Sustainable Oxidative Gold Catalysis: Ligand-Assisted Gold-Catalyzed Alkynylative Cyclization and C(sp)-C(sp) Cross-Coupling Using Hydrogen Peroxide as Oxidant

Presented by:

Hongwei Shi

From Anhui, China

December 2022

Submitted to the
Combined Faculty of Mathematics, Engineering and Natural Sciences
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Dissertation

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Prof. Dr. Michael Mastalerz

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From today, a new journey in the world of chemistry will start with strong leverage!

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Publications

1. Tao Wang, Marvin Hoffmann, Andreas Dreuw, Edina Hasagić, Chao Hu, Philipp M. Stein, Sina Witzel, **Hongwei Shi**, Yangyang Yang, Matthias Rudolph, Fabian Stuck, Frank Rominger, Marion Kerscher, Peter Comba, and A. Stephen K. Hashmi*. A Metal-Free Direct Arene C-H Amination. *Adv. Synth. Catal.* **2021**, *363*, 2783-2795.
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6. **Hongwei Shi**, Martin C. Dietl, Philipp M. Stein, Matthias Rudolph, Tao Wang, Jun Li, Petra Krämer, Frank Rominger, and A. Stephen K. Hashmi*. Ligand-Assisted Gold-Catalyzed Efficient Alkynylative Cyclization with Terminal Alkynes Using H_2O_2 as Oxidant. (*Nat. Commun.* in revision).
7. **Hongwei Shi**, Martin C. Dietl, Matthias Rudolph, Tao Wang, Jun Li, Yaowen Liu, Zuozuo Wu, and A. Stephen K. Hashmi*. Ligand-Assisted Homogeneous Gold-Catalyzed C(sp)-C(sp) Cross-Coupling Using H_2O_2 as Oxidant: Synthesis of 1,3-Diynes from Terminal Alkynes. (awaiting publication)
8. **Hongwei Shi**, Martin C. Dietl, Yu Tian, Matthias Rudolph, Petra Krämer, Frank

Rominger, and A. Stephen K. Hashmi*. Gold-Catalyzed C(sp)-C(sp) Cross-Coupling of Alkynylsilanes: Synthesis of Unsymmetrical 1,3-Diynes and Polyynes. (awaiting publication)

9. **Hongwei Shi,** Yu Tian, Hadil Alshurafa, Matthias Rudolph, Petra Krämer, Thomas Oeser, Frank Rominger, and A. Stephen K. Hashmi, Oxidative Gold-Catalyzed Selective Bicyclization/Cross-Coupling. (awaiting publication)
10. **Hongwei Shi**, Tao Wang, Jun Li, Yaowen Liu, Zuozuo Wu, Petra Krämer, Matthias Rudolph, and A. Stephen K. Hashmi*. Light-Enabled α-Oxo-C(sp^3)-H Alkenylation with Terminal Alkynes Using Benzaldehyde as HAT Photocatalyst. (awaiting publication)

List of Abbreviations

Ac	Acetyl
APCI	Atmospheric pressure chemical ionization
Ar	Aryl
ATR	Attenuated total reflection
bpy	2,2′-Bipyridine
Bu	Butyl
Calcd	Calculated
CN	Cyano
Convn.	Conversion rate
CyJohnPhos	(2-Biphenylyl)-dicyclohexylphosphin
DCM	Dichloromethane
DFT	Density functional theory
DMAP	4-Dimethylaminopyridine
DMF	Dimethyl formamide
DMS	Dimethylsulfane
DMSO	Dimethylsulfoxide
dppm	Bis(diphenylphosphino)methane
EA	Ethyl acetate
EI	Electron ionization
Equiv	Equivalent
ESI	Electrospray ionization
Et	Ethyl
GC-MS	Gas chromatography-mass spectrometry
ΔG	Gibbs free energy
h	hour
HRMS	High resolution mass spectrometry
Hz	Hertz
i	*iso*

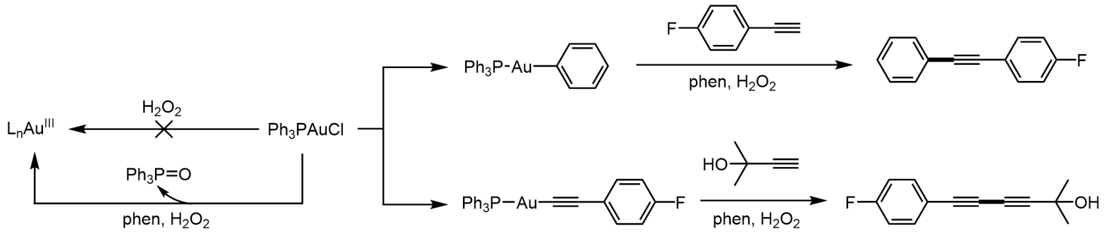
IPr	1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene
IR	Infrared
L_n	Ligand
m	*meta*
Me	Methyl
MHz	Megahertz
Min	Minute(s)
M.p.	Melting point
Ms	Mesyl
MS	Mass spectrometry
m/z	Mass per charge
ND	Not detected
NMR	Nuclear magnetic resonance
NPhth	Phthalimide
Nu	Nucleophile
o	*ortho*
p	*para*
PC	Photoexcited photosensitizer
PE	Petroleum ether
Ph	Phenyl
phen	1,10-Phenanthroline
PIDA	Phenyliodine(III) diacetate
py	Pyridin
Pr	Propyl
R_f	Retention factor
rt	Room temperature
SET	Single Electron Transfer
t	*tert*
TBHP	*tert*-Butyl hydroperoxide
TBAF	Tetrabutylammonium salt
Tf	Trifluoromethylsulfonyl

THF	Tetrahydrofuran
THT	Tetrahydrothiophene
TIPS	Triisopropylsilyl
TLC	Thin layer chromatography
TMS	Trimethyl silyl
TMEDA	Tetramethylethylenediamine
Ts	4-Toluenesulfonyl
ṽ	Wavenumber
wt	Weight

Abstract

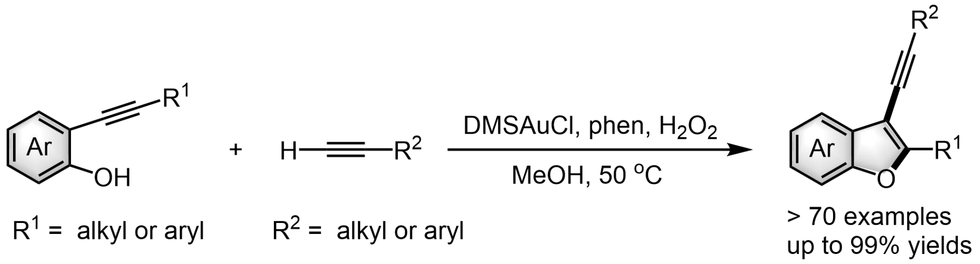
The thesis is focused on 1,10-phenanthroline (phen)-assisted homogeneous oxidative gold catalysis using hydrogen peroxide (H_2O_2) as oxidant. It is an unprecedented oxidative gold catalysis strategy with an ideal "benefit balance", not just as a more attractive substitute of common methodologies, but as an extraordinary reaction system. The efficient constructions of 3-alkynylbenzofurans, 1,3-diynes and polyynes were possible by this catalytic system (Au/phen/H_2O_2).

The thesis considers the significant advantages (ideal "benefit balance") and challenges (no-report) of H_2O_2 as an oxidant for oxidative gold catalysis. In the first part (Chapter 2), we focused on exploring the possibility of oxidative gold catalysis using H_2O_2 as oxidant and the potential application value of this reaction system. We discovered that bidentate *N*-ligands (phen) can effectively promote the oxidation of Au^I to Au^{III} in the presence of H_2O_2. Furthermore, a set of experiments with stoichiometric gold(I) complexes demonstrated that this catalytic system can be applied for homogeneous gold-catalyzed C(sp^2)-C(sp) and C(sp)-C(sp) cross-coupling reactions.



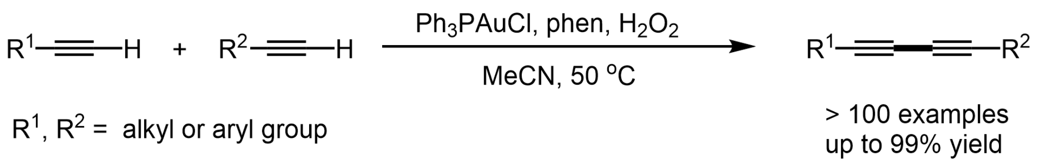
The gold-catalyzed cyclization-functionalization is a powerful approach to construct high-value organic molecules. However, current strategies mainly rely on expensive external oxidants or pre-functionalized substrates, which exhibit low atom economy and high costs. To circumvent these drawbacks, in the second part (Chapter 3), we focused on investigating the use of this catalytic system for efficient gold-catalyzed cyclization-functionalizations. A direct construction of 3-alkynylbenzofurans from terminal alkynes was possible by this gold-catalyzed process. Green and inexpensive

oxidants, simple gold catalysts, mild reaction conditions, high atom economy, remarkable selectivity, wide substrate scope, broad functional group compatibility and a facile gram-scale synthesis make this alkynylative cyclization method practical for many forms of cyclization reactions. In contrast to prior methods neither pre-functionalized alkynes nor expensive external oxidants are needed.



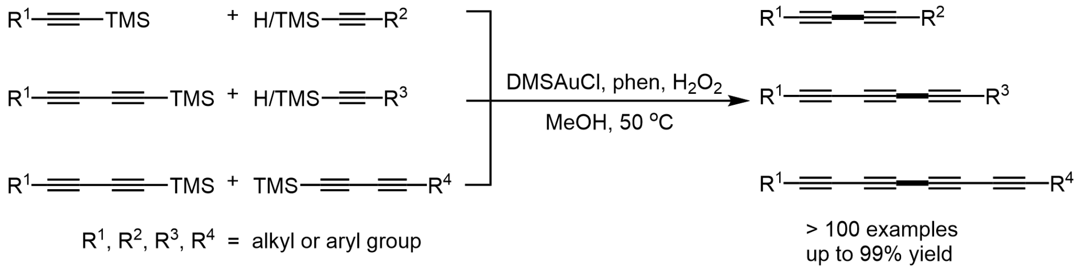
- high atom economy
  + only H_2O as by-product
- low synthetic costs:
  + inexpensive oxidant
  + simple gold catalysts and ligand
  + mild reaction conditions
- excellent synthetic efficiencies:
  + broad functionalization compatibility
  + wide substrate scope
  + remarkable selectivity
  + facile gram-scale synthesis
- green solvent and oxidant

Conjugated 1,3-diynes are unique carbon frameworks which are widely found in natural products, biologically active molecules and functional materials. Considering the importance of synthetic methods for conjugated diynes, especially unsymmetrical 1,3-diynes, we next focused on investigating the use of this catalytic system for a gold-catalyzed cross-coupling of terminal alkynes. An efficient synthesis of unnsymmetrical 1,3-diynes from terminal alkynes via this new gold catalytic system was developed (Chapter 4). A wide range of substrates, including several complex molecules and marketed drugs, were transferred with excellent functional group tolerance. Furthermore, the catalyst system was applied at a gram scale and an extension towards the synthesis of polyynes via a relay strategy was possible.



- high atom economy
  - + only H_2O as by-product
- low synthetic costs:
  - + inexpensive oxidant
  - + simple gold catalysts and ligand
  - + mild reaction conditions
- excellent synthetic efficiencies:
  - + broad functionalization compatibility
  - + wide substrate scope (including natural products and marketed drugs, substrates with similar structure or electronic properties)
  - + facile gram-scale synthesis

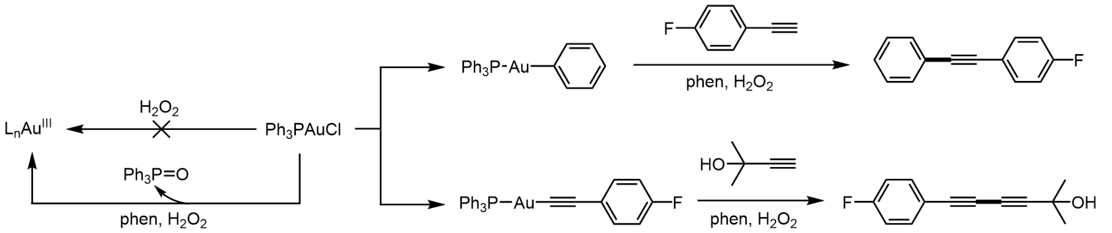
Considering the importance of polyynes in chemical and materials research, and tedious synthesis procedure of the current strategy. In the fourth part (Chapter 5), we focused on exploring gold-catalyzed C(sp)–C(sp) cross-coupling of alkynylsilanes using H_2O_2 as oxidant. Through this catalytic system, 1,3-diynes and polyynes can be successfully prepared from ethynyltrimethylsilanes without pre-functionalization or deprotection. Compared with current synthetic strategies towards polyynes, our method greatly improves the synthetic efficiency, provide new ideas for the synthesis of polyynes.



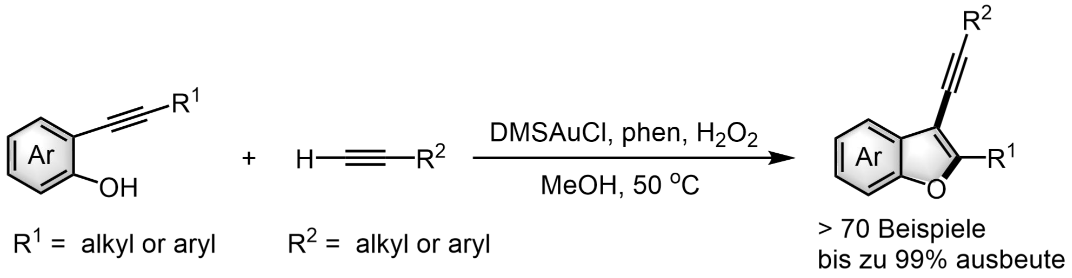
- low synthetic costs:
  - + inexpensive oxidant
  - + simple gold catalysts and ligand
  - + mild reaction conditions
  - + without pre-functionalization or deprotection
- excellent synthetic efficiencies:
  - + broad functionalization compatibility
  - + wide substrate scope
  - + direct synthesis of polyalkynes
- green solvent and oxidant

Zusammenfassung

Die Dissertation konzentriert sich auf die 1,10-Phenanthrolin (Phen)-unterstützte homogene oxidative Goldkatalyse mit Wasserstoffperoxid (H_2O_2) als Oxidationsmittel. Es ist eine beispiellose Strategie in der oxidativen Goldkatalyse mit idealer „Nutzenbilanz", nicht nur als attraktiverer Ersatz für herkömmliche Methoden, sondern als außergewöhnliches Reaktionssystem. Der effiziente Aufbau von 3-Alkinylbenzofuranen, 1,3-Diinen und Polyinen wurde durch den Einsatz dieses katalytischen System (Au/phen/H_2O_2) möglich. Die Arbeit gliedert sich in die folgenden vier Teile: Im ersten Teil (Kapitel 2) konzentrierten wir uns auf die Untersuchung der Möglichkeiten der oxidativen Goldkatalyse mit H_2O_2 als Oxidationsmittel und dem potenziellen Anwendungswert dieses Reaktionssystems. Wir entdeckten, dass zweizähnige *N*-liganden (phen) die Oxidation von Au^I zu Au^{III} effektiv fördern können. Darüber hinaus zeigte eine Reihe von stöchiometrischen Experimenten Gold(I)-komplexen, dass dieses katalytische System für homogene gold-katalysierte $C(sp^2)$-C(sp)- und C(sp)-C(sp)-Kreuzkupplungsreaktionen eingesetzt werden könnte.

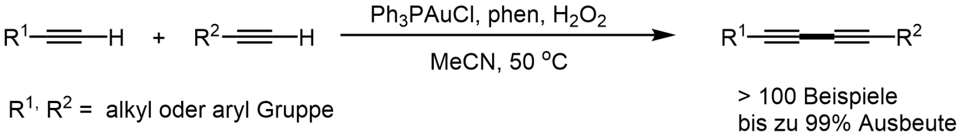


Die gold-katalysierte Zyklisierung-Funktionalisierung ist ein leistungsfähiger Ansatz zum Aufbau hochwertiger organischer Moleküle. Derzeitige Strategien beruhen jedoch hauptsächlich auf teuren externen Oxidationsmitteln oder vorfunktionalisierten Substraten, die eine geringe Atomökonomie und hohe Kosten aufweisen. Um diese Nachteile zu umgehen, konzentrierten wir uns im zweiten Teil (Kapitel 3) auf die Untersuchung der Verwendung dieses katalytischen Systems für eine Gold-katalysierte effiziente Zyklisierungs-Funktionalisierung Reaktion. Durch diesen Gold-katalysierten Prozess war ein direkter Aufbau von 3-Alkinylbenzofuranen aus terminalen Alkinen möglich. Umweltfreundliche und kostengünstige Oxidationsmittel, einfach zugängliche Goldkatalysatoren, milde Reaktionsbedingungen, hohe Atomökonomie, bemerkenswerte Selektivität, breiter Substratbereich, breite Kompatibilität mit funktionellen Gruppen und eine einfache Synthese im Grammmaßstab machen diese alkinylierende Zyklisierungsmethode für viele Formen von Zyklisierungsreaktionen praktisch. Im Gegensatz zu früheren Verfahren werden weder vorfunktionalisierte Alkine noch teure externe Oxidationsmittel benötigt.



- hohe Atomökonomie:
  - + nur wasser als Nebenprodukt
- geringe Synthesekosten:
  - + preiswertes Oxidationsmittel
  - + einfache Goldkatalysatoren und Liganden
  - + milde Reaktionsbedingungen
- hervorragende synthetische Wirkungsgrade:
  - + breite Funktionalisierungskompatibilität
  - + breites Substratspektrum
  - + bemerkenswerte Selektivität
  - + einfache Synthese im Grammmaßstab
- grünes Lösungsmittel und Oxidationsmittel

Konjugierte 1,3-Diine als einzigartige Kohlenstoffgerüste, sind in Naturprodukten, biologisch aktiven Molekülen und funktionellen Materialien weit verbreitet. In Anbetracht der Bedeutung von Synthesemethoden für konjugierte Diine, insbesondere unsymmetrischer 1,3-Diine, konzentrierten wir uns als Nächstes auf die ‚Untersuchung der Verwendung dieses katalytischen Systems für die Gold-katalysierte Kreuzkupplung von terminalen Alkinen. Eine effiziente Synthese von unsymmetrischen 1,3-Diinen aus terminalen Alkinen über dieses neue Goldkatalysesystem wurde entwickelt (Kapitel 4). Eine breite Palette von Substraten, darunter mehrere komplexe Moleküle und vermarktete Arzneimittel, wurden mit ausgezeichneter Funktionellegruppentoleranz übertragen. Darüber hinaus wurde das Katalysatorsystem im Grammmaßstab angewendet und eine Erweiterung auf die Synthese von Polyacetylenen über eine Relaisstrategie war möglich.



- hohe Atomökonomie:
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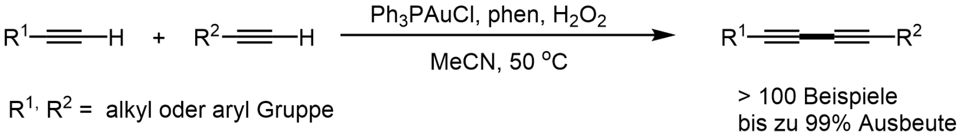
- hervorragende synthetische Wirkungsgrade:
  - breite Funktionalisierungskompatibilität
  - breites Substratspektrum (einschließlich Naturprodukten und vermarkteten Arzneimitteln, Substrate mit ähnlicher Struktur oder elektronischen Eigenschaften)
  - einfache Synthese im Grammmaßstab

Im vierten Teil (Kapitel 5) konzentrierten wir uns auf die Untersuchung der Gold-katalysierten C(sp)-C(sp)-Kreuzkupplung von Alkinylsilanen mit H_2O_2 als Oxidationsmittel. Durch dieses katalytische System können 1,3-Diine und Polyine erfolgreich aus Ethinyltrimethylsilanen ohne Vorfunktionalisierung oder Entschützung hergestellt werden. Verglichen mit den aktuellen Polyalkinsynthesestrategien verbessert unser Verfahren die Syntheseeffizienz erheblich und liefert neue Ideen für die Synthese von Polyalkinen.



- hohe Atomökonomie:
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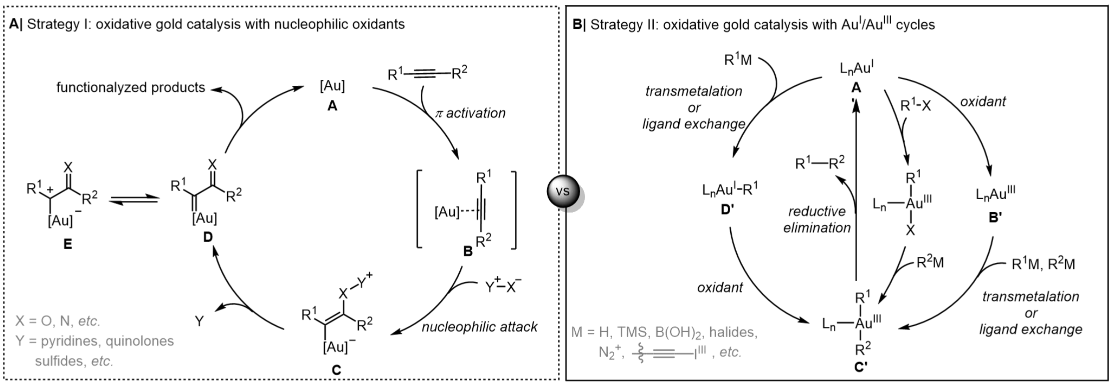
Chapter 1 General Introduction

1.1 Oxidative Gold Catalysis

Homogeneous gold catalysis has flourished since two decades, and it developed into a powerful tool for the construction of complex organic frameworks, driven by the perfect ability for the activation of C-C multiple bonds.[1] Another branch of homogeneous gold catalysis, namely gold redox chemistry has also developed rapidly.[2] Currently, two main strategies for oxidative gold catalysis have emerged (Scheme 1). The first strategy, as shown in Scheme 1A, is based on the use of *O/N*-nucleophilic oxidants to achieve an intermolecular or intramolecular *anti*-addition of the *O/N*-nucleophile across a gold-activated C-C triple bond, which then affords a highly electrophilic gold carbene **D**. This can undergo downstream transformations to give functional products. In these reactions, the oxidation state of gold remains unchanged throughout the catalysis.[3] In contrast, the second strategy involves a Au^I/Au^{III} catalytic cycle (Scheme 1B).[4] In this strategy, no matter if the first step is a transmetalation/ligand exchange progress or an oxidation progress, the common intermediate **C'** is formed, followed by reductive elimination to furnish the target products. Here, we mainly focus on the second strategy of homogeneous gold redox catalysis, which involves the Au^I/Au^{III} catalytic cycles.



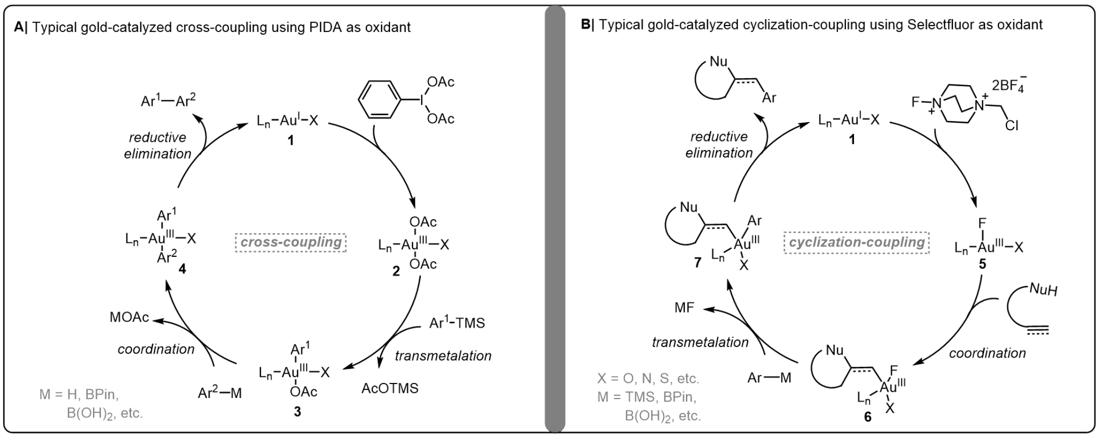
Scheme 1. Two main strategies for oxidative gold catalysis.

1.2 Oxidative Gold Catalysis Involving Au^I/Au^{III} Cycles

Homogeneous oxidative gold catalysis offers a unique balance between C-C multiple bond activation, functional-group compatibility, and molecular complexity gain of the targets. Therefore it has become a powerful and favored tool for the construction of complex functional molecules.[5] However, in this field, the main obstacle is the high oxidation potential of the Au^I/Au^{III} redox couple (+1.40 V),[6] which hinders the development of gold redox chemistry.

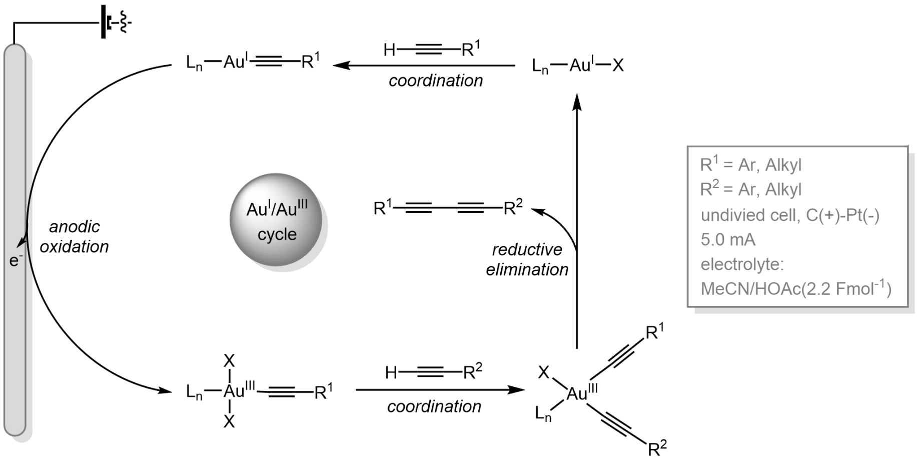
1.2.1 Au^I/Au^{III} Cycles with External Oxidants

The use of external oxidants, such as phenyliodine(III) diacetate (PIDA), Selectfluor, *etc.* can enable the switching between Au^I and Au^{III} oxidation states.[7,8] In general, oxidative gold catalysis using PIDA as the oxidant is mainly used to construct C-C coupled functional molecules (Scheme 2A).[7] Taking a C(sp^2)-C(sp^2) cross-coupling as an example, first, the linear two-coordinated Au^I complex **1** is oxidized by PIDA to form Au^{III} species **2**. Then electrophilic curation with the arylsilane takes place to afford a highly electrophilic Au^{III} intermediate **3**, followed by associative substitution to give a three-coordinate diaryl-Au^{III} intermediate **4**. Release of the biaryl products via reductive elimination then regenerates the Au^I catalyst, thereby closing the cycle. A slight difference is that the gold-catalyzed redox strategy with selectfluor as the oxidant is mostly used to construct the cyclization-coupling products (Scheme 2B).[8] As in the upper case, the L_nAu^I complex **1** is first oxidized by Selectfluor to afford cationic Au^{III} **5**. The Au^{III} complex **5** then directly activates a C-C double or triple bond, triggering the intramolecular oxidation to provide highly electrophilic Au^{III} complex **6**, followed by transmetalation to afford Au^{III} intermediate **7**. The thus generated intermediate **7** undergoes reductive elimination to furnish the corresponding functionalized cyclization products under the regeneration of the catalyst.



Scheme 2. General scheme for gold-catalyzed redox couplings with external chemical oxidants.

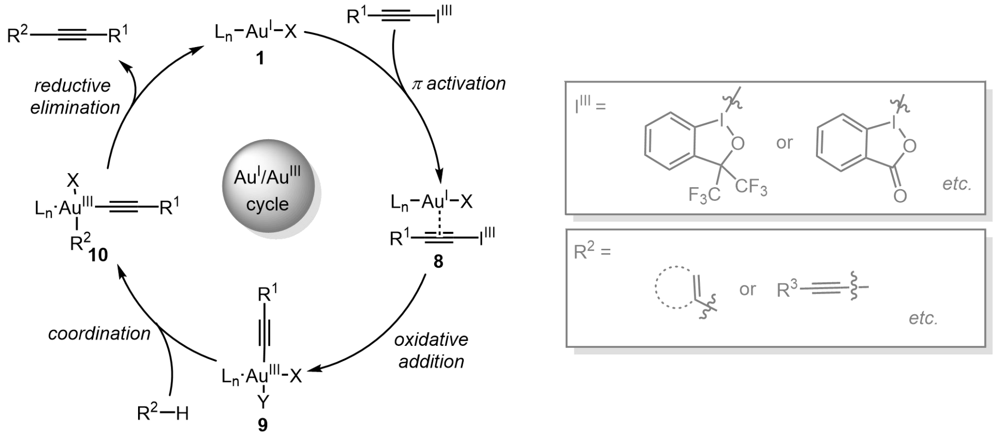
In addition, in 2019, Shi's group first reported a new strategy for electrochemically promoted gold redox catalysis. They successfully synthesized conjugated 1,3-diynes bypassing the chemical oxidant approach.[9] As shown in Scheme 3, in this strategy, the anode replaced the external oxidant, and the conversion of Au^{I} to Au^{III} was achieved through anodic oxidation. Other catalytic processes are essentially consistent with the strategy of oxidative gold catalysis using external oxidants.



Scheme 3. Electrochemically promoted oxidative gold catalysis.

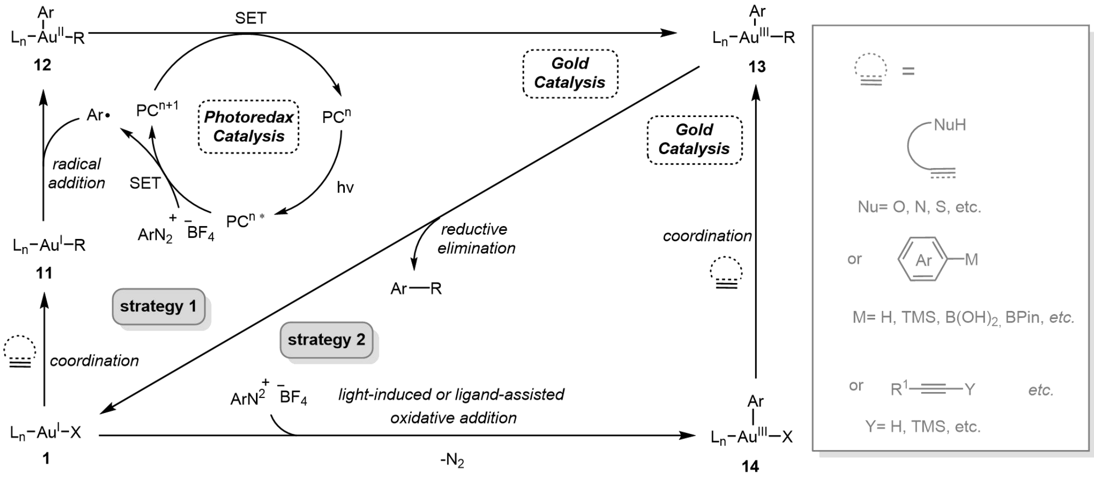
1.2.2 Au^{I}/Au^{III} Cycles without External Oxidants

In 2009, Waser's group first reported a gold-catalyzed direct alkynylation of heterocycles involving a Au^{I}/Au^{III} oxidative cycle, using alkynyl hypervalent iodine(III) reagents to bypass external oxidants, providing a new opportunity for the gold-catalyzed alkynylative functionalization.[10] In the past decade, the strategy of hypervalent iodine reagents for oxidative gold catalysis has received extensive attention, and various interesting alkynylation reactions have been reported successively.[11] Based on many relevant reports,[10,11] a summary of the widely accepted possible mechanisms is shown in Scheme 4. The linear two-coordinated Au^{I} complex **1** initially coordinates with the alkynes of the hypervalent iodine(III) reagents, triggering oxidative addition, generating the key Au^{III}-acetylide complex **9**, followed by coordination with R^2-H to provide Au^{III} intermediate **10**. This undergoes reductive elimination to deliver the corresponding products under the regeneration of the Au^{I} catalyst.



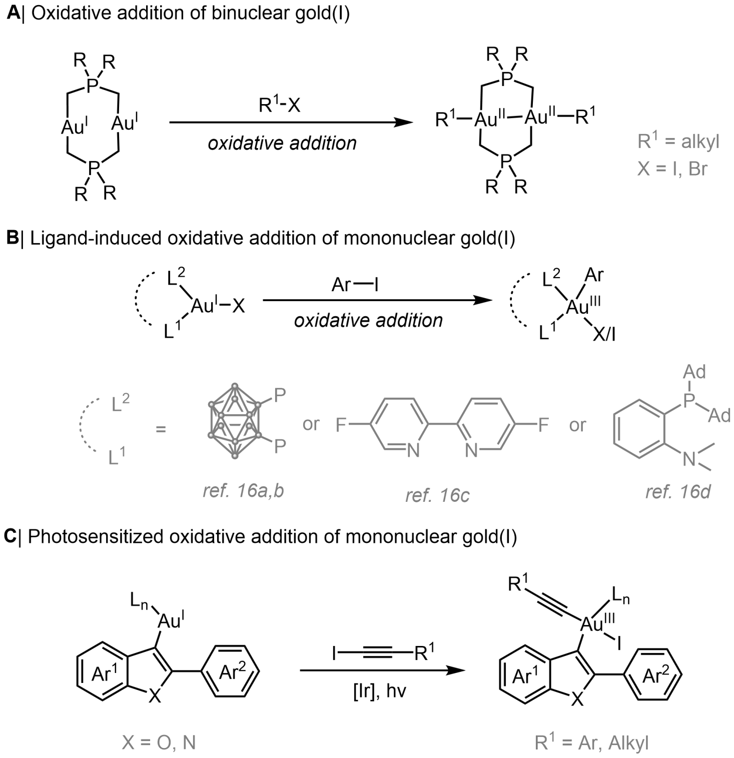
Scheme 4. Oxidative gold catalysis with alkynyl hypervalent iodine(III) reagents.

In addition, in 2013, Glorius's group first developed a strategy combining gold and a ruthenium-based photoredox catalyst with aryldiazonium salts, involving a Au^{I}/Au^{III} cycle but avoiding external oxidants.[12a] This opened up new venues for oxidative gold catalysis.[12,13] Since then, various light-induced[13a-d] or ligand-assisted[13e] strategies without photosensitizers using aryldiazonium salts as substrates have been successively developed. As shown in Scheme 5, in the first strategy, the Au^{I} complex **1** initially reacts with the alkene or alkyne substrates to furnish the Au^{I} intermediate **11** resulting from intermolecular or intramolecular nucleophiles addition. Simultaneously, the reaction of aryldiazonium salts (e.g., ArN_2BF_4) with the photoexcited photosensitizer (PC^{n*}) generates an aryl radical and PC^{n+1} via single electron transfer (SET). The thus-generated aryl radical reacts with Au^{I} complex **11** to afford the Au^{II} intermediate **12** via single-electron oxidation. At this stage, the oxidation progress may also occur before the nucleophilic addition.[12b,c] The unstable species Au^{II} **12** then prefers to afford the Au^{III} intermediate **13** via single electron oxidation with PC^{n+1}, thereby regenerating the catalyst PC^{n}. In contrast, in the second strategy, Au^{I} **1** initially reacts with aryldiazonium salts to afford the Au^{III} intermediate **14** via light-induced or ligand-assisted oxidative addition and elimination of N_2. The so-formed highly electrophilic Au^{III} complex **14** activates a C-C double or triple bond, followed by *anti*-cyclization or associative substitution to afford Au^{III} intermediate **13**.[13] Reductive elimination at this stage then delivers the corresponding products and regenerates the Au^{I} catalyst **1**, thereby completing the gold redox catalytic cycle.



Scheme 5. Oxidative gold catalysis with aryldiazonium salts.

Different from strategies using pre-functionalized substrates, the direct oxidative addition of unactivated substrates, such as alkyl halides, and aryl halides, *etc.* to Au^{I}, to generate Au^{III} has received extensive attention (Scheme 6A).[14] However, this strategy is limited to the oxidative addition of alkyl iodides or alkyl bromides to binuclear gold complexes, and its practical synthetic applications are rarely reported.[14g] This is mainly because the linear two-coordinated Au^{I} complexes are extremely stable, which are not keen on higher coordination numbers and disfavor oxidative addition.[15] In 2014, Bourissou's group first developed a new method for oxidative addition of aryl iodides to Au^{I} via diphosphine ligand-induced chelate bending, unlocking a new direction for bidentate ligand-induced oxidative addition of gold to bypass additional oxidants and pre-functionalized substrates (Scheme 6B).[16] Recently, Fensterbank's group first developed a strategy for photosensitized oxidative addition to gold(I), successfully realizing the alkynylative cyclization with iodoalkynes.[17]



Scheme 6. Oxidative gold catalysis via direct oxidative addition.

1.3 Research Purposes

Looking back at the introduced oxidative gold catalysis strategies, all of these strategies have certain drawbacks while showing their respective advantages. Drawbacks are for example low atom economy for external oxidants, impractical synthesis for alkynyl hypervalent iodine(III) reagents, potential instability for aryl diazonium salts, complicated bidentate ligands, special reaction conditions, *etc*. This all, to some extent, limits the practical application of these strategies. It is of great significance to explore a new gold catalytic system that greatly balances these advantages and disadvantages. Indeed, without taking into account the atom economy and the cost of oxidants, oxidative gold catalysis with external oxidants exhibits unparalleled reactivity in both cross-coupling and cyclization couplings, in terms of functionalization compatibility, molecular complexity and it shows a good balance between synthetic efficiencies and costs. Since Trost first proposed the concept of atom economy in 1991, ways to improve the atom efficiency of chemical reactions have become one of the main issues in all fields of synthetic chemistry,[18a] and the increasing demand for environmentally benign and atom-efficient processes has led to a growing interest on the invention of greener and more efficient synthetic strategies.[18b-e] To circumvent these drawbacks, our research focuses on exploring an unprecedented sustainable oxidative gold catalysis strategy with a green and inexpensive oxidant, not just as a more attractive substitute for common methodologies, but as an extraordinary reaction system.

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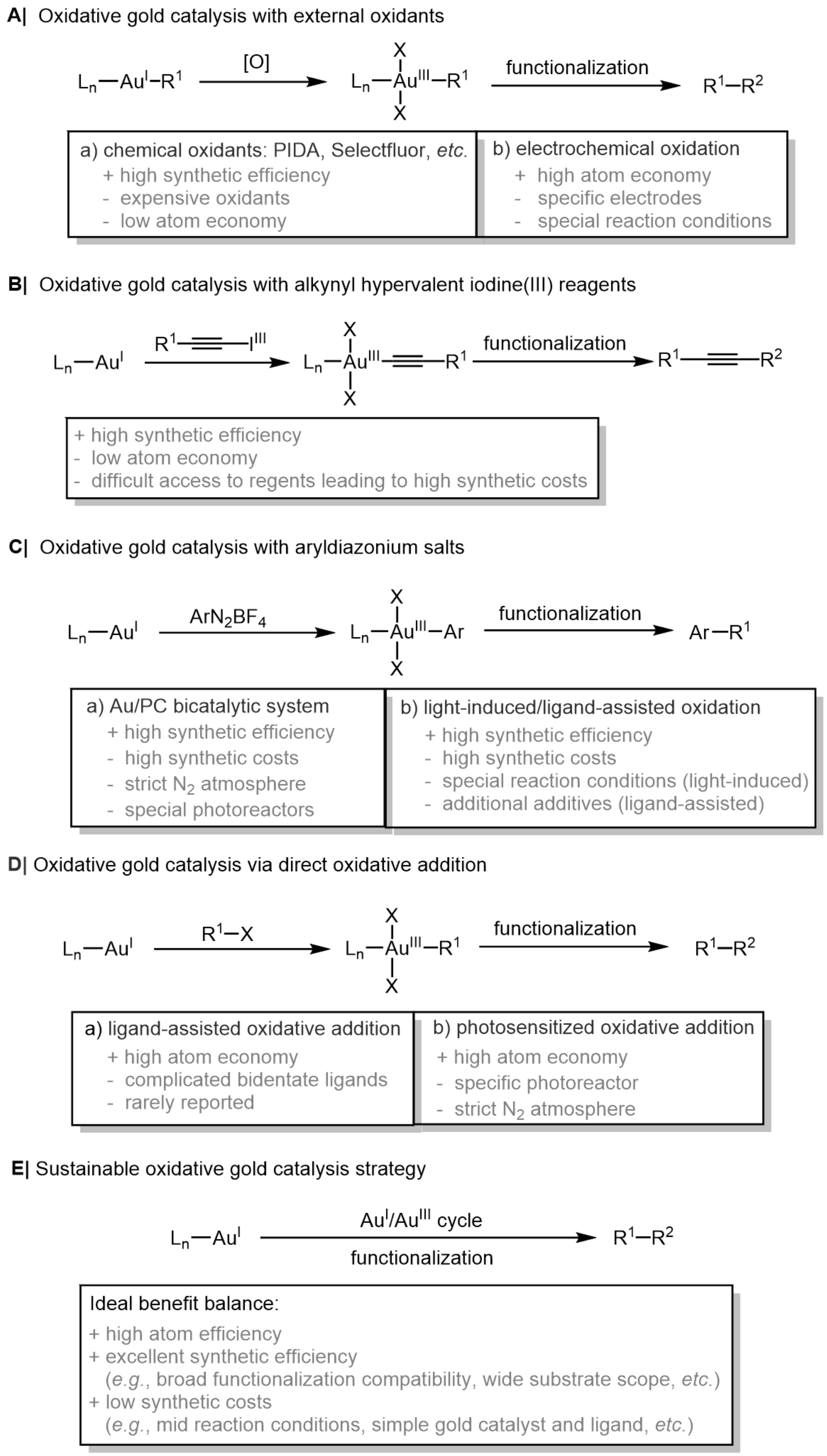
Chapter 2 A New Sustainable Oxidative Gold Catalysis Strategy

2.1 Introduction

Over the past decade, strategies for oxidative gold catalysis with external oxidants have demonstrated unparalleled synthetic efficiency, especially for C-C cross-coupling and C-H functionalizations.[1] However, the use of expensive chemical oxidants, such as PIDA, and Selectfluor not only results in higher synthetic costs but also exhibits low atom economy. Electrochemically promoted gold redox catalysis, which avoids the burden of stoichiometric oxidants, does improve the atom efficiency, but the special reaction conditions, such as specific electro-reaction devices and expensive electrodes, undoubtedly increase the synthetic costs and hinder its synthesis promotion.[2] In addition, oxidative gold catalysis with alkynyl hypervalent iodine(III) reagents has demonstrated unparalleled alkynylative functionalization efficiency.[3] The tedious synthesis progress of alkynyl hypervalent iodine(III) reagents increases the synthetic costs,[4] resulting in low atom economy, and the dissociation of aryl iodides brings difficulties to product separation (Scheme 1B). Oxidative gold catalysis with aryldiazonium salts can efficiently provide arylation products, which exhibit a high atom economy to a certain extent.[5] However, the synthesis of aryl diazonium salts is also not straightforward and has potential instability.[6] Moreover, photoredox or light-induced oxidative gold catalysis strategies usually require special reaction conditions, such as a strict N_2 atmosphere and the need for specific photoreactors, which increases the synthetic costs and limits the application (Scheme 1C).[5] Ligand-assisted gold-catalyzed direct oxidative addition strategies appear to circumvent these drawbacks perfectly, however, these practical syntheses are rarely reported and require complicated bidentate ligands.[7] Photosensitized gold oxidative addition exhibits high atom economy as well, but still requires special photoreactors and a strict N_2 atmosphere, which increases the synthetic costs (Scheme 1D).[8]

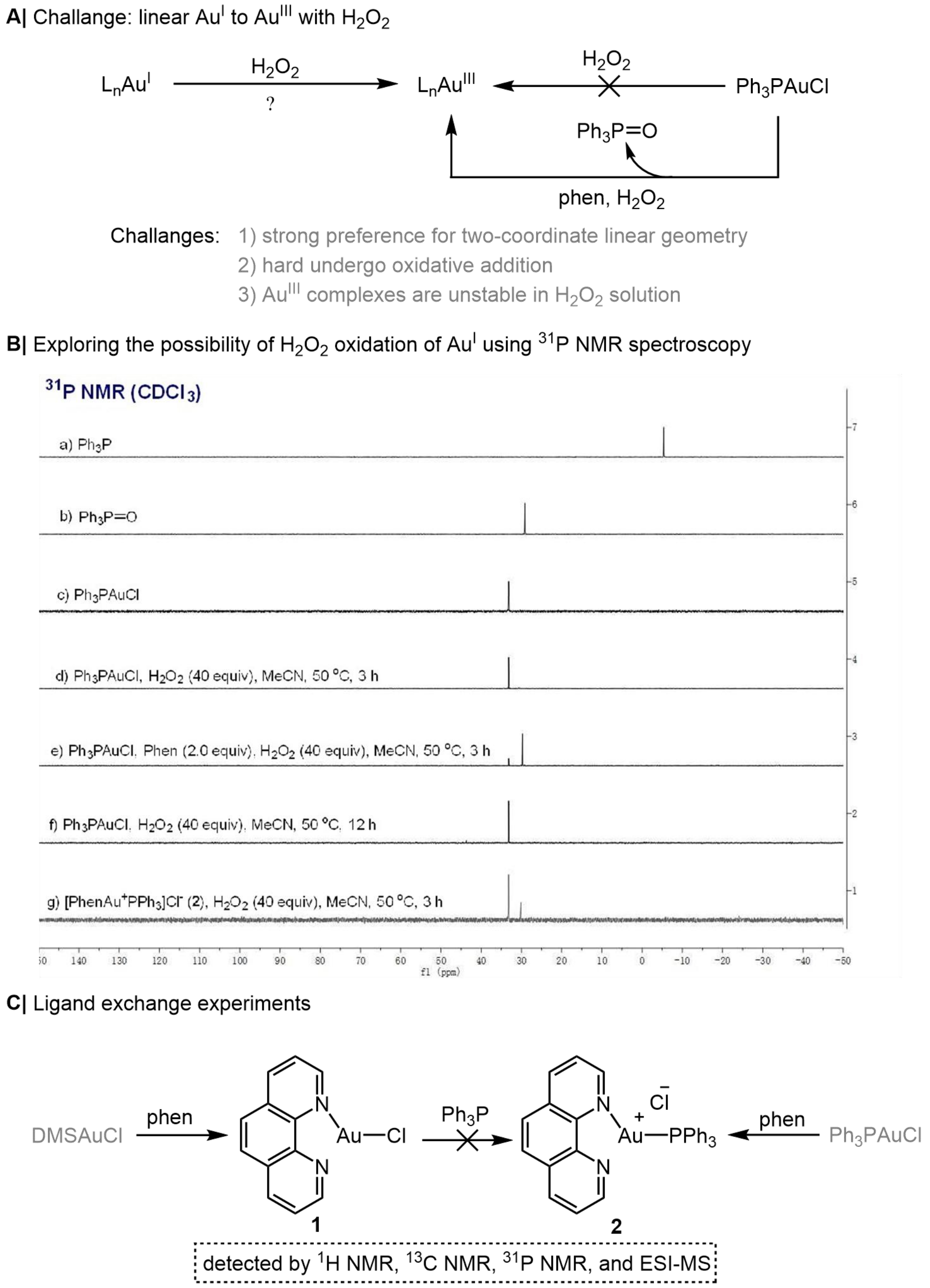
Disregarding atom economy and the cost of oxidant, oxidative gold catalysis with external oxidants bypasses the complicated synthesis of reagents, exhibiting extremely high synthetic efficiency under mild reaction conditions (without specific photoreactors, complicated bidentate ligands, and strict N_2 atmosphere, *etc.*). However, the invention of greener and more efficient synthetic strategies remains an attractive and valuable research direction.[9] While commonly used chemical oxidants, such as perchlorate, permanganate, hypervalent iodine reagents, or F^+ donors among others generate large amounts of waste, H_2O_2 can serve as an environmentally friendly and inexpensive oxidant, with H_2O being the only by-product. In addition, a high atom economy can be achieved and costs are low. As a consequence of its high oxidation potential (+1.78 V),[10] combined with its environmentally friendly properties, H_2O_2 is rapidly replacing commonly used stoichiometric oxidants.[11] Based on its redox potential, H_2O_2 can theoretically enable the conversion of Au^I to Au^{III} with an oxidation potential of +1.40 V.[12] Considering the various pros and cons of the above strategies, as shown in Scheme 1E, we set out to explore a unique sustainable oxidative gold catalysis strategy, which offers an ideal balance between atom economy, synthetic efficiency (involving wide substrate scope, broad functionalization compatibility, and remarkable selectivity, *etc.*) and synthetic costs (involving inexpensive oxidants, mild reaction conditions, simple gold catalyst, and ligand, *etc.*).



Scheme 1. Oxidative gold catalysis strategies.

2.2 Results and Discussion

As early as 2008, Wegner's group reported the first case of *t*-BuOOH (TBHP) as an oxidant in a gold-catalyzed domino cyclization/oxidative coupling reaction,[13] which confirmed the potential of peroxides as external oxidants for homogeneous oxidative gold catalysis. Surprisingly, so far there exists no homogeneous gold-catalyzed oxidative coupling using hydrogen peroxide as an oxidant in the literature.[14] The biggest challenge for a homogeneous oxidative gold catalysis cycle with H_2O_2 as the oxidant is to achieve the oxidation of Au^I to Au^{III}. Russell's group demonstrated that Ph_3P as a ligand easily dissociates from Au^{III} complexes followed by rapid oxidation to form Ph_3PO.[15] However, our initial study showed that Ph_3PAuCl was very stable in a 5 M solution of H_2O_2 in MeCN. After stirring at 50 °C for 3 h, no changes in the chemical shift were observed by ^{31}P NMR (Scheme 2B, entry d). Even after stirring the reaction mixture at 50 °C for 12 h, no Ph_3PO was detectable. However traces of $[(Ph_3P)_2Au]^+$ were formed, (^{31}P NMR: δ 43.7 ppm, *m/z*: 721.1501) and a gold mirror was observed (Scheme 2B, entry e). At first sight, it seems that the linear coordination sphere of Au^I thermodynamically disfavors the coordination of hydrogen peroxide, making it difficult to form the corresponding Au^{III} complex. It is acknowledged that linear two-coordinated Au^I complexes are extremely stable, which are not keen on higher coordination numbers and disfavor oxidative addition.[16] Bourissou's group demonstrated that the reactivity of Au^I complexes can be effectively enhanced by changing the linear state of the Au^I center, hence homovalent chelating ligands at the Au^I center were key to trigger oxidative additions.[17] Furthermore, Russell's and our group discovered that bidentate *N*-ligands, such as 2,2′-bipyridine (bpy) and 1,10-phenanthroline (phen), which enhance π back-donation from Au^I, boost the oxidative addition progress.[7c,18] Considering the above factors, we explored the possibility of the bidentate ligand phen to promote the oxidation of Ph_3PAuCl. To our delight, Ph_3PO was detected by ^{31}P NMR (Scheme 2B, entry e) from a mixture of Ph_3PAuCl, phen, and H_2O_2 which was stirred at 50 °C for 2 h. It is worth mentioning that a large amount of gold mirror was observed after a reaction time of 12 h, which indicates that the Au^{III} complex may not be stable in H_2O_2 solution. Furthermore, Ph_3PO was also detectable by ^{31}P NMR from a mixture of [PhenAu$^+$PPh$_3$]Cl$^-$ (**2**) and H_2O_2 which was stirred at 50 °C for 3 h (Scheme 2B, entry g). To further explore the possibility of the oxidation of Au^I by H_2O_2, a set of ligand exchange experiments was conducted (Scheme 2C). First, the ligand exchange reactions between DMSAuCl and phen led to the formation of PhenAuCl (**1**), which was detected by ^1H NMR, ^{13}C NMR, and ESI-MS (m/z: 377.0355). Next, Ph_3PAuCl (0.2 mmol) and phen (0.2 mmol) in MeCN were stirred at 50 °C for 1 h. No free Ph_3P was analyzed by ^{31}P NMR but [PhenAu$^+$PPh$_3$]Cl$^-$ (**2**) was detectable, and ESI-MS analysis revealed the formation of a major ion for [PhenAu$^+$PPh$_3$]: m/z 639.1284. Interestingly, gold complex **2** could not be prepared by the ligand exchange experiment of PhenAuCl with Ph_3P. This indicates that [PhenAu$^+$PPh$_3$]Cl$^-$ (**2**) is stable, at this stage, Ph_3P is unlikely to dissociate from the metal center of Au^I. In contrast, the dissociated Ph_3P was rapidly oxidized in the presence of H_2O_2 after dissociation from the metal center Au^{III},[15] which confirms that phen can effectively promote the oxidation of Au^I to Au^{III}. This series of experiments indicated that a strategy for phen-assisted oxidative gold catalysis with H_2O_2 can be achievable.

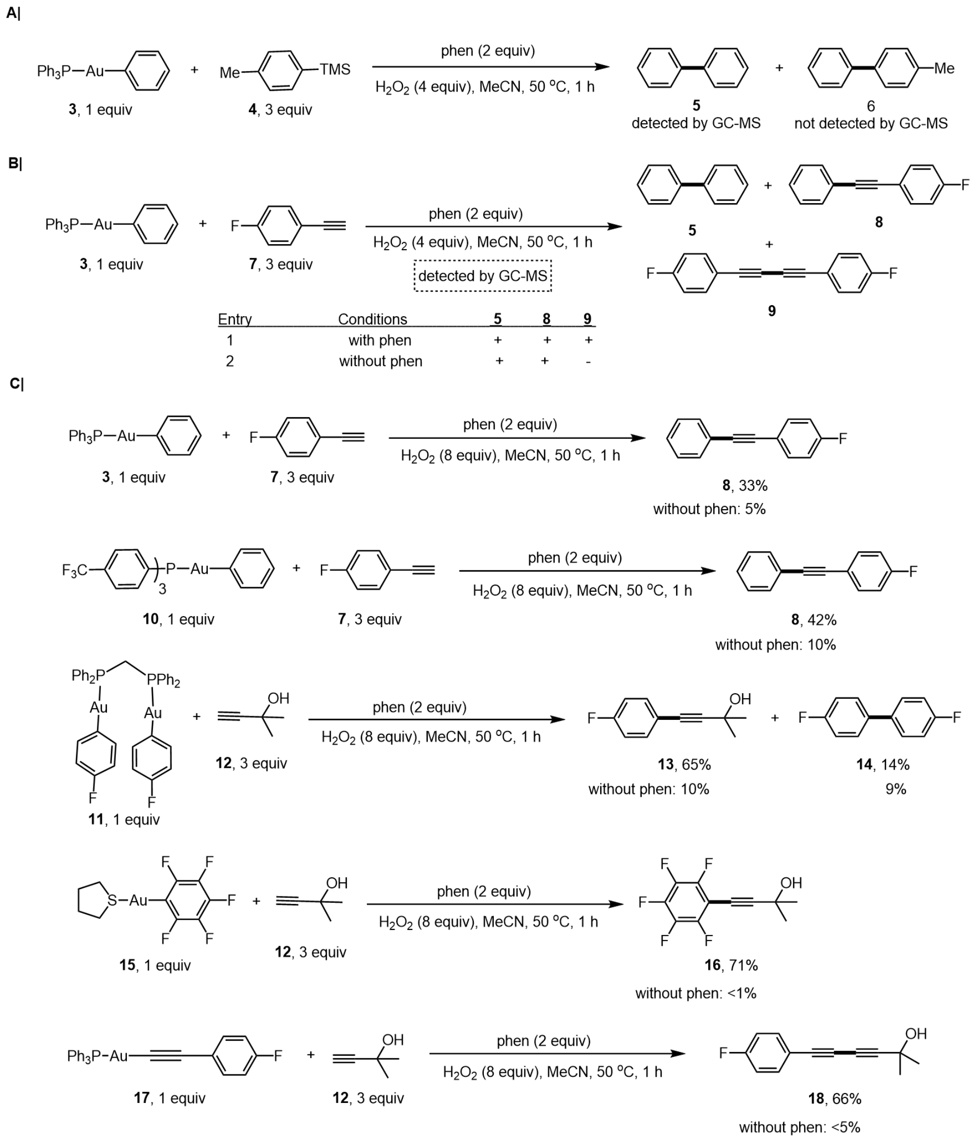

A| Challange: linear Au^I to Au^{III} with H_2O_2

B| Exploring the possibility of H_2O_2 oxidation of Au^I using ^{31}P NMR spectroscopy

C| Ligand exchange experiments

Scheme 2. Explored the possibility of oxidative gold catalysis using H_2O_2 as oxidant.

To verify the feasibility of oxidative gold catalysis with H_2O_2 as an oxidant, a set of experiments with stoichiometric Ph_3PAuPh was conducted (Scheme 3). Several examples for homogeneous gold-catalyzed oxidative C(sp^2)-C(sp^2) and C(sp^2)-C(sp) couplings with arylsilanes as coupling partners have been reported in the literature.[19] However, as shown in Scheme 3A, no cross-coupling products were detected by GC-MS in the presence or absence of phen. Interestingly, as shown in Scheme 3B, using 1-ethynyl-4-fluorobenzene **5** as the coupling partner, either homo- or cross-coupling products were detected by GC-MS. To obtain further information on the potential of hydrogen peroxide as an oxidant for oxidative gold catalysis, a set of experiments with stoichiometric Au^I species was conducted (Scheme 3C). A stoichiometric amount of arylgold(I) complex **3** was reacted with alkyne **7** to form 1-fluoro-4-(phenylethynyl)benzene **8** in 33% yield. This was achieved in the presence of phen and only a very small amount of product (5%) was observed in its absence. Interestingly, the use of a more electron-deficient phosphane in Au^I complex **10** afforded the coupled product **8** in 42% yield (10% yield without phen). Furthermore, the binuclear Au^I complex **11**, reacted with alkyne **12** in the presence of phen, delivered 65% of **13** and 14% of homocoupling by-product **14** (detected by ^{19}F NMR; 10% yield of cross-coupled product and 9% yield of homo-coupled product without phen). The stoichiometric reaction of $THTAu^I$ complex **15** with alkyne **12** formed 2-methyl-4-(perfluorophenyl)but-3-yn-2-ol **16** in 71% yield, however, in the absence of phen only a trace amount of coupled product (< 1%) was detected. In addition, the stoichiometric reaction of triphenylphosphine gold(I) alkynyl complex **17** with alkyne **12** furnished the cross-coupling product **18** in 66% yield (in the presence of phen), but only a very small amount of product was observed (< 5%). Overall, these experiments demonstrated the potential of this catalytic system for $C(sp^2)$-C(sp) and C(sp)-C(sp) cross-couplings, and phen plays a very important role.



Scheme 3. Gold-mediated C(sp^2)-C(sp) and C(sp)-C(sp) cross-couplings using H_2O_2 as oxidant.

2.3 Conclusion

As a green and inexpensive oxidant, hydrogen peroxide (H_2O_2) possesses great potential in oxidative gold catalysis, and bidentate ligand (phen) plays an irreplaceable role, which can effectively promote the oxidation of Au^I to Au^{III}. A set of experiments with stoichiometric gold(I) complex show that this catalytic system could be applied for homogeneous gold-catalyzed C(sp^2)-C(sp) and C(sp)-C(sp) cross-coupling reactions.

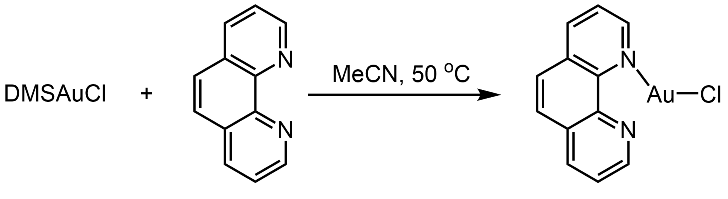
2.4 Experimental Section

2.4.1 General Materials and Methods

Chemicals were purchased from commercial suppliers and used as delivered. Dry solvents were dispensed from the solvent purification system MB SPS-800. In our conditions, MeCN can be used directly without further drying and deoxygenation. Deuterated solvents were bought from Euriso-Top. Hydrogen peroxide solution (50 wt% in water, stabilized) was bought from Sigma-Aldrich. For reactions that require heating, the heat source: aluminum heating block (less than 1 mmol scale reactions), or oil bath (more than 1 mmol scale reactions). Unless otherwise stated, all reactions were carried out under an ambient atmosphere and monitored by thin layer chromatography (TLC). Components were visualized by fluorescence quenching under UV light (254 nm) or by treatment with aqueous potassium permanganate ($KMnO_4$) solution. ^1H, $^{13}C\{^1H\}$, ^{31}P NMR, and ^{19}F NMR spectra were recorded on a Bruker Avance-III-300 (300 MHZ), or Bruker Avance-III-400 (400 MHZ) NMR spectrometer. Chemical shifts are expressed as parts per million (ppm, δ) downfield of tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.26 / 77.0 ppm) and DMSO-d_6 (2.50 / 39.5 ppm) as internal standards. Data is reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets; constants are absolute values and *J* values are expressed in Hertz (Hz). Mass spectra (HRMS) were determined in the chemistry department of the University Heidelberg under the direction of Dr. J. Gross. For ESI (+) spectra, an ApexQe FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR (IF528), IR (283), or FT-IR Vektor 22. Melting points (M.p.) were measured in open glass capillaries in a Büchi melting point apparatus.

2.4.2 General Synthesis of Gold Complexes

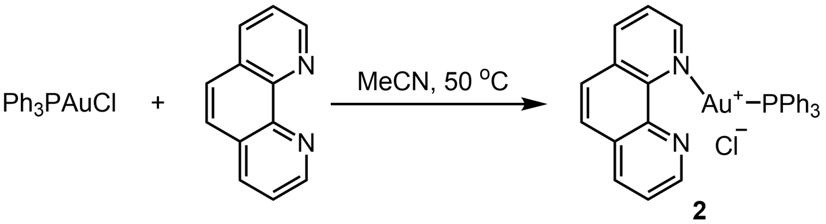
(1,10-Phenanthroline-*N*^{1},*N*^{10})gold(I) chloride (1)



1

A 25-mL round-bottomed equipped with a magnetic stir bar was charged with DMSAuCl (147.2 mg, 0.5 mmol), 1,10-phenanthroline (90 mg, 0.5 mmol) and MeCN (10 mL), the mixture was stirred at 50 °C under nitrogen. After 1 h, the solvent was removed under reduced pressure and washed sequentially with MeCN (10 mL), to obtain product **1** as colorless solid (167 mg, 81%). **^{1}H NMR** (400 MHz, DMSO) δ 9.29 (dd, *J* = 4.8, 1.5 Hz, 2H), 9.02 (dd, *J* = 8.2, 1.5 Hz, 2H), 8.33 (s, 2H), 8.18 (dd, *J* = 8.2, 4.8 Hz, 2H). **^{13}C NMR** (101 MHz, DMSO) δ 147.9, 141.2, 138.5, 129.4, 127.4, 125.4. **HRMS** (ESI) calcd for $C_{12}H_8AuN_2$ $[M]^+$: 377.0348, found: 377.0355. **IR** (ATR): ṽ = 3110, 3055, 1981, 1931, 1807, 1616, 1596, 1546, 1504, 1475, 1455, 1419, 1378, 1337, 1318, 1289, 1249, 1218, 1192, 1153, 1136, 1096, 1036, 992, 935, 884, 842, 772, 734, 716, 619. **M.p.** (amorphous): 211.5-213.8 °C.

(1,10-Phenanthroline-*N*^{1},*N*^{10})(triphenylphosphine)gold(I) (2)

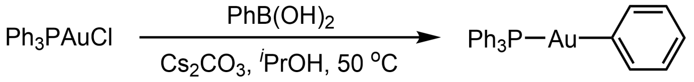


2

A 25-mL round-bottomed equipped with a magnetic stir bar was charged with Ph_3PAuCl (247.2 mg, 0.5 mmol), 1,10-phenanthroline (90 mg, 0.5 mmol) and MeCN (10 mL), the mixture was stirred at 50 °C under nitrogen. After 1 h, the solvent was removed under reduced pressure by an aspirator, without purification to give product **2** as dark solid (337 mg, 99%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.20 (dd, *J* = 4.3, 1.7 Hz, 2H), 8.27 (dd, *J* = 8.1, 1.7 Hz, 2H), 7.81 (s, 2H), 7.65 (dd, *J* = 8.1, 4.4 Hz, 2H), 7.59 – 7.38 (m, 15H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.2, 146.0, 136.1, 134.1 (d, *J*

= 13.7 Hz), 132.0 (d, *J* = 2.6 Hz), 129.2 (d, *J* = 11.9 Hz), 129.1, 128.4 (d, *J* = 28.4 Hz), 126.5, 123.1. **^{31}P NMR** (122 MHz, $CDCl_3$) δ 33.17. **HRMS** (ESI) calcd for $C_{30}H_{23}AuN_2P$ $[M]^+$: 639.1264, found: 639.1284. **IR** (ATR): ṽ = 3374, 3059, 2685, 2202, 1651, 1587, 1561, 1505, 1479, 1434, 1312, 1179, 1102, 1027, 999, 853, 740, 712, 691, 624. **M.p.** (amorphous): 119.7-121.6 °C.

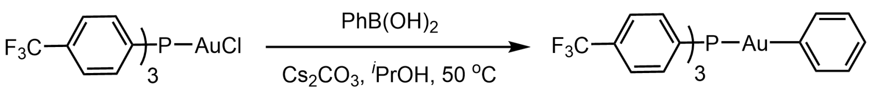
Phenyl(triphenylphosphanyl)gold (3)



3

In a 25-mL flask, Ph_3PAuCl (74 mg, 0.15 mmol) and Cs_2CO_3 (92 mg, 0.28 mmol) were added to a solution of phenyl boronic acid (35 mg, 0.29 mmol) in dry isopropanol (5 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was stirred at 50 °C for 24 h and cool the resulting solution to room temperature and concentrate in vacuo. The solid was extracted with benzene, filtered through Celite, concentrated in vacuo, washed with pentane. The solid was re-extracted into 0.5 mL benzene, filtered, and washed with methanol and pentane for three times to afford product **3** as colorless solid (57.6 mg, 72%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59 (dt, *J* = 12.3, 6.4 Hz, 8H), 7.53 – 7.40 (m, 9H), 7.34 – 7.27 (m, 2H), 7.15 – 7.01 (m, 1H). **^{31}P NMR** (122 MHz, $CDCl_3$) δ 43.53. Characterization data of **3** corresponded to the literature values.[20]

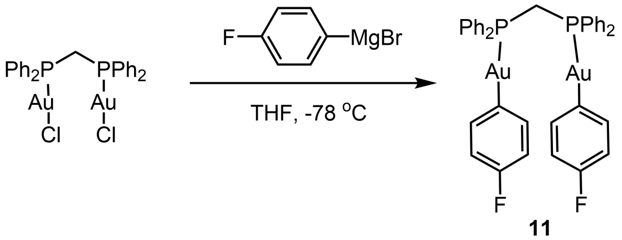
Phenyl[tris(4-(trifluoromethyl)phosphenyl)gold (10)



10

In a 25-mL flask, $(4\text{-}CF_3C_6H_4)_3PAuCl$ (140 mg, 0.2 mmol) and Cs_2CO_3 (130 mg, 0.4 mmol) were added to a solution of phenyl boronic acid (49 mg, 0.4 mmol) in dry isopropanol (10 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was stirred at 50 °C for 24 h and cool the resulting solution to room temperature and concentrate in vacuo. The solid was extracted with benzene, filtered through Celite, concentrated in vacuo, washed with pentane. The solid was re-extracted into 1 mL benzene, filtered, and washed with methanol and pentane for three times to afford product **10** as colorless solid (90 mg, 61%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.80 – 7.69 (m, 12H), 7.53 (d, *J* = 7.0, 2H), 7.32 (dd, *J* = 17.0, 9.4, 2H), 7.19 – 7.07 (m, 1H). **^{19}F NMR** (282 MHz, CDCl$_3$) δ -63.25. **^{31}P NMR** (122 MHz, CDCl$_3$) δ 43.76.

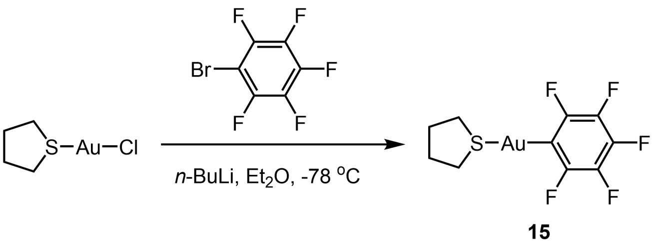
1,1-Bis(diphenylphosphino)methane) bis(4-fluorophenylgold) (11)



11

Charge a 5-mL flask equipped with a stirring bar with a solution of dppm(AuCl)$_2$ (84.8 mg, 0.1 mmol, 1 equiv) in THF (3 mL). Evacuation of the flask containing the resulting solution and flushing with N$_2$ for several times removed air. The solution was cooled at -78 °C, then 4-fluorophenylmagnesium bromide (1.0 M in THF, 0.6 mL, 0.6 mmol, 6 equiv) was added via syringe, and the mixture was stirred at -78 °C for 30 min. Then the mixture was warmed to 0 °C and stirred for 1 h. Then the mixture was quenched with 5 mL sat. aq. NH$_4$Cl and extracted with 5 mL benzene. The aqueous layer was separated and extracted with 2 x 5 mL benzene, and the combined organic layers dried over Na$_2$SO$_4$, filtered, and concentrate in vacuo. The residue was washed with 5 mL diethyl ether for two times and dried to afford product **11** as colorless solid (51.2 mg, 53%). **^{19}F NMR** (282 MHz, CDCl$_3$) δ -115.77. Characterization data of **11** corresponded to the literature values.[21]

(2,3,4,5,6-Pentafluorophenyl)(tetrahydrothiophene)gold (15)

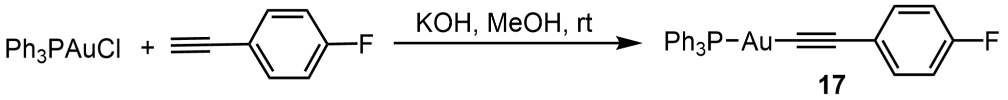


15

Charge a 25-mL flask equipped with a stirring bar with a solution of 1-bromo-2,3,4,5,6-pentafluorobenzene (123 mg, 0.5 mmol) in dry Et$_2$O (10 mL). Evacuation of the flask containing the resulting solution and flushing with N$_2$ for several times removed air. The solution was cooled at -78 °C, then *n*-butyllithium (0.4

mL, 1 mmol, 2.5 M in hexane) was added via syringe, and the solution was stirred at -78 °C or 45 min. Then THTAuCl (160 mg, 0.5 mmol) was added to the mixture. After stirred at this temperature for 15 min, then warmed to room temperature and stirred for 3 h. The solvent was removed under reduced pressure to afford product **15** as yellow solid (151.9 mg, 67 %). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 3.44 (s, 4H), 2.22 (s, 4H). **^{19}F NMR** (282 MHz, CDCl$_3$) δ -116.05 – -116.30 (m, 2F), -158.44 (t, *J* = 20.0, 1F), -162.20 – -162.54 (m, 2F). Characterization data of **15** corresponded to the literature values.[22]

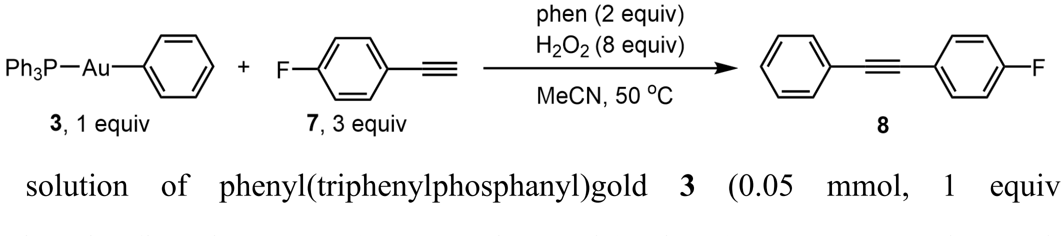
[2-(4-Fluorophenyl)ethyn-1-yl](triphenylphosphine)gold(I) (17)



In a 50-mL flask, Ph$_3$PAuCl (494.5 mg, 1 mmol) and KOH (112 mg, 2 mmol) were added to a solution of 1-ethynyl-4-fluorobenzene (172.5 mg, 1.5 mmol) in dry MeOH (25 mL) at room temperature. The mixture was stirred at room temperature in the dark for 48 h. Then the mixture was filtered and washed with 25 mL MeOH to give product **17** as colorless solid (470 mg, 81%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.66 – 7.39 (m, 17H), 6.94 (t, *J* = 8.8, 1H). **^{19}F NMR** (282 MHz, CDCl$_3$) δ -113.35. **^{31}P NMR** (122 MHz, CDCl$_3$) δ 42.29. Characterization data of **17** corresponded to the literature values.[23]

2.4.3 Gold-Mediated C(sp^2)-C(sp) and C(sp)-C(sp) Cross-Couplings Using H$_2$O$_2$ as Oxidant

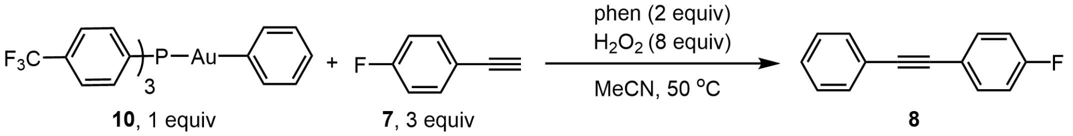
A| Preparation of 1-fluoro-4-(phenylethynyl)benzene (**8**) from gold(I) complex **3**.



A solution of phenyl(triphenylphosphanyl)gold **3** (0.05 mmol, 1 equiv), 1-ethynyl-4-fluorobenzene **7** (0.15 mmol, 3 equiv), phen (18 mg, 0.1 mmol, 2 equiv) and H$_2$O$_2$ (22.4 µL, 0.4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 1 h. After completion of the reaction, the yield of

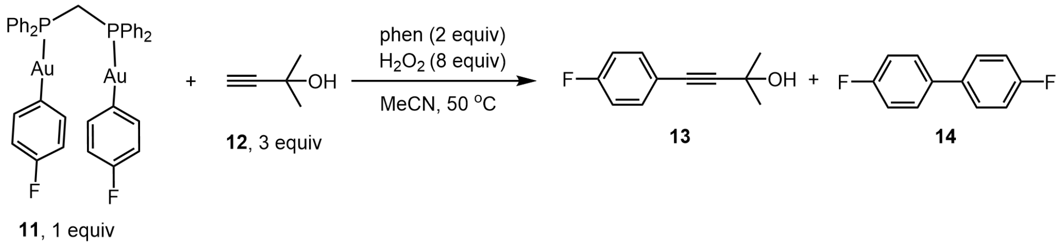
1-fluoro-4-(phenylethynyl)benzene **8** was determined by comparing the integration of the ^{19}F NMR resonance of product **8** (-110.92 ppm) with that of trifluorotoluene (-62.75 ppm). Then the solvent was removed under reduced pressure and the residue was purified by thin layer chromatography on silica gel to afford 1-fluoro-4-(phenylethynyl)benzene **8** as colorless solid (33%, yield was detected by ^{19}F NMR). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 – 7.45 (m, 4H), 7.37 (dd, *J* = 7.0, 3.5, 3H), 7.06 (t, *J* = 8.7, 2H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -110.92. Characterization data of **8** corresponded to the literature values.[24]

B| Preparation of 1-fluoro-4-(phenylethynyl)benzene (**8**) from gold(I) complex **10**.



A solution of phenyl[tris(4-(trifluoromethyl)phosphenyl)gold **10** (0.05 mmol, 1 equiv), 1-ethynyl-4-fluorobenzene **7** (0.15 mmol, 3 equiv), phen (18 mg, 0.1 mmol, 2 equiv) and H_2O_2 (22.4 µL, 0.4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 1 h. After completion of the reaction, the yield of 1-fluoro-4-(phenylethynyl)benzene **8** was determined by ^{19}F NMR using benzotrifluoride as an internal standard. The mixture was purified by thin layer chromatography on silica gel to afford 1-fluoro-4-(phenylethynyl)benzene **8** as colorless solid (42%, yield was detected by ^{19}F NMR).

