Gold-Catalyzed Cascade Cyclization of Diazo-tethered Alkynes

Presented by:

Cheng Zhang

From Jiangsu, China

August 2021

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

Prof. Dr. Milan Kivala

A dissertation submitted to the

Combined Faculty of Natural Sciences and Mathematics

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for the degree of

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Table of Contents

Publications

[1] Cheng Zhang, Kemiao Hong, Chao Pei, Su Zhou, Wenhao Hu, A. Stephen K. Hashmi,* Xinfang Xu,* “Gold(I)-catalyzed intramolecular cyclization/intermolecular cycloaddition cascade as a fast track to polycarbocycles and mechanistic insights” *Nat. Commun.* **2021**, *12*, 1182.

[2] Xianhai Tian, Lina Song, Chunyu Han, Cheng Zhang, Yufeng Wu, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi,* “Gold(III)-Catalyzed Formal [3 + 2] Annulations of N-Acyl Sulfilimines with Ynamides for the Synthesis of 4-Aminooxazoles” *Org. Lett.* **2019**, *21*, 2937-2940.

[3] Cheng Zhang, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi,* “Practical and Modular Construction of benzophenanthridine Compounds” in preparation.

[4] Cheng Zhang, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi,* “$Et_3N(HF)_3$-Controlled Regioselective Carbo-Hydroxylations and -Fluorinations of Tethered Diazo Alkynes by Gold Catalysis” in preparation.

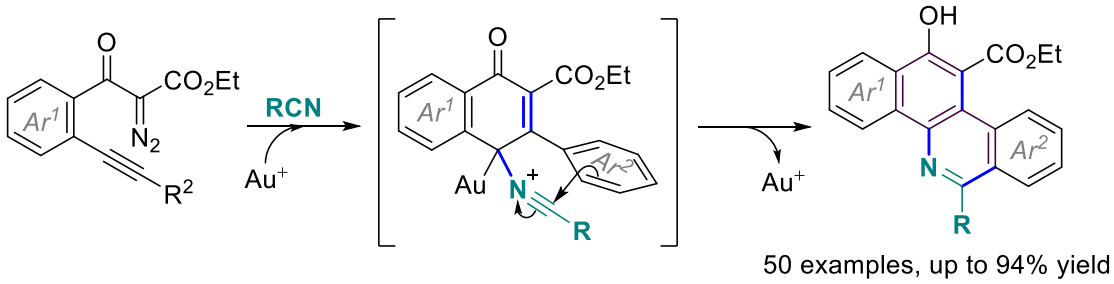
Abbreviations

Ar	Aryl
ATR	Attenuated Total Refraction
Bu	Butyl
calcd.	Calculated
Cy	Cyclohexyl
DCM	Dichloromethane
DCE	1,2-Dichloroethane
DMAP	Dimethyl amino pyridine
DMF	Dimethyl formamide
DMSO	Dimethyl sulfoxide
EDG	Electron donating group
EA	Ethyl acetate
EI	Electron ionization
eq.	Equivalent
ESI	Electrospray Ionization
Et	Ethyl
EWG	Electron withdrawing group
GC	Gas chromatography
h	hour
Hex	Hexyl
HRMS	High resolution mass spectrometry
Hz	Hertz
ICP	Inductively coupled plasma
*i*Pr	Isopropyl
IR	Infrared
m.p.	Melting point
m/z	mass per charge

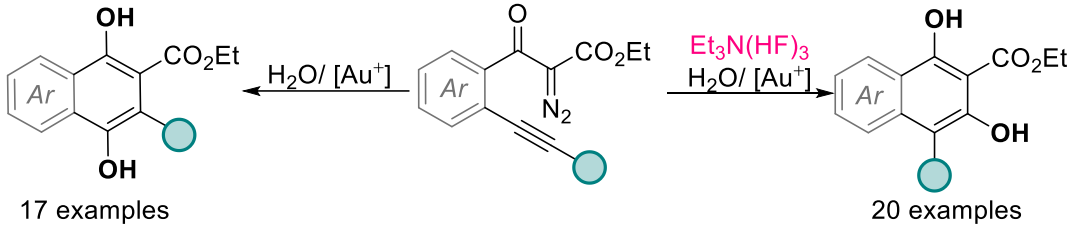
Me	Methyl
Mes	Mesityl
min	Minutes
MS	Mass spectrometry
NBS	N-bromo succinimide
NHC	N-heterocyclic carbene
NIS	N-iodosuccinimide
NMR	Nuclear magnetic resonance
Ns	4-Nitrobenzenesulfonyl
PE	Petroleum ether
Ph	Phenyl
Pr	Propyl
r.t.	Room temperature
R_f	Ratio of fronts
t	*tert*
Tf	Trifluormethylsulfonyl
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMS	Trimethyl silyl

Abstract

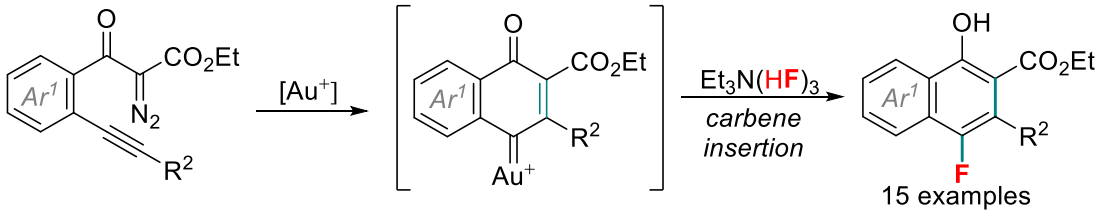
In Chapter 2, a gold-catalyzed domino annulation of diazo-tethered alkynes with nitriles proceeds through a sequential 6-*endo-dig* cyclization/nitrile insertion/C-H functionalization. This protocol offers a general and modular strategy for the rapid assembly of benzophenanthridine derivatives with a broad functional-group tolerance. Moreover, this methodology, using readily available nitriles as the nitrogen source, represent a versatile platform for the construction of benzophenanthridine frameworks.



In Chapter 3, an unprecedented dichotomy in the regioselectivity of carbohydroxylation of diazo-tethered alkynes was observed. The gold-catalyzed 6-*endo-dig* cyclization leads to the quinoid-carbene species, terminated by direct O-H insertion under additive-free conditions, while the reaction in the presence of $Et_3N(HF)_3$ undergoes an O-H *ortho*-insertion of carbene/rearrangement to give the dihydroxynaphthalene isomers as the major products.

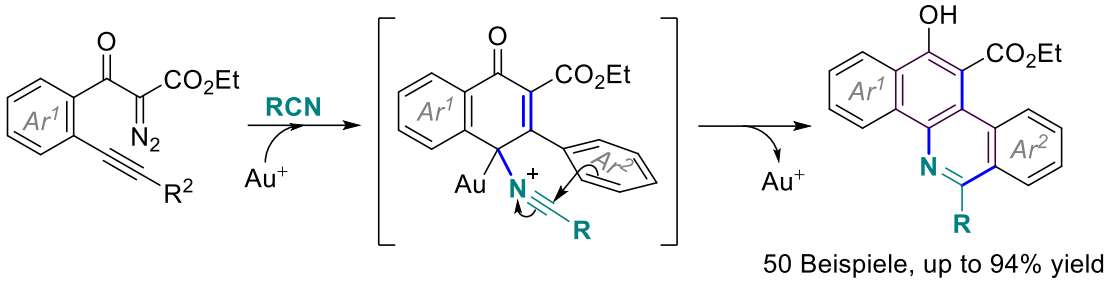


In Chapter 4, the gold-catalyzed carbofluorination of diazo-tethered alkynes provides a facile, efficient, and atom-economical route to α-fluoronaphthalene derivatives. An intermediate endocyclic gold carbene, generated by an intramolecular 6-*endo-dig* cyclization, promotes a carbene H-F insertion to afford the desired products.

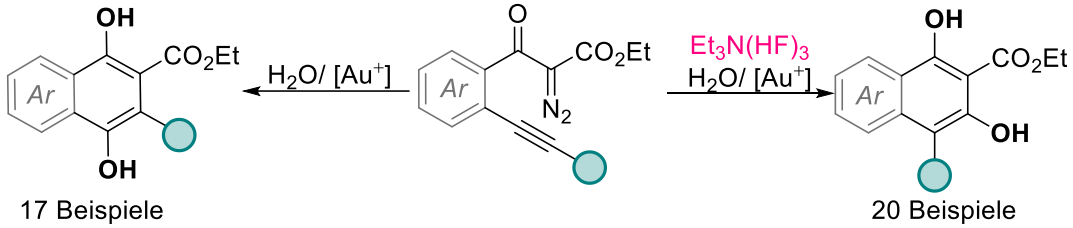


Kurzzusammenfassung

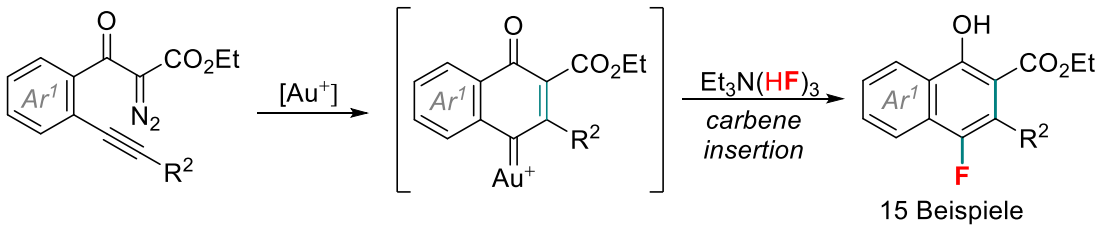
In Kapitel 2, verläuft die goldkatalysierte Dominoanellierung der diazogebundenen Alkine mit Nitrilen über eine sequentielle 6-*endo-dig*-Cyclisierung/Nitrilinsertion/ C-H-Funktionalisierung. Dieses Protokoll bietet eine allgemeine und modulare Strategie für den schnellen Aufbau von Benzophenanthridin-Derivaten mit einer breiten Toleranz von funktionellen Gruppen. Darüber hinaus stellt diese Methode, in leicht verfügbare Nitrile als Stickstoffquelle verwendet werden, eine vielseitige Plattform für den Aufbau der Gerüsten vom Benzophenanthridin dar.



In Kapitel 3, wurde eine beispiellose Dichotomie in der Regioselektivität der Carbohydroxylierung von diazo-gebundenen Alkinen beobachtet. Die goldkatalysierte 6-*endo-dig*-Cyclisierung führt zur chinoiden Carben-Spezies, die durch direkte OH-Insertion unter additiv-freien Bedingungen terminiert wird, während in der oben genannten Reaktion eine O-H-ortho-Insertion Carben/Umlagerung in Anwesenheit von $Et_3N(HF)_3$ stattfindet, mit der die Dihydroxynaphthalin-Isomere als Hauptprodukte hergestellt werden können.



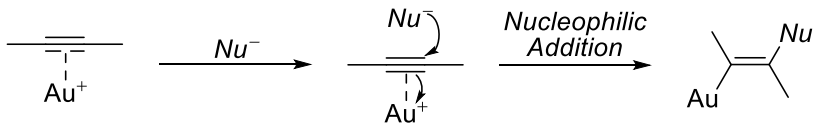
In Kapitel 4, bietet die goldkatalysierte Carbofluorierung der diazogebundenen Alkine einen einfachen, effizienten und atomökonomischen Weg zu α-Fluornaphthalin-Derivaten. Die durch die intramolekulare 6-*endo-dig*-Cyclisierung erzeugte Carben-H-F-Insertion konnte durch das intermediäre endocyclische Goldcarben gefördert werden, wodurch mehr Produkte erhalten werden konnten.



Chapter 1: General Introduction

1.1 Gold-Catalyzed Alkyne Transformations

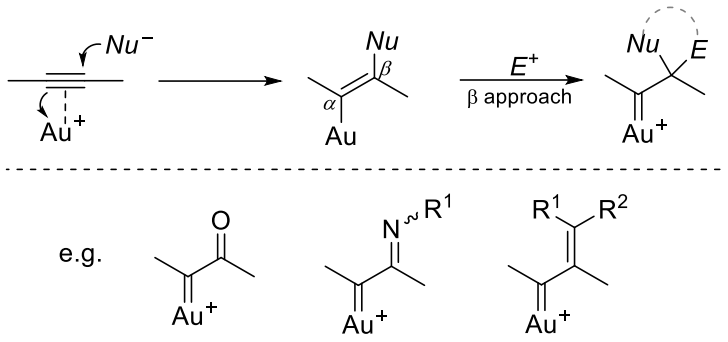
Gold was recognized as a precious, purely decorative inert metal allready thousands of years ago. However, the catalytic activity of gold complexes was ignored until the first application of homogeneous gold(I) catalysis was described by Ito and Hayashi in 1986.[1] More than a decade later, a seminal work by Teles[2] and Tanaka[3] demonstrated the utility of cationic phosphine Au(I) species in terms of the hydrolysis of alkynes, which revealed the potential of gold(I) in organic synthesis. Since the first report on the generation of a gold-carbene species by the Hashmi group,[4] the gold-catalyzed alkyne cyclization has been evolved into a powerful technique for the construction of cyclic molecules with high structural complexity.[5] In the majority of cases, homogeneous gold catalysis acts as a soft π-Lewis acid and selectively activates the alkynes in complex molecular settings toward intra- or intermolecular nucleophilic addition (Scheme 1).[6]



Scheme 1. Gold-catalyzed nucleophilic addition of alkynes.

For a long time, metal carbenes, derived from the decomposition of diazo compounds by transition metals, have been extensively used in various transformations such as cyclopropanations, cyclopropenations, X-H insertions, coupling reactions, and a myriad of ylide chemistry.[7-12] Compared to Rh^{II}, Cu^{II}-catalyzed diazo-generated carbene/alkyne metathesis (CAM) transformations,[13] gold-triggered diazo-alkyne transformations have been shown to have dramatic differences in terms of reactivity and selectivity.[14]

In this chapter, the generation of gold carbenes from alkynes involving α-oxo gold carbenes, α-imine gold carbenes and vinyl carbenes will be highlighted (Scheme 2). A series of gold-promoted intra- and intermolecular transformations as access to (hetero-)cyclic structures will be reviewed.

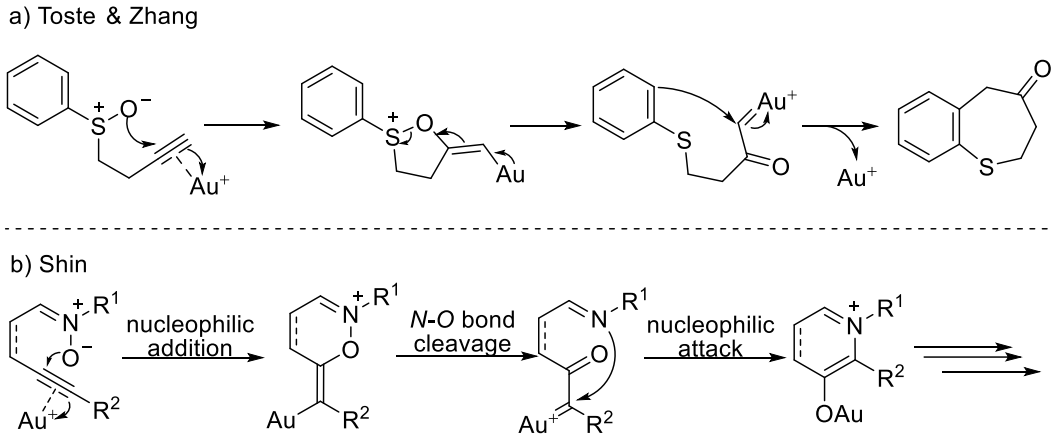


Scheme 2. Generation of gold carbenes from alkynes .

1.2 Generation of Gold Carbenes and Their Follow-up Chemistry

1.2.1 α-Oxo Gold Carbenes

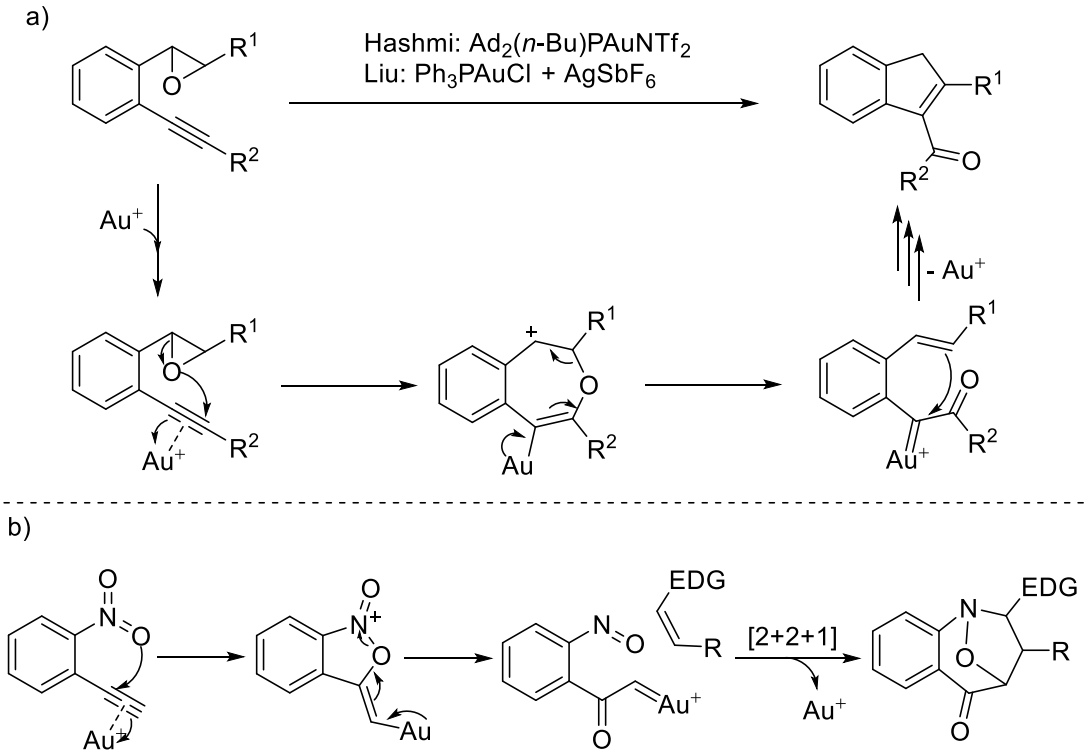
Seminal works on the generation of α-oxo gold-carbene species via the intramolecular rearrangement of sulfinyl alkynes to yield tetrahydrobenzothiepinones were reported by Toste[15] and Zhang[16], independently (Scheme 3a). In their work, a α-oxo gold carbene was obtained by an intramolecular oxygen transfer to the pendant alkyne followed by the *S*-*O* bond cleavage. The desired products were furnished via $C_{(sp2)}$-H insertion. A similar phenomenon was observed by Shin and coworkers. Shin's group reported a series of gold-catalyzed cascade cyclization of azomethine for the assembly of heterocyclic frameworks (Scheme 3b).[17] These unique α-oxo gold-carbene species, generated via gold-promoted intramolecular oxygen transfer, were the key intermediate in these transformations, terminated by an internal alkene.



Scheme 3. Sulfoxides and pyridine *N*-oxides as carbene precursors.

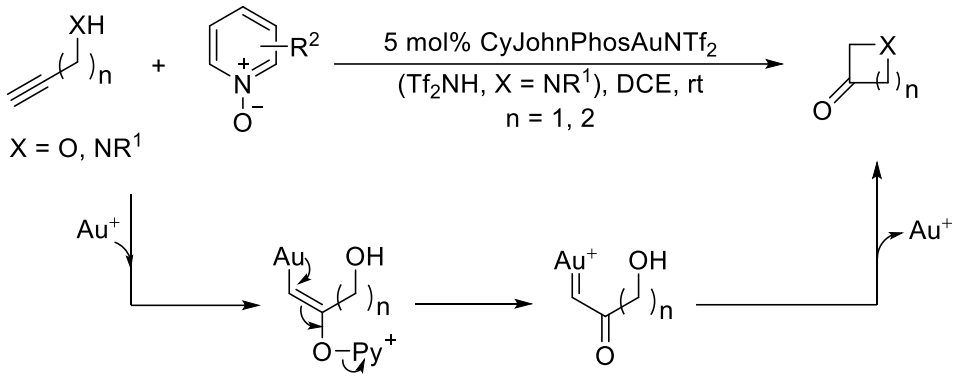
In 2008, Hashmi and Liu's group independently exploited an internal epoxide to oxidize an alkyne leading to an α-oxo gold carbene, which underwent an electrocyclization cyclization/rearrangement with the in-situ generated alkene to give

indenyl-ketone products. (Scheme 4a).[18] Similarly, Liu's group reported a redox/formal cascade cyclization of readily available 1-alkynyl-2-nitrobenzenes for bridged products in high diastereoselectivity (Scheme 4b).[19] This carbene intermediate of the resulting product was constructed through an initial intramolecular cyclization and N-O bond cleavage. Subsequently, a formal [2+2+1] cycloaddition of α-oxo gold carbene, in-situ generated nitroso, and external alkenes contributed to the desired azacyclic compounds.



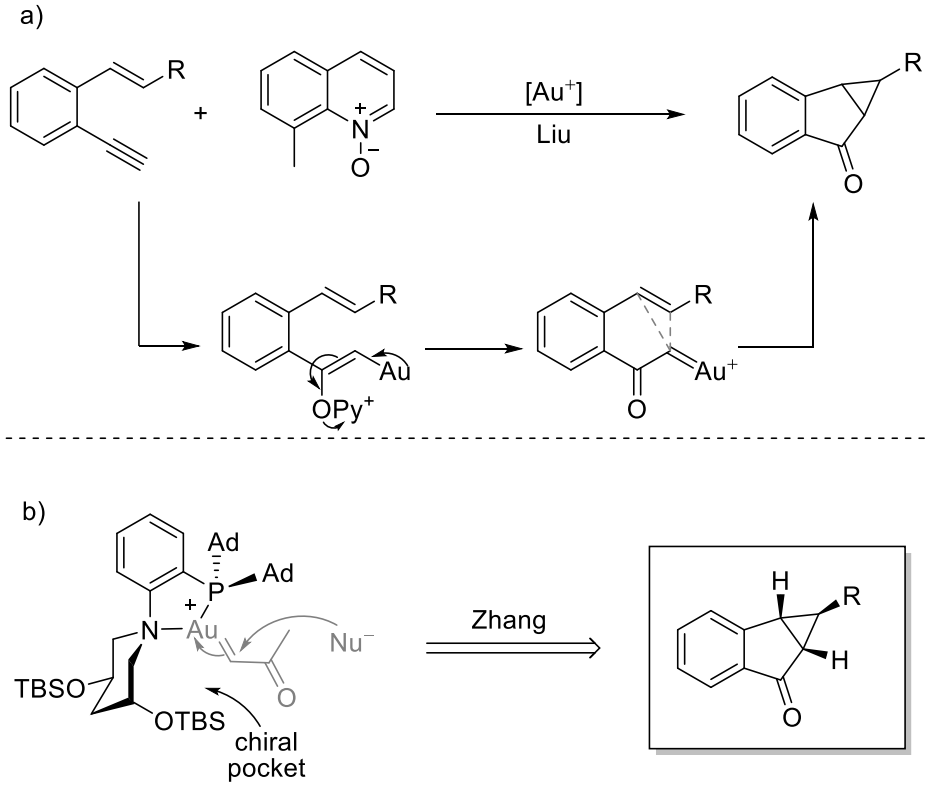
Scheme 4. The intramolecular oxygen transfer to α-oxo gold carbenes.

Compared to the gold-catalyzed intramolecular oxygen transfer for the generation of α-oxo gold carbenes, external oxidants can promote further application of the oxidative gold catalysis beyond the very bondage of the two reacting partners. [20] In 2010, Zhang's group disclosed a facile and efficient access to the α-oxo gold-carbene species through a gold-promoted intermolecular oxidation of alkynes by using pyridine *N*-oxides as external oxidants (Scheme 5).[21] The in-situ gold-carbene species could be trapped by the intramolecular hydroxyl and amino group to afford a variety of heterocyclic compounds. In particular, highly strained small rings were synthesized in good to excellent yield.



Scheme 5. X-H insertion of α-oxo gold carbenes

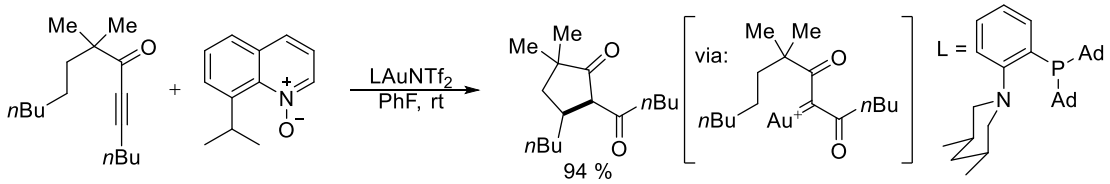
Later, Liu and Zhang et al. independently reported an intramolecular cyclopropanation of the adjacent alkene with an α-oxo gold carbene, which was in-situ generated by an external oxidant (Scheme 6a).[22] By taking full advantage of the ingeniously designed P,N-bidentate ligand, Zhang and coworkers described an enantioselective version of chiral cyclopropane derivatives (Scheme 6b).[22b]



Scheme 6. Gold-triggered oxidative cyclopropanations

Over the past decades, C–H functionalization has gradually evolved into one of the most effective strategies to synthesize complex molecules. In comparison with

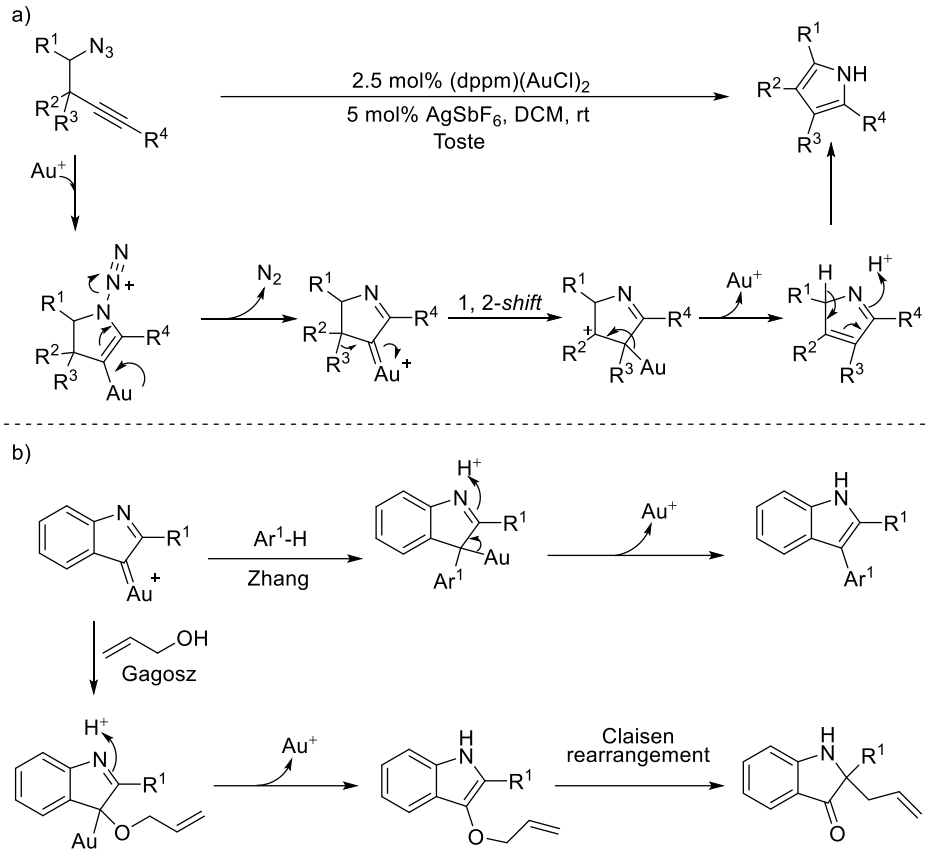
Rh-catalyzed carbene insertions of C-H bonds,[23] gold-carbene species triggered C-H bond functionalization, especially those of unactivated C(sp^3)–H bonds, were rarely reported. The most remarkable example was described by Zhang's team (Scheme 7).[24] Zhang and coworkers used an oxidative cyclization of ynones with external quinolone *N*-oxides to express this unique reactivity. The in-situ generated carbene species are highly electrophilic and capable of selective C(sp^3)-H insertion to deliver the inserted products.



Scheme 7. Insertions of the α-oxo gold-carbene species

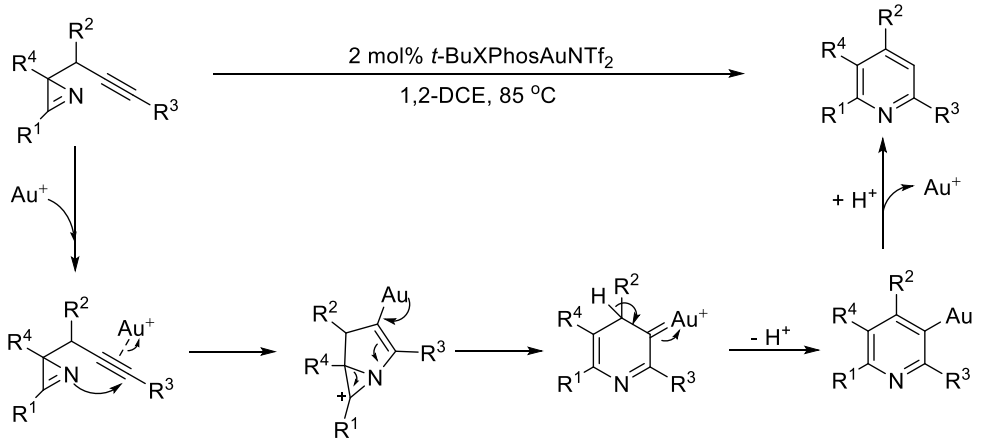
1.2.2 α-Imino Gold Carbenes

Gold-catalyzed nitrene transfer reactions from *N*-Leaving group to alkynes can yield highly electrophilic α-imino gold carbenes. In 2005, Toste and co-workers exploited a gold(I)-catalyzed acetylenic Schmidt reaction of homopropargyl azides for the preparation of substituted pyrroles, and the α-imino gold-carbene intermediate was first proposed in this report, which was formed via an intramolecular 5-*exo*-*dig* nucleophilic addition of the azide onto the pendant gold-activated alkyne followed by losing nitrogen (Scheme 8a).[25] A formal 1,2-hydride/alkyl migration regenerated the cationic gold(I) catalyst and produced the 2*H*-pyrrole that tautomerized to a substituted pyrroles. Inspired by this protocol, Gagosz and Zhang's group reported the synthesis of 3-indolinone and indole via the homologous α-imino gold-carbene species, which were trapped by allyl alcohols or nucleophilic aromatic rings (Scheme 8b).[26] Furthermore, the strategy was successfully applied to the construction of bicyclic imidazaole and quinoline derivatives.[27]



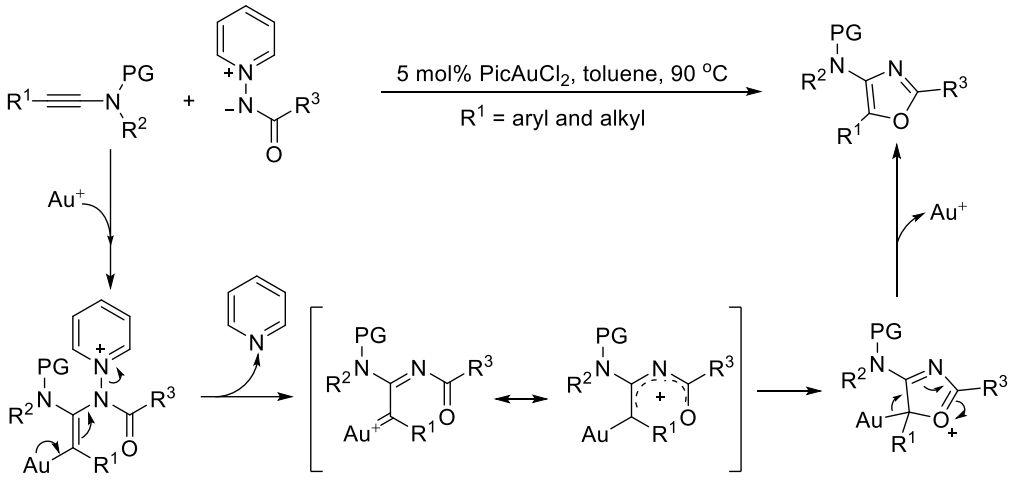
Scheme 8. Gold-catalyzed 5-*endo-dig* cyclization of azide-tethered alkynes

Instead of the azide as the nitrogen source, Gagosz reported that the 2*H*-azirine as an alternative nitrene precursor to access α-imino gold-carbenes via an intramolecular transfer of an alkenyl nitrene to an alkyne and followed by the strained ring-opening (Scheme 9).[28] Polysubstituted pyridines were synthesized with high functional-group tolerance and a wide substrate scope.



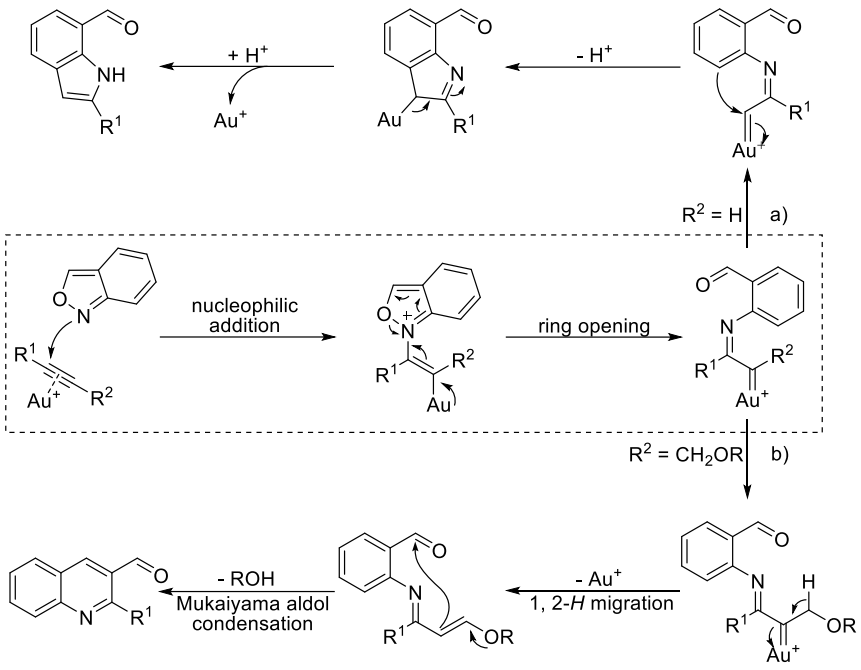
Scheme 9. α-Imino gold-carbene species from 2*H*-azirines.

In comparison with the gold-promoted intramolecular addition of the nitrogen source toward alkynes for the formation of α-imino gold-carbenes, the intermolecular nucleophilic addition for the α-imino gold carbene is more flexible and efficient without tedious steps in the synthesis of heterocyclic compounds. The first report on the generation of an α-imino gold carbene by the intermolecular incorporation of ynamides into the gold-catalyzed nitrene transfer was developed by Davies and co-workers (Scheme 10).[29] They disclosed a gold-catalyzed [3+2] cycloaddition of ynamides with iminopyridium for the preparation of polysubstituted oxazoles in the presence of the gold(III) complex.[29b]



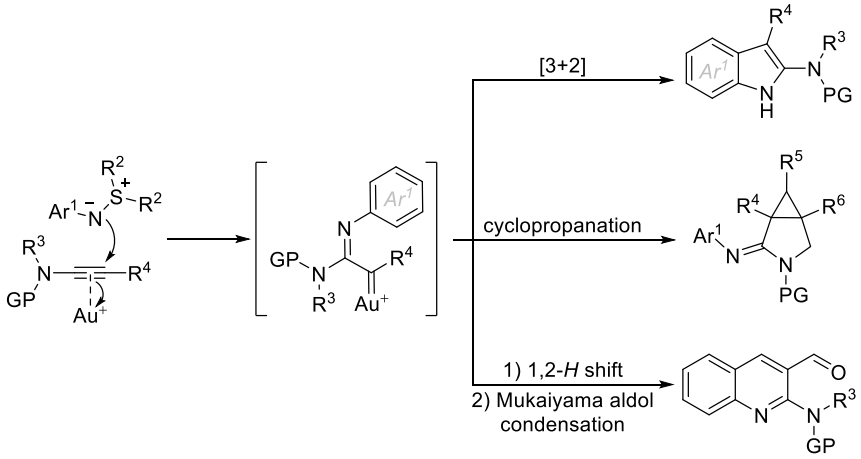
Scheme 10. α-Imino gold carbenes from an intermolecular nitrene source

In 2016, Hashmi' group contributed a gold-catalyzed C-H cascade reaction of anthranil derivatives with alkynes for the expedient synthesis of 7-acylindoles by using the potential of anthranil to act as a nitrogen source. The reaction was terminated via a tertiary C−H bond insertion.[30a] Mechanistic studies indicated that the α-imino gold-carbene species, generated via a gold-promoted intermolecular nitrogen-shift, consecutively proceeded an ortho-aryl C-H functionalization to afford the desired products (Scheme 11a). As well as alkynyl terminus, adjacent methylene moieties (R^2) were also suitable for the reaction without $C_{(sp2)}$-H insertion products, which suggested that the β-H elimination might be faster than C-H annulation (Scheme 11b).[30b] Subsequently, the methodology was expanded to the synthesis of fused quinoline derivatives, in which the Mukaiyama aldol condensation of enol/enolether with the electrophilic aldehyde derived from the ring opening of the anthranil reacted smoothly as well as ynamide substrates. Further, this strategy was successfully applied to the preparation of poly heterocyclic hydrocarbons through gold-catalyzed π-extension of anthranils with the adjacent aryls as reagents.[31]



Scheme 11. α-Imino gold carbenes from anthranils

Inspired by these milestone works on the preparation of α-imino gold-carbenes, Hashmi and coworkers continued to pursue the novel method of these carbene species for the construction of heterocyclic compounds with structural diversity. In comparison with other nucleophilic nitrenes such as azide, 2*H*-azirine and anthranil, sulfilimines are cheap and readily available to generate valuable synthetic intermediates via *N*–*S* bond cleavage. In this direction, sulfilimines were employed as α-imino gold-carbene precursors through the formal [3+2] cycloaddition with ynamides, cyclopropanations with alkene-tethered ynamides, and nucleophilic attack ynamides to afford indoles, 3-azabicyclo[3.1.0]hexan-2-imines, and quinoline derivatives (Scheme 12).[32]

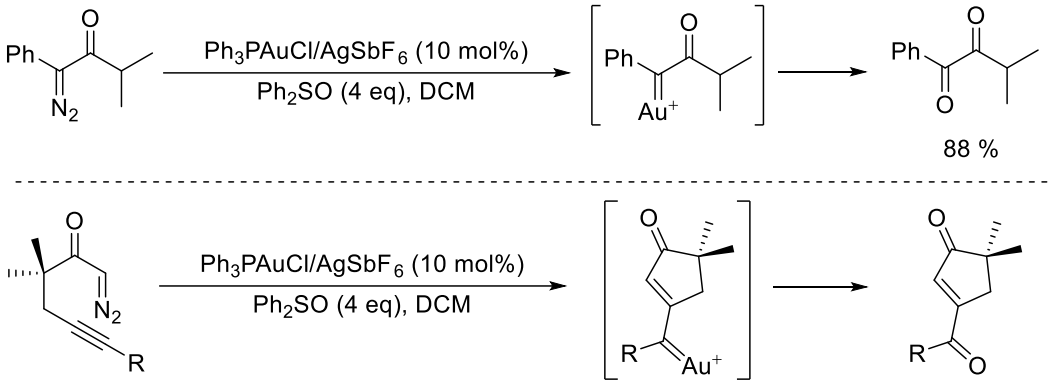


Scheme 12. α-imino gold carbene from sulfilimines.

Similarly, advances in the construction of heterocyclic compounds via α-imino gold-carbene have been also reported by Liu,[33a] Ye,[33b] Ballesteros,[33c] and Huang,[33d] independently.

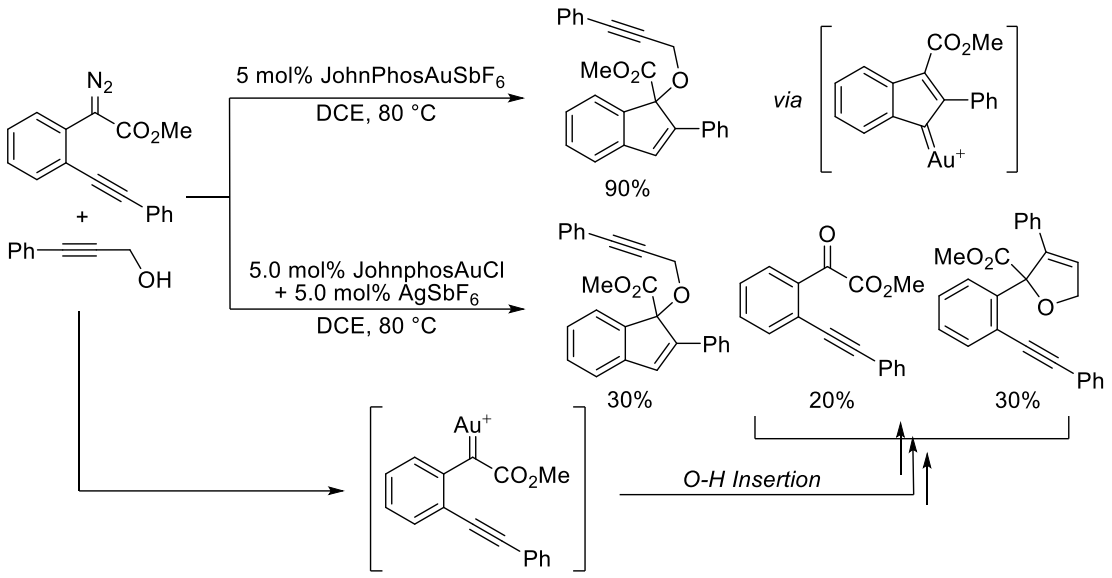
1.2.3 α-Vinyl Gold Carbenes

In 2007, Toste's group developed an unique gold-induced oxidative rearrangement of diazo-tethered alkynes. Inspired by the gold-catalyzed α-diazoketone decomposition to afford the 1,2-diketone product in the presence of diphenylsulfoxide (Scheme 13, top), the authors supposed that this cascade cyclization involved a gold-promoted intramolecular 5-*exo*-*dig* cyclization of the diazo-carbon atom towards the pendant alkyne and the subsequent loss of dinitrogen to deliver the vinyl gold-carbene species, which then underwent an oxidation process with diphenylsulfoxide to give 1,4-endione products (Scheme 13, down).[34]



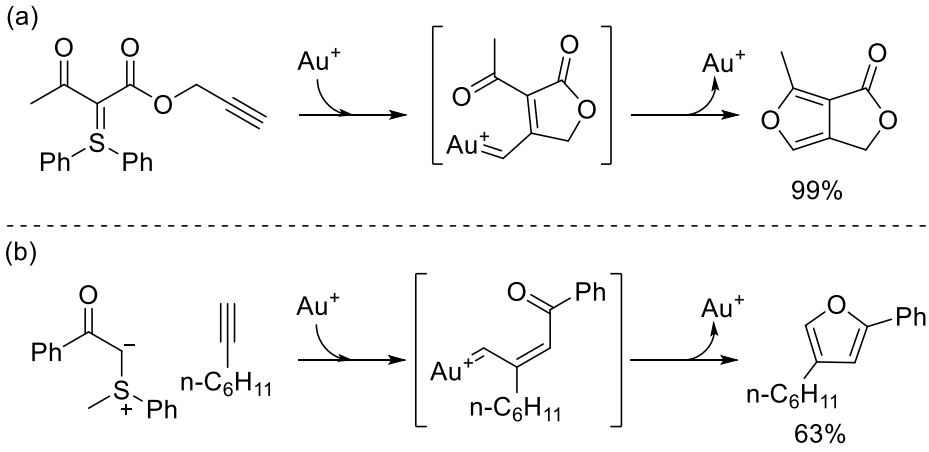
Scheme 13. Gold-catalyzed oxidative rearrangements.

However, Xu et al. recently disclosed a gold-catalyzed 5-*endo*-*dig* carbocyclization of the diazo-tethered alkynes, followed by an unprecedented vinylogous addition with an external protic nucleophile. It is noteworthy that silver activators are harmful to gold-catalyzed reactions, and the preformed cationic gold catalyst usually has a better efficiency (Scheme 14).[14b]



Scheme 14. Silver salt in homogeneous gold(I) catalysis

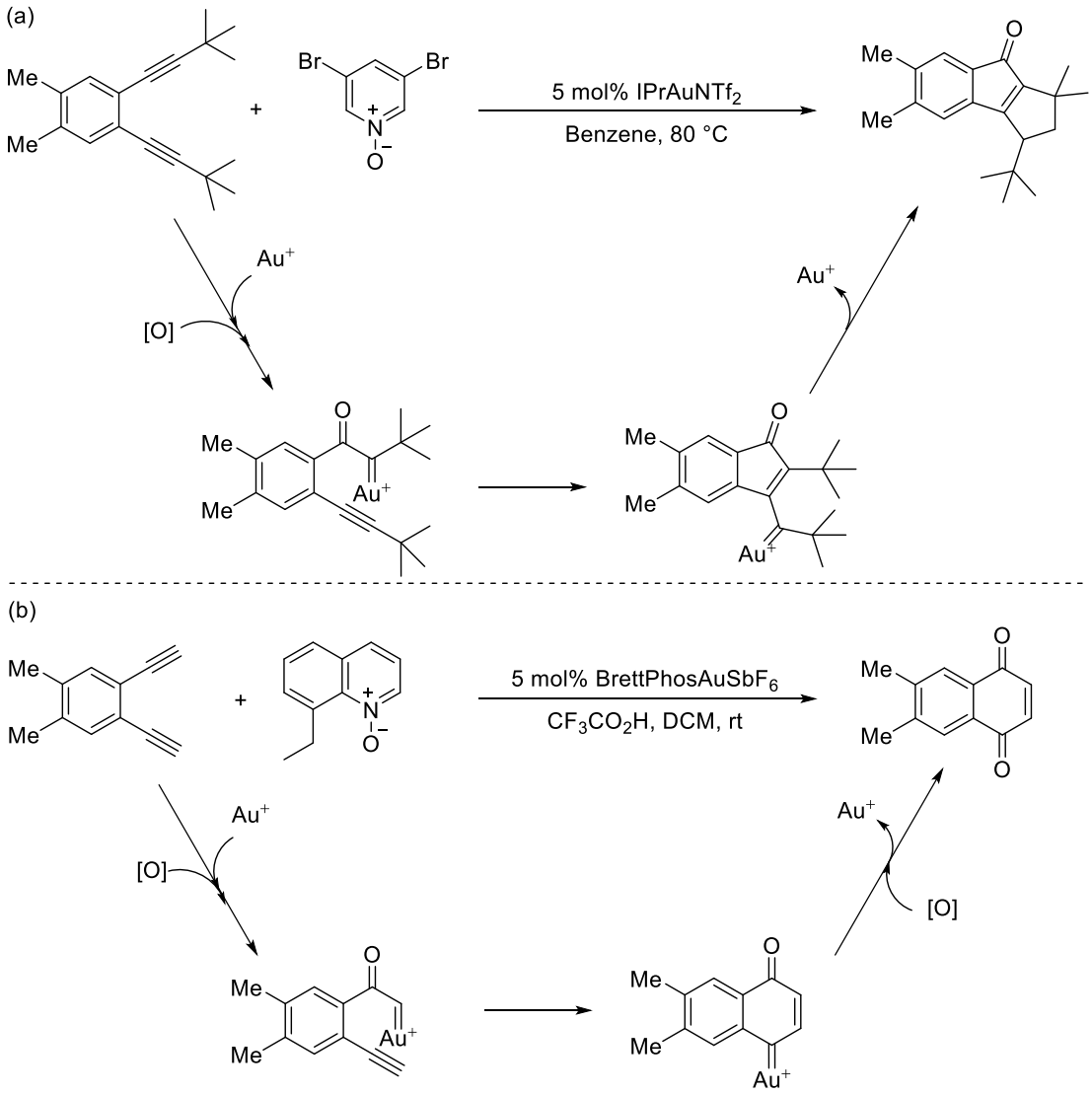
In 2012, Maulide and Skrydstrup et al. independently reported an intra- and intermolecular transfer of the carbon ylides onto terminal alkynes leading to the key intermediate vinyl gold-carbene species, which was trapped by the intramolecular carbonyl-oxygen followed by a subsequent rearrangement to the furan structures (Scheme 15).[35]



Scheme 15. Vinyl gold carbene from the carbon ylides.

