7, 159.4, 148.1, 144.2, 142.1, 141.4, 134.5, 133.2, 133.2, 130.4, 129.7, 129.0, 127.7, 125.6, 125.2, 122.6, 116.4, 116.2, 115.1, 114.8, 111.7, 110.1, 64.8, 35.7, 20.9. IR (reflection) $\tilde{\nu}$ = 1708, 1685, 1613, 1581, 1468, 1356, 1293, 1189, 1171, 1085, 1034, 1010, 936, 870, 788, 747, 703, 667, 619 cm^{-1}. HRMS (ESI) [M+Na]$^+$ (m/z) $C_{25}H_{20}FN_3NaO_5S$ calcd for 516.0999, found 516.0987.

_N_-(5'-(4-chlorophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3al)



Yield: 42 mg, 84%; yellow solid; Mp. 127.6-128.7 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.52 (s, 1H), 8.86 (s, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 7.3 Hz, 1H), 7.39 (d, J = 8.2 Hz, 2H), 7.24 (dd, J = 12.0, 4.8 Hz, 3H), 7.08 (t, J = 7.5 Hz, 1H), 6.84 (d, J = 7.4 Hz, 2H), 6.70 (d, J = 7.7 Hz, 1H), 2.82 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.2, 148.6, 144.6, 142.5, 141.9, 135.1, 133.4, 131.7, 130.9, 130.4, 130.1, 129.5, 128.3, 128.1, 125.7, 123.1, 112.3, 110.6, 65.4, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 2961, 1708, 1685, 1616, 1593, 1490, 1468, 1400, 1361, 1293, 1264, 1188, 1171, 1085, 1033, 1016, 998, 932, 889, 814, 795, 743, 704, 670, 633, 614 cm^{-1}. HRMS (ESI) [M+Na]$^+$ (m/z) $C_{25}H_{20}ClN_3N_aO_5S$ calcd for 532.0709, found 532.0712.

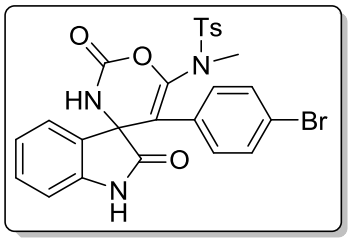
_N_-(5'-(3-chlorophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3am)



Yield: 42 mg, 83%; yellow solid; Mp. 215.7-217.2 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.60 (s, 1H), 8.90 (s, 1H), 7.59 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 7.4 Hz, 1H), 7.40 (d, J = 8.2 Hz, 2H), 7.26 (dd, J = 16.4, 8.2 Hz, 2H), 7.20 (t, J = 8.1 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 6.82 (d, J = 6.9 Hz, 2H), 6.70 (d, J =

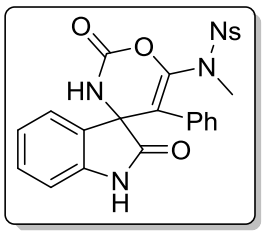
7.8 Hz, 1H), 2.82 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.2, 148.6, 144.7, 142.6, 141.9, 134.9, 133.5, 132.6, 131.0, 130.2, 130.1, 129.6, 129.4, 128.7, 128.6, 128.2, 125.7, 123.1, 112.1, 110.6, 65.4, 36.2, 21.5. IR (reflection) $\tilde{\nu}$ = 1709, 1614, 1594, 1562, 1468, 1353, 1294, 1189, 1171, 1084, 1059, 1033, 1006, 934, 786, 746, 703, 666, 619 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}ClN_3NaO_5S$ calcd for 532.0704, found 532.0712.

_N_-(5'-(4-bromophenyl)-2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3an)



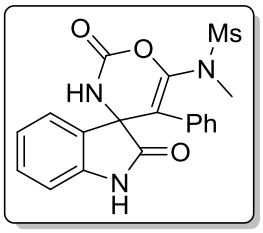
Yield: 47 mg, 85%; yellow solid; Mp. 129.7-130.9 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.55 (s, 1H), 8.88 (s, 1H), 7.57 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 7.4 Hz, 1H), 7.38 (t, J = 8.7 Hz, 4H), 7.26 – 7.22 (m, 1H), 7.08 (t, J = 7.5 Hz, 1H), 6.76 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 7.8 Hz, 1H), 2.82 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.2, 148.6, 144.7, 142.4, 141.8, 135.0, 131.9, 131.2, 130.9, 130.8, 130.1, 129.5, 128.1, 125.7, 123.1, 122.2, 112.3, 110.6, 65.3, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 1708, 1686, 1619, 1594, 1487, 1468, 1358, 1293, 1188, 1170, 1116, 1084, 1033, 1012, 998, 932, 888, 814, 794, 734, 703, 667, 630, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}BrN_3NaO_5S$ calcd for 576.0199, found 576.0210.

_N_-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_-methyl-4-nitrobenzenesulfonamide (3ao)



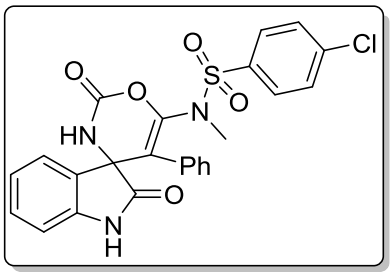
Yield: 44 mg, 88%; yellow solid; Mp. 168.7-169.5 ^{o}C; R_f= 0.2 (PE/EA = 1/1); ^{1}H NMR (300 MHz, DMSO) δ = 10.50 (s, 1H), 8.89 (s, 1H), 8.37 (d, J = 8.8 Hz, 2H), 7.95 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 7.3 Hz, 1H), 7.21 (dd, J = 14.8, 7.3 Hz, 2H), 7.16 – 7.04 (m, 3H), 6.83 (d, J = 6.9 Hz, 2H), 6.66 (d, J = 7.7 Hz, 1H), 2.91 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.7, 150.1, 148.0, 143.0, 141.4, 141.2, 130.5, 130.3, 129.3, 129.2, 129.1, 128.1, 127.7, 125.2, 124.4, 122.5, 113.2, 110.0, 65.0, 36.4. IR (reflection) $\tilde{\nu}$ = 1715, 1617, 1531, 1469, 1349, 1303, 1178, 1113, 1084, 1036, 1003, 906, 855, 797, 741, 699, 682, 644 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{24}H_{18}N_4NaO_7S$ calcd for 529.0788, found 529.0797.

***N*-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*-methylmethanesulfonamide (3ap)**



Yield: 35 mg, 87%; yellow solid; Mp. 147.9-149.1 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.49 (s, 1H), 8.87 (s, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.19 (ddd, J = 18.1, 15.3, 7.2 Hz, 4H), 7.06 (t, J = 7.5 Hz, 1H), 6.83 (d, J = 6.8 Hz, 2H), 6.65 (d, J = 7.7 Hz, 1H), 2.91 (s, 3H), 2.82 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.9, 142.7, 141.9, 131.3, 130.8, 129.8, 129.7, 128.6, 128.2, 125.6, 122.9, 112.3, 110.5, 65.4, 39.2, 36.5. IR (reflection) $\tilde{\nu}$ = 3349, 1710, 1679, 1614, 1468, 1444, 1348, 1298, 1189, 1164, 1115, 1094, 1035, 1002, 963, 936, 906, 889, 822, 798, 752, 697, 670, 641, 621, 607 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{19}H_{17}N_3NaO_5S$ calcd for 422.0781, found 422.0792.

