Gold-Catalyzed C-H Alkynylations with Hypervalent Iodine(III) Reagents

Presented by:

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From Henan, China

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A dissertation submitted to the

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Oral examination: September 29th, 2021

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

Prof. Dr. Milan Kivala

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Contents

Publications

[1] **C. Han**, X. Tian, H. Zhang, F. Rominger, A. S. K. Hashmi. "Tetrasubstituted 1,3-Enynes by Gold-Catalyzed Direct C(sp^2)−H Alkynylation of Acceptor-Substituted Enamines" *Org. Lett.* **2021**, *23*, 4764-4768.

[2] L. Hu, M. C. Dietl, **C. Han**, M. Rudolph, F. Rominger, A. S. K. Hashmi. "Au–Ag Bimetallic Catalysis: 3-Alkynyl Benzofurans from Phenols via Tandem C−H Alkynylation/Oxy-Alkynylation" *Angew. Chem., Int. Ed.* **2021**, *60*, 10637-10642.

[3] L. Song, X. Tian, **C. Han**, M. Amanpur, F. Rominger, A. S. K. Hashmi. " Catalyst-free synthesis of oxazol-2(3*H*)-ones from sulfilimines and diazo compounds through a tandem rearrangement/aziridination/ring-expansion reaction" *Org. Chem. Front.* **2021**, *8*, 3314-3319.

[4] X. Tian, L. Song, **C. Han**, C. Zhang, Y. Wu, M. Rudolph, F. Rominger, A. S. K. Hashmi. "Gold(III)-Catalyzed Formal [3 + 2] Annulations of *N*-Acyl Sulfilimines with Ynamides for the Synthesis of 4-Aminooxazoles" *Org. Lett.* **2019**, *21*, 2937–2940.

[5] **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" manuscript submitted to *Chem. Sci.* **2021**.

[6] **C. Han**, A. S. K. Hashmi. "Efficient Access to Indolizines via Gold-Catalyzed Tandem C(sp^3)–H Alkynylation/ aminoalkynylation of 2-(Pyridin-2-yl)acetate Derivatives" manuscript under preparation, **2021**.

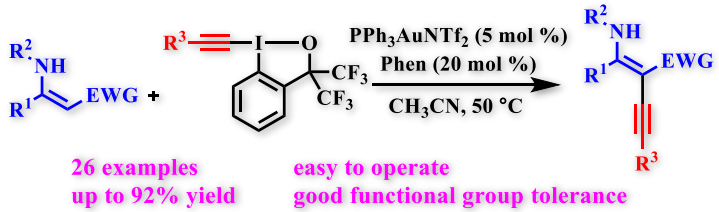
Abbreviations

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

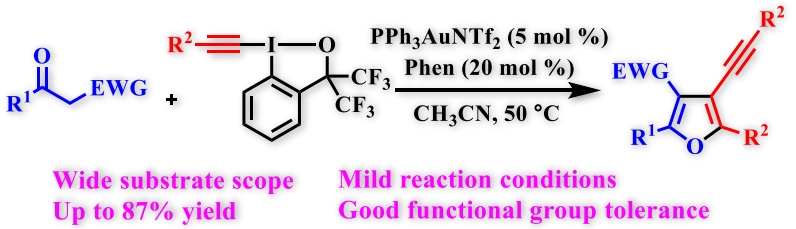
Me	methyl
Mes	Mesityl
MHz	Megahertz
min	minute
Ms	Mesyl
MS	Mass spectrometry
NBS	*N*-bromo succinimide
NHC	*N*-heterocyclic carben
NIS	*N*-iodo succinimide
NMR	Nuclear magnetic resonance
Ns	4-nitrobenzenesulfonyl
PE	Petroleum ether
Ph	Phenyl
Pr	Propyl
rt	room temperature
R_f	Ratio of fronts
t	*tert*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

Abstract

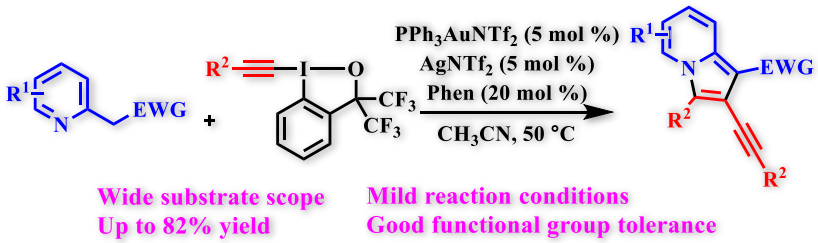
In Chapter 2, a gold-catalyzed direct alkynylation for the synthesis of 1,3-enynes using alkyl 3-aminoacrylates and hypervalent iodine reagents is reported. This reaction, which involves the formation of an alkynyl Au(III) species and a direct C-H activation of alkyl 3-aminoacrylates, reports twenty-six successful conversions in 62-92% yield with excellent functional group tolerance. In addition, only one configuration of 1,3-enynes containing enamines is produced and no further cyclization product is found.



In Chapter 3, a gold-catalyzed cascade C(sp^3)-H alkynylation/ oxy-alkynylation of *β*-keto compounds with hypervalent iodine(III) reagents for the synthesis of tetra-substituted furans is described. The alkynyl Au(III) species plays a crucial role in Au(I)/Au(III) catalytic cycles. The two operating catalytic cycles include an alkynylation of activated C(sp^3)-H bond and an oxy-alkynylation of an *β*-alkynyl ketone. This simple strategy features mild reaction conditions, high functional group tolerance, and a wide substrate scope. Furthermore, the synthetic utility of the method was demonstrated by diverse functionalizations of the final products. Gram-scale synthesis and proposed mechanism are also presented.

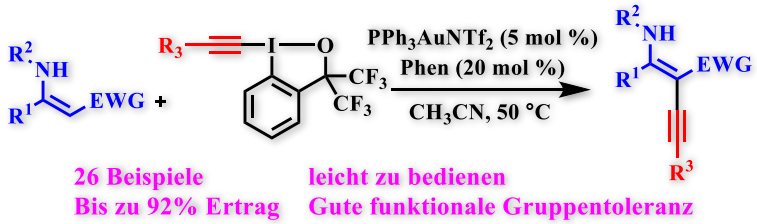


In Chapter 4, another gold-catalyzed cascade C(sp^3)–H alkynylation/Nitrogen-alkynylation of 2-pyridine compounds with hypervalent iodine(III) reagents for the synthesis of poly-substituted indolizines is described. The broad substrate scope, good functional group tolerance and good efficiency render this method useful for organic synthesis, especially for the synthesis of nitrogen-containing compounds. Gram-scale synthesis and proposed mechanism are also revealed.

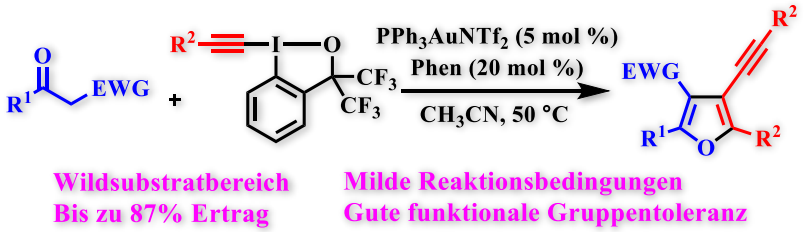

PPh3AuNTf2 (5 mol %)
AgNTf2 (5 mol %)
Phen (20 mol %)
CH3CN, 50 °C
R1
EWG
R2
CF3
CF3
Wide substrate scope
Up to 82% yield
Mild reaction conditions
Good functional group tolerance

Kurzzusammenfassung

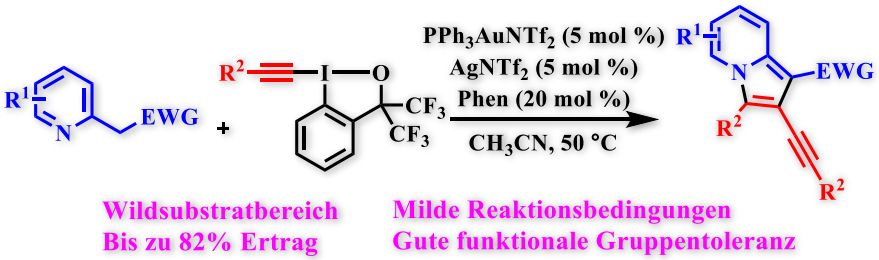
In Kapitel 2 wird eine goldkatalysierte direkte Alkinylierung zur Synthese von 1,3-Eninen mit Alkyl-3-aminoacrylaten und hypervalenten Iodreagenzien beschrieben. Diese Reaktion, die eine gebildete Alkinyl-Au(III)-Spezies und die direkte C-H-Aktivierung von Alkyl-3-aminoacrylaten umfasst, bietet 26 Substrate in 62–92 % Ausbeute mit ausgezeichneter Toleranz gegenüber funktionellen Gruppen. Außerdem wird nur eine Konfiguration von 1,3-Eninen mit Enaminen hergestellt und kein weiteres Cyclisierungsprodukt gefunden.



In Kapitel 3 wird eine goldkatalysierte C(sp^3)-H-Alkinylierung/ Oxyalkinylierung von *β*-Ketoverbindungen mit hypervalenten Iod(III)-Reagenzien zur Synthese tetrasubstituierter Furane beschrieben. Die Alkinyl-Au(III)-Spezies spielen eine entscheidende Rolle in Au(I)/Au(III)-Katalysatorzyklen und durchlaufen zwei Katalysezyklen, darunter die Alkinylierung der aktivierten C(sp^3)-H-Bindung und die Oxyalkinylierung von *β*-Alkinylketon. Diese einfache Strategie zeichnet sich durch milde Reaktionsbedingungen, hohe Toleranz gegenüber funktionellen Gruppen und große Substratbreite aus. Darüber hinaus zeigt sich der synthetische Nutzen der Methode durch vielfältige Funktionalisierungen der Endprodukte. Die Synthese im Grammmaßstab und der vorgeschlagene Mechanismus werden ebenfalls vorgestellt.



In Kapitel 4 wird eine weitere goldkatalysierte C(sp3)-H-Alkinylierung/Stickstoff-Alkinylierung von 2-Pyridinverbindungen mit hypervalenten Iod(III)-Reagenzien für die Synthese polysubstituierter Indolizine beschrieben Funktionellegruppentoleranz und gute Effizienz machen dieses Verfahren nützlich für die organische Synthese, insbesondere für die Synthese stickstoffhaltiger Verbindungen. Die Synthese im Grammmaßstab und der vorgeschlagene Mechanismus werden ebenfalls enthüllt.



Wildsubstratbereich
Bis zu 82% Ertrag

Milde Reaktionsbedingungen
Gute funktionale Gruppentoleranz

Chapter 1. General Introduction

1.1 Gold Catalysis

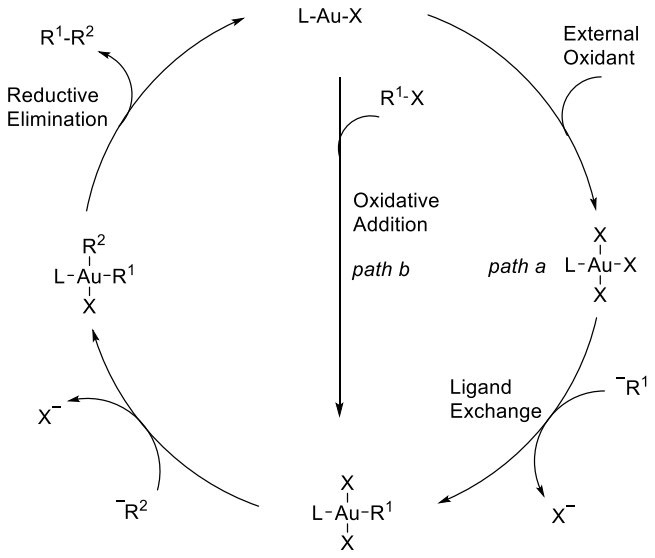
Gold has a rich coordination and organometallic chemistry,[1] but was widely considered to be catalytically inactive for a long time. Gold as a catalyst, which was later discovered to be superior to other catalysts, remained an unexplored challenge until 1973, when Bond et al. reported the hydrogenation of olefins over supported gold catalysts.[2] Later, several heterogeneous gold-catalyzed reactions were reported.[3] At about the same time, homogeneous asymmetric catalysis has developed. In 1986, Ito et al. reported the first example of an asymmetric aldol reaction catalyzed by a gold(I) complex.[4] Later reports showed that cationic gold(I) species gave excellence turnover frequencies (TOFs).[5] This chapter will focus on homogeneous gold catalysis.

The homogeneous gold-catalyzed reactions have been widely recognized as a powerful tool in the field of organic synthesis,[6] especially for the synthesis of heterocyclic[7] and complex polycyclic molecules.[8] Recently, Au(I)/Au(III) catalytic cycles have attracted increasing attention from many organic chemists.[9] Owing to the relatively high redox potential of the Au(I)/Au(III) couple (E^0 = +1.41 V),[10] it is a great challenge for the gold-catalyzed oxidative cross-coupling reactions. Unlike other transition metals, gold catalysis has a unique attraction due to mild carbophilic π acid and oxidation state stability. In this thesis, reactions using Au(I)/Au(III) catalytic cycles will be covered.

1.2 Redox Gold Catalysis

Transition metal-catalyzed coupling reactions usually involve M^n/M^{n+2} redox cycles and proceeds through a two-electron oxidation and a reduction. However, the branch of gold catalysis has been less explored, due to the high oxidation potential.[10] To solve the problem, a series of breakthroughs involving gold catalysis with/without external oxidants for Au(I)/Au(III) catalytic cycle have been reported. Generally, the main strategies for Au(I)/Au(III) catalytic cycle reactions include the use of strong external oxidants (Scheme 1-1, path a) or highly electrophilic reagents (Scheme 1-1, path b),

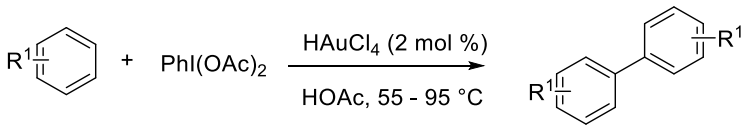
and the incorporation of a bidentate ligand. As expected, Au(I)/Au(III) catalytic cycle reactions have flourished by these strategies in the last decade.[9e, 10b]



Scheme 1-1 Modes of reactivity for oxidative gold catalysis.

1.2.1 Redox Gold Catalysis with External Oxidants

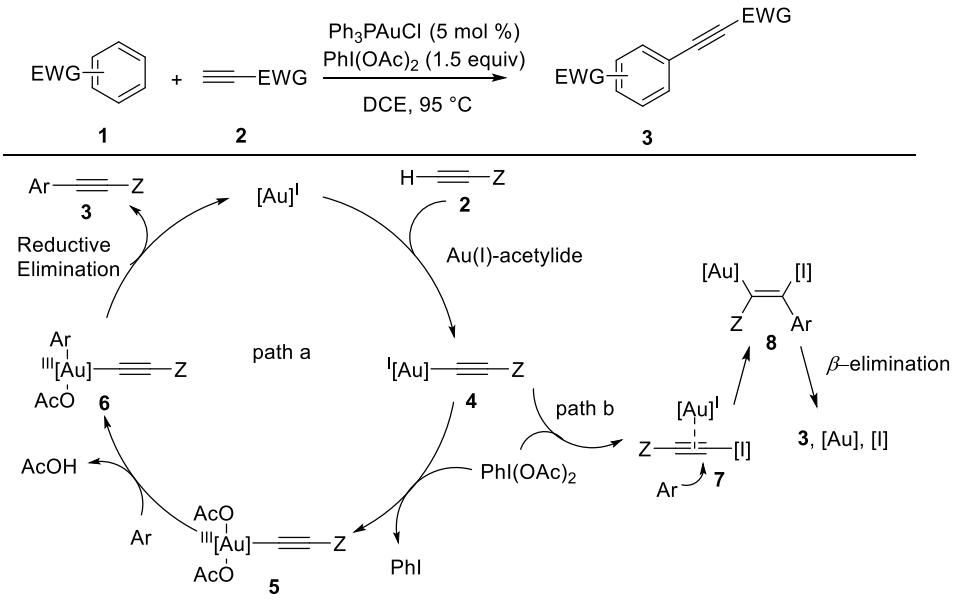
Pioneering reports by Tse's group demonstrated that a gold-catalyzed biarylation reaction of simple arenes (Scheme 1-2) is possible.[11] The biaryl compounds were accessed when simple arenes were reacted in the presence of 2 mol % $HAuCl_4$ as a catalysis and $PhI(OAc)_2$ as an external oxidant. Although, this method was limited to the synthesis of symmetric biaryl group.



Scheme 1-2 Gold-catalyzed direct oxidative coupling of non-activated arenes

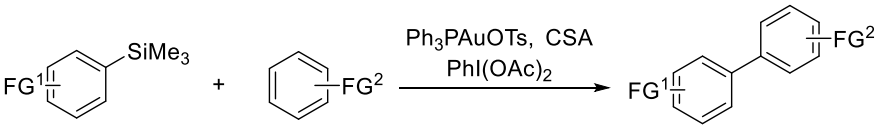
Subsequently, Nevado's group reported the first gold-catalyzed enthinylation of arenes with electron-deficient alkynes for the synthesis of aromatic propiolates.[12] Using Ph_3PAuCl as a catalysis and $PhI(OAc)_2$ as an external oxidant, a series of new Csp^2-Csp bonds could be generated (Scheme 1-3). A plausible mechanism was described as well. First, the gold(I)-acetylide complex **4** is formed in the present of Ph_3PAuCl and electron-deficient alkynes. Subsequently, **4** undergoes oxidative addition with

$PhI(OAc)_2$ to give a Au(III) complex **5**. Electrophilic aromatic substitution is occurred between Au(III) complex **5** and electron-deficient alkynes **2**, producing Au(III) complex **6**. The reductive elimination of Au(III) complex **6**, then delivers aromatic propiolates **3** (path a). Alternatively, the reaction of the gold(I) acetylide complex **4** with $PhI(OAc)_2$ could give an electrophilic alkynyl-iodonium complex **7**. A gold-catalyzed arene addition reaction to access a vinyl gold intermediate **8** then occurs, which upon *β*-elimination gives aromatic propiolates **3** (path b).



Scheme 1-3 Gold-catalyzed ethynylation of arenes

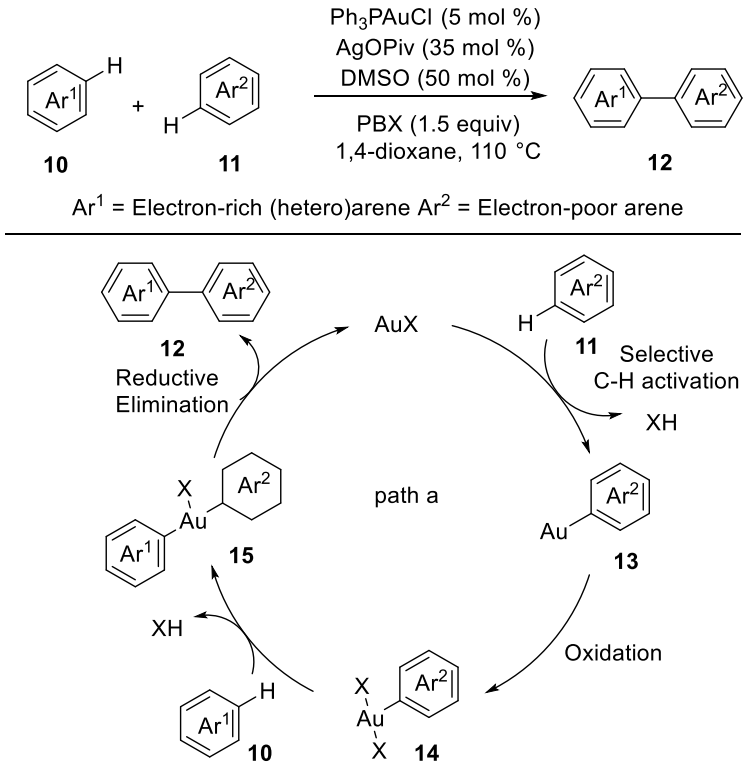
In 2012, Russell's group reported a gold-catalyzed direct C-H arylation of aryl silanes for the synthesis of biaryls (Scheme 1-4).[13] This simple strategy features mild reaction conditions, high functionality group tolerance, and a wide substrate scope. In comparison to many transition-metal-catalyzed processes, the method required low temperatures and low concentrations of one coupling partner. In 2014, initial mechanistic investigations into the gold-catalyzed intermolecular arylation were published by this group.[14] In subsequent developments, Itami's group demonstrated that gold-catalyzed oxidative direct C-H arylation of heterocycles was possible by employing a pyridylidene ligand,[15] and Lloyd-Jones's group reported a gold-catalyzed C-H arylation of heteroarenes [16] and the total synthesis of (-)-allocolchicine enabled by a gold-catalyzed biaryl coupling reaction.[17]



- *mild activation of C-H bonds*
- *site-selectivity for one C-H bond*
- *economic reactant stoichiometries*

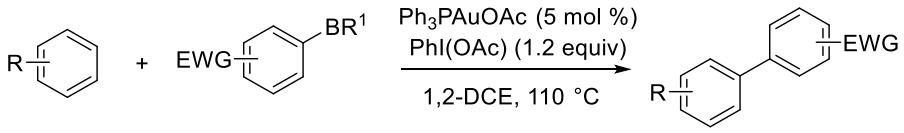
Scheme 1-4 Gold-catalyzed direct arylation

In 2015, Larrosa's group reported on the Au(I/III)-catalyzed oxidative cross-coupling of arenes via a double C−H activation strategy (Scheme 1-5).[18] An orthogonal selectivity of the C-H auration depending on the oxidation state of the Au center and the electronic properties of the arene was discovered.[10a, 10c, 19] The Au(III) species showed a high selectivity for C-H activation of electron-rich arenes, and Au(I) compounds were specific for electron-poor arenes and heteroarenes, characteristic of concerted metalation deprotonation (CMD). A plausible mechanism comprises the selective C-H activation of the electron-poor arene, which forms Au(I) species **13**. Subsequently, the species **13** undergoes an oxidative addition to produce alkynyl Au(III) complex **14**. A further selective C-H activation of the electron-rich arene with Au(III) complex **14** gives Au(III) species **15**. Then reductive elimination delivers the desired product **12**.



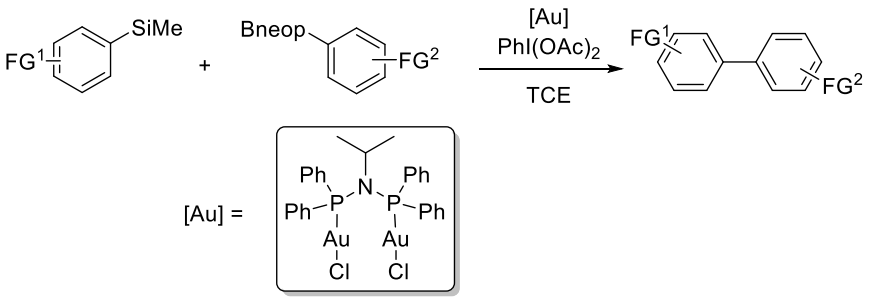
Scheme 1-5 Gold-catalyzed cross-coupling of arenes

In 2016, Nevado's group disclosed a gold-catalyzed oxidative cross-coupling of arenes with strong electron-deprived aryl boronates (Scheme 1-6).[20] Interestingly, competitive experiments indicated a higher reactivity of aryl boronates than aryl silanes, the acetato ligand as internal base played a key role and avoided the potential deactivation of aryl boranes in basic media.



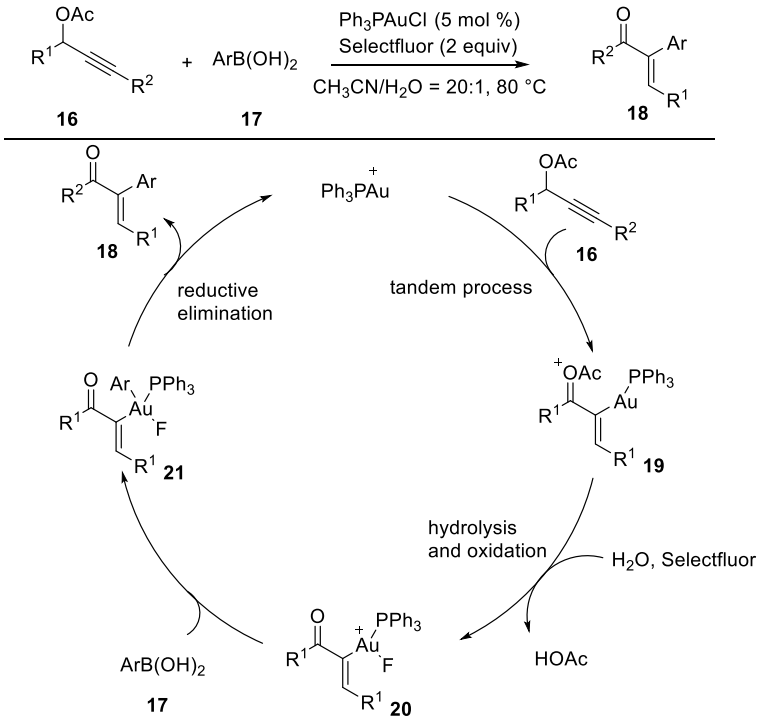
Scheme 1-6 Gold-catalyzed direct oxidative arylation with boron coupling partners

In 2020, Xie and Hashmi developed a dimeric gold-catalyzed oxidative cross-coupling of arylboronates and arylsilanes for the synthesis of biaryl compounds (Scheme 1-7).[21] The mechanism probably evolves a gold(I) center that participates in the transmetalation with an arylboronate and meanwhile a gold(III) center can activate an arylsilane. Very recently, Schoenebeck's group reported a gold-catalyzed chemoselective coupling of polyfluoroarenes with aryl germanes.[22]



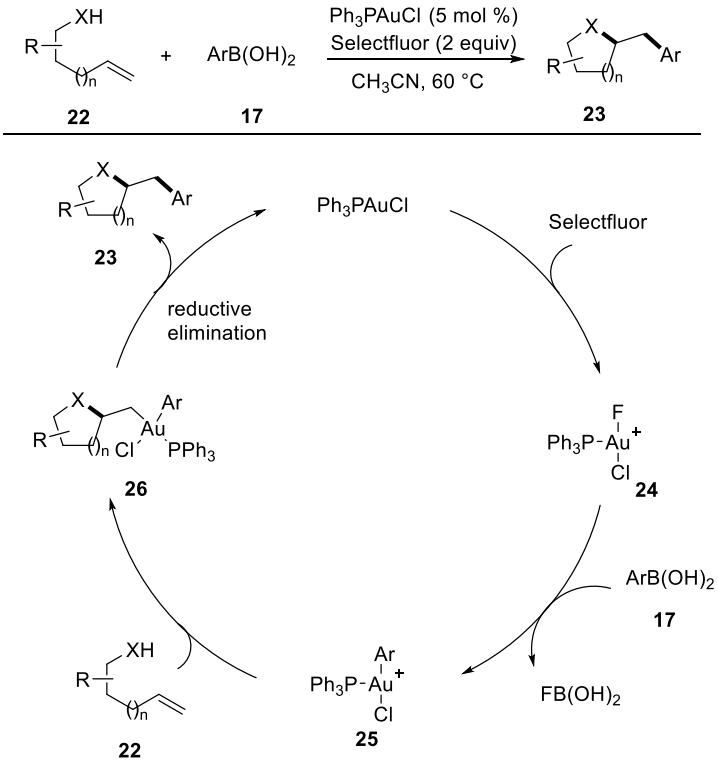
Scheme 1-7 Gold-catalyzed oxidative biaryl cross-coupling of organometallics

On the other hand, gold-catalyzed coupling can involve an in situ-formed Au(III) species by using Selectfluor as an oxidant and a subsequent attack of a nucleophile, offering new strategies for C-C bond formations. In 2009, Zhang's group reported a gold-catalyzed oxidative cross-coupling of propargylic acetates with aryl boronic acids for the synthesis of α-arylenones (Scheme 1-8).[23] First, a gold-catalyzed tandem reactions of propargylic acetate **16**, should form intermediate **19**. **19** then undergoes hydrolysis and oxidation to produce Au(III) complex **20**. Subsequently, the transmetalation could lead to the Au(III) complex **21**, which after reductive elimination give rise to the desired product **18**. Meanwhile, they demonstrated a gold-catalyzed homogeneous oxidative C-O bond-forming reaction by employing Selectfluor as an oxidant.[24]



Scheme 1-8 Gold-catalyzed oxidative cross-coupling reactions

Later on, Zhang's group developed a carboheterofunctionalization of terminal alkenes with arylboronic acids for the synthesis of substituted *N*- or *O*-heterocycles (Scheme 1-9).[25] It is assumed that an Au(III) species **24** is formed in the present of Selectfluor, subsequently, the transmetalation of **24** gives Au(III) complex **25**. Then the generated cationic complex **25** would activate the alkene for the attack of N- or O-nucleophiles. Reductive elimination then gives the desired product **23**. Interestingly, no alkenes were isolated resulting from the *β*-H elimination of **26**. This report was followed by the biamination of alkenes by using gold as a catalyst and Selectfluor as an oxidant for the synthesis of dinitrogen compounds.[26] Alkoxy-alkynylations and amino-alkoxylations of alkenes were reported by Gouverneur's group and Nevado's group via Au(I)/Au(III) catalysis.[27]

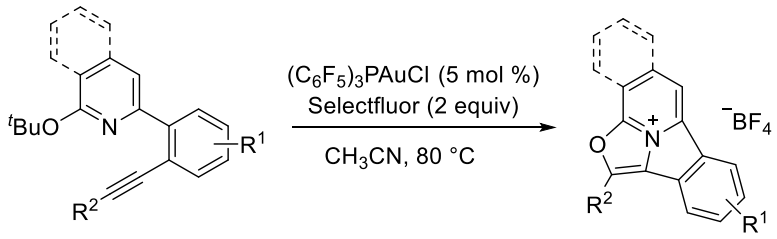


Scheme 1-9 Gold-catalyzed oxidative carboheterofunctionalization of alkenes

In 2010, Toste's group reported a three-component gold-catalyzed oxidative oxyarylation of alkenes by employing Selectfluor as an oxidant.[28] Intermolecular or intramolecular bimetallic gold(I)-catalyzed oxyarylation of terminal alkenes with

simple alcohols, water or tosylamide[29] as nucleophiles. This further developed the utility of gold-catalyzed oxidative cross-coupling by employing Selectfluor as an oxidant. Russell et al. demonstrated a gold-catalyzed oxyarylation reactions of terminal alkenes with arylsilanes affording the products in excellent isolated yield.[30]

In 2017, Patil's group reported oxidative intramolecular 1,2-amino-oxygenations of alkynes under Au(I)/Au(III) catalysis for the synthesis of ionic pyridinium-oxazole dyad with tunable emission wavelengths (Scheme 1-10)[31] and the application of these fluorophores for cell imaging. These results provided a basis for the future development of fluorescent probes for the selective detection of chemical species inside mitochondria.



Scheme 1-10 Oxidative intramolecular 1,2-amino-oxygenation of alkynes

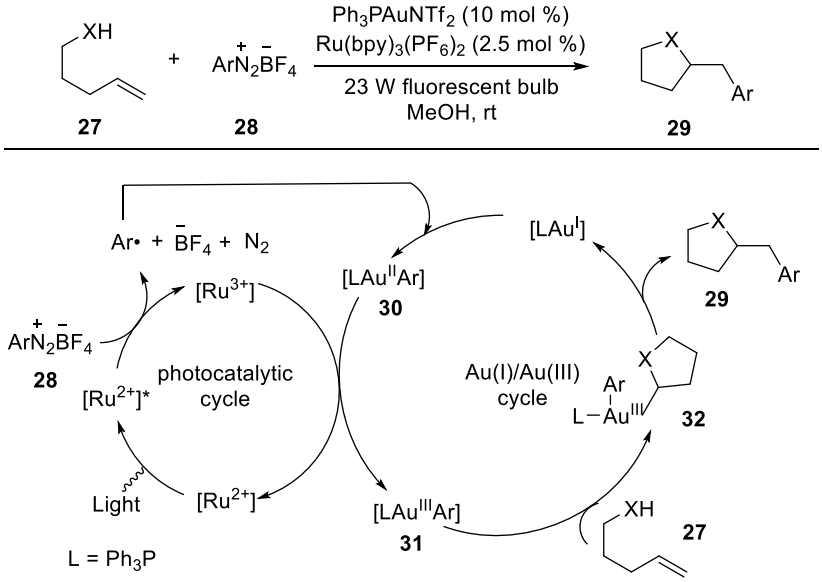
1.2.2 External Oxidant-free Oxidative Gold Catalysis

Further consideration was undertaken whether the external oxidant can be merged with the coupling partner to give a single reagent that can serve dually as an oxidant and as a coupling partner. Two significant advantages of this strategy exist: 1) no sacrificial waste due to no external oxidant and 2) the existence of other coupling partners when the Au(III) intermediate have formed. Aryldiazonium salts and ethynylbenzoiodoxolones (EBXs) have emerged as highly prospective coupling partners.

The first example of an oxidant-free oxidative gold catalysis was reported by Glorius and co-workers in 2013 (Scheme 1-11).[32] They used a novel gold and photoredox dual catalytic system for intramolecular oxy and aminoarylations of alkenes with aryldiazonium salts. Later, a gold/photoredox-catalyzed oxidative addition reaction of gold(I) with well-defined (C,N)-cyclometalated as a ligand for the synthesis of gold(III) species was reported.[33] The first experimental evidence for the involvement of a Au(I)

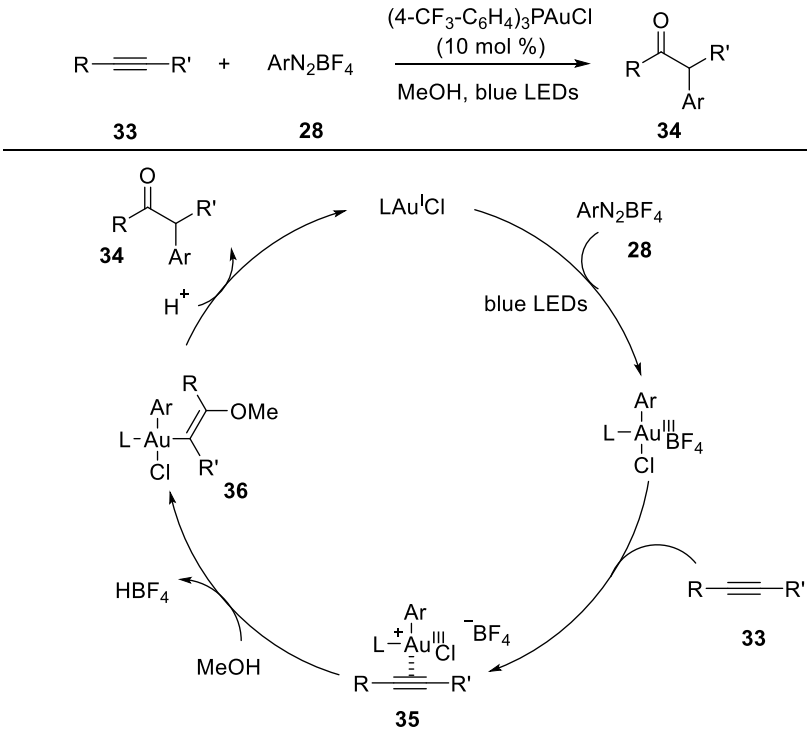
to Au(III) oxidation was provided. Subsequently, Yu's group investigated the detailed mechanism of gold/photoredox-catalyzed oxyarylation of alkenes.[34] Yu's study suggested that the oxidation of a gold(I) precatalyst occurs prior to the cyclization step. On the basis of previous studies and these experiments, a plausible mechanism is described in Scheme 11. First, a concomitant reducing excited state species $[Ru^{2+}]^*$ in the present of light. Subsequently, the key aryl radical is formed. The formed aryl radical then combines with Au(I) to give Au(II) species **30**, which is further oxidized by $[Ru^{3+}]$ to form Au(III) species **31** and initially $[Ru^{2+}]$. The Au(III) species **31** then activates the olefin **27** towards nucleophilic attack, affording Au(III) complex **32**. Reductive elimination then gives the cross-coupling product **29**. Following these initial reports, a series of related explorations were exposed.[35]

Recently, Hashmi's group reported gold(I)-catalyzed arylative cross-coupling reactions by using aryldiazonium salts in the presence of visible light without the use of photosensitizers (Scheme 1-12).[36] In contrast to previous reports on gold/photoredox-catalyzed reactions, no photosensitizer was required. The authors proposed a Au(I) activation of aryldiazonium salts **28** to form an intermediate Au(III) species. The



Scheme 1-11 Intramolecular alkoxy- and aminoarylation reactions under merged gold/photoredox catalysis.