In 2013, Hashmi' group described a gold(I)-catalyzed oxidative diyne cyclization to furnish substituted functionalized indenones (Scheme 16a).[36] The vinyl gold-carbene species, generated through an intramolecular 5-*exo*-*dig* carbene transfer of the α-oxo gold-carbene onto the pendent alkyne, was the key intermediate in this reaction, followed by a myriad of carbene transformations. Inspired by this work, Ye and coworkers reported a gold-promoted oxidative cyclization of terminal diynes to

synthesize naphthoquinones via analogous vinyl gold-carbene intermediates, in which the endocyclic gold-carbene was trapped again by the initial pyridine *N*-oxide (Scheme 16b).[37]



Scheme 16. Vinyl gold carbene from the intramolecular carbene transfer.

1.3 Research Objectives and Thesis Outline

In this doctoral thesis, the research interests focus on the development of endocyclic vinyl-carbene chemistry, generated via the gold(I)-triggered intramolecular 6-*endo*-*dig* nucleophilic addition of the diazo-carbon onto the pendent alkyne, followed by the extrusion of N_2. In contrast to diazo quinones (or so called quinone diazides) as the on-ring carbene precursors, this class of diazo-yne reagents, as carbene precursors in the presence of a gold catalyst, can provide an efficient and stable platform for the construction of cyclic molecules with high structural complexity.

In Chapter 2, a gold-catalyzed domino cyclization of diazo-tethered alkynes with nitriles to assembly benzophenanthridine derivatives in high yields is presented. Chapter 3 discloses an unprecedented gold(I)-catalyzed carbohydroxylation of diazo-tethered alkynes with high regioselectivity, controlled by the utilization of $Et_3N(HF)_3$. In Chapter 4, we also describe an intramolecular cascade-fluorination process for the synthesis of aryl fluorides in high yields.

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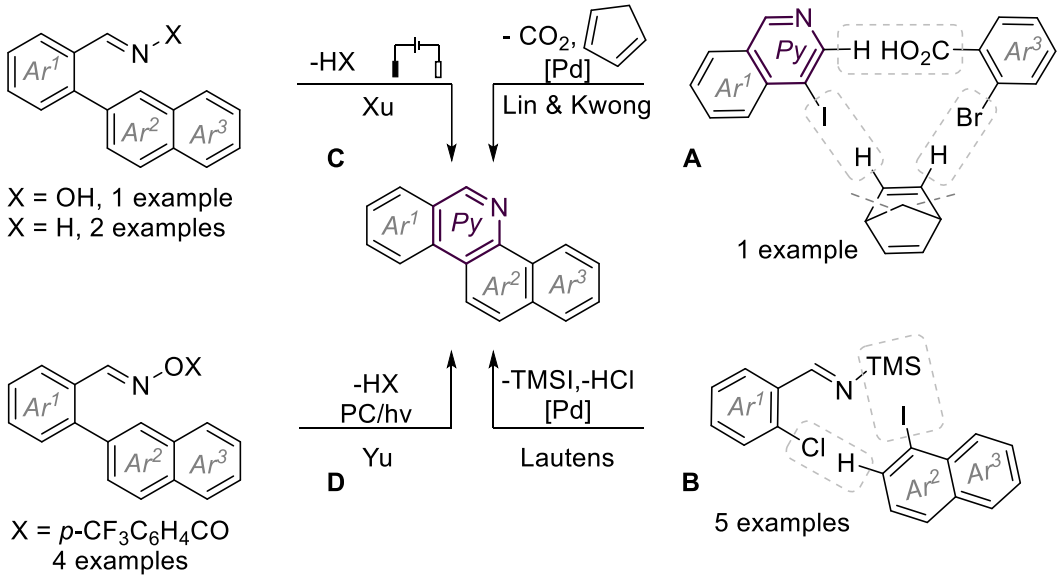
Chapter 2: Practical and Modular Construction of Benzophenanthridine Compounds

2.1 Introduction

The streamlined and efficient synthesis of complex molecules has been a long-standing challenge in organic synthesis. In this context, the search for improved techniques as flexible access to a diverse array of potential target structures is of ongoing interest with impact on natural product synthesis, pharmaceutical chemistry and material science. An important synthetic motif is the benzophenanthridine scaffold, which as a core unit is commonly found in a number of biologically active molecules which possess antimicrobial, antifungal, anti-inflammatory, antiproliferative and optoelectronic properties.[1] In addition, some derivatives are used as antiprotozoal, antibacterial and anticancer agents.[2] So far, over 80 alkaloids containing this structure have been discovered and were isolated from *Fumariaceae*, *Papaverace* and *Rutaceae* plants.[3] Recent approaches for the synthesis of the benzophenanthridine skeleton include the domino direct arylation/N-arylation,[4a] π-extensions of aryl halides,[4b] and intramolecular homolytic aromatic substitutions (HAS).[4c-4e] However, these synthetic strategies generally rely on specially preformed substrates, which often contain a naphthyl group that is imbedded into the final core by the reaction with a complex nitrogen-source (Scheme 1).[4] Still the exploration of a practical, modular, and efficient synthetic protocol to access structurally diverse and/or novel fused benzophenanthridines remains highly sought after.

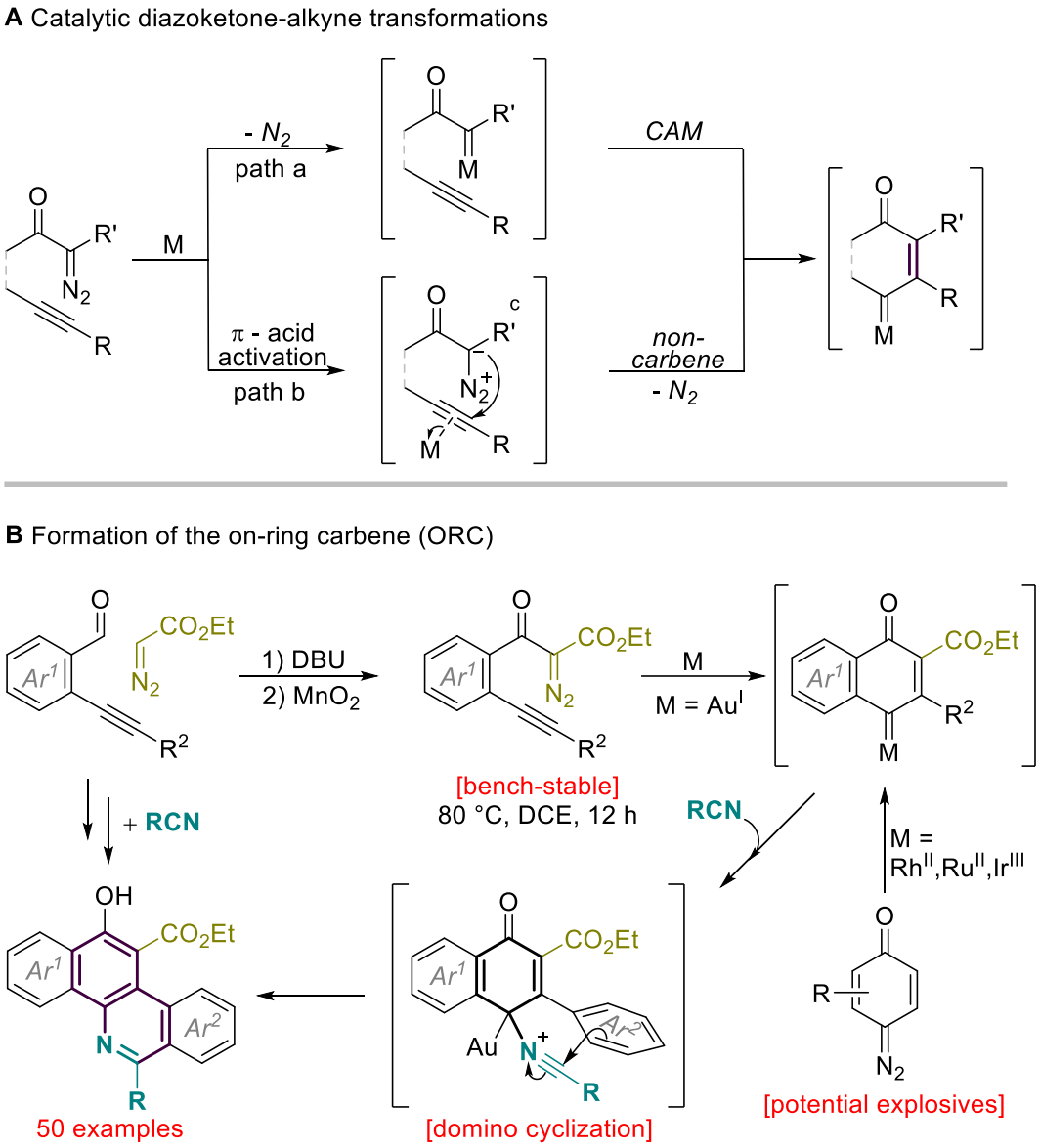


Scheme 1. One-step access to the benzophenanthridine skeletons

Cascade reactions have inspired the imagination of organic chemists because it provides an efficient and universal strategy to assemble complex molecules.[5] Instead of time-consuming and costly procedures including the purification of intermediates

and protection/ deprotection steps of functional groups, this strategy relies on a consecutive series of chemical reactions proceeding in a concurrent fashion.[6] Among these, the transition metal-catalyzed diazo-yne transformation has emerged as a powerful tool for the synthesis of polycyclic molecules.[7] Much of the early work in this context was based on a diazo-derived carbene/alkyne metathesis process (CAM), which after transfer of the initial carbene species onto the pendant alkyne gives rise for a host of transformations, including cyclopropanations, (asymmetric) C−H insertions, oxidative rearrangements and a myriad of cascade reactions (path a, Scheme 1a).[8-9] Exceptional results were observed with the combination of a variety of pendant nucleophiles, especially those containing heteroatomic substituents capable of assembling heterocyclic frameworks during the cascade event.[10] Still one drawback of this approach is the inherent features of a substrate with limited opportunity to modify the patterns of reactivity and selectivity. In recent years, this situation has changed with the development of homogeneous catalysts with different electronic and steric properties, which can overcome some of the inherent preferences for functionalization at a specific group.[11] In the catalytic diazo-yne cascade process, Rh^{I}-, Rh^{II}-, Cu^{II}-, Pd^{0}-, and Ag^{I}-complexes often directly decompose the diazo group to deliver the corresponding carbene species,[7-10] whereas the use of gold catalysts in combination of appropriate ligands can provide the opportunity to prioritize the activation of alkynes toward intra- or intermolecular nucleophiles (path b, Scheme 1a).[12] In this direction, Toste,[13a] Doyle[13b] and Xu[12a] elegantly showed examples of unparalleled selectivity and reactivity patterns in gold-catalyzed diazo-yne cascade reactions, respectively, where the gold catalyst primarily acted as a highly carbophilic π-Lewis acid to activate the alkyne rather than to decompose the diazo group.

Within the frame of our program devoted to the development of gold-catalyzed alkyne cascade cyclizations,[14] Xu and our group recently developed an efficient method for the rapid assembly of a wide set of o-alkynyl diazoacetylbenzene reagents derived from the DBU-catalyzed condensation of o-ethynylbenzaldehyde derivatives with a commercial diazoacetate.[12e] This approach circumvents previously reported material-consuming and dangerous procedures, including the use of diazomethane[15a] or diazo transfer reagents.[15b] In comparison with diazo quinones (or so called quinone diazides) as the on-ring carbene (ORC) precursors,[16] these reagents, as potential ORC precursors generated in-situ via a gold-promoted 6-*endo-dig* diazo-yne carbocyclization (Scheme 1b), can provide an ideal platform for the construction of cyclic molecules with high structural complexity. Inspired by these findings, we became interested in further exploring the reactivity of this ORC with unsaturated bonds and envisioned that the method might be applied to access biologically relevant heterocyclic frameworks. Herein, we report our discovery and development of gold-catalyzed cascade reactions of alkyne-tethered diazoketones and nitriles as modular access to benzophenanthridine derivatives with an excellent functional group compatibility.



Scheme 2. Catalytic metal carbenes

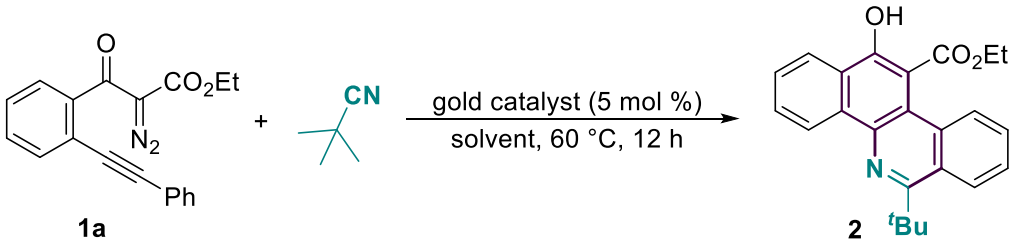
2.2 Results and Discussion

2.2.1 Optimization of the Reaction Conditions

We began with trimethylacetonitrile (2 equivalents) to test the feasibility of an intramolecular diazo-yne (**1a**) cyclization/intermolecular cascade reaction (table 1). In the first experiments, the uncatalyzed reaction between the two components did not occur, and a catalytic amount of $Ph_3PAuSbF_6$ proved to be ineffective (entries 1 and 2). Encouragingly, when the more sterically hindered $^tBu_3PAuSbF_6$ was employed, a substantial amount of decomposition of **1a** was observed, together with a small amount of the desired cascade product **3** (entry 3). The IPr ligand gave a more

efficient reaction, with the product observed in 56% yield (entry 4). Gratifyingly, the reaction with 5 mol % of JohnPhosAuSbF$_6$ in dry 1,2-dichloroethane (DCE) at 60 ˚C, proceeded smoothly to give the desired product **2** in 69% yield (entry 5), while varying the counterion of the gold catalyst from NTf_2^- to SbF_6^- showed little effect (entry 6). The use of toluene as solvent showed minimal evidence of productive cycloaddition (entry 7). Further careful optimization of the reaction parameters led to a combination of 4Å molecular sieves, giving **2a** in 80 % isolated yield with full conversion (entry 8). Notably, no O-H insertion products were observed in this reaction.

Table 1: Optimization of Reaction Conditions[a]

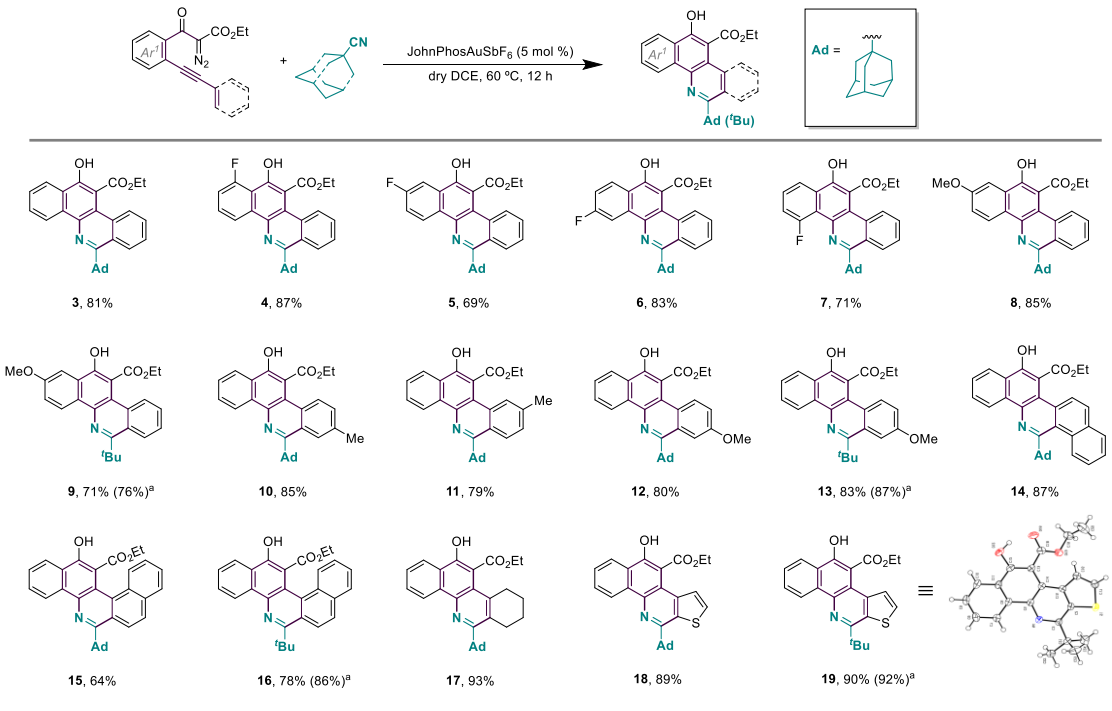


entry	catalyst	solvent	conv. (%)[b]	**2** (%)[b]
1	None	DCE	Nr	-
2	$Ph_3PAuSbF_6$	DCE	< 10	-
3	$^tBu_3PAuSbF_6$	DCE	79	31
5	IPrAuSbF$_6$	DCE	85	56
4	JohnPhosAuSbF$_6$	DCE	100	74
6	JohnPhosAuNTf$_2$	DCE	100	69
7	JohnPhosAuSbF$_6$	Toluene	< 10	-
8[c]	JohnPhosAuSbF$_6$	DCE	100	83 (80)[d]

[*a*] Reaction conditions: a solution of catalyst (5 mol %) in dry DCE (0.5 mL), was added to the solution of **1a** (63.6 mg, 0.2 mmol) and trimethylacetonitrile (45.0 µL, 0.4 mmol) in dry DCE (0.5 mL) in the glove box. Then the reaction mixture was stirred for 12 hours outside the glove box at 60 ˚C. [*b*] Yields were determined by proton NMR with 1,3,5-trimethoxybenzene as internal standard. [*c*] 4Å Molecular sieve (200 mg) was added to the reaction. [*d*] The result in the parentheses is isolated yield.

2.2.2 Substrate Scope

After identification of the optimal conditions, we first investigated the generality and utility of this gold-catalyzed domino cyclization of diazo-tethered alkynes **1** in combination with 1-adamantylnitrile using JohnPhosAuSbF$_6$ as the catalyst. As shown in Scheme 3, a series of fluorine substituents (**3**-**7**) and a methoxy group (**8**, **9**) on the linking aryl unit (Ar^1) were well tolerated, delivering the corresponding products in moderate to high yields (69%–87%). Methyl- (**10**, **11**) and methoxy- (**12**, **13**) substituted aryl alkynes were also applicable to this transformation without a noticeable yield deterioration. Additionally, we found that sterically hindered naphthalene rings (**14**-**16**) at the alkynyl terminus reacted smoothly, indicating that the steric properties of the alkynes have no obvious effects on the reaction's efficiency. Alkenyl (**17**) and thienyl (**18**, **19**) alkynes gave a higher yield than other aryl substituents, presumably because of the increased nucleophilicity of theses electron-rich aryl groups. This cascade strategy was also scalable and provided comparable yields on a 2.0 mmol scale cyclization (**9**, **13**, **16** and **19**). The structure of product **19** was unambiguously confirmed by single crystal X-ray analysis.



Scheme 3. Scope of diazo compounds **1**. *Reaction condition*: a solution of JohnPhosAuSbF$_6$ (7.32 mg, 0.01 mmol) in dry DCE (0.5 mL), was added a solution of **1** (0.2 mmol) and the nitrile (0.4 mmol) in dry DCE (0.5 mL) in the glove box, then the reaction mixture was stirred for 12.0 hours at 60 ˚C outside the glove box. Isolated yields are listed. Note: all reagents should be dried before use. [a] At 2.0 mmol scale.

Encouraged by these results, we continued to explore this protocol with respect to nitriles under the optimal reaction conditions (Scheme 4). Tertiary (**18**, **19**), secondary

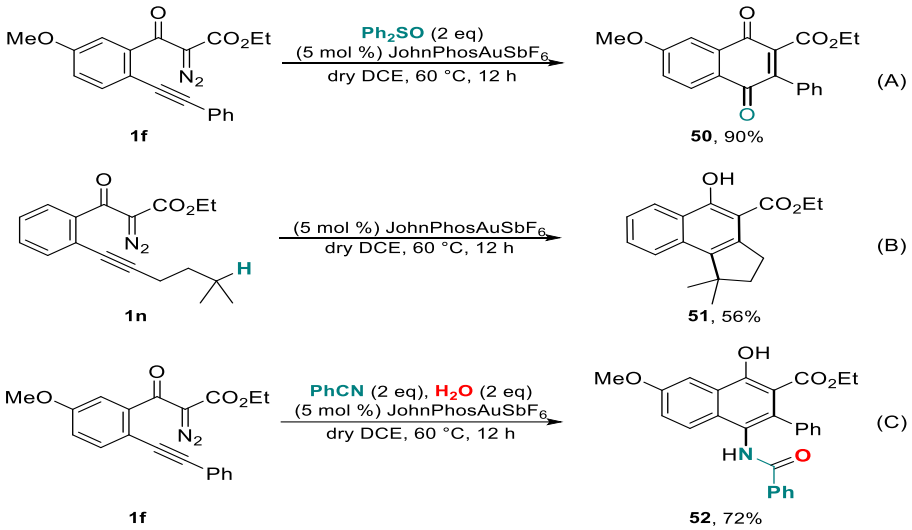
(**20**), strained-cyclic (**21**), primary (**22**, **23**) and deuterated (**24**) nitriles successfully underwent the domino cyclization with diazo-yne substrate **1n** to afford the desired products in good yields. The introduction of cyano (**25**), alkenyl (**26**) and alkynyl (**27**) groups to the nitrile were compatible with the applied conditions. Going further, a

Scheme 4. Scope of nitriles. *Reaction condition*: a solution of JohnPhosAuSbF$_6$ (7.32 mg, 0.01 mmol) in dry DCE (0.5 mL), was added to the solution of **1** (0.2 mmol) and the nitrile (0.4 mmol) in dry DCE (0.5 mL) in the glove box, then the reaction mixture was stirred for 12.0 hours at 60 ˚C. Isolated yields are listed. Note: all reagents should be dried before use.

variety of aryl nitriles bearing electron-withdrawing, electron-neutral and electron-donating substituents underwent this reaction, provided the corresponding adducts **28**–**39** in moderate to excellent yield. Substrates with *para*- (**28**-**33**), *meta*- (**34**), and *ortho*- (**35**-**40**) substituents on the aryl moiety effectively reacted with **1m** to produce the desired products in synthetically useful to high yields. The reaction also proceeded smoothly with heteroaromatic nitriles, providing the corresponding products **41** and **42** in excellent yields. Notably, substrates bearing common sensitive functional groups such as azide and unprotected phenols underwent the reaction and gave the corresponding products **44** and **43** in good to high yield. This is noteworthy as these units are known to react in traditional carbene transformations. Heteroaromatic, alkenyl and naphthyl substrates were successfully cyclized with anα-cyanonaphthalene to afford the naphthyl-benzophenanthridine compounds (**46**-**79**) in good yields, which enriched the library of biaryl axes.

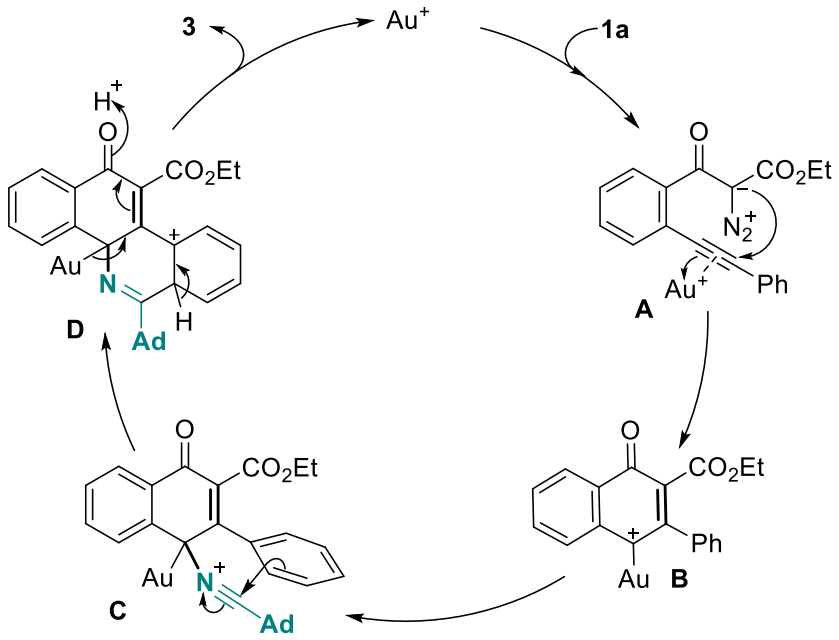
2.3 Mechanistic study

We conducted a series of control experiments to gain some insight into the mechanism. To verify the existence of the on-ring carbene (ORC) intermediate, the oxidation reaction with the substrate **1l** in the presence of diphenylsulfoxide, instead of the nitrile, was conducted under standard conditions, and the corresponding oxidation product **51** was isolated in 90% yield (Scheme 5A). As further evidence for the intermediacy of the carbene intermediate, a gold-catalyzed 6-*endo*-*dig* diazo-yne carbocyclization was terminated by a tertiary C−H bond insertion to form polycyclic product **52** in 56% yield (Scheme 5B). In addition, a non-concerted, step-wise mechanism of the intermolecular cyclization process was well supported by the interception reaction with an external acceptor. The identifiable three-component product **53** was isolated in 72% yield when the reaction was carried out in the presence of water (Scheme 5C).



Scheme 5. Control experiments. a) Oxidation of a gold carbene species with diphenylsulfoxide; b) C_{sp3}-H Insertion; c) Trapping experiment with H_2O.

Based on the above studies and the literature,[12, 13] a possible mechanism is proposed for this cascade reaction in Scheme 6.[17] Initially, Au(I) acts as a highly carbophilic π-Lewis acid, selectively activating the alkynyl group to form the gold π-complex **A**. Subsequently, an intramolecular 6-*endo-dig* nucleophilic addition of the diazo-carbon atom onto the gold-activated alkyne and then irreversible extrusion of N_2 can generate the ORC species **B**. This ORC intermediate is then trapped by the nitrile to furnish carbocation **C**,[18] followed by a domino cyclization with the pendant aryl group (**D**)/aromatization, furnishing the corresponding polycyclic product **3** under liberation of the gold catalyst.



Scheme 5. Proposed mechanism.

2.4 Conclusions

We have developed a gold-catalyzed domino reaction with high chemoselectivity, accomplished with easy avalible diazoacetate-derived substrates **1** and low cost, simple starting nitriles, leading to a variety of benzophenanthridine derivatives. The enabling feature of this reaction is the use of a nitrile as a nitrogen source through a programmed insertion/cation-transfer strategy. This methodology complements the common C_{SP2}-H insertion strategies in terms of reaction efficiency and structural diversity. As a result, we expect this protocol to have a substantial effect on drug discovery, specifically in how alkaloid replacements are designed and incorporated into targets of interest.

2.5 References

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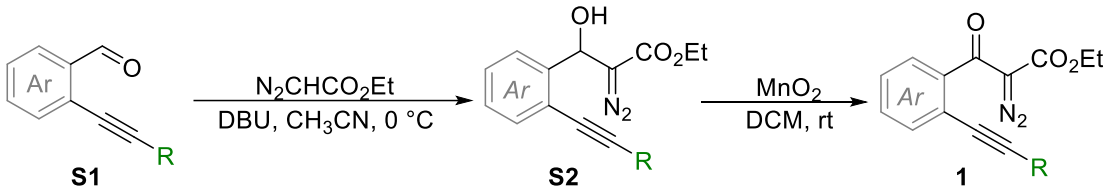
2.6 Experimental Section

2.6.1 General Information

Chemicals were purchased from commercial suppliers and used as delivered. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the

following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. Chemical shifts are given in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet) and comp (combined peaks). When combinations of multiplicities are given the first character noted refers to the biggest coupling constant. All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH_2-group), q (quartet, CH_3-group)] were determined by DEPT135 spectra. Mass spectra (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^{+}-, ESI^{-}- or $DART^{-}$-spectra a Bruker Apex-Qu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger and T. Oeser on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation

2.6.2 Experimental Procedure: Synthesis of Diazo-tethered alkynes 1.[1]



All **S1** were prepared by were prepared through Sonogashira couplings.[2]

Synthesis of S2: To a solution of ethyl diazoacetate (EDA, 1.37 g, 12.0 mmol) in CH_3CN (10.0 mL), **S1** (10.0 mmol) and 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU, 0.15 g, 1.0 mmol) were added at 0 ˚C in sequence. After the mixture was stirred overnight, the reaction was quenched with saturated aqueous NH_4Cl and then extracted with dichloromethane (3 × 20.0 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was evaporated under vacuum after filtration. The obtained product **S2** was directly used for the next step without further purification.

Synthesis of 1: To a 50-mL glass bottle containing a magnetic stirring bar, the above obtained product **S2** in DCM (20.0 mL), was added manganese dioxide (MnO_2, 8.70 g, 100.0 mmol) slowly at room temperature. The reaction mixture was stirred at overnight and then the solvent was evaporated under vacuum after filtering through Celite, and the resulting residues was purified by column chromatography on silica gel (eluent: petroleum ether/ ethyl acetate = 10:1) to give the pure diazoacetates **1**

(yield based on **S1**).

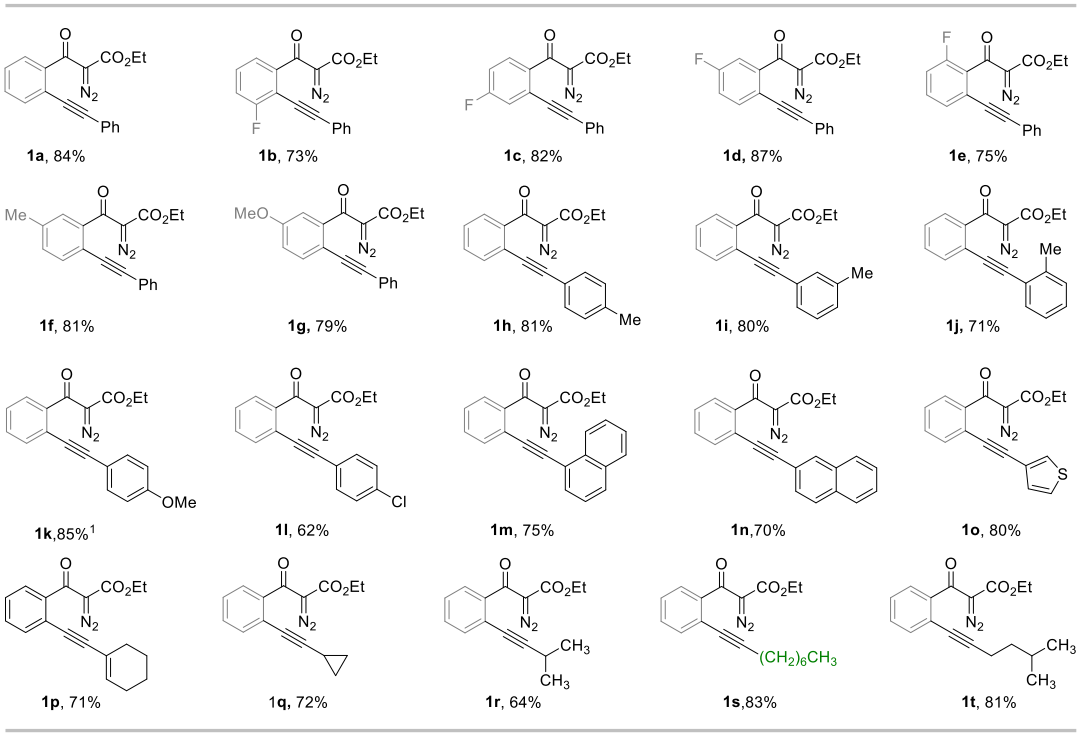
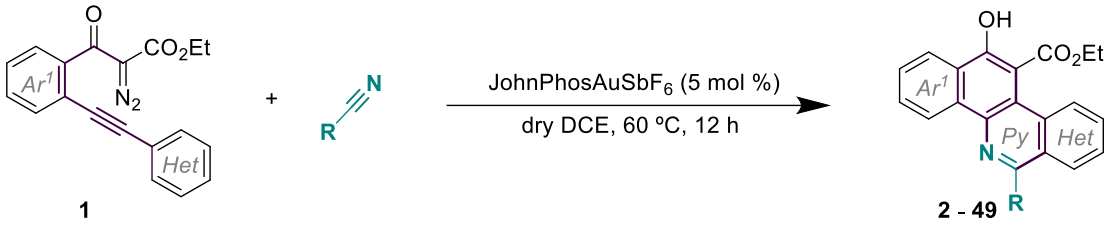


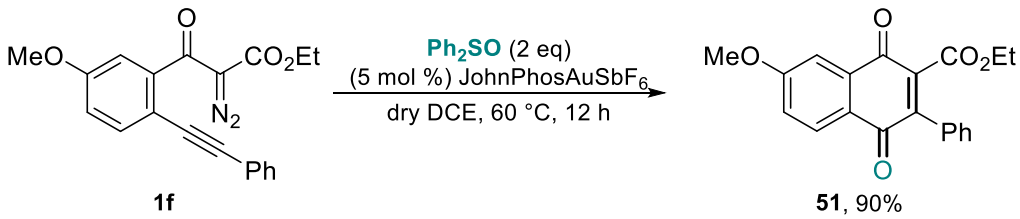
Figure S1. Scope of tethered diazo alkynes

2.6.3 Experimental Procedure: Gold-catalyzed Domino Cyclization of Diazo-ynes with Nitriles



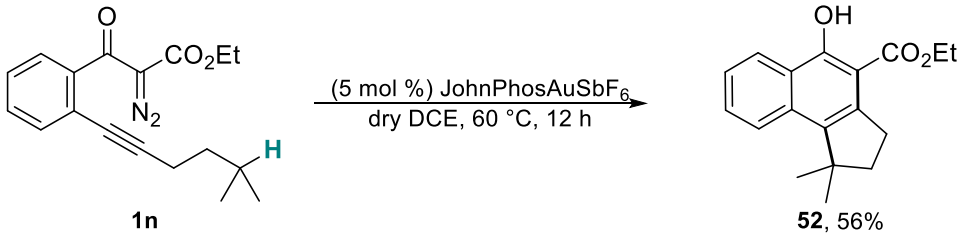
The substrate **1** (0.2 mmol), dry 1,2-dichloroethane (DCE, 0.5 mL), nitrile (0.4 mmol, dry before use), and activated 4Å molecular (30 mg) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAuSbF$_6$, 7.3 mg, 0.01 mmol) in dry DCE (0.5 mL) using a syringe was added over 2 minutes at room temperature. After the addition, the reaction mixture was stirred at 60 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/10) to afford the pure benzophenanthridine derivatives **2-49**.

2.6.4 Experimental Procedure: Gold-catalyzed oxidative rearrangements



The substrate **1f** (70 mg, 0.2 mmol), dry 1,2-dichloroethane (DCE, 0.5 mL), and phenyl sulfoxide (81.0 mg, 0.4 mmol), were mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAuSbF$_6$, 7.3 mg, 0.01 mmol) in dry DCE (0.5 mL) using a syringe was added over 2 minutes at room temperature. After the addition, the reaction mixture was stirred at 60 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/10) to afford the pure product **51** in 90% yield. white solid, mp 107.0 – 109.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.09 (d, J = 8.7 Hz, 1H), 7.55 (d, J = 2.7 Hz, 1H), 7.46 – 7.35 (m, 5H), 7.25 (dd, J = 8.7, 2.7 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.96 (s, 3H), 1.05 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 183.1 (s), 182.3 (s), 164.6 (s), 164.2 (s), 144.8 (s), 139.3 (s), 133.6 (s), 131.7 (s), 129.9 (d), 129.7 (d), 129.5 (d, 2C), 128.2 (d, 2C), 125.3 (s), 121.1 (d), 109.6 (d), 62.0 (t), 56.2 (q), 13.9 (q); HRMS (ESI) (*m/z*) $[M+H]^+$ $C_{20}H_{17}O_5$ calcd for 337.1071, found 337.1082.

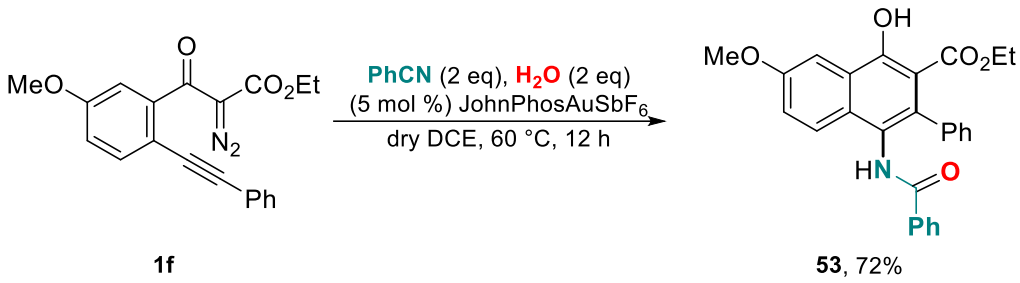
2.6.5 Experimental Procedure: Gold-catalyzed C-H annulation of Diazo-ynes



The substrate **1n** (63 mg, 0.2 mmol) and dry 1,2-dichloroethane (DCE, 0.5 mL) were added into a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAuSbF$_6$, 7.3 mg, 0.01 mmol) in dry DCE (0.5 mL) using a syringe was added over 2 minutes at room temperature. After the addition, the reaction mixture was stirred at 60 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/15) to afford the desired product **52** in 56% yield. white solid, mp 103.0 – 105.0 °C; R_f = 0.4 (EA/PE = 1/15); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.53 (s, 1H), 8.50 – 8.42 (m, 1H), 8.09 (d, J = 8.5 Hz, 1H), 7.61 – 7.55 (m, 1H), 7.47 – 7.41 (m, 1H), 4.46 (q, J = 7.2 Hz, 2H), 3.27 (t, J = 7.5 Hz, 2H), 2.02 (t, J = 7.5 Hz, 2H), 1.54 (s, 6H), 1.46 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.5 (s), 161.5 (s), 138.9 (s), 137.0 (s), 133.3 (s), 129.1

(d), 125.3 (d), 125.0 (s), 124.3 (d), 123.6 (d), 104.2 (s), 61.5 (t), 45.2 (s), 43.1 (t), 32.8 (t), 28.9 (q), 14.4 (q); HRMS (ESI) (*m/z*) $[M+Na]^+$ $C_{18}H_{20}NaO_3$ calcd for 307.1305, found 307.0969.

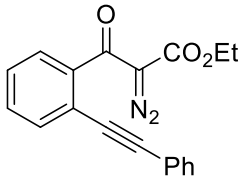
2.6.6 Experimental Procedure: Gold-catalyzed Domino Cyclization of Diazo-ynes with Nitriles



1f **53**, 72%

The substrate **1f** (70 mg, 0.2 mmol), dry 1,2-dichloroethane (DCE, 0.5 mL), benzonitrile (41 mg, 0.4 mmol), and water (7.2 mg, 0.4 mmol) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAuSbF$_6$, 7.3 mg, 0.01 mmol) in dry DCE (0.5 mL) using a syringe was added over 2 minutes at room temperature. After the addition, the reaction mixture was stirred at 60 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/3) to afford the pure product **53** in 72% yield. white solid, mp 117.8 – 120.3 °C; R_f = 0.4 (EA/PE = 1/3); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.61 (s, 1H), 7.81 – 7.73 (m, 2H), 7.48 – 7.39 (comp, 3H), 7.36 – 7.28 (comp, 6H), 7.25 – 7.19 (m, 2H), 7.13 (br, 1H), 4.01 – 3.93 (comp, 5H), 0.70 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.8 (s), 167.9 (s), 160.3 (s), 158.3 (s), 140.5 (s), 134.7 (s), 134.5 (s), 131.7 (d), 129.0 (s), 128.7 (d, 2C), 128.5 (d, 2C), 128.1 (d, 2C), 127.1 (d, 2C), 126.9 (d), 126.3 (s), 125.8 (d), 123.4 (s), 123.0 (d), 106.4 (s), 102.7 (d), 61.2 (t), 55.8 (q), 13.0 (q); IR (reflection) $\tilde{\nu}$ = 2972.13, 2932.60, 1724.13, 1649.36, 1595.63, 1502.86, 1464.27, 1446.01, 1413.21, 1374.14, 1328.50, 1224.26, 1182.26, 1095.24, 1027.78, 832.10, 757.93, 702.53, 655.09, 615.37 cm^{-1}; HRMS (ESI) (*m/z*) $[M+H]^+$ $C_{27}H_{24}NO_5^+$ calcd for 442.1649, found 442.1655.

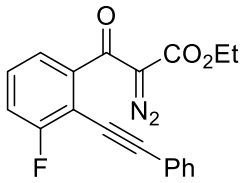
2.6.7 Characterization



Ethyl 2-diazo-3-oxo-3-(2-(phenylethynyl)phenyl)propanoate (1a)

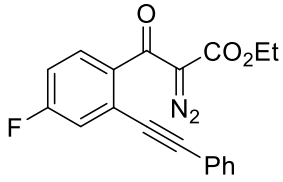
Yield: 2.67g, 84%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz,

$CDCl_3$) δ (ppm) 7.60 – 7.53 (m, 1H), 7.50 – 7.39 (comp, 5H), 7.38 – 7.30 (comp, 3H), 4.16 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.3 (s), 161.0 (s), 140.7 (s), 132.1 (d), 131.6 (d, 2C), 130.5 (d), 128.8 (d), 128.5 (d, 2C), 128.4 (d), 127.3 (d), 122.8 (s), 121.1 (s), 94.1 (s), 86.7 (s), 61.8 (t), 14.0 (q); IR (reflection) ṽ = 3060.59, 2982.34, 2936.80, 2906.09, 2216.47, 2130.81, 1969.53, 1686.79, 1624.47, 1493.00, 1474.94, 1442.99, 1394.84, 1367.27, 1245.39, 1114.36, 1012.09, 932.74, 826.19, 775.61, 749.52, 697.40, 658.00 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{14}N_2O_3$ calcd for 318.1004, found 318.1025.



Ethyl 2-diazo-3-(3-fluoro-2-(phenylethynyl)phenyl)-3-oxopropanoate (1b)

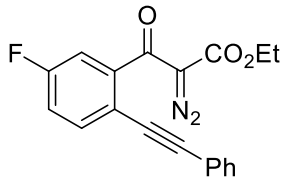
Yield: 2.46 g, 73%; Yellow liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.57 – 7.48 (comp, 2H), 7.45 – 7.32 (comp, 4H), 7.29 – 7.10 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 185.9 (d, J_{C-F} = 3.2 Hz), 162.1 (d, J_{C-F} = 253.0 Hz), 160.7 (s), 142.4 (s), 131.7 (d, 2C), 129.7 (d, J_{C-F} = 8.3 Hz), 129.1 (d), 128.5 (d, 2C), 122.8 (d, J_{C-F} = 3.6 Hz), 122.4 (s), 117.4 (d, J_{C-F} = 21.5 Hz), 110.2 (d, J_{C-F} = 17.9 Hz), 99.1 (d, J_{C-F} = 3.7 Hz), 80.0 (s), 61.8 (t), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.2 (s); IR (reflection) ṽ = 3059.81, 2983.34, 2937.48, 2907.06, 2219.76, 2132.30, 1722.46, 1698.45, 1633.71, 1567.98, 1494.13, 1458.49, 1443.87, 1393.42, 1370.09, 1301.97, 1279.36, 1251.35, 1201.76, 1171.38, 1124.40, 1069.81, 1020.55, 916.44, 873.06, 796.20, 752.43, 689.77 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FN_2O_3$ calcd for 336.0910, found 336.0914.



Ethyl 2-diazo-3-(4-fluoro-2-(phenylethynyl)phenyl)-3-oxopropanoate (1c)

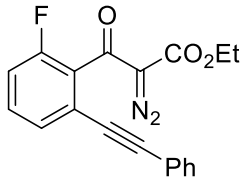
Yield: 2.76 g, 82%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.19 – 7.07 (comp, 3H), 7.08 – 6.97 (comp, 3H), 6.96 – 6.88 (m, 1H), 6.82 – 6.72 (m, 1H), 3.84 (q, *J* = 7.2 Hz, 2H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 186.1 (s), 163.4 (d, J_{C-F} = 251.6 Hz), 160.9 (s), 136.8 (d, J_{C-F} = 3.4 Hz), 131.6 (d, 2C), 129.7 (d, *J* = 9.4 Hz), 129.0 (d), 128.5 (d, 2C), 123.6 (d, J_{C-F} = 10.3 Hz), 122.1 (s), 118.8 (d, J_{C-F} = 23.5 Hz), 115.69 (d, J_{C-F} = 22.0 Hz), 95.0 (s), 85.6 (d, J_{C-F} = 3.0 Hz), 61.7 (t), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.0 (s); IR (reflection) ṽ = 3072.48, 2981.52, 2906.23, 2214.23, 2140.80, 1714.27, 1617.39, 1600.26, 1568.91, 1495.86, 1476.52, 1442.14, 1412.62, 1396.27, 1371.69,

1317.72, 1273.03, 1244.09, 1207.52, 1171.56, 1137.94, 1118.10, 1083.75, 1072.90, 1020.67, 965.48, 956.73, 932.32, 875.27, 840.36, 818.56, 761.87, 739.33, 700.82, 691.07, 630.08, 610.73 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FN_2O_3$ calcd for 336.0910, found 336.0905.



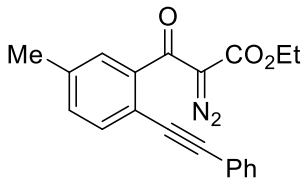
Ethyl 2-diazo-3-(5-fluoro-2-(phenylethynyl)phenyl)-3-oxopropanoate (1d)

Yield: 2.93 g, 87%; White solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.59 – 7.51 (m, 1H), 7.50 – 7.43 (comp, 2H), 7.41 – 7.29 (comp, 3H), 7.26 – 7.05 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 185.8 (d, J_{C-F} = 2.0 Hz), 162.0 (d, J_{C-F} = 251.7 Hz), 160.7 (s), 142.5 (d, J_{C-F} = 7.3 Hz), 134.0 (d, J_{C-F} = 8.1 Hz), 131.5 (d, 2C), 128.8 (d), 128.4 (d, 2C), 122.50 (s), 117.6 (d, J_{C-F} = 22.0 Hz), 117.3 (d, J_{C-F} = 3.7 Hz), 114.6 (d, J_{C-F} = 24.1 Hz), 93.7 (d, J_{C-F} = 1.6 Hz), 85.6 (s), 61.8 (t), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.9 (s); IR (reflection) ṽ = 3650.81, 3434.28, 3066.05, 2983.77, 2938.49, 2906.60, 2871.97, 2559.77, 2398.52, 2219.50, 2124.79, 1971.78, 1892.01, 1717.69, 1627.36, 1604.34, 1575.27, 1493.80, 1478.05, 1443.41, 1416.06, 1368.83, 1279.78, 1209.15, 1118.28, 1086.48, 1016.56, 979.13, 915.98, 866.59, 825.03, 805.41, 752.93, 689.20, 672.86, 617.34 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FN_2O_3$ calcd for 336.0910, found 336.0925.