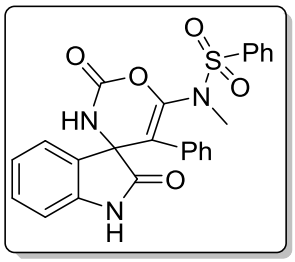
4-chloro-*N*-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*-methylbenzenesulfonamide (3aq)



Yield: 44 mg, 89%; yellow solid; Mp. 113.5-114.9 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.53 (s, 1H), 8.89 (s, 1H), 7.71 – 7.63 (m, 4H), 7.50 (d, J = 7.4 Hz, 1H), 7.25 – 7.18 (m, 2H), 7.15 (t, J = 7.4 Hz, 2H), 7.07 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 7.2 Hz, 2H), 6.67 (d, J = 7.8 Hz, 1H), 2.83 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.7, 142.0, 141.9, 139.1, 136.9, 131.2, 130.8, 130.0, 129.9, 129.8, 129.7, 128.6, 128.2, 125.7, 123.0, 113.5, 110.5, 65.5, 36.6. IR (reflection) $\tilde{\nu}$ = 1711, 1618, 1585, 1469, 1396, 1353, 1297, 1182, 1115, 1086, 1056, 1003, 906, 888, 828, 797, 762, 722, 700, 648, 630, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{24}H_{18}ClN_3NaO_5S$ calcd for 518.0548, found 518.0561.

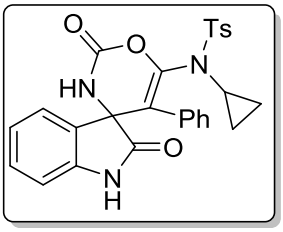
***N*-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*-methylbenzenesulfonamide (3ar)**

Yield: 41 mg, 90%; yellow solid; Mp. 143.5-144.8 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.51 (s, 1H), 8.86 (s, 1H), 7.71 (t, J = 7.4 Hz, 1H),



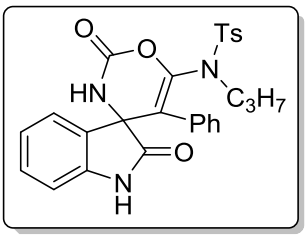
7.66 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 7.4 Hz, 1H), 7.21 (dd, *J* = 15.7, 7.6 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.3 Hz, 2H), 6.66 (d, *J* = 7.7 Hz, 1H), 2.79 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.7, 142.2, 141.9, 137.9, 134.1, 131.3, 130.8, 129.8, 129.7, 128.5, 128.2, 128.1, 125.7, 123.0, 113.3, 110.5, 65.5, 36.4. IR (reflection) $\tilde{\nu}$ = 1706, 1617, 1468, 1447, 1356, 1335, 1293, 1171, 1115, 1084, 1035, 998, 927, 905, 888, 798, 749, 726, 686, 633, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{24}H_{19}N_3NaO_5S$ calcd for 484.0938, found 484.0947.

_N_-cyclopropyl-_N_-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-4-methylbenzenesulfonamide (3as)



Yield: 44 mg, 88%; yellow solid; Mp. 165.7-166.9 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.50 (s, 1H), 8.86 (s, 1H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.41 (t, *J* = 9.8 Hz, 3H), 7.17 (tt, *J* = 8.5, 4.4 Hz, 4H), 7.07 (td, *J* = 7.6, 0.8 Hz, 1H), 6.94 – 6.78 (m, 2H), 6.65 (d, *J* = 7.6 Hz, 1H), 2.41 (s, 3H), 2.25 (d, *J* = 3.0 Hz, 1H), 0.61 (s, 2H), 0.36 (s, 2H). ^{13}C NMR (100 MHz, DMSO) δ = 175.6, 148.8, 144.9, 141.9, 141.7, 135.5, 131.1, 130.7, 130.1, 130.0, 129.7, 128.6, 128.5, 128.0, 125.6, 122.9, 113.2, 110.5, 65.7, 21.5, 7.9, 6.3. IR (reflection) $\tilde{\nu}$ = 3303, 1719, 1619, 1469, 1351, 1296, 1188, 1167, 1089, 1060, 907, 873, 815, 757, 700, 668, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{27}H_{23}N_3NaO_5S$ calcd for 524.1251, found 524.1261.

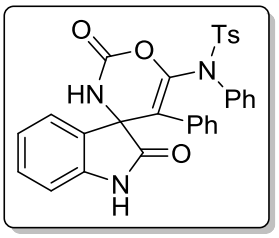
_N_-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-4-methyl-_N_-propylbenzenesulfonamide (3at)



Yield: 45 mg, 91%; yellow solid; Mp. 182.1-183.6 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.49 (s, 1H), 8.84 (s, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.41 (dd, *J* = 7.4, 3.3 Hz, 3H), 7.23 – 7.12 (m, 4H), 7.05 (td, *J* = 7.6, 0.9 Hz, 1H), 6.96 – 6.88 (m, 2H), 6.65 (d, *J* = 7.7 Hz, 1H), 2.95 – 2.82 (m, 2H), 2.41 (s, 3H), 1.40 – 1.29 (m, 2H), 0.55 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.5, 148.8, 144.6, 141.9, 140.4, 135.9, 130.9, 130.7, 130.1, 129.7, 128.5, 128.3, 127.9,

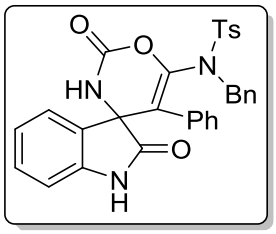
125.5, 122.9, 114.4, 110.5, 65.8, 50.0, 21.5, 20.7, 11.2. IR (reflection) $\tilde{\nu}$ = 3305, 1732, 1718, 1622, 1473, 1345, 1320, 1167, 1087, 1020, 1007, 972, 916, 806, 755, 701, 658 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{27}H_{25}N_3NaO_5S$ calcd for 526.1407, found 526.1417.

_N_-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-4-methyl-_N_-phenylbenzenesulfonamide (3au)



Yield: 45 mg, 85%; yellow solid; Mp. 140.7-142.0 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 10.47 (s, 1H), 8.96 (s, 1H), 7.48 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 7.4 Hz, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.25 – 7.17 (m, 5H), 7.12 (t, J = 7.6 Hz, 2H), 7.03 (td, J = 7.6, 0.6 Hz, 1H), 6.80 – 6.75 (m, 2H), 6.66 (dd, J = 11.4, 7.6 Hz, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.1, 148.7, 144.9, 142.2, 141.9, 138.5, 135.4, 130.8, 130.7, 129.9, 129.8, 129.6, 129.5, 128.7, 128.5, 128.4, 128.1, 126.7, 125.4, 123.0, 113.9, 110.6, 65.5, 21.5. IR (reflection) $\tilde{\nu}$ = 1692, 1619, 1594, 1490, 1469, 1353, 1266, 1167, 1087, 1059, 939, 901, 786, 748, 693, 664, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{30}H_{23}N_3NaO_5S$ calcd for 560.1251, found 560.1266.

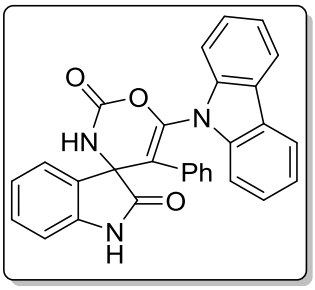
_N_-benzyl-_N_-(2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-4-methylbenzenesulfonamide (3av)



Yield: 48 mg, 87%; yellow solid; Mp. 131.7-133.1 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (500 MHz, DMSO) δ = 10.38 (d, J = 6.2 Hz, 1H), 8.82 (dd, J = 9.4, 3.7 Hz, 1H), 7.65 (d, J = 6.2 Hz, 2H), 7.46 – 7.37 (m, 3H), 7.36 (d, J = 7.1 Hz, 1H), 7.29 (t, J = 7.3 Hz, 2H), 7.15 (dd, J = 16.9, 8.1 Hz, 2H), 6.97 (t, J = 7.2 Hz, 3H), 6.92 (d, J = 5.2 Hz, 2H), 6.58 (d, J = 7.1 Hz, 1H), 6.31 (s, 2H), 4.22 (d, J = 13.6 Hz, 1H), 4.06 (d, J = 13.6 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 174.9, 148.7, 144.8, 141.7, 139.5, 135.7, 134.1, 130.7, 130.4, 130.2, 130.1, 130.0, 129.9, 129.8, 128.9, 128.6, 128.5, 128.3, 127.5, 125.3, 122.7, 114.8, 110.3, 65.6, 51.6, 21.5. IR (reflection) $\tilde{\nu}$ = 3281, 1734, 1654, 1618, 1559, 1542, 1507, 1472, 1457, 1349, 1164, 1089, 1041,

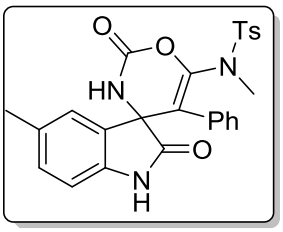
899, 875, 815, 745, 699, 662, 612 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{31}H_{25}N_3NaO_5S$ calcd for 574.1407, found 574.1423.