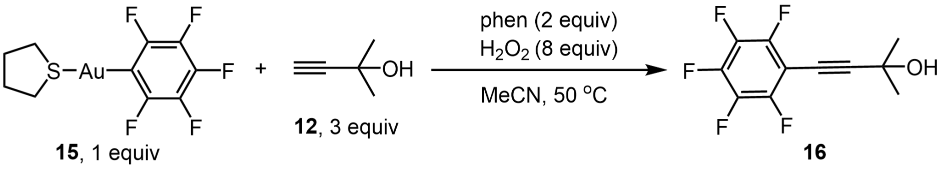
C| Preparation of 4-(4-fluorophenyl)-2-methylbut-3-yn-2-ol (**13**) from gold(I) complex **11**.



A solution of 1,1-bis(diphenylphosphino)methane) bis(4-fluorophenylgold) **11** (0.05 mmol, 1 equiv), 2-methylbut-3-yn-2-ol **12** (0.15 mmol, 3 equiv), 1,10-phenanthroline (18 mg, 0.1 mmol, 2 equiv) and H_2O_2 (22.4 µL, 0.4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 1 h. After completion of the reaction, the yield of

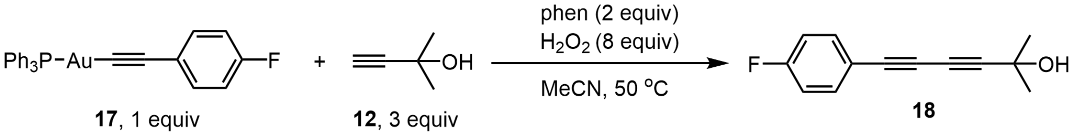
4-(4-fluorophenyl)-2-methylbut-3-yn-2-ol **13** and 4,4'-difluoro-1,1'-biphenyl **14** were determined by comparing the integration of the ^{19}F NMR resonance of product **13** (-111.12 ppm) and by-product **14** (-115.81 ppm) with that of trifluorotoluene (-62.75 ppm). Then the solvent was removed under reduced pressure and the residue was purified by thin layer chromatography on silica gel to afford 1-fluoro-4-(phenylethynyl)benzene **13** as light yellow oil (65%, yield was detected by ^{19}F NMR). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.6, 5.5, 2H), 6.97 (t, *J* = 8.6, 2H), 2.41 (br, 1H), 1.60 (s, 6H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -111.12. Characterization data of **13** corresponded to the literature values.[25]

D| Preparation of 2-methyl-4-(perfluorophenyl)but-3-yn-2-ol (**16**) from gold(I) complex **15**.



A solution of (2,3,4,5,6-pentafluorophenyl)(tetrahydrothiophene)gold **15** (0.05 mmol, 1 equiv), 2-methylbut-3-yn-2-ol **12** (0.15 mmol, 3 equiv), phen (18 mg, 0.1 mmol, 2 equiv) and H_2O_2 (22.4 μL, 0.4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 1 h. After completion of the reaction, the yield of 2-methyl-4-(perfluorophenyl)but-3-yn-2-ol **16** was determined by ^{19}F NMR using benzotrifluoride as an internal standard. The mixture was purified by thin layer chromatography on silica gel to afford 2-methyl-4-(perfluorophenyl)but-3-yn-2-ol **16** as colorless oil (71%, yield was detected by ^{19}F NMR). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.94 (br, 1H), 1.64 (s, 6H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -136.08 – -136.29 (m), -152.53 (tt, *J* = 20.8, 1.6), -161.71 – -161.97 (m).

E| Preparation of 6-(4-fluorophenyl)-2-methylhexa-3,5-diyn-2-ol (**18**) from gold(I) complex **17**.



A solution of [2-(4-fluorophenyl)ethyn-1-yl](triphenylphosphine)gold(I) **17** (0.05

mmol, 1 equiv), 2-methylbut-3-yn-2-ol **2a** (0.15 mmol, 3 equiv), phen (18 mg, 0.1 mmol, 2 equiv) and H_2O_2 (22.4 μL, 0.4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 1 h. After completion of the reaction, the yield of -(4-fluorophenyl)-2-methylhexa-3,5-diyn-2-ol **18** was determined by ^{19}F NMR using benzotrifluoride as an internal standard. The mixture was purified by thin layer chromatography on silica gel to afford -(4-fluorophenyl)-2-methylhexa-3,5-diyn-2-ol **18** as colorless solid (66%, yield was detected by ^{19}F NMR). **^{1}H NMR** (300MHz, $CDCl_3$) δ 7.69 – 7.34 (m, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 2.51 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.9 (d, *J* = 251.5 Hz, CF), 134.5 (d, *J* = 8.6 Hz), 117.6 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 22.3 Hz), 86.7, 77.6, 72.9, 66.8, 65.7, 31.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.53. Characterization data of **18** corresponded to the literature values.[26]

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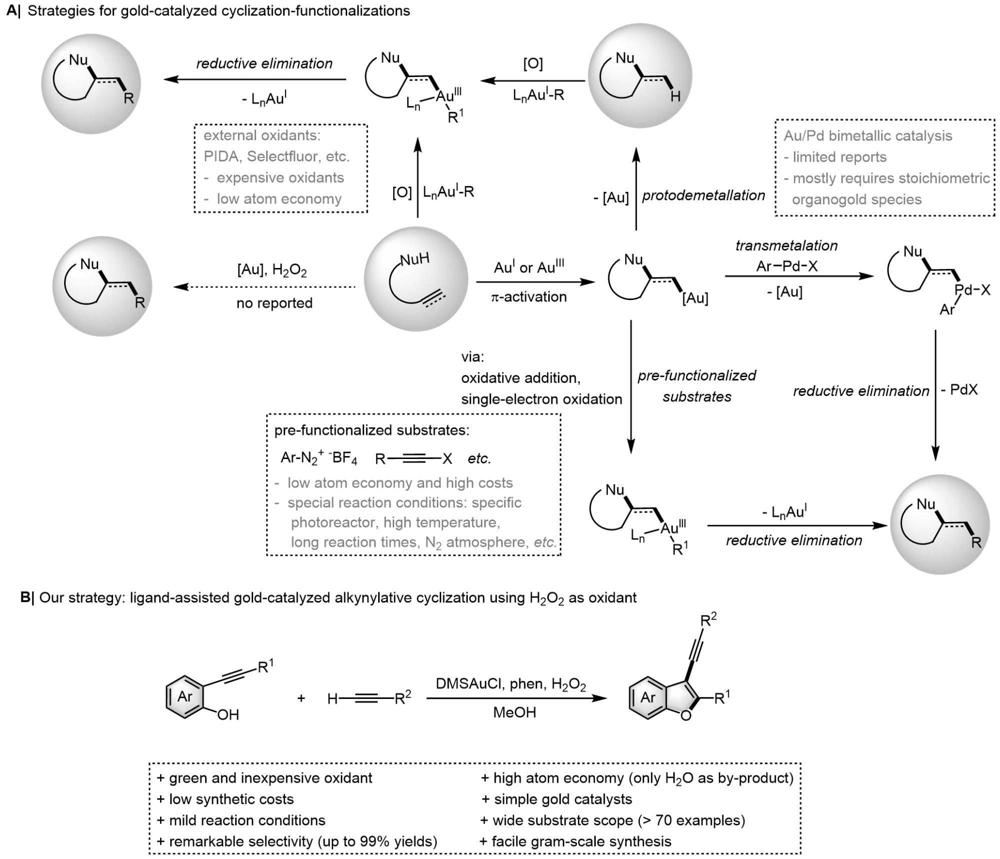
Chapter 3 Ligand-Assisted Gold-Catalyzed Efficient Alkynylative Cyclization with Terminal Alkynes Using H_2O_2 as Oxidant

In this part, Martin C. Dietl contributed the computational calculations and wrote the calculation section (**Figure 1**). Philipp M. Stein synthesized compounds **s1** and **1a**. Tao Wang synthesized compounds **1ax**, **1ba** and $(Ph_3P)_2PdCl_2$. Jun Li synthesized compounds **1aw** and **1az**. Petra Krämer analyzed IR data; Frank Rominger conducted X-ray crystal structure analysis. Matthias Rudolph corrected the manuscript and made important suggestions for mechanism investigation (Scheme 3D, equation 5). See chemrxiv, 2022, DOI: 10.26434/chemrxiv-2022-4vj3 for all calculation details, experimental details and NMR Spectra.

3.1 Introduction

As a powerful method for the preparation of high-value organic molecules, homogeneous gold catalysis has received extensive attention for its strong ability to activate C-C double or triple bonds, especially for the selective and efficient promotion of different cyclization reactions.[1] Typically, *in situ* protodeauration of organogold intermediates terminates the catalytic cycle to afford hydrogen-functionalized products.[1b-h] In recent years, more attention has been paid to the *in situ* post-functionalization of gold intermediates instead of simple protodemetallation.[1i-l] Gold-catalyzed cross-coupling reactions with strong external oxidants, such as hypervalent iodine reagents or F^+ donors have shown to be effective for the *in situ* functionalization to construct complex organic molecules.[1k-l] However, these reagents are often costly and show low atom economy. To avoid the burden of stoichiometric oxidants, a Au/Pd dual catalytic system proved to be effective for the cyclization-functionalization process, however, the only limited reports suggest that its general application remains challenging.[2] In addition, the use of special pre-functionalized substrates such as aryldiazonium salts,[3] alkynyl hypervalent iodine reagents,[4] and alkynyl halides,[5] *etc.* also gave access to Au^I/Au^{III} catalytic cycles without external oxidants to afford cyclic functionalized molecules. Although the use of external oxidants is avoided, its limitations are also significant, such as air sensitivity, and the need for specific photoreactors.[3,5a,5c] Furthermore, the synthesis of the applied reagents is not straightforward,[4] resulting in low atom economy and high synthetic costs.

In Chapter 2, we explore the possibility of oxidative gold catalysis using hydrogen peroxide (H_2O_2) as an oxidant. A series of stoichiometric experiments demonstrated the potential of phen-assisted gold-catalyzed C(sp^2)-C(sp) cross-coupling. Thus, we expected that a strategy for phen-assisted gold-catalyzed oxidative catalysis with H_2O_2 could be achievable. As a test system for a gold-catalyzed cyclization-functionalization reaction with H_2O_2 we selected an alkynylative cyclization process. 2-(Alkynyl)phenols as good cyclization coupling partners, can efficiently provide benzofuran building blocks.[4b,5a] Surprisingly, gold-catalyzed alkynylative cyclizations to provide 3-alkynylbenzofurans, based on 2-(alkynyl)phenols and terminal alkynes as coupling partners have no precedent in the literature. Herein, we describe a new ligand-assisted gold-catalyzed alkynylative cyclization with H_2O_2 as an external oxidant, to furnish 3-alkynylbenzofurans from 2-(alkynyl)phenols and terminal alkynes (Scheme 1B).

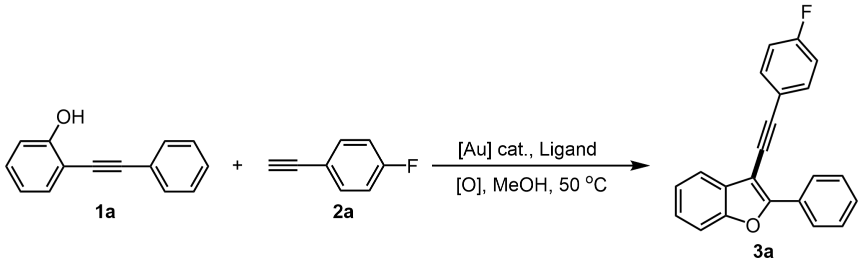


Scheme 1. Gold-catalyzed cyclization-functionalization.

3.2 Results and Discussion

We started our investigation on the gold-catalyzed alkynylative cyclization by using 2-(phenylethynyl)phenol **1a** and 1-ethynyl-4-fluorobenzene **2a** as the test system (Table 1). We first focused on the investigation of the effect of different ligands on the reaction (Table 1, entries 1-5). When DMSAuCl or Ph_3PAuCl were used as catalysts, no product was detected in the absence of a ligand (entries 1 and 2). Pyridine (py) as a monodentate ligand did not promote this reaction (entry 3), 2,2'-bipyridine (bpy) and phen as bidentate ligands furnished the product **3a** in 10 % and 99 % yield, respectively (entries 4 and 5). Next, we focused on the investigation of the effect of different gold catalysts on the reaction (entries 6-10). No products were formed without any gold catalyst (entry 5). Both mononuclear and binuclear gold complexes delivered the alkynylative cyclization product **3a** in excellent yields (entries 7-9). Interestingly, other mononuclear gold(I) complexes with significant steric bulk, such as CyJohnPhosAuCl, gave the product in only low to moderate yield (entry 10). IPrAuCl, bearing an *N*-heterocyclic carbene ligand, could not promote the reaction at all (entry 11). In addition, we also investigated the effects of other factors on the reaction such as reaction time and the equivalents of alkyne **2a**. The reaction can be completed within 3 h (entry 12), and the alkynylative cyclization efficiency of 2-(phenylethynyl)phenol **1a** can be maximized by adding 1.5 equivalents of alkyne **2a** (entry 13). Reducing the equivalents of H_2O_2 also delivered the product in good yield (entry 14). Other peroxides, such as TBHP led to only moderate yield (entry 15). Surprisingly, no product was detected if other oxidants, that were previously used in gold-catalyzed redox couplings such as phenyliodine(III) diacetate (PIDA) or Selectfluor,[1k-l] were applied (entries 16 and 17). Also, the ratio of DMSAuCl to phen had a significant effect on the reaction. It is worth pointing out, that although the catalytic combination of 1 mol% DMSAuCl and 4 mol% phen only gave product **3a** in moderate yield within 3 h, the yield could be improved to 97% by extending the reaction time to 16 h (entries 19 and 20). Considering the comprehensive efficiency, the optimal catalytic system consists of 2.5 mol% DMSAuCl, 10 mol% phen, and 8 equivalents of H_2O_2 (entry 18).

Table 1. Optimization of the conditions.[a,b]



Entry	Au cat. (mol%)	ligand (mol%)	**2a** (equiv)	[O] (equiv)	time (h)	**3a** (%)
1	Ph_3PAuCl (7.5)	-	2	H_2O_2 (8)	12	ND
2	DMSAuCl (7.5)	-	2	H_2O_2 (8)	12	ND
3	DMSAuCl (7.5)	py (30)	2	H_2O_2 (8)	12	ND
4	DMSAuCl (7.5)	bpy (30)	2	H_2O_2 (8)	12	10
5	DMSAuCl (7.5)	phen (30)	2	H_2O_2 (8)	12	99
6	-	phen (30)	2	H_2O_2 (8)	12	ND
7	Ph_3PAuCl (7.5)	phen (30)	2	H_2O_2 (8)	12	99
8	Dppm$(AuCl)_2$ (3.75)	phen (30)	2	H_2O_2 (8)	12	99
9	$AuCl_3$ (7.5)	phen (30)	2	H_2O_2 (8)	12	88
10	CyJohnPhosAuCl (7.5)	phen (30)	2	H_2O_2 (8)	12	42
11	IPrAuCl (7.5)	phen (30)	2	H_2O_2 (8)	12	ND
12	DMSAuCl (7.5)	phen (30)	2	H_2O_2 (8)	3	99
13	DMSAuCl (7.5)	phen (30)	1.5	H_2O_2 (8)	3	99
14	DMSAuCl (7.5)	phen (30)	1.5	H_2O_2 (4)	3	85
15	DMSAuCl (7.5)	phen (30)	1.5	TBHP (4)	3	25
16	DMSAuCl (7.5)	phen (30)	1.5	PIDA (4)	3	ND
17	DMSAuCl (7.5)	phen (30)	1.5	Selectfluor (4)	3	ND
18	**DMSAuCl (2.5)**	phen **(10)**	**1.5**	H_2O_2 (8)	**3**	**99**
19	DMSAuCl (1)	phen (4)	1.5	H_2O_2 (8)	3	38
20	DMSAuCl (1)	phen (4)	1.5	H_2O_2 (8)	16	97

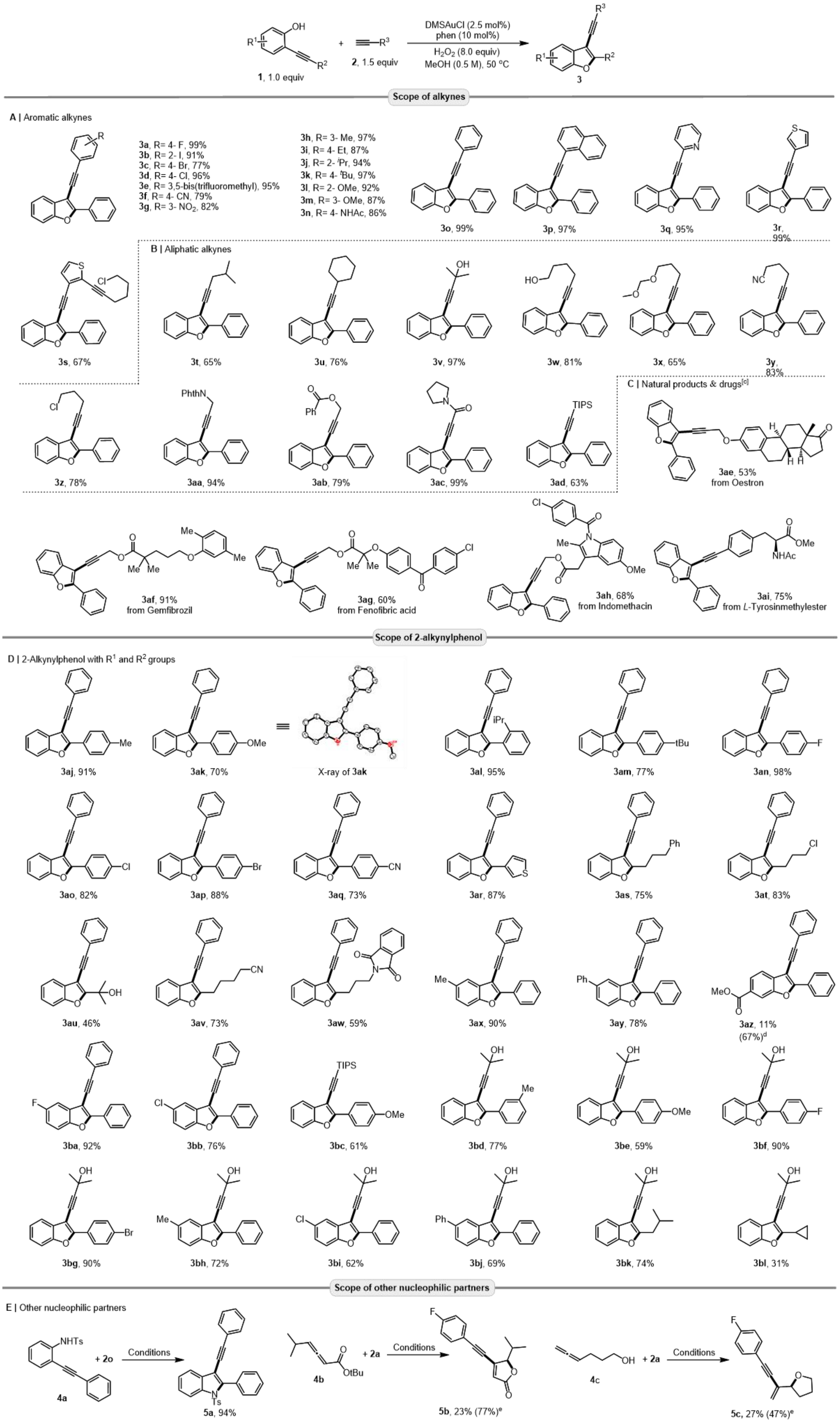
[a] Reaction conditions: 2-(phenylethynyl)phenol **1a** (0.05 mmol), 1-ethynyl-4-fluorobenzene **2a**, gold catalyst, ligand and [O] (oxidant) in MeOH (0.1 mL), 50 °C. [b] Determined by ^{19}F NMR using benzotrifluoride as internal standard. py = pyridine; phen = 1,10-phenanthroline; CyJohnPhos = (2-biphenylyl)-dicyclohexylphosphin; dppm = bis(diphenylphosphino)methane; IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene.

With the optimized conditions in hand, we explored the scope of different terminal alkyne **2** to form 3-alkynylbenzofuran **3**, using 2-alkynylphenol **1** as the alkynylative cyclization partners. As shown in Table 2A, we first focused on alkynylative cyclization with aromatic terminal alkynes. Aryl alkynes bearing electron-withdrawing groups, such as -F, -I, -Br, -Cl, $-CF_3$, -CN, and $-NO_2$, were tolerated well, furnishing the alkynylbenzofurans in yields ranging from 77% to 99% (**3a**-**3g**). A variety of electron-rich aryl alkynes, with electron-donating groups such as -Me, -Et, -^{i}Pr, -^{t}Bu, -OMe, and - NHAc, reacted smoothly as well, affording the target alkynylative cyclization products in very good to excellent yields (**3h**-**3n**, 84-97%). It is worth pointing out that the bulky hindered aryl acetylenes **2b** and **2l**, and even the more sterically hindered 1-ethynyl-2-isopropylbenzene **2j**, still reacted well, forming the corresponding products (**3b**, **3l**, and **3j**) in excellent yields (91-94%). The above results show that the electronic properties and the position of the substituents on the aromatic ring of terminal aryl alkynes have no significant effect on this reaction. Phenylacetylene and naphthylacetylene without substitution at the aromatic moiety proved to be also suitable substrates, providing **3o** and **3p** in 99% and 97% yields, respectively. As expected, heteroaromatic alkynes, including both electron-poor pyridine and electron-rich thiophene substituents, reacted very smoothly as well, affording the corresponding alkynylbenzofurans in excellent yield (**3q**, 95%, **3r**, 99%). Surprisingly, enediynes were tolerated well by the catalytic system to afford alkynylbenzofuran **3s** in a yield of 61%. In addition, as shown in Table 2B, great functional group tolerance was also observed with aliphatic alkynes. Alkylalkynes bearing isobutyl (**3t**), cyclohexyl (**3u**), functional groups such as alcohols (**3v, 3w**), ether (**3x**), cyano (**3y**), chloro (**3z**), phthalimide (**3aa**), ester (**3ab**), amide (**3ac**), and TIPS (**3ad**) were all tolerated in this reaction leading to the target products in good to excellent yields (63-99%). To underline the synthetic utility of the method, we next evaluated the potential to use this methodology for the introduction of benzofuran units into natural products and synthetic drugs (Table 2C). This gold-catalyzed alkynylative cyclization worked well with the substrate **2ae**, derived from Oestrone (a weak estrogen), delivering the alkynylative cyclization product **3ae** in decent yield. **2af** and **2ag** as derivatives of small molecule hypolipidemic drugs Gemfibrozil and Fenofibric acid, were amenable to this reaction forming **3af** and **3ag** in 91% and 60% yields, respectively. The derivative **2ah** of Indomethacin, a common non-steroidal anti-inflammatory drug, was also successfully employed to form **3ah** in a 68% yield. *L*-Tyrosine derivative **2ai** reacted smoothly as well, to afford alkynylbenzofuran **3ai** in good yield.

Encouraged by these results, the scope for a range of 2-alkynylphenols was further explored (Table 2D). First, we varied the R^2 groups of the 2-alkynylphenol partners, both aryl- and alkyl- groups performed efficiently. The electronic properties of the aryl substituents (R^2 groups) had only little influence, electron-donating groups such as Me-, MeO-, ^{i}Pr-, and ^{t}Bu-, electron-withdrawing groups such as F-, Cl-, Br-, and CN-, both smoothly afforded the corresponding products **3aj**-**3aq** in good to excellent yields (70-98%). Among them, the structure of alkynylbenzofuran **3ak** was confirmed by X-ray crystallographic analysis. Steric hindrance of the 2-alkynylphenols had no significant effect on the reaction. For example, the large sterically hindered 2-((2-isopropylphenyl)ethynyl)phenol **2al**, reacted very well, forming the corresponding product (**3al**) in 95% yield. Excitingly, 2-alkynylphenol **1** bearing heteroaromatics, such as thiophene, was tolerated as well, to give 3-(phenylethynyl)-2-(thiophen-3-yl)benzofuran **3ar** in 86% yield. Furthermore, 2-alkyl-3-(phenylethynyl)benzofurans (**3as**-**3aw**) bearing functional groups such as Ph-, Cl-, HO-, CN-, and NPhth- groups, were accessible in moderate to good yields. Next, we varied the R^1 groups at the benzene core of the 2-alkynylphenol partners (**3ax**-**3bb**), introducing both electron-rich (Me-, Ph-) and electron-poor (F-, Cl-) functional groups. Both groups were suitable substrates, affording the corresponding alkynylbenzofurans in good to excellent yields (76-92%). However, the benzene ring with a stronger electron deficient group (MeOCO-) of the 2-alkynylphenol partner, showed a low reactivity, even after extending the reaction time to 48 h, a low yield of alkynylbenzofuran **3az** was obtained (11%, and 65% recovered 2-alkynylphenol **1az**). In addition, by using aliphatic alkynes as coupling partners, a range of 2-alkynylphenols with different functional groups (R^1 and R^2) showed a good tolerance as well, furnishing the target alkynylbenzofurans with yields ranging from 31% to 99% yield (**3bc**-**3bl**). Of particular note is that no cyclopropane ring-opening product was observed (**3bl**), which implies that a free radical pathway is not involved.[6]

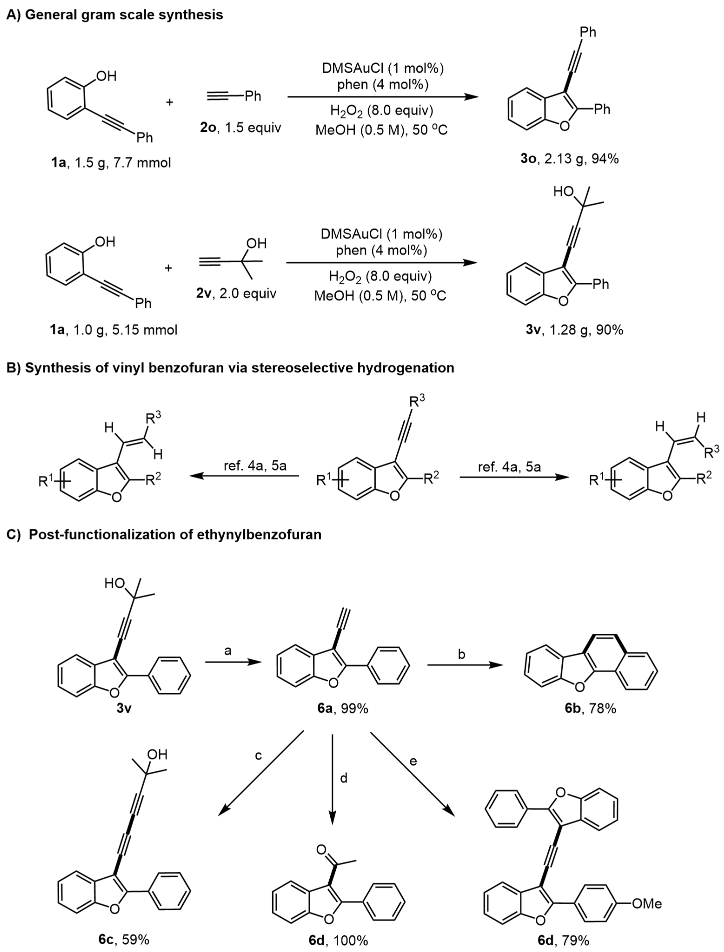
To further emphasize the general applicability of our strategy, other nucleophilic partners were tested as well. As shown in Table 2E, 2-alkynyl tosylaniline **4a** as a nucleophilic partner, under standard conditions, furnishing the corresponding alkynylative cyclization product **5a** in 94% yield. Moreover, *tert*-butyl-dienoate **4b** as a good nucleophilic precursor, reacted smoothly as well, affording the corresponding product **5b** in a 23% yield under standard conditions. Hexa-4,5-dien-1-ol **4c** showed a good tolerance as well, giving the corresponding alkynylation product **5c** in a poor yield. It is noteworthy that the efficiency of these reactions can also be improved by optimizing some conditions. For example, by increasing the amount of Au catalyst, phen ligand and coupling partner **2a**, the yields of **5b** and **5c** were significantly higher. This further illustrates the generality and feasibility of the gold-catalyzed alkynylative cyclization strategy by using H_2O_2 as an oxidant.

Table 2. Scope for the gold-catalyzed alkynylative cyclization.[a,b]



[a] Reaction conditions: 2-alkynylphenol **1** (0.2 mmol), alkyne **2** (0.3 mmol), DMSAuCl (2.5 mol%), phen (10 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C. [b] Isolated yields are reported. [c] alkyne **2** (0.21 mmol). [d] Recovered 2-alkynylphenol **1az**. [e] Alkyne **2** (0.4 mmol), DMSAuCl (7.5 mol%), phen (30 mol%).

An upscaling of the reaction to a gram scale was easily possible, which was demonstrated by the synthesis of alkynylbenzofurans **3o** and **3v** that were obtained in yields of 94% and 90% respectively (Scheme 2a). The structural modification of benzofuran as a ubiquitous skeleton of bioactive natural products and pharmaceuticals,[7] remains an important field of research. The introduced alkyne moiety in the obtained products of our strategy offers an attractive synthetic handle for modifications which further multiplies the potential applications. As shown in Scheme 2b, the palladium-catalyzed stereoselective hydrogenation of benzofurans is reported to deliver the corresponding vinylbenzofurans.[4a,5a] In addition, ethynylbenzofurans as valuable scaffolds, were easily obtained by deprotection of 3-(3-hydroxy-3-methyl)alkynylbenzofurans, such as **3v**. Considering the importance of benzofuran derivatives, we demonstrated a range of post-functional applications to demonstrate the synthetic utility of alkynylbenzofurans (Scheme 2c). The heterotetracene **6b** was efficiently obtained via a $PtCl_2$-catalyzed cyclization.[4c] 1,3-Diynylbenzofuran **6c** was successfully obtained by a copper-catalyzed Glaser coupling.[8] In addition, 3-acetylbenzofuran was efficiently synthesized by water addition using $AuCl_3$ as a catalyst. Notably, the unsymmetrical dibenzofuranoacetylene **6d** can also be efficiently prepared in a 79% yield under our standard conditions.



Scheme 2. Comprehensive application. Reagents and conditions: ^{a} NaOH (2 equiv), 1,4-dioxane, 60 °C, 24 h. ^{b} $PtCl_2$ (10 mol%), toluene, 100 °C, 12 h. ^{c} 2-methylbut-3-yn-2-ol **2v** (1.3 equiv), Cu (5 mol%), TMEDA (20 mol%), $CHCl_3$/1,4-dioxane (3:1), air, 50 °C, 24 h. ^{d} $AuCl_3$ (10 mol%), H_2O (8 equiv), ^{i}PrOH, 65 °C, 24 h. ^{e} 2-((4-methoxyphenyl)ethynyl)phenol **1ak** (1 equiv), ethynyl-benzofuran **6a** (1.5 equiv), DMSAuCl (2.5 mol%), phen (10 mol%), and H_2O_2 (8 equiv, 50 wt% in water), MeCN (0.5 M), 50 °C, 12 h.

To obtain further insight into the operating mechanism, a set of control experiments was conducted (Scheme 3). First, as shown in Scheme 3A, C3-unsubstituted benzofuran **7a** was reacted with 1-ethynyl-4-fluorobenzene **2a** under normal conditions. This only afforded homocoupling product **7b** after stirring for 72 h, and no alkynylation product **3a** was observed. This finding suggests that an alkynylation of the unfunctionalized benzofuran formed via a prior cyclization/ protodemetalation is unlikely.[4c-f]

When stoichiometric amounts of AuCl and phen were reacted with **1a** and **2a** (without any oxidants), neither the alkynylative cyclization product **3a** nor the homocoupling product **7b** was detected after stirring for 24 h (Scheme 3B, entry 1). By using $AuCl_3$

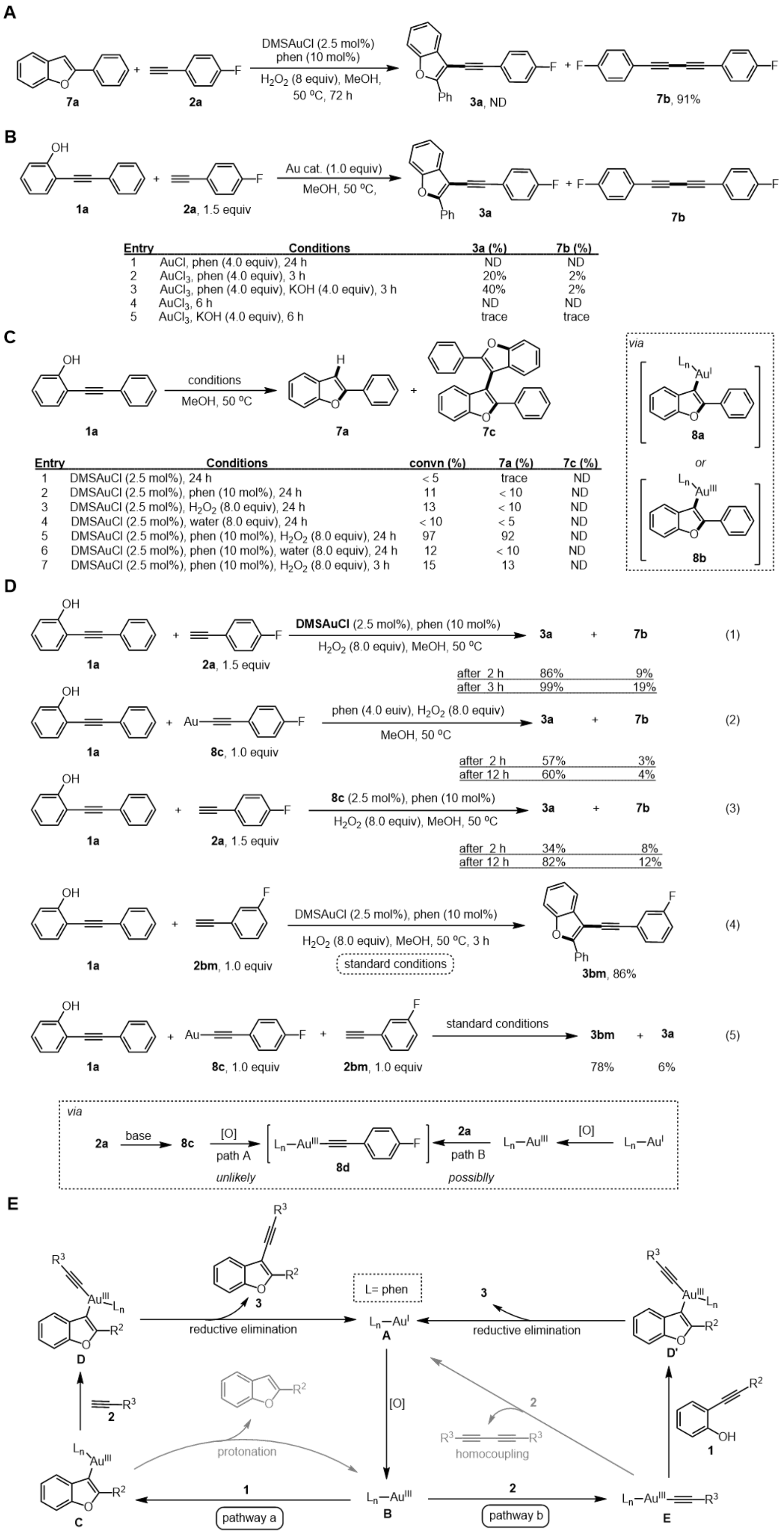
instead of AuCl, a 20% yield of product **3a** was detected (entry 2). Further addition of excess hydroxide ions via adding KOH, significantly improved the reaction performance, providing **3a** in a 40% yield (entry 3). Interestingly, without phen, no product was detected, and even with the addition of excess KOH formed only trace amounts of product (entries 4 and 5). These results suggest that the gold-catalyzed alkynylative cyclization reaction involves oxidation of Au^{I} to Au^{III} and a reductive elimination in the catalytic cycle. Additionally, the bidentate ligand phen plays a very important role in the oxidation of Au^{I} to Au^{III}.

Considering that the catalytic cycle presumably involves vinylgold(I)[3d,3e,5,9] or vinylgold(III)[3c,4a,10] intermediates, we next focused on the formation of the hydrogen-functionalized product **7a**. As shown in Scheme 3C, when DMSAuCl was added (without any ligand and/or additive), only traces of benzofuran **7a** were detected after stirring for 24 h. Interestingly, the addition of phen or H_2O_2, only led to a small amount of product (entries 2 and 3). Under standard conditions (in the absence of a terminal alkyne), the benzofuran **7a** was obtained in a yield of 92% after stirring for 24 h (entry 5). However, after the standard reaction time of 3 h only a small amount of product **7a** was obtained (entry 7). In addition, the replacement of H_2O_2 with H_2O was inefficient (entries 4 and 6). No dimerization product **7c** was detected under these conditions. These results suggest that the catalytic process rather proceeds through a vinylgold(III) intermediate, and the rate of protonation is presumably much slower than the rate of alkynylation.

Several examples of gold-catalyzed oxidative C–C(sp) couplings from terminal alkynes have been reported in the literature.[11] There are currently two acceptable mechanisms proposed. One is that the initial *in situ* generations of gold(I)-acetylide **8c** is followed by an oxidation step to form the gold(III)-acetylide intermediate **8d**. As an alternative, Au^{I} is directly oxidized to Au^{III} followed by alkynylation to give the same gold(III)-acetylide **8d**. Considering these two possible pathways, a set of control experiments was carried out (Scheme 3D). Equation 1 shows the experimental results under standard conditions. The stoichiometric reaction of gold(I)-acetylide **8c** (prepared from DMSAuCl and 1-ethynyl-4-fluorobenzene) with

2-(phenylethynyl)phenol **1a**, afforded the product **3a** in 57% yield after stirring for 2 h (equation 2). Even by prolonging the reaction time to 12 h, the yield of **3a** was not significantly improved. Interestingly, when using gold(I)-acetylide **8c** instead of DMSAuCl as the sole gold source, only a low reaction rate was observed after stirring for 2 h, well below the efficiency under standard conditions (equation 3). Furthermore, under standard conditions, the alkynylative cyclization product **3bm** was obtained in a 86% isolated yield, while the stoichiometric reaction of gold(I)-acetylide **8c** with 2-(phenylethynyl)phenol **1a** and 1-ethynyl-3-fluorobenzene **2bm**, delivered NMR yield in 78% for the product **3bm** and 6% for the product **3a** (equations 4 and 5). Based on the above results, and considering that no additional base was added in the catalytic system, the *in situ* generations of gold(I)-acetylide **8c** is unlikely (path A), and Au^{I} is presumably oxidized directly to Au^{III}, which affords vinylgold(III) or gold(III)-acetylide intermediates.

With these preliminary mechanistic investigations in mind, our proposed catalytic cycle is presented in Scheme 3E. Starting with L_nAu^{I} salt **A**, oxidation might occur at the stage of the Au^{I} salt, to afford L_nAu^{III} intermediate **B**. In pathway a, L_nAu^{III} **B** directly activates the alkynes of 2-alkynylphenols **1**, triggering intramolecular cyclization to provide vinylgold(III) intermediate **C**, followed by acetylide formation with alkyne **2** to afford the alkynylgold(III) complex **D**. Reductive elimination from intermediate **D**, would afford the alkynylation product **3** and regenerate the catalyst. As an alternative, L_nAu^{III} **B** favors forming the gold(III)-acetylide **E** first, followed by activation of the triple bond of 2-alkynylphenols **1** to give the common intermediate **D** (pathway b), which provides product **3** following reductive elimination.



B

Entry	Conditions	3a (%)	7b (%)
1	AuCl, phen (4.0 equiv), 24 h	ND	ND
2	$AuCl_3$, phen (4.0 equiv), 3 h	20%	2%
3	$AuCl_3$, phen (4.0 equiv), KOH (4.0 equiv), 3 h	40%	2%
4	$AuCl_3$, 6 h	ND	ND
5	$AuCl_3$, KOH (4.0 equiv), 6 h	trace	trace

C

Entry	Conditions	convn (%)	7a (%)	7c (%)
1	DMSAuCl (2.5 mol%), 24 h	< 5	trace	ND
2	DMSAuCl (2.5 mol%), phen (10 mol%), 24 h	11	< 10	ND
3	DMSAuCl (2.5 mol%), H_2O_2 (8.0 equiv), 24 h	13	< 10	ND
4	DMSAuCl (2.5 mol%), water (8.0 equiv), 24 h	< 10	< 5	ND
5	DMSAuCl (2.5 mol%), phen (10 mol%), H_2O_2 (8.0 equiv), 24 h	97	92	ND
6	DMSAuCl (2.5 mol%), phen (10 mol%), water (8.0 equiv), 24 h	12	< 10	ND
7	DMSAuCl (2.5 mol%), phen (10 mol%), H_2O_2 (8.0 equiv), 3 h	15	13	ND

D

(1)

	3a	7b
after 2 h	86%	9%
after 3 h	99%	19%

(2)

	3a	7b
after 2 h	57%	3%
after 12 h	60%	4%

(3)

	3a	7b
after 2 h	34%	8%
after 12 h	82%	12%

Scheme 3. Mechanistic investigation and proposal catalytic cycle.

Based on our findings we propose a possible reaction mechanism in Scheme 3E, which is in line with the thermodynamic data obtained by DFT calculations (Figure 1). The geometries of all possible intermediates were first optimized, followed by frequency analyses on a B3LYP[12]/def2-SVP[13] level of theory. For gold, additionally, the basis set def2-TZVP[13] was applied. Two potential pathways were considered, both beginning with a ligand replacement of dimethylsulfide by phen in DMSAuCl to form complex **I** in an exergonic reaction step (ΔG = -2.30 kcal/mol). Oxidation with H_2O_2 then yields the *cis*-bishydroxy Au^{III} complex **II** (ΔG = - 19.8 kcal/mol), which is thermodynamically more stable than the corresponding *trans*-complex (ΔG = -17.1 kcal/mol). In pathway a, first the ethynylphenol is deprotonated by one hydroxide ligand of **II**, which dissociates as water. Next, the deprotonated ethynylphenol π-coordinates to the free site *trans* to the phen ligand to furnish **IIIa** in an endergonic reaction step (ΔG = 1.64 kcal/mol). A barrier-free cyclization of **IIIa** (ΔG = - 41.9 kcal/mol) than delivers the *σ*-coordinated benzofuryl Au^{III} organyl species **IVa**. Next the exergonic formation of Au^{III} acetylide complex **Va (**ΔG = -5.61 kcal/mol) takes place, triggered by the deprotonation of phenylacetylene by the hydroxy ligand, which dissociates as water. At this stage, a three-membered transition state **TS-a** (ΔG = 15.3 kcal/mol) leads to the formation of a covalent bond between the former acetylide and the benzofuran unit to generate the final product **VI** (ΔG = - 52.6 kcal/mol) and regenerate the catalyst **I**. In the pathway b, the *cis*-bishydroxy Au^{III} complex **II** first deprotonates phenylacetylene, which yields a gold(III)-acetylide **IIIb** in an exergonic reaction step (ΔG = -6.01 kcal/mol). In analogy to pathway a, the second hydroxy ligand then triggers the formation of π-complex **IVb** (ΔG = - 6.66 kcal/mol), and a barrier-free cyclization of the ethynylphenol moiety then furnishes complex **Vb** (ΔG = - 33.1 kcal/mol). A related three-membered transition state **TS-b** (ΔG = 17.5 kcal/mol) then delivers the product and regenerates catalyst **I** via reductive elimination (ΔG = -54.9 kcal/mol). As a competing pathway, Au^{III} complex **IIIb** can also form bis-acetylide complex **IVc** (ΔG = -6.50 kcal/mol) in an exergonic reaction, instead of σ,π-complex **IVb**. Transition state **TS-c** (ΔG = 13.7 kcal/mol) then delivers homocoupling product **V** via reductive elimination (ΔG = -56.2 kcal/mol).

Indeed, this species was detected as a side product under some conditions (such as Scheme. 3d).

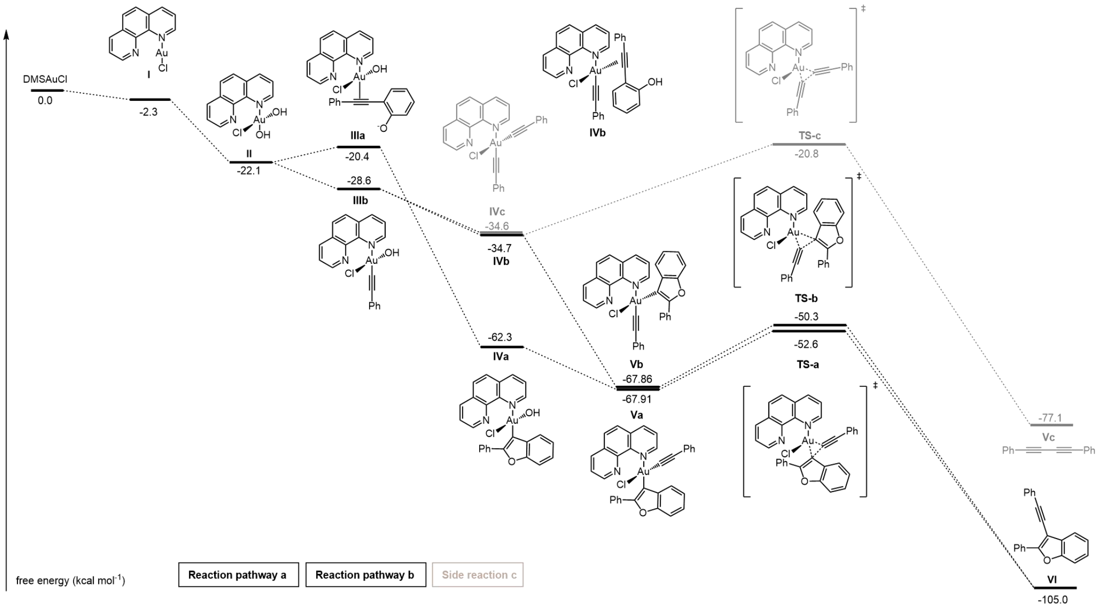


Figure 1. Calculated reaction pathways and energy landscape for gold-catalyzed alkynylative cyclization.

3.3 Conclusion

In conclusion, we develop the first example of using H_2O_2 as an oxidant to achieve a gold-catalyzed alkynylative cyclization with terminal alkynes. Through this method, an efficient synthesis of 3-alkynylbenzofurans from terminal alkynes was achieved. The reaction system exhibits the advantages of high atom economy, low-cost synthesis, mild reaction conditions, remarkable selectivity, wide substrate scope, and good functional group tolerance. Control experiments with other commonly used oxidants were not effective with revealed that this process is not only a more attractive substitute for common methodologies but instead offers a unique tool for gold catalysis. In addition, this method was not only limited to the synthesis of 3-alkynylbenzofurans it could also be applied to other forms of alkynylative cyclization reactions. We propose two possible reaction mechanisms based on mechanistic experiments, which are consistent with the results of DFT calculations. This reaction involves the Au^I/Au^{III} catalytic cycle, and 1,10-phenanthroline (phen) as a bidentate ligand is crucial for the catalytic cycle, since it shows a significant influence on the oxidation process of Au^{I} to Au^{III} and reductive eliminations of Au^{III} intermediates.

3.4 Experimental Section

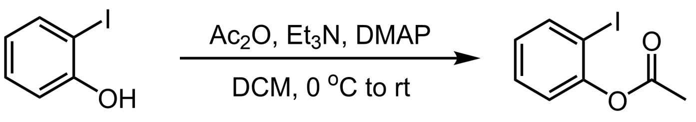
3.4.1 General Materials and Methods

Chemicals were purchased from commercial suppliers and used as delivered. Dry solvents were dispensed from the solvent purification system MB SPS-800. In our conditions, MeOH can be used directly without further drying and deoxygenation. Deuterated solvents were bought from Euriso-Top. Hydrogen peroxide solution (50 wt% in water, stabilized) was bought from Sigma-Aldrich. For reactions that require heating, the heat source: aluminum heating block (less than 0.5 mmol scale reactions), or oil bath (more than 0.5 mmol scale reactions). Unless otherwise stated, all reactions were carried out under an ambient atmosphere and monitored by thin layer chromatography (TLC). Components were visualized by fluorescence quenching under UV light (254 nm) or by treatment with aqueous potassium permanganate ($KMnO_4$) solution. ^{1}H, $^{13}C\{^{1}H\}$, ^{19}F NMR spectra were recorded on a Bruker Avance-III-300 (300 MHZ), Bruker Avance-III-400 (400 MHZ), or Bruker Avance-III-600 (600 MHZ) NMR spectrometer. Chemical shifts are expressed as parts per million (ppm, δ) downfield of tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.26 / 77.0 ppm) and DMSO-d_6 (2.50 / 39.5 ppm) as internal standards. Data is reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentalet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, dp = doublet of pentalets, td = triplet of doublets, qd = quartet of doublets, pd = pentalet of doublets, ddd = doublet of doublet of doublets, dtd = doublet of triplets of doublets, tdd = triplet of doublet of doublets; constants are absolute values and *J* values are expressed in Hertz (Hz). Mass spectra (MS and HRMS) were determined in the chemistry department of the University Heidelberg under the direction of Dr. J. Gross. For ESI (+) spectra, an ApexQe FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR (IF528), IR (283), or FT-IR Vektor 22. Melting points

(M.p.) were measured in open glass capillaries in a Büchi melting point apparatus. X-ray data were collected at a temperature of 200 K on the Bruker APEX-II Quazar area detector. For computational analysis, all geometry optimizations and subsequent frequency analyses were performed in the gas phase using Orca 5.0.1 on the bwForCluster JUSTUS2 on a B3LYP/def2-SVP level of theory. For gold, the def2-TZVP basis set was employed. Also, the RIJCOSX approximation and Grimme's DFT-D3 dispersion correction were used. Transition states were determined based on geometry optimizations of relaxed surface scans of initial geometries, their truthfulness was determined by subsequent frequency analysis.

3.4.2 General Procedure for 2-Alkynylphenols

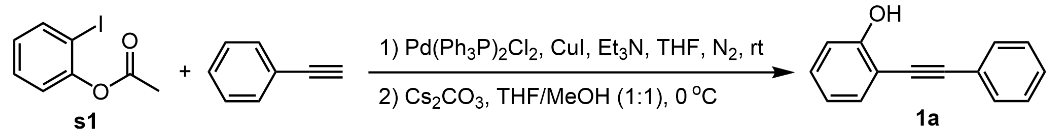
2-Iodophenyl acetate (s1)



s1

To a solvent of 2-iodophenol (11.0 g, 50 mmol, 1 equiv), triethylamine (Et_3N) (10.4 mL, 75 mmol, 1.5 equiv) and 4-dimethylaminopyridine (DMAP) (300 mg, 2.5 mmol, 0.05 equiv) in 100 mL DCM was added dropwise acetic anhydride (Ac_2O) (5.7 mL, 60 mmol, 1.2 equiv) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, 50 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 50 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-iodophenyl acetate **s1** as light yellow oil (12.8 g, 98%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.37 (ddd, *J* = 8.0, 7.5, 1.5 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.5 Hz, 1H), 6.98 (td, *J* = 7.8, 1.5 Hz, 1H), 2.37 (s, 3H). Characterization data of **s1** corresponded to the literature values.[14]

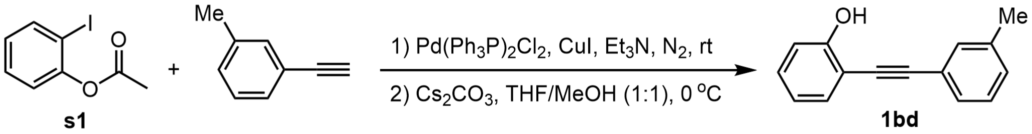
2-(Phenylethynyl)phenol (1a)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (13.1 g, 50 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (225 mg, 0.5 mol%) and CuI (190 mg, 2 mol%) in 60 mL dry THF were added phenylacetylene (6 mL, 55 mmol, 1.1 equiv) and Et_3N (27 mL, 200 mmol, 4 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air.. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 50 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 50 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(phenylethynyl)phenyl acetate **1a-1** as light yellow oil .

Step 2: To a solvent of 2-(phenylethynyl)phenyl acetate **1a-1** in 200 mL THF/MeOH (1:1) was added Cs_2CO_3 (17.8 g, 55 mmol, 1.1 equiv) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 50 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 50 mL DCM, the organic phases were combined, and concentrated in vacuo. Then 50 mL ethyl acetate was added and the mixture was washed with 25 mL sat. brine for two times, the aqueous phases were combined and extracted three times with 25 mL ethyl acetate, and the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was free from silica gel chromatography to give 2-(phenylethynyl)phenol **1a** as light yellow solid (8.68 g, 89% over 2 steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 2H), 7.44 (dd, J = 7.7, 1.6 Hz, 1H), 7.41 – 7.36 (m, 3H), 7.28 (ddd, J = 7.5, 4.9, 1.9 Hz, 1H), 7.00 (dd, J = 8.3, 0.8 Hz, 1H), 6.92 (td, J = 7.6, 1.1 Hz, 1H), 5.84 (s, 1H). Characterization data of **1a** corresponded to the literature values.[15]

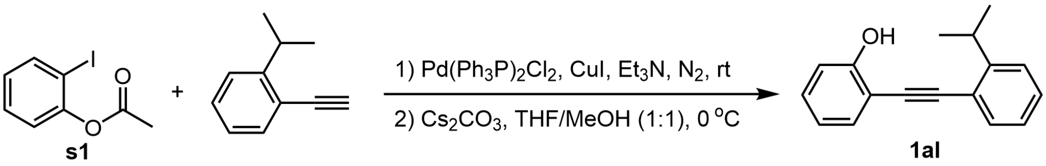
2-(3-Tolylethynyl)phenol (1bd)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (524.1 mg, 2 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 1 mol%) and CuI (7.6 mg, 2 mol%) in 4 mL Et_3N was added 1-ethynyl-3-methylbenzene (278.4 mg, 2.4 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (10:1) as eluting solvent to afford 2-(3-tolylethynyl)phenyl acetate **1bd-1** as light yellow oil .

Step 2: To a solvent of 2-(3-tolylethynyl)phenyl acetate **1bd-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.4 g, 4.2 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 40 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(3-tolylethynyl)phenol **1bd** as light yellow oil (394 mg, 95% over 2 steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.33 – 7.24 (m, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.02 (dd, *J* = 8.2, 0.5 Hz, 1H), 6.93 (td, *J* = 7.6, 1.1 Hz, 1H), 5.91 (br, 1H), 2.39 (s, 3H). Characterization data of **1bd** corresponded to the literature values.[16]

2-((2-Isopropylphenyl)ethynyl)phenol (1al)

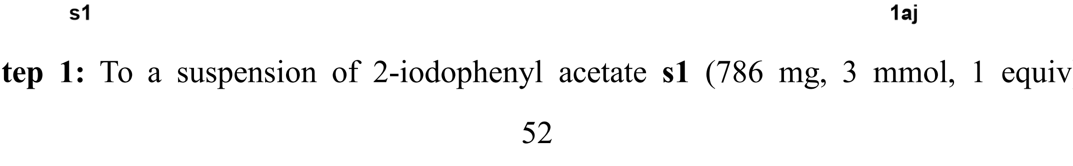


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv),

$(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 1-ethynyl-2-isopropylbenzene (475 mg, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (10:1) as eluting solvent to afford 2-((2-isopropylphenyl)ethynyl)phenyl acetate **1al-1** as light yellow oil .

Step 2: To a solvent of 2-((2-isopropylphenyl)ethynyl)phenyl acetate **1al-1** in 30 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol, 1.5 equiv) at 0 °C. The mixture was stirred at this temperature for 15 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 40 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((2-isopropylphenyl)ethynyl)phenol **1al** as light yellow oil (517 mg, 73% over 2 steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.54 (d, J = 7.4 Hz, 1H), 7.45 (dd, J = 7.7, 1.1 Hz, 1H), 7.41 – 7.32 (m, 2H), 7.32 – 7.25 (m, 1H), 7.25 – 7.17 (m, 1H), 7.01 (d, J = 8.3 Hz, 1H), 6.94 (dd, J = 11.6, 4.1 Hz, 1H), 5.86 (s, 1H), 3.52 (dt, J = 13.8, 6.9 Hz, 1H), 1.34 (d, J = 6.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.4, 150.3, 132.4, 131.5, 130.4, 129.2, 125.7, 125.1, 121.1, 120.4, 114.7, 109.9, 95.2, 86.6, 31.9, 23.1. **HRMS** (EI) calcd for $C_{17}H_{16}O$ $[M]^+$: 236.11957, found: 236.11939. **IR** (Reflection): ṽ = 3516, 3062, 2962, 2869, 1613, 1574, 1491, 1479, 1461, 1445, 1384, 1362, 1344, 1289, 1238, 1193, 1094, 1078, 1031, 939, 865, 807, 753.

2-(4-Tolylethynyl)phenol (1aj)

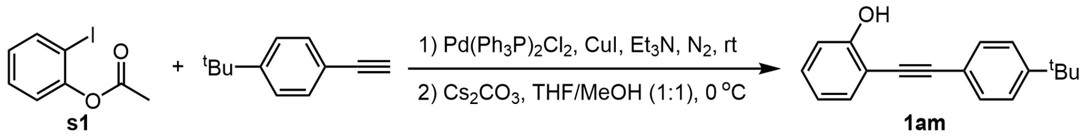


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv),

$(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 1-ethynyl-4-methylbenzene (383 mg, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(4-tolylethynyl)phenyl acetate **1aj-1** as light yellow oil .

Step 2: To a solvent of 2-(4-tolylethynyl)phenyl acetate **1aj-1** in 30 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol, 1.5 equiv) at 0 °C. The mixture was stirred at this temperature for 15 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 40 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(4-tolylethynyl)phenol **1aj** as light yellow oil (315 mg, 50% over 2 steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42 (dd, J = 10.6, 4.7 Hz, 3H), 7.31 – 7.23 (m, 1H), 7.19 (d, J = 7.9 Hz, 2H), 6.99 (d, J = 7.7 Hz, 1H), 6.91 (td, J = 7.6, 1.0 Hz, 1H), 5.85 (s, 1H), 2.39 (s, 3H). Characterization data of **1aj** corresponded to the literature values.[17]

2-((4-(*tert*-Butyl)phenyl)ethynyl)phenol (1am)

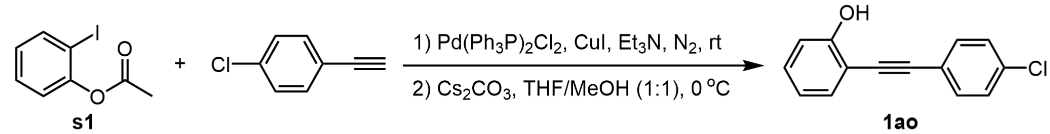


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 1-(*tert*-butyl)-4-ethynylbenzene (600 μL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase

was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((4-(*tert*-butyl)phenyl)ethynyl)phenyl acetate **1am-1** as light yellow oil .

Step 2: To a solvent of 2-((4-(*tert*-butyl)phenyl)ethynyl)phenyl acetate **1am-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 10 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((4-(*tert*-butyl)phenyl)ethynyl)phenol **1am** as dark yellow oil (516 mg, 69% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 (d, J = 8.4 Hz, 2H), 7.30 (dd, J = 12.7, 4.7 Hz, 3H), 7.15 (dd, J = 11.2, 4.2 Hz, 1H), 6.87 (d, J = 8.2 Hz, 1H), 6.79 (t, J = 7.5 Hz, 1H), 5.79 (s, 1H), 1.22 (s, 9H). Characterization data of **1am** corresponded to the literature values.[18]

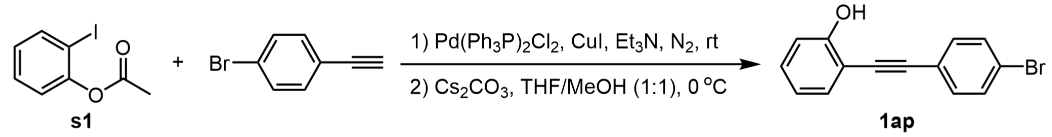
2-((4-Chlorophenyl)ethynyl)phenol (1ao)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 1-chloro-4-ethynylbenzene (450 mg, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((4-chlorophenyl)ethynyl)phenyl acetate **1ao-1** as light yellow oil .

Step 2: To a solvent of 2-((4-chlorophenyl)ethynyl)phenyl acetate **1ao-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 10 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((4-chlorophenyl)ethynyl)phenol **1ao** as light yellow solid (566 mg, 86% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.44 (ddd, *J* = 31.7, 19.8, 7.5 Hz, 7H), 7.02 (dd, *J* = 16.6, 7.5 Hz, 2H), 5.83 (s, 1H). Characterization data of **1ao** corresponded to the literature values.[14]

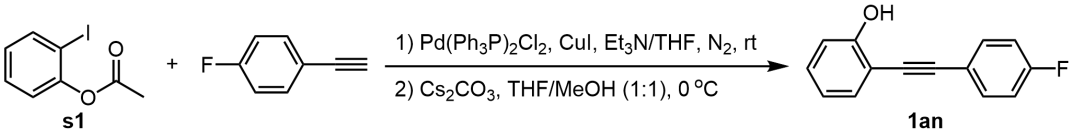
2-((4-Bromophenyl)ethynyl)phenol (1ap)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (524.1 mg, 2 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 1 mol%) and CuI (7.6 mg, 2 mol%) in 5 mL Et_3N was added 1-bromo-4-ethynylbenzene (434.4 mg, 2.4 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-((4-bromophenyl)ethynyl)phenyl acetate **1ap-1** as light yellow oil (412 mg, 66%).

Step 2: To a solvent of 2-((4-bromophenyl)ethynyl)phenyl acetate **1ap-1** (314 mg, 1 mmol) in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (652 mg, 2 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 10 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-((4-bromophenyl)ethynyl)phenol **1ap** as light yellow solid (267 mg, 98%). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.41 (dd, *J* = 7.0, 5.0 Hz, 3H), 7.34 – 7.20 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 5.76 (s, 1H). Characterization data of **1ap** corresponded to the literature values.[19]

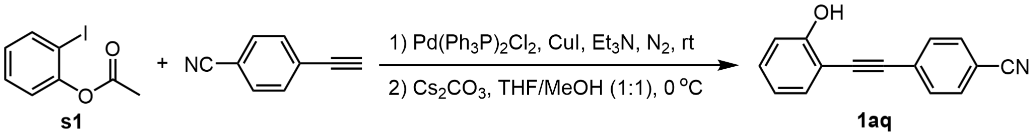
2-((4-Fluorophenyl)ethynyl)phenol (1an)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (1.31 g, 5 mmol, 1 equiv), (Ph$_3$P)$_2$PdCl$_2$ (35 mg, 1 mol%) and CuI (19 mg, 2 mol%) in 25 mL Et$_3$N/THF (1:1) was added 1-ethynyl-4-fluorobenzene (584 μL, 6 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N$_2$ for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 30 mL saturated NH$_4$Cl was added and the aqueous phase was extracted three times with 30 mL DCM, the organic phases were combined, dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-((4-fluorophenyl)ethynyl)phenyl acetate **1an-1** as light yellow oil .

Step 2: To a solvent of 2-((4-fluorophenyl)ethynyl)phenyl acetate **1an-1** in 40 mL THF/MeOH (1:1) was added Cs$_2$CO$_3$ (3.26 g, 10 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 40 mL saturated NH$_4$Cl was added, and the aqueous phase was extracted three times with 40 mL DCM, the organic phases were combined, dried over Na$_2$SO$_4$, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-((4-fluorophenyl)ethynyl)phenol **1an** as light yellow solid (784 mg, 74% over two steps). **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.53 (dd, *J* = 8.0, 5.6 Hz, 2H), 7.42 (d, *J* = 7.4 Hz, 1H), 7.28 (dd, *J* = 11.2, 3.8 Hz, 1H), 7.08 (t, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.92 (t, *J* = 7.4 Hz, 1H), 5.82 (s, 1H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -109.85. Characterization data of **1an** corresponded to the literature values.[20]

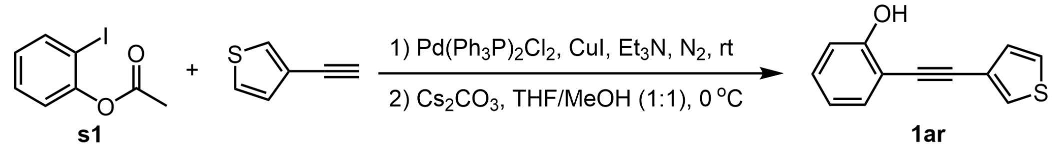
4-((2-Hydroxyphenyl)ethynyl)benzonitrile (1aq)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (21 mg, 1 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 4-ethynylbenzonitrile (419.1 mg, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (8:1) as eluting solvent to afford 2-((4-cyanophenyl)ethynyl)phenyl acetate **1aq-1** as light yellow oil .

Step 2: To a solvent of 2-((4-cyanophenyl)ethynyl)phenyl acetate **1aq-1** in 40 mL THF/MeOH (1:1) was added Cs_2CO_3 (652 mg, 2 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (8:1) as eluting solvent to afford 4-((2-hydroxyphenyl)ethynyl)benzonitrile **1aq** as yellow solid (495 mg, 75% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.62 (s, 4H), 7.43 (d, *J* = 6.9 Hz, 1H), 7.30 (d, *J* = 7.0 Hz, 1H), 7.08 – 6.82 (m, 2H), 5.82 (s, 1H). Characterization data of **1aq** corresponded to the literature values.[21]

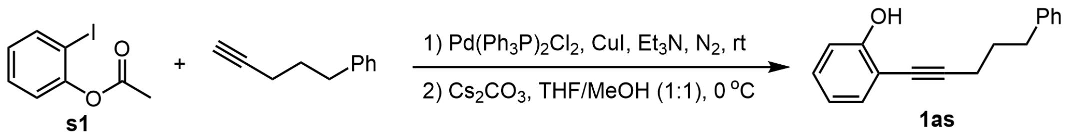
2-(Thiophen-3-ylethynyl)phenol (1ar)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (524 mg, 2 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (7.0 mg, 0.5 mol%) and CuI (7.6 mg, 2 mol%) in 4 mL Et_3N was added 3-ethynylthiophene (217 µL, 2.2 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(thiophen-3-ylethynyl)phenyl acetate **1ar-1** as light yellow oil .

Step 2: To a solvent of 2-(thiophen-3-ylethynyl)phenyl acetate **1ar-1** in 16 mL THF/MeOH (1:1) was added Cs_2CO_3 (978 mg, 3 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 10 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(thiophen-3-ylethynyl)phenol **1ar** as light yellow solid (357 mg, 89% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.41 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.34 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.31 – 7.23 (m, 1H), 7.21 (dd, *J* = 5.0, 1.1 Hz, 1H), 6.98 (dd, *J* = 8.3, 0.7 Hz, 1H), 6.91 (td, *J* = 7.6, 1.1 Hz, 1H), 5.80 (s, 1H). Characterization data of **1ar** corresponded to the literature values.[22]

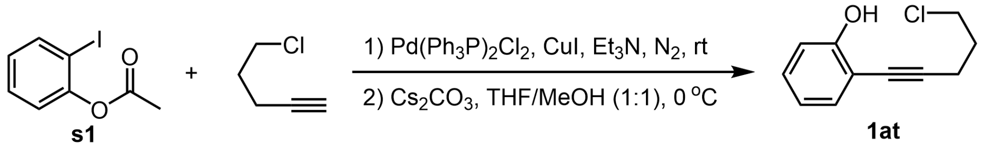
2-(5-Phenylpent-1-yn-1-yl)phenol (1as)



Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added pent-4-yn-1-ylbenzene (501 μL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(5-phenylpent-1-yn-1-yl)phenyl acetate **1as-1** as light yellow oil .

Step 2: To a solvent of 2-(5-phenylpent-1-yn-1-yl)phenyl acetate **1as-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(5-phenylpent-1-yn-1-yl)phenol **1as** as light yellow oil (585 mg, 83% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.33 – 7.23 (m, 3H), 7.22 – 7.12 (m, 4H), 6.91 (dd, *J* = 8.2, 0.8 Hz, 1H), 6.82 (td, *J* = 7.5, 1.1 Hz, 1H), 5.77 (s, 1H), 2.75 (t, *J* = 7.5 Hz, 2H), 2.45 (t, *J* = 7.1 Hz, 2H), 1.98 – 1.87 (m, 2H). Characterization data of **1as** corresponded to the literature values.[23]

2-(5-Chloropent-1-yn-1-yl)phenol (1at)

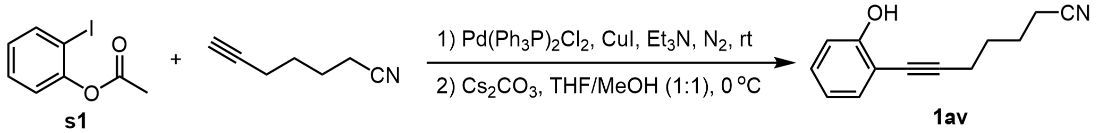


Step 1: To a suspension of 2-iodophenyl acetate **s1** (524 mg, 2 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 1 mol%) and CuI (7.6 mg, 2 mol%) in 5 mL Et_3N was added 5-chloropent-1-yne (254 μL, 2.4 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture

was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(5-chloropent-1-yn-1-yl)phenyl acetate **1at-1** as light yellow oil (473 mg, 100%).

Step 2: To a solvent of 2-(5-chloropent-1-yn-1-yl)phenyl acetate **1at-1** (473 mg, 2 mmol) in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.4 g, 4.2 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(5-chloropent-1-yn-1-yl)phenoll **1at** as light yellow solid (365.5 mg, 94%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.26 – 7.15 (m, 1H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 5.78 (s, 1H), 3.72 (t, *J* = 6.2 Hz, 2H), 2.70 (t, *J* = 6.9 Hz, 2H), 2.09 (p, *J* = 6.6 Hz, 2H). Characterization data of **1at** corresponded to the literature values.[23]

7-(2-Hydroxyphenyl)hept-6-ynenitrile (1av)

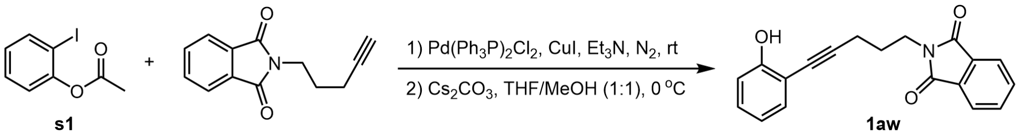


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added hept-6-ynenitrile (400 μL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel

chromatography with PE/EA (2:1) as eluting solvent to afford 2-(6-cyanohex-1-yn-1-yl)phenyl acetate **1av-1** as light yellow oil .

Step 2: To a solvent of 2-(6-cyanohex-1-yn-1-yl)phenyl acetate **1av-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (2:1) as eluting solvent to afford 7-(2-hydroxyphenyl)hept-6-ynenitrile **1av** as light yellow solid (388 mg, 65% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.29 (dd, J = 7.7, 1.3 Hz, 1H), 7.25 – 7.18 (m, 1H), 6.93 (d, J = 8.2 Hz, 1H), 6.85 (t, J = 7.5 Hz, 1H), 5.72 (s, 1H), 2.57 (t, J = 6.4 Hz, 2H), 2.43 (t, J = 6.6 Hz, 2H), 1.93 – 1.75 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.5, 131.6, 129.9, 120.3, 119.3, 114.5, 109.7, 95.9, 75.7, 27.5, 24.5, 18.9, 16.9. **HRMS** (EI) calcd for $C_{13}H_{13}NO$ $[M]^+$: 199.09917, found: 199.09890. **IR** (ATR): ṽ = 3303, 2944, 2874, 2259, 1910, 1732, 1602, 1588, 1506, 1461, 1448, 1417, 1372, 1347, 1289, 1258, 1227, 1197, 1160, 1107, 1040, 1012, 977, 937, 921, 830, 759, 737, 683. **M.p.** (amorphous): 67.7-69.8 °C.

2-(5-(2-Hydroxyphenyl)pent-4-yn-1-yl)isoindoline-1,3-dione (1aw)

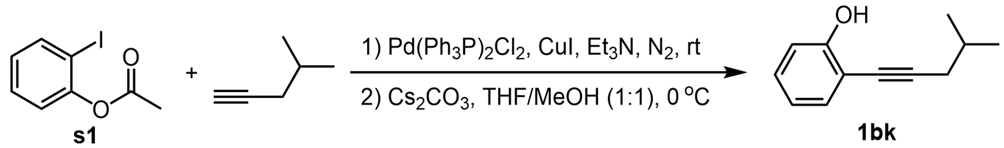


Step 1: To a suspension of 2-iodophenyl acetate **s1** (524 mg, 2 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (14 mg, 1 mol%) and CuI (7.6 mg, 2 mol%) in 5 mL Et_3N was added 2-(pent-4-yn-1-yl)isoindoline-1,3-dione (512 mg, 2.4 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by

silica gel chromatography with PE/EA (5:1) as eluting solvent to afford 2-(5-(1,3-dioxoisoindolin-2-yl)pent-1-yn-1-yl)phenyl acetate **1aw-1** as light yellow oil .

Step 2: To a solvent of 2-(5-(1,3-dioxoisoindolin-2-yl)pent-1-yn-1-yl)phenyl acetate **1aw-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.4 g, 4.2 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(5-(2-hydroxyphenyl)pent-4-yn-1-yl)isoindoline-1,3-dione **1aw** as colorless solid (357 mg, 58% over two steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.0 Hz, 2H), 7.20 (ddd, *J* = 13.9, 7.6, 1.5 Hz, 2H), 6.95 (dd, *J* = 8.1, 0.5 Hz, 1H), 6.86 (s, 1H), 6.80 (td, *J* = 7.5, 1.0 Hz, 1H), 3.99 – 3.91 (m, 2H), 2.50 (t, *J* = 6.5 Hz, 2H), 2.04 – 1.96 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.6, 157.4, 134.1, 131.8, 131.4, 129.7, 123.4, 119.8, 114.9, 109.8, 95.3, 76.2, 36.4, 26.9, 16.8. **HRMS** (EI) calcd for $C_{19}H_{15}NO_3$ $[M]^+$: 305.10464, found: 305.10460. **IR** (Reflection): ṽ = 3427, 2945, 2897, 2836, 1770, 1758, 1694, 1612, 1573, 1488, 1459, 1429, 1401, 1373, 1327, 1293, 1234, 1209, 1166, 1111, 1032, 882, 829, 798, 763, 725, 715, 694, 621. **M.p.** (amorphous): 125.8-127.5 °C.

2-(4-Methylpent-1-yn-1-yl)phenol (1bk)

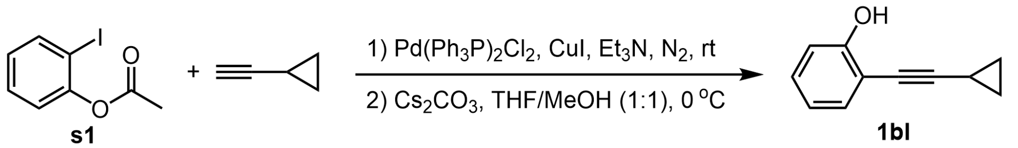


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added 4-methylpent-1-yne (388 µL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted

three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(4-methylpent-1-yn-1-yl)phenyl acetate **1bk-1** as light yellow oil .

Step 2: To a solvent of 2-(4-methylpent-1-yn-1-yl)phenyl acetate **1bk-1** (3 mmol) in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-(4-methylpent-1-yn-1-yl)phenol **1bk** as light yellow oil (382 mg, 73% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.25 – 7.16 (m, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.85 (td, *J* = 7.6, 0.9 Hz, 1H), 5.80 (s, 1H), 2.38 (d, *J* = 6.5 Hz, 2H), 1.94 (dp, *J* = 13.2, 6.6 Hz, 1H), 1.06 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.50, 131.43, 129.56, 120.14, 114.26, 110.26, 96.88, 77.00, 75.38, 28.72, 28.12, 22.03. **HRMS** (EI) calcd for $C_{12}H_{14}O$ $[M]^+$: 174.10392, found: 174.10318. **IR** (Reflection): ṽ = 3506, 3045, 2959, 2927, 2870, 2226, 1614, 1577, 1487, 1463, 1426, 1385, 1368, 1346, 1288, 1237, 1207, 1181, 1152, 1103, 1032, 937, 827, 752, 699.