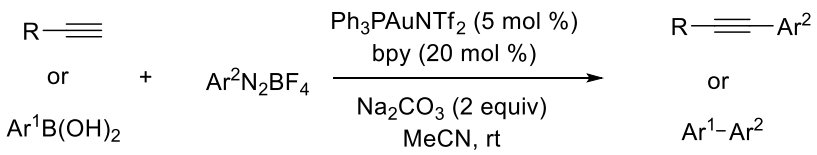
alkynyl moiety of **33** coordinates with the Au(III) complex, subsequently, the intramolecular nucleophilic attack of the oxygen atom takes place to afford Au(III) complex **36**. Upon reductive elimination of **36**, the desired product **34** is formed, meanwhile the Au(I) species is regenerated to complete the catalytic cycle. Later, Wong's group reported a photosensitizer-free visible light-mediated gold-catalyzed bifunctionalization reaction for the synthesis of silyl-substituted quinolizinium compounds.[37] This was followed by a report of Bandini's group replaced the aryldiazonium salts with bench-stable arylazosulfones with arylboronic acids under light irradiation without using any photocatalyst for the synthesis of diverse biaryls.[38]



Scheme 1-12 Photosensitizer-free gold-catalyzed 1,2-difunctionalization of alkynes

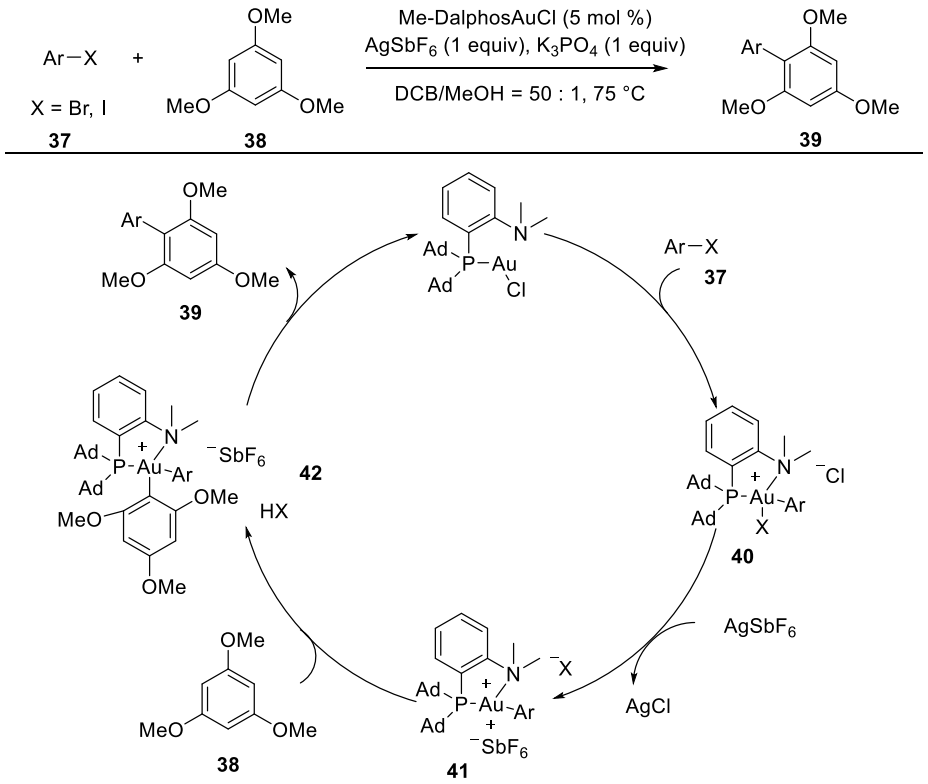
Further development, Shi's group reported a gold-catalyzed C(sp)–C(sp^2) and C(sp^2)–C(sp^2) cross-coupling reaction with aryldiazonium salts as the coupling partner without light (Scheme 1-13).[39] Strong evidence for the bipyridine assisted nitrogen extrusion was gained via NMR and ESI-MS studies. Subsequently, the same group showed that gold-catalyzed Sandmeyer-type reactions without the addition of a ligand are possible.[40] In 2018, Dughera's group reported a gold-catalyzed Heck-coupling of arenediazonium *o*-benzenedisulfonimides for the synthesis of diverse C–H arylated

products.[41] Later on, the activation of aryldiazonium salts (ArN_2X) without the need of light, ligands or nucleophiles was reported by Porcel and Patil et al.[42]



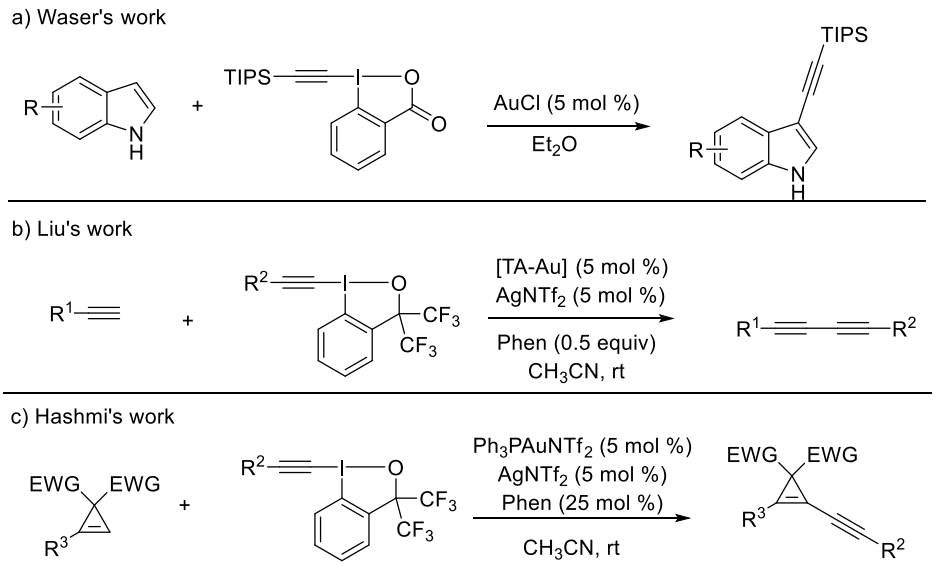
Scheme 1-13 Ligand-assisted gold-catalyzed cross-coupling with aryldiazonium salts

The stability of aryldiazonium salts is dictated, however due to the energetic of the aryldiazonium salts, their reactivity cannot be predicted. Therefore, the development of alternative methods is urgently needed. In 2019, Bourissou's group reported the hemilabile (P,N) MeDalphos ligand to trigger oxidative addition of iodoarenes to gold.[43] Competition experiments and Hammett correlations substantiate indicated electron-enriched substrates both in stoichiometric oxidative addition reactions and in catalytic C–C cross-coupling with 1,3,5-trimethoxybenzene of gold. They also showed that gold(I) complexes can also add oxidatively into Si–Si[44] and Sn–Sn[45] bonds. It is not easy to provide a suitable coordination environment around the organo-halides. The formed aryl–gold(III) complexes are too stable to exploit for further reactivity. In 2017, Bourissou's group reported the gold(I)-catalyzed $C(sp^2)$–$C(sp^2)$ cross-coupling with aryl halides via modification of the ancillary ligand on Au to facilitate the oxidative addition step to the gold center (Scheme 1-14). This work used (Me-Dalphos)AuCl as the ancillary (P,N) ligand which not only stabilizes the gold(III) species but also provides the perfect environment for transmetalation with various nucleophilic coupling partners. Biaryl compounds were obtained by a gold-catalyzed arylation of 1,3,5-trimethoxybenzene with aryl halides. The reaction involves a $C(sp^2)$–X oxidative addition, $C(sp^2)$–H auration and reductive elimination, giving direct arylation of arenes. The gold(III) complex **40** was isolated and characterized.



Scheme 1-14 Gold-catalyzed direct C–H arylation of arenes with aryl halides

Recently, alkynyl gold(III) species have attracted increasing attention from many organic chemists by reacting alkynyl-substituted hypervalent iodine reagents with gold(I) catalysts.[9] In 2009, Waser's group reported the first regioselective C3-alkynylation of indoles and C2-alkynylation of pyrroles by employing gold as a catalyst (Scheme 1-15a).[46] Subsequently, the same group reported several applications of alkynyl gold(III) species, which introduced alkyne moieties on the heterocycles by using alkynyl-substituted hypervalent iodine reagents.[46-47] Liu's group disclosed a gold-catalyzed alkynylation reaction of terminal alkynes using alkynyl-substituted hypervalent iodine reagents (Scheme 1-15b).[48] Interestingly, 1,10-phenanthroline was essential. Later, Hashmi's group successfully demonstrated alkynyl gold(III) complexes as key to the further alkynylation of various substrates, such as *N*-propargylcarboxamides,[49] cyclopropenes (Scheme 1-15c),[50] phenols[51] and acceptor-substituted enamines.[52] The mechanistic data indicated that alkynyl Au(III) species play a crucial role in Au(I)/Au(III) catalytic cycles.



Scheme 1-15 Gold-catalyzed alkynylation reactions.

1.3 Research Objectives

This thesis will further explore Au(I)/Au(III) catalytic cycles by employing hypervalent iodine reagent as a oxidant. By utilizing the unique redox property and carbophilic π acidity of gold, we will explore 1) direct C(sp^2)-H functionalization of alkenes, 2) cascade C(sp^3)–H alkynylation/oxy-alkynylations of acceptor-substituted carbonyl compounds and 3) tandem C(sp^3)–H alkynylation/ nitrogen-alkynylation of pyridine compounds. And this study also will enhance our knowledge of the gold-catalyzed redox reaction.

1.4 References

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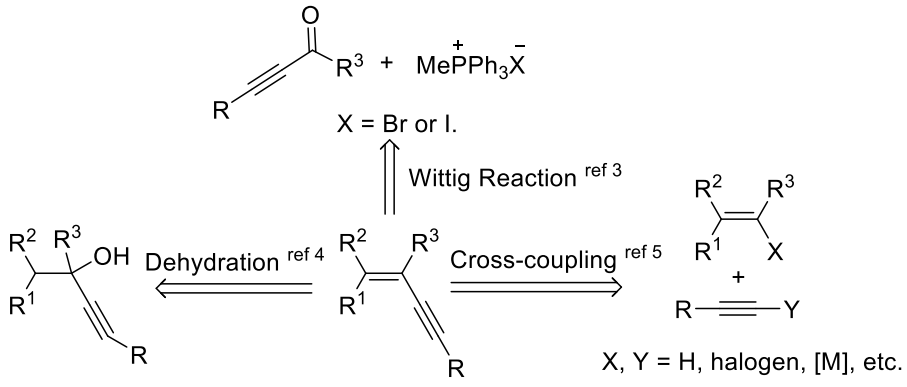
Chapter 2. Tetrasubstituted 1,3-Enynes by Gold-Catalyzed Direct C(sp^2)–H Alkynylation of Acceptor-Substituted Enamines

2.1 Introduction

Conjugated 1,3-enynes are important subunits present in natural products, pharmacologically active molecules and functional materials for optics and electronics.[1] They often serve as extremely valuable synthetic intermediates to participate in diverse downstream transformations in organic synthesis.[2] Thus, it is not surprising that considerable efforts have been expended in seeking methods for the preparation of conjugated 1,3-enynes. Classical synthetic strategies for the construction of 1,3-enynes include Wittig olefination of propargyl aldehyde,[3] dehydration of propargyl alcohols,[4] and cross-dimerization of alkynes as well as Sonogashira and Suzuki-Miyaura coupling reactions (Scheme 2-1).[2a, 5] During the past decades, the direct alkynylation of alkenes has gained considerable more attention.[6] Usually, alkynylations of alkenes to give 1,3-enynes have been limited to electronically activated substrates or require the introduction of a proper directing group.[7] Consequently, there is still a high demand to develop efficient and simple methods for the direct stereo- and regioselective synthesis of conjugated, highly substituted enynes.



Scheme 2-1 Previous reports on the synthesis of 1,3-enynes

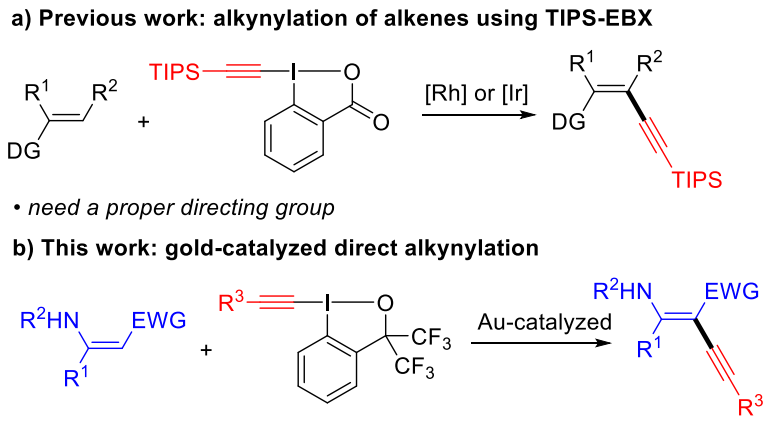
Alkyl 3-aminoacrylates are also important subunits in nitrogen-containing natural products possessing important biological properties.[8] They are highly versatile intermediates in synthetic chemistry.[9] In comparison with simple olefins, the carbon-

carbon double bond of enamines is more electron-rich because of the π-donating capacity of the nitrogen atom.[10] The unique property of enamines, has enabled the development of several efficient strategies for C-H functionalization catalyzed by transition metals over the past decades,[11] such as arylation,[10, 12] alkenylation[13] and arylation.[14] However, to the best of our knowledge, no examples of direct C(sp^2)-H alkynylations of enamines have been reported based on these strategies so far.

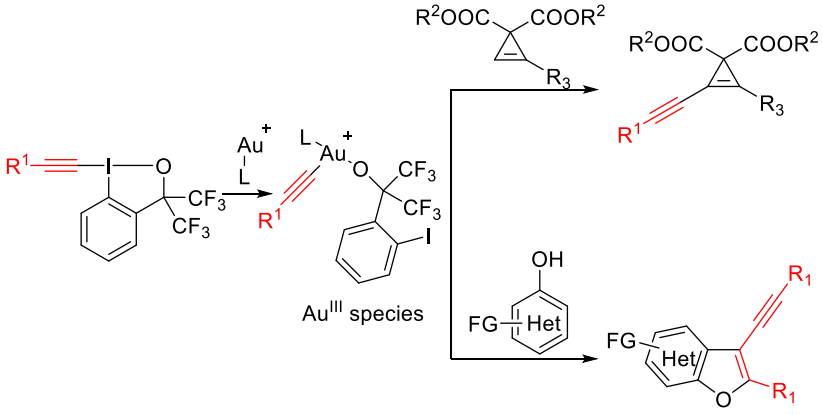
On the other hand, owning to the non-classical bond character and the excellent reactivity,[15] alkynyl-substituted hypervalent iodine reagents have attracted increasing attention from many organic chemists.[16] Various electrophilic alkynylation reactions based on alkynyl-substituted hypervalent iodine reagents have been developed.[17] In 2009, Waser's group reported the first direct C-H alkynylation for the synthesis of indole and pyrrole derivatives from [(triisopropylsilyl)ethynyl]benziodoxolone (TIPS-EBX (**2a**)) by employing AuCl as a catalyst.[18] Later, a series of C-H alkynylation based TIPS-EBX and electron-rich aryls have been demonstrated,[17a, 17b, 19] such as thiophenes,[20] anilines,[21] furans[22] and benzofurans.[23] In 2011, Waser's group reported that phenols can undergo Wacker cyclization toward Pd(II) species, followed by an alkynylation process using TIPS-EBX reagent to provide oxy-alkynylation products.[24] Therewith, Patil's group used AuCl to catalyze the aminoalkynylation reaction of alkynes with TIPS-EBX.[25] Liu's group developed a new method for the synthesis of unsymmetrical 1,3-butadiynes by employing gold-catalyzed a C-H alkynylation reaction with hypervalent iodine reagents from terminal alkynes.[26] Even so, alkynylation of alkenes for the synthesis of 1,3-enynes using TIPS-EBX are only reported by employing rhodium and iridium catalysts (Scheme 2-2a).[7b, 27]

In this context, our group is interested in Au(I)/Au(III) catalytic cycle reactions,[28] and we reported Au-catalyzed domino cyclization/alkynylation reaction,[29] dual Au/Ag catalysis direct alkynylation of cyclopropenes[30] and C-H alkynylation/oxy-alkynylation of phenols reaction (Scheme 2-3).[31] Based on our previous in-depth mechanistic study, we demonstrated that the Au(III) species are useful intermediates for the C-C bonds formation. We herein report the first gold-catalyzed C(sp^2)-H

alkynylation of alkyl 3-aminoacrylates with hypervalent iodine reagents (Scheme 2-2b).



Scheme 2-2 Metal-catalyzed alkynylations of alkenes



Scheme 2-3 Preliminary study of Au(III) species C-H activations

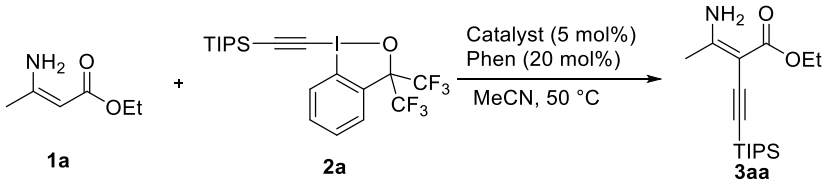
2.2 Result and Discussion

2.2.1 Optimization of the Reaction Conditions

We began our study by using 3-aminoacrylate **1a** and TIPS-EBX **2a** as model substrate (Table 2). As expected, the desired product **3aa** was isolated in 88% yield when the reaction was performed at 50 °C in the presence of 5 mol% $Ph_3PAuNTf_2$, 5 mol % $AgNTf_2$ and 20 mol % Phen in CH_3CN (entry 1). By comparison with our previous work, silver was not essential (entry 2). Control experiments showed that gold is essential for the reaction (entries 3 and 4) and the yield is lower without Phen (entry 3). Further screenings of gold catalysts did not provide any improvement (entries 5−8), and no product was detected when we employed JohnPhosAuCl as a catalyst (entry 8).

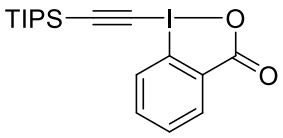
Other solvents also worked well, but the yields were lower than CH_3CN (entries 9−13). Other transition metal catalysts were ineffective (Table 1), such as aryl- and alkyl-substituted alkynes.

Table 1 Optimization of the Reaction Conditions[a]



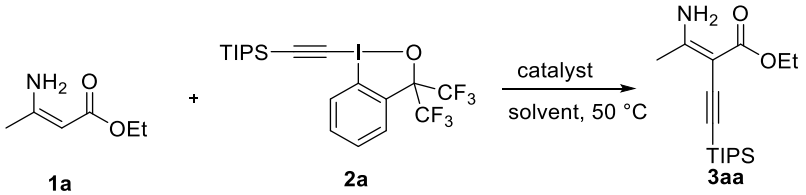
Entry	Catalyst	Yield (%)
1	$Cu(OTf)_2$	n.d.[c]
2	$Bi(OTf)_3$	n.d.
3	$Zn(OTf)_2$	n.d.
4	$In(OTf)_3$	n.d.
5[d]	$Ph_3PAuNTf_2$	72

[a]**1a** (0.10 mmol), **2a** (0.12 mmol), Catalyst (5 mol %), Phen (20 mol %) in solvent (1 mL) at 50 ℃. [b]Phen: 1,10-phenanthroline. [c]n.d.: not detected. [d]Replacement of **2a** with **2a′**.



2a'

Table 2 Optimization of the reaction conditions[a]



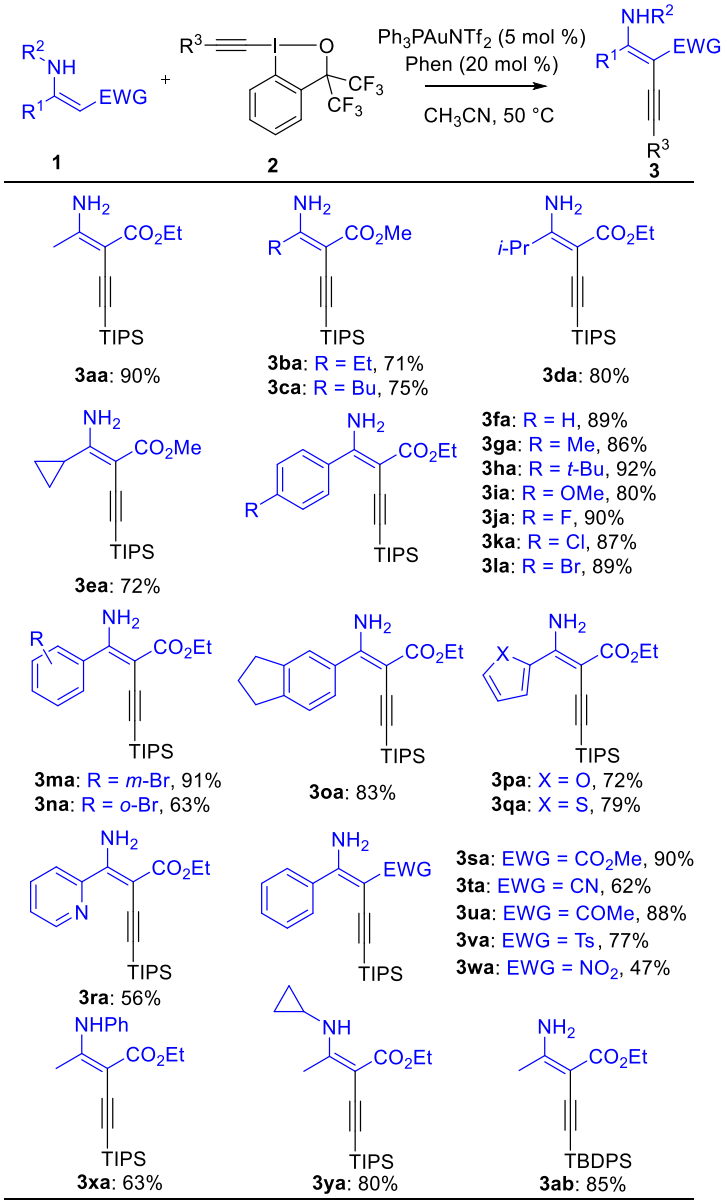
Entry	Catalyst	Ligand	Solvent	Yield (%)[b]
1	$Ph_3PAuNTf_2/AgNTf_2$	Phen[c]	CH_3CN	87 (88)[d]
2	**$Ph_3PAuNTf_2$**	**Phen**	**CH_3CN**	**90**
3	-	Phen	CH_3CN	n.d.[e]
4	$Ph_3PAuNTf_2$	-	CH_3CN	31
5	Ph_3PAuCl	Phen	CH_3CN	84
6	$(C_6F_5)_3PAuNTf_2$	Phen	CH_3CN	81

7	IPrAuCl	Phen	CH_3CN	12
8	JohnPhosAuCl	Phen	CH_3CN	n.d.[e]
9	$Ph_3PAuNTf_2$	Phen	DCE[f]	76
10	$Ph_3PAuNTf_2$	Phen	CH_3Cl	56
11	$Ph_3PAuNTf_2$	Phen	THF[g]	83
12	$Ph_3PAuNTf_2$	Phen	toluene	42
13	$Ph_3PAuNTf_2$	Phen	CH_2Cl_2	85

[a]**1a** (0.10 mmol), **2a** (0.12 mmol), catalyst (5 mol %), Phen (20 mol %) in solvent (1 mL) at 50 °C. [b]NMR yield with CH_2Br_2 as an internal standard. [c]Phen: 1,10-phenanthroline. [d]Isolated yield. [e]n.d.: not detected. [f]DCE : 1,2-dichloroethane. [g]THF : tetrahydrofuran.

Under the optimized reaction conditions (Table 2, entry 2) we investigated the substrate scope of this reaction. As shown in Scheme 2-4, a series of electron-donating groups such as Me-, Et-, Bu-, *i*-Pr-, cyclopropyl- on the alkyl 3-aminoacrylates were tolerated (**3aa**−**ea**). The structure of **3aa** was confirmed by single-crystal X-ray structure analysis (Figure 2). Also, an alkyl-substituted alkyl 3-aminoacrylates **1f** was tolerated and the product **3fa** could be obtained in 89% yield. Electron-donating groups such as Me-, *t*-Bu, OMe-, and cyclopentane- on the phenyl ring all converted to the corresponding products (**3ga**−**ia, 3oa**) in 80−92% yields. Additionally, the phenyl-substituted alkyl 3-aminoacrylates bearing electron-withdrawing groups (i.e., 4-F-, 4-Cl-, 4-Br-, 3-Br-, and 2-Br-) afforded the targets products (**3ja**−**na**) in 63−92% yields.

2.2.2 Substrate Scope



[a]Reaction conditions: **1** (0.10 mmol), **2** (0.12 mmol), $Ph_3PAuNTf_2$ (5 mol %), Phen (20 mol %) in CH_3CN (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 2-4 Reaction scope[a,b]

Furthermore, the corresponding products (**3pa**−**ra**) were obtained in 63−92% yields when the substrates such as furan, thiophene and pyridine were used. Notably, the ester moieties of **1a** were replaced by other ester, cyano, keto, *p*-toluenesulfonyl and nitro groups, underwent equally well, giving the corresponding functionalized products (**3sa**−**wa**) in good yields (47−90 %). Phenyl and cyclopropyl substituted amine **1x** and **1y** were well-tolerated, giving the product **3xa** and **3ya** in good yield. On the other hand, the TIPS group of **2a** could be replaced by TBDPS, giving the product **3ab** in 85% yield.

Furthermore, a gram-scale synthesis was conducted by a 4.0 mmol scale reaction of **1a** and **2a**. As shown in Scheme 2-5, the desired product **3aa** was obtained in 83% yield.

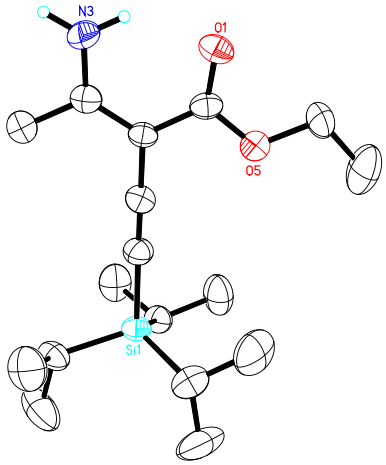
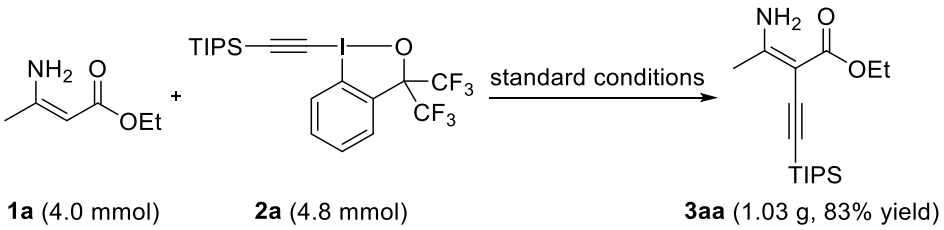
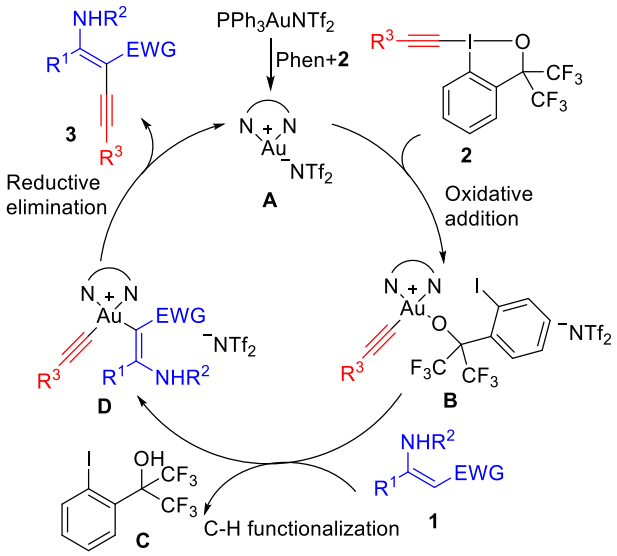


Figure 1. Solid state molecular structure of **3aa**



Scheme 2-5 Gram-scale synthesis



Scheme 2-6 Proposed reaction mechanism

According to previous reports in the literature,[30a, 31] a plausible mechanism is

described in Scheme 2-6. First, Au(I) species **A** is formed under the optimized reaction conditions. Subsequently, the species **A** undergoes an oxidative addition with hypervalent iodine reagent **2** to produce alkynyl Au(III) complex **B**. In comparison with simple olefins, the carbon-carbon double bond of alkyl 3-aminoacrylate **1** is more electron-rich because of the π-donating capacity of the nitrogen atom.[10] Then a Au(III) complex **D** is formed via direct C-H activation of Au(III) complex **B** with alkyl 3-aminoacrylates **1**. Finally, reductive elimination of Au(III) complex **D**, the desired product **3** is released meanwhile Au(I) species **A** is regenerated to complete the catalytic cycle.

2.3 Conclusions

In summary, we further revealed the applicability of Au(III) species by employing gold-catalyzed direct C(sp^2)-H alkynylation of alkyl 3-aminoacrylates with hypervalent iodine reagents for the synthesis of 1,3-enynes. The broad substrate scope, good functional group tolerance and excellent yields obtained render this method practical for organic synthesis especially total synthesis of nitrogen-containing natural products.

2.4 References

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2.5 Experimental Section

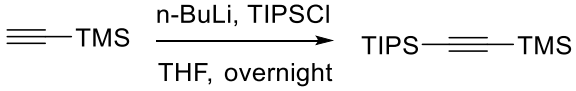
2.5.1 General Remarks

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

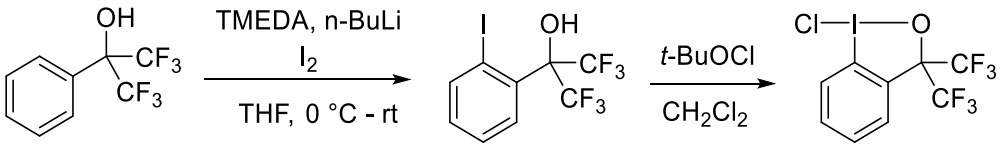
Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection 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: Preparation of **2a**



To a solution of trimethysilylacetylene (11 mmol) in THF (15 mL) was added n-BuLi (2.5 M in hexane, 10 mmol, 1 equiv) at -78 °C. After being stirred at -78 °C for 15 min, the reaction was further stirred at 0 °C for 10 min. After being cooled down to -78 °C again, TIPSCl (10 mmol, 1 equiv) was added. The reaction mixture was then allowed to warm to room temperature and stirred overnight. The reaction was quenched with saturated NH_4Cl solution. The resulting mixture was extracted with Et_2O (2 × 20 mL), the organic layers were combined, washed with saturated brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was afforded as a yellow oil (87% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12-1.08 (m, 21H), 0.20 (s, 9H). The spectroscopic data was consistent with the literature.[1]



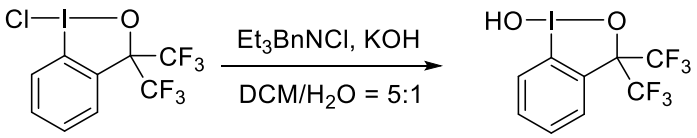
Under argon, TMEDA (465 mg, 4 mmol, 0.2 equiv) was added to a solution of n-BuLi (2.5 M in hexane, 44 mmol, 2.2 equiv). After 15 min, the cloudy solution was cooled to 0 °C and 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (20 mmol, 1 equiv) in THF (3 mL) was added dropwise. The reaction was stirred at 0 °C for 30 min and then at room

temperature overnight. I_2 (22 mmol, 1.1 equiv) in THF (10 mL) was added at 0 °C and the mixture was stirred at 0 °C for 30 minutes and room temperature for 4 h. The reaction was quenched with saturated NH_4Cl (aq). Ethyl acetate was added and the layers were separated. The aqueous layer was then extracted twice with ethyl acetate. The organic layers were combined, washed twice with saturated $Na_2S_2O_3$ (aq), dried over Na_2SO_4, and filtered. The resulting solvent was evaporated under the reduced pressure to afford 1,1,1,3,3,3-hexafluoro-2-(2-iodophenyl)propan-2-ol as an brown oil which was used without further purification.

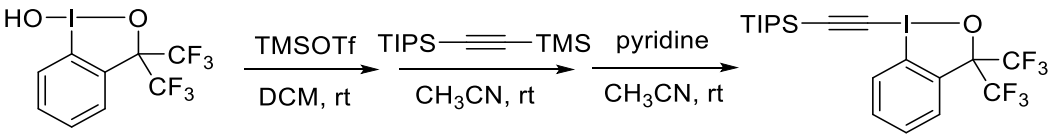
The crude product was dissolved in CH_2Cl_2 (20 mL) under air. *t*-BuOCl (21 mmol, 1.05 equiv) was then added dropwise at 0 °C. The resulting suspension was stirred under room temperature for 30 min. Then, the reaction mixture was filtered and washed with CH_2Cl_2 to afford in 45% yield as a yellow solid.

_t_-BuOCl

tert-Butyl alcohol (100 mmol) was dissolved in AcOH (6 mL) and cooled to 0 °C. To this reaction mixture an 12 % aqueous solution of sodium hypochlorite (130 mL) was added. After 10 min the organic phase was separated, washed with sat. $NaHCO_3$ (3 x 10 mL) and brine (10 mL) and dried over $CaCl_2$. The product was obtained as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 9H). The spectroscopic data was consistent with the literature.[2]

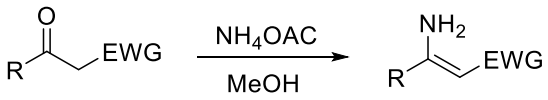


Under air, to a stirred solution of previous product (10 mmol, 1 equiv) in CH_2Cl_2 (20 mL) were added Et_3BnNCl (0.05 equiv) and KOH (10 mmol, 1 equiv) in water (4 mL). After stirring at room temperature for 12 h, the resulting suspension was filtered and washed with CH_2Cl_2 to afford desirable product in 74% yield as a colorless solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.03 – 7.85 (m, 2H), 7.78 – 7.69 (m, 2H). The spectroscopic data was consistent with the literature.[3]



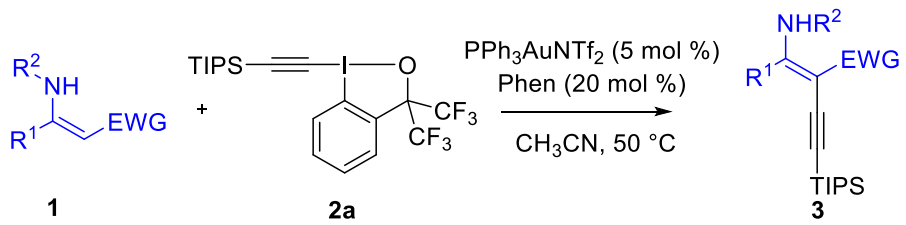
Under argon, to a solution of TMSOTf (1.1 equiv) was a suspension of previous chemical (1 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) at room temperature. After 30 min, the solvent was removed at 0 °C under vacuum, and then CH_3CN (3 mL) was added. Trimethyl(phenylethynyl)silane (1.3 equiv) was added to the mixture dropwise at 0 °C. Then, the resulting solution was warmed up to room temperature and stirred for 12 h. After that, a solution of pyridine (1.1 equiv) was added slowly, and the resulting mixture was stirred at room temperature for 3 h. The solvent was then evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford **2a** in 86% yield as a colorless solid.

Procedure B: Synthesis of **1**



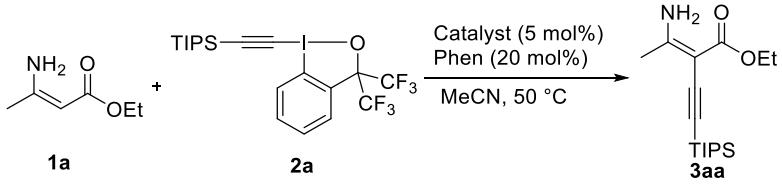
A solution of *β*-keto (2 mmol) and NH_4OAc (10 mmol) in methanol (2 mL) was stirred under reflux in oil bath for overnight. After the solvent was vaporated under reduced pressure, the residue was diluted with CH_2Cl_2 (10 mL). The organic solution was filtered and the solid was washed with CH_2Cl_2 (2 x 5 mL). The combined filtrate was washed with water and brine and then dried over anhydrous $MgSO_4$. Evaporation of the solvent with the aid of rotary evaporator afforded the desired product **1**, which was further purified by a silica gel column chromatography. The spectroscopic data has been previously reported.[4]

Procedure C: Synthesis of **3**



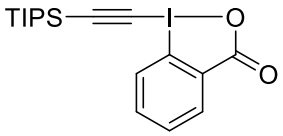
A mixture of **1** (0.10 mmol) and **2a** (0.12 mmol) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol %) and then heated to 50 °C in an oil bath. The reaction was monitored by TLC and upon completion, the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to afford the desired product **3**.

Table S1 Optimization of the Reaction Conditions[a]



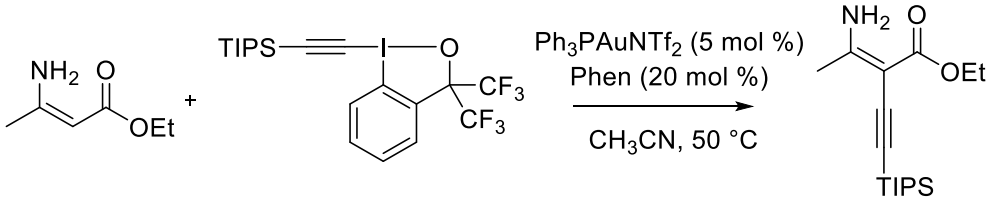
Entry	Catalyst	Yield (%)
1	$Cu(OTf)_2$	n.d.[c]
2	$Bi(OTf)_3$	n.d.
3	$Zn(OTf)_2$	n.d.
4	$In(OTf)_3$	n.d.
5[d]	$Ph_3PAuNTf_2$	72

[a]**1a** (0.10 mmol), **2a** (0.12 mmol), Catalyst (5 mol %), Phen (20 mol %) in solvent (1 mL) at 50 °C. [b]Phen: 1,10-phenanthroline. [c]n.d.: not detected. [d]Replacement of **2a** with **2a′**.



2a'

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



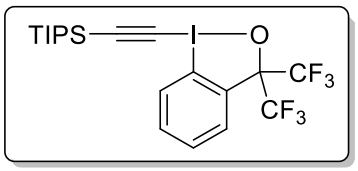
1a (4.0 mmol) **2a** (4.8 mmol) **3aa** (1.03 g, 83% yield)

A mixture of **1** (4 mmol) and **2a** (1.2 equiv) in 15 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol %) and then heated to 50 °C in an oil bath. The reaction was monitored by TLC and upon completion, the solvent was removed under

reduced pressure. The residue was purified by silica gel column chromatography to give product **3aa** in 83% yield.

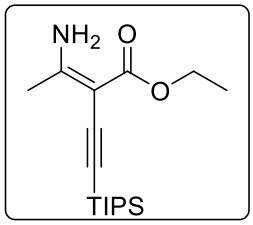
2.5.3 Characterization Data

((3,3-bis(trifluoromethyl)-1λ^3-benzo[d][1,2]iodaoxol-1(3H)-yl)ethynyl)triisopropylsilane 2a



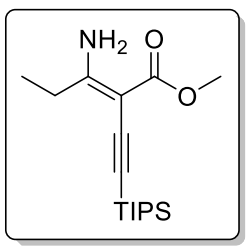
Yield: 472 mg, 0.86 mmol, 86%; colorless solid, mp 120-121 °C; R_f = 0.72 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 – 8.29 (m, 1H), 7.84 (m, 1H), 7.74 – 7.59 (m, 2H), 1.17 – 1.11 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 132.7 (d), 131.0 (d), 129.9 (s), 129.8 (m), 128.1 (d), 123.5 (q, $^1J_{C\text{-}F}$ = 290.0 Hz), 112.1 (s), 110.7 (s), 81.5 (m), 69.7 (s), 18.5 (q), 11.2 (d). IR (reflection) $\tilde{\nu}$ = 2948, 2894, 2867, 1566, 1464, 1440, 1368, 1265, 1217, 1181, 1164, 1150, 1135, 1118, 1070, 1045, 1018, 991, 964, 948, 882, 757, 729, 693, 678, 662 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{20}H_{26}F_6IOSi$ $[M+H]^+$: 551.0696, found: 551.0691.

ethyl (Z)-3-amino-2-((triisopropylsilyl)ethynyl)but-2-enoate (3aa)



Yield: 28 mg, 90 μmol, 90%; colorless solid, mp 64-65 °C; R_f = 0.65 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (brs, 1H), 5.05 (brs, 1H), 4.13 (q, J = 7.1 Hz, 2H), 2.22 (s, 3H), 1.28 (t, J = 7.1 Hz, 3H), 1.10 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1 (s), 165.5 (s), 103.9 (s), 92.0 (s), 82.4 (s), 59.6 (t), 22.4 (q), 18.7 (q, 6C), 14.2 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3389, 3299, 3219, 2941, 2891, 2864, 2147, 1643, 1624, 1515, 1462, 1367, 1271, 1159, 1110, 1075, 1017, 996, 961, 919, 884, 830, 789, 737, 675 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{17}H_{31}NO_2Si$ $[M]^+$: 309.2119, found: 309.2111.