6'-(9*H*-carbazol-9-yl)-5'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (3aw)



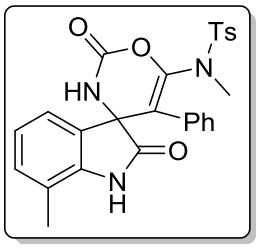
Yield: 37 mg, 82%; yellow solid; Mp. 158.7-159.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (500 MHz, DMSO) δ = 10.78 (s, 1H), 9.13 (s, 1H), 8.07 (t, J = 7.3 Hz, 2H), 7.87 (d, J = 7.3 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H), 7.53 (dd, J = 16.9, 8.4 Hz, 2H), 7.47 (t, J = 7.7 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.24 (dd, J = 14.7, 7.5 Hz, 2H), 7.09 (t, J = 7.5 Hz, 1H), 6.87 – 6.78 (m, 5H), 6.75 (d, J = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, DMSO) δ = 180.9, 153.9, 147.0, 144.4, 143.5, 135.7, 134.2, 133.4, 133.2, 132.9, 131.8, 131.1, 128.1, 127.9, 126.4, 125.7, 118.8, 115.9, 115.4, 115.1, 70.7. IR (reflection) $\tilde{\nu}$ = 1707, 1666, 1617, 1468, 1444, 1327, 1301, 1192, 1167, 1100, 1039, 1017, 975, 927, 814, 792, 750, 723, 697, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{29}H_{19}N_3NaO_3$ calcd for 480.1319, found 480.1326.

***N*,4-dimethyl-*N*-(5-methyl-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)benzenesulfonamide (3ba)**



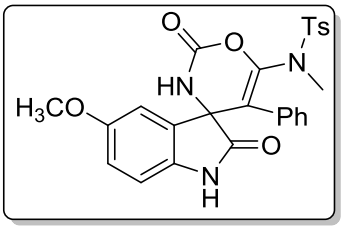
Yield: 41 mg, 85%; yellow solid; Mp. 153.9-154.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (500 MHz, DMSO) δ = 10.41 (s, 1H), 8.85 (s, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.31 (s, 1H), 7.21 (t, J = 7.3 Hz, 1H), 7.16 (t, J = 7.4 Hz, 2H), 7.03 (d, J = 7.9 Hz, 1H), 6.87 (d, J = 7.2 Hz, 2H), 6.57 (d, J = 7.9 Hz, 1H), 2.77 (s, 3H), 2.39 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.8, 144.6, 142.3, 139.5, 135.1, 132.0, 131.5, 131.0, 130.1, 129.9, 129.8, 128.5, 128.3, 128.2, 126.1, 113.4, 110.3, 65.6, 36.3, 21.5, 21.1. IR (reflection) $\tilde{\nu}$ = 1735, 1625, 1597, 1493, 1444, 1349, 1305, 1250, 1190, 1172, 1157, 1084, 1051, 1006, 913, 881, 814, 761, 699, 656, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_5S$ calcd for 512.1250, found 512.1255.

***N*,4-dimethyl-*N*-(7-methyl-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)benzenesulfonamide (3ca)**



Yield: 42 mg, 86%; yellow solid; Mp. 217.9-219.2 ^{o}C; R_f= 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.57 (s, 1H), 8.85 (s, 1H), 7.53 (d, J = 7.8 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.2 Hz, 1H), 7.21 (t, J = 7.0 Hz, 1H), 7.15 (t, J = 7.5 Hz, 2H), 7.05 (d, J = 7.6 Hz, 1H), 7.00 (t, J = 7.4 Hz, 1H), 6.86 (d, J = 7.6 Hz, 2H), 2.77 (s, 3H), 2.39 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.7, 148.8, 144.6, 142.3, 140.6, 139.9, 135.1, 131.9, 131.5, 130.1, 129.8, 129.6, 128.5, 128.2, 128.1, 122.9, 119.8, 113.4, 65.7, 36.3, 21.5, 16.5. IR (reflection) $\tilde{\nu}$ = 1733, 1707, 1629, 1463, 1362, 1106, 996, 839, 803, 744, 700, 665, 637, 619 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_5S$ calcd for 512.1250, found 512.1257.

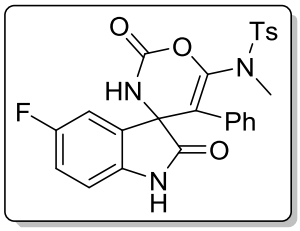
***N*-(5-methoxy-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*,4-dimethylbenzenesulfonamide (3da)**



Yield: 42 mg, 84%; yellow solid; Mp. 219.9-220.9 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.36 (s, 1H), 8.89 (d, J = 6.7 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.18 (ddd, J = 25.0, 16.0, 8.9 Hz, 4H), 6.93 – 6.85 (m, 2H), 6.83 – 6.77 (m, 1H), 6.61 (dd, J = 8.4, 4.3 Hz, 1H), 3.74 (s, 3H), 2.78 (d, J = 1.6 Hz, 3H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 155.9, 148.8, 144.6, 142.3, 135.1, 131.5, 131.0, 130.1, 129.8, 128.5, 128.2, 115.8, 113.2, 112.1, 111.1, 65.9, 56.1, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 3297, 2941, 1732, 1598, 1491, 1441, 1346, 1299, 1268, 1200, 1159, 1084, 1050, 1006, 969, 913, 880, 814, 760, 699, 657 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_6S$ calcd for 528.1199, found 528.1203.

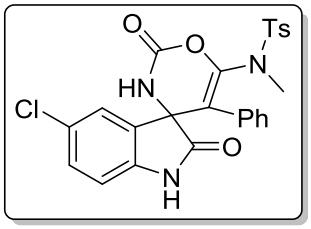
***N*-(5-fluoro-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-*N*,4-dimethylbenzenesulfonamide (3ea)**

Yield: 42 mg, 87%; yellow solid; Mp. 233.9-234.5 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.54 (s, 1H), 8.88 (s, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.45 (dd, J = 7.7, 2.0 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.25 – 7.15 (m, 3H), 7.05 (td,



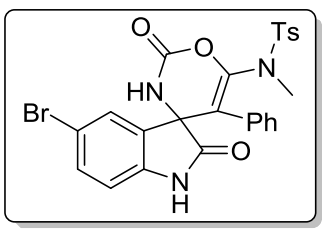
J = 9.3, 2.7 Hz, 1H), 6.95 – 6.88 (m, 2H), 6.66 (dd, *J* = 8.4, 4.1 Hz, 1H), 2.79 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.5, 159.9, 157.6, 148.7, 144.6, 142.5, 138.3, 138.2, 135.1, 131.4, 131.3, 130.1, 129.8, 128.6, 128.3, 128.2, 117.3, 117.1, 113.6, 113.4, 112.7, 111.5, 111.4, 65.9, 36.3, 21.4. IR (reflection) $\tilde{\nu}$ = 3177, 3072, 2943, 2882, 2834, 1710, 1676, 1611, 1594, 1480, 1374, 1292, 1271, 1224, 1189, 1178, 1113, 1083, 1038, 1023, 909, 863, 847, 816, 797, 762, 726, 705, 669, 624, 616 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{20}FN_3NaO_5S$ calcd for 516.0999, found 516.1008.