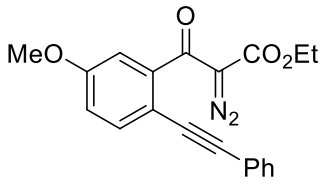
Ethyl 2-diazo-3-(2-fluoro-6-(phenylethynyl)phenyl)-3-oxopropanoate (1e)

Yield: 2.52 mg, 75%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.50 – 7.42 (comp, 2H), 7.42 – 7.29 (comp, 5H), 7.14 – 7.04 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 182.9 (d, J_{C-F} = 1.3 Hz), 160.4 (s), 157.1 (s), 131.7 (d, 2C), 131.2 (d, J_{C-F} = 9.1 Hz), 129.0 (d), 128.5 (d, 2C), 128.0 (d, J_{C-F} = 3.2 Hz), 122.7 (d, J_{C-F} = 4.9 Hz), 122.4 (s), 115.8 (d, J_{C-F} = 21.5 Hz), 94.4 (s), 85.4 (d, J_{C-F} = 4.0 Hz), 61.8 (t), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -115.68 (s); IR (reflection) ṽ = 3079.05, 2983.48, 2937.61, 2213.06, 2135.61, 1955.72, 1700.86, 1627.36, 1604.58, 1562.01, 1492.30, 1458.91, 1394.53, 1367.82, 1238.09, 1113.77, 1065.16, 1011.16, 975.74, 929.95, 829.39, 794.13, 751.97, 689.72 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FN_2O_3$ calcd for 336.0910, found 336.0928.



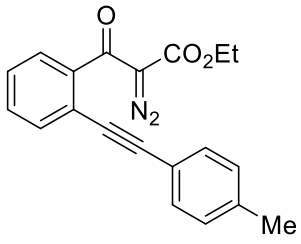
Ethyl 2-diazo-3-(5-methyl-2-(phenylethynyl)phenyl)-3-oxopropanoate (1f)

Yield: 2.69 g, 81%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.57 – 7.47 (comp, 2H), 7.47 – 7.31 (comp, 5H), 7.29 – 7.21 (m, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.1 (s), 161.0 (s), 140.9 (s), 137.7 (s), 132.6 (d), 131.5 (d, 2C), 129.2 (d), 128.6 (d), 128.4 (d, 2C), 127.5 (d), 122.8 (s), 121.1 (s), 93.6 (s), 86.9 (s), 61.6 (t), 21.2 (q), 14.0 (q); IR (reflection) ṽ =3059, 2982, 2926, 2872, 2139, 1726, 1695, 1629, 1600, 1496, 1443, 1396, 1370, 1307, 1280, 1252, 1208, 1177, 1124, 1096, 1015, 944, 921, 827, 758, 691, 627 cm^{-1}; HRMS (EI) [M-2N] $C_{20}H_{16}O_3$ calcd for 304.1099, found 304.1124.



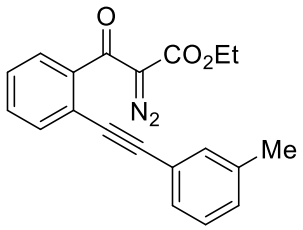
Ethyl 2-diazo-3-(5-methoxy-2-(phenylethynyl)phenyl)-3-oxopropanoate (1g)

Yield: 2.75 g, 79%; Yellow solid; R_f = 0.5 (EA/PE = 1/5); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.55 – 7.43 (comp, 3H), 7.41 – 7.29 (comp, 3H), 7.05 – 6.96 (m, 2H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 186.9 (s), 160.9 (s), 159.5 (s), 141.9 (s), 133.5 (d), 131.3 (d, 2C), 128.38 (d, 2C), 128.35 (d), 123.0 (s), 116.6 (d), 113.2 (s), 112.4 (d), 92.7 (s), 86.6 (s), 61.7 (t), 55.5 (q), 14.0 (q); IR (reflection) ṽ = 3073.31, 2982.93, 2938.26, 2842.27, 2128.61, 1717.45, 1618.59, 1593.61, 1497.69, 1464.34, 1450.93, 1415.10, 1393.06, 1371.08, 1325.34, 1298.23, 1275.90, 1248.11, 1233.20, 1188.56, 1169.28, 1138.04, 1087.69, 1019.59, 983.29, 909.08, 881.57, 867.45, 833.49, 792.25, 762.12, 747.97, 716.38, 683.57, 669.76, 624.81 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{16}N_2O_3$ calcd for 348.1110, found 348.1105.



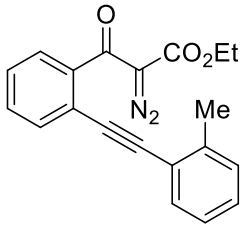
Ethyl 2-diazo-3-oxo-3-(2-(*p*-tolylethynyl)phenyl)propanoate (1h)

Yield: 2.69 g, 81%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.57 – 7.51 (m, 1H), 7.48 – 7.32 (comp, 5H), 7.21 – 7.12 (m, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.4 (s), 161.0 (s), 140.6 (s), 139.0 (s), 132.0 (d), 131.5 (d, 2C), 130.4 (d), 129.2 (d, 2C), 128.2 (d), 127.2 (d), 121.3 (s), 119.7 (s), 94.4 (s), 86.1 (s), 61.7 (t), 21.6 (q), 14.0 (q); IR (reflection) ṽ = 2990, 2213, 2139, 1721, 1617, 1591, 1510, 1474, 1445, 1387, 1366, 1320, 1281, 1244, 1176, 1134, 1118, 1093, 1041, 1018, 950, 937, 819, 776, 750, 738, 706, 675, 646 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{16}N_2O_3$ calcd for 332.1161, found 332.1147.



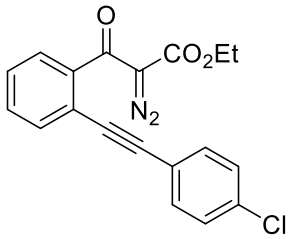
Ethyl 2-diazo-3-oxo-3-(2-(*m*-tolylethynyl)phenyl)propanoate (1i)

Yield: 2.66 g, 80%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.58 – 7.53 (m, 1H), 7.49 – 7.39 (comp, 3H), 7.31 – 7.23 (comp, 3H), 7.19 – 7.13 (m, 1H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 187.4 (s), 161.1 (s), 140.8 (s), 138.3 (s), 132.3 (d), 132.2 (d), 130.6 (d), 129.8 (d), 128.8 (d), 128.5 (d), 128.4 (d), 127.3 (d), 122.6 (s), 121.3 (s), 94.5 (s), 86.5 (s), 61.8 (t), 21.4 (q), 14.1 (q); IR (reflection) ṽ = 3062, 2983, 2925, 2139, 1727, 1696, 1633, 1600, 1489, 1445, 1394, 1370, 1305, 1250, 1176, 1121, 1095, 1015, 936, 877, 830, 784, 755, 690, 656 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{16}N_2O_3$ calcd for 332.1161, found332.1185.



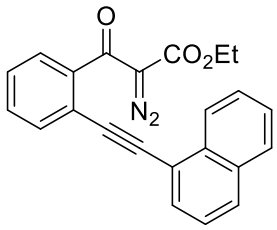
Ethyl 2-diazo-3-oxo-3-(2-(*o*-tolylethynyl)phenyl)propanoate (1j)

Yield: 2.36 g, 71%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.64 – 7.56 (m, 1H), 7.55 – 7.32 (comp, 4H), 7.31 – 7.16 (comp, 3H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.50 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.4 (s), 160.8 (s), 140.5 (s), 140.1 (s), 132.2 (d), 132.1 (d), 130.3 (d), 129.6 (d), 128.8 (d), 128.2 (d), 126.9 (d), 125.7 (d), 122.6 (s), 121.2 (s), 93.0 (s), 90.5 (s), 61.7 (t), 20.5 (q), 14.0 (q), 0.2 (d); IR (reflection) ṽ = 3062, 3022, 2983, 2908, 2213, 2141, 1726, 1696, 1634, 1593, 1491, 1445, 1370, 1320, 1249, 1176, 1124, 1092, 1015, 936, 863, 828, 757, 715, 691, 656 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{16}N_2O_3$ calcd for 332.1161, found 332.1144.



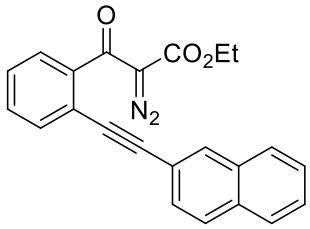
Ethyl 3-(2-((4-chlorophenyl)ethynyl)phenyl)-2-diazo-3-oxopropanoate (1l)

Yield: 2.19 g, 62%; Yellow solid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.59 – 7.53 (m, 1H), 7.50 – 7.37 (comp, 5H), 7.37 – 7.28 (comp, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.1 (s), 161.0 (s), 140.6 (s), 134.8 (s), 132.8 (d, 2C), 132.1 (d), 130.5 (d), 128.8 (d,2C), 128.5 (d), 127.3 (d), 121.2 (s), 120.7 (s), 92.8 (s), 87.7 (s), 61.7 (t), 14.0 (q); IR (reflection) ṽ = 2988.97, 2138.39, 1719.99, 1674.22, 1618.43, 1593.12, 1490.71, 1474.45, 1444.13, 1395.23, 1365.60, 1318.08, 1279.98, 1244.68, 1176.52, 1162.65, 1134.05, 1117.31, 1087.03, 1067.48, 1041.83, 1013.85, 938.34, 867.59, 854.24, 827.90, 778.35, 767.79, 754.01, 736.84, 717.39, 706.60, 695.43, 659.83, 648.09 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}ClN_2O_3$ calcd for 352.0615, found 352.0589.



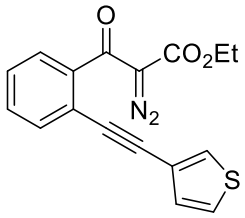
Ethyl 2-diazo-3-(2-(naphthalen-1-ylethynyl)phenyl)-3-oxopropanoate (1m)

Yield: 2.76 g, 75%; Yellow liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.32 (d, *J* = 8.3 Hz, 1H), 7.95 – 7.83 (comp, 2H), 7.79 – 7.68 (comp, 2H), 7.65 – 7.59 (m, 1H), 7.59 – 7.42 (comp, 5H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.06 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 187.6 (s), 160.8 (s), 140.7 (s), 133.3 (s), 133.3 (s), 132.3 (d), 130.7 (d), 130.5 (d), 129.3 (d), 128.5 (d), 128.4 (d), 127.1 (d, 2C), 126.6 (d), 126.1 (d), 125.4 (d), 121.2 (s), 120.5 (s), 92.3 (s), 91.6 (s), 61.7 (s), 14.0 (s); IR (reflection) ṽ = 3059, 2982, 2936, 2905, 2140, 1725, 1696, 1632, 1593, 1507, 1479, 1444, 1396, 1369, 1301, 1256, 1173, 1123, 1098, 1012, 934, 863, 801, 773, 754, 681, 654 cm^{-1}; HRMS (EI) (*m/z*) $C_{32}H_{16}O_3$ calcd for 340.1099, found 340.1193.



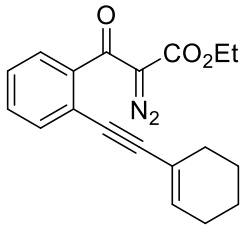
Ethyl 2-diazo-3-(2-(naphthalen-2-ylethynyl)phenyl)-3-oxopropanoate (1n)

Yield: 2.58 g, 70%; Yellow solid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.99 (s, 1H), 7.87 – 7.75 (comp, 3H), 7.64 – 7.58 (m, 1H), 7.54 – 7.39 (comp, 6H), 4.17 (q, *J* = 7.1 Hz, 2H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.3 (s), 161.0 (s), 140.7 (s), 133.0 (s), 133.0 (s), 132.2 (d), 131.7 (d), 130.5 (d), 128.4 (d), 128.20 (d), 128.16 (d), 127.91 (d), 127.86 (d), 127.3 (d), 127.0 (d), 126.8 (d), 121.2 (s), 120.0 (s), 94.5 (s), 87.1 (s), 61.8 (t), 14.1 (q); IR (reflection) ṽ = 3058, 2982, 2936, 2904, 2139, 1725, 1694, 1631, 1597, 1502, 1476, 1443, 1393, 1369, 1304, 1250, 1173, 1115, 1090, 1015, 955, 933, 894, 859, 817, 747, 671, 647 cm^{-1}; HRMS (EI) (*m/z*) $C_{32}H_{16}O_3$ calcd for 340.1099, found 340.1231.

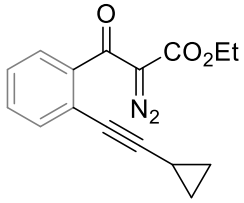


Ethyl 2-diazo-3-oxo-3-(2-(thiophen-3-ylethynyl)phenyl)propanoate (1o)

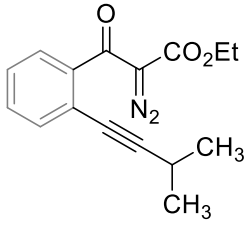
Yield: 2.59 g, 80%; Brown liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.54 – 7.50 (m, 1H), 7.50 – 7.47 (m, 1H), 7.47 – 7.38 (comp, 3H), 7.29 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.12 (dd, *J* = 5.0, 1.1 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.3 (s), 161.1 (s), 140.6 (s), 132.0 (d), 130.5 (d), 129.8 (d), 129.3 (d), 128.3 (d), 127.3 (d), 125.7 (d), 121.8 (s), 121.1 (s), 89.3 (s), 86.3 (s), 61.8 (t), 14.0 (q); IR (reflection) ṽ = 3107, 3063, 2982, 2937, 2905, 2871, 2209, 2138, 1721, 1694, 1628, 1593, 1562, 1523, 1475, 1445, 1393, 1369, 1296, 1247, 1205, 1174, 1122, 1094, 1039, 1014, 932, 870, 836, 780, 755, 698, 662, 624 cm^{-1}; HRMS (EI) (*m/z*) $C_{17}H_{12}N_2O_3S$ calcd for 324.0569, found 324.0537.



Ethyl 3-(2-(cyclohex-1-en-1-ylethynyl)phenyl)-2-diazo-3-oxopropanoate (1p)
Yield: 2.29 g, 71%; Brown liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.44 – 7.31 (comp, 4H), 6.22 – 6.12 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.19 – 2.08 (comp, 4H), 1.72 – 1.57 (comp, 4H), 1.13 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.5 (s), 161.1 (s), 140.5 (s), 136.1 (d), 131.8 (d), 130.4 (d), 127.8 (d), 127.1 (d), 121.7 (s), 120.5 (s), 96.2 (s), 84.1 (s), 61.7 (t), 29.0 (t), 25.9 (t), 22.3 (t), 21.5 (t), 14.1 (q); IR (reflection) ṽ = 3294.50, 3061.78, 2981.27, 2933.56, 2860.77, 2199.56, 2132.60, 1719.58, 1697.89, 1626.39, 1592.91, 1561.87, 1476.95, 1444.55, 1394.04, 1368.46, 1292.01, 1174.93, 1116.71, 1013.66, 933.26, 841.90, 798.58, 752.83, 700.84, 660.04 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{18}N_2O_3$ calcd for 322.1317, found 322.1303.

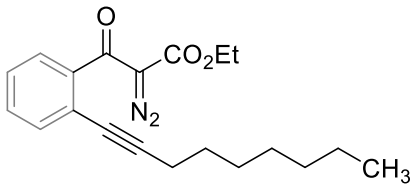


Ethyl 3-(2-(cyclopropylethynyl)phenyl)-2-diazo-3-oxopropanoate (1q)
Yield: 2.03 g, 72%; Green liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.39 – 7.30 (comp, 2H), 7.30 – 7.25 (comp, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 1.46 – 1.30 (m, 1H), 1.12 (t, *J* = 7.1 Hz, 3H), 0.87 – 0.80 (m, 2H), 0.74 – 0.65 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.4 (s), 160.9 (s), 140.7 (s), 132.0 (d), 130.2 (d), 127.4 (d), 126.8 (d), 121.7 (s), 98.6 (s), 72.9 (s), 61.6 (d), 14.0 (q), 8.8 (t, 2C), 0.2 (d); IR (reflection) ṽ = 3300, 3092, 3064, 2984, 2938, 2907, 2871, 2230, 2139, 1729, 1697, 1633, 1595, 1563, 1478, 1445, 1393, 1370, 1307, 1263, 1175, 1115, 1054, 1016, 954, 934, 839, 814, 757, 689, 652 cm^{-1}; HRMS (EI) (*m/z*) $C_{16}H_{14}N_2O_3$ calcd for 282.1004, found 282.1015.



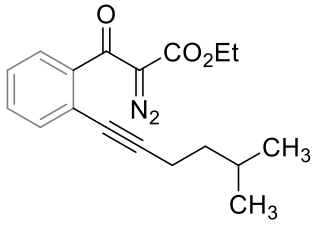
Ethyl 2-diazo-3-(2-(3-methylbut-1-yn-1-yl)phenyl)-3-oxopropanoate (1r)

Yield: 1.82 g, 64%; Green liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.40 – 7.33 (comp, 2H), 7.32 – 7.29 (comp, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.72 (hept, *J* = 6.9 Hz, 1H), 1.19 (d, *J* = 6.9 Hz, 6H), 1.12 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.7 (s), 161.1 (s), 140.9 (s), 131.8 (d), 130.2 (d), 127.7 (d), 126.8 (d), 121.7 (s), 100.8 (s), 77.2 (s), 61.6 (t), 22.8 (q, 2C), 21.2 (d), 14.0 (q); IR (reflection) ṽ = 3399, 3064, 2986, 2938, 2145, 1726, 1630, 1478, 1445, 1371, 1305, 1250, 1175, 1151, 1126, 1097, 1013, 935, 858, 757, 680 cm^{-1}; HRMS (EI) (*m/z*) $C_{16}H_{16}N_2O_3$ calcd for 284.1161, found 284.1136.



Ethyl 2-diazo-3-(2-(non-1-yn-1-yl)phenyl)-3-oxopropanoate (1s)

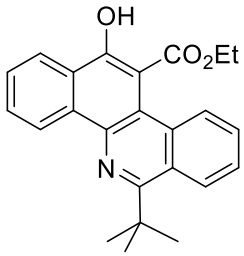
Yield: 2.83 g, 83%; Green liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.43 – 7.33 (comp, 2H), 7.33 – 7.28 (comp, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.36 (t, *J* = 7.0 Hz, 2H), 1.59 – 1.48 (m, 2H), 1.44 – 1.35 (m, 2H), 1.33 – 1.25 (comp, 6H), 1.13 (t, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.7 (s), 161.0 (s), 140.8 (s), 132.1 (d), 130.2 (d), 127.5 (d), 126.8 (d), 121.8 (s), 95.6 (s), 77.9 (s), 61.6 (t), 31.8 (t), 28.92 (t), 28.91 (t), 28.7 (t), 22.7 (t), 19.6 (t), 14.1 (q), 14.1 (q); IR (reflection) ṽ = 3064, 2930, 2857, 2230, 2138, 1730, 1698, 1635, 1595, 1466, 1445, 1395, 1370, 1305, 1261, 1176, 1121, 1099, 1016, 934, 829, 755, 695, 654 cm^{-1}; HRMS (EI) [M-2N] $C_{20}H_{24}O_3$ calcd for 312.1725, found 312.1763.



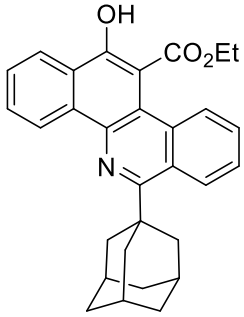
Ethyl 2-diazo-3-(2-(5-methylhex-1-yn-1-yl)phenyl)-3-oxopropanoate (1t)

Yield: 2.53 g, 81%; Green liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.50 – 7.13 (comp, 4H), 4.12 (qd, *J* = 7.1, 3.6 Hz, 2H), 2.35 (td, *J* = 7.3, 2.8 Hz, 2H), 1.67 (dpd, *J* = 13.4, 6.6, 2.5 Hz, 1H), 1.41 (qd, *J* = 7.3, 2.8 Hz, 2H), 1.09 (td, *J* = 7.1, 3.6 Hz, 3H), 0.88 (dd, *J* = 6.6, 2.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 187.2 (s), 160.6 (s), 140.6 (s), 131.7 (d), 129.9 (d), 127.3 (d), 126.5 (d), 121.5 (s), 95.2 (s), 77.7 (s), 61.3 (t), 37.2 (t), 26.9 (d), 21.9 (q), 17.3 (t), 13.8 (q); IR (reflection) ṽ = 3063.99, 2957.39, 2933.11, 2869.85, 2230.16, 2138.16, 1729.88, 1697.69, 1634.61, 1594.79, 1563.45, 1467.96, 1444.62, 1385.96, 1369.37, 1304.17,

1238.23, 1174.66, 1120.74, 1099.22, 1042.93, 1014.90, 933.17, 868.66, 828.07, 755.20, 695.59, 654.52 cm^{-1}; HRMS (EI) [M-2H] $C_{18}H_{20}O_3$ calcd for 284.1412, found 284.1407.

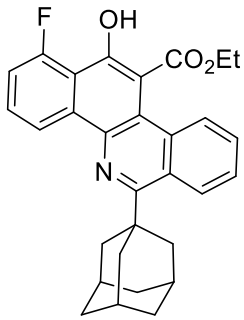


Compound **2**: Yield: 59.8 mg, 80%; white solid, mp 175.0 – 177.0 °C; R_f = 0.2 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.49 (s, 1H), 9.50 – 9.21 (m, 1H), 8.69 – 8.60 (m, 1H), 8.56 – 8.46 (m, 1H), 8.11 – 7.97 (m, 1H), 7.90 – 7.80 (m, 1H), 7.73 – 7.65 (m, 1H), 7.63 – 7.53 (m, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.87 (s, 9H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.1 (s), 163.8 (s), 159.6 (s), 135.3 (s), 135.2 (s), 133.6 (s), 130.3 (d), 129.3 (d), 127.5 (d), 127.0 (d), 126.7 (d), 125.9 (s), 125.31 (d), 125.29 (s), 125.0 (d), 123.9 (d), 118.4 (s), 101.8 (s), 61.9 (t), 40.5 (s), 31.5 (3C, q), 14.0 (q); IR (reflection) $\tilde{\nu}$ = 2912.37, 2856.24, 2251.85, 2229.36, 2218.45, 1454.10, 1346.40, 1316.55, 1186.42, 1101.13, 1082.72, 976.95, 934.22, 812.63, 772.09, 692.99 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{24}NO_3^+$ calcd for 374.1751, found 374.1751.

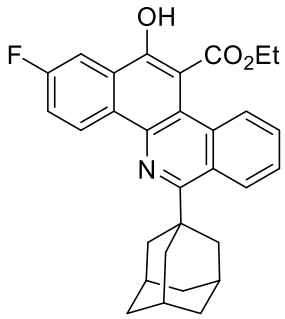


Compound **3**: Yield: 73.2 mg, 81%; white solid, mp 175.0 – 177.0 °C; R_f = 0.2 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.41 (s, 1H), 9.38 – 9.27 (m, 1H), 8.87 – 8.77 (m, 1H), 8.52 – 8.41 (m, 1H), 8.04 – 7.96 (m, 1H), 7.84 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.60 – 7.52 (comp, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.59 (d, *J* = 2.4 Hz, 6H), 2.28 (br, 3H), 2.01 – 1.90 (m, 6H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.2 (s), 163.3 (s), 159.6 (s), 135.5 (s), 135.4 (s), 133.7 (s), 130.3 (d), 129.4 (d), 127.6 (d), 126.8 (d), 126.6 (d), 125.6 (s), 125.5 (s), 125.1 (d), 125.1 (d), 124.0 (d), 118.25 (s), 101.9 (s), 61.7 (t), 43.3 (s), 42.5 (t, 3C), 37.4 (t, 3C), 29.5 (d, 3C), 14.0 (q); IR (reflection) $\tilde{\nu}$ = 2912.37, 2856.24, 2251.85, 2229.36, 2218.45, 1454.10, 1346.40, 1316.55, 1186.42, 1101.13, 1082.72, 976.95, 934.22, 812.63, 772.09, 692.99 cm^{-1}; HRMS (ESI) $[M+H]^+$

$C_{30}H_{30}NO_3^+$ calcd for 452.2220, found 452.2213.

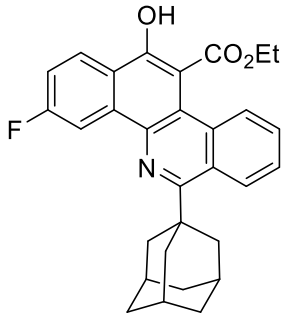


Compound **4**: Yield: 81.7 mg, 87%; white solid, mp 236.0 – 238.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.37 (s, 1H), 9.25 – 9.10 (m, 1H), 8.90 – 8.77 (m, 1H), 8.07 – 7.97 (m, 1H), 7.79 – 7.70 (m, 1H), 7.63 – 7.53 (comp, 2H), 7.37 – 7.28 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 2.57 (d, J = 2.6 Hz, 6H), 2.27 (br, 3H), 2.03 – 1.88 (m, 6H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 163.8 (s), 160.5 (d, J_{C-F} = 258.9 Hz), 158.3 (d, J_{C-F} = 3.6 Hz), 137.8 (d, J_{C-F} = 1.9 Hz), 134.7 (d, J_{C-F} = 3.2 Hz), 133.4 (s), 130.6 (d, J_{C-F} = 1.1 Hz), 130.4 (s), 129.1 (s), 127.0 (d), 126.9 (d), 125.7 (s), 125.6 (d), 121.3 (d, J_{C-F} = 4.0 Hz), 118.9 (s), 115.0 (d, J_{C-F} = 8.5 Hz), 114.1 (d, J_{C-F} = 22.0 Hz), 103.4 (s), 61.9 (t), 43.4 (s), 42.5 (t, 3C), 37.4 (t, 3C), 29.4 (d, 3C), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -111.59 (s); IR (reflection) $\tilde{\nu}$ = 2902.30, 2846.51, 1738.62, 1645.37, 1621.38, 1586.34, 1514.96, 1453.83, 1410.93, 1394.80, 1372.13, 1343.42, 1302.82, 1263.07, 1240.10, 1214.90, 1182.11, 1167.77, 1131.42, 1108.93, 1049.69, 1028.51, 999.33, 968.80, 937.35, 899.89, 840.96, 820.60, 793.80, 772.42, 760.32, 731.43, 684.32, 673.31, 656.42, 641.86 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{29}FNO_3^+$ calcd for 470.2126, found 470.2120.

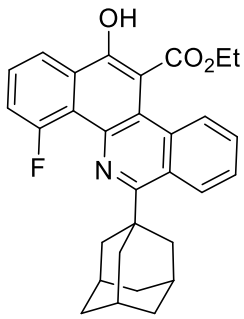


Compound **5**: Yield: 64.8 mg, 69%; white solid, mp 160.0 – 162.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 11.27 (s, 1H), 9.37 – 9.25 (m, 1H), 8.86 – 8.77 (m, 1H), 8.15 – 8.01 (m, 1H), 8.02 – 7.91 (m, 1H), 7.61 – 7.51 (comp, 3H), 4.39 (q, J = 7.1 Hz, 2H), 2.58 – 2.56 (m, 6H), 2.27 (br, 3H), 1.99 – 1.90 (m, 6H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 172.0 (s), 163.8 (s), 162.3 (d, J_{C-F} = 247.5 Hz), 158.4 (d, J_{C-F} = 4.0 Hz), 135.1 (s), 133.6 (s), 132.1 (s), 129.2 (d), 127.9 (d, J_{C-F} = 8.6 Hz), 126.9 (d, J_{C-F} = 9.3 Hz), 126.9 (d), 126.8 (d), 125.4

(s), 125.2 (d), 119.3 (d, $J_{C\text{-}F}$ = 23.7 Hz), 117.6 (d, $J_{C\text{-}F}$ = 1.3 Hz), 108.7 (d, $J_{C\text{-}F}$ = 23.1 Hz), 103.0 (s), 61.9 (t), 43.3 (s), 42.4 (t, 3C), 37.4 (t, 3C), 29.4 (d, 3C), 14.0 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -112.55 (s); IR (reflection) ṽ = 2922.51, 2854.60, 2229.34, 1648.86, 1595.00, 1518.35, 1504.96, 1453.63, 1401.68, 1373.18, 1345.27, 1313.37, 1262.92, 1228.14, 1210.91, 1184.61, 1158.60, 1095.22, 1029.94, 996.67, 976.15, 879.06, 858.25, 842.96, 813.50, 771.56, 737.27, 713.03, 697.81, 674.66, 613.67 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{29}FNO_3^+$ calcd for 470.2126, found 470.2119.

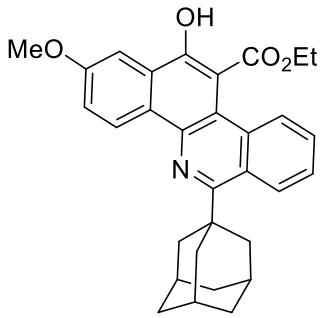


Compound **6**: Yield: 77.9 mg, 83%; white solid, mp 181.0 – 183.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 11.46 (s, 1H), 8.91 – 8.86 (m, 1H), 8.84 – 8.80 (m, 1H), 8.52 – 8.42 (m, 1H), 8.04 – 7.95 (m, 1H), 7.61 – 7.56 (comp, 2H), 7.43 – 7.37 (m, 1H), 4.38 (q, J = 7.2 Hz, 2H), 2.58 – 2.53 (m, 6H), 2.27 (br, 3H), 1.99 – 1.90 (m, 6H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 172.1 (s), 164.2 (d, $J_{C\text{-}F}$ = 249.9 Hz), 161.4 (d, $J_{C\text{-}F}$ = 533.2 Hz), 137.9 (d, $J_{C\text{-}F}$ = 9.4 Hz), 134.7 (d, $J_{C\text{-}F}$ = 4.4 Hz), 133.6 (s), 129.5 (d), 127.0 (d, $J_{C\text{-}F}$ = 9.3 Hz), 126.9 (d), 126.8 (d), 125.8 (s), 125.5 (d), 122.3 (d, $J_{C\text{-}F}$ = 1.5 Hz), 119.2 (s), 116.7 (d, $J_{C\text{-}F}$ = 24.5 Hz), 109.9 (d, $J_{C\text{-}F}$ = 23.2 Hz), 101.3 (d, $J_{C\text{-}F}$ = 1.7 Hz), 61.8 (t), 43.3 (s), 42.4 (t, 3C), 37.4 (t, 3C), 29.4 (d, 3C), 14.0 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -107.87 (s); IR (reflection) ṽ = 3079.22, 2907.95, 2855.62, 2659.67, 2252.37, 2229.95, 2219.40, 1739.03, 1657.82, 1621.53, 1587.27, 1499.69, 1453.69, 1401.70, 1368.42, 1345.35, 1329.76, 1309.21, 1294.65, 1260.85, 1226.07, 1182.44, 1144.81, 1098.21, 1024.83, 997.15, 976.74, 956.44, 896.77, 853.96, 834.23, 821.02, 809.69, 765.71, 740.69, 695.98, 682.44, 652.60, 609.02 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{29}FNO_3^+$ calcd for 470.2126, found 470.2119.

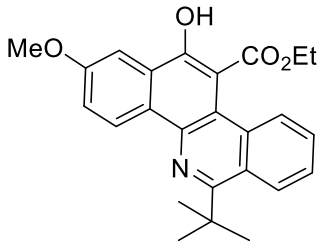


Compound **7**: Yield: 66.7 mg, 71%; white solid, mp 98.0 – 99.0 °C; R_f = 0.3 (EA/PE =

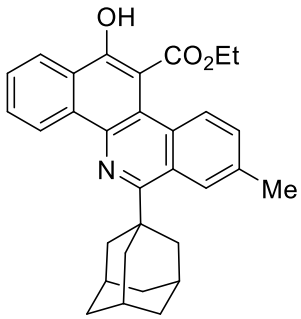
1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.45 (s, 1H), 8.90 – 8.79 (m, 1H), 8.37 (d, *J* = 7.9 Hz, 1H), 8.05 – 7.93 (m, 1H), 7.67 – 7.49 (m, 4H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.59 (d, *J* = 1.4 Hz, 6H), 2.28 (br, 3H), 1.97 (q, *J* = 12.3 Hz, 6H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.0 (s), 163.2 (d, J_{C-F} = 1.4 Hz), 160.8 (d, J_{C-F} = 261.9 Hz), 158.7 (d, J_{C-F} = 3.7 Hz), 135.0 (d, J_{C-F} = 8.9 Hz), 133.3 (s), 129.5 (d), 128.2 (d, J_{C-F} = 3.3 Hz), 127.8 (d, J_{C-F} = 8.8 Hz), 126.6 (d, *J* = 3.9 Hz), 125.5 (d), 124.7 (d, J_{C-F} = 2.0 Hz), 123.6 (d, J_{C-F} = 6.2 Hz), 120.2 (d, J_{C-F} = 4.5 Hz), 118.8 (d, J_{C-F} = 0.7 Hz), 118.0 (d, *J* = 22.6 Hz), 102.6 (d, J_{C-F} = 0.8 Hz), 61.9 (t), 43.3 (d, J_{C-F} = 1.8 Hz), 42.4 (t, 3C), 37.4 (t, 3C), 29.5 (d, 3C), 14.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -106.80 (s); IR (reflection) ṽ = 2898.12, 2843.82, 1726.61, 1645.90, 1584.46, 1518.47, 1497.84, 1452.24, 1406.98, 1373.15, 1310.25, 1264.54, 1209.18, 1181.96, 1157.24, 1102.33, 1088.94, 1029.21, 986.17, 928.54, 909.87, 887.04, 868.34, 819.63, 796.90, 774.30, 754.47, 734.32, 718.50, 696.33, 673.96, 656.55 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{29}FNO_3^+$ calcd for 470.2126, found 470.2122.



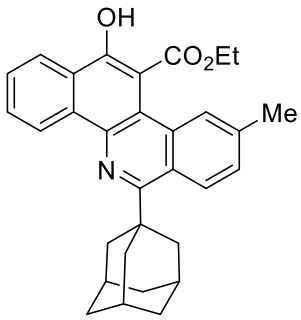
Compound **8**: Yield: 81.9 mg, 85%; white solid, mp 187.0 – 188.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.35 (s, 1H), 9.22 (d, *J* = 9.0 Hz, 1H), 8.81 (dd, *J* = 6.9, 2.6 Hz, 1H), 8.03 – 7.93 (m, 1H), 7.80 (d, *J* = 2.6 Hz, 1H), 7.59 – 7.49 (comp, 2H), 7.45 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 4.01 (s, 3H), 2.58 (d, *J* = 1.8 Hz, 6H), 2.27 (s, 3H), 2.02 – 1.88 (m, 6H), 1.20 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.3 (s), 163.4 (s), 159.4 (s), 158.7 (s), 135.5 (s), 133.8 (s), 130.0 (s), 129.2 (d), 127.0 (d), 126.8 (d), 126.6 (d), 125.1 (s), 124.7 (d), 121.3 (d), 116.7 (s), 103.5 (d), 102.5 (s), 61.8 (t), 55.7 (q), 43.3 (s), 42.5 (t, 3C), 37.4 (t, 3C), 29.5 (d, 3C), 14.0 (q); IR (reflection) ṽ = 2901.49, 2848.46, 1655.58, 1619.66, 1585.69, 1518.10, 1503.58, 1433.60, 1415.75, 1402.88, 1371.20, 1312.40, 1272.37, 1227.59, 1203.38, 1179.90, 1132.53, 1097.92, 1077.13, 1029.53, 997.28, 973.00, 936.32, 920.34, 882.96, 854.97, 833.41, 797.74, 758.55, 734.67, 714.55, 697.34, 675.42, 657.65, 616.06 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{31}H_{32}NO_4^+$ calcd for 482.2326, found 482.2320.



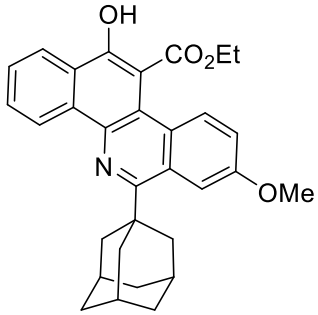
Compound **9**: Yield: 57.3 mg, 71%; white solid, mp 131.0 – 133.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.41 (s, 1H), 9.21 (d, *J* = 9.0 Hz, 1H), 8.69 – 8.52 (m, 1H), 8.06 – 7.95 (m, 1H), 7.76 (d, *J* = 2.6 Hz, 1H), 7.62 – 7.51 (comp, 2H), 7.44 (dd, *J* = 9.0, 2.6 Hz, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.94 (s, 3H), 1.86 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.2 (s), 163.8 (s), 159.9 (s), 158.6 (s), 135.9 (s), 133.6 (s), 129.8 (s), 129.0 (d), 127.0 (d), 126.8 (d), 126.7 (s), 126.6 (d), 124.9 (d), 124.8 (s), 121.2 (d), 116.7 (s), 103.2 (d), 102.4 (s), 61.7 (t), 55.5 (q), 40.5 (s), 31.4 (3C, q), 13.9 (q); IR (reflection) ṽ = 2976, 2928, 1654, 1587, 1520, 1438, 1395, 1373, 1313, 1277, 1237, 1217, 1184, 1162, 1142, 1099, 1031, 993, 851, 831, 804, 769, 757, 740, 722, 699, 680 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{25}H_{26}NO_4^+$ calcd for 404.1857, found 404.1857.



Compound **10**: Yield: 79.2 mg, 85%; white solid, mp 172.0 – 175.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.38 (s, 1H), 9.31 (d, *J* = 7.8 Hz, 1H), 8.60 (s, 1H), 8.47 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.90 (d, *J* = 8.6 Hz, 1H), 7.83 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.67 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.41 (dd, *J* = 8.6, 1.3 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.62 (s, 3H), 2.60 (d, *J* = 2.4 Hz, 6H), 2.29 (br, 3H), 2.02 – 1.91 (m, 6H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.3 (s), 162.8 (s), 159.4 (s), 135.5 (s), 134.9 (s), 134.7 (s), 131.7 (s), 130.3 (d), 129.3 (d), 128.5 (d), 127.3 (d), 126.2 (d), 125.7 (s), 125.4 (s), 125.0 (d), 123.9 (d), 118.3 (s), 101.9 (s), 61.7 (t), 43.3 (s), 42.5 (t, 3C), 37.5 (t, 3C), 29.5 (d, 3C), 22.4 (q), 14.1 (q); IR (reflection) ṽ = 2901.64, 2848.57, 1653.97, 1617.83, 1584.67, 1521.22, 1496.95, 1444.54, 1400.70, 1371.16, 1334.24, 1309.55, 1263.14, 1230.41, 1205.33, 1154.43, 1097.69, 1020.66, 998.68, 970.07, 939.71, 906.30, 883.28, 861.98, 833.91, 819.46, 800.65, 767.39, 716.14, 693.18, 665.34 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{31}H_{32}NO_3^+$ calcd for 466.2377, found 466.2370.

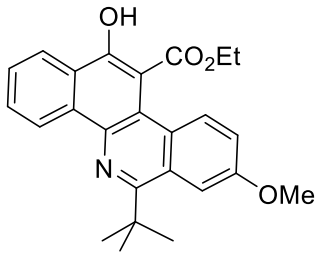


Compound **11**: Yield: 73.6 mg, 79%; white solid, mp 164.0 – 165.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.37 (s, 1H), 9.32 (d, *J* = 8.2 Hz, 1H), 8.72 (d, *J* = 8.7 Hz, 1H), 8.48 (d, *J* = 7.7 Hz, 1H), 7.88 – 7.80 (m, 1H), 7.76 (s, 1H), 7.72 – 7.64 (m, 1H), 7.39 (dd, *J* = 8.7, 1.5 Hz, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 2.66 – 2.56 (m, 6H), 2.54 (s, 3H), 2.28 (br, 3H), 2.02 – 1.89 (m, 6H), 1.22 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.3 (s), 163.2 (s), 159.4 (s), 136.4 (s), 135.6 (s), 135.5 (s), 134.0 (s), 130.3 (d), 128.9 (d), 128.8 (s), 127.5 (d), 127.0 (d), 126.7 (d), 125.6 (s), 125.1 (d), 123.9 (d), 123.7 (s), 118.0 (s), 101.9 (s), 61.6 (t), 43.2 (s), 42.5 (t, 3C), 37.4 (t, 3C), 29.5 (d, 3C), 22.0 (q), 14.0 (q); IR (reflection) ṽ = 2979.30, 2899.45, 2846.96, 1737.75, 1641.60, 1620.13, 1583.78, 1498.37, 1440.50, 1405.61, 1370.90, 1313.80, 1265.77, 1233.36, 1213.83, 1178.75, 1157.86, 1140.18, 1097.90, 1021.62, 997.19, 969.20, 902.74, 860.63, 829.56, 819.44, 793.26, 766.97, 695.42, 678.22, 662.38 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{31}H_{32}NO_3^+$ calcd for 466.2377, found 466.2370.

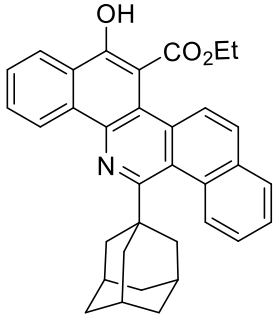


Compound **12**: Yield: 77.1 mg, 80%; white solid, mp 215.0 – 217.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.41 (s, 1H), 9.28 (d, *J* = 8.2 Hz, 1H), 8.46 (d, *J* = 7.4 Hz, 1H), 8.16 (d, *J* = 2.6 Hz, 1H), 7.92 (d, *J* = 9.2 Hz, 1H), 7.86 – 7.78 (m, 1H), 7.70 – 7.62 (m, 1H), 7.25 (dd, *J* = 9.2, 2.6 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 3H), 2.60 (d, *J* = 2.4 Hz, 6H), 2.28 (s, 3H), 2.02 – 1.89 (m, 6H), 1.21 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.2 (s), 162.1 (s), 159.7 (s), 156.5 (s), 135.6 (s), 134.4 (s), 130.8 (d), 130.3 (d), 128.5 (s), 127.2 (d), 126.6 (s), 125.2 (s), 124.8 (d), 124.0 (d), 118.4 (s), 117.7 (d), 107.1 (d), 101.7 (s), 61.7 (t), 55.5 (q), 43.2 (s), 42.2 (t, 3C), 37.5 (t, 3C), 29.5 (d, 3C), 14.1 (q); IR (reflection) ṽ = 3069.35, 2899.66, 2847.81, 1650.90, 1614.57, 1584.37, 1520.63, 1497.33, 1454.09, 1405.76, 1372.17, 1333.89, 1312.88, 1266.13, 1251.22, 1230.65,

1205.78, 1177.60, 1153.32, 1091.27, 1029.92, 968.18, 944.21, 915.96, 879.32, 855.94, 835.80, 819.28, 799.52, 767.57, 716.20, 692.78, 678.58, 665.34 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{31}H_{32}NO_4^+$ calcd for 482.2326, found 482.2321.

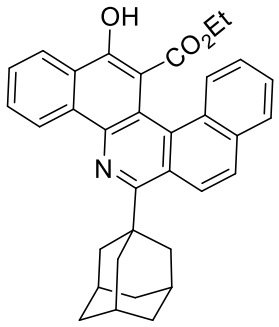


Compound **13**: Yield: 67.0 mg, 83%; white solid, mp 163.0 – 165.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.54 (s, 1H), 9.35 (d, *J* = 8.0 Hz, 1H), 8.53 (dd, *J* = 8.0, 0.5 Hz, 1H), 8.04 – 7.93 (comp, 2H), 7.86 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.30 (dd, *J* = 9.3, 2.6 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 4.02 (s, 3H), 1.91 (s, 9H), 1.27 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.1 (s), 162.6 (s), 159.6 (s), 156.6 (s), 135.5 (s), 134.2 (s), 130.6 (d), 130.2 (d), 128.4 (s), 127.1 (d), 126.5 (s), 125.1 (s), 124.7 (d), 123.9 (d), 118.5 (s), 117.8 (d), 106.9 (d), 101.6 (s), 61.6 (t), 55.8 (q), 40.3 (s), 31.2 (q), 14.0 (q); IR (reflection) $\tilde{\nu}$ = 3071, 2980, 2932, 1650, 1615, 1583, 1522, 1455, 1408, 1371, 1312, 1268, 1227, 1190, 1170, 1156, 1134, 1100, 1078, 1037, 1023, 948, 916, 853, 836, 802, 766, 721, 690, 672 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{25}H_{26}NO_4^+$ calcd for 404.1857, found 404.1855.

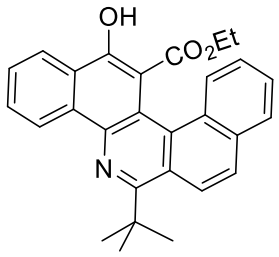


Compound **14**: Yield: 87.3 mg, 87%; white solid, mp > 350 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.03 (s, 1H), 9.40 (d, *J* = 8.1 Hz, 1H), 8.75 (d, *J* = 9.2 Hz, 1H), 8.68 (d, *J* = 8.1 Hz, 1H), 8.55 (d, *J* = 8.0 Hz, 1H), 7.95 – 7.81 (comp, 3H), 7.79 – 7.71 (m, 1H), 7.62 – 7.49 (comp, 2H), 3.71 (dq, *J* = 10.7, 7.2 Hz, 1H), 3.32 (dq, *J* = 10.7, 7.2 Hz, 1H), 2.73 – 2.52 (m, 6H), 2.30 (br, 3H), 2.05 – 1.91 (m, 6H), 0.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 162.3 (s), 159.4 (s), 137.6 (s), 135.4 (s), 133.8 (s), 132.5 (s), 131.9 (s), 130.4 (d), 127.8 (d), 127.6 (d), 127.3 (d), 126.5 (d), 126.2 (d), 125.9 (s), 125.8 (d), 125.3 (d), 124.13 (s), 124.05 (d), 123.7 (d), 116.7 (s), 104.2 (s), 61.3 (t), 43.3 (s), 42.6 (t, 3C), 37.4 (t, 3C), 29.5 (d, 3C), 12.9 (q); IR (reflection) $\tilde{\nu}$ = 2928.05, 2903.68, 2851.07,

1653.10, 1617.08, 1584.67, 1517.57, 1489.12, 1456.53, 1399.74, 1368.81, 1312.66, 1270.35, 1258.48, 1229.05, 1197.19, 1178.11, 1154.78, 1100.92, 1092.07, 1068.17, 1014.46, 976.24, 904.25, 876.38, 849.34, 831.82, 807.10, 790.97, 756.31, 730.06, 690.63, 661.49, 634.92 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{34}H_{32}NO_3$ calcd for 502.2377, found 502.2368.

