Gold-Catalyzed Intermolecular Annulation to Access Heterocyclic Compounds

Presented by:
Hongming Jin
From Anhui, China

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Oral examination: November 10th , 2017

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

Prof. Dr. UweH. F. Bunz

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Table of Contents

Publications

[1] **Hongming Jin,** Long Huang, Jin Xie, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi, "Gold-Catalyzed C-H Annulation of Anthranils with Alkynes: A Facile, Flexible and Atom-Economical Synthesis of Unprotected 7-Acyl Indoles" *Angew. Chem. Int. Ed.* **2016**, *54*, 794-797.

[2] **Hongming Jin,** Bing Tian, Xinlong Song, Jin Xie, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi, "Gold-Catalyzed Synthesis of Quinolines from Propargyl Silyl Ethers and Anthranils *via* the Umpolung of a Gold Carbene Carbon" *Angew. Chem. Int. Ed.* **2016**, *55*, 12688-12692.

[3] **Hongming Jin,** Zhongyi Zeng, Matthias Rudolph, Frank Rominger and A. Stephen K. Hashmi, "Counteranion-Directed Divergent [4+2] Annulation of Benzofurazans with Ynamides by Gold and Platinum Catalysis: Switchable Access to Quinoxaline *N*-Oxides/ Quinoxalines" (to be submitted).

[4] **Hongming Jin**, Yufeng Wu, Matthias Rudolph, Frank Rominger and A. Stephen K. Hashmi, "Gold-Catalyzed Oxidative [2+2+1] Annulation of Ynamides with Quinoxaline *N*-Oxides toward Fully-Functionalized Furans" (to be submitted).

[5] Zhongyi Zeng, **Hongming Jin**, Jin Xie, Bing Tian, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi, "alpha-Imino Gold Carbenes from 1,2,4-Oxadiazoles: Atom-Economical Access to Fully Substituted 4-Aminoimidazoles" *Org. Lett.* **2017**, *19*, 1020-1023.

[6] Zhongyi Zeng, **Hongming Jin**, Xinlong Song, Qian Wang, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi, "Gold-Catalyzed Intermolecular Cyclocarboamination of Ynamides with 1,3,5-Triazinanes: En Route to Tetrahydropyrimidines" *Chem. Commun.* **2017**, *53*, 4304-4307.

[7] Jin Xie, **Hongming Jin**, A. Stephen K. Hashmi, "The recent achievements of redox-neutral radical C–C cross-coupling enabled by visible-light" *Chem. Soc. Rev.* **2017**, *46*, 5193-5203.

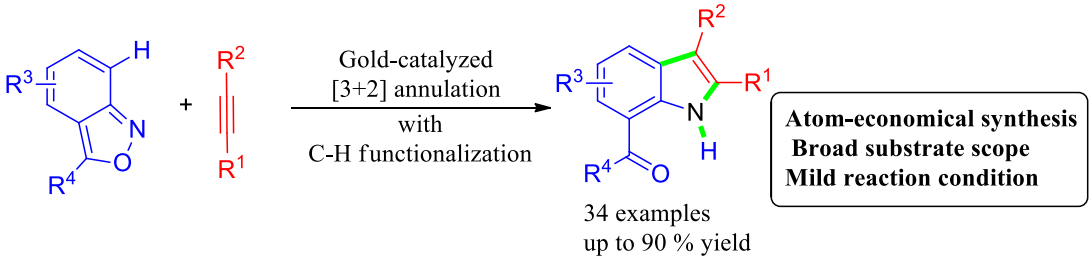
Abbreviations

Ar	Aryl
ATR	Attenuated Total Refraction
Bu	Butyl
calcd.	Calculated
Cy	Cyclohexyl
DCM	Dichloromethane
DCE	1,2-Dichloroethane
DMAP	Dimethyl amino pyridine
DME	1 2-Dimethoxyethane
DMF	Dimethyl formamide
DMS	Dimethyl sulfide
DMSO	Dimethyl sulfoxide
EDG	Electron donating group
EA	Ethyl acetate
EI	Electron ionization
eq.	Equivalent
ESI	Electrospray Ionization
Et	Ethyl
EWG	Electron withdrawing group
FAB	Fast atom bombardment
GC	Gas chromatography
h	hour
Hex	Hexyl
HRMS	High resolution mass spectrometry
Hz	Hertz
ICP	Inductively coupled plasma
IR	Infrared
m.p.	Melting point
m/z	mass per charge
Me	Methyl
Mes	Mesityl
MHz	Megahertz
min	Minutes
Ms	Mesyl

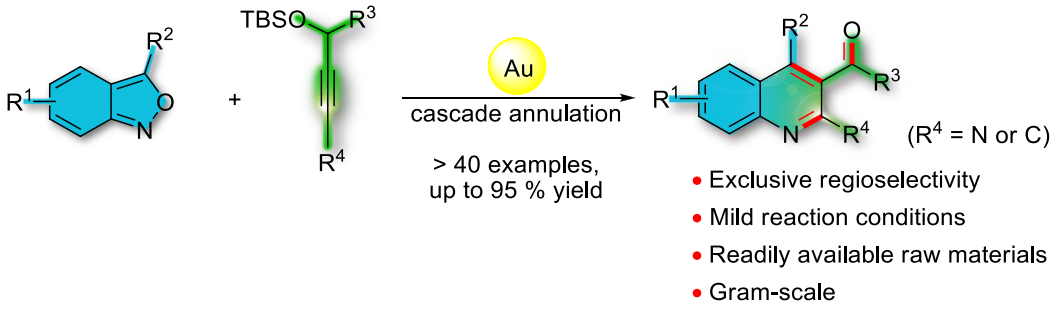
MS	Mass spectrometry
NBS	N-bromo succinimide
NHC	N-heterocyclic carbene
NIS	N-iodosuccinimide
NMR	Nuclear magnetic resonance
Ns	4-Nitrobenzenesulfonyl
PE	Petroleum ether
Ph	Phenyl
Pr	Propyl
r.t.	Room temperature
R_f	Ratio of fronts
t	*tert*
Tf	Triflate
THF	Tetrahydrofuran
TLC	Thin layer chromatography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

Abstract

In chapter 2, the gold-catalyzed C-H annulation of anthranil derivatives with alkynes offers a facile, flexible, and atom-economical one-step route to unprotected 7-acylindoles. An intermediate a-imino gold carbene, generated by an intermolecular reaction, promotes ortho-aryl C-H functionalization to afford the target products. The transformation proceeds with a broad range of substrates under mild conditions. Moreover, the obtained functionalized indole products represent a versatile platform for the construction of diverse indolyl frameworks.

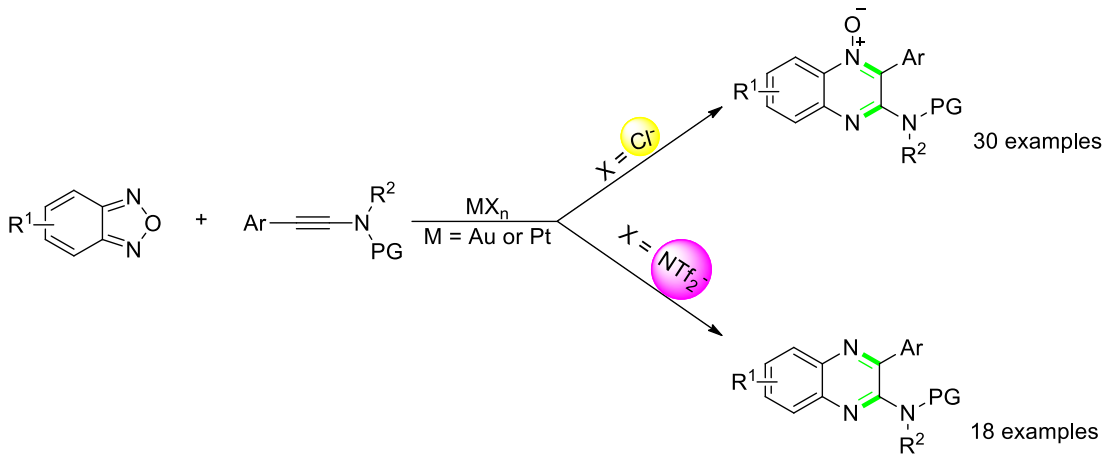


In chapter 3, a gold-catalyzed cascade annulation of propargylic silyl ethers with anthranils proceeds through a sequential ring opening/1,2-H-shift/protodeauration/Mukaiyama aldol cyclization. This method offers a regiospecific and modular access to 2-aminoquinolines and other quinoline derivatives under mild conditions and with a broad functional-group tolerance. The conversion is possible on a gram scale, which underlines the synthetic practicability of this methodology. The versatility of the obtained scaffold has been demonstrated by useful postfunctionalization.

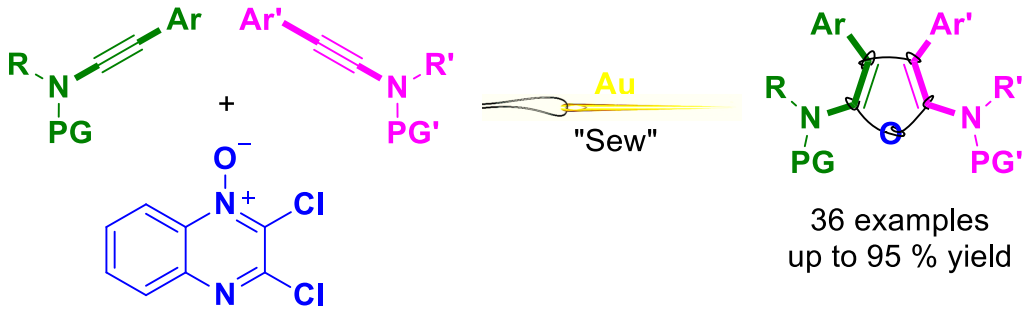


In chapter 4, gold and platinum-catalyzed counteranion-directed divergent [4+2]

annulations have been described, enabling the convergent assembly of densely substituted quinoxaline and quinoxaline *N*-oxide from benzofurazans and ynamides. A broad scope of functional groups was well tolerated, delivering high regioselectivity. The quinoxaline *N*-oxides were suitable for the further C-H functionalization. Mechanism studies suggested the counteranion-tuned distinct cyclization pathways toward the corresponding product.

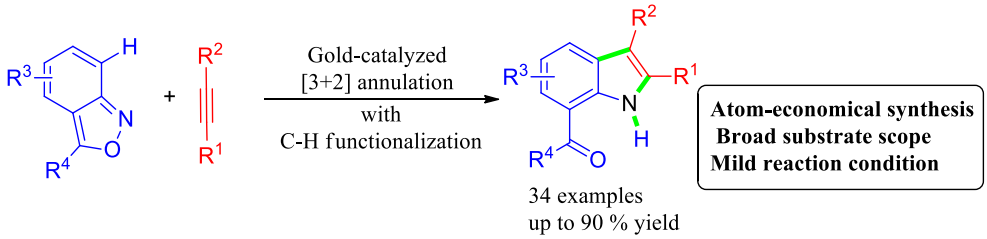


In chapter 5, the gold-catalyzed oxidative [2+2+1] annulation of two molecules of ynamide with 2, 3-quinoxaline *N*-oxide, enables the facile and convergent assembly of fully-substituted symmetric and unsymmetric furan frameworks. A wide range of functional groups is well compatible due to the mild condition. The strategy works also for the intramolecular macrocyclization of di-ynamides for the synthesis of macrocyclic furan derivatives.

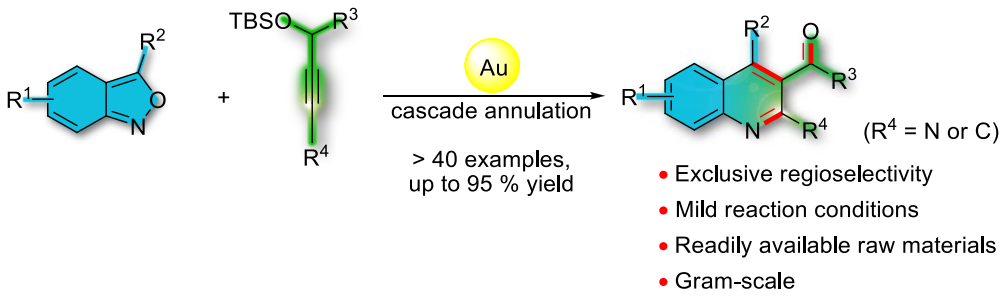


Kurzzusammenfassung

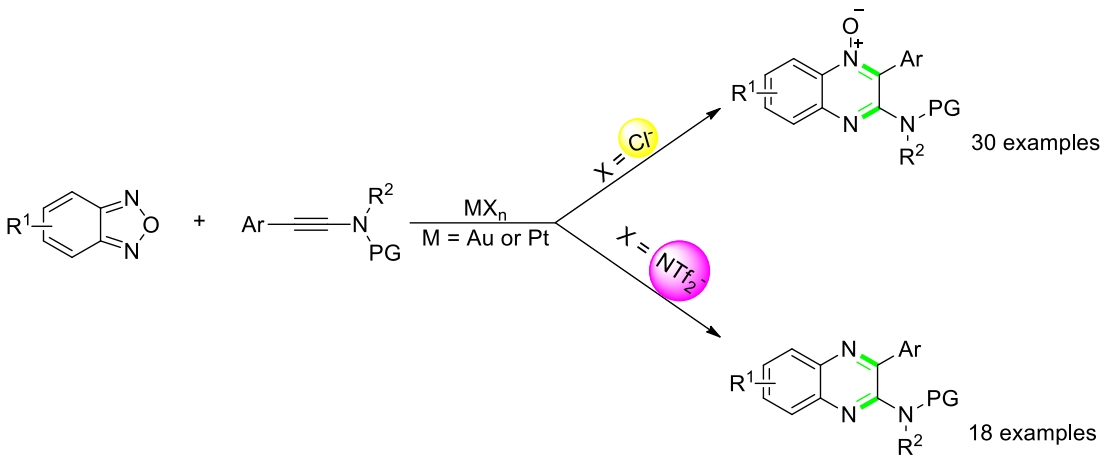
In Kapitel 2, die goldkatalysierte C-H-Anellierung von Anthranilderivaten mit Alkinen eröffnet eine einfache, flexible und atomökonomische einstufige Route zu ungeschützten 7-Acylindolen. Über eine α-Iminogoldcarben-Zwischenstufe, die in einer intermolekularen Reaktion generiert wird, erfolgt eine ortho-Aryl-C-H-Funktionalisierung zur Zielverbindung. Die Transformation zeichnet sich durch ein breites Substratspektrum und milde Bedingungen aus. Darüber hinaus stellen die erhaltenen Indole eine vielseitige Plattform für den Aufbau verschiedenster Indolyl-Grundgerüste dar.