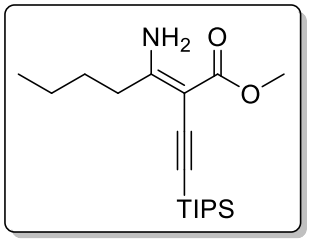
methyl (Z)-3-amino-2-((triisopropylsilyl)ethynyl)pent-2-enoate (3ba)



Yield: 22 mg, 71 μmol, 71%; yellow solid, mp 42-44 °C; R_f = 0.52 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (brs, 1H), 5.09 (brs, 1H), 3.70 (s, 3H), 2.57 (q, J = 7.6 Hz, 2H), 1.23 (t, J = 7.6 Hz, 3H), 1.10 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (s), 170.7 (s), 103.3 (s), 92.1 (s), 81.2 (s), 50.9 (q), 29.1 (t), 18.6

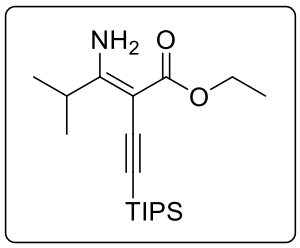
(q, 6C), 11.7 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3412, 3310, 2943, 2865, 2145, 1734, 1648, 1621, 1518, 1463, 1440, 1383, 1275, 1190, 1114, 1072, 1019, 996, 920, 883, 811, 793, 727, 676 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{17}H_{31}NO_2Si$ $[M]^+$: 309.2119, found: 309.2124.

methyl (Z)-3-amino-2-((triisopropylsilyl)ethynyl)hept-2-enoate (3ca)



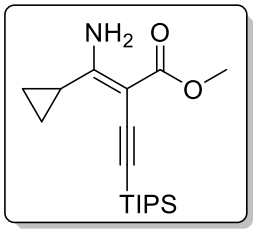
Yield: 25 mg, 75 μmol, 75%; colorless liquid; R_f = 0.64 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.85 (brs, 1H), 5.07 (brs, 1H), 3.69 (s, 3H), 2.60 – 2.45 (m, 2H), 1.70 – 1.57 (m, 2H), 1.40 (dt, J = 15.1, 7.4 Hz, 2H), 1.10 (m, 21H), 0.92 (t, J = 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8 (s), 169.9 (s), 103.6 (s), 92.1 (s), 81.6 (s), 51.0 (q), 35.9 (t), 29.8 (t), 22.6 (t), 18.7 (q, 6C), 13.8 (q), 11.6 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3426, 3313, 2943, 2864, 2143, 1672, 1616, 1517, 1463, 1437, 1382, 1365, 1271, 1189, 1115, 1083, 1015, 995, 919, 883, 824, 790, 728, 673 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{19}H_{36}NO_2Si$ $[M+H]^+$: 338.2510, found: 338.2502.

ethyl (Z)-3-amino-4-methyl-2-((triisopropylsilyl)ethynyl)pent-2-enoate (3da)



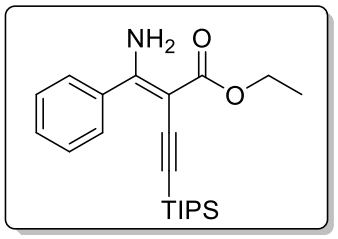
Yield: 27 mg, 80 μmol, 80%; colorless liquid; R_f = 0.63 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (brs, 1H), 5.12 (brs, 1H), 4.14 (q, J = 7.1 Hz, 2H), 3.51 – 3.33 (m, 1H), 1.28 (t, J = 7.1 Hz, 3H), 1.20 (s, 3H), 1.17 (s, 3H), 1.10 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (s), 170.6 (s), 103.3 (s), 92.5 (s), 81.0 (s), 59.6 (t), 32.2 (d), 19.8 (q, 2C), 18.7 (q, 6C), 14.2 (q), 11.5 (s, 3C). IR (reflection) $\tilde{\nu}$ = 3445, 3305, 2959, 2942, 2892, 2864, 2142, 1748, 1666, 1607, 1507, 1463, 1366, 1328, 1262, 1168, 1100, 1081, 1017, 995, 943, 919, 882, 859, 792, 731, 673 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{19}H_{35}NO_2Si$ $[M]^+$: 337.2432, found: 337.2435.

methyl (Z)-2-(amino(cyclopropyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ea)



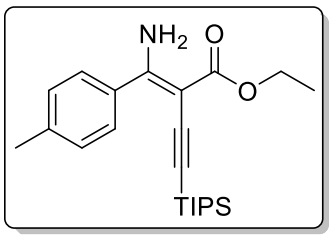
Yield: 26 mg, 72 μmol, 72%; yellow solid, mp 60-61 °C; R_f = 0.68 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (brs, 1H), 4.60 (brs, 1H), 3.70 (s, 3H), 2.53 – 2.35 (m, 1H), 1.09 (s, 21H), 1.03 – 0.97 (m, 2H), 0.78 (q, J = 5.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6 (s), 169.5 (s), 103.8 (s), 92.3 (s), 82.7 (s), 51.1 (q), 18.8 (q, 6C), 15.2 (d), 11.6 (d, 3C), 7.7 (t, 2C). IR (reflection) $\tilde{\nu}$ = 3430, 3309, 2943, 2891, 2864, 2142, 1659, 1608, 1510, 1462, 1441, 1383, 1342, 1281, 1244, 1194, 1091, 989, 932, 882, 849, 813, 787, 768, 726, 673, 658 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{32}NO_2Si$ $[M+H]^+$: 322.2197, found: 322.2189.

ethyl (Z)-2-(amino(phenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3fa)



Yield: 33 mg, 89 μmol, 89%; yellow liquid; R_f = 0.70 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (brs, 1H), 7.65 – 7.58 (m, 2H), 7.42 – 7.33 (m, 3H), 5.08 (brs, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.32 (t, J = 7.1 Hz, 3H), 0.95 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 (s), 166.1 (s), 137.2 (s), 129.8 (d), 128.18 (d, 2C), 128.16 (d, 2C), 104.1 (s), 91.3 (s), 82.9 (s), 60.1 (t), 18.6 (q, 6C), 14.3 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3418, 3304, 2941, 2864, 2141, 1652, 1605, 1576, 1519, 1488, 1463, 1366, 1267, 1146, 1097, 1023, 998, 908, 883, 794, 776, 734, 701, 676, 656 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{22}H_{33}NO_2Si$ $[M]^+$: 371.2275, found: 371.2259.

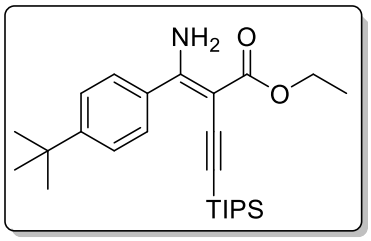
ethyl (Z)-2-(amino(p-tolyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ga)



Yield: 33 mg, 86 μmol, 86%; yellow solid, mp 74-75 °C; R_f = 0.74 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.00 (brs, 1H), 7.55 – 7.48 (m, 2H), 7.17 (dd, J = 8.4, 0.6 Hz, 2H), 5.10 (brs, 1H), 4.19 (q, J = 7.1 Hz, 2H), 2.36 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 0.95 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (s), 166.2 (s), 140.0 (s), 134.2 (s), 128.7 (d, 2C), 128.0 (d, 2C), 104.3 (s), 91.0 (s), 82.4 (s), 59.9 (t), 21.3 (q), 18.5 (q, 6C), 14.2 (q), 11.4 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3387, 3295, 3248, 3204, 2941, 2864, 2359, 2137, 1650, 1613, 1571, 1525, 1493, 1464, 1366, 1264,

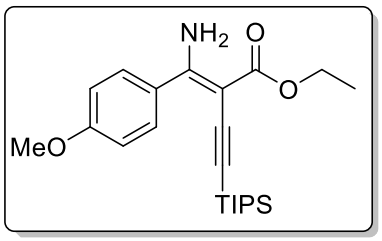
1144, 1117, 1097, 1022, 995, 909, 883, 829, 791, 747, 718, 674 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{23}H_{36}NO_2Si$ $[M+H]^+$: 386.2510, found: 386.2504.

ethyl (Z)-2-(amino(4-(tert-butyl)phenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ha)



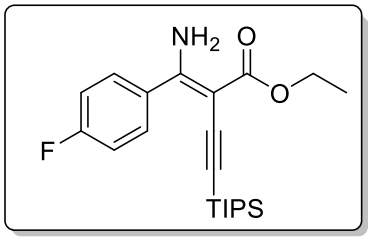
Yield: 39 mg, 92 μmol, 92%; colorless solid, mp 109-110 °C; R_f = 0.66 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.98 (brs, 1H), 7.62 – 7.49 (m, 2H), 7.44 – 7.34 (m, 2H), 5.10 (brs, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.34 – 1.28 (m, 12H), 0.94 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (s), 166.4 (s), 153.1 (s), 134.3 (s), 128.0 (d, 2C), 125.1 (d, 2C), 104.4 (s), 91.0 (s), 82.6 (s), 60.0 (t), 34.8 (s), 31.2 (q, 3C), 18.6 (q, 6C), 14.3 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3473, 3416, 3300, 2958, 2941, 2863, 2143, 1656, 1644, 1595, 1558, 1528, 1494, 1462, 1365, 1264, 1156, 1105, 1017, 995, 909, 882, 846, 835, 791, 734, 672, 659 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{42}NO_2Si$ $[M+H]^+$: 428.2979, found: 428.2963.

ethyl (Z)-2-(amino(4-methoxyphenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ia)



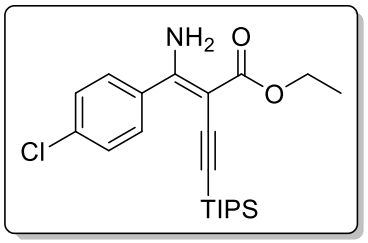
Yield: 32 mg, 80 μmol, 80%; yellow liquid; R_f = 0.60 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (brs, 1H), 7.64 – 7.58 (m, 2H), 6.91 – 6.85 (m, 2H), 5.07 (brs, 1H), 4.19 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 0.97 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8 (s), 165.8 (s), 160.9 (s), 129.8 (d, 2C), 129.4 (s), 113.5 (d, 2C), 104.6 (s), 91.1 (s), 82.4 (s), 60.0 (t), 55.4 (q), 18.7 (q, 6C), 14.3 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3425, 3298, 2941, 2863, 2139, 1739, 1664, 1605, 1572, 1494, 1463, 1366, 1251, 1177, 1146, 1096, 1030, 995, 882, 835, 810, 789, 747, 670 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{23}H_{35}NO_3Si$ $[M]^+$: 401.2381, found: 401.2402.

ethyl (Z)-2-(amino(4-fluorophenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ja)



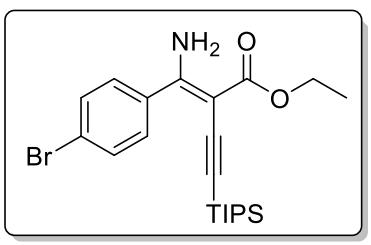
Yield: 35 mg, 90 μmol, 90%; colorless liquid; R_f = 0.61 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (brs, 1H), 7.69 – 7.55 (m, 2H), 7.12 – 6.98 (m, 2H), 5.03 (brs, 1H), 4.20 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.96 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5 (s), 164.8 (s), 163.6 (d, ^1J = 249.8 Hz), 133.2 (d, ^4J = 3.3 Hz), 130.4 (d, ^3J = 8.5 Hz, 2C), 115.2 (d, ^2J = 21.8 Hz, 2C), 103.9 (s), 91.6 (s), 83.2 (s), 60.1 (t), 18.6 (q, 6C), 14.3 (q), 11.4 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3492, 3419, 3303, 2942, 2864, 2143, 1668, 1609, 1586, 1498, 1465, 1366, 1267, 1234, 1159, 1145, 1097, 1016, 995, 882, 841, 789, 748, 673 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{33}FNO_2Si$ $[M+H]^+$: 390.2259, found: 390.2248.

ethyl (Z)-2-(amino(4-chlorophenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ka)



Yield: 35 mg, 87 μmol, 87%; yellow liquid; R_f = 0.74 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.96 (brs, 1H), 7.59 – 7.52 (m, 2H), 7.38 – 7.31 (m, 2H), 5.05 (brs, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.95 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 (s), 164.5 (s), 135.8 (s), 135.4 (s), 129.6 (d, 2C), 128.4 (d, 2C), 103.6 (s), 91.7 (s), 83.2 (s), 60.1 (t), 18.5 (q, 6C), 14.2 (q), 11.3 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3419, 3302, 2942, 2892, 2864, 2143, 1668, 1605, 1566, 1520, 1486, 1464, 1366, 1266, 1145, 1090, 1016, 995, 908, 883, 835, 789, 742, 721, 674 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{22}H_{32}ClNO_2Si$ $[M]^+$: 405.1885, found: 405.1891.

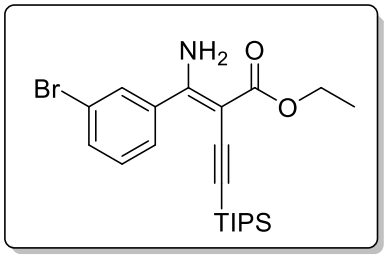
ethyl (Z)-2-(amino(4-bromophenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3la)



Yield: 40 mg, 89 μmol, 89%; yellow liquid; R_f = 0.55 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (brs, 1H), 7.61 – 7.41 (m, 4H), 5.04 (brs, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H), 0.95 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4 (s), 164.6 (s), 136.0

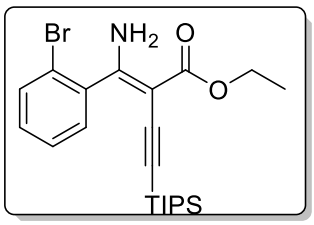
(s), 131.5 (d, 2C), 129.9 (d, 2C), 124.1 (s), 103.7 (s), 91.8 (s), 83.3 (s), 60.2 (t), 18.6 (q, 6C), 14.2 (q), 11.4 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3415, 3297, 2958, 2941, 2864, 2147, 1642, 1616, 1563, 1514, 1483, 1366, 1272, 1146, 1070, 1013, 992, 910, 885, 844, 790, 778, 742, 722, 676, 661 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{22}H_{32}BrNO_2Si$ $[M]^+$: 449.1380, found: 449.1395.

ethyl (Z)-2-(amino(3-bromophenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ma)



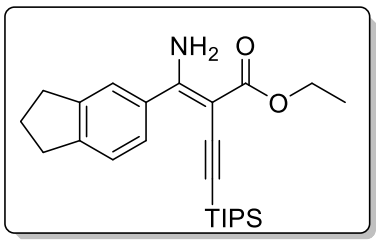
Yield: 41 mg, 91 μmol, 91%; yellow liquid; R_f = 0.72 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.94 (brs, 1H), 7.76 (t, *J* = 1.7 Hz, 1H), 7.58 – 7.49 (m, 2H), 7.26 (t, *J* = 7.9 Hz, 1H), 5.03 (brs, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H), 0.96 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3 (s), 164.0 (s), 139.1 (s), 132.8 (d), 131.2 (d), 129.9 (d), 126.7 (d), 122.2 (s), 103.4 (s), 92.0 (s), 83.5 (s), 60.2 (t), 18.6 (q, 6C), 14.2 (q), 11.4 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3419, 3300, 2941, 2891, 2864, 2143, 1669, 1604, 1561, 1518, 1469, 1402, 1366, 1261, 1149, 1099, 1073, 1018, 996, 917, 883, 863, 786, 738, 673 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{22}H_{32}BrNO_2Si$ $[M]^+$: 449.1380, found: 449.1394.

ethyl (Z)-2-(amino(2-bromophenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3na)



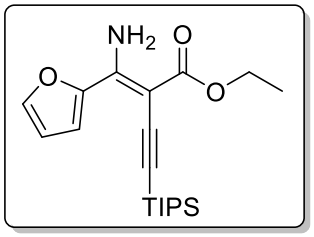
Yield: 28 mg, 63 μmol, 63%; yellow liquid; R_f = 0.75 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (brs, 1H), 7.58 (d, *J* = 8.1 Hz, 1H), 7.40 – 7.28 (m, 2H), 7.25 – 7.16 (m, 1H), 5.01 (brs, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.88 (m, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0 (s), 164.7 (s), 138.5 (s), 133.0 (d), 130.4 (d), 129.8 (d), 127.4 (d), 121.2 (s), 102.8 (s), 91.4 (s), 84.8 (s), 60.2 (t), 18.6 (q, 6C), 14.2 (q), 11.3 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3413, 3304, 3196, 3059, 2941, 2891, 2864, 2722, 2146, 1670, 1602, 1524, 1470, 1383, 1366, 1280, 1253, 1154, 1101, 1044, 1027, 995, 908, 883, 861, 790, 763, 740, 718, 673 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{22}H_{32}BrNO_2Si$ $[M]^+$: 449.1380, found: 449.1386.

ethyl (Z)-2-(amino(2,3-dihydro-1H-inden-5-yl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3oa)



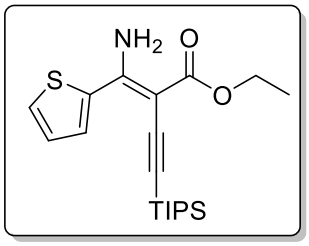
Yield: 34 mg, 83 μmol, 83%; yellow liquid; R_f = 0.68 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.01 (brs, 1H), 7.49 (s, 1H), 7.33 (d, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 7.7 Hz, 1H), 5.11 (brs, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.89 (td, *J* = 7.3, 4.3 Hz, 4H), 2.07 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 0.94 (m, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.8 (s), 167.0 (s), 146.4 (s), 144.0 (s), 135.1 (s), 125.8 (d), 124.4 (d), 124.1 (d), 104.5 (s), 90.9 (s), 82.4 (s), 60.0 (t), 32.82 (t), 32.76 (t), 25.6 (t), 18.6 (q, 6C), 14.3 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3420, 3299, 2941, 2863, 2144, 1731, 1666, 1601, 1572, 1517, 1482, 1365, 1266, 1217, 1184, 1089, 1018, 995, 882, 826, 790, 747, 672 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{25}H_{37}NO_2Si$ $[M]^+$: 411.2588, found: 411.2572.

ethyl (Z)-2-(amino(furan-2-yl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3pa)



Yield: 26 mg, 72 μmol, 72%; yellow liquid; R_f = 0.72 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.06 (brs, 1H), 7.98 (d, *J* = 3.6 Hz, 1H), 7.61 – 7.46 (m, 1H), 6.53 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.86 (brs, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1 (s), 152.0 (s), 147.4 (s), 143.5 (d), 117.2 (d), 112.3 (d), 104.7 (s), 96.3 (s), 79.5 (s), 60.2 (t), 18.8 (q, 6C), 14.4 (q), 11.6 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3500, 3304, 2943, 2865, 2138, 1663, 1598, 1576, 1508, 1463, 1366, 1258, 1176, 1140, 1085, 1020, 935, 883, 744, 669 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{20}H_{32}NO_3Si$ $[M+H]^+$: 362.2146, found: 362.2142.

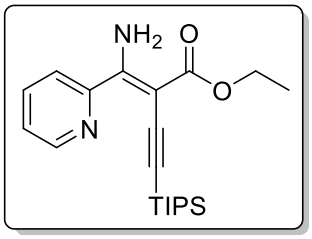
ethyl (Z)-2-(amino(thiophen-2-yl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3qa)



Yield: 30 mg, 79 μmol, 79%; yellow liquid; R_f = 0.76 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 3.8, 1.2 Hz, 1H), 7.43 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.06 (dd, *J* = 5.0, 3.8 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1

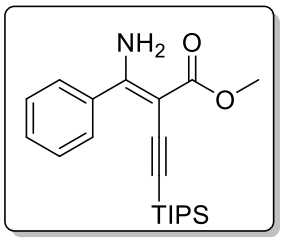
Hz, 3H), 1.06 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (s), 157.3 (s), 137.2 (s), 130.7 (d), 128.0 (d), 127.1 (d), 104.0(s), 94.2 (s), 82.7 (s), 60.2 (t), 18.6 (q, 6C), 14.2 (q), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3385, 3301, 3243, 3201, 3111, 2940, 2862, 2140, 1657, 1611, 1525, 1492, 1478, 1389, 1365, 1341, 1259, 1226, 1121, 1061, 1047, 1024, 996, 917, 881, 857, 848, 785, 756, 737, 722, 672, 653, 608 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{20}H_{31}NO_2SSi$ $[M]^+$: 377.1839, found: 377.1863.

ethyl (Z)-2-(amino(pyridin-2-yl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3ra)



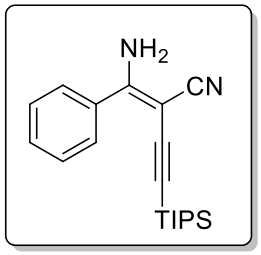
Yield: 21 mg, 56 μmol, 56%; yellow solid, mp 103-104 °C; R_f = 0.48 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.12 (brs, 1H), 8.80 (d, J = 8.1 Hz, 1H), 8.65 (d, J = 4.4 Hz, 1H), 7.69 (td, J = 7.9, 1.7 Hz, 1H), 7.34 (dd, J = 7.5, 4.9 Hz, 1H), 6.76 (brs, 1H), 4.23 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H), 1.06 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1 (s), 160.8 (s), 151.9 (s), 148.9 (d), 136.0 (d), 125.7 (d), 124.8 (d), 104.6 (s), 94.3 (s), 81.8 (s), 60.2 (t), 18.7 (q, 6C), 14.3 (q), 11.6 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3340, 3262, 3183, 2941, 2891, 2864, 2136, 1671, 1624, 1589, 1568, 1528, 1463, 1364, 1257, 1174, 1154, 1086, 1016, 995, 914, 881, 803, 776, 748, 732, 676, 655, 619 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{21}H_{32}N_2O_2Si$ $[M]^+$: 372.2228, found: 372.2233.

methyl (Z)-2-(amino(phenyl)methylene)-4-(triisopropylsilyl)but-3-ynoate (3sa)



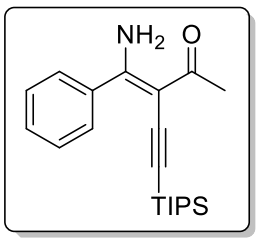
Yield: 32 mg, 90 μmol, 90%; yellow solid, mp 84-85 °C; R_f = 0.74 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (brs, 1H), 7.64 – 7.57 (m, 2H), 7.44 – 7.31 (m, 3H), 5.11 (brs, 1H), 3.76 (s, 3H), 0.94 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0 (s), 166.2 (s), 137.1 (s), 129.9 (d), 128.20 (d, 2C), 128.16 (d, 2C), 104.0 (s), 91.4 (s), 82.6 (s), 51.3 (q), 18.6 (q, 6C), 11.5 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3420, 3306, 2939, 2890, 2862, 2146, 1656, 1603, 1578, 1519, 1488, 1462, 1445, 1386, 1364, 1274, 1188, 1145, 1095, 1076, 987, 919, 883, 854, 795, 776, 729, 704, 674, 657 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{21}H_{31}NO_2Si$ $[M]^+$: 357.2119, found: 357.2124.

(Z)-2-(amino(phenyl)methylene)-4-(triisopropylsilyl)but-3-ynenitrile (3ta)



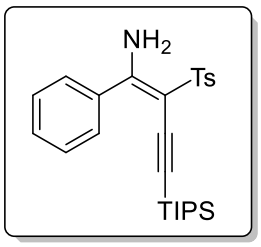
Yield: 20 mg, 62 μmol, 62%; yellow liquid; R_f = 0.52 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, J = 5.1, 2.6 Hz, 2H), 7.54 – 7.41 (m, 3H), 5.43 (s, 2H), 1.13 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3 (s), 133.2 (s), 131.3 (d), 128.9 (d, 2C), 127.6 (d, 2C), 118.6 (s), 98.9 (s), 98.6 (s), 64.7 (s), 18.6 (q, 6C), 11.2 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3446, 3326, 3219, 2943, 2891, 2865, 2205, 2143, 1623, 1539, 1496, 1463, 1409, 1244, 1181, 1074, 996, 920, 883, 773, 728, 699, 676, 660 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{20}H_{29}N_2Si$ $[M+H]^+$: 325.2095, found: 325.2087.

(Z)-3-(amino(phenyl)methylene)-5-(triisopropylsilyl)pent-4-yn-2-one (3ua)



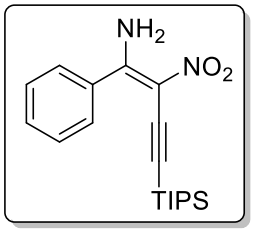
Yield: 30 mg, 88 μmol, 88%; colorless solid, mp 144-145 °C; R_f = 0.21 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.96 (brs, 1H), 7.86 – 7.78 (m, 2H), 7.40 – 7.27 (m, 3H), 5.73 (brs, 1H), 2.33 (s, 3H), 0.97 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7 (s), 169.7 (s), 140.9 (s), 129.9 (d), 128.2 (d, 2C), 127.4 (d, 2C), 106.3 (s), 94.3 (s), 92.2 (s), 23.7 (q), 18.7 (q, 6C), 11.4 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3306, 3166, 2941, 2890, 2863, 2141, 1591, 1572, 1461, 1383, 1315, 1300, 1282, 1253, 1177, 1138, 1072, 993, 882, 860, 669 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{21}H_{31}NOSi$ $[M]^+$: 341.2169, found: 341.2180.

(Z)-1-phenyl-2-tosyl-4-(triisopropylsilyl)but-1-en-3-yn-1-amine (3va)



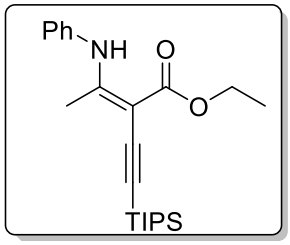
Yield: 35 mg, 77 μmol, 77%; yellow liquid; R_f = 0.33 (PE/EA = 3/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.2 Hz, 2H), 7.55 (dd, J = 7.7, 1.6 Hz, 2H), 7.41 – 7.27 (m, 5H), 2.42 (s, 3H), 0.84 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.5 (s), 143.5 (s), 139.0 (s), 136.8 (s), 130.2 (d), 129.3 (d, 2C), 128.3 (d, 2C), 128.1 (d, 2C), 127.5 (d, 2C), 100.7 (s), 95.1 (s), 92.9 (s), 21.6 (q), 18.5 (q, 6C), 11.2 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3435, 3334, 3221, 3062, 2942, 2890, 2864, 2131, 1733, 1617, 1533, 1495, 1463, 1444, 1404, 1283, 1226, 1183, 1153, 1128, 1079, 1018, 995, 919, 882, 811, 776, 735, 703, 671 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{26}H_{35}NO_2SSi$ $[M]^+$: 453.2153, found: 453.2166.

(Z)-2-nitro-1-phenyl-4-(triisopropylsilyl)but-1-en-3-yn-1-amine (3wa)



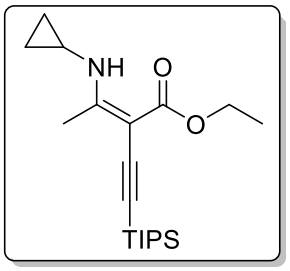
Yield: 16 mg, 47 μmol, 47%; yellow solid, mp 123-124 °C; R_f = 0.38 (PE/EA = 2/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.66 (brs, 1H), 7.66 – 7.57 (m, 2H), 7.54 – 7.38 (m, 3H), 5.95 (brs, 1H), 0.93 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0 (s), 134.9 (s), 131.1 (d), 128.7 (d, 2C), 128.1 (d, 2C), 100.4 (s), 97.0 (s), 18.5 (q, 6C), 11.2 (d, 3C). IR (reflection) $\tilde{\nu}$ = 3329, 3172, 2958, 2943, 2889, 2864, 2160, 1626, 1543, 1435, 1390, 1273, 1229, 1212, 1149, 1073, 1016, 998, 969, 917, 881, 846, 777, 758, 719, 698, 675, 644 cm^{-1}. HRMS (EI, m/z) calc'd for $C_{19}H_{28}N_2O_2Si$ $[M]^+$: 344.1915, found: 344.1926.

ethyl (Z)-3-(phenylamino)-2-((triisopropylsilyl)ethynyl)but-2-enoate (3xa)



Yield: 24 mg, 63 μmol, 63%; yellow solid, mp 43-44 °C; R_f = 0.83 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.29 (s, 1H), 7.35 (t, J = 7.7 Hz, 2H), 7.21 (t, J = 7.4 Hz, 1H), 7.08 (d, J = 7.8 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 2.29 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.11 (d, J = 2.5 Hz, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (s), 164.8 (s), 138.6 (s), 129.2 (d, 2C), 125.9 (d), 125.2 (d, 2C), 104.1 (s), 93.4 (s), 83.8 (s), 59.9 (t), 18.9 (q), 18.8 (q, 6C), 14.3(q), 11.6 (d, 3C). IR (reflection) $\tilde{\nu}$ = 2941, 2864, 2138, 1656, 1621, 1595, 1578, 1501, 1464, 1441, 1426, 1385, 1359, 1264, 1184, 1074, 1020, 994, 972, 918, 883, 854, 786, 760, 732, 697, 676 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{23}H_{36}NO_2Si$ $[M+H]^+$: 386.2510, found: 386.2509.

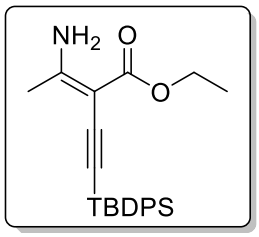
ethyl (Z)-3-(cyclopropylamino)-2-((triisopropylsilyl)ethynyl)but-2-enoate (3ya)



Yield: 28 mg, 80 μmol, 80%; colorless solid, mp 46-47 °C; R_f = 0.80 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 4.10 (q, J = 7.1 Hz, 2H), 2.60 (dt, J = 6.9, 3.0 Hz, 1H), 2.41 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H), 1.09 (m, 21H), 0.83 – 0.76 (m, 2H), 0.64 – 0.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8 (s), 169.1 (s), 104.7 (s), 92.0 (s), 81.2 (s), 59.5 (t), 25.4 (q), 18.8 (q, 6C), 18.2 (d), 14.3 (q), 11.6 (d, 3C), 7.8 (t, 2C). IR (reflection) $\tilde{\nu}$ = 3255, 2942, 2864, 2131, 1662, 1596, 1455, 1365, 1333, 1275, 1227, 1200, 1158, 1113, 1076, 1027, 993,

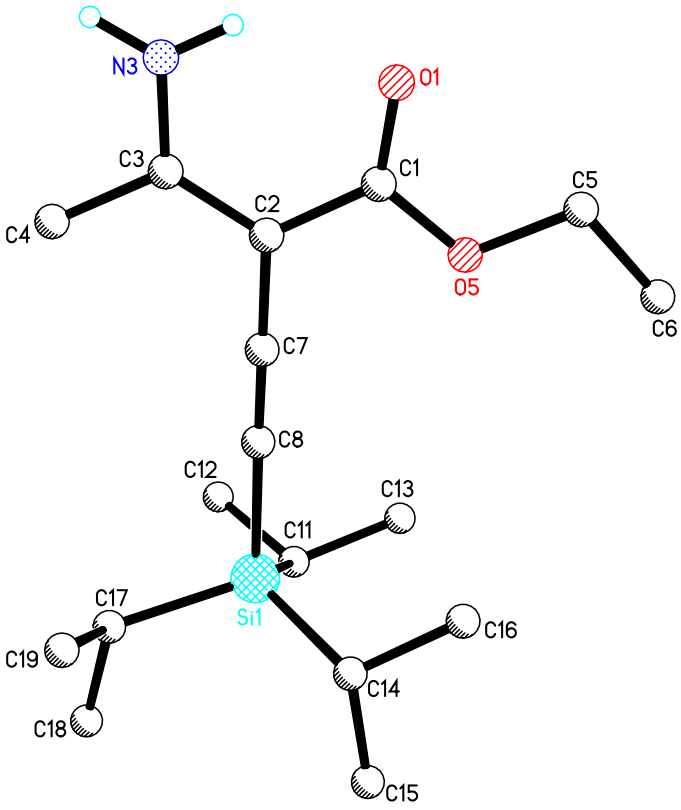
957, 935, 883, 843, 780, 733, 663 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{20}H_{36}NO_2Si$ $[M+H]^+$: 350.2510, found: 350.2500.

ethyl (Z)-3-amino-2-((tert-butyldiphenylsilyl)ethynyl)but-2-enoate (3ab)



Yield: 33 mg, 85 µmol, 85%; yellow solid, mp 94-95 °C; R_f = 0.42 (PE/EA = 5/1); ^1H NMR (300 MHz, $CDCl_3$) δ 8.93 (brs, 1H), 7.97 – 7.79 (m, 4H), 7.37 (dd, *J* = 5.2, 1.7 Hz, 6H), 5.16 (brs, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H), 1.11 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1 (s), 166.3 (s), 135.7 (d, 4C), 134.6 (s, 2C), 129.2 (d, 2C), 127.5 (d, 4C), 106.8 (s), 91.1 (s), 82.3 (s), 59.8 (t), 27.2 (q, 3C), 22.6 (q), 18.8 (s), 14.4 (q). IR (reflection) $\tilde{\nu}$ = 3411, 3308, 3215, 3073, 2961, 2898, 2860, 2149, 1644, 1619, 1515, 1472, 1428, 1371, 1272, 1108, 1019, 960, 909, 866, 834, 788, 735, 702, 609 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{30}NO_2Si$ $[M+H]^+$: 392.2040, found: 392.2055.

2.5.4 Solid state molecular structure of 3aa



2.5.5 References

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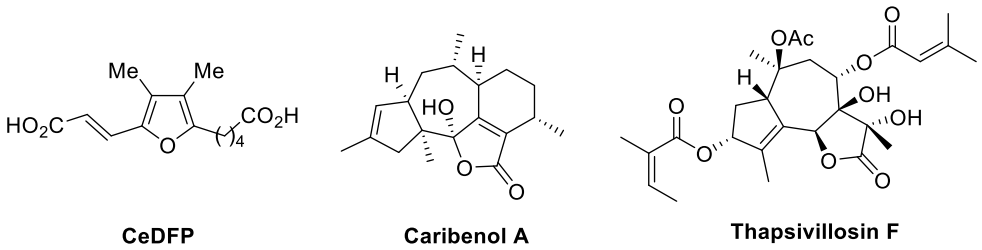
Chapter 3. Tetra-Substituted Furans by a Gold-Catalyzed Tandem C(sp^3)–H Alkynylation/Oxy-Alkynylation Reaction

3.1 Introduction

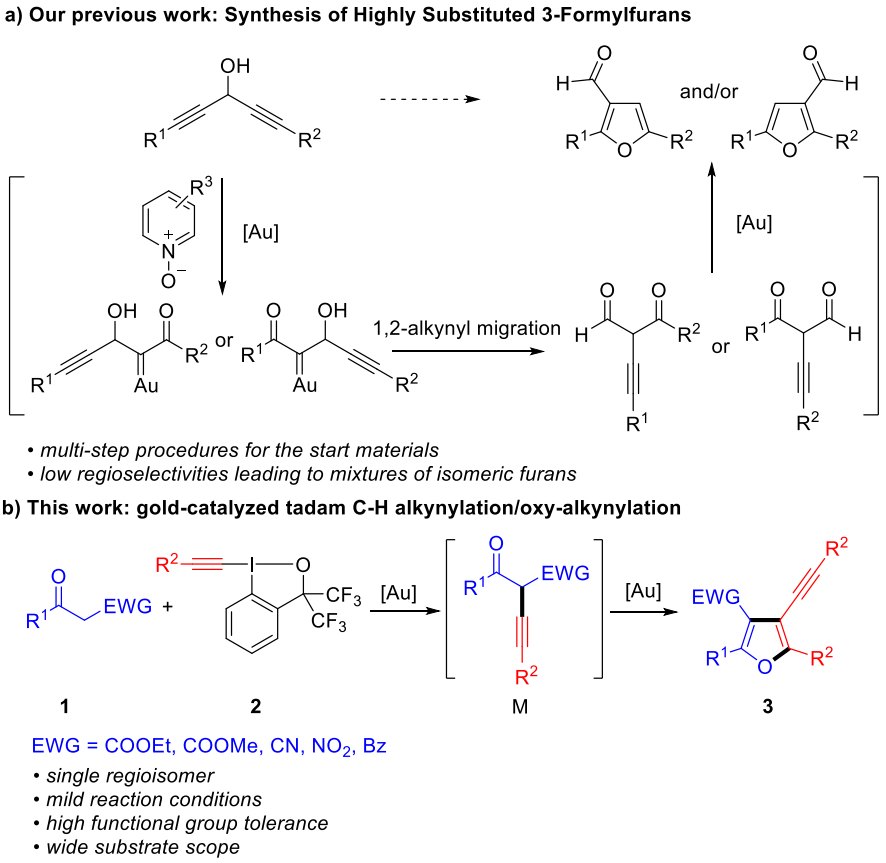
Poly-substituted Furans are important scaffold found in bioactive natural products, pharmacologically active molecules and polymer materials.[1] They are also valuable intermediates in synthetic chemistry (Scheme 3-1).[2] Generally, the main strategies for the synthesis of poly-substituted furans include the direct functionalization of existing furans[3] and intramolecular cyclization of acyclic compounds.[4] Because of the limitation of reaction scope, the direct functionalization of exiting furans is still a great challenge. For the latter method, intramolecular cyclization of acyclic compounds to give poly-substituted furans has been limited to multistep procedures. Furthermore, both methods need functionalization of precursors for the synthesis of tetrasubstituted furans.[5] Gold-catalyzed cyclization reactions have provided convenience for the synthesis of poly-substituted furans.[6] In 2014, our group reported a gold(I)-catalyzed cascade reaction for the synthesis of 3-formylfurans (Schema 3-2a), despite the efficiency of this strategy, the regioselectivities of substituted furans were still disadvantageous.[7] Thus, the development of efficient and simple method for the construction of tetrasubstituted furans is still an important subject.



Scheme 3-1 Selected bioactive compounds containing tetra-substituted furans

Gold-catalyzed reactions have been widely recognized as a powerful tool in the field of organic synthesis,[8] especially for the synthesis of heterocyclic[9] and complex polycyclic molecules.[10] Recently, alkynyl gold(III) species have attracted increasing attention from many organic chemists by reacting alkynyl-substituted hypervalent

iodine reagents with the aid of gold(I) catalyst.[11] For instance, Waser's group reported several



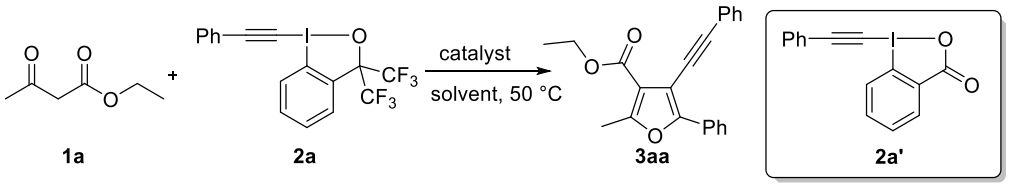
Scheme 3-2 Gold-catalyzed synthesis of poly-substituted furans

applications of alkynyl gold(III) species which introduced alkyne moieties on the heterocycles by using alkynyl-substituted hypervalent iodine reagents.[12] Liu's group disclosed a gold-catalyzed alkynylation reaction of terminal alkynes using alkynyl-substituted hypervalent iodine reagents.[13] Recently, we successfully demonstrated alkynyl gold(III) complexes as key to the further alkynylation of various substrates, such as *N*-propargylcarboxamides,[14] cyclopropenes,[15] phenols[16] and acceptor-substituted enamines. Further consideration, gold-catalyzed direct C(sp^3)-H alkynylation should be involved. Therein gold acts as a carbophilic Lewis acid to activate π-bonds by π-coordination, we envisioned that the acetylene-containing molecules by direct C(sp^3)-H alkynylation could further intramolecular cyclize in the present of alkynyl gold(III) complexes. Two reasons have made the construction of tetrasubstituted furans highly challenging by using alkynyl gold(III) complexes: 1) the

homocoupling side reaction of alkynyl gold(III) complexes and 2) the low stability of gold(III) intermediates.[15a, 16] Herein, we report the first gold-catalyzed tandem C-H alkynylation/oxy-alkynylation of *β*-keto compounds with hypervalent iodine reagents accessing tetrasubstituted furans (Scheme 3-2b).