2-(Cyclopropylethynyl)phenol (1bl)

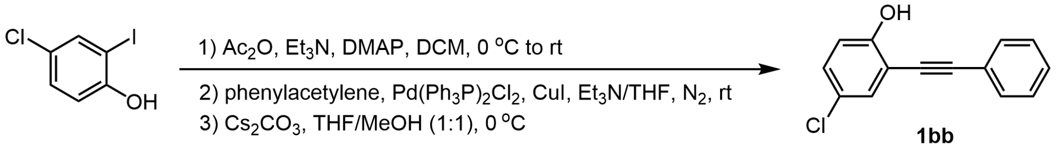


Step 1: To a suspension of 2-iodophenyl acetate **s1** (786 mg, 3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N was added ethynylcyclopropane (280 µL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 20 mL saturated NH_4Cl was added and the aqueous phase was extracted

three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(cyclopropylethynyl)phenyl acetate **1bl-1** as light yellow oil .

Step 2: To a solvent of 2-(cyclopropylethynyl)phenyl acetate **1bl-1** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.3 g, 4.5 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-(cyclopropylethynyl)phenol **1bl** as light yellow oil (339 mg, 71% over two steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.23 – 7.11 (m, 1H), 6.92 (dd, *J* = 8.2, 0.7 Hz, 1H), 6.82 (td, *J* = 7.6, 1.1 Hz, 1H), 5.80 (s, 1H), 1.51 (tt, *J* = 8.2, 5.1 Hz, 1H), 0.97 – 0.88 (m, 2H), 0.84 (ddd, *J* = 7.7, 5.4, 2.5 Hz, 2H). Characterization data of **1bl** corresponded to the literature values.[24]

4-Chloro-2-(phenylethynyl)phenol (1bb)

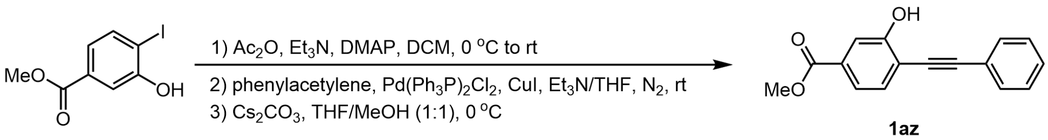


Step 1: To a solvent of 4-chloro-2-iodophenol (763 mg, 3 mmol, 1 equiv), Et_3N (0.62 mL, 4.5 mmol, 1.5 equiv) and DMAP (18.3 mg, 0.15 mmol, 0.05 equiv) in 6 mL DCM was added dropwise Ac_2O (0.34 mL, 3.6 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 4-chloro-2-iodophenyl acetate **1bb-1** as light yellow oil .

Step 2: To a suspension of 4-chloro-2-iodophenyl acetate **1bb-1**, $(Ph_3P)_2PdCl_2$ (21 mg, 1 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N/THF (1:1) was added phenylacetylene (0.39 mL, 3.6 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 4-chloro-2-(phenylethynyl)phenyl acetate **1bb-2** as light yellow oil .

Step 3: To a solvent of 4-chloro-2-(phenylethynyl)phenyl acetate **1bb-2** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.0 g, 3.3 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 4-chloro-2-(phenylethynyl)phenol **1bb** as light yellow solid (567 mg, 83% over three steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.66 – 7.48 (m, 2H), 7.40 (d, *J* = 1.5 Hz, 4H), 7.22 (dd, *J* = 8.7, 2.2 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 1H), 5.81 (s, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.1, 131.7, 130.9, 130.4, 129.2, 128.5, 125.1, 121.8, 116.0, 111.0, 97.3, 81.8. Characterization data of **1bb** corresponded to the literature values.[16]

Methyl 3-hydroxy-4-(phenylethynyl)benzoate (1az)



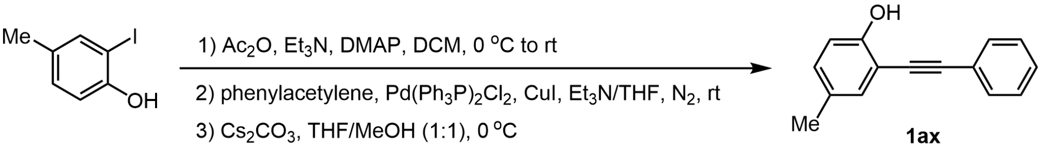
1az

Step 1: To a solvent of methyl 3-hydroxy-4-iodobenzoate (834 mg, 3 mmol, 1 equiv), Et_3N (0.62 mL, 4.5 mmol, 1.5 equiv) and DMAP (18.3 mg, 0.15 mmol, 0.05 equiv) in 6 mL DCM was added dropwise Ac_2O (0.34 mL, 3.6 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (8:1) as eluting solvent to afford methyl 3-acetoxy-4-iodobenzoate **1az-1** as light yellow oil .

Step 2: To a suspension of methyl 3-acetoxy-4-iodobenzoate **1az-1** (3 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (21 mg, 1 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N/THF (1:1) was added phenylacetylene (0.39 mL, 3.6 mmol, 1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (8:1) as eluting solvent to afford methyl 3-acetoxy-4-(phenylethynyl)benzoate **1az-2** as light yellow oil .

Step 3: To a solvent of methyl 3-acetoxy-4-(phenylethynyl)benzoate **1az-2** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1 g, 3.3 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford methyl 3-hydroxy-4-(phenylethynyl)benzoate **1az** as light yellow solid (643 mg, 85% over three steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.65 (d, J = 1.4 Hz, 1H), 7.62 – 7.52 (m, 3H), 7.48 (d, J = 8.0 Hz, 1H), 7.39 (dd, J = 5.1, 1.8 Hz, 3H), 5.95 (s, 1H), 3.92 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.3, 156.3, 131.72, 131.70, 131.6, 129.3, 128.6, 121.8, 121.5, 115.8, 114.2, 98.7, 82.5, 52.3. Characterization data of **1az** corresponded to the literature values.[3c]

4-Methyl-2-(phenylethynyl)phenol (1ax)



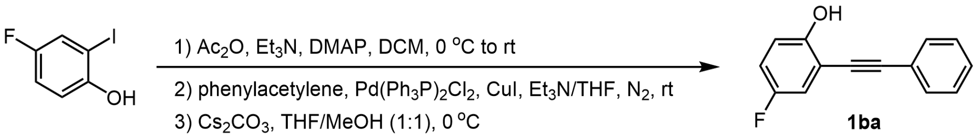
Step 1: To a solvent of 4-chloro-2-iodophenol (702 mg, 3 mmol, 1 equiv), Et_3N (0.62 mL, 4.5 mmol, 1.5 equiv) and DMAP (18.3 mg, 0.15 mmol, 0.05 equiv) in 6 mL DCM was added dropwise Ac_2O (0.34 mL, 3.6 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (15:1) as eluting solvent to afford 2-iodo-4-methylphenyl acetate **1ax-1** as light yellow oil .

Step 2: To a suspension of 2-iodo-4-methylphenyl acetate **1ax-1**, $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N/THF (1:1) was added phenylacetylene (0.36 mL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 4-methyl-2-(phenylethynyl)phenyl acetate **1ax-2** as light yellow oil .

Step 3: To a solvent of 4-methyl-2-(phenylethynyl)phenyl acetate **1ax-2** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.0 g, 3.3 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford

4-methyl-2-(phenylethynyl)phenol **1ax** as light yellow solid (583 mg, 93% over three steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 10.6, 4.7 Hz, 2H), 7.31 – 7.23 (m, 3H), 7.19 (d, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 7.7 Hz, 1H), 6.91 (td, *J* = 7.6, 1.0 Hz, 1H), 5.85 (s, 1H), 2.39 (s, 3H). Characterization data of **1ax** corresponded to the literature values.[19]

4-Fluoro-2-(phenylethynyl)phenol (1ba)

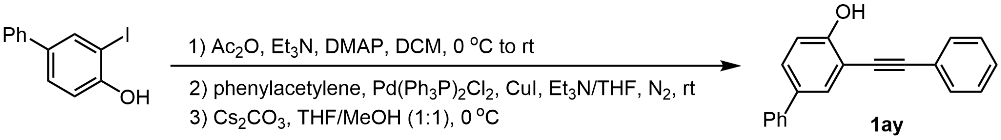


Step 1: To a solvent of 4-fluoro-2-iodophenol (476 mg, 2 mmol, 1 equiv), Et_3N (0.41 mL, 3 mmol, 1.5 equiv) and DMAP (12.2 mg, 0.1 mmol, 0.05 equiv) in 4 mL DCM was added dropwise Ac_2O (0.23 mL, 2.4 mmol, 1.2 equiv) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, products were detected by TLC. 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 4-fluoro-2-iodophenyl acetate **1ba-1** as light yellow oil .

Step 2: To a suspension of 4-fluoro-2-iodophenyl acetate **1ba-1**, $(Ph_3P)_2PdCl_2$ (7.0 mg, 0.5 mol%) and CuI (7.6 mg, 2 mol%) in 4 mL Et_3N/THF (1:1) was added phenylacetylene (0.24 mL, 2.2 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 10 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 10 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 4-fluoro-2-(phenylethynyl)phenyl acetate **1ba-2** as light yellow oil .

Step 3: To a solvent of 4-fluoro-2-(phenylethynyl)phenyl acetate **1ba-2** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (978 mg, 3 mmol) at 0 °C. The mixture was stirred at this temperature for 10 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 4-fluoro-2-(phenylethynyl)phenol **1ba** as light yellow solid (358 mg, 84% over three steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 (dd, J = 6.6, 3.0 Hz, 2H), 7.40 – 7.38 (m, 3H), 7.12 (dd, J = 8.5, 2.9 Hz, 1H), 7.04 – 6.85 (m, 2H), 5.68 (s, 1H). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -123.83. Characterization data of **1ba** corresponded to the literature values.[19]

3-(Phenylethynyl)-[1,1'-biphenyl]-4-ol (1ay)

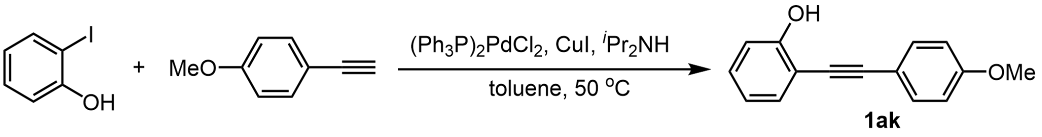


Step 1: To a solvent of 3-iodo-[1,1'-biphenyl]-4-ol (885 mg, 3 mmol, 1 equiv), triethylamine (0.62 mL, 4.5 mmol, 1.5 equiv) and DMAP (4-dimethylaminopyridine) (18.3 mg, 0.15 mmol, 0.05 equiv) in 6 mL DCM was added dropwise Ac_2O (0.34 mL, 3.6 mmol, 1.2 equiv) at 0 °C. The mixture was stirred at this temperature for 30 min and then warmed up to room temperature and stirred overnight. After completion of the reaction, products were detected by TLC. 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 3-iodo-[1,1'-biphenyl]-4-yl acetate **1ay-1** as light yellow oil .

Step 2: To a suspension of 3-iodo-[1,1'-biphenyl]-4-yl acetate **1ay-1**, $(Ph_3P)_2PdCl_2$ (10.5 mg, 0.5 mol%) and CuI (11.4 mg, 2 mol%) in 6 mL Et_3N/THF (1:1) was added phenylacetylene (0.36 mL, 3.3 mmol, 1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, 15 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 15 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 3-(phenylethynyl)-[1,1'-biphenyl]-4-yl acetate **1ay-2** as light yellow oil .

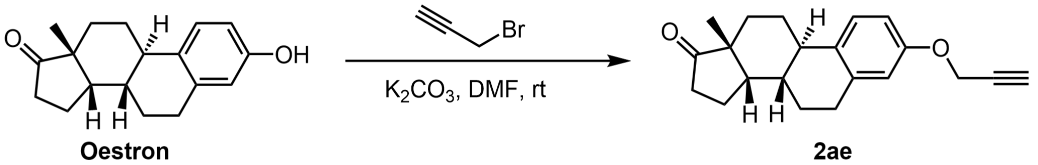
Step 3: To a solvent of 3-(phenylethynyl)-[1,1'-biphenyl]-4-yl acetate **1ay-2** in 20 mL THF/MeOH (1:1) was added Cs_2CO_3 (1.0 g, 3.3 mmol) at 0 °C. The mixture was stirred at this temperature for 30 min. After completion of the reaction, 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL DCM, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 3-(phenylethynyl)-[1,1'-biphenyl]-4-ol **1ay** as light yellow solid (590 mg, 73% over three steps). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.68 (d, J = 2.2 Hz, 1H), 7.62 – 7.48 (m, 5H), 7.47 – 7.37 (m, 5H), 7.33 (t, J = 7.3 Hz, 1H), 7.06 (d, J = 8.5 Hz, 1H), 5.86 (s, 1H). Characterization data of **1ay** corresponded to the literature values.[18]

2-((4-Methoxyphenyl)ethynyl)phenol (1ak)



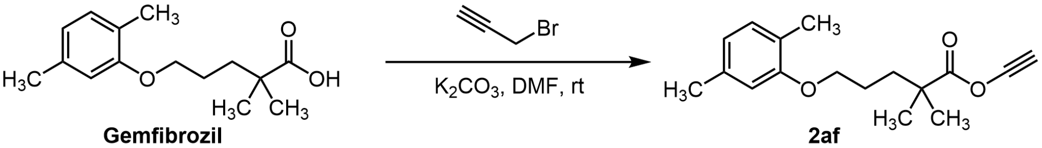
To a suspension of 2-iodophenol **s1** (3.85 g, 17.5 mmol, 1 equiv), $(Ph_3P)_2PdCl_2$ (306 mg, 2.5 mol%) and CuI (166 mg, 5 mol%) in 40 mL toluene were added 1-ethynyl-4-methoxybenzene (2.5 mL, 19.25 mmol, 1.1 equiv) and diisopropylamine (2.45 mL, 17.5 mmol, 1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 50 °C for 2 h. After completion of the reaction, 40 mL saturated NH_4Cl was added and the aqueous phase was extracted three times with 40 mL ethyl acetate, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford 2-((4-methoxyphenyl)ethynyl)phenol **1ak** as a brown solid (3.08 g, 79%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 – 7.45 (m, 2H), 7.40 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.30 – 7.19 (m, 1H), 6.98 (dd, *J* = 8.3, 0.8 Hz, 1H), 6.94 – 6.86 (m, 3H), 5.84 (br, 1H), 3.84 (s, 3H). Characterization data of **1ak** corresponded to the literature values.[25]

(*8S,9R,13R,14S*)-13-Methyl-3-(prop-2-yn-1-yloxy)-6,7,8,9,11,12,13,14,15,16-decahydro-*17H*-cyclopenta[*a*]phenanthren-17-one (2ae)



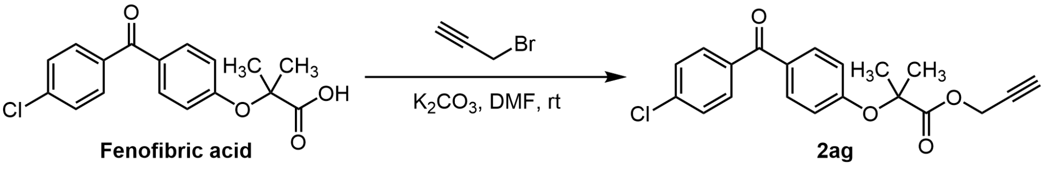
In a 25-mL flask, 3-bromopropyne (0.17 mL, 1.5 mmol, 1.5 equiv, 80 wt% in toluene) was added to a solution of Oestrone (270.4 mg, 1 mmol, 1 equiv) and K_2CO_3 (552 mg, 4 mmol, 4 equiv) in DMF (10 mL) at room temperature. The mixture was stirred at room temperature overnight. Then the reaction was diluted with 30 mL ethyl acetate and washed three times with 30 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EA (8:1) as eluting solvent to afford target product **2ae** as colorless oil (252.0 mg, 82%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 1H), 6.79 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 4.66 (d, *J* = 2.4 Hz, 2H), 2.91 – 2.88 (m, 2H), 2.55 – 2.38 (m, 3H), 2.33 – 2.20 (m, 1H), 2.19 – 1.89 (m, 3H), 1.70 – 1.34 (m, 6H), 0.91 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.8, 155.5, 137.8, 133.0, 126.3, 114.9, 112.3, 78.8, 75.3, 55.7, 50.4, 48.0, 44.0, 38.3, 35.8, 31.6, 29.6, 26.5, 25.9, 21.6, 13.8. **HRMS** (EI) calcd for $C_{21}H_{14}O_2$ $[M]^+$: 308.17708, found: 308.17775. **IR** (Reflection): ṽ =3309, 2944, 2863, 2131, 1731, 1463, 1386, 1363, 1253, 1232, 1205, 1156, 1121, 1085, 1032, 995, 815, 755, 678, 638. **M.p.** (amorphous): 147.8-148.4 °C.

Prop-2-yn-1-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (2af)



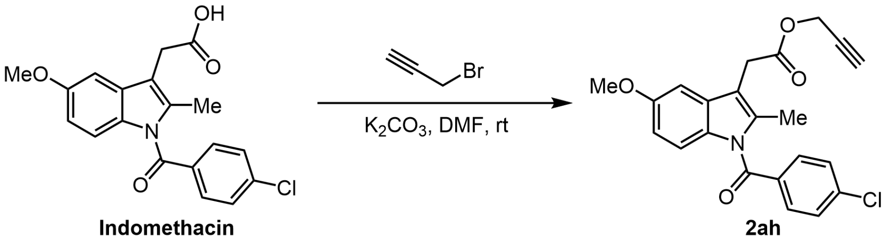
In a 10 mL flask, 3-bromopropyne (0.17 mL, 1.5 mmol, 1.5 equiv, 80 wt% in toluene) was added to a solution of Gemfibrozil (250.3 mg, 1 mmol, 1 equiv) and K_2CO_3 (552 mg, 4 mmol, 4 equiv) in DMF (5 mL) at room temperature. The mixture was stirred at room temperature for 3 h. Then the reaction was diluted with 15 mL ethyl acetate and washed three times with 15 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EA (20:1) as eluting solvent to afford target product **2af** as colorless oil (285.2 mg, 99%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.01 (d, *J* = 7.4 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.62 (s, 1H), 4.68 (d, *J* = 2.4 Hz, 2H), 3.93 (d, *J* = 3.0 Hz, 2H), 2.44 (t, *J* = 2.4 Hz, 1H), 2.32 (s, 3H), 2.19 (s, 3H), 1.77 – 1.76 (m, 4H), 1.26 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 176.9, 156.9, 136.4, 130.3, 123.6, 120.7, 111.9, 77.9, 74.5, 67.8, 51.9, 42.1, 37.0, 25.1, 25.0, 21.4, 15.7. **HRMS** (EI) calcd for $C_{18}H_{24}O_3$ $[M]^+$: 288.17200, found: 288.17283. **IR** (Reflection): ṽ = 3290, 2950, 2924, 2871, 2128, 1731, 1613, 1584, 1508, 1472, 1453, 1413, 1390, 1310, 1261, 1187, 1125, 1045, 991, 843, 802, 634.

Prop-2-yn-1-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (2ag)



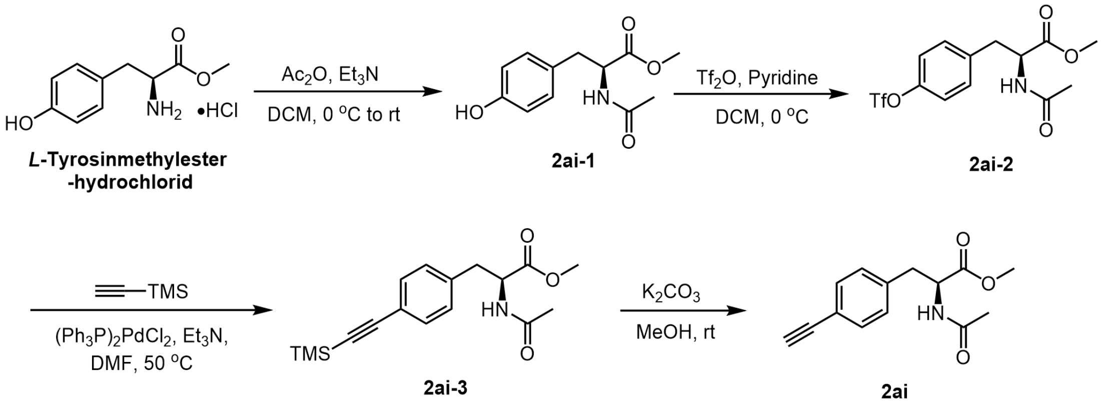
In a 25 mL flask, 3-bromopropyne (0.34 mL, 3 mmol, 1.5 equiv, 80 wt% in toluene) was added to a solution of Fenofibric acid (637.5 mg, 2 mmol, 1 equiv) and K_2CO_3 (1.1 g, 8 mmol, 4 equiv) in DMF (10 mL) at room temperature. The mixture was stirred at room temperature for 3 h. Then the reaction was diluted with 30 mL ethyl acetate and washed three times with 30 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EA (10:1) as eluting solvent to afford target product **2ag** as light yellow oil (713.5 mg, 100%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 4H), 7.43 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.76 (d, J = 2.4 Hz, 2H), 2.48 (t, J = 2.4 Hz, 1H), 1.68 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 194.1, 172.8, 159.2, 138.3, 136.3, 131.9, 131.1, 130.6, 128.5, 117.6, 79.2, 76.7, 75.5, 52.9, 25.3. **HRMS** (EI) calcd for $C_{20}H_{17}ClO_4$ $[M]^+$: 356.08099, found: 356.08069. **IR** (Reflection): ṽ = 3292, 3071, 2994, 2943, 2558, 2129, 1921, 1738, 1650, 1589, 1505, 1486, 1467, 1436, 1418, 1387, 1367, 1301, 1240, 1165, 1116, 1089, 1013, 967, 924, 852, 791, 760, 740, 722, 678.

Prop-2-yn-1-yl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-*1H*-indol-3-yl)acetate (2ah)



In a 25 mL flask, 3-bromopropyne (0.34 mL, 3 mmol, 1.5 equiv, 80 wt% in toluene) was added to a solution of Indomethacin (715.6 mg, 2 mmol, 1 equiv) and K_2CO_3 (1.1 g, 8 mmol, 4 equiv) in DMF (10 mL) at room temperature. The mixture was stirred at room temperature overnight. Then the reaction was diluted with 30 mL ethyl acetate and washed three times with 30 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography with PE/EA (10:1) as eluting solvent to afford target product **2ah** as light yellow solid (644.2 mg, 81%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 2H), 7.55 – 7.40 (m, 2H), 6.97 (d, J = 2.5 Hz, 1H), 6.88 (d, J = 9.0 Hz, 1H), 6.67 (dd, J = 9.0, 2.5 Hz, 1H), 4.71 (d, J = 2.5 Hz, 2H), 3.84 (s, 3H), 3.71 (s, 2H), 2.48 (t, J = 2.5 Hz, 1H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 168.2, 156.0, 139.2, 136.0, 133.8, 131.1, 130.7, 130.4, 129.1, 114.9, 111.9, 111.8, 101.2, 77.4, 75.1, 55.6, 52.4, 30.0, 13.3. **HRMS** (EI) calcd for $C_{22}H_{18}NO_4Cl$ $[M]^+$: 395.09189, found: 395.09170. **IR** (Reflection): ṽ = 3284, 3089, 2932, 2129, 1741, 1681, 1591, 1477, 1456, 1400, 1357, 1316, 1222, 1142, 1088, 1067, 1014, 925, 833, 754, 688. **M.p.** (amorphous): 86.9-88.8 °C.

Methyl (*S*)-2-acetamido-3-(4-ethynylphenyl)propanoate (2ai)



Step 1: To a suspension of *L*-Tyrosinmethylester-hydrochlorid (926.7 mg, 4 mmol) in 15 mL DCM was added Et_3N (0.59 mL, 4.2 mmol) at 0 °C and the reaction was stirred at this temperature for 10 min. Then Ac_2O (0.4 mL, 4.2 mmol) was added and the mixture was warmed up to room temperature and stirred overnight. The mixture was filtered and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (1:1) as eluting solvent to afford methyl acetyl-*L*-Tyrosinate **2ai-1** as colorless solid (950 mg, 100%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 (d, *J* = 8.5 Hz, 2H), 6.73 (d, *J* = 8.5 Hz, 2H), 6.11 (br, 1H), 5.97 (d, *J* = 8.0 Hz, 1H), 4.87 (dt, *J* = 8.0, 5.9 Hz, 1H), 3.74 (s, 3H), 3.04 (ddd, *J* = 31.9, 14.0, 5.8 Hz, 2H), 1.99 (s, 3H).

Step 2: To a solvent of acetyl-*L*-Tyrosinate **2ai-1** (950 mg, 4 mmol) and pyridine (0.97 mL, 12 mmol) in 16 mL dry DCM was added dropwise trifluoromethanesulfonic anhydride (Tf_2O) (0.81 mL, 4.8 mmol) at 0 °C. The reaction was warmed up to room temperature and stirred for 1 h. After completion of the reaction, the mixture was washed with 15 mL sat. brine, and the aqueous phase was extracted three times with 15 mL ethyl acetate, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with DCM/MeOH (10:1) as eluting solvent to afford the methyl (*S*)-2-acetamido-3-(4-(((trifluoromethyl)sulfonyl)oxy)phenyl)propanoate **2ai-2** as colorless solid (1.29 g, 87%). **^{1}H NMR** (300MHz, $CDCl_3$) δ 7.23 – 7.06 (m, 4H), 5.95 (d, *J* = 7.4 Hz, 1H), 4.89 (dt, *J* = 7.5, 5.9 Hz, 1H), 3.72 (s, 3H), 3.16 (qd, *J* = 14.0, 5.9

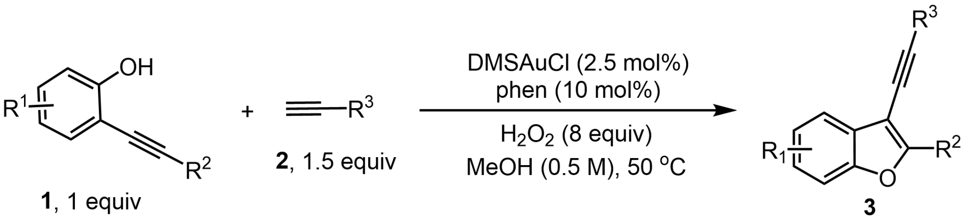
Hz, 2H), 2.00 (s, 3H).

Step 3: To a suspension of $(Ph_3P)_2PdCl_2$ (84 mg, 0.12 mmol) in 7 mL DMF/Et_3N (5:2) were added compound **2ai-2** (738.6 mg, 2 mmol) and Et_3N (0.34 mL, 2.4 mmol). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 50 °C overnight. After completion of the reaction, the resulting solution was cooled to room temperature, then the solution was filtered and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (1:1) as eluting solvent to afford methyl (*S*)-2-acetamido-3-(4-((trimethylsilyl)ethynyl)phenyl)propanoate **2ai-3** as dark yellow oil (516.9 mg, 81%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.3, 2H), 7.02 (d, *J* = 8.2, 2H), 5.87 (d, *J* = 7.6, 1H), 4.87 (dt, *J* = 7.7, 5.8, 1H), 3.71 (s, 3H), 3.21 – 3.03 (m, 2H), 1.98 (s, 3H), 0.24 (s, 9H).

Step 4: To a solvent of compound **2ai-3** (450 mg, 1.42 mmol) in 20 mL DCM/MeOH (1:1) was added K_2CO_3 (587 mg, 4.2 mmol). The mixture was stirred at room temperature. After completion of the reaction, the solution was filtered and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE/EA (1:1) to afford target product **2ai** as dark yellow oil (235.2 mg, 68%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 5.96 (d, *J* = 6.8 Hz, 1H), 4.87 (dd, *J* = 13.5, 5.8 Hz, 1H), 3.71 (s, 3H), 3.21 – 3.02 (m, 3H), 1.98 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.9, 169.6, 136.8, 132.3, 129.2, 120.9, 83.2, 77.4, 52.9, 52.4, 37.7, 23.1. **HRMS** (EI) calcd for $C_{14}H_{15}NO_3$ $[M]^+$: 245.10464, found: 245.10497. **IR** (Reflection): ṽ = 3282, 3065, 3001, 2953, 2848, 2107, 1917, 1744, 1655, 1540, 1508, 1436, 1373, 1273, 1217, 1130, 1019, 844, 826, 666.

3.4.3 General Procedure for the Gold-Catalyzed Alkynylative Cyclization

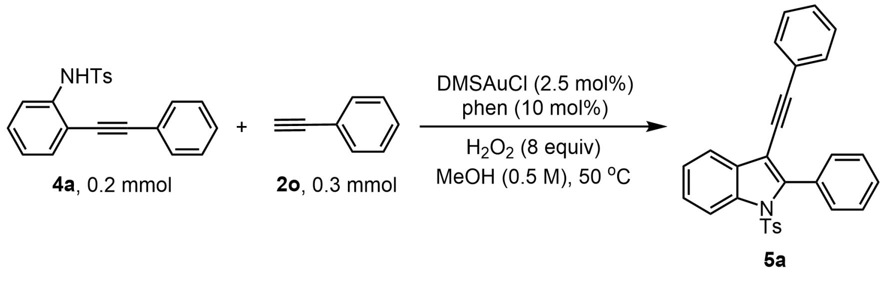
3.4.3.1 General Procedure for the Synthesis of 3-Alkynylbenzofurans



A 4-mL vial equipped with a magnetic stir bar was charged with DMSAuCl (1.5 mg, 2.5 mol%), phen (3.6 mg, 10 mol%), 2-(alkynyl)phenol **1** (0.2 mmol, if as solid), terminal alkynes **2** (0.3 mmol, 1.5 equiv, if as solid) in MeOH (0.4 mL), then 2-(alkynyl)phenol **1** (0.2 mmol, if as oil), terminal alkynes **2** (0.3 mmol, 1.5 equiv, if as oil) and H_2O_2 (89.6 μL, 1.6 mmol, 50 wt% in water) were added. The mixture was stirred at 50 °C. After completion of the reaction (monitored by TLC), the resulting solution was cooled to room temperature. 2 mL DCM was added, the solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by column chromatography on silica gel, to afford the crude products.

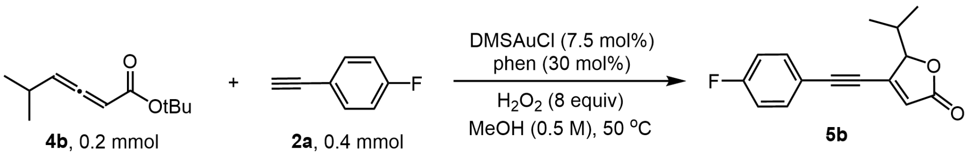
3.4.3.2 General Procedure for the Synthesis of Other Alkynylative Cyclization Products

2-Phenyl-3-(phenylethynyl)-1-tosyl-*1H*-indole (5a)



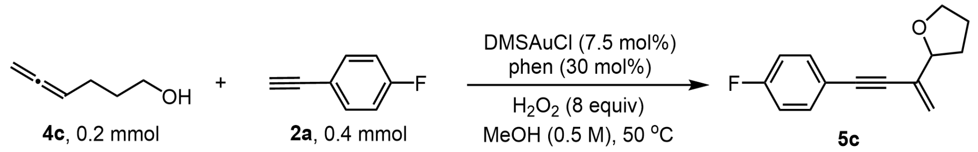
A solution of the 4-methyl-*N*-(2-(phenylethynyl)phenyl)benzenesulfonamide **4a** (69.5 mg, 0.2 mmol), ethynylbenzene **2o** (32.9 μL, 0.3 mmol, 1.5 equiv), DMSAuCl (1.5 mg, 2.5 mol%), phen (3.6 mg, 10 mol%) and H_2O_2 (89.6 μL, 1.6 mmol, 50 wt% in water) in MeOH (0.4 mL) was stirred at 50 °C. After completion of the reaction, the solvent was removed under reduced pressure by an aspirator, the residual mixture was purified by silica gel chromatography with PE/EA (5:1) as eluting solvent to afford product **5a** as colorless solid (84.4 mg, 94%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.37 (d, *J* = 8.1 Hz, 1H), 7.75 – 7.63 (m, 3H), 7.56 – 7.49 (m, 3H), 7.49 – 7.35 (m, 4H), 7.31 (dd, *J* = 7.2, 4.0 Hz, 5H), 7.06 (d, *J* = 8.2 Hz, 2H), 2.29 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.9 143.5, 137.1, 134.4, 131.4, 131.2, 130.7, 130.7, 129.3, 129.1, 128.3, 127.2, 126.8, 125.7, 124.7, 123.0, 120.1, 116.6, 108.2, 94.7, 81.4, 21.5. **HRMS** (EI) calcd for $C_{29}H_{21}NO_2S$ $[M]^+$: 447.12875, found: 447.12725. **IR** (Reflection): ṽ = 3063, 2924, 2853, 2249, 2205, 1733, 1597, 1493, 1474, 1450, 1374, 1305, 1253, 1213, 1188, 1178, 1122, 1091, 1071, 1026, 957, 912, 838, 812, 756, 733, 695, 665. **M.p.** (amorphous): 59.7-63.9 °C.

4-((4-Fluorophenyl)ethynyl)-5-isopropylfuran-2(*5H*)-one (5b)



A solution of the *tert*-butyl 5-methylhexa-2,3-dienoate **4b** (36.5 mg, 0.2 mmol), 1-ethynyl-4-fluorobenzene **2a** (46 μL, 0.4 mmol, 2 equiv), DMSAuCl (4.4 mg, 7.5 mol%), phen (10.8 mg, 30 mol%) and H_2O_2 (89.6 μL, 1.6 mmol, 50 wt% in water) in MeOH (0.4 mL) was stirred at 50 °C. After completion of the reaction, the solvent was removed under reduced pressure by an aspirator, the residual mixture was purified by silica gel chromatography with PE/DCM (1:1) as eluting solvent to afford product **5b** as colorless solid (37.8 mg, 77%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 – 7.44 (m, 2H), 7.16 – 7.04 (m, 2H), 6.23 (d, *J* = 1.7 Hz, 1H), 4.94 (dd, *J* = 2.9, 1.8 Hz, 1H), 2.30 (dtd, *J* = 13.8, 6.9, 3.0 Hz, 1H), 1.17 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 172.7, 163.6 (d, *J* = 253.2 Hz), 149.6, 134.2 (d, *J* = 8.8 Hz), 122.9, 117.1 (d, *J* = 3.6 Hz), 116.1 (d, *J* = 22.3 Hz), 104.6, 88.2, 79.7 (d, *J* = 1.4 Hz), 30.8, 19.0, 14.7. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -107.11. **HRMS** (EI) calcd for $C_{15}H_{13}O_2F$ $[M]^+$: 244.08941, found: 244.08897. **IR** (ATR): ṽ = 3105, 2965, 2930, 2203, 1786, 1742, 1610, 1587, 1504, 1461, 1370, 1353, 1319, 1296, 1274, 1255, 1228, 1218, 1164, 1154, 1092, 1024, 973, 911, 893, 876, 834, 820, 746, 730, 707. **M.p.** (amorphous): 87.2-89.1 °C.

2-(4-(4-Fluorophenyl)but-1-en-3-yn-2-yl)tetrahydrofuran (5c)

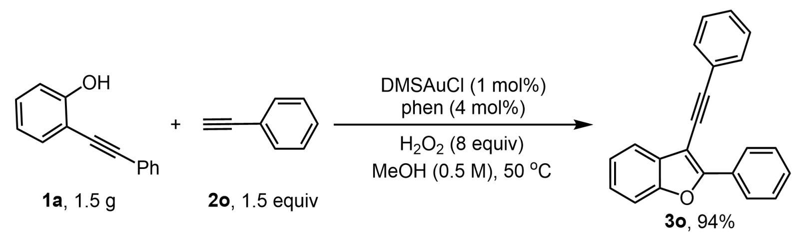


A solution of the hexa-4,5-dien-1-ol **4c** (19.7 mg, 0.2 mmol), 1-ethynyl-4-fluorobenzene **2a** (46 µL, 0.4 mmol, 2 equiv), DMSAuCl (4.4 mg, 7.5 mol%), phen (10.8 mg, 30 mol%) and H_2O_2 (89.6 µL, 1.6 mmol, 50 wt% in water) in MeOH (0.4 mL) was stirred at 50 °C. After completion of the reaction, products were monitored by TLC. The solvent was removed under reduced pressure by an aspirator, the residual mixture was purified by silica gel chromatography with PE/DCM (1:1) as eluting solvent to afford product **5c** as colorless oil (20.4 mg, 47%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.46 – 7.36 (m, 2H), 7.09 – 6.87 (m, 2H), 5.58 (t, *J* = 1.5 Hz, 1H), 5.51 (s, 1H), 4.48 (dd, *J* = 6.8, 5.8 Hz, 1H), 4.06 – 3.96 (m, 1H), 3.92 – 3.83 (m, 1H), 2.23 – 2.09 (m, 1H), 2.08 – 1.85 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.5 (d, *J* = 249.6 Hz), 133.5 (d, *J* = 8.3 Hz), 133.1, 120.7, 119.2 (d, *J* = 3.5 Hz), 115.6 (d, *J* = 22.1 Hz), 89.4, 87.1 (d, *J* = 1.4 Hz), 80.6, 68.9, 31.5, 25.6. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -110.88. **HRMS** (EI) calcd for $C_{14}H_{13}OF$ $[M]^+$: 216.09449, found: 216.09326. **IR** (Reflection): ṽ = 3436, 3073, 2955, 2927, 2875, 2204, 1729, 1674, 1600, 1508, 1460, 1411, 1233, 1157, 1070, 930, 838.

3.4.4 Comprehensive Application

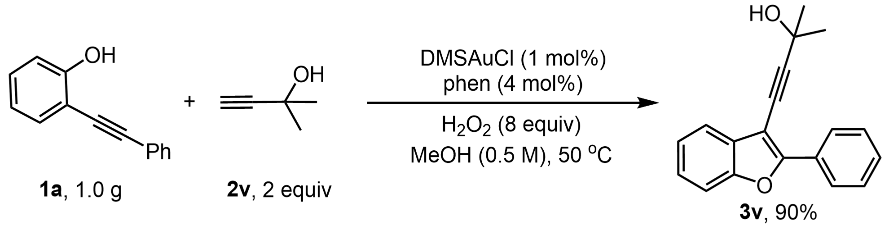
3.4.4.1 General Procedure for Gram Scale Synthesis

A. Gram scale synthesis of 2-phenyl-3-(phenylethynyl)benzofuran (3o)



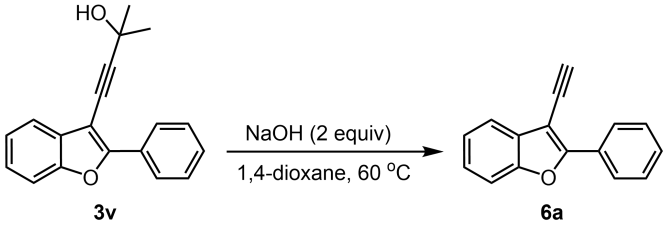
A round-bottomed of 50 mL equipped with a magnetic stir bar was charged with DMSAuCl (22.7 mg, 1 mol%), phen (55.4 mg, 4 mol%), 2-(phenylethynyl)phenol **1a** (1.5 g, 7.7 mmol) in MeOH (15 mL), then ethynylbenzene **2o** (1.27 mL, 11.55 mmol, 1.5 equiv) and H_2O_2 (3.45 mL, 61.6 mmol, 50 wt% in water) were added. The mixture was stirred at 50 °C for 16 h. After completion of the reaction, the solvent was removed under reduced pressure, then diluted with 5 mL ethyl acetate. The residual aqueous phase was extracted three times with 5 mL ethyl acetate, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with petroleum ether as eluting solvent to afford product **3o** as light yellow solid (2.13 g, 94%).

B. Gram scale synthesis of 2-methyl-4-(2-phenylbenzofuran-3-yl)but-3-yn-2-ol (3v)



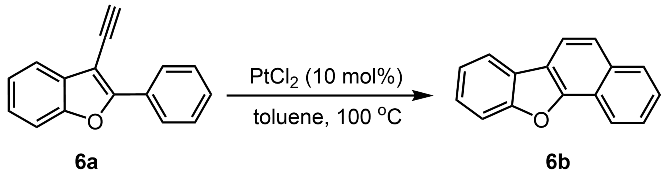
A round-bottomed of 25 mL equipped with a magnetic stir bar was charged with DMSAuCl (15.2 mg, 1 mol%), phen (37.1 mg, 4 mol%), 2-(phenylethynyl)phenol **1a** (1.0 g, 5.15 mmol) in MeOH (10 mL), then 2-methylbut-3-yn-2-ol **2v** (0.75 mL, 7.72 mmol, 1.5 equiv) and H_2O_2 (2.3 mL, 41.2 mmol, 50 wt% in water) were added. The mixture was stirred at 50 °C. After 12 h, 2-(phenylethynyl)phenol **1a** was not complected (monitored by TLC), 2-methylbut-3-yn-2-ol **2v** (0.25 mL, 2.57 mmol, 0.5 equiv) was added, then the mixture was stirred at 50 °C for an additional 12 h. After completion of the reaction, the solvent was removed under reduced pressure, then diluted with 5 mL ethyl acetate. And the residual aqueous phase was extracted three times with 5 mL ethyl acetate, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography with PE:DCM (1:1) as eluting solvent to afford product **3v** as light yellow solid (1.28 g, 90%).

3.4.4.2 Post-functionalization of Ethynylbenzofuran



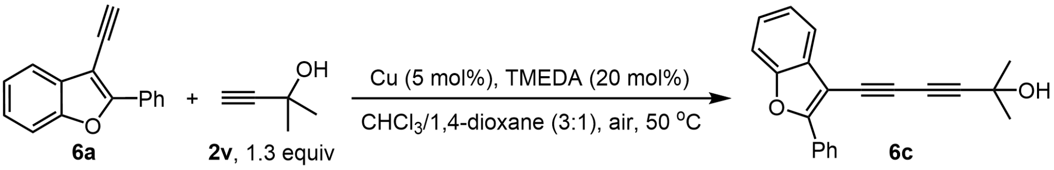
3-Ethynyl-2-phenylbenzofuran (6a)

In a 50-mL flask, 2-methyl-4-(2-phenylbenzofuran-3-yl)but-3-yn-2-ol **3v** (552 mg, 2 mmol) was added to a solution of well-ground anhydrous NaOH (160 mg, 4 mmol, 2 equiv) in 1,4-dioxane (20 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 60 °C overnight. After completion of the reaction, the resulting solution was cooled to room temperature. Then 20 mL saturated NH_4Cl was added, and the aqueous phase was extracted three times with 20 mL ethyl acetate, the organic phases were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography with PE as eluting solvent to afford product **6a** as dark yellow oil (432 mg, 99 %). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.46 – 8.23 (m, 2H), 7.77 – 7.66 (m, 1H), 7.55 – 7.49 (m, 3H), 7.46 – 7.40 (m, 1H), 7.40 – 7.29 (m, 2H), 3.63 (s, 1H). Characterization data of **6a** corresponded to the literature values.[4c]



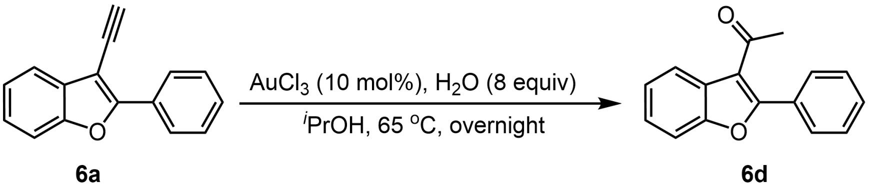
Naphtho[1,2-*b*]benzofuran (6b)

A solution of the 3-ethynyl-2-phenylbenzofuran **6a** (43.6 mg, 0.2 mmol) and $PtCl_2$ (5.3 mg, 10 mol%) in toluene (1.5 mL) was stirred at 100 °C overnight. After completion of the reaction, the solvent was removed under reduced pressure by an aspirator, the residual mixture was purified by silica gel chromatography with PE as eluting solvent to afford product **6b** as colorless solid (34.1 mg, 78%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.2 Hz, 1H), 8.09 – 7.97 (m, 3H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.73 (d, J = 8.1 Hz, 1H), 7.70 – 7.62 (m, 1H), 7.58 (ddd, J = 8.2, 7.0, 1.3 Hz, 1H), 7.53 – 7.45 (m, 1H), 7.41 (td, J = 7.5, 1.0 Hz, 1H). Characterization data of **6b** corresponded to the literature values.[4c]



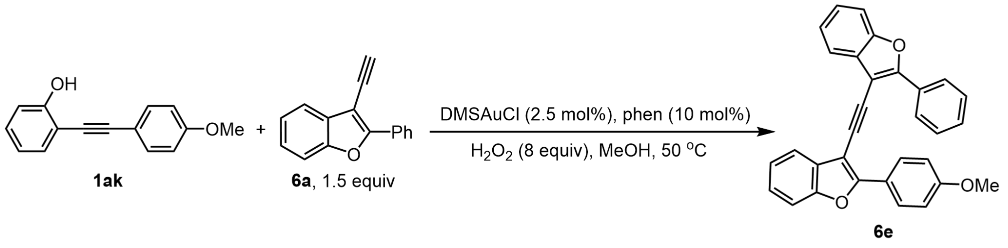
2-Methyl-6-(2-phenylbenzofuran-3-yl)hexa-3,5-diyn-2-ol (6c)

A solution of the 3-ethynyl-2-phenylbenzofuran **6a** (43.6 mg, 0.2 mmol), 2-methylbut-3-yn-2-ol **2v** (25.3 µL, 0.26 mmol), copper powder (0.6 mg, 5 mol%), TMEDA (5.9 µL, 20 mol%) in 0.4 mL $CHCl_3$/1,4-dioxane (3:1) was stirred at 50 °C overnight. After completion of the reaction, the resulting solution was cooled to room temperature. The solvent was removed under reduced pressure by an aspirator, then the residual mixture was purified by silica gel chromatography with PE/DCM (1:1) as eluting solvent to afford product **6c** as colorless solid (35.3 mg, 59%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.27 – 8.22 (m, 2H), 7.73 – 7.63 (m, 1H), 7.56 – 7.47 (m, 3H), 7.46 – 7.40 (m, 1H), 7.39 – 7.27 (m, 2H), 2.18 (br, 1H), 1.65 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 159.0, 153.3, 129.9, 129.7, 129.6, 128.8, 125.9, 125.6, 123.6, 120.3, 111.3, 97.7, 88.3, 80.4, 70.7, 67.4, 65.9, 31.1. **HRMS** (EI) calcd for $C_{21}H_{16}O_2$ $[M]^+$: 300.11448, found: 300.11359. **IR** (Reflection): ṽ = 3061, 2151, 1957, 1888, 1737, 1593, 1559, 1497, 1455, 1443, 1400, 1337, 1293, 1272, 1257, 1202, 1180, 1151, 1100, 1069, 1028, 962, 897, 847, 827, 771, 744, 685, 644, 624. **M.p.** (amorphous): 128.9-130.2 °C.



1-(2-Phenylbenzofuran-3-yl)ethan-1-one (6d)

A solution of the 3-ethynyl-2-phenylbenzofuran **6a** (21.8 mg, 0.1 mmol), $AuCl_3$ (3.0 mg, 10 mol%) and H_2O (14.4 µL, 8 equiv) in ^{i}PrOH (0.5 mL) was stirred at 65 °C overnight. After completion of the reaction, the solvent was removed under reduced pressure by an aspirator. The residual mixture was purified by silica gel chromatography with PE as eluting solvent to afford product **6d** as light yellow oil (23.6 mg, 100%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 – 8.09 (m, 1H), 7.81 – 7.72 (m, 2H), 7.56 – 7.48 (m, 4H), 7.42 – 7.32 (m, 2H), 2.39 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.4, 160.3, 153.9, 130.5, 130.2, 129.7, 128.6, 126.8, 125.4, 124.2, 122.4, 118.4, 111.1, 30.5. **HRMS** (EI) calcd for $C_{16}H_{12}O_2$ $[M]^+$: 236.08318, found: 236.08278. **IR** (Reflection): ṽ = 3059, 2925, 1904, 1736, 1664, 1607, 1561, 1490, 1475, 1451, 1381, 1287, 1255, 1202, 1185, 1110, 1089, 1072, 1025, 956, 893, 825, 772, 750, 700, 665, 631.

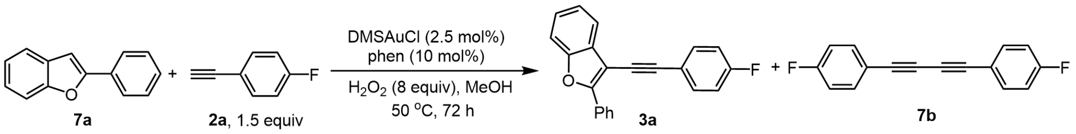


2-(4-Methoxyphenyl)-3-((2-phenylbenzofuran-3-yl)ethynyl)benzofuran (6e)

A 4-mL vial equipped with a magnetic stir bar was charged with DMSAuCl (0.7 mg, 2.5 mol%), phen (1.8 mg, 10 mol%) and 2-((4-methoxyphenyl)ethynyl)phenol **1ak** (22.4 mg, 0.1 mmol) in MeOH (0.2 mL), then 3-ethynyl-2-phenylbenzofuran **6a** (32.7 mg, 0.15 mmol, 1.5 equiv) and H_2O_2 (44.8 μL, 0.8 mmol, 50 wt% in water) were added. The mixture was stirred at 50 °C. After completion of the reaction, the resulting solution was cooled to room temperature. 1 mL DCM was added, the solution was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was purified by flash column chromatography on silica gel with PE/DCM (5:1) as eluting solvent to afford product **6e** as yellow solid (34.8 mg, 79%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 5.3, 3.3 Hz, 2H), 8.41 – 8.36 (m, 2H), 7.87 – 7.78 (m, 2H), 7.58 – 7.49 (m, 4H), 7.44 (dt, *J* = 4.5, 1.8 Hz, 1H), 7.42 – 7.34 (m, 4H), 7.05 – 6.97 (m, 2H), 3.88 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.5, 156.6, 156.1, 153.6, 153.4, 130.2, 130.1, 130.0, 129.3, 128.7, 127.7, 126.0, 125.5, 125.0, 123.6, 123.5, 123.0, 120.2, 119.9, 114.2, 111.3, 111.1, 99.6, 97.7, 89.0, 88.1, 55.4. **HRMS** (EI) calcd for $C_{31}H_{20}O_3$ $[M]^+$: 440.14070, found: 440.14065. **IR** (ATR): ṽ = 3056, 2925, 2837, 2184, 1733, 1606, 1509, 1454, 1422, 1302, 1249, 1202, 1176, 1104, 1068, 1029, 897, 828, 785, 740, 686, 607. **M.p.** (amorphous): 125.9-127.6 °C.

3.4.5 Mechanistic Study

A| The experiment of gold-catalyzed cascade cyclization-alkynylation.



A 4-mL vial equipped with a magnetic stir bar was charged with DMSAuCl (0.7 mg, 2.5 mol%), phen (1.8 mg, 10 mol%), 2-phenylbenzofuran **7a** (19.4 mg, 0.1 mmol) in MeOH (0.2 mL), then 1-ethynyl-4-fluorobenzene **2a** (16.6 μL, 0.15 mmol) and H_2O_2 (44.8 μL, 1.6 mmol, 50 wt% in water) were added. The mixture was stirred at 50 °C for 72 h, then the solvent was removed under reduced pressure. 0.5 mL $CDCl_3$ was added and removed the mixture into a NMR tube. As shown in Figure 2, no alkynyl cyclization product **3a** (-110.53 ppm, ^{19}F NMR) was observed. Then recovery of the mixture, the residual mixture was purified by flash column chromatography on silica gel with PE as eluting solvent to afford homocoupling product **7b** as light yellow solid (32.8 mg, 92%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.71 – 7.38 (m, 4H), 7.10 – 6.91 (m, 4H); **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.49. Characterization data of **7b** corresponded to the literature values.[26]

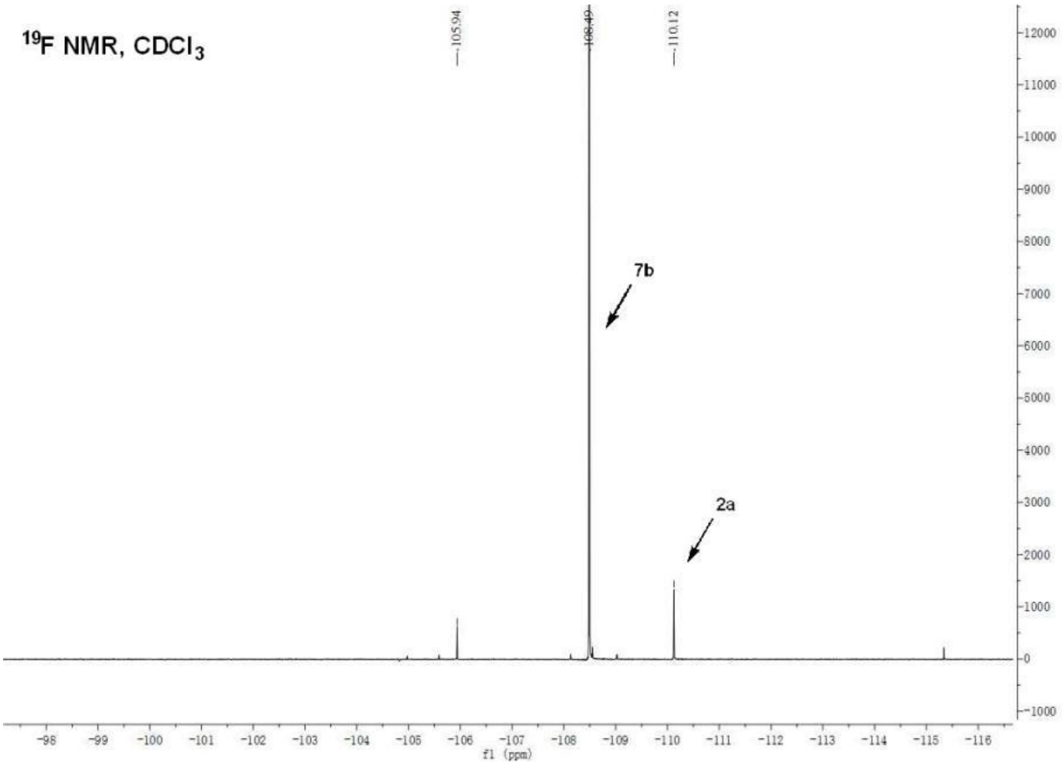
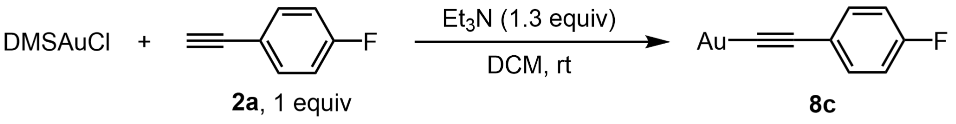


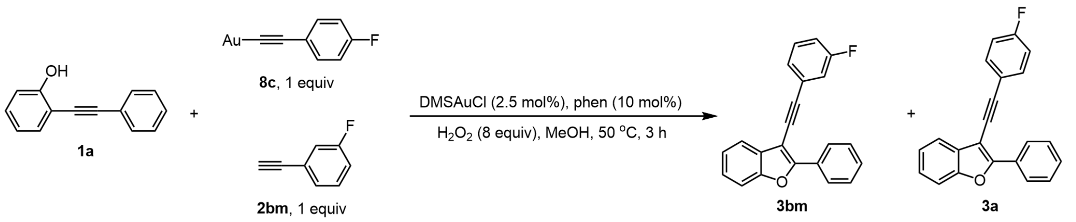
Figure 2. ^{19}F NMR (282 MHz, $CDCl_3$) spectra of gold-catalyzed cascade cyclization-alkynylation.

B| The general synthesis of ((4-fluorophenyl)ethynyl)gold (**8c**).



((4-Fluorophenyl)ethynyl)gold **8c** was prepared according to a published procedure.[27] A round-bottomed of 50 mL equipped with a magnetic stir bar was charged with DMSAuCl (147 mg, 0.5 mmol) in 15 mL DCM, 1-ethynyl-4-fluorobenzene **2a** (57.2 µL, 0.5 mmol, 1 equiv) was added. While stirring, Et_3N (90 µL, 0.65 mmol, 1.3 equiv) was added. The mixture was stirred at room temperature in the dark. After 12 h, the solvent was removed under reduced pressure, the precipitate was filtered, washed with DCM and dried under vacuum to obtain the product **8c** as yellow solid (121 mg, 77%). **Note:** the gold complex **8c** is insoluble in solvents such as DCM, acetone, MeCN, EtOH, MeOH, THF, Et_2O, water, and DMSO. The IR data was in agreement with literature values.[27] **IR** (ATR): ṽ = 2963, 2008, 1651, 1596, 1501, 1260, 1226, 1095, 835, 800, 740.

C| The stoichiometric reaction of gold(I)-acetylide (**8c**) with 2-(phenylethynyl)phenol (**1a**) and 1-ethynyl-3-fluorobenzene (**2bm**)



A 4-mL vial equipped with a magnetic stir bar was charged with DMSAuCl (0.7 mg, 2.5 mol%), phen (1.8 mg, 10 mol%), 2-(phenylethynyl)phenol **1a** (19.4 mg, 0.1 mmol), ((4-fluorophenyl)ethynyl)gold **8c** (31.6 mg, 0.1 mmol, 1 equiv) in MeOH (0.2 mL), then 3-ethynyl-4-fluorobenzene **2bm** (11.6 µL, 0.1 mmol, 1 equiv) and H_2O_2 (44.8 µL, 1.6 mmol, 50 wt% in water, 8 equiv) were added. The mixture was stirred at 50 °C for 3 h, then the solvent was removed under reduced pressure. The yields of product **3bm** (78%) and product **3a** (6%) were determined by comparing the integration of the ^{19}F NMR resonance of products **3am** (-112.62 ppm) and **3a** (-110.53 ppm) with that of trifluorotoluene (-62.75 ppm).

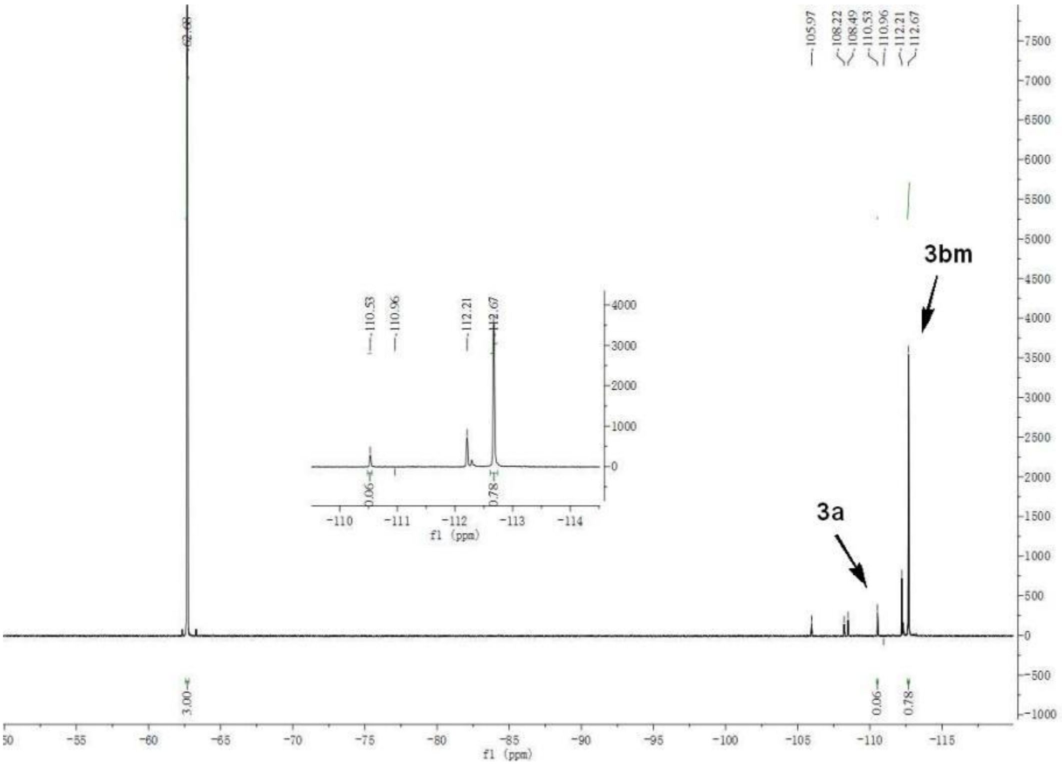
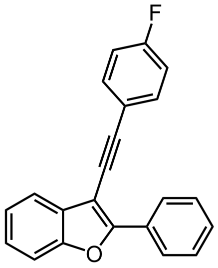


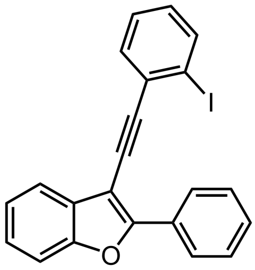
Figure 3. ^{19}F NMR (282 MHz, CDCl$_3$) spectra of the stoichiometric reaction of gold(I)-acetylide (**8c**) with 2-(phenylethynyl)phenol (**1a**) and 1-ethynyl-3-fluorobenzene (**2bm**).

3.5 Characterization of Products



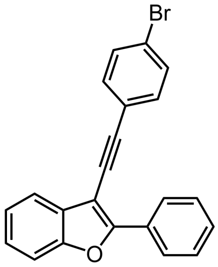
3-((4-Fluorophenyl)ethynyl)-2-phenylbenzofuran

3a, light yellow solid, 62.2 mg, 99% yield. R$_f$ = 0.4 (*n*-Hexane), chromatography eluent: *n*-Hexane. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.37 – 8.29 (m, 2H), 7.74 (dd, *J* = 6.4, 2.3 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.56 – 7.48 (m, 3H), 7.46 – 7.39 (m, 1H), 7.35 (tt, *J* = 7.3, 5.8 Hz, 2H), 7.16 – 7.06 (m, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 162.6(d, *J* = 250.0 Hz), 156.4, 153.5, 133.4 (d, *J* = 8.4 Hz), 130.1, 129.9, 129.2, 128.7, 126.0, 125.4, 123.4, 120.3, 119.5 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 22.1 Hz), 111.2, 99.0, 95.6, 80.9 (d, *J* = 1.4 Hz). **^{19}F NMR** (282 MHz, $CDCl_3$) δ -110.53. **HRMS** (EI) calcd for $C_{22}H_{13}OF$ $[M]^+$: 312.09449, found: 312.09432. **IR** (ATR): ṽ = 3063, 1891, 1600, 1507, 1492, 1456, 1443, 1293, 1256, 1232, 1201, 1110, 1090, 1027, 832, 767, 742, 682, 624. **M.p.** (amorphous): 89.3-91.6 °C.



3-((2-Iodophenyl)ethynyl)-2-phenylbenzofuran

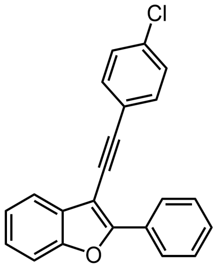
3b, light yellow solid, 76.8 mg, 91% yield. R_f = 0.5 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.1 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 7.4 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.43 (t, *J* = 7.3 Hz, 1H), 7.37 (dq, *J* = 14.6, 7.5 Hz, 3H), 7.06 (t, *J* = 7.7 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 156.6, 153.5, 138.8, 132.8, 130.02, 130.00, 129.9, 129.4, 129.3, 128.7, 127.9, 126.2, 125.4, 123.5, 120.7, 111.2, 100.0, 98.9, 98.5, 85.0. **HRMS** (EI) calcd for $C_{22}H_{13}OI$ $[M]^+$: 420.00056, found: 420.00282. **IR** (ATR): ṽ = 3058, 2207, 2191, 1551, 1456, 1442, 1426, 1383, 1291, 1254, 1230, 1202, 1121, 1093, 1068, 1016, 930, 897, 829, 769, 744, 705, 682, 643, 626. **M.p.** (amorphous): 99.7-102.0 °C.



3-((4-Bromophenyl)ethynyl)-2-phenylbenzofuran

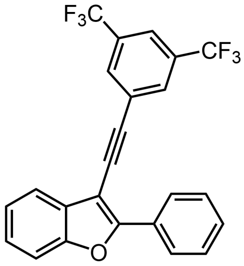
3c, light yellow solid, 57.1 mg, 77% yield. R_f = 0.5 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.39 – 8.26 (m, 2H), 7.78 – 7.70 (m, 1H), 7.58 – 7.41 (m, 8H), 7.41 – 7.30

(m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.5, 153.5, 132.9, 131.7, 130.0, 129.7, 129.3, 128.7, 126.0, 125.4, 123.4, 122.6, 122.3, 120.3, 111.2, 98.9, 95.6, 82.4. **HRMS** (EI) calcd for $C_{22}H_{13}OBr$ $[M]^+$: 372.01443, found: 372.01347. **IR** (ATR): ṽ = 3049, 2216, 1897, 1737, 1595, 1558, 1483, 1474, 1457, 1443, 1391, 1342, 1294, 1258, 1239, 1203, 1113, 1093, 1067, 1027, 1009. 957, 930, 895, 818, 766, 740, 681, 626. **M.p.** (amorphous): 125.8-127.1 °C.



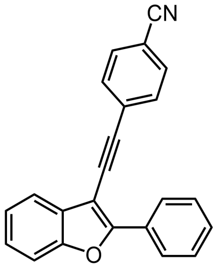
3-((4-Chlorophenyl)ethynyl)-2-phenylbenzofuran

3d, light yellow solid, 62.8 mg, 96% yield. $R_f = 0.7$ (PE:EA = 10:1), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.44 – 8.25 (m, 2H), 7.81 – 7.71 (m, 1H), 7.58 – 7.50 (m, 5H), 7.46 – 7.41 (m, 1H), 7.41 – 7.31 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 153.5, 134.4, 132.6, 129.2, 128.8, 128.7, 126.0, 125.4, 123.4, 121.8, 120.3, 111.2, 98.9, 95.6, 82.2. **HRMS** (EI) calcd for $C_{22}H_{13}OCl$ $[M]^+$: 328.06494, found: 328.06451. **IR** (ATR): ṽ = 3049, 2219, 1897, 1732, 1597, 1561, 1486, 1475, 1457, 1444, 1396, 1294, 1258, 1240, 1204, 1114, 1086, 1070, 1027, 1013, 957, 930, 909, 898, 824, 766, 751, 740, 681, 628. **M.p.** (amorphous): 112.6-114.5 °C.



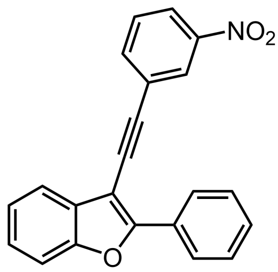
3-((3,5-Bis(trifluoromethyl)phenyl)ethynyl)-2-phenylbenzofuran

3e, light yellow solid, 81.9 mg, 95% yield. $R_f = 0.8$ (PE:DCM = 10:1), chromatography eluent: 1% Dichloromethane in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.5 Hz, 2H), 8.01 (s, 2H), 7.87 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 3H), 7.46 (t, *J* = 7.4 Hz, 1H), 7.41 – 7.34 (m, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 157.6, 153.5, 132.1 (q, *J* = 33.8 Hz), 131.2 (d, *J* = 3.0 Hz), 129.7 (d, *J* = 6.4 Hz), 129.4, 128.8, 126.2, 125.7, 123.9, 123.7, 122.1, 121.6 (dt, *J* = 7.4, 3.6 Hz), 120.2, 97.9, 93.4, 85.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.07. **HRMS** (EI) calcd for $C_{24}H_{12}OF_6$ $[M]^+$: 430.07869, found: 430.07935. **IR** (ATR): ṽ = 3067, 2212, 1613, 1559, 1458, 1443, 1402, 1358, 1280, 1201, 1172, 1130, 1097, 1071, 1028, 905, 890, 847, 828, 769, 742, 683, 628. **M.p.** (amorphous): 137.4-138.6 °C.



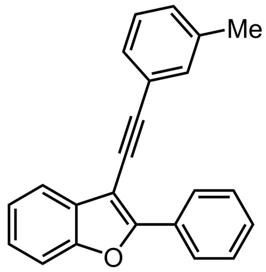
4-((2-Phenylbenzofuran-3-yl)ethynyl)benzonitrile

3f, light yellow solid, 50.3 mg, 79% yield. R_f = 0.3 (PE:DCM = 2:1), chromatography eluent: 50% Petroleum ether in dichlormethan. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.75 – 7.69 (m, 1H), 7.65 (s, 4H), 7.56 – 7.49 (m, 3H), 7.48 – 7.42 (m, 1H), 7.41 – 7.31 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.3, 153.5, 132.1, 131.8, 129.8, 129.5, 129.4, 128.7, 128.1, 126.1, 125.6, 123.6, 120.1, 118.4, 111.5, 111.3, 98.3, 95.0, 85.9. **HRMS** (EI) calcd for $C_{23}H_{13}NO$ $[M]^+$: 319.09917, found: 319.09856. **IR** (ATR): ṽ = 3063, 2223, 2204, 1922, 1782, 1681, 1604, 1583, 1561, 1508, 1489, 1475, 1456, 1444, 1407, 1393, 1342, 1293, 1258, 1241, 1203, 1176, 1114, 1092, 1070, 1026, 1007, 967, 929, 912, 898, 837, 767, 750, 737, 682, 634, 623. **M.p.** (amorphous): 166.4-167.2 °C.



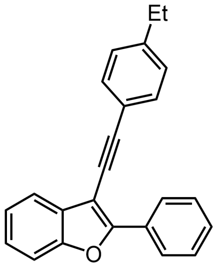
3-((3-Nitrophenyl)ethynyl)-2-phenylbenzofuran

3g, yellow solid, 55.4 mg, 82% yield. R_f = 0.4 (PE:DCM = 2:1), chromatography eluent: 30% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.47 – 8.40 (m, 1H), 8.35 – 8.27 (m, 2H), 8.26 – 8.17 (m, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.60-7.51 (m, 4H), 7.45 (dd, *J* = 8.4, 6.2 Hz, 1H), 7.42 – 7.30 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.2, 153.5, 148.2, 137.0, 129.8, 129.6, 129.50, 129.45, 128.8, 126.1, 125.6, 125.1, 123.6, 122.9, 120.2, 111.3, 98.2, 94.1, 84.0. **HRMS** (EI) calcd for $C_{22}H_{13}NO_3$ $[M]^+$: 339.08899, found: 339.08792. **IR** (ATR): ṽ = 3083, 2924, 2863, 2214, 1731, 1585, 1524, 1498, 1472, 1455, 1443, 1349, 1302, 1277, 1256, 1235, 1200, 1127, 1111, 1090, 1071, 1028, 999, 910, 896, 827, 811, 802, 766, 739, 700, 673, 655, 626. **M.p.** (amorphous): 136.4-137.1 °C.



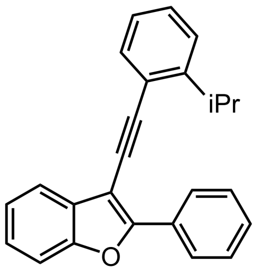
2-Phenyl-3-(m-tolylethynyl)benzofuran

3h, light yellow oil, 59.9 mg, 97% yield. R_f = 0.4 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.40 (d, *J* = 7.5 Hz, 2H), 7.80 (dd, *J* = 5.9, 3.0 Hz, 1H), 7.59 – 7.43 (m, 6H), 7.43 – 7.29 (m, 3H), 7.23 (d, *J* = 7.5 Hz, 1H), 2.44 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.2, 153.5, 138.1, 132.0, 130.2, 129.9, 129.3, 129.1, 128.63, 128.61, 128.35, 126.0, 125.3, 123.3, 123.2, 120.3, 111.2, 99.3, 97.0, 80.8, 21.3. **HRMS** (EI) calcd for $C_{23}H_{16}O$ $[M]^+$: 308.11957, found: 308.12046. **IR** (Reflection): ṽ = 3057, 2920, 2859, 2210, 1734, 1682, 1602, 1561, 1482, 1455, 1443, 1382, 1340, 1291, 1256, 1203, 1181, 1112, 1096, 1070, 1028, 1006, 896, 826, 782, 769, 745, 689, 664, 625.



3-((4-Ethylphenyl)ethynyl)-2-phenylbenzofuran

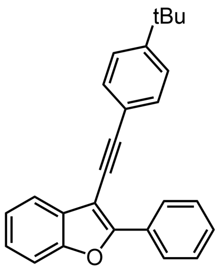
3i, light yellow solid, 56.2 mg, 87% yield. R_f = 0.5 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.0 Hz, 2H), 7.79 (dd, *J* = 6.0, 2.3 Hz, 1H), 7.61 – 7.49 (m, 5H), 7.48 – 7.31 (m, 3H), 7.27 (d, *J* = 7.9 Hz, 2H), 2.73 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.1, 153.5, 144.9, 131.5, 130.2, 130.0, 129.0, 128.6, 128.0, 126.0, 125.3, 123.3, 120.5, 120.4, 111.1, 99.4, 97.0, 80.4, 28.9, 15.4. **HRMS** (EI) calcd for $C_{24}H_{18}O$ $[M]^+$: 322.13522, found: 322.13391. **IR** (ATR): ṽ = 2964, 2930, 2871, 2205, 1886, 1735, 1601, 1509, 1488, 1474, 1455, 1442, 1386, 1290, 1257, 1232, 1202, 1113, 1096, 1069, 1028, 919, 897, 829, 771, 741, 688, 624. **M.p.** (amorphous): 73.6-75.5 °C.



3-((2-Isopropylphenyl)ethynyl)-2-phenylbenzofuran

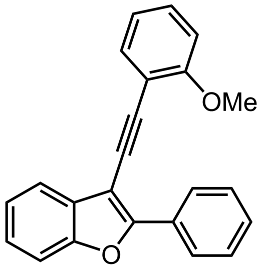
3j, light yellow oil, 63.4 mg, 94% yield. R_f = 0.6 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 7.8 Hz, 2H), 7.86 – 7.74 (m, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.46 (d, *J* = 7.3 Hz, 1H), 7.41 – 7.37 (m, 4H), 7.31 – 7.24 (m, 1H), 3.76 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.43 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.9, 153.5, 150.2, 132.5, 130.2, 130.1, 129.1, 128.9, 128.6, 126.0, 125.7, 125.3, 125.0, 123.4, 122.1, 120.3, 111.2, 99.5, 95.7, 84.6, 31.8, 23.3. **HRMS** (EI) calcd for $C_{25}H_{20}O$ $[M]^+$:

336.15087, found: 336.15184. **IR** (Reflection): ṽ = 3062, 2961, 2928, 2867, 1591, 1482, 1456, 1444, 1384, 1362, 1340, 1291, 1257, 1234, 1203, 1119, 1095, 1069, 1028, 1006, 895, 828, 744, 689, 660, 625.



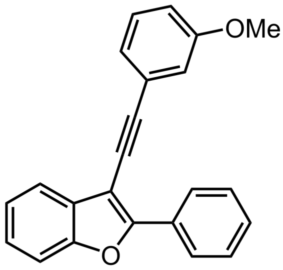
3-((4-(*tert*-Butyl)phenyl)ethynyl)-2-phenylbenzofuran

3k, light yellow solid, 68.1 mg, 97% yield. R$_f$ = 0.6 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.51 – 8.18 (m, 2H), 7.85 – 7.75 (m, 1H), 7.65 – 7.59 (m, 2H), 7.59 – 7.50 (m, 3H), 7.50 – 7.41 (m, 3H), 7.41 – 7.30 (m, 2H), 1.40 (s, 9H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 156.1, 153.5, 151.8, 131.3, 130.2, 130.0, 129.1, 128.6, 126.0, 125.5, 125.3, 123.3, 120.4, 111.1, 99.4, 96.9, 80.5, 34.8, 31.2. **HRMS** (EI) calcd for $C_{26}H_{22}O$ $[M]^+$: 350.16652, found: 350.16545. **IR** (Reflection): ṽ = 2963, 2864, 2360, 1592, 1492, 1456, 1443, 1392, 1257, 1239, 1203, 1103, 1091, 1067, 1013, 897, 833, 769, 745, 701, 685, 623. **M.p.** (amorphous): 113.8-115.0 °C.



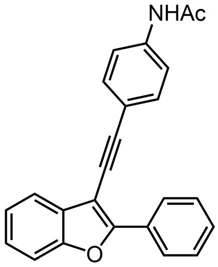
3-((2-Methoxyphenyl)ethynyl)-2-phenylbenzofuran

3l, light yellow solid, 59.9 mg, 97% yield. R$_f$ = 0.5 (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.62 – 8.40 (m, 2H), 7.89 – 7.78 (m, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.58 – 7.48 (m, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.32 (m, 3H), 7.02 (t, *J* = 7.5 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 4.01 (s, 3H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 160.1, 156.0, 153.5, 133.0, 130.2, 130.0, 129.8, 129.0, 128.5, 126.0, 125.2, 123.3, 120.5, 120.5, 112.8, 111.1, 110.7, 99.6, 93.7, 85.2, 55.8. **HRMS** (EI) calcd for $C_{23}H_{16}O_2$ $[M]^+$: 324.11448, found: 324.11289. **IR** (Reflection): ṽ = 3062, 2960, 2937, 2834, 2204, 1895, 1715, 1598, 1573, 1488, 1456, 1442, 1434, 1386, 1339, 1289, 1278, 1256, 1228, 1203, 1180, 1162, 1126, 1106, 1093, 1070, 1044, 1025, 931, 896, 832, 768, 745, 690, 660, 625. **M.p.** (amorphous): 96.2-97.8 °C.