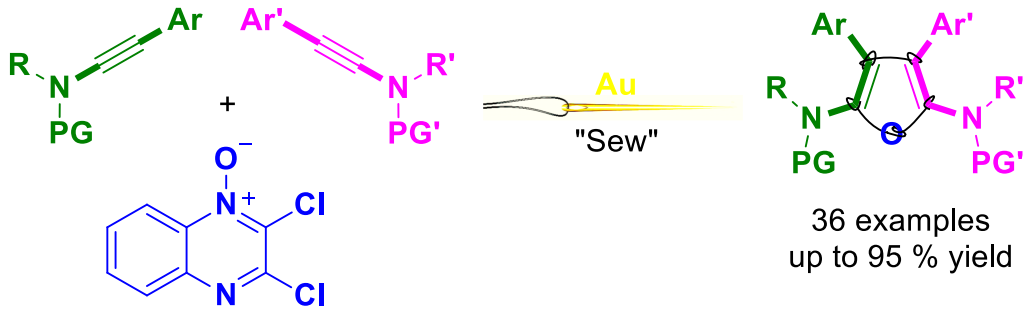
In Kapitel 3, die Gold-katalysierte Kaskaden-Anellierung propargylischer Silylether mit Anthranilen verläuft sequenziell über eine Ringöffnung/1,2-H-Verschiebung/Protodesaurierung/Mukaiyama-Aldol-Cyclisierung. Dieses Protokoll bietet einen regiospezifischen und modularen Zugang zu 2-Aminochinolinen und anderen Chinolinderivaten unter milden Bedingungen bei guter Kompatibilität mit funktionellen Gruppen. Die Reaktionen gelingen im Gramm-Maßstab, was den präparativen Nutzen der Methode unterstreicht. Die Vielseitigkeit der erhaltenen Molekülgerüste wurde anhand nützlicher Folgereaktionen demonstriert.



In Kapitel 4, sind die Gold- und Platinkatalysierte Gegenanion-dirigierenden divergenten [4+2] Anellierungen beschrieben, die den konvergenten Aufbau von dicht-substituierten Chinoxalin und Chinoxalin *N*-Oxiden von Benzofurazanen und Ynamiden ermöglicht. Ein breites Substratspektrum von funktionellen Gruppen wurde sehr gut toleriert und lieferte eine hohe Regioselektivität. Die Chinoxalin *N*-Oxide waren für weitere C-H Funktionalisierungen geeignet. Mechanistische Studien wiesen auf einen Gegenanion-abgestimmten eindeutigen Cyclisierungspfad gegenüber dem korrespondierenden Produkt hin.



In Kapitel 5, ermöglicht die gold-katalysierte oxidative [2+2+1] Anellierung von zwei Ynamid Molekülen mit Chinoxalin *N*-Oxid den leichten und konvergenten Aufbau von durchgehend substituierten symmetrischen und unsymmetrischen Furan Grundgerüsten. Eine große Bandbreite von funktionellen Gruppen ist aufgrund der milden Reaktionsbedingungen gut kompatibel. Die Strategie funktioniert auch für intramolekulare Macrocyclisierungen von di-Ynamiden für die Synthese von macrocyclischen Furan-Derivaten.



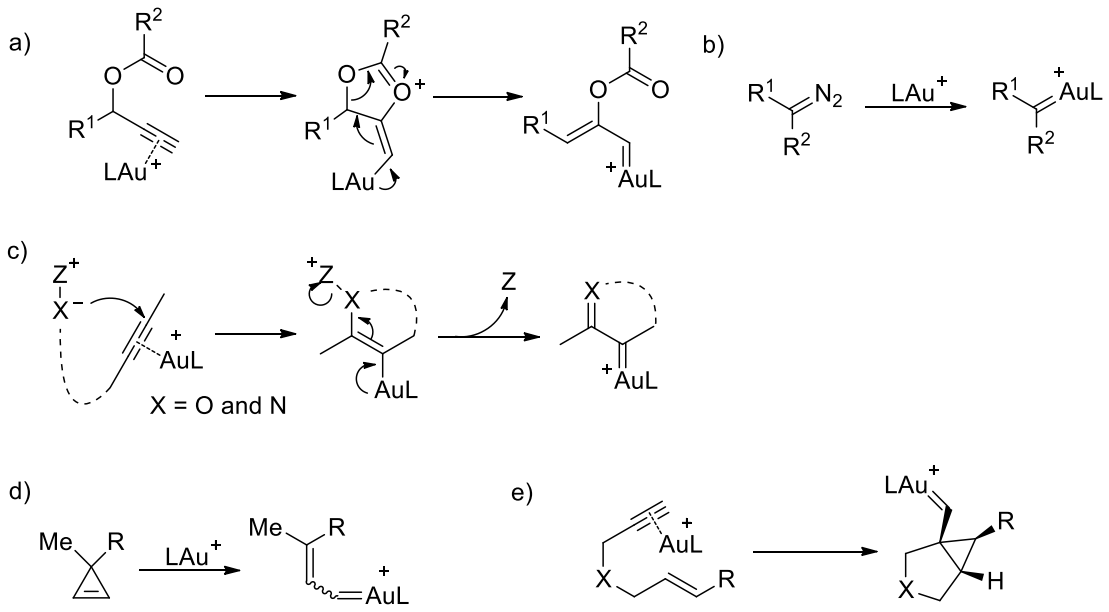
Chapter 1: General Introduction

1.1 Gold Carbene Species in Homogeneous Gold Catalysis

Gold was recognized as currency decoration thousands of years ago. However, the catalytic activity of gold compounds has been ignored until the last century.[1] During the past decades, homogeneous gold catalysis has been booming and afforded various flexible, versatile and atom-economic strategies for the construction of complex molecular frameworks.[2] Due to the pronounced carbophilicity of gold complexes, enormous efforts in this field referred to gold-catalyzed alkyne activation and transformation[3], with high functional group tolerance and mild reaction condition. In these reaction mechanisms, gold carbenes are often involved and considered as a key electrophilic intermediate despite still continuing debates on their structure and nature.[4]

The first reaction involving gold carbene intermediates was the furan-yne transformation for Hashmi phenol synthesis.[5a] Subsequently, the nature of gold carbenoid, carbene versus carbocation, was fully discussed by Hashmi[5b,c], Fürstners[5d] and Echavarren[5e,f] et al. A bonding model for gold carbenes was described by Toste's group in 2009.[5g] The gold core can accept two pairs of electrons from the ligand and carbene respectively to produce a three-center four-electron σ-hyperbond. Meanwhile, two π-backdonations are formed by electrons transfer from two filled 5d orbitals on gold to empty π*-antibonding orbitals of the ligand and the carbene. The most common approaches to gold carbenes are summarized in Scheme 1, including: a) 1, 2-acyloxy migration of propargylic carboxylates;[6] b) the decomposition of diazo compounds;[7] c) the direct alkyne oxidation and amination;[8] d) ring-opening of cyclopropenes;[9] e) intramolecular cycloisomerization of enynes.[10] The bonding of some gold carbenes has been investigated in great detail by DFT computations.[10e,f]

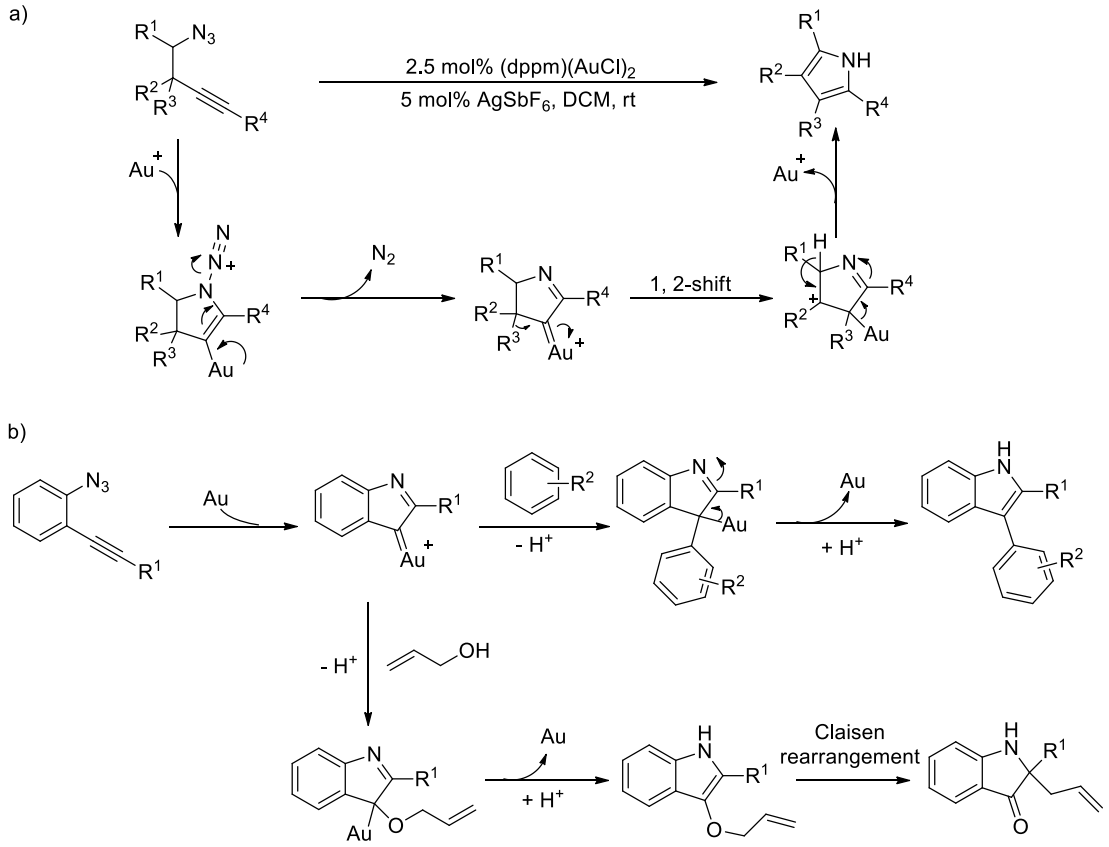
In this chapter, gold carbenes resulting from alkyne amination and oxidation are highlighted (Scheme 1, c). A range of gold carbene-triggered intramolecular and intermolecular cyclizations to access heterocyclic compounds will be reviewed.



Scheme 1. General approaches to gold carbenes.

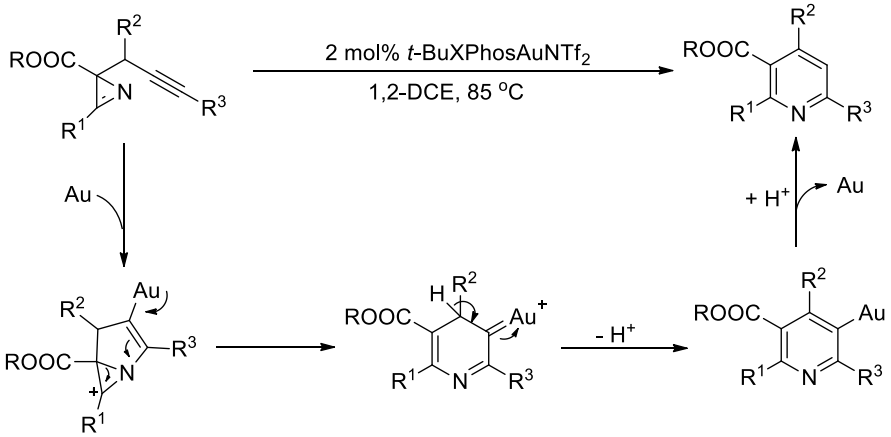
1.2 α-Imino Gold Carbene-Mediated Syntheses of Heterocyclic Compounds

The first report on the generation of an α-imino gold carbene by the intramolecular acetylenic Schmidt reaction of alkynes with an tethered azide was developed by Toste and co-workers (Scheme 2, a).[11] In this work, the α-imino gold carbene was invoked by the intramolecular nucleophilic azide addition to an alkyne followed by losing nitrogen. Through 1,2-hydride/alkyl migration pyrrole products were furnished. Inspired by this reaction, Zhang and Gagosa's group reported indole and 3-indolinone synthesis *via* analogous α-imino gold carbene intermediates, in which the gold carbene was trapped by aryl nucleophiles or allyl alcohols (Scheme 2, b).[12] Further, the strategy was successfully applied to the preparation of bicyclic imidazaole[13] and quinoline[14] derivatives.



Scheme 2. α-Imino gold carbene generated *via* intramolecular azide addition.

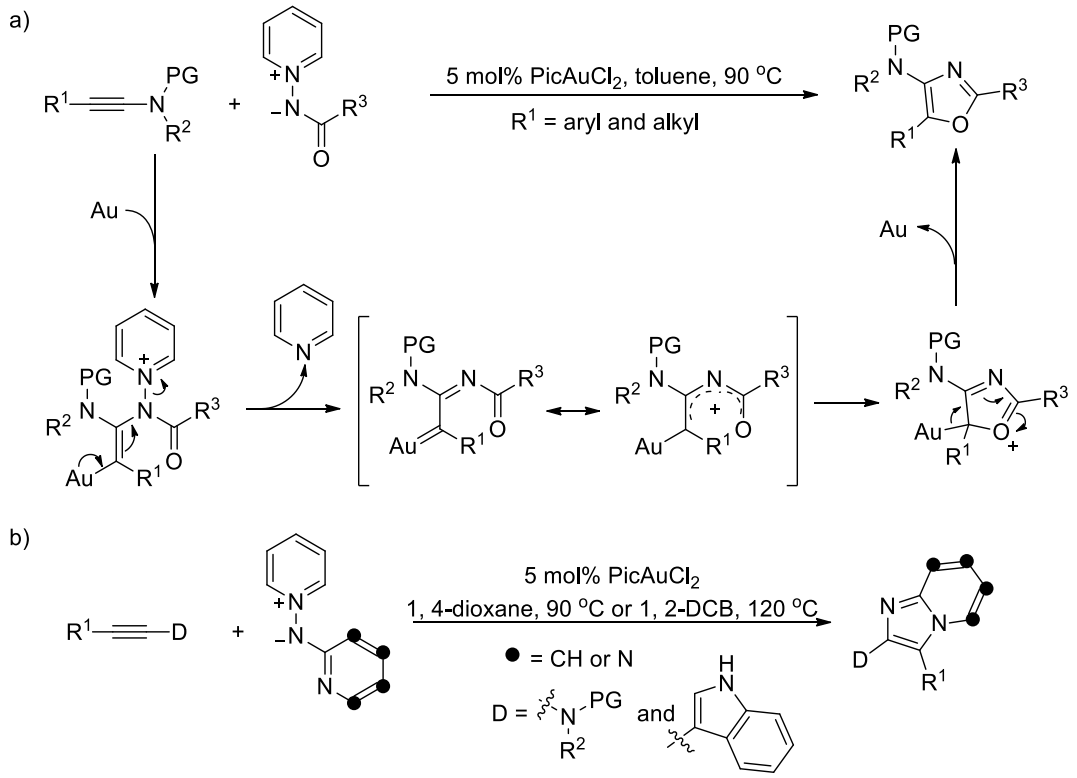
Instead of azides, Gagosz et al. found 2*H*-azirines as alternative nitrene precursor to access α-imino gold carbene *via* intramolecular cyclization followed by strained ring-opening (Scheme 3).[15] A broad scope of functionalized pyridines was obtained in excellent yields.



Scheme 3. α-Imino gold carbene generated *via* intramolecular 2*H*-azirines attack.