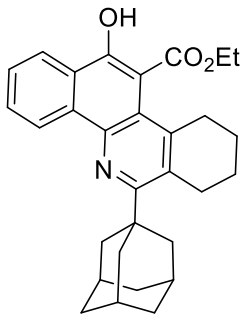


Compound **15**: Yield: 64.2 mg, 64%; white solid, mp 145.0 – 147.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.39 (s, 1H), 9.39 (s, 1H), 9.36 – 9.27 (m, 1H), 8.55 – 8.45 (comp, 2H), 8.18 – 8.10 (m, 1H), 7.99 – 7.92 (m, 1H), 7.88 – 7.82 (m, 1H), 7.72 – 7.66 (m, 1H), 7.61 – 7.54 (comp, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 2.70 (d, *J* = 1.9 Hz, 6H), 2.34 (br, 3H), 2.01 (q, *J* = 12.3 Hz, 6H), 1.10 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.5 (s), 164.5 (s), 159.4 (s), 135.4 (s), 134.0 (s), 131.5 (s), 130.5 (s), 130.4 (s), 130.3 (d), 129.3 (d), 128.40 (s), 128.36 (d), 127.7 (d), 127.41 (d), 127.38 (d), 126.6 (d), 126.2 (d), 125.5 (s), 125.1 (d), 124.0 (d), 123.6 (s), 118.1 (s), 102.5 (s), 61.7 (t), 43.9 (s), 42.7 (t, 3C), 37.5 (t, 3C), 29.5 (d, 3C), 14.1 (q); IR (reflection) ṽ = 2930.17, 2904.40, 2888.17, 2847.47, 1645.39, 1583.84, 1542.72, 1498.61, 1448.82, 1401.28, 1373.71, 1332.74, 1312.83, 1273.78, 1254.95, 1232.88, 1191.44, 1156.39, 1095.05, 1014.86, 989.72, 960.98, 905.59, 886.44, 835.83, 804.27, 768.28, 759.10, 730.19, 686.91, 661.85, 630.89, 615.13 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{34}H_{32}NO_3$ calcd for 502.2377, found 502.2368.

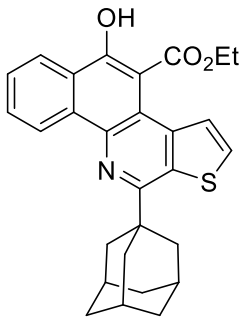


Compound **16**: Yield: 66.1 mg, 78%; white solid, mp 177.0 – 179.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.17 (s, 1H), 9.48 (d, *J* = 8.2 Hz, 1H), 8.79 – 8.70 (m, 1H), 8.66 – 8.54 (comp, 2H), 7.97 – 7.89 (comp, 2H), 7.86 (d, *J* = 9.1 Hz, 1H), 7.81 – 7.73 (m, 1H), 7.63 – 7.53 (m, 2H), 3.76 (dq, *J* = 10.7, 7.1 Hz, 1H), 3.40 (dq, *J* = 10.7, 7.1 Hz, 1H), 1.93 (s, 9H), 0.41 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.6 (s), 162.8 (s), 159.4 (s), 137.3 (s), 135.3 (s),

133.7 (s), 132.3 (s), 131.9 (s), 130.4 (d), 127.8 (d), 127.7 (d), 127.3 (d), 126.4 (d), 126.2 (d), 126.1 (d), 125.9 (s), 125.2 (d), 124.0 (d), 123.9 (s), 123.8 (d), 116.9 (s), 104.1 (s), 61.3 (t), 40.4 (s), 31.6 (q), 12.8 (q); IR (reflection) $\tilde{\nu}$ = 2981, 2966, 2932, 2870, 1648, 1615, 1586, 1518, 1492, 1464, 1442, 1401, 1369, 1324, 1267, 1234, 1194, 1150, 1140, 1118, 1093, 1013, 963, 937, 852, 832, 793, 761, 738, 696, 645, 612 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{28}H_{26}NO_3$ calcd for 424.1908, found 424.1908.

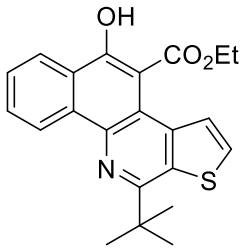


Compound **17**: Yield: 84.7 mg, 93%; white solid, mp 166.0 – 168.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.34 (s, 1H), 9.25 (d, *J* = 8.1 Hz, 1H), 8.39 (dd, *J* = 8.1, 0.8 Hz, 1H), 7.82 – 7.76 (m, 1H), 7.68 – 7.61 (m, 1H), 4.43 (q, *J* = 7.1 Hz, 2H), 3.16 (br, 2H), 2.74 (t, *J* = 6.5 Hz, 2H), 2.37 (d, *J* = 2.0 Hz, 6H), 2.20 (br, 3H), 2.04 – 2.02 (m, 2H), 1.91 – 1.83 (m, 6H), 1.81 – 1.74 (m, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.9 (s), 160.7 (s), 159.5 (s), 146.5 (s), 138.6 (s), 135.8 (s), 132.3 (s), 130.3 (d), 127.7 (d), 125.7 (s), 124.8 (d), 123.9 (d), 120.5 (s), 101.5 (s), 61.8 (t), 41.9 (s), 41.3 (t, 3C), 37.3 (t, 3C), 29.4 (d, 3C), 29.3 (t), 25.7 (t), 20.7 (t), 20.4 (t), 14.3 (q); IR (reflection) $\tilde{\nu}$ = 2912.55, 2855.98, 2661.23, 2251.64, 2229.24, 1640.99, 1453.98, 1346.20, 1316.26, 1231.48, 1185.97, 1100.89, 976.83, 934.12, 812.45, 771.38, 692.71, 647.17 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{34}NO_3^+$ calcd for 456.2533, found 456.2527.

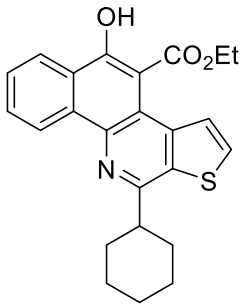


Compound **18**: Yield: 81.5 mg, 89%; white solid, mp 227.0 – 229.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.45 (s, 1H), 9.41 – 9.30 (m, 1H), 8.51 – 8.41 (m, 1H), 7.83 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.60 (d, *J* = 5.7 Hz, 1H), 7.54 (d, *J* = 5.7 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.52 (d, *J* = 2.8 Hz, 6H), 2.26 (br, 3H), 1.93 (br, 6H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.5 (s), 159.8 (s), 159.5 (s), 141.9 (s), 136.9

(s), 135.7 (s), 131.2 (s), 130.4 (d), 127.6 (d), 127.1 (d), 125.41 (d), 125.39 (s), 125.3 (d), 123.9 (d), 117.8 (s), 102.90 (s), 61.9 (d), 42.0 (s), 41.1 (t), 37.3 (t), 29.2 (d), 14.1 (q); IR (reflection) $\tilde{\nu}$ = 2897.98, 2843.14, 1641.89, 1586.82, 1495.36, 1473.86, 1445.75, 1403.15, 1372.77, 1340.04, 1299.79, 1234.40, 1159.87, 1110.47, 1097.40, 1028.01, 975.15, 861.52, 832.81, 807.01, 765.30, 713.44, 678.70, 660.78, 650.77, 634.49 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{28}H_{28}NO_3S$ calcd for 458.1784, found 458.1775.

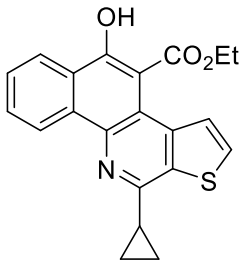


Compound **19**: Yield: 68.3 mg, 90%; white solid, mp 153.0 – 155.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.48 (s, 1H), 9.47 – 9.29 (m, 1H), 8.47 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.83 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.69 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.62 (d, *J* = 5.6 Hz, 1H), 7.56 (d, *J* = 5.6 Hz, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 1.77 (s, 9H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.5 (s), 159.8 (s), 159.6 (s), 141.9 (s), 136.8 (s), 135.7 (s), 131.6 (s), 130.4 (d), 127.6 (d), 127.4 (d), 125.6 (d), 125.4 (s), 125.3 (d), 124.0 (d), 117.9 (s), 102.0 (s), 61.9 (t), 39.9 (s), 29.7 (q, 3C), 14.2 (q); IR (reflection) $\tilde{\nu}$ = 2973.30, 2951.46, 2925.99, 2899.02, 2861.39, 1643.29, 1587.85, 1548.23, 1493.40, 1478.19, 1461.26, 1443.62, 1404.31, 1386.52, 1365.76, 1337.53, 1320.97, 1300.71, 1280.80, 1260.86, 1229.31, 1194.16, 1157.47, 1116.94, 1094.68, 1033.56, 1020.30, 972.58, 914.41, 852.59, 835.30, 799.22, 766.30, 726.34, 687.58, 664.02, 636.38, 608.20 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{22}H_{22}NO_3S$ calcd for 380.1315, found 380.1311.

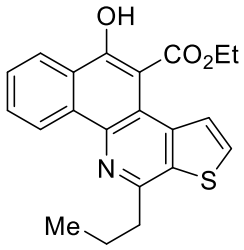


Compound **20**: Yield: 71.4 mg, 88%; white solid, mp 125.0 – 127.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.33 (s, 1H), 9.31 (d, *J* = 8.2 Hz, 1H), 8.37 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.74 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.56 – 7.44 (comp, 2H), 4.41 (q, *J* = 7.2 Hz, 2H), 3.19 – 3.05 (m, 1H), 2.14 – 2.05 (m, 2H), 2.03 – 1.87 (comp, 4H), 1.82 – 1.74 (m, 1H), 1.52 – 1.35 (comp, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm)

171.5 (s), 159.3 (s), 157.5 (s), 140.6 (s), 138.0 (s), 135.5 (s), 134.3 (s), 130.4 (d), 127.7 (d), 127.6 (d), 126.5 (d), 125.4 (d), 125.3 (s), 123.9 (d), 118.0 (s), 102.2 (s), 62.0 (t), 46.1 (d), 32.0 (t, 2C), 26.8 (t, 2C), 26.4 (t), 14.2 (q); IR (reflection) $\tilde{\nu}$ = 2926.58, 2851.05, 1726.78, 1658.57, 1615.15, 1585.45, 1548.34, 1499.34, 1444.01, 1407.27, 1368.75, 1293.81, 1230.73, 1162.56, 1093.20, 1029.08, 892.86, 836.28, 763.89, 714.61, 654.95, 634.97 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{24}NO_3S$ calcd for 406.1471, found 406.1466.

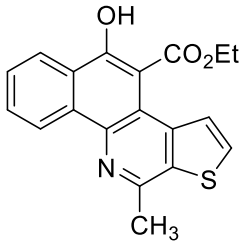


Compound **21**: Yield: 61.1 mg, 84%; white solid, mp 115.0 – 117.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.39 (s, 1H), 9.28 – 9.18 (m, 1H), 8.65 – 8.19 (m, 1H), 7.79 (M, 1H), 7.72 – 7.59 (comp, 2H), 7.59 – 7.49 (m, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.51 – 2.36 (m, 1H), 1.57 – 1.50 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.24 – 1.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 158.9 (s), 154.1 (s), 140.2 (s), 138.0 (s), 135.3 (s), 135.2 (s), 130.2 (d), 127.8 (d), 127.6 (d), 126.5 (d), 125.3 (s), 125.1 (d), 123.9 (d), 117.6 (s), 102.2 (s), 61.9 (t), 16.4 (d), 14.1 (q), 10.1 (t, 2C); IR (reflection) $\tilde{\nu}$ = 3078.41, 2998.06, 1649.19, 1616.78, 1587.59, 1568.32, 1549.37, 1503.77, 1442.78, 1407.57, 1369.78, 1296.79, 1226.85, 1165.32, 1132.19, 1097.07, 1036.97, 1017.98, 995.60, 959.17, 902.43, 853.57, 832.37, 809.27, 759.73, 712.89, 666.77, 644.93, 631.56 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{21}H_{18}NO_3S$ calcd for 364.1002, found 364.0998.

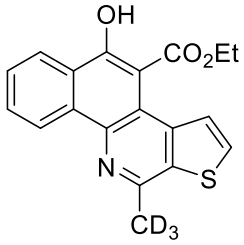


Compound **22**: Yield: 58.5 mg, 80%; white solid, mp 66.0 – 68.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.44 (s, 1H), 9.37 (d, *J* = 8.2 Hz, 1H), 8.47 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.82 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.68 (ddd, *J* = 8.2, 7.1, 1.2 Hz, 1H), 7.62 (d, *J* = 5.5 Hz, 1H), 7.55 (d, *J* = 5.5 Hz, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 3.27 – 3.15 (m, 2H), 2.22 – 2.09 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 159.2 (s), 153.4 (s), 140.5 (s), 138.1(s), 135.3 (s), 135.1 (s), 130.4 (d), 127.7 (d), 127.6 (d), 126.5 (d), 125.3 (s),

125.3 (d), 123.9 (d), 118.0 (s), 102.2 (s), 61.9 (t), 39.5 (t), 21.4 (t), 14.4 (q), 14.1 (q); IR (reflection) ṽ = 3098.67, 2955.98, 2932.58, 2870.53, 1755.10, 1647.47, 1617.13, 1589.26, 1567.57, 1502.73, 1481.79, 1464.87, 1444.76, 1432.43, 1405.65, 1367.50, 1306.50, 1287.98, 1264.46, 1231.90, 1165.04, 1129.45, 1093.59, 1035.03, 957.23, 928.28, 894.72, 861.31, 831.35, 809.26, 793.01, 757.15, 733.95, 711.75, 682.48, 645.87 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{21}H_{20}NO_3S$ calcd for 366.1158, found 366.1154.

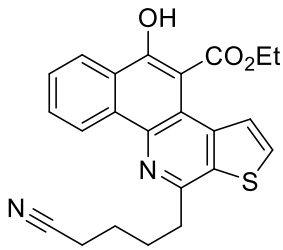


Compound **23**: Yield: 55.3 mg, 82%; white solid, mp 71.0 – 72.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.42 (s, 1H), 9.34 (d, *J* = 8.2 Hz, 1H), 8.47 (dd, *J* = 8.2, 0.7 Hz, 1H), 7.83 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.69 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.65 (d, *J* = 5.5 Hz, 1H), 7.56 (d, *J* = 5.5 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 2.99 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 159.3 (s), 150.0 (s), 140.5 (s), 138.1 (s), 135.2 (s), 135.0 (s), 130.5 (d), 128.0 (d), 127.7 (d), 126.6 (d), 125.3 (s), 125.1 (d), 124.0 (d), 118.2 (s), 102.2 (s), 61.9 (t), 23.9 (q), 14.1 (q); IR (reflection) ṽ =3088.88, 2981.74, 2913.99, 1754.76, 1692.75, 1645.93, 1589.80, 1556.99, 1504.67, 1479.89, 1440.33, 1404.83, 1369.39, 1306.96, 1282.13, 1231.37, 1167.80, 1095.05, 1032.78, 927.08, 889.72, 863.58, 829.71, 809.87, 768.84, 718.76, 684.03, 649.85, 635.56 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{19}H_{16}NO_3S$ calcd for 338.0845, found 338.0853.

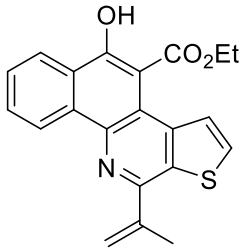


Compound **24**: Yield: 54.7 mg, 81%; white solid, mp 73.0 – 75.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.43 (s, 1H), 9.35 (d, *J* = 8.2 Hz, 1H), 8.47 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.83 (ddd, *J* = 8.2, 7.0, 1.4 Hz, 1H), 7.73 – 7.64 (comp, 2H), 7.57 (d, *J* = 5.5 Hz, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 159.4 (s), 150.0 (s), 140.5 (s), 138.1 (s), 135.3 (s), 135.0 (s), 130.5 (d), 128.2 (d), 127.8 (d), 126.6 (d), 125.4 (s), 125.2 (d), 124.0 (d), 118.2 (s), 102.2 (s), 62.0 (t), 14.1 (q); IR (reflection) ṽ = 2987.73, 1651.23, 1617.22, 1587.10, 1566.13, 1499.09, 1445.49, 1406.31, 1370.45, 1320.58, 1306.80, 1251.45, 1229.45, 1171.82, 1098.97, 1031.07, 982.57, 957.49, 927.43, 893.74, 860.13, 829.17, 805.17, 764.87, 748.60, 703.21, 675.17, 655.89, 642.03, 626.20 cm^{-1}; HRMS

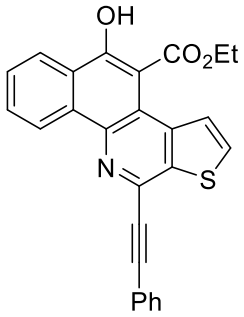
(ESI) $[M+H]^+$ $C_{19}H_{13}D_3NO_3S$ calcd for 341.1034, found 341.1031.



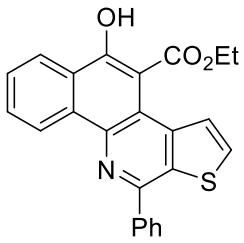
Compound **25**: Yield: 63.1 mg, 78%; white solid, mp 137.0 – 139.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.44 (s, 1H), 9.29 (d, *J* = 8.1 Hz, 1H), 8.45 (d, *J* = 7.6 Hz, 1H), 7.86 – 7.76 (m, 1H), 7.72 – 7.65 (m, 1H), 7.63 (d, *J* = 5.5 Hz, 1H), 7.54 (d, *J* = 5.5 Hz, 1H), 4.49 (q, *J* = 7.2 Hz, 2H), 3.25 (t, *J* = 7.2 Hz, 2H), 2.49 (t, *J* = 7.2 Hz, 2H), 2.34 – 2.22 (m, 2H), 1.89 (dt, *J* = 9.9, 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.2 (s), 159.4 (s), 151.8 (s), 140.6 (s), 137.9 (s), 135.2 (s), 134.8 (s), 130.5 (d), 127.8 (d), 127.7 (d), 126.6 (d), 125.3 (s), 125.1 (d), 123.9 (d), 119.8 (s), 118.2 (s), 102.1 (s), 61.9 (t), 35.9 (t), 26.5 (t), 25.2 (t), 17.2 (t), 14.01 (q); IR (reflection) $\tilde{\nu}$ = 2958.51, 2935.56, 2872.27, 2245.48, 1755.55, 1693.26, 1638.43, 1598.53, 1553.22, 1500.71, 1460.14, 1409.41, 1368.77, 1289.84, 1225.39, 1167.07, 1094.40, 1054.61, 1032.65, 933.84, 853.94, 828.19, 795.08, 765.11, 729.92, 702.73, 684.25, 649.60, 618.10 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{23}H_{21}N_2O_3S$ calcd for 405.1267, found 405.1269.



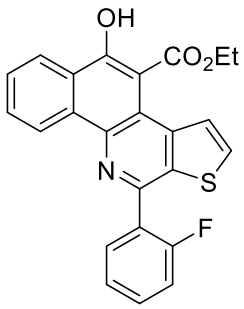
Compound **26**: Yield: 59.6 mg, 82%; white solid, mp 191.0 – 193.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.32 (d, *J* = 8.3 Hz, 1H), 8.47 (d, *J* = 8.3 Hz, 1H), 7.83 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.74 – 7.68 (m, 1H), 7.66 (d, *J* = 5.6 Hz, 1H), 7.56 (d, *J* = 5.6 Hz, 1H), 6.09 (s, 1H), 5.77 (s, 1H), 4.50 (q, *J* = 7.2 Hz, 2H), 2.57 (s, 3H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.1 (s), 151.6 (s), 145.2 (s), 141.6 (s), 137.4 (s), 135.4 (s), 132.9 (s), 130.6 (d), 129.0 (d), 127.8 (d), 126.3 (d), 125.5 (s), 125.2 (d), 124.0 (d), 118.7 (s), 118.2 (t), 102.0 (s), 62.0 (t), 22.1 (q), 14.14 (q); IR (reflection) $\tilde{\nu}$ = 2981.17, 2937.01, 1739.60, 1674.88, 1597.53, 1544.44, 1499.19, 1444.72, 1409.06, 1370.43, 1298.41, 1205.98, 1097.73, 1025.21, 910.59, 855.92, 832.30, 767.39, 729.84, 643.99 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{21}H_{18}NO_3S$ calcd for 364.1002, found 364.0999.



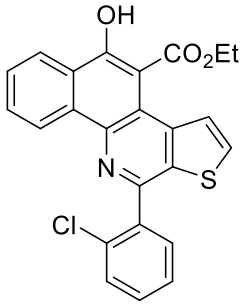
Compound **27**: Yield: 45.7 mg, 54%; white solid, mp 158.0 – 160.0 °C; R_f = 0.2 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.60 (s, 1H), 9.38 (d, *J* = 8.2 Hz, 1H), 8.48 (d, *J* = 7.9 Hz, 1H), 7.86 (t, *J* = 7.3 Hz, 1H), 7.80 – 7.68 (comp, 4H), 7.58 (d, *J* = 5.5 Hz, 1H), 7.49 – 7.38 (comp, 3H), 4.51 (q, *J* = 7.1 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.2 (s), 160.5 (s), 140.3 (s), 138.9 (s), 138.6 (s), 135.2 (s), 134.8 (s), 132.4 (d, 2C), 130.8 (d), 129.5 (d), 129.3 (d), 128.6 (d, 2C), 128.2 (d), 126.4 (d), 125.6 (d), 125.5 (s), 124.0 (d), 122.3 (s), 119.5 (s), 102.1 (s), 93.6 (s), 87.4 (s), 62.1 (t), 14.1 (q); IR (reflection) ṽ = 3352.07, 3095.05, 3074.97, 3060.49, 2993.80, 2979.89, 2933.59, 2213.71, 1677.22, 1614.86, 1586.66, 1560.55, 1495.53, 1442.72, 1408.14, 1372.44, 1315.31, 1258.74, 1213.90, 1159.73, 1125.07, 1092.26, 1044.13, 1028.76, 904.72, 862.77, 831.52, 804.41, 750.92, 717.91, 706.11, 685.53, 669.74, 628.68 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{26}H_{16}NO_3S$ calcd for 422.0856, found 422.0857.



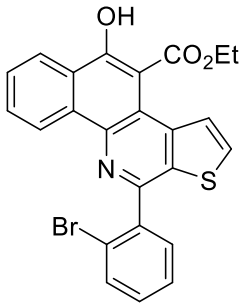
Compound **28**: Yield: 66.3 mg, 83%; white solid, mp 159.0 – 160.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.62 (s, 1H), 9.42 (d, *J* = 8.2 Hz, 1H), 8.56 – 8.42 (m, 1H), 8.42 – 8.23 (comp, 2H), 7.88 – 7.80 (m, 1H), 7.74 – 7.52 (comp, 6H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.1 (s), 150.4 (s), 142.0 (s), 139.8 (s), 138.1 (s), 135.3 (s), 133.6 (s), 130.6 (d), 129.6 (d), 129.1 (d), 128.9 (d, 2C), 128.8 (d, 2C), 127.9 (d), 126.4 (d), 125.5 (s), 125.3 (d), 124.0 (d), 118.5 (s), 101.9 (s), 62.0 (s), 14.2 (s); IR (reflection) ṽ = 3100.94, 3062.85, 2977.99, 2935.22, 1639.45, 1586.58, 1561.90, 1493.76, 1473.97, 1445.30, 1411.07, 1398.91, 1372.04, 1303.88, 1286.69, 1261.14, 1225.96, 1174.71, 1152.79, 1114.34, 1094.56, 1081.20, 1029.03, 962.81, 917.60, 876.84, 855.08, 829.40, 810.86, 793.55, 771.06, 753.69, 729.61, 694.51, 660.38, 647.28, 634.71 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{18}NO_3S$ calcd for 400.1002, found 400.0999.



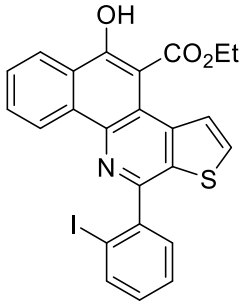
Compound **29**: Yield: 76.8 mg, 92%; white solid, mp 165.0 – 167.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.66 (s, 1H), 9.36 (d, J = 7.8 Hz, 1H), 8.55 – 8.45 (m, 1H), 7.99 – 7.91 (m, 1H), 7.86 – 7.79 (m, 1H), 7.73 – 7.66 (comp, 2H), 7.61 – 7.50 (comp, 2H), 7.41 – 7.28 (comp, 2H), 4.53 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.4 (d, $J_{C\text{-}F}$ = 250.5 Hz), 160.3 (s), 146.7 (s), 141.3 (s), 138.1 (s), 135.4 (d, J = 46.6 Hz), 131.9 (d, $J_{C\text{-}F}$ = 3.2 Hz), 131.2 (d, $J_{C\text{-}F}$ = 8.3 Hz), 130.7 (d), 129.1 (d), 128.0 (d), 127.7 (d, $J_{C\text{-}F}$ = 14.1 Hz), 126.1 (s), 125.4 (s), 125.3 (d), 124.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 124.0 (d), 119.0 (s), 116.5 (d, $J_{C\text{-}F}$ = 21.7 Hz), 101.9 (s), 62.1 (t), 14.2 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -112.35 (s); IR (reflection) ṽ = 3086.90, 2927.11, 2853.67, 1637.82, 1587.65, 1498.54, 1474.90, 1446.41, 1406.30, 1372.35, 1345.66, 1311.89, 1285.23, 1264.79, 1236.60, 1179.19, 1160.11, 1118.42, 1095.90, 1028.22, 1013.96, 945.53, 881.35, 854.87, 829.17, 803.42, 766.95, 752.21, 687.67, 660.87, 642.58 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}FNO_3S$ calcd for 418.0908, found 418.0904.



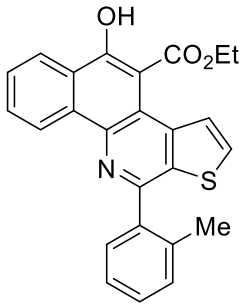
Compound **30**: Yield: 78.1 mg, 90%; thick liquid; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.62 (s, 1H), 9.40 – 9.31 (m, 1H), 8.56 – 8.45 (m, 1H), 7.85 – 7.78 (m, 1H), 7.77 – 7.67 (comp, 3H), 7.65 – 7.59 (comp, 2H), 7.51 – 7.45 (comp, 2H), 4.54 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.3 (s), 149.5 (s), 141.2 (s), 138.7 (s), 138.2 (s), 135.7 (s), 135.4 (s), 133.4 (s), 131.4 (d), 130.7 (d), 130.6 (d), 130.4 (d), 129.3 (d), 128.0 (d), 127.0 (d), 126.2 (d), 125.6 (d), 125.5 (s), 124.0 (d), 119.1 (s), 102.1 (s), 62.1 (t), 14.2 (q); IR (reflection) ṽ = 2979.35, 2933.09, 2871.86, 1754.97, 1732.78, 1693.54, 1651.47, 1588.74, 1546.62, 1499.36, 1461.81, 1441.49, 1408.87, 1371.58, 1307.49, 1289.13, 1231.90, 1179.48, 1160.37, 1097.86, 1057.21, 1030.08, 909.59, 880.74, 830.99, 765.29, 732.75, 665.61, 640.79 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}ClNO_3S$ calcd for 434.0612, found 434.0630.



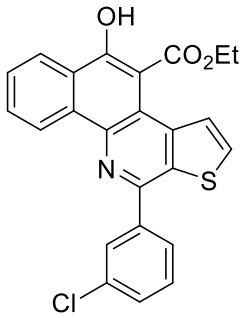
Compound **31**: Yield: 81.3 mg, 85%; thick liquid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.62 (s, 1H), 9.37 (d, *J* = 7.8 Hz, 1H), 8.50 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.88 – 7.77 (comp, 2H), 7.77 – 7.66 (comp, 3H), 7.63 (d, *J* = 5.6 Hz, 1H), 7.52 (td, *J* = 7.5, 1.2 Hz, 1H), 7.41 (td, *J* = 7.8, 1.7 Hz, 1H), 4.55 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.3 (s), 150.7 (s), 141.3 (s), 140.5 (s), 138.1 (s), 135.5 (s), 135.4 (s), 133.8 (d), 131.3 (d), 130.7 (d), 130.6 (d), 129.4 (d), 128.0 (d), 127.6 (d), 126.3 (d), 125.7 (d), 125.5 (s), 124.0 (d), 122.9 (s), 119.1 (s), 102.1 (s), 62.1 (t), 14.2 (q); IR (reflection) $\tilde{\nu}$ = 2963.97, 2932.85, 2872.64, 1756.13, 1694.10, 1655.24, 1597.58, 1547.23, 1458.35, 1409.73, 1366.78, 1288.73, 1228.90, 1173.62, 1097.04, 1051.46, 1027.48, 934.44, 851.37, 828.84, 769.03, 710.01, 656.36, 641.40 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{24}H_{15}BrNO_3S$ calcd for 475.9962, found 475.9962.



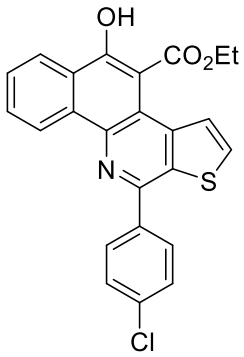
Compound **32**: Yield: 91.4 mg, 87%; thick liquid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.63 (s, 1H), 9.42 (d, *J* = 8.3 Hz, 1H), 8.51 (dd, *J* = 8.0, 0.8 Hz, 1H), 8.12 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.87 – 7.80 (m, 1H), 7.78 – 7.69 (comp, 2H), 7.68 (d, *J* = 5.6 Hz, 1H), 7.63 (d, *J* = 5.6 Hz, 1H), 7.54 (td, *J* = 7.6, 0.9 Hz, 1H), 7.23 (td, *J* = 7.6, 1.6 Hz, 1H), 4.55 (q, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 160.3 (s), 152.5 (s), 143.8 (s), 141.4 (s), 140.5 (s), 138.0 (s), 135.4 (s), 135.1 (s), 130.7 (d), 130.6 (d), 130.3 (d), 129.4 (d), 128.3 (d), 128.0 (d), 126.4 (d), 125.8 (d), 125.5 (s), 124.0 (d), 119.0 (s), 102.08 (s), 97.5 (s), 62.1 (t), 14.2 (q); IR (reflection) $\tilde{\nu}$ = 2958.03, 1752.32, 1688.40, 1650.21, 1587.30, 1544.50, 1498.50, 1457.31, 1444.50, 1407.65, 1371.50, 1349.96, 1306.41, 1230.74, 1179.52, 1159.80, 1119.34, 1097.04, 1029.22, 1015.92, 879.66, 853.85, 830.55, 762.50, 725.22, 638.37 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}INO_3S$ calcd for 525.9968, found 525.9979.



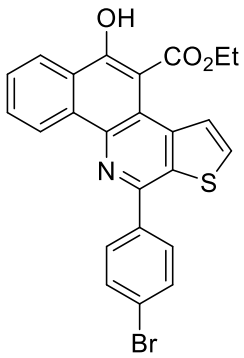
Compound **33**: Yield: 77.7 mg, 94%; white solid, mp 125.0 – 127.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.60 (s, 1H), 9.35 (d, *J* = 7.9 Hz, 1H), 8.67 – 8.42 (m, 1H), 7.86 – 7.78 (m, 1H), 7.77 – 7.58 (comp, 4H), 7.52 – 7.33 (comp, 3H), 4.56 (q, *J* = 7.2 Hz, 2H), 2.47 (s, 3H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 159.9 (s), 152.0 (s), 141.2 (s), 139.2 (s), 138.1 (s), 137.2 (s), 135.9 (s), 135.4 (s), 131.3 (d), 130.6 (d), 129.5 (d), 129.4 (d), 129.2(d), 127.9 (d), 126.3 (d), 125.9 (d), 125.5 (s), 125.4 (d), 124.0 (d), 118.5 (s), 102.1 (s), 62.0 (t), 20.4 (q), 14.2(q); IR (reflection) ṽ = 3081.85, 2963.09, 1635.16, 1588.76, 1561.32, 1496.15, 1476.16, 1445.61, 1408.17, 1372.44, 1343.72, 1306.44, 1284.52, 1258.71, 1235.21, 1179.38, 1160.75, 1096.54, 1029.17, 1016.41, 963.44, 945.69, 878.98, 853.66, 826.81, 808.97, 768.77, 758.06, 742.51, 725.45, 687.78, 662.91, 646.38, 636.40 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{25}H_{20}NO_3S$ calcd for 414.1158, found 414.1159.



Compound **34**: Yield: 65.1 mg, 75%; white solid, mp 170.0 – 171.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.64 (s, 1H), 9.37 (d, *J* = 8.1 Hz, 1H), 8.48 (dd, *J* = 8.1, 0.9 Hz, 1H), 8.40 – 8.24 (m, 1H), 8.24 – 8.15 (m, 1H), 7.89 – 7.82 (m, 1H), 7.78 – 7.67 (comp, 2H), 7.65 – 7.58 (m, 1H), 7.57 – 7.47 (comp, 2H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 160.4 (s), 148.9 (s), 142.2 (s), 141.6 (s), 138.1 (s), 135.3 (s), 135.0 (s), 133.4 (s), 130.8 (d), 130.1 (s), 129.6 (s), 129.1 (d), 129.1 (s), 129.0 (d), 128.1 (s), 126.9 (s), 126.53 (s), 126.50 (d), 126.48 (s), 125.3 (s), 124.2 (s), 118.9 (s), 101.9 (s), 62.1 (t), 14.2 (q); IR (reflection) ṽ = 2955.68, 2924.54, 2853.72, 1727.78, 1643.57, 1589.36, 1570.29, 1496.18, 1463.82, 1444.47, 1410.13, 1372.49, 1303.33, 1253.99, 1233.25, 1175.86, 1156.90, 1118.71, 1096.03, 1079.27, 1031.45, 958.47, 895.88, 834.52, 792.88, 758.23, 730.90, 706.12, 660.43, 635.42 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}ClNO_3S$ calcd for 434.0612, found 434.0617.

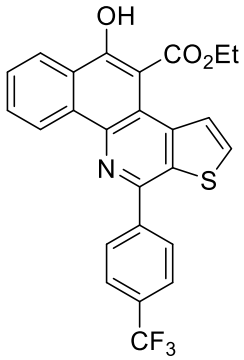


Compound **35**: Yield: 70.3 mg, 81%; white solid, mp 179.0 – 180.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.63 (s, 1H), 9.35 (d, *J* = 8.0 Hz, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.5 Hz, 2H), 7.87 – 7.79 (m, 1H), 7.75 – 7.65 (m, 2H), 7.65 – 7.47 (comp, 3H), 4.52 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 1171.3 (s), 160.3 (s), 149.1 (s), 142.2 (s), 138.2 (s), 138.1 (s), 135.6 (s), 135.2 (s), 133.2 (s), 130.7 (d), 130.1 (d, 2C), 129.1 (d, 2C), 129.0 (d), 128.0 (d), 126.5 (d), 125.6 (s), 125.2 (d), 124.1 (d), 118.7 (s), 101.9 (s), 62.1 (t), 14.2 (q); IR (reflection) ṽ = 3077.97, 2987.10, 2900.89, 1642.94, 1587.82, 1561.50, 1496.55, 1470.17, 1443.29, 1408.04, 1371.48, 1295.42, 1257.87, 1222.72, 1172.59, 1159.00, 1140.05, 1118.77, 1089.09, 1030.48, 1011.22, 959.73, 879.85, 833.89, 791.97, 758.19, 722.46, 692.59, 659.86, 636.92, 626.81 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}ClNO_3S$ calcd for 434.0612, found 434.0616.

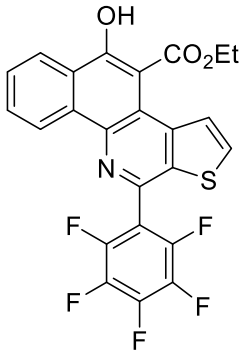


Compound **36**: Yield: 73.7 mg, 77%; white solid, mp 159.0 – 161.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.63 (s, 1H), 9.36 (d, *J* = 8.2 Hz, 1H), 8.48 (d, *J* = 8.2 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 2H), 7.84 (t, *J* = 7.4 Hz, 1H), 7.80 – 7.63 (comp, 4H), 7.63 – 7.54 (m, 1H), 4.52 (q, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 160.3 (s), 149.1 (s), 142.1 (s), 138.6 (s), 138.1 (s), 135.2 (s), 133.2 (s), 132.0 (d, 2C), 130.7 (d), 130.4 (d, 2C), 129.1 (d), 128.0 (d), 126.5 (d), 125.6 (s), 125.2 (d), 124.1 (d), 124.0 (s), 118.7 (s), 101.9 (s), 62.1 (t), 14.2 (q); IR (reflection) ṽ = 3094.00, 2977.05, 2921.37, 2851.27, 1898.17, 1655.06, 1618.02, 1586.41, 1560.74, 1496.36, 1473.59, 1442.73, 1407.18, 1372.30, 1321.24, 1291.64, 1258.39, 1229.84, 1174.52, 1145.39, 1123.34, 1099.20, 1030.34, 1008.47, 957.28, 922.57, 877.98, 856.16, 829.14, 787.76, 758.83, 745.45,

716.22, 705.63, 688.93, 678.20, 656.72, 648.20, 634.10, 621.71 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}BrNO_3S$ calcd for 478.0107, found 478.0119.

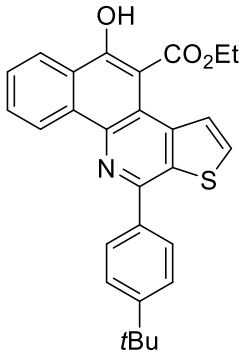


Compound **37**: Yield: 58.0 mg, 62%; white solid, mp 115.0 – 117.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.66 (s, 1H), 9.36 (d, *J* = 8.1 Hz, 1H), 8.49 (d, *J* = 8.1 Hz, 1H), 8.43 (d, *J* = 8.1 Hz, 2H), 7.91 – 7.80 (comp, 3H), 7.79 – 7.66 (comp, 2H), 7.61 (d, *J* = 5.6 Hz, 1H), 4.53 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 160.6 (s), 148.8 (s), 143.2 (d, J_{C-F} = 1.3 Hz), 142.3 (s), 138.2 (s), 135.2 (s), 133.4 (s), 131.6 (s), 131.1 (s), 130.8 (d), 129.2 (d, 2C), 129.1 (d), 128.2 (d), 126.5 (d), 125.9 (q, J_{C-F} = 3.8 Hz, 2C), 125.7 (s), 125.2 (d), 124.2 (d), 101.9 (s), 62.1 (t), 14.2 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -62.55 (s); IR (reflection) $\tilde{\nu}$ = 2977.23, 2935.75, 1757.84, 1695.30, 1650.35, 1617.63, 1587.63, 1545.74, 1497.90, 1473.74, 1415.77, 1372.50, 1322.80, 1228.69, 1167.27, 1112.22, 1066.15, 1030.14, 1015.62, 852.22, 830.19, 793.63, 770.93, 713.80, 693.49, 629.72 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{13}F_5NO_3S$ calcd for 490.0531, found 490.0533.

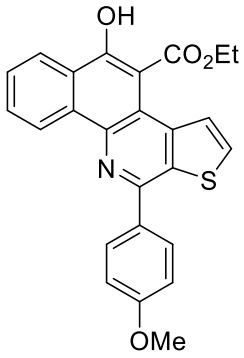


Compound **38**: Yield: 56.8 mg, 58%; white solid, mp 86.0 – 88.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 11.73 (s, 1H), 9.24 (d, *J* = 8.3 Hz, 1H), 8.53 – 8.48 (m, 1H), 7.86 – 7.82 (m, 1H), 7.76 – 7.71 (comp, 2H), 7.64 (d, *J* = 5.5 Hz, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 171.2 (s), 161.1 (s), 141.5 (s), 138.5 (s), 136.3 (s), 135.0 (s), 131.1 (d), 129.2 (d), 128.4 (d), 126.4 (d), 125.6 (s), 125.3 (d), 124.2 (d), 120.0 (s), 101.8 (s), 62.3 (t), 14.2 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -139.41 – -139.55 (m, 2F), -152.19 –

-152.99 (m, 1F), -160.87 – -161.41 (m, 2F); IR (reflection) ṽ = 2983.12, 1651.06, 1587.67, 1523.96, 1494.47, 1445.56, 1407.71, 1371.78, 1318.31, 1290.04, 1230.27, 1164.81, 1131.12, 1098.59, 1082.42, 1034.50, 1016.17, 985.86, 902.57, 859.00, 831.45, 761.44, 731.62, 653.06, 640.87, 622.20 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{13}F_5NO_3S$ calcd for 490.0531, found 490.0533.

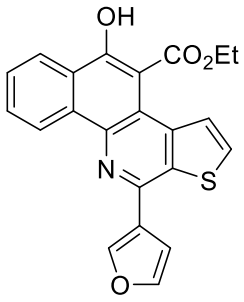


Compound **39**: Yield: 72.9 mg, 80%; white solid, mp 181.0 – 183.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.61 (s, 1H), 9.43 (d, *J* = 7.8 Hz, 1H), 8.48 (dd, *J* = 8.1, 0.7 Hz, 1H), 8.35 – 8.22 (comp, 2H), 7.87 – 7.79 (m, 1H), 7.74 – 7.62 (comp, 4H), 7.59 (d, *J* = 5.6 Hz, 1H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.46 (s, 9H), 1.36 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.0 (s), 152.8 (s), 150.4 (s), 142.0 (s), 138.1 (s), 137.0 (s), 135.4 (s), 133.5 (s), 130.5 (d), 129.0 (d), 128.6 (d, 2C), 127.9 (d), 126.3 (d), 125.8 (d, 2C), 125.5 (s), 125.4 (d), 124.0 (d), 118.4 (s), 102.0 (s), 62.0 (t), 35.0 (s), 31.5 (q, 3C), 14.2 (q); IR (reflection) ṽ = 3093.27, 3072.05, 2988.24, 2957.59, 2924.44, 2900.81, 2864.80, 1651.29, 1588.49, 1495.78, 1467.45, 1412.09, 1364.13, 1300.29, 1285.78, 1263.80, 1226.72, 1197.80, 1174.43, 1160.83, 1144.56, 1118.59, 1097.72, 1080.46, 1028.73, 967.31, 924.57, 878.44, 855.94, 844.37, 829.13, 791.57, 773.53, 765.25, 742.97, 717.31, 673.83, 663.11, 653.71, 630.08 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{28}H_{26}NO_3S$ calcd for 456.1628, found 456.1631.

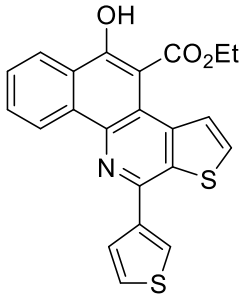


Compound **40**: Yield: 73.9 mg, 86%; white solid, mp 154.0 – 156.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.40 (d, *J* = 8.1 Hz, 1H), 8.46 (d, *J* = 8.1 Hz, 1H), 8.29 (d, *J* = 8.7 Hz, 2H), 7.82 (t, *J* = 7.3 Hz, 1H),

7.70 (d, *J* = 7.3 Hz, 1H), 7.65 (d, *J* = 5.6 Hz, 1H), 7.56 (d, *J* = 5.6 Hz, 1H), 7.13 (d, *J* = 8.7 Hz, 2H), 4.51 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.8 (s), 159.8 (s), 150.0 (s), 142.0 (s), 138.0 (s), 135.3 (s), 133.2 (s), 132.4 (s), 130.4 (d), 130.2 (d, 2C), 128.9 (d), 127.8 (d), 126.4 (d), 125.5 (s), 125.3 (d), 124.0 (d), 118.2 (s), 114.2 (d, 2C), 102.0 (s), 62.0 (t), 55.5 (q), 14.1 (q); IR (reflection) ṽ = 3082.59, 2961.36, 2928.93, 2834.54, 1754.19, 1650.22, 1605.72, 1584.81, 1561.68, 1539.70, 1511.46, 1494.04, 1471.78, 1456.76, 1440.94, 1409.36, 1373.02, 1345.96, 1326.84, 1308.71, 1292.53, 1231.12, 1182.83, 1171.46, 1116.93, 1099.09, 1081.96, 1027.79, 963.09, 891.03, 875.67, 847.55, 836.14, 787.05, 760.95, 716.27, 695.69, 661.08, 634.96, 624.47 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{25}H_{20}NO_4S$ calcd for 430.1108, found 430.1126.

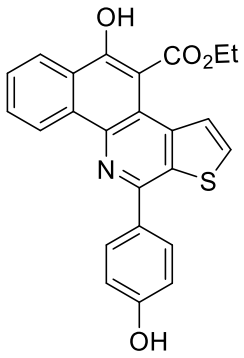


Compound **41**: Yield: 70.1 mg, 90%; white solid, mp 145.0 – 147.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.55 (s, 1H), 9.38 (d, *J* = 8.1 Hz, 1H), 8.48 (d, *J* = 8.1 Hz, 1H), 8.40 (s, 1H), 7.89 – 7.82 (m, 1H), 7.75 – 7.68 (comp, 2H), 7.67 – 7.63 (m, 1H), 7.63 – 7.57 (m, 1H), 7.53 – 7.41 (m, 1H), 4.51 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 159.9 (s), 143.7 (d), 143.5 (s), 142.7 (d), 141.6 (s), 138.0 (s), 135.2 (s), 132.6 (s), 130.6 (d), 128.2 (d), 128.0 (d), 127.0 (s), 126.5 (d), 125.6 (s), 125.3 (d), 124.1 (d), 118.5 (s), 110.3 (d), 102.1 (s), 62.0 (t), 14.2 (q); IR (reflection) ṽ = 3139.07, 2984.18, 2924.96, 2853.33, 1659.35, 1586.57, 1519.22, 1497.59, 1477.65, 1446.20, 1401.66, 1370.26, 1341.21, 1307.08, 1263.75, 1221.28, 1193.64, 1159.39, 1120.78, 1090.74, 1074.79, 1034.73, 987.93, 921.16, 866.54, 830.89, 807.70, 760.59, 710.64, 658.53, 638.90 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{22}H_{16}NO_4S$ calcd for 390.0795, found 390.0801.

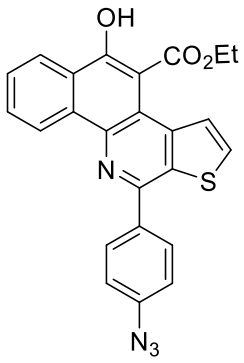


Compound **42**: Yield: 68.1 mg, 84%; white solid, mp 154.0 – 156.0 °C; R_f = 0.3

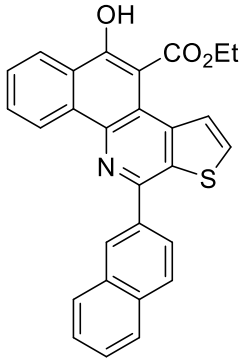
(EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.41 (d, *J* = 8.1 Hz, 1H), 8.49 (dd, *J* = 8.1, 0.8 Hz, 1H), 8.29 (dd, *J* = 2.9, 1.2 Hz, 1H), 8.18 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.90 – 7.82 (m, 1H), 7.80 – 7.66 (comp, 2H), 7.61 (d, *J* = 5.6 Hz, 1H), 7.54 (dd, *J* = 5.0, 2.9 Hz, 1H), 4.52 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.0 (s), 145.8 (s), 142.0 (s), 141.8 (s), 137.8 (s), 135.1 (s), 132.9 (s), 130.6 (d), 128.8 (d), 128.4 (d), 128.0 (d), 126.4 (d), 126.1 (d), 125.7 (d), 125.6 (s), 125.3 (d), 124.1 (d), 118.5 (s), 102.0 (s), 62.1 (t), 14.2 (q); IR (reflection) ṽ = 3113.96, 3092.68, 2984.22, 2922.48, 2853.03, 1649.48, 1589.18, 1563.18, 1542.84, 1497.07, 1476.16, 1403.51, 1370.15, 1321.29, 1297.03, 1259.21, 1229.80, 1204.21, 1168.83, 1140.51, 1098.92, 1082.31, 1032.04, 971.34, 907.58, 883.35, 862.59, 843.29, 829.99, 767.21, 754.81, 710.20, 697.17, 659.14, 639.23 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{22}H_{16}NO_3S_2$ calcd for 406.0566, found 406.0573.