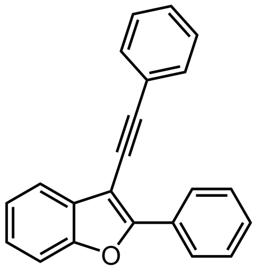
3-((3-Methoxyphenyl)ethynyl)-2-phenylbenzofuran

3m, light yellow oil, 56.4 mg, 87% yield. $R_f = 0.3$ (PE:DCM = 10:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.38 (d, *J* = 7.4 Hz, 2H), 7.79 (dd, *J* = 6.0, 2.7 Hz, 1H), 7.60 – 7.49 (m, 3H), 7.46 – 7.41 (m, 1H), 7.40 – 7.31 (m, 3H), 7.30 – 7.23 (m, 1H), 7.19 (s, 1H), 7.01 – 6.92 (m, 1H), 3.88 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 159.4, 156.4, 153.5, 130.1, 129.9, 129.5, 129.2, 128.6, 126.0, 125.3, 124.3, 124.1, 123.4, 120.3, 116.5, 114.8, 111.2, 99.1, 96.6, 81.0, 55.3. **HRMS** (EI) calcd for $C_{23}H_{16}O_2$ $[M]^+$: 324.11448, found: 324.11515. **IR** (Reflection): ṽ = 3064, 3001, 2937, 2833, 2210, 1734, 1574, 1485, 1474, 1455, 1442, 1426, 1384, 1316, 1284, 1257, 1203, 1176, 1166, 1111, 1095, 1069, 1045, 1006, 993, 917, 896, 869, 850, 826, 770, 744, 686, 625.



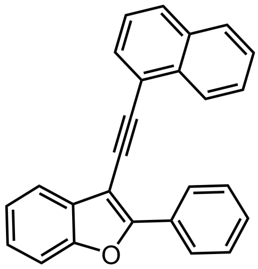
***N*-(4-((2-Phenylbenzofuran-3-yl)ethynyl)phenyl)acetamide**

3n, light yellow solid, 60.6 mg, 86% yield. $R_f = 0.3$ (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, DMSO) δ 10.17 (s, 1H), 8.37 – 8.12 (m, 2H), 7.80 – 7.75 (m, 1H), 7.73 – 7.69 (m, 3H), 7.67 – 7.57 (m, 4H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.47 – 7.36 (m, 2H), 2.09 (s, 3H). **^{13}C NMR** (101 MHz, DMSO) δ 168.6, 155.3, 152.9, 140.0, 132.1, 129.7, 129.2, 129.2, 128.9, 126.0, 125.4, 123.9, 120.1, 118.9, 116.2, 111.5, 98.7, 97.3, 79.5, 24.1. **HRMS** (EI) calcd for $C_{24}H_{17}NO_2$ $[M]^+$: 351.12538, found: 351.12666. **IR** (ATR): ṽ = 3293, 3064, 2208, 1662, 1586, 1524, 1493, 1456, 1442, 1403, 1370, 1312, 1292, 1257, 1237, 1202, 1111, 1093, 1069, 1028, 970, 896, 828, 797, 768, 741, 685, 626. **M.p.** (amorphous): 212.6-213.2 °C.



2-Phenyl-3-(phenylethynyl)benzofuran

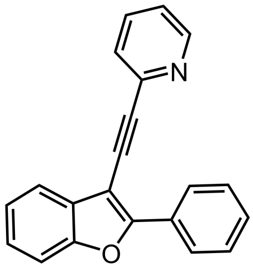
3o, colorless solid, 58.3 mg, 99% yield. $R_f = 0.4$ (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.48 – 8.33 (m, 2H), 7.85 – 7.76 (m, 1H), 7.68 (dd, *J* = 7.3, 2.1 Hz, 2H), 7.60 – 7.50 (m, 3H), 7.49 – 7.41 (m, 4H), 7.37 (ddd, *J* = 8.8, 5.1, 1.7 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.3, 153.5, 131.5, 130.1, 129.9, 129.1, 128.6, 128.5, 128.4, 126.0, 125.3, 123.4, 120.3, 111.2, 99.2, 96.8, 81.2. **HRMS** (EI) calcd for $C_{22}H_{14}O$ $[M]^+$: 294.10392, found: 294.10420. **IR** (ATR): ṽ = 3060, 2215, 1733, 1592, 1561, 1485, 1474, 1456, 1443, 1385, 1291, 1256, 1232, 1203, 1114, 1093, 1069, 1026, 1008, 915, 897, 827, 769, 742, 687, 665, 627. **M.p.** (amorphous): 81.3-82.6 °C.



3-(Naphthalen-1-ylethynyl)-2-phenylbenzofuran

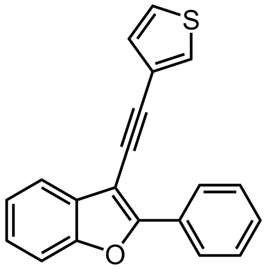
3p, light yellow solid, 66.9 mg, 97% yield. $R_f = 0.7$ (PE:EA = 10:1), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.2 Hz, 1H), 8.47

(d, *J* = 7.4 Hz, 2H), 8.00 – 7.84 (m, 4H), 7.71 – 7.50 (m, 6H), 7.49 – 7.35 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.4, 153.6, 133.3, 133.1, 130.5, 130.2, 130.0, 129.2, 128.9, 128.7, 128.4, 126.9, 126.5, 126.2, 126.1, 125.4, 125.3, 123.5, 121.0, 120.4, 111.3, 99.4, 95.0, 85.9. **HRMS** (EI) calcd for $C_{26}H_{16}O$ $[M]^+$: 344.11957, found: 344.11860. **IR** (ATR): ṽ = 3054, 2927, 2852, 2203, 1738, 1587, 1556, 1507, 1456, 1441, 1406, 1375, 1291, 1258, 1234, 1203, 1180, 1129, 1109, 1068, 1027, 1008, 897, 827, 793, 765, 744, 683, 657, 626. **M.p.** (amorphous):113.5-115.6 °C.



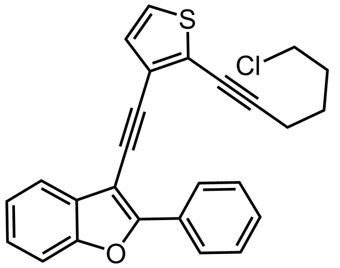
2-((2-Phenylbenzofuran-3-yl)ethynyl)pyridine

3q, light yellow oil, 59.9 mg, 97% yield. R_f = 0.6 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.5 Hz, 1H), 8.47 – 8.26 (m, 2H), 7.88 – 7.81 (m, 1H), 7.73 (td, *J* = 7.7, 1.6 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.57-7.52 (m, 3H), 7.48 – 7.33 (m, 3H), 7.31 – 7.24 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.4, 153.4, 150.1, 143.4, 136.1, 129.8, 129.6, 129.4, 128.7, 127.2, 126.1, 125.4, 123.5, 122.8, 120.5, 111.1, 98.3, 95.9, 81.3. **HRMS** (EI) calcd for $C_{21}H_{13}NO$ $[M]^+$: 295.09917, found: 295.09945. **IR** (Reflection): ṽ = 3058, 2220, 1733, 1579, 1560, 1496, 1460, 1443, 1427, 1386, 1339, 1292, 1249, 1202, 1150, 1123, 1090, 1070, 1045, 1027, 1006, 988, 917, 896, 829, 776, 746, 690, 624.



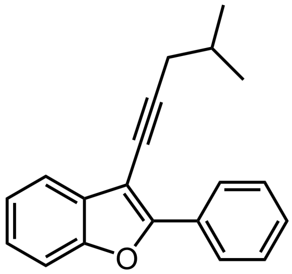
2-Phenyl-3-(thiophen-3-ylethynyl)benzofuran

3r, light yellow solid, 59.6 mg, 99% yield. R_f = 0.4 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.44 – 8.24 (m, 2H), 7.83 – 7.72 (m, 1H), 7.63 (dd, *J* = 2.9, 1.0 Hz, 1H), 7.58 – 7.48 (m, 3H), 7.46 – 7.40 (m, 1H), 7.39 – 7.30 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.2, 153.5, 130.1, 129.9, 129.8, 129.1, 128.7, 128.6, 125.9, 125.5, 125.3, 123.4 122.4, 120.3, 111.2, 99.1, 91.8, 80.6. **HRMS** (EI) calcd for $C_{20}H_{12}OS$ $[M]^+$: 300.06034, found: 300.05967. **IR** (Reflection): ṽ = 3108, 1731, 1590, 1487, 1455, 1441, 1352, 1290, 1256, 1226, 1202, 1184, 1109, 1093, 1068, 1027, 1007, 929, 914, 896, 870, 827, 777, 742, 720, 684, 621. **M.p.** (amorphous): 86.5-88.1 °C.



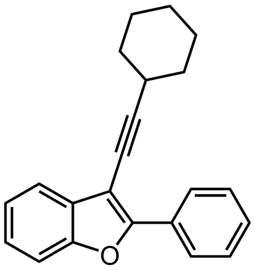
3-((2-(6-Chlorohex-1-yn-1-yl)thiophen-3-yl)ethynyl)-2-phenylbenzofuran

3s, yellow solid, 55.8 mg, 67% yield. R_f = 0.4 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.45 – 8.37 (m, 2H), 7.82 – 7.73 (m, 1H), 7.58 – 7.47 (m, 3H), 7.46 – 7.29 (m, 3H), 7.16 (dd, *J* = 12.2, 5.3 Hz, 2H), 3.44 (t, *J* = 6.4 Hz, 2H), 2.55 (t, *J* = 6.9 Hz, 2H), 1.95 – 1.84 (m, 2H), 1.73 (tt, *J* = 7.0, 3.8 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.2, 153.5, 130.1, 129.9, 129.1, 128.6, 127.1, 126.0, 125.9, 125.4, 125.1, 123.3, 120.3, 111.2, 99.1, 98.2, 91.5, 84.3, 73.8, 44.4, 31.5, 25.6, 19.3. **HRMS** (EI) calcd for $C_{26}H_{19}OSCl$ $[M]^+$: 414.08397, found: 414.07951. **IR** (ATR): ṽ = 3059, 2952, 2867, 2226, 2204, 1734, 1565, 1492, 1457, 1443, 1404, 1332, 1255, 1200, 1129, 1093, 1065, 1029, 910, 898, 831, 765, 733, 715, 682, 635. **M.p.** (amorphous): 80.1-82.2 °C.



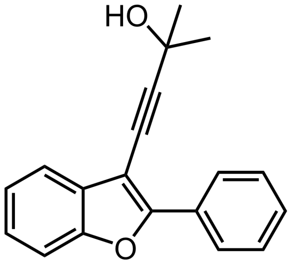
3-(4-Methylpent-1-yn-1-yl)-2-phenylbenzofuran

3t, light yellow oil, 35.4 mg, 65% yield. R_f = 0.4 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.37 – 8.22 (m, 2H), 7.75 – 7.64 (m, 1H), 7.48 (t, *J* = 7.9 Hz, 3H), 7.43 – 7.35 (m, 1H), 7.36 – 7.27 (m, 2H), 2.52 (d, *J* = 6.4 Hz, 2H), 2.04 (dp, *J* = 13.2, 6.6 Hz, 1H), 1.15 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.5, 153.4, 130.5, 130.4, 128.8, 128.5, 125.8, 125.1, 123.1, 120.3, 111.0, 99.8, 97.2, 72.8, 29.2, 28.3, 22.1. **HRMS** (EI) calcd for $C_{20}H_{18}O$ $[M]^+$: 274.13522, found: 274.13543. **IR** (Reflection): ṽ = 3063, 2926, 2869, 2227, 1946, 1892, 1736, 1682, 1592, 1562, 1495, 1456, 1443, 1426, 1383, 1368, 1339, 1291, 1276, 1257, 1205, 1164, 1107, 1089, 1067, 1028, 1006, 968, 916, 896, 826, 768, 747, 690, 625.



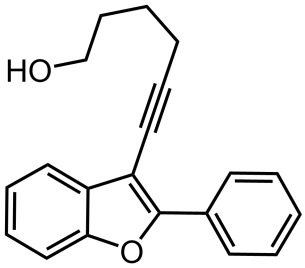
3-(Cyclohexylethynyl)-2-phenylbenzofuran

3u, light yellow oil, 45.9 mg, 76% yield. R_f = 0.4 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.42 – 8.17 (m, 2H), 7.73 – 7.60 (m, 1H), 7.52 – 7.47 (m, 3H), 7.43 – 7.36 (m, 1H), 7.37 – 7.27 (m, 2H), 2.93 – 2.73 (m, 1H), 2.09 – 1.95 (m, 2H), 1.87 (dt, *J* = 9.9, 6.2 Hz, 2H), 1.78 – 1.56 (m, 3H), 1.54 – 1.41 (m, 3H). **^{13}C NMR** (75MHz, $CDCl_3$) δ 155.4, 153.4, 130.4, 130.4, 128.7, 128.5, 125.7, 125.1, 123.1, 120.3, 111.0, 102.3, 99.9, 72.0, 32.7, 30.1, 25.9, 24.8. **HRMS** (EI) calcd for $C_{22}H_{20}O$ $[M]^+$: 300.15087, found: 300.15252. **IR** (Reflection): ṽ = 3063, 2936, 2853, 2662, 2223, 1947, 1892, 1735, 1681, 1593, 1562, 1494, 1475, 1444, 1383, 1349, 1314, 1290, 1256, 1233, 1205, 1166, 1132, 1109, 1066, 1028, 1006, 936, 915, 895, 860, 827, 769, 751, 689, 624.



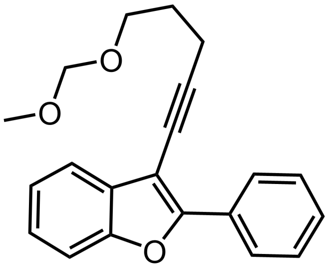
2-Methyl-4-(2-phenylbenzofuran-3-yl)but-3-yn-2-ol

3v, colorless solid, 53.5 mg, 97% yield. R_f = 0.2 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.33-8.18 (m, 2H), 7.71-7.61 (m, 1H), 7.51-7.46 (m, 3H), 7.44-7.37 (m, 1H), 7.37-7.27 (m, 2H), 2.32 (br, 1H), 1.75 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.3, 153.4, 130.0, 129.8, 129.1, 128.6, 125.8, 125.3, 123.3, 120.1, 111.1, 101.3, 98.5, 74.1, 66.0, 31.5. **HRMS** (EI) calcd for $C_{19}H_{16}O_2$ $[M]^+$: 276.11448, found: 276.11453. **IR** (ATR): ṽ = 3198, 2982, 2931, 2226, 1738, 1494, 1455, 1442, 1407, 1378, 1361, 1292, 1256, 1227, 1202, 1159, 1138, 1095, 1066, 1030, 1008, 961, 911, 897, 826, 776, 766, 737, 683, 625. **M.p.** (crystal) 87.5-89.3 °C.



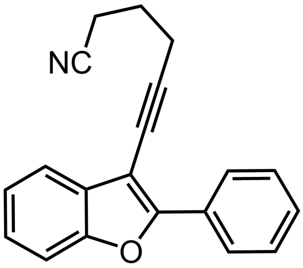
6-(2-Phenylbenzofuran-3-yl)hex-5-yn-1-ol

3w, light yellow oil, 47.0 mg, 81% yield. R_f = 0.2 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.36 – 8.21 (m, 2H), 7.73 – 7.57 (m, 1H), 7.53 – 7.45 (m, 3H), 7.43 – 7.36 (m, 1H), 7.31 (pd, *J* = 7.2, 1.4 Hz, 2H), 3.76 (t, *J* = 5.8 Hz, 2H), 2.66 (t, *J* = 6.5 Hz, 2H), 1.93 – 1.75 (m, 4H), 1.62 (br, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.6, 153.4, 130.4, 130.3, 128.8, 128.5, 125.7, 125.1, 123.1, 120.2, 111.0, 99.6, 97.6, 72.4, 62.4, 31.9, 25.1, 19.8. **HRMS** (EI) calcd for $C_{20}H_{18}O_2$ $[M]^+$: 290.13013, found: 290.13023. **IR** (Reflection): ṽ = 3353, 3062, 2935, 2864, 2226, 1894, 1733, 1592, 1562, 1494, 1475, 1455, 1443, 1381, 1339, 1290, 1257, 1204, 1165, 1108, 1067, 1029, 1007, 983, 917, 895, 826, 769, 745, 690, 624.



3-(4-(Methoxymethoxy)but-1-yn-1-yl)-2-phenylbenzofuran

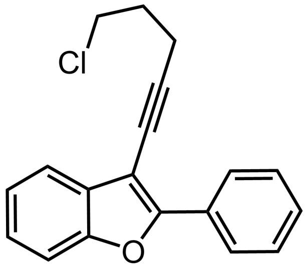
3x, light yellow oil, 39.8 mg, 65% yield. R_f = 0.4 (PE:DCM = 2:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.5 Hz, 2H), 7.72 – 7.62 (m, 1H), 7.51 – 7.46 (m, 3H), 7.43 – 7.36 (m, 1H), 7.38 – 7.26 (m, 2H), 4.75 (s, 2H), 3.87 (t, *J* = 6.8 Hz, 2H), 3.42 (s, 3H), 2.92 (t, *J* = 6.8 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.9, 153.3, 130.3, 130.2, 128.9, 128.5, 125.8, 125.1, 123.2, 120.2, 111.1, 99.3, 96.6, 94.6, 73.1, 66.2, 55.4, 21.6. **HRMS** (EI) calcd for $C_{20}H_{18}O_3$ $[M]^+$: 306.12505, found: 306.12633. **IR** (Reflection): ṽ = 3062, 2931, 2883, 2822, 2768, 2231, 1947, 1895, 1733, 1683, 1592, 1562, 1495, 1475, 1456, 1443, 1381, 1335, 1291, 1257, 1205, 1150, 1112, 1071, 1030, 1006, 989, 968, 918, 895, 876, 826, 770, 749, 691, 624.



6-(2-Phenylbenzofuran-3-yl)hex-5-ynenitrile

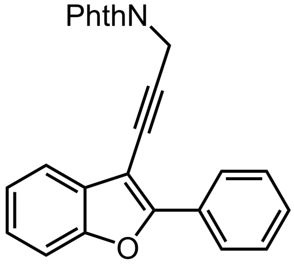
3y, light yellow oil, 47.4 mg, 83% yield. R_f = 0.3 (DCM), chromatography eluent: Dichloromethane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 – 8.17 (m, 2H), 7.68 – 7.60 (m, 1H), 7.57 – 7.47 (m, 3H), 7.45 – 7.38 (m, 1H), 7.38 – 7.27 (m, 2H), 2.81 (t, *J* = 6.8 Hz, 2H), 2.63 (t, *J* = 7.1 Hz, 2H), 2.06 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.1, 153.3, 130.1, 129.1, 128.6, 125.7, 125.3, 123.3, 120.0, 119.0, 111.1, 98.9, 94.5, 74.1, 24.6, 19.0, 16.2. **HRMS** (EI) calcd for $C_{20}H_{15}NO$ $[M]^+$: 285.11482, found:

285.11462. **IR** (Reflection): ṽ = 3062, 2940, 2836, 2248, 1732, 1683, 1592, 1562, 1493, 1475, 1455, 1443, 1429, 1381, 1341, 1290, 1257, 1204, 1165, 1108, 1068, 1028, 1006, 917, 895, 826, 770, 746, 690, 624.



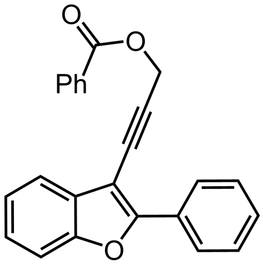
3-(5-Chloropent-1-yn-1-yl)-2-phenylbenzofuran

3z, light yellow oil, 46.1 mg, 78% yield. R_f = 0.6 (PE:EA = 10:1), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 – 8.22 (m, 2H), 7.68 – 7.59 (m, 1H), 7.52 – 7.46 (m, 3H), 7.40 (ddd, *J* = 7.4, 3.8, 1.1 Hz, 1H), 7.36 – 7.27 (m, 2H), 3.81 (t, *J* = 6.3 Hz, 2H), 2.82 (t, *J* = 6.8 Hz, 2H), 2.17 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.0, 153.4, 130.3, 130.2, 129.0, 128.6, 125.8, 125.2, 123.2, 120.2, 111.1, 99.3, 95.7, 73.2, 43.7, 31.4, 17.4. **HRMS** (EI) calcd for $C_{19}H_{15}OCl$ $[M]^+$: 294.08059, found: 294.08058. **IR** (Reflection): ṽ = 3062, 2958, 2840, 2231, 1755, 1592, 1562, 1495, 1475, 1455, 1442, 1382, 1341, 1289, 1257, 1204, 1166, 1108, 1067, 1028, 1006, 949, 914, 895, 850, 826, 769, 746, 690, 666, 624.



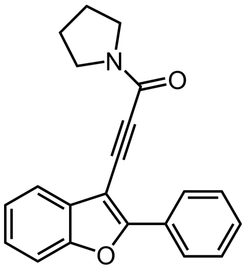
2-(3-(2-Phenylbenzofuran-3-yl)prop-2-yn-1-yl)isoindoline-1,3-dione

3aa, colorless solid, 70.6 mg, 94% yield. R_f = 0.2 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.89 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.74 – 7.68 (m, 2H), 7.68 – 7.64 (m, 1H), 7.50 – 7.44 (m, 3H), 7.41 – 7.35 (m, 1H), 7.29 (tdd, *J* = 12.1, 7.1, 1.3 Hz, 2H), 4.85 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.0, 157.1, 153.3, 134.1, 132.0, 129.8, 129.7, 129.2, 128.6, 125.9, 125.2, 123.5, 123.4, 120.3, 111.0, 98.1, 90.4, 75.2, 28.3. **HRMS** (EI) calcd for $C_{25}H_{15}NO_3$ $[M]^+$: 377.10464, found: 377.10430. **IR** (ATR): ṽ = 2227, 1770, 1703, 1612, 1457, 1444, 1418, 1396, 1380, 1336, 1307, 1257, 1205, 1168, 1113, 1089, 1069, 1028, 938, 826, 797, 770, 745, 723, 708, 685, 625. **M.p.** (amorphous): 149.4-150.9 °C.



3-(2-Phenylbenzofuran-3-yl)prop-2-yn-1-yl benzoate

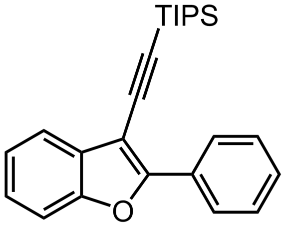
3ab, light yellow solid, 55.4 mg, 79% yield. R_f = 0.4 (PE:EA = 10:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.37 – 8.24 (m, 2H), 8.24 – 8.11 (m, 2H), 7.75 – 7.68 (m, 1H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.55 – 7.45 (m, 5H), 7.44 – 7.38 (m, 1H), 7.38 – 7.28 (m, 2H), 5.34 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.9, 157.3, 153.3, 133.3, 129.8, 129.6, 129.3, 128.6, 128.4, 126.0, 125.3, 123.4, 120.3, 111.2, 98.1, 90.7, 78.7, 53.6. **HRMS** (EI) calcd for $C_{24}H_{16}O_3$ $[M]^+$: 352.10940, found: 352.10974. **IR** (ATR): ṽ = 3059, 2928, 2236, 1720, 1601, 1492, 1454, 1389, 1359, 1315, 1266, 1204, 1171, 1109, 1068, 1026, 963, 936, 920, 895, 854, 826, 769, 748, 706, 689, 659, 627. **M.p.** (amorphous): 61.7-63.0 °C.



3-(2-Phenylbenzofuran-3-yl)-1-(pyrrolidin-1-yl)prop-2-yn-1-one

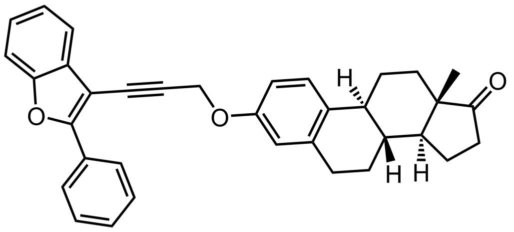
3ac, light yellow solid, 62.5 mg, 99% yield. R_f = 0.4 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.1 Hz, 2H), 7.72 – 7.63 (m, 1H), 7.57 – 7.39 (m, 4H), 7.38 – 7.29 (m, 2H), 3.80 (t, *J* = 6.4 Hz, 2H), 3.58 (t, *J* = 6.4 Hz, 2H), 2.13 – 1.84 (m, 4H). **^{13}C NMR** (75 MHz,

$CDCl_3$) δ 158.9, 153.4, 152.5, 129.9, 129.3, 129.3, 128.7, 126.3, 125.6, 123.7, 120.2, 111.3, 96.7, 90.1, 81.0, 48.1, 45.4, 25.4, 24.6. **IR** (ATR): ṽ = 2966, 2879, 2203, 1625, 1603, 1558, 1443, 1413, 1370, 1335, 1290, 1256, 1199, 1157, 1068, 1029, 1006, 910, 826, 756, 741, 719, 706, 680, 620. **HRMS** (EI) calcd for $C_{21}H_{17}NO_2$ $[M]^+$: 315.12538, found: 315.12457. **M.p.** (amorphous): 158.1-159.8 °C.



Triisopropyl((2-phenylbenzofuran-3-yl)ethynyl)silane

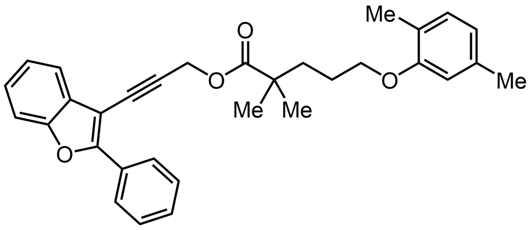
3ad, light yellow solid, 46.8 mg, 63% yield. R_f = 0.6 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.3 Hz, 2H), 7.73 – 7.64 (m, 1H), 7.53 – 7.40 (m, 4H), 7.39 – 7.28 (m, 2H), 1.24 (s, 21H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.8, 153.3, 130.3, 130.1, 129.1, 128.5, 126.0, 125.3, 123.4, 120.3, 111.1, 99.6, 99.6, 98.3, 18.7, 11.4. **HRMS** (EI) calcd for $C_{25}H_{30}OSi$ $[M]^+$: 374.20604, found: 374.20685. **IR** (ATR): ṽ = 3066, 2941, 2889, 2863, 2158, 1458, 1442, 1366, 1291, 1257, 1203, 1135, 1096, 1072, 1018, 995, 914, 883, 828, 767, 741, 681, 633. **M.p.** (amorphous): 59.2-60.4 °C.



***(8R,9S,13S,14S)*-13-Methyl-3-((3-(2-phenylbenzofuran-3-yl)prop-2-yn-1-yl)oxy)-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one**

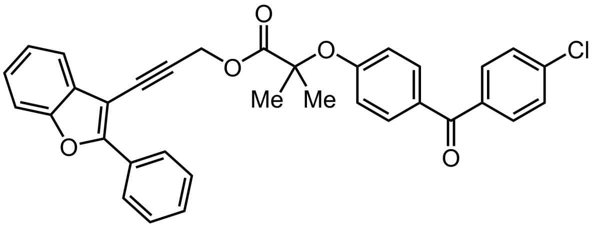
3ae, colorless solid, 51.5 mg, 53% yield. R_f = 0.2 (PE:DCM = 1:2), chromatography eluent: 50% Petroleum ether in dichlormethan. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.22 – 8.04 (m, 2H), 7.66 – 7.55 (m, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.42 – 7.33 (m, 3H), 7.32 – 7.22 (m, 3H), 6.91 (dd, *J* = 8.6, 2.7 Hz, 1H), 6.84 (d, *J* = 2.5 Hz, 1H), 5.05 (s, 2H), 3.04 – 2.78 (m, 2H), 2.49 (dd, *J* = 18.4, 8.2 Hz, 1H), 2.43 – 2.35 (m, 1H), 2.28 (dd, *J* = 18.8, 9.5 Hz, 1H), 2.14 (dd, *J* = 18.0, 9.2 Hz, 1H), 2.09 – 1.92 (m, 3H), 1.71 – 1.32

(m, 6H), 0.90 (s, 3H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 220.8, 156.9, 155.7, 153.4, 137.8, 132.9, 129.9, 129.8, 129.2, 128.6, 126.4, 126.0, 125.3, 123.4, 120.2, 115.2, 112.8, 111.2, 98.2, 91.9, 79.0, 56.7, 50.4, 48.0, 44.0, 38.3, 35.8, 31.6, 29.7, 26.5, 25.9, 21.6, 13.8. **HRMS** (EI) calcd for $C_{35}H_{32}O_3$ $[M]^+$: 500.23460, found: 500.23406. **IR** (Reflection): ṽ = 3453, 3286, 3060, 2929, 2862, 2249, 2225, 2120, 1737, 1608, 1576, 1498, 1455, 1405, 1374, 1340, 1307, 1281, 1256, 1231, 1187, 1163, 1101, 1084, 1055, 1030, 1008, 965, 912, 871, 844, 818, 771, 732, 691, 648. **M.p.** (amorphous): 74.1-75.3 °C.



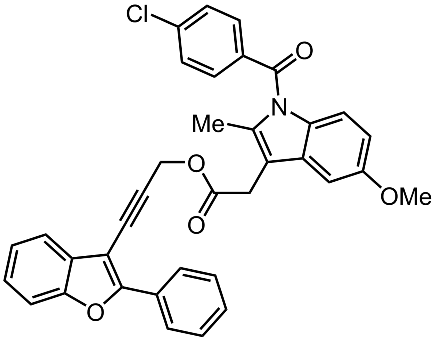
3-(2-Phenylbenzofuran-3-yl)prop-2-yn-1-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate

3af, light yellow oil, 87.3 mg, 91% yield. R$_f$ = 0.2 (PE:DCM = 5:1), chromatography eluent: 25% Dichlormethan in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.29 (d, *J* = 7.5 Hz, 2H), 7.75 – 7.62 (m, 1H), 7.51 (t, *J* = 7.5 Hz, 3H), 7.45 – 7.38 (m, 1H), 7.33 (dq, *J* = 7.3, 6.3 Hz, 2H), 7.00 (d, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.56 (s, 1H), 5.10 (s, 2H), 3.90 (t, *J* = 2.9 Hz, 2H), 2.30 (s, 3H), 2.16 (s, 3H), 1.83 (s, 4H), 1.34 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 177.1, 157.1, 156.8, 153.3, 136.3, 130.2, 129.8, 129.3, 128.6, 126.0, 125.3, 123.5, 123.4, 120.6, 120.2, 111.8, 111.1, 98.1, 91.0, 78.2, 67.7, 60.3, 53.0, 42.2, 37.1, 25.12, 25.10, 21.3, 15.7. **HRMS** (EI) calcd for $C_{32}H_{32}O_4$ $[M]^+$: 480.22951, found: 480.23130. **IR** (Reflection): ṽ = 3057, 2950, 2924, 2870, 2229, 1735, 1614, 1585, 1509, 1473, 1456, 1443, 1388, 1311, 1263, 1203, 1186, 1157, 1129, 1068, 1047, 983, 934, 895, 845, 826, 803, 770, 745, 689, 625.



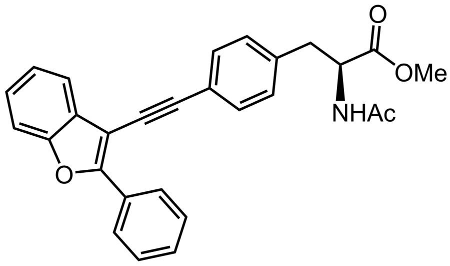
3-(2-Phenylbenzofuran-3-yl)prop-2-yn-1-yl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate

3ag, light yellow oil, 65.4 mg, 60% yield. R_f = 0.4 (PE:DCM = 1:2), chromatography eluent: 5% Petroleum ether in dichlormethan. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.26 – 8.15 (m, 2H), 7.64 – 7.59 (m, 1H), 7.59 – 7.50 (m, 5H), 7.47 (t, *J* = 7.3 Hz, 2H), 7.39 (dd, *J* = 8.8, 4.2 Hz, 1H), 7.37 – 7.24 (m, 4H), 6.92 (d, *J* = 8.8 Hz, 2H), 5.20 (s, 2H), 1.77 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 193.9, 173.1, 159.2, 157.4, 153.3, 138.1, 136.1, 132.0, 130.9, 130.4, 129.6, 129.5, 128.7, 128.3, 125.9, 125.5, 123.5, 120.0, 117.4, 111.3, 97.7, 89.9, 79.3, 79.0, 54.0, 25.4. **HRMS** (EI) calcd for $C_{34}H_{25}O_5Cl$ $[M]^+$: 548.13850, found: 548.14040. **IR** (Reflection): ṽ = 3064, 2994, 2940, 2229, 1741, 1654, 1598, 1504, 1487, 1456, 1443, 1386, 1363, 1303, 1276, 1249, 1202, 1170, 1130, 1090, 1069, 1014, 965, 927, 852, 837, 791, 746, 689, 664, 625.



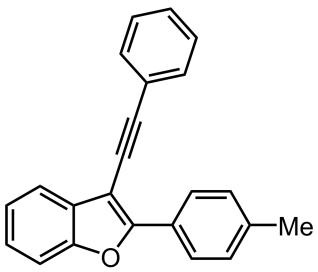
3-(2-Phenylbenzofuran-3-yl)prop-2-yn-1-yl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate

3ah, light yellow solid, 79.6 mg, 68% yield. R_f = 0.6 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.23 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.65 – 7.57 (m, 3H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.37 (m, 5H), 7.36 – 7.31 (m, 1H), 7.31 – 7.25 (m, 1H), 7.02 (d, *J* = 2.5 Hz, 1H), 6.88 (d, *J* = 9.0 Hz, 1H), 6.66 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.11 (s, 2H), 3.79 (s, 2H), 3.75 (s, 3H), 2.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 168.2, 157.2, 156.1, 153.3, 139.2, 136.0, 133.8, 131.1, 130.8, 130.5, 129.8, 129.7, 129.4, 129.0, 128.6, 125.9, 125.4, 123.5, 120.1, 114.9, 112.1, 111.7, 111.2, 101.2, 97.9, 90.5, 78.7, 55.6, 53.6, 30.2, 13.4. **HRMS** (EI) calcd for $C_{36}H_{26}NO_5Cl$ $[M]^+$: 587.14940, found: 587.14793. **IR** (ATR): ṽ = 2925, 2230, 1733, 1668, 1610, 1477, 1457, 1444, 1398, 1374, 1354, 1320, 1289, 1235, 1215, 1166, 1152, 1089, 1072, 1036, 1025, 1014, 992, 954, 913, 868, 847, 826, 806, 774, 753, 692, 662, 627. **M.p.** (amorphous): 153.5-154.4 °C.



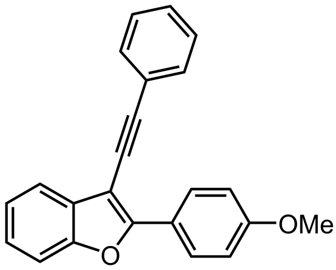
Methyl (*S*)-2-acetamido-3-(4-((2-phenylbenzofuran-3-yl)ethynyl)phenyl)propanoate

3ai, light yellow solid, 65.2 mg, 75% yield. R_f = 0.3 (DCM:EA = 2:1), chromatography eluent: 50% Ethyl acetate in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.82 – 7.68 (m, 1H), 7.58 – 7.47 (m, 5H), 7.45 – 7.39 (m, 1H), 7.38 – 7.29 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.08 (s, 1H), 4.93 (dd, *J* = 13.5, 5.8 Hz, 1H), 3.76 (s, 3H), 3.21 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.13 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.02 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.9, 169.6, 156.3, 153.5, 136.4, 131.6, 130.1, 129.8, 129.4, 129.1, 128.6, 126.0, 125.3, 123.3, 122.2, 120.3, 111.2, 99.1, 96.4, 81.4, 53.0, 52.4, 37.8, 23.1. **HRMS** (EI) calcd for $C_{28}H_{23}NO_4$ $[M]^+$: 437.16216, found: 437.16488. **IR** (ATR): ṽ = 3289, 2953, 2207, 1741, 1649, 1540, 1512, 1490, 1455, 1373, 1351, 1297, 1255, 1216, 1168, 1111, 1069, 1052, 1028, 1007, 959, 913, 828, 771, 744, 686, 625, 615. **M.p.** (amorphous): 155.4-158.8 °C.



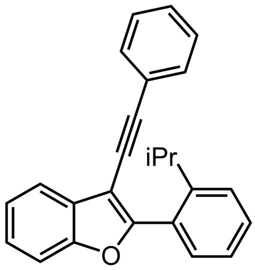
3-(Phenylethynyl)-2-(*p*-tolyl)benzofuran

3aj, colorless solid, 55.9 mg, 91% yield. $R_f = 0.6$ (PE:EA = 20:1), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.8 Hz, 2H), 7.78 (dd, *J* = 7.1, 0.5 Hz, 1H), 7.66 (d, *J* = 6.7 Hz, 2H), 7.55 (dd, *J* = 4.5, 4.0 Hz, 1H), 7.47 – 7.40 (m, 3H), 7.39 – 7.33 (m, 4H), 2.45 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.7, 153.4, 139.3, 131.5, 130.0, 129.4, 128.4, 128.3, 127.4, 126.0, 125.1, 123.5, 123.3, 120.2, 111.1, 98.4, 96.5, 81.4, 21.5. **HRMS** (EI) calcd for $C_{23}H_{16}O$ $[M]^+$: 308.11957, found: 308.11975. **IR** (ATR): ṽ = 3061, 3031, 2920, 2859, 2215, 1609, 1587, 1510, 1487, 1474, 1453, 1388, 1341, 1291, 1255, 1231, 1202, 1188, 1098, 1068, 1018, 909, 896, 835, 818, 785, 751, 737, 687, 667, 654, 608. **M.p.** (amorphous): 118.7-119.9 °C.



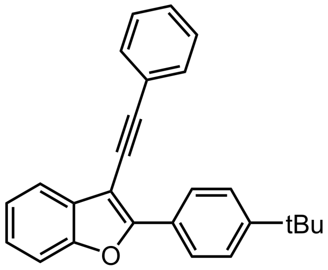
2-(4-Methoxyphenyl)-3-(phenylethynyl)benzofuran

3ak, light yellow solid, 45.7 mg, 70% yield. $R_f = 0.4$ (PE:DCM = 10:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.31 (d, *J* = 8.9 Hz, 2H), 7.74 (dd, *J* = 6.0, 3.0 Hz, 1H), 7.64 (dd, *J* = 7.4, 2.0 Hz, 2H), 7.55 – 7.48 (m, 1H), 7.47 – 7.37 (m, 3H), 7.37 – 7.28 (m, 2H), 7.04 (d, *J* = 9.0 Hz, 2H), 3.89 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.4, 156.6, 153.3, 131.5, 130.1, 128.4, 128.3, 127.6, 124.8, 123.5, 123.3, 123.0, 120.0, 114.1, 111.0, 97.4, 96.2, 81.5, 55.3. **HRMS** (EI) calcd for $C_{23}H_{16}O_2$ $[M]^+$: 324.11448, found: 324.11613. **IR** (ATR): ṽ = 2213, 1456, 1403, 1357, 1279, 1249, 1201, 1171, 1129, 1119, 1095, 1023, 905, 889, 847, 829, 783, 740, 682, 629, 607. **M.p.** (amorphous): 103.6-105.7 °C.



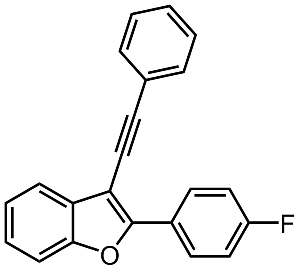
2-(2-Isopropylphenyl)-3-(phenylethynyl)benzofuran

3al, colorless oil, 62.9 mg, 94% yield. R_f = 0.7 (PE:EA = 10:1), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 – 7.82 (m, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.59 – 7.55 (m, 1H), 7.54 – 7.47 (m, 4H), 7.42 – 7.39 (m, 2H), 7.38 – 7.32 (m, 4H), 3.46 (dt, *J* = 13.6, 6.8 Hz, 1H), 1.33 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.0, 153.9, 148.8, 131.5, 130.8, 130.1, 129.2, 128.4, 128.3, 128.2, 126.0, 125.5, 125.0, 123.4, 123.3, 120.4, 111.3, 101.9, 94.8, 80.5, 30.4, 24.2. **HRMS** (EI) calcd for $C_{25}H_{20}O$ $[M]^+$: 336.15087, found: 336.15175. **IR** (Reflection): ṽ = 3061, 2964, 2928, 2868, 2219, 1755, 1587, 1493, 1452, 1384, 1363, 1293, 1273, 1253, 1231, 1196, 1160, 1099, 1069, 1050, 1028, 1007, 903, 828, 811, 747, 689, 660, 626.



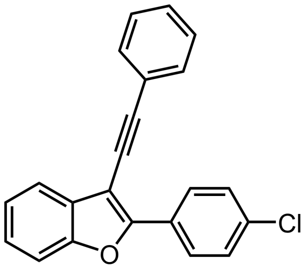
2-(4-(*tert*-Butyl)phenyl)-3-(phenylethynyl)benzofuran

3am, light yellow oil, 53.6 mg, 77% yield. R_f = 0.4 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.4 Hz, 2H), 7.78 (dd, *J* = 4.8, 3.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.58 – 7.53 (m, 3H), 7.48 – 7.38 (m, 3H), 7.38 – 7.30 (m, 2H), 1.41 (s, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.6, 153.4, 152.5, 131.5, 130.0, 128.4, 128.3, 127.4, 125.8, 125.6, 125.1, 123.5, 123.3, 120.2, 111.1, 98.5, 96.5, 81.4, 34.9, 31.2. **HRMS** (EI) calcd for $C_{26}H_{22}O$ $[M]^+$: 350.16652, found: 350.16500. **IR** (Reflection): ṽ = 3062, 2961, 2903, 2867, 2216, 1755, 1579, 1513, 1487, 1474, 1453, 1409, 1387, 1363, 1293, 1268, 1256, 1231, 1204, 1108, 1095, 1069, 1014, 897, 836, 746, 688.



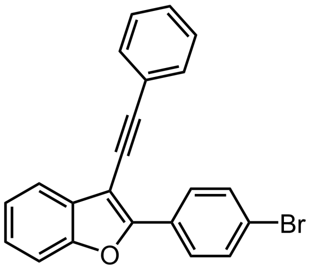
2-(4-Fluorophenyl)-3-(phenylethynyl)benzofuran

3an, colorless solid, 60.9 mg, 98% yield. $R_f = 0.6$ (PE:DCM = 10:1), chromatography eluent: 5% Dichlormethan in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 – 8.27 (m, 2H), 7.83 – 7.73 (m, 1H), 7.69 – 7.60 (m, 2H), 7.57 – 7.49 (m, 1H), 7.49 – 7.40 (m, 3H), 7.40 – 7.32 (m, 2H), 7.25 – 7.16 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 163.0 (d, *J* = 250.3 Hz), 155.4 (d, *J* = 1.0 Hz), 153.4, 131.5, 129.8, 128.5, 129.0 (d, *J* = 8.3 Hz), 126.5(d, *J* = 3.3 Hz), 125.3, 123.4, 123.2, 120.3, 115.9, 115.6, 111.1, 98.9 (d, *J* = 1.6 Hz), 96.7, 81.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -110.67. **HRMS** (EI) calcd for $C_{22}H_{13}OF$ $[M]^+$: 312.09449, found: 312.09563. **IR** (ATR): ṽ = 3064, 2925, 2853, 2216, 1893, 1595, 1570, 1507, 1488, 1475, 1453, 1411, 1388, 1342, 1290, 1255, 1229, 1201, 1161, 1116, 1093, 1012, 896, 836, 798, 755, 741, 689, 668, 629, 606. **M.p.** (amorphous): 99.8-101.5 °C.



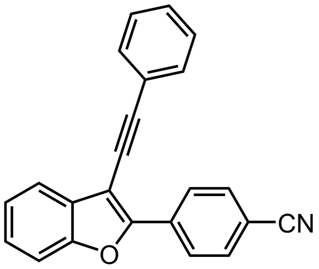
2-(4-Chlorophenyl)-3-(phenylethynyl)benzofuran

3ao, light yellow solid, 53.6 mg, 82% yield. $R_f = 0.4$ (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.38 – 8.21 (m, 2H), 7.79 – 7.72 (m, 1H), 7.63 (dd, *J* = 6.5, 3.2 Hz, 2H), 7.55 – 7.39 (m, 6H), 7.38 – 7.30 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.1, 153.5, 134.9, 131.5, 129.7, 128.9, 128.6, 128.6, 128.5, 127.2, 125.6, 123.5, 123.1, 120.4, 111.2, 99.7, 97.2, 80.9. **HRMS** (EI) calcd for $C_{22}H_{13}OCl$ $[M]^+$: 336.15087, found: 336.15175. **IR** (ATR): ṽ = 3056, 3035, 2219, 1925, 1898, 1734, 1645, 1577, 1496, 1483, 1453, 1405, 1387, 1343, 1308, 1293, 1256, 1234, 1202, 1182, 1124, 1114, 1092, 1071, 1012, 925, 895, 825, 738, 726, 684, 669, 642, 625. **M.p.** (amorphous): 132.1-133.7 °C.



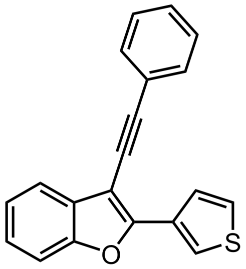
2-(4-Bromophenyl)-3-(phenylethynyl)benzofuran

3ap, colorless solid, 65.2 mg, 88% yield. $R_f = 0.6$ (PE:DCM = 10:1), chromatography eluent: 5% Dichlormethan in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.6 Hz, 2H), 7.75 (dd, *J* = 6.5, 2.3 Hz, 1H), 7.67 – 7.58 (m, 4H), 7.51 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.38 – 7.31 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.1, 153.5, 131.8, 131.5, 129.7, 129.0, 128.6, 128.5, 127.3, 125.6, 123.5, 123.2, 123.1, 120.4, 111.2, 99.8, 97.3, 80.9. **HRMS** (EI) calcd for $C_{22}H_{13}OBr$ $[M]^+$: 372.01443, found: 372.01255. **IR** (ATR): ṽ = 3054, 3036, 2925, 2854, 2219, 1898, 1737, 1574, 1553, 1494, 1483, 1452, 1401, 1386, 1342, 1293, 1256, 1234, 1201, 1182, 1156, 1124, 1094, 1071, 1009, 925, 894, 848, 822, 751, 738, 709, 685, 667, 638. **M.p.** (amorphous): 139.6-141.1°C.



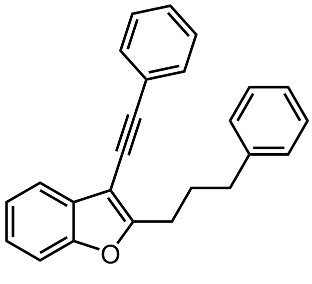
4-(3-(Phenylethynyl)benzofuran-2-yl)benzonitrile

3aq, light yellow solid, 46.7 mg, 73% yield. $R_f = 0.3$ (PE:DCM = 2:1), chromatography eluent: 50% Petroleum ether in dichlormethan. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.6 Hz, 2H), 7.79 – 7.73 (m, 3H), 7.67 – 7.59 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.42 (m, 3H), 7.40 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.35 (td, *J* = 7.4, 1.1 Hz, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 153.8, 153.5, 134.0, 132.4, 131.6, 129.5, 128.9, 128.6, 126.5, 125.9, 123.8, 122.7, 120.8, 118.7, 111.8, 111.4, 102.3, 98.5, 80.3. **HRMS** (EI) calcd for $C_{23}H_{13}NO$ [M]$^+$: 319.09917, found: 319.09744. **IR** (ATR): ṽ = 3047, 2925, 2224, 1730, 1604, 1573, 1546, 1487, 1474, 1450, 1412, 1342, 1293, 1256, 1234, 1203, 1172, 1095, 1073, 1033, 1016, 910, 897, 840, 813, 756, 738, 684, 647, 614. **M.p.** (amorphous): 175.2-176.7 °C.



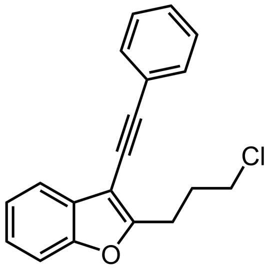
3-(Phenylethynyl)-2-(thiophen-3-yl)benzofuran

3ar, light yellow solid, 52.5 mg, 87% yield. R$_f$ = 0.4 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.24 – 8.13 (m, 1H), 8.00 (d, *J* = 5.1 Hz, 1H), 7.82 – 7.73 (m, 1H), 7.66 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.52 (dd, *J* = 5.7, 3.3 Hz, 1H), 7.48 – 7.40 (m, 4H), 7.39 – 7.30 (m, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 153.8, 153.3, 131.6, 131.5, 129.5, 128.5, 128.4, 126.2, 125.6, 125.1, 123.7, 123.4, 123.3, 120.2, 111.1, 98.2, 96.6, 81.0. **HRMS** (EI) calcd for $C_{20}H_{12}OS$ [M]$^+$: 300.06034, found: 300.06066. **IR** (ATR): ṽ = 3104, 2208, 1588, 1487, 1474, 1454, 1351, 1285, 1263, 1239, 1203, 1190, 1097, 1008, 925, 906, 868, 832, 784, 767, 742, 685, 661, 643. **M.p.** (amorphous): 111.5-112.4 °C.



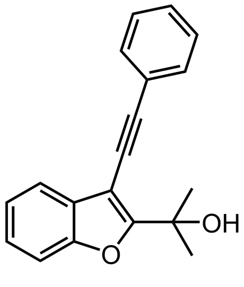
3-(Phenylethynyl)-2-(3-phenylpropyl)benzofuran

3as, light yellow oil, 50.6 mg, 75% yield. R$_f$ = 0.3 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.76 – 7.65 (m, 1H), 7.63 – 7.53 (m, 2H), 7.51 – 7.45 (m, 1H), 7.44 – 7.36 (m, 3H), 7.36 – 7.18 (m, 7H), 3.03 (t, *J* = 7.3 Hz, 2H), 2.78 (t, *J* = 7.6 Hz, 2H), 2.22 (p, *J* = 7.5 Hz, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 162.3, 153.8, 141.6, 131.4, 128.7, 128.6, 128.3, 128.1, 125.9, 124.2, 123.5, 123.1, 119.8, 111.0, 100.4, 94.8, 79.9, 35.1, 29.2, 27.1. **HRMS** (EI) calcd for $C_{25}H_{20}O$ $[M]^+$: 336.15087, found: 336.15110. **IR** (Reflection): ṽ = 3061, 3027, 2932, 2860, 2219, 1945, 1891, 1732, 1588, 1491, 1475, 1454, 1387, 1324, 1277, 1235, 1177, 1108, 1090, 1071, 1028, 1008, 928, 867, 846, 811, 746, 690, 652.



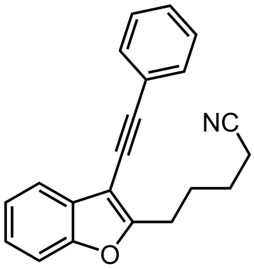
2-(3-Chloropropyl)-3-(phenylethynyl)benzofuran

3at, light yellow oil, 48.8 mg, 83% yield. R$_f$ = 0.4 (PE:DCM = 20:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.72 – 7.65 (m, 1H), 7.63 – 7.56 (m, 2H), 7.49 – 7.43 (m, 1H), 7.42 – 7.35 (m, 3H), 7.35 – 7.28 (m, 2H), 3.67 (t, *J* = 6.5 Hz, 2H), 3.18 (t, *J* = 7.2 Hz, 2H), 2.33 (p, *J* = 6.8 Hz, 2H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 160.7, 153.8, 131.5, 128.6, 128.4, 128.2, 124.5, 123.3, 123.2, 120.0, 111.0, 101.0, 95.1, 79.4, 44.0, 30.6, 25.0. **HRMS** (EI) calcd for $C_{19}H_{15}OCl$ $[M]^+$: 294.08059, found: 294.08011. **IR** (Reflection): ṽ = 3060, 2959, 2923, 2869, 2220, 1946, 1895, 1733, 1589, 1491, 1475, 1454, 1443, 1387, 1276, 1235, 1177, 1108, 1087, 1069, 1028, 1008, 971, 929, 916, 867, 842, 810, 747, 690, 652.



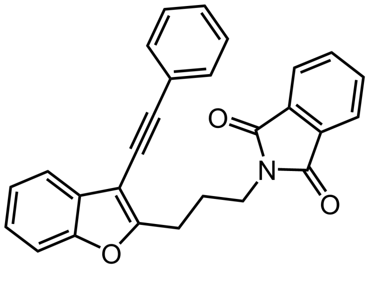
2-(3-(Phenylethynyl)benzofuran-2-yl)propan-2-ol

3au, light yellow oil, 25.6 mg, 46% yield (unstable). R$_f$ = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.76 – 7.67 (m, 1H), 7.56 (dd, *J* = 6.5, 3.2 Hz, 2H), 7.51 – 7.44 (m, 1H), 7.41 – 7.35 (m, 3H), 7.35 – 7.29 (m, 2H), 2.54 (br, 1H), 1.82 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 164.2, 153.1, 131.4, 129.1, 128.44, 128.43, 125.0, 123.3, 123.1, 120.3, 111.2, 98.0, 96.3, 79.5, 71.1, 29.0. **HRMS** (EI) calcd for $C_{19}H_{16}O_2$ [M]$^+$: 276.11448, found: 276.11475. **IR** (Reflection): ṽ = 3450, 3061, 2981, 2929, 2218, 1805, 1730, 1597, 1490, 1475, 1454, 1382, 1334, 1259, 1236, 1132, 1109, 1081, 1007, 960, 912, 865, 806, 748, 690.



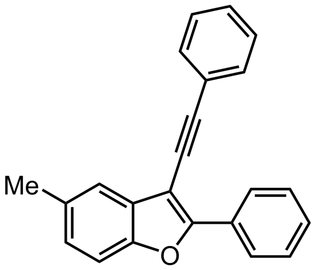
5-(3-(Phenylethynyl)benzofuran-2-yl)pentanenitrile

3av, light yellow oil, 43.6 mg, 73% yield. R$_f$ = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.70 – 7.64 (m, 1H), 7.61 – 7.54 (m, 2H), 7.48 – 7.42 (m, 1H), 7.42 – 7.35 (m, 3H), 7.34 – 7.27 (m, 2H), 3.04 (t, *J* = 7.1 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 2.02 (ddd, *J* = 19.5, 9.8, 5.1 Hz, 2H), 1.85 – 1.71 (m, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 160.9, 153.8, 131.4, 128.5, 128.4, 128.3, 124.5, 123.2, 123.2, 119.9, 119.3, 111.0, 100.8, 95.0, 79.4, 26.6, 26.5, 24.5, 16.8. **HRMS** (EI) calcd for $C_{21}H_{17}NO$ [M]$^+$: 299.13047, found: 299.13030. **IR** (Reflection): ṽ = 3059, 2949, 2868, 2246, 2219, 1731, 1588, 1491, 1475, 1454, 1427, 1328, 1270, 1235, 1178, 1110, 1093, 1069, 1045, 1008, 930, 848, 750, 691, 651.



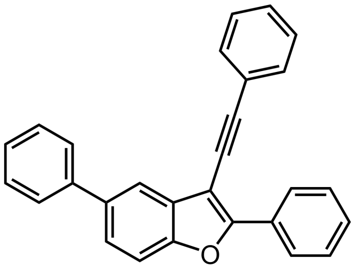
2-(3-(3-(Phenylethynyl)benzofuran-2-yl)propyl)isoindoline-1,3-dione

3aw, light yellow oil, 48.1 mg, 59% yield. R$_f$ = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.80 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.67 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.56 – 7.51 (m, 2H), 7.41 – 7.32 (m, 4H), 7.29 – 7.22 (m, 2H), 3.87 (t, *J* = 7.1 Hz, 2H), 3.07 (t, *J* = 7.6 Hz, 2H), 2.34 – 2.24 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.2, 160.9, 153.7, 133.8, 132.0, 131.4, 128.5, 128.3, 128.1, 124.3, 123.3, 123.1, 123.1, 119.8, 111.0, 100.6, 95.1, 79.5, 37.6, 26.4, 25.3. **HRMS** (EI) calcd for $C_{27}H_{19}NO_3$ $[M]^+$: 405.13594, found: 405.13705. **IR** (Reflection): ṽ = 3466, 3060, 2934, 2849, 2253, 2220, 1773, 1717, 1588, 1491, 1467, 1454, 1397, 1370, 1236, 1173, 1105, 1078, 1021, 910, 885, 793, 752, 719, 691, 651.



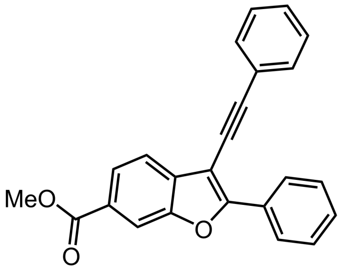
5-Methyl-2-phenyl-3-(phenylethynyl)benzofuran

3ax, colorless solid, 55.6 mg, 90% yield. $R_f = 0.5$ (PE:DCM = 10:1), chromatography eluent: 5% Petroleum ether in dichlormethan. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 – 8.25 (m, 2H), 7.68 (d, *J* = 6.6 Hz, 2H), 7.56 – 7.51 (m, 3H), 7.48 – 7.38 (m, 5H), 7.18 (d, *J* = 8.3 Hz, 1H), 2.52 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.4, 152.0, 133.0, 131.5, 130.3, 129.9, 129.0, 128.6, 128.45, 128.36, 126.6, 126.0, 123.5, 120.1, 110.7, 98.9, 96.6, 81.4, 21.3. **HRMS** (EI) calcd for $C_{23}H_{16}O$ $[M]^+$: 308.11957, found: 308.11779. **IR** (ATR): ṽ = 3055, 3027, 2921, 2214, 1944, 1736, 1599, 1561, 1474, 1443, 1383, 1321, 1262, 1243, 1204, 1178, 1163, 1113, 1096, 1069, 1027, 998, 940, 913, 871, 832, 821, 794, 765, 750, 686, 655, 619. **M.p.** (amorphous): 126.5-128.2 °C.



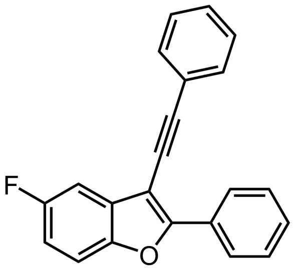
2,5-Diphenyl-3-(phenylethynyl)benzofuran

3by, light yellow solid, 57.7 mg, 78% yield. R_f = 0.4 (PE:DCM = 30:1), chromatography eluent: 2% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.49 – 8.32 (m, 2H), 7.95 (s, 1H), 7.76 – 7.64 (m, 4H), 7.60 (d, *J* = 1.0 Hz, 2H), 7.58 – 7.36 (m, 9H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.9, 153.1, 141.4, 137.2, 131.6, 130.4, 130.1, 129.2, 128.7, 128.7, 128.5, 127.5, 127.0, 126.0, 125.0, 123.3, 118.8, 111.3, 99.4, 97.0, 81.1. **HRMS** (EI) calcd for $C_{28}H_{18}O$ $[M]^+$: 370.13522, found: 370.13275. **IR** (ATR): ṽ = 3055, 3032, 2211, 1954, 1877, 1739, 1600, 1555, 1485, 1463, 1442, 1385, 1272, 1253, 1222, 1199, 1133, 1113, 1072, 1024, 913, 880, 817, 759, 747, 688, 665, 629. **M.p.** (amorphous): 101.1-101.8 °C.



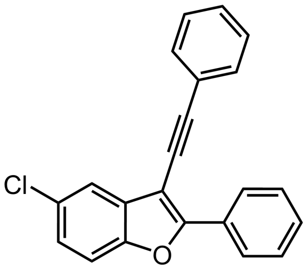
Methyl 2-phenyl-3-(phenylethynyl)benzofuran-6-carboxylate

3az, light yellow solid, 7.8 mg, 11% yield, 67% recovered yield of starting substrate **1az.** R_f = 0.5 (PE:DCM = 1:1), chromatography eluent: 30% Dichlormethan in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.34 (d, *J* = 7.3 Hz, 2H), 8.19 (s, 1H), 8.02 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.63 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.52 (t, *J* = 7.3 Hz, 2H), 7.47 – 7.38 (m, 4H), 3.96 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.9, 158.8, 152.8, 134.1, 131.5, 129.8, 129.6, 128.7, 128.6, 128.5, 127.2, 126.3, 124.7, 123.0, 119.9, 112.8, 99.3, 97.2, 80.4, 52.2. **HRMS** (EI) calcd for $C_{24}H_{16}O_3$ $[M]^+$: 352.10940, found: 352.11079. **IR** (Reflection): ṽ = 3063, 2950, 2926, 2850, 2217, 1717, 1619, 1584, 1485, 1434, 1389, 1292, 1221, 1198, 1114, 1082, 984, 762, 688. **M.p.** (amorphous): 133.4-135.1 °C.



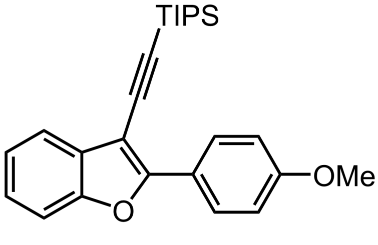
5-Fluoro-2-phenyl-3-(phenylethynyl)benzofuran

3ba, colorless solid, 57.5 mg, 92%. R_f = 0.3 (*n*-Hexane), chromatography eluent: *n*-Hexane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.43 – 8.23 (m, 2H), 7.64 (dt, *J* = 4.3, 2.5 Hz, 2H), 7.52 (dd, *J* = 10.4, 4.7 Hz, 2H), 7.48 – 7.37 (m, 6H), 7.07 (td, *J* = 9.0, 2.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.7 (d, *J* = 239.9 Hz), 157.8, 149.7, 131.5, 130.9 (d, *J* = 10.6 Hz), 129.9, 129.4, 128.7, 128.6, 128.5, 126.1, 123.1, 113.0 (d, *J* = 26.5 Hz), 111.9 (d, *J* = 9.5 Hz), 106.0 (d, *J* = 25.5 Hz), 99.4 (d, *J* = 3.9 Hz), 97.1, 80.5. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -119.69. **HRMS** (EI) calcd for $C_{22}H_{13}OF$ $[M]^+$: 312.09449, found: 312.09405. **IR** (ATR): ṽ = 3058, 2219, 1956, 1887, 1854, 1732, 1697, 1598, 1561, 1488, 1470, 1444, 1385, 1334, 1277, 1247, 1198, 1179, 1159, 1116, 1096, 1070, 1026, 999, 952, 916, 848, 835, 823, 801, 777, 759, 739, 686, 660, 616. **M.p.** (amorphous): 101.3-102.9 °C.



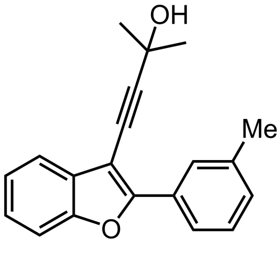
5-Chloro-2-phenyl-3-(phenylethynyl)benzofuran

3bb, colorless solid, 49.7 mg, 76% yield. R_f = 0.6 (PE:DCM = 10:1), chromatography eluent: 5% Dichlormethan in petroleum ether.**^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.46 – 8.28 (m, 2H), 7.71 (d, *J* = 2.1 Hz, 1H), 7.64 (dd, *J* = 6.5, 3.2 Hz, 2H), 7.56 – 7.47 (m, 2H), 7.48 – 7.39 (m, 5H), 7.30 (dd, *J* = 8.7, 2.1 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.5, 151.8, 131.5, 131.3, 129.7, 129.5, 129.1, 128.7, 128.6, 128.5, 126.1, 125.5, 123.1, 120.0, 112.2, 98.8, 97.2, 80.3. **HRMS** (EI) calcd for $C_{22}H_{13}OCl$ $[M]^+$: 328.06494, found: 328.06435. **IR** (ATR): ṽ = 3059, 2925, 1945, 1860, 1728, 1603, 1585, 1573, 1559, 1500, 1485, 1441, 1385, 1322, 1258, 1232, 1201, 1111, 1092, 1068, 1048, 1027, 998, 919, 862, 831, 818, 802, 763, 750, 715, 680, 646, 611. **M.p.** (amorphous): 108.6-109.9 °C.



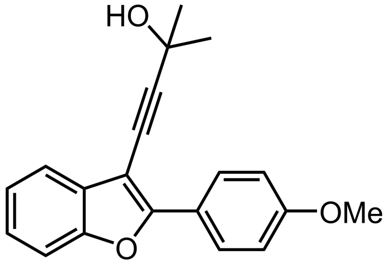
Triisopropyl((2-(4-methoxyphenyl)benzofuran-3-yl)ethynyl)silane

3bc, light yellow solid, 49.5 mg, 61% yield. R_f = 0.4 (PE:DCM = 10:1), chromatography eluent: 5% Petroleum ether in dichlormethan. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.9 Hz, 2H), 7.65 (dd, *J* = 6.2, 2.8 Hz, 1H), 7.48 (dd, *J* = 6.2, 2.9 Hz, 1H), 7.35 – 7.28 (m, 2H), 6.99 (d, *J* = 8.9 Hz, 2H), 3.89 (s, 3H), 1.23 (s, 21H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.4, 157.1, 153.1, 130.4, 127.7, 124.8, 123.3, 123.0, 120.0, 113.9, 110.9, 98.8, 98.7, 97.8, 55.3, 18.7, 11.4. **HRMS** (EI) calcd for $C_{26}H_{32}O_2Si$ $[M]^+$: 404.21661, found: 404.21954. **IR** (Reflection): ṽ = 3066, 2942, 2891, 2864, 2152, 1735, 1609, 1565, 1508, 1454, 1422, 1370, 1305, 1255, 1203, 1178, 1136, 1105, 1071, 1033, 996, 920, 883, 833, 807, 786, 772, 745, 677, 660, 635, 624, 606. **M.p.** (amorphous): 57.6-58.7 °C.



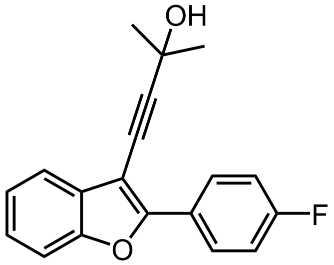
2-Methyl-4-(2-(m-tolyl)benzofuran-3-yl)but-3-yn-2-ol

3bd, light yellow solid, 44.6 mg, 77% yield. R_f = 0.3 (PE:DCM = 1:2), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.65 (dd, *J* = 6.6, 2.2 Hz, 1H), 7.50 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.43 – 7.27 (m, 3H), 7.22 (d, *J* = 7.6 Hz, 1H), 2.45 (s, 3H), 2.29 (br, 1H), 1.75 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 156.6, 153.4, 138.2, 130.0, 129.9, 129.8, 128.5, 126.5, 125.2, 123.3, 123.0, 120.1, 111.1, 101.2, 98.3, 74.2, 66.0, 31.5, 21.5. **HRMS** (EI) calcd for $C_{20}H_{18}O_2$ $[M]^+$: 290.13013, found: 290.13042. **IR** (ATR): ṽ = 3308, 3040, 2980, 2926, 2222, 1933, 1889, 1850, 1609, 1565, 1452, 1371, 1293, 1259, 1228, 1185, 1161, 1141, 1109, 1092, 1068, 1042, 1006, 955, 909, 872, 787, 772, 743, 697, 678, 646, 628. **M.p.** (amorphous): 71.0-72.1 °C.



4-(2-(4-Methoxyphenyl)benzofuran-3-yl)-2-methylbut-3-yn-2-ol

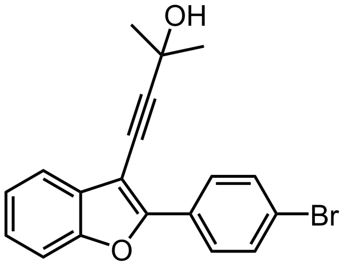
3be, light yellow oil, 35.9 mg, 59% yield. $R_f = 0.2$ (PE:DCM = 1:2), chromatography eluent: 30% Petroleum ether in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.28 – 8.14 (m, 2H), 7.67 – 7.57 (m, 1H), 7.51 – 7.40 (m, 1H), 7.34 – 7.24 (m, 2H), 7.06 – 6.95 (m, 2H), 3.87 (s, 3H), 2.15 (br, 1H), 1.74 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.4, 156.7, 153.2, 130.0, 127.5, 124.8, 123.2, 122.9, 119.8, 114.1, 110.9, 100.8, 96.7, 74.4, 66.0, 55.3, 31.6. **HRMS** (EI) calcd for $C_{20}H_{18}O_3$ $[M]^+$: 306.12505, found: 306.12563. **IR** (Reflection): ṽ = 3390, 2979, 2933, 2837, 2223, 1731, 1608, 1509, 1455, 1422, 1379, 1304, 1253, 1223, 1203, 1178, 1105, 1067, 1030, 957, 896, 833, 785, 772, 745.



4-(2-(4-Fluorophenyl)benzofuran-3-yl)-2-methylbut-3-yn-2-ol

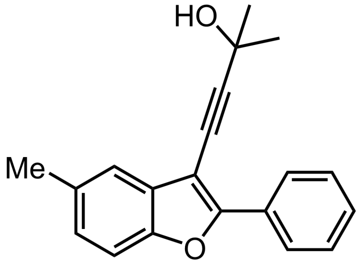
3bf, colorless solid, 52.7 mg, 90% yield. $R_f = 0.3$ (PE:DCM = 1:2), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.23 (dd, J = 8.7, 5.4 Hz, 2H), 7.63 (d, J = 7.4 Hz, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.31 (ddd, J = 21.3, 11.0, 4.1 Hz, 2H), 7.16 (t, J = 8.6 Hz, 2H), 2.34 (br, 1H), 1.74 (s, 6H). **^{13}C**

NMR (151 MHz, $CDCl_3$) δ 163.0 (d, *J* = 250.4 Hz), 155.4, 153.3, 129.7, (d, *J* = 8.2 Hz), 126.31 (d, *J* = 3.3 Hz), 125.3, 123.4, 120.1, 115.8, 115.6, 111.1, 101.3, 98.11 (d, *J* = 1.3 Hz), 73.9, 66.0, 31.5. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.07. **HRMS** (EI) calcd for $C_{19}H_{15}O_2F$ $[M]^+$: 294.10506, found: 294.10474. **IR** (ATR): ṽ = 3284, 3064, 2977, 2929, 2861, 2232, 1731, 1601, 1574, 1505, 1477, 1454, 1377, 1361, 1303, 1257, 1228, 1203, 1156, 1110, 1098, 1064, 1013, 953, 897, 834, 798, 773, 738, 659, 627, 606. **M.p.** (amorphous): 84.6-86.9 °C.



4-(2-(4-Bromophenyl)benzofuran-3-yl)-2-methylbut-3-yn-2-ol

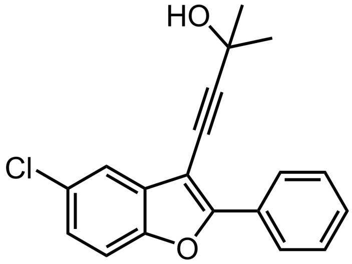
3bg, light yellow solid, 63.8 mg, 90% yield. R_f = 0.3 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 – 7.99 (m, 2H), 7.62 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.60 – 7.55 (m, 2H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37 – 7.23 (m, 2H), 2.41 (br, 1H), 1.73 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 153.4, 131.8, 129.7, 128.9, 127.2, 125.6, 123.5, 123.2, 120.2, 111.2, 102.0, 99.1, 73.8, 66.0, 31.5. **HRMS** (EI) calcd for $C_{19}H_{15}O_2Br$ $[M]^+$: 354.02499, found: 354.02361. **IR** (ATR): ṽ = 3295, 2979, 2928, 2221, 1579, 1489, 1450, 1399, 1375, 1340, 1253, 1225, 1200, 1142, 1103, 1075, 1061, 1007, 959, 893, 828, 775, 743, 707, 651, 632. **M.p.** (amorphous): 105.4-107.2 °C.



2-Methyl-4-(5-methyl-2-phenylbenzofuran-3-yl)but-3-yn-2-ol

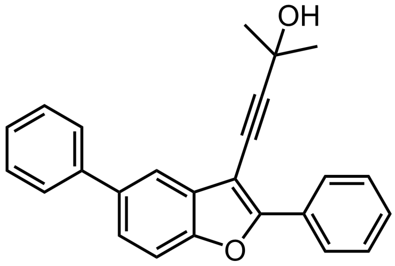
3bh, colorless solid, 41.9 mg, 72% yield. R_f = 0.3 (PE:DCM = 1:2), chromatography eluent: 30% Petroleum ether in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35

– 8.16 (m, 2H), 7.52 – 7.45 (m, 2H), 7.44 – 7.34 (m, 3H), 7.13 (dd, *J* = 8.4, 1.3 Hz, 1H), 2.48 (s, 3H), 2.17 (br, 1H), 1.75 (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 156.5, 151.9, 132.9, 130.2, 129.9, 129.0, 128.5, 126.6, 125.8, 119.9, 110.6, 101.2, 98.2, 74.3, 66.0, 31.5, 21.3. **HRMS** (EI) calcd for $C_{20}H_{18}O_2$ [M]$^+$: 290.13013, found: 290.13149. **IR** (ATR): ṽ = 3453, 2980, 2922, 2863, 2227, 1600, 1562, 1475, 1443, 1371, 1314, 1282, 1260, 1230, 1205, 1159, 1121, 1098, 1065, 1026, 957, 940, 915, 891, 873, 831, 792, 769, 748, 680, 645, 620. **M.p.** (amorphous): 116.0-118.2 °C.



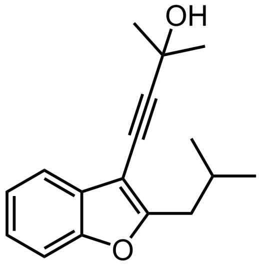
4-(5-Chloro-2-phenylbenzofuran-3-yl)-2-methylbut-3-yn-2-ol

3bi, light yellow solid, 38.6 mg, 62% yield. R$_f$ = 0.3 (PE:DCM = 1:2), chromatography eluent: 30% Petroleum ether in dichloromethane. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.22 (dd, *J* = 5.3, 3.3 Hz, 2H), 7.58 (d, *J* = 2.1 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.42 (dt, *J* = 4.7, 1.9 Hz, 1H), 7.38 (d, *J* = 8.7 Hz, 1H), 7.26 (dd, *J* = 8.7, 2.1 Hz, 1H), 2.25 (br, 1H), 1.74 (s, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 157.6, 151.7, 131.2, 129.57, 129.55, 129.1, 128.6, 126.0, 125.5, 119.8, 112.1, 101.8, 98.1, 73.4, 66.0, 31.5. **HRMS** (EI) calcd for $C_{19}H_{15}O_2Cl$ [M]$^+$: 310.07551, found: 310.07484. **IR** (ATR): ṽ = 3464, 2980, 2359, 2251, 1583, 1452, 1441, 1375, 1318, 1259, 1223, 1204, 1165, 1079, 1052, 1027, 958, 908, 872, 831, 800, 782, 770, 735, 703, 683, 650. **M.p.** (amorphous): 93.9-95.7 °C.



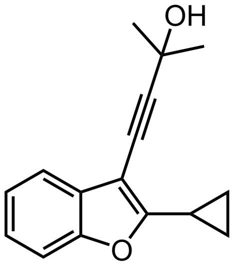
4-(2,5-Diphenylbenzofuran-3-yl)-2-methylbut-3-yn-2-ol

3bj, light yellow oil, 48.9 mg, 69% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.35 – 8.23 (m, 2H), 7.81 (s, 1H), 7.71 – 7.63 (m, 2H), 7.57 – 7.45 (m, 6H), 7.40 (ddd, *J* = 10.7, 8.4, 6.2 Hz, 2H), 2.23 (br, 1H), 1.76 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 157.0, 153.0, 141.3, 137.1, 130.3, 130.0, 129.2, 128.7, 128.6, 127.5, 127.0, 125.9, 125.0, 118.5, 111.2, 101.5, 98.7, 74.0, 66.0, 31.5. **HRMS** (EI) calcd for $C_{25}H_{20}O_2$ $[M]^+$: 352.14578, found: 352.14501. **IR** (ATR): ṽ = 3338, 3061, 2980, 2931, 2224, 1951, 1879, 1737, 1601, 1495, 1465, 1445, 1375, 1243, 1217, 1162, 1065, 1028, 958, 915, 881, 814, 785, 762, 749, 690, 625.