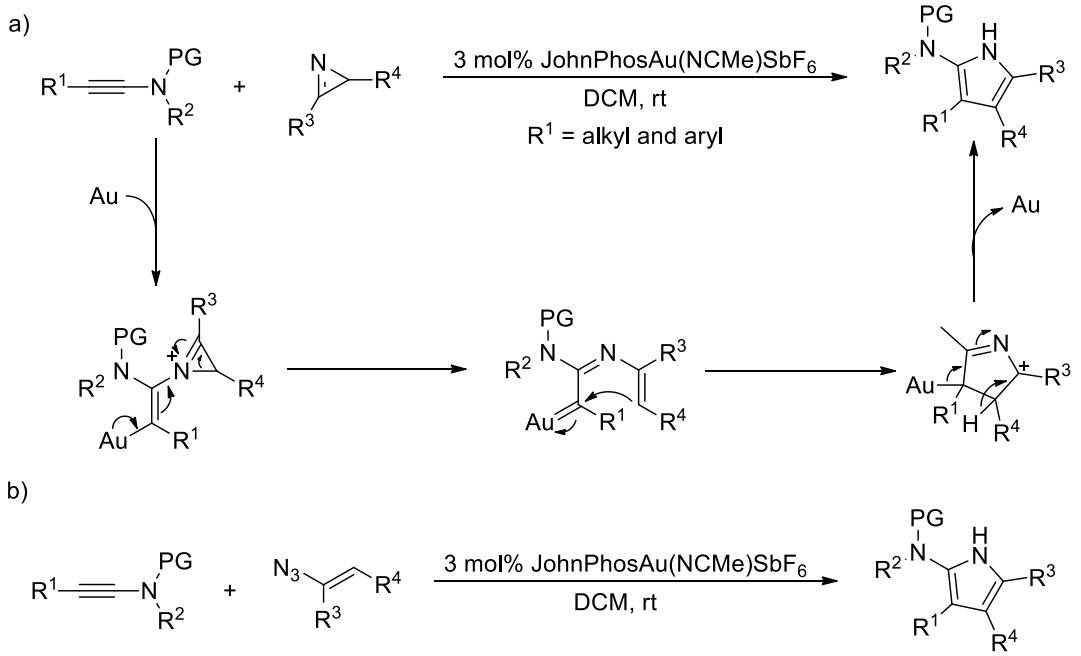
Compared with intramolecular cyclizations toward heterocyclic compounds, the intermolecular formal cycloaddition for heterocycle construction is more flexible and

versatile without tedious steps in the synthesis of substrates. In 2011, by incorporation of ynamides into the gold-catalyzed nitrene transfer, Davies's group reported the gold-catalyzed [3+2] annulation of ynamides with iminopyridium yields densely substituted oxazoles[16a] with the gold(III) complex[16b] as catalyst (Scheme 4, a). As well as aryl substituents, alkyl substituted (R^1) ynamides were also suitable for the reaction without α-H elimination products, which suggested that the C-O bond formation might be faster than N-N bond cleavage. Subsequently, the methodology was expanded to the synthesis of fused imidazodiazines and imidazopyridines, in which electron-rich internal alkynes reacted smoothly as well as ynamids (Scheme 4, b).[17]



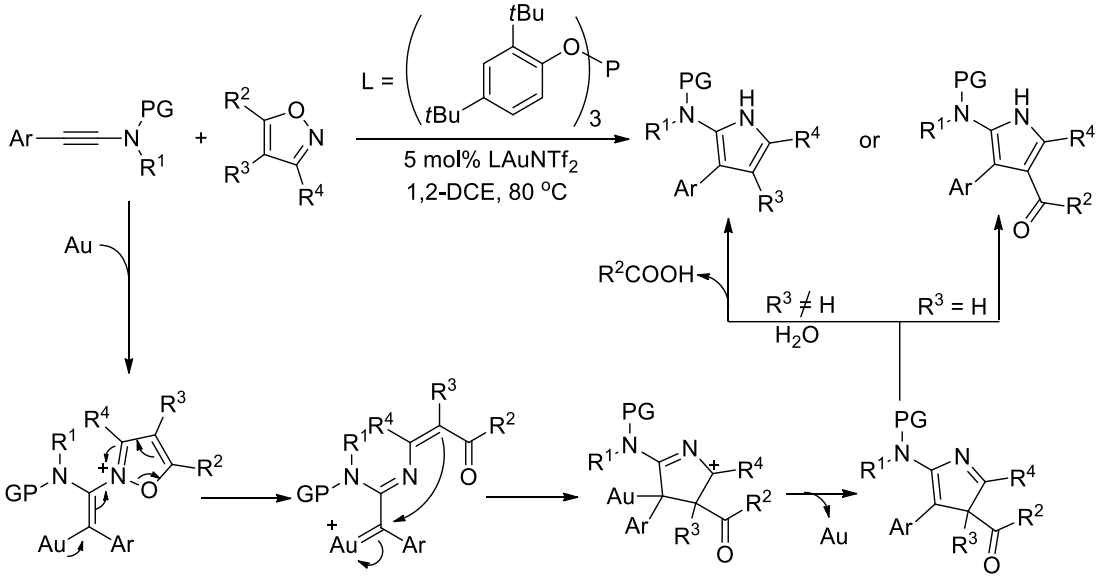
Scheme 4. α-Imino gold carbenes generated *via* intermolecular nitrene transfer.

In 2015, Huang and Liu's group exploited the intermolecular [3+2] annulation of ynamides with 2*H*-azirines, enabling the atom-economic synthesis of various 2-aminopyrroles (Scheme 5, a).[18] Furthermore, the nucleophilic vinyl azide turned out to be a well suitable equivalent of 2*H*-azirines (Scheme 5, b).[19]



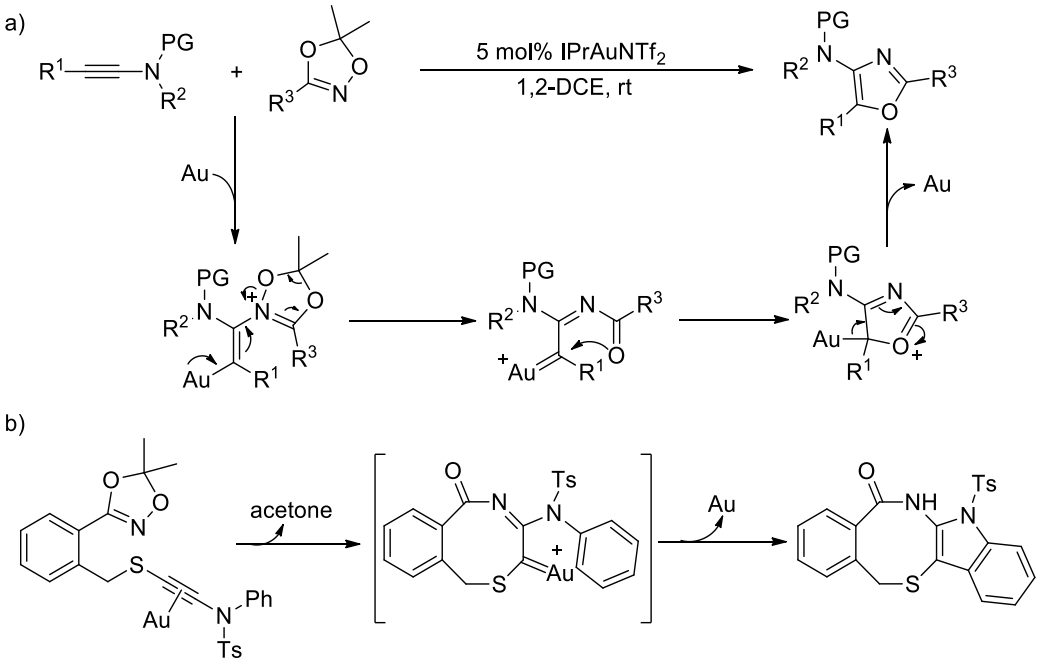
Scheme 5. 2*H*-azirines as a nitrene equivalent.

In the same year, Ye's group published an alternative intermolecular [3+2] annulation towards 2-aminopyrroles taking advantage of isoxazoles as a nitrene equivalent (Scheme 6).[20] The α-imino gold carbene was produced by gold-promoted N-O bond cleavage and then underwent a 4π-electrocyclization/deauration processes. The structure of the final product was depended on the R^3-substitutents. 3-Acyl pyrroles were gained followed by 1, 3 H-shift, while water-assisted deacylated products were observed in the case of alkyl and aryl substituents.



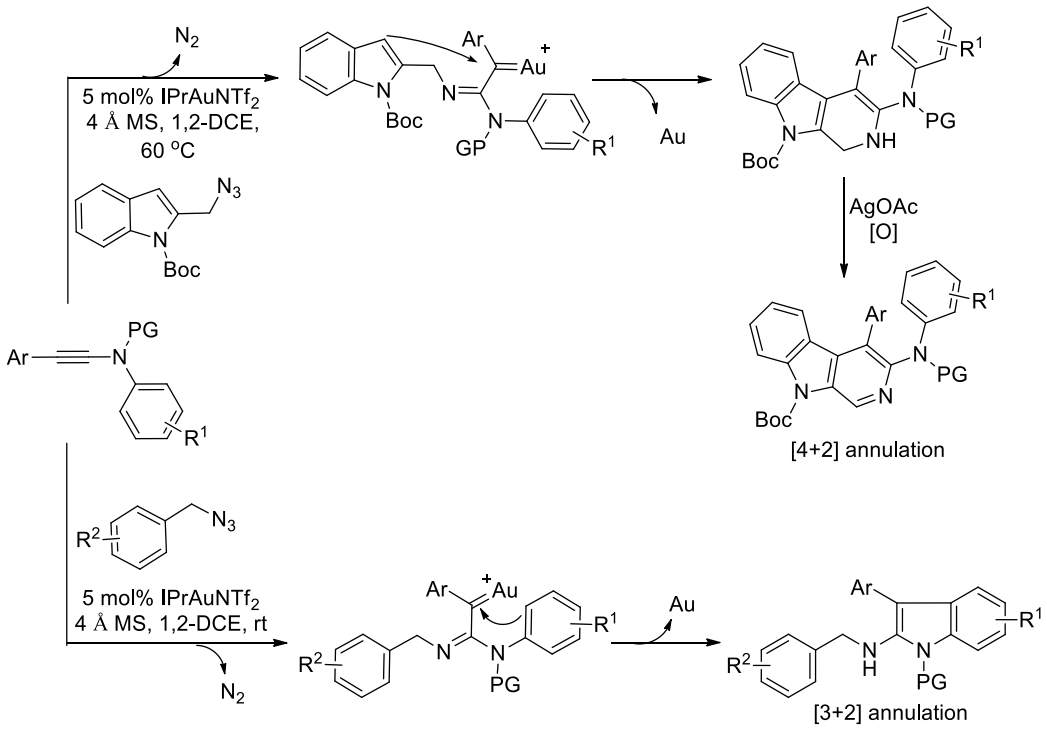
Scheme 6. Isoxazoles as a nitrene equivalent.

In 2016, another intermolecular nitrene transfer reagent, dioxazole, was described by Liu's group.[21] The α-imino gold carbene might be produced *via* a tandem N-O bond cleavage/ acetone releasing process. The gold-catalyzed intermolecular formal [3+2] cycloaddition provided a novel protocol to oxazole derivatives under mild conditions (Scheme 7, a). Moreover, an intramolecular cascade cyclization was conducted to demonstrate the generation of an α-imino gold carbene intermediate (Scheme 7, b).

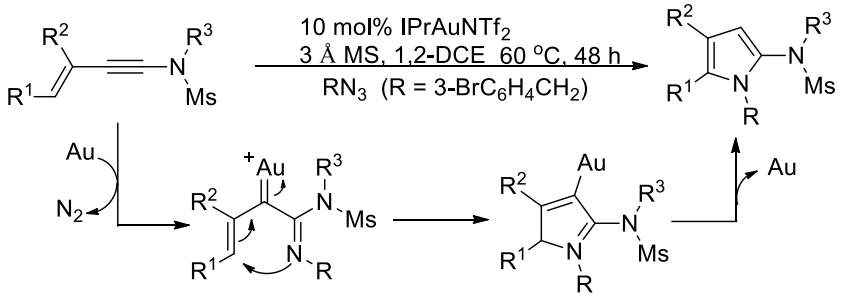


Scheme 7. Dioxazoles as a nitrene equivalent.

Ye and co-workers reported the first instance on gold-catalyzed intermolecular transformation of ynamides with benzyl azides.[22] Remarkably, the kind of benzyl azides has a crucial influence on final products and yields. Generally, treatment of 3-bromobenzyl azide and *N*-aryl substituted ynamides led to 2-aminoindoles in good to excellent yields even at room temperature, whereas Boc-protected indolyl azides offered a [4+2] annulation toward 3-amino-β-carbolines proceeded by AgOAc oxidation (Scheme 8). Subsequently, the benzyl azide was employed to the reaction with 3-en-1-ynamides to initiate aza-Nazarov cyclization for the synthesis of 2-aminopyrroles (Scheme 9).[23]

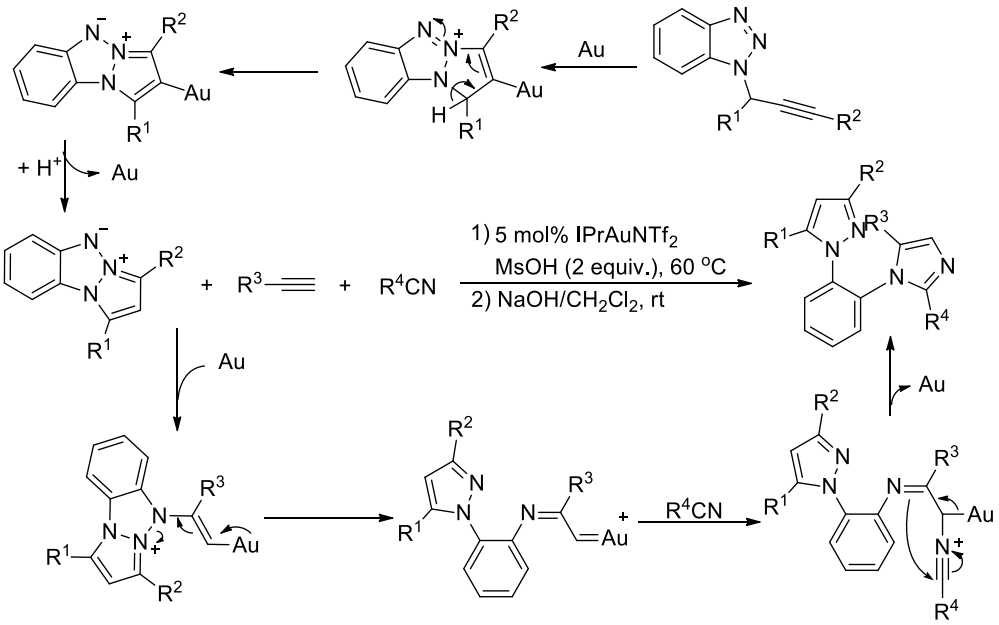


Scheme 8. Gold-catalyzed intermolecular reaction of ynamides with azides.