3.2 Result and Discussion

3.2.1 Optimization of the Reaction Conditions



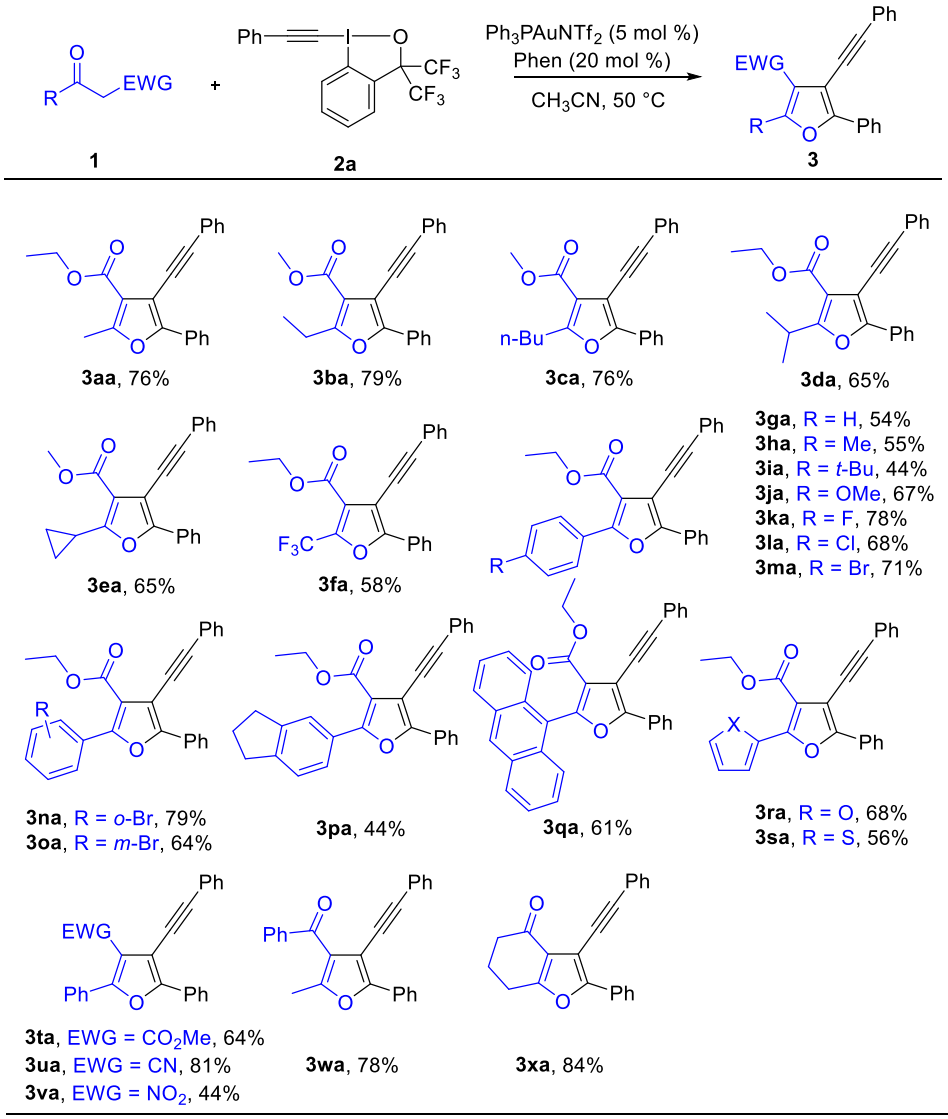
Entry	Catalyst	Ligand	Solvent	Yield (%)[b]
1[c]	$Ph_3PAuNTf_2/AgNTf_2$	Phen[d]	CH_3CN	55
2	$Ph_3PAuCl/AgNTf_2$	Phen	CH_3CN	73
3	**$Ph_3PAuNTf_2$**	**Phen**	**CH_3CN**	**78 (76)[e]**
4	-	Phen	CH_3CN	n.d.[f]
5	$Ph_3PAuNTf_2$	-	CH_3CN	trace
6	$(C_6F_5)_3PAuNTf_2$	Phen	CH_3CN	8
7	Ph_3PAuCl	Phen	CH_3CN	68
8	JohnPhosAuCl	Phen	CH_3CN	trace
9[g]	$Ph_3PAuNTf_2$	Phen	CH_3CN	74
10	$Ph_3PAuNTf_2$	Phen	DCE[h]	74
11	$Ph_3PAuNTf_2$	Phen	$CHCl_3$	50
12	$Ph_3PAuNTf_2$	Phen	THF[i]	22
13	$Ph_3PAuNTf_2$	Phen	toluene	28
14	$Ph_3PAuNTf_2$	Phen	CH_2Cl_2	64
15[j]	$Ph_3PAuNTf_2$	Phen	CH_3CN	27

[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.22 mmol), catalyst (5 mol %), Phen (20 mol %) in solvent (1.0 mL) at 50 °C. [b]NMR yield with CH_2Br_2 as an internal standard. [c]Room temperature. [d]Phen: 1,10-phenanthroline. [e]Isolated yield. [f]n.d.: not detected. [g]0.25 mmol **2a** was used. [h]DCE : 1,2-dichloroethane. [i]THF : tetrahydrofuran. [j]Replacement of **2a** with alkynylbenziodoxolone (**2a'**).

We began our study by using ethyl acetoacetate **1a** and alkynylbenziodoxole **2a** as model substrates (Table 1). Though the reaction was found to be slow at room temperature, the desired furan **3aa** was formed in 73% yield by using

$Ph_3PAuCl/AgNTf_2$ as catalyst and 1,10-phenanthroline as ligand in CH_3CN at 50 °C (entries 1−2). Control experiments indicated that silver was not essential (entry 3) and none or only trace product was detected in the absence of either gold catalyst or ligand (entries 4 and 5). Other gold catalysts like $(C_6F_5)_3PAuNTf_2$, IPrAuCl, or JohnPhosAuCl gave lower yields or only traces of the product (entries 6−8). Increasing the amount of **2a** did not result in any remarkable change in yield (entry 9). Furthermore, no improvement of the reaction was obtained by using other solvents (entries 10−14). Replacement of **2a** with alkynylbenziodoxolone led to a lower yield (27%) of the desired product **3aa** (entry 15).

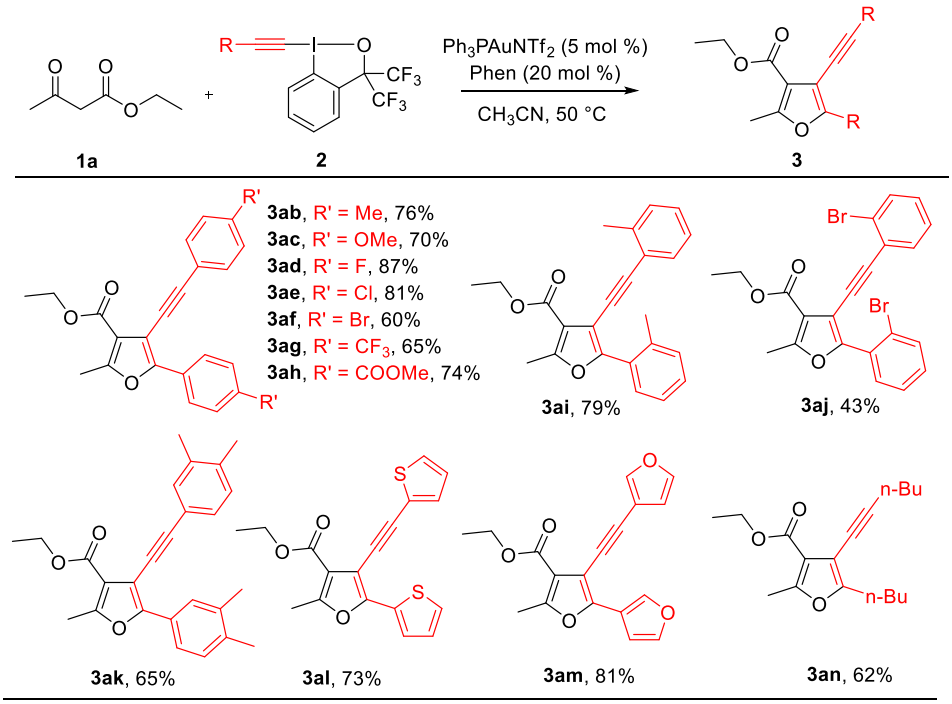
3.2.2 Substrate Scope



[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.22 mmol), $Ph_3PAuNTf_2$ (5 mol %), Phen (20 mol %) in CH_3CN (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 3-3 Scope with respect to different α-acceptor substituted ketones[a,b]

With the optimized reaction conditions in hand, the substrate scope of this reaction was investigated. We first examined various 1,3-dicarbonyl compounds and their variants. As shown in Scheme 3-3, a wide variety of alkyl substituents such as Me, Et, *n*-Bu, *i*-Pr, cyclopropyl, and CF_3 were well tolerated, affording the corresponding tetrasubstituted furans products (**3aa**−**fa**) in 58−79% yield. In addition, aryl-substituted 1,3-dicarbonyl compounds containing either electron-donating or electron-withdrawing groups such as H-, Me-, *t*-Bu-, OMe-, cyclopentane-, F-, Cl-, and Br- (*o*-, *m*-, or *p*-position) on the phenyl ring could smoothly convert to the target products (**3ga**−**pa**) in 44−79% yield. Anthracene-substituted 1,3-dicarbonyl **1q** delivered product **3qa** in 61% yield. Furthermore, heteroaromatic products (**3ra** and **3sa**) performed well under these reaction conditions. Notably, the ester moiety of **1g** was replaced by COOMe, CN, and NO_2 groups as well as dicarbonyl substrates **1w** and **1x**, giving the corresponding functionalized products (**3ta**−**xa**) in 44−84% yield.

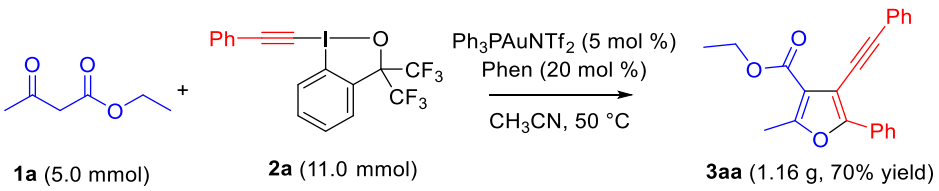


[a]Reaction conditions: **1a** (0.10 mmol), **2** (0.22 mmol), $Ph_3PAuNTf_2$ (5 mol %), Phen (20 mol %) in CH_3CN (1.0 mL) at 50 °C. [b]Isolated yield.

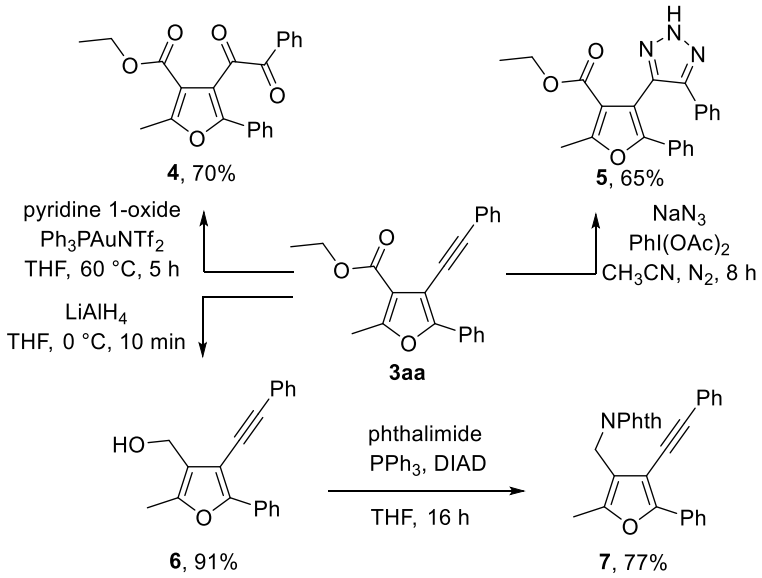
Scheme 3-4 Scope with respect to the hypervalent iodine reagents[a,b]

We next investigated the scope of hypervalent iodine reagents. As shown in Scheme 3-

4, aryl-substituted ethynylbenziodoxoles bearing electron-donating and electron-withdrawing groups such as Me-, OMe-, F-, Cl-, Br, CF_3-, and COOMe- on the *para* position of the phenyl ring react with ethyl acetoacetate **1a** to obtain corresponding products (**3ab**–**ah**) in 60–87% yield. Ethynylbenziodoxoles substituted on the *ortho* or *meta* position also smoothly convert to the target products (**3ai**–**ak**). Heteroaryl-derived products (**3al** and **3am**) were well tolerated under the standard reaction conditions. Notable, alkyl-substituted ethynylbenziodoxoles such as *n*-Bu group were also applicable in this transition, and the desired product **3an** was obtained in 62% yield. Moreover, a gram-scale synthesis of **3aa** was also possible (Scheme 3-5, 1.16 g of **3aa** was isolated).



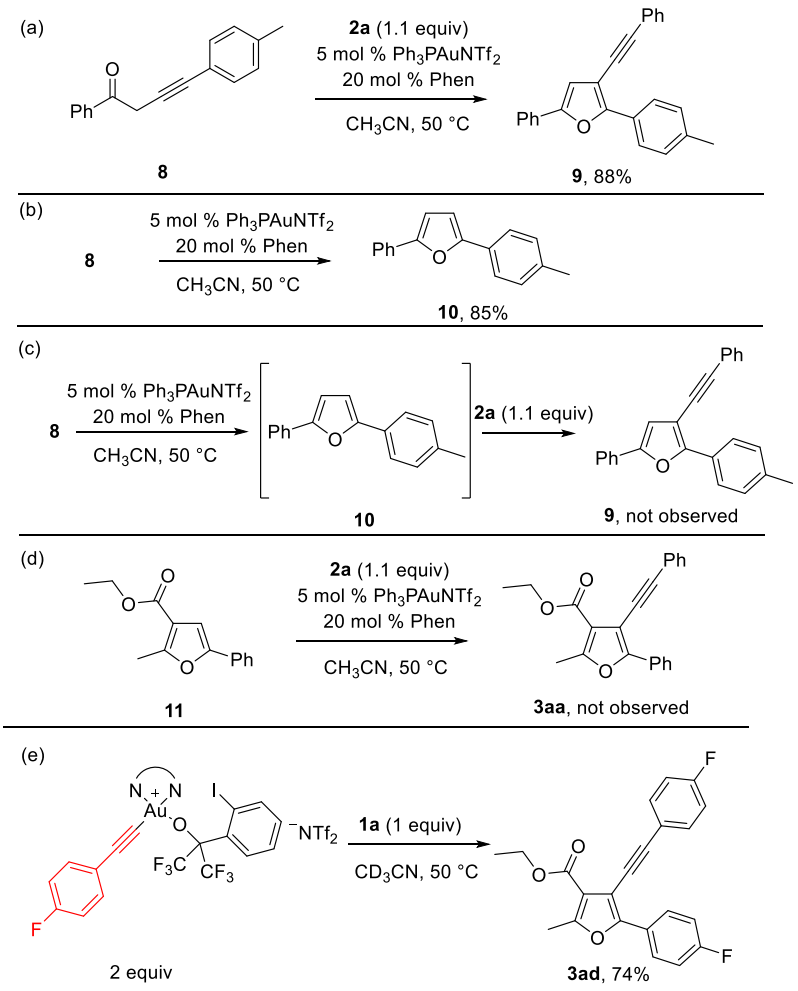
Scheme 3-5 Gram-scale synthesis



Scheme 3-6 Diverse transformations of **3aa**

To demonstrate the synthetic utility of the products, a variety of transformations were revealed (Scheme 3-6). A gold-catalyzed diketonization of tetrasubstituted furan **3aa** was tested by employing pyridine 1-oxide as an oxidant, and the desired product **4** was obtained in 70% yield. The PhI(OAc) promoted oxidative "click reaction" between **3aa**

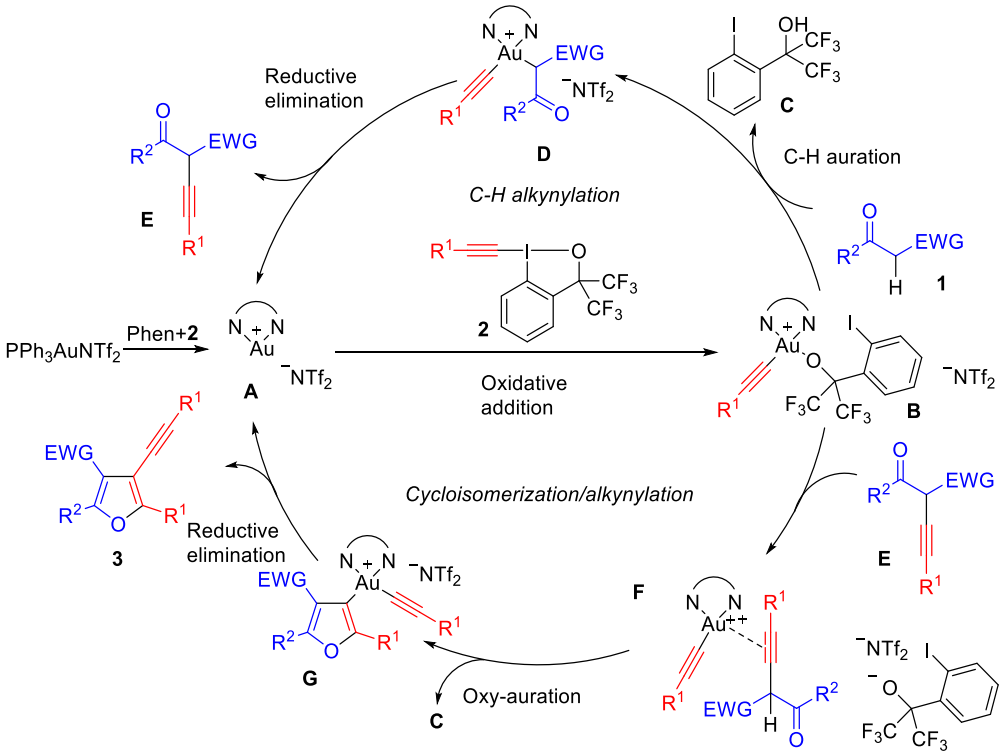
and sodium azide gave NH-1,2,3-triazole **5** in 65% yield. The reduction of **3aa** in the presence of $LiAlH_4$ provided product **6** in 91% yield. Next, the alcohol product **6** was directly converted to amine **7** in 77% yield through Mitsunobu reaction.



Scheme 3-7 Mechanistic experiments

To investigate the mechanism of this reaction, a series of mechanistic experiments were performed to gain further insight into the Au(I)/Au(III) catalytic cycle. The reaction of *β*-alkynyl ketone **8** and **2a** afforded the desired trisubstituted furan **9** in 85% yield under the standard reaction conditions (Scheme 3-7a), which indicated that this reaction first underwent C(sp^3)-H alkynylation, although many attempts to isolate the *β*-alkynyl ketone compound failed. In addition, *β*-alkynyl ketone **8** could smoothly convert to C3-unsubstituted furan **10** in the absence of **2a** (Scheme 3-7b), further adding **2a** to reaction b, no conversions were observed (Scheme 3-7c), thus suggesting that the alkynylation of the gold(I) 3-furyl complex is not involved in this reaction process. We reacted C3-

unsubstituted furan **11** and **2a** under the standard reaction conditions and the reaction failed to deliver tetrasubstituted furan **3aa** (Scheme 3-7d). This excludes a scenario of a direct C-H functionalization of the C3-unsubstituted furan, instead the alkynyl moiety of *β*-alkynyl ketone coordinates with the gold(III) complex followed by oxy-alkynylation and reductive elimination. The stoichiometric reaction of Au(III) complex with **1a** afforded tetrasubstituted furan **3ad** in 74% yield (Scheme 3-7e). The result implies that a Au(III) complex is formed and participates in the Au(I)/Au(III) catalytic cycle.



Scheme 3-8 Proposed reaction mechanism

On the basis of previous studies[15-16] and these experiments, a plausible mechanism[17] is described in Scheme 6. First, Au(I) species **A** is formed in the presence of 1,10-phenanthroline and hypervalent iodine reagent **2**. Subsequently, **A** undergoes an oxidative addition with hypervalent iodine reagent **2** to give alkynyl Au(III) complex **B**. C-H alkynylation of the activated C(sp^3)-H bond then occur between *β*- keto **1** and alkynyl Au(III) complex **B**, producing Au(III) complex **D**. The reductive elimination of Au(III) complex **D**, delivers alkynyl ketone **E**. In the second cycle, the alkynyl moiety

of **E** coordinates with alkynyl Au(III) complex **B**, subsequently, the intramolecular nucleophilic attack of the oxygen atom afford sAu(III) 3-furyl complex **G**. Upon reductive elimination of **G**, the desired product **3** is formed, meanwhile Au(I) species **A** is regenerated to complete the catalytic cycle.

3.3 Conclusions

In summary, by utilizing the unique redox property and carbophilic π acidity of gold, we reported the synthesis of tetrasubstituted furans by employing gold-catalyzed C(sp^3)-H alkynylation/oxy-alkynylation of *β*-keto compounds with hypervalent iodine reagents. The protocol offers a simple approach to tetrasubstituted furans, and features mild reaction conditions, high functional group tolerance, and a wide substrate scope. Moreover, diverse transformations of the tetrasubstituted furans were conducted highlighting potential applications of the prepared complex compounds. Gram-scale synthesis and proposed mechanism are also revealed.

3.4 References

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3.5 Experimental Section

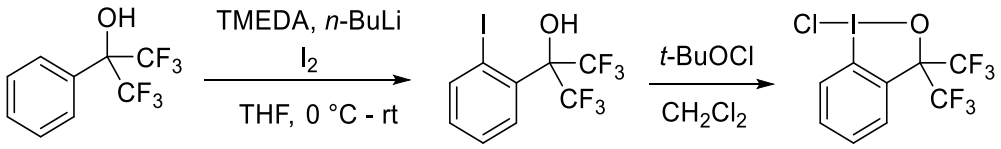
3.5.1 General Remarks

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: Preparation of **2**



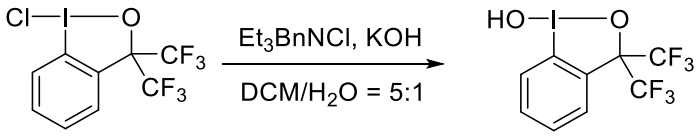
Under argon, TMEDA (4 mmol, 0.2 equiv) was added to a solution of n-BuLi (2.5 M in hexane, 44 mmol, 2.2 equiv). After 15 min, the cloudy solution was cooled to 0 °C and 1,1,1,3,3,3-hexafluoro-2-phenylpropan-2-ol (20 mmol, 1 equiv) in THF (3 mL) was added dropwise. The reaction was stirred at 0 °C for 30 min and then at room temperature overnight. I_2 (22 mmol, 1.1 equiv) in THF (10 mL) was added at 0 °C and the mixture was stirred at 0 °C for 30 min and room temperature for 4 h. The reaction was quenched with saturated NH_4Cl (aq). Ethyl acetate was added and the layers were separated. The aqueous layer was then extracted twice with ethyl acetate. The organic layers were combined, washed twice with saturated $Na_2S_2O_3$ (aq), dried over Na_2SO_4, and filtered. The resulting solvent was evaporated under the reduced pressure to afford 1,1,1,3,3,3-hexafluoro-2-(2-iodophenyl)propan-2-ol as a brown oil which was used without further purification.

The crude product was dissolved in CH_2Cl_2 (20 mL) under air. *t*-BuOCl (21 mmol, 1.05 equiv) was then added dropwise at 0 °C. The resulting suspension was stirred under room temperature for 30 min. Then, the reaction mixture was filtered and washed with CH_2Cl_2 to afford in 45% yield as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d,

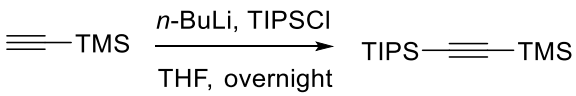
J = 8.5 Hz, 1H), 7.89 – 7.80 (m, 1H), 7.77 – 7.70 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.8 (d), 132.1 (s), 131.6 (d), 129.7 (m), 128.5 (d), 122.9 (q, $^1J_{C\text{-}F}$ = 289.6 Hz), 113.4 (s), 85.2 (m). IR (reflection) $\tilde{\nu}$ = 3100, 1738, 1593, 1564, 1462, 1442, 1289, 1263, 1237, 1193, 1155, 1136, 1119, 1102, 1043, 1007, 969, 950, 765, 757, 727, 690, 682, 667 cm^{-1}. The spectroscopic data is in agreement with that previously reported.[1]

_t_-BuOCl

tert-Butyl alcohol (100 mmol) was dissolved in AcOH (6 mL) and cooled to 0 °C. To this reaction mixture an 12 % aqueous solution of sodium hypochlorite (130 mL) was added. After 10 min the organic phase was separated, washed with sat. $NaHCO_3$ (3 x 10 mL) and brine (10 mL) and dried over $CaCl_2$. The product was obtained as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 9H). The spectroscopic data is in agreement with that previously reported.[2]

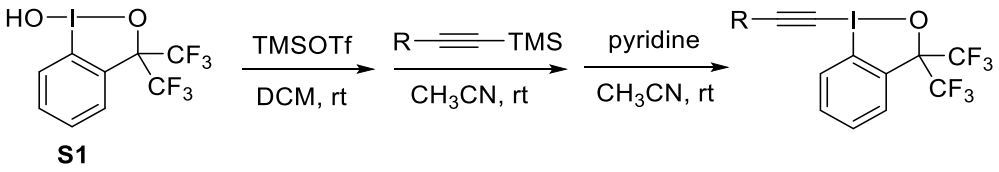


Under air, to a stirred solution of previous chemical (10 mmol, 1 equiv) in CH_2Cl_2 (20 mL) were added Et_3BnNCl (0.5 mmol, 0.05 equiv) and KOH (10 mmol, 1 equiv) in water (4 mL). After stirring at room temperature for 12 h, the resulting suspension was filtered and washed with CH_2Cl_2 to afford desirable product in 74% yield as a colorless solid. ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.03 – 7.85 (m, 2H), 7.78 – 7.69 (m, 2H). The spectroscopic data is in agreement with that previously reported.[1]



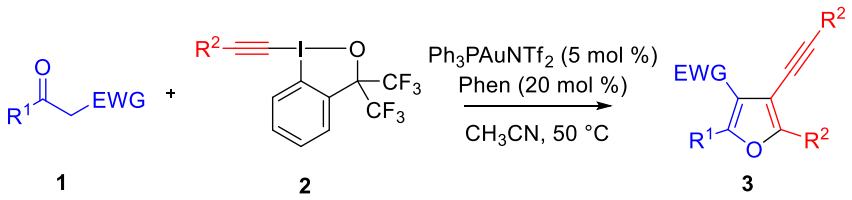
To a solution of trimethysilylacetylene (11 mmol) in THF (15 mL) was added n-BuLi (2.5 M in hexane, 10 mmol, 1 equiv) at -78 °C. After being stirred at -78 °C for 15 min, the reaction was further stirred at 0 °C for 10 min. After being cooled down to -78 °C again, TIPSCl (10 mmol, 1 equiv) was added. The reaction mixture was then allowed to warm to room temperature and stirred overnight. The reaction was quenched with

saturated NH_4Cl solution. The resulting mixture was extracted with Et_2O (2 × 20 mL), the organic layers were combined, washed with saturated brine (20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the crude product was afforded as a yellow oil (87% yield); ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 – 1.08 (m, 21H), 0.20 (s, 9H). The spectroscopic data is in agreement with that previously reported.[1]



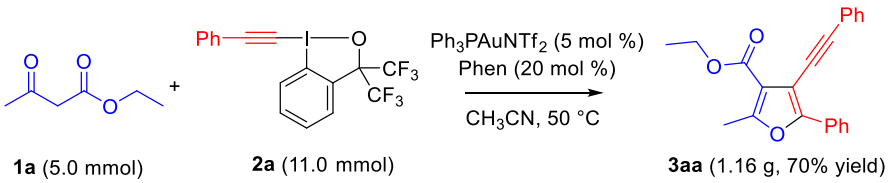
Under argon, TMSOTf (1.1 equiv) was added dropwise to a suspension of **S1** (1 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) at room temperature. After 30 min, the solvent was removed at 0 °C under vacuum, and then CH_3CN (3 mL) was added. Trimethyl(phenylethynyl)silane (1.3 equiv) was added to the mixture dropwise at 0 °C. Then, the resulting solution was warmed up to room temperature and stirred for 12 h. After that, a solution of pyridine (1.1 equiv) was added slowly, and the resulting mixture was stirred at room temperature for 3 h. The solvent was then evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel to afford **2a** in 86% yield as a colorless solid.

Procedure B: Synthesis of chemical **3**



A mixture of **1** (0.10 mmol) and **2** (0.22 mmol) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 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.

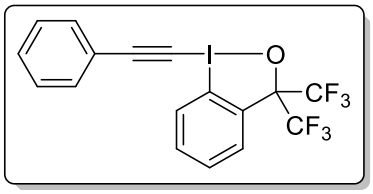
Procedure C: Gram-Scale Synthesis **3aa**



A mixture of **1a** (5.0 mmol) and **2** (11.0 mmol) in 15.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 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 solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3aa** in 70% yield (1.16 g).

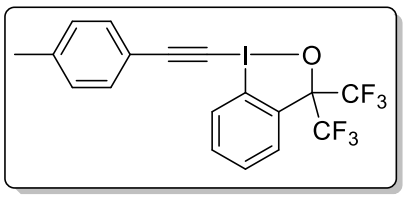
3.5.3 Characterization Data

1-(phenylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodaoxole (2a)



Yield: 405 mg, 86%; colorless solid, mp 132-133 °C; R_f = 0.46 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 – 8.23 (m, 1H), 7.86 (m, 1H), 7.77 – 7.65 (m, 2H), 7.63 – 7.52 (m, 2H), 7.49 – 7.35 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 133.1 (d), 132.8 (d, 2C), 131.4 (d), 130.3 (d), 130.1 (s), 130.0 (m), 128.8 (d, 2C), 128.5 (d), 123.7 (q, $^1J_{C\text{-}F}$ = 290.8 Hz), 121.4 (s), 111.5 (s), 105.4 (s), 81.8 (m), 54.5 (s). IR (reflection) $\tilde{\nu}$ = 2139, 1738, 1595, 1567, 1488, 1466, 1442, 1290, 1259, 1182, 1151, 1137, 1071, 1048, 1026, 964, 947, 873, 794, 754, 728, 691, 664, 641 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_{10}F_6IO$ $[M+H]^+$: 470.9675, found: 470.9680.

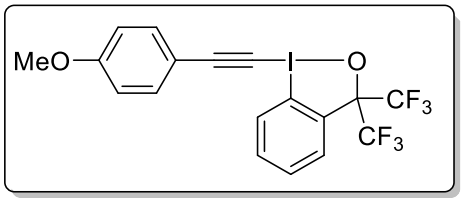
1-(*p*-tolylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodaoxole (2b)



Yield: 364 mg, 75%; colorless solid, mp 124-125 °C; R_f = 0.70 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 – 8.25 (m, 1H), 7.90 – 7.82 (m, 1H), 7.73 – 7.64 (m, 2H), 7.45 (m, 2H), 7.21 (m, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 140.8 (s), 132.9 (d), 132.6 (d, 2C), 131.2 (d),

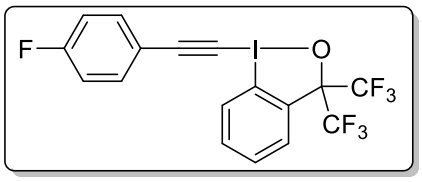
130.1 (s) 129.9 (m), 129.4 (d, 2C), 128.3 (d), 123.6 (q, $^{1}J_{C\text{-}F}$ = 290.6 Hz), 118.2 (s), 111.5 (s), 105.7 (s), 81.7 (m), 53.5 (s), 21.6 (q). IR (reflection) $\tilde{\nu}$ = 3079, 3030, 2930, 2139, 1738, 1606, 1565, 1505, 1464, 1440, 1379, 1289, 1255, 1183, 1148, 1046, 1019, 963, 949, 814, 761, 753, 727, 691, 662, 640 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{12}F_6IO$ $[M+H]^+$: 484.9832, found: 484.9826.

1-((4-methoxyphenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2c)



Yield: 165 mg, 33%; pale yellow solid, mp 91-92 °C; R_f = 0.42 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 – 8.24 (m, 1H), 7.89 – 7.80 (m, 1H), 7.74 – 7.63 (m, 2H), 7.55 – 7.46 (m, 2H), 6.97 – 6.87 (m, 2H), 3.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 161.1 (s), 134.4 (d, 2C), 132.9 (d), 131.1 (d), 130.1 (s), 129.9 (m), 128.3 (d), 123.6 (q, $^{1}J_{C\text{-}F}$ = 290.6 Hz), 114.3 (d, 2C), 113.2 (s), 111.6 (s), 105.9 (s), 81.6 (m), 55.4 (q), 52.7 (s). IR (reflection) $\tilde{\nu}$ = 3076, 2966, 2843, 2135, 1738, 1603, 1565, 1508, 1464, 1440, 1295, 1253, 1219, 1183, 1165, 1150, 1138, 1029, 965, 946, 832, 762, 728, 690, 663, 641 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{12}F_6IO_2$ $[M+H]^+$: 500.9781, found: 500.9787.

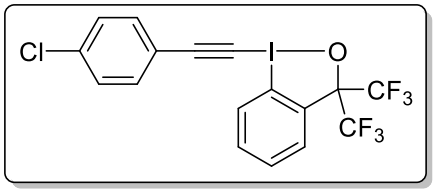
1-((4-fluorophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2d)



Yield: 321 mg, 64%; colorless solid, mp 136-137 °C; R_f = 0.62 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 – 8.21 (m, 1H), 7.85 (m, 1H), 7.76 – 7.64 (m, 2H), 7.61 – 7.49 (m, 2H), 7.16 – 7.04 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 163.5 (d, $^{1}J_{C\text{-}F}$ = 252.8 Hz), 134.7 (d, $^{3}J_{C\text{-}F}$ = 8.7 Hz), 132.9 (d), 131.2 (d), 129.94 (s), 129.86 (m), 128.2 (d), 123.5 (q, $^{1}J_{C\text{-}F}$ = 290.5 Hz), 117.4 (d, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 116.0 (d, $^{2}J_{C\text{-}F}$ = 22.3 Hz), 111.3 (s), 104.0 (s), 81.6 (m), 54.3 (s). IR (reflection) $\tilde{\nu}$ = 2144, 1748, 1599, 1566, 1505, 1465, 1441, 1289, 1266, 1205, 1184, 1166, 1146, 1118, 1094, 1048, 1017, 968, 949, 837, 763, 739, 728, 691, 663, 641 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_9F_7IO$ $[M+H]^+$: 488.9581, found:

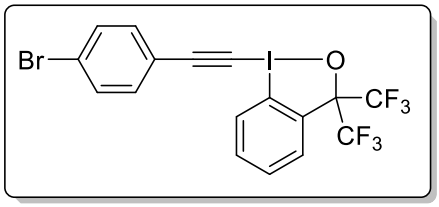
488.9584.

1-((4-chlorophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2e)



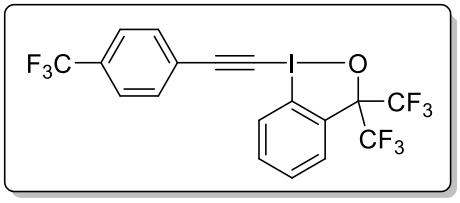
Yield: 479 mg, 95%; pale yellow solid, mp 118-119 °C; R_f = 0.55 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.21 (m, 1H), 7.89 – 7.81 (m, 1H), 7.74 – 7.66 (m, 2H), 7.52 – 7.45 (m, 2H), 7.41 – 7.35 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 136.4 (s), 133.8 (d, 2C), 133.0 (d), 131.3 (d), 130.02(s), 129.97 (m), 129.1 (d, 2C), 128.3 (d), 123.6 (q, $^1J_{C\text{-}F}$ = 290.6 Hz), 119.8 (s), 111.4 (s), 103.9 (s), 81.7 (m), 55.9 (s). IR (reflection) $\tilde{\nu}$ = 2133, 1738, 1563, 1487, 1462, 1439, 1399, 1295, 1262, 1219, 1185, 1164, 1148, 1118, 1095, 1045, 1015, 964, 947, 827, 800, 761, 729, 691, 664, 645 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_9ClF_6IO$ $[M+H]^+$: 504.9285, found: 504.9280.

1-((4-bromophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2f)



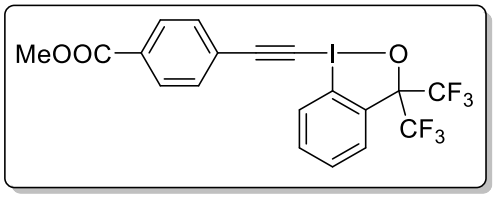
Yield: 467 mg, 85%; pale yellow solid, mp 149-150 °C; R_f = 0.54 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.20 (m, 1H), 7.85 (m, 1H), 7.75 – 7.65 (m, 2H), 7.58 – 7.50 (m, 2H), 7.45 – 7.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.9 (d, 2C), 133.0 (d), 132.0 (d, 2C), 131.3 (d), 130.0 (s), 129.9 (m), 128.3 (d), 124.7 (s), 123.6 (q, $^1J_{C\text{-}F}$ = 291.0 Hz), 120.2 (s), 111.3 (s), 103.9 (s), 81.5 (m), 56.1 (s). IR (reflection) $\tilde{\nu}$ = 2131, 1738, 1564, 1484, 1462, 1440, 1394, 1263, 1219, 1185, 1165, 1148, 1132, 1070, 1045, 1012, 964, 947, 824, 796, 762, 729, 691, 664, 641, 612 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_9BrF_6IO$ $[M+H]^+$: 548.8780, found: 548.8778.

3,3-bis(trifluoromethyl)-1-((4-(trifluoromethyl)phenyl)ethynyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2g)



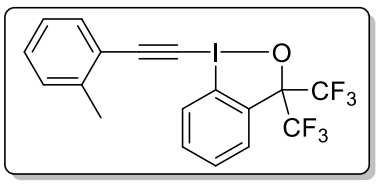
Yield: 422 mg, 78%; colorless solid, mp 124-125 °C; R_f = 0.60 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.22 (m, 1H), 7.87 (m, 1H), 7.76 – 7.68 (m, 2H), 7.67 (s, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.1 (d), 132.8 (d, 2C), 131.7 (q, $^2J_{C\text{-}F}$ = 33.0 Hz), 131.4 (d), 130.04 (m), 130.01 (s), 125.6 (q, $^3J_{C\text{-}F}$ = 3.7 Hz), 125.12 (s), 125.11 (s) 123.6 (q, $^1J_{C\text{-}F}$ = 272.4 Hz), 123.5 (q, $^1J_{C\text{-}F}$ = 291.5 Hz), 111.3 (s), 103.1 (s), 81.7 (m), 57.8 (s). IR (reflection) $\tilde{\nu}$ = 3072, 2146, 1747, 1615, 1566, 1465, 1440, 1405, 1321, 1296, 1264, 1183, 1148, 1123, 1106, 1066, 1047, 1017, 964, 948, 841, 820, 755, 728, 691, 664, 641, 608 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_9F_9IO$ $[M+H]^+$: 538.9549, found: 538.9546.

4-((3,3-bis(trifluoromethyl)-1λ^3-benzo[*d*][1,2]iodaoxol-1(3H)-yl)ethynyl)benzoate (2h)



Yield: 386 mg, 73%; colorless solid, mp 195-196 °C; R_f = 0.58 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 – 8.22 (m, 1H), 8.10 – 8.04 (m, 2H), 7.89 – 7.83 (m, 1H), 7.75 – 7.67 (m, 2H), 7.64 – 7.58 (m, 2H), 3.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 166.1 (s), 133.1 (d), 132.5 (d, 2C), 131.4 (d), 131.2 (s), 130.0 (m), 129.7 (d, 2C), 128.4 (d), 125.8 (s), 123.5 (q, ^1J = 290.6 Hz), 111.3 (s), 103.9 (s), 81.7 (m), 58.0 (s), 52.4 (q). IR (reflection) $\tilde{\nu}$ = 3066, 3005, 2953, 2847, 2148, 1702, 1605, 1563, 1466, 1435, 1405, 1314, 1286, 1267, 1180, 1150, 1133, 1118, 1048, 1019, 970, 952, 881, 862, 843, 776, 766, 754, 732, 693, 683, 664, 644, 620 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{19}H_{12}F_6IO_3$ $[M+H]^+$: 528.9730, found: 528.9738.