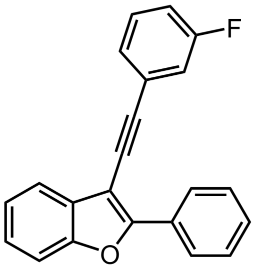
4-(2-Isobutylbenzofuran-3-yl)-2-methylbut-3-yn-2-ol

3bk, light yellow oil, 37.9 mg, 74% yield. R_f = 0.3 (PE:DCM = 1:1), chromatography eluent: 50% Petroleum ether in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.53 (m, 1H), 7.44 – 7.37 (m, 1H), 7.29 – 7.22 (m, 2H), 2.76 (d, *J* = 7.1 Hz, 2H), 2.20 (dp, *J* = 13.6, 6.8 Hz, 1H), 2.08 (br, 1H), 1.68 (s, 6H), 1.01 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.3, 153.7, 128.7, 124.1, 122.9, 119.6, 110.9, 100.2, 99.2, 73.0, 65.9, 36.5, 31.7, 28.2, 22.4. **HRMS** (EI) calcd for $C_{17}H_{20}O_2$ $[M]^+$: 256.14578, found: 256.14706. **IR** (Reflection): ṽ = 3346, 3064, 2958, 2931, 2870, 2228, 1731, 1596, 1455, 1368, 1275, 1231, 1167, 1103, 1070, 1007, 958, 926, 897, 870, 774, 746, 658, 638.



4-(2-Cyclopropylbenzofuran-3-yl)-2-methylbut-3-yn-2-ol

3bl, colorless oil, 14.9 mg, 31% yield. R_f = 0.2 (PE:DCM = 1:1), chromatography eluent: 50% Petroleum ether in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 1H), 7.35 – 7.29 (m, 1H), 7.25 – 7.16 (m, 2H), 2.24 (tt, *J* = 8.4, 5.1 Hz, 1H), 2.04 (br, 1H), 1.68 (s, 6H), 1.24 – 1.18 (m, 2H), 1.08 (ddd, *J* = 11.2, 6.9, 4.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.0, 152.9, 129.2, 123.8, 123.0, 119.1, 110.7, 99.4, 98.1, 72.8, 65.9, 31.7, 9.4, 7.9. **HRMS** (EI) calcd for $C_{16}H_{16}O_2$ $[M]^+$: 240.11448, found: 240.11643. **IR** (ATR): ṽ = 3349, 3091, 2980, 2931, 2866, 2227, 1893, 1731, 1594, 1475, 1457, 1401, 1362, 1326, 1282, 1265, 1223, 1199, 1163, 1096, 1048, 1026, 1007, 958, 943, 894, 868, 830, 811, 786, 773, 744, 687, 640, 625.



3-((3-fluorophenyl)ethynyl)-2-phenylbenzofuran

3bm, light yellow solid, 53.8 mg, 86% yield. R_f = 0.4 (*n*-Hexane), chromatography eluent: *n*-Hexane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.34 (dd, *J* = 5.3, 3.4 Hz, 1H), 7.79 – 7.72 (m, 1H), 7.57 – 7.50 (m, 2H), 7.48 – 7.30 (m, 3H), 7.11 (tdd, *J* = 8.5, 2.6, 1.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.5 (d, *J* = 246.8 Hz), 156.7, 153.5, 130.1, 130.0 (d, *J* = 2.9 Hz), 129.7, 129.3, 128.7, 127.4 (d, *J* = 3.0 Hz), 126.1, 125.4, 125.2 (d, *J* = 9.5 Hz), 123.5, 120.3, 118.2 (d, *J* = 22.7 Hz), 115.7 (d, *J* = 21.2 Hz), 111.2, 98.8, 95.4 (d, *J* = 3.4 Hz), 82.2. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -112.62. **HRMS** (EI) calcd for $C_{22}H_{13}OF$ $[M]^+$: 312.09449, found: 312.09613. **IR** (ATR): ṽ = 3069, 2211, 1935, 1781, 1739, 1609, 1578, 1483, 1456, 1432, 1384, 1342, 1293, 1262, 1203, 1176, 1155, 1109, 1094, 1070, 1027, 1008, 931, 897, 873, 828, 785, 745, 686, 661, 627.

M.p. (amorphous): 92.5-93.8 °C.

3.6 X-Ray Crystallographic Data of 3ak

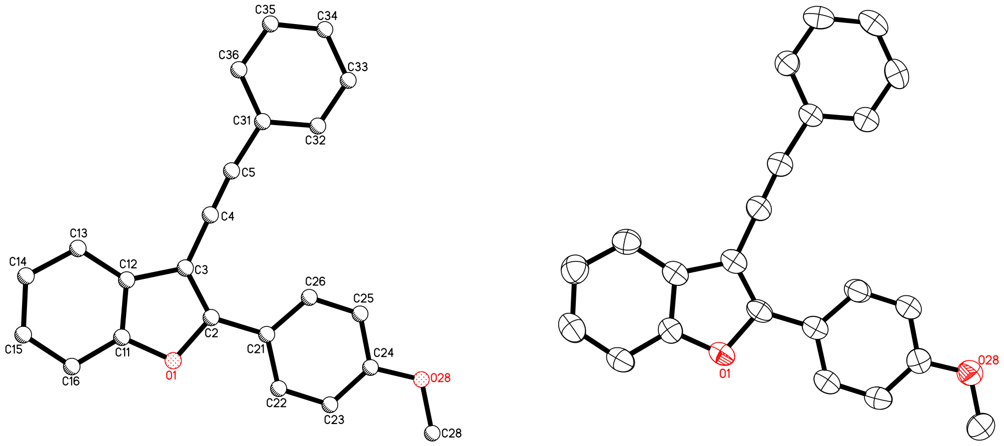


Figure 4. The ORTEP projection of crystal structure of **3ak**.

Table 3. Crystal Data and Structure Refinement for **3ak.**

Identification code	hws12 (**3ak**)	
Empirical formula	$C_{23}H_{16}O_2$	
Formula weight	324.36	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Z	4	
Unit cell dimensions	a = 16.084(2) Å	α = 90 deg.
	b = 5.0200(7) Å	β = 104.717(4) deg.
	c = 21.009(3) Å	γ = 90 deg.
Volume	1640.6(4) Å^3	
Density (calculated)	1.31 g/cm^3	
Absorption coefficient	0.08 mm^{-1}	
Crystal shape	plank	
Crystal size	0.321 x 0.040 x 0.035 mm^3	
Crystal colour	colourless	
Theta range for data collection	1.3 to 25.0 deg.	
Index ranges	$-19 \le h \le 19$, $-5 \le k \le 5$, $-25 \le l \le 25$	
Reflections collected	14479	
Independent reflections	2873 (R(int) = 0.0827)	
Observed reflections	1770 ($I > 2\sigma(I)$)	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.96 and 0.90	

Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2873 / 0 / 227
Goodness-of-fit on F^2	1.04
Final R indices (I > 2sigma(I))	R1 = 0.048, wR2 = 0.100
Largest diff. peak and hole	0.16 and -0.25 eÅ^{-3}

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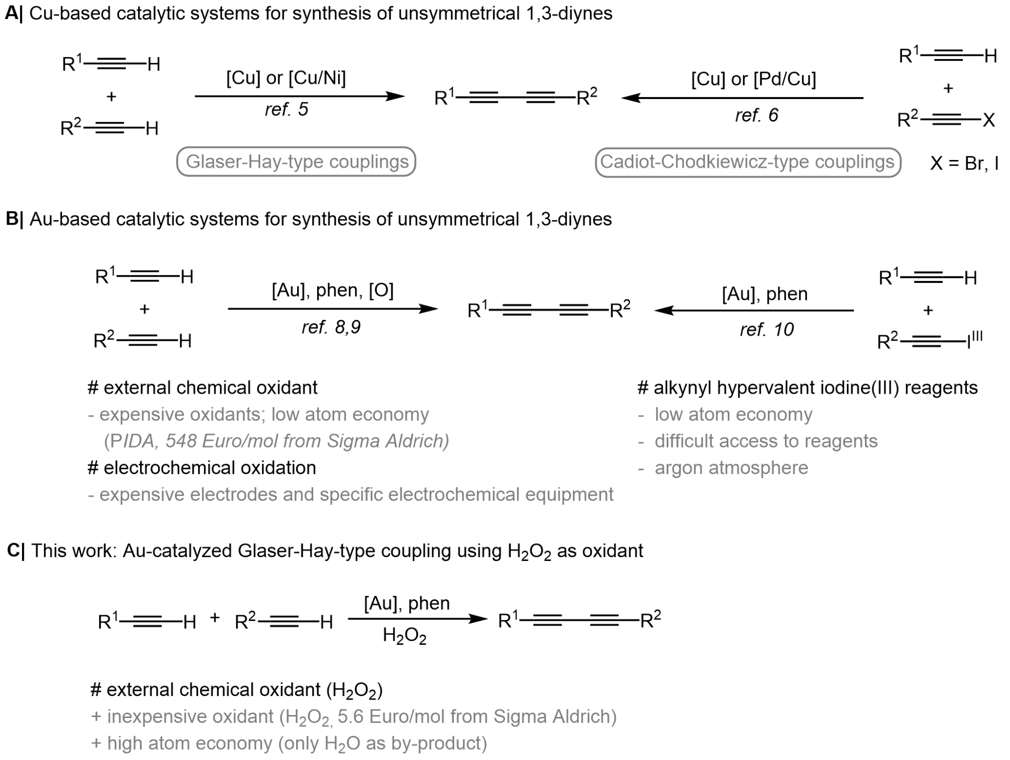
Chapter 4 Ligand-Assisted Homogeneous Gold-Catalyzed C(sp)-C(sp) Cross-Coupling Using H_2O_2 as Oxidant: Synthesis of 1,3-Diynes from Terminal Alkynes

4.1 Introduction

Conjugated 1,3-diynes bear an attractive carbon framework that is widely found in natural products, biologically active molecules, and functional materials.[1] The development of efficient methods for conjugated diynes, especially unsymmetrical 1,3-diynes, has attracted much attention.[1a,2] At present, the general methods for the synthesis of conjugated 1,3-diynes mainly include copper-based catalytic systems and gold-based catalytic systems. The classical copper-based catalytic systems, include Glaser-Hay coupling[3] and Cadiot-Chodkiewicz coupling[4]. Based on these copper-based catalytic systems, several landmark strategies, such as Cu- or Cu/Ni-catalyzed Glaser-Hay-type couplings,[5] Pd/Cu-catalyzed Cadiot-Chodkiewicz-type couplings,[6] have demonstrated to efficiently construct unsymmetrical 1,3-diynes (Scheme 1A). Early gold-based catalytic strategies with external chemical oxidants, such as Selectfluor and phenyliodine(III) diacetate (PIDA), were usually used for homo-coupling.[7] Until 2014, Shi et al. developed a new Au/phen catalytic system using PIDA as an oxidant, first achieving selective heterocoupling of terminal alkynes.[8] After that, several new gold-based catalytic systems (Au/phen) for the synthesis of unsymmetrical 1,3-diynes have been developed, such as electrochemical-promoted gold-catalyzed Glaser-Hay-type couplings[9] and gold-catalyzed Cadiot-Chodkiewicz-type couplings[10]. However, these gold-based catalytic strategies contain significant disadvantages, such as the use of expensive external oxidants,[8] the need for expensive electrodes and specific electrochemical equipment,[9] reliance on hard-to-obtain reagents,[10] resulting in low atom economy and high costs. To circumvent these drawbacks, we aimed the development green and efficient gold-catalyzed C(sp)-C(sp) cross-coupling to construct conjugated diynes.

In Chapter 2, we found that H_2O_2 as an external oxidant can efficiently achieve the oxidation of Au^I to Au^{III} in the presence of a bidentate ligand (phen). A set of gold-mediated cross-coupling reactions also demonstrated the potential of gold-catalyzed C(sp)-C(sp) cross-coupling using H_2O_2 as an oxidant. In addition, considering that symmetrical 1,3-diynes as side products were detected in gold-catalyzed alkynylative cyclization (Chapter 3), we believe that this new catalytic system (Au/phen/H_2O_2) can also be applied to the efficient synthesis of unsymmetrical 1,3-butadiynes via C(sp)-C(sp) cross-coupling. Herein, we developed a ligand-assisted gold-catalyzed C(sp)-C(sp) cross-coupling of terminal alkynes using H_2O_2 as an oxidant (Scheme 1C).

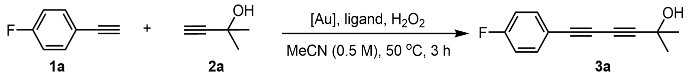


Scheme 1. Synthetic strategy of unsymmetrical 1,3-diynes.

4.2 Results and Discussion

We initiated our investigation on the gold-catalyzed C(sp)-C(sp) cross-coupling of terminal alkynes with 1-ethynyl-4-fluorobenzene **1a** and 2-methyl-3-butyn-2-ol **2a** (Table 1). We first focused on the investigation of the effect of different gold catalysts on the reaction. No coupled products were formed without Au catalyst (entry 1). The tested different gold complexes delivered yields in the range between 8-95% for the coupled diyne **3a** and 3-10% for the homo-coupling by-product **4a** (analyzed by ^{19}F NMR, entries 2-7). Both simple mononuclear and binuclear gold(I) complexes delivered the coupled product **3a** in good yields (entries 2-5). CyJohnPhosAuCl with significant steric bulk, forming the cross-coupling product **3a** and the homo-coupling by-product **4a** in 50% and 10% yields, respectively (entry 6). Interestingly, IPrAuCl, bearing an *N*-heterocyclic carbene ligand, only giving small amounts of products (entry 7). Au^{III} complex ($AuCl_3$) was tested, affording the target cross-coupling product in low yield (entry 8). In addition, to eliminate the possibility that trace amounts of Cu or Pd in the Au salt could catalyze the reaction, using CuCl and $(Ph_3P)_2PdCl_2$ instead of gold catalyst in this catalytic system. The results showed that Cu did not catalyze the reaction at all (entry 9), and Pd catalyst only formed only trace amounts of product **3a** (entry 10). Other bidentate ligands, such as 2,2'-bipyridyl (bpy), affording product **3a** only in low yield (entry 11). Pyridine (py) as a monodentate ligand did not promote this reaction (entry 12). No products were formed without the ligand (entry 13). Different concentrations of hydrogen peroxide, such as H_2O_2 (35 wt% in water) also worked well, affording the coupled diyne **3a** and the homo-coupling by-product **4a** in 87% and 8% yields, respectively (entry 14). No products were detected with the replacement of H_2O_2 by H_2O (entry 15), indicating that the key to the reaction is hydrogen peroxide instead of water. In addition, reducing the equivalents of H_2O_2 also delivered the product in good yield (entry 16). It is worth mentioning that decreasing the 1:3 ratio of the alkynes to a 1:1 ratio gave the cross-coupling product **3a** with 67% yield (entry 17). Reducing the amount of Au catalyst and ligand, the target product **3a** was still obtained in good yield (entry 18).

Table 1. Evaluation of reaction conditions for the cross-coupling of terminal alkynes **1a** with **2a**.[a]

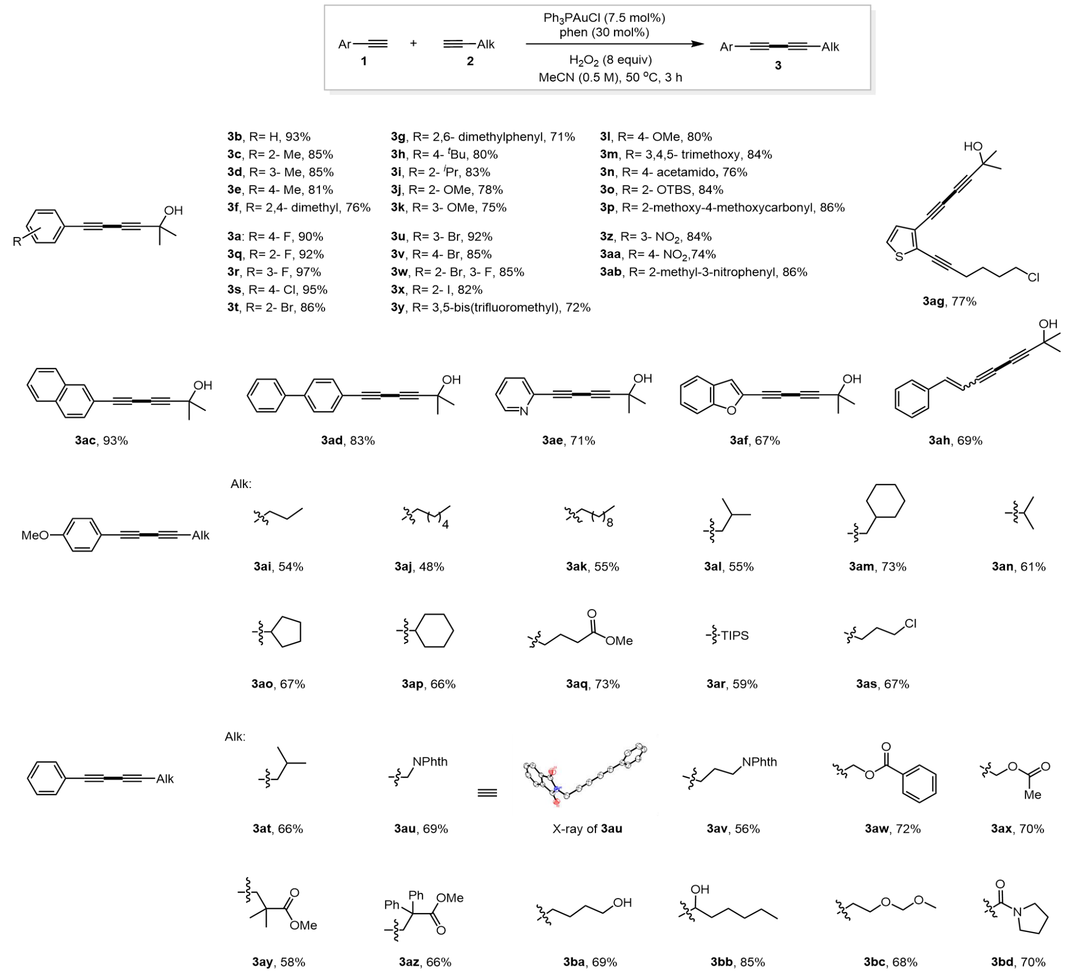


Entry	Gold catalyst (%)	Ligand (%)	**1a** Convn. (%)[b]	**3a** (%)[b]	**4a** (%)[b]
1	-	phen (30)	97	0	0
2	DMSAuCl (7.5)	phen (30)	100	90	5
3	**Ph_3PAuCl** (7.5)	phen (30)	**100**	**95**	**4**
4	PhenAuCl (7.5)	phen (30)	100	91	7
5	Dppm$(AuCl)_2$ (3.75)	phen (30)	100	86	7
6	CyJohnphosAuCl (7.5)	phen (30)	99	50	10
7	IPrAuCl (7.5)	phen (30)	97	8	7
8	$AuCl_3$ (7.5)	phen (30)	99	11	3
9	CuCl (7.5)	phen (30)	97	0	0
10	$(Ph_3P)_2PdCl_2$ (7.5)	phen (30)	99	trace	trace
11	Ph_3PAuCl (7.5)	bpy (30)	100	5	8
12	Ph_3PAuCl (7.5)	py (30)	100	0	0
13	Ph_3PAuCl (7.5)	-	91	0	0
14[c]	Ph_3PAuCl (7.5)	phen (30)	100	87	6
15[d]	Ph_3PAuCl (7.5)	phen (30)	53	0	0
16[e]	Ph_3PAuCl (7.5)	phen (30)	99	81	8
17[f]	Ph_3PAuCl (7.5)	phen (30)	99	65	17
18	Ph_3PAuCl (5)	phen (20)	100	85	8

[a] Reaction conditions: a solution of the terminal alkynes **1a** (0.1 mmol), terminal alkynes **2a** (0.3 mmol), Ph_3PAuCl (3.7 mg, 7.5 mol%), phen (5.4 mg, 30 mol%) and H_2O_2 (22.4 µL, 0.8 mmol, 50 wt% in water) in MeCN (0.2 mL) was stirred at 50 °C for 3 h. [b] Determined by ^{19}F NMR using benzotrifluoride as internal standard. [c] H_2O_2 (35 wt% in water). [d] H_2O instead of H_2O_2. [e] H_2O_2 (11.2 µL, 0.4 mmol, 50 wt% in water). [f] terminal alkynes **2a** (0.1 mmol).

With the optimal conditions in hand, we set up to explore the scope of different aromatic alkynes to form 1,3-diynes. As shown in Table 2, the catalytic system showed excellent substrate compatibility, and various 1,3-diynes were accessible in excellent isolated yields. The electronic properties of the aryl substituents had only little influence. First, a series of aromatic alkynes bearing electron-donating groups in 2-, 3- and 4-position, including alkyl, alkoxy, acyloxy, or amide groups were investigated. All of the corresponding 1,3-diynes (**3b**-**3p**) were obtained in high yields. The same reaction efficiency was observed with aryl acetylenes bearing electron-withdrawing groups such as fluoro, chloro, bromo, iodo, trifluoromethyl, and nitro, which delivered the diynes in excellent yields (**3a**, **3q**-**3ab**). 2-Ethynylnaphthalene and 4-ethynyl-1,1'-biphenyl reacted smoothly as well, furnishing 1,3-diynes **3ac** and **3ad** in high yields. Heteroaromatic alkynes such as pyridine (**3ae**), benzofuran (**3af**), and thiophene (**3ag**) were also suitable substrates. In addition, but-1-en-3-yn-1-ylbenzene as a substrate was well tolerated by the catalytic system to afford **3ah** showing the same Z/E ratio as the starting material (1:6). Apart from 2-methyl-3-butyn-2-ol **2a**, a variety of different aliphatic alkynes were tested (Table 2). Alkynes with alkyl chains provided the conjugated diacetylenes (**3ai**-**3ap** and **3at**) in good yields. Furthermore, aliphatic chains containing functional groups such as esters (**3aq**, **3aw**-**3az**), TIPS (**3ar**), chlorine (**3as**), phthalimide (**3au**, **3av**), alcohols (**3ba**, **3bb**), ether (**3bc**), and amide (**3bd**) were all tolerated in this reaction.

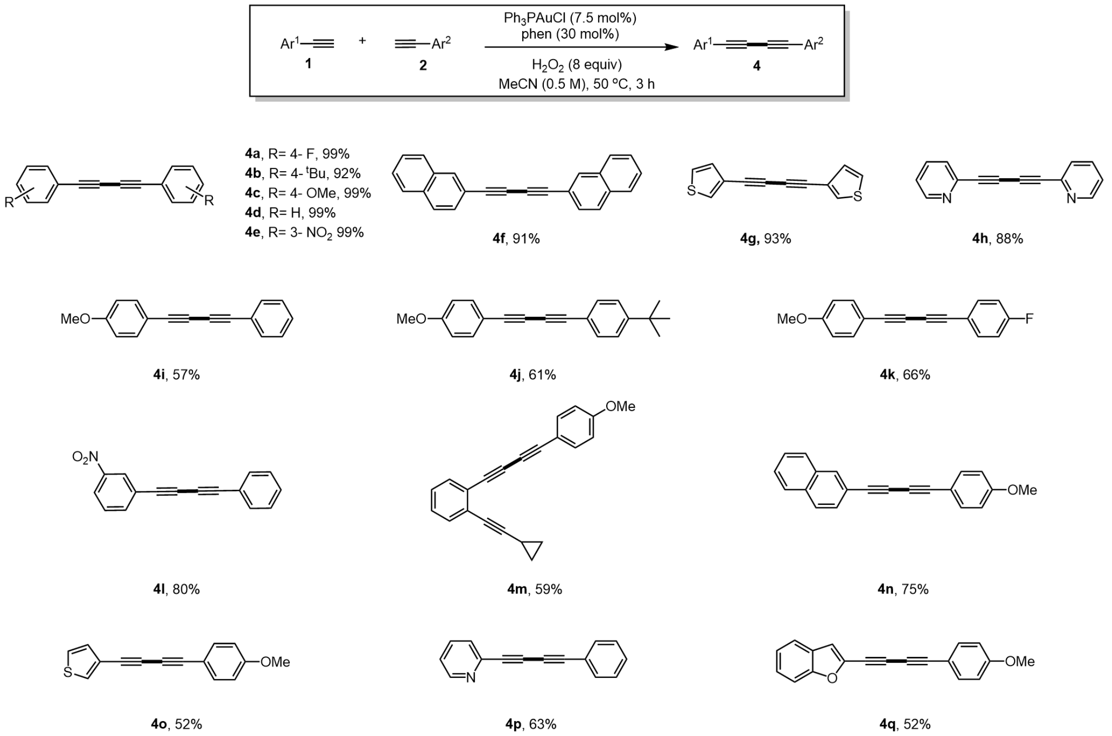
Table 2. Substrate scope for the cross-couplings of aromatic alkynes with aliphatic alkynes.[a,b]



[a] Reaction conditions: aromatic alkyne **1** (0.2 mmol), aliphatic alkyne **2** (0.6 mmol), PPh_3AuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeCN (0.4 mL), 50 °C, 3 h. [b] Yield of isolated product.

As shown in Table 3, with the same catalytic system, both electron-donating and electron-withdrawing groups were tolerated, furnishing the homo-coupling products in excellent yields (**4a**–**4e**). 2-Ethynylnaphthalene and heteroaromatic alkynes, such as pyridine and thiophene, reacted smoothly as well (**4f**–**4h**). To verify the feasibility of our method for the selective cross-coupling of two different terminal aromatic alkynes with similar structures or electronic properties, we next investigated the substrate scope for two different aromatic alkynes. To our delight, direct cross-coupling of various aryl and heteroaryl-substituted terminal alkynes was also suitable. Different terminal aromatic alkynes, bearing either electron-withdrawing or electron-donating groups can be coupled to each other to form the corresponding products (**4i-4m**) in moderate to good yields (57-80%). It is worth mentioning that no cyclopropane ring-opening product was observed (**4m**), which implies that a free radical pathway is not involved.[11] Naphthalene acetylene and heteroaromatics alkynes such as thiophene, benzofuran, and pyridine were also suitable substances, forming the coupled products in moderate yields (**4n**-**4q**).

Table 3. Substrate scope for the cross-couplings of aromatic alkynes.[a,b,c]

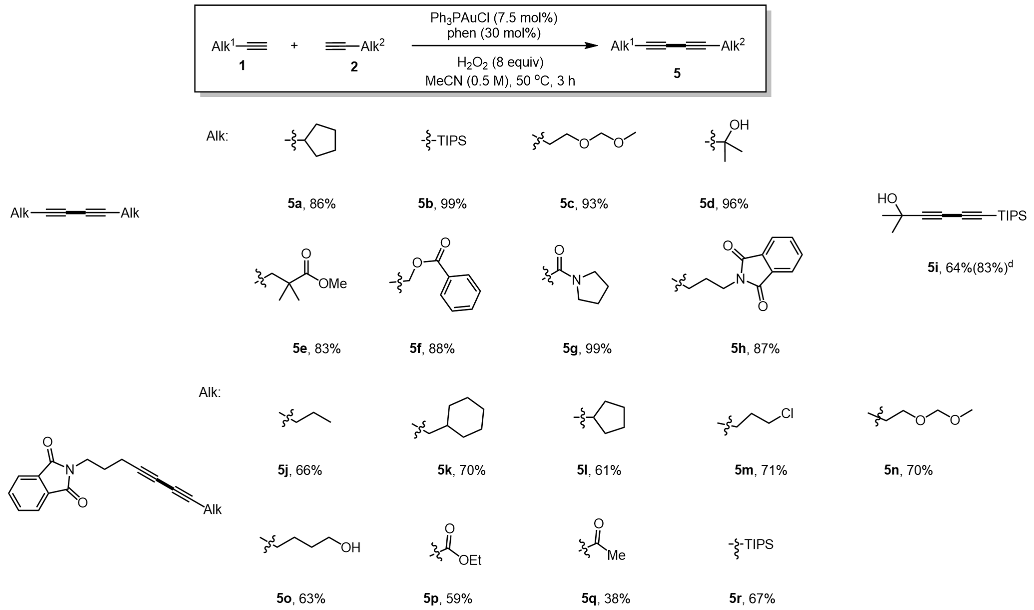


[a] Reaction conditions: aromatic alkyne **1** (0.2 mmol), aromatic alkyne **2** (0.6 mmol), PPh_3AuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeCN (0.4 mL), 50 °C, 3 h. [b] Reaction conditions of homo-coupling: aromatic alkyne (0.4 mmol). [c] Yield of isolated product.

In addition to the cross-coupling of different aromatic alkynes, a variety of aliphatic alkynes provided the 1,3-diynes under very mild conditions, too (Table 4). Homo-coupling of aliphatic alkynes including functional groups such as TIPS (**5b**), ether (**5c**), alcohol (**5d**), esters (**5e**, **5f**), amide (**5g**), and phthalimide (**5h**) were realized in excellent yields (83-99%). Furthermore, we explored the feasibility of the cross-coupling of different terminal alkyl alkynes. It is worth pointing out that free fatty alcohols and silane group (TIPS) both did not interfere (**5i**). The reaction of 5-phthalimido-1-pentyne with unsubstituted alkylacetylenes also proceeded to afford 1,3-diynes in 61-70% yield (**5j**-**5l**). Different aliphatic chains containing functional groups, such as chlorine (**5m**), ether (**5n**), alcohol (**5o**), ester (**5p**), ketone (**5q**), and

TIPS (**5r**) were tolerated in this reaction as well.

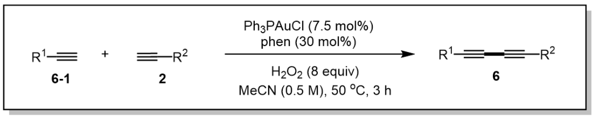
Table 4. Substrate scope for the cross-couplings of aliphatic alkynes.[a,b,c]

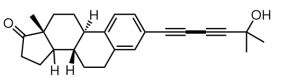


[a] Reaction conditions: aliphatic alkyne **1** (0.2 mmol), aliphatic alkyne **2** (0.6 mmol), PPh_3AuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeCN (0.4 mL), 50 °C, 3 h. [b] Reaction conditions of homo-coupling: aromatic alkyne (0.4 mmol). [c] Yield of isolated product. [d] aliphatic alkyne **1** (0.6 mmol), aliphatic alkyne **2** (0.2 mmol).

As demonstrated above, our methodology allows cross-couplings between a wide array of terminal alkynes achieved under very mild conditions. The resulting 1,3-diyne unit is an attractive target that can serve as starting material for further downstream transformations.[12] To underline the synthetic utility of the method, we next evaluated the potential to use this methodology for the introduction of diyne units onto natural products and synthetic drugs (Table 5), which not only increases the complexity of the molecule but also delivers a synthetic handle for modifications in various ways to release more potential applications. Indeed, the gold-catalyzed cross-coupling of 1,3-diynes worked well with substrates **6a-1** and **6b-1** that are derived from Oestrone (a weak estrogen) delivering the corresponding products **6a** and **6b** in decent yield. *L*-Tyrosine derivative **6c-1** could also be applied to afford the 1,3-diyne product **6c** in high yield. The derivatives **6d-1** and **6e-1** of Ibuprofen and Indomethacin as common non-steroidal anti-inflammatory drugs, were suitable substances, providing target coupled derivatives **6a** and **6e** in good yields. In addition, Gemfibrozil and Fenofibric acid used as small-molecule hypolipidemic drugs and their derivatives **6f-1** and **6g-1** reacted smoothly as well, affording the corresponding products **6f** and **6g** in high yields. Interestingly, **6h-1** as a derivative of Ethisterone delivered the product in moderate yield (47%), which may be attributed to its poor solubility. Moreover, as a natural product of triterpenoids, Oleanic acid has a variety of biological activities such as hypolipidemic, anti-inflammatory, cardiotonic, diuretic, and anti-tumor properties. Its derivative **6i-1** was also tolerated, forming coupled product **6i** in 61% yield.

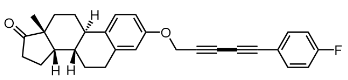
Table 5. Cross-couplings of alkynes containing biologically or pharmaceutically relevant skeletons.[a,b]





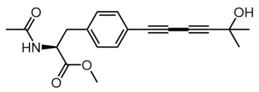
from Oestron

6a, 68%



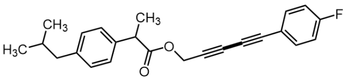
from Oestron

6b, 69%



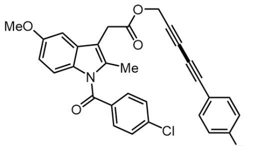
from *L*-Tyrosinmethylester

6c, 85%



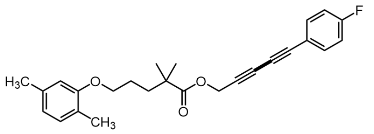
from Ibuprofen

6d, 75%



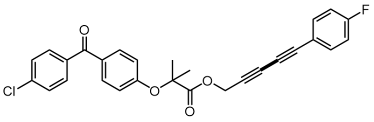
from Indomethacin

6e, 68%



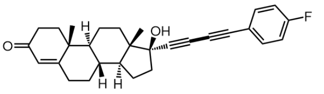
from Gemfibrozil

6f, 82%



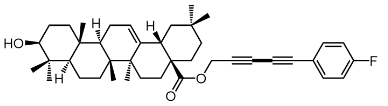
from Fenofibric acid

6g, 70%



from Ethisterone

6h, 47%



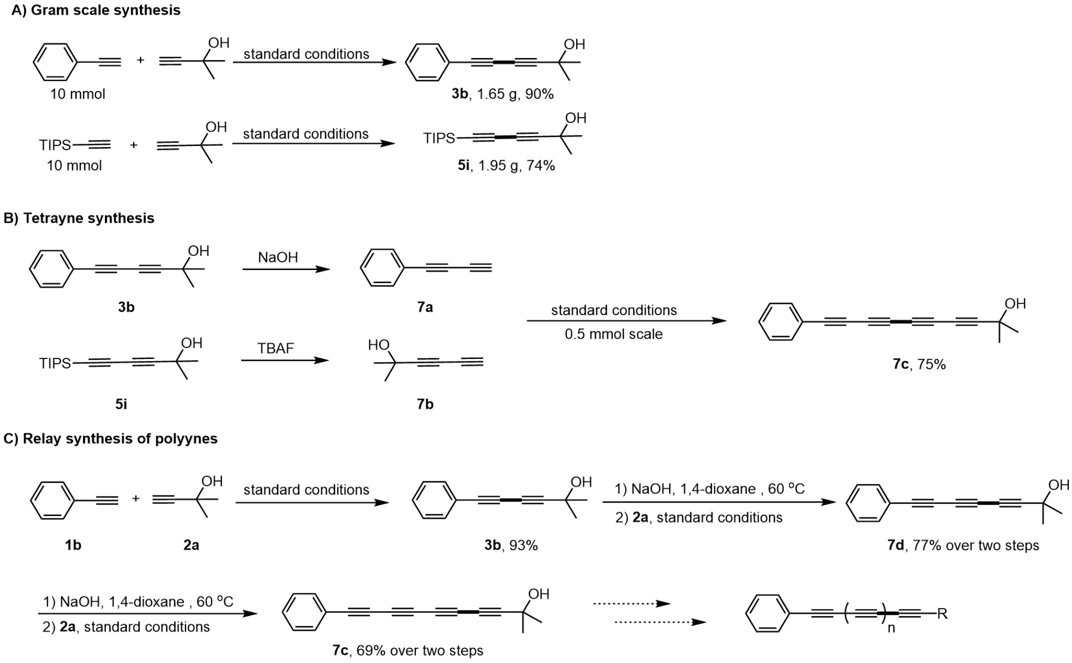
from Oleanic acid

6i, 61%

[a] Reaction conditions: alkyne **1** (0.2 mmol), alkyne **2** (0.6 mmol), PPh_3AuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeCN (0.4 mL), 50 °C, 3 h. [b] Yield of isolated product.

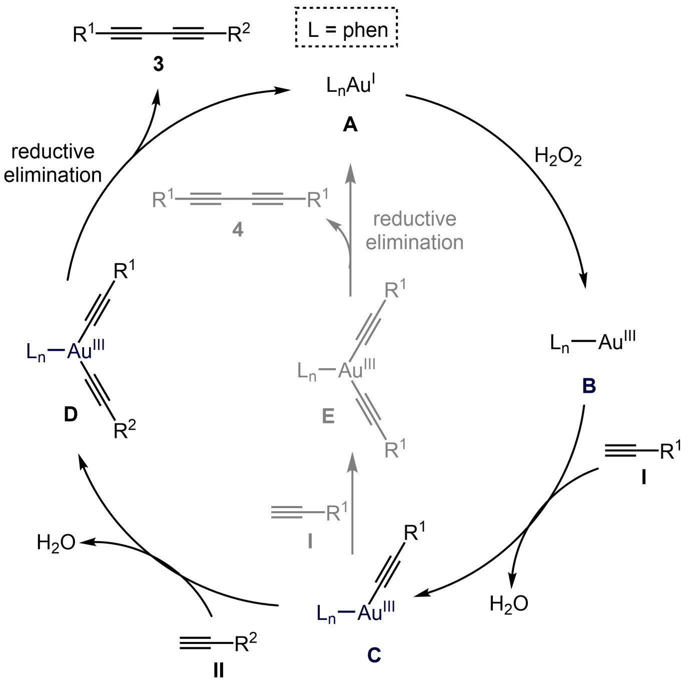
An upscaling of the reaction to a gram scale was easily possible, which was demonstrated by the synthesis of diynes **3b** and **5i** that were obtained in 90% and 74% yields, respectively (Scheme 2A). In addition, treatment of **7a** with **7b** under standard conditions produced tetrayne **7c** in a 75% yield (Scheme 2B). Tetraynes can be obtained by this strategy in good yield, however, these reactions usually require a large excess of one of the diynes. As an alternative to the construction of polyynes by the cross-coupling of diynes, we designed a strategy based on the consecutive use of

2-methyl-3-butyn-2-ol **2a** (0.06 Euro/mL, from Sigma Aldrich) as a very cheap commercial raw material that can be used in an excessive amount to speed up the conversion rate and increase the yield of the target product. After deprotection, the obtained products can then be used with the same alkyne (**2a**) for the introduction of the next alkyne unit. The feasibility of this relay strategy was demonstrated by the effective construction of tetrayne **7c** (Scheme 2C). This method could serve as a useful tool for applications, especially for materials science.[1d]



Scheme 2. Comprehensive application.

Based on previous studies on the mechanism of gold-catalyzed alkynylative cyclization with hydrogen peroxide as oxidant (Chapter 3), we propose the possible reaction mechanism as shown in Scheme 3. Starting with $\mathrm{L_nAu^{I}}$ salt **A**, the oxidation of $\mathrm{L_nAu^{I}}$ complex **A** to afford $\mathrm{L_nAu^{III}}$ complex **B**, directly activates the alkyne **I** to generate the acetylenic $\mathrm{Au^{III}}$ species **C**, followed by coordination of terminal alkyne **II** to afford gold(III)alkynyl complex **D,** which provides target coupled product **3** and regenerates the catalyst via reductive elimination. As an alternative, the acetylenic $\mathrm{Au^{III}}$ species **C** activates the triple bond of terminal alkyne **II** to furnish the gold(III) alkynyl complex **E**. Reductive elimination from intermediate **E**, would afford the homo-coupling by-product **4.**



Scheme 5. Possible mechanism.

4.3 Conclusion

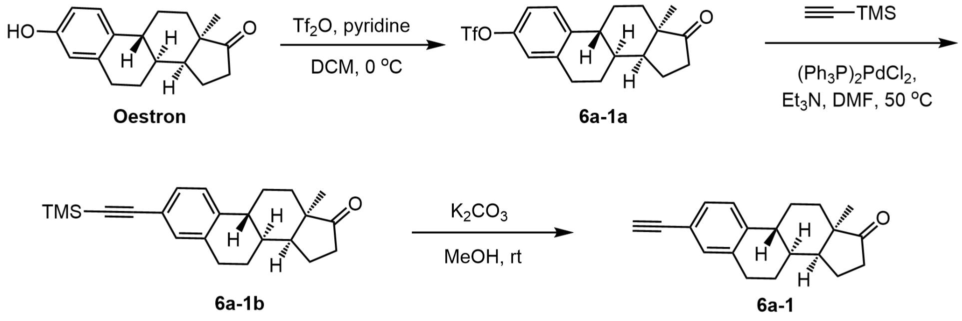
An efficient synthesis of unsymmetrical 1,3-diynes from terminal alkynes via homogeneous gold-catalyzed oxidative C(sp)-C(sp) cross-coupling with H_2O_2 as oxidant was developed. A wide range of substrates, including several complex molecules and marketed drugs, were transferred with excellent functional group tolerance. Furthermore, the catalyst system was applied at a gram scale and an extension towards the synthesis of polyacetylenes was possible.

4.4 Experimental Section

4.4.1 General Materials and Methods

Chemicals were purchased from commercial suppliers and used as delivered. Dry solvents were dispensed from the solvent purification system MB SPS-800. MeCN can be used directly without further drying and deoxygenation. Deuterated solvents were bought from Euriso-Top. Hydrogen peroxide solution (50 wt% in water, stabilized) was bought from Sigma-Aldrich. Unless otherwise stated, all reactions were carried out under an ambient atmosphere and monitored by thin layer chromatography (TLC). For reactions that require heating, the heat source: aluminum heating block (less than 0.5 mmol scale reactions), or oil bath (more than 0.5 mmol scale reactions). Components were visualized by treatment with aqueous potassium permanganate ($KMnO_4$) solution or by fluorescence quenching under UV light (254 nm). ^{1}H, ^{13}C{^{1}H} and ^{19}F NMR spectra were recorded on a Bruker Avance-III-300 (300 MHZ), Bruker Avance-III-400 (400 MHZ), Bruker Avance-III-500 (500 MHZ), Bruker Avance-III-600 (600 MHZ), Bruker Avance NEO 700 (700 MHZ) NMR spectrometer. Chemical shifts are expressed as parts per million (ppm, δ) downfield of tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.26 / 77.0 ppm) and CD_3OD (3.31 / 49.3 ppm) as internal standards. Data is reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentalet, m = multiplet, br = broad, dd = doublet of doublets, dp = doublet of pentalets, td = triplet of doublets, qd = quartet of doublets, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, hept = heptet; constants are absolute values and *J* values are expressed in Hertz (Hz). Mass spectra (MS and HRMS) were determined in the chemistry department of the University Heidelberg under the direction of Dr. J. Gross. For ESI (+) spectra, an ApexQe FT-ICR-MS spectrometer was applied. For ESI+ -spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR (IF528), IR (283), or FT-IR Vektor 22. Melting points (M.p.) were measured in open glass capillaries in a Büchi melting point apparatus. X-ray data were collected at a temperature of 200 K on the Bruker APEX-II Quazar area detector.

4.4.2 Preparation of Substrates

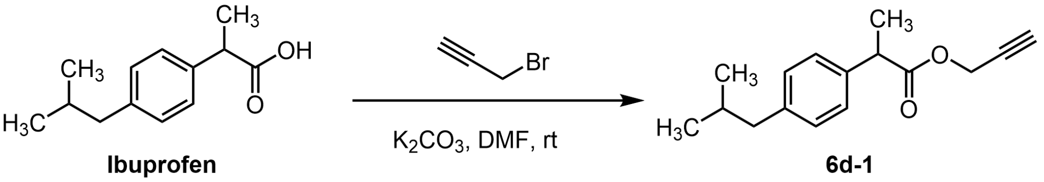


(*8S,9R,13R*)-3-Ethynyl-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-*17H*-cyclopenta[*a*]phenanthren-17-one (6a-1)

Step 1: To a solvent of Oestrone (1.0 g, 3.7 mmol) and pyridine (0.6 mL, 7.4 mmol) in 20 mL dry DCM was added dropwise Tf_2O (0.75 mL, 4.4 mmol) at 0 °C. The reaction was warmed up to room temperature and stirred for 2 h. Then the mixture was washed with 20 mL sat. brine, the aqueous phase was extracted with 3×20 mL EA, and the organic phases were combined, dried over Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography to afford product **6a-1a** as colorless solid (1.37 g, 92%).

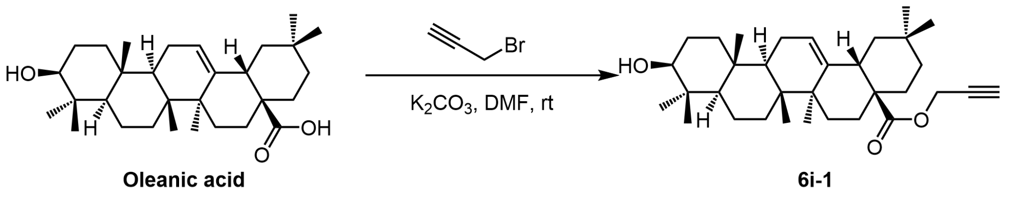
Step 2: To a suspension of $(Ph_3P)_2PdCl_2$ (50.5 mg, 0.072 mmol) in 4 mL DMF/Et_3N (1:1) were added **6a-1a** (483 mg, 1.2 mmol) and trimethylsilylacetylene (0.2 mL, 1.4 mmol). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 50 °C overnight. Then filtered, concentrated, and purified by silica gel chromatography to afford product **6a-2a** as light yellow solid (257.4 mg, 61%).

Step 3: To a solvent of **6a-2a** (240 mg, 0.7 mmol) in 12 mL DCM/MeOH (1:1) was added K_2CO_3 (304 mg, 2.2 mmol). The mixture was stirred at room temperature. After 30 min, filtered, concentrated, and purified by silica gel chromatography to afford target product **6a-1** as light yellow solid (176 mg, 86%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 – 7.11 (m, 3H), 3.02 (s, 1H), 2.89 (dd, *J* = 8.7, 4.1, 2H), 2.52 (dd, *J* = 18.3, 8.4, 1H), 2.46 – 2.37 (m, 1H), 2.37 – 2.25 (m, 1H), 2.17 (dd, *J* = 18.2, 9.3, 1H), 2.11 – 1.94 (m, 3H), 1.71 – 1.39 (m, 6H), 0.92 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.6, 140.8, 136.6, 132.6, 129.4, 125.4, 119.4, 83.7, 76.4, 50.5, 47.9, 44.4, 37.9, 35.8, 31.5, 29.0, 26.3, 25.6, 21.6, 13.8. **IR** (Reflection): ṽ = 3304, 2934, 2870, 2105, 1732, 1493, 1454, 1432, 1407, 1370, 1254, 1214, 1081, 1051, 1009, 944, 925, 825, 781, 655. **HRMS** (APCI) calcd for $C_{20}H_{23}O$ $[M+H]^+$: 279.1743, found: 279.1740. **M.p.** (amorphous): 208.8-211.6 °C



(+/-)-Prop-2-yn-1-yl 2-(4-isobutylphenyl)propanoate (6d-1)

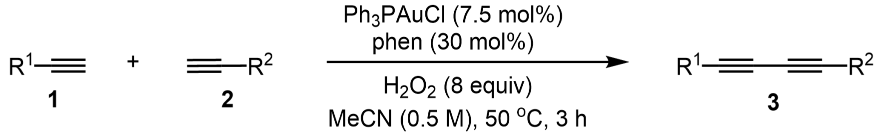
3-Bromopropyne (81 μL, 0.73 mmol) was added to a solution of Ibuprofen (100 mg, 0.485 mmol) and K_2CO_3 (268 mg, 1.94 mmol) in DMF (3 mL) at room temperature. The mixture was stirred at room temperature overnight. Then the reaction was diluted with 10 mL EA and washed 3×10 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography to afford target product **6d-1** as colorless oil (114.7 mg, 97%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 4.66 (ddd, *J* = 35.9, 15.6, 2.4 Hz, 2H), 3.74 (q, *J* = 7.2 Hz, 1H), 2.46 – 2.43 (m, 3H), 1.91 – 1.78 (m, 1H), 1.51 (d, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.9, 140.7, 137.2, 129.4, 127.2, 77.6, 74.8, 52.2, 45.0, 44.9, 30.2, 22.4, 18.5. **HRMS** (EI) calcd for $C_{16}H_{20}O_2$ $[M]^+$: 244.14578, found: 244.14482. **IR** (Reflection): ṽ = 3289, 2954, 2933, 2869, 2130, 1904, 1742, 1512, 1455, 1367, 1329, 1232, 1198, 1154, 1090, 1021, 929, 848, 799, 633.



Prop-2-yn-1-yl (*4aS,6aS,6bR,8aR,10S,12aR,12bR,14bS*)-10-hydroxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(*2H*)-carboxylate (6i-1)

3-Bromopropyne (0.26 mL, 2.3 mmol) was added to a solution of Oleanic acid (685 mg) and K_2CO_3 (828 mg, 6 mmol) in DMF (8 mL) at room temperature. The reaction mixture was stirred at room temperature for 3 h. Then the reaction was diluted with 15 mL ethyl acetate and washed with 3×15 mL sat. brine. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography to afford target product **6ai** as colorless solid (601.1 mg, 81%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.30 (t, *J* = 3.3, 1H), 4.62 (qd, *J* = 15.6, 2.4, 2H), 3.20 (dd, *J* = 10.6, 5.1, 1H), 2.86 (dd, *J* = 13.8, 4.0, 1H), 2.41 (t, *J* = 2.4, 1H), 1.96 (dd, *J* = 13.7, 4.6, 1H), 1.91 – 1.81 (m, 2H), 1.76 – 1.47 (m, 11H), 1.46 – 1.15 (m, 8H), 1.13 (s, 3H), 1.07 – 1.03 (m, 1H), 0.98 (s, 3H), 0.92 (s, 3H), 0.90 (s, 6H), 0.76 (d, *J* = 5.0, 3H), 0.72 (d, *J* = 9.6, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 176.8, 143.4, 122.6, 79.0, 78.1, 74.4, 55.2, 51.6, 47.6, 46.8, 45.8, 41.7, 41.3, 39.4, 38.7, 38.4, 37.0, 33.8, 33.1, 32.7, 32.2, 30.6, 28.1, 27.7, 27.2, 25.8, 23.6, 23.4, 23.0, 18.3, 17.1, 15.6, 15.3. **HRMS** (EI) calcd for $C_{33}H_{50}O_3$ $[M]^+$: 494.37545, found: 494.37728. **IR** (Reflection): ṽ = 3309, 2944, 2863, 2131, 1731, 1463, 1386, 1362, 1252, 1157, 1122, 1086, 1032, 995, 815, 755, 678, 638. **M.p.** (amorphous): 121.1-122.8 °C.

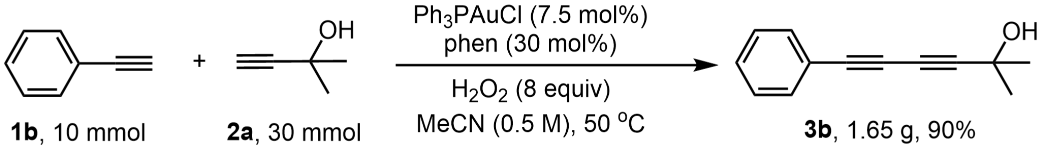
4.4.3 General Procedure for the Cross-Coupling of Terminal Alkynes



A solution of the terminal alkynes **1** (0.2 mmol), terminal alkynes **2** (0.6 mmol), Ph_3PAuCl (7.4 mg, 7.5 mol%), phen (10.8 mg, 30 mol%) and H_2O_2 (44.8 μL, 0.8 mmol, 50 wt% in water) in MeCN (0.4 mL) was stirred at 50 °C for 3 h. After completion of the reaction, products were detected by TLC. The solvent was removed under reduced pressure by an aspirator, the pure product was obtained by flash column chromatography on silica gel.

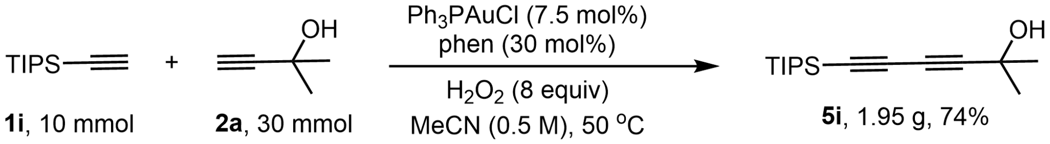
4.4.4 General Procedure for Gram Scale Reaction

A. Gram Scale Synthesis of 2-Methyl-6-phenylhexa-3,5-diyn-2-ol



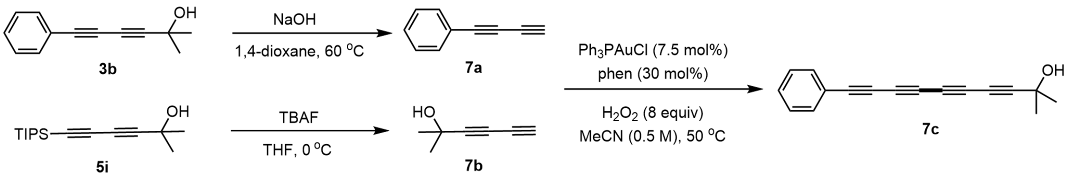
A solution of **1b** (10 mmol), **2a** (30 mmol), Ph_3PAuCl (373 mg, 7.5 mol%), phen (540 mg, 30 mol%) and H_2O_2 (4.5 mL, 80 mmol, 50 wt% in water) in MeCN (20 mL) was stirred at 50 °C for 5 h. After completion of the reaction, removed the solvent, the residue was purified by silica gel chromatography to afford **3b** as light yellow solid (1.65 g, 90%).

B. Gram Scale Synthesis of 2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol



A solution of **1b** (10 mmol), 2-methylbut-3-yn-2-ol **2a** (30 mmol), Ph_3PAuCl (373 mg, 7.5 mol%), phen (540 mg, 30 mol%) and H_2O_2 (4.5 mL, 80 mmol, 50 wt% in water) in MeCN (20 mL) was stirred at 50 °C for 5 h. After completion of the reaction, removed the solvent, the residue was purified by silica gel chromatography to afford **5i** as light yellow solid (1.95 g, 74%).

4.4.5 Tetrane Synthesis



Buta-1,3-diyn-1-ylbenzene (7a)

In a 50-mL flask, **3b** (368 mg, 2 mmol) was added to a solution of NaOH (160 mg, 4 mmol) in 1,4-dioxane (20 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air, stirred at 60 °C overnight, cooled the resulting solution to room temperature, concentrated, and purified by silica gel chromatography to afford **7a** as yellow oil (220 mg, 87%).

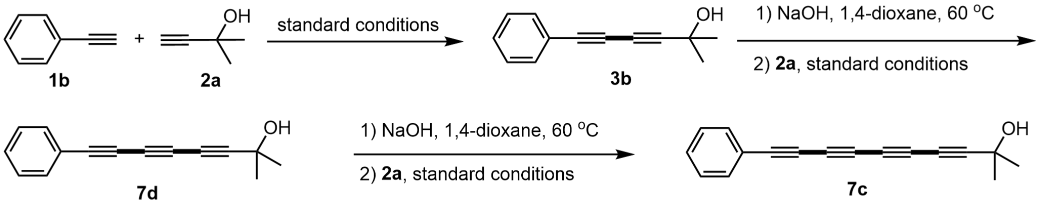
2-Methylhexa-3,5-diyn-2-ol (7b)

Compound **5i** (1.32 g, 5 mmol) in dry THF (50 mL). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The solution was cooled at 0 °C, then 6 mL of TBAF solution (1.0 M in THF, 6 mmol) was added and the resulting yellow solution was stirred at 0 °C for 45 min. Then the mixture was quenched with 50 mL water and extracted with 50 mL ether. The aqueous layer was separated and extracted with 50 mL Et_2O, and the combined organic layers dried over Na_2SO_4, filtered, concentrated, and purified by silica gel chromatography to afford **7b** as a red oil (459 mg, 85%).

2-Methyl-10-phenyldeca-3,5,7,9-tetrayn-2-ol (7c)

A solution of **7a** (63 mg, 0.5 mmol), **7b** (162 mg, 1.5 mmol), Ph_3PAuCl (18.5 mg, 7.5 mol%), phen (27 mg, 30 mol%) and H_2O_2 (224 μL, 4 mmol, 50 wt% in water) in MeCN (1 mL) was stirred at 50 °C for 3 h. Removed the solvent and the residue was purified by silica gel chromatography to afford **7c** as dark yellow oil (87.5 mg, 75%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 – 7.47 (m, 2H), 7.44 – 7.28 (m, 3H), 2.28 (br, 1H), 1.55 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.2, 130.0, 128.5, 120.4, 83.3, 77.0, 74.3, 67.4, 67.0, 65.7, 64.2, 63.1, 62.2, 30.9. **HRMS** (APCI) calcd for $C_{17}H_{11}$ $[M-OH]^+$: 215.0854, found: 215.0855; calcd for $C_{17}H_{11}O$ $[M-H]^+$: 231.0802, found: 231.0804. **IR** (Reflection): ṽ = 3346, 3063, 2983, 2933, 2212, 2181, 2150, 1732, 1491, 1442, 1377, 1364, 1254, 1165, 1019, 954, 861, 754, 686.

4.4.6 Relay Synthesis of Polyynes

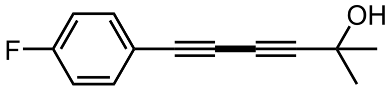


Step 1: According to standard conditions, 2-methyl-6-phenylhexa-3,5-diyn-2-ol **3a** could be obtained in 90-93% yields.

Step 2: In a 50-mL flask, **3b** (368 mg, 2 mmol) was added to a solution of NaOH (160 mg, 4 mmol) in 1,4-dioxane (20 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 60 °C overnight, cooled to room temperature, concentrated, and purified by flash silica gel chromatography to afford **7a** as yellow oil . Dissolve crude product **7a** with 4 mL MeCN immediately, then **2a** (584 μL, 6 mmol), Ph_3PAuCl (54 mg, 7.5 mol%), phen (108 mg, 30 mol%) and H_2O_2 (0.9 mL, 16 mmol, 50 wt% in water) were added, the mixture was stirred at 50 °C. After completion, removing the solvent and the residue was purified by silica gel chromatography to afford **7d** as dark yellow oil (321.3 mg, 77%).

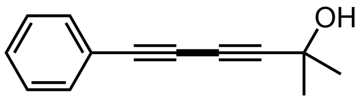
Step 3: In a 50-mL flask, **7d** (211 mg, 1 mmol) was added to a solution of NaOH (80 mg, 2 mmol) in 1,4-dioxane (10 mL) at room temperature. Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was stirred at 60 °C. After completion, cooled to room temperature, concentrated, and purified by silica gel chromatography to afford the crude product as dark yellow oil. Dissolve the crude product with 2 mL MeCN immediately, then **2a** (292 µL, 3 mmol), Ph_3PAuCl (37 mg, 7.5 mol%), phen (54 mg, 30 mol%) and H_2O_2 (450 µL, 8 mmol, 50 wt% in water) were added, and the mixture was stirred at 50 °C. After completion, purified by silica gel chromatography to afford **7c** as dark yellow oil (160 mg, 69%).

4.5 Characterization of Products



6-(4-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

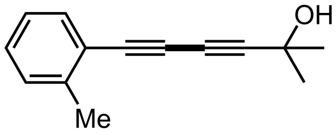
3a, colorless solid, 36.2 mg, 90% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.69 – 7.34 (m, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 2.51 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 162.9 (d, *J* = 251.5 Hz, CF), 134.5 (d, *J* = 8.6 Hz), 117.6 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 22.3 Hz), 86.7, 77.6, 72.9, 66.8, 65.7, 31.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.53. Characterization data of **3a** corresponded to the literature values.[6c]



2-Methyl-6-phenylhexa-3,5-diyn-2-ol

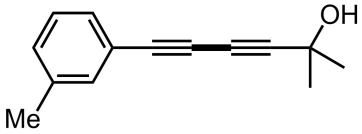
3b, light yellow solid, 34.2 mg, 93% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.32 – 7.15 (m, 3H), 2.13 (br, 1H), 1.51 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.2, 128.4, 121.5, 86.7, 78.7, 73.1, 67.0, 65.7, 31.1.

Characterization data of **3b** corresponded to the literature values.[6c]



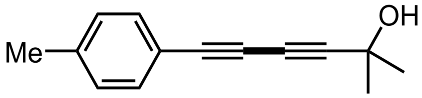
2-Methyl-6-(o-tolyl)hexa-3,5-diyn-2-ol

3c, light yellow oil, 37.6 mg, 95% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.6 Hz, 1H), 7.26 – 6.95 (m, 3H), 2.36 (s, 3H), 2.14 (br, 1H), 1.50 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 141.7, 132.9, 129.5, 129.1, 125.6, 121.3, 87.1, 77.8 76.7, 67.1, 65.8, 31.1, 20.6. Characterization data of **3c** corresponded to the literature values.[8]



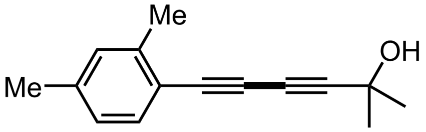
2-Methyl-6-(m-tolyl)hexa-3,5-diyn-2-ol

3d, light yellow oil, 33.6 mg, 85% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30 – 7.28 (m, 2H), 7.23 – 7.15 (m, 2H), 2.32 (s, 3H), 2.18 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.1, 133.0, 130.2, 129.6, 128.3, 121.3, 86.5, 79.0, 72.8, 67.1, 65.7, 31.1, 21.1. Characterization data of **3d** corresponded to the literature values.[5a]



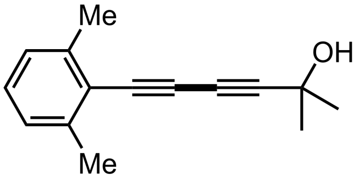
2-Methyl-6-(p-tolyl)hexa-3,5-diyn-2-ol

3e, colorless solid, 32.0 mg, 81% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 2.35 (s, 3H), 2.20 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 139.6, 132.4, 129.2, 118.3, 86.3, 79.1, 72.5, 67.1, 65.7, 31.1, 21.6. Characterization data of **3e** corresponded to the literature values.[6c]



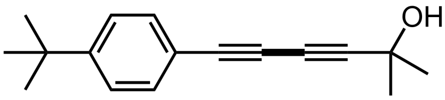
6-(2,4-Dimethylphenyl)-2-methylhexa-3,5-diyn-2-ol

3f, light yellow oil, 32.4 mg, 76% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 2.41 (s, 3H), 2.31 (s, 3H), 2.18 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 141.5, 139.5, 132.9, 130.4, 126.4, 118.2, 86.8, 78.1, 76.0, 67.3, 65.8, 31.1, 21.5, 20.5. **HRMS** (EI) calcd for $C_{15}H_{16}O$ $[M]^+$: 212.11957, found: 212.11954. **IR** (Reflection): ṽ = 1902, 1718, 1610, 1494, 1454, 1377, 1312, 1209, 1165, 1036, 952, 926, 855, 817, 703.



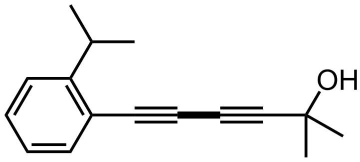
6-(2,6-Dimethylphenyl)-2-methylhexa-3,5-diyn-2-ol

3g, light yellow solid, 30.2 mg, 71% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 8.3, 6.8 Hz, 1H), 7.03 (d, *J* = 7.6 Hz, 2H), 2.44 (s, 6H), 2.15 (br, 1H), 1.61 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 142.0, 128.5, 126.7, 121.3, 87.7, 80.8, 67.2, 65.8, 31.1, 21.0. **HRMS** (EI) calcd for $C_{15}H_{16}O$ $[M]^+$: 212.11957, found: 212.11993. **IR** (Reflection): ṽ = 1935, 1573, 1467, 1377, 1363, 1303, 1203, 1164, 1033, 949, 860, 770, 729. **M.p.** (amorphous): 56.6-58.8 °C.



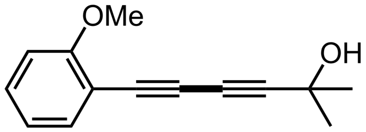
6-(4-(*tert*-Butyl)phenyl)-2-methylhexa-3,5-diyn-2-ol

3h, light yellow solid, 38.3 mg, 80% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent:10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 2.16 (br, 1H), 1.58 (s, 3H), 1.31 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.7, 132.3, 125.4, 118.4, 86.3, 79.1, 72.5, 67.2, 65.7, 34.9, 31.1, 31.0. Characterization data of **3h** corresponded to the literature values.[6c]



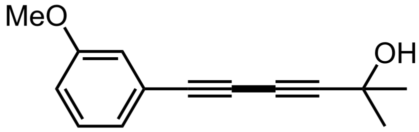
6-(2-Isopropylphenyl)-2-methylhexa-3,5-diyn-2-ol

3i, light yellow oil, 37.4 mg, 83% yield. R_f = 0.6 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.39 – 7.22 (m, 2H), 7.15 (td, *J* = 7.5, 1.5 Hz, 1H), 3.46 (hept, *J* = 6.9 Hz, 1H), 2.18 (br, 1H), 1.62 (s, 6H), 1.29 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.1, 133.5, 129.5, 125.6, 125.1, 120.3, 87.0, 77.6, 76.5, 67.2, 65.8, 31.7, 31.1, 23.2. **HRMS** (EI) calcd for $C_{16}H_{18}O$ $[M]^+$: 226.13522, found: 226.13596. **IR** (Reflection): ṽ = 1483, 1446, 1363, 1213, 1164, 950, 860, 756.



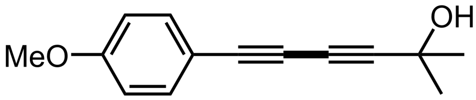
6-(2-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

3j, light yellow oil, 33.5 mg, 78% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.4 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.35 – 7.28 (m, 1H), 6.93 – 6.82 (m, 2H), 3.87 (s, 3H), 2.17 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.4, 134.4, 130.7, 120.4, 110.7, 110.6, 87.1, 76.9, 75.3, 67.3, 65.7, 55.8, 31.0. Characterization data of **3j** corresponded to the literature values.[13]



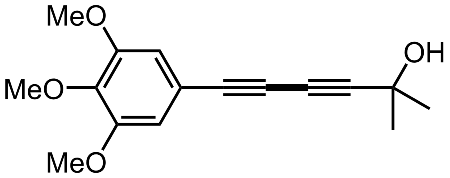
6-(3-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

3k, colorless solid, 32.1 mg, 75% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.21 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.99 (s, 1H), 6.91 (dd, *J* = 8.3, 2.5 Hz, 1H), 3.78 (s, 3H), 2.34 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.2, 129.5, 125.0, 122.4, 117.1, 116.0, 86.7, 78.6, 72.9, 66.9, 65.7, 55.2, 31.0. Characterization data of **3k** corresponded to the literature values.[13]



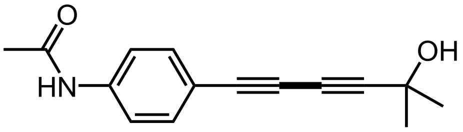
6-(4-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

3l, colorless solid, 34.4 mg, 80% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 6.85 – 6.80 (m, 2H), 3.80 (s, 3H), 2.24 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.3, 134.1, 114.1, 113.4, 86.1, 79.0, 71.9, 67.2, 65.7, 55.3, 31.1. Characterization data of **3l** corresponded to the literature values.[6c]



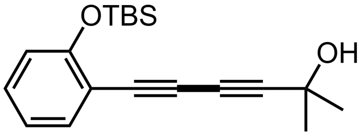
2-Methyl-6-(3,4,5-trimethoxyphenyl)hexa-3,5-diyn-2-ol

3m, light yellow solid, 45.9 mg, 84% yield. R_f = 0.5 (PE:EA = 2:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.70 (s, 2H), 3.84 (s, 3H), 3.82 (s, 6H), 2.21 (br, 1H), 1.56 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.0, 139.8, 116.3, 109.7, 86.7, 78.8, 72.3, 66.9, 65.6, 60.9, 56.1, 31.1. Characterization data of **3m** corresponded to the literature values.[14]



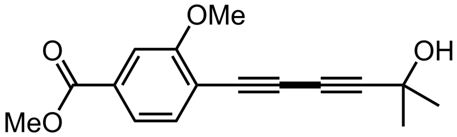
***N*-(4-(5-Hydroxy-5-methylhexa-1,3-diyn-1-yl)phenyl)acetamide**

3n, light yellow solid, 36.4 mg, 76% yield. R_f = 0.3 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CD_3OD) δ 7.52 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.7 Hz, 2H), 2.08 (s, 3H), 1.46 (s, 6H). **^{13}C NMR** (101 MHz, CD_3OD) δ 172.0, 141.3, 134.4, 121.0, 118.1, 88.4, 79.3, 73.9, 67.5, 66.2, 31.7, 24.2. **HRMS** (EI) calcd for $C_{15}H_{15}NO_2$ $[M]^+$: 241.10973, found: 241.10958. **IR** (Reflection): ṽ = 1650, 1599, 1513, 1454, 1398, 1317, 1210, 1175, 1144, 1016, 970, 930, 842, 826, 734. **M.p.** (amorphous): 212.4-214.6 °C.



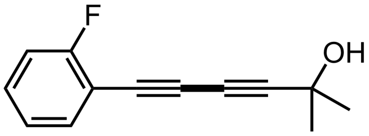
6-(2-((*tert*-Butyldimethylsilyl)oxy)phenyl)-2-methylhexa-3,5-diyn-2-ol

3o, light yellow oil, 52.6 mg, 84% yield. $R_f = 0.6$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.22 (td, *J* = 8.2, 1.7 Hz, 1H), 6.89 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 2.11 (br, 1H), 1.57 (s, 6H), 1.04 (s, 9H), 0.23 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 158.1, 134.0, 130.4, 121.2, 119.8, 114.3, 86.7, 76.8, 76.5, 67.4, 65.7, 31.1, 25.6, 18.2, -4.4. **HRMS** (EI) calcd for $C_{19}H_{26}SiO_2$ $[M]^+$: 314.16966, found: 31417020. **IR** (Reflection): ṽ = 1735, 1594, 1567, 1486, 1446, 1363, 1287, 1252, 1203, 1164, 1114, 913, 840, 782, 759.



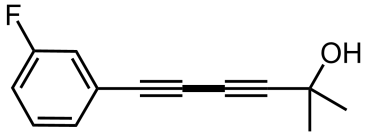
Methyl 4-(5-hydroxy-5-methylhexa-1,3-diyn-1-yl)-3-methoxybenzoate

3p, light yellow solid, 46.6 mg, 86% yield. $R_f = 0.3$ (PE:EA = 2:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.09 (d, *J* = 2.0 Hz, 1H), 7.98 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 2.36 (br, 1H), 1.56 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.9, 164.6, 136.0, 132.4, 122.6, 111.0, 110.2, 87.6, 74.0, 66.9, 65.6, 56.1, 52.1, 31.0. **HRMS** (EI) calcd for $C_{16}H_{16}O_4$ $[M]^+$: 272.10431, found: 272.10415. **IR** (Reflection): ṽ = 1900, 1705, 1599, 1500, 1435, 1411, 1378, 1320, 1257, 1196, 1167, 1135, 1111, 1051, 1016, 973, 953, 912, 841, 763, 737, 634. **M.p.** (amorphous): 92.4-93.6 °C.



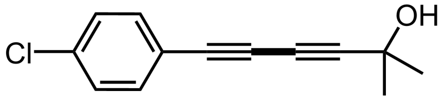
6-(2-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

3q, light yellow oil, 37.1 mg, 92% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (td, *J* = 7.1, 1.5 Hz, 1H), 7.33 (tdd, *J* = 8.2, 5.3, 1.7 Hz, 1H), 7.13 – 6.99 (m, 2H), 2.19 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.8 (d, *J* = 253.4 Hz), 134.3, 130.9 (d, *J* = 8.0 Hz), 124.1 (d, *J* = 3.8 Hz), 115.6 (d, *J* = 20.6 Hz), 110.4 (d, *J* = 15.6 Hz), 87.8, 77.9 (d, *J* = 3.2 Hz), 72.0, 66.8, 65.7, 31.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.76. **HRMS** (APCI) calcd for $C_{13}H_{10}F$ $[M-OH]^+$: 185.0761, found: 185.0760; calcd for $C_{13}H_{12}FO$ $[M+H]^+$: 203.0867, found: 203.0866. **IR** (Reflection): ṽ = 3258, 2980, 2934, 1609, 1573, 1490, 1450, 1377, 1321, 1265, 1224, 1206, 1166, 1108, 956, 865, 819, 750.



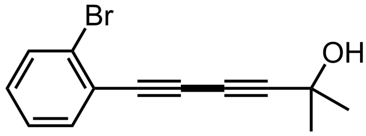
6-(3-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

3r, light yellow oil, 39.4 mg, 97% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.24 (m, 2H), 7.21 – 7.14 (m, 1H), 7.13 – 7.04 (m, 1H), 2.25 (br, 1H), 1.60 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2 (d, *J* = 247.4 Hz), 130.0 (d, *J* = 8.6 Hz), 128.4 (d, *J* = 3.1 Hz), 123.4 (d, J = 9.5 Hz), 119.2 (d, *J* = 23.1 Hz), 116.7 (d, *J* = 21.3 Hz), 87.4, 77.3 (d, *J* = 3.6 Hz), 74.0, 66.7, 65.7, 31.0. **^{19}F NMR** (282 MHz, CDCl3) δ -112.31. Characterization data of **3r** corresponded to the literature values.[15]



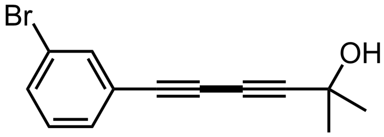
6-(4-Chlorophenyl)-2-methylhexa-3,5-diyn-2-ol

3s, light yellow solid, 41.7 mg, 95% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 2.17 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.4 133.7, 128.8, 120.0, 87.3, 77.5, 74.1, 66.8, 65.7, 31.0. Characterization data of **3s** corresponded to the literature values.[6c]



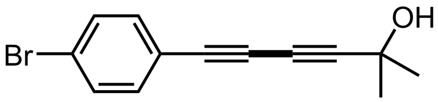
6-(2-Bromophenyl)-2-methylhexa-3,5-diyn-2-ol

3t, light yellow oil, 45.1 mg, 86% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.57 (dd, J = 8.0, 0.7 Hz, 1H), 7.49 (dd, J = 7.7, 1.7 Hz, 1H), 7.25 (td, J = 7.6, 1.0 Hz, 1H), 7.19 (td, J = 7.8, 1.7 Hz, 1H), 2.26 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 134.4, 132.5, 130.2, 127.0, 126.1, 123.9, 88.2, 77.3, 66.8, 65.7, 31.0. **HRMS** (APCI) calcd for $C_{13}H_{10}Br$ $[M-OH]^+$: 244.9960, found: 244.9958. **IR** (Reflection): ṽ = 3354, 3066, 2982, 2934, 2237, 2151, 1732, 1557, 1469, 1433, 1364, 1319, 1250, 1209, 1165, 1065, 1027, 952, 860, 753, 708, 663.