Scheme 9. Ynamide amination-initiated aza-Nazarov cyclization

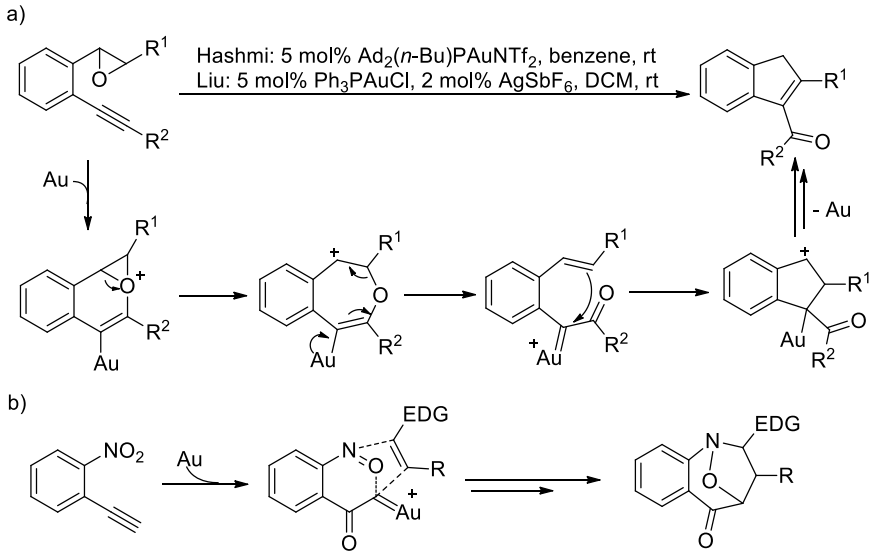
Besides of ynamides, Ballesteros et al. reported an α-imino gold carbene-mediated three component cascade reaction involving common terminal alkynes (Scheme 10).[24] A highly nucleophilic dipolar triazapentalene derivative was *in-situ* generated *via* gold-aided *5-endo-dig* cyclization of the propargylic benzotriazole and enabled the reaction with gold-activated terminal alkyne to provide α-imino gold carbene intermediates. Then, the gold carbene could be easily captured by the external nitrile following an intramolecular cyclization. Both pyrazole and imidazoles were formed in one-pot.



Scheme 10. Gold-catalyzed three component cascade reaction of alkyne, nitrile and propargylic benzotriazole.

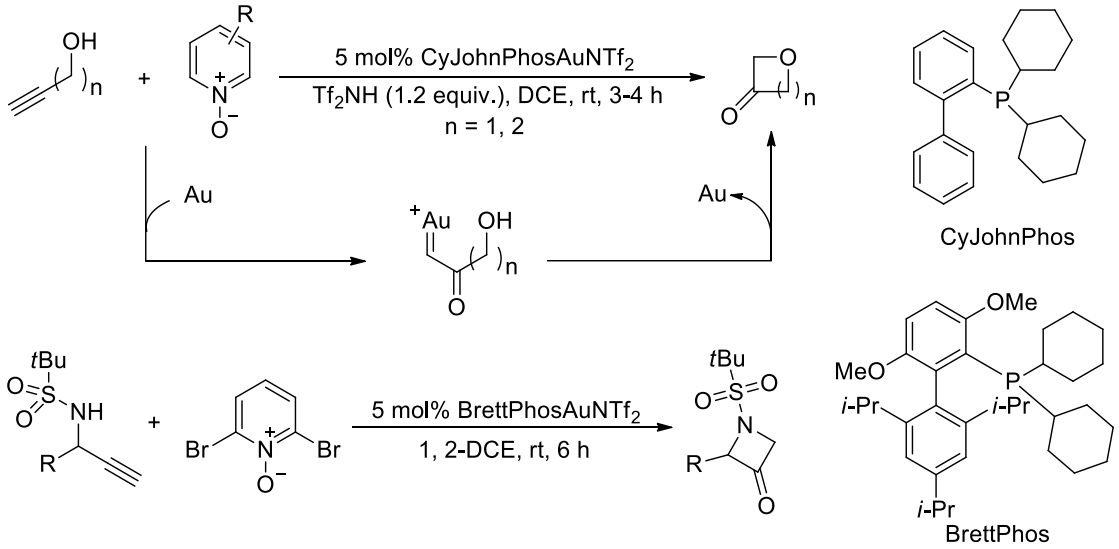
1.3 α-Oxo Gold Carbene-Mediated Syntheses of Cyclic Compounds

In 2008, Hashmi and Liu et al. independently reported that an internal epoxide can oxidize an alkyne leading to an α-oxo gold carbene, which is involved by in a further cyclization with the nascent C–C double bond. (Scheme 11, a).[25] Subsequently, Liu's group disclosed a formal [2+2+1] cycloaddition of a nitroso species, external alkenes and α-oxo gold carbenoids, which results from intramolecular oxidation *via* nitro groups, delivering bridged products with excellent diastereoselectivity. (Scheme 11, b).[26]



Scheme 11. Intramolecular generation of a presumed α-oxo gold carbene.

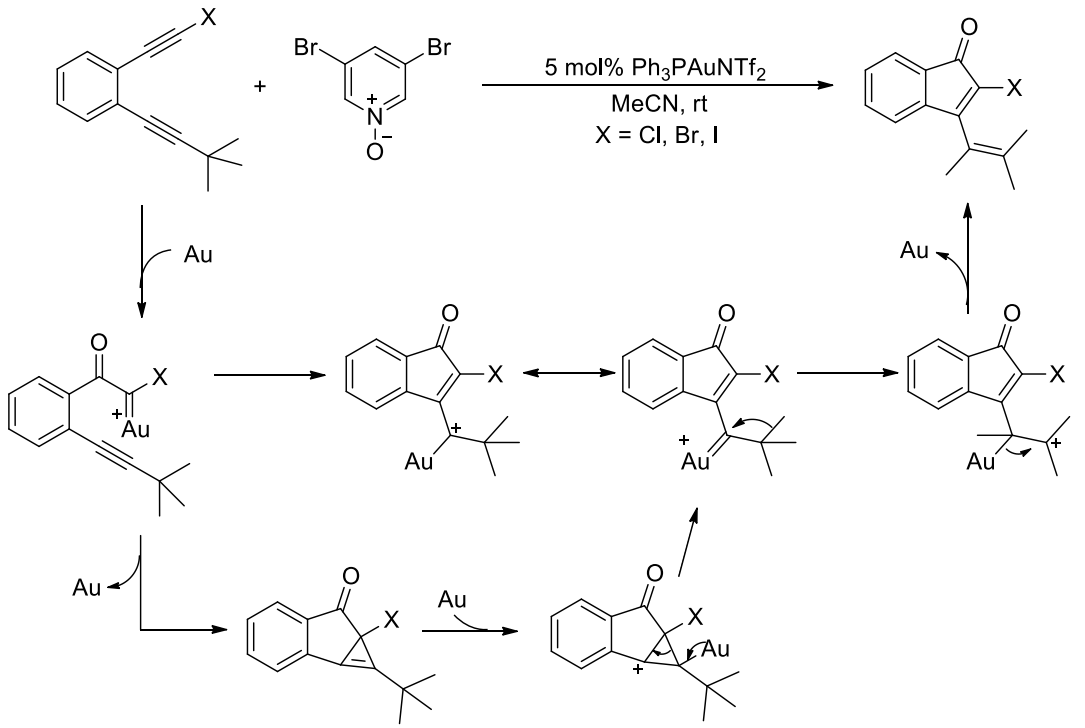
In 2010, Zhang's group reported the intermolecular generation of α-oxo gold carbenes *via* the reaction of alkynes with pyridine *N*-oxides (Scheme 12). The resulting gold carbene could be trapped by the tethered O- and N-nucleophile to give a variety of functionalized heterocyclic compounds.[27] Especially, highly strained 4-member rings were afforded in good to excellent yields.



Scheme 12. Intramolecular trapping of α-oxo gold carbene by heteroatom-nucleophiles

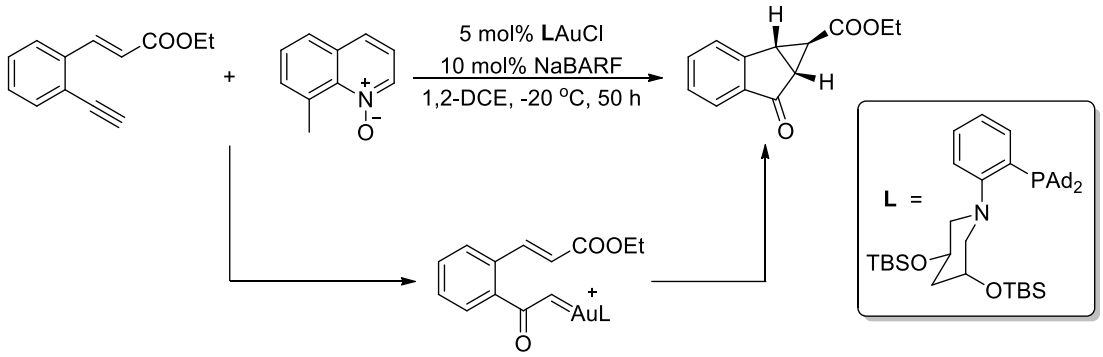
In 2013, Hashmi and co-workers described the gold-catalyzed oxidative cyclization of diynes (Scheme 13).[28] The α-oxo gold carbene accessed by alkyne oxidation was

transferred across the adjacent alkyne undergoing a 1, 5-carbene shift. The resulting vinyl gold carbene could be quenched by 1, 2-alkyl migration. Moreover, the oxidation of the vinyl carbene intermediate proved the 1, 5-carbene shift process.



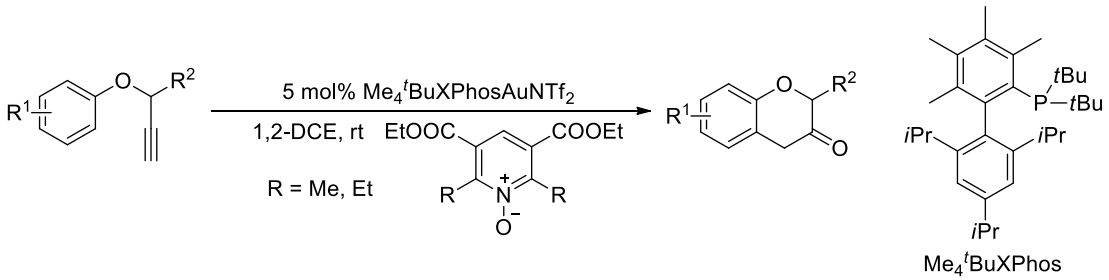
Scheme 13. α-Oxo gold carbene-initiated intramolecular 1, 5-carbene shift.

Lately, Zhang et al successfully achieved the intramolecular cyclopropanation of an alkene with an α-oxo gold carbene.[29] Taking advantage of a newly designed chiral *P*, *N*-bidentate ligand enabled the gold-catalyzed enantioselective synthesis of polycyclic cyclopropane derivatives (Scheme 14).



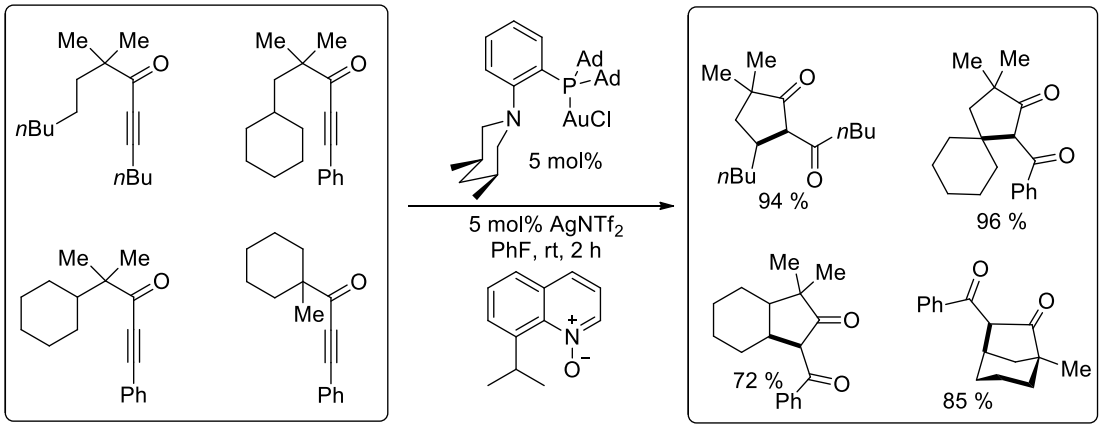
Scheme 14. Intramolecular trapping of α-oxo gold carbene by double bond.

Due to the high electrophilicity, α-oxo gold carbenes can also induce a sp^2-C-H insertion. Zhang's group reported the intramolecular attack of an electron-rich benzene onto a presumed gold carbene in the aryl propargyl ether oxidation (Scheme 15).[30] A large array of valuable chroman-3-ones was gained in moderate to good yields with sterically hindered ligands on the gold catalyst.



Scheme 15. Intramolecular trapping of α-oxo gold carbenes by electron-rich arenes.

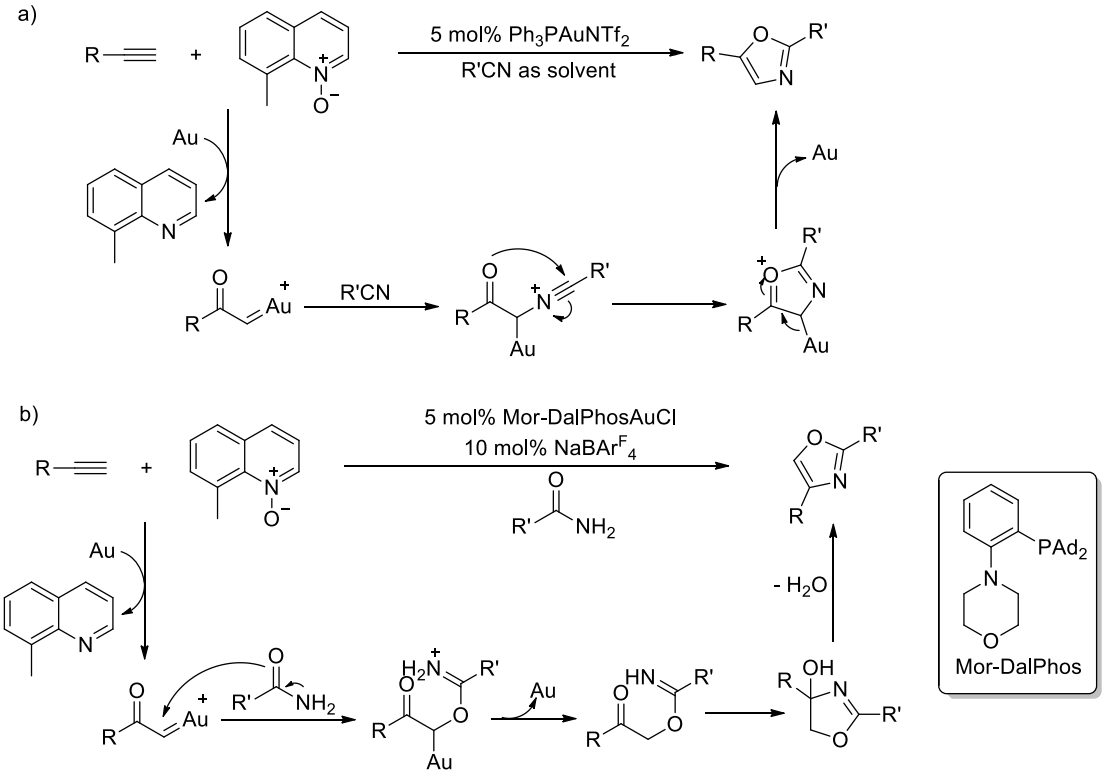
Recently, a notable progress in α-oxo gold carbene-triggered the unactivated sp^3-C-H bond functionalization was disclosed by Zhang's group.[31] Ynones were used as substrates to generate β-diketone-α-gold carbenes. These highly electrophilic carbene species are capable of common sp^3-C-H insertion to offer versatile spiro-, bridged and fused cyclopentanones (Scheme 16). The Thorpe-Ingold effect on substrate conformation is a key factor for cyclized efficiency.