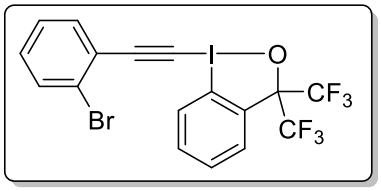
1-(*o*-tolylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2] iodaoxole (2i)



Yield: 382 mg, 79%; colorless solid, mp 147-148 °C; R_f = 0.52 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37 – 8.28 (m, 1H), 7.91 – 7.81 (m, 1H), 7.76 – 7.64 (m, 2H), 7.53 (dd, J = 7.6, 0.9 Hz, 1H), 7.38 – 7.17 (m,

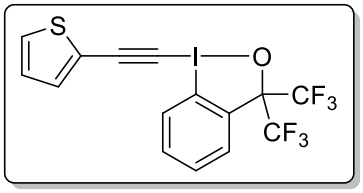
3H), 2.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.5 (s), 133.1 (d), 132.8 (d), 131.1 (d), 130.1 (d), 129.99 (s), 129.86 (m), 129.8 (d), 128.2 (d), 125.8 (d), 123.5 (q, $^1J_{C\text{-}F}$ = 291.0 Hz), 121.1 (s), 111.5 (s), 104.3 (s), 81.6 (m), 57.4 (s), 20.8 (q). IR (reflection) $\tilde{\nu}$ = 3075, 2928, 2136, 1739, 1562, 1481, 1464, 1438, 1381, 1287, 1264, 1219, 1176, 1149, 1132, 1043, 1017, 962, 952, 943, 833, 759, 750, 728, 712, 692, 681, 660, 641 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{12}F_6IO$ $[M+H]^+$: 484.9832, found: 484.9832.

1-((2-bromophenyl)ethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2j)



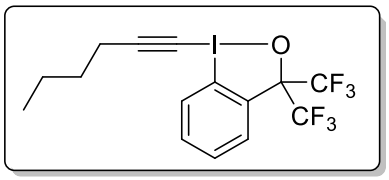
Yield: 452 mg, 83%; colorless solid, mp 140-141 °C; R_f = 0.53 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 – 8.42 (m, 1H), 7.86 (m, 1H), 7.78 – 7.61 (m, 3H), 7.57 (dd, J = 7.6, 1.9 Hz, 1H), 7.40 – 7.23 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 134.3 (d), 133.0 (d), 132.6 (d), 131.2 (d), 131.0 (d), 129.8 (m), 128.7 (d), 127.2 (d), 126.0 (s), 123.7 (s), 123.5 (q, $^1J_{C\text{-}F}$ = 291.0 Hz), 111.4 (s), 102.8 (s), 81.6 (m), 59.4 (s). IR (reflection) $\tilde{\nu}$ = 3077, 2145, 1738, 1563, 1465, 1438, 1287, 1262, 1251, 1220, 1194, 1176, 1150, 1135, 1045, 1027, 962, 952, 944, 808, 752, 728, 691, 681, 660, 641 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_9BrF_6IO$ $[M+H]^+$: 548.8780, found: 548.8781.

1-(thiophen-2-ylethynyl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2l)



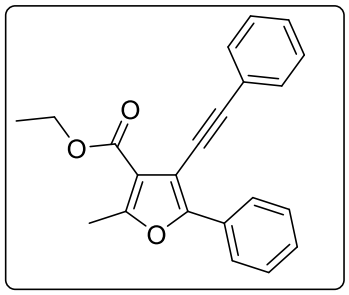
Yield: 123 mg, 26%; yellow solid, mp 112-113 °C; R_f = 0.42 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 – 8.19 (m, 1H), 7.85 (m, 1H), 7.76 – 7.64 (m, 2H), 7.45 – 7.38 (m, 2H), 7.10 – 7.03 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.0 (d), 132.9 (d), 131.2 (d), 129.92 (s), 129.85 (m), 129.7 (d), 128.3 (d), 127.2 (d), 123.5 (q, $^1J_{C\text{-}F}$ = 291.0 Hz), 121.1 (s), 111.6 (s), 98.2 (s), 81.6 (m), 59.5 (s). IR (reflection) $\tilde{\nu}$ = 2123, 1564, 1462, 1439, 1421, 1258, 1221, 1178, 1164, 1148, 1132, 1117, 1077, 1044, 1021, 964, 947, 855, 835, 763, 728, 706, 689, 663, 640 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{15}H_8F_6IOS$ $[M+H]^+$: 476.9239, found: 476.9231.

1-(hex-1-yn-1-yl)-3,3-bis(trifluoromethyl)-1,3-dihydro-1λ^3-benzo[*d*][1,2]iodaoxole (2n)



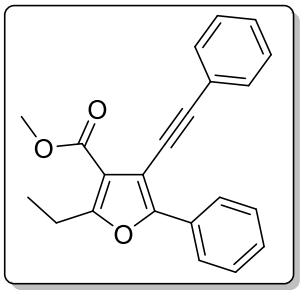
Yield: 266 mg, 60%; colorless solid, mp 106-107 °C; R_f = 0.52 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 – 8.18 (m, 1H), 7.87 – 7.78 (m, 1H), 7.73 – 7.61 (m, 2H), 2.53 (t, J = 7.1 Hz, 2H), 1.64 – 1.58 (m, 2H), 1.47 (dt, J = 14.3, 7.3 Hz, 2H), 0.96 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 132.7 (d), 131.0 (d), 130.1 (s), 129.8 (m), 128.2 (d), 123.65 (q, $^1J_{C\text{-}F}$ = 290.8 Hz), 110.9 (s), 107.9 (s), 81.6 (m), 43.4 (s), 30.4 (t), 22.0 (t), 20.0 (t), 13.5 (q). IR (reflection) $\tilde{\nu}$ = 3076, 2968, 2944, 2879, 2160, 1739, 1566, 1464, 1440, 1382, 1263, 1215, 1181, 1167, 1155, 1135, 1048, 1009, 963, 950, 868, 760, 731, 691, 663, 642 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{15}H_{14}F_6IO$ $[M+H]^+$: 450.9988, found: 450.9987.

ethyl 2-methyl-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3aa)



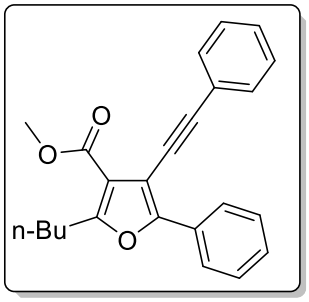
Yield: 25 mg, 76%; yellow solid, mp 70-71 °C; R_f = 0.72 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (dt, J = 8.2, 1.6 Hz, 2H), 7.61 – 7.54 (m, 2H), 7.48 – 7.41 (m, 2H), 7.40 – 7.31 (m, 4H), 4.38 (q, J = 7.1 Hz, 2H), 2.67 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.3 (s), 158.4 (s), 153.5 (s), 131.3 (d, 2C), 129.7 (s), 128.5 (d, 2C), 128.32 (d, 2C), 128.28 (d), 128.2 (d), 124.9 (d, 2C), 123.6 (s), 115.6 (s), 102.7 (s), 95.6 (s), 82.2 (s), 60.3 (t), 14.3 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3338, 3061, 2982, 2928, 2216, 1950, 1880, 1708, 1605, 1499, 1485, 1444, 1422, 1370, 1336, 1248, 1212, 1148, 1098, 1072, 1044, 1014, 964, 947, 927, 830, 783, 757, 730, 692, 667, 647 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{19}O_3$ $[M+H]^+$: 331.1329, found: 331.1327.

methyl 2-ethyl-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ba)



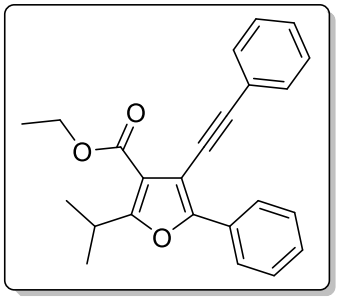
Yield: 26 mg, 79%; yellow solid, mp 73-75 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.10 (m, 2H), 7.60 – 7.54 (m, 2H), 7.49 – 7.43 (m, 2H), 7.41 – 7.31 (m, 4H), 3.92 (s, 3H), 3.09 (q, J = 7.6 Hz, 2H), 1.34 (t, J = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (s), 163.3 (s), 153.5 (s), 131.4 (d, 2C), 129.9 (s), 128.6 (d, 2C), 128.40 (d, 2C), 128.39 (d), 128.3 (d), 125.0 (d, 2C), 123.6 (s), 114.7 (s), 102.8 (s), 95.9 (s), 82.2 (s), 51.5 (q), 21.5 (t), 12.2 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2977, 2948, 2879, 2215, 1950, 1881, 1713, 1604, 1557, 1499, 1484, 1440, 1412, 1348, 1322, 1247, 1228, 1200, 1118, 1100, 1072, 1029, 1019, 965, 945, 913, 837, 812, 787, 755, 730, 689, 656 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{19}O_3$ $[M+H]^+$: 331.1329, found: 331.1327.

methyl 2-butyl-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ca)



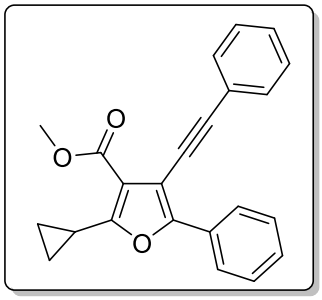
Yield: 27 mg, 76%; yellow liquid; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dt, J = 8.3, 1.7 Hz, 2H), 7.59 – 7.53 (m, 2H), 7.49 – 7.42 (m, 2H), 7.41 – 7.32 (m, 4H), 3.92 (s, 3H), 3.10 – 3.04 (m, 2H), 1.80 – 1.69 (m, 2H), 1.43 (dq, J = 14.7, 7.4 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (s), 162.6 (s), 153.5 (s), 131.4 (d, 2C), 129.9 (s), 128.6 (d, 2C), 128.40 (d, 2C), 128.38 (d), 128.3 (d), 125.0 (d, 2C), 123.6 (s), 115.2 (s), 102.7 (s), 95.9 (s), 82.2 (s), 51.4 (q), 30.1 (t), 27.6 (t), 22.3 (t), 13.8 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2955, 2931, 2871, 2216, 1949, 1879, 1800, 1714, 1603, 1558, 1498, 1484, 1439, 1379, 1346, 1325, 1244, 1200, 1110, 1071, 1034, 962, 912, 848, 814, 784, 755, 688 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{23}O_3$ $[M+H]^+$: 359.1642, found: 359.1646.

ethyl 2-isopropyl-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3da)



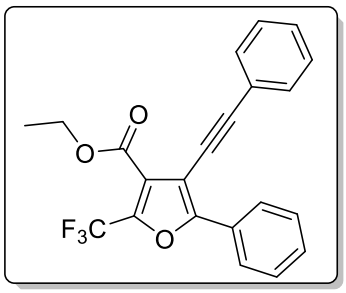
Yield: 23 mg, 65%; yellow solid, mp 67-68 °C; R_f = 0.64 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dt, *J* = 8.3, 1.7 Hz, 2H), 7.62 – 7.55 (m, 2H), 7.51 – 7.44 (m, 2H), 7.43 – 7.33 (m, 4H), 4.40 (q, *J* = 7.1 Hz, 2H), 3.89 – 3.80 (m, 1H), 1.43 (t, *J* = 7.1 Hz, 3H), 1.39 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (s), 163.3 (s), 153.3 (s), 131.4 (d, 2C), 130.0 (s), 128.6 (d, 2C), 128.4 (d, 2C), 128.3 (d), 128.2 (d), 125.0 (d, 2C), 123.7 (s), 113.9 (s), 102.7 (s), 95.6 (s), 82.3 (s), 60.4 (t), 27.5 (d), 20.7 (q, 2C), 14.4 (q). IR (reflection) $\tilde{\nu}$ = 3064, 2982, 2937, 2873, 2215, 1703, 1602, 1556, 1498, 1484, 1443, 1413, 1368, 1340, 1310, 1271, 1248, 1211, 1161, 1116, 1089, 1058, 1025, 1007, 913, 841, 788, 766, 754, 689, 650 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{23}O_3$ $[M+H]^+$: 359.1642, found: 359.1638.

methyl 2-cyclopropyl-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ea)



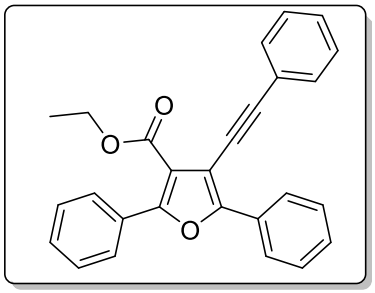
Yield: 22 mg, 65%; yellow solid, mp 109-110 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.60 – 7.54 (m, 2H), 7.46 – 7.29 (m, 6H), 3.94 (s, 3H), 2.85 (m, 1H), 1.21 – 1.09 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (s), 162.5 (s), 152.1 (s), 131.4 (d, 2C), 129.8 (s), 128.5 (d, 2C), 128.4 (d, 2C), 128.3 (d, 2C), 124.8 (d, 2C), 123.6 (s), 115.0 (s), 103.1 (s), 95.8 (s), 82.2 (s), 51.4 (q), 9.4 (d), 9.0 (t, 2C). IR (reflection) $\tilde{\nu}$ = 3007, 2945, 1705, 1594, 1561, 1498, 1485, 1443, 1404, 1371, 1281, 1246, 1209, 1184, 1119, 1084, 1058, 1027, 1015, 956, 905, 881, 831, 816, 782, 755, 681, 650 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{23}H_{19}O_3$ $[M+H]^+$: 343.1329, found: 343.1322.

ethyl 5-phenyl-4-(phenylethynyl)-2-(trifluoromethyl)furan-3-carboxylate (3fa)



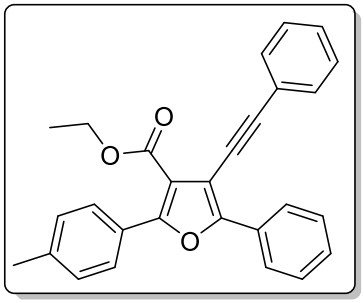
Yield: 22 mg, 58%; colorless solid, mp 94-95 °C; R_f = 0.65 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.14 (m, 2H), 7.57 (tdd, *J* = 5.2, 3.2, 2.0 Hz, 2H), 7.52 – 7.35 (m, 6H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2 (s), 155.8 (s), 141.4 (d, $^2J_{C\text{-}F}$ = 43.0 Hz), 131.6 (d, 2C), 129.9 (d), 128.9 (d), 128.8 (d, 2C), 128.5 (d, 2C), 128.4 (s), 125.7 (d, 2C), 122.7 (s), 122.0 (d, $^3J_{C\text{-}F}$ = 2.4 Hz), 118.5 (q, $^1J_{C\text{-}F}$ = 269.6 Hz), 104.4 (s), 97.0 (s), 79.5 (s), 61.7 (t), 14.0 (q). IR (reflection) $\tilde{\nu}$ = 2992, 2940, 2905, 1958, 1886, 1727, 1613, 1552, 1499, 1483, 1445, 1412, 1367, 1350, 1306, 1246, 1228, 1163, 1142, 1079, 1020, 999, 981, 914, 872, 842, 788, 758, 719, 687, 626 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{16}F_3O_3$ $[M+H]^+$: 385.1046, found: 385.1040.

ethyl 2,5-diphenyl-4-(phenylethynyl)furan-3-carboxylate (3ga)



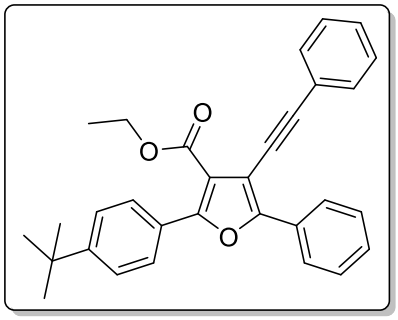
Yield: 21 mg, 54%; yellow solid, mp 80-81 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.0 Hz, 2H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 2H), 7.46 (dt, *J* = 14.0, 7.6 Hz, 5H), 7.41 – 7.35 (m, 4H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 163.3 (s), 155.4 (s), 154.3 (s), 131.5 (d, 2C), 129.7 (d), 129.6 (s), 129.3 (s), 128.8 (d), 128.7 (d, 2C), 128.49 (d, 2C), 128.46(d), 128.41 (d, 2C), 128.3 (d, 2C), 125.4 (d, 2C), 123.4 (s), 116.4 (s), 104.5 (s), 96.0 (s), 81.8 (s), 61.0 (t), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3057, 2984, 2935, 2902, 2219, 1952, 1883, 1712, 1599, 1571, 1552, 1483, 1445, 1390, 1367, 1337, 1319, 1296, 1239, 1158, 1130, 1112, 1070, 1026, 965, 914, 838, 789, 769, 757, 688, 610 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{21}O_3$ $[M+H]^+$: 393.1485, found: 393.1492.

ethyl 5-phenyl-4-(phenylethynyl)-2-(*p*-tolyl)furan-3-carboxylate (3ha)



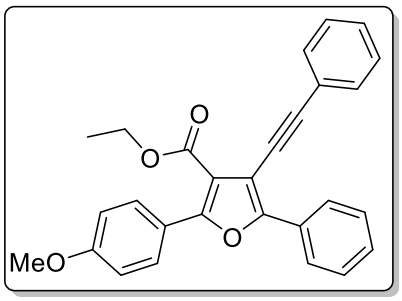
Yield: 22 mg, 55%; yellow solid, mp 83-84 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.62 – 7.55 (m, 2H), 7.51 – 7.44 (m, 2H), 7.43 – 7.34 (m, 4H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.42 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (s), 155.8 (s), 154.0 (s), 139.9 (s), 131.4 (d, 2C), 129.7 (s), 128.9 (d, 2C), 128.7 (d), 128.6 (d, 2C), 128.5 (d, 2C), 128.4 (d), 128.3 (d, 2C), 126.5 (s), 125.3 (d, 2C), 123.5 (s), 115.9 (s), 104.5 (s), 95.9 (s), 81.9 (s), 60.9 (t), 21.5 (q), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3058, 2987, 2928, 2217, 1713, 1601, 1505, 1483, 1442, 1412, 1366, 1336, 1314, 1292, 1234, 1219, 1188, 1159, 1107, 1070, 1021, 965, 911, 842, 824, 783, 757, 717, 686, 666, 646 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{28}H_{23}O_3$ $[M+H]^+$: 407.1642, found: 407.1638.

ethyl 2-(4-(tert-butyl)phenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ia)



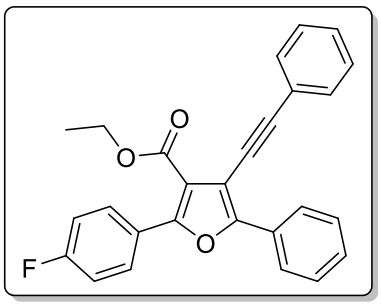
Yield: 20 mg, 45%; yellow liquid; R_f = 0.62 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.86 – 7.78 (m, 2H), 7.54 – 7.47 (m, 2H), 7.44 – 7.37 (m, 4H), 7.34 – 7.25 (m, 4H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.32 – 1.26 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (s), 155.8 (s), 154.0 (s), 153.0 (s), 131.4 (d, 2C), 129.7 (s), 128.7 (d), 128.6 (d, 2C), 128.5 (d, 2C), 128.4 (d), 128.2 (d, 2C), 126.5 (s), 125.3 (d, 2C), 125.2 (d, 2C), 123.5 (s), 115.9 (s), 104.4 (s), 95.9 (s), 82.0 (s), 60.9 (t), 34.9 (s), 31.2 (q, 3C), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3060, 2963, 2904, 2868, 1950, 1879, 1718, 1601, 1578, 1501, 1483, 1463, 1444, 1413, 1367, 1337, 1317, 1293, 1269, 1236, 1201, 1122, 1098, 1071, 1020, 967, 913, 839, 787, 756, 730, 690 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{31}H_{29}O_3$ $[M+H]^+$: 449.2111, found: 449.2113.

ethyl 2-(4-methoxyphenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ja)



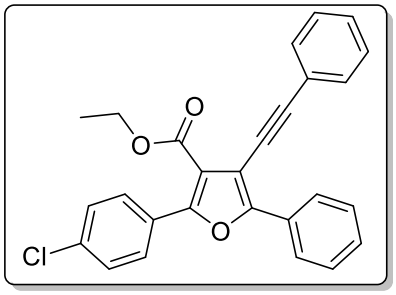
Yield: 28 mg, 67%; yellow solid, mp 138-139 °C; R_f = 0.44 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 8.18 (m, 2H), 7.96 – 7.89 (m, 2H), 7.61 – 7.55 (m, 2H), 7.50 – 7.44 (m, 2H), 7.42 – 7.33 (m, 4H), 7.01 – 6.96 (m, 2H), 4.39 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4 (s), 160.7 (s), 155.9 (s), 153.8 (s), 131.4 (d, 2C), 130.1 (d, 2C), 129.7 (s), 128.61 (d, 2C), 128.59 (d), 128.5 (d, 2C), 128.4 (d), 125.3 (d, 2C), 123.6 (s), 121.9 (s), 115.1 (s), 113.7 (d, 2C), 104.4 (s), 95.9 (s), 82.1 (s), 60.8 (t), 55.4 (q), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3063, 2976, 2934, 1707, 1610, 1581, 1503, 1484, 1461, 1439, 1403, 1390, 1365, 1339, 1303, 1263, 1237, 1178, 1125, 1111, 1071, 1022, 964, 910, 837, 816, 785, 763, 753, 683, 666, 645, 617 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{28}H_{23}O_4$ $[M+H]^+$: 423.1591, found: 423.1591.

ethyl 2-(4-fluorophenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ka)



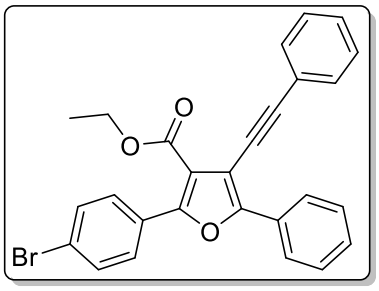
Yield: 32 mg, 78%; yellow solid, mp 120-121 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 7.9 Hz, 2H), 8.01 – 7.93 (m, 2H), 7.58 (dd, J = 7.4, 1.9 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.39 (q, J = 5.8 Hz, 4H), 7.16 (t, J = 8.7 Hz, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5 (d, $^1J_{C\text{-}F}$ = 250.3 Hz), 163.2 (s), 154.7 (s), 154.3 (s), 131.4 (d, 2C), 130.6 (d, $^3J_{C\text{-}F}$ = 8.6 Hz, 2C), 129.5 (s), 128.9 (d), 128.7 (d, 2C), 128.5 (d, 3C), 125.5 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 125.4 (d, 2C), 123.4 (s), 116.2 (s), 115.39 (d, $^2J_{C\text{-}F}$ = 21.9 Hz, 2C), 104.5 (s), 96.1 (s), 81.8 (s), 61.0 (t), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 2988, 1710, 1600, 1503, 1482, 1443, 1413, 1366, 1334, 1292, 1235, 1161, 1127, 1112, 1099, 1070, 1024, 963, 910, 840, 805, 785, 757, 686, 665, 644 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}FO_3$ $[M+H]^+$: 411.1391, found: 411.1388.

ethyl 2-(4-chlorophenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3la)



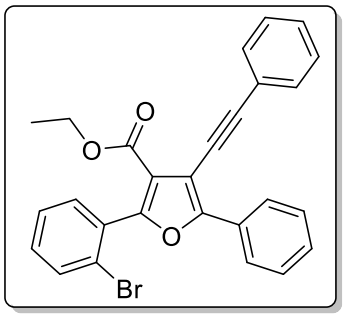
Yield: 29 mg, 68%; colorless solid, mp 100-101 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.95 – 7.88 (m, 2H), 7.61 – 7.54 (m, 2H), 7.51 – 7.37 (m, 8H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (s), 154.4 (s), 154.2 (s), 135.7 (s), 131.4 (d, 2C), 129.7 (d, 2C), 129.5 (s), 128.9 (d), 128.7 (d, 2C), 128.53 (d, 2C), 128.49 (d, 3C), 127.7 (s), 125.4 (d, 2C), 123.4 (s), 116.8 (s), 104.7 (s), 96.1 (s), 81.6 (s), 61.1 (t), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3062, 2989, 2925, 1711, 1601, 1579, 1549, 1481, 1440, 1406, 1367, 1333, 1305, 1281, 1235, 1184, 1129, 1114, 1104, 1092, 1071, 1014, 963, 910, 834, 784, 756, 685, 664, 633, 623 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}ClO_3$ $[M+H]^+$: 427.1095, found: 427.1092.

ethyl 2-(4-bromophenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3ma)



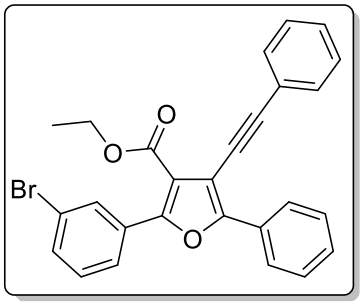
Yield: 33 mg, 71%; yellow solid, mp 92-93 °C; R_f = 0.62 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.16 (m, 2H), 7.89 – 7.80 (m, 2H), 7.63 – 7.54 (m, 4H), 7.51 – 7.45 (m, 2H), 7.42 – 7.33 (m, 4H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (s), 154.5 (s), 154.2 (s), 131.5 (d, 2C), 131.4 (d, 2C), 129.8 (d, 2C), 129.4 (s), 128.9 (d), 128.7 (d, 2C), 128.5 (d, 3C), 128.2 (s), 125.4 (d, 2C), 124.0 (s), 123.4 (s), 116.9 (s), 104.7 (s), 96.2 (s), 81.6 (s), 61.1 (t), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3058, 2985, 1714, 1602, 1577, 1549, 1479, 1440, 1406, 1367, 1334, 1304, 1279, 1235, 1184, 1113, 1076, 1024, 1010, 964, 910, 831, 784, 756, 717, 685, 663, 615 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}BrO_3$ $[M+H]^+$: 471.0590, found: 471.0593.

ethyl 2-(2-bromophenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3na)



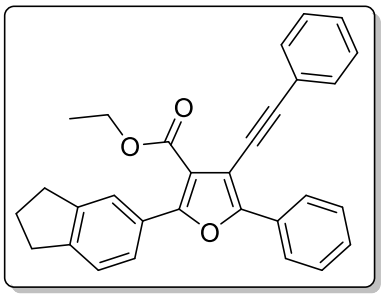
Yield: 37 mg, 79%; yellow solid, mp 108-109 °C; R_f = 0.50 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dt, *J* = 8.3, 1.7 Hz, 2H), 7.71 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.64 – 7.58 (m, 2H), 7.55 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.50 – 7.31 (m, 8H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (s), 155.1 (s), 155.0 (s), 132.9 (d), 132.4 (d), 131.5 (d, 2C), 131.4 (s), 131.1 (d), 129.6 (s), 128.9 (d), 128.7 (d, 2C), 128.4 (d, 3C), 126.9 (d), 125.4 (d, 2C), 124.0 (s), 123.5 (s), 118.6 (s), 103.5 (s), 96.3 (s), 81.5 (s), 60.7 (t), 14.0 (q). IR (reflection) $\tilde{\nu}$ = 2978, 1713, 1622, 1567, 1469, 1432, 1365, 1336, 1277, 1239, 1156, 1112, 1076, 1047, 1026, 966, 945, 919, 865, 838, 785, 766, 756, 728, 684, 657, 646, 610 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}BrO_3$ $[M+H]^+$: 471.0590, found: 471.0593.

ethyl 2-(3-bromophenyl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3oa)



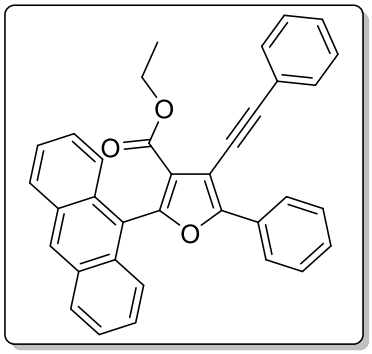
Yield: 30 mg, 64%; yellow solid, mp 91-92 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.19 (m, 2H), 8.10 (t, *J* = 1.8 Hz, 1H), 7.90 (m, 1H), 7.64 – 7.54 (m, 3H), 7.52 – 7.46 (m, 2H), 7.42 – 7.31 (m, 5H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (s), 154.7 (s), 153.4 (s), 132.4 (d), 131.5 (d, 2C), 131.2 (s), 131.1 (d), 129.7 (d), 129.4 (s), 129.0 (d), 128.7 (d, 2C), 128.5 (d), 128.48 (d, 2C), 126.9 (d), 125.4 (d, 2C), 123.3 (s), 122.3 (s), 117.3 (s), 104.8 (s), 96.3 (s), 81.5 (s), 61.2 (t), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3069, 2975, 1709, 1598, 1574, 1558, 1498, 1469, 1441, 1426, 1390, 1368, 1330, 1243, 1131, 1117, 1069, 1027, 997, 972, 903, 893, 844, 776, 749, 715, 687, 662, 610 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}BrO_3$ $[M+H]^+$: 471.0590, found: 471.0593.

ethyl 2-(2,3-dihydro-1*H*-inden-5-yl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3pa)



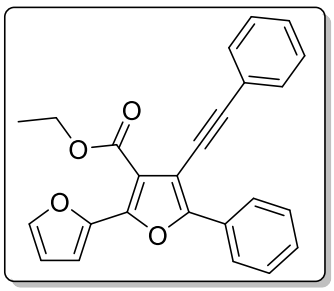
Yield: 19 mg, 44%; yellow liquid; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.19 (m, 2H), 7.77 (s, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.58 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.35 (m, 4H), 7.32 (d, *J* = 7.8 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.98 (m, 4H), 2.17 – 2.09 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.4 (s), 156.3 (s), 153.9 (s), 146.4 (s), 144.3 (s), 131.4 (d, 2C), 129.7 (s), 128.6 (d, 3C), 128.5 (d, 2C), 128.4 (d), 127.2 (s), 126.7 (d), 125.3 (d, 2C), 124.4 (d), 124.2 (d), 123.5 (s), 115.7 (s), 104.4 (s), 95.9 (s), 82.0 (s), 60.9 (t), 33.0 (t), 32.9 (t), 25.5 (t), 14.3 (q). IR (reflection) $\tilde{\nu}$ = 3060, 2954, 2842, 2217, 1951, 1888, 1716, 1600, 1553, 1483, 1443, 1367, 1337, 1235, 1219, 1087, 1070, 1026, 979, 913, 888, 824, 787, 756, 690 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{30}H_{25}O_3$ $[M+H]^+$: 433.1798, found: 433.1796.

ethyl 2-(anthracen-9-yl)-5-phenyl-4-(phenylethynyl)furan-3-carboxylate (3qa)



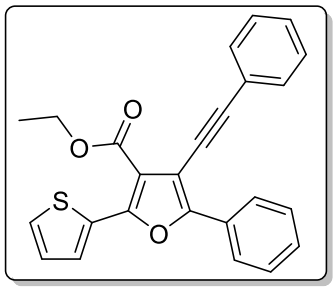
Yield: 30 mg, 61%; yellow liquid; R_f = 0.44 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.25 (dd, *J* = 5.3, 3.4 Hz, 2H), 8.11 – 8.05 (m, 2H), 7.82 – 7.74 (m, 2H), 7.72 – 7.64 (m, 2H), 7.53 – 7.36 (m, 10H), 3.89 (q, *J* = 7.1 Hz, 2H), 0.57 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.1 (s), 155.8 (s), 154.7 (s), 131.61 (s, 2C), 131.58 (d, 2C), 131.1 (s, 2C), 129.7 (s), 129.5 (d), 128.9 (d), 128.7 (d, 2C), 128.54 (d, 2C), 128.49 (d), 128.47 (d, 2C), 126.6 (d, 2C), 125.7 (d, 2C), 125.4 (d, 4C), 124.0 (s), 123.5 (s), 121.1 (s), 103.6 (s), 96.7 (s), 81.6 (s), 60.2 (t), 13.3 (q). IR (reflection) $\tilde{\nu}$ = 3054, 2981, 2250, 2198, 1951, 1720, 1603, 1554, 1522, 1483, 1444, 1425, 1371, 1322, 1205, 1117, 1080, 1045, 1014, 909, 894, 845, 790, 757, 737, 692, 607 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{35}H_{25}O_3$ $[M+H]^+$: 493.1798, found: 493.1800.

ethyl 5-phenyl-4-(phenylethynyl)-[2,2'-bifuran]-3-carboxylate (3ra)



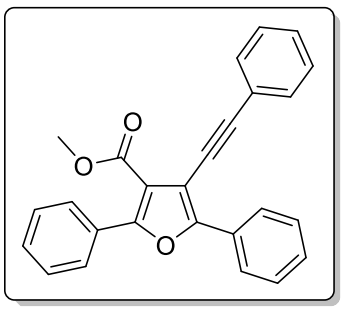
Yield: 26 mg, 68%; yellow solid, mp 90-91 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.19 (m, 2H), 7.64 – 7.54 (m, 3H), 7.52 – 7.44 (m, 3H), 7.43 – 7.34 (m, 4H), 6.58 (dd, J = 3.5, 1.8 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (s), 154.1 (s), 147.4 (s), 144.0 (s), 143.8 (d), 131.4 (d, 2C), 129.5 (s), 128.8 (d), 128.6 (d, 2C), 128.48 (d, 2C), 128.45 (d), 125.5 (d, 2C), 123.4 (s), 114.8 (s), 113.9 (d), 112.0 (d), 104.1 (s), 96.1 (s), 81.8 (s), 60.9 (t), 14.4 (q). IR (reflection) $\tilde{\nu}$ = 3161, 3116, 3058, 2981, 2905, 1701, 1598, 1539, 1498, 1478, 1443, 1367, 1326, 1255, 1164, 1130, 1080, 1022, 971, 905, 886, 834, 783, 766, 750, 688, 668, 629 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{19}O_4$ $[M+H]^+$: 383.1278, found: 383.1275.

ethyl 5-phenyl-4-(phenylethynyl)-2-(thiophen-2-yl)furan-3-carboxylate (3sa)



Yield: 22 mg, 56%; yellow solid, mp 106-107 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.19 (m, 2H), 8.06 (m, 1H), 7.57 (m, 2H), 7.48 (m, 3H), 7.43 – 7.34 (m, 4H), 7.15 (dd, J = 5.0, 3.8 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.44 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (s), 153.6 (s), 151.5 (s), 131.4 (d, 2C), 131.0 (s), 129.4 (s), 129.3 (d), 128.8 (d), 128.7 (d, 2C), 128.51 (d), 128.48 (d, 2C), 128.4 (d), 127.5 (d), 125.4 (d, 2C), 123.5 (s), 114.4 (s), 104.4 (s), 96.1 (s), 81.9 (s), 60.9 (t), 14.4 (q). IR (reflection) $\tilde{\nu}$ = 2981, 2211, 1703, 1598, 1572, 1482, 1429, 1371, 1314, 1248, 1211, 1129, 1104, 1073, 1048, 1026, 913, 855, 784, 755, 706, 687, 637, 609 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{19}O_3S$ $[M+H]^+$: 399.1049, found: 399.1046.

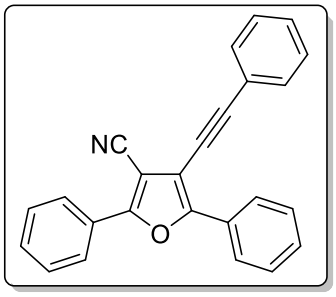
methyl 2,5-diphenyl-4-(phenylethynyl)furan-3-carboxylate (3ta)



Yield: 24 mg, 64%; yellow solid, mp 121-122 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.20 (m, 2H), 7.96 – 7.90 (m, 2H), 7.62 – 7.56 (m, 2H), 7.52 – 7.43 (m, 5H), 7.42 – 7.35 (m, 4H), 3.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (s), 155.6 (s), 154.2 (s),

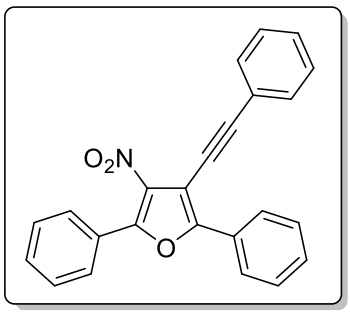
131.5 (d), 129.7 (d), 129.6 (s), 129.3 (s), 128.8 (d), 128.7 (d, 2C), 128.5 (d, 4C), 128.4 (d, 2C), 128.3 (d, 2C), 125.3 (d, 2C), 123.4 (s), 116.3 (s), 104.5 (s), 96.2 (s), 81.7 (s), 51.8 (q). IR (reflection) $\tilde{\nu}$ = 3076, 2997, 2949, 2213, 1709, 1598, 1583, 1569, 1483, 1433, 1341, 1321, 1294, 1238, 1190, 1132, 1116, 1070, 1027, 987, 940, 924, 816, 788, 762, 687, 610 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{19}O_3$ $[M+H]^+$: 379.1329, found: 379.1330.

2,5-diphenyl-4-(phenylethynyl)furan-3-carbonitrile (3ua)



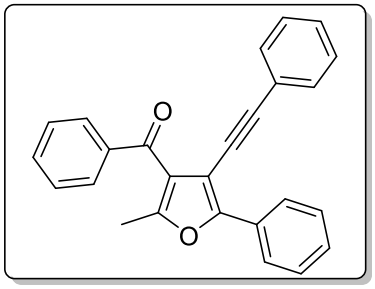
Yield: 28 mg, 81%; yellow solid, mp 177-178 °C; R_f = 0.64 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.14 (m, 2H), 8.11 – 8.05 (m, 2H), 7.66 – 7.60 (m, 2H), 7.56 – 7.47 (m, 5H), 7.44 – 7.37 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6 (s), 153.7 (s), 131.8 (d, 2C), 130.6 (d), 129.4 (d), 129.2 (d, 2C), 129.1 (d), 128.9 (d, 2C), 128.7 (s), 128.5 (d, 2C), 127.5 (s), 125.6 (d, 2C), 125.2 (d, 2C), 122.4 (s), 113.6 (s), 105.9 (s), 98.1 (s), 96.6 (s), 78.7 (s). IR (reflection) $\tilde{\nu}$ = 3060, 2229, 1956, 1888, 1808, 1600, 1559, 1484, 1444, 1345, 1231, 1153, 1119, 1101, 1070, 1027, 999, 965, 923, 841, 771, 758, 686, 638 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{16}NO$ $[M+H]^+$: 346.1226, found: 346.1224.

3-nitro-2,5-diphenyl-4-(phenylethynyl)furan (3va)



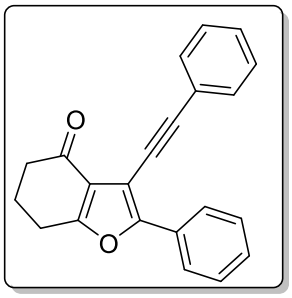
Yield: 16 mg, 44%; yellow solid, mp 188-189 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.18 (m, 2H), 7.95 – 7.88 (m, 2H), 7.66 – 7.59 (m, 2H), 7.56 – 7.49 (m, 5H), 7.46 – 7.36 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6 (s), 150.9 (s), 131.7 (d, 2C), 131.0 (d), 129.7 (d), 129.0 (d), 128.9 (d, 2C), 128.7 (d, 6C), 128.5 (d, 2C), 127.1 (s), 125.4 (d, 2C), 122.6 (s), 100.9 (s), 98.1 (s), 78.6 (s). IR (reflection) $\tilde{\nu}$ = 3064, 2220, 1987, 1963, 1605, 1572, 1553, 1509, 1483, 1446, 1410, 1357, 1233, 1189, 1145, 1119, 1072, 1028, 999, 967, 925, 833, 761, 688, 622 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{16}NO_3$ $[M+H]^+$: 366.1125, found: 366.1128.

(2-methyl-5-phenyl-4-(phenylethynyl)furan-3-yl)(phenyl)methanone (3wa)



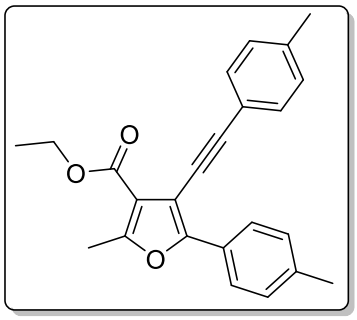
Yield: 28 mg, 78%; yellow solid, mp 88-89 °C; R_f = 0.62 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2H), 7.89 – 7.83 (m, 2H), 7.54 – 7.46 (m, 1H), 7.44 – 7.35 (m, 4H), 7.31 – 7.23 (m, 1H), 7.19 – 7.12 (m, 3H), 6.99 – 6.91 (m, 2H), 2.45 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.3 (s), 156.6 (s), 153.1 (s), 138.4 (s), 132.7 (d), 131.0 (d, 2C), 129.8 (d, 2C), 129.7 (s), 128.5 (d, 2C), 128.4 (d), 128.1 (d, 3C), 128.0 (d, 2C), 124.9 (d, 2C), 123.6 (s), 122.9 (s), 102.9 (s), 97.2 (s), 81.9 (s), 13.6 (q). IR (reflection) $\tilde{\nu}$ = 3060, 1650, 1598, 1578, 1498, 1484, 1451, 1440, 1396, 1379, 1341, 1265, 1243, 1212, 1183, 1164, 1152, 1133, 1115, 1096, 1068, 1023, 999, 933, 910, 858, 838, 803, 762, 753, 729, 687, 673, 626 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{19}O_2$ $[M+H]^+$: 363.1380, found: 363.1378.