_N_-(5-chloro-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3fa)



Yield: 44 mg, 87%; yellow solid; Mp. 223.5-224.3 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.66 (s, 1H), 8.86 (s, 1H), 7.61 (d, *J* = 1.9 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.26 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.20 (dt, *J* = 14.2, 6.9 Hz, 3H), 6.88 (d, *J* = 6.8 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 1H), 2.78 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.2, 148.6, 144.6, 142.5, 140.9, 135.0, 131.7, 131.2, 130.6, 130.1, 129.8, 128.6, 128.3, 128.2, 126.8, 125.9, 112.5, 112.0, 65.6, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 3166, 2864, 2239, 1711, 1674, 1607, 1473, 1448, 1373, 1295, 1215, 1178, 1102, 1079, 1036, 1018, 914, 874, 845, 820, 799, 765, 725, 701, 667, 622, 613 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{20}ClN_3NaO_5S$ calcd for 532.0704, found 532.0710.

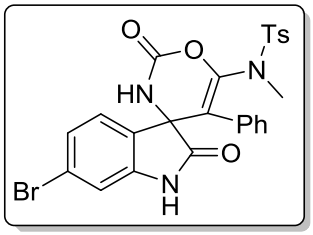
_N_-(5-bromo-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ga)



Yield: 47 mg, 86%; yellow solid; Mp. 225.6-226.8 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (300 MHz, DMSO) δ = 10.65 (s, 1H), 8.85 (s, 1H), 7.72 (d, *J* = 1.9 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.38 (m, 1H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.24 – 7.15 (m, 3H), 6.93 – 6.86 (m, 2H), 6.63 (d, *J* = 8.3 Hz, 1H), 2.79 (s, 3H), 2.39 (s,

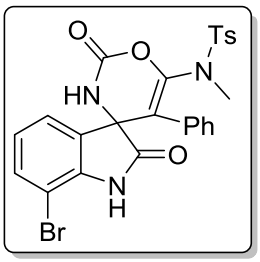
3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.1, 148.6, 144.6, 142.6, 141.3, 135.1, 133.5, 132.1, 131.2, 130.4, 130.1, 129.8, 128.6, 128.3, 128.2, 114.4, 112.6, 112.5, 65.6, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 1712, 1674, 1610, 1469, 1371, 1297, 1170, 1085, 1016, 933, 902, 867, 816, 765, 724, 703, 668, 622, 613 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{25}H_{20}BrN_3NaO_5S$ calcd for 576.0199, found 576.0205.

_N_-(6-bromo-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ha)



Yield: 47 mg, 86%; yellow solid; Mp. 137.2-138.5 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.69 (s, 1H), 8.86 (s, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.26 (dd, J = 8.0, 1.5 Hz, 1H), 7.24 – 7.16 (m, 3H), 6.88 (d, J = 7.0 Hz, 2H), 6.83 (d, J = 1.4 Hz, 1H), 2.77 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.6, 144.6, 143.6, 142.5, 135.0, 131.2, 130.1, 129.8, 129.1, 128.6, 128.3, 128.2, 127.6, 125.7, 123.3, 113.3, 112.6, 65.2, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 3344, 1715, 1606, 1477, 1445, 1362, 1291, 1252, 1187, 1170, 1124, 1085, 1064, 1032, 1004, 913, 896, 867, 813, 762, 723, 698, 668, 622, 613 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}BrN_3NaO_5S$ calcd for 576.0199, found 576.0204.

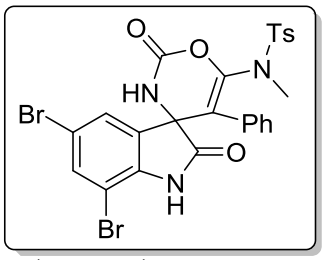
_N_-(7-bromo-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ia)



Yield: 46 mg, 84%; yellow solid; Mp. 218.9-219.7 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 10.87 (s, 1H), 8.92 (s, 1H), 7.53 (t, J = 6.9 Hz, 3H), 7.43 (d, J = 8.1 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.18 (t, J = 7.3 Hz, 2H), 7.04 (t, J = 7.8 Hz, 1H), 6.88 (d, J = 7.2 Hz, 2H), 2.78 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.3, 148.6, 144.6, 142.5, 141.5, 135.0, 133.6, 131.6, 131.1, 130.1, 129.8, 128.7, 128.3, 128.2, 124.8, 124.7, 112.8, 102.8, 66.4, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 3335, 3111, 1749, 1719, 1620, 1597, 1471, 1444, 1345, 1305, 1257, 1184, 1158, 1134, 1089, 1059, 1007, 964, 921, 867, 803, 777,

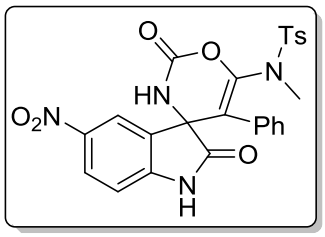
741, 717, 699, 658, 618 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}BrN_3NaO_5S$ calcd for 576.0199, found 576.0206.

_N_-(5,7-dibromo-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3ja)



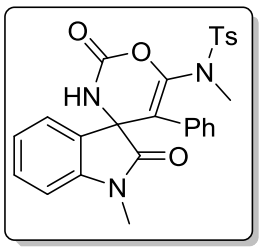
Yield: 52 mg, 83%; yellow solid; Mp. 198.2-199.1 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (300 MHz, DMSO) δ = 11.03 (s, 1H), 8.85 (s, 1H), 7.80 (d, J = 1.5 Hz, 1H), 7.68 (d, J = 1.7 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.22 (q, J = 5.7 Hz, 3H), 6.93 – 6.84 (m, 2H), 2.79 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (75 MHz, DMSO) δ = 174.7, 147.8, 144.1, 142.2, 140.6, 134.8, 134.5, 132.6, 130.5, 129.6, 129.3, 128.3, 127.9, 127.7, 127.4, 114.4, 111.4, 103.1, 65.9, 35.7, 20.9. IR (reflection) $\tilde{\nu}$ = 3078, 1711, 1683, 1610, 1595, 1569, 1493, 1453, 1356, 1290, 1212, 1188, 1171, 1106, 1082, 1037, 1020, 932, 903, 875, 856, 812, 801, 761, 726, 700, 671, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{19}Br_2N_3NaO_5S$ calcd for 655.9283, found 655.9291.

_N_,4-dimethyl-N-(5-nitro-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)benzenesulfonamide (3ka)



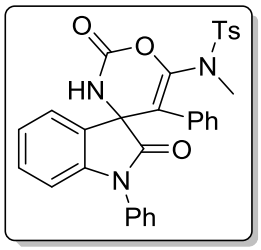
Yield: 42 mg, 82%; yellow solid; Mp. 174.2-175.0 °C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 11.27 (s, 1H), 8.91 (s, 1H), 8.48 (s, 1H), 8.16 (dd, J = 8.7, 2.3 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.19 (ddd, J = 15.9, 7.7, 2.2 Hz, 3H), 6.90 (d, J = 7.0 Hz, 2H), 6.86 (d, J = 8.7 Hz, 1H), 2.82 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 176.1, 148.5, 148.3, 144.7, 143.2, 142.7, 134.9, 130.9, 130.7, 130.1, 129.8, 128.7, 128.4, 128.2, 127.8, 121.8, 111.8, 110.8, 65.4, 36.2, 21.5. IR (reflection) $\tilde{\nu}$ = 1712, 1666, 1596, 1521, 1461, 1365, 1336, 1294, 1266, 1162, 1122, 1088, 1054, 1018, 938, 890, 874, 813, 748, 728, 705, 666, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{25}H_{20}N_4NaO_7S$ calcd for 543.0945, found 543.1503.