Scheme 16. Intramolecular trapping of α-oxo gold carbene by unactivated sp^3 C-H.

Compared to the myriad of intramolecular trapping pathways, intermolecular cycloadditions of α-oxo gold carbenes is still limited to the cascade reaction with nitriles and amides. In 2011, Zhang's group reported the first instance on

intermolecular trapping of α-oxo gold carbenes by nitrile solvents, enabling a convergent [2+2+1] synthesis of 2, 5-disubstituted oxazoles from terminal alkynes, nitriles and quinoline *N*-oxides (Scheme 17, a).[32] Owing to the high electrophilicity, gold carbenes are easily over-oxidized by *N*-oxides, which disable the subsequent reaction. In 2012, a bidentate ligand was developed to temper the reactivity of terminal α-oxo gold carbenes suitable for trapping by stoichiometric external amides.[33] A [3+2] annulation was furnished to access diverse 2, 4-disubstituted oxazoles (Scheme 17, b).



Scheme 17. Intermolecular trapping of α-oxo gold carbene by nitriles and amides.

1.4 Research Objectives and Thesis Outline

The research projects exhibited in this thesis focus on gold carbene-mediated intermolecular annulations toward various heterocyclic compounds, which are difficult to prepare by conventional methods. Novel and atom-economy approaches to α-imino gold carbenes are also described. Moreover, platinum carbenes will be discussed under some special conditions.

In chapter 2, a gold-catalyzed formal [3+2] cycloaddition of alkynes with anthranils is

presented to offer synthetically valuable *N*-unprotected 7-acylindoles. Chapter 3 describes a gold-catalyzed [4+2] annulation towards the 2-aminoquinoline framework *via* the umpolung of a gold carbene carbon. Chapter 4 discloses a counteranion-controlled gold and platinum-catalyzed divergent [4+2] annulation of ynamides with benzofurazans to selectively access quinoxaline *N*-oxides and quinoxalines. In chapter 5, the α-oxo gold carbene-triggered oxidative [2+2+1] approach to full-substituted furans and macrocyclic furan derivates is developed by taking advantage of the amphoteric character of ynamides. 2, 3-dichloroquinoxaline *N*-oxide is found to suit the cascade reaction.

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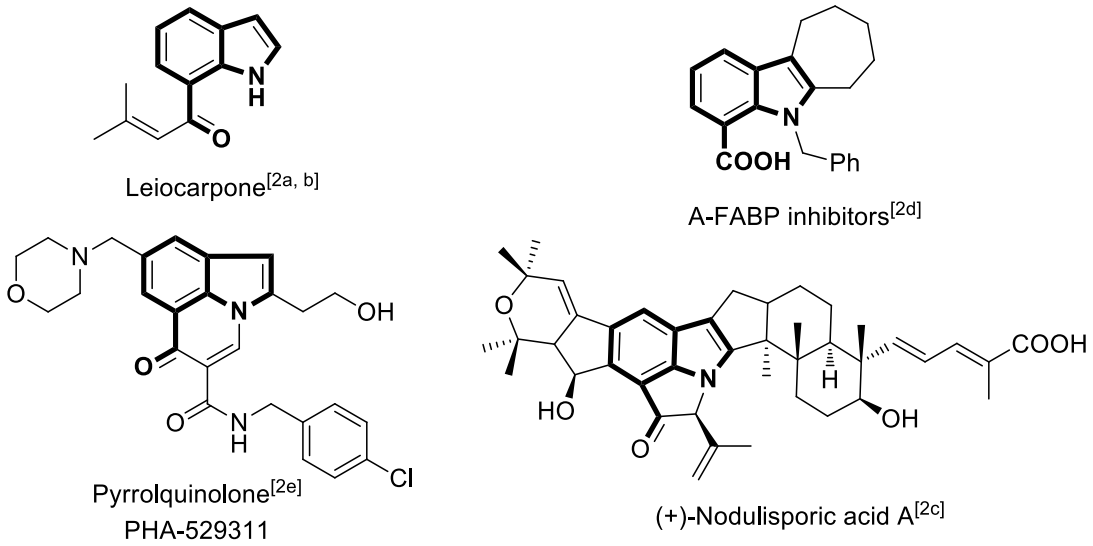
Chapter 2: Gold-Catalyzed C-H Annulation of Anthranils with Alkynes: a Facile, Flexible and Atom-Economical Synthesis of *N*-unprotected 7-Acyl Indoles

2.1 Introduction

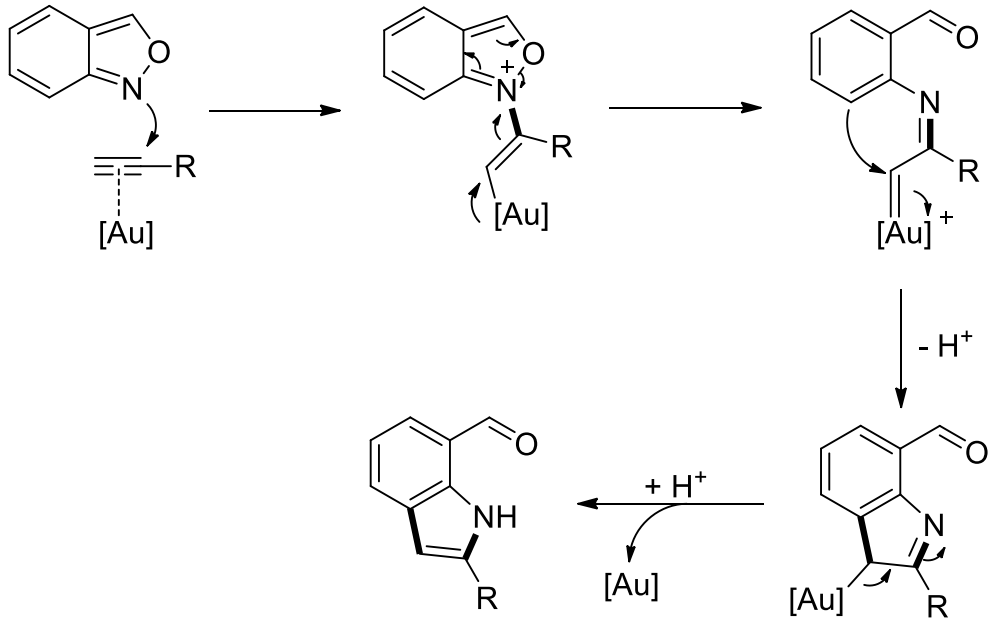
Indoles have attracted immense attention owing to their ubiquitous presence in natural products, drug molecular and materials.[1] Among indoles, 7-acylindoles serve not only as a class of bioactive molecules (Scheme 1), but also as key building blocks with orthogonal chemical reactivity.[2] However, conventional methodologies,[3] such as the Fischer, Larock and Bartoli syntheses, usually show low functional group tolerance and difficulties in installing aldehydes and ketones make it a challenge to construct 7-acylindoles. Hence, the development of a general synthetic strategy for the efficient construction of a diversified scaffold of 7-acylindole would be highly desirable.



Scheme 1. Selected bioactive compounds based on 7-acylindoles

In recent years, transition metal-catalyzed synthesis of functional indoles has experienced significant development.[1f,4] Gold catalysis[5,6,7e] especially has had a strong impact on this field of synthetic chemistry. For example, gold-catalyzed intramolecular annulation[5] of 2-alkynyl arylazides has afforded an efficient access to

indolyl[6b,d] and pseudoindoxyl[6a,c] skeletons, based on α-imino gold carbenoids as electrophilic key intermediates. However, the access towards α-imino gold carbenoids by intramolecular nitrene transfer can limit the generality and flexibility of the obtained products. Regarding this drawback, an intermolecular approach for the generation of an imino gold carbene species en route to functionalized heterocyclic compounds would represent an attractive strategy. In line with this principle, Davies et al. and Ye et al. successfully accomplished gold-catalyzed intermolecular cycloaddition for the preparation of polysubstituted oxazoles[7a, b] and pyrroles[7c]. Very recently, the gold-catalyzed intermolecular transformation of benzyl azides with ynamides was also reported by Ye's group.[7d] However, the α-imino gold carbenes that are produced through the intermolecular approach have so far been limited to polarized alkynes. Inspired by these reports and in continuation of our work on indole chemistry,[8] we envisioned that a gold-catalyzed intermolecular transformation of anthranil with alkynes could produce α-imino gold carbene intermediates. Based on the high electrophilicity of the α-imino gold carbenoid, an intramolecular *ortho*-aryl C-H insertion could then afford the desired 7-formyl indoles (Scheme 2). Herein, we report our results on the unprecedented gold-catalyzed C-H annulation of anthranils with alkynes under mild reaction condition. Remarkably, the reaction also proceeds smoothly with ynamides, non-polarized alkynes, and non-terminal alkynes. The process enables a facile, flexible and atom-economical synthesis of 7-acylindolyl frameworks.



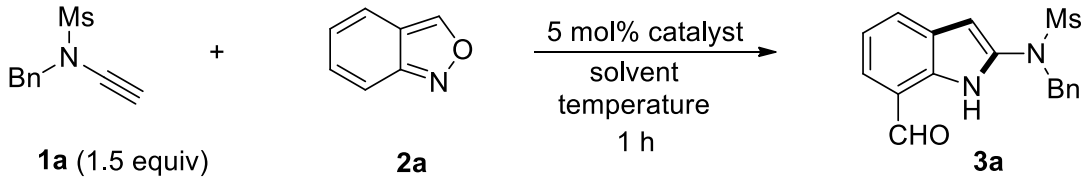
Scheme 2. Planned gold-catalyzed annulation of anthranils with alkynes.

2.2 Results and Discussion

2.2.1 Optimization of the Reaction Conditions

Initially, we conducted a screening of the reaction conditions with ynamide **1a**, since such substrates usually possess high reactivity in gold catalyzed reaction as a result of their electronic properties[7a-d,9] (Table 1). Treatment of ynamide **1a** and anthranil **2a** with $Ph_3PAuCl/AgNTf_2$ at 0 ^oC provided the expected product **3a** in 36 % yield (entry 1). Among the screened gold catalysts, the catalyst with an NHC ligand (entry 6) showed higher activity than those with phosphane and phosphite ligands (entries 2-4). $AuBr_3$ was less efficient as well (entry 5). The yield increased to 84 % upon decreasing the reaction temperature to - 20 ^oC (entry 7). Further, improvement was achieved by taking advantage of different silver salts (entry 8, 9) and solvents (entry 10-17). Finally, up to 90 % yield of **3a** was gained by employing 5 mol% $IPrAuCl/AgNTf_2$ as catalyst in $PhCF_3$ at - 20 ^oC (entry 11). The control experiment without catalyst showed no reaction even at room temperature (entry 18).

Table 1: Optimization of Reaction Conditions[a]



1a (1.5 equiv) **2a** **3a**

Entry	Catalyst	Solvent	Temperature	Yield % [b]
1	$Ph_3PAuCl/AgNTf_2$	$ClCH_2CH_2Cl$	0 ^oC	36
2	$JohnPhosAuCl/AgNTf_2$	$ClCH_2CH_2Cl$	0 ^oC	49
3	$^tBuXPhosAuCl/AgNTf_2$	$ClCH_2CH_2Cl$	0 ^oC	33
4[c]	$(ArO)_3PAuCl /AgNTf_2$	$ClCH_2CH_2Cl$	0 ^oC	64
5	$AuBr_3$	$ClCH_2CH_2Cl$	0 ^oC	35
6	$IPrAuCl/AgNTf_2$	$ClCH_2CH_2Cl$	0 ^oC	73
7	$IPrAuCl/AgNTf_2$	$ClCH_2CH_2Cl$	-20 ^oC	84

8	IPrAuCl/$AgSbF_6$	$ClCH_2CH_2Cl$	-20 ^oC	74
9	IPrAuCl/$AgBF_4$	$ClCH_2CH_2Cl$	-20 ^oC	58
10	IPrAuCl/AgOTf	$ClCH_2CH_2Cl$	-20 ^oC	32
11	**IPrAuCl/$AgNTf_2$**	**$PhCF_3$**	**-20 ^oC**	**90 (85[d])**
12	IPrAuCl/$AgNTf_2$	PhMe	-20 ^oC	81
13	IPrAuCl/$AgNTf_2$	PhCl	-20 ^oC	71
14	IPrAuCl/$AgNTf_2$	CH_2Cl_2	-20 ^oC	72
15	IPrAuCl/$AgNTf_2$	CH_3CN	-20 ^oC	22
16	IPrAuCl/$AgNTf_2$	THF	-20 ^oC	46
17	IPrAuCl/$AgNTf_2$	Et_2O	-20 ^oC	30
18	none	$ClCH_2CH_2Cl$	rt	ND

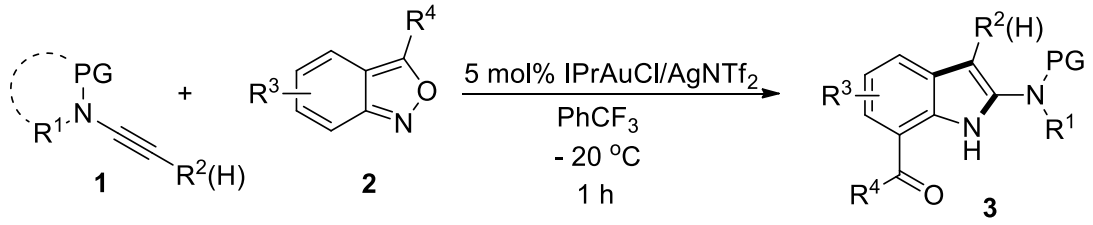
[a] Reaction conditions: **1a** (0.3 mmol), **1b** (0.2 mmol); a solution (1 ml) of **1a** was added over 3 mins to a solution (1 ml) of **1b** and the catalyst at the according temperature, reaction time 1 h. [b] Measured by ^1H NMR using 4-(dimethylamino)benzaldehyde as the internal standard. [c] Ar = 2, 4-di-*tert*-butylphenyl. [d] Isolated yield.

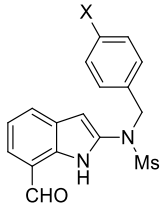
2.2.2 Scope and Limitation

With the optimized condition in hand, the scope of the reaction was explored (Table 2). Ynamides reacted with excellent to moderate yields (**3a**-**3j**). A broad set of substitutents at the ynamide nitrogen atom turned out to be compatible. 7-Formyl indole **3e** which was prepared from *N*-(2-bromophenyl) ynamide in good yield, is a potential precursor for the synthesis of 1,2-fused indoles according to a method from Perumal's group.[4g] Among the tested protecting groups on the ynamides, besides tosyl and mesyl, the oxazolidinone-derived ynamide also underwent the annulation to afford the product **3j** in moderate yield. Non-terminal ynamides were also investigated and the targeted product (**3k**) was prepared from phenyl-substituted ynamide in good yield, the alkyl-substituted ynamide afforded the H elimination product **3l'** rather than **3l**. Various substituted anthranils were empolyed for the synthesis of diversified 7-acylindoles (**3m**-**3y**). Owing to the mild reaction conditions,

a large array of functional groups, including ester (**3n)**, acetal (**3o)**, chloride **3p**, bromide (**3q**, **3r**), alkene (**3v)** and α, β-unsaturaed ketones (**3w-3y**) were all tolerated, which enormously enhances the range of the obtained substrates. The reaction of anthranils with electron-donating groups usually proceeded with higher yields, which suggests an electrophilic aromatic substitution mechanism. For a structural confirmation of the 7-acylindolyl framework, a single crystal X-ray structure analysis[10] of **3q** was performed (Figure 1).