2-phenyl-3-(phenylethynyl)-6,7-dihydrobenzofuran-4(5*H*)-one (3xa)



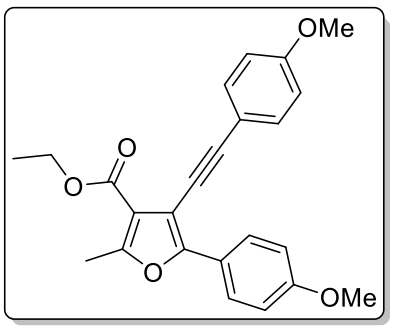
Yield: 26 mg, 84%; colorless solid, mp 110-111 °C; R_f = 0.26 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (dd, J = 5.3, 3.3 Hz, 2H), 7.62 (m, 2H), 7.46 (m 2H), 7.41 – 7.31 (m, 4H), 2.96 (t, J = 6.3 Hz, 2H), 2.59 – 2.52 (m, 2H), 2.29 – 2.17 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2 (s), 165.5 (s), 154.8 (s), 131.7 (d, 2C), 129.6 (s), 128.7 (d, 3C), 128.4 (d), 128.3 (d, 2C), 125.1 (d, 2C), 123.4 (s), 122.1 (s), 100.0 (s), 96.3 (s), 81.4 (s), 38.1 (t), 23.6 (t), 22.3 (t). IR (reflection) $\tilde{\nu}$ = 3062, 2935, 1676, 1600, 1558, 1499, 1482, 1454, 1435, 1415, 1357, 1223, 1175, 1157, 1145, 1091, 1063, 1023, 1010, 905, 884, 766, 752, 688, 652 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{17}O_2$ $[M+H]^+$: 313.1223, found: 313.1222.

ethyl 2-methyl-5-(*p*-tolyl)-4-(*p*-tolylethynyl)furan-3-carboxylate (3ab)



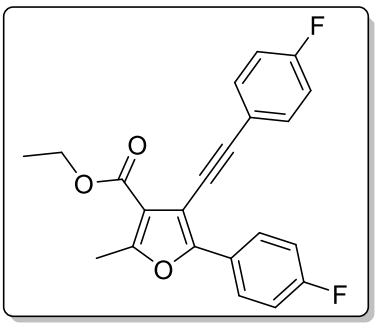
Yield: 27 mg, 76%; yellow solid, mp 132-133 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 2.68 (s, 3H), 2.42 (s, 3H), 2.41 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (s), 158.1 (s), 153.7 (s), 138.3 (s, 2C), 131.2 (d, 2C), 129.23 (d, 2C), 129.15 (d, 2C), 127.2 (s), 125.0 (d, 2C), 120.7 (s), 115.5 (s), 102.2 (s), 95.7 (s), 81.7 (s), 60.3 (t), 21.5 (q), 21.4 (q), 14.4 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2989, 2923, 1704, 1602, 1517, 1498, 1441, 1417, 1368, 1332, 1269, 1248, 1207, 1182, 1159, 1098, 1038, 975, 842, 811, 777, 717, 686, 656 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{23}O_3$ $[M+H]^+$: 359.1642, found: 359.1643.

ethyl 5-(4-methoxyphenyl)-4-((4-methoxyphenyl)ethynyl)-2-methylfuran-3-carboxylate (3ac)



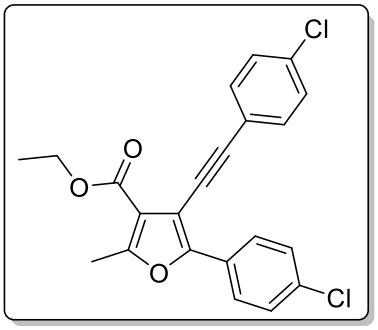
Yield: 27 mg, 70%; yellow solid, mp 93-94 °C; R_f = 0.31 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.03 (m, 2H), 7.53 – 7.45 (m, 2H), 6.99 – 6.93 (m, 2H), 6.93 – 6.87 (m, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.84 (s, 3H), 2.64 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (s), 159.6 (s), 159.6 (s), 157.8 (s), 153.4 (s), 132.8 (d, 2C), 126.5 (d, 2C), 122.9 (s), 116.0 (s), 115.4 (s), 114.1 (d, 2C), 114.0 (d, 2C), 101.3 (s), 95.1 (s), 81.1 (s), 60.3 (t), 55.34 (q), 55.32 (q), 14.4 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2971, 2840, 1887, 1696, 1602, 1567, 1516, 1499, 1462, 1444, 1404, 1370, 1329, 1289, 1244, 1210, 1173, 1095, 1025, 979, 829, 811, 783, 724, 684, 654 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{23}O_5$ $[M+H]^+$: 391.1540, found: 391.1533.

ethyl 5-(4-fluorophenyl)-4-((4-fluorophenyl)ethynyl)-2-methylfuran-3-carboxylate (3ad)



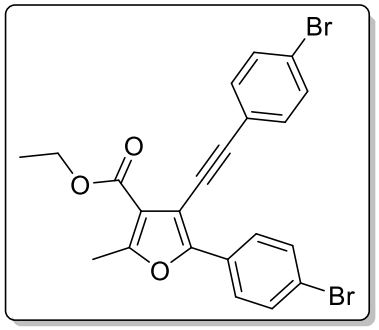
Yield: 32 mg, 87%; yellow solid, mp 94-95 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2H), 7.57 – 7.48 (m, 2H), 7.17 – 7.02 (m, 4H), 4.36 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (s), 162.59 (d, $^1J_{C\text{-}F}$ = 249.8 Hz), 162.58 (d, $^1J_{C\text{-}F}$ = 249.8 Hz), 158.4 (s), 152.7 (s), 133.2 (d, $^3J_{C\text{-}F}$ = 8.4 Hz, 2C), 126.9 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 126.1 (d, $^4J_{C\text{-}F}$ = 3.3 Hz), 119.6 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 22.6 Hz, 2C), 115.7 (d, $^2J_{C\text{-}F}$ = 21.7 Hz, 2C), 115.6 (s), 102.4 (s), 94.5 (s), 81.7 (d, $^5J_{C\text{-}F}$ = 1.2 Hz), 60.4 (t), 14.4 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3069, 2989, 2910, 1884, 1704, 1599, 1513, 1496, 1449, 1419, 1368, 1332, 1269, 1226, 1160, 1116, 1100, 1035, 1018, 974, 828, 779, 717, 681, 655, 624 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{17}F_2O_3$ $[M+H]^+$: 367.1140, found: 367.1135.

ethyl 5-(4-chlorophenyl)-4-((4-chlorophenyl)ethynyl)-2-methylfuran-3-carboxylate (3ae)



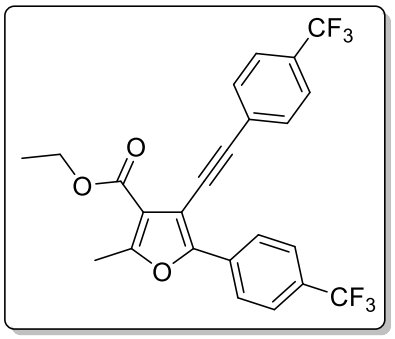
Yield: 32 mg, 81%; yellow solid, mp 127-128 °C; R_f = 0.62 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 2H), 7.50 – 7.44 (m, 2H), 7.43 – 7.38 (m, 2H), 7.37 – 7.32 (m, 2H), 4.36 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (s), 158.7 (s), 152.6 (s), 134.5 (s), 134.2 (s), 132.5 (d, 2C), 128.8 (d, 4C), 128.2 (s), 126.2 (d, 2C), 121.9 (s), 115.7 (s), 103.1 (s), 95.0 (s), 82.9 (s), 60.5 (t), 14.4 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 2986, 2907, 1896, 1707, 1604, 1496, 1480, 1449, 1416, 1398, 1366, 1331, 1264, 1247, 1210, 1176, 1092, 1034, 1013, 973, 854, 823, 771, 713, 681, 637, 618 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{17}Cl_2O_3$ $[M+H]^+$: 399.0549, found: 399.0545.

ethyl 5-(4-bromophenyl)-4-((4-bromophenyl)ethynyl)-2-methylfuran-3-carboxylate (3af)



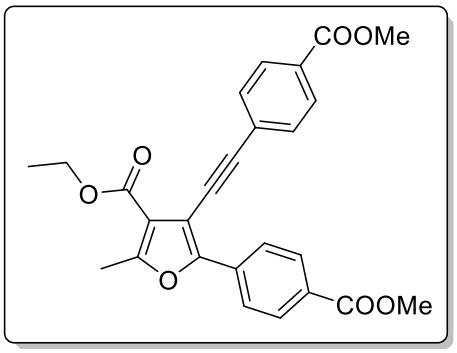
Yield: 29 mg, 60%; yellow solid, mp 126-127 °C; R_f = 0.63 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.93 (m, 2H), 7.59 – 7.54 (m, 2H), 7.54 – 7.48 (m, 2H), 7.42 – 7.37 (m, 2H), 4.36 (q, J = 7.1 Hz, 2H), 2.65 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (s), 158.8 (s), 152.7 (s), 132.7 (d, 2C), 131.79 (d, 2C), 131.76 (d, 2C), 128.6 (s), 126.4 (d, 2C), 122.7 (s), 122.5 (s), 122.3 (s), 115.8 (s), 103.2 (s), 95.2 (s), 83.1 (s), 60.5 (t), 14.4 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3090, 3054, 2984, 2905 ,1897, 1708, 1605, 1589, 1492, 1479, 1419, 1393, 1367, 1330, 1263, 1246, 1211, 1178, 1102, 1071, 1034, 1009, 973, 821, 779, 765, 711, 697, 681, 666, 636 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{17}Br_2O_3$ $[M+H]^+$: 486.9539, found: 486.9537.

ethyl 2-methyl-5-(4-(trifluoromethyl)phenyl)-4-((4-(trifluoromethyl)phenyl) ethynyl)furan-3-carboxylate (3ag)



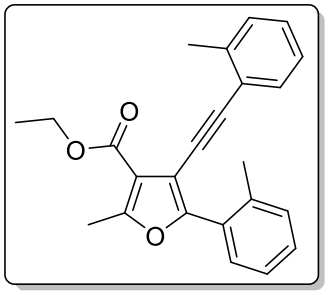
Yield: 30 mg, 65%; colorless solid, mp 110-111 °C; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, J = 8.2 Hz, 2H), 7.74 – 7.60 (m, 6H), 4.39 (q, J = 7.1 Hz, 2H), 2.69 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (s), 159.5 (s), 152.3 (s), 132.7 (s), 131.62 (d, 2C), 130.31 (q, $^2J_{C\text{-}F}$= 33.0 Hz), 130.09 (q, $^2J_{C\text{-}F}$= 33.0 Hz), 126.95 (s), 125.64 (q, $^3J_{C\text{-}F}$= 3.8 Hz, 2C), 125.46 (q, $^3J_{C\text{-}F}$ = 3.8 Hz, 2C), 125.02 (d, 2C), 123.96 (q, $^1J_{C\text{-}F}$= 271.9 Hz), 123.88 (q, $^1J_{C\text{-}F}$= 272.0 Hz), 116.0 (s), 104.3 (s), 95.2 (s), 84.0 (s), 60.6 (t), 14.4 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 2980, 2933, 2908, 2218, 1923, 1710, 1615, 1503, 1480, 1409, 1370, 1322, 1244, 1212, 1173, 1160, 1116, 1100, 1067, 1015, 971, 839, 781, 766, 739, 687 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{17}F_6O_3$ $[M+H]^+$: 467.1076, found: 467.1075.

ethyl 5-(4-(methoxycarbonyl)phenyl)-4-((4-(methoxycarbonyl)phenyl)ethynyl)-2-methylfuran-3-carboxylate (3ah)



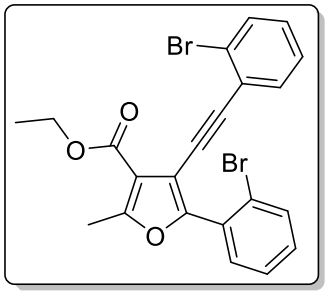
Yield: 33 mg, 74%; colorless solid, mp 149-150 °C; R_f = 0.46 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 – 8.14 (m, 2H), 8.12 – 8.01 (m, 4H), 7.60 (d, *J* = 8.5 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 3.93 (s, 3H), 2.67 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6 (s), 166.5 (s), 162.9 (s), 159.5 (s), 152.7 (s), 133.5 (s), 131.3 (d, 2C), 129.9 (d, 2C), 129.8 (s), 129.7 (d, 2C), 129.5 (s), 127.9 (s), 124.6 (d, 2C), 116.0 (s), 104.6 (s), 96.0 (s), 84.9 (s), 60.6 (t), 52.3 (q), 52.2 (q), 14.4 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 2992, 2954, 2916, 2843, 2213, 1925, 1726, 1706, 1606, 1574, 1488, 1434, 1405, 1367, 1333, 1308, 1270, 1249, 1211, 1193, 1180, 1117, 1098, 1038, 1015, 967, 850, 825, 809, 782, 763, 697, 668 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{23}O_7$ $[M+H]^+$: 447.1438, found: 447.1442

ethyl 2-methyl-5-(*o*-tolyl)-4-(*o*-tolylethynyl)furan-3-carboxylate (3ai)



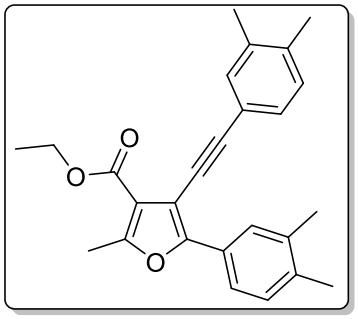
Yield: 28 mg, 79%; yellow liquid; R_f = 0.61 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.34 – 7.22 (m, 3H), 7.21 – 7.14 (m, 2H), 7.14 – 7.08 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 2.45 (s, 3H), 2.37 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (s), 158.6 (s), 155.5 (s), 140.1 (s), 137.2 (s), 131.8 (d), 130.8 (d), 130.0 (d), 129.4 (d), 129.2 (d), 128.9 (s), 128.1 (d), 125.5 (d), 125.4 (d), 123.4 (s), 114.8 (s), 105.2 (s), 93.1 (s), 85.4 (s), 60.4 (t), 20.8 (q), 20.6 (q), 14.5 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3059, 3019, 2979, 2926, 2867, 2216, 1953, 1919, 1707, 1602, 1477, 1456, 1416, 1367, 1330, 1287, 1240, 1211, 1191, 1120, 1089, 1030, 973, 943, 841, 783, 755, 721, 657 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{23}O_3$ $[M+H]^+$: 359.1642, found: 359.1642.

ethyl 5-(2-bromophenyl)-4-((2-bromophenyl)ethynyl)-2-methylfuran-3-carboxylate (3aj)



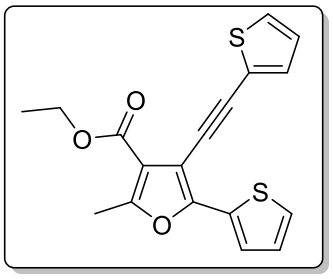
Yield: 21 mg, 43%; yellow liquid; R_f = 0.59 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.54 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.25 – 7.20 (m, 1H), 7.16 – 7.09 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.68 (s, 3H), 1.40 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (s), 159.3 (s), 154.1 (s), 133.6 (d), 133.5 (d), 132.39 (d), 132.38 (d), 130.6 (d), 130.3 (s), 129.3 (d), 127.1 (d), 126.9 (d), 125.7 (s), 125.1 (s), 122.6 (s), 114.9 (s), 106.0 (s), 92.8 (s), 85.5 (s), 60.5 (t), 14.5 (q), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 2977, 2219, 1699, 1595, 1567, 1477, 1457, 1428, 1369, 1331, 1257, 1235, 1210, 1095, 1065, 1023, 975, 835, 781, 751, 722, 685, 665, 638 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{17}Br_2O_3$ $[M+H]^+$: 486.9539, found: 486.9522.

ethyl 5-(3,4-dimethylphenyl)-4-((3,4-dimethylphenyl)ethynyl)-2-methylfuran-3-carboxylate (3ak)



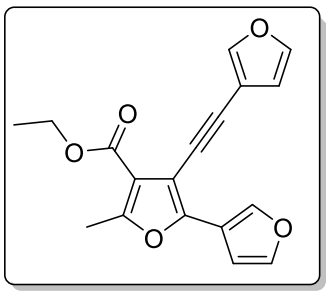
Yield: 25 mg, 65%; colorless solid, mp 152-153 °C; R_f = 0.60 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.86 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.35 (s, 1H), 7.30 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.65 (s, 3H), 2.33 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H), 2.28 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (s), 158.0 (s), 153.8(s), 137.1 (s), 137.0 (s), 136.7 (s), 136.6 (s), 132.4 (d), 129.8 (d), 129.7 (d), 128.7 (d), 127.6 (s), 126.2 (d), 122.6 (d), 121.1 (s), 115.4 (s), 102.2 (s), 95.8 (s), 81.6 (s), 60.3 (t), 20.0 (q), 19.8 (q), 19.7 (q), 19.6 (q), 14.4 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2971, 2920, 1718, 1597, 1503, 1487, 1446, 1407, 1382, 1337, 1287, 1233, 1207, 1179, 1165, 1126, 1098, 1022, 976, 884, 816, 780, 713, 688, 650, 628 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{27}O_3$ $[M+H]^+$: 387.1955, found: 387.1951.

ethyl 2-methyl-5-(thiophen-2-yl)-4-(thiophen-2-ylethynyl)furan-3-carboxylate (3al)



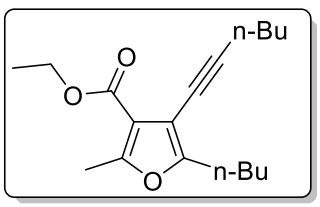
Yield: 25 mg, 73%; yellow solid, mp 73-74 °C; R_f = 0.56 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.34 (dd, *J* = 7.6, 2.7 Hz, 3H), 7.10 (dd, *J* = 5.0, 3.7 Hz, 1H), 7.07 – 7.02 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.64 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (s), 158.3 (s), 150.7 (s), 131.7 (s), 131.65 (d), 127.5 (d), 127.4 (d), 127.2 (d), 125.8 (d), 124.7 (d), 123.6 (s), 115.0 (s), 101.5 (s), 90.3 (s), 85.5 (s), 60.5 (t), 14.3 (q), 14.0 (q). IR (reflection) $\tilde{\nu}$ = 3116, 2982, 2904, 1704, 1605, 1480, 1436, 1406, 1377, 1350, 1315, 1244, 1227, 1173, 1098, 1041, 855, 820, 778, 701, 612 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{15}O_3S_2$ $[M+H]^+$: 343.0457, found: 343.0456.

ethyl 3-(furan-3-ylethynyl)-5-methyl-[2,3'-bifuran]-4-carboxylate (3am)



Yield: 25 mg, 81%; colorless solid, mp 62-63 °C; R_f = 0.55 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 0.6 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.46 (t, *J* = 1.7 Hz, 1H), 7.42 (t, *J* = 1.7 Hz, 1H), 6.94 (dd, *J* = 1.8, 0.6 Hz, 1H), 6.54 (dd, *J* = 1.7, 0.5 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.61 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (s), 158.0 (s) 149.0 (s), 145.3 (d), 143.3 (d), 143.0 (d), 139.9 (d), 116.7 (s), 114.8 (s), 112.4 (d), 107.9 (s), 107.6 (d), 102.1 (s), 86.9 (s), 82.9 (s), 60.4 (t), 14.2 (q), 14.0 (q). IR (reflection) $\tilde{\nu}$ = 3137, 2994, 2227, 1700, 1597, 1512, 1475, 1444, 1414, 1377, 1333, 1260, 1236, 1161, 1148, 1103, 1085, 1056, 1017, 977, 937, 873, 840, 803, 782, 735, 695, 634 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{15}O_5$ $[M+H]^+$: 311.0914, found: 311.0918.

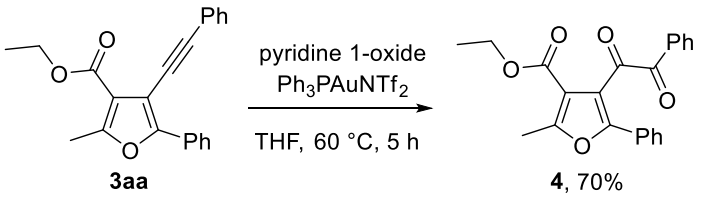
ethyl 5-butyl-4-(hex-1-yn-1-yl)-2-methylfuran-3-carboxylate (3an)



Yield: 18 mg, 62%; yellow liquid; R_f = 0.82 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.29 (q, *J* = 7.1 Hz, 2H), 2.66 (t, *J* = 7.4 Hz, 2H), 2.50 (s, 3H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.66 – 1.56 (m, 4H), 1.52 – 1.44 (m, 2H), 1.38 – 1.31 (m, 5H), 0.93 (dd, *J* = 13.6, 7.3 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (s), 158.4

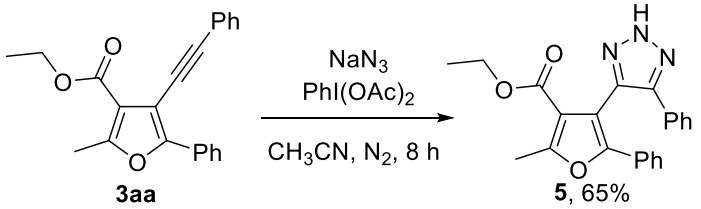
(s), 157.2 (s), 113.8 (s), 103.6 (s), 94.2 (s), 71.4 (s), 60.0 (t), 31.0 (t), 29.9 (t), 26.3 (t), 22.1 (t), 22.0 (t), 19.4 (t), 14.3 (q), 14.0 (q), 13.7 (q), 13.6 (q). IR (reflection) $\tilde{\nu}$ = 2959, 2933, 2873, 2222, 1711, 1610, 1585, 1465, 1429, 1378, 1296, 1228, 1192, 1144, 1085 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{18}H_{27}O_3$ $[M+H]^+$: 291.1955, found: 291.1960.

3.5.4 Diverse transformations of 3aa



3aa **4**, 70%

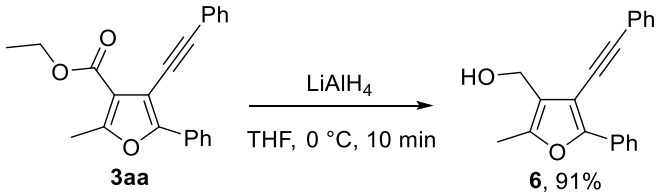
A mixture of **3aa** (0.1 mmol), pyridine 1-oxide (0.2 mmol) and PPh_3AuNTf_2 (5 mol %) in 1.0 mL THF and then heated to 60 °C in an oil bath. The reactions were monitored by TLC analysis and the **3aa** was consumed completely (about 5 h). The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **4**. Yield: 27.0 mg, 70%; yellow liquid; R_f = 0.45 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.11 (m, 2H), 7.87 – 7.80 (m, 2H), 7.66 – 7.59 (m, 1H), 7.56 – 7.48 (m, 2H), 7.44 – 7.36 (m, 3H), 3.99 (q, J = 7.1 Hz, 2H), 2.66 (s, 3H), 1.07 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.3 (s), 188.9 (s), 163.1 (s), 158.2 (s), 155.5 (s), 133.8 (d), 133.0 (s), 130.7 (d, 2C), 129.9 (d), 128.7 (s), 128.45 (d, 2C), 128.43 (d, 2C), 127.7 (d, 2C), 118.9 (s), 114.9 (s), 60.9 (t), 14.1 (q), 13.8 (q). IR (reflection) $\tilde{\nu}$ = 2982, 1701, 1676, 1597, 1580, 1559, 1489, 1449, 1426, 1331, 1265, 1232, 1154, 1100, 1067, 1025, 974, 914, 849, 787, 756, 696 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{19}O_5$ $[M+H]^+$: 363.1227, found: 363.1224.



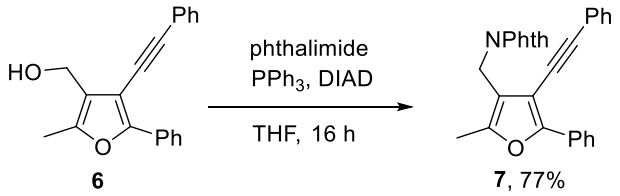
3aa **5**, 65%

The mixture of **3aa** (0.1 mmol), NaN_3 (1.5 equiv), and $PhI(OAc)_2$ (1.5 equiv) in MeCN (2.0 mL) was stirred at room temperature under ambient nitrogen for 8 h, The solvent

was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired product **5**. Yield: 24 mg, 65%; yellow liquid; R_f = 0.40 (PE/EA = 3/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.08 (brs, 1H), 7.66 – 7.60 (m, 2H), 7.38 – 7.33 (m, 2H), 7.31 – 7.27 (m, 1H), 7.26 – 7.24 (m, 2H), 7.23 – 7.17 (m, 3H), 3.95 (q, J = 7.1 Hz, 2H), 2.72 (s, 3H), 0.93 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (s), 159.6 (s), 150.3 (s), 145.43 (s), 145.37 (s), 130.3 (s), 129.4 (s), 128.64 (d, 2C), 128.59 (d, 2C), 128.28 (d), 128.27 (d), 126.6 (d, 2C), 125.4 (d, 2C), 115.6 (s), 119.9 (s), 60.1 (t), 14.2 (q), 13.6 (q). IR (reflection) $\tilde{\nu}$ = 2983, 2927, 2250, 2113, 1714, 1597, 1446, 1382, 1322, 1239, 1212, 1180, 1101, 984, 948, 912, 768, 734, 694, 665, 648 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{22}H_{20}N_3O_3$ $[M+H]^+$: 374.1488, found: 374.1488.



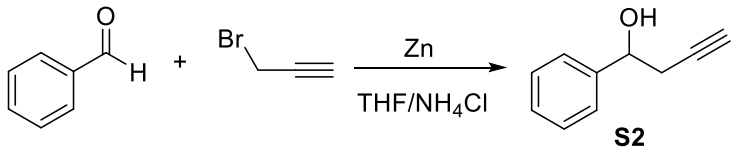
The solution of **3aa** (0.1 mmol) in 1.0 mL THF at 0 °C was slowly added $LiAlH_4$ (0.2 mmol). The resulting solution was warmed to room temperature and stirred for 30 min. The solvent was diluted with water (2.0 mL) and extracted with ethyl acetate and dried over anhydrous $MgSO_4$. After the solvent was evaporated, the crude product was purified by column chromatography give **6**. Yield: 26 mg, 91%; colorless solid, mp 99-100 °C; R_f = 0.23 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dt, J = 8.2, 1.6 Hz, 2H), 7.55 (m, 2H), 7.46 – 7.34 (m, 5H), 7.33 – 7.28 (m, 1H), 4.63 (s, 2H), 2.40 (s, 3H), 1.77 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9 (s), 148.9 (s), 131.4 (d, 2C), 130.4 (s), 128.6 (d, 2C), 128.5 (d, 2C), 128.4 (d), 127.8 (d), 124.5 (d, 2C), 123.3 (s), 122.2 (s), 103.5 (s), 96.0 (s), 81.6 (s), 55.6 (t), 11.8 (q). IR (reflection) $\tilde{\nu}$ = 3237, 3058, 2924, 2871, 2215, 1629, 1603, 1561, 1485, 1443, 1372, 1324, 1256, 1125, 1073, 993, 910, 797, 765, 747, 725, 682, 645 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{20}H_{17}O_2$ $[M+H]^+$: 289.1223, found: 289.1217.



Alcohol **6** (0.1 mmol) was dissolved in anhydrous THF (1.0 mL) and the solution was cooled in an ice-bath. Triphenylphosphane (0.2 mmol), diisopropylazodicarboxylate (DIAD, 0.2 mmol) and phthalimide (0.2 mmol) were added sequentially into the solution. The reaction was stirred at 0 °C for 3 h and then warmed to room temperature. After stirring at room temperature for 12 h, the solution was extracted by EtOAc and washed with water. The organic phase was combined, dried over Na_2SO_4, and concentrated in vacuum. The residue was purified by flash chromatography. Yield: 32 mg, 77%; colorless solid, mp 193-194 °C; R_f = 0.38 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.81 – 7.75 (m, 2H), 7.67 – 7.61 (m, 2H), 7.57 (dt, *J* = 8.3, 2.2 Hz, 2H), 7.42 – 7.31 (m, 5H), 7.29 – 7.24 (m, 1H), 4.79 (s, 2H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8 (s, 2C), 152.9 (s), 150.2 (s), 133.8 (d, 2C), 132.2 (s, 2C), 131.5 (d, 2C), 130.4 (s), 128.4 (d, 2C), 128.2 (d, 2C), 128.1 (d), 127.7 (d), 124.5 (d, 2C), 123.6 (s), 123.2 (d, 2C), 117.2 (s), 103.8 (s), 96.3 (s), 81.8 (s), 32.1 (t), 12.1 (q). IR (reflection) $\tilde{\nu}$ = 3472, 3082, 2921, 1774, 1713, 1633, 1597, 1498, 1485, 1469, 1436, 1396, 1359, 1313, 1252, 1189, 1149, 1112, 1088, 1071, 1040, 1025, 938, 912, 870, 793, 761, 727, 715, 688, 660, 643, 615 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{28}H_{20}NO_3$ $[M+H]^+$: 418.1438, found: 418.1439.

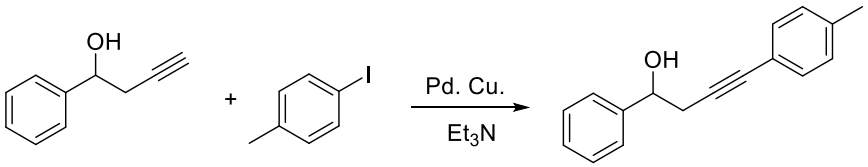
3.5.5 Mechanistic experiments

Preparation of substrates 8:



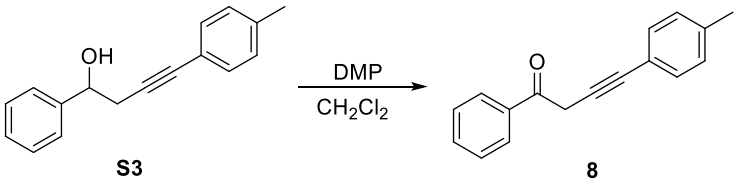
Propargyl bromide (2 equiv) was added to a mixture of the zinc dust (2 equiv) and the aldehydes (1 mmol) in THF/NH_4Cl (1:1) (6 mL) at room temperature. Then, the mixture was stirred at room temperature and monitored by TLC analysis. When the start

material was disappeared, the mixture was extracted with diethyl ether (3 × 5 mL) and the organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography to obtain **S2**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 4.86 (td, *J* = 6.4, 3.5 Hz, 1H), 2.64 (dd, *J* = 6.4, 2.6 Hz, 2H), 2.58 (d, *J* = 3.6 Hz, 1H), 2.07 (t, *J* = 2.6 Hz, 1H). The spectroscopic data is in agreement with that previously reported.[3]



S2 **S3**

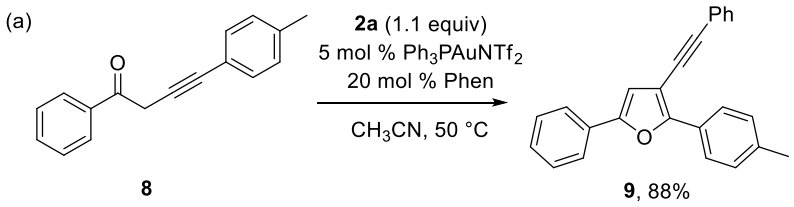
To a dried schlenk flask was added $Pd(PPh_3)_2Cl_2$ (5 mol %), CuI (10 mol %), 4-Iodotoluene (1.1 mmol), **S2** (1.0 mmol) and Et_3N under argon. The resulting mixture was stirred for 16 h at rt. EtOAc were added and the mixture filtered. After removal of solvent using rotary evaporator, the crude compound was purified by silica gel column chromatography to obtain **S3**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 – 7.27 (m, 7H), 7.10 (d, *J* = 7.9 Hz, 2H), 4.95 (t, *J* = 6.4 Hz, 1H), 2.91 – 2.80 (m, 2H), 2.51 (dd, *J* = 9.2, 5.0 Hz, 1H), 2.34 (s, 3H). The spectroscopic data is in agreement with that previously reported.[3]



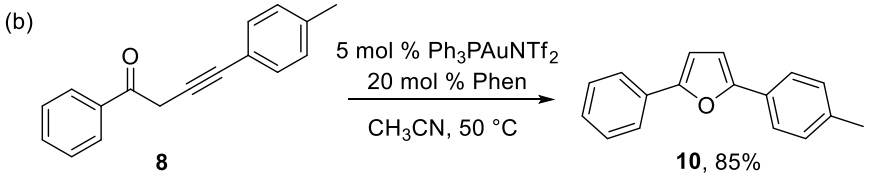
S3 **8**

A solution of the above prepared alcohol **S3** (1.0 mmol) in dichloromethane (5.0 mL) was added to Dess-Martin periodinane (DMP) (1.5 mmol) stirring at room temperature. After disappearance of the starting material (TLC), the reaction mixture was poured into a saturated aqueous $Na_2S_2O_3$ solution and neutralized with saturated with Na_2CO_3 solution. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated. The crude extracts were purified by silica gel column chromatography to obtain **8**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2H), 7.61 (dt, *J* = 2.7, 1.8 Hz, 1H), 7.53 (dd, *J* = 6.3, 1.4 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.9 Hz, 2H),

4.09 (s, 2H), 2.35 (s, 3H). The spectroscopic data is in agreement with that previously reported.[4]



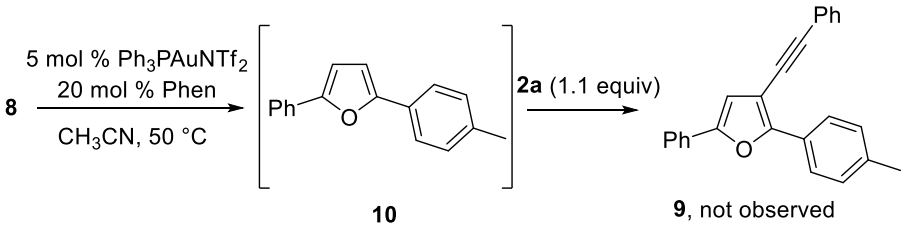
A mixture of **8** (0.1 mmol) and **2a** (1.1 equiv) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol%) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **8** was consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **9**. Yield: 28 mg, 84%; colorless solid, mp 120-121 °C; R_f = 0.78 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.08 (m, 2H), 7.75 (dd, J = 5.2, 3.3 Hz, 2H), 7.62 – 7.56 (m, 2H), 7.48 – 7.35 (m, 5H), 7.34 – 7.27 (m, 3H), 6.84 (s, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4 (s), 152.0 (s), 138.2 (s), 131.4 (d, 2C), 130.1 (s), 129.3 (d, 2C), 128.8 (d, 2C), 128.4 (d, 2C), 128.2 (d), 127.82 (d), 127.75 (s), 124.9 (d, 2C), 123.9 (d, 2C), 123.5 (s), 109.9 (d), 104.1 (s), 93.8 (s), 83.0 (s), 21.4 (q). IR (reflection) $\tilde{\nu}$ = 3031, 2917, 2855, 2207, 1598, 1509, 1482, 1442, 1262, 1157, 1113, 1056, 1028, 930, 915, 818, 799, 754, 714, 691, 684, 656, 644, 614 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{19}O$ $[M+H]^+$: 335.1430, found: 335.1429.



A chemical of **8** (0.1 mmol) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol%) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the chemical **8** was consumed completely. The solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **10**. Yield: 22 mg, 94%; colorless solid,

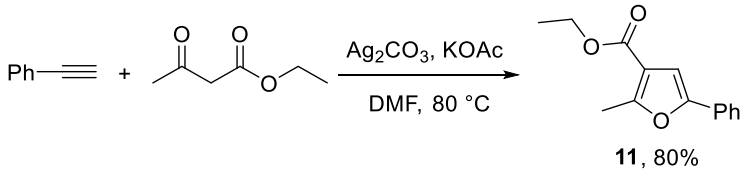
mp 98-99 °C; R_f = 0.80 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 – 7.62 (m, 2H), 7.62 – 7.52 (m, 2H), 7.37 – 7.27 (m, 2H), 7.24 – 7.08 (m, 3H), 6.64 (d, J = 3.5 Hz, 1H), 6.59 (d, J = 3.5 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6 (s), 153.0 (s), 137.3 (s), 130.9 (s), 129.4 (d, 2C), 128.7 (d, 2C), 128.1 (s), 127.2 (d), 123.72 (d, 2C), 123.66 (d, 2C), 107.2 (d), 106.5 (d), 21.3 (q). IR (reflection) $\tilde{\nu}$ = 3039, 3023, 2912, 2856, 2722, 1891, 1811, 1605, 1567, 1545, 1497, 1482, 1446, 1375, 1310, 1289, 1210, 1177, 1156, 1114, 1065, 1024, 967, 928, 910, 821, 794, 758, 715, 691, 672, 639, 619 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{17}H_{15}O$ $[M+H]^+$: 235.1117, found: 235.1119.

(c)

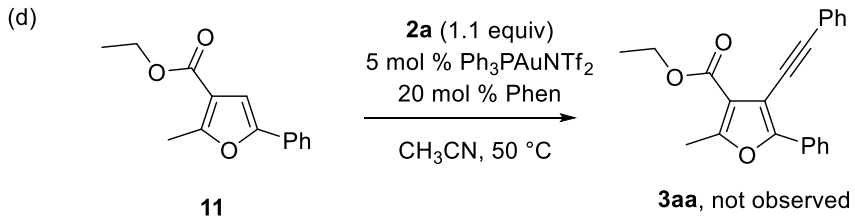


A mixture of **8** (0.1 mmol) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol%) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and the furan **10** was generated then added **2a**. The trisubstituted furan **9** not observed.

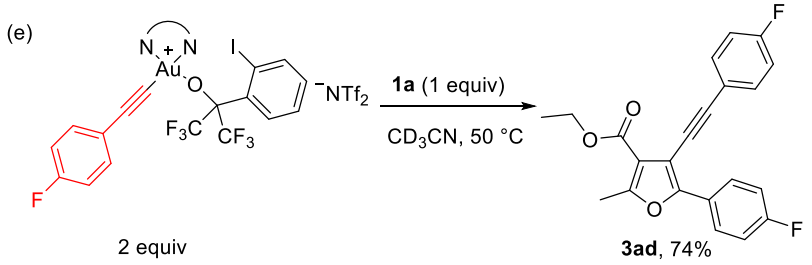
Preparation of substrates 11:



A mixture of phenylacetylene (0.25 mmol), ethyl acetoacetate (0.75 mmol), Ag_2CO_3 (0.50 mmol), and KOAc (0.50 mmol) in DMF was stirred in N_2 at 80 °C in an oil bath for 12 h. After completion of the reaction, the mixture was quenched with diluted hydrochloride, the solution was extracted with ethyl acetate. The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel to afford **11** in 80% yield. ^{1}H NMR (301 MHz, $CDCl_3$) δ 7.57 – 7.41 (m, 2H), 7.21 (dd, J = 10.8, 4.2 Hz, 2H), 7.10 (dd, J = 9.1, 5.6 Hz, 1H), 6.74 (s, 1H), 4.20 (q, J = 7.0 Hz, 2H), 2.49 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H). The spectroscopic data is in agreement with that previously reported.[5]



A mixture of **11** (0.1 mmol) and **2a** (1.1 equiv) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), Phen (20 mol%) and then heated to 50 °C in an oil bath. The reactions were monitored by TLC analysis and not observed chemical **3aa**.