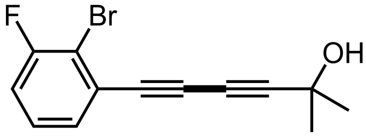
6-(3-Bromophenyl)-2-methylhexa-3,5-diyn-2-ol

3u, light yellow oil, 48.6 mg, 92% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.48 (d, J = 8.1 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 7.9 Hz, 1H), 2.19 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.1, 132.4, 131.0, 129.8, 123.6, 122.1, 87.5, 76.9, 74.4, 66.7, 65.7, 31.0. Characterization data of **3u** corresponded to the literature values.[16]



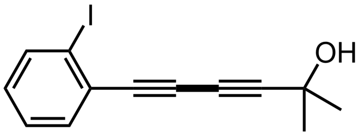
6-(4-Bromophenyl)-2-methylhexa-3,5-diyn-2-ol

3v, light yellow solid, 44.9 mg, 85% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45 (d, J = 8.5 Hz, 2H), 7.32 (d, J = 8.5 Hz, 2H), 2.11 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.8, 131.7, 123.7, 120.5, 87.3, 77.6, 74.3, 66.8, 65.7, 31.0. Characterization data of **3v** corresponded to the literature values.[6c]



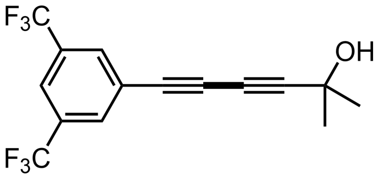
6-(2-Bromo-3-fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

3w, light yellow oil, 46.2 mg, 82% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.18 (td, *J* = 8.3, 5.8 Hz, 1H), 7.04 (td, *J* = 8.5, 0.9 Hz, 1H), 2.20 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.4 (d, *J* = 256.9 Hz), 130.7 (d, *J* = 8.9 Hz), 128.2 (d, *J* = 3.6 Hz), 127.0 (d, *J* = 0.7 Hz), 114.3 (d, *J* = 21.2 Hz), 113.7 (d, *J* = 17.9 Hz), 89.4, 82.3 (d, *J* = 4.2 Hz), 70.3, 66.7 (d, *J* = 1.0 Hz), 65.8, 30.9. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -104.14. **HRMS** (EI) calcd for $C_{13}H_{10}BrFO$ $[M]^+$: 279.98936, found: 279.99042. **IR** (Reflection): ṽ = 1596, 1560, 1461, 1444, 1364, 1279, 1254, 1209, 1163, 952, 873, 777, 717.



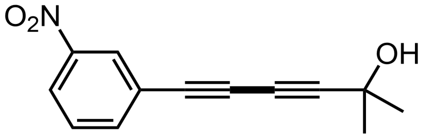
6-(2-Iodophenyl)-2-methylhexa-3,5-diyn-2-ol

3x, light yellow oil, 50.8 mg, 82% yield. R_f = 0.5 (PE:EA = 5:1) , chromatography eluent:10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.0, 0.5 Hz, 1H), 7.48 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.30 (td, *J* = 7.7, 0.9 Hz, 1H), 7.03 (td, *J* = 7.8, 1.6 Hz, 1H), 2.20 (br, 1H), 1.60 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.8, 133.9, 130.2, 128.4, 127.8, 100.7, 88.3, 79.9, 66.9, 65.8, 31.0. **HRMS** (EI) calcd for $C_{13}H_{11}OI$ $[M]^+$: 309.98491, found: 309.98502. **IR** (Reflection): ṽ = 1579, 1553, 1462, 1429, 1364, 1209, 1165, 1016, 952, 860, 753, 706, 650.



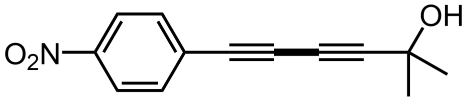
6-(3,5-Bis(trifluoromethyl)phenyl)-2-methylhexa-3,5-diyn-2-ol

3y, light yellow oil, 46.2 mg, 72% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent:10% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.89 (s, 2H), 7.83 (s, 1H), 2.13 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 132.2 (s), 132.1 (q, J = 120.0 Hz), 124.1 (s), 122.7 (q, J = 273.0 Hz), 122.5 (dd, J = 7.3, 3.7 Hz), 88.8, 76.5, 75.1, 66.2, 65.7, 30.9. **^{19}F NMR** (282 MHz, CDCl3) δ -63.28. **HRMS** (EI) calcd for $C_{15}H_{10}OF_6$ [M]$^+$: 320.06304, found: 320.06296. **IR** (Reflection): $\tilde{\nu}$ = 1614, 1461, 1390, 1278, 1175, 1136, 1067, 957, 897, 848, 723, 699, 683.



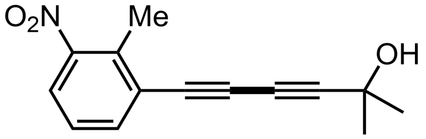
2-Methyl-6-(3-nitrophenyl)hexa-3,5-diyn-2-ol

3z, dark yellow oil, 38.4 mg, 84% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.33 – 8.26 (m, 1H), 8.24 – 8.12 (m, 1H), 7.75 (d, J = 7.7 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 2.24 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 148.1, 138.0, 129.5, 127.2, 123.8, 123.5, 88.3, 75.8, 75.6, 66.3, 65.7, 31.0. **HRMS** (APCI) calcd for $C_{13}H_{10}NO_2$ [M-OH]$^+$: 212.0706, found: 212.0723; calcd for $C_{13}H_{12}NO_3$ [M+H]$^+$: 230.0812, found: 230.0806. **IR** (Reflection): $\tilde{\nu}$ = 3362, 3083, 2984, 2240, 2152, 1533, 1472, 1354, 1210, 1166, 955, 898, 849, 807, 769, 735, 671.



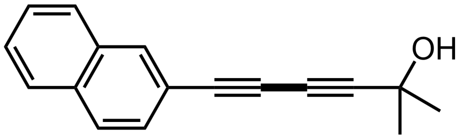
2-Methyl-6-(4-nitrophenyl)hexa-3,5-diyn-2-ol

3aa, dark yellow solid, 34.1 mg, 74% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.18 (d, J = 8.8 Hz, 2H), 7.60 (d, J = 8.8 Hz, 2H), 2.20 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 147.5, 133.2, 128.5, 123.6, 89.5, 78.1, 76.3, 66.3, 65.7, 30.9. Characterization data of **3aa** corresponded to the literature values.[5a]



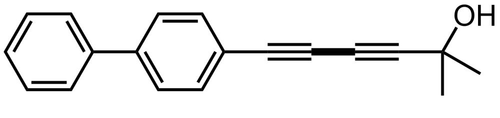
2-Methyl-6-(2-methyl-3-nitrophenyl)hexa-3,5-diyn-2-ol

3ab, light yellow oil, 41.8 mg, 86% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 7.7 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 2.81 (s, 3H), 2.42 (br, 1H), 1.77 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.3, 137.0, 136.0, 126.4, 125.0, 124.7, 78.9, 75.3, 66.4, 65.7, 31.0, 17.5. **HRMS** (EI) calcd for $C_{14}H_{13}NO_3$ $[M]^+$: 243.08899, found: 243.08837. **IR** (Reflection): ṽ = 3356, 2984, 2934, 2237, 2149, 1603, 1536, 1455, 1354, 1225, 1206, 1191, 1166, 1083, 954, 888, 852, 807, 761, 735, 701, 649.



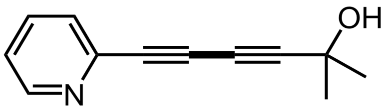
2-Methyl-6-(naphthalen-2-yl)hexa-3,5-diyn-2-ol

3ac, light yellow solid, 43.4 mg, 93% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.87 – 7.70 (m, 3H), 7.54 – 7.44 (m, 3H), 2.25 (br, 1H), 1.62 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.1, 133.0, 132.7, 128.4, 128.1, 127.8, 127.7, 127.2, 126.7, 118.7, 86.9, 79.2, 73.4, 67.2, 65.7, 31.1. **HRMS** (EI) calcd for $C_{17}H_{14}O$ $[M]^+$: 234.10392, found: 234.10234. **IR** (Reflection): ṽ = 1727, 1595, 1498, 1455, 1409, 1376, 1362, 1304, 1269, 1241, 1208, 1163, 961, 946, 904, 863, 822, 745, 627. **M.p.** (amorphous): 96.8-97.4 °C.



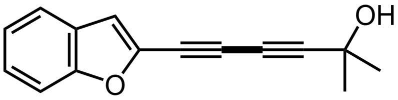
6-([1,1'-Biphenyl]-4-yl)-2-methylhexa-3,5-diyn-2-ol

3ad, light yellow solid, 43.1 mg, 83% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 6H), 7.48 – 7.42 (m, 2H), 7.40 – 7.34 (m, 1H), 2.16 (br, 1H), 1.60 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.0, 140.0, 132.9, 128.9, 127.8, 127.1, 127.0, 120.3, 87.0, 78.7, 73.8, 67.1, 65.7, 31.1. Characterization data of **3ad** corresponded to the literature values.[6c]



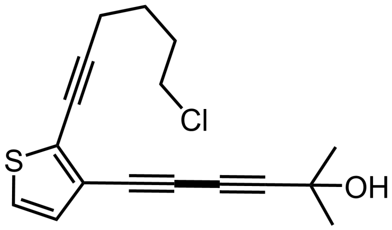
2-Methyl-6-(pyridin-2-yl)hexa-3,5-diyn-2-ol

3ae, dark yellow solid, 26.4 mg, 71% yield. $R_f = 0.4$ (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.8 Hz, 1H), 7.59 (td, *J* = 7.7, 1.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.12 (m, 1H), 3.02 (br, 1H), 1.52 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.0, 142.0, 136.3, 128.1, 123.5, 88.2, 73.6, 66.4, 65.4, 31.0. Characterization data of **3ae** corresponded to the literature values.[5a]



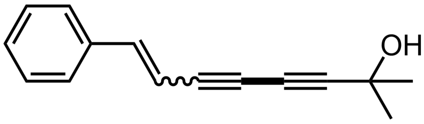
6-(Benzofuran-2-yl)-2-methylhexa-3,5-diyn-2-ol

3af, light yellow solid, 30.1 mg, 67% yield. $R_f = 0.6$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.7 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.32 – 7.24 (m, 1H), 7.23 – 7.08 (m, 1H), 6.97 (s, 1H), 2.12 (br, 1H), 1.52 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 155.0, 137.6, 127.1, 126.3, 123.5, 121.4, 114.3, 111.3, 90.1, 79.3, 68.5, 66.4, 65.8, 30.9. **HRMS** (EI) calcd for $C_{15}H_{12}O_2$ $[M]^+$: 224.08318, found: 224.08306. **IR** (Reflection): ṽ = 1611, 1561, 1475, 1447, 1346, 1307, 1258, 1229, 1190, 1162, 1143, 1042, 1008, 954, 924, 884, 851, 816, 797, 751, 640, 612. **M.p.** (amorphous): 82.4-83.2 °C.



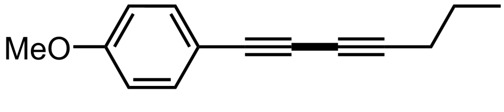
6-(2-(6-Chlorohex-1-yn-1-yl)thiophen-3-yl)-2-methylhexa-3,5-diyn-2-ol

3ag, dark yellow oil, 46.8 mg, 77% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.06 (d, *J* = 5.3 Hz, 1H), 6.96 (d, *J* = 5.3 Hz, 1H), 3.63 (t, *J* = 6.5 Hz, 2H), 2.55 (t, *J* = 6.8 Hz, 2H), 2.19 (br, 1H), 2.06 – 1.96 (m, 2H), 1.85 – 1.74 (m, 2H), 1.57 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 129.7, 129.6, 125.0, 124.2, 99.0, 87.6, 76.2, 73.3, 73.2, 67.0, 65.7, 44.6, 31.3, 31.0, 25.4, 19.1. **HRMS** (EI) calcd for $C_{17}H_{17}OSCl$ $[M]^+$: 304.06831, found: 304.06826. **IR** (Reflection): ṽ = 1731, 1509, 1454, 1427,1364, 1329, 1293, 1224, 1201, 1166, 1097,1078, 958, 911, 846, 815, 728, 642.



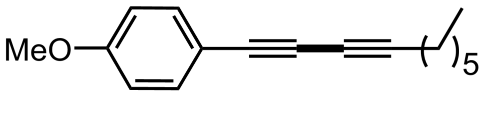
2-Methyl-8-phenylocta-7-en-3,5-diyn-2-ol

3ah, Z:E = 1:6, light yellow oil, 28.9 mg, 69% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.1 Hz, 0.34H), 7.49 – 7.27 (m, 5.50H), 7.08 (d, *J* = 16.3 Hz, 1H), 6.76 (d, *J* = 12.1 Hz, 0.17 H), 6.18 (d, *J* = 16.3 Hz, 1H), 5.73 (d, *J* = 12.1 Hz, 0.17H), 2.12 (br, 1H), 1.58 (s, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.7, 142.4(Z), 135.9(Z), 135.6, 129.3, 129.1(Z), 128.8, 128.5(Z), 128.4(Z), 126.4, 106.5, 105.6(Z), 88.5(Z), 87.3, 79.6(Z), 78.5, 77.3(Z), 75.2, 67.3, 67.2(Z), 65.8(Z), 65.7, 31.1. **HRMS** (EI) calcd for $C_{15}H_{14}O$ $[M]^+$: 210.10392, found: 210.10387. **IR** (Reflection): ṽ = 1732, 1605, 1574, 1491, 1448, 1363, 1257, 1207, 1160, 1074, 1027, 952, 913, 851, 808, 784, 747, 689, 647.



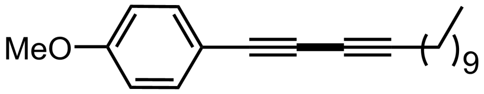
1-(Hepta-1,3-diyn-1-yl)-4-methoxybenzene

3ai, light yellow oil, 21.3 mg, 73% yield. R_f = 0.5 (PE:EA = 50:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 2.33 (t, *J* = 7.0 Hz, 2H), 1.60 (dd, *J* = 14.4, 7.2 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.0, 134.0, 114.0, 114.2, 84.0, 74.8, 73.1, 65.3, 55.3, 21.8, 21.5, 13.5. **HRMS** (EI) calcd for $C_{14}H_{14}O$ $[M]^+$: 198.10392, found: 198.10357. **IR** (Reflection): ṽ = 1733, 1604, 1568, 1509, 1462, 1341, 1303, 1287, 1251, 1173, 1107, 1031, 832.



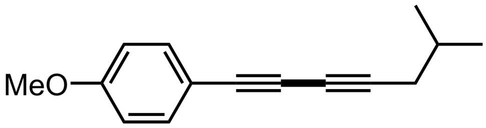
1-(Deca-1,3-diyn-1-yl)-4-methoxybenzene

3aj, light yellow oil, 23.0 mg, 48% yield. R_f = 0.6 (PE:EA = 50:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.38 (m, 2H), 6.87 – 6.78 (m, 2H), 3.80 (s, 3H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.63 – 1.51 (m, 2H), 1.47 – 1.38 (m, 2H), 1.36 – 1.24 (m, 4H), 0.90 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.0, 134.0, 114.1, 114.0, 84.2, 74.8, 73.1, 65.2, 55.3, 31.3, 28.5, 28.3, 22.5, 19.6, 14.0. **HRMS** (EI) calcd for $C_{17}H_{20}O$ $[M]^+$: 240.15087, found: 240.14999. **IR** (Reflection): ṽ = 1734, 1604, 1568, 1509, 1464, 1287, 1251, 1173, 1106, 1032, 831.



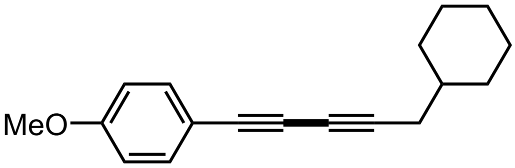
1-Methoxy-4-(tetradeca-1,3-diyn-1-yl)benzene

3ak, light yellow oil, 32.7 mg, 55% yield. $R_f = 0.5$ (PE:EA = 50:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 – 7.33 (m, 2H), 6.98 – 6.64 (m, 2H), 3.80 (s, 3H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.57 (dt, *J* = 14.6, 7.0 Hz, 2H), 1.40 (dd, *J* = 13.8, 6.9 Hz, 2H), 1.31 – 1.24 (m, 12H), 0.88 (t, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.0, 134.0, 114.1, 114.0, 84.2, 74.8, 73.2, 65.2, 55.3, 31.9, 29.6, 29.5, 29.3, 29.1, 28.9, 28.3, 22.7, 19.6, 14.1. **HRMS** (EI) calcd for $C_{21}H_{28}O$ $[M]^+$: 296.21347, found: 296.21348. **IR** (Reflection): ṽ = 2929, 2854, 2538, 2148, 1734, 1604, 1568, 1510, 1465, 1336, 1303, 1287, 1252, 1173, 1106, 1033, 832, 722, 644.



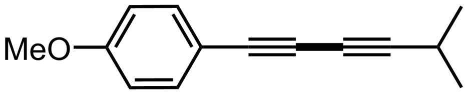
1-Methoxy-4-(6-methylhepta-1,3-diyn-1-yl)benzene

3al, light yellow oil, 23.3 mg, 55% yield. $R_f = 0.5$ (PE:EA = 50:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.33 (m, 2H), 6.92 – 6.69 (m, 2H), 3.80 (s, 3H), 2.25 (d, *J* = 6.5 Hz, 2H), 1.95 – 1.82 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.0, 134.0, 114.1, 114.0, 83.1, 74.8, 73.2, 66.0, 55.3, 28.7, 28.1, 22.0. **HRMS** (EI) calcd for $C_{15}H_{16}O$ $[M]^+$: 212.11957, found: 212.11962. **IR** (Reflection): ṽ = 1604, 1566, 1509, 1462, 1385, 1346, 1288, 1250, 1172, 1107, 1030, 830.



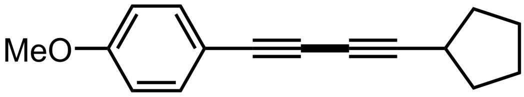
1-(5-Cyclohexylpenta-1,3-diyn-1-yl)-4-methoxybenzene

3am, light yellow oil, 37.2 mg, 73% yield. $R_f = 0.6$ (PE:EA = 50:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.8 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 2.25 (d, *J* = 6.6 Hz, 2H), 1.82 (d, *J* = 12.9 Hz, 2H), 1.78 – 1.62 (m, 3H), 1.60 – 1.47 (m, 1H), 1.36 – 1.15 (m, 3H), 1.15 – 0.95 (m, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.0, 134.0, 114.1, 114.0, 83.2, 74.8, 73.2, 66.0, 55.3, 37.3, 32.7, 27.4, 26.12, 26.06. **HRMS** (EI) calcd for $C_{18}H_{20}O$ $[M]^+$: 252.15087, found: 252.15094. **IR** (Reflection): ṽ = 1889, 1734, 1606, 1568, 1510, 1446, 1421, 1371, 1350, 1331, 1304, 1290, 1259, 1175, 1106, 1065, 1031, 895, 831, 773, 644.



1-Methoxy-4-(5-methylhexa-1,3-diyn-1-yl)benzene

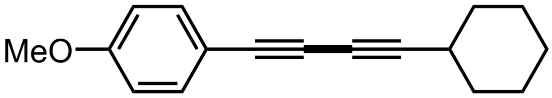
3an, light yellow oil, 24.1 mg, 61% yield. $R_f = 0.4$ (PE:EA = 50:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.31 (m, 2H), 6.86 – 6.75 (m, 2H), 3.80 (s, 3H), 2.71 (hept, *J* = 6.9 Hz, 1H), 1.23 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.0, 134.0, 114.1, 114.0, 89.0, 75.6, 72.9, 64.5, 55.3, 22.5, 21.3. **HRMS** (EI) calcd for $C_{14}H_{14}O$ $[M]^+$: 198.10392, found: 198.10415. **IR** (Reflection): ṽ = 1603, 1568, 1509, 1464, 1332, 1285, 1251, 1174, 1106, 1030, 831.



1-(Cyclopentylbuta-1,3-diyn-1-yl)-4-methoxybenzene

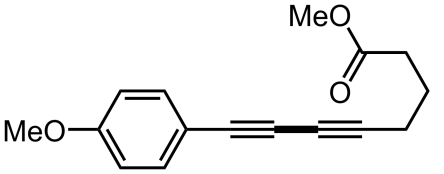
3ao, light yellow solid, 30.0 mg, 67% yield. $R_f = 0.4$ (PE:EA = 50:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 2H), 6.89 – 6.70 (m, 2H), 3.80 (s, 3H), 2.77 (p, *J* = 7.5 Hz, 1H), 2.02 – 1.89 (m, 2H), 1.82 – 1.64 (m, 4H), 1.64 – 1.50 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ

160.0, 134.0, 114.1, 114.0, 88.1, 75.6, 73.1, 64.7, 55.3, 33.6, 30.8, 25.1. **HRMS** (EI) calcd for $C_{16}H_{16}O$ $[M]^+$: 224.11957, found: 224.11960. **IR** (Reflection): ṽ = 1601, 1567, 1509, 1450, 1353, 1286, 1249, 1173, 1108, 1036, 941, 834, 629. **M.p.** (amorphous): 67.4-68.2 °C.



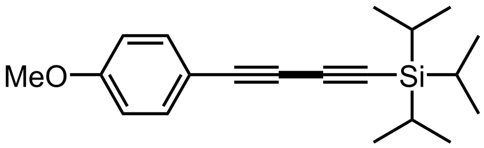
1-(Cyclohexylbuta-1,3-diyn-1-yl)-4-methoxybenzene

3ap, light yellow solid, 31.5 mg, 66% yield. R_f = 0.7 (PE:EA = 20:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 3.80 (s, 2H), 2.53 (t, *J* = 8.5 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.73 (d, *J* = 3.6 Hz, 1H), 1.51 (d, *J* = 9.2 Hz, 1H), 1.32 (t, *J* = 8.0 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.0, 134.0 114.1, 114.0, 87.9, 75.4, 73.0, 65.1, 55.3, 32.2, 29.7, 25.7, 24.7. **HRMS** (APCI) calcd for $C_{17}H_{19}O$ $[M+H]^+$: 239.1430, found: 239.1427. **IR** (Reflection): ṽ = 2931, 2856, 2235, 2140, 1604, 1567, 1509, 1447, 1283, 1250, 1175, 1110, 1033, 891, 831, 809, 764, 627. **M.p.** (amorphous): 43.5-44.6 °C.



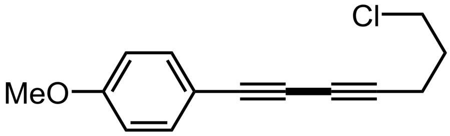
Methyl 8-(4-methoxyphenyl)octa-5,7-diynoate

3aq, light yellow solid, 37.2 mg, 73% yield. R_f = 0.4 (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.9 Hz, 2H), 6.82 (d, *J* = 8.9 Hz, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 2.46 (dt, *J* = 12.2, 7.1 Hz, 4H), 1.89 (p, *J* = 7.1 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 173.3, 160.1, 134.0, 114.0, 113.8, 82.5, 75.2, 72.9, 66.1, 55.3, 51.6, 32.7, 23.5, 19.0. **HRMS** (EI) calcd for $C_{16}H_{16}O_3$ $[M]^+$: 256.10940, found: 256.10909. **IR** (Reflection): ṽ = 1736, 1603, 1567, 1510, 1459, 1439, 1340, 1287, 1250, 1173, 1107, 1029, 832. **M.p.** (amorphous): 54.4-56.0 °C.



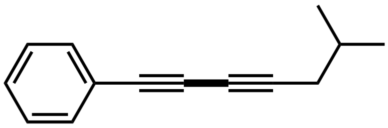
Triisopropyl((4-methoxyphenyl)buta-1,3-diyn-1-yl)silane

3ar, light yellow oil, 36.6 mg, 59% yield. $R_f = 0.5$ (PE:EA = 40:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H), 1.11 (s, 21H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.3, 134.3, 114.1, 113.4, 89.8, 87.0, 75.8, 73.5, 55.3, 18.6, 11.3. **HRMS** (APCI) calcd for $C_{20}H_{29}OSi$ $[M+1]^+$: 313.1981, found: 313.1982. **IR** (Reflection): ṽ = 2943, 2891, 2865, 2201, 2098, 1603, 1567, 1509, 1462, 1384, 1297, 1252, 1172, 1107, 1072, 1017, 882, 831, 678.



1-(7-Chlorohepta-1,3-diyn-1-yl)-4-methoxybenzene

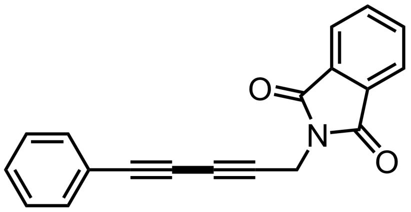
3as, light yellow oil, 31.0 mg, 67% yield. $R_f = 0.2$ (PE:EA = 50:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.35 (m, 2H), 6.89 – 6.77 (m, 2H), 3.81 (s, 2H), 3.68 (t, *J* = 6.3 Hz, 2H), 2.56 (t, *J* = 6.8 Hz, 2H), 2.02 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.2, 134.1, 114.1, 113.7, 81.7, 75.4, 72.8, 66.3, 55.3, 43.4, 31.0, 17.0. **HRMS** (EI) calcd for $C_{14}H_{13}OCl$ $[M]^+$: 232.06494, found: 232.06511. **IR** (Reflection): ṽ = 1732, 1603, 1567, 1509, 1461, 1441, 1355, 1304, 1286, 1250, 1173, 1107, 1030, 832, 656.



(6-Methylhepta-1,3-diyn-1-yl)benzene

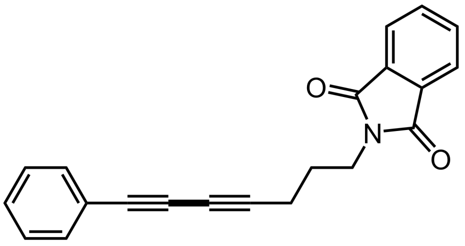
3at, light yellow oil, 24.1 mg, 66% yield. R_f = 0.7 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.38 – 7.26 (m, 3H), 2.26 (d, *J* = 6.5 Hz, 2H), 1.90 (dp, *J* = 13.2, 6.6 Hz, 1H), 1.03 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 128.8, 128.3, 122.1, 83.9, 74.6, 74.4, 65.9, 28.7, 28.1, 22.0. **HRMS** (EI) calcd for $C_{14}H_{14}$ $[M]^+$:182.10900, found:

182.10850. **IR** (Reflection): ṽ = 1611, 1561, 1475, 1447, 1346, 1307, 1258, 1229, 1190, 1162, 1143, 1042, 1008, 954, 924, 884, 851, 816, 797, 751, 640, 612.



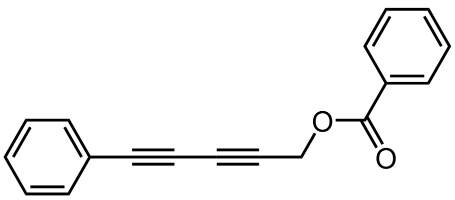
2-(5-Phenylpenta-2,4-diyn-1-yl)isoindoline-1,3-dione

3au, light yellow solid, 39.6 mg, 69% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.39 – 7.31 (m, 2H), 7.26 – 7.14 (m, 3H), 4.51 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 166.8, 134.2, 132.6, 131.9, 129.3, 128.3, 123.6, 121.2, 77.5, 75.9, 73.3, 67.9, 27.8. Characterization data of **3au** corresponded to the literature values.[8]



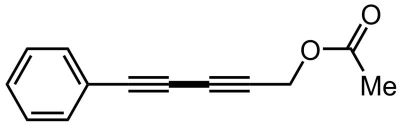
2-(7-Phenylhepta-4,6-diyn-1-yl)isoindoline-1,3-dione

3av, light yellow oil, 35.2 mg, 56% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 – 7.79 (m, 2H), 7.75 – 7.63 (m, 2H), 7.45 – 7.37 (m, 2H), 7.36 – 7.23 (m, 3H), 3.82 (t, *J* = 6.9 Hz, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.98 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.3, 133.9, 132.5, 132.1, 128.8, 128.3, 123.3, 121.9, 82.9, 75.0, 74.0, 65.7, 37.2, 27.0, 17.5. Characterization data of **3av** corresponded to the literature values.[5a]



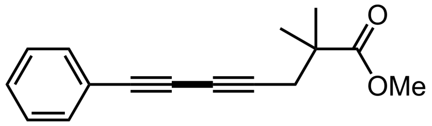
5-Phenylpenta-2,4-diyn-1-yl benzoate

3aw, light yellow oil, 37.3 mg, 72% yield. R_f = 0.5 (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.14 – 8.02 (m, 2H), 7.59 (t, J = 7.4 Hz, 1H), 7.47 (dd, J = 15.1, 7.5 Hz, 4H), 7.42 – 7.29 (m, 3H), 5.07 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.7, 133.4, 132.6, 129.8, 129.4, 129.3, 128.4, 128.4, 121.2, 78.8, 76.2, 73.1, 71.3, 53.1. Characterization data of **3aw** corresponded to the literature values.[5a]



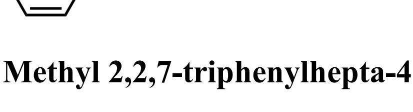
5-Phenylpenta-2,4-diyn-1-yl acetate

3ax, light yellow solid, 27.8 mg, 70% yield. R_f = 0.6 (PE:EA = 10:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.49 (dd, J = 7.9, 1.4 Hz, 2H), 7.42 – 7.27 (m, 3H), 4.81 (s, 2H), 2.12 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.0, 132.6, 129.5, 128.4, 121.2, 78.8, 76.1, 73.0, 71.1, 52.5, 20.6. Characterization data of **3ax** corresponded to the literature values.[6a]



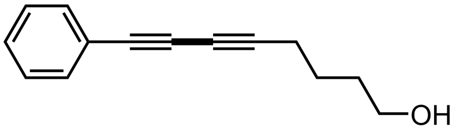
Methyl 2,2-dimethyl-7-phenylhepta-4,6-diynoate

3ay, light yellow oil, 28.1 mg, 58% yield. R_f = 0.7 (PE:EA = 10:1), chromatography eluent: 1% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (dd, J = 7.6, 1.7 Hz, 2H), 7.38 – 7.25 (m, 3H), 3.71 (s, 3H), 2.63 (s, 2H), 1.32 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 176.8, 132.5, 128.9, 128.3, 121.9, 81.0, 75.2, 74.2, 67.1, 52.2, 42.4, 30.6, 24.7. **HRMS** (EI) calcd for $C_{16}H_{16}O_2$ $[M]^+$: 240.11448, found: 240.11401. **IR** (Reflection): ṽ = 1733, 1596, 1571, 1490, 1470, 1442, 1388, 1367, 1328, 1304, 1254, 1199, 1134, 1024, 997, 859, 755, 689.



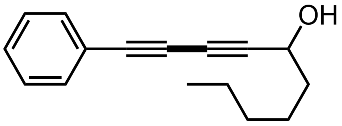
Methyl 2,2,7-triphenylhepta-4,6-diynoate

3az, light yellow oil, 48.3 mg, 66% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.2 Hz, 2H), 7.39 – 7.23 (m, 13H), 3.76 (s, 3H), 3.47 (s, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 173.6, 141.1, 132.5, 128.9, 128.7, 128.3, 128.0, 127.4, 121.8, 80.6, 75.3, 74.2, 68.3, 60.1, 52.8, 30.5. **HRMS** (EI) calcd for $C_{26}H_{20}O_2$ $[M]^+$: 364.14578, found: 364.14590. **IR** (Reflection): ṽ = 1953, 1883, 1803, 1731, 1597, 1492, 1444, 1433, 1227, 1020, 755, 698.



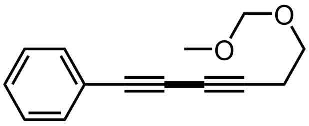
8-Phenylocta-5,7-diyn-1-ol

3ba, light yellow oil, 27.2 mg, 69% yield. R_f = 0.4 (DCM:MeOH = 50:1) , chromatography eluent: 10% Methanol in dichloromethane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.6, 1.9 Hz, 2H), 7.38 – 7.25 (m, 3H), 3.69 (t, *J* = 6.0 Hz, 2H), 2.41 (t, *J* = 6.6 Hz, 2H), 1.79 – 1.61 (m, 4H), 1.55 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 128.8, 128.3, 122.0, 84.2, 74.9, 74.2, 65.4, 62.2, 31.7, 24.5, 19.3. Characterization data of **3ba** corresponded to the literature values.[15]



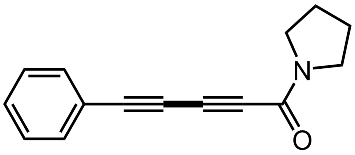
1-Phenyldeca-1,3-diyn-5-ol

3bb, light yellow oil, 38.5 mg, 85% yield. R_f = 0.6 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 8.1, 1.5 Hz, 2H), 7.39 – 7.27 (m, 3H), 4.51 (t, *J* = 6.6 Hz, 1H), 1.98 (br, 1H), 1.81 – 1.72 (m, 2H), 1.55 – 1.44 (m, 2H), 1.37 – 1.25 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.5, 129.2, 128.4, 121.5, 83.5, 78.5, 73.2, 69.5, 63.1, 37.5, 31.4, 24.7, 22.5, 14.0. **HRMS** (APCI) calcd for $C_{16}H_{17}$ $[M-OH]^+$: 209.1325, found: 209.1323; calcd for $C_{16}H_{17}O$ $[M-H]^-$: 225.1274, found: 225.1272. **IR** (Reflection): ṽ = 3368, 2955, 2859, 2240, 2210, 1707, 1596, 1490, 1443, 1378, 1338, 1177, 1128, 1025, 915, 755, 689.



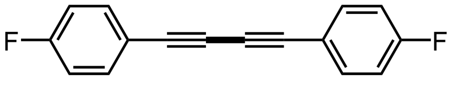
(6-(Methoxymethoxy)hexa-1,3-diyn-1-yl)benzene

3bc, light yellow oil, 29.2 mg, 68% yield. R_f = 0.4 (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.37 – 7.27 (m, 3H), 4.67 (s, 2H), 3.70 (t, *J* = 6.7 Hz, 2H), 3.39 (s, 3H), 2.67 (t, *J* = 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.5, 128.9, 128.3, 121.9, 96.5, 81.1, 75.1, 74.1, 66.1, 65.4, 55.3, 21.2. **HRMS** (EI) calcd for $C_{14}H_{14}O_2$ $[M]^+$: 214.09883, found: 214.09930. **IR** (Reflection): ṽ = 1722, 1596, 1490, 1443, 1380, 1342, 1207, 1150, 1111, 1069, 1029, 961, 917, 756, 690.



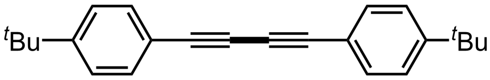
5-Phenyl-1-(pyrrolidin-1-yl)penta-2,4-diyn-1-one

3bd, light yellow solid, 31.1 mg, 70% yield. R_f = 0.3 (PE:EA = 2:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 – 7.46 (m, 2H), 7.44 – 7.28 (m, 3H), 3.67 (t, *J* = 6.5 Hz, 2H), 3.49 (t, *J* = 6.5 Hz, 2H), 1.99 – 1.86 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 151.3, 132.8, 130.0, 128.5, 120.4, 83.3, 73.8, 73.2, 72.3, 47.9, 45.5, 25.3, 24.5. **HRMS** (EI) calcd for $C_{15}H_{13}NO$ $[M]^+$: 223.09917, found: 223.09953. **IR** (Reflection): ṽ = 1624, 1440, 1414, 1341, 1225, 1192, 1175, 1119, 1026, 973, 902, 851, 757, 722, 690, 614. **M.p.** (amorphous): 100.5-101.4 °C.



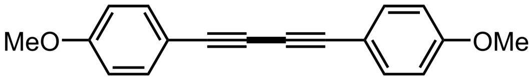
1,4-Bis(4-fluorophenyl)buta-1,3-diyne

4a, colorless solid, 47.4 mg, 99% yield. R_f = 0.6 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 – 7.47 (m, 4H), 7.09 – 6.98 (m, 4H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.0 (d, *J* = 251.6 Hz, CF), 134.5 (d, *J* = 8.7 Hz), 117.8 (d, *J* = 3.5 Hz), 115.9 (d, *J* = 22.2 Hz), 80.4, 73.5. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.50. Characterization data of **4a** corresponded to the literature values.[17]



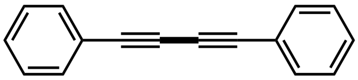
1,4-Bis(4-(tert-butyl)phenyl)buta-1,3-diyne

4b, colorless solid, 57.8 mg, 92% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.4 Hz, 4H), 7.37 (d, *J* = 8.4 Hz, 4H), 1.33 (s, 18H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 152.5, 132.2, 125.5, 118.8, 81.5, 73.5, 34.9, 31.1. Characterization data of **4b** corresponded to the literature values.[18]



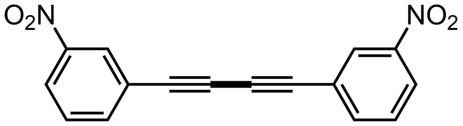
1,4-Bis(4-methoxyphenyl)buta-1,3-diyne

4c, light yellow solid, 26.1 mg, 99% yield. R_f = 0.2 (PE: EA = 10:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.9 Hz, 4H), 6.85 (d, *J* = 8.9 Hz, 4H), 3.82 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.2, 134.0, 114.1, 113.9, 81.2, 72.9, 55.3. Characterization data of **4c** corresponded to the literature values.[17]



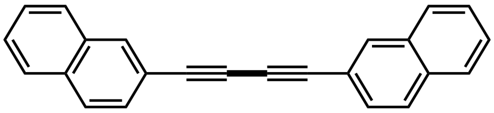
1,4-Diphenylbuta-1,3-diyne

4d, colorless solid, 40.2 mg, 99% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.6, 1.9 Hz, 4H), 7.43 – 7.30 (m, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.2, 128.4, 121.8, 81.5, 73.9. Characterization data of **4d** corresponded to the literature values.[18]



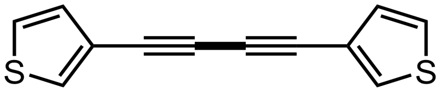
1,4-Bis(3-nitrophenyl)buta-1,3-diyne

4e, yellow solid, 58.0 mg, 99% yield. R_f = 0.5 (PE: EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 – 8.38 (m, 1H), 8.25 (ddd, *J* = 8.3, 2.2, 0.9 Hz, 1H), 7.88 – 7.78 (m, 1H), 7.57 (t, *J* = 8.0 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.1, 138.1, 129.7, 127.4, 124.2, 123.1, 79.9, 75.5. Characterization data of **4e** corresponded to the literature values.[19]



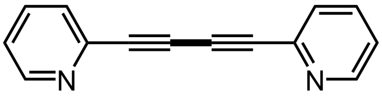
1,4-Di(naphthalen-2-yl)buta-1,3-diyne

4f, light yellow solid, 54.8 mg, 91% yield. R$_f$ = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.10 (s, 1H), 7.85 – 7.80 (m, 3H), 7.57 (dd, *J* = 8.6, 1.3 Hz, 1H), 7.52 (dd, *J* = 6.3, 3.2 Hz, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 133.2, 133.1, 132.8, 128.5, 128.2, 127.9, 127.8, 127.2, 126.8, 119.1, 82.2, 74.4. **HRMS** (APCI) calcd for $C_{24}H_{15}$ [M+H]$^+$: 303.1168, found: 303.1165. **IR** (Reflection): ṽ = 3055, 1958, 1925, 1624, 1593, 1567, 1498, 1381, 1272, 1208, 1164, 1146, 1122, 1019, 952, 904, 867, 826, 740, 643. **M.p.** (amorphous): 204.1-205.9 °C.



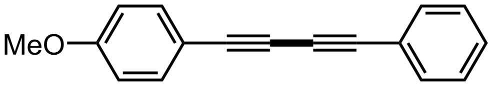
1,4-Di(thiophen-3-yl)buta-1,3-diyne

4g, dark yellow solid, 40.1 mg, 93% yield. R$_f$ = 0.7 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.59 (d, *J* = 2.4 Hz, 2H), 7.28 (dt, *J* = 5.7, 2.9 Hz, 2H), 7.18 (d, *J* = 5.0 Hz, 2H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 131.2, 130.1, 125.6, 120.8, 76.6, 73.5. Characterization data of **4g** corresponded to the literature values.[18]



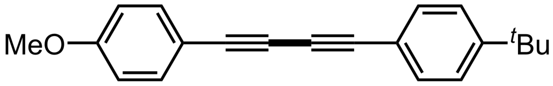
1,4-Di(pyridin-2-yl)buta-1,3-diyne

4h, dark yellow solid, 71.6 mg, 88% yield. R$_f$ = 0.3 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 8.60 (d, *J* = 4.2 Hz, 2H), 7.68 (td, *J* = 7.7, 1.4 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.29 (dd, *J* = 6.9, 5.1 Hz, 2H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 150.2, 141.6, 136.2, 128.3, 123.7, 80.7, 73.0. Characterization data of **4h** corresponded to the literature values.[20]



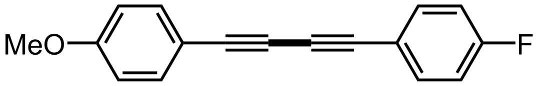
1-Methoxy-4-(phenylbuta-1,3-diyn-1-yl)benzene

4i, light yellow solid, 26.4 mg, 57% yield. R$_f$ = 0.5 (PE:EA = 20:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.48 (d, *J* = 8.8 Hz, 2H), 7.39 – 7.30 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 160.3, 134.1, 132.4, 129.0, 128.4, 121.9, 114.1, 113.6, 81.8, 81.0, 74.1, 72.7, 55.3. Characterization data of **4i** corresponded to the literature values.[21]



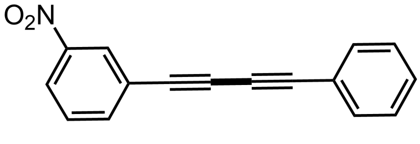
1-(*tert*-Butyl)-4-((4-methoxyphenyl)buta-1,3-diyn-1-yl)benzene

4j, light yellow solid, 34.9 mg, 61% yield. R_f = 0.7 (PE:EA = 10:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.52 – 7.43 (m, 4H), 7.36 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 1.32 (s, 9H). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 160.3, 152.5, 134.1, 132.2, 125.4, 118.9, 114.1, 113.8, 81.4, 81.3, 73.5, 72.9, 55.3, 34.9, 31.1. Characterization data of **4j** corresponded to the literature values.[22]



1-Fluoro-4-((4-methoxyphenyl)buta-1,3-diyn-1-yl)benzene

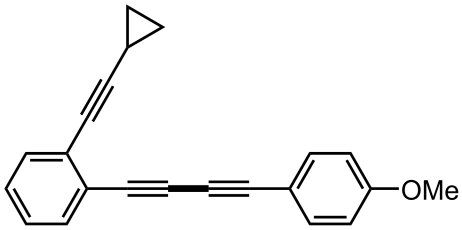
4k, colorless solid, 32.9 mg, 66% yield. R_f = 0.5 (PE:DCM = 4:1), chromatography eluent: 10% Dichloromethane in petroleum ether. ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.53 – 7.44 (m, 4H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 162.9 (d, *J* = 251.2 Hz), 160.4, 134.4 (d, *J* = 8.5 Hz), 134.1, 118.1 (d, *J* = 3.6 Hz), 115.8 (d, *J* = 22.2 Hz), 114.1, 113.5, 81.8, 79.9, 73.9 (d, *J* = 1.6 Hz), 72.5, 55.3. **HRMS** (APCI) calcd for $C_{17}H_{12}FO$ $[M+H]^+$: 251.0867, found: 251.0865. **IR** (Reflection): ṽ = 2964, 2840, 2211, 2139, 1891, 1599, 1568, 1504, 1455, 1295, 1228, 1173, 1159, 1038, 832, 799, 694. **M.p.** (amorphous): 122.3-124.9 °C.



1-Nitro-3-(phenylbuta-1,3-diyn-1-yl)benzene

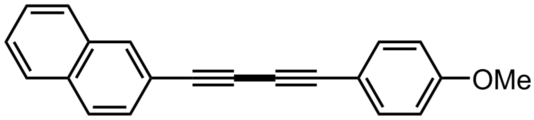
4l, light yellow solid, 39.7 mg, 80% yield. R_f = 0.7 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 8.37 –

8.33 (m, 1H), 8.21 (ddd, *J* = 8.3, 2.2, 0.9 Hz, 1H), 7.83 – 7.79 (m, 1H), 7.57 – 7.52 (m, 3H), 7.43 – 7.39 (m, 1H), 7.38 – 7.34 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 148.1, 137.9, 132.6, 129.7, 129.5, 128.5, 127.2, 123.8, 123.7, 121.1, 83.1, 78.5, 76.4, 73.1. Characterization data of **4l** corresponded to the literature values.[22]



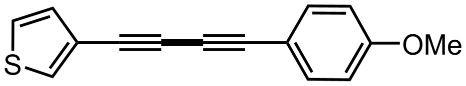
1-(Cyclopropylethynyl)-2-((4-methoxyphenyl)buta-1,3-diyn-1-yl)benzene

4m, light yellow oil, 34.9 mg, 59% yield. R_f = 0.7 (PE:DCM = 2:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.9 Hz, 2H), 7.46 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.37 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.25 (td, *J* = 7.6, 2.0 Hz, 1H), 7.20 (td, *J* = 7.6, 1.4 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 3.82 (s, 3H), 1.53 (dt, *J* = 11.3, 6.6 Hz, 1H), 0.95 – 0.90 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.3, 134.1, 132.5, 131.6, 128.5, 127.6, 127.1, 124.5, 114.1, 113.8, 99.0, 82.6, 79.9, 77.4, 74.1, 72.9, 55.3, 9.1, 0.5. **HRMS** (EI) calcd for $C_{22}H_{16}O[M]^+$: 296.11957, found: 296.11974. **IR** (Reflection): ṽ = 3059, 3009, 2959, 2934, 2837, 2543, 2211, 2139, 1730, 1601, 1566, 1509, 1479, 1441, 1343, 1291, 1251, 1171, 1107, 1030, 952, 831, 809, 756, 620.



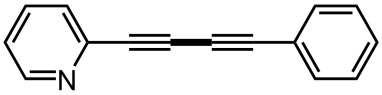
2-((4-Methoxyphenyl)buta-1,3-diyn-1-yl)naphthalene

4n, colorless solid, 42.5 mg, 75% yield. R_f = 0.7 (PE:DCM = 2:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.92 – 7.71 (m, 3H), 7.61 – 7.42 (m, 5H), 6.88 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.4, 134.1, 133.1, 132.8, 128.5, 128.1, 127.8, 127.8, 127.1, 126.7, 119.2, 114.2, 113.7, 82.0, 81.5, 74.5, 72.9, 55.3. Characterization data of **4n** corresponded to the literature values.[23]



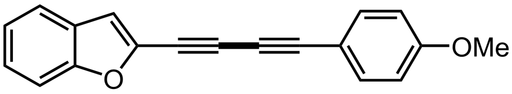
3-((4-Methoxyphenyl)buta-1,3-diyn-1-yl)thiophene

4o, light yellow solid, 34.9 mg, 59% yield. R_f= 0.8 (PE:DCM = 2:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 2.9, 0.9 Hz, 1H), 7.39 (d, *J* = 8.8 Hz, 2H), 7.20 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.09 (dd, *J* = 5.0, 0.9 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 3.74 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.3, 134.1, 130.9, 130.1, 125.5, 121.1, 114.1, 113.7, 81.6, 76.2, 73.8, 72.7, 55.3. Characterization data of **4o** corresponded to the literature values.[23]



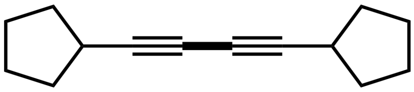
2-(Phenylbuta-1,3-diyn-1-yl)pyridine

4p, light yellow solid, 25.6 mg, 63% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.8 Hz, 1H), 7.68 (td, *J* = 7.7, 1.7 Hz, 1H), 7.54 (dt, *J* = 11.0, 4.4 Hz, 3H), 7.43 – 7.32 (m, 3H), 7.28 (ddd, *J* = 7.6, 4.7, 0.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.2, 142.2, 136.2, 132.6, 129.5, 128.4, 128.1, 123.4, 121.3, 82.5, 80.1, 73.9, 73.5. Characterization data of **4p** corresponded to the literature values.[22]



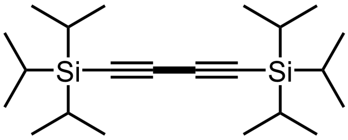
2-((4-Methoxyphenyl)buta-1,3-diyn-1-yl)benzofuran

4q, light yellow solid, 28.1 mg, 52% yield. R_f= 0.7 (PE:DCM = 2:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.29 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.23 – 7.17 (m, 1H), 7.12 – 7.06 (m, 1H), 6.91 (d, *J* = 0.8 Hz, 1H), 6.76 – 6.66 (m, 2H), 3.67 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 160.7, 155.0, 138.0, 134.3, 127.3, 126.2, 123.5, 121.3, 114.2, 114.0, 112.9, 111.3, 85.2, 80.3, 72.1, 70.7, 55.4. **HRMS** (EI) calcd for $C_{19}H_{12}O_2[M]^+$: 272.08318, found: 272.08272. **IR** (Reflection): ṽ = 3130, 2961, 2932, 2849, 2203, 2138, 1890, 1735, 1604, 1568, 1508, 1475, 1449, 1417, 1350, 1306, 1293, 1251, 1184, 1150, 1138, 1108, 1031, 1012, 991, 920, 886, 826, 810, 744, 734, 664, 639, 614. **M.p.** (amorphous): 136.8-138.6 °C.



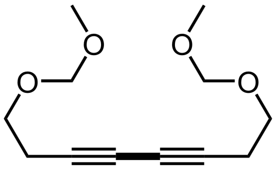
1,4-Dicyclopentylbuta-1,3-diyne

5a, colorless oil, 32.2 mg, 86 % yield. R_f = 0.8 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 2.75 – 2.58 (m, 2H), 1.95 – 1.84 (m, 4H), 1.74 – 1.49 (m, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 82.2, 64.7, 33.6, 30.5, 25.0. **HRMS** (APCI) calcd for $C_{14}H_{17}$ $[M-H]^-$: 185.1325, found: 185.1323. **IR** (Reflection): ṽ = 3405, 2961, 2871, 2251, 2231, 2152, 1711, 1451, 1325, 1262, 1204, 972, 856.



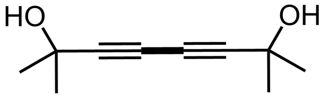
1,4-Bis(triisopropylsilyl)buta-1,3-diyne

5b, light green solid, 72.3 mg, 99% yield. R_f = 0.8 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 1.10 (s, 42H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 90.2, 81.6, 18.6, 11.3. Characterization data of **5b** corresponded to the literature values.[17]



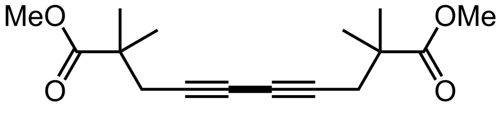
2,4,13,15-Tetraoxahexadeca-7,9-diyne

5c, colorless oil, 42.2 mg, 93% yield. R_f= 0.7 (PE:EA = 2:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.62 (s, 4H), 3.63 (t, J = 6.6 Hz, 4H), 3.35 (s, 6H), 2.54 (t, J = 6.6 Hz, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 96.4, 74.4, 66.1, 65.4, 55.3, 20.7. **HRMS** (APCI) calcd for $C_{12}H_{19}O_4$ $[M+H]^+$: 227.1278, found: 227.1275. **IR** (Reflection): ṽ = 2935, 2887, 2237, 1733, 1467, 1442, 1383, 1210, 1149, 1109, 1068, 1029, 917.



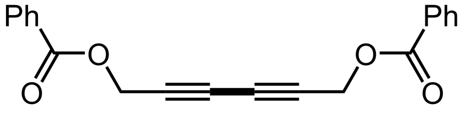
2,7-Dimethylocta-3,5-diyne-2,7-diol

5d, colorless solid, 31.8 mg, 96% yield. $R_f = 0.2$ (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CD_3OD) δ 1.46 (s, 12H). **^{13}C NMR** (75 MHz, CD_3OD) δ 85.3, 67.0, 66.0, 31.6. Characterization data of **5d** corresponded to the literature values.[17]



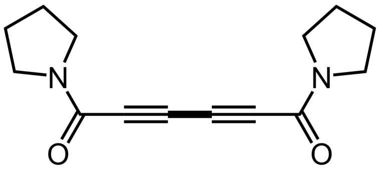
Dimethyl 2,2,9,9-tetramethyldeca-4,6-diynedioate

5e, light yellow oil, 46.2 mg, 83% yield. $R_f = 0.2$ (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.67 (s, 6H), 2.50 (s, 4H), 1.25 (s, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 176.8, 74.2, 67.2, 52.1, 42.3, 30.2, 24.6. **HRMS** (EI) calcd for $C_{16}H_{22}O_4$ $[M]^+$: 278.15126, found: 278.15150. **IR** (Reflection): ṽ = 2974, 2953, 2234, 2148, 1733, 1471, 1435, 1389, 1367, 1314, 1252, 1199, 1133, 986, 859, 770.



Hexa-2,4-diyne-1,6-diyl dibenzoate

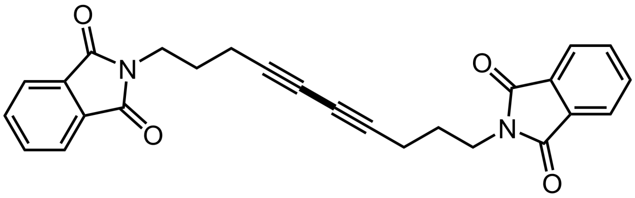
5f, light yellow solid, 56.1 mg, 88% yield. $R_f = 0.3$ (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.10 – 7.97 (m, 4H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 4.99 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.6, 133.4, 129.8, 129.1, 128.4, 73.7, 70.5, 52.7. Characterization data of **5f** corresponded to the literature values.[24]



1,6-Di(pyrrolidin-1-yl)hexa-2,4-diyne-1,6-dione

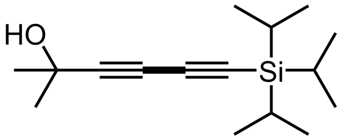
5g, colorless solid, 45.3 mg, 99% yield. $R_f = 0.2$ (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.62 (t, *J*

= 6.4 Hz, 1H), 3.47 (t, *J* = 6.4 Hz, 1H), 2.00 – 1.85 (m, 2H). ^{13}**C NMR** (126 MHz, $CDCl_3$) δ 150.3, 74.8, 71.0, 47.9, 45.6, 25.2, 24.4. Characterization data of **5g** corresponded to the literature values.[25]



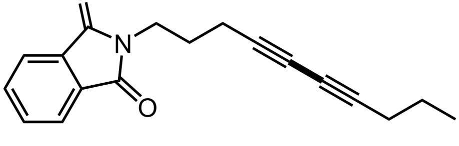
2,2'-(Deca-4,6-diyne-1,10-diyl)bis(isoindoline-1,3-dione)

5h, colorless solid, 74.2 mg, 87% yield. R_f = 0.2 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 5.5, 3.0 Hz, 4H), 7.68 (dd, *J* = 5.4, 3.1 Hz, 4H), 3.72 (t, *J* = 6.9 Hz, 4H), 2.25 (t, *J* = 7.0 Hz, 4H), 1.85 (p, *J* = 7.0 Hz, 4H). ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 168.2, 133.8, 132.0, 123.2, 75.9, 65.6, 37.1, 26.9, 17.0. Characterization data of **5h** corresponded to the literature values.[26]



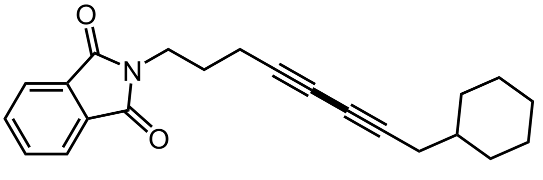
2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol

5i, light yellow solid, 33.6 mg, 66% yield. R_f = 0.6 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 2.02 (br, 1H), 1.54 (s, 6H), 1.08 (s, 21H). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 88.9, 84.8, 80.6, 67.7, 65.6, 31.0, 18.5, 11.2. Characterization data of **5i** corresponded to the literature values.[27]



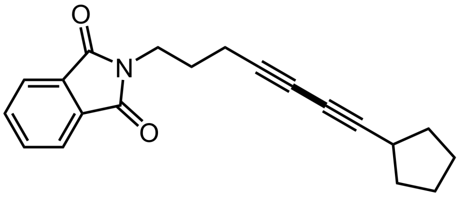
2-(Deca-4,6-diyn-1-yl)isoindoline-1,3-dione

5j, light yellow oil, 36.6 mg, 66% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.76 (t, *J* = 6.9 Hz, 2H), 2.33 (t, *J* = 7.0 Hz, 2H), 2.16 (t, *J* = 7.0 Hz, 2H), 1.91 (p, *J* = 7.0 Hz, 2H), 1.59 – 1.39 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 133.8, 132.1, 123.2, 77.7, 75.5, 66.0, 65.0, 37.2, 27.1, 21.7, 21.08, 17.1, 13.4. **HRMS** (EI) calcd for $C_{18}H_{17}NO_2$ $[M]^+$: 279.12538, found: 279.12589. **IR** (Reflection): ṽ = 2963, 2935, 2873, 2232, 1771, 1703, 1614, 1467, 1437, 1396, 1371, 1188, 1114, 1088, 1024, 884, 793, 717.



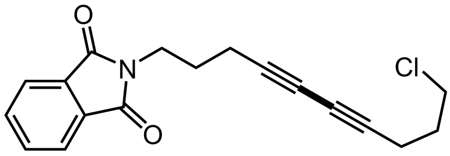
2-(8-Cyclohexylocta-4,6-diyn-1-yl)isoindoline-1,3-dione

5k, light yellow oil, 46.8 mg, 70% yield. R_f = 0.2 (PE:EA = 10:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.0 Hz, 2H), 3.76 (t, *J* = 7.0 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 2.07 (d, *J* = 6.6 Hz, 2H), 1.91 (p, *J* = 7.0 Hz, 2H), 1.74 (d, *J* = 13.1 Hz, 2H), 1.71 – 1.66 (m, 2H), 1.65 – 1.59 (m, 1H), 1.47 – 1.38 (m, 1H), 1.25 – 1.17 (m, 2H), 1.15 – 1.06 (m, 1H), 0.94 (qd, *J* = 12.4, 3.1 Hz, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 168.3, 133.9, 132.1, 123.2, 76.9, 75.5, 66.0, 65.7, 37.2, 37.1, 32.6, 27.1, 26.9, 26.1, 26.0, 17.1. **HRMS** (EI) calcd for $C_{22}H_{23}NO_2$ $[M]^+$: 333.17233, found: 333.17167. **IR** (Reflection): ṽ = 1773, 1720, 1615, 1467, 1438, 1395, 1371, 1188, 1115, 1025, 885, 722.



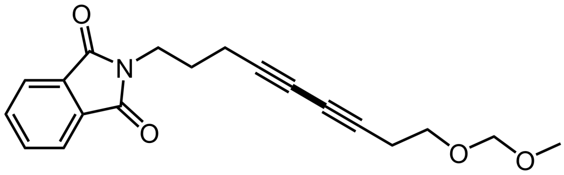
2-(7-Cyclopentylhepta-4,6-diyn-1-yl)isoindoline-1,3-dione

5l, light yellow oil, 37.4 mg, 61% yield. R_f = 0.2 (PE:EA = 10:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.1 Hz, 2H), 3.76 (t, *J* = 6.9 Hz, 2H), 2.59 (p, *J* = 7.0 Hz, 1H), 2.33 (t, *J* = 7.0 Hz, 2H), 2.01 – 1.79 (m, 4H), 1.77 – 1.62 (m, 2H), 1.62 – 1.44 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 133.8, 132.1, 123.2, 81.8, 76.3, 66.0, 64.5, 37.2, 33.5, 30.3, 27.1, 25.0, 17.2. **HRMS** (EI) calcd for $C_{20}H_{19}NO_2$ $[M]^+$: 305.14103, found: 305.14049. **IR** (Reflection): ṽ = 1772, 1720, 1615, 1468, 1438, 1398, 1372, 1188, 1115, 1088, 1025, 886, 794, 720.



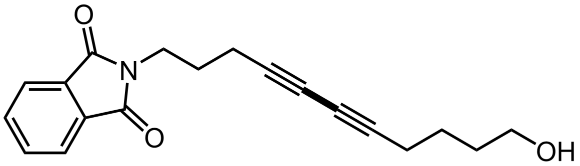
2-(10-Chlorodeca-4,6-diyn-1-yl)isoindoline-1,3-dione

5m, light yellow solid, 44.3 mg, 71% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.77 (t, *J* = 6.9 Hz, 2H), 3.59 (t, *J* = 6.3 Hz, 2H), 2.42 – 2.26 (m, 4H), 1.96 – 1.87 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 133.9, 132.1, 123.2, 76.2, 75.5, 65.9, 65.7, 43.4, 37.2, 30.9, 26.96, 17.1, 16.6. **HRMS** (EI) calcd for $C_{18}H_{16}NO_2Cl$ $[M]^+$: 313.08641, found: 313.08530. **IR** (Reflection): ṽ = 3463, 2954, 2234, 1771, 1702, 1614, 1467, 1437, 1397, 1372, 1188, 1114, 1025, 884, 794, 719. **M.p.** (amorphous): 56.7-58.6 °C.



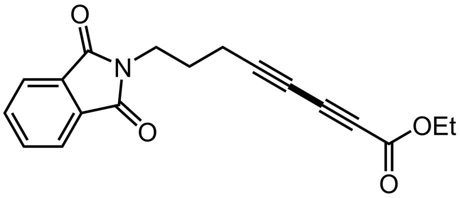
2-(9-(Methoxymethoxy)nona-4,6-diyn-1-yl)isoindoline-1,3-dione

5n, light yellow oil, 45.3 mg, 70% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.70 (dd, *J* = 5.5, 3.1 Hz, 2H), 4.61 (s, 2H), 3.75 (t, *J* = 6.9 Hz, 2H), 3.59 (t, *J* = 6.8 Hz, 2H), 3.35 (s, 3H), 2.48 (t, *J* = 6.8 Hz, 2H), 2.32 (t, *J* = 7.0 Hz, 2H), 1.90 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.2, 133.9, 132.1, 123.2, 96.3, 76.1, 74.2, 66.0, 65.8, 65.4, 55.3, 37.1, 27.0, 20.7, 17.1. **HRMS** (EI) calcd for $C_{19}H_{19}NO_4$ $[M]^+$: 325.13086, found: 325.12507. **IR** (Reflection): ṽ = 3465, 2939, 2886, 2825, 1771, 1702, 1614, 1467, 1438, 1395, 1372, 1148, 1110, 1025, 916, 794, 717.



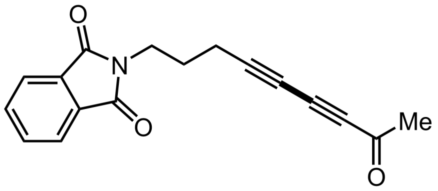
2-(11-Hydroxyundeca-4,6-diyn-1-yl)isoindoline-1,3-dione

5o, light yellow oil, 39.0 mg, 63% yield. R_f = 0.3 (PE:EA = 1:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.75 (t, *J* = 6.9 Hz, 2H), 3.64 (t, *J* = 6.1 Hz, 2H), 2.31 (t, *J* = 7.0 Hz, 2H), 2.23 (t, *J* = 6.6 Hz, 2H), 1.96 – 1.84 (m, 2H), 1.81 (br, 1H), 1.70 – 1.49 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 133.9, 132.0, 123.2, 77.3, 75.8, 65.9, 65.3, 62.2, 37.1, 31.6, 27.01, 24.5, 18.9, 17.0. **HRMS** (EI) calcd for $C_{19}H_{19}NO_3$ $[M]^+$: 309.12812, found: 309.12673. **IR** (Reflection): ṽ = 3524, 3466, 2941, 2871, 2242, 2156, 1771, 1723, 1614, 1468, 1438, 1402, 1372, 1282, 1173, 1115, 1025, 885, 795, 724.



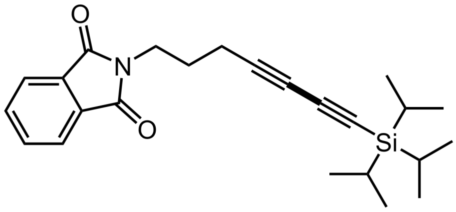
Ethyl 8-(1,3-dioxoisoindolin-2-yl)octa-2,4-diynoate

5p, light yellow solid, 36.7 mg, 59% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.71 (dd, *J* = 5.4, 3.1 Hz, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.78 (t, *J* = 6.8 Hz, 2H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.97 (p, *J* = 6.9 Hz, 2H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 152.8, 134.0, 132.0, 123.3, 85.8, 71.0, 65.6, 64.2, 62.2, 37.0, 26.5, 17.4, 13.9. **HRMS** (EI) calcd for $C_{18}H_{15}NO_4$ $[M]^+$: 309.09956, found: 309.09766. **IR** (Reflection): ṽ = 3466, 2982, 2939, 2238, 2156, 1771, 1694, 1614, 1467, 1436, 1392, 1364, 1272, 1151, 1114, 1014, 885, 794, 744, 714. **M.p.** (amorphous): 58.8-59.9 °C.



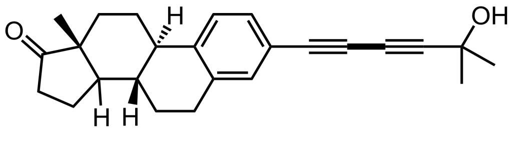
2-(8-Oxonona-4,6-diyn-1-yl)isoindoline-1,3-dione

5q, dark yellow oil, 21.1 mg, 38% yield. $R_f = 0.3$ (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.5, 3.0 Hz, 1H), 7.72 (dd, *J* = 5.4, 3.1 Hz, 1H), 3.79 (t, *J* = 6.8 Hz, 1H), 2.46 (t, *J* = 7.0 Hz, 1H), 2.30 (s, 1H), 1.98 (p, J = 6.9 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 183.4, 168.3, 134.1, 132.0, 123.3, 89.0, 75.3, 72.7, 64.3, 37.0, 32.6, 26.6, 17.6. **HRMS** (EI) calcd for $C_{17}H_{13}NO_3$ $[M]^+$: 279.08899, found: 279.08646. **IR** (Reflection): ṽ = 3464, 2940, 2230, 2151, 1771, 1715, 1615, 1467, 1437, 1398, 1372, 1266, 1188, 1116, 1088, 1025, 913,795, 719.



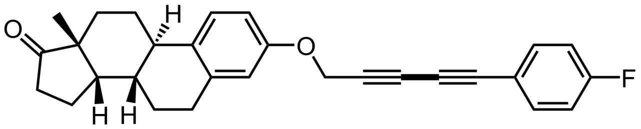
2-(7-(Triisopropylsilyl)hepta-4,6-diyn-1-yl)isoindoline-1,3-dione

5r, colorless oil, 54.1 mg, 67% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.69 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.76 (t, *J* = 6.9 Hz, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 1.93 (p, *J* = 7.0 Hz, 2H), 1.03 (s, 21H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.2, 133.9, 132.0, 123.2, 89.7, 80.5, 76.9, 66.4, 37.2, 27.0, 18.5, 17.2, 11.2. **HRMS** (EI) calcd for $C_{24}H_{31}NO_2Si$ $[M]^+$: 393.21186, found: 393.21272. **IR** (Reflection): ṽ = 2943, 2865, 2223, 2104, 1773, 1711, 1466, 1395, 1369, 1185, 1114, 1022, 995, 882, 718.



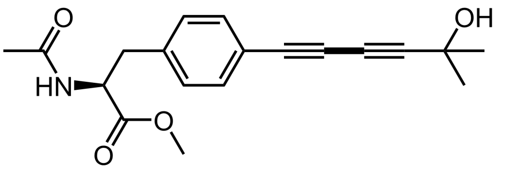
(*8S,9R,13R*)-3-(5-Hydroxy-5-methylhexa-1,3-diyn-1-yl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one

6a, colorless solid, 49.3 mg, 68% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 3H), 2.90 – 2.79 (m, 2H), 2.51 (dd, *J* = 19.2, 8.8 Hz, 1H), 2.41 – 2.36 (m, 1H), 2.26 (dd, *J* = 13.9, 7.1 Hz, 1H), 2.19 – 2.12 (m, 1H), 2.08 – 2.02 (m, 1H), 2.02 – 1.98 (m, 1H), 1.97 (d, *J* = 11.2 Hz, 1H), 1.67 – 1.55 (m, 2H), 1.57 (s, 6H), 1.50 (ddd, *J* = 15.2, 10.9, 4.2 Hz, 3H), 1.41 (dt, *J* = 11.9, 9.9 Hz, 1H), 0.90 (s, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 220.9, 1415, 136.8, 132.9, 129.8, 125.5, 118.7, 86.4, 78.9, 72.5, 67.1, 65.6, 50.4, 47.9, 44.4, 37.8, 35.8, 31.5, 31.1, 31.1, 29.0, 26.2, 25.5, 21.5, 13.8. **HRMS** (EI) calcd for $C_{25}H_{28}O_2$ $[M]^+$: 360.20838, found: 360.20711. **IR** (Reflection): ṽ = 3442, 2979, 2939, 2856, 2805, 1719, 1497, 1469, 1452, 1407, 1362, 1265, 1213, 1171, 1127, 1088, 1009, 956, 895, 824, 732. **M.p.** (amorphous): 212.5-214.2 °C.



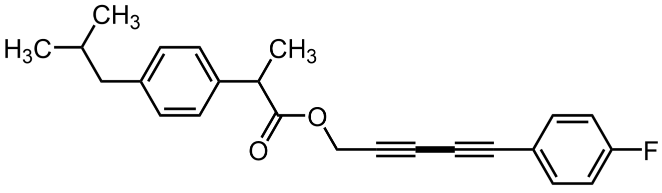
(*8S,9R,13R,14S*)-3-((5-(4-Fluorophenyl)penta-2,4-diyn-1-yl)oxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-*17H*-cyclopenta[a]phenanthren-17-one

6b, light yellow solid, 58.5 mg, 69% yield. $R_f = 0.3$ (PE:EA = 10:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.42 (m, 2H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.05 – 6.95 (m, 2H), 6.80 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.72 (d, *J* = 2.7 Hz, 1H), 4.80 (s, 2H), 2.92 (dd, *J* = 9.5, 4.7 Hz, 2H), 2.50 (dd, *J* = 18.7, 8.5 Hz, 1H), 2.43 – 2.36 (m, 1H), 2.25 (dd, *J* = 13.5, 7.2 Hz, 1H), 2.15 (dd, *J* = 18.4, 9.4 Hz, 1H), 2.08 (dd, *J* = 10.2, 5.0 Hz, 1H), 2.05 – 1.93 (m, 3H), 1.71 – 1.36 (m, 7H), 0.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 220.7, 163.1 (d, *J* = 251.9 Hz), 155.5, 137.9, 134.6 (d, *J* = 8.6 Hz), 133.1, 126.4, 117.3 (d, *J* = 3.5 Hz), 115.8 (d, *J* = 22.4 Hz), 115.0, 112.3, 77.54, 77.50, 73.0 (d, *J* = 1.5 Hz), 71.5, 56.3, 50.4, 47.9, 43.9, 38.2, 35.8, 31.5, 29.6, 26.4, 25.8, 21.5, 13.8. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.11. **HRMS** (EI) calcd for $C_{29}H_{27}O_2F$ $[M]^+$: 426.19896, found: 426.19744. **IR** (Reflection): ṽ = 2931, 2254, 1734, 1598, 1506, 1371, 1280, 1225, 1157, 1097, 1054, 1021, 916, 864, 835, 819, 799, 732. **M.p.** (amorphous): 154.1-155.8 °C.



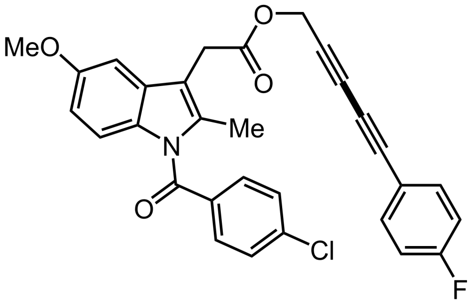
Methyl (*S*)-2-acetamido-3-(4-(5-hydroxy-5-methylhexa-1,3-diyn-1-yl)phenyl)propanoate

6c, light yellow oil, 55.4 mg, 85% yield. R_f = 0.2 (PE:EA= 1:2) , chromatography eluent: 40% Petroleum ether in Ethyl acetate. **^{1}H NMR** (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 8.1 Hz, 2H), 7.04 (d, *J* = 8.2 Hz, 2H), 6.13 (t, *J* = 6.2 Hz, 1H), 4.85 (dd, *J* = 13.5, 5.9 Hz, 1H), 3.70 (s, 3H), 3.15 (dd, *J* = 13.9, 6.0 Hz, 1H), 3.06 (dd, *J* = 13.9, 5.8 Hz, 1H), 2.79 (br, 1H), 1.98 (s, 3H), 1.56 (s, 6H). **^{13}C NMR** (126 MHz, CDCl$_3$) δ 171.9, 169.9, 137.3, 132.6, 129.3, 120.3, 87.1, 78.2, 73.4, 66.7, 65.5, 53.0, 52.4, 37.7, 31.0, 23.0. **HRMS** (EI) calcd for C$_{19}$H$_{21}$NO$_4$ [M]$^+$: 327.11651, found: 327.14636. **IR** (Reflection): ṽ = 3294, 3067, 2982, 2953, 2933, 2863, 2236, 1745, 1658, 1543, 1438, 1375, 1211, 1171, 1132, 1017, 954, 911, 861, 732.



(+/-)-5-(4-Fluorophenyl)penta-2,4-diyn-1-yl 2-(4-isobutylphenyl)propanoate

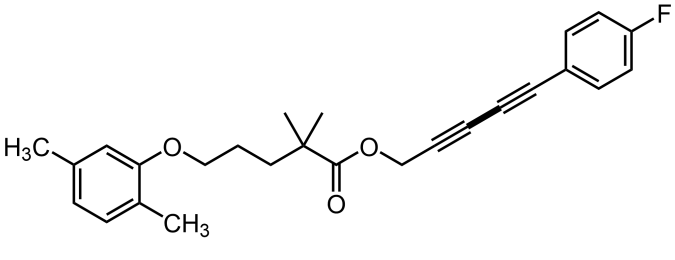
6d, light yellow oil, 54.4 mg, 75% yield. R_f = 0.4 (PE:DCM = 10:1), chromatography eluent: 5% Dichloromethane in petroleum ether. **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.48 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.02 (t, *J* = 8.6 Hz, 2H), 4.86 (d, *J* = 16.4 Hz, 1H), 4.74 (d, *J* = 16.4 Hz, 1H), 3.76 (q, *J* = 7.1 Hz, 1H), 2.46 (d, *J* = 7.2 Hz, 2H), 1.88 – 1.82 (m, 1H), 1.53 (d, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 173.8, 163.1 (d, *J* = 251.5 Hz), 140.7, 137.1, 134.7 (d, *J* = 8.3 Hz), 129.4, 127.1, 117.3 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.1 Hz), 77.6, 76.2, 72.9, 71.0, 52.8, 45.0, 44.9, 30.1, 22.4, 18.5. **^{19}F NMR** (282 MHz, CDCl$_3$) δ -108.25 (d, *J* = 100.3 Hz). **HRMS** (EI) calcd for C$_{24}$H$_{23}$O$_2$F [M]$^+$: 362.16766, found: 362.16761. **IR** (Reflection): ṽ = 2955, 2932, 2869, 2249, 1744, 1599, 1508, 1464, 1368, 1330, 1233, 1155, 1091, 1014, 957, 836, 791.



5-(4-Fluorophenyl)penta-2,4-diyn-1-yl

2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-*1H*-indol-3-yl)acetate

6e, light yellow solid, 69.7 mg, 68% yield. $R_f = 0.5$ (PE:DCM = 1:1), chromatography eluent: 20% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.63 (m, 2H), 7.51 – 7.43 (m, 4H), 7.06 – 6.99 (m, 2H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.90 (d, *J* = 9.0 Hz, 1H), 6.68 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.84 (s, 2H), 3.85 (s, 3H), 3.73 (s, 2H), 2.39 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 168.2, 163.18 (d, *J* = 252.2 Hz), 156.1, 139.3, 136.0, 134.71 (d, *J* = 8.6 Hz), 133.8, 131.2, 130.8, 130.4, 129.1, 117.2 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.3 Hz), 115.0, 111.89, 111.87, 101.1, 77.8, 75.9, 72.8 (d, *J* = 1.3 Hz), 71.3, 55.7, 53.0, 30.0, 13.4. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -107.87 (d, *J* = 1.1 Hz). **HRMS** (EI) calcd for $C_{30}H_{21}NO_4FCl$ $[M]^+$: 513.11377, found: 513.11180. **IR** (Reflection): ṽ = 3071, 2933, 2834, 2249, 1744, 1684, 1598, 1507, 1478, 1401, 1358, 1323, 1226, 1155, 1089, 1067, 1037, 1015, 980, 925, 836, 754, 735. **M.p.** (amorphous): 98.1-100.2 °C.