Table 2: Reaction scope of anthranils with ynamides[a,b]



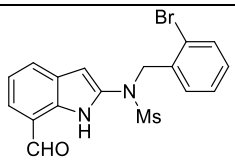


3a, X = H, 85 %

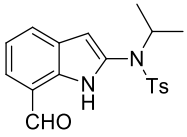
3b, X = Me, 80 %

3c, X = OMe, 74 %

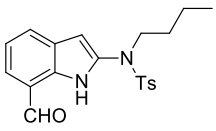
3d, X = Cl, 77 %



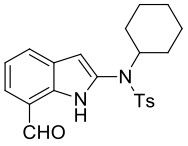
3e, 74 %



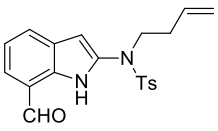
3f, 88 %



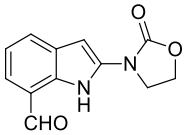
3g, 84 %



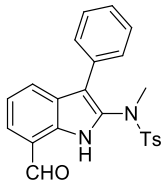
3h, 86 %



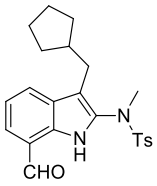
3i, 83 %



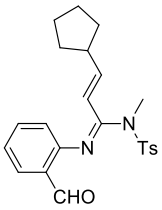
3j, 50 %



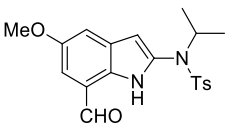
3k[c], 84 %



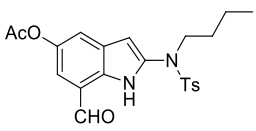
3l, 0 %

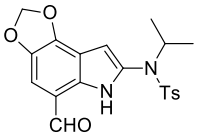


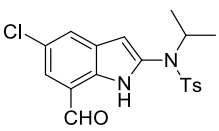
3l'[c], 81 %

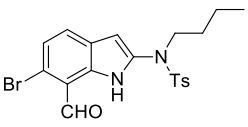


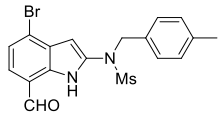
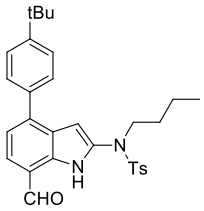
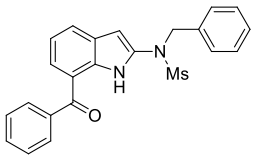
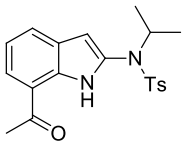
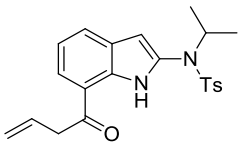
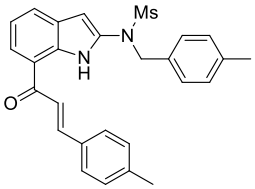
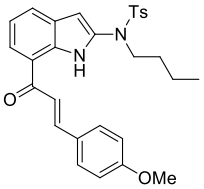
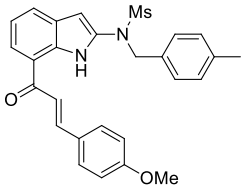
3m, 74 %









3n, 81 %	**3o,** 75%	**3p**, 61 %	**3q**, 64 %
			
3r, 53 %	**3s,** 80 %	**3t,** 85 %	**3u**, 83 %
			
3v, 74 %	**3w** [d], 73 %	**3x** [d], 79 %	**3y** [d], 65 %

[a] Reaction conditions: **1** (0.3 mmol), **2** (0.2 mmol); a solution (1 ml) of **1** was added over 3 mins to a solution (1 ml) of **2** and 5 mol% IPrAuCl/$AgNTf_2$ at -20 ^oC, then stirred for an additional 1 h. [b] Isolated yields. [c] Reaction temperature: 65 ^oC, 4 Å MS was added. [d] a mixture of $ClCH_2CH_2Cl$ (0.5 ml) and $PhCF_3$ (1.5 ml) was as solvent.

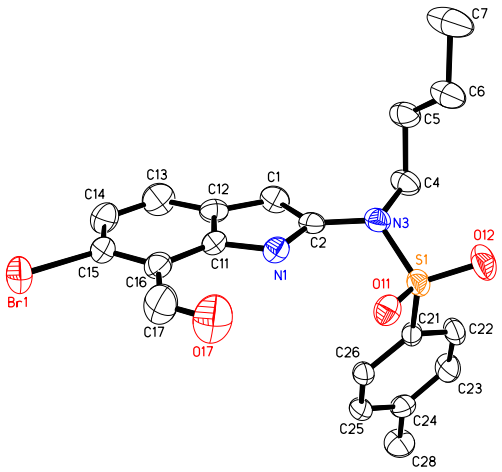
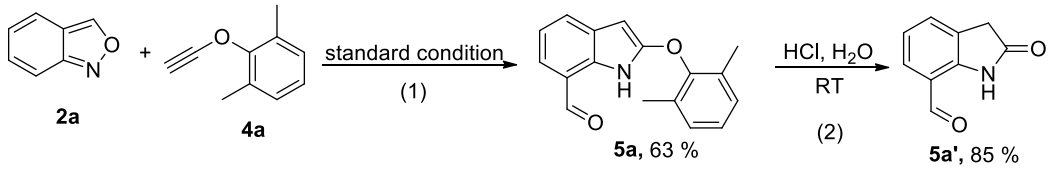


Figure 1. Solid-state molecular structure of **3q**.

The transformation was not only limited to ynamides. The reaction of anthranil and aryl alkynyl ether **4a** under the standard reaction condition furnished 2-oxyl product **5a** in 63 % yield (Scheme 3, Step 1). 7-Formyl oxindole **5a'**, a promising novel antioxidant[11], was easily gained by the hydrolysis of **5a** under acid condition

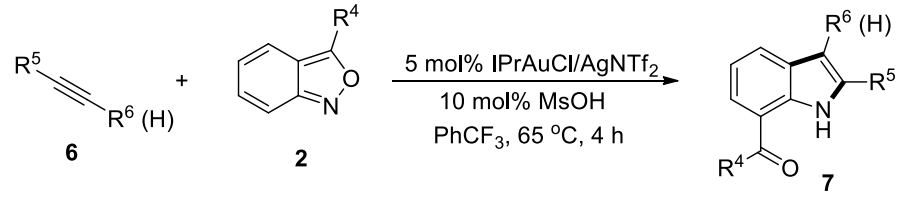
(Scheme 3, Step 2).

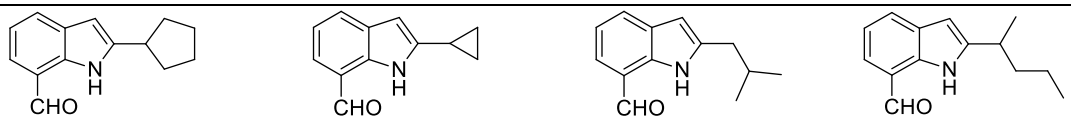


Scheme 3. The reaction of anthranil with aryl alkynyl ether

To extend the scope of substrates further, the non-polarized alkynes were used as well. However, owing to their decreased reactivity, the reaction did not work under the standard condition. But by raising the temperature and extending the reaction time, the yield of the expected product could be gradually increased.[12] By the addition of 10 mol% MsOH, which might facilitate the deauration process and by using an excess of alkyne (MsOH alone is not catalytically active) enabled a more efficient conversion rate of anthranil, delivering the products in moderate yields. Under the adjusted conditions, both alkyl and aryl alkynes were suitable for the construction of C2-functionalyzed and C2, C3-diarylated products (Table 3, **7a**-**7i**). The 7-substituted indole **7j**, which is a key precursor for synthesizing pyrrolquinolone derivatives,[13] could facilely be prepared despite the conjugated double bond.

Table 3: Reaction scope of alkynes[a, b]



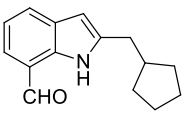


7a, 68 %

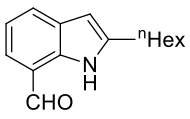
7b, 68 %

7c, 65 %

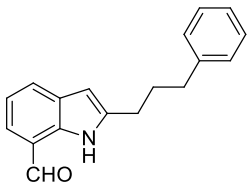
7d, 74 %



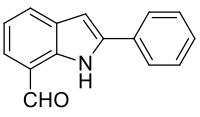
7e, 56 %



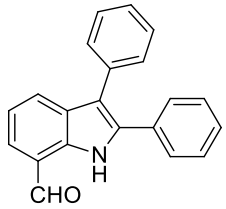
7f, 67 %



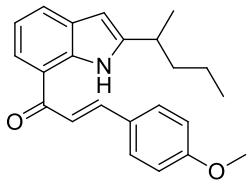
7g, 63 %



7h, 61 %

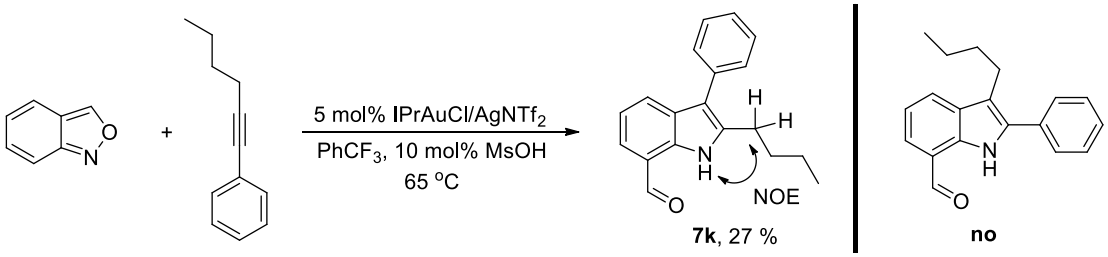


7i, 50 %



7j, 66 %

[a] Reaction conditions: **6** (0.8 mmol) and **2** (0.2 mmol) were heated for 4 h at 65 ^{o}C in 2 ml $PhCF_3$. [b] Isolated yields.

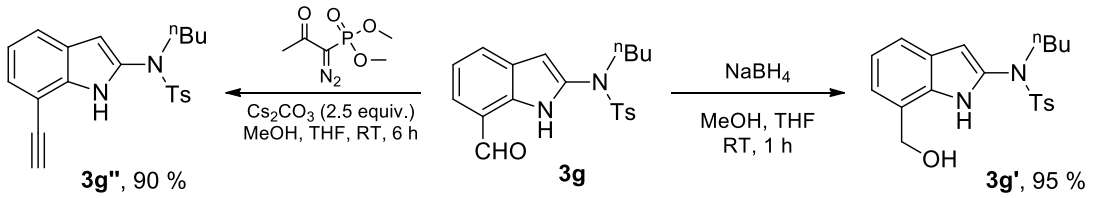


Scheme 4. Conversion of an unsymmetrical alkyne.

Finally, an unsymmetrically alkyl/aryl-substituted alkyne was used. In this case, a low yield of 2-alkyl-3-aryl indol **7k** was obtained (assigned by NOE) and no other indole isomer was formed (Scheme 4). The low yield might result from a competing hyride-shift pathway if the carbenoid is formed next to the alkyl tether (similar to the formation of **3l'**).

2.2.3 Further Derivatisation

Owing to the presence of both electrophilic and nuclephilic sites, 7-formly indoles have been utilized as flexible scaffolds for the syntheses of 1, 7-fused indoles, most of which exhibit significant biological activity.[13,14] While numerous studies have focused on the reactions of indoles with electrophiles, we turned our attention on nucleophilic transformations of 7-acyl indoles. For instance, the reduction of **3g** afforded the 7-alkylated product **3g'** and the unprotected 7-alkynyl indole **3g"** could be obtained easily in excellent yield through Seyferth-Gilbert homologation (Scheme 5).



Scheme 5. Application to the preparation of diverse 7-substituted indoles

2.3 Summary

In summary, we decribed a novel, short, and atom-economical synthesis of 7-acyl indoles through gold-catalyzed C-H annulation of anthranils with alkynes. The substrate scope is remarkably broad and the benign reaction conditions tolerate a diverse set of functional groups, which further strengthens the synthetic impact of this method. The obtained indoles are highly interesting building blocks for the synthesis of 7-substiuted indolyl and fused indolyl frameworks. Based on the availability of the starting materials and the enormous gain in molecular complexity, we believe that this method will serve as powerful tool for organic synthesis.

2.4 References

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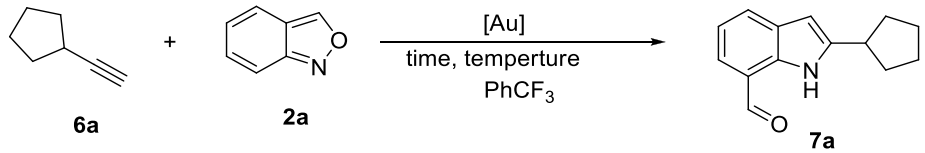
2.5 Experimental Section

General information: Chemicals were purchased from commercial suppliers and used as delivered. The reagents **1**[1,2], **4a**[3,4] have been prepared according to the literature. Dry solvents were dispensed from the solvent purification system MB SPS-800. Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance DRX-300, Bruker-Avance DRX-500 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) and m (multiplet) as well as combinations of them. 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 and HSQC 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^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-K_α-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Heavy atom diffractions were solved by direct methods and refined against F2 with full matrix least square algorithm. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Gas Chromatography / Mass

Spectrometry (GC/MS) spectra were measured on two different hardware systems: 1. HP 5972 Mass Selective Detector, coupled with a HP 5890 SERIES II plus gas chromatograph. 2. Agilent 5975C Mass Selective Detector, coupled with an Agilent 7890A gas chromatograph. In both cases, as a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and helium was used as the carrier gas. Gas Chromatography (GC) was carried out on a HP 5890 SERIES II plus gas chromatograph. As a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and nitrogen was used as the carrier gas. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not corrected. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400 mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and diethylether (Et_2O) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)), molybdatophosphoric acid (5 % in ethanol), vanillin/H_2SO_4 (in ethanol) or anisaldehyde/HOAc (in ethanol). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

Optimization of the Reaction Conditions (Table S1)

Table S1: Optimization of reaction conditions[a]



6a **2a** **7a**

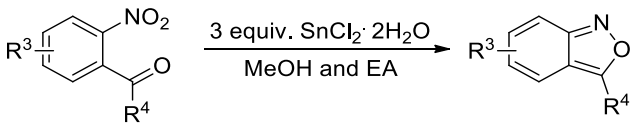
Entry	Catalyst (5 mol%)	Additives	Amount of **6a**	Time	T °C	Yield (%)[b]
1	IPrAuCl/$AgNTf_2$	none	1.5 equiv.	1 h	-20	0
2	IPrAuCl/$AgNTf_2$	none	4 equiv.	1 h	-20	0

3	IPrAuCl/$AgNTf_2$	none	4 equiv.	1 h	rt	trace
4	IPrAuCl/$AgNTf_2$	none	4 equiv.	4 h	rt	8
5	IPrAuCl/$AgNTf_2$	none	4 equiv.	24 h	rt	17
6	IPrAuCl/$AgNTf_2$	none	4 equiv.	1 h	50	18
7	IPrAuCl/$AgNTf_2$	none	4 equiv.	4 h	50	28
8	IPrAuCl/$AgNTf_2$	none	4 equiv.	4 h	65	36
9	IPrAuCl/$AgNTf_2$	none	4 equiv.	24 h	65	29
10[c]	$(ArO)_3PAuCl/AgNTf_2$	none	4 equiv.	4 h	65	29
11	IPrAuCl/$AgSbF_6$	none	4 equiv.	4 h	65	30
12	IPrAuCl/$AgNTf_2$	10 mol% $AgNTf_2$	4 equiv.	4 h	65	63
13	IPrAuCl/$AgNTf_2$	10 mol% $Zn(OTf)_2$	4 equiv.	4 h	65	57
14	IPrAuCl/$AgNTf_2$	10 mol% $Fe(OTf)_3$	4 equiv.	4 h	65	13
15	IPrAuCl/$AgNTf_2$	20 mol% $Zn(OTf)_2$	4 equiv.	4 h	65	64
16	**IPrAuCl/$AgNTf_2$**	**10 mol% MsOH**	**4 equiv.**	**4 h**	**65**	**68**
17	IPrAuCl/$AgNTf_2$	10 mol% $HNTf_2$	4 equiv.	4 h	65	34
18	IPrAuCl/$AgNTf_2$	20 mol% MsOH	4 equiv.	4 h	65	60
19	IPrAuCl/$AgNTf_2$	1 equiv. MsOH	4 equiv.	4 h	65	trace
20	none	10 mol% MsOH	4 equiv	4 h	65	0

[a] Reaction conditions: **6a** and **2a** (0.2 mmol) were heated in $PhCF_3$ (2ml). [b] isolated yield. [c] Ar = 2, 4-di-*tert*-butylphenyl.