A J. Young tube was charge with PPh_3AuNTf_2 and Phen in CD_3CN. Then alkynyliodonium reagents was added. The reaction was monitored by ^1H and ^{19}F NMR.[6] After determining the formation of **A**, **1a** were added. The reaction mixture was stirred at 50 °C in an oil bath. The reactions were monitored by TLC analysis and the desired products **3ad** was obtain.

3.5.6 References

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(2) von Eckardstein, L.; Petras, D.; Dang, T.; Cociancich, S.; Sabri, S.; Grätz, S.; Kerwat, D.; Seidel, M.; Pesic, A.; Dorrestein, P. C.; Royer, M.; Weston, J. B.; Süssmuth, R. D. *Chem. Eur. J.* **2017**, *23*, 15316–15321.

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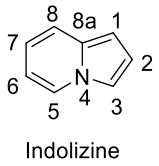
(5) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766–5769.

(6) (a) Yang, Y.; Antoni, P.; Zimmer, M.; Sekine, K.; Mulks, F. F.; Hu, L.; Zhang, L.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2019**, *58*, 5129–5133. (b) Hu, L.; Dietl, M. C.; Han, C.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2021**, *60*, 10637–10642.

Chapter 4. Efficient Access to Indolizines via Gold-Catalyzed Tandem C(sp^3)–H Alkynylation/ aminoalkynylation of 2-(Pyridin-2-yl)acetate Derivatives

4.1 Introduction

Indolizines are important scaffolds found in many natural products and synthetic bioactive compounds.[1] They are constituted by two condensed rings containing a pyrrole-type five-membered ring and a pyridine-type six-membered ring (Fig. 1). For derivatives of indolizine wide applications can be found such as biologically active compounds, such as antitubercular,[2] anticancer,[3] and the usage as molecular probes.[4] Generally, the main strategies for the synthesis of indolizines include intramolecular cyclizations of pyridine derivatives,[5] intermolecular cyclizations of 2-alkylpyridine derivatives[6] and 1,3-dipolar cycloadditions.[7] However, these methods suffer from one or more drawbacks such as the use of less readily available reagents, vigorous reaction conditions and low selectivity that limit these methods to small range synthesis. Due to the importance of these indolizine derivatives in organic synthesis, the development of facile and green synthetic methods to indolizines under mild reaction conditions is still worthwhile.

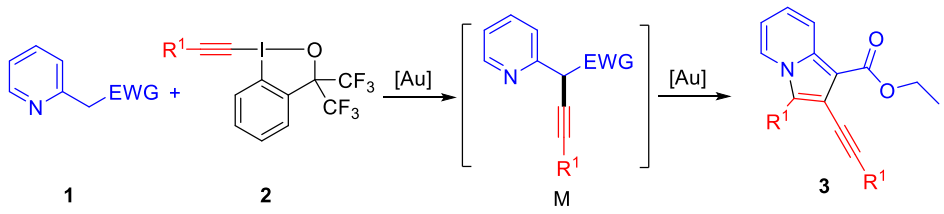


Indolizine

Figure 2 Structure and numbering system of the indolizine skeleton

Recently, several approaches using gold-catalyzed direct C-H functionalization have been reported (see Chapter 2 and 3). Our group reported alkynyl gold(III) complexes as key to the further alkynylation of various substrates, such as *N*-propargylcarboxamides,[8] cyclopropenes,[9] phenols[10] and acceptor-substituted enamines.[11] To further develop the strategy of alkynylations with alkynyl gold(III) complexes, ethyl 2-pyridylacetate was used as a partner for the synthesis of indolizine.

By combining the characteristics of gold(III) species, this reaction will involve two Au(I)/Au(III) catalytic cycles and proceeds through a C(sp^3)–H alkynylation of a substituted pyridine and a subsequent nitro-alkynylation of the generated *β*-alkynyl ester. Two challenges need to be solved by using alkynyl gold(III) complexes: 1) the homocoupling side reaction of alkynyl gold(III) complexes and 2) the control of the active of gold(III) intermediates. Herein, we communicate our efforts in the gold-catalyzed synthesis of poly-substituted indolizines through C(sp^3)–H alkynylation/ nitrogen-alkynylation between ethyl 2-pyridylacetate derivatives and hypervalent iodine reagents (Scheme 4-1).

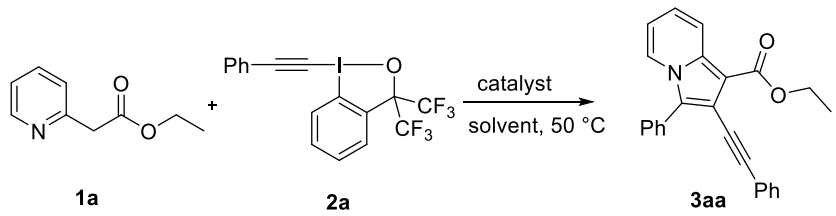


Scheme 4-1 Gold-catalyzed synthesis of poly-substituted indolizines

4.2 Result and Discussion

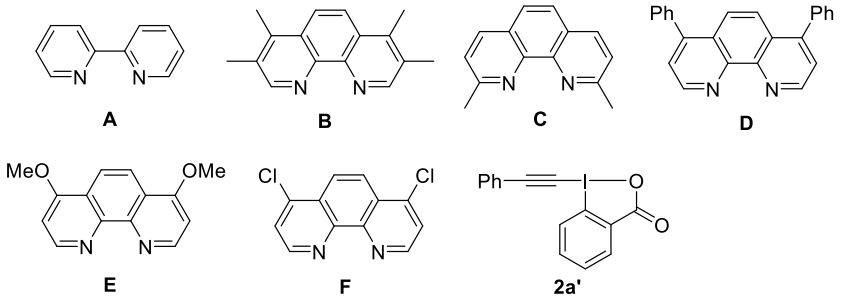
4.2.1 Optimization of the Reaction Conditions

Table 1 Optimization of the Reaction Conditions[a]



Entry	Catalyst	Ligand	Solvent	Yield (%)[b]
1[c]	$Ph_3PAuNTf_2/AgNTf_2$	Phen[d]	CH_3CN	11
2	**$Ph_3PAuNTf_2/AgNTf_2$**	**Phen**	**CH_3CN**	**78 (78)[e]**
3	$Ph_3PAuNTf_2$	Phen	CH_3CN	12
4	-	Phen	CH_3CN	n.d.[f]
5	$Ph_3PAuNTf_2/AgNTf_2$	-	CH_3CN	trace
6	$(C_6F_5)_3PAuNTf_2/AgNTf_2$	Phen	CH_3CN	49
7	$Ph_3PAuCl/AgNTf_2$	Phen	CH_3CN	30
8	JohnPhosAuCl/$AgNTf_2$	Phen	CH_3CN	13

9	IPrAuCl/$AgNTf_2$	Phen	CH_3CN	6
10	$Ph_3PAuNTf_2$/AgOTf	Phen	CH_3CN	31
11	$Ph_3PAuNTf_2$/$AgSbF_6$	Phen	CH_3CN	73
12	$Ph_3PAuNTf_2$/AgOTs	Phen	CH_3CN	45
13	$Ph_3PAuNTf_2$/$AgBF_4$	Phen	CH_3CN	trace
14	$Ph_3PAuNTf_2$/$AgNTf_2$	Phen	DCE[g]	56
15	$Ph_3PAuNTf_2$/$AgNTf_2$	Phen	THF[h]	19
16	$Ph_3PAuNTf_2$/$AgNTf_2$	Phen	toluene	59
17	$Ph_3PAuNTf_2$/$AgNTf_2$	Phen	EtOH	16
18	$Ph_3PAuNTf_2$/$AgNTf_2$	A	CH_3CN	18
19	$Ph_3PAuNTf_2$/$AgNTf_2$	B	CH_3CN	32
20	$Ph_3PAuNTf_2$/$AgNTf_2$	C	CH_3CN	30
21	$Ph_3PAuNTf_2$/$AgNTf_2$	D	CH_3CN	55
22	$Ph_3PAuNTf_2$/$AgNTf_2$	E	CH_3CN	trace
23	$Ph_3PAuNTf_2$/$AgNTf_2$	F	CH_3CN	26
24[i]	$Ph_3PAuNTf_2$/$AgNTf_2$	Phen	CH_3CN	55

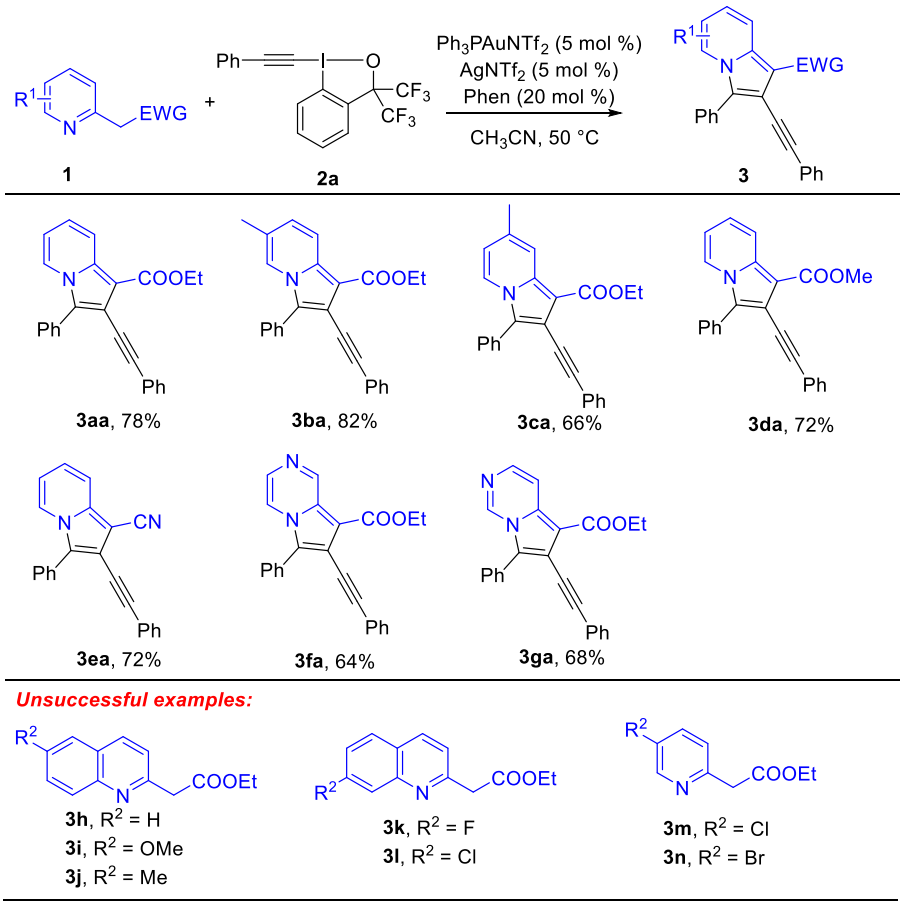


[a]Reaction conditions: **1a** (0.10 mmol), **2a** (0.25 mmol), catalyst (5 mol %), Phen (20 mol %) in solvent (1.0 mL) at 50 ℃. [b]NMR yield with CH_2Br_2 as an internal standard. [c]Room temperature. [d]Phen: 1,10-phenanthroline. [e]Isolated yield. [f]n.d.: not detected. [g]DCE : 1,2-dichloroethane. [h]THF : tetrahydrofuran. [i]Replacement of **2a** with alkynylbenziodoxolone (**2a'**).

We initially optimized the reaction conditions by employing ethyl 2-pyridylacetate **1a** and alkynylbenziodoxole **2a** as model substrates (Table 1). It was found that this reaction takes place at room temperature given the desired product **3aa** in 11% yield (entry 1). By raising the temperature to 50 ℃, we could obtain **3aa** in 78% yield (entry 2). Control experiments indicated that silver is essential (entry 3), none or only trace of product was detected in the absence of either catalyst or ligand (entries 4 and 5).

Subsequently, several other gold catalysts ($(C_6F_5)_3PAuNTf_2$, Ph_3PAuCl, JohnPhosAuCl, IPrAuCl) were tested, but the yield of the desired product **3aa** did not improve (entries 6−9). Other silver catalysts such as AgOTf, $AgSbF_6$, AgOTs and $AgBF_4$ resulted in lower yield (entries 10−13). Furthermore, no improvement was observed when other solvents were used instead of CH_3CN (entries 14−17). Other Phen-type ligands did not improve the reaction efficiency (entries 18–23). When the alkynylbenziodoxolone **2a** was replaced by **2a'**, a lower yield of product **3aa** was detected (entry 24).

4.2.2 Substrate Scope

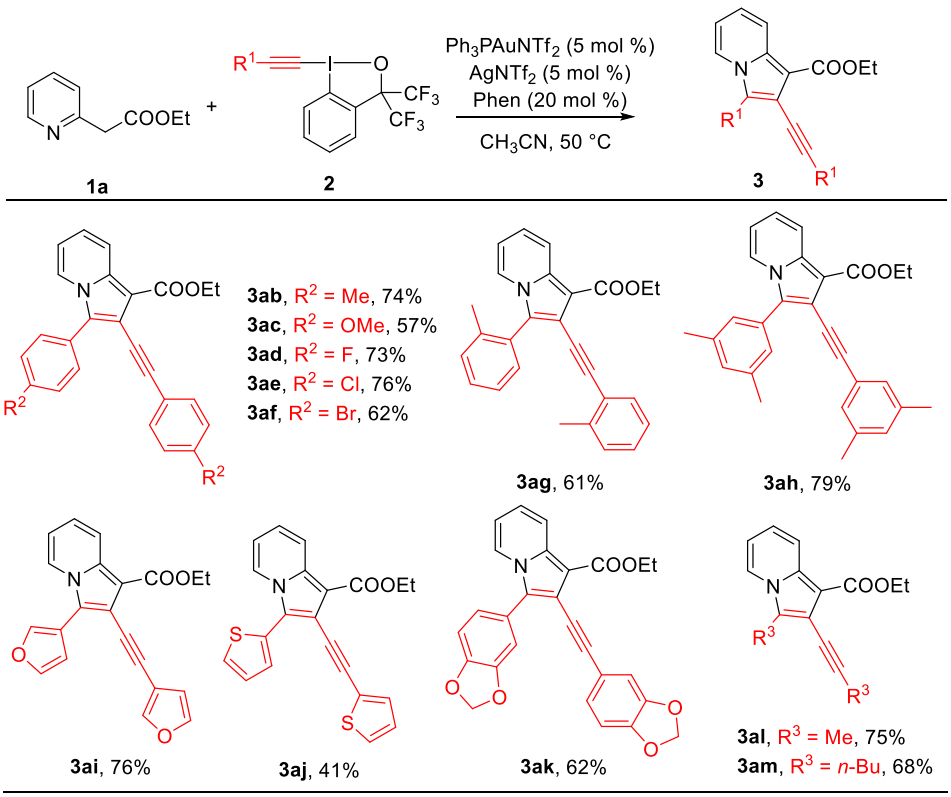


[a]Reaction conditions: **1** (0.10 mmol), **2a** (0.25 mmol), $Ph_3PAuNTf_2$ (5 mol %), $AgNTf_2$ (5 mol %), Phen (20 mol %) in CH_3CN (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 4-2 Scope with respect to different α-acceptor-substituted pyridines[a,b]

Under the optimized reaction conditions (Table 1, entry 2), we first tested different pyridine derivatives. As shown in Scheme 4-2, methyl-substituted 2-pyridylacetate were well tolerated, affording the corresponding products (**3ba**−**ca**) in 66−82% yield.

The structure of **3aa** was confirmed by single crystal X-ray structure analysis (Figure 2). Replacement of the ester group of **2a** by COOMe or CN gave products **3da** and **3ea** in 72% yield. Heteroaryl-derived products (**3fa** and **3ga**) were readily prepared in good yield under the standard conditions. Unfortunately, electron-withdrawing substituents on the pyridine ring did not give the desired products. In addition, quinoline derivatives (**3h**−**l**) failed to transform to the corresponding products.



[a]Reaction conditions: **1a** (0.10 mmol), **2** (0.25 mmol), $Ph_3PAuNTf_2$ (5 mol %), $AgNTf_2$ (5 mol %), Phen (20 mol %) in CH_3CN (1.0 mL) at 50 °C. [b]Isolated yield.

Scheme 4-3 Scope with respect to hypervalent iodine reagents[a,b]

As a next step we investigated the scope of the hypervalent iodine reagents. As shown in Scheme 4-3, aryl-substituted ethynylbenziodoxoles bearing either electron-donating (Me, OMe) or halide (F, Cl, Br) groups successfully reacted with ethyl 2-pyridylacetate **1a** to produce the corresponding products **3ab**−**ah** in 57−79% yield. The use of heteroaryl alkynes enabled the synthesis of products **3ai**−**aj** bearing three heterocyclic units in good yield. Notable, alkyl-substituted ethynylbenziodoxoles such as Me or *n*-Bu groups were also applicable for the transformation yielding the desired products

3al in 75% yield and **3am** in 68% yield. Moreover a gram-scale synthesis of **3aa** was possible (Scheme 4-4, 1.03 g of **3aa** was isolated).

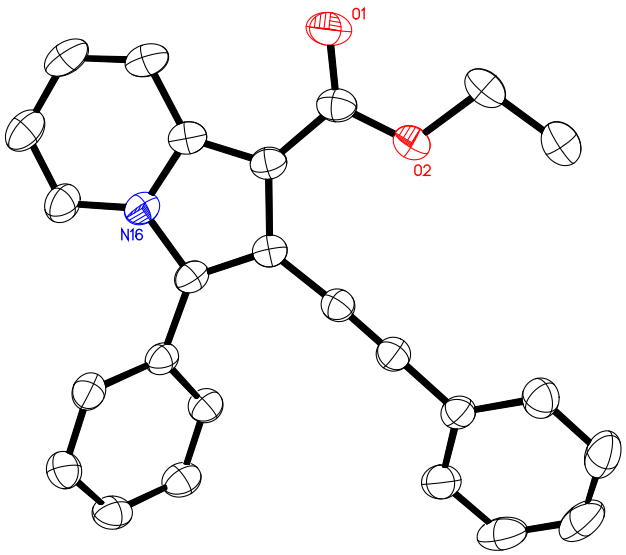
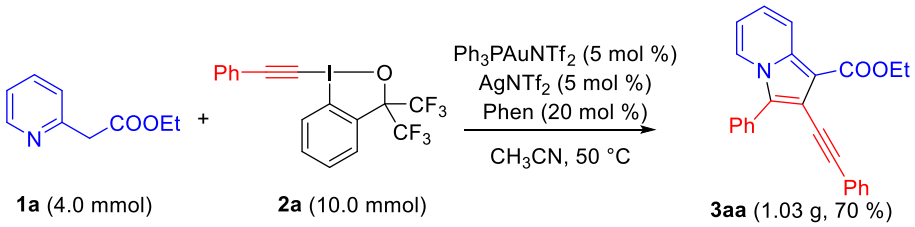
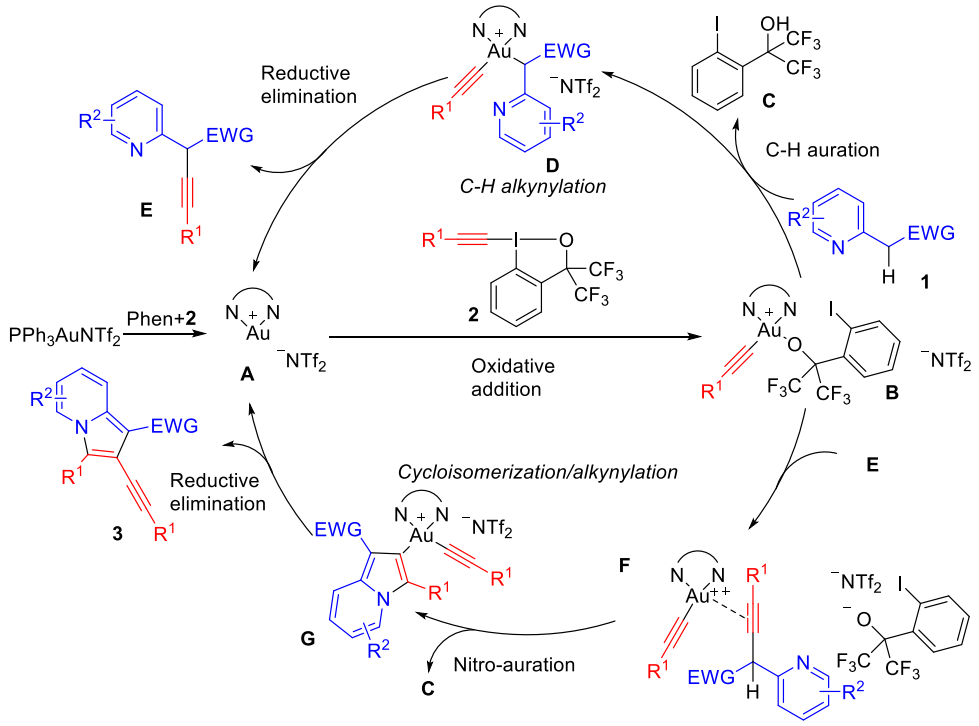


Figure 2 Solid state molecular structure of **3aa**



Scheme 4-4 Gram-scale synthesis



Scheme 4-5 Proposed reaction mechanism

On the basis of previous reports,[9-11] a plausible mechanism[12] is described in Scheme 4-5. First, Au(I) species **A** is formed in the presence of 1,10-phenanthroline and hypervalent iodine reagent **2**. Subsequently, alkynyl Au(III) complex **B** is formed by oxidative addition of **A** with hypervalent iodine reagent **2**. The C-H auration of 2-pyridine derivatives **1** with Au(III) complex **B** then occurs to produce Au(III) complex **D** and a subsequent reductive elimination gives compound **E**. In the second catalytic cycle, the alkynyl moiety of **E** coordinates with alkynyl Au(III) complex **B**, subsequently, the intramolecular nucleophilic attack of the nitrogen atom affords Au(III) 3-furyl complex **G**. Upon reductive elimination of **G**, the desired product **3** is formed, and meanwhile Au(I) species **A** is regenerated to complete the catalytic cycle.

4.3 Conclusions

In summary, we reported the synthesis of indolizines by employing a gold-catalyzed C(sp^3)-H alkynylation/nitrogen-alkynylation sequence of 2-pyridine compounds with hypervalent iodine reagents. The broad substrate scope, good functional group tolerance and good efficiency render this method useful for organic synthesis,

especially for the synthesis of nitrogen-containing compounds. Gram-scale synthesis and proposed mechanism are also revealed.

4.4 References

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4.5 Experimental Section

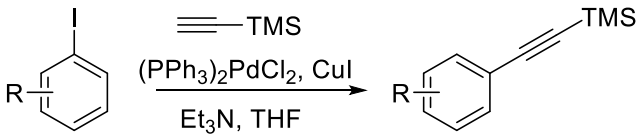
4.5.1 General Remarks

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®.

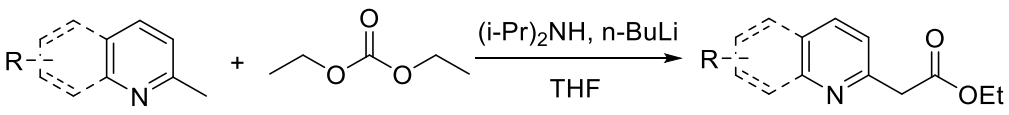
4.5.2 Experiment Procedures

Procedure A: Trimethylsilyl alkynes



To a mixture of 4-iodotoluene (10 mmol), $(PPh_3)_2PdCl_2$ (30 mg, 0.04 mmol), and CuI (15 mg, 0.08 mmol) in Et_3N (1.7 mL) and THF (15 mL) was added (trimethylsilyl)acetylene (1.7 mL, 12 mmol), and the reaction mixture was stirred under nitrogen atmosphere at room temperature for 3 h. After filtration, the filtrate was evaporated under reduced pressure. The residue was then diluted with diethyl ether (15 mL) and the ethereal layer was washed with water and dried over $MgSO_4$. After filtration, the solvent was evaporated and the resulting crude product was subjected to silica gel column chromatography.

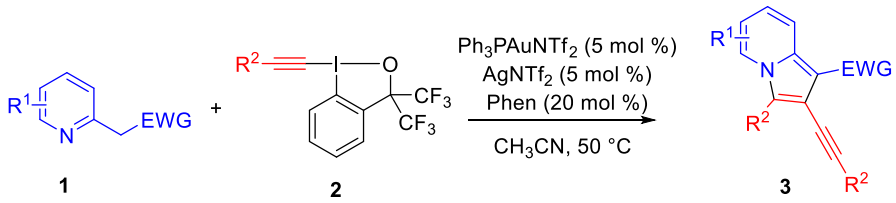
Procedure B: The synthesis of 2-pyridines derivatives



A mixture of 1.52 g of diisopropylamine (2.1 mL, 15 mmol) and 5 mL of dried THF was added to a three-necked flask by syringe under N_2. After being cooled down to -78 °C, 5.6 mL of n-butyllithium (2.5 M in hexane, 14 mmol) was slowly added. The mixture was stirred for 30 min. Then 2-methylquinoline (5 mmol) was slowly added.

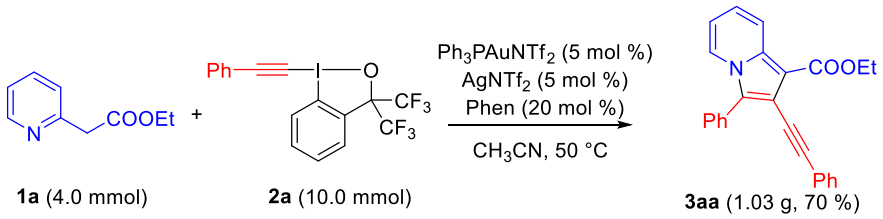
The color turned to orange rapidly and then to dark brown. After 30 min, 2.19 g of diethyl carbonate (2.3 mL, 18.5 mmol) was added, and the mixture was stirred for 2 h. The reaction was quenched by 10 mL of water followed by extraction by EtOAc. The combined organic layers were dried over Na_2SO_4 and evaporated in vacuo. The crude residue was purified by silica gel column chromatography to give the desired products.

Procedure C: Synthesis of **3**



A mixture of **1** (0.10 mmol) and **2** (0.25 mmol) in 1.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), $AgNTf_2$ (5 mol %), Phen (20 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.

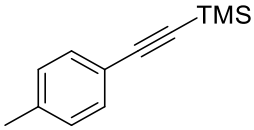
Procedure D: Gram-Scale Synthesis **3aa**



A mixture of **1a** (4.0 mmol) and **2a** (10.0 mmol) in 15.0 mL CH_3CN was treated with PPh_3AuNTf_2 (5 mol %), $AgNTf_2$ (5 mol %), Phen (20 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 solvent was removed under vacuum and the crude residue was purified by silica gel column chromatography to give the desired products **3aa** in 70% yield (1.03 g).

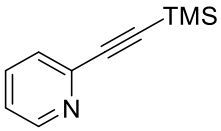
4.5.3 Characterization Data

trimethyl(p-tolylethynyl)silane (cy-1-122)



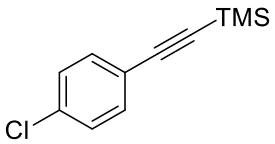
Yield: 1.585 g, 85%; pale yellow liquid; R_f = 0.78 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 2.36 (s, 3H), 0.29 (s, 9H). The spectroscopic data is in agreement with that previously reported.[1]

2-((trimethylsilyl)ethynyl)pyridine (cy-1-124)



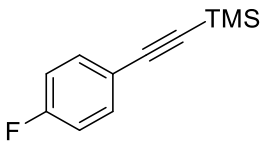
Yield: 1.51 g, 87%; brown oil; R_f = 0.23 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 4.8, 0.9 Hz, 1H), 7.54 (td, *J* = 7.7, 1.8 Hz, 1H), 7.35 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.12 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 0.19 (s, 9H). The spectroscopic data is in agreement with that previously reported.[2]

((4-chlorophenyl)ethynyl)trimethylsilane (cy-1-125)



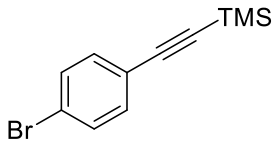
Yield: 2.01 g, 97%; pale yellow solid; R_f = 0.78 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.36 (m, 2H), 7.34 – 7.26 (m, 2H), 0.27 (s, 9H). The spectroscopic data is in agreement with that previously reported.[3]

((4-fluorophenyl)ethynyl)trimethylsilane (cy-1-131)



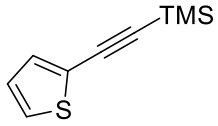
Yield: 1.687 g, 88%; pale yellow liquid; R_f = 0.88 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.39 (m, 2H), 7.05 – 6.93 (m, 2H), 0.25 (s, 9H). The spectroscopic data is in agreement with that previously reported.[4]

((4-bromophenyl)ethynyl)trimethylsilane (cy-1-130)



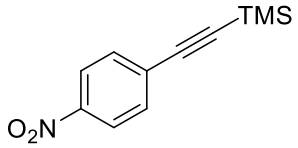
Yield: 2.18 g, 87%; pale yellow solid; R_f = 0.83 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.39 (m, 2H), 7.36 – 7.29 (m, 2H), 0.25 (s, 9H). The spectroscopic data is in agreement with that previously reported.[1]

trimethyl(thiophen-2-ylethynyl)silane (cy-1-135)



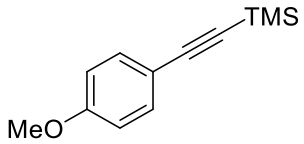
Yield: 1.56 g, 87%; colorless liquid; R_f = 0.72 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.20 (m, 2H), 6.97 (dd, J = 5.1, 3.7 Hz, 1H), 0.28 (s, 9H). The spectroscopic data is in agreement with that previously reported.[5]

trimethyl((4-nitrophenyl)ethynyl)silane (cy-1-134)



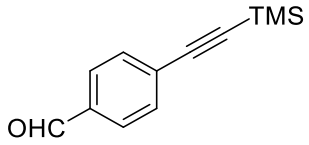
Yield: 1.92 g, 88%; yellow solid; R_f = 0.23 (PE); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, J = 8.9 Hz, 2H), 7.58 (d, J = 8.9 Hz, 2H), 0.27 (s, 9H). The spectroscopic data is in agreement with that previously reported.[6]

((4-methoxyphenyl)ethynyl)trimethylsilane (cy-1-138)



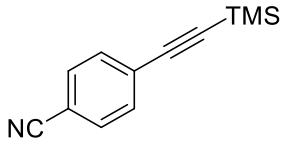
Yield: 1.82 g, 90%; yellow liquid; R_f = 0.17 (PE); ^{1}H NMR (301 MHz, $CDCl_3$) δ 7.48 – 7.36 (m, 2H), 6.88 – 6.77 (m, 2H), 3.79 (s, 3H), 0.26 (s, 9H). The spectroscopic data is in agreement with that previously reported.[7]

4-((trimethylsilyl)ethynyl)benzaldehyde (cy-1-139)



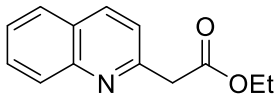
Yield: 1.92 g, 95%; yellow solid; R_f = 0.81 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.85 – 7.76 (m, 2H), 7.63 – 7.54 (m, 2H), 0.26 (s, 9H). The spectroscopic data is in agreement with that previously reported.[8]

4-((trimethylsilyl)ethynyl)benzonitrile (cy-177)



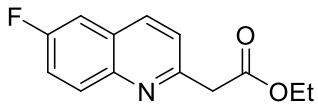
Yield: 1.92 g, 95%; yellow solid; R_f = 0.78 (PE/EA = 10/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 – 7.56 (m, 2H), 7.55 – 7.50 (m, 2H), 0.26 (s, 9H). The spectroscopic data is in agreement with that previously reported.[9]

ethyl 2-(quinolin-2-yl)acetate (cy-196)



Yield: 704 mg, 66%; light yellow oil; R_f = 0.36 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.69 (m, 1H), 7.56 – 7.47 (m, 1H), 7.43 (d, J = 8.4 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 4.03 (s, 2H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.5 (s), 154.9 (s), 147.9 (s), 136.6 (d), 129.6 (d), 129.1 (d), 127.5 (d), 127.1 (s), 126.4 (d), 121.8 (d), 61.1 (t), 44.9 (t), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3451, 3059, 2981, 2936, 2905, 2873, 1733, 1648, 1620, 1599, 1566, 1505, 1464, 1427, 1390, 1369, 1328, 1261, 1150, 1115, 1030, 941, 829, 768, 745, 706, 619 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{14}NO_2$ $[M+H]^+$: 216.1019, found: 216.1020.

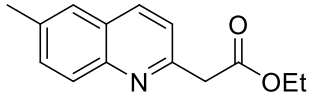
ethyl 2-(6-fluoroquinolin-2-yl)acetate (cy-238)



Yield: 680 mg, 59%; yellow solid; R_f = 0.40 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 – 8.01 (m, 2H), 7.43 (m, 3H), 4.20 (q, J = 7.1 Hz, 2H), 4.01 (s, 2H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.4 (s), 160.4 (d, ^1J = 247.8 Hz), 154.2 (d, ^4J = 2.8 Hz), 145.0 (s), 135.9 (d, ^4J = 5.3 Hz), 131.6 (d, ^3J = 9.1 Hz), 127.6 (d, ^3J = 10.1 Hz), 122.5 (d), 119.7 (d, ^2J = 25.6 Hz), 110.5 (d, ^2J = 21.7 Hz), 61.2 (t), 44.77 (t),

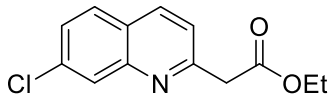
14.2 (q). IR (reflection) $\tilde{\nu}$ = 3435, 3062, 2992, 2961, 2941, 2907, 1977, 1898, 1725, 1630, 1611, 1566, 1508, 1478, 1410, 1397, 1371, 1334, 1304, 1258, 1224, 1176, 1142, 1109, 1031, 964, 939, 919, 874, 826, 782, 742, 681 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{13}FNO_2$ $[M+H]^+$: 234.0925, found: 234.0927.

ethyl 2-(6-methylquinolin-2-yl)acetate (cy-240)



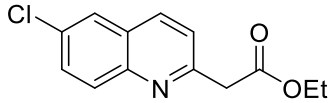
Yield: 638 mg, 59%; yellow liquid; R_f = 0.34 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.5 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.52 (dd, *J* = 10.8, 2.1 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 2.52 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.5 (s), 153.8 (s), 146.4 (s), 136.1 (s), 135.9 (d), 131.8 (d), 128.7 (d), 127.0 (s), 126.3 (d), 121.6 (d), 61.0 (t), 44.7 (t), 21.4 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2983, 2919, 2876, 1731, 1600, 1565, 1497, 1464, 1417, 1369, 1321, 1270, 1239, 1190, 1154, 1032, 958, 897, 880, 828, 743, 679, 624 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{14}H_{16}NO_2$ $[M+H]^+$: 230.1176, found: 230.1177.

ethyl 2-(7-chloroquinolin-2-yl)acetate (cy-241)



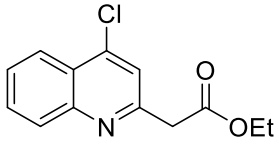
Yield: 432 mg, 35%; yellow solid; R_f = 0.28 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 11.0, 5.3 Hz, 2H), 7.73 (d, *J* = 8.7 Hz, 1H), 7.47 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.2 (s), 156.0 (s), 148.1 (s), 136.3 (d), 135.4 (s), 128.6 (d), 128.1 (d), 127.4 (d), 125.3 (s), 121.9 (d), 61.1 (t), 44.7 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3077, 3054, 2987, 2943, 2905, 2878, 1732, 1612, 1597, 1564, 1542, 1498, 1477, 1450, 1406, 1367, 1339, 1325, 1246, 1231, 1184, 1163, 1116, 1069, 1027, 944, 902, 881, 847, 812, 788, 766, 731, 652, 639, 619 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{13}ClNO_2$ $[M+H]^+$: 250.0629, found: 250.0631.

ethyl 2-(6-chloroquinolin-2-yl)acetate (cy-256)



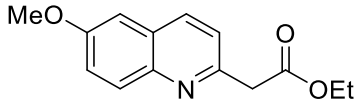
Yield: 622 mg, 50%; yellow solid; R_f = 0.32 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.78 (d, *J* = 2.3 Hz, 1H), 7.63 (dd, *J* = 9.0, 2.3 Hz, 1H), 7.45 (d, *J* = 8.5 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.2 (s), 155.1 (s), 146.2 (s), 135.6 (d), 132.0 (s), 130.7 (d), 130.4 (d), 127.6 (s), 126.1 (d), 122.6 (d), 61.1 (t), 44.7 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2989, 2943, 2907, 1981, 1906, 1722, 1683, 1605, 1562, 1495, 1476, 1408, 1391, 1366, 1349, 1331, 1305, 1263, 1230, 1206, 1171, 1126, 1113, 1082, 1035, 986, 937, 892, 879, 826, 814, 785, 756, 727, 645 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{13}ClNO_2$ $[M+H]^+$: 250.0629, found: 250.0631.

ethyl 2-(4-chloroquinolin-2-yl)acetate (cy-258)



Yield: 689 mg, 56%; yellow liquid; R_f = 0.36 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 – 8.17 (m, 1H), 8.10 – 8.03 (m, 1H), 7.75 (m, 1H), 7.61 (m, 1H), 7.55 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 4.00 (s, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.0 (s), 154.6 (s), 148.5 (s), 142.9 (s), 130.4 (d), 129.4 (d), 127.3 (d), 125.2 (s), 123.9 (d), 121.8 (d), 61.2 (t), 44.4 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3449, 3066, 2982, 2936, 2906, 1962, 1739, 1617, 1589, 1555, 1520, 1495, 1463, 1445, 1410, 1369, 1343, 1303, 1258, 1155, 1118, 1096, 1030, 988, 955, 917, 872, 834, 760, 654 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{13}ClNO_2$ $[M+H]^+$: 250.0629, found: 250.0631.