Compound **43**: Yield: 74.0 mg, 89%; thick liquid; R_f = 0.5 (EA/PE = 1/10); ^{1}H NMR (300 MHz, DMSO) δ (ppm) (s, 1H), 9.99 (br, 1H), 9.53 – 9.23 (m, 1H), 8.42 (d, *J* = 7.6 Hz, 1H), 8.25 (d, *J* = 5.6 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 2H), 7.91 – 7.76 (m, 2H), 7.72 (d, *J* = 5.6 Hz, 1H), 7.07 (d, *J* = 8.6 Hz, 2H), 4.56 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO) δ (ppm) 169.1 (s), 158.9 (s), 150.0 (s), 149.4 (s), 140.0 (s), 136.9 (s), 132.7 (s), 132.6 (s), 132.3 (d), 130.2 (s), 129.8 (d, 2C), 128.4 (d), 127.6 (d), 126.90 (s), 125.0 (d), 123.1 (d), 122.7 (d), 117.4 (s), 115.6 (d, 2C), 111.1 (s), 61.6 (t), 13.9 (q); IR (reflection) ṽ = 2256.61, 2126.80, 1719.62, 1649.81, 1609.84, 1588.68, 1541.63, 1519.36, 1496.82, 1471.59, 1445.28, 1409.79, 1372.23, 1308.85, 1277.04, 1233.06, 1171.45, 1097.45, 1026.55, 1003.56, 880.14, 842.78, 767.54, 663.85, 632.65 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{18}NO_4S$ calcd for 416.0951, found 416.0951.

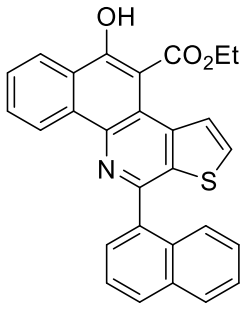


Compound **44**: Yield: 75.8 mg, 86%; white solid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.34 (d, *J* = 8.1 Hz, 1H), 8.44 (d, *J* = 8.1 Hz, 1H), 8.30 (d, *J* = 8.5 Hz, 2H), 7.85 – 7.77 (m, 1H), 7.71 – 7.63 (m, 2H), 7.56 (d, *J* = 5.6 Hz, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 4.49 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.3 (s), 160.2 (s), 149.2 (s), 142.1 (s), 141.3 (s), 138.0 (s), 136.5 (s), 135.2 (s), 133.2 (s), 130.6 (d), 130.3 (d, 2C), 129.0 (d), 128.0 (d), 126.5 (d), 125.6 (s), 125.2 (d), 124.1 (d), 119.4 (d, 2C), 118.6 (s), 101.92 (s), 62.0 (t), 14.2 (q); IR (reflection) ṽ = 2980.56, 2122.69, 2083.15, 1648.97, 1587.62, 1562.95, 1541.68, 1497.20, 1469.98, 1441.91, 1411.66, 1371.57, 1344.45, 1326.27, 1292.51, 1260.78, 1228.54, 1173.32, 1156.65, 1142.58, 1112.68, 1097.61, 1029.07, 1012.81, 960.75, 921.81, 879.03, 840.34, 832.08, 806.18, 789.88, 760.23, 744.27, 730.45, 714.35, 690.14, 672.15, 658.74, 636.99, 628.30 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{24}H_{17}N_4O_3S^+$ calcd for 441.1016, found 441.1017.

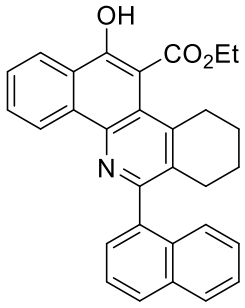


Compound **45**: Yield: 69.2 mg, 77%; thick liquid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.65 (s, 1H), 9.46 (d, *J* = 8.1 Hz, 1H), 8.77 (s, 1H), 8.60 – 8.40 (comp, 2H), 8.07 (d, *J* = 8.6 Hz, 1H), 8.05 – 7.99 (m, 1H), 7.99 – 7.92 (m, 1H), 7.90 – 7.82 (m, 1H), 7.77 – 7.66 (comp, 2H), 7.64 – 7.51 (comp, 3H), 4.53 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.2 (s), 150.3 (s), 142.1 (s), 138.1 (s), 137.2 (s), 135.3 (s), 134.0 (s), 133.8 (s), 133.4 (s), 130.6 (d), 129.1 (d), 128.7 (d), 128.6 (d), 128.3 (d), 127.9 (d, 2C), 126.9 (d), 126.5 (d, 2C), 126.5 (d), 125.6 (s), 125.3 (d), 124.1 (d), 118.6 (s), 102.0 (s), 62.0 (t), 14.2 (q); IR (reflection) ṽ = 3455.08, 3063.31, 2975.68, 2936.09, 2873.77, 1757.75, 1694.50, 1598.61, 1543.97, 1482.34, 1456.70, 1411.84, 1366.91, 1330.50, 1289.58,

1233.32, 1192.34, 1167.65, 1153.05, 1140.00, 1096.41, 1054.45, 1023.43, 966.37, 934.89, 899.35, 861.39, 828.48, 773.31, 753.79, 706.86, 645.34 cm^{-1}; HRMS (ESI) $[M+K]^+$ $C_{28}H_{19}KNO_3S$ calcd for 488.0717, found 488.0934.

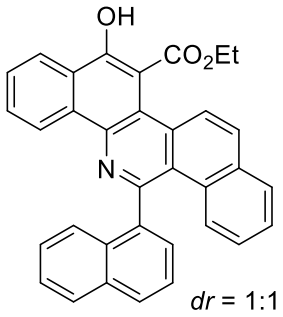


Compound **46**: Yield: 76.4 mg, 85%; thick liquid; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.65 (s, 1H), 9.33 (dd, *J* = 8.1, 0.9 Hz, 1H), 8.53 (dd, *J* = 8.1, 0.9 Hz, 1H), 8.22 (d, *J* = 8.5 Hz, 1H), 8.07 – 7.98 (comp, 3H), 7.79 (ddd, *J* = 8.2, 6.9, 1.5 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.69 – 7.62 (comp, 3H), 7.56 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.46 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 4.57 (q, *J* = 7.2 Hz, 2H), 1.40 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.1 (s), 151.0 (s), 141.6 (s), 138.2 (s), 137.2 (s), 136.7 (s), 135.5 (s), 134.3 (s), 131.7 (s), 130.7 (d), 129.8 (d), 129.4 (d), 128.5 (d), 128.0 (d), 127.7 (d), 126.5 (d), 126.28 (d, 2C), 126.26 (d), 125.5 (d), 125.3 (d), 124.0 (d), 118.7 (s), 102.1 (s), 62.1 (t), 14.2 (q); IR (reflection) $\tilde{\nu}$ = 2977.05, 2934.74, 2872.42, 1755.19, 1693.70, 1653.34, 1587.50, 1543.95, 1508.72, 1496.74, 1457.94, 1406.18, 1370.75, 1351.31, 1304.26, 1289.61, 1230.45, 1160.67, 1094.27, 1050.97, 1025.83, 935.41, 910.18, 830.39, 801.99, 777.79, 736.90, 706.30, 666.69, 641.71 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{28}H_{19}NO_3S$ calcd for 448.1013, found 448.1015.

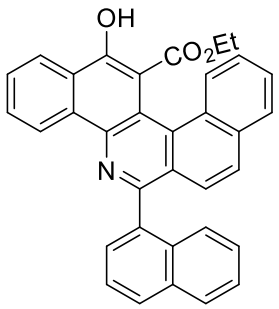


Compound **47**: Yield: 78.8 mg, 88%; white solid, mp 137.0 – 138.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.15 (s, 1H), 9.27 – 9.15 (m, 1H), 8.52 – 8.40 (m, 1H), 8.00 – 7.93 (commp, 2H), 7.74 – 7.58 (comp, 5H), 7.52 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 2.99 (t, *J* = 5.1 Hz, 2H), 2.73 – 2.45 (m, 2H), 1.81 – 1.64 (comp, 4H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.4 (s), 171.5 (s), 159.3 (s), 155.8 (s), 143.8 (s), 140.2 (s), 139.0 (s), 135.2 (s), 133.9 (s), 132.0 (s),

131.0 (s), 130.3 (d), 128.5 (d), 128.3 (d), 128.1 (d), 127.0 (d), 126.3 (d), 125.9 (d), 125.7 (s), 125.6 (d), 125.2 (d), 123.8 (d), 122.9 (s), 102.2 (s), 62.0 (t), 30.5 (t), 26.5 (t), 22.5 (t), 22.3 (t), 14.4 (q); IR (reflection) ṽ = 2939.05, 2863.36, 1650.02, 1586.77, 1568.48, 1498.73, 1445.30, 1403.10, 1373.14, 1311.07, 1231.54, 1206.43, 1158.31, 1095.43, 1016.03, 962.74, 909.17, 882.91, 856.55, 802.14, 781.67, 769.01, 751.03, 725.86, 686.35, 657.83, 636.37, 615.71 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{30}H_{26}NO_3$ calcd for 448.1907, found 448.1904.

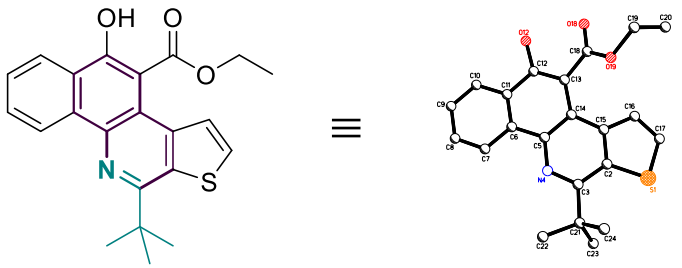


Compound **48**: The desired product was isolated as a mixture of two diastereoisomers Yield: 80.0 mg, 81%; white solid, mp > 350 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $Cl_2CDCDCl_2$) δ (ppm) *with two isomers*: 12.33 (s, 1H), 9.48 – 9.31 (m, 1H), 8.94 – 8.83 (m, 1H), 8.74 – 8.64 (m, 1H), 8.17 – 8.07 (comp, 2H), 8.01 – 7.95 (m, 1H), 7.92 – 7.58 (comp, 10H), 7.46 – 7.37 (m, 1H), 3.96 – 3.75 (m, 1H), 3.64 – 3.42 (m, 1H), 0.62 – 0.30 (m, 3H); ^{13}C NMR (150 MHz, $Cl_2CDCDCl_2$) δ (ppm) *with two isomers*: 171.3 (s), 159.8 (s), 156.0 (s) and 155.7 (s), 138.7 (s), 137.3 (s) and 137.2 (s), 134.49 (s) and 134.48 (s), [133.6 – 125.1 combined with 35 peaks] 133.6 (s), 133.4 (s), 132.6 (s), 132.48 (s), 132.46 (s), 132.3 (s), 132.2 (s), 131.2 (s), 131.1 (s), 130.6 (d), 130.5 (d), 128.73 (d), 128.70 (d), 128.3 (d), 128.2 (d), 128.12 (d), 128.08 (d), 128.06 (d), 127.8 (d), 127.7 (d), 126.5 (d), 126.4 (d), 126.3 (d), 126.2 (d), 126.1 (d), 125.99 (d), 125.95 (d), 125.61 (s), 125.59 (s), 125.5 (d), 125.4 (s), 125.3 (s), 125.21 (d), 125.15 (d), 125.1 (d), 124.02 (d) and 124.01 (d), 123.91 (d), 117.8 (s) and 117.7 (s), 103.6 (s) and 103.8 (s), 61.6 (t) and 61.5 (t), 12.6 (q).; IR (reflection) ṽ = 3404.81, 3061.60, 2927.57, 2257.22, 2127.88, 1719.00, 1649.81, 1616.95, 1586.39, 1567.40, 1497.42, 1467.64, 1443.48, 1404.91, 1370.27, 1322.54, 1303.84, 1269.31, 1236.96, 1202.10, 1162.15, 1119.72, 1100.83, 1055.37, 1024.20, 856.40, 833.98, 774.23, 734.72, 696.03, 662.23, 633.77 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{34}H_{24}NO_3$ calcd for 494.1751, found 494.1744.



Compound **49**: Yield: 72.1 mg, 73%; white solid, mp 125.0 – 126.0 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.65 (s, 1H), 9.09 – 8.94 (m, 1H), 8.40 – 8.30 (m, 1H), 7.90 – 7.78 (comp, 3H), 7.74 – 7.63 (comp, 3H), 7.58 – 7.40 (comp, 5H), 7.36 – 7.29 (m, 1H), 7.24 – 7.10 (comp, 2H), 6.87 – 6.73 (m, 1H), 4.27 (q, J = 7.1 Hz, 2H), 1.06 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 172.1 (s), 160.8 (s), 154.7 (s), 142.2 (s), 137.5 (s), 134.6 (s), 134.4 (s), 134.0 (s), 132.7 (s), 131.8 (s), 130.7 (d), 129.5 (s), 129.1 (d), 128.6 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.7 (d), 127.2 (d), 126.6 (d), 126.5 (d), 126.3 (d), 126.3 (d), 126.2 (d), 126.1 (d), 126.0 (d), 125.3 (d), 124.2 (s), 124.1 (d), 119.5 (s), 101.6 (s), 61.9 (t), 14.1 (q); IR (reflection) $\tilde{\nu}$ = 3054.31, 2971.76, 2931.51, 1729.90, 1650.36, 1586.06, 1509.86, 1446.10, 1403.59, 1370.47, 1322.44, 1293.75, 1271.50, 1235.01, 1159.83, 1118.05, 1104.79, 1018.91, 985.55, 836.60, 806.40, 777.14, 738.06, 696.57, 669.93, 636.57 cm^{-1}; HRMS (ESI) $[M+H]^+$ $C_{34}H_{24}NO_3$ calcd for 494.1751, found 494.1746.