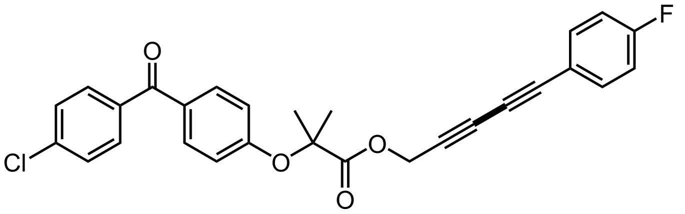


5-(4-Fluorophenyl)penta-2,4-diyn-1-yl

5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate

6f, light yellow oil, 66.5 mg, 82% yield. $R_f = 0.4$ (PE:EA = 40:1), chromatography eluent: 2% Ethyl acetate in petroleum ether. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 8.4, 5.5 Hz, 2H), 7.05 – 6.96 (m, 3H), 6.67 (d, *J* = 7.4 Hz, 1H), 6.62 (s, 1H), 4.81 (s, 2H), 3.94 (s, 2H), 2.31 (s, 3H), 2.20 (s, 3H), 1.78 (s, 4H), 1.27 (s, 6H). **^{13}C NMR**

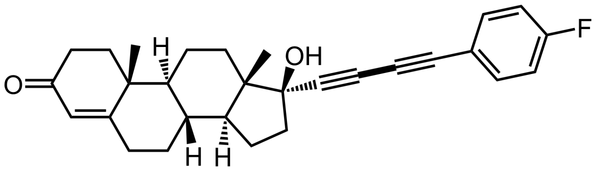
(176 MHz, $CDCl_3$) δ 176.8, 163.1 (d, *J* = 252.3 Hz), 156.9, 136.4, 134.7 (d, *J* = 9.0 Hz), 130.2, 123.5, 120.6, 117.3 (d, *J* = 3.1 Hz) 115.8 (d, *J* = 22.7 Hz), 111.8, 77.5, 76.4, 72.9, 70.8, 67.7, 52.5, 42.2, 37.0, 25.1, 25.0, 21.4, 15.7. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.12 (d, *J* = 1.1 Hz). **HRMS** (EI) calcd for $C_{26}H_{27}O_3F$ $[M]^+$: 406.19387, found: 406.19272. **IR** (Reflection): ṽ = 2972, 2951, 2926, 2870, 2249, 1736, 1599, 1508, 1473, 1391, 1367, 1312, 1264, 1233, 1187, 1156, 1129, 1048, 977, 837, 805.



5-(4-Fluorophenyl)penta-2,4-diyn-1-yl

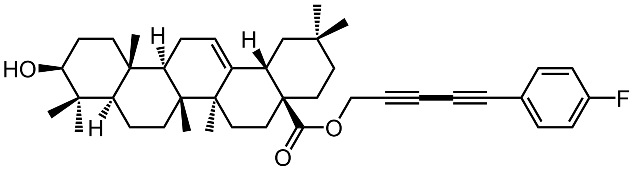
2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate

6g, light yellow oil, 66.9 mg, 70% yield. R_f = 0.4 (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.6 Hz, 2H), 7.69 (d, *J* = 8.3 Hz, 2H), 7.41 (dd, *J* = 8.2, 5.6 Hz, 2H), 7.38 (d, *J* = 8.3 Hz, 2H), 7.00 (t, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 4.90 (s, 2H), 1.70 (s, 6H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 194.1, 172.9, 163.2 (d, *J* = 252.0 Hz), 159.2, 138.3, 136.2, 134.7 (d, *J* = 9.2 Hz), 132.0, 131.2, 130.6, 128.4, 117.4, 116.9 (d, *J* = 3.8 Hz), 115.9 (d, *J* = 21.8 Hz), 79.2, 78.1, 75.1, 72.5, 71.6, 53.5, 25.3. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.08 (d, J = 195.5 Hz). **HRMS** (EI) calcd for $C_{28}H_{20}O_4FCl$ $[M]^+$: 474.10287, found: 474.09721. **IR** (Reflection): ṽ = 3072, 2994, 2942, 2248, 1746, 1655, 1599, 1506, 1366, 1304, 1275, 1248, 1171, 1130, 1090, 1014, 953, 928, 837, 792, 762, 660.



***(8R,9S,10R,13S,14S,17S)*-17-((4-Fluorophenyl)buta-1,3-diyn-1-yl)-17-hydroxy-10,13-dimethyl-1,2,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-*3H*-cyclopenta[a]phenanthren-3-one**

6h, colorless solid, 40.2 mg, 47% yield. R_f = 0.2 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 8.9, 5.3 Hz, 2H), 7.02 (q, *J* = 8.9 Hz, 2H), 5.74 (s, 1H), 2.55 – 2.16 (m, 5H), 2.09 – 1.99 (m, 2H), 1.91 (br, 1H), 1.88 – 1.81 (m, 1H), 1.79 – 1.63 (m, 5H), 1.62 – 1.44 (m, 2H), 1.44 – 1.32 (m, 2H), 1.20 (s, 3H), 1.05 (tdd, *J* = 15.4, 12.6, 3.7 Hz, 2H), 0.91 (s, 3H). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 199.5, 171.0, 163.0 (d, *J* = 251.6 Hz), 134.5 (d, *J* = 8.5 Hz), 123.9, 117.6 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.3 Hz), 85.6, 80.5, 78.0, 73.1 (d, *J* = 1.4 Hz), 70.7, 53.2, 50.3, 47.5, 38.9, 38.6, 36.3, 35.7, 33.9, 32.8, 32.7, 31.4, 23.2, 20.7, 17.4, 12.8. ^{19}**F NMR** (282 MHz, $CDCl_3$) δ -108.43. **HRMS** (EI) calcd for $C_{29}H_{31}O_2F$ $[M]^+$: 430.23026, found: 430.22917. **IR** (Reflection): ṽ = 3542, 3064, 2977, 2935, 2910, 2854, 2143, 1671, 1597, 1507, 1451, 1432, 1330, 1290, 1233, 1161, 1126, 1068, 1052, 1028, 952, 869, 838, 820, 680. **M.p.** (amorphous): 222.5-226.2 °C.



5-(4-Fluorophenyl)penta-2,4-diyn-1-yl (*4aS,6aS,6bR,8aR,10S,12aR,12bR,14bS*)-10-hydroxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-4a(*2H*)-carboxylate

6i, light yellow solid, 74.8 mg, 61% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. ^{1}**H NMR** (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.01 (dd, *J* = 12.0, 5.2 Hz, 2H), 5.31 (t, *J* = 3.5 Hz, 1H), 4.80 (d, *J* = 16.3 Hz, 1H), 4.72 (d, *J* = 16.3 Hz, 1H), 3.20 (dd, *J* = 11.3, 4.6 Hz, 1H), 2.87 (dd, *J* = 13.8, 4.2 Hz, 1H), 2.05 – 1.95 (m, 1H), 1.94 – 1.80 (m, 2H), 1.77 – 1.46 (m, 12H), 1.34 (ddd, *J* = 27.3, 16.8, 9.7 Hz, 4H), 1.24 – 1.16 (m, 2H), 1.13 (s, 3H), 1.11 – 1.05 (m, 1H), 0.97 (s, 3H), 0.93 (s, 3H), 0.90 (s, 3H), 0.88 (s, 3H), 0.79 (s, 3H), 0.75 (s, 3H). ^{13}**C NMR** (101 MHz, $CDCl_3$) δ 176.7, 163.1 (d, *J* = 251.9 Hz), 143.4, 134.6 (d, *J* = 8.5 Hz), 122.7, 117.4 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.4 Hz), 79.0, 77.4, 76.7, 73.2 (d, *J* = 1.4 Hz), 70.7, 55.2, 52.2, 47.6, 46.9, 45.8, 41.7, 41.3, 39.4, 38.7, 38.4, 37.0, 33.8, 33.05, 32.7, 32.2, 30.6, 28.1, 27.7, 27.2, 25.8, 23.6, 23.4, 23.0, 18.3, 17.1, 15.5, 15.3. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.15. **HRMS** (EI) calcd for $C_{41}H_{53}O_3F$ $[M]^+$: 612.39733, found: 612.39567. **IR** (Reflection): ṽ = 2946, 2867, 2250, 1730, 1599, 1507, 1460, 1365, 1232, 1155, 1118, 1029, 1011, 910, 834, 792, 734, 655. **M.p.** (amorphous): 155.4-156.7 °C.

4.6 X-Ray Crystallographic Data of 3au

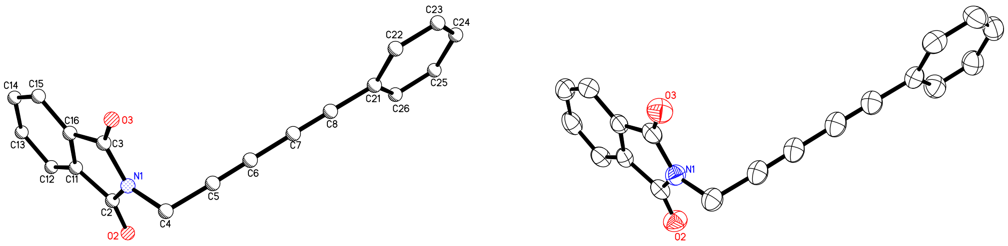


Figure 4. The ORTEP projection of crystal structure of **3au**.

Table 6. Crystal Data and Structure Refinement for **3au.**

Identification code	hws18 (**3au**)	
Empirical formula	$C_{19}H_{11}NO_2$	
Formula weight	285.29	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	triclinic	
Space group	$P\bar{1}$	
Z	2	
Unit cell dimensions	a = 5.3942(6) Å	α =84.034(3) deg.
	b = 8.6436(9) Å	β =82.049(3) deg.
	c = 15.2985(17) Å	γ =86.200(3) deg.
Volume	701.64(13) Å^3	
Density (calculated)	1.35 g/cm^3	
Absorption coefficient	0.09 mm^{-1}	
Crystal shape	plank	
Crystal size	0.094 x 0.086 x 0.048 mm^3	
Crystal colour	colourless	
Theta range for data collection	1.4 to 25.7 deg.	
Index ranges	$-6 \leq h \leq 6$, $-10 \leq k \leq 9$, $-18 \leq l \leq 18$	
Reflections collected	9390	
Independent reflections	2647 (R(int) = 0.0514)	
Observed reflections	1637 ($I > 2\sigma(I)$)	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.96 and 0.90	

Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2647 / 0 / 199
Goodness-of-fit on F^2	1.01
Final R indices (I>2sigma(I))	R1 = 0.051, wR2 = 0.097
Largest diff. peak and hole	0.16 and -0.17 eÅ^{-3}

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Chapter 5 Gold-Catalyzed C(sp)-C(sp) Cross-Coupling of Alkynylsilanes Using H_2O_2 as Oxidant: Synthesis of 1,3-Diynes and Polyynes

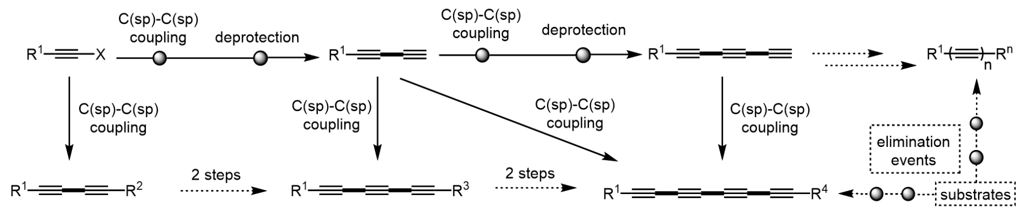
5.1 Introduction

Conjugated 1,3-diynes, especially polyynes, depending on the unique chemical structures and properties, are widely applied in the fields of chemistry and materials,[1] and thus their synthetic strategies have received extensive attention.[2] At present, the synthetic strategies of polyynes can be mainly divided into two categories (Scheme 1A). One is Cu-, or Au-based catalyzed C(sp)-C(sp) couplings of deprotected terminal polyalkenoic precursors.[3,2a,e] Another is to furnish polyynes via elimination events in the last step, utilizing strategies such as Fritsch-Buttenberg-Wiechell rearrangements,[4a] alkylidene carbene rearrangements,[4b] solution-spray flash vacuum pyrolysis,[4c] *etc*. However, these strategies involve cumbersome multi-steps, which exhibited low atom economy and high synthetic costs. Moreover, due to the instability of terminal polyynes species,[5] corresponding polyacetylene compounds are often prepared by one-pot method or by direct next-step coupling,[2c] which limits the application of terminal polyynes in these coupling reactions. In Chapter 4, we proposed a relay synthesis strategy for the preparation of polyynes, which saved the synthetic costs to a certain extent, however, it still exhibited lower atom economy and synthetic efficiency due to the cumbersome steps.

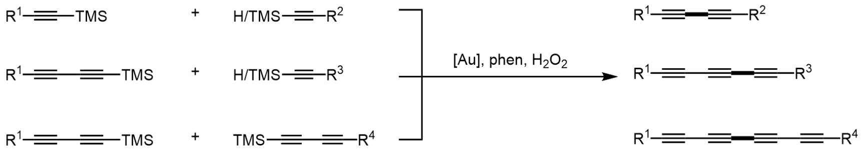
Direct synthesis of target molecules from initial starting materials without pre-functionalization maximizes synthetic efficiency.[6] It is acknowledged that several methods for the synthesis of terminal alkynes exist, involving the preparation of 1-trimethylsilyl alkynes via Sonogashira reaction,[7] followed by silyl-group deprotection.[8] The direct synthesis of unsymmetrical 1,3-diynes and polyynes from alkynylsilanes is extremely attractive. Surprisingly, so far there are only a few synthetic strategies for the direct synthesis of unsymmetrical 1,3-diynes from alkynylsilanes without pre-functionalization found in the literature.[9] The existing strategies for the synthesis of 1,3-diynes from alkynylsilanes mainly involve deprotection of the silyl group to provide terminal alkynes coupling partners,[10] pre-functionalization of alkynylsilanes,[11] and one-pot desilylation,[12] *etc*. Copper salts[13] and Au^{III} complexes[14] were revealed to have more specific reactivity for transmetallation of alkynylsilanes. However, silyl groups, such as TMS and TIPS, are tolerated in Cu-, or Au-based catalyzed Glaser-Hay-type couplings.[15] Therefore, exploring the synthetic strategy of 1,3-diynes and polyynes via direct C(sp)-C(sp) cross-coupling of alkynylsilanes without deprotection or pre-functionalization is extremely challenging but significant.

For the transition metal-catalyzed oxidative C-C(sp) coupling of organosilanes, the formation of $[L_nM(C\equiv CR)]^{n+}$ intermediates undergoing transmetalation with organosilanes is the key to achieving these oxidative coupling reactions.[16] This process often requires additives, such as K_2CO_3,[17a] CsF,[17b] and tetrabutylammonium salt (TBAF),[17c-e] e*tc.* to activate alkynyl silanes. In the first two parts (Chapters 3 and 4), we successfully achieved gold-catalyzed C(sp^2)-C(sp) and C(sp)-C(sp) cross-coupling of terminal alkynes using H_2O_2 as an oxidant. We expected that the L_nAu^{III} complex formed by the reaction of L_nAu^I with H_2O_2 can afford a L_nAu^{III}-acetylide and trimethylsilanol via associative substitution with alkynyl silanes. Herein, we developed a new strategy for the direct synthesis of 1,3-diynes and polyynes from trimethylsilyl alkynes via gold-catalyzed oxidative C(sp)-C(sp) cross-coupling using H_2O_2 as oxidant (Scheme 1B).

A| Previous classical synthetic strategies for unsymmetrical polyynes



B| This work: Directly synthesis of unsymmetrical 1,3-diynes and polyynes from alkynylsilanes



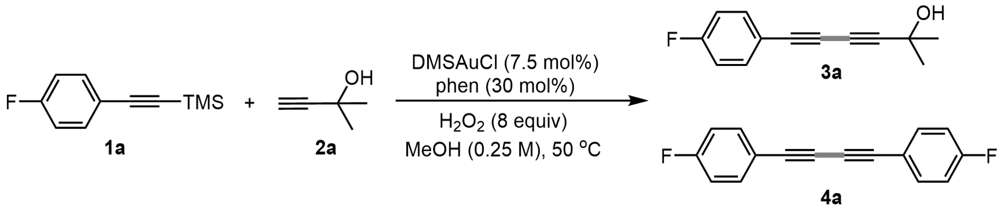
Scheme 1. Synthetic strategies of unsymmetrical polyynes.

5.2 Results and Discussion

To examine the feasibility of the approach and to optimize the reaction conditions, we started investigating the reaction parameters using (4-fluorophenylethynyl)trimethylsilane **1a** and 2-methylbut-3-yn-2-ol **2a** as model substrates. We first focused on the investigation of the effect of different gold catalysts on the reaction. The tested other Au^I complexes such as DMSAuCl, Ph_3PAuCl, $(4\text{-}MeOC_6H_4)_3PAuCl$, and $(4\text{-}CF_3C_6H_4)_3PAuCl$ delivered yields in the range between 60-91% for the cross-coupled diyne **3a** and 7-19% for the homo-coupled by-product **4a** (entries 1-4). No coupled products were detected without Au catalyst (entry 5). Considering the possible residual traces of Cu or Pd salts from the Sonogashira reaction, to eliminate the possibility that Cu-, or Pd-catalyzed the reaction, we used CuI and $(Ph_3P)_2PdCl_2$ instead of DMSAuCl in this catalytic system. The results showed that Cu or Pd salts did not catalyze the reaction at all (entries 6 and 7). In the case of using Ph_3P (entry 8) and pyridine (entry 9) instead of phen or without ligand (entry 10), no coupled products were detected. Using 2,2'-bipyridin (bpy) instead of phen as the ligand, only forms small amounts of products (entry 11). Interestingly, different equivalents or concentrations of H_2O_2 also have a significant influence on the reaction (entries 12-14). In addition, other oxidants such as PIAD and TBHP were tested, only furnishing 1,3-diyne **3a** in 9% and 24% yields, respectively (entries 15 and 16). It is noteworthy that reducing the amount of

DMSAuCl (2.5 mol%) and phen (10 mol%) can also efficiently afford the coupled product **3a** (64%, entry 17).

Table 1. Evaluation of reaction conditions for the cross-coupling of alkynylsilane **1a** with terminal alkyne **2a**.[a,b]



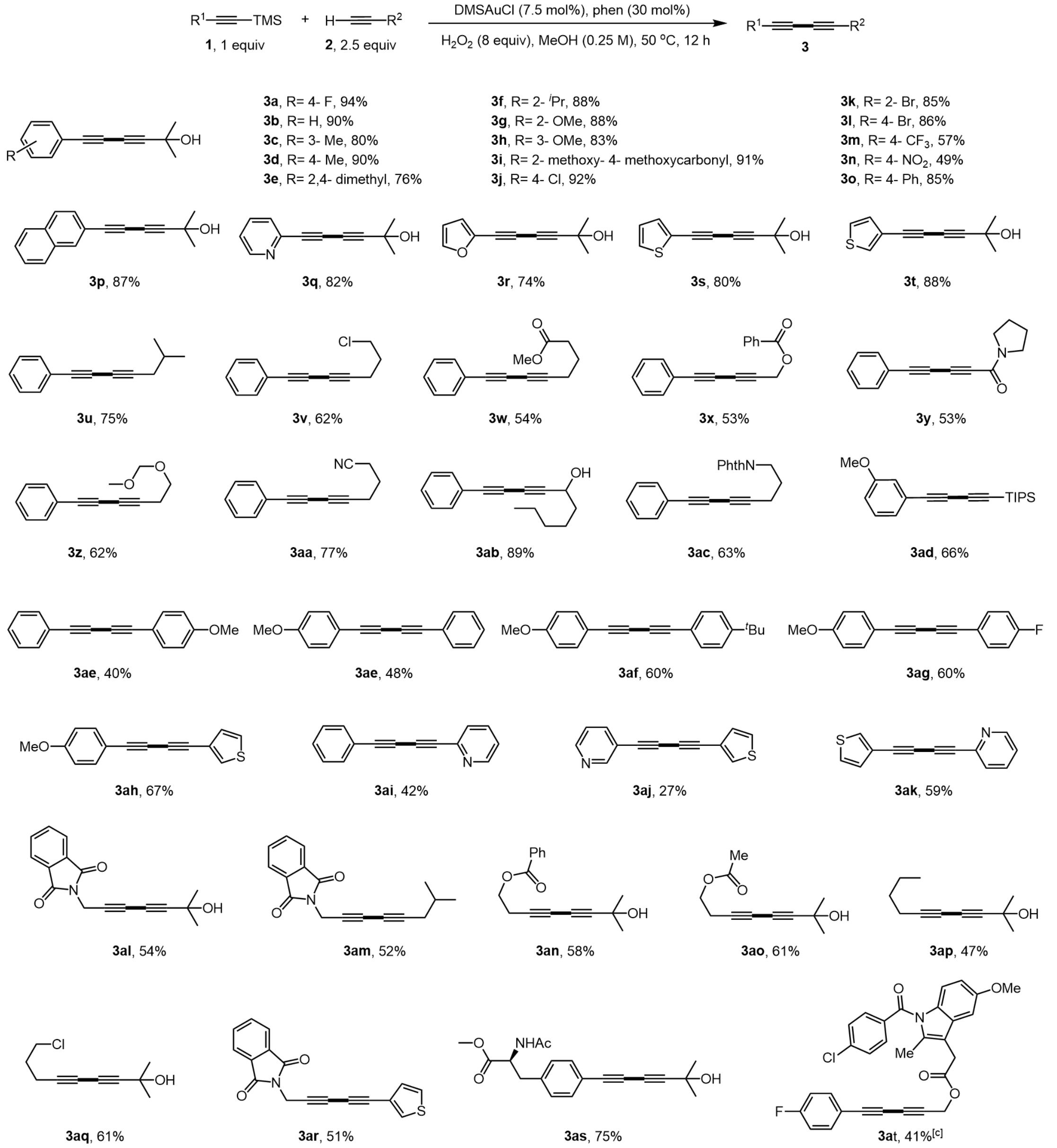
Entry	Deviation on reaction conditions	Convn. (%)	**3a** (%)	**4a** (%)
1	**DMSAuCl**	**100**	**91**	**7**
2	Ph_3PAuCl instead of DMSAuCl	87	70	8
3	$(4\text{-}MeOC_6H_4)_3PAuCl$ instead of DMSAuCl	100	67	15
4	$(4\text{-}CF_3C_6H_4)_3PAuCl$ instead of DMSAuCl	100	60	19
5	without Au catalysis	18	0	0
6	CuI instead of DMSAuCl	29	0	0
7	$(Ph_3P)_2PdCl_2$ instead of DMSAuCl	30	0	0
8	without phen	95	0	0
9	Ph_3P instead of phen	87	0	0
10	Pyridine instead of phen	27	0	0
11	bpy instead of phen	22	1	2
12	H_2O_2 (4 equiv)	67	35	6
13	H_2O_2 (10 equiv)	100	78	13
14	H_2O_2 (8 equiv, 35 wt% in water)	100	85	8
15	TBHP (8 equiv) instead of H_2O_2	31	24	6
16	PIDA (4 equiv) instead of H_2O_2	89	9	1
17	DMSAuCl (2.5 mol%), phen (10 mol%), 24 h	100	64	19

[a] Reaction conditions: alkynylsilane **1a** (0.1 mmol), terminal alkyne **2a** (0.25 mmol), DMSAuCl (7.5 mol%), phen (30 mol%) and H_2O_2 (0.8 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C, 3 h. [b] Determined by ^{19}F NMR using benzotrifluoride as internal standard.

With the optimized conditions in hand, we set up to explore the scope of different alkynylsilanes **1** with terminal alkynes **2** to form 1,3-diynes **3** (Table 2). We first focused on the cross-couplings of aromatic trimethylsilyl alkynes with terminal alkynes. A variety of electron-rich aryl alkynylsilanes, with electron-donating groups such as -Me, -^{i}Pr, and -OMe, reacted smoothly as well, affording the coupled products in good to excellent yields (**3c-3i**). It is worth pointing out that aryl alkynylsilanes with steric hindrance had no significant effect on the reaction, and reacted very smoothly, forming the corresponding 1,3-diynes (**3e-3g**) in good yields

(76-88%). Aryl alkynylsilanes bearing electron-withdrawing groups, such as -F, -Cl, -Br were tolerated well, furnishing the coupled products in excellent yields (**3a**, **3j-3l**). Interestingly, aryl alkynylsilanes containing strong electron-withdrawing groups such as -CF_3 and -NO_2, only form the target 1,3-diynes in moderate yields (**3m, 3n**). In addition, phenyl alkynylsilanes, biphenyl alkynylsilanes, and naphthyl alkynylsilanes without substitution at the aromatic moiety reacted smoothly as well, giving the coupled products **3b, 3o,** and **3p** in very good yields (85-90%). Heteroaromatic alkynes such as pyridine (**3q**), furan (**3r**), and thiophene (**3s**, **3t**) proved to be also suitable substrates, furnishing the target 1,3-diynes in high yields (74-88%). In addition, a variety of different aliphatic alkynes were tested, aliphatic chains containing functional groups such as chlorine (**3v**), esters (**3w** and **3x**), amide (**3y**), ether (**3z**), cyano (**3aa**), alcohols (**3ab**), phthalimide (**3ac**), and TIPS (**3ad**) were all tolerated in this reaction, providing the corresponding 1,3-diynes with yields ranging from 53% to 89%. The cross-couplings between aryl alkynylsilanes and terminal aromatic alkynes with similar structural or electronic properties were performed efficiently as well, affording the target coupled products in moderate yields (**3ae**-**3ag**, 40-60%). Good reactivity was also observed in the reactions of aromatic trimethylsilyl alkynes with heteroaromatic alkynes such as thiophene and pyridine, forming the target 1,3-diynes **3ah** and **3ai** in 42% and 67% yields, respectively. Cross-couplings of heteroaromatic trimethylsilyl alkynes with heteroaromatic alkynes also proceed smoothly (**3aj**, **3ak**). Furthermore, a variety of aliphatic trimethylsilyl alkynes were tested, and reacted smoothly with aliphatic alkynes under very mild conditions as well, furnishing the corresponding 1,3-diynes (**3al-3aq**) in moderate yields (47-61%). Interestingly, treatment of trimethylsilyl aliphatic alkynes with heteroaromatic alkynes (3-ethynylthiophene) under standard conditions also afforded 1,3-diyne **3r** in 51% yield. It is worth mentioning that this catalytic system was also suitable for the introduction of conjugated 1,3-diyne units into natural products and synthetic drugs. For example, *L*-Tyrosine and Indomethacin derivatives reacted very smoothly, affording 1,3-diynes **3as** and **3at** in 75% and 41% yields, respectively.

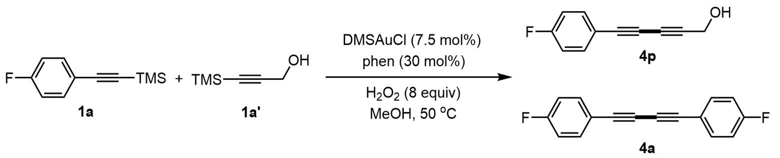
Table 2. Substrate scope for the cross-couplings of alkynylsilanes with terminal alkynes.[a,b]



[a] Reaction conditions: trimethylsilyl alkynes **1** (0.2 mmol), terminal alkyne **2** (0.5 mmol), DMSAuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.8 mL), 50 °C, 12 h. [b] Yield of isolated product. [c] trimethylsilyl alkynes **1** (0.3 mmol), terminal alkyne **2** (0.2 mmol).

Encouraged by gold-catalyzed C(sp)-C(sp) cross-couplings of trimethylsilyl alkynes with terminal alkynes. As shown in Table 3, using ((4-fluorophenyl)ethynyl)trimethylsilane **1a** and 3-(trimethylsilyl)prop-2-yn-1-ol **1a'** as coupling partners, we started investigating the reaction parameters of gold-catalyzed cross-couplings of different trimethylsilyl alkynes. Interestingly, under standard conditions, the coupled product **4p** and the homo-coupling product **4a** were obtained only in low yields even when the reaction time was extended to 24 h (entry 1). Based on the optimization of the conditions for gold-catalyzed cross-coupling of alkynylsilanes with terminal alkynes (Table 1), we further screened the mole ratio of cross-coupling partners (trimethylsilyl alkynes). Different equivalents of alkyne **1a’** were tested, delivering yields in the range between 17-51% for the cross-coupled diyne **4p** and 12-26% for the homo-coupled by-product **4a** (entries 1-4), and we determined that the optimal molar ratio of trimethylsilyl alkynes is 1:1.5 (entry 3). Considering Ph_3PAuCl served as the optimal catalyst for gold-catalyzed C(sp)-C(sp) cross-coupling of two different terminal alkynes (see Chapter 4), however, Ph_3PAuCl instead of DMSAuCl did not perform more efficient catalytic performance (entry 5). In addition, we investigated the effect of different reaction concentrations on this reaction and determined the optimal reaction concentration to be 0.5 M (entries 6-8).

Table 3. Evaluation of reaction conditions for the cross-couplings of different alkynylsilanes.[a,b]

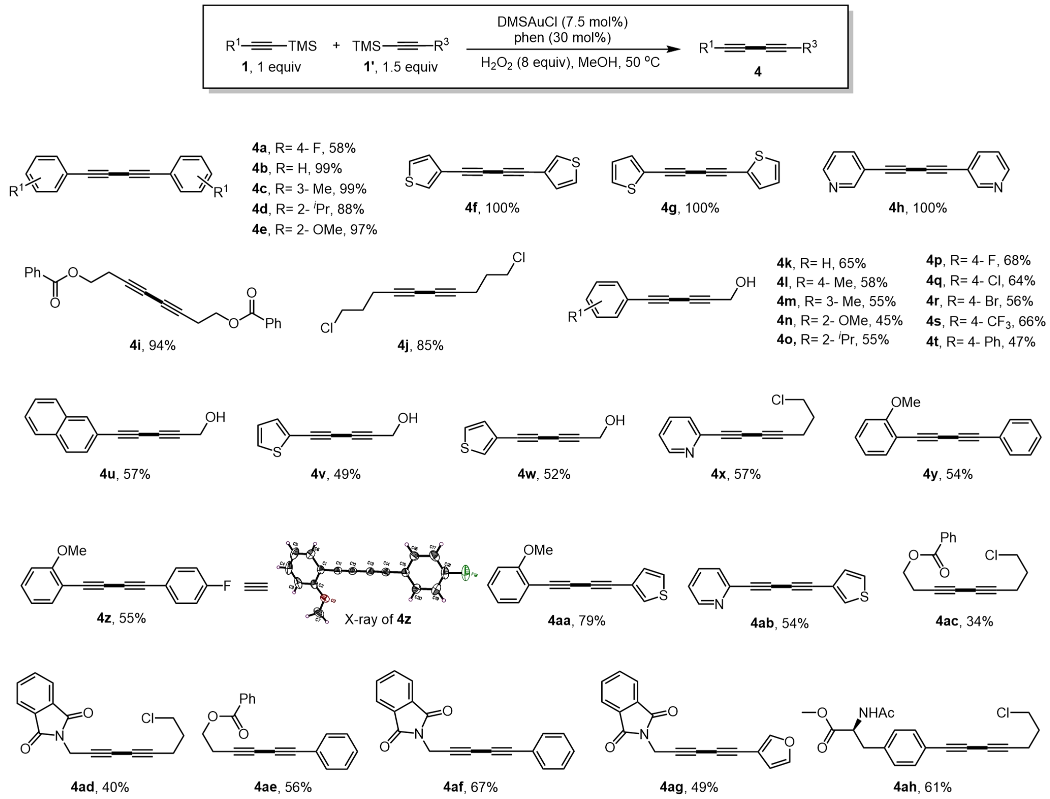


Entry	Deviation on reaction conditions	Convn. (%)	**4p** (%)	**4a** (%)
1	-	69	17	25
2	**1a’** (2 equiv)	73	49	12
3	**1a’** (1.5 equiv)	85	50	16
4	**1a’** (1 equiv)	100	51	26
5	**1a’** (1.5 equiv), Ph_3PAuCl (7.5 mol%)	100	41	26
6	**1a’** (1.5 equiv), MeOH (0.33 M)	100	57	16
7	**1a’ (1.5 equiv), MeOH (0.5 M)**	**100**	**61**	**12**
8	**1a’** (1.5 equiv), MeOH (1 M)	100	54	20

[a] Reaction conditions: ((4-fluorophenyl)ethynyl)trimethylsilane **1a** (0.05 mmol), 3-(trimethylsilyl)prop-2-yn-1-ol **1a’** (0.125 mmol, 2.5 equiv), DMSAuCl (7.5 mol%), phen (30 mol%) and H_2O_2 (0.4 mmol, 50 wt% in water) in MeOH (0.2 mL, 0.25 M), 50 °C, 24 h. [b] Determined by ^{19}F NMR using benzotrifluoride as internal standard.

With the optimized conditions in hand, we next initiated our investigation on the substrate scope of gold-catalyzed C(sp)-C(sp) homo- and cross-coupling of trimethylsilyl alkynes (Table 4). Aromatic alkynylsilanes without substitution (**4b**) or with electron-donating groups, such as -Me (**4c**), -^{i}Pr (**4d**), and -OMe (**4e**), furnishing the symmetrical 1,3-diynes in excellent yields (88-99%). Surprisingly, aromatic alkynylsilanes bearing electron-withdrawing group such as -F, only furnishing the symmetrical 1,3-diyne **4a** in 58% yield, even if the reaction time was prolonged to 48 h, the starting material **1a** was still not completely converted. Heteroaromatic ethynyl trimethylsilanes such as thiophene (**4f** and **4g**), and pyridine (**4h**) were also suitable substrates, affording the target heteroaromatic 1,3-diynes in excellent yields. The homo-coupling reaction of aliphatic alkynylsilanes (**4i** and **4j**) was smooth as well, providing the symmetrical 1,3-diynes in excellent yields. Interestingly, the electronic properties of the aryl substituents had only little influence on this reaction. Aromatic alkynylsilanes with electron-donating groups, such as -Me (**4l** and **4m**), -OMe (**4n**), and -^{i}Pr (**4o**), electron-withdrawing groups, such as -F (**4p**), -Cl (**4q**), -Br (**4r**), and -CF_3 (**4s**), both reacted smoothly, affording the 1,3-diynes in moderated yields (45-68%). In addition, aromatic alkynylsilanes without substitution, such as phenylacetylene (**4k**), biphenylacetylene (**4t**), and naphthyl acetylene (**4u**) were all suitable substrates, furnishing the corresponding 1,3-diynes in 47-65% yields. Heteroaromatic substrates, such as thiophene (**4v** and **4w**), and pyridine (**4x**) coupled smoothly with aliphatic alkynylsilanes as well, affording the target products in moderated yields (49-57%). This gold-catalyzed cross-coupling strategy was also practical for two different trimethylsilyl alkynes with similar structure or electronic properties, such as two aromatic alkynes (**4y** and **4z**), aromatic alkyne with heteroaromatic alkyne (**4aa**), two heteroaromatic alkynes (**4ab**), and two aliphatic alkynes (**4ac** and **4ad**), affording the corresponding 1,3-diynes in poor to good yields (34-79%). To our delight, the cross-coupling reactions of aliphatic alkynes with aromatic alkynes or heteroaromatic alkynes be performed smoothly as well (**4ae-4ag**, 49-67%). *L*-Tyrosine derivative **1ah** also smoothly furnished the target 1,3-diyne **4ah** in 61% yield, which proved the synthetic utility of the method.

Table 4. Substrate scope for the cross-couplings of alkynylsilanes.[a,b,c]



4a, R= 4- F, 58%
4b, R= H, 99%
4c, R= 3- Me, 99%
4d, R= 2- ^{i}Pr, 88%
4e, R= 2- OMe, 97%

4f, 100%

4g, 100%

4h, 100%

4i, 94%

4j, 85%

4k, R= H, 65%
4l, R= 4- Me, 58%
4m, R= 3- Me, 55%
4n, R= 2- OMe, 45%
4o, R= 2- ^{i}Pr, 55%
4p, R= 4- F, 68%
4q, R= 4- Cl, 64%
4r, R= 4- Br, 56%
4s, R= 4- CF_3, 66%
4t, R= 4- Ph, 47%

4u, 57%

4v, 49%

4w, 52%

4x, 57%

4y, 54%

4z, 55%

4aa, 79%

4ab, 54%

4ac, 34%

4ad, 40%

4ae, 56%

4af, 67%

4ag, 49%

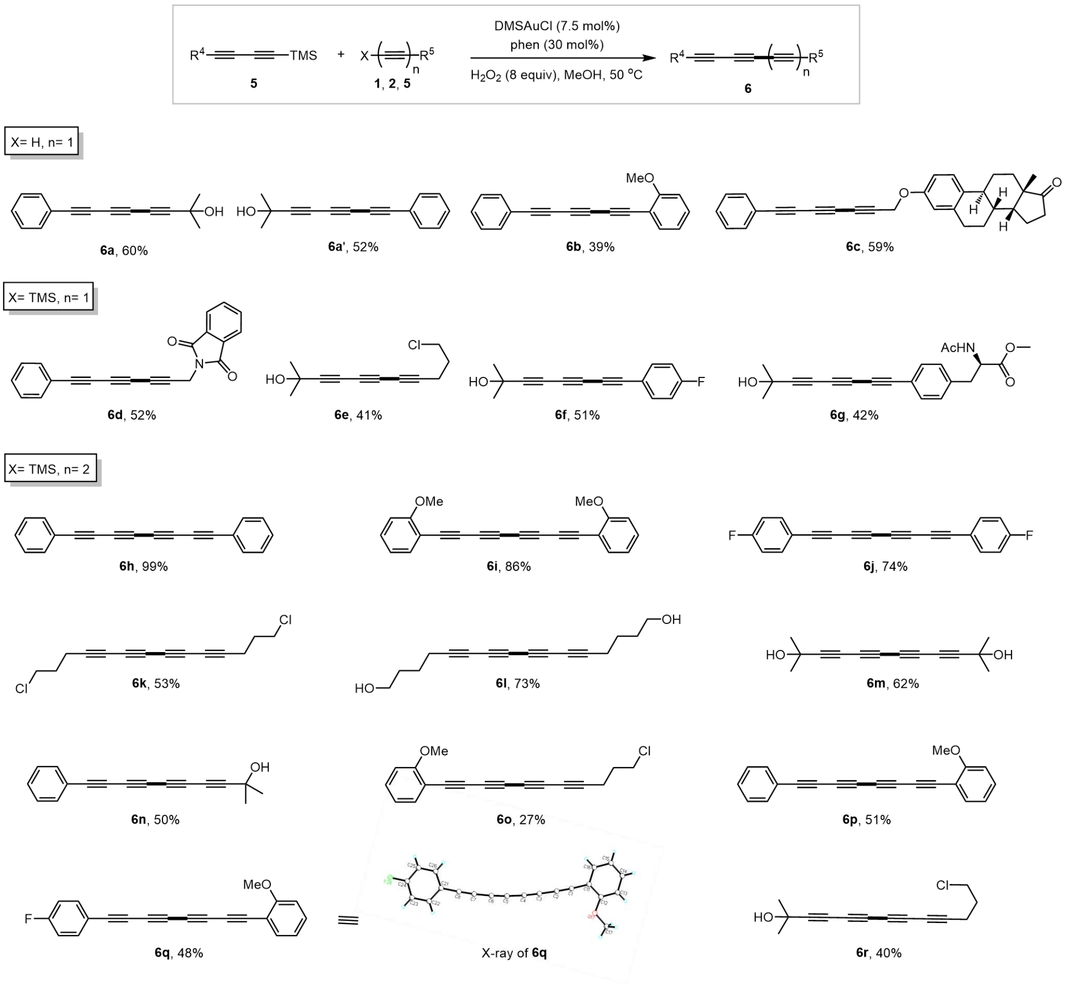
4ah, 61%

[a] Reaction conditions: trimethylsilyl alkynes **1** (0.2 mmol), trimethylsilyl alkynes **1'** (0.3 mmol), DMSAuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C, 24 h. [b] For homo-coupling reaction conditions: trimethylsilyl alkynes **1** (0.4 mmol), DMSAuCl (5 mol%), phen (20 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C, 24 h. [c] Yield of isolated product.

Considering the importance of polyynes in the fields of chemistry and materials,[1] and the challenges of their synthesis, we initiated our investigation of the substrate range for polyalkyne synthesis (Table 5). We first focused on the synthetic strategy of triynes via this gold-catalyzed cross-coupling of 1,3-diynyltrimethylsilanes with terminal alkynes. 1,3-Diynylsilanes and terminal alkynes reacted smoothly, furnishing the target trialkynes (**6a-6c**) in poor to moderated yields (39-60%). In addition, the cross-coupling reactions of 1,3-diynylsilanes with alkynyl trimethylsilanes performed smoothly as well, affording the corresponding triynes in moderated yields (**6d-6g**). Both strategies were suitable for the cross-coupling of alkynes with similar structural or electronic properties (**6b** and **6e**), and derivatives of complex drug molecules were tolerated as well (**6c** and **6g**). Next, we initiated our investigation on the feasibility of this gold-catalyzed cross-coupling strategy for tetrayne synthesis. Both aromatic

1,3-diynylsilanes and aliphatic 1,3-diynylsilanes could efficiently provide symmetrical tetraynes through homo-coupling in moderate to excellent yields (**6h-6m**). Cross-coupling of 1,3-diynylsilanes, including aromatic 1,3-diynylsilanes with aliphatic 1,3-diynylsilanes (**6n** and **6o**), different aromatic 1,3-diynylsilanes (**6p** and **6q**), different aliphatic 1,3-diynylsilanes (**6r**), performed smoothly as well, furnishing unsymmetrical tetraynes in poor to moderate yields.

Table 5. Substrate scope for the synthesis of polyacetylene.[a,b,c]



[a] Reaction conditions A (X = H): trimethylsilyl alkynes **5** (0.2 mmol), terminal alkyne **2** (0.5 mmol), DMSAuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.8 mL), 50 °C, 12 h. Reaction conditions B (X = TMS): trimethylsilyl alkynes **5** (0.2 mmol), trimethylsilyl alkynes **1** (0.3 mmol), DMSAuCl (7.5 mol%), phen (30 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C, 24 h. [b] For homo-coupling reaction conditions: trimethylsilyl alkynes **5** (0.4 mmol), DMSAuCl (5 mol%), phen (20 mol%), and H_2O_2 (1.6 mmol, 50 wt% in water) in MeOH (0.4 mL), 50 °C, 24 h. [c] Yield of isolated product.

5.3 Conclusion

We developed a gold-catalyzed strategy for C(sp)–C(sp) cross-coupling of alkynylsilanes using H_2O_2 as oxidant, which once again demonstrated the potential of hydrogen peroxide as an oxidant for oxidative gold catalysis. This catalytic system was successfully applied to the synthesis of 1,3-diynes and polyynes, which exhibits the advantages of high atom economy, wide substrate range, mild reaction conditions, and good functional group tolerance. Compared with the current polyalkyne synthetic strategies, our method greatly improves the synthetic efficiency, and provide new ideas for the synthesis of polyynes.

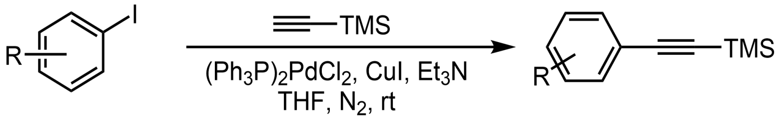
5.4 Experimental Section

5.4.1 General Materials and Methods

Chemicals were purchased from commercial suppliers and used as delivered. Dry solvents were dispensed from the solvent purification system MB SPS-800. In our conditions, MeOH can be used directly without further drying and deoxygenation. Deuterated solvents were bought from Euriso-Top. Hydrogen peroxide solution (50 wt% in water, stabilized) was bought from Sigma-Aldrich. For reactions that require heating, the heat source: aluminum heating block (less than 0.5 mmol scale reactions), or oil bath (more than 0.5 mmol scale reactions). Unless otherwise stated, all reactions were carried out under an ambient atmosphere and monitored by thin layer chromatography (TLC). Components were visualized by fluorescence quenching under UV light (254 nm) or by treatment with aqueous potassium permanganate ($KMnO_4$) solution. ^1H, $^{13}C\{^1H\}$ and ^{19}F NMR spectra were recorded on a Bruker Avance-III-300 (300 MHZ), Bruker Avance-III-400 (400 MHZ), or Bruker Avance-III-600 (400 MHZ) NMR spectrometer. Chemical shifts are expressed as parts per million (ppm, δ) downfield of tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.26 / 77.0 ppm) as internal standards. Data is reported as follows: s = singlet, d = doublet, t = triplet, p = pentalet, q = quartet, m = multiplet, br = broad, dd = doublet of doublets, dt = doublet of triplets, dp = doublet of pentalets, td = triplet of doublets, ddd = doublet of doublet of doublets, hept = heptet; constants are absolute values and *J* values are expressed in Hertz (Hz). Mass spectra (MS and HRMS) were determined in the chemistry department of the University Heidelberg under the direction of Dr. J. Gross. For ESI (+) spectra, an ApexQe FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR (IF528), IR (283), or FT-IR Vektor 22. Melting points (M.p.) were measured in open glass capillaries in a Büchi melting point apparatus. X-ray data were collected at a temperature of 200 K on the Bruker APEX-II Quazar area detector.

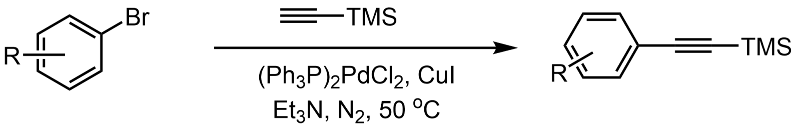
5.4.2 General Procedure for Trimethylsilyl Alkynes

A. General procedure for trimethylsilyl aromatic alkynes from aromatic iodine



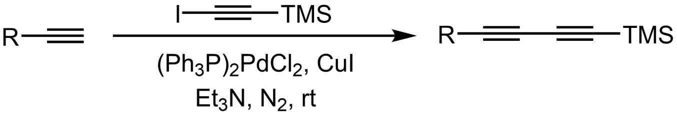
To a suspension of $(Ph_3P)_2PdCl_2$ (1 mol%) and CuI (4 mol%) in THF (0.5 M) were added Et_3N (3.5 equiv) aromatic iodine (1 equiv) and trimethylsilylacetylene (1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature, and products were detected by TLC. After completion of the reaction, the mixture was filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography to afford trimethylsilyl aromatic alkynes.

B. General procedure for trimethylsilyl aromatic alkynes from aromatic bromide

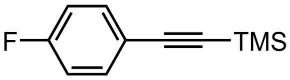


To a suspension of $(Ph_3P)_2PdCl_2$ (1 mol%) and CuI (4 mol%) in Et_3N (0.5 M) were added aromatic bromide (1 equiv) and trimethylsilylacetylene (1.2 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at 50 °C overnight. After completion of the reaction, cooling the mixture to room temperature, filtered, and concentrated in vacuo. The residual mixture was purified by silica gel chromatography to afford trimethylsilyl aromatic alkynes.

C. General procedure for trimethyl(1,3-diyn-1-yl)silanes



To a suspension of $(Ph_3P)_2PdCl_2$ (1 mol%) and CuI (4 mol%) in Et_3N (0.5 M) were added 1-iod-2-(trimethylsilyl)-acetylen (1 equiv) and terminal alkyne (1.1 equiv). Evacuation of the flask containing the resulting solution and flushing with N_2 for several times removed air. The mixture was allowed to stir at room temperature overnight. After completion of the reaction, the mixture was filtered and concentrated in vacuo. The residual mixture was purified by silica gel chromatography to afford trimethyl(1,3-diyn-1-yl)silanes.

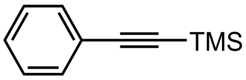


((4-Fluorophenyl)ethynyl)trimethylsilane (1a)

General Procedure A, the spectral data were in agreement with literature values.[16c]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.37 (m, 2H), 7.10 – 6.89 (m, 2H), 0.24 (s, 9H).

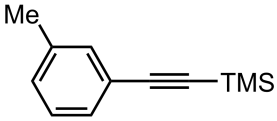
^{19}F NMR (282 MHz, $CDCl_3$) δ -110.50.



Trimethyl(phenylethynyl)silane (1b)

General Procedure A, the spectral data were in agreement with literature values.[18]

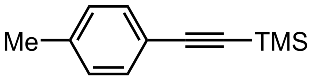
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.34 – 7.27 (m, 3H), 0.25 (s, 9H).



Trimethyl(m-tolylethynyl)silane (1c)

General Procedure A, the spectral data were in agreement with literature values.[19]

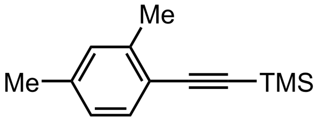
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.3, 3.8 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 2.32 (s, 3H), 0.25 (s, 9H).



Trimethyl(p-tolylethynyl)silane (1d)

General Procedure A, the spectral data were in agreement with literature values.[20]

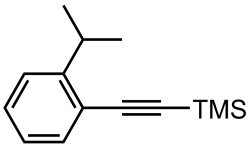
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 7.9 Hz, 2H), 2.34 (s, 3H), 0.24 (s, 9H).



((2,4-Dimethylphenyl)ethynyl)trimethylsilane (1e)

General Procedure A, the spectral data were in agreement with literature values.[21]

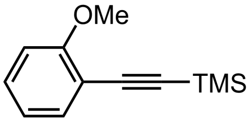
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, J = 7.8 Hz, 1H), 7.00 (s, 1H), 6.92 (d, J = 7.7 Hz, 1H), 2.39 (s, 3H), 2.30 (s, 3H), 0.25 (s, 9H).



((2-Isopropylphenyl)ethynyl)trimethylsilane (1f)

General Procedure A, the spectral data were in agreement with literature values.[22]

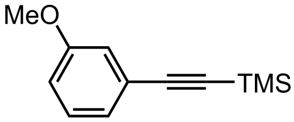
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 1H), 7.33 – 7.22 (m, 2H), 7.11 (ddd, J = 7.6, 6.5, 2.3 Hz, 1H), 3.45 (hept, J = 6.9 Hz, 1H), 1.26 (d, J = 6.9 Hz, 6H), 0.26 (s, 9H).



((2-Methoxyphenyl)ethynyl)trimethylsilane (1g)

General Procedure A, the spectral data were in agreement with literature values.[23]

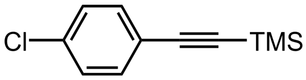
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (dd, J = 7.5, 1.7 Hz, 1H), 7.28 (ddd, J = 8.3, 7.6, 1.8 Hz, 1H), 6.87 (ddd, J = 8.3, 6.7, 3.0 Hz, 2H), 3.88 (s, 3H), 0.27 (s, 9H).



((3-Methoxyphenyl)ethynyl)trimethylsilane (1h)

General Procedure A, the spectral data were in agreement with literature values.[24]

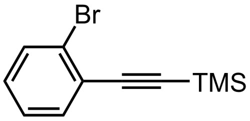
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.9 Hz, 1H), 7.06 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.99 (dd, *J* = 2.5, 1.4 Hz, 1H), 6.87 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 3.80 (s, 3H), 0.25 (s, 9H).



((4-Chlorophenyl)ethynyl)trimethylsilane (1j)

General Procedure A, the spectral data were in agreement with literature values.[25]

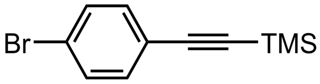
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 – 7.34 (m, 2H), 7.31 – 7.24 (m, 2H), 0.25 (s, 9H).



((2-Bromophenyl)ethynyl)trimethylsilane (1k)

General Procedure A, the spectral data were in agreement with literature values.[26]

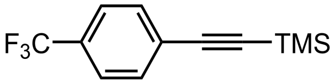
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.49 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.24 (dt, *J* = 7.6, 1.6 Hz, 1H), 7.15 (td, *J* = 7.7, 1.8 Hz, 1H), 0.28 (s, 9H).



((4-Bromophenyl)ethynyl)trimethylsilane (1l)

General Procedure A, the spectral data were in agreement with literature values.[27]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.34 – 7.28 (m, 2H), 0.24 (s, 9H).

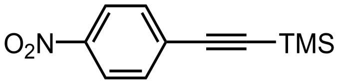


Trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (1m)

General Procedure A, the spectral data were in agreement with literature values.[28]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 4H), 0.26 (s, 9H).

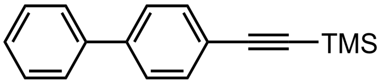
^{19}F NMR (282 MHz, $CDCl_3$) δ -62.85.



Trimethyl((4-nitrophenyl)ethynyl)silane (1n)

General Procedure A, the spectral data were in agreement with literature values.[29]

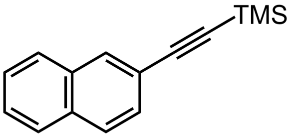
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 – 8.08 (m, 2H), 7.65 – 7.50 (m, 2H), 0.27 (s, 9H).



([1,1'-Biphenyl]-4-ylethynyl)trimethylsilane (1o)

General Procedure A, the spectral data were in agreement with literature values.[30]

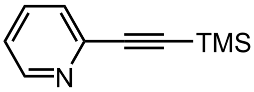
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.64 – 7.51 (m, 6H), 7.45 (t, J = 7.4 Hz, 2H), 7.36 (t, J = 7.2 Hz, 1H), 0.28 (s, 9H).



Trimethyl(naphthalen-2-ylethynyl)silane (1p)

General Procedure B, the spectral data were in agreement with literature values.[31]

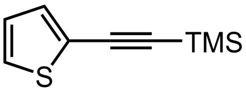
^{1}H NMR (300 MHz, CDCl$_3$) δ 8.00 (s, 1H), 7.78 (td, J = 9.0, 6.0 Hz, 3H), 7.54 – 7.42 (m, 3H), 0.29 (s, 9H).



2-((Trimethylsilyl)ethynyl)pyridine (1q)

General Procedure B, the spectral data were in agreement with literature values.[32]

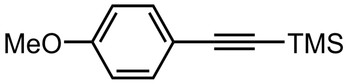
^{1}H NMR (300 MHz, CDCl$_3$) δ 8.56 (ddd, J = 4.9, 1.7, 0.9 Hz, 1H), 7.63 (td, J = 7.7, 1.8 Hz, 1H), 7.45 (dt, J = 7.8, 1.1 Hz, 1H), 7.22 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 0.27 (s, 9H).



Trimethyl(thiophen-2-ylethynyl)silane (1s)

General Procedure B, the spectral data were in agreement with literature values.[33]

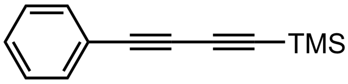
^{1}H NMR (300 MHz, CDCl$_3$) δ 7.23 (d, J = 4.4 Hz, 2H), 6.98 – 6.92 (m, 1H), 0.25 (s, 9H).



((4-Methoxyphenyl)ethynyl)trimethylsilane (1ae)

General Procedure A, the spectral data were in agreement with literature values.[34]

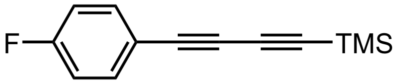
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 – 7.34 (m, 2H), 6.87 – 6.76 (m, 2H), 3.81 (s, 3H), 0.24 (s, 9H).



Trimethyl(phenylbuta-1,3-diyn-1-yl)silane (5a)

General Procedure C, the spectral data were in agreement with literature values.[35]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.43 – 7.28 (m, 3H), 0.24 (s, 9H).



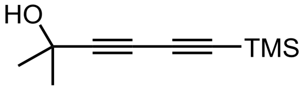
((4-Fluorophenyl)buta-1,3-diyn-1-yl)trimethylsilane (5b)

General Procedure C, the spectral data were in agreement with literature values.[36]

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.44 (m, 2H), 7.04 – 6.97 (m, 2H), 0.23 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 163.1 (d, *J* = 251.8 Hz), 134.7 (d, *J* = 8.5 Hz), 117.5 (d, *J* = 3.7 Hz), 115.9 (d, *J* = 22.4 Hz), 90.7, 87.6, 75.6, 73.9, -0.4.

^{19}F NMR (282 MHz, $CDCl_3$) δ -108.35.

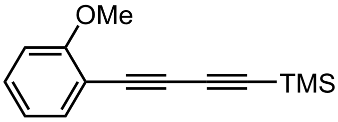


2-Methyl-6-(trimethylsilyl)hexa-3,5-diyn-2-ol (5c)

General Procedure C, the spectral data were in agreement with literature values.[37]

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (s, 6H), 0.19 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 87.8, 87.1, 81.9, 67.3, 65.5, 31.0, -0.5.

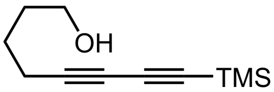


((2-Methoxyphenyl)buta-1,3-diyn-1-yl)trimethylsilane (5d)

General Procedure C, the spectral data were in agreement with literature values.[38]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.36 – 7.28 (m, 1H), 6.92 – 6.83 (m, 2H), 3.87 (s, 3H), 0.23 (s, 9H).

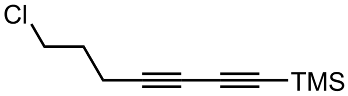
^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7, 134.6, 130.8, 120.5, 110.7, 91.0, 88.1, 77.9, 73.3, 55.8, -0.4.



8-(Trimethylsilyl)octa-5,7-diyn-1-ol (5e)

General Procedure C, the spectral data were in agreement with literature values.[39]

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (t, *J* = 6.0 Hz, 1H), 2.32 (t, *J* = 6.5 Hz, 1H), 1.76 – 1.56 (m, 2H), 1.49 (s, 1H), 0.17 (s, 5H).

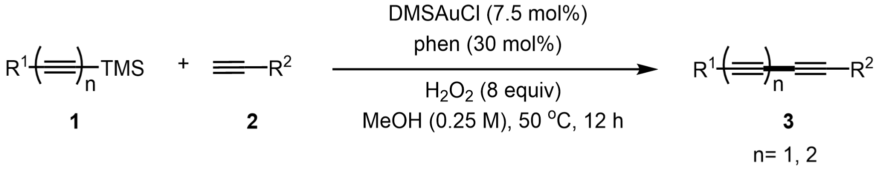


(7-Chlorohepta-1,3-diyn-1-yl)trimethylsilane (5f)

General Procedure C, the spectral data were in agreement with literature values.[40]

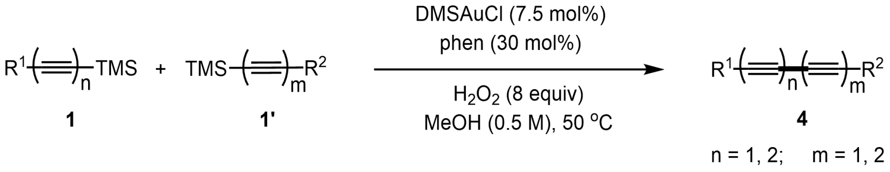
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.3 Hz, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.98 (p, *J* = 6.6 Hz, 2H), 0.19 (s, 9H).

5.4.3 General Procedure for the Cross-Coupling of Alkynylsilanes with Terminal Alkynes



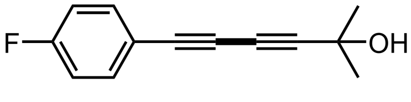
A solution of the alkynylsilanes **1** (0.2 mmol), terminal alkynes **2** (0.5 mmol, 2.5 equiv), DMSAuCl (4.4 mg, 7.5 mol%), phen (10.8 mg, 30 mol%) and H_2O_2 (89.6 μL, 1.6 mmol, 50 wt% in water) in MeOH (0.8 mL) was stirred at 50 °C for 12 h. After completion of the reaction, products were detected by TLC. The solvent was removed under reduced pressure by an aspirator, the pure product was obtained by flash column chromatography on silica gel.

5.4.4 General Procedure for the Cross-Coupling of Alkynylsilanes



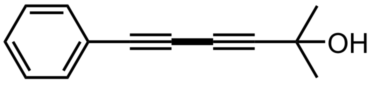
A solution of the alkynylsilanes **1** (0.2 mmol), terminal alkynes **2** (0.3 mmol, 1.5 equiv), DMSAuCl (4.4 mg, 7.5 mol%), phen (10.8 mg, 30 mol%) and H_2O_2 (89.6 µL, 1.6 mmol, 50 wt% in water) in MeOH (0.4 mL) was stirred at 50 °C for 24 h. After completion of the reaction, products were detected by TLC. The solvent was removed under reduced pressure by an aspirator, the pure product was obtained by flash column chromatography on silica gel.

5.5 Characterization of Products



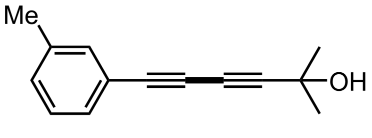
6-(4-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

3a, colorless solid, 37.8 mg, 94% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.55 – 7.36 (m, 2H), 7.00 (t, *J* = 8.7 Hz, 2H), 2.20 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 163.0 (d, *J* = 251.5 Hz), 134.5 (d, *J* = 8.6 Hz), 117.6 (d, *J* = 3.6 Hz), 115.8 (d, *J* = 22.3 Hz), 86.7, 77.7, 72.9, 72.9, 66.9, 65.7, 31.1. Characterization data of **3a** corresponded to the literature values.[41]



2-Methyl-6-phenylhexa-3,5-diyn-2-ol

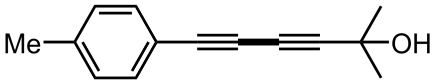
3b, light yellow solid, 33.2 mg, 90% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.40 – 7.27 (m, 3H), 2.16 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.2, 128.4, 121.5, 86.7, 78.8, 73.1, 67.0, 65.7, 31.1. Characterization data of **3b** corresponded to the literature values.[41]



2-Methyl-6-(m-tolyl)hexa-3,5-diyn-2-ol

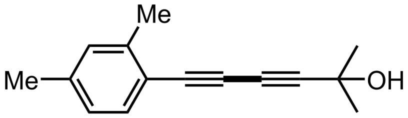
3c, light yellow oil, 31.8 mg, 80% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30 – 7.28 (m, 2H), 7.23 – 7.15 (m, 2H), 2.32 (s, 3H), 2.13 (br, 1H), 1.58 (s, 6H). **^{13}C NMR**

(75 MHz, $CDCl_3$) δ 138.1, 133.0, 130.2, 129.6, 128.3, 121.3, 86.5, 79.0, 72.8, 67.1, 65.7, 31.1, 21.1. Characterization data of **3c** corresponded to the literature values.[41]



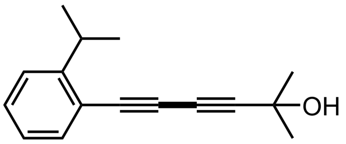
2-Methyl-6-(p-tolyl)hexa-3,5-diyn-2-ol

3d, colorless solid, 32.0 mg, 81% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 2.35 (s, 3H), 2.22 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 139.6, 132.4, 129.2, 118.4, 86.3, 79.0, 72.5, 67.2, 65.7, 31.1, 21.5. Characterization data of **3d** corresponded to the literature values.[41]



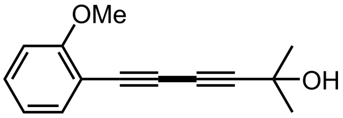
6-(2,4-Dimethylphenyl)-2-methylhexa-3,5-diyn-2-ol

3e, light yellow oil, 32.5 mg, 76% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.8 Hz, 1H), 7.01 (s, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 2.41 (s, 3H), 2.31 (s, 3H), 2.19 (s, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 141.6, 139.5, 132.9, 130.4, 126.4, 118.2, 86.8, 78.1, 76.0, 67.3, 65.8, 31.1, 21.5, 20.5. Characterization data of **3e** corresponded to the literature values.[41]



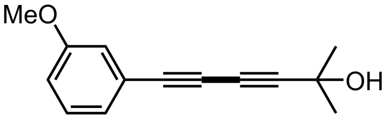
6-(2-Isopropylphenyl)-2-methylhexa-3,5-diyn-2-ol

3f, light yellow oil, 39.7 mg, 88% yield. R_f = 0.6 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.6 Hz, 1H), 7.38 – 7.24 (m, 2H), 7.13 (td, *J* = 7.6, 1.6 Hz, 1H), 3.43 (hept, *J* = 6.9 Hz, 1H), 2.21 (br, 1H), 1.60 (s, 6H), 1.26 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 152.1, 133.5, 129.5, 125.6, 125.1, 120.3, 87.0, 77.6, 76.4, 67.2, 65.8, 31.7, 31.1, 23.2. Characterization data of **3f** corresponded to the literature values.[41]



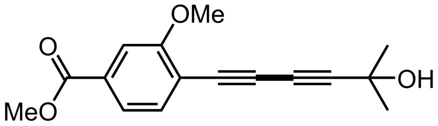
6-(2-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

3g, light yellow oil, 37.7 mg, 88% yield. $R_f = 0.3$ (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.31 (td, *J* = 8.4, 1.6 Hz, 1H), 6.96 – 6.79 (m, 2H), 3.87 (s, 3H), 2.13 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.4, 134.4, 130.7, 120.5, 110.7, 110.6, 87.2, 76.9, 75.3, 67.3, 65.7, 55.8, 31.1. Characterization data of **3g** corresponded to the literature values.[41]



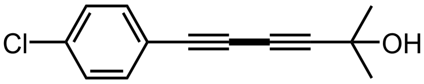
6-(3-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

3h, colorless solid, 35.6 mg, 83% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.22 (t, *J* = 7.9 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 7.03 – 6.96 (m, 1H), 6.95 – 6.87 (m, 1H), 3.78 (s, 3H), 2.20 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 159.2, 129.5, 125.0, 122.4, 117.1, 116.0, 78.7, 72.9, 67.0, 65.7, 55.3, 31.1. Characterization data of **3h** corresponded to the literature values.[41]



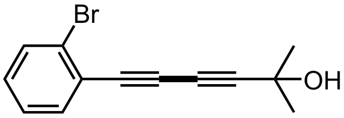
Methyl 4-(5-hydroxy-5-methylhexa-1,3-diyn-1-yl)-3-methoxybenzoate

3i, light yellow solid, 49.3 mg, 91% yield. $R_f = 0.3$ (PE:EA = 2:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.12 (d, *J* = 2.1 Hz, 1H), 8.00 (dd, *J* = 8.8, 2.1 Hz, 1H), 6.89 (d, *J* = 8.8 Hz, 1H), 3.93 (s, 3H), 3.88 (s, 3H), 2.11 (s, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.9, 164.6, 136.1, 132.5, 122.7, 111.1, 110.2, 87.6, 74.1, 67.0, 65.7, 56.1, 52.1, 31.1. Characterization data of **3i** corresponded to the literature values.[41]



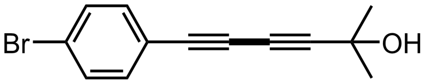
6-(4-Chlorophenyl)-2-methylhexa-3,5-diyn-2-ol

3j, light yellow solid, 40.2 mg, 92% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.6 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 2.11 (s, 1H), 1.58 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 135.4, 133.7, 128.8, 120.0, 87.2, 77.5, 74.1, 66.8, 65.7, 31.1. Characterization data of **3j** corresponded to the literature values.[41]



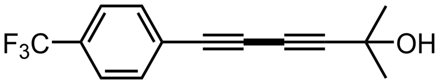
6-(2-Bromophenyl)-2-methylhexa-3,5-diyn-2-ol

3k, light yellow oil, 44.8 mg, 85% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.50 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.26 (td, *J* = 7.5, 1.3 Hz, 1H), 7.20 (td, *J* = 7.7, 1.9 Hz, 1H), 2.24 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 134.4, 132.5, 130.2, 127.0, 126.1, 123.9, 88.2, 773, 76.8, 66.9, 65.7, 31.0. Characterization data of **3k** corresponded to the literature values.[41]



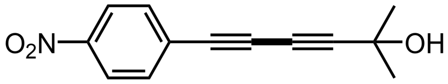
6-(4-Bromophenyl)-2-methylhexa-3,5-diyn-2-ol

3l, light yellow solid, 45.3 mg, 86% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 2.10 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.8, 131.7, 123.7, 120.5, 87.3, 77.6, 74.3, 66.8, 65.7, 31.0. Characterization data of **3l** corresponded to the literature values.[41]



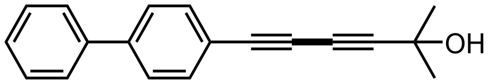
2-Methyl-6-(4-(trifluoromethyl)phenyl)hexa-3,5-diyn-2-ol

3m, light yellow solid, 28.5 mg, 57% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (br, 4H), 2.16 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 132.7, 130.8 (q, *J* = 32.8 Hz), 125.5 (d, *J* = 1.3 Hz), 125.4 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 272.3 Hz), 88.0, 77.1, 75.4, 66.6, 65.8, 31.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.01. Characterization data of **3m** corresponded to the literature values.[15a]



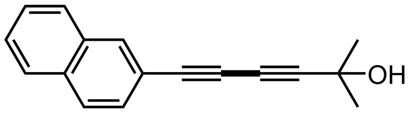
2-Methyl-6-(4-nitrophenyl)hexa-3,5-diyn-2-ol

3n, light yellow solid, 22.6 mg, 49 % yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.9 Hz, 2H), 7.61 (d, *J* = 8.9 Hz, 2H), 2.02 (br, 1H), 1.59 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 147.5, 133.2, 128.5, 123.6, 89.5, 78.1, 76.3, 66.4, 65.8, 31.0. Characterization data of **3n** corresponded to the literature values.[41]



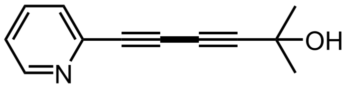
6-([1,1'-Biphenyl]-4-yl)-2-methylhexa-3,5-diyn-2-ol

3o, light yellow solid, 44.0 mg, 85% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 – 7.53 (m, 6H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.41 – 7.33 (m, 1H), 2.27 (br, 1H), 1.61 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 141.9, 140.0, 132.9, 128.9, 127.8, 127.04, 126.98, 120.3, 87.0, 78.7, 73.8, 67.1, 65.7, 31.1. Characterization data of **3o** corresponded to the literature values.[41]



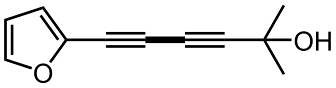
2-Methyl-6-(naphthalen-2-yl)hexa-3,5-diyn-2-ol

3p, light yellow solid, 40.6 mg, 87% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.85 – 7.73 (m, 3H), 7.54 – 7.46 (m, 3H), 2.16 (br, 1H), 1.61 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.1, 133.0, 132.7, 128.4, 128.1, 127.79, 127.77, 127.2, 126.7, 118.7, 86.8, 79.2, 73.4, 67.2, 65.8, 31.1. Characterization data of **3p** corresponded to the literature values.[41]



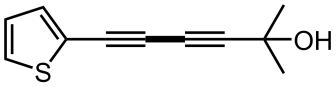
2-Methyl-6-(pyridin-2-yl)hexa-3,5-diyn-2-ol

3q, dark yellow solid, 30.2 mg, 82% yield. R_f = 0.8 (DCM:EA = 1:1), chromatography eluent: 20% Ethyl acetate in Dichloromethane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.3 Hz, 1H), 7.67 (td, *J* = 7.8, 1.7 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.24 (m, 1H), 3.12 (br, 1H), 1.60 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.1, 142.0, 136.3, 128.1, 123.5, 88.2, 73.5, 66.5, 65.4, 31.0. Characterization data of **3q** corresponded to the literature values.[41]



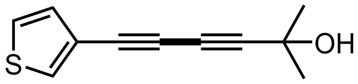
6-(Furan-2-yl)-2-methylhexa-3,5-diyn-2-ol

3r, dark yellow oil, 25.8 mg, 74% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 1.4 Hz, 1H), 6.70 (d, *J* = 3.4 Hz, 1H), 6.39 (dd, *J* = 3.4, 1.9 Hz, 1H), 2.08 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 144.6, 136.2, 118.1, 111.1, 89.4, 77.9, 68.3, 66.6, 65.8, 31.0. **HRMS** (APCI) calcd for $C_{11}H_9O$ $[M-OH]^+$: 157.0648, found: 157.0648; calcd for $C_{11}H_{11}O_2$ $[M+H]^+$: 175.0754, found: 175.0751. **IR** (Reflection): ṽ = 3376, 2984, 2934, 2230, 1735, 1482, 1460, 1364, 1292, 1204, 1164, 1078, 1010, 953, 914, 885, 848, 818, 746, 650.



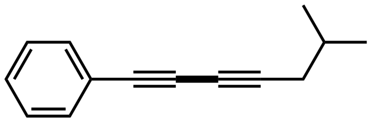
2-Methyl-6-(thiophen-2-yl)hexa-3,5-diyn-2-ol

3s, dark yellow oil, 30.4 mg, 80% yield. R_f = 0.5 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 6.97 (dd, *J* = 5.1, 3.8 Hz, 1H), 2.17 (br, 1H), 1.57 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 134.3, 128.6, 127.1, 121.7, 88.8, 77.2, 71.8, 66.9, 65.8, 31.0. **HRMS** (APCI) calcd for $C_{11}H_9S$ $[M-OH]^+$: 173.0419, found: 173.0418. **IR** (Reflection): ṽ = 3226, 2981, 2934, 1458, 1421, 1376, 1361, 1282, 1221, 1186, 1163, 1081, 1049, 1005, 949, 856, 845, 832, 734, 710, 697, 623.



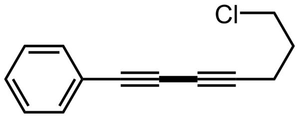
2-Methyl-6-(thiophen-3-yl)hexa-3,5-diyn-2-ol

3t, dark yellow oil, 33.6 mg, 88% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 1H), 7.29 – 7.23 (m, 1H), 7.13 (dd, J = 4.9, 0.7 Hz, 1H), 2.21 (br, 1H), 1.58 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 131.3, 130.1, 125.6, 120.6, 86.5, 74.0, 72.8, 67.0, 65.7, 31.1. **HRMS** (APCI) calcd for $C_{11}H_9S$ $[M-OH]^+$: 173.0419, found: 173.0423; calcd for $C_{11}H_{11}OS$ $[M+H]^+$: 191.0525, found: 191.0521. **IR** (Reflection): ṽ = 3223, 2981, 2933, 2237, 2186, 1658, 1458, 1414, 1376, 1359, 1278, 1213, 1164, 1082, 1051, 960, 913, 870, 849, 812, 779, 734, 689, 622.