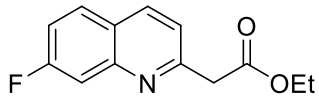
ethyl 2-(6-methoxyquinolin-2-yl)acetate (cy-260)



Yield: 721 mg, 59%; yellow liquid; R_f = 0.34 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.43 – 7.29 (m, 2H), 7.04 (d, *J* = 2.8 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.99 (s, 2H), 3.90 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.7 (s), 157.7 (s), 152.2 (s), 143.9 (s), 135.4 (d), 130.4 (d), 128.0 (s), 122.2 (d), 122.0 (d), 105.1 (d), 61.1 (t), 55.5 (q), 44.5 (t), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2990, 2943, 2902, 2836, 2358, 1722, 1682, 1626, 1606, 1570, 1502, 1485, 1456, 1441, 1401,

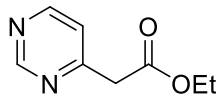
1368, 1330, 1311, 1265, 1227, 1195, 1167, 1115, 1037, 953, 937, 915, 885, 855, 830, 786, 739, 677, 621 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{14}H_{16}NO_3$ $[M+H]^+$: 246.1125, found: 246.1124.

ethyl 2-(7-fluoroquinolin-2-yl)acetate (cy-262)



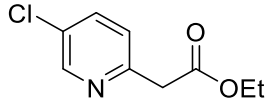
Yield: 485 mg, 42%; yellow liquid; R_f = 0.52 (PE/EA = 5/1); ^{1}H NMR (301 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 1H), 7.78 (dd, *J* = 9.0, 6.1 Hz, 1H), 7.69 (dd, *J* = 10.2, 2.5 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 1H), 7.36 – 7.27 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.3 (s), 163.2 (d, ^1J = 249.9 Hz), 156.0 (s), 148.8 (d, ^3J = 12.7 Hz), 136.5 (d, ^6J = 0.9 Hz), 129.5 (d, ^3J = 10.0 Hz), 124.1 (d, ^4J = 1.1 Hz), 121.2 (d, ^5J = 2.6 Hz), 116.9 (d, ^2J = 25.4 Hz), 112.8 (d, ^2J = 20.4 Hz), 61.2 (t), 44.7 (t), 14.2 (q). IR (reflection) $\tilde{\nu}$ = 2978, 2933, 1721, 1629, 1510, 1436, 1394, 1371, 1336, 1255, 1210, 1193, 1161, 1112, 1028, 961, 922, 863, 846, 824, 796, 775, 744, 690, 651, 628 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{13}H_{13}FNO_2$ $[M+H]^+$: 234.0925, found: 234.0927.

ethyl 2-(pyrimidin-4-yl)acetate (cy-265)



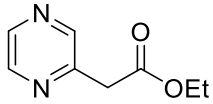
Yield: 297 mg, 36%; yellow liquid; R_f = 0.38 (PE/EA = 1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (d, *J* = 0.8 Hz, 1H), 8.69 (d, *J* = 5.2 Hz, 1H), 7.37 (dd, *J* = 5.2, 1.3 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.1 (s), 162.9 (s), 158.8 (d), 157.1 (d), 121.4 (d), 61.5 (t), 43.4 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3043, 2983, 2937, 2908, 1737, 1583, 1552, 1476, 1389, 1370, 1338, 1257, 1183, 1158, 1029, 993, 831, 708 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_8H_{11}N_2O_2$ $[M+H]^+$: 167.0815, found: 167.0811.

ethyl 2-(5-chloropyridin-2-yl)acetate (cy-267)



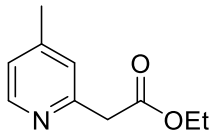
Yield: 212 mg, 22%; colorless liquid; R_f = 0.50 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 2.3 Hz, 1H), 7.64 (dd, *J* = 8.3, 2.5 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.2 (s), 152.6 (s), 148.2 (d), 136.5 (d), 130.7 (s), 124.7 (d), 61.2 (t), 43.2 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2982, 2935, 1737, 1580, 1561, 1471, 1370, 1335, 1255, 1180, 1156, 1109, 1030, 1016, 822, 633 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_9H_{11}ClNO_2$ $[M+H]^+$: 200.0473, found: 200.0465.

ethyl 2-(pyrazin-2-yl)acetate (cy-272)



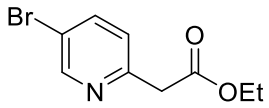
Yield: 522 mg, 63%; yellow liquid; R_f = 0.32 (PE/EA = 1/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (d, *J* = 1.2 Hz, 1H), 8.55 – 8.51 (m, 1H), 8.48 (d, *J* = 2.5 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.7 (s), 150.5 (s), 145.3 (d), 144.2 (d), 143.1 (d), 61.4 (t), 41.3 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 2983, 2937, 1735, 1580, 1529, 1476, 1405, 1369, 1337, 1253, 1177, 1058, 1020, 832, 768 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_8H_{11}N_2O_2$ $[M+H]^+$: 167.0815, found: 167.0812.

ethyl 2-(4-methylpyridin-2-yl)acetate (cy-275)



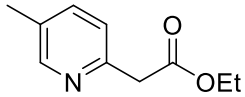
Yield: 482 mg, 54%; colorless liquid; R_f = 0.40 (PE/EA = 2/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, *J* = 5.1 Hz, 1H), 7.08 (s, 1H), 6.96 (d, *J* = 5.0 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.75 (s, 2H), 2.29 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.8 (s), 154.2 (s), 149.1 (d), 147.8 (s), 124.7 (d), 123.1 (d), 60.9 (t), 43.8 (t), 20.9 (q), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3055, 2982, 2931, 2873, 1737, 1606, 1562, 1479, 1447, 1368, 1333, 1265, 1154, 1100, 1032, 828 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{10}H_{14}NO_2$ $[M+H]^+$: 180.1019, found: 180.1017.

ethyl 2-(5-bromopyridin-2-yl)acetate (cy-280)



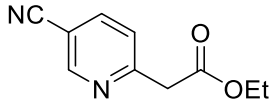
Yield: 524 mg, 43%; colorless liquid; R_f = 0.48 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, *J* = 2.3 Hz, 1H), 7.78 (dd, *J* = 8.3, 2.4 Hz, 1H), 7.21 (d, *J* = 8.3 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1 (s), 153.0 (s), 150.5 (d), 139.3 (d), 125.2 (d), 119.3 (s), 61.2 (t), 43.2 (t), 14.1 (q). IR (reflection) $\tilde{\nu}$ = 3452, 3049, 2982, 2936, 2906, 1736, 1575, 1557, 1469, 1412, 1369, 1335, 1256, 1181, 1093, 1030, 1009, 941, 887, 820, 769, 695, 660, 630 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_9H_{11}BrNO_2$ $[M+H]^+$: 243.9968, found: 243.9965.

ethyl 2-(5-methylpyridin-2-yl)acetate (cy-307)



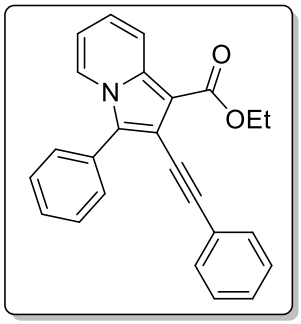
Yield: 525 mg, 59%; yellow liquid; R_f = 0.21 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 1.9 Hz, 1H), 7.46 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.80 (s, 2H), 2.32 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.9 (s), 151.5 (s), 149.7 (d), 137.3 (d), 131.5 (s), 123.3 (d), 61.0 (t), 43.5 (t), 18.1 (q), 14.2 (q). HRMS (ESI, m/z) calc'd for $C_{10}H_{14}NO_2$ $[M+H]^+$: 180.1019, found: 180.1016.

ethyl 2-(5-cyanopyridin-2-yl)acetate (cy-312)



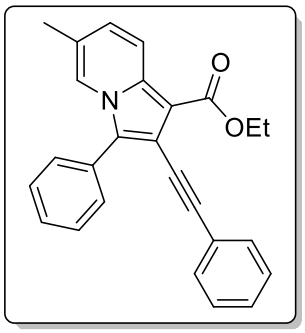
Yield: 225 mg, 24%; yellow liquid; R_f = 0.32 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, *J* = 1.8 Hz, 1H), 7.94 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.92 (s, 2H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.5 (s), 158.8 (s), 152.2 (d), 139.7 (d), 124.1 (d), 116.6 (s), 108.5 (s), 61.5 (t), 44.0 (t), 14.1 (q). HRMS (ESI, m/z) calc'd for $C_{10}H_{11}N_2O_2$ $[M+H]^+$: 191.0815, found: 191.0812.

ethyl 3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (cy-316)(cy-574) (3aa)



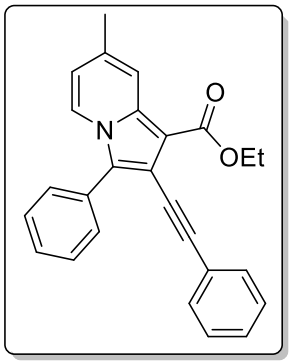
Yield: 30 mg, 78%; yellow solid; R_f = 0.48 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 9.1 Hz, 1H), 8.18 (d, J = 7.0 Hz, 1H), 7.70 (d, J = 7.6 Hz, 2H), 7.55 (t, J = 7.3 Hz, 2H), 7.45 (dd, J = 15.8, 7.5 Hz, 3H), 7.29 (d, J = 6.2 Hz, 3H), 7.13 – 7.05 (m, 1H), 6.70 (t, J = 6.7 Hz, 1H), 4.47 (q, J = 7.0 Hz, 2H), 1.49 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 164.6 (s), 135.9 (s), 131.5 (d, 2C), 129.9 (d, 2C), 129.7 (s), 129.5 (s), 128.9 (d, 2C), 128.7 (d), 128.2 (d, 2C), 128.0 (d), 123.9 (s), 123.2 (d), 123.0 (d), 120.3 (d), 113.4 (d), 110.3 (s), 104.4 (s), 94.1 (s), 84.2 (s), 59.8 (t), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 3078, 3056, 3024, 2985, 2950, 2904, 1678, 1633, 1600, 1537, 1525, 1508, 1479, 1440, 1407, 1383, 1346, 1323, 1274, 1247, 1215, 1185, 1157, 1139, 1123, 1071, 1027, 965, 904, 830, 780, 749, 738, 703, 684, 666, 618 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{20}NO_2$ $[M+H]^+$: 366.1489, found: 366.1489.

ethyl 6-methyl-3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (cy-454) (3ba)



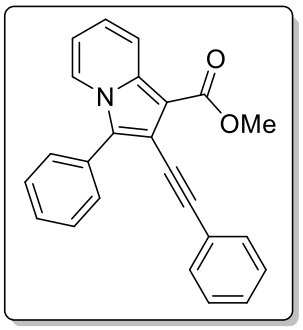
Yield: 31 mg, 82%; yellow solid; R_f = 0.46 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 9.2 Hz, 1H), 7.88 (d, J = 1.1 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.53 – 7.45 (m, 2H), 7.40 (dt, J = 4.7, 1.8 Hz, 1H), 7.36 – 7.30 (m, 2H), 7.22 – 7.17 (m, 3H), 6.88 (dd, J = 9.3, 1.3 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 2.17 (d, J = 0.7 Hz, 3H), 1.40 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5 (s), 134.7 (s), 131.3 (d, 2C), 129.9 (d, 2C), 129.7 (s), 129.2 (s), 128.7 (d, 2C), 128.5 (d), 128.1 (d, 2C), 127.8 (d), 126.3 (d), 123.9 (s), 122.9 (s), 120.5 (d), 119.6 (d), 109.8 (s), 104.1 (s), 93.7 (s), 84.3 (s), 59.6 (t), 18.4 (q), 14.6 (q). IR (reflection) $\tilde{\nu}$ = 2982, 2953, 2212, 1672, 1597, 1542, 1510, 1441, 1425, 1381, 1337, 1309, 1276, 1251, 1215, 1127, 1068, 964, 911, 802, 774, 753, 721, 703, 688, 664, 643 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{21}NNaO_2$ $[M+Na]^+$: 402.1465, found: 402.1459.

ethyl 7-methyl-3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (cy-455) (3ca)



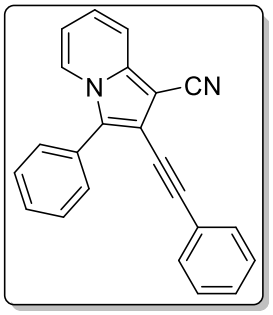
Yield: 25 mg, 66%; yellow solid; R_f = 0.46 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.05 (m, 2H), 7.72 – 7.66 (m, 2H), 7.54 (dd, *J* = 10.7, 4.4 Hz, 2H), 7.49 – 7.38 (m, 3H), 7.32 – 7.26 (m, 3H), 6.55 (dd, *J* = 7.2, 1.8 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7 (s), 136.6 (s), 134.2 (s), 131.4 (d, 2C), 129.9 (d, 2C), 129.7 (s), 129.2 (s), 128.8 (d, 2C), 128.5 (d), 128.2 (d, 2C), 127.8 (d), 124.0 (s), 122.6 (d), 118.6 (d), 116.0 (d), 109.9 (s), 102.9 (s), 93.8 (s), 84.4 (s), 59.7 (t), 21.4 (q), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2982, 2214, 1739, 1677, 1598, 1512, 1439, 1399, 1379, 1341, 1275, 1252, 1220, 1183, 1166, 1124, 1062, 1037, 913, 876, 770, 749, 721, 704, 688, 655 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{26}H_{21}NNaO_2$ $[M+Na]^+$: 402.1465, found: 402.1462.

methyl 3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (cy-522) (3da)



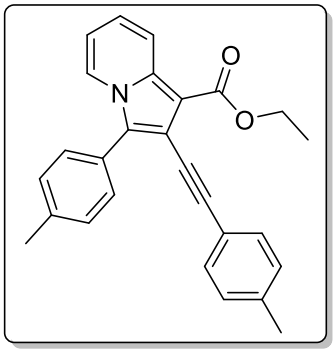
Yield: 25 mg, 72%; yellow solid; R_f = 0.44 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 9.1, 1.2 Hz, 1H), 8.19 (dt, *J* = 7.1, 1.1 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.60 – 7.52 (m, 2H), 7.50 – 7.39 (m, 3H), 7.29 (dd, *J* = 5.0, 1.9 Hz, 3H), 7.10 (ddd, *J* = 9.1, 6.6, 1.1 Hz, 1H), 6.72 (td, *J* = 7.0, 1.3 Hz, 1H), 4.00 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.8 (s), 135.9 (s), 131.4 (d, 2C), 129.8 (d, 2C), 129.5 (s), 129.4 (s), 128.8 (d, 2C), 128.6 (d), 128.1 (d, 2C), 127.9 (d), 123.8 (s), 123.1 (d), 123.0 (d), 120.2 (d), 113.3 (d), 110.3 (s), 104.2 (s), 94.2 (s), 83.9 (s), 51.0 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2947, 2836, 2248, 2218, 1692, 1633, 1599, 1572, 1526, 1509, 1476, 1443, 1398, 1327, 1272, 1249, 1217, 1188, 1125, 1072, 1018, 967, 912, 835, 783, 757, 742, 692, 666, 618 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{24}H_{18}NO_2$ $[M+H]^+$: 352.1332, found: 352.1330.

3-phenyl-2-(phenylethynyl)indolizine-1-carbonitrile (cy-483) (3ea)



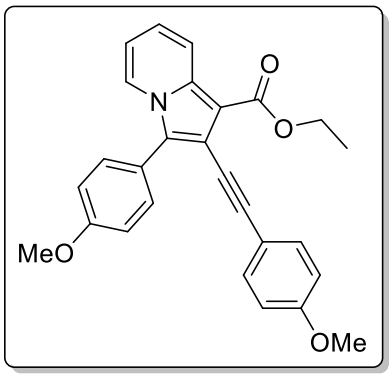
Yield: 23 mg, 72%; yellow liquid; R_f = 0.44 (PE/EA = 5/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 – 8.19 (m, 1H), 7.72 – 7.62 (m, 3H), 7.61 – 7.54 (m, 2H), 7.52 – 7.44 (m, 3H), 7.35 – 7.28 (m, 3H), 7.11 (ddd, *J* = 9.0, 6.7, 0.9 Hz, 1H), 6.75 (td, *J* = 6.9, 1.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2 (s), 131.6 (d, 2C), 129.4 (d, 2C), 129.03 (d, 2C), 129.00 (d), 128.6 (s), 128.5 (s), 128.5 (d), 128.2 (d, 2C), 123.6 (d), 123.2 (d), 122.7 (s), 117.9 (d), 115.5 (s), 113.6 (d), 111.9 (s), 95.2 (s), 85.4 (s), 80.9 (s). IR (reflection) $\tilde{\nu}$ = 2208, 1633, 1597, 1509, 1442, 1396, 1346, 1326, 1261, 1149, 1071, 1026, 913, 830, 806, 756, 742, 702, 689, 616 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{23}H_{15}N_2$ $[M+H]^+$: 319.1230, found: 319.1230.

ethyl 3-(*p*-tolyl)-2-(*p*-tolylethynyl)indolizine-1-carboxylate (cy-903) (3ab)



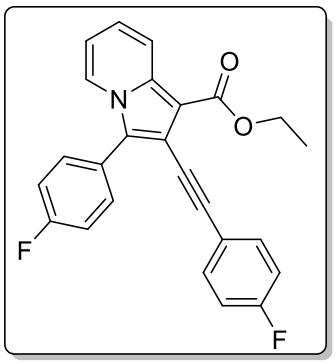
Yield: 29 mg, 74%; yellow solid; R_f = 0.48 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 9.1, 1.1 Hz, 1H), 8.17 (dd, *J* = 7.1, 0.9 Hz, 1H), 7.58 (d, *J* = 8.1 Hz, 2H), 7.40 – 7.30 (m, 4H), 7.14 – 7.03 (m, 3H), 6.69 (td, *J* = 6.9, 1.3 Hz, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 2.46 (s, 3H), 2.34 (s, 3H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 138.5 (s), 138.0 (s), 135.8 (s), 131.3 (d, 2C), 129.7 (d, 2C), 129.6 (s), 129.5 (d, 2C), 129.0 (d, 2C), 126.6 (s), 123.1 (d), 122.9 (d), 120.9 (s), 120.3 (d), 113.1 (d), 110.2 (s), 104.3 (s), 94.2 (s), 83.5 (s), 59.7 (t), 21.50 (q), 21.47 (q), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 3027, 2971, 2918, 1680, 1633, 1538, 1510, 1461, 1437, 1405, 1383, 1342, 1323, 1307, 1271, 1249, 1209, 1186, 1141, 1119, 1065, 1028, 963, 930, 908, 839, 813, 781, 739, 727, 704, 689, 647 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{24}NO_2$ $[M+H]^+$: 394.1802, found: 394.1791.

ethyl 3-(4-methoxyphenyl)-2-((4-methoxyphenyl)ethynyl)indolizine-1-carboxylate (cy-962) (3ac)



Yield: 24 mg, 57%; yellow liquid; R_f = 0.44 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dt, J = 9.1, 1.2 Hz, 1H), 8.13 (dt, J = 7.1, 1.0 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.40 – 7.33 (m, 2H), 7.12 – 7.03 (m, 3H), 6.86 – 6.80 (m, 2H), 6.69 (td, J = 6.9, 1.3 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 3.90 (s, 3H), 3.81 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 159.8 (s), 159.4 (s), 135.7 (s), 132.9 (d, 2C), 131.3 (d, 2C), 129.3 (s), 123.0 (d), 122.8 (d), 121.9 (s), 120.2 (d), 116.2 (s), 114.3 (d, 2C), 113.9 (d, 2C), 113.1 (d), 110.3 (s), 104.1 (s), 94.0 (s), 82.8 (s), 59.7 (t), 55.4 (q), 55.3 (q), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2977, 2936, 2905, 2836, 2538, 2215, 2182, 2050, 1680, 1632, 1605, 1572, 1540, 1514, 1462, 1440, 1406, 1385, 1325, 1291, 1250, 1217, 1188, 1125, 1107, 1070, 1031, 967, 833, 807, 783, 743, 691, 646 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{24}NO_4$ $[M+H]^+$: 426.1700, found: 426.1692.

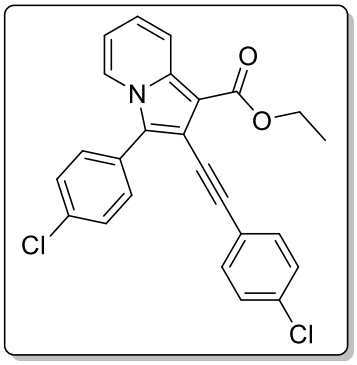
ethyl 3-(4-fluorophenyl)-2-((4-fluorophenyl)ethynyl)indolizine-1-carboxylate (cy-1000) (3ad)



Yield: 29 mg, 73%; brown solid; R_f = 0.48 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dt, J = 9.2, 1.1 Hz, 1H), 8.09 (dt, J = 7.1, 1.0 Hz, 1H), 7.70 – 7.60 (m, 2H), 7.39 (m, 2H), 7.29 – 7.23 (m, 2H), 7.10 (m, 1H), 7.04 – 6.96 (m, 2H), 6.73 (td, J = 6.9, 1.3 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 1.47 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4 (s), 162.8 (d, $^1J_{C\text{-}F}$ = 250.2 Hz), 162.4 (d, $^1J_{C\text{-}F}$ = 250.0 Hz), 135.8 (s), 133.3 (d, $^3J_{C\text{-}F}$ = 8.3 Hz, 2C), 131.9 (d, $^3J_{C\text{-}F}$ = 8.3 Hz, 2C), 128.5 (s), 125.6 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 123.2 (d), 122.8 (d), 120.4 (d), 119.8 (d, $^4J_{C\text{-}F}$ = 3.5 Hz), 116.1 (d, $^2J_{C\text{-}F}$ = 21.7 Hz, 2C), 115.6 (d, $^2J_{C\text{-}F}$ = 22.1 Hz, 2C), 113.5 (d), 110.4 (s), 104.5 (s), 93.1 (s), 83.5 (d, $^5J_{C\text{-}F}$ = 1.3 Hz), 59.8 (t), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2986, 1669, 1635, 1599, 1539, 1510, 1481, 1442, 1412, 1385, 1340, 1327, 1274, 1218, 1185, 1160, 1125, 1096, 1072,

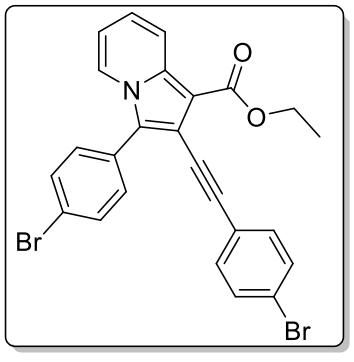
1036, 1013, 967, 840, 831, 812, 781, 739, 729, 710, 687, 650, 624 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{18}F_2NO_2$ $[M+H]^+$: 402.1300, found: 402.1302.

ethyl 3-(4-chlorophenyl)-2-((4-chlorophenyl)ethynyl)indolizine-1-carboxylate (cy-957) (3ae)



Yield: 33 mg, 76%; yellow solid; R_f = 0.55 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (dt, *J* = 9.2, 1.1 Hz, 1H), 8.12 (dt, *J* = 7.1, 1.0 Hz, 1H), 7.67 – 7.59 (m, 2H), 7.56 – 7.50 (m, 2H), 7.37 – 7.27 (m, 4H), 7.11 (m, 1H), 6.74 (td, *J* = 6.9, 1.3 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3 (s), 136.0 (s), 134.6 (s), 134.1 (s), 132.6 (d, 2C), 131.2 (d, 2C), 129.2 (d, 2C), 128.6 (d, 2C), 128.3 (s), 127.9 (s), 123.3 (d), 122.8 (d), 122.2 (s), 120.5 (d), 113.7 (d), 110.3 (s), 104.7 (s), 93.2 (s), 84.8 (s), 59.9 (t), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2982, 2936, 2906, 2219, 1675, 1633, 1593, 1536, 1509, 1496, 1481, 1441, 1411, 1399, 1384, 1339, 1324, 1277, 1249, 1217, 1183, 1146, 1125, 1092, 1075, 1033, 1014, 967, 820, 780, 765, 738, 719, 700, 684, 639 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{18}Cl_2NO_2$ $[M+H]^+$: 434.0709, found: 434.0698.

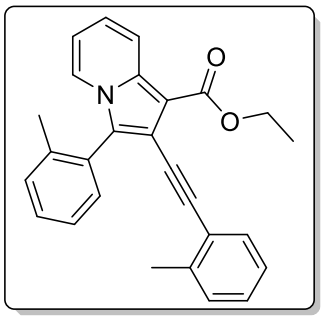
ethyl 3-(4-bromophenyl)-2-((4-bromophenyl)ethynyl)indolizine-1-carboxylate (cy-1002) (3af)



Yield: 32 mg, 62%; yellow solid; R_f = 0.45 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 9.2, 1.1 Hz, 1H), 8.12 (dd, *J* = 6.2, 0.9 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.58 – 7.53 (m, 2H), 7.46 – 7.42 (m, 2H), 7.31 – 7.26 (m, 2H), 7.11 (ddd, *J* = 9.1, 6.6, 1.0 Hz, 1H), 6.74 (td, *J* = 6.9, 1.3 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.2 (s), 136.1 (s), 132.8 (d, 2C), 132.2 (d, 2C), 131.6 (d, 2C), 131.4 (d, 2C), 128.4 (s), 128.3 (s), 123.4 (d), 122.82 (s), 122.78 (d), 122.6 (s), 122.3 (s), 120.5 (d), 113.7 (d), 110.3 (s), 104.8 (s), 93.3 (s), 84.9 (s), 59.9 (t), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2979, 2903, 2217, 1675, 1633, 1588, 1535, 1508, 1492, 1442,

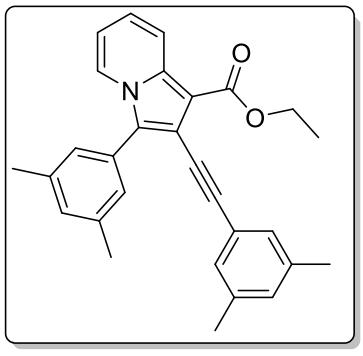
1410, 1393, 1384, 1338, 1324, 1275, 1248, 1216, 1184, 1125, 1069, 1032, 1010, 966, 907, 817, 781, 760, 738, 713, 693, 680, 664, 636 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{25}H_{18}Br_2NO_2$ $[M+H]^+$: 521.9699, found: 521.9686.

ethyl 3-(*o*-tolyl)-2-(*o*-tolylethynyl)indolizine-1-carboxylate (cy-956) (3ag)



Yield: 24 mg, 61%; yellow liquid; R_f = 0.60 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (dt, *J* = 9.1, 1.1 Hz, 1H), 7.55 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.44 – 7.28 (m, 5H), 7.17 – 7.04 (m, 4H), 6.69 (td, *J* = 6.8, 1.3 Hz, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.14 (s, 3H), 2.11 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 140.2 (s), 139.2 (s), 135.6 (s), 131.9 (d), 131.7 (d), 130.5 (d), 129.6 (s and d, 2C), 129.2 (d), 129.0 (s), 127.9 (d), 126.3 (d), 125.3 (d), 123.6 (s), 123.3 (d), 122.7 (d), 120.2 (d), 113.2 (d), 111.1 (s), 103.7 (s), 93.4 (s), 87.6 (s), 59.7 (t), 20.2 (q), 19.5 (q), 14.8 (q). IR (reflection) $\tilde{\nu}$ = 3059, 2978, 2248, 2213, 1926, 1684, 1633, 1599, 1571, 1525, 1508, 1456, 1444, 1403, 1384, 1341, 1324, 1272, 1247, 1218, 1183, 1117, 1065, 1043, 966, 907, 837, 813, 783, 757, 742, 714, 694, 659, 623 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{24}NO_2$ $[M+H]^+$: 394.1802, found: 394.1791.

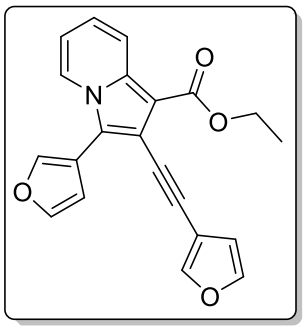
ethyl 3-(3,5-dimethylphenyl)-2-((3,5-dimethylphenyl)ethynyl)indolizine-1-carboxylate (cy-1003) (3ah)



Yield: 33 mg, 79%; yellow liquid; R_f = 0.67 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 9.1, 1.1 Hz, 1H), 8.22 (d, *J* = 7.1 Hz, 1H), 7.33 (s, 2H), 7.07 (ddd, *J* = 9.0, 4.8, 2.4 Hz, 4H), 6.92 (s, 1H), 6.70 (td, *J* = 6.9, 1.3 Hz, 1H), 4.47 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 6H), 2.28 (s, 6H), 1.49 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 138.3 (s), 137.6 (s), 135.8 (s), 130.3 (d), 129.9 (s), 129.8 (d), 129.4 (s), 129.2 (d, 2C), 127.5 (d, 2C), 123.7 (s), 123.3 (d), 122.9 (d), 120.3 (d), 113.1 (d), 110.3 (s), 104.3 (s), 94.6 (s), 83.7 (s), 59.7 (t), 21.4 (q, 2C), 21.1 (q, 2C), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2978, 2918, 2861, 2732, 2248, 2218, 1684, 1633, 1598, 1507, 1444,

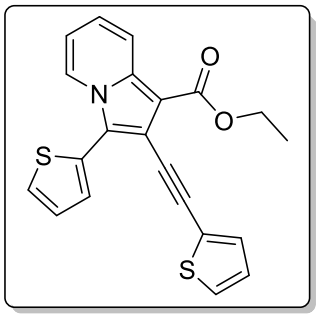
1419, 1384, 1331, 1302, 1273, 1255, 1238, 1223, 1184, 1160, 1127, 1092, 1040, 970, 907, 849, 783, 741, 688 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{29}H_{28}NO_2$ $[M+H]^+$: 422.2115, found: 422.2106.

ethyl 3-(furan-3-yl)-2-(furan-3-ylethynyl)indolizine-1-carboxylate (cy-1001) (3ai)



Yield: 26 mg, 76%; yellow solid; R_f = 0.43 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dt, *J* = 9.1, 1.2 Hz, 1H), 8.16 (dt, *J* = 7.1, 1.0 Hz, 1H), 7.91 (dd, *J* = 1.4, 0.8 Hz, 1H), 7.67 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.62 (t, *J* = 1.7 Hz, 1H), 7.39 (t, *J* = 1.7 Hz, 1H), 7.08 (m, 1H), 6.85 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.76 (m, 1H), 6.51 (m, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 1.44 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3 (s), 145.4 (d), 143.4 (d), 142.8 (d), 141.9 (d), 136.0 (s), 123.3 (d), 122.9 (d), 121.4 (s), 120.3 (d), 114.4 (s), 113.5 (d), 112.5 (d), 110.4 (s), 110.3 (d), 108.2 (s), 104.5 (s), 86.0 (s), 85.3 (s), 59.8 (t), 14.5 (q). IR (reflection) $\tilde{\nu}$ = 3131, 3104, 2989, 2974, 2926, 1660, 1525, 1508, 1484, 1434, 1406, 1385, 1360, 1325, 1289, 1233, 1210, 1159, 1126, 1099, 1067, 1030, 983, 923, 872, 834, 793, 781, 728, 687, 647, 632 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{21}H_{16}NO_4$ $[M+H]^+$: 346.1074, found: 346.1070.

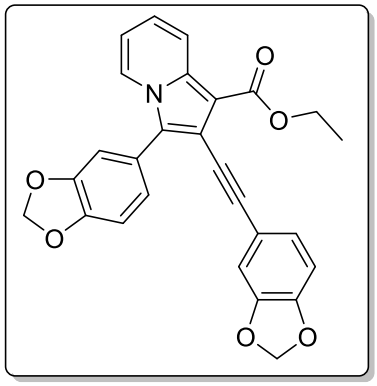
ethyl 3-(thiophen-2-yl)-2-(thiophen-2-ylethynyl)indolizine-1-carboxylate (cy-963) (3aj)



Yield: 14 mg, 41%; yellow liquid; R_f = 0.45 (PE/EA = 5/1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.38 (d, *J* = 7.1 Hz, 1H), 8.31 (d, *J* = 9.1 Hz, 1H), 7.53 (dd, *J* = 5.2, 1.0 Hz, 1H), 7.44 (dd, *J* = 3.6, 1.0 Hz, 1H), 7.28 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.24 (td, *J* = 3.4, 2.1 Hz, 2H), 7.13 (ddd, *J* = 9.1, 6.6, 0.9 Hz, 1H), 7.00 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.79 (td, *J* = 6.9, 1.2 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.48 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3 (s), 136.3 (s), 131.6 (d), 130.0 (s), 128.5 (d), 127.4 (d), 127.3 (d), 127.05 (d), 127.04 (d), 123.9 (s), 123.49 (d), 123.43 (d), 122.7 (s), 120.2 (d), 113.7 (d), 111.3 (s), 104.6 (s), 88.7 (s), 87.8 (s), 59.9 (t), 14.6 (q). IR (reflection) $\tilde{\nu}$ = 3087, 2983, 2934, 1735, 1665,

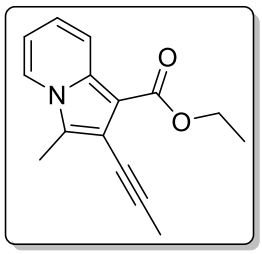
1633, 1530, 1511, 1444, 1426, 1386, 1337, 1317, 1270, 1251, 1233, 1192, 1164, 1117, 1086, 1054, 946, 909, 848, 826, 779, 733, 700, 619 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{21}H_{16}NO_2S_2$ $[M+H]^+$: 378.0617, found: 378.0608.

ethyl 3-(benzo[*d*][1,3]dioxol-5-yl)-2-(benzo[*d*][1,3]dioxol-5-ylethynyl)indolizine-1-carboxylate (cy-1005) (3ak)



Yield: 28 mg, 62%; yellow liquid; R_f = 0.32 (PE/EA = 5/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.1 Hz, 1H), 8.13 (d, *J* = 7.1 Hz, 1H), 7.14 (dt, *J* = 4.7, 1.5 Hz, 2H), 7.07 (m, 1H), 7.02 – 6.95 (m, 2H), 6.89 (d, *J* = 1.5 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.70 (td, *J* = 6.9, 1.3 Hz, 1H), 6.07 (s, 2H), 5.96 (s, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5 (s), 148.1 (s), 147.9 (s), 147.7 (s), 147.3 (s), 135.7 (s), 129.1 (s), 126.1 (d), 124.0 (d), 123.0 (d and s, 2C), 122.9 (d), 120.3 (d), 117.2 (s), 113.2 (d), 111.4 (d), 110.3 (s), 110.1(d), 108.8 (d), 108.4 (d), 104.2 (s), 101.4 (t), 101.2 (t), 94.2 (s), 82.5 (s), 59.7 (t), 14.7 (q). IR (reflection) $\tilde{\nu}$ = 2985, 2918, 1680, 1632, 1602, 1539, 1504, 1481, 1459, 1445, 1425, 1408, 1378, 1356, 1327, 1240, 1204, 1186, 1154, 1139, 1109, 1062, 1031, 929, 896, 864, 852, 835, 802, 779, 758, 734, 691, 665, 610 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{27}H_{20}NO_6$ $[M+H]^+$: 454.1285, found: 454.1279.

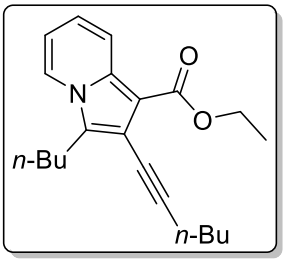
ethyl 3-methyl-2-(prop-1-yn-1-yl)indolizine-1-carboxylate (cy-1010) (3al)



Yield: 18 mg, 75%; yellow solid; R_f = 0.30 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (dt, *J* = 9.1, 1.1 Hz, 1H), 7.72 (d, *J* = 7.0 Hz, 1H), 7.02 (ddd, *J* = 9.1, 6.7, 1.0 Hz, 1H), 6.76 (td, *J* = 6.8, 1.3 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 2.17 (s, 3H), 1.43 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 134.8 (s), 125.4 (s), 122.3 (d), 121.6 (d), 120.0 (d), 112.8 (d), 110.7 (s), 103.3 (s), 91.4 (s), 73.2 (s), 59.4 (t), 14.5 (q), 10.1 (q), 4.8 (q). IR (reflection) $\tilde{\nu}$ = 3101, 2982, 2911, 2851, 1737, 1672, 1634, 1524, 1505, 1434, 1412, 1387, 1348, 1320, 1269, 1240,

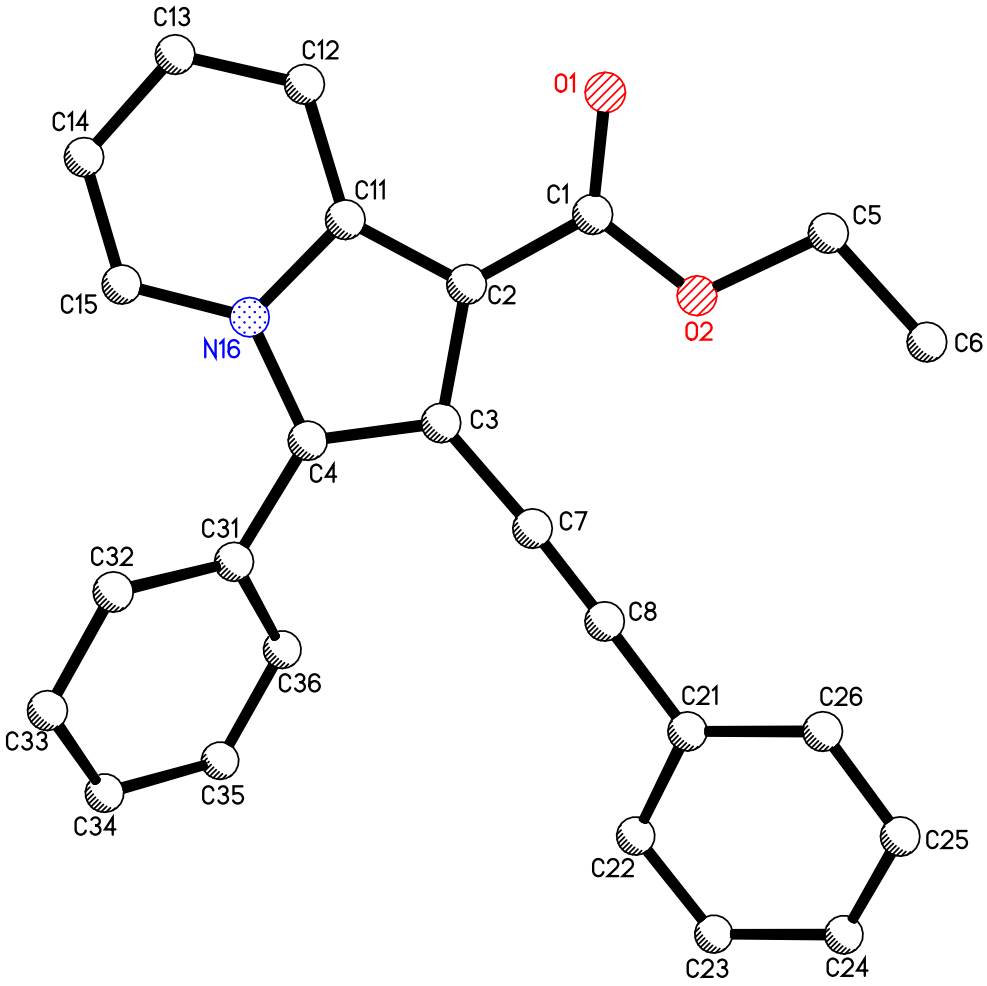
1174, 1150, 1130, 1067, 1043, 1013, 996, 853, 834, 781, 763, 728, 669, 649 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{15}H_{16}NO_2$ $[M+H]^+$: 242.1176, found: 242.1173.

ethyl 3-butyl-2-(hex-1-yn-1-yl)indolizine-1-carboxylate (cy-1011) (3am)



Yield: 22 mg, 68%; yellow liquid; R_f = 0.58 (PE/EA = 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.15 (m, 1H), 7.80 (d, *J* = 7.0 Hz, 1H), 6.99 (ddd, *J* = 9.1, 6.6, 1.0 Hz, 1H), 6.73 (td, *J* = 6.9, 1.3 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.99 (t, *J* = 7.5 Hz, 2H), 2.53 (t, *J* = 7.0 Hz, 2H), 1.70 – 1.59 (m, 4H), 1.58 – 1.49 (m, 2H), 1.45 – 1.36 (m, 5H), 0.99 – 0.92 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (s), 135.0 (s), 130.1 (s), 122.3 (d), 121.5 (d), 120.2 (d), 112.7 (d), 110.5 (s), 103.2 (s), 95.9 (s), 74.1 (s), 59.4 (t), 31.0 (t), 29.3 (t), 24.1 (t), 22.4 (t), 22.1 (t), 19.6 (t), 14.6 (q), 13.8 (q), 13.6 (q). IR (reflection) $\tilde{\nu}$ = 2957, 2932, 2871, 2234, 1683, 1632, 1586, 1523, 1505, 1453, 1409, 1384, 1357, 1318, 1299, 1263, 1240, 1225, 1172, 1142, 1130, 1103, 1040, 963, 931, 844, 783, 739, 693, 638 cm^{-1}. HRMS (ESI, m/z) calc'd for $C_{21}H_{28}NO_2$ $[M+H]^+$: 326.2115, found: 326.2112.

4.5.4 Solid state molecular structure of 3aa



4.5.5 References

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