Experimental Procedure 1: Synthesis of substituted anthranils

The syntheses of substituted anthranils was referred to the report of S. Fletcher's group [5] with a little modification.



A round bottom flask equipped with a magnetic stirrer bar was charged with the substituted 2-nitroacylbenzene (3.00 mmol) in EtOAc–MeOH (1:1; 20 mL). $SnCl_2 \cdot H_2O$ (9.00 mmol) was added and the reaction was stirred at room temperature

for 24 h. The reaction was quenched by saturated $NaHCO_3$ (20 ml), and filtered. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the organic portions combined, washed with H_2O (20 mL), saturated aqueous NaCl (20 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization of unknown compounds has been listed in part 4.

Experimental Procedure 2: Gold-catalyzed C-H annulation of anthranils with ynamides or aryl alkynyl ethers 4a

A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (5 mol%, 6.2 mg), $AgNTf_2$ (5 mol%, 4 mg), and solvent (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the reaction was cooled to -20 ^oC and the anthranil (0.2 mmol) was added. The alkyne (0.2 mmol) dissolved in solvent (1 ml) was added dropwise over 3 minutes at -20 ^oC, and reacted at -20 ^oC for 1h. The solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. For the non-terminal ynamides, 4 Å MS was added and reacted at 65 ^oC for 1 h. The characterization of products has been listed in part 4.

Experimental Procedure 4: Gold-catalyzed C-H annulation of alkynes with anthranils

A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (5 mol%, 6.2 mg), $AgNTf_2$ (5 mol%, 4 mg), MsOH (10 mol%, 2 mg) and solvent (1 ml). The mixture was stirred 5 minutes at room temperature. Then the anthranil (0.2 mmol) and alkyne (0.2 mmol) dissolved in solvent (1 ml) were added. The reaction was stirred at 65 ^oC for 4 h. The solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization of products has been listed in part 4.

Experimental Procedure 5: The hydrolysis of 5a

To the solution of **5a** in MeOH (1 ml) was added dropwise 2 N HCl (1 ml). The reaction was stirred at room temperature until the reagent disappeared, monitored by TLC. The reaction was quenched by saturated $NaHCO_3$. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the organic portions combined, washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization of product has been listed in part 4.

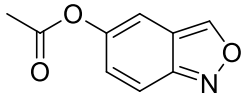
Experimental Procedure 6: Seyferth-Gilbert homologation of 3g

To the mixture of **3g** (0.2 mmol), Cs_2CO_3 (0.5 mmol), MeOH (1 ml) and THF (1 ml) was added dropwise the dimethyl (1-diazo-2-oxopropyl)phosphonate (0.4 mmol) at 0 ^oC. Then, the reaction was stirred 6 h at room temperature. The mixture was washed with H_2O (10 mL), and extracted with EtOAc (3 × 5 mL). The organic portions were combined and washed with saturated aqueous NaCl (10 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexane/EtOAc) to provide the title compound. The characterization of product has been listed in part 4.

Experimental Procedure 7: Reduction reaction of 3g

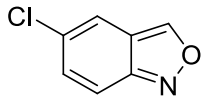
To the solvent of **3g** (0.2 mmol) and EtOH (2 ml) was added the $NaBH_4$ (0.4 mmol), then stirred 2 h at room temperature. The reaction was quenched by H_2O (10 ml), and filtered. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the organic portions combined, washed with H_2O (10 mL), saturated aqueous NaCl (10 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexane/EtOAc) to provide the title compound. The characterization of product has been listed in part 4.

Characterization



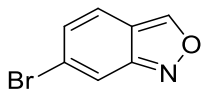
Compound **2c**: Yield 88 %, colourless soild, mp: 78-80 ^oC; R_f = 0.20 (PE/EA = 5:1);

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.13 (s, 1 H), 7.66 (d, *J* = 9 Hz, 1 H), 7.31 (s, 1 H), 7.08 (d, *J* = 9.5 Hz, 1 H), 2.34 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 169.4 (s), 154.8 (d), 154.6 (s), 146.9 (s), 128.3 (d), 117.7 (s), 116.7 (d), 109.3 (d), 21.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3142, 3080, 2939, 1750, 1652, 1619, 1567, 1523, 1473, 1432, 1413, 1372, 1360, 1328, 1259, 1216, 1176, 1140, 1104, 1048, 1016, 954, 926, 08, 872, 808, 785, 754, 736, 681, 611 cm^{-1}; HRMS (EI) m/z calcd for $C_9H_7NO_3$: 177.0413; found: 177.0413.



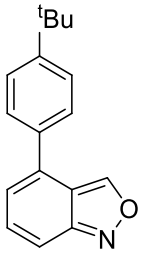
Compound **2e**: Yield 78 %, colourless soild, mp: 76-78 ^{o}C; R_f = 0.54 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.03 (s, 1 H), 7.57-7.45 (m, 2 H), 7.21-7.14 (m, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 154.6 (s), 154.1 (d), 132.8 (d), 130.3 (s), 118.4 (s), 117.8 (d), 116.8 (d) ppm; IR (reflection): $\tilde{\nu}$ = 3109, 1911, 1728, 1638, 1546, 1515, 1462, 1408, 1317, 1252, 1231, 1154, 1115, 1057, 1043, 923, 879, 864, 857, 803, 772, 733, 692, 644, 627, 610 cm^{-1}; HRMS (EI) m/z calcd for C_7H_4ClNO: 152.9981; found: 152.9964.

Compound **2f**: Yield 88 %, light yellow soild, mp: 98-99 ^{o}C; R_f = 0.60 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.07 (s, 1 H), 7.55-7.47 (m, 1 H), 7.15-7.06 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156.2 (s), 156.1 (d), 131.5 (d), 126.8 (d), 121.0 (s), 114.3 (d), 112.5 (s) ppm; IR (reflection): $\tilde{\nu}$ = 3178, 3120, 3096, 1767, 1633, 1546, 1512, 1438, 1398, 1349, 1255, 1198, 1184, 1157, 120, 1014, 946, 912, 868, 819, 782, 729, 616 cm^{-1}; HRMS (EI) m/z calcd for C_7H_4BrNO: 196.9476; found: 196.9478.

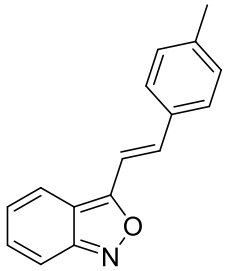


Compound **2g**: Yield 84 %, light yellow soild, mp: 55-56 ^{o}C; R_f = 0.46 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.06 (s, 1 H), 7.79 (s, 1 H), 7.40 (d, *J* = 9 Hz, 1 H), 7.02 (d, J = 9.5 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156.6 (s), 155.3 (d),

128.8 (d), 125.8 (s), 121.0 (d), 117.2 (d), 116.7 (s) ppm; IR (reflection): $\tilde{\nu}$ = 3124, 3106, 3089, 1897, 1741, 1684, 1658, 1634, 1541, 1499, 1456, 1431, 1406, 1375, 1289, 1232, 1203, 1145, 1115, 1031, 917, 866, 855, 843, 828, 789, 771, 757, 734, 669, 627, 609 cm^{-1}; HRMS (EI) m/z calcd for C_7H_4BrNO: 196.9476; found: 196.9470.

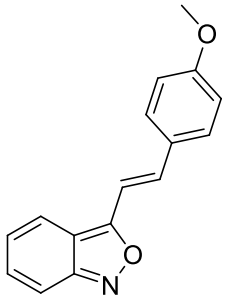


Compound **2h**: Yield 85 %, colourless soild, mp: 171-173 ^oC; R_f = 0.46 (PE/EA = 5:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 9.15 (s, 1 H), 7.80-7.78 (m, 1 H), 7.67-7.61 (m, 3 H), 7.56-7.52 (m, 2 H), 7.37-7.34 (m, 1 H), 1.40 (s, 9 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156.9 (s), 154.3 (d), 151.6 (s), 143.6 (s), 137.2 (s), 127.0 (d, 2 C), 126.0 (d, 2 C), 125.8 (d), 119.8 (d), 117.6 (s), 111.4 (d), 34.7 (s), 31.3 (q, 3C) ppm; IR (reflection): $\tilde{\nu}$ = 3137, 3122, 3061, 2960, 2901, 1738, 1643, 1562, 1520, 1461, 1405, 1382, 1363, 1307, 1269, 1203, 1151, 1123, 1105, 1024, 950, 926, 862, 841, 825, 797, 780, 741, 667, 649, 632 cm^{-1}; HRMS (ESI) m/z calcd for $C_{17}H_{17}NO$ $[M+H]^+$: 252.1383; found: 252.1382.

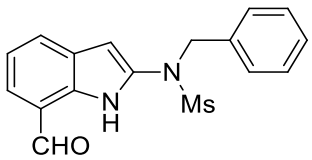


Compound **2l**: Yield 83 %, yellow soild, mp: 122-123 ^oC; R_f = 0.5 (PE/EA = 5:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.61-7.56 (m, 1 H), 7.56-7.47 (m, 2 H), 7.46-7.42 (m, 2 H), 7.26-7.14 (m, 4 H), 6.97-6.93 (m, 1 H), 2.32 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.8 (s), 157.4 (s), 139.8 (s), 135.2 (d), 133.0 (s), 130.9 (d), 129.7 (d, 2 C), 127.3 (d, 2 C), 123.9 (d), 119.9 (d), 115.6 (s), 115.3 (d), 111.1 (d), 21.5 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3070, 3025, 2919, 1903, 1737, 1638, 1605, 1571, 1522, 143, 1412, 1397, 1378, 1308, 1277, 1226, 1181, 1152, 1139, 1112, 1060, 1038, 962, 944, 918, 857, 835, 803, 753, 742,711, 669, 649, 626, 610 cm^{-1}; HRMS (ESI) m/z calcd for

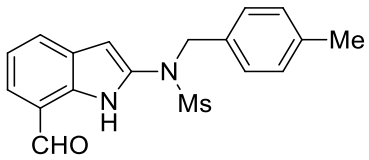
$C_{16}H_{13}NO$ $[M+H]^+$: 236.1070; found: 236.1069.



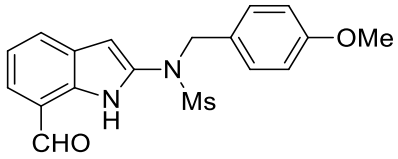
Compound **2m**: Yield 80 %, yellow soild, mp: 122-124 ^oC; R_f = 0.3 (PE/EA = 5:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.59-7.53 (m, 1 H), 7.53-7.44 (m, 4 H), 7.25-7.17 (m, 1 H), 7.14-7.07 (m, 1 H), 6.95-6.90 (m, 1 H), 6.89-6.84 (m, 2 H), 3.78 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 164.0 (s), 160.7 (s), 157.4 (s), 134.9 (d), 130.9 (d), 128.8 (d, 2 C), 128.5 (s), 123.7 (d), 120.0 (d), 115.4 (s), 115.2 (d), 114.5 (d, 2 C), 109.9 (d), 55.4 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3009, 2841, 1658, 1636, 1602, 1574, 1548, 1511, 1452, 1422, 1401, 1309, 1280, 1254, 1180, 1152, 1137, 1112, 1056, 1020, 985, 965, 907, 841, 825, 813, 788, 746, 718, 637, 609 cm^{-1}; HRMS (ESI) m/z calcd for $C_{16}H_{13}NO_2$ $[M+H]^+$: 252.1019; found: 252.1018.



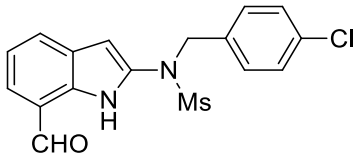
Compound **3a**: Yield 85 %, colourless solid, mp: 132-133 ^oC; R_f = 0.36 (PE/EA = 5:2); ^1H NMR (300 MHz, $CDCl_3$) δ = 10.24 (brs, 1 H), 9.93 (s, 1 H), 7.70-7.65 (m, 1 H), 7.51-7.45 (m, 1 H), 7.32-7.08 (m, 6 H), 6.23 (d, *J* = 2.4 Hz, 1 H), 4.82 (s, 2 H), 2.89 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 135.6 (s), 135.5 (s), 131.4 (s), 128.8 (d, 2C), 128.7 (d), 128.22 (d), 128.18 (d, 2C), 128.1 (s), 127.4 (d), 120.2 (s), 120.0 (d), 95.5 (d), 54.5 (t), 38.0 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3403, 3012, 2870, 1670, 1608, 1592, 1544, 1454, 1437, 1357, 1328, 1289, 1272, 1238, 1199, 1187, 1149, 1088, 1049, 1027, 974, 957, 903, 881, 850, 791, 771, 732, 721, 693, 665, 621, 610 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{16}N_2O_3S$: 328.0882; found: 328.0888.



Compound **3b**: Yield 80 %, colourless solid, mp: 131-132 ^{o}C; R_f = 0.44 (PE/EA = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.22 (brs, 1 H), 9.94 (s, 1 H), 7.70-7.65 (m, 1 H), 7.51-7.46 (m, 1 H), 7.20-7.08 (m, 3 H), 7.03-6.97 (m, 2 H), 6.23 (d, *J* = 2.4 Hz, 1 H), 4.78 (s, 2 H), 2.88 (s, 3 H), 2.19 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 138.0 (s), 135.6 (s), 132.5 (s), 131.4 (s), 129.4 (d, 2C), 128.7 (d), 128.2 (d, 2C), 128.1 (s), 127.3 (d), 120.2 (s), 120.0 (d), 95.6 (d), 54.3 (t), 38.0 (q), 21.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 346, 3349, 3124, 3023,2928, 2818, 2735, 1709, 1672, 1609, 1592, 1546, 1516, 1491, 1451,1412, 1358, 236, 1221, 1195, 1153, 1119, 1047, 1021, 957, 882, 89, 806, 769, 747, 726, 684, 657 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{18}N_2O_3S$: 342.1038; found: 342.1025.