_N_,4-dimethyl-_N_-(1-methyl-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)benzenesulfonamide (3la)



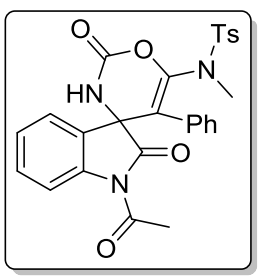
Yield: 41 mg, 84%; yellow solid; Mp. 168.9-169.7 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 8.79 (s, 1H), 7.53 (dd, J = 11.1, 8.0 Hz, 3H), 7.37 (d, J = 8.1 Hz, 2H), 7.30 (d, J = 7.7 Hz, 1H), 7.15 (ddd, J = 19.6, 9.9, 4.7 Hz, 4H), 6.86 (d, J = 7.8 Hz, 1H), 6.81 (d, J = 7.1 Hz, 2H), 2.94 (s, 3H), 2.78 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 173.8, 148.8, 144.6, 143.3, 142.4, 135.1, 131.2, 130.9, 130.1, 129.6, 129.1, 128.5, 128.2, 128.1, 125.3, 123.6, 113.1, 109.4, 65.2, 36.3, 26.7, 21.5. IR (reflection) $\tilde{\nu}$ = 1729, 1705, 1608, 1492, 1470, 1350, 1297, 1188, 1171, 1086, 1061, 1028, 993, 907, 815, 794, 749, 699, 670, 613 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{26}H_{23}N_3NaO_5S$ calcd for 512.1251, found 512.1255.

_N_-(2,2'-dioxo-1,5'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_, 4-dimethylbenzenesulfonamide (3ma)



Yield: 46 mg, 85%; yellow solid; Mp. 137.6-138.5 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 9.01 (s, 1H), 7.68 (d, J = 7.0 Hz, 1H), 7.59 – 7.51 (m, 4H), 7.45 (t, J = 7.4 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.30 – 7.18 (m, 5H), 6.97 (d, J = 7.6 Hz, 2H), 6.87 (d, J = 7.3 Hz, 2H), 6.50 (d, J = 7.6 Hz, 1H), 2.82 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 173.2, 148.7, 144.7, 143.2, 142.3, 135.0, 133.9, 131.0, 130.3, 130.2, 129.9, 129.1, 129.0, 128.7, 128.3, 128.2, 126.6, 125.8, 124.3, 113.2, 109.7, 65.5, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ =3063, 1712, 1685, 1596, 1498, 1464, 1364, 1294, 1245, 1221, 1187, 1167, 1113, 1084, 1046, 1007, 958, 930, 884, 814, 750, 700, 668, 645, 623, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{31}H_{25}N_3NaO_5S$ calcd for 574.1407, found 574.1413.

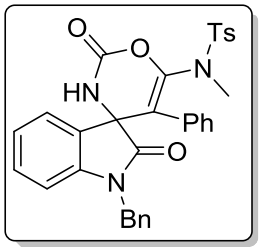
_N_-(1-acetyl-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3na)



Yield: 44 mg, 86%; yellow solid; Mp. 157.2-158.3 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 8.90 (s, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.42 – 7.34 (m, 4H), 7.21 (t, J = 7.3 Hz, 1H), 7.16 (t, J = 7.4 Hz, 2H), 6.80 (d, J = 7.2 Hz, 2H), 2.81 (s, 3H), 2.48 (s,

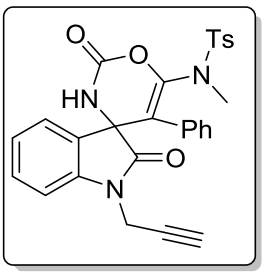
3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 175.4, 170.2, 148.2, 144.7, 142.4, 139.5, 134.9, 131.1, 130.6, 130.2, 129.7, 128.9, 128.4, 128.2, 126.5, 125.7, 116.2, 112.6, 65.9, 36.3, 26.3, 21.5. IR (reflection) $\tilde{\nu}$ = 1734, 1706, 1683, 1656, 1595, 1491, 1459, 1443, 1414, 1371, 1340, 1280, 1171, 1084, 1060, 1039, 1021, 1007, 956, 919, 860, 810, 794, 759, 705, 675, 664, 622, 612 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{27}H_{23}N_3NaO_6S$ calcd for 540.1199, found 540.1208.

_N_-(1-benzyl-2,2'-dioxo-5'-phenyl-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3oa)



Yield: 47 mg, 84%; yellow solid; Mp. 120.6-121.4 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 9.01 (s, 1H), 7.62 (d, J = 7.3 Hz, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.30 (t, J = 7.5 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.22 – 7.09 (m, 6H), 6.81 (d, J = 7.5 Hz, 2H), 6.78 (d, J = 7.1 Hz, 2H), 6.65 (d, J = 7.8 Hz, 1H), 4.86 (d, J = 16.1 Hz, 1H), 4.61 (d, J = 16.1 Hz, 1H), 2.79 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 173.8, 148.6, 144.6, 142.6, 142.5, 135.5, 135.0, 131.0, 130.9, 130.2, 130.1, 129.3, 128.9, 128.7, 128.3, 128.2, 127.6, 127.1, 125.5, 123.8, 112.9, 110.2, 65.3, 43.6, 36.3, 21.5. IR (reflection) $\tilde{\nu}$ = 3061, 1703, 1606, 1494, 1483, 1468, 1354, 1305, 1244, 1172, 1107, 1086, 1045, 1029, 1018, 975, 926, 888, 815, 747, 717, 698, 671, 637, 623, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{32}H_{27}N_3NaO_5S$ calcd for 588.1563, found 588.1569.

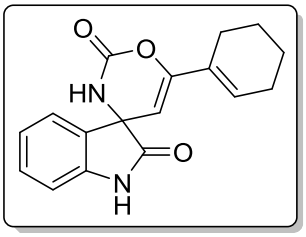
_N_-(2,2'-dioxo-5'-phenyl-1-(prop-2-yn-1-yl)-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)-_N_,4-dimethylbenzenesulfonamide (3pa)



Yield: 44 mg, 87%; yellow solid; Mp. 140.7-142.0 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (500 MHz, DMSO) δ = 8.96 (d, J = 7.7 Hz, 1H), 7.58 (d, J = 7.2 Hz, 2H), 7.52 (d, J = 7.3 Hz, 1H), 7.38 (d, J = 7.7 Hz, 2H), 7.32 (t, J = 7.7 Hz, 1H), 7.19 – 7.09 (m, 4H), 6.96 (d, J = 7.7 Hz, 1H), 6.85 (d, J = 7.0 Hz, 2H), 4.43 (q, J = 17.9 Hz, 2H), 3.23 (d, J = 1.0 Hz, 1H), 2.79 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, DMSO) δ = 173.3, 148.8, 144.6, 142.6, 141.6, 135.1, 131.1, 130.7, 130.1, 129.5,

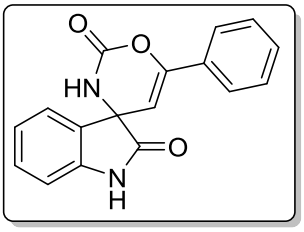
128.8, 128.5, 128.2, 125.6, 123.9, 113.1, 110.0, 77.3, 75.1, 65.0, 36.3, 29.6, 21.5. IR (reflection) $\tilde{\nu}$ = 3284, 3058, 2124, 1707, 1683, 1606, 1483, 1468, 1444, 1427, 1350, 1294, 1242, 1170, 1106, 1086, 1050, 1018, 979, 922, 894, 813, 795, 748, 718, 701, 668, 622, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{28}H_{23}N_3NaO_5S$ calcd for 536.1250, found 536.1254.