2.6.8 Single-crystal X-ray diffraction of 19



Datablock: cz8

```
Bond precision:  C-C = 0.0030 A          Wavelength=0.71073

Cell:            a=10.1686(10)    b=13.3227(13)     c=13.8293(14)
                 alpha=90         beta=90.329(2)    gamma=90
Temperature:     200 K

                 Calculated                Reported
Volume           1873.5(3)                 1873.5(3)
Space group      P 21/n                    P 21/n
Hall group       -P 2yn                    -P 2yn
Moiety formula   C22 H21 N O3 S            ?
Sum formula      C22 H21 N O3 S            C22 H21 N O3 S
Mr               379.46                    379.46
Dx,g cm-3        1.345                     1.345
Z                4                         4
Mu (mm-1)        0.195                     0.195
F000             800.0                     800.0
F000'            800.84
h,k,lmax         13,17,17                  13,17,17
Nref             4296                      4177
Tmin,Tmax        0.978,0.992               0.898,0.959
Tmin'            0.971

Correction method= # Reported T Limits: Tmin=0.898 Tmax=0.959
AbsCorr = MULTI-SCAN

Data completeness= 0.972          Theta(max)= 27.482

R(reflections)= 0.0459( 2937)     wR2(reflections)= 0.1169( 4177)

S = 1.026                  Npar= 252
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

2.6.9 References

[1] C. Zhang, K. Hong, S. Dong, C. Pei, X. Zhang, C. He, W. Hu, X. Xu, *iScience* **2019**, *21*, 499–508.

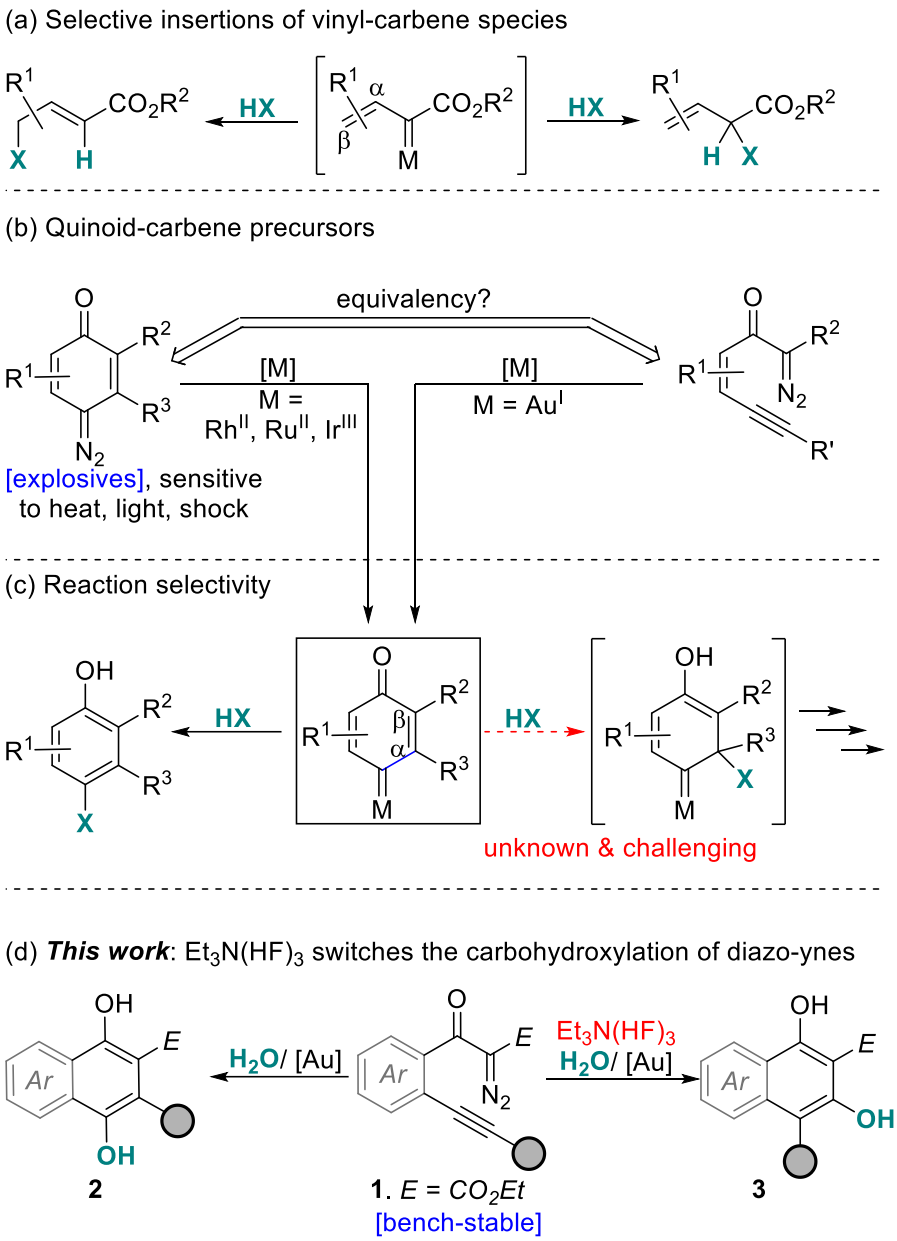
[2] J. Wang, H.-T. Zhu, Y.-X. Li, L.-J. Wang, Y.-F. Qiu, Z.-H. Qiu, M.-J. Zhong, X.-Y. Liu, Y.-M. Liang, *Org. Lett.* **2014**, *16*, 2236 – 2239.

Chapter 3: $Et_3N(HF)_3$-Controlled Regioselective Carbo-Hydroxylations of Diazo-tethered Alkynes by Gold Catalysis

3.1 Introduction

Over the past two decades, gold-catalyzed alkyne transformations have been extensively applied for the construction of carbon–carbon and carbon–heteroatom bonds in chemical synthesis.[1] In this direction, considerable effort has been devoted to the development of hydroxylation reactions that deliver valuable carbonyl compounds from alkynes.[2] To date, a number of reports in improving reaction efficiency and selectivity by using either ligands coordinated to the metal center or external acids have been disclosed.[3] By comparison, the arguably more compelling site-selective variants, which can furnish each member capable of functionalizing a specific site in a particular substrate, are discernibly less established.[4]

Vinyl-carbene species are prominent intermediates for organic reactions.[5] Their dipolar nature makes them susceptible to nucleophilic addition in carbene or vinylogous position (Scheme 1a).[6] Quinone diazides have been used to prepare quinoid carbene by transition metal-catalyzed diazo decomposition,[7] but those substrates are in general potential explosives, and sensitive to heat, light, and shock (Scheme 1b, left).[7a] Very recently, Xu and our group have cooperatively developed a practical and efficient synthesis of the quinoid-carbene species via a gold-triggered 6-*endo*-*dig* diazo-yne carbocyclization.[8] This strategy would render diazo-tethered alkynes equivalent to quinone diazides in accessing quinoid carbene chemistry (Scheme 1b, right), as a result, readily available diazo-tethered alkynes could serve as direct substrates. Inspired by these advances, we hypothesized that the quinoid-carbene intermediate could undergo a Michael reaction with an external donor that delivers the corresponding on-ring carbene for subsequent transformations.



Scheme 1. Catalytic metal carbene insertions.

A key challenge to realise this pathway, is finding a catalytic system capable of the selective vinylogous position rather than direct carbene insertions.[7, 8b] Here, we report our discovery and development of the $Et_3N(HF)_3$-controlled divergent, chemoselective carbohydroxylations of diazo-tethered alkynes, where the regioselectivity would not rely on the inherent reactivity features of the substrates(Scheme 1c). Moreover, a toolbox of additives could be employed in each member capable of functionalizing a specific site in a particular substrate.

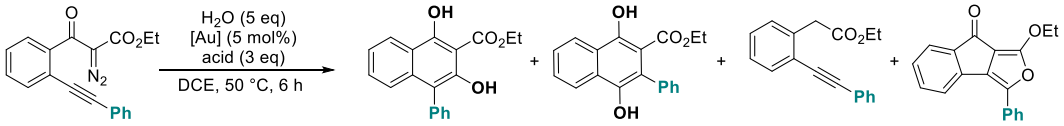
3.2 Results and Discussion

3.2.1 Optimization of the Reaction Conditions

On the basis of this vision, the feasibility of an acid-controlled selectivity switch was initially evaluated by examining the effect of exogenous acids on gold-catalyzed carbohydroxylations of the tethered diazo alkyne **1a** (Table 1), which has already been used for the construction of cyclic molecules with high structural complexity in the presence of rhodium or gold catalysts, respectively.[9] Indeed, an experiment in which **1a** and water were mixed with the gold catalyst at 50 ˚C showed no evidence of a reaction diversity (entry 1) and only the normal product **3a** (derived from the attack of the nucleophilic center onto the activated alkyne, path X) was obtained. But when the same reaction was carried out in the presence of various Brønsted acidic additives, besides the formation of trivial product **3a**, the formation of a regioisomeric cycloadduct **2a** in low to good yields was isolated depending on the applied acid (entries 2 to 6). [$Et_3N(HF)_3$] turned out to be the best choice, which delivered **2a** in a very good yield of 87% and almost perfect regioselectivity. In contrast, with Lewis acids, such as $Sc(OTf)_3$, $Y(OTf)_3$, $Yb(OTf)_3$, $La(OTf)_3$, and $Zn(OTf)_2$, only trace product **2a** was observed, and most of the starting material was transferred into trivial product **3a**, arising from the direct diazo/alkyne cascade and subsequent O–H insertion (entry 7). Upon omission of the catalyst or “HF”, no transformation was observed (entry 8 and 9). Control experiments indicated that **1a** decomposed when strong acid was used in the reaction (entry 10). Other ligands in combination with [$Et_3N(HF)_3$] were screened next. Notably, the use of PPh_3 as the ligand instead of JohnPhos, resulted in no product formation and complete recovery of the substrate **1a** (entry 11) was possible. The IPr ligand was less efficient and only 48% of product **2a** were obtained (entry 12). Other transition metal catalysts involving Cu^{II}-, Ag^{I}-, Rh^{II}- and Pd^{0}-complexes, predominantly underwent intramolecular [3+2] cycloaddition to deliver the indenofuranone **5a** (entry 13).[15a,15b[9]] While DCE was found to be the optimal solvent for the reaction, the carbohydroxylation proceeded with a slightly lower yield of 73% in chloroform-*d*, which is commonly used in control experiments (entry 14).

As a next step, we sought to understand the concentrated influence of $Et_3N(HF)_3$ as additive on the regioselectivity. NMR tube experiments were conducted to qualitatively evaluate the dependency of the selectivity on the concentration of this acid (Scheme 2). By increasing the amount of $Et_3N(HF)_3$, the amount of the cascade product **3a** decreased, and it disappeared at about 1 equivalent of $Et_3N(HF)_3$. At the same time, the amount of regioisomer **2a** kept increasing, with a good selectivity being observed for more than 2 equivalents of $Et_3N(HF)_3$. From these screens, 3 equivalents of $Et_3N(HF)_3$ turned out to be optimal to selectively deliver **2a** in high yield.

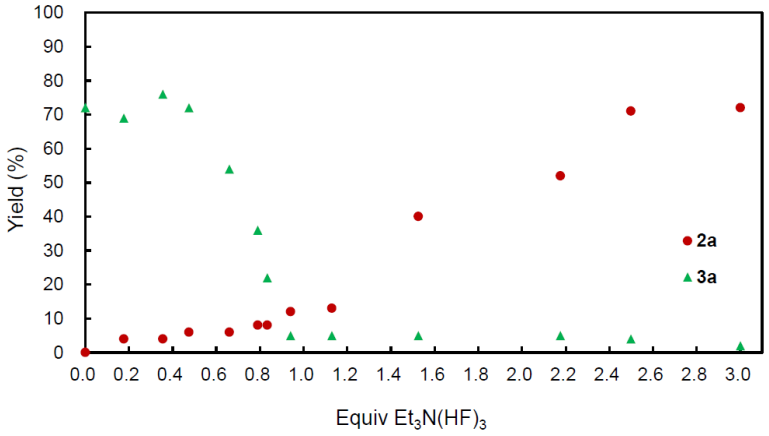
Table 1: Optimization of Reaction Conditions[a]



1a **2a** **3a** **4a** **5a**

entry	acid	note	**2a** (%)[b]	**3a** (%)[b]	**4a** (%)[b]	**5a** (%)[b]
1	None	—	0	83	0	0
2	Py(HF)x	—	<5	63	0	0
3	Py(TsOH)	—	11	64	0	0
4	$Et_3N(H_2SO_4)$	—	19	71	0	0
5	$Et_3N(H_3PO_4)$	—	38	25	0	0
6	$Et_3N(HF)_3$	—	87	<5	0	0
7[c]	Lewis acid	$Sc(OTf)_3$, $Y(OTf)_3$, $Yb(OTf)_3$, $La(OTf)_3$, $Zn(OTf)_2$	<10	40-81	0	0
8[d]	$Et_3N(HF)_3$	No catalyst	0	0	0	0
9[d]	Et_3N	—	0	0	0	0
10[e]	TfOH	No catalyst	0	0	54	0
11[d]	$Et_3N(HF)_3$	PPh_3 instead of JohnPhos	<5	<5	0	0
12	$Et_3N(HF)_3$	IPr instead of JohnPhos	48	<5	0	0
13[c]	$Et_3N(HF)_3$	$Cu(OTf)_2$, $AgSbF_6$, $Rh_2(OAc)_4$, $Pd_2(dba)_3$ instead of [Au]	<5	0	0	75-95
14	$Et_3N(HF)_3$	$CDCl_3$ as solvent	73	<5	0	0

[*a*] Reaction conditions: to a solution of catalyst (0.005 mmol) in DCE (0.25 mL), was added the solution of **1a** (32.0 mg, 0.1 mmol), H_2O (9.0 uL, 0.5 mmol), and acid (0.3 mmol) in DCE (0.25 mL) at room temperature, and the reaction mixture was stirred for 6 hours at 50 ˚C. [*b*] Yields were determined by proton NMR analysis using mesitylene as internal standard. [*c*] See Table S1 in SI for more details. [*d*] Most of **1a** was recovered. [Au] = $JohnPhosAu(CH_3CN)SbF_6$.

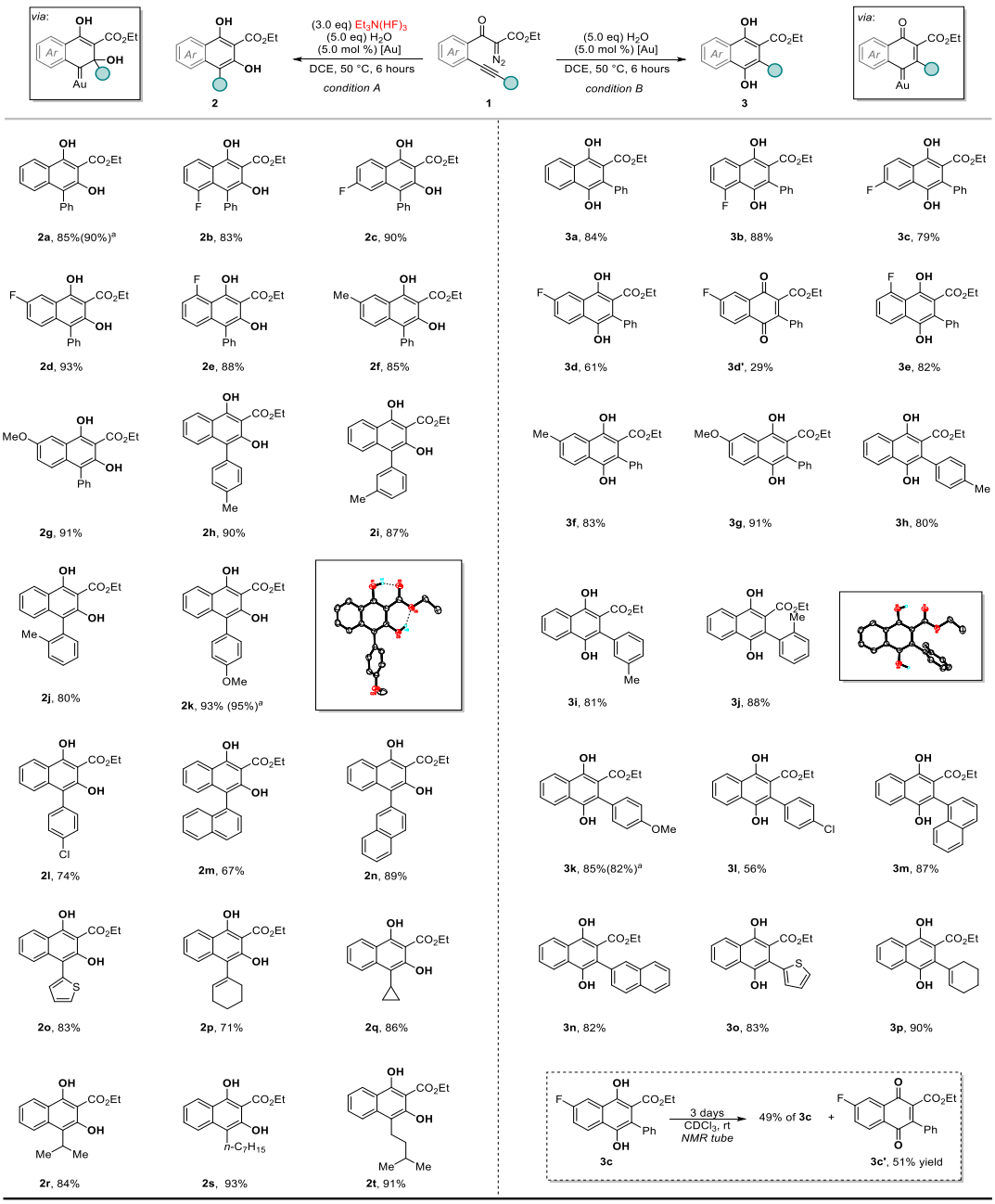


Scheme 2. Plot of the acid concentration *vs* the reaction yield of **2a** and **3a**.

3.2.2 Substrate Scope

Next, the scope of the transformation was investigated, beginning with the examination in the presence of 3 equivalents of $Et_3N(HF)_3$. As summarized on the left side of Scheme 3, a series of fluorine substituents on the aromatic ring (Ar) were well tolerated, delivering the cyclized products **2b**–**2e** in moderate to high yields (83%–93%). Electron-rich (**2f**, **2g**), electron-neutral (**2a**) and electron-poor (**2b**–**2e**) aryl linkers (Ar) were also applicable to this transformation without a noticeable yield deterioration. Going further, substrates with *para*-, *meta*-, and *ortho*-substituents on the phenyl substituent on the alkyne underwent reactions in good yields (**2h**–**2j**). An electron-donating group on the phenyl substituent (**2k**) showed higher reactivity than in the case of a substitution with an electron-withdrawing group (**2l**), presumably because of the weaker coordination of electron-deficient alkynes with a gold(I) catalyst. Naphthyl (**2m**, **2n**) and heteroaryl (**2o**) groups were also easily accommodated using this protocol. Substitution of the alkenyl moiety was tolerated (**2p**) as long as this substituent did not interfere with the putative gold-activated alkyne for nucleophilic addition. The introduction of alkyl groups and even a strained ring to the diazo-tethered alkyne were compatible under *condition A* (**2q**–**2t**). However, the same substrates with alkyl substituents showed no reactivity in the absence of the additive (see section below, *condition B*). Notably, product **2t** a core structure for the preparation of anti-HCV drugs was easily synthesized by our current method in 91% yield.[10]

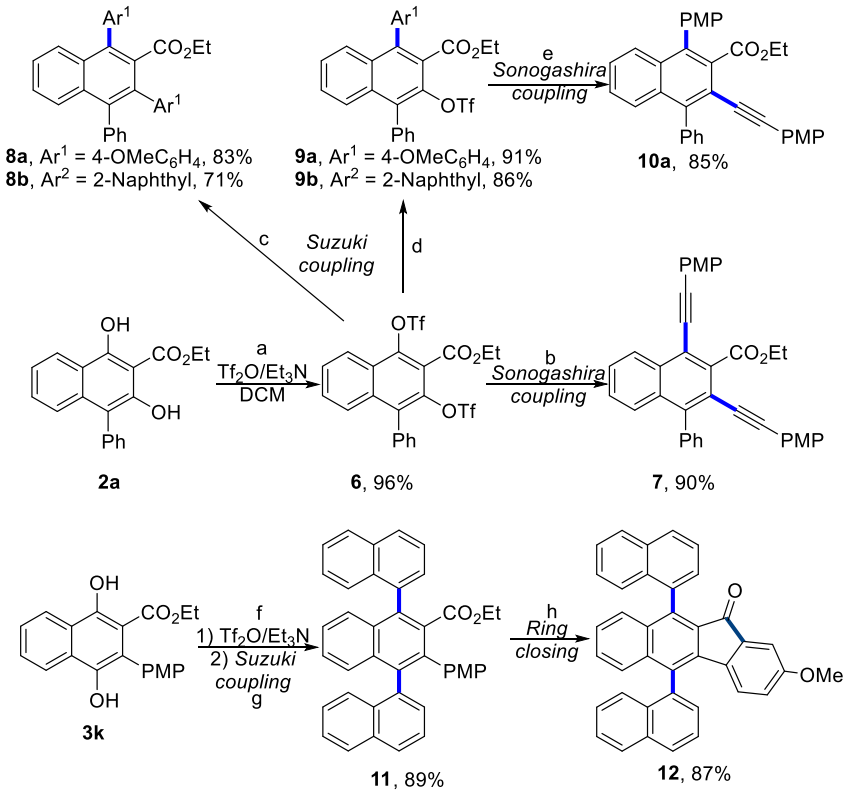
The corresponding cyclization/insertion via the nucleophilic attack onto the alkyne in the absence of an additive (*condition B*) is shown on the right section of Scheme 3. In general, the electronic nature or positions of the substituents on the aromatic ring did not significantly affect the efficiency of the reaction, all substrates generated the corresponding *para*-dinaphthols as single regioisomers (**3a**−**3l**). Specifically, when the aryl linker was combined with a fluorine substituent, we not only discovered the desired product **3d** in 61% yield, but also detected naphthoquinone **3d'** in 29% yield. A control experiment suggested that the oxidation product in this methodology was derived from the dehydrogenation of the target product **3d**. Gratifyingly, this transformation tolerated naphthyl (**3m**, **3n**), heterocyclic (**3o**), and alkenyl (**3p**) groups as well. Besides, gram-scale reactions were carried out under both *condition A* and *condition B*, affording **2a** and **3k** in 90% and 82% yield, respectively. The structures of products **2k** and **3j** were unambiguously confirmed by single-crystal X-ray analysis.[11]



Scheme 3. Regioselective carbohydroxylation. Reaction conditions: to a solution of JohnPhosAu(CH_3CN)SbF_6 (7.7 mg, 0.01 mmol) in DCE (0.5 mL), was added the solution of **1** (0.2 mmol), H_2O (18.0 uL, 1.0 mmol), and $Et_3N(HF)_3$ (98.0 uL, 0.6 mmol, for *condition A*; *condition B* without $Et_3N(HF)$) in DCE (0.5 mL) at 50 ˚C, and the reaction mixture was stirred for 6.0 hours to give isolated yield. [a] The reaction was conducted on a 4.0-mmol scale.

3.2.3 Application

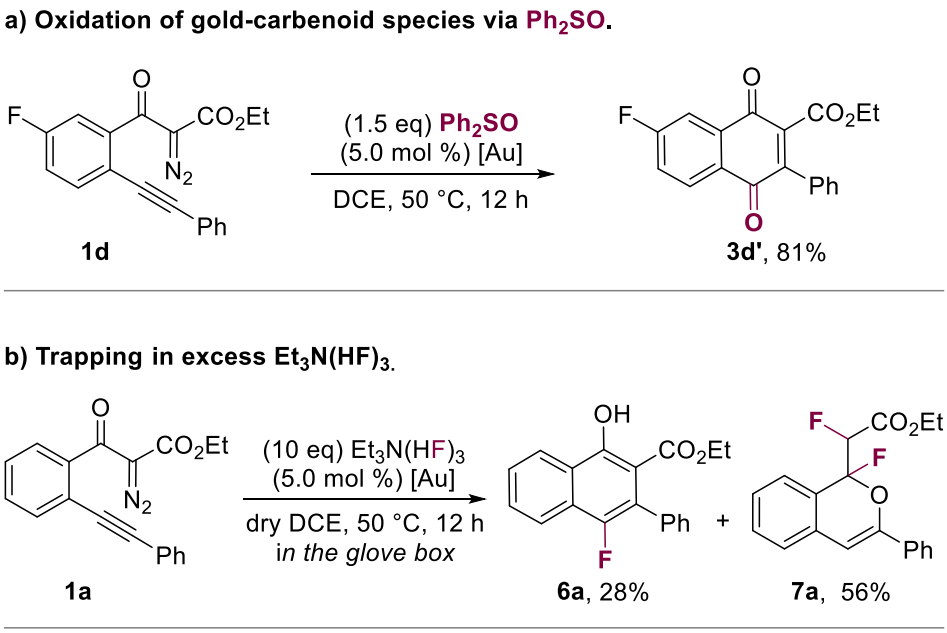
A triflate group as an excellent leaving group was extensively applied in palladium-catalyzed cross-coupling reactions. As showed in Scheme 4, this module **6** was readily established by the trifluoromethanesulfonation of the product **2a**. Facile manipulation of this unit **6** undergoes a Sonogashira coupling reaction with 4-ethynylanisole to deliver the dialkynyl product **7** in high yield. When the Tf-protected substrate **6** was employed to react with 4-anisylboronic acid or 1-naphthylboronic acid at 60 ˚C for 2 hours, Suzuki coupling reactions can provide the monoaryl-functionalized products **8**; the biarylations of the building block were easily achieved in high yield at elevated temperature overnight. Moreover, the monoaryl product **9a** could react with an alkyne again to provide the cross-coupling product **10a**. On the other hand, trifluoromethanesulfonation of the product **3k** with trifluoromethanesulfonic anhydride, followed by a Suzuki coupling reaction, delivered the ternaphthalene **11** in a total 89% yield for the two steps. This tri-naphthalene then underwent an acid-promoted F-C type cyclization to give the polycyclic hydrocarbon **12** in 87% yield.



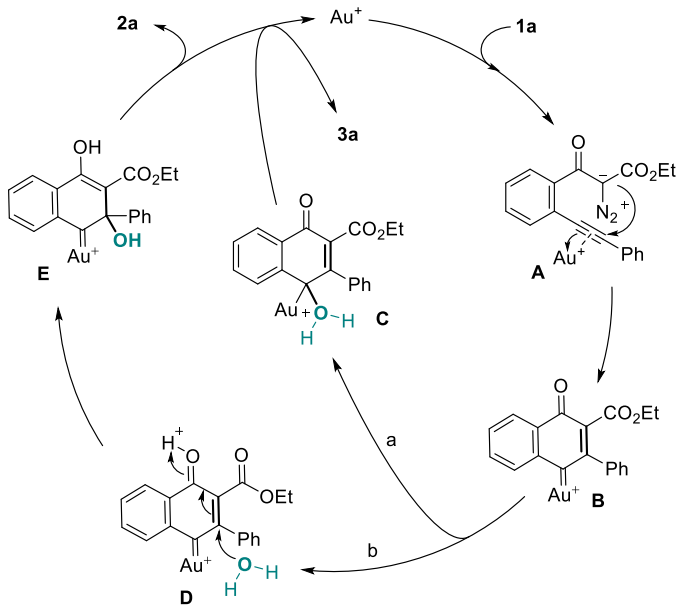
Scheme 4. Applications in coupling reaction.

3.3 Mechanistic study

Based on the reported literature,[8,9c,12] two distinct mechanisms are proposed to explain the chemo- and regioselectivity in the Au(I)-catalyzed carbohydroxylation of diazo-tethered alkynes (Scheme 6). In both cases, the gold(I) catalyst coordinates the alkyne to form a gold π-complex **A**, followed by an intramolecular nucleophilic addition of diazo-carbon onto the activated-alkyne and subsequent loss of N_2 to produce the carbene species **B**. An oxidative experiment of the substrate **1d** in the presence of diphenylsulfoxide affords the naphthoquinone product **3d'**, which also give the certification of the intermediate **B** (Scheme 5). And the direct carbene insertion with carbene give the desired product **2a** under additive-free conditions (path a). For the $Et_3N(HF)_3$ system (path b), the quinoid-carbene species exposed in Brønsted acid undergoes a Michael addition with water to generate the intermediate **D**, followed by a 1,2-phenyl migration to generate the desired product **3a** and to turn over the Au-cycle.



Scheme 5. Control experiments. a) Oxidation of a gold carbene species with diphenylsulfoxide; b) Trapping experiment with excess $Et_3N(HF)_3$.



Scheme 6. Proposed mechanism.

3.4 Conclusions

We have developed an unprecedented dichotomy in the regioselectivity of carbohydroxylation of diazo-tethered alkynes was observed. The gold-catalyzed 6-*endo*-*dig* cyclization leads to the quinoid-carbene species, terminated by direct O-H insertion under additive-free conditions, while reactions in the presence of $Et_3N(HF)_3$ undergo an O-H *ortho*-insertion of carbene/rearrangement to give the dihydroxynaphthalene isomers as the major products. Mechanistic studies indicate that the additive acid promotes a Michael addition of the quinoid-carbene species by protonation of para-carbonyl group. This protocol complements the carbene insertion strategies from the view of chemo- and regioselectivity.

3.5 References

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3.6 Experimental Section

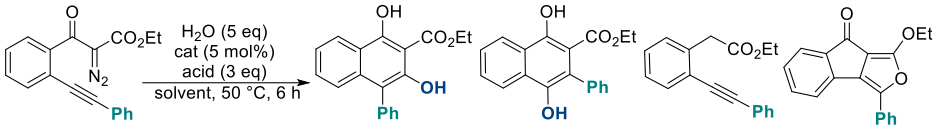
3.6.1 General Information

Chemicals were purchased from commercial suppliers and used as delivered. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. Chemical shifts are given in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet) and comp (combined peaks). When combinations of multiplicities are given the first character noted refers to the biggest coupling constant. All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH2-group), q (quartet, CH3-group)] were determined by DEPT135 spectra. Mass spectra (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^{+}-, ESI^{-}- or $DART^{-}$-spectra a Bruker Apex-Qu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger and T. Oeser on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation.

3.6.2 Optimization of the Reaction Conditions (Table S1)

1a (32.0 mg, 0.1 mmol), solvent (0.25 mL), water (9.0 uL, 0.5 mmol), and acid (0.3 mmol) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the catalyst (0.005 mmol) in 1,2-dichloroethane (0.25 mL) using a syringe was added over 5 minutes at room temperature. After the addition, the reaction mixture was stirred at 50 ˚C for 6 hours. Then, the solvent was removed under reduced pressure and the crude products was analyzed by ^{1}H *NMR* with mesitylene as internal standard in $CDCl_3$.

Table S1. Reaction optimization.



1a **2a** **3a** **4a** **5a**

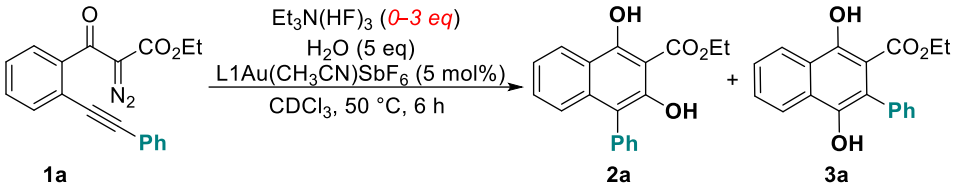
entry	cat	acid	solvent	yield **2a**	yield **3a**	yield **4a**	yield **5a**
1	$L1Au(CH_3CN)SbF_6$	none	DCE	-	83%	< 5%	< 5%
2	$L1Au(CH_3CN)SbF_6$	$Py(HF)_x$	DCE	< 5%	63%	< 5%	< 5%
3	$L1Au(CH_3CN)SbF_6$	Py(TsOH)	DCE	11%	64%	< 5%	< 5%
4	$L1Au(CH_3CN)SbF_6$	$Et_3N+H_2SO_4$	DCE	19%	71%	< 5%	< 5%
5	$L1Au(CH_3CN)SbF_6$	$Et_3N+H_3PO_4$	DCE	38%	25%	< 5%	< 5%
6	$L1Au(CH_3CN)SbF_6$	$Et_3N(HF)_3$	DCE	87%	< 5%	< 5%	< 5%
7	$L1Au(CH_3CN)SbF_6$	$Sc(OTf)_3$	DCE	< 10%	69%	< 5%	< 5%
8	$L1Au(CH_3CN)SbF_6$	$Sc(OTf)_3$ (10 mol %)	DCE	< 10%	81%	< 5%	< 5%
9	$L1Au(CH_3CN)SbF_6$	$Y(OTf)_3$	DCE	< 10%	40%	< 5%	< 5%
10	$L1Au(CH_3CN)SbF_6$	$Yb(OTf)_3$	DCE	< 10%	53%	< 5%	< 5%
11	$L1Au(CH_3CN)SbF_6$	$La(OTf)_3$	DCE	< 10%	42%	< 5%	< 5%
12	$L1Au(CH_3CN)SbF_6$	$Zn(OTf)_2$	DCE	< 10%	57%	< 5%	< 5%
13[a]	none	$Et_3N(HF)_3$	DCE	-	-	-	-
14[a]	$L1Au(CH_3CN)SbF_6$	Et_3N	DCE	-	-	-	-
15	none	TfOH	DCE	-	-	54%	< 5%
16[a]	$PPh_3Au(CH_3CN)SbF_6$	$Et_3N(HF)_3$	DCE	-	-	-	-
17	$IprAu(CH_3CN)SbF_6$	$Et_3N(HF)_3$	DCE	48%	< 5%	< 5%	< 5%
18	$Cu(OTf)_2$	$Et_3N(HF)_3$	DCE	< 5%	< 5%	< 5%	95%
19	$AgSbF_6$	$Et_3N(HF)_3$	DCE	< 5%	< 5%	< 5%	91%
20	$Rh_2(OAc)_4$	$Et_3N(HF)_3$	DCE	< 5%	< 5%	< 5%	75%
21	$Pd_2(dba)_3$	$Et_3N(HF)_3$	DCE	< 5%	< 5%	< 5%	87%
22	$L1Au(CH_3CN)SbF_6$	$Et_3N(HF)_3$	$CDCl_3$	73%	< 5%	< 5%	< 5%

[a] Most of **1a** was recovered. L1 = JohnPhos.

3.6.3 Role of $Et_3N(HF)_3$ (Table S1)

1a (32.0 mg, 0.1 mmol), $CDCl_3$ (0.25 mL), water (9.0 uL, 0.5 mmol), and $Et_3N(HF)_3$ (0 ~ 0.3 mmol) were successively mixed in the NMR tube containing a magnetic stirring bar. Then, $JohnphosAu(CH_3CN)SbF_6$ (3.9 mg, 0.005 mmol) in $CDCl_3$ (0.25 mL) using a syringe was added over 5 minutes at room temperature. After the addition, the reaction mixture was stirred at 50 ˚C for 6 hours. Then, the magnetic stirring bar was taken out and the crude product was analyzed by ^1H *NMR* with mesitylene as internal standard.

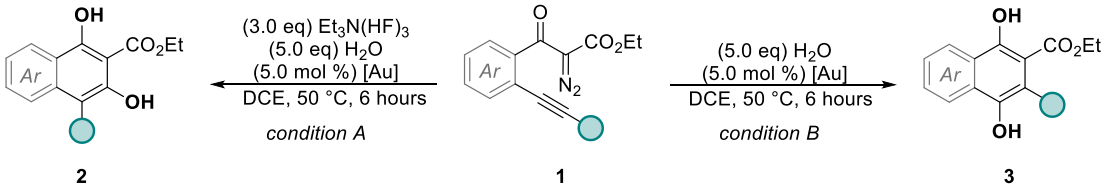
Table S2. Plot of [$Et_3N(HF)_3$] *vs* the yield of 2a and 3a.



entry	$Et_3N(HF)_3$ (***n*** eq)	yield **2a** (%)	yield **3a** (%)
1	0	0	72
2	0.18	4	69
3	0.36	4	76
4	0.48	6	72
5	0.66	6	54
6	0.79	8	36
7	0.83	8	22
8[a]	0.94	12	5
9[a]	1.13	13	5
10	1.53	40	5
11	2.18	52	5
12	2.50	71	4
13	3.00	72	3

[a] The reaction mixture was stirred at 50 ˚C for 18 hours.

3.6.4 Experimental Procedure: Gold-catalyzed Selective Carbohydroxylations of Diazo-ynes



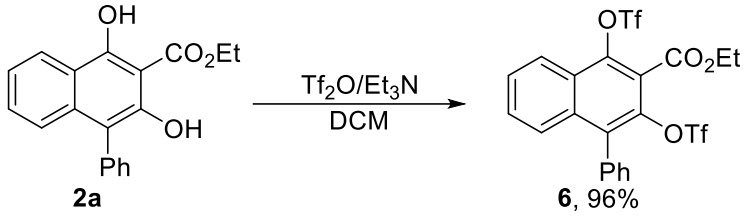
Condition A: The substrate **1** (0.2 mmol), 1,2-dichloroethane (0.5 mL), water (18.0 uL, 1.0 mmol), and $Et_3N(HF)_3$ (98.0 uL, 0.6 mmol) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAu(CH_3CN)SbF_6, 7.7 mg, 0.01 mmol) in 1,2-dichloroethane (0.5 mL) using a syringe was added over 5 minutes at room temperature. After the addition, the reaction mixture was stirred at 50 ˚C for 6 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/20 to 1/10) to afford the pure products **2** in 67%-93% yields.

Condition B: The substrate **1** (0.2 mmol), 1,2-dichloroethane (0.5 mL), and water (18.0 uL, 1.0 mmol) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAu(CH_3CN)SbF_6, 7.7 mg,

0.01 mmol) in 1,2-dichloroethane (0.5 mL) using a syringe was added over 5 minutes at room temperature. After the addition, the reaction mixture was stirred at 50 ˚C for 6 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/20 to 1/10) to afford the pure products **3** in 56%-91% yields.

3.6.5 Experimental Procedure: Applications

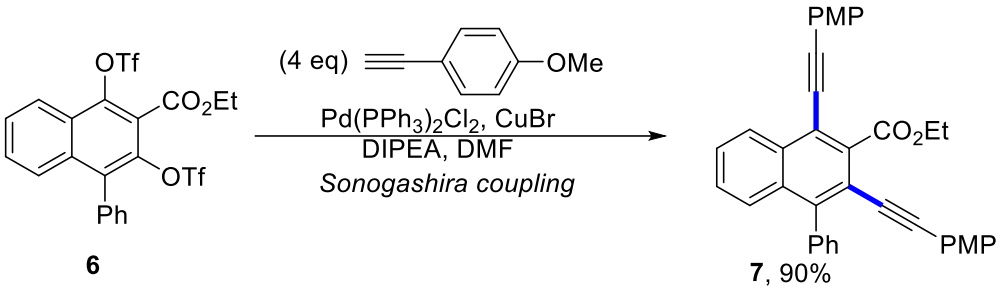
OTf-protection:



2a **6**, 96%

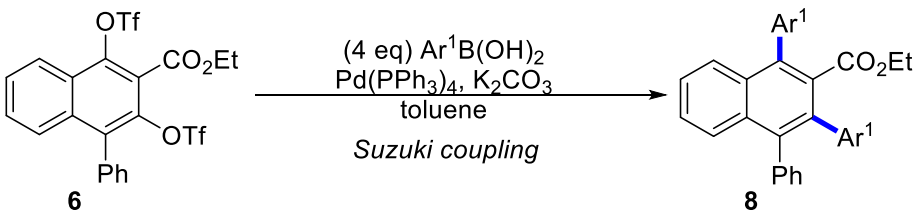
2a (308.3 mg, 1.0 mmol) was dissolved in dry dichloromethane (5.0 mL) and then cooled to -78 ˚C. Triethylamine (Et_3N, 253.0 μL, 1.5 mmol) was added, and then trifluoromethanesulfonic anhydride (Tf_2O, 208.0 μL, 1.5 mmol) was added over 5 minutes via a syringe. The reaction was gradually warmed to room temperature and stirred for about 2 hours until **2a** was completely consumed by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (eluted by ethyl acetate/petroleum ether = 1:50) to give the pure product **6** in 96% yield. White solid, mp 91.0 – 92.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.25 (d, J = 8.5 Hz, 1H), 7.81 – 7.73 (m, 2H), 7.68 – 7.63 (m, 1H), 7.61 – 7.53 (comp, 3H), 7.51 – 7.39 (m, 2H), 4.49 (q, J = 7.2 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 161.7 (s), 142.7 (s), 139.3 (s), 135.4 (s), 134.2 (s), 131.69 (s), 131.3 (d, 2C), 130.2 (d), 129.5 (d), 129.4 (d), 128.7 (d, 2C), 127.5 (d), 126.1 (s), 122.6 (d), 120.5 (s), 118.6 (q, $J_{C\text{-}F}$ = 320.6 Hz), 118.1 (q, $J_{C\text{-}F}$ = 320.7 Hz), 63.6 (t), 13.7 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -72.70 (s), -74.06 (s); IR (reflection) ṽ = 2999.19, 1730.50, 1620.27, 1596.57, 1504.96, 1431.98, 1397.70, 1360.97, 1290.97, 1241.30, 1224.58, 1207.59, 1132.17, 1068.33, 1017.26, 988.94, 945.20, 915.70, 868.95, 842.42, 831.08, 802.90, 770.21, 759.17, 739.25, 729.02, 706.12, 678.90, 659.86, 639.17, 606.33 cm^{-1}; HRMS (EI) (*m/z*) $C_{21}H_{14}F_6O_8S_2$ calcd for 572.0034, found 572.0052.

Sonogashira coupling:



6 (57.2 mg, 0.1 mmol), 1-ethynyl-4-methoxybenzene (53.0 mg, 0.4 mmol), copper(I) bromide (2.1 mg, 0.015 mmol), bis(triphenylphosphine)palladium(II) dichloride (28.0 mg, 0.04 mmol), diisopropylethylamine (DIPEA, 0.2 mL, 1.2 mmol) and DMF (2.0 mL) were added to a 5-mL glass bottle. The reaction was capped and then backfilled with nitrogen. Then, the reaction mixture was heated to 60 °C for 5 hours until **6** was completely consumed as determined by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (eluted by ethyl acetate/petroleum ether = 1:10) to give the pure product **7** in 90% yield. White solid, mp 209.0 – 210.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.51 (d, *J* = 8.3 Hz, 1H), 7.65 – 7.44 (comp, 10H), 7.10 – 7.02 (m, 2H), 6.98 – 6.91 (m, 2H), 6.80 – 6.72 (m, 2H), 4.57 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 1.46 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 168.4 (s), 160.2 (s), 159.8 (s), 143.4 (s), 138.4 (s), 136.5 (s), 133.4 (d, 2C), 133.0 (d, 2C), 132.3 (s), 132.1 (s), 130.8 (d, 2C), 128.2 (d, 2C), 127.9 (d), 127.8 (d), 127.7 (d), 127.2 (d), 127.1 (d), 118.8 (s), 117.6 (s), 115.3 (s), 115.2 (s), 114.3 (d, 2C), 114.0 (d, 2C), 98.8 (s), 96.9 (s), 85.6 (s), 83.5 (s), 61.9 (t), 55.5 (q), 55.4 (q), 14.7 (q); IR (reflection) $\tilde{\nu}$ = 3064.03, 2956.43, 2839.66, 2204.49, 1721.80, 1604.22, 1568.57, 1552.81, 1508.80, 1463.97, 1442.26, 1411.70, 1376.46, 1312.71, 1293.40, 1250.27, 1237.69, 1199.56, 1170.45, 1153.92, 1131.29, 1105.61, 1067.86, 1026.61, 939.78, 901.71, 847.36, 821.37, 794.94, 753.97, 742.07, 698.00, 668.64, 637.13, 616.79 cm^{-1}; HRMS (EI) (*m/z*) $C_{37}H_{28}O_4$ calcd for 536.1988, found 536.1964.

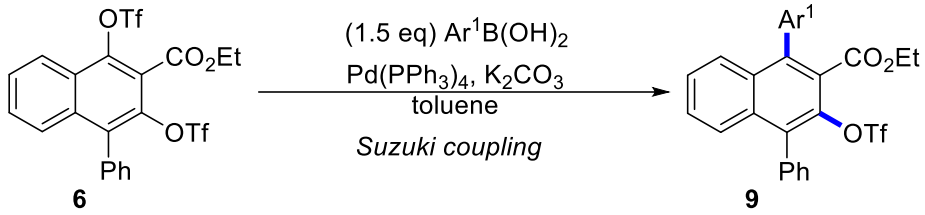
Suzuki coupling:



6 (57.2 mg, 0.1 mmol), aryl-boronic acid (0.4 mmol), tetrakis(triphenylphosphine) palladium(0) (23.0 mg, 0.02 mmol), potassium carbonate (42.5 mg, 0.3 mmol) and

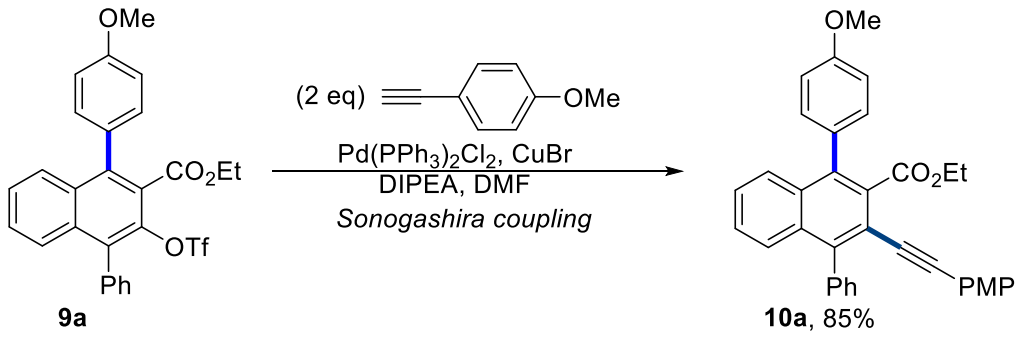
toluene (2.0 mL) were added to a 5-mL glass bottle. The reaction was capped and then backfilled with nitrogen. Then, the reaction mixture was heated to 80 °C for 12 hours until **6** was completely consumed as determined by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (eluted by ethyl acetate/petroleum ether = 1:10) to give the pure product **8a** and **8b** in 83% and 71% yields, respectively.

Suzuki coupling:



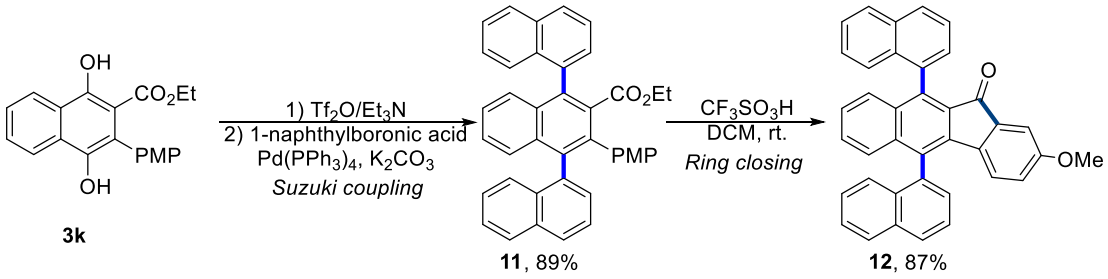
6 (114.4 mg, 0.2 mmol), aryl-boronic acid (0.3 mmol), tetrakis(triphenylphosphine) palladium (0) (11.5 mg, 0.01 mmol), potassium carbonate (21.5 mg, 0.15 mmol) and toluene (1.0 mL) were added to a 5-mL glass bottle. The reaction was capped and then backfilled with nitrogen. Then, the reaction mixture was heated to 60 °C for 2 hours until most of **6** was completely consumed as determined by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (eluted by ethyl acetate/petroleum ether = 1:15) to give the pure product **9a** and **9b** in 91% and 86% yields, respectively.

Sonogashira coupling:



9a (53.0 mg, 0.1 mmol), 1-ethynyl-4-methoxybenzene (27.0 mg, 0.2 mmol), copper(I) bromide (0.7 mg, 0.005 mmol), bis(triphenylphosphine)palladium(II) dichloride (14.0 mg, 0.02 mmol), diisopropylethylamine (DIPEA, 0.1 mL, 0.6 mmol) and DMF (1.0 mL) were added to a 5-mL glass bottle. The reaction was capped and then backfilled with nitrogen. Then, the reaction mixture was heated to 60 °C for 5 hours until **9a** was completely consumed as determined by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography

on silica gel (eluted by ethyl acetate/petroleum ether = 1:10) to give the pure product **10a** in 85% yield. White solid, mp 160.0 – 163.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.70 – 7.64 (m, 2H), 7.58 – 7.48 (comp, 5H), 7.44 – 7.35 (comp, 4H), 7.10 – 6.97 (comp, 4H), 6.76 (d, *J* = 7.9 Hz, 2H), 4.18 (q, *J* = 6.9 Hz, 2H), 3.90 (s, 3H), 3.77 (s, 3H), 1.12 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 168.8 (s), 159.7 (s), 159.4 (s), 142.7 (s), 138.8 (s), 136.8 (s), 133.6 (s), 133.0 (d, 2C), 132.6 (s), 132.0 (s), 131.6 (d, 2C), 130.9 (d, 2C), 129.6 (s), 128.1 (d, 2C), 127.7 (d), 127.1 (d, 2C), 127.0 (d), 126.9 (d), 117.2 (s), 115.4 (s), 113.9 (d, 2C), 113.7 (d, 2C), 96.6 (s), 86.1 (s), 61.3 (t), 55.5 (q), 55.4 (q), 14.2 (q); IR (reflection) ṽ = 2976.46, 2934.58, 2838.59, 2207.67, 1732.22, 1603.50, 1576.95, 1509.63, 1460.82, 1443.99, 1381.35, 1308.20, 1290.43, 1247.32, 1223.66, 1177.29, 1137.14, 1109.07, 1054.40, 1025.57, 945.20, 904.74, 868.25, 830.10, 813.57, 777.55, 740.33, 702.29, 683.31, 640.99, 611.42 cm^{-1}; HRMS (EI) (*m/z*) $C_{35}H_{28}O_4$ calcd for 512.1988, found 512.1964.



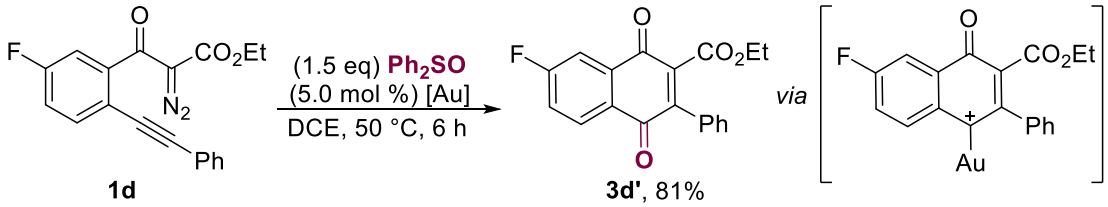
OTf-protected* 3k: 3k** (170.0 mg, 0.5 mmol) was dissolved in dry dichloromethane (4.0 mL) and then cooled to -78 ˚C. Triethylamine (Et_3N, 130.0 μL, 0.75 mmol) was added, and then trifluoromethanesulfonic anhydride (Tf_2O, 104.0 μL, 0.75 mmol) was added over 10 minutes via a syringe. The reaction was gradually warmed to room temperature and stirred for about 2 hours until **2a** was completely consumed by TLC. Afterwards, the solvent was evaporated under vacuum after filtering through Celite, and the obtained **3k-*OTf was directly used for the next step without further purification.

Suzuki coupling*:** To a 10-mL oven-dried round-bottom flask containing a magnetic stirring bar, the above **3k-*OTf, 1-naphthylboronic acid (344mg, 2.0 mmol), tetrakis(triphenylphosphine)palladium(0) (57.8 mg, 0.05 mmol), and potassium carbonate (276.0 mg, 2.0 mmol) in toluene (10.0 mL), were mixed under argon at room temperature. Then, the reaction mixture was heated to 80 °C for 12 hours until **3k-*OTf*** was completely consumed as determined by TLC. Afterwards, the solvent was removed under reduced pressure and the mixture was purified by flash column chromatography on silica gel (eluted by ethyl acetate/petroleum ether = 1:30) to give the pure product **11** in 89%yield. White solid, mp 204.0 – 205.0 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) *with two diastereoisomers*: 8.07 – 8.00 (comp, 2H), 7.94 – 7.84 (comp, 2H), 7.78 – 7.73 (comp, 1H), 7.72 – 7.65 (comp, 2H), 7.64 – 7.29 (comp, 12H), 7.14 – 6.89 (br, 1H), 6.82 – 6.61 (br, 1H), 6.56 – 6.29 (br,

1H), 3.67 – 3.54 (comp, 5H), 0.56 – 0.43 (comp, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) *with two diastereoisomers*: 168.9 (s) and 168.8 (s), 158.3 (s) and 158.2 (s), [*138 – 125 with 54 signals*: 137.5 (s), 137.4 (s), 136.6 (s), 136.5 (s), 136.33 (s), 136.27 (s), 135.82 (s), 135.78 (s), 135.63 (s), 135.61 (s), 134.7 (s), 134.6 (s), 133.6 (s), 133.5 (s), 133.42 (s), 133.36 (s), 133.31 (s), 133.27 (s), 133.22 (s), 133.16 (s), 131.9 (s), 131.8 (s), 131.7 (s), 131.5 (s), 129.4 (d), 129.2 (d), 128.7 (d), 128.52 (d), 128.50 (d), 128.3 (d), 128.2 (d), 128.1 (d), 127.8 (d), 127.7 (d), 127.4 (d), 127.33 (d), 127.28 (d), 127.2 (d), 127.1 (d), 127.0 (d), 126.8 (d), 126.6 (d), 126.5 (d), 126.4 (d), 126.3 (d), 126.2 (d), 126.13 (d), 126.07 (d), 126.0 (d), 125.7 (d), 125.33 (d), 125.31 (d), 125.3 (d), 125.2 (d)] 112.6 (d) and 112.5 (d), 60.44 (t), 54.92 (q), 13.23 (q) and 13.18 (q); IR (reflection) ṽ = 3060.08, 2961.12, 1728.52, 1611.07, 1514.21, 1460.79, 1409.08, 1362.94, 1300.73, 1246.34, 1231.00, 1176.44, 1137.46, 1121.02, 1077.52, 1030.36, 928.33, 858.92, 826.63, 799.53, 774.82, 738.17, 698.00, 666.22 cm^{-1}; HRMS (EI) (*m/z*) C40H30O3 calcd for 558.2195, found 558.2179.

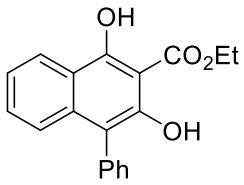
Ring closing: A solution of trifluoromethanesulfonic acid (87.0 μL, 1.0 mmol) in dry dichloromethane (1.0 mL) was added over 5 min to a 10-mL glass bottle containing a magnetic stirring bar, and **11** (112.0 mg, 0.2 mmol) in dry dichloromethane (1.0 mL) using a syringe at room temperature. After the addition, the reaction mixture was stirred for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/15) to afford the polycyclic product **12** in 87% yield. White solid, mp 198.0 – 199.0 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) *with two diastereoisomers*: 8.15 (d, *J* = 8.2 Hz, 1H), 8.11 – 8.05 (comp, 2H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.78 – 7.74 (m, 1H), 7.74 – 7.67 (comp, 2H), 7.65 – 7.59 (comp, 2H), 7.59 – 7.55 (m, 1H), 7.53 – 7.45 (comp, 3H), 7.40 – 7.36 (m, 1H), 7.35 – 7.28 (comp, 3H), 7.25 – 7.20 (m, 1H), 7.02 (d, *J* = 2.6 Hz, 1H), 6.53 (dd, *J* = 8.6, 2.6 Hz, 1H), 5.86 (d, *J* = 8.6 Hz, 1H), 3.68 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 192.0 (s), 160.4 (s), 139.1 (s), 138.5 (s), 137.3 (s), 137.1 (s), 136.8 (s), 135.4 (s), 134.2 (s), 134.1 (s), 133.8 (s), 133.7 (s), 132.8 (s), 132.5 (s), 131.0 (s), 130.4 (s), 129.3 (d), 129.0 (d), 128.9 (d), 128.59 (d), 128.57 (d), 128.5 (d), 128.0 (d), 127.3 (d), 127.1 (d), 126.9 (d), 126.63 (d), 126.62 (d), 126.3 (d, 2C), 126.0 (d), 125.9 (d), 125.7 (d), 125.6 (d), 124.9 (s), 121.1 (d), 108.0 (d), 55.6 (q); IR (reflection) ṽ = 3065.53, 2996.60, 2959.08, 2935.23, 2834.87, 1708.88, 1599.26, 1506.95, 1484.86, 1453.33, 1436.92, 1350.75, 1290.33, 1232.34, 1195.91, 1160.15, 1081.43, 1054.49, 1034.87, 1023.91, 1004.99, 956.68, 888.13, 866.86, 827.93, 809.78, 794.84, 775.03, 726.50, 688.70, 666.13, 648.39, 636.66, 623.39 cm^{-1}; HRMS (EI) (*m/z*) $C_{38}H_{24}O_2$ calcd for 512.1776, found 512.1757.

3.6.6 Experimental Procedure: Trapped Experiment with Phenylsulfoxide.



The diazo-yne **1d** (67.0 mg, 0.2 mmol), 1,2-dichloroethane (0.5 mL), and Phenyl sulfoxide (60.7 mg, 0.3 mmol) were successively mixed in a 5-mL glass bottle containing a magnetic stirring bar. Then, the gold catalyst (JohnphosAu(CH_3CN)SbF_6, 7.7 mg, 0.01 mmol) in 1,2-dichloroethane (0.5 mL) using a syringe was added over 5 minutes at room temperature. After the addition, the reaction mixture was stirred at 50 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/30) to give the pure products **3d'** in 81% yield. Yellow solid, mp 97 – 99 ˚C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.21 (dd, *J* = 8.6, 5.2 Hz, 1H), 7.79 (dd, *J* = 8.4, 2.6 Hz, 1H), 7.50 – 7.33 (comp, 6H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 181.1 (d, *J* = 1.4 Hz), 166.5 (d, *J* = 258.6 Hz), 163.9 (s), 144.9 (s), 139.7 (s), 134.2 (d, *J* = 8.0 Hz), 131.3 (s), 130.6 (d, *J* = 9.0 Hz), 130.1 (d), 129.4 (d, 2C), 128.4 (d, *J* = 3.2 Hz), 128.3 (d, 2C), 121.8 (d, *J* = 22.5 Hz), 113.3 (d, *J* = 23.6 Hz), 62.2 (t), 13.9 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -100.70; IR (reflection) ṽ = 3067.08, 2984.41, 1717.62, 1659.74, 1602.17, 1587.87, 1487.11, 1462.41, 1444.94, 1392.56, 1371.57, 1347.72, 1299.34, 1259.92, 1239.92, 1213.70, 1191.57, 1130.38, 1079.30, 1012.05, 964.52, 938.56, 911.05, 853.10, 814.87, 795.38, 763.59, 734.50, 706.23, 636.86 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FO_4$ calcd for 324.0798, found 324.0807.

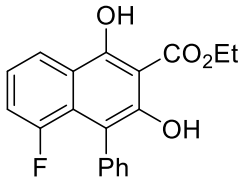
3.6.7 Characterization



Ethyl 1,3-dihydroxy-4-phenyl-2-naphthoate (2a).

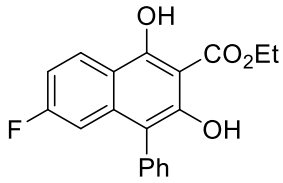
Yield: 52.4 mg, 85%; white solid, mp 117.8 – 120.3 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.61 (s, 1H), 9.29 (s, 1H), 8.36 (d, *J* = 8.4 Hz, 1H), 7.56 – 7.50 (comp, 2H), 7.48 – 7.42 (comp, 2H), 7.40 – 7.30 (comp, 4H), 4.62 (q, *J* = 7.1 Hz, 2H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.4 (s), 150.2 (s), 137.3 (s), 136.1 (s), 131.4 (d, 2C), 130. 6 (d), 128.6 (d, 2C), 127.3 (d), 124.7 (d), 124.3 (d), 123.1 (d), 119.6 (s), 114.9 (s), 97.2 (s), 63.2 (t), 14.4 (q); IR

(reflection) ṽ = 3426, 2984, 1736, 1657, 1640, 1599, 1575, 1506, 1471, 1452, 1442, 1402, 1371, 1333, 1302, 1232, 1194, 1158, 1094, 1081, 1013, 946, 924, 912, 868, 802, 773, 755, 730, 703, 674, 651, 607 cm^{-1}; HRMS (ESI) (*m/z*) $[M-H]^-$ $C_{19}H_{15}O_4$ calcd for 307.0976, found 307.0969.



Ethyl 5-fluoro-1,3-dihydroxy-4-phenyl-2-naphthoate (2b).

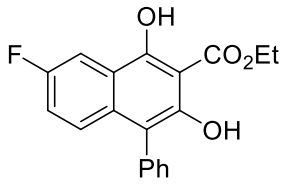
Yield: 54.2 mg, 83%; white solid, mp 156.8 – 157.8 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.69 (s, 1H), 9.28 (s, 1H), 8.32 – 8.13 (m, 1H), 7.53 – 7.40 (comp, 3H), 7.40 – 7.34 (comp, 2H), 7.28 – 7.20 (m, 1H), 7.18 – 7.06 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 1.51 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.2 (s), 161.2 (d, J_{C-F} = 3.9 Hz), 158.3 (d, J_{C-F} = 253.6 Hz), 151.4 (s), 138.1 (d, J_{C-F} = 3.8 Hz), 130.2 (d, J_{C-F} = 3.7 Hz, 2C), 127.8 (d, 2C), 126.9 (d), 126.8 (d, J_{C-F} = 10.4 Hz), 122.9 (d, J_{C-F} = 8.1 Hz), 121.8 (d, J_{C-F} = 4.7 Hz), 120.5 (d, J_{C-F} = 4.4 Hz, d), 116.1 (d, J_{C-F} = 21.8 Hz), 111.7 (d, J_{C-F} = 2.2 Hz), 97.8 (d, J_{C-F} = 1.1 Hz), 63.5 (t), 14.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.53 (s); IR (reflection) ṽ = 3415, 3082, 2995, 1904, 1737, 1664, 1637, 1604, 1576, 1505, 1460, 1445, 1399, 1388, 1332, 1302, 1275, 1231, 1202, 1168, 1142, 1093, 1011, 991, 927, 870, 855, 794, 767, 750, 733, 704, 673, 658, 614 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{19}H_{14}FO_4$ calcd for 325.0882, found 325.0876.



Ethyl 6-fluoro-1,3-dihydroxy-4-phenyl-2-naphthoate (2c).

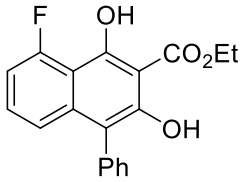
Yield: 58.7 mg, 90%; white solid, mp 102.0 – 104.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.60 (s, 1H), 9.38 (s, 1H), 8.35 (dd, *J* = 9.2, 6.0 Hz, 1H), 7.65 – 7.50 (m, 2H), 7.49 – 7.42 (m, 1H), 7.37 (d, *J* = 7.4 Hz, 2H), 7.16 – 6.88 (comp, 2H), 4.62 (q, *J* = 7.1 Hz, 2H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.3 (s), 164.2 (d, J_{C-F} = 250.4 Hz), 161.3 (s), 151.4 (s), 139.2 (d, J_{C-F} = 10.3 Hz), 135.6 (s), 131.2 (d, 2C), 128.7 (d, 2C), 127.52 (d), 127.45 (d, J_{C-F} = 11.2 Hz), 116.5 (d, J_{C-F} = 0.5 Hz), 114.6 (d, *J* J_{C-F} = 4.8 Hz), 113.1 (d, J_{C-F} = 25.3 Hz), 108.4 (d, J_{C-F} = 22.9 Hz), 96.6 (d, J_{C-F} = 1.8 Hz, s), 63.3 (t), 14.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -107.42 (s); IR (reflection) ṽ = 3416, 2993, 1737, 1664, 1635, 1604, 1575, 1505, 1469, 1459, 1398, 1387, 1332, 1301, 1273, 1231, 1201, 1167, 1142, 1092, 1010, 991, 927, 917, 869, 854, 794, 766, 750, 733, 703, 672, 614 cm^{-1};