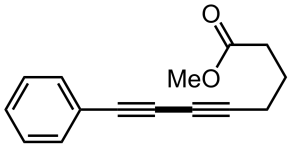
(6-Methylhepta-1,3-diyn-1-yl)benzene

3u, light yellow oil, 27.3 mg, 75% yield. $R_f = 0.7$ (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (dd, J = 7.5, 2.0 Hz, 2H), 7.38 – 7.26 (m, 3H), 2.26 (d, J = 6.5 Hz, 2H), 1.90 (dp, J = 13.2, 6.6 Hz, 1H), 1.03 (d, J = 6.7 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 128.8, 128.3, 122.1, 83.9, 74.6, 74.4, 65.9, 28.7, 28.1, 22.0. Characterization data of **3u** corresponded to the literature values.[41]



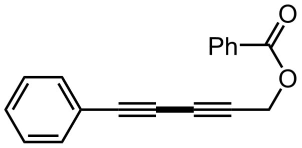
(7-Chlorohepta-1,3-diyn-1-yl)benzene

3v, colorless oil, 25.3 mg, 62% yield. $R_f = 0.4$ (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (dd, J = 7.7, 1.8 Hz, 2H), 7.40 – 7.27 (m, 3H), 3.68 (t, J = 6.3 Hz, 2H), 2.58 (t, J = 6.8 Hz, 2H), 2.03 (p, J = 6.6 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.0, 128.4, 121.8, 82.4, 75.2, 74.0, 66.1, 43.4, 31.0, 17.0. Characterization data of **3v** corresponded to the literature values.[42]



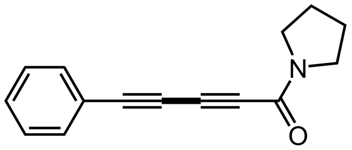
Methyl 9-phenylnona-6,8-diynoate

3w, light yellow oil, 25.8 mg, 54% yield. $R_f = 0.4$ (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.37 – 7.27 (m, 3H), 3.69 (s, 3H), 2.52 – 2.41 (m, 4H), 1.90 (p, *J* = 7.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.3, 132.5, 128.9, 128.3, 121.9, 83.2, 75.1, 74.1, 66.0, 51.6, 32.7, 23.4, 19.0. Characterization data of **3w** corresponded to the literature values.[43]



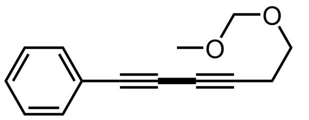
5-Phenylpenta-2,4-diyn-1-yl benzoate

3x, light yellow oil, 27.5 mg, 53% yield. $R_f = 0.5$ (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.12 – 8.04 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.47 (dd, *J* = 15.1, 7.1 Hz, 4H), 7.41 – 7.28 (m, 3H), 5.07 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 165.7, 133.4, 132.6, 129.8, 129.5, 129.3, 128.4, 128.4, 121.2, 78.8, 76.2, 73.1, 71.3, 53.1. Characterization data of **3x** corresponded to the literature values.[41]



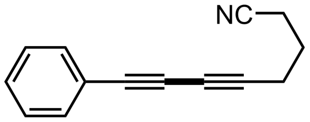
5-Phenyl-1-(pyrrolidin-1-yl)penta-2,4-diyn-1-one

3y, light yellow solid, 23.5 mg, 53% yield. $R_f = 0.3$ (PE:EA = 2:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 – 7.48 (m, 2H), 7.45 – 7.30 (m, 3H), 3.67 (t, *J* = 6.4 Hz, 2H), 3.50 (t, *J* = 6.5 Hz, 2H), 1.99 – 1.89 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 151.4, 132.8, 130.1, 128.5, 120.4, 83.3, 73.8, 73.3, 72.3, 47.9, 45.5, 25.3, 24.5. Characterization data of **3y** corresponded to the literature values.[41]



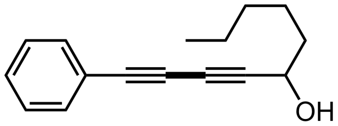
(6-(Methoxymethoxy)hexa-1,3-diyn-1-yl)benzene

3z, light yellow oil, 29.2 mg, 68% yield. $R_f = 0.4$ (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.39 – 7.25 (m, 3H), 4.67 (s, 2H), 3.70 (t, *J* = 6.7 Hz, 2H), 3.39 (s, 3H), 2.67 (t, *J* = 6.7 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 128.9, 128.3, 121.9, 96.4, 81.1, 75.1, 74.1, 66.1, 65.4, 55.3, 21.2. Characterization data of **3z** corresponded to the literature values.[41]



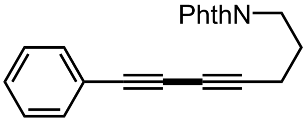
8-Phenylocta-5,7-diynenitrile

3aa, light yellow oil, 31.1 mg, 70% yield. $R_f = 0.3$ (PE:EA = 2:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.39 – 7.27 (m, 3H), 2.61 – 2.47 (m, 4H), 1.94 (p, *J* = 7.0 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.1, 128.4, 121.6, 118.8, 81.1, 75.7, 73.7, 67.0, 24.2, 18.7, 16.2. Characterization data of **3aa** corresponded to the literature values.[11]



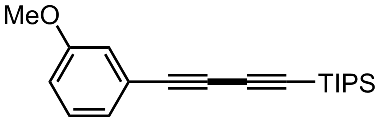
1-Phenyldeca-1,3-diyn-5-ol

3ab, light yellow oil, 40.3 mg, 89% yield. $R_f = 0.6$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.8, 1.6 Hz, 2H), 7.40 – 7.28 (m, 3H), 4.51 (t, *J* = 6.6 Hz, 1H), 2.02 (s, 1H), 1.82 – 1.71 (m, 2H), 1.49 (td, *J* = 13.8, 6.9 Hz, 2H), 1.37 – 1.28 (m, 4H), 0.91 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.5, 129.3, 128.4, 121.5, 83.4, 78.5, 73.2, 69.5, 63.1, 37.5, 31.4, 24.7, 22.5, 14.0. Characterization data of **3ab** corresponded to the literature values.[41]



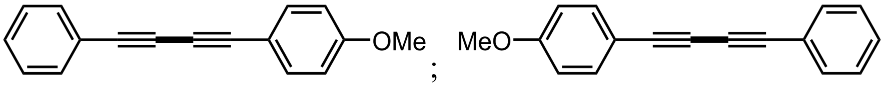
2-(7-Phenylhepta-4,6-diyn-1-yl)isoindoline-1,3-dione

3ac, light yellow oil, 35.2 mg, 56% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.68 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.41 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.35 – 7.22 (m, 3H), 3.82 (t, *J* = 6.9 Hz, 2H), 2.45 (t, *J* = 7.0 Hz, 2H), 1.98 (p, *J* = 6.9 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.3, 133.9, 132.4, 132.1, 128.8, 128.2, 123.2, 121.9, 82.9, 75.0, 74.0, 65.7, 37.2, 26.9, 17.5. Characterization data of **3ac** corresponded to the literature values.[41]



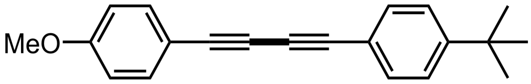
Triisopropyl((3-methoxyphenyl)buta-1,3-diyn-1-yl)silane

3ad, light yellow oil, 41.2 mg, 66% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 13.7, 5.8 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 2.3 Hz, 1H), 6.99 – 6.92 (m, 1H), 3.83 (s, 3H), 1.16 (s, 22H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 159.3, 129.5, 125.2, 122.5, 117.2, 116.1, 89.4, 87.9, 75.5, 74.4, 55.3, 18.6, 11.3. **HRMS** (EI) calcd for $C_{20}H_{28}OSi$ $[M]^+$: 312.19039, found: 312.19105. **IR** (Reflection): ṽ = 2943, 2891, 2866, 2206, 2100, 1734, 1596, 1574, 1488, 1463, 1428, 1384, 1366, 1319, 1297, 1220, 1178, 1047, 1029, 995, 919, 881, 869, 784, 700, 679, 659.



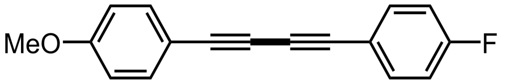
1-Methoxy-4-(phenylbuta-1,3-diyn-1-yl)benzene

3ae, light yellow solid, 18.6 mg, 40% yield; **3ae'**, light yellow solid, 22.4 mg, 48% yield. R_f = 0.4 (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 – 7.43 (m, 4H), 7.41 – 7.28 (m, 3H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.4, 134.1, 132.4, 129.0, 128.4, 122.0, 114.1, 113.7, 81.8, 81.0, 74.2, 72.7, 55.3. Characterization data of **3ae** corresponded to the literature values.[41]



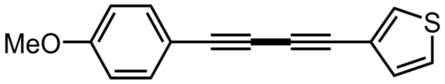
1-(*tert*-Butyl)-4-((4-methoxyphenyl)buta-1,3-diyn-1-yl)benzene

3af, light yellow solid, 34.5 mg, 60% yield. $R_f = 0.4$ (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.7, 2.1 Hz, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 1H), 3.82 (s, 1H), 1.32 (s, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 160.3, 152.5, 134.1, 132.2, 125.4, 118.9, 114.1, 113.8, 81.4, 81.3, 73.5, 72.9, 55.3, 34.9, 31.1. Characterization data of **3af** corresponded to the literature values.[41]



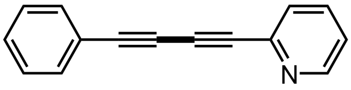
1-Fluoro-4-((4-methoxyphenyl)buta-1,3-diyn-1-yl)benzene

3ag, light yellow solid, 26.5 mg, 60% yield. $R_f = 0.4$ (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.52 – 7.45 (m, 4H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.9 (d, *J* = 251.2 Hz), 160.4, 134.4 (d, *J* = 8.5 Hz), 134.1, 118.1 (d, *J* = 3.6 Hz), 115.8 (d, *J* = 22.3 Hz), 114.2, 113.6, 81.8, 79.9, 73.9 (d, *J* = 1.5 Hz), 72.6, 55.3. Characterization data of **3ag** corresponded to the literature values.[41]



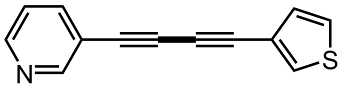
3-((4-Methoxyphenyl)buta-1,3-diyn-1-yl)thiophene

3ah, light yellow oil, 31.9 mg, 67% yield. $R_f = 0.4$ (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.48 – 7.44 (m, 2H), 7.28 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 (dd, *J* = 5.0, 1.1 Hz, 1H), 6.87 – 6.84 (m, 2H), 3.82 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 160.3, 134.1, 130.9, 130.1, 125.5, 121.0, 114.1, 113.6, 81.6, 76.2, 73.7, 72.6, 55.3. Characterization data of **3ah** corresponded to the literature values.[41]



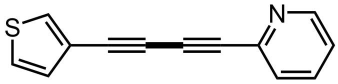
2-(Phenylbuta-1,3-diyn-1-yl)pyridine

3ai, light yellow solid, 25.6 mg, 63% yield. $R_f = 0.4$ (PE:EA = 5:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.61 (d, *J* = 4.7 Hz, 1H), 7.68 (td, *J* = 7.7, 1.7 Hz, 1H), 7.61 – 7.48 (m, 3H), 7.44 – 7.27 (m, 4H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 150.1, 142.1, 136.3, 132.7, 129.5, 128.4, 128.1, 123.5, 121.3, 82.6, 80.0, 74.1, 73.5. Characterization data of **3ai** corresponded to the literature values.[41]



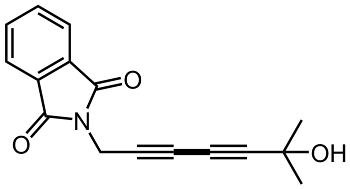
3-(Thiophen-3-ylbuta-1,3-diyn-1-yl)pyridine

3aj, light yellow solid, 11.1 mg, 29% yield. R$_f$ = 0.5 (PE:EA = 2:1), chromatography eluent: 40% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.72 (d, *J* = 1.4 Hz, 1H), 8.54 (dd, *J* = 4.9, 1.6 Hz, 1H), 7.76 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.60 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.27 (dd, *J* = 5.1, 3.1 Hz, 1H), 7.25 – 7.22 (m, 1H), 7.16 (dd, *J* = 5.0, 1.1 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 153.1, 149.2, 139.3, 131.8, 130.1, 125.8, 123.0, 120.5, 119.3, 78.0 77.8, 77.2, 73.1. **HRMS** (EI) calcd for $C_{13}H_7NS$ [M]$^+$: 209.02937, found: 209.02945. **IR** (Reflection): ṽ = 3109, 3084, 2220, 2147, 1722, 1580, 1561, 1476, 1408, 1357, 1216, 1192, 1171, 1122, 1080, 1023, 1004, 910, 867, 783, 739, 700, 622. **M.p.** (amorphous): 112.1-113.7 °C.



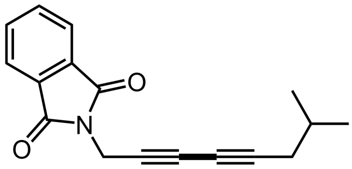
2-(Thiophen-3-ylbuta-1,3-diyn-1-yl)pyridine

3ak, light yellow solid, 24.7 mg, 59% yield. R$_f$ = 0.6 (PE:EA = 2:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 8.66 – 8.51 (m, 1H), 7.72 – 7.58 (m, 2H), 7.51 (t, *J* = 7.1 Hz, 1H), 7.32 – 7.23 (m, 2H), 7.18 (dd, *J* = 5.0, 1.1 Hz, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 150.3, 142.3, 136.1, 131.9, 130.2, 128.0, 125.7, 123.4, 120.4, 80.1, 77.6, 73.7, 73.2. **HRMS** (EI) calcd for $C_{13}H_7NS$ [M]$^+$: 209.02937, found: 209.02790. **IR** (Reflection): ṽ = 3110, 3095, 3079, 3045, 2992, 2215, 1966, 1929, 1859, 1577, 1561, 1462, 1431, 1361, 1319, 1174, 1156, 1051, 1020, 986, 900, 869, 775, 737, 700, 617. **M.p.** (amorphous): 95.4-96.3 °C.



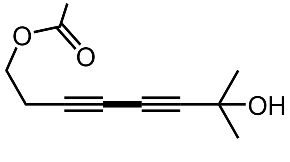
2-(6-Hydroxy-6-methylhepta-2,4-diyn-1-yl)isoindoline-1,3-dione

3al, yellow oil, 28.8 mg, 54% yield. $R_f = 0.5$ (DCM:EA = 20:1), chromatography eluent: 4% Ethyl acetate in dichloromethane. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.4, 3.1 Hz, 2H), 4.51 (s, 1H), 2.14 (br, 1H), 1.48 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.8, 134.3, 131.8, 123.6, 82.7, 73.2, 67.2, 66.4, 65.4, 30.9, 27.6. Characterization data of **3al** corresponded to the literature values.[44]



2-(7-Methylocta-2,4-diyn-1-yl)isoindoline-1,3-dione

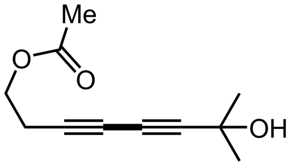
3am, light yellow solid, 27.5 mg, 52% yield. $R_f = 0.7$ (PE:EA = 3:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.73 (dd, *J* = 5.5, 3.0 Hz, 2H), 4.50 (s, 2H), 2.12 (d, *J* = 6.5 Hz, 2H), 1.80 (dp, *J* = 13.3, 6.6 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 166.8, 134.2, 131.9, 123.5, 79.7, 68.9, 68.3, 65.2, 28.2, 27.8, 27.6, 21.9. **HRMS** (APCI) calcd for $C_{17}H_{16}NO_2$ $[M+H]^+$: 266.1176, found: 266.1174. **IR** (Reflection): ṽ = 3476, 2962, 2919, 2870, 2258, 1769, 1718, 1467, 1417, 1388, 1344, 1319, 1281, 1187, 1170, 1117, 1087, 940, 723, 706, 618. **M.p.** (amorphous): 85.6-86.4 °C.



7-Hydroxy-7-methylocta-3,5-diyn-1-yl benzoate

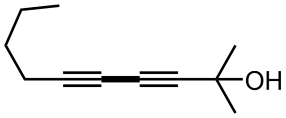
3an, light yellow oil, 29.8 mg, 58% yield.

$R_f = 0.4$ (PE:EA = 3:1), chromatography eluent: 25% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.62 – 7.53 (m, 1H), 7.49 – 7.38 (m, 2H), 4.41 (t, *J* = 6.7 Hz, 2H), 2.77 (t, *J* = 6.7 Hz, 2H), 2.06 (br, 1H), 1.52 (s, 6H). **^{13}C NMR** (151 MHz, CDCl$_3$) δ 166.3, 133.2, 129.7, 129.7, 128.4, 80.6, 76.9, 67.0, 65.9, 65.5, 62.2, 31.1, 19.9. **HRMS** (APCI) calcd for $C_{16}H_{15}O_3$ [M+H]$^+$: 255.1016, found: 255.1008; calcd for $C_{16}H_{15}O_2$ [M-OH]$^+$: 239.1067, found: 239.1057. **IR** (Reflection): ṽ = 3436, 2982, 2933, 2255, 1720, 1602, 1452, 1379, 1315, 1273, 1156, 1113, 1070, 1027, 955, 881, 710.



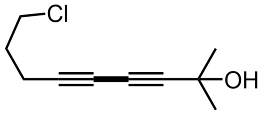
7-Hydroxy-7-methylocta-3,5-diyn-1-yl acetate

3ao, colorless oil, 23.6 mg, 61% yield. R$_f$ = 0.3 (PE:EA = 3:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 4.15 (t, *J* = 6.7 Hz, 2H), 2.62 (t, *J* = 6.7 Hz, 2H), 2.07 (s, 3H), 2.03 (br, 1H), 1.52 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 170.8, 80.6, 76.9, 66.9, 65.8, 65.5, 61.7, 31.1, 20.8, 19.8. **HRMS** (APCI) calcd for $C_{11}H_{15}O_3$ [M+H]$^+$: 195.1016, found: 195.1015; calcd for $C_{11}H_{13}O_2$ [M-OH]$^+$: 177.0910, found: 177.0904. **IR** (Reflection): ṽ = 3267, 3110, 2917, 2854, 2238, 1730, 1450, 1352, 1312, 1196, 1097, 1076, 1005, 928, 871, 832, 783, 692, 624.



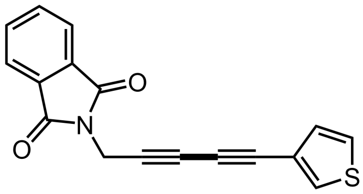
2-Methyldeca-3,5-diyn-2-ol

3ap, light yellow oil, 16.5 mg, 47% yield. R$_f$ = 0.4 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 2.28 (t, *J* = 6.9 Hz, 2H), 1.92 (br, 1H), 1.59 – 1.34 (m, 10H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 81.9, 79.8, 67.4, 65.5, 64.2, 31.2, 30.2, 21.9, 18.9, 13.5. **HRMS** (APCI) calcd for $C_{11}H_{17}O$ [M+H]$^+$: 165.1274, found: 165.1267; calcd for $C_{11}H_{15}$ [M-OH]$^+$: 147.1168, found: 147.1163. **IR** (Reflection): ṽ = 3356, 2981, 2960, 2934, 2873, 2252, 1733, 1666, 1457, 1427, 1364, 1263, 1154, 956, 902, 862.



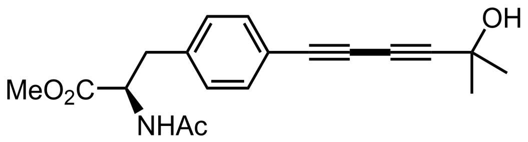
9-Chloro-2-methylnona-3,5-diyn-2-ol

3aq, colorless oil, 22.6 mg, 61% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.3 Hz, 2H), 2.49 (t, *J* = 6.8 Hz, 2H), 2.05 – 1.92 (m, 3H), 1.52 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 80.3, 79.6, 67.1, 65.5, 65.3, 43.3, 31.1, 30.8, 16.7. **HRMS** (APCI) calcd for $C_{10}H_{12}Cl$ $[M-OH]^+$: 167.0622, found: 167.0617; calcd for $C_{10}H_{14}ClO$ $[M+H]^+$: 185.0728, found: 185.0722. **IR** (Reflection): ṽ = 3280, 3064, 3000, 2954, 2848, 2244, 2153, 1915, 1745, 1656, 1542, 1510, 1436, 1373, 1214, 1139, 1018, 889, 827.



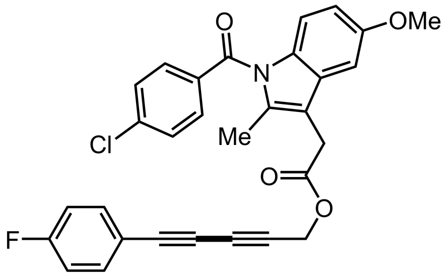
2-(5-(Thiophen-3-yl)penta-2,4-diyn-1-yl)isoindoline-1,3-dione

3ar, light yellow solid, 29.7 mg, 51% yield. R_f = 0.5 (PE:DCM = 1:1), chromatography eluent: 30% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 5.4, 3.1 Hz, 1H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 1H), 7.53 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.24 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.09 (dd, *J* = 5.0, 1.1 Hz, 1H), 4.59 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 134.2, 131.9, 131.7, 130.1, 125.5, 123.6, 120.4, 75.8, 73.0, 72.7, 68.0, 27.9. **HRMS** (EI) calcd for $C_{17}H_{19}NO_2S$ $[M]^+$: 291.03485, found: 291.03378. **IR** (Reflection): ṽ = 3464, 3119, 3084, 2953, 2241, 2152, 1772, 1705, 1468, 1416, 1391, 1338, 1315, 1191, 1111, 932, 872, 785, 747, 718, 708, 634, 617. **M.p.** (amorphous): 161.8-163.2 °C.



Methyl (*R*)-2-acetamido-3-(4-(5-hydroxy-5-methylhexa-1,3-diyn-1-yl)phenyl)propanoate

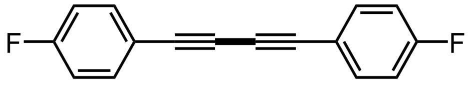
3as, light yellow oil, 49.1 mg, 75% yield. R_f = 0.2 (PE:EA = 1:2), chromatography eluent: 50% Petroleum ether in ethyl acetate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.8 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.10 (s, 1H), 4.85 (dd, *J* = 13.0, 6.1 Hz, 1H), 3.70 (s, 3H), 3.14 (dd, *J* = 13.8, 6.0 Hz, 1H), 3.06 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.79 (br, 1H), 1.97 (s, 3H), 1.56 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.9, 169.8, 137.4, 132.6, 129.3, 120.3, 87.1, 78.2, 73.5, 66.7, 65.5, 53.0, 52.4, 37.8, 31.0, 23.0. Characterization data of **3as** corresponded to the literature values.[41]



5-(4-Fluorophenyl)penta-2,4-diyn-1-yl

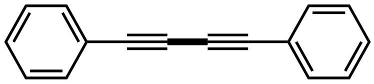
2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetate

3at, light yellow solid, 42.4 mg, 41% yield. R_f = 0.5 (PE:DCM = 1:1), chromatography eluent: 20% Dichloromethane in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.72 – 7.63 (m, 2H), 7.49 – 7.46 (m, 4H), 7.07 – 6.99 (m, 2H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.89 (d, *J* = 9.0 Hz, 1H), 6.68 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.84 (s, 2H), 3.85 (s, 3H), 3.73 (s, 2H), 2.39 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.90, 168.25, 163.17 (d, *J* = 252.3 Hz), 156.06, 139.27, 136.05, 134.72 (d, *J* = 8.7 Hz), 133.8, 131.2, 130.7, 130.4, 129.1, 117.2 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.4 Hz), 115.0, 111.9, 111.9, 101.0, 77.8, 75.9, 72.7 (d, *J* = 1.2 Hz), 71.2, 55.7, 53.0, 30.0, 13.4. Characterization data of **3at** corresponded to the literature values.[41]



1,4-Bis(4-fluorophenyl)buta-1,3-diyne

4a, colorless solid, 19.1 mg, 80% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.57 – 7.42 (m, 4H), 7.13 – 6.91 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 163.1 (d, *J* = 251.6 Hz), 134.5 (d, *J* = 8.6 Hz), 117.8 (d, *J* = 3.6 Hz), 115.9 (d, *J* = 22.3 Hz), 80.4, 73.5. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -108.49. Characterization data of **4a** corresponded to the literature values.[41]

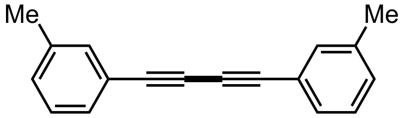


1,4-Diphenylbuta-1,3-diyne

4b, colorless solid, 20.2 mg, 99% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether.

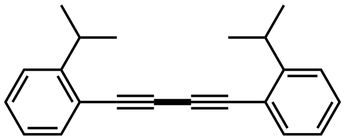
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.5, 1.8 Hz, 4H), 7.42 – 7.29 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 132.5, 129.2, 128.4, 121.8, 81.5, 73.9. Characterization data of **4b** corresponded to the literature values.[41]



1,4-Di-*m*-tolylbuta-1,3-diyne

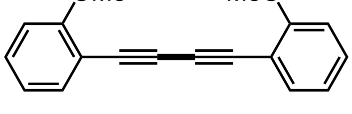
4c, light yellow solid, 23.1 mg, 99% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.34 (d, *J* = 6.9 Hz, 4H), 7.28 – 7.15 (m, 4H), 2.35 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 138.1, 133.0, 130.1, 129.6, 128.3, 121.6, 81.6, 73.6, 21.2. Characterization data of **4c** corresponded to the literature values.[41]



1,4-Bis(2-isopropylphenyl)buta-1,3-diyne

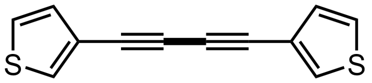
4d, light yellow oil, 25.1 mg, 88% yield. R_f = 0.5 (PE), chromatography eluent: Petroleum ether.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.4 Hz, 2H), 7.39 – 7.28 (m, 4H), 7.21 – 7.13 (m, 2H), 3.51 (dt, *J* = 13.8, 6.9 Hz, 2H), 1.31 (d, *J* = 6.9 Hz, 12H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 152.0, 133.4, 129.4, 125.6, 125.1, 120.7, 80.9, 77.4, 31.7, 23.3. Characterization data of **4d** corresponded to the literature values.[41]



1,4-Bis(2-methoxyphenyl)buta-1,3-diyne

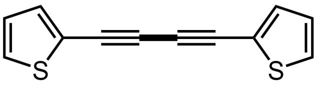
4e, colorless solid, 25.5 mg, 97% yield. R_f = 0.4 (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.32 (ddd, *J* = 8.4, 7.6, 1.7 Hz, 2H), 6.91 (td, *J* = 7.5, 0.9 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 3.90 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 161.3, 134.4, 130.5, 120.5, 111.2, 110.6, 78.6, 77.9, 55.8. Characterization data of **4e** corresponded to the literature values.[41]



1,4-Di(thiophen-3-yl)buta-1,3-diyne

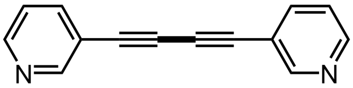
4f, yellow solid, 21.3 mg, 99% yield. R_f = 0.6 (PE), chromatography eluent: Petroleum ether.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 3.0, 1.1 Hz, 2H), 7.28 (dd, *J* = 5.0, 3.0 Hz, 2H), 7.17 (dd, *J* = 5.0, 1.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 131.2, 130.1, 125.6, 120.9, 76.6, 73.5. Characterization data of **4f** corresponded to the literature values.[41]



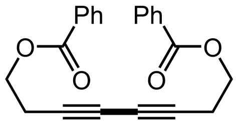
1,4-Di(thiophen-2-yl)buta-1,3-diyne

4g, yellow solid, 21.1 mg, 99% yield. R_f = 0.6 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 3.7, 1.0 Hz, 1H), 7.33 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.00 (dd, *J* = 5.1, 3.7 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 134.4, 128.9, 127.2, 121.9, 77.8, 76.6. Characterization data of **4g** corresponded to the literature values.[45]



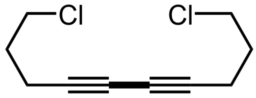
1,4-Di(pyridin-3-yl)buta-1,3-diyne

4h, yellow solid, 20.2 mg, 99% yield. R_f = 0.6 (PE:EA = 1:2), chromatography eluent: 50% Petroleum ether in ethyl acetate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 1.0 Hz, 2H), 8.67 – 8.45 (m, 2H), 7.81 (dd, *J* = 7.9, 1.8 Hz, 2H), 7.28 (dd, *J* = 7.9, 4.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.0, 149.4, 139.4, 123.1, 118.8, 79.1, 76.6. Characterization data of **4h** corresponded to the literature values.[46]



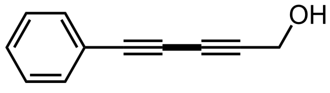
Octa-3,5-diyne-1,8-diyl dibenzoate

4i, colorless solid, 32.7 mg, 94% yield. R_f = 0.3 (PE:EA = 10:1), chromatography eluent: 10% Petroleum ether in ethyl acetate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 7.98 (m, 2H), 7.64 – 7.51 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 4.41 (t, *J* = 6.7 Hz, 2H), 2.74 (t, *J* = 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 133.1, 129.8, 129.7, 128.4, 73.5, 66.6, 62.2, 19.9. Characterization data of **4i** corresponded to the literature values.[47]



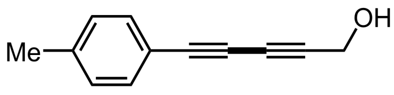
1,10-Dichlorodeca-4,6-diyne

4j yellow oil, 17.3 mg, 85% yield. R_f = 0.3 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 3.64 (t, *J* = 6.3 Hz, 4H), 2.46 (t, *J* = 6.8 Hz, 4H), 1.98 (p, *J* = 6.6 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 75.8, 66.1, 43.4, 31.0, 16.6. Characterization data of **4j** corresponded to the literature values.[48]



5-Phenylpenta-2,4-diyn-1-ol

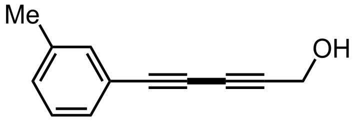
4k, light yellow oil, 20.2 mg, 65% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.42 – 7.28 (m, 3H), 4.42 (s, 2H), 1.82 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.6, 129.3, 128.4, 121.3, 80.4, 78.6, 73.1, 70.5, 51.7. Characterization data of **4k** corresponded to the literature values.[5a]



5-(4-Tolyl)penta-2,4-diyn-1-ol

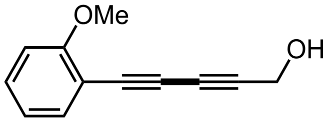
4l, light yellow solid, 19.8 mg, 58% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.1 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 4.42 (s, 2H), 2.36 (s, 3H), 1.79 (br, 1H). **^{13}C**

NMR (101 MHz, $CDCl_3$) δ 139.8, 132.5, 129.2, 118.2, 80.1, 78.9, 72.5, 70.6, 51.7, 21.7. Characterization data of **4l** corresponded to the literature values.[49]



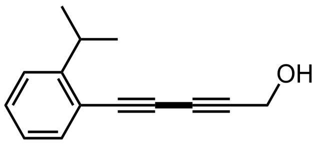
5-(3-Tolyl)penta-2,4-diyn-1-ol

4m, light yellow oil, 18.6 mg, 55% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.29 (m, 2H), 7.24 – 7.15 (m, 2H), 4.42 (s, 2H), 2.32 (s, 3H), 1.96 (br, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.2, 133.1, 130.3, 129.7, 128.3, 121.1, 80.2, 78.8, 72.8, 70.5, 51.6, 21.1. **HRMS** (APCI) calcd for $C_{12}H_{11}O$ $[M+H]^+$: 171.0804, found: 171.0798; calcd for $C_{12}H_9$ $[M-OH]^+$: 153.0699, found: 153.0696. **IR** (Reflection): ṽ = 3394, 2919, 2859, 2240, 1726, 1599, 1578, 1484, 1440, 1356, 1197, 1105, 1087, 1011, 907, 879, 779, 685, 673, 664.



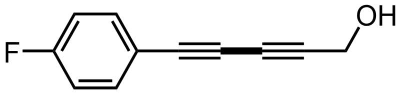
5-(2-Methoxyphenyl)penta-2,4-diyn-1-ol

4n, light yellow oil, 16.9 mg, 45% yield. R_f = 0.2 (PE:EA = 4:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.37 – 7.28 (m, 1H), 6.94 – 6.82 (m, 2H), 4.42 (s, 2H), 3.88 (s, 3H), 1.89 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.5, 134.5, 130.8, 120.5, 110.7, 110.6, 81.0, 76.9, 75.2, 70.7, 55.8, 51.7. **HRMS** (APCI) calcd for $C_{12}H_{11}O_2$ $[M+H]^+$: 187.0754, found: 187.0737; calcd for $C_{12}H_9O$ $[M-OH]^+$: 169.0648, found: 169.0640. **IR** (Reflection): ṽ = 3402, 2936, 2838, 2240, 1729, 1594, 1573, 1489, 1460, 1434, 1274, 1242, 1181, 1163, 1128, 1085, 1004, 839, 747.



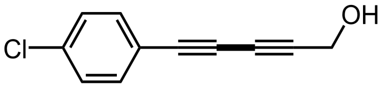
5-(2-Isopropylphenyl)penta-2,4-diyn-1-ol

4o, light yellow oil, 21.7 mg, 55% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.35 – 7.26 (m, 2H), 7.14 (td, *J* = 7.5, 1.4 Hz, 1H), 4.44 (s, 2H), 3.42 (dt, *J* = 13.8, 6.9 Hz, 1H), 1.92 (br, 1H), 1.26 (d, *J* = 6.9 Hz, 6H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 152.3, 133.5, 129.7, 125.6, 125.1, 120.1, 80.8, 77.5, 76.5, 70.6, 51.7, 31.7, 23.2. **HRMS** (APCI) calcd for $C_{14}H_{15}O$ [M+H]$^+$: 199.1117, found: 199.1109; calcd for $C_{14}H_{13}$ [M-OH]$^+$: 181.1012, found: 181.1006. **IR** (Reflection): ṽ = 3347, 2962, 2927, 2868, 2239, 1731, 1483, 1445, 1362, 1073, 1011, 757.



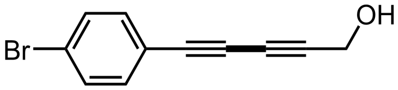
5-(4-Fluorophenyl)penta-2,4-diyn-1-ol

4p, light yellow solid, 26.3 mg, 56% yield. R$_f$ = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.61 – 7.39 (m, 2H), 7.11 – 6.90 (m, 2H), 4.42 (s, 2H), 1.90 (br, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 164.7, 161.4, 134.7, 134.6, 117.5, 117.4, 116.0, 115.7, 80.4, 77.5, 72.9, 72.9, 70.3, 51.6. **^{19}F NMR** (282 MHz, CDCl$_3$) δ -108.33. Characterization data of **4p** corresponded to the literature values.[49]



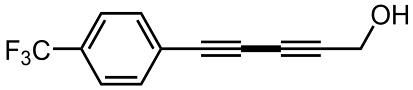
5-(4-Chlorophenyl)penta-2,4-diyn-1-ol

4q, light yellow solid, 24.5 mg, 64% yield. R$_f$ = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (700 MHz, CDCl$_3$) δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 4.42 (s, 2H), 1.82 (br, 1H). **^{13}C NMR** (176 MHz, CDCl$_3$) δ 135.5, 133.8, 128.9, 128.8, 119.8, 80.9, 77.3, 74.1, 70.2, 51.6. **HRMS** (APCI) calcd for $C_{11}H_8ClO$ [M+H]$^+$: 191.0258, found: 191.0252; calcd for $C_{11}H_6Cl$ [M-OH]$^+$: 173.0153, found: 173.0146. **IR** (Reflection): ṽ = 3505, 2925, 2901, 2868, 2243, 1899, 1644, 1589, 1488, 1434, 1397, 1268, 1100, 1088, 1013, 823, 708. **M.p.** (amorphous): 126.4-127.7 °C.



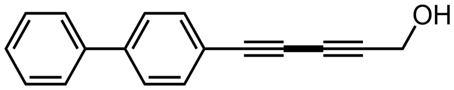
5-(4-Bromophenyl)penta-2,4-diyn-1-ol

4r, light yellow solid, 26.3 mg, 56% yield. R$_f$ = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 4.42 (s, 2H), 1.79 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.9, 131.8, 123.9, 120.3, 81.0, 74.3, 70.3, 51.6. Characterization data of **4r** corresponded to the literature values.[50]



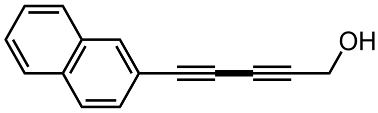
5-(4-(Trifluoromethyl)phenyl)penta-2,4-diyn-1-ol

4s, light yellow solid, 29.5 mg, 66% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (s, 4H), 4.44 (s, 2H), 1.87 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 132.8, 130.9 (q, *J* = 32.8 Hz), 125.3 (dd, *J* = 7.6, 3.8 Hz), 125.2, 123.7 (q, *J* = 272.4 Hz), 81.7, 76.8, 75.4, 70.0, 51.6. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -63.02. **HRMS** (APCI) calcd for $C_{12}H_8F_3O$ $[M+H]^+$: 225.0522, found: 225.0514; calcd for $C_{12}H_6F_3$ $[M-OH]^+$: 207.0416, found: 207.0409. **IR** (Reflection): ṽ = 3247, 2922, 2861, 2634, 1732, 1614, 1446, 1405, 1367, 1309, 1181, 1116, 1105, 1062, 1009, 839, 682. **M.p.** (amorphous): 115.7-116.4 °C.



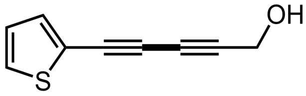
5-([1,1'-Biphenyl]-4-yl)penta-2,4-diyn-1-ol

4t, light yellow solid, 21.7 mg, 47% yield. R_f = 0.2 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59 – 7.56 (m, 6H), 7.45 (t, *J* = 7.3 Hz, 2H), 7.38 (d, *J* = 7.2 Hz, 1H), 4.44 (s, 2H), 1.92 (br, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 142.1, 140.0, 133.0, 128.9, 127.9, 127.1, 127.0, 120.1, 80.7, 78.5, 73.8, 70.5, 51.7. **HRMS** (APCI) calcd for $C_{17}H_{13}O$ $[M+H]^+$: 233.0961, found: 233.0951; calcd for $C_{17}H_{11}$ $[M-OH]^+$: 215.0855, found: 215.0852. **IR** (Reflection): ṽ = 3310, 3028, 2856, 2240, 1598, 1484, 1444, 1405, 1350, 1102, 1076, 1005, 917, 840, 762, 725, 698, 644. **M.p.** (amorphous): 114.6-116.4 °C.



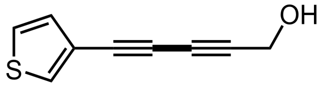
5-(Naphthalen-2-yl)penta-2,4-diyn-1-ol

4u, light yellow solid, 23.6 mg, 57% yield. R_f = 0.2 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 8.04 (s, 1H), 7.84 – 7.72 (m, 3H), 7.58 – 7.41 (m, 3H), 4.45 (s, 2H), 1.87 (br, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 133.2, 132.7, 128.4, 128.1, 127.8, 127.8, 127.3, 126.8, 118.6, 80.6, 79.0, 73.4, 70.6, 51.7. **HRMS** (APCI) calcd for $C_{15}H_{11}O$ [M+H]$^+$: 207.0804, found: 207.0797; calcd for $C_{15}H_9$ [M-OH]$^+$: 189.0699, found: 189.0692. **IR** (Reflection): ṽ = 3324, 3060, 2911, 2859, 2241, 1597, 1503, 1352, 1269, 1234, 1133, 1084, 1017, 953, 890, 860, 819, 740, 639. **M.p.** (amorphous): 87.1-88.9 °C.



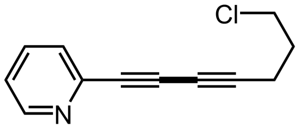
5-(Thiophen-2-yl)penta-2,4-diyn-1-ol

4v, light yellow solid, 15.8 mg, 49% yield. R_f = 0.3 (PE:EA = 4:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, CDCl$_3$) δ 7.32 (dd, *J* = 3.7, 1.0 Hz, 1H), 7.30 (dd, *J* = 5.1, 1.0 Hz, 1H), 6.98 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.43 (s, 2H), 1.86 (br, 1H). **^{13}C NMR** (101 MHz, CDCl$_3$) δ 134.6, 128.8, 127.1, 121.6, 82.6, 77.3, 71.7, 70.3, 51.7. **HRMS** (APCI) calcd for C_9H_7OS [M+H]$^+$: 163.0212, found: 163.0206; calcd for C_9H_5S [M-OH]$^+$: 145.0106, found: 145.0101. **IR** (Reflection): ṽ = 3258, 2854, 2233, 1450, 1424, 1360, 1309, 1212, 1089, 1062, 1036, 1005, 911, 854, 711. **M.p.** (amorphous): 75.2-77.5 °C.



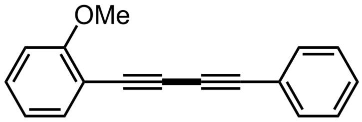
5-(Thiophen-3-yl)penta-2,4-diyn-1-ol

4w, light yellow oil, 16.9 mg, 52% yield. R_f = 0.2 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.58 – 7.55 (m, 1H), 7.27 – 7.24 (m, 1H), 7.13 (d, *J* = 5.0 Hz, 1H), 4.40 (s, 2H), 1.85 (br, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 147.4, 131.6, 130.1, 125.6, 120.4, 80.3, 73.8, 72.8, 70.4, 51.6. **HRMS** (APCI) calcd for C_9H_7OS [M+H]$^+$: 163.0212, found: 163.0207; calcd for C_9H_5S [M-OH]$^+$: 145.0106, found: 145.0103. **IR** (Reflection): ṽ = 3440, 2982, 2934, 2255, 1722, 1454, 1363, 1227, 1153, 1036, 953, 875, 808, 764.



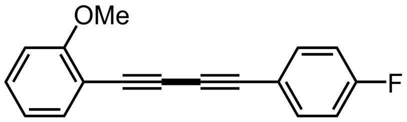
2-(7-Chlorohepta-1,3-diyn-1-yl)pyridine

4x, dark yellow oil, 23.1 mg, 57% yield. R_f = 0.5 (PE:EA = 2:1), chromatography eluent: 30% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.69 (d, *J* = 1.4 Hz, 1H), 8.54 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.74 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.34 – 7.08 (m, 1H), 3.67 (t, *J* = 6.3 Hz, 2H), 2.58 (t, *J* = 6.8 Hz, 2H), 2.03 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.1, 149.0, 139.3, 123.0, 119.3, 83.8, 77.3, 71.7, 65.6, 43.3, 30.8, 17.0. **HRMS** (EI) calcd for $C_{12}H_{10}NCl$ $[M]^+$: 203.04963, found: 203.04968. **IR** (Reflection): ṽ = 3031, 2960, 2918, 2848, 2247, 1733, 1582, 1560, 1476, 1439, 1407, 1355, 1285, 1186, 1123, 1022, 861, 804, 765, 703, 650, 621.



1-Methoxy-2-(phenylbuta-1,3-diyn-1-yl)benzene

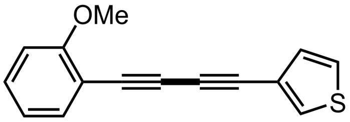
4y, light yellow oil, 25.1 mg, 54% yield. R_f = 0.4 (PE:DCM = 4:1), chromatography eluent: 20% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.7, 1.8 Hz, 2H), 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.40 – 7.30 (m, 4H), 6.98 – 6.84 (m, 2H), 3.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.4, 134.4, 132.4, 130.7, 129.0, 128.4, 122.0, 120.5, 111.1, 110.7, 82.1, 78.1, 77.7, 74.2, 55.8. Characterization data of **4y** corresponded to the literature values.[51]



1-((4-Fluorophenyl)buta-1,3-diyn-1-yl)-2-methoxybenzene

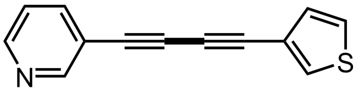
4z, light yellow solid, 27.7 mg, 55% yield. R_f = 0.4 (PE:DCM = 4:1), chromatography eluent: 20% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 – 7.45 (m, 3H), 7.34 (td, *J* = 8.5, 1.7 Hz, 1H), 7.08 – 6.99 (m, 2H), 6.95 – 6.84 (m, 2H), 3.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.94 (d, *J* = 251.3 Hz), 161.5, 134.4 (d, *J* = 2.5 Hz), 130.7, 120.5, 118.2 (d, *J* = 3.6 Hz), 115.8 (d, *J* = 22.3 Hz), 111.0, 110.7, 81.0, 78.1, 77.5, 74.0 (d, *J* = 1.5 Hz), 55.8. **^{19}F NMR** (282 MHz, $CDCl_3$)

δ -108.90. **HRMS** (EI) calcd for $C_{17}H_{11}OF$ $[M]^+$: 250.07884, found: 250.07932. **IR** (Reflection): ṽ = 3005, 2976, 2936, 2836, 2145, 1735, 1597, 1574, 1507, 1491, 1460, 1433, 1286, 1249, 1231, 1177, 1158, 1120, 1096, 1050, 1023, 943, 834, 795, 762. **M.p.** (amorphous): 97.8-98.9 °C.



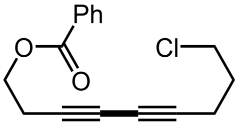
3-((2-Methoxyphenyl)buta-1,3-diyn-1-yl)thiophene

4aa, light yellow oil, 37.8 mg, 79% yield. R_f = 0.6 (PE:DCM = 4:1), chromatography eluent: 20% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.48 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.33 (ddd, *J* = 8.4, 7.6, 1.7 Hz, 1H), 7.28 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 (dd, *J* = 5.0, 1.1 Hz, 1H), 6.95 – 6.86 (m, 2H), 3.90 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.43, 134.37, 130.98, 130.64, 130.14, 125.49, 121.13, 120.51, 111.06, 110.68, 77.94, 77.61, 77.28, 77.00, 73.83, 55.82. **HRMS** (EI) calcd for $C_{15}H_{10}OS$ $[M]^+$: 238.04469, found: 238.04510. **IR** (Reflection): ṽ = 3101, 2999, 2965, 2917, 2832, 2144, 1594, 1573, 1517, 1488, 1458, 1429, 1355, 1296, 1277, 1247, 1179, 1157, 1116, 1081, 1048, 1024, 1002, 927, 865, 822, 787, 777, 742, 697, 622.



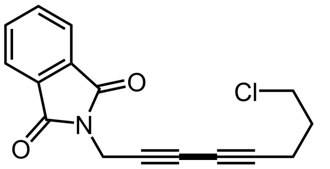
3-(Thiophen-3-ylbuta-1,3-diyn-1-yl)pyridine

4ab, light yellow solid, 22.5 mg, 54% yield. Characterization data see **3aj**.



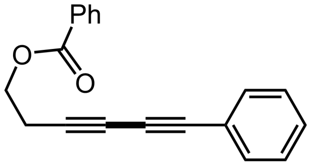
9-Chloronona-3,5-diyn-1-yl benzoate

4ac, colorless oil, 18.6 mg, 34% yield. R_f = 0.5 (PE:EA = 10:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 7.98 (m, 2H), 7.63 – 7.51 (m, 1H), 7.50 – 7.40 (m, 2H), 4.41 (t, *J* = 6.8 Hz, 2H), 3.64 (t, *J* = 6.3 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 2H), 2.46 (t, *J* = 6.8 Hz, 2H), 1.98 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 133.1, 129.9, 129.7, 128.4, 76.1, 73.2, 66.7, 66.0, 62.3, 43.4, 31.0, 19.9, 16.6. **HRMS** (EI) calcd for $C_{16}H_{15}O_2Cl$ $[M]^+$: 274.07551, found: 274.07503. **IR** (Reflection): ṽ = 3423, 3064, 2960, 2915, 2848, 2261, 2165, 1914, 1717, 1602, 1584, 1492, 1452, 1384, 1340, 1314, 1263, 1176, 1109, 1070, 1027, 973, 937, 849, 805, 767, 709, 687, 676, 660.



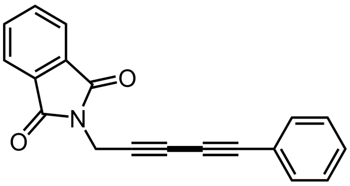
2-(8-Chloroocta-2,4-diyn-1-yl)isoindoline-1,3-dione

4ad, colorless solid, 22.8 mg, 40% yield. R_f = 0.4 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.74 (dd, *J* = 5.5, 3.1 Hz, 2H), 4.50 (s, 2H), 3.60 (t, *J* = 6.3 Hz, 2H), 2.44 (t, *J* = 6.8 Hz, 2H), 1.95 (p, *J* = 6.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 134.2, 132.0, 123.6, 78.4, 69.6, 68.0, 65.5, 43.3, 30.8, 27.6, 16.6. **HRMS** (EI) calcd for $C_{16}H_{12}NO_2Cl$ $[M]^+$: 285.05511, found: 285.05479. **IR** (Reflection): ṽ = 3064, 2960, 2915, 1718, 1601, 1583, 1491, 1452, 1384, 1314, 1269, 1176, 1111, 1070, 1026, 972, 847, 709, 687, 663. **M.p.** (amorphous): 95.3-96.9 °C.



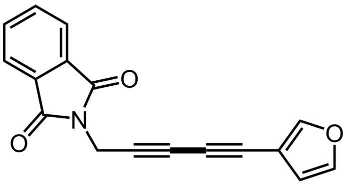
6-Phenylhexa-3,5-diyn-1-yl benzoate

4ae, light yellow oil, 30.8 mg, 56% yield. R_f = 0.5 (PE:EA = 10:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 7.90 (m, 2H), 7.61 – 7.54 (m, 1H), 7.51 – 7.42 (m, 4H), 7.38 – 7.28 (m, 3H), 4.47 (t, *J* = 6.7 Hz, 2H), 2.86 (t, *J* = 6.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.2, 133.1, 132.6, 129.8, 129.7, 129.0, 128.4, 128.4, 121.7, 79.8, 75.5, 74.0, 66.7, 62.2, 20.3. **HRMS** (EI) calcd for $C_{19}H_{14}O_2$ $[M]^+$: 274.09883, found: 274.10005. **IR** (Reflection): ṽ = 3062, 2960, 2915, 2246, 1726, 1601, 1490, 1452, 1384, 1344, 1314, 1279, 1176, 1114, 1070, 1026, 805, 755, 709, 688.



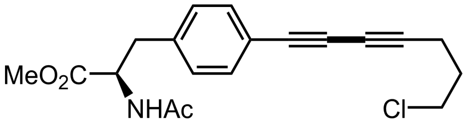
2-(5-Phenylpenta-2,4-diyn-1-yl)isoindoline-1,3-dione

4af, light yellow solid, 38.2 mg, 67% yield. R_f = 0.4 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 – 7.83 (m, 2H), 7.79 – 7.69 (m, 2H), 7.44 (d, J = 7.2 Hz, 2H), 7.39 – 7.25 (m, 3H), 4.60 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 134.2, 132.6, 131.9, 129.3, 128.4, 123.6, 121.2, 77.5, 76.0, 73.3, 68.0, 27.9. **HRMS** (EI) calcd for $C_{19}H_{11}NO_2$ $[M]^+$: 285.07843, found: 285.07583. **IR** (Reflection): ṽ = 3464, 3032, 2949, 2919, 2249, 1771, 1707, 1488, 1465, 1414, 1389, 1342, 1302, 1188, 1109, 1087, 1025, 935, 847, 796, 755, 722, 707, 688, 620. **M.p.** (amorphous): 172.5-173.6 °C.



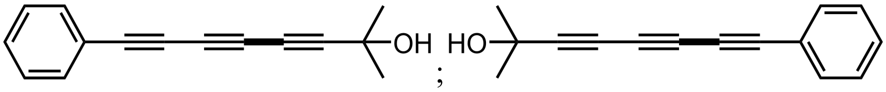
2-(5-(Furan-3-yl)penta-2,4-diyn-1-yl)isoindoline-1,3-dione

4ag, colorless solid, 27.0 mg, 49% yield. R_f = 0.5 (PE:DCM = 1:1), chromatography eluent: 50% Dichloromethane in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dd, J = 5.5, 3.1 Hz, 2H), 7.74 (dd, J = 5.5, 3.0 Hz, 2H), 7.65 (d, J = 0.7 Hz, 1H), 7.33 (t, J = 1.7 Hz, 1H), 6.42 (dd, J = 1.8, 0.5 Hz, 1H), 4.58 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.8, 148.0, 142.9, 134.2, 132.0, 123.6, 112.7, 106.1, 75.7, 75.1, 69.0, 67.9, 27.8. **HRMS** (EI) calcd for $C_{17}H_9NO_3$ $[M]^+$: 275.05769, found: 275.05731. **IR** (Reflection): ṽ = 3144, 2958, 2241, 1769, 1717, 1605, 1561, 1506, 1468, 1417, 1391. 1343, 1319, 1190, 1169, 1116, 1081, 1018, 940, 869, 805, 750, 721, 708, 628. **M.p.** (amorphous): 154.5-156.5 °C.



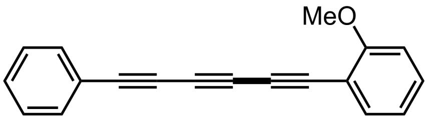
Methyl (*R*)-2-acetamido-3-(4-(7-chlorohepta-1,3-diyn-1-yl)phenyl)propanoate

4ah, light yellow oil, 42.1 mg, 61% yield. R_f = 0.4 (DCM:EA = 2:1), chromatography eluent: 50% Ethyl acetate in dichloromethane. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 8.2 Hz, 2H), 6.06 (s, 1H), 4.93 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.77 (s, 3H), 3.73 (t, *J* = 6.3 Hz, 2H), 3.21 (dd, *J* = 14.2, 5.9 Hz, 1H), 3.13 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.63 (t, *J* = 6.8 Hz, 2H), 2.08 (dd, *J* = 13.8, 7.3 Hz, 2H), 2.04 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.8, 169.6, 137.1, 132.6, 129.3, 120.6, 82.6, 74.8, 74.3, 66.0, 52.9, 52.4, 43.4, 37.8, 30.9, 23.0, 17.0. **HRMS** (EI) calcd for $C_{19}H_{20}NO_3Cl$ $[M]^+$: 345.11262, found: 345.11246. **IR** (Reflection): ṽ = 3556, 3359, 2983, 2931, 2253, 1730, 1440, 1364, 1291, 1260, 1156, 955.



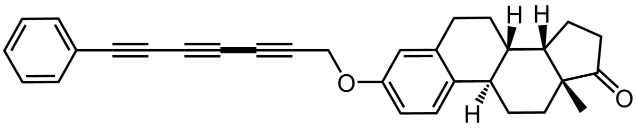
2-Methyl-8-phenylocta-3,5,7-triyn-2-ol

6a, light yellow oil, 24.8 mg, 60% yield; **6a’**, dark yellow oil, 21.8 mg, 52% yield. R_f = 0.4 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.44 – 7.28 (m, 3H), 2.06 (br, 1H), 1.56 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 133.0, 129.7, 128.5, 120.8, 83.9, 77.2, 74.2, 67.5, 65.8, 65.7, 63.6, 31.0. Characterization data of **6a** corresponded to the literature values.[41]



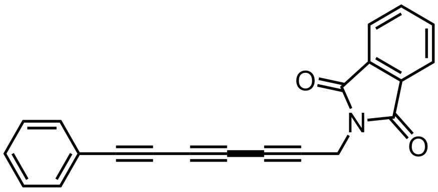
1-Methoxy-2-(phenylhexa-1,3,5-triyn-1-yl)benzene

6b, dark yellow solid, 19.9 mg, 39% yield. R_f = 0.4 (PE:EA = 20:1), chromatography eluent: 5% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 – 7.51 (m, 2H), 7.49 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.42 – 7.30 (m, 4H), 6.95 – 6.86 (m, 2H), 3.90 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.1, 134.9, 132.9, 131.2, 129.6, 128.5, 121.1, 120.6, 110.7, 110.3, 78.8, 78.1, 75.3, 74.6, 67.1, 66.8, 55.8. **HRMS** (EI) calcd for $C_{19}H_{12}O$ $[M]^+$: 256.08827, found: 256.08682. **IR** (Reflection): ṽ = 3059, 3032, 3008, 2981, 2946, 2838, 2245, 2194, 1944, 1731, 1592, 1571, 1492, 1460, 1432, 1280, 1257, 1177, 1164, 1127, 1086, 1066, 1044, 1025, 929, 908, 846, 787, 743, 713, 681. **M.p.** (amorphous): 58.6-60.3 °C.



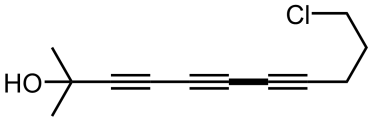
(*8S,9R,13R,14S*)-13-Methyl-3-((7-phenylhepta-2,4,6-triyn-1-yl)oxy)-6,7,8,9,11,12,13,14,15,16-decahydro-*17H*-cyclopenta[a]phenanthren-17-one

6c, light yellow solid, 25.4 mg (0.1 mmol scale), 59 % yield. R_f = 0.2 (PE:DCM = 1:1), chromatography eluent: 50% Petroleum ether in dichloromethane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 – 7.47 (m, 2H), 7.44 – 7.28 (m, 3H), 7.23 (d, *J* = 8.6 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.70 (d, *J* = 2.6 Hz, 1H), 4.77 (s, 2H), 2.99 – 2.81 (m, 2H), 2.51 (dd, *J* = 18.3, 8.4 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.35 – 2.20 (m, 1H), 2.16 (dd, *J* = 18.2, 9.3 Hz, 1H), 2.11 – 1.92 (m, 3H), 1.74 – 1.37 (m, 6H), 0.91 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 220.9, 155.4, 138.0, 133.3, 133.0, 129.9, 128.5, 126.4, 115.0, 112.4, 77.2, 75.0, 74.0, 72.0, 65.8, 63.6, 56.4, 50.4, 48.0, 44.0, 38.3, 35.9, 31.6, 29.6, 26.5, 25.9, 21.6, 13.8. **HRMS** (EI) calcd for $C_{31}H_{28}O_2$ $[M]^+$: 432.20838, found: 432.20897. **IR** (ATR): ṽ = 3060, 3045, 2973, 2934, 2878, 2860, 2195, 1732, 1605, 1497, 1448, 1377, 1346, 1311, 1286, 1231, 1163, 1101, 1084, 1053, 1025, 918, 863, 843, 818, 789, 763, 692. **M.p.** (amorphous): 164.1-165.8 °C.



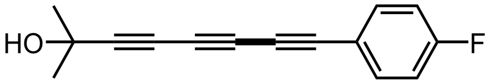
2-(7-Phenylhepta-2,4,6-triyn-1-yl)isoindoline-1,3-dione

6d, dark yellow oil, 29.8 mg, 52% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.76 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.54 – 7.46 (m, 2H), 7.42-7.35 (m, 1H), 7.35 – 7.28 (m, 2H), 4.58 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.7, 134.3, 133.1 131.9, 129.8, 128.5, 123.7, 120.7, 76.8, 74.1, 73.5, 68.4, 66.0, 62.4, 27.8. **HRMS** (EI) calcd for $C_{21}H_{11}NO_2$ $[M]^+$: 309.07843, found: 309.07702. **IR** (Reflection): ṽ = 3467, 2958, 2926, 2191, 1772, 1709, 1614, 1491, 1468, 1413, 1389, 1360, 1330, 1313, 1193, 1174, 1111, 1090, 936, 794, 756, 720, 709, 686, 635.



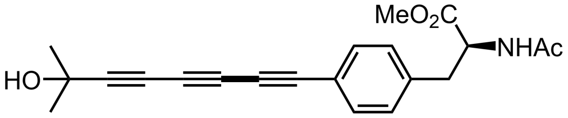
11-Chloro-2-methylundeca-3,5,7-triyn-2-ol

6e, dark yellow oil, 17.1 mg, 41% yield. $R_f = 0.6$ (PE:EA = 4:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.2 Hz, 2H), 2.52 (t, *J* = 6.8 Hz, 2H), 2.04 – 1.95 (m, 3H), 1.53 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 81.2, 78.9, 67.5, 66.3, 65.6, 64.0, 59.4, 43.3, 31.0, 30.7, 16.9. **HRMS** (EI) calcd for $C_{12}H_{13}OCl$ $[M]^+$: 208.06494, found: 208.06546. **IR** (Reflection): ṽ = 3357, 2984, 2932, 2218, 2113, 1732, 1662, 1440, 1360, 1200, 1165, 956, 843, 656.



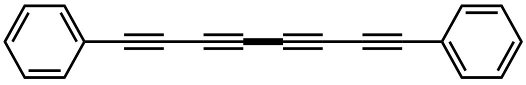
8-(4-Fluorophenyl)-2-methylocta-3,5,7-triyn-2-ol

6f, light yellow solid, 23.1 mg, 51% yield. $R_f = 0.6$ (PE:EA = 4:1), chromatography eluent: 15% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.54 – 7.46 (m, 2H), 7.06 – 6.99 (m, 2H), 1.90 (br, 1H), 1.56 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 163.3 (d, *J* = 252.6 Hz), 135.1 (d, *J* = 8.8 Hz), 116.9 (d, *J* = 3.5 Hz), 116.0 (d, *J* = 22.3 Hz), 84.0, 76.1, 74.0 (d, *J* = 1.3 Hz), 67.4, 65.8, 65.7, 63.4, 31.0. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -107.35. **HRMS** (EI) calcd for $C_{15}H_{11}OF$ $[M]^+$: 226.07884, found: 226.07935. **IR** (Reflection): ṽ = 3232, 2982, 2937, 2195, 1887, 1736, 1596, 1504, 1365, 1228, 1156, 1126, 1013, 955, 911, 830, 793, 653. **M.p.** (amorphous): 115.3-116.4 °C.



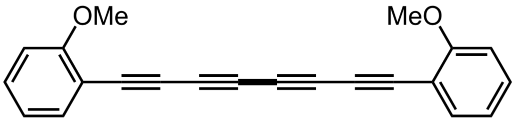
Methyl (*R*)-2-acetamido-3-(4-(7-hydroxy-7-methylocta-1,3,5-triyn-1-yl)phenyl) propanoate

6g, light yellow oil, 29.4 mg, 42% yield. $R_f = 0.3$ (DCM:EA = 2:1), chromatography eluent: 50% Ethyl acetate in dichloromethane. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.1 Hz, 2H), 7.13 (d, *J* = 8.1 Hz, 2H), 6.10 (d, *J* = 7.6 Hz, 1H), 4.94 (dd, *J* = 13.4, 5.8 Hz, 1H), 3.78 (s, 3H), 3.24 (dd, *J* = 13.8, 5.9 Hz, 1H), 3.15 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.69 (br, 1H), 2.06 (s, 3H), 1.62 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 171.8, 169.8, 138.0, 133.1, 129.5, 119.6, 84.4, 76.8, 74.4, 67.2, 66.0, 65.5, 63.4, 53.0, 52.5, 37.9, 30.9, 30.9, 23.1. **HRMS** (EI) calcd for $C_{21}H_{21}NO_4$ [M]$^+$: 351.14651, found: 351.14731. **IR** (Reflection): ṽ = 3294, 3069, 2983, 2953, 2933, 2851, 2191, 1743, 1655, 1542, 1509, 1436, 1373, 1218, 1170, 1131, 1018, 962, 907, 826, 729.



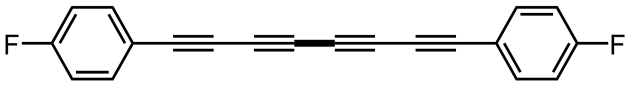
1,8-Diphenylocta-1,3,5,7-tetrayne

6h, light yellow solid, 25.2 mg, 99% yield. R$_f$ = 0.6 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.62 – 7.50 (m, 4H), 7.46 – 7.29 (m, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 133.2, 130.0, 128.5, 120.5, 77.7, 74.4, 67.2, 63.6. Characterization data of **6h** corresponded to the literature values.[5b]



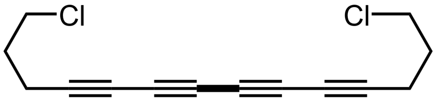
1,8-Bis(2-methoxyphenyl)octa-1,3,5,7-tetrayne

6i, brown solid, 26.8 mg, 86% yield. R$_f$ = 0.2 (PE:EA = 10:1), chromatography eluent: 10% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.48 (dd, *J* = 7.6, 1.5 Hz, 2H), 7.41 – 7.31 (m, 2H), 6.96 – 6.82 (m, 4H), 3.89 (s, 6H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 162.4, 135.1, 131.5, 120.6, 110.7, 109.8, 78.2, 74.5, 68.0, 64.1, 55.8. **HRMS** (EI) calcd for $C_{22}H_{14}O_2$ [M]$^+$: 310.09883, found: 310.09879. **IR** (ATR): ṽ = 3073, 3006, 2941, 2838, 2200, 1944, 1594, 1571, 1489, 1463, 1432, 1299, 1273, 1242, 1182, 1164, 1120, 1046, 1024, 931, 841, 791, 741, 676. **M.p.** (amorphous): 146.5-148.1 °C.



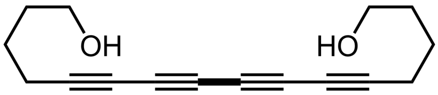
1,8-Bis(4-fluorophenyl)octa-1,3,5,7-tetrayne

6j, light yellow solid, 21.2 mg, 74% yield. R$_f$ = 0.6 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, CDCl$_3$) δ 7.61 – 7.45 (m, 1H), 7.11 – 6.97 (m, 1H). **^{13}C NMR** (75 MHz, CDCl$_3$) δ 163.49 (d, *J* = 253.3 Hz), 135.36 (d, *J* = 8.7 Hz), 116.63 (d, *J* = 3.6 Hz), 116.11 (d, *J* = 22.4 Hz), 77.2, 74.23 (d, *J* = 1.6 Hz), 67.1, 63.5. **IR** (ATR): ṽ = 3102, 3072, 2954, 2924, 2854, 2204, 1889, 1639, 1595, 1505, 1464, 1401, 1377, 1297, 1279, 1225, 1159, 1095, 1015, 830, 809, 642, 616. M.p. (amorphous): 154.6-157.2 °C.



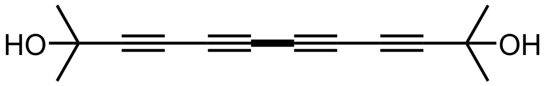
1,14-Dichlorotetradeca-4,6,8,10-tetrayne

6k, brown oil, 13.3 mg, 53% yield. R_f = 0.3 (PE), chromatography eluent: Petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.2 Hz, 4H), 2.53 (t, *J* = 6.8 Hz, 4H), 2.00 (p, *J* = 6.6 Hz, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 78.4, 66.6, 61.3, 60.9, 43.2, 30.7, 16.9. **HRMS** (EI) calcd for $C_{14}H_{12}Cl_2$ $[M]^+$: 250.03105, found: 250.03050. **IR** (Reflection): ṽ =2958, 2925, 2853, 2227, 1731, 1596, 1465, 1441, 1359, 1288, 1179, 1101, 968, 826, 723, 656.



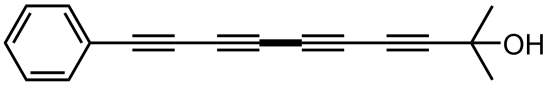
Hexadeca-5,7,9,11-tetrayne-1,16-diol

6l, dark yellow oil, 17.7 mg, 73% yield. R_f = 0.5 (EA), chromatography eluent: Ethyl acetate. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 3.66 (t, *J* = 6.0 Hz, 4H), 2.36 (t, *J* = 6.6 Hz, 4H), 1.71 – 1.59 (m, 8H), 1.54 (br, 2H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 80.0, 66.0, 62.1, 61.3, 60.7, 31.6, 24.3, 19.3. **HRMS** (EI) calcd for $C_{16}H_{18}O_2$ $[M]^+$: 242.13013, found: 242.13100. **IR** (Reflection): ṽ = 3361, 2938, 2868, 2536, 2225, 2156, 1721, 1602, 1584, 1453, 1316, 1274, 1157, 1115, 1063, 713.



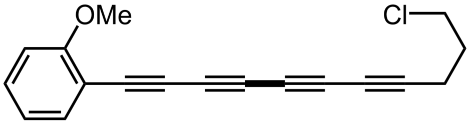
2,11-Dimethyldodeca-3,5,7,9-tetrayne-2,11-diol

6m, dark yellow oil, 13.2 mg, 62% yield. R_f = 0.5 (PE:EA = 2:1), chromatography eluent: 50% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, CD_3OD) δ 1.37 (s, 12H). **^{13}C NMR** (151 MHz, CD_3OD) δ 85.2, 67.1, 66.1, 64.1, 62.7, 31.3. **HRMS** (EI) calcd for $C_{14}H_{14}O_2$ $[M]^+$: 214.09883, found: 214.09760. **IR** (Reflection): ṽ = 3332, 2984, 2934, 2224, 2161, 1710, 1455, 1378, 1364, 1230, 1164, 955, 842.



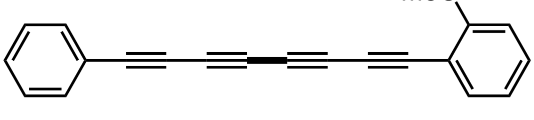
2-Methyl-10-phenyldeca-3,5,7,9-tetrayn-2-ol

6n, dark yellow oil, 23.2 mg, 50% yield. $R_f = 0.5$ (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.56 – 7.50 (m, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.33 (t, J = 7.6 Hz, 2H), 2.03 (br, 1H), 1.55 (s, 6H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 133.2, 130.0, 128.5, 120.4, 83.2, 74.3, 67.5, 67.0, 65.7, 64.2, 63.0, 62.2, 30.9. Characterization data of **6n** corresponded to the literature values.[41]



1-(11-Chloroundeca-1,3,5,7-tetrayn-1-yl)-2-methoxybenzene

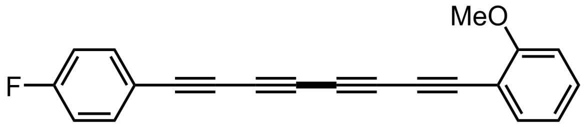
6o, brown oil, 15.2 mg, 27% yield. $R_f = 0.5$ (PE:DCM = 1:1), chromatography eluent: 30% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.47 (dd, J = 7.6, 1.6 Hz, 1H), 7.43 – 7.30 (m, 1H), 6.98 – 6.82 (m, 2H), 3.88 (s, 3H), 3.64 (t, J = 6.2 Hz, 2H), 2.55 (t, J = 6.8 Hz, 2H), 2.02 (p, J = 6.6 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.5, 135.1, 131.5, 120.6, 110.7, 109.8, 79.8, 78.1, 73.0, 68.0, 66.7, 64.4, 61.0, 60.9, 55.8, 43.2, 30.7, 17.0. **HRMS** (EI) calcd for $C_{18}H_{13}OCl$ $[M]^+$: 280.06494, found: 280.06400. **IR** (ATR): ṽ = 3072, 3006, 2941, 2838, 2200, 1944, 1732, 1594, 1571, 1489, 1432, 1299, 1273, 1242, 1182, 1120, 1046, 930, 841, 790, 741, 676.



1-Methoxy-2-(phenylocta-1,3,5,7-tetrayn-1-yl)benzene

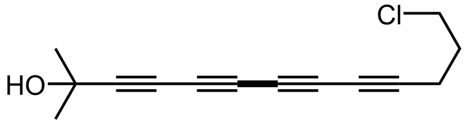
6p, dark yellow solid, 28.7 mg, 51% yield. $R_f = 0.5$ (PE:DCM = 5:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 – 7.51 (m, 2H), 7.48 (dd, J = 7.6, 1.6 Hz, 1H), 7.45 – 7.29 (m, 4H), 6.90 (dd, J = 12.7, 8.0 Hz, 2H), 3.89 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.5, 135.1, 133.2, 131.5, 129.9, 128.5, 120.6, 120.6, 110.7, 109.8, 78.1, 77.7, 74.5, 67.8, 67.3, 63.9, 63.8, 55.8. **HRMS** (EI) calcd for $C_{21}H_{12}O$ $[M]^+$: 280.08827, found: 280.08824. **IR** (Reflection): ṽ

= 2925, 2853, 2198, 2127, 1736, 1594, 1572, 1493, 1458, 1432, 1298, 1274, 1248, 1180, 1163, 1115, 1047, 1024, 999, 917, 845, 811, 749, 683. **M.p.** (amorphous): 85.9-87.6 °C.



1-((4-Fluorophenyl)octa-1,3,5,7-tetrayn-1-yl)-2-methoxybenzene

6q, yellow solid, 28.5 mg, 48% yield. R_f = 0.5 (PE:DCM = 5:1), chromatography eluent: 10% Dichloromethane in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.60 – 7.44 (m, 3H), 7.43 – 7.31 (m, 1H), 7.03 (t, *J* = 8.7 Hz, 2H), 6.96 – 6.83 (m, 2H), 3.88 (d, *J* = 4.7 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 163.4 (d, *J* = 253.1 Hz), 162.5, 135.3 (d, *J* = 8.7 Hz), 135.1, 131.6, 120.6, 116.8 (d, *J* = 3.6 Hz), 116.07 (d, *J* = 22.4 Hz), 110.7, 109.7, 78.0, 74.6, 74.4, 74.3, 67.7, 67.4, 64.0, 63.7, 55.8. **^{19}F NMR** (282 MHz, $CDCl_3$) δ -106.82. **HRMS** (EI) calcd for $C_{21}H_{10}OF$ $[M]^+$: 297.07102, found: 297.07265. **IR** (Reflection): ṽ = 3072, 2925, 2853, 2201, 2132, 1733, 1596, 1573, 1506, 1492, 1458, 1434, 1404, 1299, 1274, 1248, 1227, 1180, 1156, 1114, 1094, 1048, 1023, 931, 832, 801, 741, 649. **M.p.** (amorphous): 121.9-123.2 °C.



13-Chloro-2-methyltrideca-3,5,7,9-tetrayn-2-ol

6r, brown oil, 18.6 mg, 40% yield. R_f = 0.3 (PE:EA = 5:1), chromatography eluent: 20% Ethyl acetate in petroleum ether. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.2 Hz, 2H), 2.54 (t, *J* = 6.8 Hz, 2H), 2.08 – 1.95 (m, 2H), 1.92 (br, 1H), 1.54 (s, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 81.8, 79.2, 67.5, 66.5, 65.7, 64.4, 62.8, 60.6, 60.2, 43.2, 30.9, 30.6, 16.9. **HRMS** (EI) calcd for $C_{14}H_{13}OCl$ $[M]^+$: 232.06494, found: 232.06556. **IR** (Reflection): ṽ = 3393, 2983, 2932, 2225, 2181, 1713, 1441, 1364, 1288, 1221, 1166, 957, 656.

5.6 X-Ray Crystallographic Data of 4z and 6q

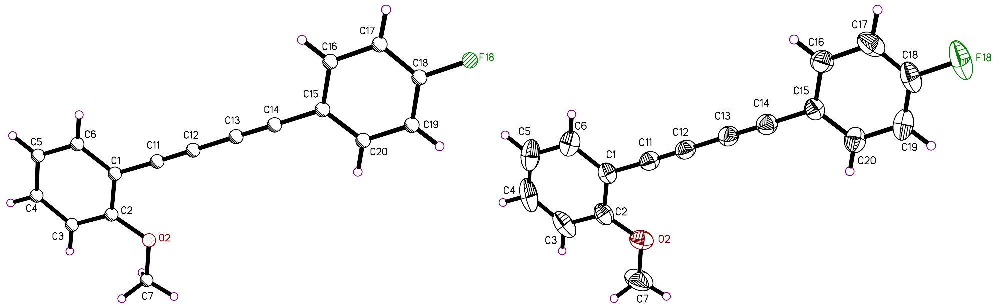


Figure 1. The ORTEP projection of crystal structure of **4z**.

Table 6. Crystal Data and Structure Refinement for **4z.**

Identification code	hws11 (**4z**)	
Empirical formula	$C_{17}H_{11}FO$	
Formula weight	250.26	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/n$	
Z	4	
Unit cell dimensions	a = 7.1021(7) Å	α = 90 deg.
	b = 24.963(2) Å	β = 104.066(2) deg.
	c = 7.5156(7) Å	γ = 90 deg.
Volume	1292.5(2) Å^3	
Density (calculated)	1.29 g/cm^3	
Absorption coefficient	0.09 mm^{-1}	
Crystal shape	brick	
Crystal size	0.164 x 0.131 x 0.060 mm^3	
Crystal colour	yellow	
Theta range for data collection	1.6 to 26.5 deg.	
Index ranges	$-8 \le h \le 8$, $-31 \le k \le 31$, $-9 \le l \le 9$	
Reflections collected	13331	
Independent reflections	2675 (R(int) = 0.0530)	
Observed reflections	1734 (I > 2\s(I))	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.75 and 0.70	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	2675 / 0 / 184	
Goodness-of-fit on F^2	1.01	
Final R indices ($I > 2\sigma(I)$)	R1 = 0.050, wR2 = 0.106	
Largest diff. peak and hole	0.15 and -0.16 eÅ^{-3}	

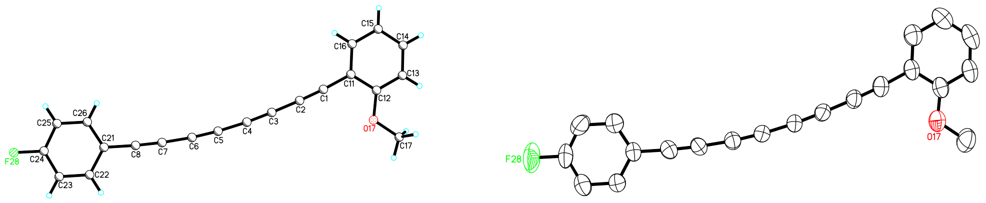


Figure 2. The ORTEP projection of crystal structure of **6q**.

Table 7. Crystal Data and Structure Refinement for **6q.**

Identification code	hws10 (**6q**)	
Empirical formula	$C_{21}H_{11}FO$	
Formula weight	298.30	
Temperature	200(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	$P2_1/c$	
Z	4	
Unit cell dimensions	a = 3.939(3) Å	α = 90 deg.
	b = 16.108(11) Å	β = 90.903(17) deg.
	c = 24.645(16) Å	γ = 90 deg.
Volume	1563.5(19) $Å^3$	
Density (calculated)	1.27 g/cm^3	
Absorption coefficient	0.09 mm^{-1}	
Crystal shape	plank	
Crystal size	0.096 x 0.048 x 0.022 mm^3	
Crystal colour	yellow	
Theta range for data collection	1.5 to 21.7 deg.	
Index ranges	$-4 \le h \le 4$, $-16 \le k \le 16$, $-25 \le l \le 25$	
Reflections collected	10243	
Independent reflections	1837 (R(int) = 0.0620)	
Observed reflections	1209 ($I > 2\sigma(I)$)	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.96 and 0.88	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	1837 / 0 / 209	
Goodness-of-fit on F^2	1.05	
Final R indices (I > 2sigma(I))	R1 = 0.047, wR2 = 0.084	
Largest diff. peak and hole	0.13 and -0.12 $eÅ^{-3}$	

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