6'-(cyclohex-1-en-1-yl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5aa)



Yield: 22 mg, 74%; yellow solid; Mp. 194.5-196.1 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (600 MHz, DMSO) δ = 10.56 (s, 1H), 8.39 (s, 1H), 7.27 (dd, J = 13.6, 7.3 Hz, 2H), 7.02 (t, J = 7.5 Hz, 1H), 6.86 (d, J = 7.7 Hz, 1H), 6.33 (s, 1H), 4.97 (s, 1H), 2.15 (d, J = 3.1 Hz, 2H), 1.97 (dd, J = 17.9, 11.6 Hz, 2H), 1.57 (dd, J = 11.8, 5.8 Hz, 2H), 1.53 (dd, J = 11.9, 6.5 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) δ = 177.2, 150.5, 149.7, 142.1, 131.9, 130.6, 128.5, 127.6, 125.5, 123.2, 110.9, 96.4, 62.8, 25.5, 24.1, 22.5, 22.2. IR (reflection) $\tilde{\nu}$ = 3276, 2930, 2861, 2247, 1721, 1620, 1472, 1394, 1350, 1326, 1281, 1243, 1188, 1136, 1105, 1060, 898, 752, 672, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{17}H_{16}N_2NaO_3$ calcd for 319.1053, found 319.1054.

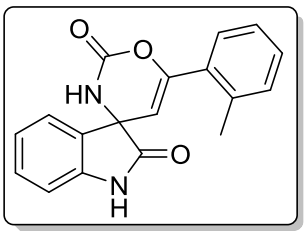
6'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ab)



Yield: 22 mg, 76%; yellow solid; Mp. 161.9-162.8 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 10.63 (s, 1H), 8.57 (s, 1H), 7.71 – 7.67 (m, 2H), 7.46 – 7.41 (m, 3H), 7.35 (d, J = 7.4 Hz, 1H), 7.31 (td, J = 7.7, 1.1 Hz, 1H), 7.08 – 7.03 (m, 1H), 6.91 (d, J = 7.7 Hz, 1H), 5.83 (d, J = 1.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 176.7, 149.4, 141.8, 131.6, 131.5, 130.4, 130.0, 129.1, 125.4, 124.8, 122.9, 118.4, 110.7, 97.6, 62.7. IR (reflection) $\tilde{\nu}$ = 2974, 1716, 1622, 1472, 1348, 1275, 1189, 1134, 1058, 792, 753, 688, 652, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{17}H_{12}N_2NaO_3$ calcd for 315.0740, found 315.0741.

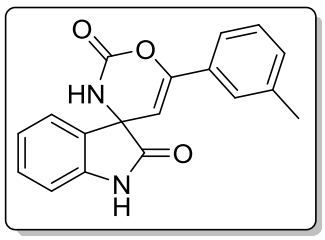
6'-(*o*-tolyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ac)

Yield: 23 mg, 77%; yellow solid; Mp. 177.2-178.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (700 MHz, DMSO) δ = 10.60 (s, 1H), 8.53 (s, 1H), 7.41 (d, J = 7.3 Hz, 1H),



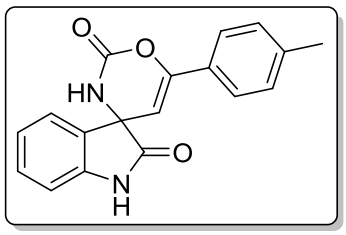
7.34 (dd, *J* = 9.3, 7.8 Hz, 2H), 7.29 (dd, *J* = 16.8, 7.9 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 5.20 (d, *J* = 1.5 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (175 MHz, DMSO) δ = 176.6, 150.9, 149.5, 141.8, 136.4, 132.6, 131.5, 131.1, 130.4, 130.0, 129.0, 126.4, 125.3, 122.9, 110.7, 101.4, 62.8, 20.3. IR (reflection) $\tilde{\nu}$ = 3300, 2246, 1723, 1620, 1472, 1350, 1326, 1292, 1261, 1198, 1135, 1056, 937, 898, 753, 681, 652 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_3$ calcd for 329.0896, found 329.0898.

6'-(*m*-tolyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ad)



Yield: 24 mg, 78%; yellow solid; Mp. 129.2-130.1 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (700 MHz, DMSO) δ = 10.64 (s, 1H), 8.56 (s, 1H), 7.52 (s, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.31 (td, *J* = 7.6, 3.4 Hz, 2H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.80 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (175 MHz, DMSO) δ = 176.7, 149.4, 141.8, 138.4, 131.6, 131.5, 130.7, 130.4, 129.0, 125.4, 122.9, 121.9, 120.8, 119.0, 110.7, 97.5, 62.7, 21.4. IR (reflection) $\tilde{\nu}$ = 1725, 1620, 1471, 1325, 1280, 1199, 1134, 1060, 895, 786, 744, 682, 648 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_3$ calcd for 329.0897, found 329.0896.

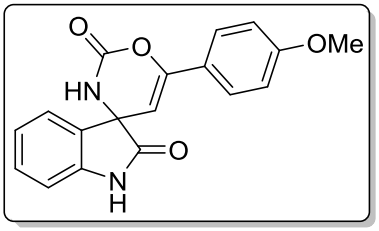
6'-(*p*-tolyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ae)



Yield: 21 mg, 71%; yellow solid; Mp. 183.4-184.8 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.61 (s, 1H), 8.54 (s, 1H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.32 (dd, *J* = 15.6, 7.6 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 7.7 Hz, 1H), 5.74 (d, *J* = 1.2 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 176.8, 149.5, 149.4, 141.8, 139.7, 131.5, 130.4, 129.7, 128.9, 125.4, 124.8, 122.9, 110.7, 96.7, 62.7, 21.3. IR (reflection) $\tilde{\nu}$ = 3291, 1722, 1619, 1514, 1472, 1350, 1326, 1273, 1227, 1185, 1135, 1105, 1057, 1019, 936, 899,

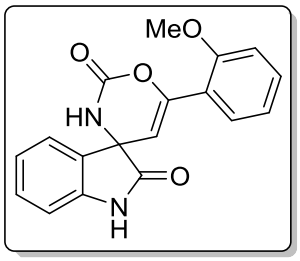
824, 791, 752, 679, 651, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_3$ calcd for 329.0896, found 329.0900.

6'-(4-methoxyphenyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5af)



Yield: 22 mg, 65%; yellow solid; Mp. 143.5-144.3 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 10.61 (s, 1H), 8.53 (s, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.32 (dd, J = 14.9, 7.4 Hz, 2H), 7.05 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 7.7 Hz, 1H), 5.65 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 176.9, 160.7, 149.5, 149.3, 141.8, 131.6, 130.4, 126.4, 125.3, 124.0, 122.9, 114.5, 110.7, 95.6, 62.7, 55.7. IR (reflection) $\tilde{\nu}$ = 3282, 3106, 2997, 2974, 2936, 2838, 1728, 1696, 1617, 1575, 1514, 1471, 1438, 1421, 1323, 1275, 1254, 1227, 1179, 1153, 1107, 1060, 1032, 979, 958, 942, 902, 875, 836, 820, 800, 764, 678, 641, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_4$ calcd for 345.0845, found 345.0850.

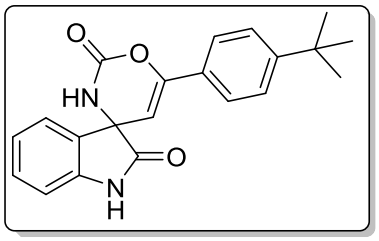
6'-(2-methoxyphenyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ag)



Yield: 20 mg, 62%; yellow solid; Mp. 170.4-171.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (600 MHz, DMSO) δ = 10.75 (s, 1H), 8.67 (d, J = 1.4 Hz, 1H), 7.75 (dd, J = 7.8, 1.7 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.47 (d, J = 7.3 Hz, 1H), 7.44 (td, J = 7.7, 1.1 Hz, 1H), 7.25 (d, J = 8.1 Hz, 1H), 7.21 – 7.16 (m, 2H), 7.03 (d, J = 7.8 Hz, 1H), 5.87 (d, J = 1.7 Hz, 1H), 3.91 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ = 177.1, 157.6, 149.8, 146.9, 142.0, 131.9, 131.5, 130.7, 127.8, 125.6, 123.3, 121.2, 120.1, 112.7, 111.0, 102.2, 63.0, 56.4. IR (reflection) $\tilde{\nu}$ = 3292, 2844, 1723, 1620, 1580, 1495, 1470, 1435, 1354, 1324, 1297, 1249, 1225, 1183, 1128, 1104, 1062, 1048, 1020, 938, 899, 827, 755, 681, 618 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_4$ calcd for 345.0845, found 345.0848.