HRMS (ESI) $[M-H]^-$ $C_{19}H_{14}FO_4$ calcd for 325.0882, found 325.0875.



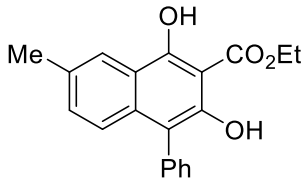
Ethyl 7-fluoro-1,3-dihydroxy-4-phenyl-2-naphthoate (2d).

Yield: 60.7 mg, 93%; white solid, mp 121.3 – 123.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.50 (s, 1H), 9.22 (s, 1H), 7.94 (dd, *J* = 10.0, 2.7 Hz, 1H), 7.57 – 7.49 (m, 2H), 7.46 – 7.41 (m, 1H), 7.39 – 7.30 (comp, 3H), 7.24 – 7.16 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 1.52 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.3 (s), 160.7 (s), 160.3 (d, J_{C-F} = 5.1 Hz), 157.5 (s), 149.7 (d, J_{C-F} = 2.2 Hz), 135.8 (s), 134.1 (s), 131.3 (d, 2C), 128.6 (d, 2C), 127.5 (d), 127.2 (d, J_{C-F} = 8.1 Hz), 120.5 (d, J_{C-F} = 24.8 Hz), 120.0 (d, J_{C-F} = 8.7 Hz), 115.1 (s), 107.8 (d, J_{C-F} = 22.5 Hz), 98.0 (s), 63.4 (t), 14.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -118.36 (s); IR (reflection) ṽ = 3153, 2986, 1738, 1665, 1634, 1615, 1581, 1510, 1468, 1448, 1409, 1389, 1364, 1319, 1300, 1286, 1233, 1222, 1190, 1166, 1137, 1086, 1068, 1008, 976, 943, 875, 828, 799, 784, 764, 753, 728, 712, 695, 660, 627 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{19}H_{14}FO_4$ calcd for 325.0882, found 325.0876.



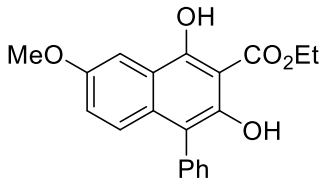
Ethyl 8-fluoro-1,3-dihydroxy-4-phenyl-2-naphthoate (2e).

Yield: 57.4 mg, 88%; Yellow solid, mp 138.2 – 142.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.94 (d, *J* = 3.5 Hz, 1H), 9.27 (s, 1H), 7.45 – 7.37 (m, 2H), 7.35 – 7.29 (m, 1H), 7.25 – 7.14 (comp, 3H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.86 – 6.76 (m, 1H), 4.51 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.3 (s), 162.0 (d, J_{C-F} = 4.3 Hz), 161.0 (d, J_{C-F} = 261.8 Hz), 151.2 (d, J_{C-F} = 1.4 Hz), 139.5 (d, J_{C-F} = 2.4 Hz), 136.0 (s), 131.2 (d, 2C), 130.4 (d, J_{C-F} = 10.0 Hz), 128.7 (d, 2C), 127.5 (d), 120.7 (d, J_{C-F} = 4.4 Hz), 115.0 (d, J_{C-F} = 2.7 Hz), 109.9 (d, J_{C-F} = 9.1 Hz), 108.9 (d, J_{C-F} = 22.3 Hz), 97.8 (d, J_{C-F} = 1.8 Hz), 63.5 (t), 14.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.35; IR (reflection) ṽ = 3447, 3076, 2987, 1738, 1637, 1603, 1582, 1505, 1472, 1451, 1402, 1369, 1321, 1293, 1227, 1215, 1167, 1155, 1140, 1118, 1089, 1058, 1013, 918, 868, 845, 818, 806, 779, 756, 719, 702, 682 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{19}H_{14}FO_4$ calcd for 325.0882, found 325.0876.



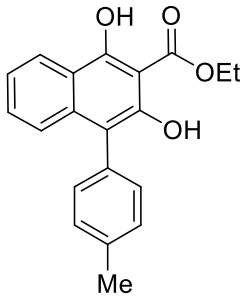
Ethyl 1,3-dihydroxy-7-methyl-4-phenyl-2-naphthoate (2f).

Yield: 54.8 mg, 85%; Yellow solid, mp 118.0 – 120.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.58 (s, 1H), 9.30 (s, 1H), 8.27 (d, *J* = 8.4 Hz, 1H), 7.60 – 7.51 (comp, 2H), 7.50 – 7.43 (m, 1H), 7.43 – 7.35 (comp, 2H), 7.22 – 7.12 (comp, 2H), 4.62 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.4 (s), 150.4 (s), 141.0 (s), 137.5 (s), 136.3 (s), 131.4 (d, 2C), 128.5 (d, 2C), 127.2 (d), 125.3 (d), 124.2 (d), 123.7 (d), 117.8 (s), 114.4 (s), 96.5 (s), 63.0 (t), 22.3 (q), 14.3 (q); IR (reflection) $\tilde{\nu}$ = 3438, 2970, 1738, 1661, 1639, 1619, 1578, 1509, 1467, 1445, 1400, 1376, 1310, 1248, 1216, 1178, 1142, 1089, 1072, 1032, 941, 872, 858, 824, 797, 779, 761, 741, 698, 661, 638 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_4$ calcd for 322.1205, found 322.1210.



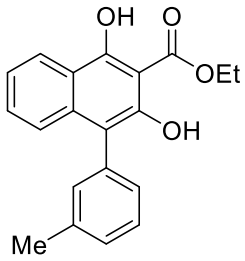
Ethyl 1,3-dihydroxy-7-methoxy-4-phenyl-2-naphthoate (2g).

Yield: 61.6 mg, 91%; Yellow solid, mp 138.7 – 139.5 °C; R_f = 0.4 (EA/PE = 1/5);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.07 (s, 1H), 7.63 (d, *J* = 2.7 Hz, 1H), 7.55 – 7.48 (m, 2H), 7.46 – 7.35 (comp, 3H), 7.30 (d, *J* = 9.2 Hz, 1H), 7.15 – 7.08 (m, 1H), 4.62 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 3H), 1.50 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.6 (s), 159.9 (s), 155.9 (s), 148.6 (s), 136.2 (s), 132.7 (s), 131.4 (d, 2C), 128.6 (d, 2C), 127.3 (d), 126.4 (d), 123.2 (d), 120.2 (s), 115.1 (s), 102.1 (d), 97.6 (s), 63.2 (t), 55.5 (q), 14.4 (q); IR (reflection) $\tilde{\nu}$ = 3438, 3419, 3002, 2828, 1661, 1639, 1619, 1578, 1509, 1467, 1445, 1400, 1376, 1309, 1248, 1216, 1185, 1178, 1142, 1089, 1071, 1032, 941, 871, 858, 824, 797, 779, 761, 741, 698, 661, 637 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{20}H_{17}O_5$ calcd for 337.1081, found 337.1076.



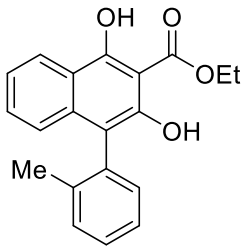
Ethyl 1,3-dihydroxy-4-(*p*-tolyl)-2-naphthoate (2h).

Yield: 58.0 mg, 90%; Yellow solid, mp 125.6 – 128.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.48 (s, 1H), 9.14 (s, 1H), 8.29 – 8.19 (m, 1H), 7.36 – 7.27 (comp, 2H), 7.27 – 7.19 (comp, 3H), 7.18 – 7.14 (comp, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.5 (s), 161.3 (s), 150.3 (s), 137.4 (s), 136.9 (s), 133.0 (s), 131.2 (d, 2C), 130.5 (d), 129.4 (d, 2C), 124.7 (d), 124.2 (d), 123.1 (d), 119.6 (s), 114.9 (s), 97.2 (s), 63.2 (t), 21.5 (q), 14.3 (q); IR (reflection) $\tilde{\nu}$ = 3429, 3046, 3008, 2985, 2918, 2864, 1976, 1737, 1665, 1639, 1577, 1516, 1497, 1474, 1452, 1441, 1422, 1402, 1368, 1335, 1299, 1245, 1228, 1214, 1194, 1156, 1094, 1079, 1013, 948, 935, 919, 869, 814, 801, 772, 751, 738, 702, 666, 650 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{20}H_{17}O_4$ calcd for 321.1132, found 321.1127.



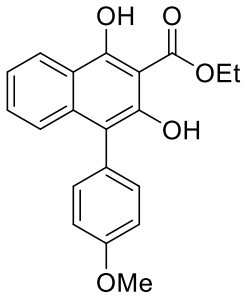
Ethyl 1,3-dihydroxy-4-(*m*-tolyl)-2-naphthoate (2i).

Yield: 56.1 mg, 97%; Yellow solid, mp 125.0 – 126.8 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.48 (s, 1H), 9.14 (s, 1H), 8.41 – 8.11 (m, 1H), 7.34 – 7.23 (comp, 3H), 7.22 – 7.16 (m, 1H), 7.15 – 7.10 (m, 1H), 7.10 – 6.94 (comp, 2H), 4.48 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.4 (s), 150.1 (s), 138.1 (s), 137.3 (s), 136.0 (s), 131.9 (d), 130.5 (d), 128.5 (d), 128.3 (d), 128.1 (d), 124.7 (d), 124.2 (d), 123.0 (d), 119.6 (s), 115.1 (s), 97.2 (s), 63.1 (t), 21.6 (q), 14.3 (q); IR (reflection) $\tilde{\nu}$ = 3434, 2985, 2913, 2862, 1945, 1737, 1657, 1635, 1605, 1574, 1504, 1473, 1453, 1402, 1371, 1328, 1302, 1229, 1155, 1096, 1013, 959, 927, 882, 859, 804, 793, 771, 751, 729, 704, 675, 651, 614 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{20}H_{17}O_4$ calcd for 321.1132, found 321.1127.



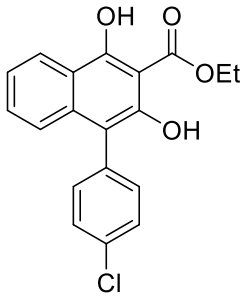
Ethyl 1,3-dihydroxy-4-(*o*-tolyl)-2-naphthoate (2j).

Yield: 51.6 mg, 80%; Yellow solid, mp 127.0 – 128.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.61 (s, 1H), 9.22 (s, 1H), 8.50 – 8.26 (m, 1H), 7.46 – 7.29 (comp, 5H), 7.25 – 7.18 (m, 1H), 7.18 – 7.11 (m, 1H), 4.70 – 4.57 (m, 2H), 2.07 (s, 3H), 1.52 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.5 (s), 161.5 (s), 150.0 (s), 138.2 (s), 137.1 (s), 135.6 (s), 131.4 (d), 130.7 (d), 130.2 (d), 127.9 (d), 126.1 (d), 124.5 (d), 124.4 (d), 123.1 (d), 119.7 (s), 114.1 (s), 97.3 (s), 63.2 (t), 19.8 (q), 14.4 (q); IR (reflection) ṽ = 3434, 2983, 1738, 1663, 1640, 1578, 1504, 1472, 1454, 1441, 1400, 1371, 1333, 1301, 1231, 1188, 1158, 1117, 1094, 1075, 1016, 949, 934, 922, 867, 803, 773, 736, 700, 672, 651, 616 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{20}H_{17}O_4$ calcd for 321.1132, found 321.1126.



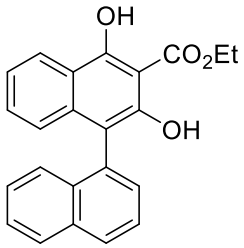
Ethyl 1,3-dihydroxy-4-(4-methoxyphenyl)-2-naphthoate (2k).

Yield: 62.9 mg, 93%; Yellow solid, mp 144.0 – 147.0 °C; R_f = 0.4 (EA/PE = 1/5);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.59 (s, 1H), 9.29 (s, 1H), 8.36 (d, *J* = 8.3 Hz, 1H), 7.48 – 7.39 (comp, 2H), 7.37 – 7.28 (comp, 3H), 7.12 – 7.03 (m, 2H), 4.61 (q, *J* = 7.1 Hz, 2H), 3.90 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.41 (s), 161.24 (s), 158.82 (s), 150.38 (s), 137.53 (s), 132.35 (d, 2C), 130.46 (d), 128.07 (s), 124.68 (d), 124.22 (d), 123.02 (d), 119.60 (s), 114.50 (s), 114.08 (d, 2C), 97.17 (s), 77.58 (s), 77.16 (s), 76.74 (s), 63.14 (t), 55.35 (q), 14.31 (q); IR (reflection) ṽ = 3429, 2986, 2952, 2933, 2833, 1741, 1661, 1635, 1605, 1577, 1516, 1499, 1463, 1402, 1371, 1332, 1302, 1241, 1228, 1195, 1179, 1151, 1110, 1093, 1074, 1035, 1012, 965, 951, 936, 919, 868, 842, 807, 787, 774, 746, 705, 666, 649, 634 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{20}H_{17}O_5$ calcd for 337.1081, found 337.1076.



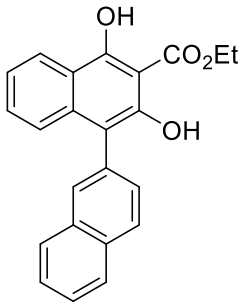
Ethyl 4-(4-chlorophenyl)-1,3-dihydroxy-2-naphthoate (2l).

Yield: 50.7 mg, 74%; Yellow solid, mp 142.0 – 143.0 °C; R_f = 0.4 (EA/PE = 1/8);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.56 (s, 1H), 9.34 (s, 1H), 8.47 – 8.21 (m, 1H), 7.53 – 7.41 (comp, 3H), 7.39 – 7.26 (comp, 4H), 4.63 (q, *J* = 7.1 Hz, 2H), 1.52 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.3 (s), 161.6 (s), 150.4 (s), 137.0 (s), 134.6 (s), 133.3 (s), 132.8 (d, 2C), 130.8 (d), 128.8 (d, 2C), 124.4 (d), 124.3 (d), 123.3 (d), 119.7 (s), 113.6 (s), 97.2 (s), 63.3 (t), 14.4 (q); IR (reflection) ṽ = 3430, 3078, 2991, 2915, 2863, 1739, 1672, 1632, 1577, 1504, 1473, 1449, 1395, 1369, 1307, 1262, 1227, 1197, 1154, 1095, 1086, 1075, 1029, 1013, 949, 937, 922, 869, 836, 811, 800, 775, 759, 727, 699, 680, 655, 628 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{19}H_{14}ClO_4$ calcd for 341.0586, found 341.0581.



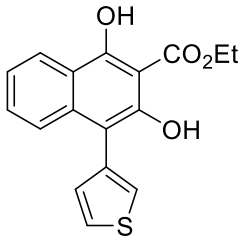
Ethyl 2,4-dihydroxy-[1,1'-binaphthalene]-3-carboxylate (2m).

Yield: 48.0 mg, 67%; Yellow solid, mp 144.7 – 145.7 °C; R_f = 0.4 (EA/PE = 1/8);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.75 (s, 1H), 9.19 (s, 1H), 8.53 – 8.34 (m, 1H), 8.03 – 7.89 (comp, 2H), 7.68 – 7.60 (m, 1H), 7.56 – 7.40 (comp, 3H), 7.40 – 7.27 (comp, 3H), 7.20 – 6.93 (m, 1H), 4.74 – 4.53 (m, 2H), 1.49 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.5 (s), 162.0 (s), 150.9 (s), 137.9 (s), 134.1 (s), 134.0 (s), 133.2 (s), 130.7 (d), 129.1 (d), 128.5 (d), 128.1 (d), 126.2 (d), 126.1 (d), 126.0 (d), 125.9 (d), 125.0 (d), 124.3 (d), 123.2 (d), 119.8 (s), 112.5 (s), 97.4 (s), 63.2 (t), 14.4 (q); IR (reflection) ṽ = 3411, 3041, 2988, 2937, 2861, 1942, 1740, 1668, 1634, 1575, 1503, 1474, 1456, 1411, 1388, 1371, 1324, 1305, 1258, 1245, 1225, 1158, 1113, 1092, 1008, 936, 923, 870, 844, 802, 768, 745, 701, 681, 651, 629, 613 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{23}H_{17}FO_4$ calcd for 357.1132, found 357.1128.



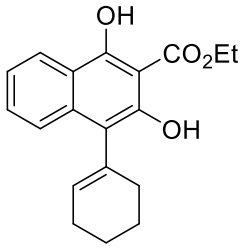
Ethyl 2,4-dihydroxy-[1,2'-binaphthalene]-3-carboxylate (2n).

Yield: 63.8 mg, 89%; Yellow solid, mp 168.6 – 170.1 °C; R_f = 0.4 (EA/PE = 1/9); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.65 (s, 1H), 9.36 (s, 1H), 8.42 (d, *J* = 8.3 Hz, 1H), 8.04 – 7.87 (comp, 4H), 7.59 – 7.50 (comp, 3H), 7.49 – 7.40 (comp, 2H), 7.39 – 7.30 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 1.51 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.5 (s), 150.5 (s), 137.3 (s), 133.7 (s), 133.6 (s), 132.8 (s), 130.6 (d), 130.2 (d), 129.7 (d), 128.1 (d), 128.1 (d), 127.9 (d), 126.1 (d), 126.0 (d), 124.7 (d), 124.3 (d), 123.2 (d), 119.7 (s), 114.8 (s), 97.2 (s), 63.2 (t), 14.3 (q); IR (reflection) ṽ = 3428, 3054, 2982, 2911, 2863, 1737, 1660, 1636, 1609, 1577, 1504, 1473, 1455, 1403, 1370, 1348, 1325, 1302, 1245, 1229, 1201, 1180, 1159, 1095, 1075, 1007, 966, 948, 936, 923, 901, 875, 854, 819, 803, 772, 752, 721, 699, 678, 648 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{23}H_{17}FO_4$ calcd for 357.1132, found 357.1128.



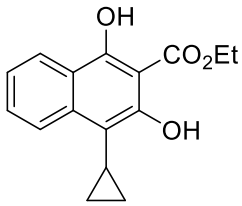
Ethyl 1,3-dihydroxy-4-(thiophen-3-yl)-2-naphthoate (2o).

Yield: 52.2 mg, 83%; Yellow solid, mp 103.2 – 106.0 °C; R_f = 0.4 (EA/PE = 1/10); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.57 (s, 1H), 9.36 (s, 1H), 8.86 – 7.75 (m, 1H), 7.54 – 7.44 (comp, 3H), 7.34 – 7.30 (comp, 2H), 7.22 – 7.13 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 1.52 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.4 (s), 161.5 (s), 150.9 (s), 137.5 (s), 135.4 (s), 130.7 (d), 130.6 (d), 125.1 (d), 124.8 (d), 124.6 (d), 124.3 (d), 123.2 (d), 119.7 (s), 109.6 (s), 97.2 (s), 63.2 (t), 14.4 (q); IR (reflection) ṽ = 3412, 3128, 3086, 3008, 2986, 2927, 1737, 1642, 1577, 1536, 1499, 1465, 1449, 1418, 1390, 1369, 1344, 1296, 1274, 1258, 1246, 1231, 1212, 1174, 1161, 1149, 1130, 1107, 1086, 1052, 1011, 962, 946, 912, 894, 880, 851, 826, 798, 760, 738, 717, 695, 664, 649, 620, 605 cm^{-1}; HRMS (ESI) $[M-H]^-$ $C_{17}H_{13}O_4S$ calcd for 313.0540, found 313.0534.



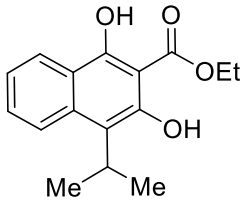
Ethyl 4-(cyclohex-1-en-1-yl)-1,3-dihydroxy-2-naphthoate (2p).

Yield: 44.4 mg, 71%; Yellow solid, mp 85.7 – 87.4 °C; R_f = 0.4 (EA/PE = 1/10);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.40 (s, 1H), 9.08 (s, 1H), 8.42 – 8.01 (m, 1H), 7.76 – 7.63 (m, 1H), 7.48 – 7.40 (m, 1H), 7.25 – 7.19 (m, 1H), 5.87 – 5.41 (m, 1H), 4.61 – 4.45 (m, 2H), 2.40 – 2.29 (m, 1H), 2.25 – 2.18 (m, 2H), 2.05 – 1.94 (m, 1H), 1.82 – 1.67 (comp, 4H), 1.44 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.6 (s), 160.7 (s), 149.4 (s), 136.8 (s), 133.7 (s), 130.4 (d), 128.5 (d), 124.4 (d), 124.3 (d), 122.9 (d), 119.7 (s), 117.3 (s), 97.3 (s), 63.0 (t), 29.5 (t), 25.8 (t), 23.4 (t), 22.5 (t), 14.5 (q); IR (reflection) ṽ = 3435, 2982, 2926, 2831, 1730, 1666, 1637, 1575, 1503, 1474, 1442, 1402, 1371, 1323, 1304, 1244, 1228, 1175, 1159, 1148, 1093, 1067, 1015, 958, 917, 868, 800, 771, 748, 706, 682, 645 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{19}H_{19}O_4$ calcd for 311.1289, found 311.1283.



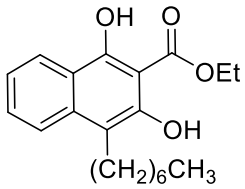
Ethyl 4-cyclopropyl-1,3-dihydroxy-2-naphthoate (2q).

Yield: 46.8 mg, 86%; Yellow solid, mp 95.4 – 97.8 °C; R_f = 0.6 (EA/PE = 1/20);; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.38 (s, 1H), 9.53 (s, 1H), 8.37 – 8.28 (comp, 2H), 7.64 – 7.58 (m, 1H), 7.36 – 7.30 (m, 1H), 4.65 (q, J = 7.1 Hz, 2H), 1.85 – 1.75 (m, 1H), 1.56 (t, J = 7.1 Hz, 3H), 1.20 – 1.12 (m, 2H), 0.75 – 0.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.54 (s), 160.85 (s), 152.92 (s), 138.66 (s), 130.28 (d), 124.51 (d), 124.26 (d), 122.81 (d), 119.76 (s), 112.13 (s), 97.31 (s), 63.07 (t), 14.46 (q), 7.98 (t), 7.15 (d); IR (reflection) ṽ = 3434, 3088, 2998, 2967, 2905, 1736, 1660, 1637, 1577, 1503, 1471, 1454, 1407, 1372, 1303, 1229, 1163, 1138, 1091, 1075, 1057, 1017, 989, 932, 909, 889, 871, 805, 783, 765, 735, 692, 672, 651 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{16}H_{15}O_4$ calcd for 271.0976, found 271.0968.



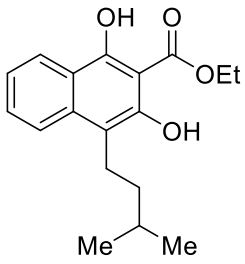
Ethyl 1,3-dihydroxy-4-isopropyl-2-naphthoate (2r).

Yield: 46.1 mg, 84%; Yellow solid, mp 99.6 – 102.0 °C; R_f = 0.6 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.19 (s, 1H), 9.63 (s, 1H), 8.40 – 8.30 (m, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.59 – 7.52 (m, 1H), 7.32 – 7.26 (m, 1H), 4.63 (q, *J* = 7.1 Hz, 2H), 3.98 – 3.72 (m, 1H), 1.54 (t, *J* = 7.1 Hz, 3H), 1.48 (d, *J* = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.6 (s), 159.8 (s), 151.6 (s), 136.6 (s), 130.2 (d), 125.0 (d), 123.0 (d), 122.4 (d), 120.0 (s), 117.6 (s), 97.6 (s), 63.1 (t), 26.1 (d), 21.0 (q), 14.5 (q); IR (reflection) ṽ = 3366, 2982, 2970, 2940, 2909, 2875, 1737, 1665, 1639, 1608, 1547, 1472, 1409, 1382, 1351, 1328, 1302, 1227, 1170, 1157, 1123, 1091, 1022, 995, 980, 964, 903, 849, 803, 776, 756, 681, 650 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{16}H_{17}O_4$ calcd for 273.1132, found 273.1129.



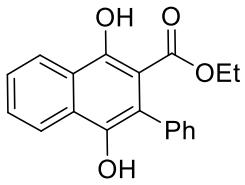
Ethyl 4-heptyl-1,3-dihydroxy-2-naphthoate (2s).

Yield: 60.1 mg, 93%; Yellow liquid; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.22 (s, 1H), 9.44 (s, 1H), 8.38 – 8.26 (m, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.34 – 7.27 (m, 1H), 4.60 (q, *J* = 7.1 Hz, 2H), 3.00 – 2.92 (m, 2H), 1.67 – 1.58 (m, 2H), 1.53 (t, *J* = 7.1 Hz, 3H), 1.48 – 1.30 (comp, 8H), 0.91 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.5 (s), 159.8 (s), 150.6 (s), 136.8 (s), 130.4 (d), 124.7 (d), 122.8 (d), 122.6 (d), 119.8 (s), 113.2 (s), 97.2 (s), 63.0 (t), 32.1 (t), 30.1 (t), 29.9 (t), 29.5 (t), 24.6 (t), 22.8 (t), 14.4 (q), 14.3 (q); IR (reflection) ṽ = 3459, 2955, 1732, 1673, 1636, 1612, 1555, 1507, 1466, 1411, 1378, 1357, 1304, 1227, 1158, 1126, 1089, 1021, 960, 909, 847, 805, 775, 657 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{20}H_{25}O_4$ calcd for 329.1758, found 329.1753.



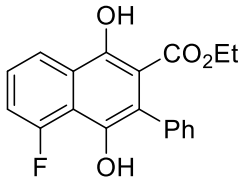
Ethyl 1,3-dihydroxy-4-isopentyl-2-naphthoate (2t).

Yield: 55.0 mg, 91%; Yellow liquid; R_f = 0.4 (EA/PE = 1/20) ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.23 (s, 1H), 9.42 (s, 1H), 8.37 – 8.29 (m, 1H), 7.80 (d, *J* = 8.6 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.34 – 7.28 (m, 1H), 4.61 (q, *J* = 7.1 Hz, 2H), 2.99 – 2.92 (m, 2H), 1.80 – 1.69 (m, 1H), 1.57 – 1.46 (comp, 5H), 1.04 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 170.5 (s), 159.8 (s), 150.4 (s), 136.8 (s), 130.4 (d), 124.8 (d), 122.7 (d), 122.6 (d), 119.8 (s), 113.3 (s), 97.2 (s), 63.0 (t), 38.9 (t), 28.8 (d), 22.8 (q), 22.6 (t), 14.4 (q); IR (reflection) ṽ = 3456, 2957, 1678, 1642, 1613, 1556, 1468, 1451, 1412, 1382, 1357, 1303, 1247, 1229, 1199, 1170, 1097, 1075, 1020, 917, 847, 810, 778, 686, 657 cm^{-1}; HRMS (ESI) [M-H]$^-$ $C_{18}H_{22}O_4$ calcd for 301.1445, found 301.1439.



Ethyl 1,4-dihydroxy-3-phenyl-2-naphthoate (3a).

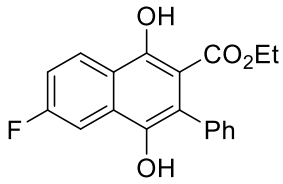
Yield: 51.8 mg, 84%; Yellow solid, mp 112.5 – 115.0 °C; R_f = 0.4 (EA/PE = 1/8); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.08 (s, 1H), 8.45 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 8.2 Hz, 1H), 7.70 – 7.65 (m, 1H), 7.61 – 7.56 (m, 1H), 7.51 – 7.46 (m, 2H), 7.45 – 7.41 (m, 1H), 7.33 – 7.28 (m, 2H), 5.05 (s, 1H), 3.97 (q, *J* = 7.2 Hz, 2H), 0.71 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 156.0 (s), 141.2 (s), 137.3 (s), 130.2 (d, 2C), 129.5 (d), 129.1 (d, 2C), 127.9 (d), 127.8 (s), 126.6 (d), 125.3 (s), 124.1 (d), 122.5 (d), 118.3 (s), 105.1 (s), 60.93 (t), 13.08 (q); IR (reflection) ṽ = 3502, 2983, 1948, 1737, 1655, 1633, 1589, 1488, 1475, 1442, 1401, 1386, 1372, 1333, 1270, 1240, 1212, 1159, 1099, 1065, 1020, 953, 920, 845, 804, 766, 748, 718, 702, 690, 662, 617 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{16}O_4$ calcd for 308.1049, found 308.1036.



Ethyl 5-fluoro-1,4-dihydroxy-3-phenyl-2-naphthoate (3b).

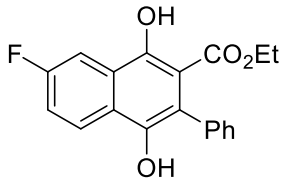
Yield: 57.4 mg, 88%; Yellow solid, mp 118 – 119 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.93 (s, 1H), 8.40 – 8.21 (m, 1H), 7.51 – 7.38 (comp, 4H), 7.34 – 7.25 (comp, 3H), 5.91 (d, *J* = 12.6 Hz, 1H), 3.97 (q, *J* = 7.2 Hz, 2H), 0.72 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 159.0 (d, *J* = 249.3 Hz), 154.5 (d, *J* = 4.2 Hz), 140.5 (d, *J* = 3.4 Hz), 137.4 (s), 130.0 (d, 2C), 128.5 (d, 2C), 127.6 (d, *J* = 4.2 Hz), 127.5 (d), 126.3 (d, *J* = 9.2 Hz), 121.1 (d, *J* = 2.6

Hz), 120.8 (d, *J* = 4.2 Hz), 117.2 (d, *J* = 9.4 Hz), 114.8 (d, *J* = 22.8 Hz), 107.1 (d, *J* = 1.3 Hz), 61.2 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -117.18; IR (reflection) ṽ = 3523.40, 2989.58, 2901.01, 1729.55, 1650.51, 1589.62, 1493.00, 1470.04, 1443.09, 1397.44, 1374.20, 1317.56, 1288.35, 1234.76, 1188.04, 1152.97, 1086.86, 1051.48, 1025.92, 988.77, 933.48, 911.63, 877.06, 843.30, 789.57, 758.21, 725.67, 701.42, 691.42 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{15}FO_4$ calcd for 326.0954, found 326.0961.



Ethyl 6-fluoro-1,4-dihydroxy-3-phenyl-2-naphthoate (3c).

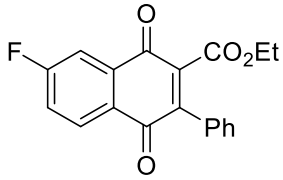
Yield: 51.6 mg, 79%; Yellow solid, mp 163 – 165.0 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.45 (dd, *J* = 9.2, 5.6 Hz, 1H), 7.78 (dd, *J* = 10.3, 2.5 Hz, 1H), 7.52 – 7.43 (comp, 3H), 7.35 – 7.27 (comp, 3H), 5.02 (s, 1H), 3.96 (q, *J* = 7.2 Hz, 2H), 0.70 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.6 (s), 163.5 (d, *J* = 250.0 Hz), 156.1 (d, *J* = 1.0 Hz), 140.7 (d, *J* = 4.5 Hz), 137.0 (s), 130.0 (d, 2C), 129.4 (d, *J* = 9.7 Hz), 129.2 (d, 2C), 128.1 (d), 127.2 (d, *J* = 9.5 Hz), 122.2 (d, *J* = 1.1 Hz), 119.5 (s), 116.5 (d, *J* = 24.9 Hz), 106.9 (d, *J* = 22.8 Hz), 104.6 (d, *J* = 1.9 Hz), 61.0 (t), 13.1 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.10. IR (reflection) ṽ = 3502.00, 3102.36, 2984.35, 2937.99, 1641.37, 1601.01, 1490.75, 1473.22, 1442.05, 1402.04, 1383.32, 1333.19, 1267.23, 1244.11, 1168.34, 1150.41, 1103.45, 1058.00, 1023.24, 959.44, 884.32, 846.78, 794.27, 735.77, 702.54, 675.69 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{15}FO_4$ calcd for 326.0954, found 326.0935.



Ethyl 7-fluoro-1,4-dihydroxy-3-phenyl-2-naphthoate (3d).

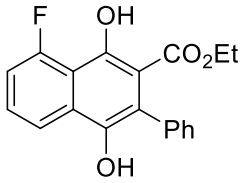
Yield: 39.8 mg, 61%; Yellow solid, mp 88 – 89 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 11.97 (s, 1H), 8.19 (dd, *J* = 9.2, 5.5 Hz, 1H), 8.04 (dd, *J* = 10.1, 2.6 Hz, 1H), 7.50 – 7.37 (comp, 4H), 7.32 – 7.27 (comp, 2H), 5.07 (s, 1H), 3.97 (q, *J* = 7.2 Hz, 2H), 0.71 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.5 (s), 161.5 (d, *J* = 246.9 Hz), 155.0 (d, *J* = 4.8 Hz), 141.3 (d, *J* = 0.9 Hz), 137.0 (s), 130.2 (d, 2C), 129.2 (d, 2C), 128.0 (d), 126.5 (d, *J* = 9.1 Hz), 125.3 (d, *J* = 8.6 Hz), 124.6 (d, *J* = 1.0 Hz), 119.2 (d, *J* = 24.8 Hz), 117.7 (d, *J* = 2.4 Hz), 108.2 (d, *J* = 22.7 Hz), 106.2 (s), 61.1 (t), 13.1 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -113.24; IR (reflection) ṽ = 3532.30, 3059.09, 2984.99, 2936.35, 2905.43, 1738.61, 1667.82,

1597.47, 1494.13, 1443.89, 1399.55, 1380.75, 1327.94, 1297.21, 1260.36, 1236.90, 1212.76, 1180.85, 1127.20, 1067.42, 1020.71, 981.69, 845.37, 828.04, 756.77, 701.56, 660.02 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{15}FO_4$ calcd for 326.0954, found 326.0946.



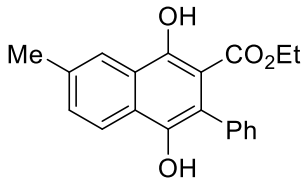
Ethyl 7-fluoro-1,4-dioxo-3-phenyl-1,4-dihydronaphthalene-2-carboxylate (3d').

Yield: 18.8 mg, 29%; Yellow solid, mp 97 – 99 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 8.21 (dd, *J* = 8.6, 5.2 Hz, 1H), 7.79 (dd, *J* = 8.4, 2.6 Hz, 1H), 7.50 – 7.33 (comp, 6H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.05 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 181.1 (d, *J* = 1.4 Hz), 166.5 (d, *J* = 258.6 Hz), 163.9 (s), 144.9 (s), 139.7 (s), 134.2 (d, *J* = 8.0 Hz), 131.3 (s), 130.6 (d, *J* = 9.0 Hz), 130.1 (d), 129.4 (d, 2C), 128.4 (d, *J* = 3.2 Hz), 128.3 (d, 2C), 121.8 (d, *J* = 22.5 Hz), 113.3 (d, *J* = 23.6 Hz), 62.2 (t), 13.9 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -100.70; IR (reflection) ṽ = 3067.08, 2984.41, 1717.62, 1659.74, 1602.17, 1587.87, 1487.11, 1462.41, 1444.94, 1392.56, 1371.57, 1347.72, 1299.34, 1259.92, 1239.92, 1213.70, 1191.57, 1130.38, 1079.30, 1012.05, 964.52, 938.56, 911.05, 853.10, 814.87, 795.38, 763.59, 734.50, 706.23, 636.86 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{13}FO_4$ calcd for 324.0798, found 324.0807.



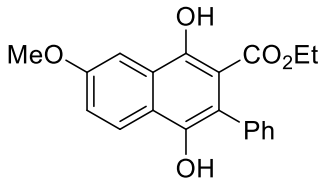
Ethyl 8-fluoro-1,4-dihydroxy-3-phenyl-2-naphthoate (3e).

Yield: 54.0 mg, 82%; Yellow solid, mp 138 – 140 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.35 (d, *J* = 3.2 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.59 – 7.43 (comp, 4H), 7.33 – 7.26 (comp, 2H), 7.20 (ddd, *J* = 12.9, 7.8, 1.0 Hz, 1H), 5.09 (s, 1H), 3.95 (q, *J* = 7.2 Hz, 2H), 0.69 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 160.6 (d, *J* = 260.6 Hz), 155.7 (d, *J* = 4.2 Hz), 140.8 (d, *J* = 4.2 Hz), 136.8 (s), 129.90 (d, *J* = 3.4 Hz), 129.85 (d, 2C), 129.7 (d, *J* = 9.2 Hz), 129.2 (d, 2C), 128.1 (d), 119.6 (d, *J* = 1.5 Hz), 118.5 (d, *J* = 4.6 Hz), 115.2 (d, *J* = 10.0 Hz), 112.7 (d, *J* = 22.2 Hz), 106.1 (d, *J* = 1.9 Hz), 61.1 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.93; IR (reflection) ṽ = 3057.25, 2977.23, 2933.49, 1730.08, 1662.94, 1598.43, 1459.30, 1443.84, 1371.40, 1327.55, 1278.94, 1230.72, 1157.70, 1130.78, 1095.69, 1008.64, 907.28, 833.80, 798.95, 785.24, 763.17, 719.84, 699.01, 632.24 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{15}FO_4$ calcd for 326.0954, found 326.0946.



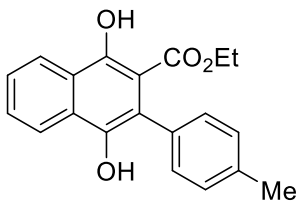
Ethyl 1,4-dihydroxy-7-methyl-3-phenyl-2-naphthoate (3f).

Yield: 53.5 mg, 83%; Yellow solid, mp 107 – 108 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.10 (s, 1H), 8.34 (d, *J* = 8.5 Hz, 1H), 7.97 (s, 1H), 7.50 – 7.40 (comp, 4H), 7.32 – 7.27 (m, 2H), 5.01 (s, 1H), 3.95 (q, *J* = 7.2 Hz, 2H), 2.56 (s, 3H), 0.70 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 156.2 (s), 140.8 (s), 139.9 (s), 137.4 (s), 130.2 (d, 2C), 129.1 (d, 2C), 128.7 (d), 128.0 (s), 127.8 (d), 124.0 (d), 123.4 (s), 121.6 (d), 118.3 (s), 104.3 (s), 60.8 (t), 22.2 (q), 13.1 (q); IR (reflection) ṽ = 3532.29, 3062.41, 2988.61, 2977.44, 2934.79, 2920.32, 1737.00, 1652.65, 1595.59, 1488.01, 1471.91, 1441.93, 1400.75, 1377.52, 1320.74, 1264.94, 1235.09, 1207.13, 1161.21, 1107.64, 1067.42, 1023.70, 951.88, 892.03, 844.76, 821.32, 795.74, 733.72, 697.47, 660.04 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_4$ calcd for 322.1205, found 322.1188.



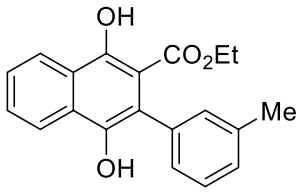
Ethyl 1,4-dihydroxy-7-methoxy-3-phenyl-2-naphthoate (3g).

Yield: 61.6 mg, 91%; Yellow solid, mp 122 – 123 °C; R_f = 0.3 (EA/PE = 1/10); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.02 (s, 1H), 8.10 (d, *J* = 9.1 Hz, 1H), 7.73 (d, *J* = 2.6 Hz, 1H), 7.50 – 7.38 (comp, 3H), 7.35 – 7.27 (comp, 3H), 5.02 (s, 1H), 4.01 – 3.92 (comp, 5H), 0.70 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.8 (s), 158.6 (s), 154.8 (s), 141.4 (s), 137.4 (s), 130.3 (d, 2C), 129.1 (d, 2C), 127.8 (d), 126.5 (s), 124.3 (d), 122.8 (s), 121.7 (d), 116.3 (s), 105.7 (s), 102.5 (d), 60.9 (t), 55.7 (q), 13.1 (q); IR (reflection) ṽ = 3543.02, 2997.34, 2953.24, 1641.21, 1597.59, 1494.88, 1439.49, 1399.40, 1378.66, 1333.98, 1303.60, 1250.89, 1224.70, 1179.36, 1099.03, 1070.47, 1029.53, 979.45, 909.10, 846.67, 827.52, 796.27, 755.56, 700.98, 679.95, 651.47, 609.71 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_5$ calcd for 338.1154, found 338.1141.



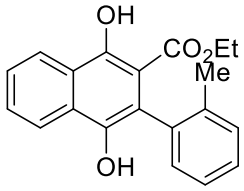
Ethyl 1,4-dihydroxy-3-(*p*-tolyl)-2-naphthoate (3h).

Yield: 51.5 mg, 80%; Yellow solid, mp 113 – 114 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.05 (s, 1H), 8.44 (d, *J* = 8.3 Hz, 1H), 8.19 (d, *J* = 8.1 Hz, 1H), 7.66 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 5.11 (s, 1H), 3.98 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 0.73 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 155.9 (s), 141.3 (s), 137.7 (s), 134.1 (s), 130.0 (d, 2C), 129.8 (d, 2C), 129.4 (d), 127.7 (s), 126.5 (d), 125.3 (s), 124.1 (d), 122.4 (d), 118.2 (s), 105.3 (s), 61.0 (t), 21.4 (q), 13.1 (q); IR (reflection) ṽ = 3502.37, 2991.39, 2942.94, 2902.50, 2836.42, 1737.48, 1643.86, 1584.56, 1474.73, 1438.85, 1394.30, 1370.96, 1322.01, 1258.83, 1230.38, 1204.60, 1181.12, 1151.83, 1097.04, 1057.53, 1022.38, 964.85, 921.61, 854.57, 802.33, 775.43, 751.21, 684.70, 657.86 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_4$ calcd for 322.1205, found 322.1205.



Ethyl 1,4-dihydroxy-3-(*m*-tolyl)-2-naphthoate (3i).

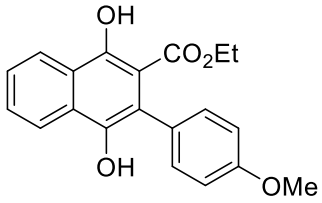
Yield: 52.2 mg, 81%; Yellow solid, mp 105 – 106 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.06 (s, 1H), 8.48 – 8.42 (m, 1H), 8.23 – 8.16 (m, 1H), 7.66 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.26 – 7.20 (m, 1H), 7.14 – 7.07 (comp, 2H), 5.12 (s, 1H), 4.05 – 3.92 (m, 2H), 2.41 (s, 3H), 0.72 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 155.9 (s), 141.2 (s), 138.8 (s), 137.1 (s), 130.8 (d), 129.4 (d), 129.0 (d), 128.6 (d), 127.8 (s), 127.1 (d), 126.5 (d), 125.3 (s), 124.1 (d), 122.4 (d), 118.4 (s), 105.1 (s), 60.9 (t), 21.5 (q), 13.1 (q); IR (reflection) ṽ = 3521.67, 2993.67, 2923.72, 1737.74, 1647.06, 1583.08, 1470.52, 1440.58, 1396.76, 1371.20, 1325.09, 1297.23, 1258.14, 1238.47, 1203.25, 1177.64, 1153.59, 1099.05, 1067.39, 1019.00, 959.40, 912.72, 888.19, 776.69, 711.68, 677.06, 660.53 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_4$ calcd for 322.1205, found 322.1188.



Ethyl 1,4-dihydroxy-3-(*o*-tolyl)-2-naphthoate (3j).

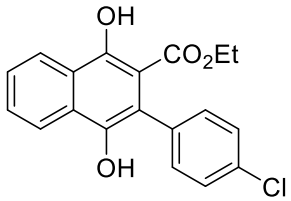
Yield: 56.7 mg, 88%; Yellow solid, mp 115 – 116 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.20 (s, 1H), 8.47 (d, *J* = 7.7 Hz, 1H), 8.19 (d, *J* =

7.7 Hz, 1H), 7.67 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.36 – 7.31 (comp, 2H), 7.30 – 7.26 (m, 1H), 7.18 – 7.13 (m, 1H), 4.85 (s, 1H), 4.04 – 3.91 (m, 2H), 2.09 (s, 3H), 0.72 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 156.3 (s), 140.8 (s), 138.0 (s), 136.3 (s), 130.5 (d), 130.2 (d), 129.4 (d), 128.4 (d), 127.9 (s), 126.6 (d), 126.5 (d), 125.3 (s), 124.1 (d), 122.4 (d), 117.4 (s), 104.8 (s), 60.9 (t), 19.9 (q), 13.1 (q); IR (reflection) ṽ = 3523.67, 3490.41, 2979.15, 1738.13, 1656.80, 1631.02, 1588.07, 1487.25, 1440.73, 1397.69, 1371.24, 1327.35, 1266.49, 1238.08, 1211.10, 1157.75, 1097.53, 1061.32, 1017.98, 952.78, 848.83, 804.70, 764.54, 690.27, 656.22 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{18}O_4$ calcd for 322.1205, found 322.1187.



Ethyl 1,4-dihydroxy-3-(4-methoxyphenyl)-2-naphthoate (3k).

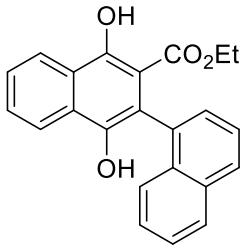
Yield: 57.5 mg, 85%; Yellow solid, mp 133 – 134.0 °C; R_f = 0.3 (EA/PE = 1/15); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.08 (s, 1H), 8.45 (d, *J* = 7.9 Hz, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.66 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.58 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.25 – 7.13 (m, 2H), 7.07 – 6.95 (m, 2H), 5.13 (s, 1H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 0.78 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.7 (s), 159.5 (s), 155.9 (s), 141.6 (s), 131.3 (d, 2C), 129.4 (d), 129.1 (s), 127.7 (s), 126.5 (d), 125.2 (s), 124.0 (d), 122.4 (d), 117.8 (s), 114.6 (d, 2C), 105.4 (s), 60.9 (t), 55.6 (q), 13.3 (q); IR (reflection) ṽ = 3072.83, 2978.26, 2934.50, 2838.93, 1734.63, 1668.06, 1604.43, 1510.99, 1461.92, 1443.18, 1370.43, 1344.17, 1325.96, 1290.96, 1273.66, 1254.51, 1231.24, 1179.93, 1137.67, 1095.65, 1068.87, 1027.70, 926.79, 898.25, 855.13, 833.06, 817.82, 791.65, 751.90, 714.74, 651.87, 630.69 cm^{-1}; HRMS (ESI$^-$) [M-H] $C_{20}H_{17}O_5$ calcd for 337.1081, found 337.1082.



Ethyl 3-(4-chlorophenyl)-1,4-dihydroxy-2-naphthoate (3l).

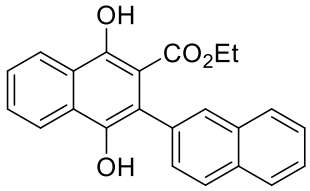
Yield: 38.4 mg, 56%; Yellow solid, mp 109 – 110 °C; R_f = 0.4 (EA/PE = 1/15); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.14 (s, 1H), 8.49 – 8.41 (m, 1H), 8.24 – 8.14 (m, 1H), 7.68 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.52 – 7.44 (m, 2H), 7.27 – 7.24 (m, 2H), 4.91 (s, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 0.79 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.4 (s), 156.4 (s), 141.2 (s), 135.8 (s), 134.1 (s), 131.7 (d, 2C), 129.7 (d), 129.3 (d, 2C), 127.8 (s), 126.9 (d), 125.5

(s), 124.1 (d), 122.5 (d), 116.9 (s), 104.7 (s), 61.2 (t), 13.2 (q); IR (reflection) ṽ = 3532.05, 2989.37, 2959.19, 2925.03, 1652.14, 1586.54, 1492.49, 1441.06, 1397.70, 1371.31, 1324.23, 1293.10, 1257.07, 1235.85, 1200.00, 1157.83, 1086.82, 1063.98, 1018.26, 950.95, 845.05, 822.22, 800.92, 768.06, 691.87, 655.18 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{21}O_4$ calcd for 342.0659, found 342.0640.



Ethyl 1',4'-dihydroxy-[1,2'-binaphthalene]-3'-carboxylate (3m).

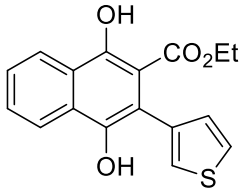
Yield: 62.4 mg, 87%; Yellow solid, mp 137 – 139 °C; R_f = 0.4 (EA/PE = 1/20); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.31 (s, 1H), 8.58 – 8.46 (m, 1H), 8.28 – 8.19 (m, 1H), 7.94 (t, *J* = 7.8 Hz, 2H), 7.75 – 7.61 (comp, 2H), 7.60 – 7.47 (comp, 3H), 7.45 – 7.34 (comp, 2H), 4.97 (s, 1H), 3.68 (q, *J* = 7.2 Hz, 2H), 0.16 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.5 (s), 156.4 (s), 141.8 (s), 134.7 (s), 134.0 (s), 133.4 (s), 129.6 (d), 128.5 (d), 128.3 (d), 128.0 (s), 127.7 (d), 126.8 (d), 126.4 (d), 125.8 (d), 125.6 (d), 124.2 (d), 122.7 (d), 115.9 (s), 105.6 (s), 60.7 (t), 12.4 (q); IR (reflection) ṽ = 3510.08, 3046.42, 2985.13, 2932.33, 1648.45, 1626.95, 1578.90, 1505.93, 1466.70, 1441.76, 1397.32, 1371.73, 1325.35, 1292.34, 1259.38, 1236.02, 1204.26, 1178.42, 1157.77, 1107.06, 1093.66, 1058.85, 1024.23, 960.79, 872.03, 849.01, 799.51, 783.24, 768.64, 737.96, 695.96, 681.25, 652.19 cm^{-1}; HRMS (ESI^-) [M-H] $C_{23}H_{17}O_4$ calcd for 357.1132, found 357.1133.



Ethyl 1,4-dihydroxy-[2,2'-binaphthalene]-3-carboxylate (3n).

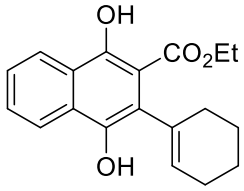
Yield: 58.8 mg, 82%; Yellow solid, mp 135 – 137 °C; R_f = 0.4 (EA/PE = 1/20); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.15 (s, 1H), 8.51 – 8.46 (m, 1H), 8.24 – 8.20 (m, 1H), 7.98 – 7.91 (comp, 2H), 7.88 – 7.85 (m, 1H), 7.82 (s, 1H), 7.75 – 7.60 (comp, 2H), 7.58 – 7.54 (comp, 2H), 7.41 – 7.37 (m, 1H), 5.19 (s, 1H), 3.89 (q, *J* = 7.1 Hz, 2H), 0.42 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.6 (s), 156.2 (s), 141.4 (s), 134.8 (s), 133.7 (s), 132.9 (s), 129.6 (d), 128.7 (d), 128.6 (d), 128.5 (d), 128.0 (d), 127.90 (d), 127.86 (s), 126.7 (d), 126.6 (d), 125.4 (s), 124.1 (d), 122.5 (d), 118.1 (s), 105.1 (s), 61.0 (t), 12.9 (q); IR (reflection) ṽ = 3508.17, 3048.62, 2980.13, 1647.99, 1587.32, 1503.80, 1470.86, 1439.86, 1396.38, 1370.16, 1322.11, 1256.20,

1226.59, 1203.30, 1178.26, 1152.25, 1099.05, 1062.43, 1014.29, 967.65, 894.72, 876.60, 822.32, 803.10, 792.83, 766.64, 753.46, 683.61, 655.52, 638.68 cm^{-1}; HRMS (EI) (*m/z*) $C_{23}H_{18}O_4$ calcd for 358.1205, found 358.1211.



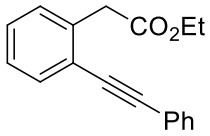
Ethyl 1,4-dihydroxy-3-(thiophen-3-yl)-2-naphthoate (3o).

Yield: 52.2 mg, 83%; Yellow solid, mp 137 – 138 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.11 (s, 1H), 8.47 – 8.41 (m, 1H), 8.22 – 8.16 (m, 1H), 7.67 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.9, 1.4 Hz, 1H), 7.48 (dd, *J* = 4.9, 4.0 Hz, 1H), 7.25 (dd, *J* = 3.0, 1.3 Hz, 1H), 7.02 (dd, *J* = 4.9, 1.3 Hz, 1H), 5.35 (s, 1H), 4.05 (q, *J* = 7.2 Hz, 2H), 0.89 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.6 (s), 156.0 (s), 142.0 (s), 136.9 (s), 130.1 (d), 129.5 (d), 127.6 (s), 126.8 (d), 126.6 (d), 125.4 (s), 124.1 (d), 123.5 (d), 122.5 (d), 112.6 (s), 105.2 (s), 61.0 (t), 13.3 (q); IR (reflection) ṽ = 3519.67, 3112.53, 3075.84, 2991.33, 2976.72, 2932.43, 1650.37, 1626.71, 1587.06, 1529.96, 1470.12, 1437.14, 1399.12, 1370.81, 1326.48, 1257.64, 1232.15, 1177.78, 1151.89, 1098.50, 1063.42, 1018.65, 966.76, 855.24, 832.14, 800.48, 763.16, 679.53, 654.24, 631.89, 620.66 cm^{-1}; HRMS (EI) (*m/z*) $C_{17}H_{14}O_4S$ calcd for 314.0613, found 314.0610.



Ethyl 3-(cyclohex-1-en-1-yl)-1,4-dihydroxy-2-naphthoate (3p).

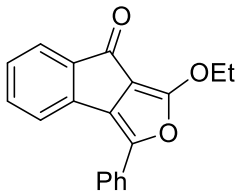
Yield: 56.2 mg, 90%; Yellow solid, mp 101 – 103 °C; R_f = 0.4 (EA/PE = 1/20); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.23 (s, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.60 (m, 1H), 7.57 – 7.49 (m, 1H), 6.04 (s, 1H), 5.83 – 5.77 (m, 1H), 4.48 – 4.35 (m, 2H), 2.37 – 2.07 (comp, 4H), 1.90 – 1.68 (comp, 4H), 1.41 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.9 (s), 156.3 (s), 140.0 (s), 136.2 (s), 129.3 (d), 127.8 (s), 127.7 (d), 126.2 (d), 124.8 (s), 124.0 (d), 122.5 (d), 120.0 (s), 104.1 (s), 61.6 (t), 30.5 (t), 25.7 (t), 23.2 (t), 22.2 (t), 14.6 (q); IR (reflection) ṽ = 3502.57, 2990.98, 2944.11, 2836.48, 1737.78, 1643.67, 1584.37, 1474.67, 1439.23, 1394.03, 1370.83, 1321.89, 1286.72, 1258.48, 1230.44, 1204.39, 1180.92, 1151.77, 1096.90, 1057.28, 1022.46, 965.57, 921.81, 892.44, 854.50, 826.65, 802.49, 776.07, 751.18, 707.09, 684.55, 657.61 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{20}O_4$ calcd for 312.1362, found 312.1349.