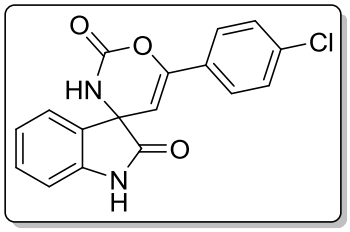
6'-(4-(*tert*-butyl)phenyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ah)

Yield: 24 mg, 70%; yellow solid; Mp. 164.2-165.3 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 10.61 (s, 1H), 8.54 (s, 1H), 7.61 (d, J = 8.5 Hz, 2H),



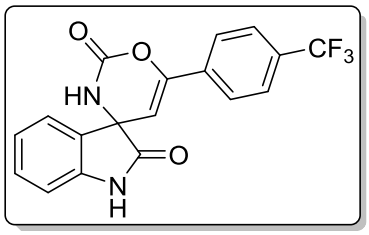
7.45 (d, *J* = 8.5 Hz, 2H), 7.36 – 7.27 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 5.75 (s, 1H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, DMSO) δ = 176.8, 152.8, 149.5, 141.8, 131.6, 130.4, 128.9, 125.9, 125.3, 124.7, 122.9, 110.7, 96.9, 62.7, 34.9, 31.4. IR (reflection) $\tilde{\nu}$ = 3360, 2964, 2906, 2870, 1724, 1620, 1516, 1472, 1349, 1326, 1276, 1186, 1135, 1114, 1058, 1016, 936, 899, 842, 793, 752, 675, 652, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{21}H_{20}N_2NaO_3$ calcd for 371.1366, found 371.1366.

6'-(4-chlorophenyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5ai)



Yield: 23 mg, 72%; yellow solid; Mp. 185.6-186.3 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.65 (s, 1H), 8.60 (s, 1H), 7.71 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 5.92 (d, *J* = 1.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 176.6, 149.2, 148.4, 141.8, 134.6, 131.3, 130.5, 129.2, 126.7, 125.4, 122.9, 110.7, 98.4, 62.8. IR (reflection) $\tilde{\nu}$ = 2248, 1723, 1620, 1492, 1472, 1348, 1273, 1190, 1134, 1093, 1056, 1013, 936, 898, 836, 793, 752, 708, 673, 652, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{17}H_{11}ClN_2NaO_3$ calcd for 349.0350, found 349.0352.

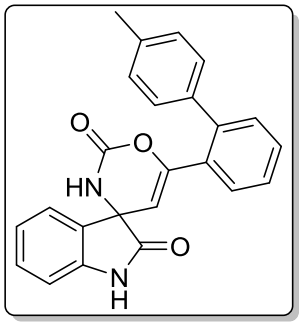
6'-(4-(trifluoromethyl)phenyl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5aj)



Yield: 25 mg, 69%; yellow solid; Mp. 156.8-157.9 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.68 (s, 1H), 8.65 (s, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.7 Hz, 1H), 7.06 (t, *J* = 7.3 Hz, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.10 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 176.4, 149.0, 148.1, 141.9, 135.5, 131.2, 130.6, 126.1, 125.6, 125.5, 123.0, 118.3, 110.8, 100.2, 62.8, 28.8. IR (reflection) $\tilde{\nu}$ = 3321, 2970, 2935, 1721, 1620, 1472, 1414, 1349, 1323, 1279, 1227, 1190, 1130, 1068, 1014, 900,

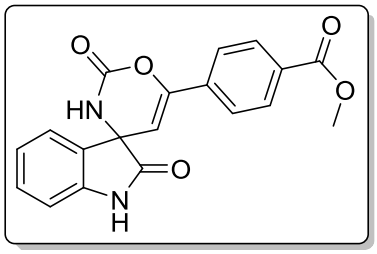
851, 789, 752, 686, 652, 614 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{11}F_3N_2NaO_3$ calcd for 383.0614, found 383.0617.

6'-(4'-methyl-[1,1'-biphenyl]-2-yl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dion e (5ak)



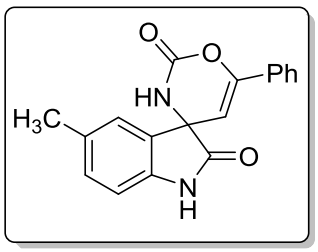
Yield: 28 mg, 73%; yellow solid; Mp. 175.7-176.6 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 10.49 (s, 1H), 8.36 (s, 1H), 7.52 – 7.47 (m, 2H), 7.45 – 7.42 (m, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.33 (s, 1H), 7.31 (s, 1H), 7.23 (d, J = 8.0 Hz, 3H), 7.10 (d, *J* = 7.1 Hz, 1H), 7.03 (d, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 4.76 (d, *J* = 1.6 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 176.3, 150.8, 149.3, 141.6, 140.7, 137.8, 136.8, 131.5, 131.2, 130.7, 130.3, 129.6, 129.4, 128.7, 127.7, 125.3, 122.6, 110.5, 101.9, 62.7, 21.2. IR (reflection) $\tilde{v}$ = 3362, 2245, 1725, 1620, 1472, 1326, 1197, 1134, 1060, 937, 897, 821, 801, 753, 679, 648 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{24}H_{18}N_2NaO_3$ calcd for 405.1209, found 405.1212.

methyl 4-(2,2'-dioxo-2',3'-dihydrospiro[indoline-3,4'-[1,3]oxazin]-6'-yl)benzoate (5al)



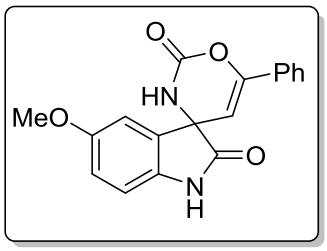
Yield: 23 mg, 68%; yellow solid; Mp. 189.1-190.2 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (600 MHz, DMSO) δ = 10.99 (s, 1H), 8.94 (d, *J* = 1.0 Hz, 1H), 8.29 (d, *J* = 8.6 Hz, 2H), 8.13 (d, *J* = 8.6 Hz, 2H), 7.66 (d, *J* = 7.3 Hz, 1H), 7.61 (td, *J* = 7.8, 1.1 Hz, 1H), 7.34 (td, *J* = 7.6, 0.7 Hz, 1H), 7.20 (d, *J* = 7.8 Hz, 1H), 6.37 (d, *J* = 1.6 Hz, 1H), 4.15 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ = 176.7, 166.4, 149.4, 148.7, 142.1, 136.2, 131.5, 130.9, 130.8, 130.2, 125.8, 125.4, 123.3, 111.0, 100.4, 63.1, 53.0. IR (reflection) $\tilde{v}$ = 3306, 2981, 1716, 1620, 1472, 1439, 1350, 1325, 1278, 1228, 1189, 1134, 1057, 1017, 959, 899, 863, 754, 694, 653, 613 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{19}H_{14}N_2NaO_5$ calcd for 373.0794, found 373.0798.

5-methyl-6'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5bb)



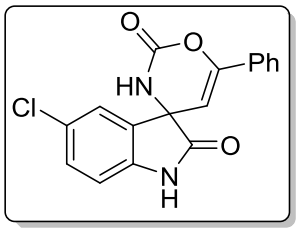
Yield: 23 mg, 78%; yellow solid; Mp. 180.2-181.0 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (700 MHz, DMSO) δ = 10.54 (s, 1H), 8.56 (s, 1H), 7.70 – 7.67 (m, 2H), 7.43 (q, J = 5.5 Hz, 3H), 7.18 (s, 1H), 7.11 (d, J = 7.8 Hz, 1H), 6.79 (d, J = 7.9 Hz, 1H), 5.82 (d, J = 1.1 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (175 MHz, DMSO) δ = 176.7, 149.4, 149.2, 139.3, 132.0, 131.6, 131.5, 130.6, 130.0, 129.1, 125.9, 124.8, 110.5, 97.8, 62.8, 20.9. IR (reflection) $\tilde{\nu}$ = 3352, 2923, 1720, 1626, 1494, 1349, 1274, 1191, 1134, 1057, 1029, 886, 816, 755, 741, 694, 651, 615 cm^{-1}. HRMS (ESI) $[M+H]^+$ (m/z) $C_{18}H_{14}N_2NaO_3$ calcd for 329.0896, found 329.0900.

5-methoxy-6'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5db)



Yield: 24 mg, 77%; yellow solid; Mp. 175.6-176.5 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (600 MHz, DMSO) δ = 10.76 (s, 1H), 8.87 (s, 1H), 7.98 (dd, J = 7.7, 1.7 Hz, 2H), 7.74 – 7.70 (m, 3H), 7.29 (d, J = 2.4 Hz, 1H), 7.16 (dd, J = 8.5, 2.6 Hz, 1H), 7.11 (d, J = 8.5 Hz, 1H), 6.11 (d, J = 1.5 Hz, 1H), 4.00 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ = 177.0, 156.3, 149.7, 149.6, 135.2, 132.8, 131.9, 130.3, 129.4, 125.1, 116.1, 111.9, 111.6, 97.9, 63.5, 56.4. IR (reflection) $\tilde{\nu}$ = 3306, 2838, 2184, 1721, 1610, 1490, 1439, 1351, 1298, 1272, 1196, 1136, 1057, 1028, 885, 813, 753, 694, 650, 615 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_4$ calcd for 345.0845, found 345.0849.

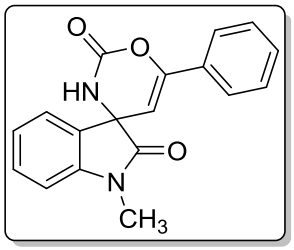
5-chloro-6'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5fb)



Yield: 25 mg, 79%; yellow solid; Mp. 165.3-166.0 ^{o}C; R_f = 0.2 (PE/EA = 1/1); ^{1}H NMR (400 MHz, DMSO) δ = 10.76 (s, 1H), 8.58 (s, 1H), 7.71 – 7.67 (m, 2H), 7.49 (d, J = 1.6 Hz, 1H), 7.44 (d, J = 3.5 Hz, 3H), 7.36 (dd, J = 8.3, 1.9 Hz, 1H), 6.92 (d, J = 8.3 Hz, 1H), 5.86 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 176.5, 149.6, 149.2, 140.8, 133.4, 131.6, 130.3, 130.0 129.1, 126.9, 125.7, 124.9, 112.2, 96.9, 62.9. IR (reflection) $\tilde{\nu}$ = 3282, 2980, 2935, 1733, 1620, 1475, 1349, 1272, 1192, 1135, 1055,

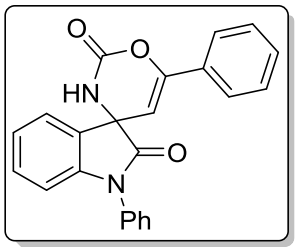
885, 821, 757, 693, 651, 617 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{17}H_{11}N_2NaO_3$ calcd for 349.0350, found 349.0352.

1-methyl-6'-phenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5lb)



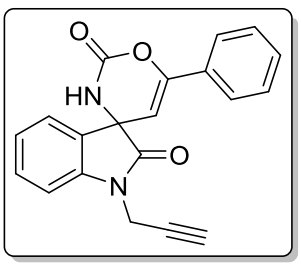
Yield: 23 mg, 76%; yellow solid; Mp. 105.2-106.5 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 8.52 (s, 1H), 7.70 – 7.66 (m, 2H), 7.44 (d, J = 1.7 Hz, 1H), 7.43 (d, J = 1.9 Hz, 2H), 7.40 (s, 1H), 7.13 (t, J = 8.0 Hz, 3H), 5.82 (d, J = 1.5 Hz, 1H), 3.18 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ = 175.1, 149.3, 143.3, 131.5, 130.8, 130.6 130.1, 129.1, 125.0, 124.9, 123.6, 121.5, 109.6, 97.4, 62.3, 27.0. IR (reflection) $\tilde{\nu}$ = 2964, 1725, 1613, 1493, 1470, 1349, 1271, 1227, 1189, 1131, 1094, 1052, 1028, 974, 937, 897, 856, 805, 752, 693, 616 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{18}H_{14}N_2NaO_3$ calcd for 329.0896, found 329.0901.

1,6'-diphenylspiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5mb)



Yield: 27 mg, 75%; yellow solid; Mp. 204.1-205.6 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (600 MHz, DMSO) δ = 8.70 (d, J = 0.9 Hz, 1H), 7.71 (dd, J = 7.8, 1.5 Hz, 2H), 7.62 (t, J = 7.8 Hz, 2H), 7.54 – 7.50 (m, 2H), 7.49 – 7.43 (m, 5H), 7.36 (td, J = 7.9, 1.0 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 7.9 Hz, 1H), 6.06 (d, J = 1.5 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ = 174.9, 149.9, 149.5, 143.5, 134.7, 131.8, 131.0, 130.9, 130.5, 129.5, 129.2, 127.4, 125.9, 125.2, 124.5, 110.3, 97.6, 62.9. IR (reflection) $\tilde{\nu}$ = 3120, 2944, 1724, 1614, 1595, 1497, 1466, 1368, 1328, 1267, 1235, 1192, 1175, 1106, 1055, 1027, 929, 897, 850, 812, 751, 694, 627, 611 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{23}H_{16}N_2NaO_3$ calcd for 391.1053, found 391.1062.

6'-phenyl-1-(prop-2-yn-1-yl)spiro[indoline-3,4'-[1,3]oxazine]-2,2'(3'*H*)-dione (5pb)



Yield: 25 mg, 77%; yellow solid; Mp. 125.3-126.1 ^oC; R_f = 0.2 (PE/EA = 1/1); ^1H NMR (400 MHz, DMSO) δ = 8.68 (s, 1H), 7.69 (dd, J = 6.7, 3.0 Hz, 2H), 7.48 – 7.41 (m, 5H), 7.19 (dd, J = 16.2, 8.1 Hz, 2H), 5.82 (d, J = 1.6 Hz, 1H),

4.56 (d, J = 1.8 Hz, 2H), 3.36 (t, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ = 174.4, 149.8, 149.2, 141.5, 131.4, 130.6, 130.2, 129.1, 125.3, 124.9, 124.0, 110.4, 97.1, 78.0, 75.5, 62.3, 29.9. IR (reflection) $\tilde{\nu}$ = 3284, 2933, 2125, 1728, 1612, 1487, 1467, 1449, 1351, 1269, 1176, 1107, 1079, 1051, 1029, 1005, 973, 934, 895, 845, 752, 692, 637, 610 cm^{-1}. HRMS (ESI) $[M+Na]^+$ (m/z) $C_{20}H_{14}N_2NaO_3$ calcd for 353.0896, found 353.0903.

4.5.4. Referneces

1. a) Urban, M.; Franc, M.; Hofmanova, M.; Cisarova, I.; Vesely, J. *Org. Biomol. Chem.*, **2017**, *15*, 9071–9076. b) Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R. *Org. Lett.*, **2012**, *10*, 2512-2515.

2. Tian, X., Song, L., Rudolph, M., Rominger, F., Oeser, T., Hashmi, A. S. K. Sulfilimines as Versatile Nitrene Transfer Reagents: Facile Access to Diverse Aza-Heterocycles. *Angew. Chem., Int. Ed.* **2019**, *58*, 3589−3593.

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