Ethyl 2-(2-(phenylethynyl)phenyl)acetate (4a).

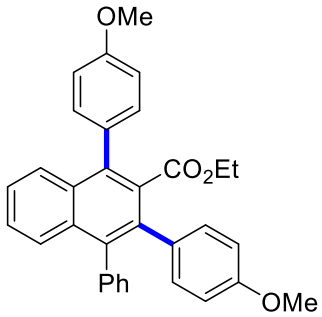
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.66 – 7.52 (comp, 3H), 7.50 – 7.18 (comp, 6H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 2H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.2 (s), 136.5 (s), 132.1 (d), 131.6 (d, 2C), 130.0 (d), 128.6 (d), 128.43 (d), 128.41 (d, 2C), 127.2 (d), 123.6 (s), 123.3 (s), 94.0 (s), 87.6 (s), 60.9 (t), 40.3 (t), 14.2 (q).

The spectroscopic properties correspond to the data available in the literature.[1]



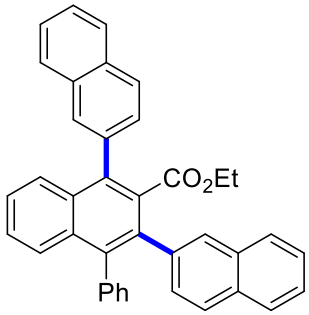
1-Ethoxy-3-phenyl-8*H*-indeno[1,2-*c*]furan-8-one (5a)

^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.82 – 7.72 (comp, 4H), 7.55 – 7.46 (comp, 3H), 7.42 – 7.30 (m, 2H), 4.90 (q, *J* = 7.1 Hz, 2H), 1.53 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 182.6 (s), 157.4 (s), 142.1 (s), 138.2 (s), 137.3 (s), 133.5 (d), 129.8 (s), 129.0 (d, 2C), 128.5 (d), 128.3 (d), 125.5 (d, 2C), 125.3 (s), 124.8 (d), 122.5 (d), 101.1 (s), 70.9 (t), 15.1 (q).

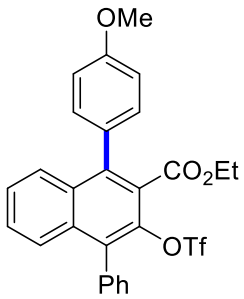


Compound **8a**: Yield: 40.6 mg, 83%; White solid, mp 183.0 – 184.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.73 – 7.67 (m, 1H), 7.62 – 7.57 (m, 1H), 7.44 – 7.37 (comp, 4H), 7.30 – 7.24 (comp, 3H), 7.19 – 7.14 (m, 2H), 7.11 – 7.05 (m, 2H), 7.04 – 6.97 (m, 2H), 6.72 – 6.62 (m, 2H), 3.89 (s, 3H), 3.80 – 3.65 (comp, 5H), 0.79 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 169.3 (s), 159.3 (s), 158.3 (s), 138.89 (s), 138.85 (s), 136.5 (s), 134.9 (s), 133.8 (s),

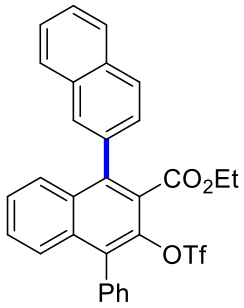
132.9 (s), 131.8 (s), 131.7 (d, 2C)), 131.62 (s), 131.60 (d, 2C)), 131.3 (d, 2C)), 130.1 (s), 127.8 (d, 2C)), 127.1 (d), 127.0 (d), 126.84 (d), 126.80 (d), 126.2 (d), 113.6 (d, 2C), 112.8 (d, 2C)), 60.7 (t), 55.4 (q), 55.2 (q), 13.8 (q); IR (reflection) $\tilde{\nu}$ = 2950.46, 2901.71, 2837.35, 1736.25, 1609.78, 1574.67, 1513.29, 1457.21, 1442.60, 1403.93, 1380.22, 1300.35, 1288.31, 1244.30, 1222.55, 1182.00, 1106.88, 1032.72, 924.68, 873.04, 847.75, 832.07, 766.58, 740.40, 704.54, 638.00, 626.52 cm^{-1}; HRMS (EI) (*m/z*) $C_{33}H_{28}O_4$ calcd for 488.1988, found 488.1982.



Compound **8b**: Yield: 37.5 mg, 71%; White solid, mp 172.0 – 173.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) *with two diastereoisomers*: 8.08 – 7.87 (comp, 4H), 7.82 – 7.65 (comp, 6H), 7.64 – 7.53 (comp, 3H), 7.49 – 7.28 (comp, 7H), 7.25 – 7.08 (comp, 3H), 3.60 – 3.45 (m, 2H), 0.52 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) *with two diastereoisomers*: 169.0 (s), 139.2 (s), 138.50 (s) and138.47 (s), 137.1 (s), 136.91 (s), 136.88 (s), 135.7 (s), 135.4 (s), 135.1 (s), 133.8 (s), 133.7 (s), 133.3 (s), 133.2 (s), 132.97 (s) and 132.95 (s), 132.9 (s), 132.81 (s) and 132.78 (s), 132.1 (s), 131.8 (s), 131.4 (d) and 131.32 (d), 131.26 (d) and 131.1 (d), 129.7 (d) and 129.6 (d), 129.3 (d) and 129.2 (d), 128.9 (d), 128.7 (d) and 128.6 (d), 128.3 (d) and 128.2 (d), 128.1 (d) and 128.0 (d), 128.0 (d), 127.9 (d), 127.8 (d), 127.7 (d), 127.5 (d), 127.2 (d), 127.14 (d) and 127.10 (d), 127.0 (d), 126.82 (d) and 126.75 (s), 126.6 (d), 126.44 (d), 126.39 (d), 125.92 (d) and 125.86 (d), 60.8 (s), 13.4 (s); IR (reflection) $\tilde{\nu}$ = 3056.09, 2976.86, 1727.34, 1629.83, 1600.51, 1503.67, 1462.61, 1441.77, 1406.24, 1376.42, 1300.71, 1270.99, 1237.23, 1222.91, 1197.19, 1169.08, 1129.88, 1099.92, 1018.42, 961.81, 929.07, 900.45, 859.98, 820.00, 746.99, 725.78, 701.60, 668.62, 654.31, 634.10, 624.10 cm^{-1}; HRMS (EI) (*m/z*) $C_{39}H_{28}O_2$ calcd for 528.2089, found 528.2070.



Compound **9a**: Yield: 96.6 mg, 91%; White solid, mp 146.0 – 147.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.77 – 7.63 (m, 2H), 7.61 – 7.52 (comp, 3H), 7.52 – 7.43 (comp, 4H), 7.41 – 7.32 (m, 2H), 7.11 – 7.01 (m, 2H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 3H), 0.99 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 165.5 (s), 159.8 (s), 140.9 (s), 139.5 (s), 133.8 (s), 133.3 (s), 133.0 (s), 132.1 (s), 131.4 (d, 4C), 130.0 (s), 129.0 (d), 128.6 (d, 2C), 128.3 (d), 127.59 (d), 127.56 (d), 127.2 (s), 126.7 (s), 113.8 (d, 2C), 61.9 (t), 55.5 (q), 13.7 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -74.11 IR (reflection) ṽ = 2960.54, 2935.75, 2840.34, 1731.59, 1610.01, 1573.55, 1505.00, 1452.01, 1415.56, 1383.38, 1347.56, 1283.47, 1221.96, 1205.10, 1171.67, 1136.69, 1108.79, 1073.85, 1040.12, 1009.06, 948.21, 912.83, 899.63, 835.02, 816.74, 804.98, 773.87, 760.49, 736.03, 701.38, 684.69, 648.95, 609.70 cm^{-1}; HRMS (EI) (*m/z*) $C_{27}H_{21}F_3O_6S$ calcd for 530.1011, found 530.0990.



Compound **9b**: Yield: 94.7 mg, 86%; White solid, mp 196.0 – 198.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.00 (d, *J* = 8.4 Hz, 1H), 7.98 – 7.95 (m, 1H), 7.92 – 7.87 (m, 2H), 7.72 – 7.67 (m, 2H), 7.62 – 7.56 (comp, 6H), 7.54 – 7.49 (comp, 3H), 7.48 – 7.44 (m, 1H), 3.94 (dtt, *J* = 10.8, 7.1, 3.6 Hz, 2H), 0.74 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 165.3 (s), 141.0 (s), 139.5 (s), 134.4 (s), 133.8 (s), 133.7 (s), 133.1 (s), 133.0 (s), 132.9 (s), 131.8 (s), 131.5 (d), 131.3 (d), 129.2 (d), 129.0 (d), 128.7 (d), 128.6 (d), 128.4 (d), 128.2 (d), 128.1 (d), 128.0 (d), 127.9 (d), 127.72 (d), 127.69 (d), 127.3 (d), 126.8 (d,2C), 126.6 (s), 118.2 (q, *J* = 320.6 Hz), 61.9 (t), 13.4 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -74.10; IR (reflection) ṽ = 3064.21, 2990.19, 1732.26, 1596.14, 1561.20, 1502.62, 1446.06, 1416.57, 1349.08, 1286.89, 1242.97, 1211.94, 1168.67, 1134.88, 1074.23, 1044.86, 1013.57, 965.89, 942.24, 913.01, 898.29, 862.51, 820.92, 799.86, 775.37, 754.28, 720.25, 697.79, 684.81, 647.52, 628.78, 613.75 cm^{-1}; HRMS (EI) (*m/z*) $C_{30}H_{21}F_3O_5S$ calcd for 550.1062, found 550.1047.

3.6.8 References:

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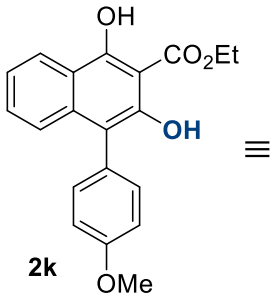
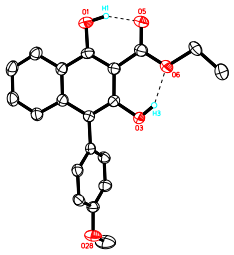
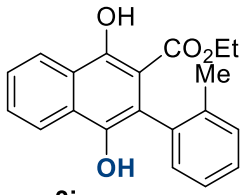
3.6.9 Single-crystal X-ray diffractions

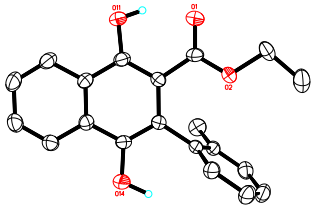


2k ≡





3j ≡

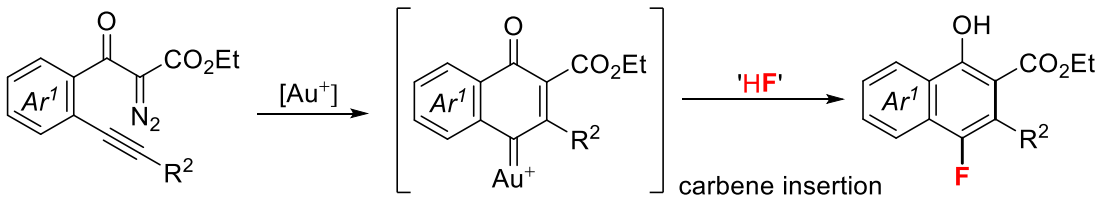


Chapter 4: Carbofluorination via a Gold-catalyzed Cascade Reaction

4.1 Introduction

Gold-catalyzed cascade reactions are valuable transformations in organic synthesis that provide efficient and rapid access to molecular complexity.[1] Among these, cascades initiated by gold-activated alkynes toward intra- or intermolecular nucleophiles have been applied extensively to achieve alkyne difunctionalization,[2] including classic examples of the H-X insertion into gold-carbene species,[3] the oxidative coupling involving a dual-metal system,[4] and a myriad of cycloadditions.[5] Notably, related gold-triggered carbofluorinations have still to be described.[6] Since fluorine substitution has found widespread application in nearly every aspect of the chemical industry,[7] such a cascade cyclization would be of great value because it would grant access to organofluorine compounds by the modular combination of a nucleophile, an alkyne, and a fluoride source. Herein, we report the development of an intramolecular gold(I)-catalyzed carbofluorination of alkynes for the preparation of α-fluoronaphthalene derivatives.

Prior work has demonstrated that a transition metal-catalyzed C−F bond-formation is challenging. For the synthesis of aryl fluorides, one important method is the reductive elimination from a fluorometal complex.[8] Another C−F bond-forming mechanism is the nucleophilic attack of a fluorine source to an aryl palladium complex.[9] In general, these transformations proceed under harsh reaction conditions with specialized ligands/reagents, such as strong oxidants and high temperature. therefore, it is highly desirable to discover a simple, rapid, and efficient C−F bond-forming strategy. Recently, we questioned whether the H-F insertion of an in-situ generated carbene species that is generated via a gold-promoted 6-*endo-dig* diazo-yne cyclization,[10] could enable the design of a carbofluorination reaction between readily available fluoride. As outlined in Scheme 1, it was envisioned that the exposure of diazo-ynes to a gold catalyst would afford the gold-carbene species, which could readily engage a fluorine source by a carbene insertion.[11]



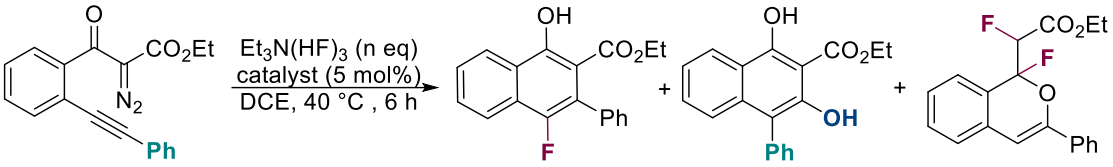
Scheme 1. Proposed carbofluorination of diazo-ynes

4.2 Results and Discussion

4.2.1 Optimization of the Reaction Conditions

We used the carbofluorination of the diazo-yne **1a** as a model reaction to investigate the HF insertion (Table1). And $EtN_3(HF)_3$ was used as our fluorine source. No reaction took place over 12 hours when JohnPhosAuCl was the catalyst (entry 1), probably due to coordination of the chloride ion with this gold catalyst. Then we

Table 1: Optimization of the Reaction Conditions.[a]



1a **2a** **3a** **4a**

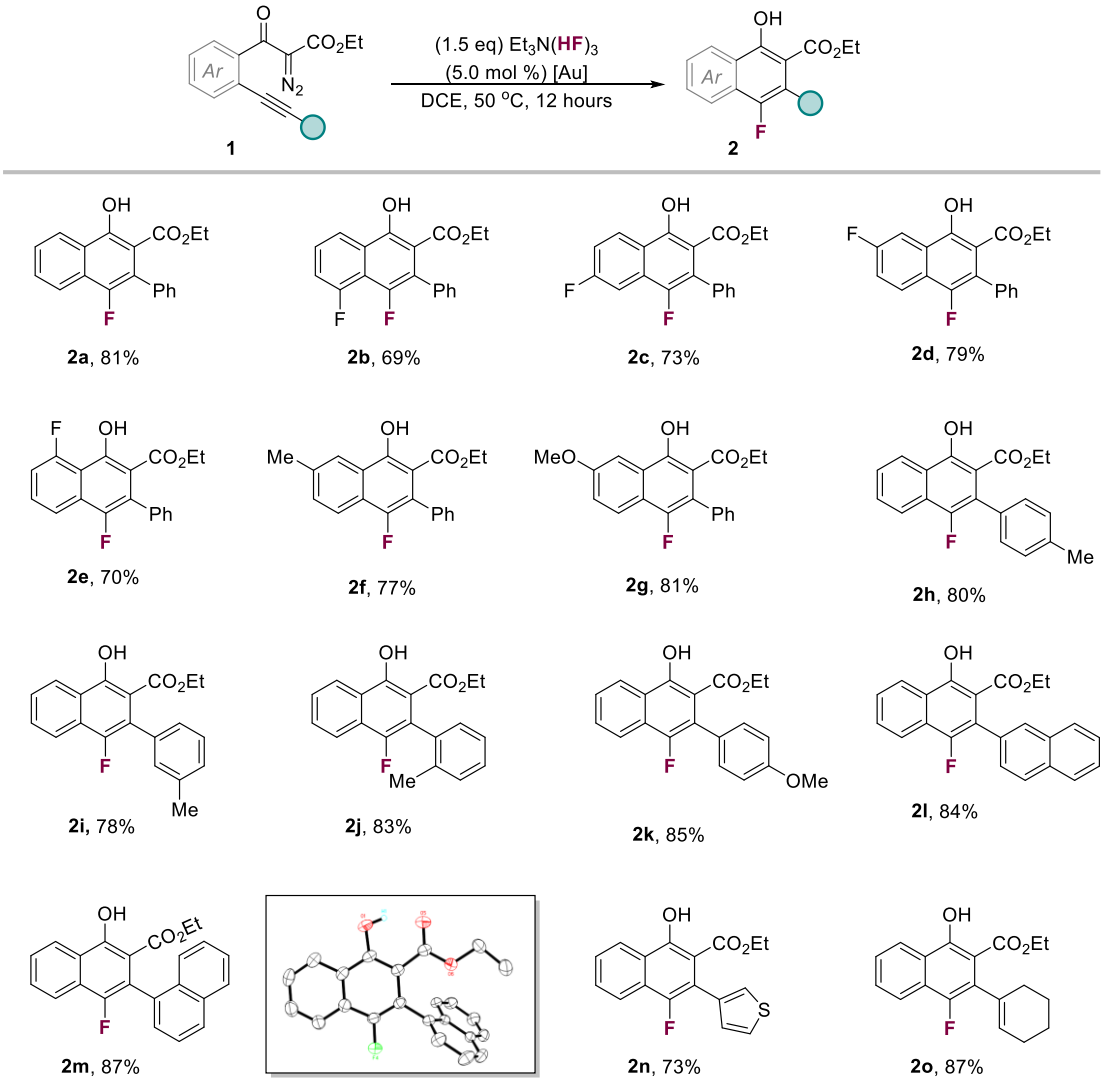
entry	catalyst	n	note	yield **2a**	yield **3a**	yield **4a**
1	JohnPhosAuCl	3.0	dry DCE	< 5%	< 5%	< 5%
2	CyJohnPhosAuSbF$_6$	3.0	dry DCE	44%	< 10%	28%
3	JohnPhosAuSbF$_6$	3.0	dry DCE	51%	< 10%	19%
4	*t*BuXPhosAuSbF$_6$	3.0	dry DCE	45%	< 10%	26%
5	IPrAuSbF$_6$	3.0	dry DCE	39%	< 10%	22%
6	Ph_3PAuSbF$_6$	3.0	dry DCE	< 10%	< 10%	< 10%
7	JohnPhosAuSbF$_6$	3.0	DCE (AR)	16%	64%	< 5%
8	JohnPhosAuSbF$_6$	3.0	dry DCE, **1a** with 4Å MS	62%	< 10%	29%
9[b]	JohnPhosAuSbF$_6$	3.0	dry DCE, **1a** with 4Å MS	-	-	-
10	JohnPhosAuSbF$_6$	10.0	dry DCE, **1a** with 4Å MS	28%	< 10%	56%
11	JohnPhosAuSbF$_6$	1.5	dry DCE, **1a** with 4Å MS	81%	< 10%	< 5%
12	JohnPhosAuSbF$_6$	1.0	dry DCE, **1a** with 4Å MS	69%	< 10%	< 5%

[*a*] In a nitrogen-filled glovebox: A solution of catalyst (0.01 mmol) in dry DCE (0.5 mL) was added over 5 min to a 10-mL oven-dried flask containing a magnetic stirring bar, the diazo-yne **1a** (64 mg, 0.2 mmol) and $Et_3N(HF)_3$ (n mmol) in dry DCE (0.5 mL) using a syringe at room temperature under argon atmosphere. After the addition, the reaction mixture was stirred at 40 ˚C for 12 hours. Yields were determined by proton NMR with 1,3,5-trimethoxybenzene as internal standard. [b] Pyridine-HF instead of $EtN_3(HF)_3$

explored the ligand effects (entries 2–5). Generally, gold catalysts derived from IPr- or Buchwald-type ligands gave good results, and the JohnPhosAuSbF_6 gave the best chemical yield (entry 3). It was interesting that the triphenylphosphine-based (Ph_3P) gold catalyst only gave a trace of product (entry 6). Notably, the O-H insertion product was detected with analytical reagent DCE (entry 7), thus, the reaction efficiency and product yield were improved by using dry DCE and 4Å molecular Sieves (entry 8), giving **2a** in 62 % isolated yield with full conversion. We also investigated another fluorination reagent pyridine-HF, but no reaction occurred (entry 9). The low reactivity of the Py-HF complex may be due to its high basicity. By increasing the amount of $Et_3N(HF)_3$, the amount of the difluoride product **4a** increased (entries 10–12). At the same time, the amount of the desired **2a** kept decreasing, with an optimal result being observed with 1.5 equivalents of $Et_3N(HF)_3$.

4.2.2 Substrate Scope

After a series of optimization experiments, we were pleased to find that the use of 1.5 equivalents of $Et_3N(HF)_3$ as the nucleophile in the glovebox at 50 ˚C provided α-naphthyl fluoride **2a** in 81% yield. With this fluorination strategy, substrates **1** were converted under standard conditions, generating the corresponding products in 69–87% yield (Scheme 2). Both electron-withdrawing and electron-donating groups were well-tolerated (**2b**–**2k**). Comparatively, carbofluorinations of the substrates with naphthyl groups delivered fluorinated products in excellent yields (**2l**, **2m**), probably owing to the reduction of other nucleophiles' attack with their bulky substituents. Heteroaryl- and alkenyl-substituted substrates also underwent the carbofluorination smoothly, leading to α-fluoronaphthalenes **2n** and **2o** in 73% and 87% yields, respectively. The structure of **2m** was confirmed by single-crystal X-ray diffraction analysis.[17]



Scheme 3. Reaction conditions: to a solution of JohnPhosAuSbF$_6$ (7.7 mg, 0.01 mmol) in dry DCE (0.5 mL), was added the solution of **1** (0.2 mmol), and Et$_3$N(HF)$_3$ (49.0 uL, 0.24 mmol) in dry DCE (0.5 mL) at 50 ˚C, and the reaction mixture was stirred for 12.0 hours to give isolated yield. *Note*: diazo compounds were dried over 4 Å molecular sieves in dry DCE before use; Et$_3$N(HF)$_3$ was stored in the glovebox.

4.3 Conclusions

We have developed a gold-catalyzed carbofluorination of diazo-tethered alkynes, accomplished with the commercially available Et$_3$N(HF)$_3$. Our novel synthesis of aryl fluorides is enabled by the H-F insertion of the in-situ generated gold-carbene species, derived from a gold-triggered 6-*endo-dig* diazo-yne cyclization. This methodology complements the common palladium-catalyzed oxidative-coupling strategies in terms of reaction efficiency and atom economy. As a result, we expect this protocol to have a substantial effect on drug discovery and materials research.

4.4 References

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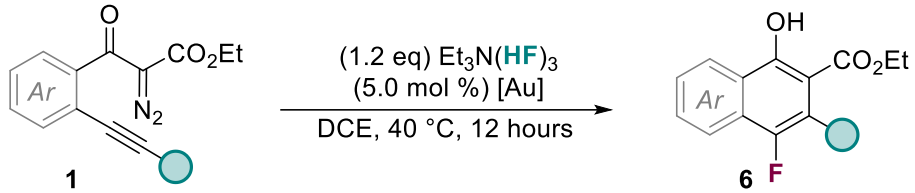
4.5 Experimental Section

4.5.1 General Information

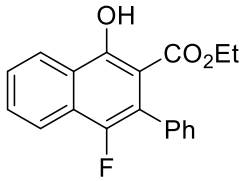
Chemicals were purchased from commercial suppliers and used as delivered. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance III 400, and Bruker Avance-III-500. Chemical shifts are given in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet) and comp (combined peaks). When combinations of multiplicities are given the first character noted refers to the biggest coupling constant. All ^{13}C NMR spectra were measured with ^{1}H-decoupling. The multiplicities mentioned in these spectra [s (singlet, quaternary carbon), d (doublet, CH-group), t (triplet, CH_2-group), q (quartet, CH_3-group)] were determined by DEPT135 spectra. Mass spectra (MS and HRMS) were determined at the chemistry department of the University of Heidelberg under the direction of Dr. J. Gross. EI-spectra were measured on a JOEL JMS-700 spectrometer. For ESI^+-, ESI^-- or $DART^-$-spectra a Bruker Apex-Qu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger and T. Oeser on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-Kα-radiation

2.5.2 Experimental Procedure: Gold-Catalyzed Carbofluorinations of Diazo-ynes

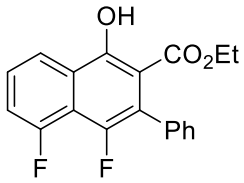


In a nitrogen-filled glove-box: A solution of JohnphosAu(CH_3CN)SbF_6 (7.7 mg, 0.01 mmol) in dry 1,2-dichloroethane (0.5 mL) was added over 5 min to a 10-mL oven-dried flask containing a magnetic stirring bar, the diazo-yne **1** (0.2 mmol) and $Et_3N(HF)_3$ (39.0 uL, 0.24 mmol) in dry 1,2-dichloroethane (0.5 mL) using a syringe at room temperature under argon atmosphere. After the addition, the reaction mixture was stirred at 40 ˚C for 12 hours. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on a silica gel (solvents: ethyl acetate/petroleum ether = 1/30) to afford the α-fluoronaphthalene derivatives **6** in 69%-87% yields.

2.5.3 Characterization

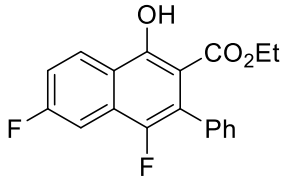


Ethyl 4-fluoro-1-hydroxy-3-phenyl-2-naphthoate (2a).
Yield: 50.3 mg, 81%; Yellow solid, mp 51.3 – 53.5 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.23 (s, 1H), 8.47 (d, J = 8.3 Hz, 1H), 8.03 (d, J = 8.3 Hz, 1H), 7.71 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.61 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 7.44 – 7.37 (comp, 3H), 7.33 – 7.28 (m, 2H), 4.00 (q, J = 7.2 Hz, 2H), 0.74 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm) 171.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 157.9 (s), 148.4 (d, $J_{C\text{-}F}$ = 240.4 Hz), 136.6 (s), 130.2 (d), 129.5 (d), 127.7 (d, 2C), 127.0 (d, $J_{C\text{-}F}$ = 32.5 Hz, 2C), 126.9 (d, $J_{C\text{-}F}$ = 20.5 Hz), 125.1 (d, $J_{C\text{-}F}$ = 5.0 Hz), 124.2 (d, $J_{C\text{-}F}$ = 2.3 Hz), 122.0 (d, $J_{C\text{-}F}$ = 18.3 Hz), 120.7 (d, $J_{C\text{-}F}$ = 5.3 Hz), 105.2 (d, $J_{C\text{-}F}$ = 2.3 Hz), 61.2 (t), 13.0 (q); ^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -133.74 (s); IR (reflection) ṽ = 2986, 2905, 1954, 1739, 1655, 1597, 1579, 1499, 1475, 1447, 1401, 1377, 1329, 1294, 1274, 1238, 1191, 1158, 1136, 1103, 1059, 1027, 951, 922, 886, 844, 805, 770, 750, 701, 661, 618 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{15}FO_3$ calcd for 310.1005, found 310.1003.



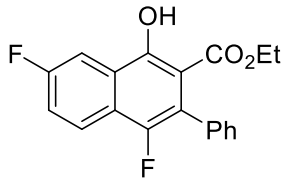
Ethyl 4,5-difluoro-1-hydroxy-3-phenyl-2-naphthoate (2b)

Yield: 42.5 mg, 65%; Yellow solid, mp 79.5 – 82.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.18 (s, 1H), 8.31 – 8.22 (m, 1H), 7.54 – 7.49 (m, 1H), 7.43 – 7.33 (comp, 4H), 7.32 – 7.27 (m, 2H), 3.99 (q, J = 7.2 Hz, 2H), 0.74 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.2 (d, $J_{C\text{-}F}$ = 2.8 Hz), 157.5 (dd, $J_{C\text{-}F}$ = 256.7, 2.1 Hz), 157.1 (dd, $J_{C\text{-}F}$ = 3.7, 2.8 Hz), 146.9 (dd, $J_{C\text{-}F}$ = 245.2, 2.2 Hz), 135.9 (d, $J_{C\text{-}F}$ = 1.2 Hz), 129.5 (d, $J_{C\text{-}F}$ = 1.6 Hz, 2C), 127.8 (d, 2C), 127.5 (t, $J_{C\text{-}F}$ = 3.6 Hz), 127.3 (d), 127.1 (dd, $J_{C\text{-}F}$ = 8.0, 1.3 Hz), 123.8 (dd, $J_{C\text{-}F}$ = 18.6, 2.1 Hz), 120.2 (dd, $J_{C\text{-}F}$ = 4.6, 2.2 Hz), 117.1 (dd, $J_{C\text{-}F}$ = 16.5, 12.5 Hz), 115.7 (dd, $J_{C\text{-}F}$ = 20.6, 1.0 Hz), 106.4 (t, $J_{C\text{-}F}$ = 1.5 Hz), 61.5 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -115.54 (d, J = 65.8 Hz, 1F), -126.68 (d, J = 66.3 Hz, 1F); IR (reflection) ṽ = 2993, 1731, 1650, 1601, 1501, 1474, 1443, 1400, 1388, 1376, 1350, 1328, 1290, 1248, 1237, 1201, 1175, 1159, 1114, 1087, 1075, 1047, 1024, 987, 925, 879, 822, 802, 764, 751, 731, 708, 689, 617 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{14}F_2O_3$ calcd for 328.0911, found 328.0895.



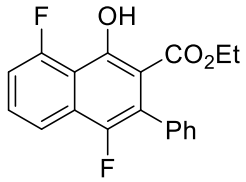
Ethyl 4,6-difluoro-1-hydroxy-3-phenyl-2-naphthoate (2c).

Yield: 48.0 mg, 73%; Yellow solid, mp 39.4 – 41.6 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.29 (s, 1H), 8.51 – 8.44 (m, 1H), 7.64 – 7.58 (m, 1H), 7.45 – 7.33 (comp, 4H), 7.32 – 7.27 (m, 2H), 3.99 (q, J = 7.2 Hz, 2H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.4 (d, $J_{C\text{-}F}$ = 3.0 Hz), 163.8 (d, $J_{C\text{-}F}$ = 252.6 Hz), 157.94 – 157.89 (m, 1C), 147.9 (dd, $J_{C\text{-}F}$ = 240.0, 4.7 Hz), 136.1 (s), 129.4 (d, $J_{C\text{-}F}$ = 1.4 Hz, 2C), 128.5 (dd, $J_{C\text{-}F}$ = 21.0, 10.0 Hz), 127.8 (d, 2C), 127.6 (dd, $J_{C\text{-}F}$ = 9.7, 2.4 Hz), 127.6 (d), 123.7 (d, $J_{C\text{-}F}$ = 17.9 Hz), 122.1 (d, $J_{C\text{-}F}$ = 5.1 Hz), 116.9 (d, $J_{C\text{-}F}$ = 25.0 Hz), 105.3 (dd, $J_{C\text{-}F}$ = 23.5, 5.9 Hz), 104.9 (t, $J_{C\text{-}F}$ = 2.0 Hz), 61.4 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -107.46 (d, J = 4.1 Hz, 1F), -133.28 (d, J = 3.5 Hz, 1F); IR (reflection) ṽ = 2991, 1738, 1646, 1584, 1499, 1479, 1441, 1408, 1378, 1358, 1327, 1279, 1243, 1192, 1150, 1104, 1067, 1048, 1022, 958, 948, 886, 859, 846, 807, 758, 733, 696, 676, 655, 622 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{14}F_2O_3$ calcd for 328.0911, found 328.0895.



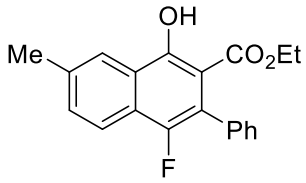
Ethyl 4,7-difluoro-1-hydroxy-3-phenyl-2-naphthoate (2d).

Yield: 52.0 mg, 79%; Yellow solid, mp 107.2 – 108.6 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.11 (s, 1H), 8.13 – 7.97 (comp, 2H), 7.49 – 7.36 (comp, 4H), 7.33 – 7.26 (m, 2H), 4.00 (q, *J* = 7.2 Hz, 2H), 0.74 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.3 (d, *J* = 3.0 Hz), 161.5 (d, *J* = 248.1 Hz), 156.9 (dd, *J* = 4.9, 2.2 Hz), 148.5 (dd, *J* = 240.7, 1.1 Hz), 136.1 (s), 129.5 (d, *J* = 1.0 Hz, 2C), 127.8 (d, 2C), 127.3 (d), 126.4 (dd, *J* = 9.1, 4.8 Hz), 123.8 – 123.3 (m, 1C), 121.5 (dd, *J* = 18.2, 2.6 Hz), 120.2 (d, *J* = 25.6 Hz), 108.6 (dd, *J* = 23.0, 1.9 Hz), 106.4 (d, *J* = 2.4 Hz), 61.4 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -112.04 (d, *J* = 3.8 Hz, 1F), -132.90 (d, *J* = 4.1 Hz, 1F); IR (reflection) ṽ = 2989, 1931, 1740, 1654, 1599, 1504, 1476, 1446, 1423, 1399, 1377, 1328, 1268, 1233, 1192, 1181, 1115, 1090, 1076, 1062, 1024, 983, 933, 909, 872, 849, 832, 814, 797, 753, 736, 702, 678, 658, 647, 609 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{14}F_2O_3$ calcd for 328.0911, found 328.0917.

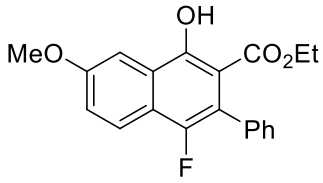


Ethyl 4,8-difluoro-1-hydroxy-3-phenyl-2-naphthoate (2e)

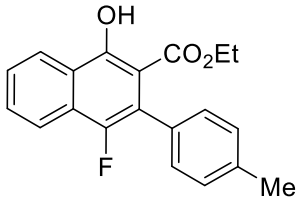
Yield: 50.5 mg, 77%; Yellow solid, mp 90.8 – 93.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.47 (d, *J* = 3.0 Hz, 1H), 7.89 – 7.75 (m, 1H), 7.66 – 7.57 (m, 1H), 7.45 – 7.36 (comp, 3H), 7.30 – 7.26 (m, 2H), 7.26 – 7.19 (m, 1H), 3.99 (q, *J* = 7.2 Hz, 2H), 0.72 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.2 (d, $J_{C\text{-}F}$ = 3.0 Hz), 160.5 (dd, $J_{C\text{-}F}$ = 262.2, 4.3 Hz), 157.8 (dd, $J_{C\text{-}F}$ = 4.2, 2.3 Hz), 148.0 (dd, $J_{C\text{-}F}$ = 239.9, 4.8 Hz), 136.0 (s), 130.7 (dd, $J_{C\text{-}F}$ = 9.4, 0.6 Hz), 129.3 (d, $J_{C\text{-}F}$ = 1.4 Hz), 129.2 (dd, $J_{C\text{-}F}$ = 21.1, 3.2 Hz, 2C), 127.9 (d, 2C), 127.4 (d), 123.5 (dd, $J_{C\text{-}F}$ = 18.4, 1.5 Hz), 116.8 (dd, $J_{C\text{-}F}$ = 6.7, 4.9 Hz), 115.2 (dd, $J_{C\text{-}F}$ = 10.4, 4.7 Hz), 113.1 (d, $J_{C\text{-}F}$ = 22.1 Hz), 106.4 (t, $J_{C\text{-}F}$ = 2.1 Hz), 61.5 (t), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -109.33 (d, *J* = 3.8 Hz, 1F), -131.51 (d, *J* = 3.9 Hz, 1F); IR (reflection) ṽ = 2982, 1946, 1742, 1643, 1598, 1579, 1500, 1472, 1443, 1403, 1380,1329, 1292, 1240, 1201, 1150, 1120, 1070, 1023, 961, 918, 885, 845, 833, 810, 787, 762, 751, 724, 698, 658, 644 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{14}F_2O_3$ calcd for 328.0911, found 328.0916.



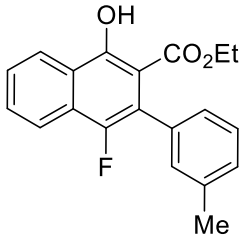
Ethyl 4-fluoro-1-hydroxy-7-methyl-3-phenyl-2-naphthoate (2f).
Yield: 50.0 mg, 77%; Yellow solid, mp 97.5 – 99.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.21 (s, 1H), 8.38 – 8.31 (m, 1H), 7.79 (s, 1H), 7.46 – 7.35 (comp, 4H), 7.31 – 7.26 (comp, 2H), 3.98 (q, J = 7.2 Hz, 2H), 2.57 (s, 3H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.6 (d, J_{C-F} = 3.0 Hz), 158.0 (d, J_{C-F} = 1.9 Hz), 148.3 (d, J_{C-F} = 239.9 Hz), 140.8 (d, J_{C-F} = 1.3 Hz), 136.6 (s), 129.6 (d, J_{C-F} = 1.3 Hz, 2C), 129.1 (d), 127.7 (d, 2C), 127.2 (d, J_{C-F} = 20.3 Hz), 127.1 (d), 124.2 (d, J_{C-F} = 2.5 Hz), 123.4 (d, J_{C-F} = 5.2 Hz), 122.2 (d, J_{C-F} = 18.3 Hz), 119.9 (d, J_{C-F} = 5.2 Hz), 104.6 (d, J_{C-F} = 2.4 Hz), 61.1 (t), 22.3 (q), 13.1 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -134.33 (s); IR (reflection) $\tilde{\nu}$ = 2979, 1945, 1868, 1739, 1642, 1600, 1493, 1466, 1444, 1400, 1372, 1356, 1330, 1294, 1247, 1203, 1186, 1165, 1109, 1072, 1060, 1021, 967, 953, 937, 897, 882, 843, 798, 758, 729, 695, 676, 658 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_3$ calcd for 324.1162, found 324.1146.



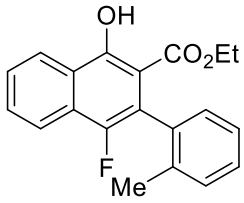
Ethyl 4-fluoro-1-hydroxy-7-methoxy-3-phenyl-2-naphthoate (2g).
Yield: 55.1 mg, 81%; Yellow solid, mp 130.6 – 132.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.13 (s, 1H), 7.97 – 7.90 (m, 1H), 7.76 – 7.71 (m, 1H), 7.42 – 7.27 (comp, 6H), 4.01 – 3.95 (comp, 5H), 0.73 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.62 (d, J_{C-F} = 3.0 Hz), 158.80 (s), 156.59 (d, J_{C-F} = 2.1 Hz), 148.79 (d, J_{C-F} = 240.1 Hz), 136.52 (s), 129.70 (d, J_{C-F} = 1.3 Hz, 2C), 127.73 (d, 2C), 127.03 (d), 126.55 (d, J_{C-F} = 5.1 Hz), 122.62 (d), 122.58 (d, J_{C-F} = 3.5 Hz), 122.01 (d, J_{C-F} = 20.9 Hz), 119.79 (d, J_{C-F} = 18.3 Hz), 105.93 (d, J_{C-F} = 2.7 Hz), 102.66 (d, J_{C-F} = 2.1 Hz), 61.24 (t), 55.71 (q), 13.04 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -133.71 (s); IR (reflection) $\tilde{\nu}$ = 3002, 2966, 1737, 1644, 1601, 1578, 1504, 1479, 1446, 1412, 1401, 1379, 1358, 1333, 1250, 1224, 1180, 1160, 1117, 1102, 1069, 1027, 979, 904, 878, 853, 826, 799, 779, 752, 731, 697, 683, 667, 653, 611 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_4$ calcd for 340.1111, found 340.1099.



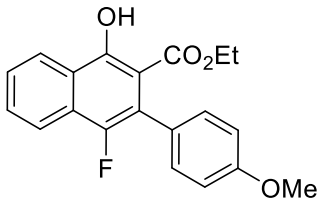
Ethyl 4-fluoro-1-hydroxy-3-(*p*-tolyl)-2-naphthoate (2h).
Yield: 51.9 mg, 80%; Yellow solid, mp 86.9 – 88.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.16 (s, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.70 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.25 – 7.16 (comp, 4H), 4.01 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 0.76 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.6 (d, J_{C-F} = 3.0 Hz), 157.8 (d, J_{C-F} = 2.1 Hz), 148.6 (d, J_{C-F} = 240.0 Hz), 136.8 (s), 133.3 (s), 130.2 (d, J_{C-F} = 1.3 Hz), 129.4 (d, J_{C-F} = 1.3 Hz, 2C), 128.5 (d, 2C), 127.0 (d, J_{C-F} = 20.7 Hz), 126.8 (d), 125.2 (d, *J* = 5.0 Hz), 124.2 (d, J_{C-F} = 2.5 Hz), 122.2 (d, J_{C-F} = 18.3 Hz), 120.8 (d, J_{C-F} = 5.4 Hz), 105.6 (d, J_{C-F} = 2.5 Hz), 61.3 (t), 21.4 (q), 13.1 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -133.93 (s); IR (reflection) ṽ = 2994, 1905, 1739, 1650, 1596, 1578, 1515, 1475, 1440, 1401, 1375, 1330 1299, 1243, 1154, 1103, 1059, 1017, 954, 890, 867, 847, 835, 805, 784, 762 ,686, 654, 627 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_3$ calcd for 324.1162, found 324.1163.



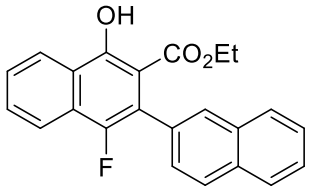
Ethyl 4-fluoro-1-hydroxy-3-(*m*-tolyl)-2-naphthoate (2i).
Yield: 50.6 mg, 78%; Yellow solid, mp 78.5 – 79.3 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.20 (s, 1H), 8.46 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.70 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.61 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.17 – 7.01 (comp, 2H), 4.01 (q, *J* = 7.1 Hz, 2H), 2.40 (s, 3H), 0.75 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.5 (d, J_{C-F} = 3.0 Hz), 157.8 (d, J_{C-F} = 2.1 Hz), 148.5 (d, J_{C-F} = 240.1 Hz), 137.2 (s), 136.23 (s), 130.207 (d, J_{C-F} = 3.0 Hz), 130.206 (d), 127.9 (d), 127.7 (d), 127.0 (d, J_{C-F} = 20.4 Hz), 126.9 (d), 126.6 (d, J_{C-F} = 1.4 Hz), 125.2 (d, J_{C-F} = 5.0 Hz), 124.2 (d, J_{C-F} = 2.5 Hz), 122.3 (d, J_{C-F} = 18.3 Hz), 120.8 (d, J_{C-F} = 5.4 Hz), 105.4 (d, J_{C-F} = 2.4 Hz), 61.2 (t), 21.5 (q), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -133.76 (s); IR (reflection) ṽ = 2980, 1932, 1736, 1637, 1596, 1579, 1490, 1474, 1441, 1399, 1377, 1328, 1243, 1178, 1150, 1107, 1095, 1064, 1034, 1022, 958, 889, 849, 793, 782, 764, 750, 707, 678, 666, 652 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_3$ calcd for 324.1162, found 324.1437.



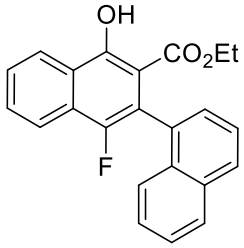
Ethyl 4-fluoro-1-hydroxy-3-(*o*-tolyl)-2-naphthoate (2j).
Yield: 53.8 mg, 83%; Yellow solid, mp 68.0 – 69.3 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.43 (s, 1H), 8.50 (d, *J* = 8.3 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.72 (ddd, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.62 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.33 – 7.26 (comp, 2H), 7.26 – 7.18 (m, 1H), 7.15 – 7.05 (m, 1H), 4.05 – 3.94 (m, 2H), 2.14 (s, 3H), 0.74 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.5 (d, J_{C-F} = 3.0 Hz), 158.3 (d, J_{C-F} = 2.0 Hz), 148.2 (d, J_{C-F} = 239.1 Hz), 136.5 (d, J_{C-F} = 0.6 Hz), 136.1 (s), 130.2 (d, J_{C-F} = 1.3 Hz), 129.4 (d), 129.3 (d, J_{C-F} = 1.1 Hz), 127.5 (d), 127.1 (d, J_{C-F} = 20.7 Hz), 126.8 (d), 125.295 (d), 125.287 (d, J_{C-F} = 4.8 Hz), 124.3 (d, J_{C-F} = 2.5 Hz), 121.4 (d, J_{C-F} = 19.7 Hz), 120.8 (d, J_{C-F} = 5.2 Hz), 105.2 (d, J_{C-F} = 2.7 Hz), 61.2 (t), 20.1 (q), 13.0 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -132.65 (s); IR (reflection) ṽ = 2986, 1953, 1908, 1738, 1645, 1596, 1577, 1491, 1475, 1442, 1400, 1375, 1326, 1240, 1188, 1158, 1102, 1057, 1016, 952, 889, 869, 845, 810, 787, 759, 745, 725, 686, 656 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_3$ calcd for 324.1162, found 324.1143.



Ethyl 4-fluoro-1-hydroxy-3-phenyl-2-naphthoate (2k).
Yield: 57.9 mg, 85%; Yellow solid, mp 84.2 – 85.1 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.16 (s, 1H), 8.52 – 8.41 (m, 1H), 8.04 – 8.00 (m, 1H), 7.70 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.60 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.25 – 7.18 (m, 2H), 6.99 – 6.92 (m, 2H), 4.03 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 0.82 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.6 (d, J_{C-F} = 3.1 Hz), 159.1 (s), 157.8 (d, J_{C-F} = 2.1 Hz), 148.8 (d, J_{C-F} = 239.6 Hz), 130.6 (d, J_{C-F} = 1.3 Hz, 2C), 130.2 (d, J_{C-F} = 1.3 Hz), 128.6 (s), 127.0 (d, *J* = 20.8 Hz), 126.8 (d), 125.1 (d, J_{C-F} = 5.0 Hz), 124.3 (d, J_{C-F} = 2.5 Hz), 121.8 (d, J_{C-F} = 18.1 Hz), 120.8 (d, J_{C-F} = 5.3 Hz), 113.3 (d, 2C), 105.6 (d, J_{C-F} = 2.2 Hz), 61.3 (t), 55.5 (q), 13.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -133.99 (s); IR (reflection) ṽ = 2934, 2839, 1887, 1737, 1654, 1607, 1577, 1512, 1467, 1440, 1401, 1376, 1331, 1300, 1286, 1238, 1176, 1157, 1105, 1061, 1033, 1017, 954, 890, 848, 822, 806, 784, 762, 689, 678, 653, 628 cm^{-1}; HRMS (EI) (*m/z*) $C_{20}H_{17}FO_4$ calcd for 340.1111, found 340.1104.

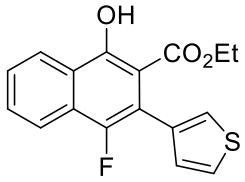


Ethyl 1-fluoro-4-hydroxy-[2,2'-binaphthalene]-3-carboxylate (2l).
Yield: 60.5 mg, 84%; Yellow solid, mp 93.9 – 94.8 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.29 (s, 1H), 8.50 (d, *J* = 8.2 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.83 (comp, 3H), 7.78 (s, 1H), 7.73 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.63 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.55 – 7.49 (m, 2H), 7.47 – 7.39 (m, 1H), 3.92 (q, *J* = 7.1 Hz, 2H), 0.46 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.5 (d, J_{C-F} = 3.0 Hz), 158.1 (d, J_{C-F} = 2.0 Hz), 148.8 (d, J_{C-F} = 240.7 Hz), 133.8 (s), 133.2 (s), 132.6 (s), 130.3 (d, J_{C-F} = 1.3 Hz), 128.2 (d, J_{C-F} = 1.8 Hz), 128.1 (d, J_{C-F} = 0.7 Hz), 128.1 (d), 127.8 (d), 127.1 (d), 127.02 (d, J_{C-F} = 20.5 Hz), 127.01 (d), 126.2 (d), 126.0 (d), 125.3 (d, J_{C-F} = 5.0 Hz), 124.3 (d, J_{C-F} = 2.5 Hz), 122.0 (d, J_{C-F} = 18.2 Hz), 120.8 (d, J_{C-F} = 5.4 Hz), 105.4 (d, J_{C-F} = 2.3 Hz), 61.3 (t), 12.9 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -133.57 (s); IR (reflection) ṽ = 2985, 1651, 1596, 1577, 1505, 1475, 1444, 1400, 1375, 1327, 1242, 1181, 1153, 1126, 1104, 1057, 1014, 969, 943, 898, 847, 823, 789, 755, 679, 656, 637 cm^{-1}; HRMS (EI) (*m/z*) $C_{23}H_{17}FO_3$ calcd for 360.1162, found 360.1152.

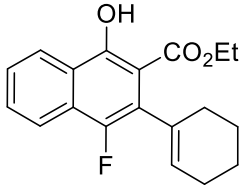


Ethyl 1'-fluoro-4'-hydroxy-[1,2'-binaphthalene]-3'-carboxylate (2m).
Yield: 57.7 mg, 87%; Yellow solid, mp 138.0 – 139.0 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.53 (s, 1H), 8.54 (d, *J* = 8.2 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 2H), 7.74 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.66 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.53 (dd, *J* = 8.2, 7.0 Hz, 2H), 7.46 (ddd, *J* = 8.0, 7.0, 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.0, 4.7, 1.3 Hz, 2H), 3.70 (qd, *J* = 7.1, 0.8 Hz, 2H), 0.18 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 171.4 (d, J_{C-F} = 3.0 Hz), 158.4 (d, J_{C-F} = 2.0 Hz), 149.0 (d, J_{C-F} = 240.2 Hz), 134.3 (d, J_{C-F} = 1.0 Hz), 133.5 (s), 133.1 (d, J_{C-F} = 0.7 Hz), 130.4 (d, J_{C-F} = 1.5 Hz), 128.2 (d), 127.7 (d), 127.1 (d, J_{C-F} = 20.6 Hz), 127.1 (d), 126.8 (d, J_{C-F} = 1.6 Hz), 125.9 (d, J_{C-F} = 32.3 Hz), 125.61 (d), 125.57 (d, J_{C-F} = 5.1 Hz), 125.3 (d), 124.4 (d, J_{C-F} = 2.6 Hz), 120.9 (d, J_{C-F} = 5.2 Hz), 120.1 (d, J_{C-F} = 19.2 Hz), 105.8 (d, J_{C-F} = 2.4 Hz), 61.0 (t), 12.4 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -131.45 (s); IR (reflection) ṽ = 3054, 2976, 1739, 1652, 1593, 1578, 1507, 1471, 1439, 1402, 1374, 1329, 1244, 1182, 1155, 1105, 1090, 1057, 1017,

948, 890, 847, 814, 800, 782, 768, 694, 685, 652 cm^{-1}; HRMS (EI) (*m/z*) $C_{23}H_{17}FO_3$ calcd for 360.1162, found 360.1160.



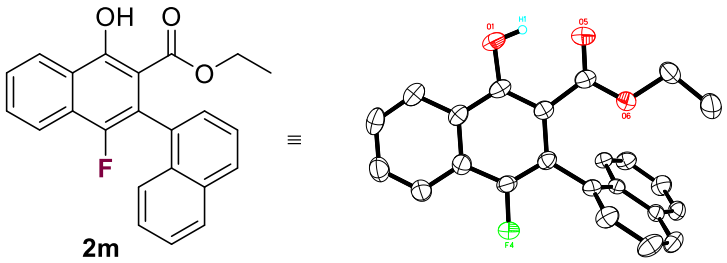
Ethyl 4-fluoro-1-hydroxy-3-(thiophen-2-yl)-2-naphthoate (2n).
Yield: 46.2 mg, 73%; Yellow solid, mp 105.8 – 107.1 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 12.16 (s, 1H), 8.45 (d, *J* = 8.3 Hz, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.70 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.60 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.35 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.21 (dd, *J* = 3.0, 0.9 Hz, 1H), 7.05 (dd, *J* = 4.9, 0.9 Hz, 1H), 4.08 (q, *J* = 7.2 Hz, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.5 (d, J_{C-F} = 3.2 Hz), 157.8 (d, J_{C-F} = 2.0 Hz), 149.0 (d, J_{C-F} = 241.3 Hz), 135.2 (s), 130.3 (d), 129.7 (d), 127.0 (d), 126.9 (d, J_{C-F} = 19.8 Hz), 125.3 (d, J_{C-F} = 5.0 Hz), 124.3 (d, J_{C-F} = 2.3 Hz), 124.1 (d), 123.2 (d, J_{C-F} = 2.3 Hz), 120.8 (d, J_{C-F} = 5.3 Hz), 117.0 (d, J_{C-F} = 18.2 Hz), 105.5 (d, J_{C-F} = 2.2 Hz), 61.4 (t), 13.3 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -132.65 (s); IR (reflection) ṽ = 3116, 2990, 1976, 1733, 1645, 1597, 1580, 1535, 1495, 1474, 1435, 1405, 1377, 1332, 1287, 1248, 1217, 1183, 1156, 1103, 1059, 1021, 968, 924, 868, 840, 821, 796, 768, 718, 692, 677, 659, 634, 620 cm^{-1}; HRMS (EI) (*m/z*) $C_{17}H_{13}FO_3S$ calcd for 316.0569, found 316.0588.



Ethyl 3-(cyclohex-1-en-1-yl)-4-fluoro-1-hydroxy-2-naphthoate (2o).
Yield: 54.7 mg, 87%; Yellow solid, mp 67.8 – 68.9 °C; R_f = 0.4 (EA/PE = 1/100); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.21 (s, 1H), 8.40 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.65 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 7.53 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1H), 5.84 – 5.06 (m, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 2.33 – 2.28 (m, 2H), 2.23 – 2.15 (m, 2H), 1.87 – 1.79 (m, 2H), 1.79 – 1.72 (m, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 171.8 (d, J_{C-F} = 3.1 Hz), 157.7 (d, J_{C-F} = 1.9 Hz), 148.1 (d, J_{C-F} = 237.7 Hz), 133.3 (s), 129.9 (d, J_{C-F} = 1.3 Hz), 127.1 (d, J_{C-F} = 20.9 Hz), 126.3 (d), 125.7 (d, J_{C-F} = 1.8 Hz), 124.7 (d, J_{C-F} = 5.0 Hz), 124.5 (d, J_{C-F} = 19.3 Hz), 124.13 (d, J_{C-F} = 2.5 Hz), 120.48 (d, J_{C-F} = 5.3 Hz), 105.31 (d, J_{C-F} = 3.1 Hz), 61.69 (t), 30.11 (d, J_{C-F} = 1.0 Hz), 25.63 (t), 23.16 (t), 22.15 (t), 14.52 (q); ^{19}F NMR (283 MHz, $CDCl_3$) δ (ppm) -135.63 (s); IR (reflection) ṽ = 2933, 1732, 1651, 1594, 1580, 1474, 1436, 1402, 1378, 1331, 1266, 1237, 1181, 1155 1098, 1057, 1028, 1020, 970,

921, 891, 855, 827, 805, 763, 707, 679, 656, 612 cm^{-1}; HRMS (EI) (*m/z*) $C_{19}H_{19}FO_3$ calcd for 314.1318, found 314.1307.

2.5.4 Single-crystal X-ray diffraction of 2m



Datablock: cz2

Bond precision: C-C = 0.0046 A Wavelength=0.71073

Cell: a=7.4955(12) b=11.1487(18) c=11.2502(18)
alpha=82.087(3) beta=78.707(3) gamma=77.257(3)
Temperature: 200 K

	Calculated	Reported
Volume	894.8(2)	894.8(2)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C23 H17 F O3	?
Sum formula	C23 H17 F O3	C23 H17 F O3
Mr	360.37	360.36
Dx,g cm-3	1.337	1.337
Z	2	2
Mu (mm-1)	0.095	0.095
F000	376.0	376.0
F000'	376.21	
h,k,lmax	8,13,13	8,13,13
Nref	3197	3168
Tmin,Tmax	0.986,0.992	0.877,0.958
Tmin'	0.986	

Correction method= # Reported T Limits: Tmin=0.877 Tmax=0.958
AbsCorr = MULTI-SCAN

Data completeness= 0.991 Theta(max)= 25.116

R(reflections)= 0.0564(2512) wR2(reflections)= 0.1792(3168)

S = 1.228 Npar= 249