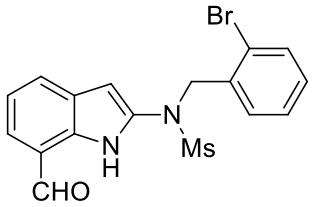


Compound **3c**: Yield 74 %, colourless solid, mp: 137-139 ^{o}C; R_f = 0.30 (PE/EA = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.18 (brs, 1 H), 9.97 (s, 1 H), 7.74-7.68 (m, 1 H), 7.55-7.50 (m, 1 H), 7.25-7.12 (m, 3 H), 6.79-6.71 (m, 2 H), 6.24 (d, *J* = 2.4 Hz, 1 H), 4.77 (s, 2 H), 3.67 (s, 3 H), 2.89 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 159.5 (s), 135.5 (s), 131.4 (s), 129.7 (d, 2C), 128.7 (d), 128.1 (s), 127.5 (s), 127.3 (d), 120.2 (s), 120.0 (d), 114.1 (d, 2C), 95.8 (d), 55.3 (q), 54.1 (t), 38.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3425, 3355, 3011, 2932, 2837, 2737, 1670, 1610, 1591, 1544, 1514, 1490, 1453, 1411, 1357, 1304, 1249, 1195, 1178, 1157, 1113, 1048, 957, 882, 846, 768, 746, 704, 684, 656 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{18}N_2O_4S$: 358.0987; found: 358.1000.

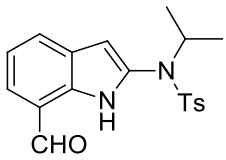


Compound **3d**: Yield 77 %, colourless solid, mp: 126-128 ^{o}C; R_f = 0.30 (PE/EA = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.26 (brs, 1 H), 9.95 (s, 1 H), 7.71-7.66 (m, 1

H), 7.54-7.49 (m, 1 H), 7.24-7.10 (m, 5 H), 6.22 (d, *J* = 2.4 Hz, 1 H), 4.79 (s, 2 H), 2.92 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 135.2 (s), 134.1 (s), 131.4 (s), 129.5 (d, 2C), 128.94 (d, 2C), 128.9 (d), 128.0 (s), 127.4 (d), 120.2 (s), 120.1 (d), 114.1 (s), 95.6 (d), 53.7 (t), 37.9 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3444, 3376, 3057, 2954, 2927, 2856, 2731, 1666, 1606, 1592, 1555, 1489, 1454, 1383, 1350, 1290, 1232, 1201, 1175, 1141, 1107, 1046, 1004, 797, 742, 688, 660 cm^{-1} ; HRMS (EI) m/z calcd for $C_{17}H_{15}ClN_2O_3S$: 362.0492; found: 362.0477.

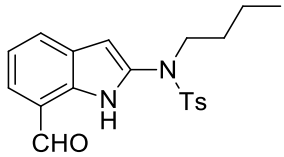


Compound **3e**: Yield 74 %, colourless solid, mp: 151-153 ^{o}C; R_f = 0.54 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.39 (brs, 1 H), 9.97 (s, 1 H), 7.69-7.64 (m, 1 H), 7.53-7.48 (m, 1 H), 7.45-7.38 (m, 2 H), 7.18-7.09 (m, 2 H), 7.03-6.96 (m, 1 H), 6.20 (d, *J* = 2.4 Hz, 1 H), 4.99 (s, 2 H), 2.99 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 135.4 (s), 134.6 (s), 132.8 (d), 131.5 (s), 129.4 (d), 129.1 (d), 128.7 (d), 128.1 (s), 127.9 (d), 127.3 (d), 123.0 (s), 120.2 (s), 120.1 (d), 94.8 (d), 53.7 (t), 37.8 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3419, 3356, 3018, 2930, 220, 2736, 1667, 1608, 1592, 1543, 1491, 1471, 1442, 1412, 1351, 1236, 1195, 1152, 1046, 1024, 956, 882, 838, 799, 733, 701, 682, 656 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{15}BrN_2O_3S$: 405.9987; found: 405.9976.

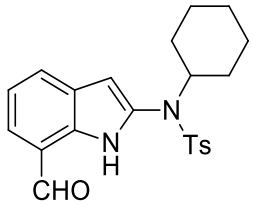


Compound **3f**: Yield 88 %, colourless solid, mp: 142-143 ^{o}C; R_f = 0.24 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.87 (brs, 1 H), 7.79-7.73 (m, 1 H), 7.60 (d, *J* = 8.4Hz, 3 H), 7.20 (dd, *J = 2.7*, 8.1Hz, 3 H), 6.14 (d, *J* = 2.4 Hz, 1 H), 4.51 (m, 1 H), 2.34 (s, 3 H), 1.01 (d, *J* = 6.6Hz, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 143.8 (s), 137.2 (s), 131.7 (s), 130.8 (s), 129.6 (d, 2C), 129.5 (d), 128.0 (d), 127.9 (s), 127.5 (d, 2C), 120.3 (s), 119.8 (d), 102.7 (d), 52.0 (d), 21.8 (q, 2C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ =3323, 2982, 2929, 2815, 2739, 1670, 1611, 1592,

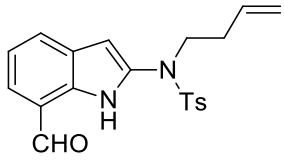
1544, 1493, 1447, 1387, 1368, 1346, 1304, 1238, 1208, 1187, 1173, 1157, 1112, 1086, 1050, 1029, 991, 93, 862,812, 782, 750, 711, 670, 641 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{20}N_2O_3S$: 356.1195; found: 356.1172.



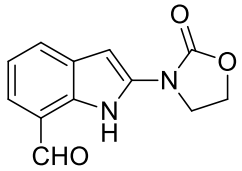
Compound **3g**: Yield 84 %, colourless solid, mp: 147-148 ^oC; R_f = 0.28 (PE/EA = 5:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 10.29 (brs, 1 H), 10.01 (s, 1 H), 7.70-7.64 (m, 1 H), 7.56-7.52 (m, 1 H), 7.46-7.40 (m, 2 H), 7.18-7.10 (m, 3 H), 5.91 (d, *J* = 2.4 Hz, 1 H), 3.46 (t, *J* = 6.9Hz, 2 H), 2.30 (s, 3 H), 1.52-1.40 (m, 2 H), 1.34-1.21(m, 2 H), 0.79 (t, *J* = 7.2Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 144.1 (s), 136.0 (s), 134.2 (s), 131.3 (s), 129.6 (d, 2C), 128.6 (d), 128.2 (s), 127.6 (d, 2C), 127.3 (d), 120.2 (s), 119.8 (d), 95.2 (d), 50.5 (t), 30.1 (t), 21.6 (q), 19.7 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3425, 2953, 2932, 2870, 2804, 2724, 1672, 1610, 1595, 1535, 1490, 1454, 1414, 1382, 1354, 1309, 1293, 1237, 1197, 1162, 1089, 1060, 1048, 1007, 974, 945, 873, 852, 816, 797, 733, 714, 666, 647 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{22}N_2O_3S$: 370.1351; found: 370.1327.



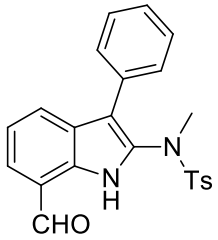
Compound **3h**: Yield 86 %, colourless solid, mp: 152-153 ^oC; R_f = 0.34 (PE/EA = 5:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.79 (brs, 1 H), 7.78-7.72 (m, 1 H), 7.65-7.55 (m, 3 H), 7.24-7.14 (m, 3 H), 6.12 (d, *J* = 2.1 Hz, 1 H), 4.13-3.99 (m, 1 H), 2.35 (s, 3 H), 1.86-1.39 (m, 5 H), 1.33-0.97(m, 4 H), 0.85-0.67 (m, 1 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 143.7 (s), 137.6 (s), 131.7 (s), 131.4 (s), 129.7 (d, 2C), 129.5 (d), 128.0 (d), 127.9 (s), 127.4 (d, 2C), 120.3 (s), 119.8 (d), 102.9 (d), 59.8 (d), 32.5 (t, 2C), 25.8 (t, 2C), 25.0 (t), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3351, 2935, 2856, 2810, 2731, 1663, 1608, 1590, 1492, 1449, 1397, 1382, 1352, 1298, 1266, 1234, 1201, 1162, 1120, 1092, 1067, 1047, 120, 1003, 93, 882, 842, 807, 738, 709, 668, 639 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{24}N_2O_3S$: 396.1508; found: 396.1498.



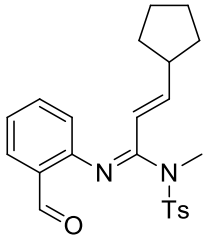
Compound **3i**: Yield 83 %, colourless solid, mp: 146-148 ^{o}C; R_f = 0.26 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.26 (brs, 1 H), 10.01 (s, 1 H), 7.72-7.65 (m, 1 H), 7.59-7.52 (m, 1 H), 7.49-7.41 (m, 2 H), 7.21-7.10 (m, 3 H), 5.93 (d, *J* = 2.7 Hz, 1 H), 5.74-5.59 (m, 1 H), 5.01-4.90 (m, 2 H), 3.54 (t, *J* = 6.9Hz, 2 H), 2.30 (s, 3 H), 2.29-2.20(m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.0 (d), 144.2 (s), 135.7 (s), 134.3 (s), 134.1 (d), 131.3 (s), 129.7 (d, 2C), 128.7 (d), 128.1 (s), 127.6 (d, 2C), 127.4 (d), 120.2 (d), 119.9 (d), 117.6 (t), 95.7 (d), 50.3 (t), 32.6 (t), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3435, 3341, 3067, 2979, 2925, 2816, 2735, 1920, 1671, 1608, 1592, 1543, 1492, 1452, 1408, 1362, 1306, 1235, 1197, 1164, 1120, 1090, 1047, 1019, 993, 973, 916, 883, 862, 812, 747, 719, 688, 671 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{20}N_2O_3S$: 368.1195; found: 368.1213.



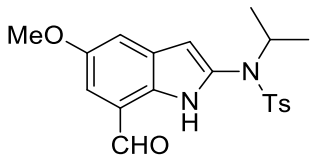
Compound **3j**: Yield 50 %, colourless solid, mp: 190-192 ^{o}C; R_f = 0.53 (CH_2Cl_2/EA = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 11.40 (brs, 1 H), 10.04 (s, 1 H), 7.07-7.66 (m, 1 H), 7.52-7.47 (m, 1 H), 7.19-7.14 (m, 1 H), 5.77 (d, *J* = 2.5 Hz, 1 H), 4.55 (t, *J* = 8 Hz, 2 H), 4.03 (t, *J* = 8 Hz, 2 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.9 (d), 154.8 (s), 136.0 (s), 130.9 (s), 128.3 (s), 127.1 (d), 126.0 (d), 120.0 (s), 119.9 (d), 85.0 (d), 62.7 (t), 44.4 (t) ppm; IR (reflection): $\tilde{\nu}$ = 3415, 3115, 2990, 287, 2739, 1739, 1676, 1616, 1594, 1574 1491, 1473, 1460, 1436, 1417, 1390, 1372, 1304, 1252, 1216, 1184, 1119, 1063, 1045, 978, 908, 877, 793, 764, 732, 667, 643 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{10}N_2O_3$: 230.0691; found: 230.092.



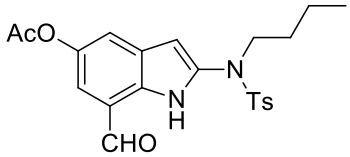
Compound **3k**: Yield 84 %, colourless solid, mp: 216-218 ^{o}C; R_f = 0.24 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.14 (brs, 1 H), 10.06 (s, 1 H), 7.77-7.73 (m, 1 H), 7.65-7.61 (m, 1 H), 7.57-7.51 (m, 2 H), 7.23-7.13 (m, 6 H), 6.87-6.82 (m, 2 H), 3.01 (s, 3 H), 2.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.0 (d), 144.4 (s), 134.6 (s), 132.3 (s), 132.1 (s), 130.8 (s), 130.0 (d, 2 C), 129.6 (d), 129.4 (d, 2 C), 128.4 (d, 2 C), 127.8 (s), 127.6 (d, 2 C), 127.1 (d), 126.8 (d), 120.1 (s), 120.0 (d), 112.3 (s), 38.6 (q), 21.7 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3346, 2941, 2847, 1736, 1666, 1603, 1574, 1495, 1448, 1427, 1408, 1367, 1333, 1216, 1184, 1151, 1107, 1089, 1072, 1050, 1034, 989, 883, 812, 798, 778, 753, 741, 722, 703, 676, 646 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{20}N_2O_3S$: 404.1195; found: 404.1182.



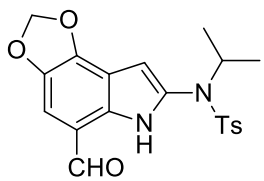
Compound **3l'**: Yield 81 %, colourless liquid; R_f = 0.4 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ =, 9.68 (s, 1 H), 7.74-7.63 (m, 3 H), 7.43-7.34 (m, 1 H), 7.28-7.20 (m, 2 H), 7.10-7.00 (m, 1 H), 6.60 (d, *J* = 8.1 Hz, 1 H), 6.21 (dd, *J* = 8.1 and 15.6 Hz, 1 H), 5.71 (d, *J* = 15.6 Hz, 1 H), 3.13 (s, 3 H), 2.43-2.25 (m, 4 H), 1.68-1.55 (m, 2H), 1.54-1.34 (m, 4 H), 1.22-1.05 (m, 2 H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 190.8 (d), 157.2 (s), 152.3 (d), 151.3 (s), 144.4 (s), 134.77 (d), 134.72 (s), 129.5 (d, 2 C), 128.2 (d), 128.1 (d, 2 C), 126.4 (s), 123.8 (d), 121.3 (d), 118.7 (d), 43.3 (q), 36.3 (d), 32.3 (t, 2 C), 25.2 (t, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 2953, 2917, 2868, 1689, 1644, 1595, 1450, 1357, 1276, 1161, 1088, 915, 834, 814, 771, 718, 669, 611 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{26}N_2O_3S$: 410.1664; found: 410.1663.



Compound **3m**: Yield 74 %, yellow solid, mp: 145-147 ^{o}C; R_f = 0.56 (PE/EA = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.06 (s, 1 H), 9.76 (brs, 1 H), 7.71-7.67 (m, 2 H), 7.38-7.28 (m, 4 H), 6.16 (d, *J* = 2.5 Hz, 1 H), 4.60 (m, 1 H), 3.91 (s, 3 H), 2.45 (s, 3H), 1.11 (d, *J* = 7.0 Hz, 6 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.7 (d), 153.8 (s), 143.8 (s), 137.2 (s), 131.2 (s), 129.7 (d, 2 C), 128.5 (s), 127.5 (d, 2 C), 127.1 (s), 120.4 (s), 117.9 (d), 111.2 (d), 102.2 (d), 56.3 (q), 52.0 (d), 21.9 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3437, 3336, 3137, 3054, 2963,2927, 2853, 2305,1676, 1616, 1597, 1550, 1482, 1458, 1420, 1386, 1349, 1336, 1265, 1242, 1213, 1185, 1163, 1118, 1088, 1071, 1040, 996, 940, 891, 855, 813, 733, 704, 671 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{22}N_2O_4S$: 386.1300; found: 386.1297.

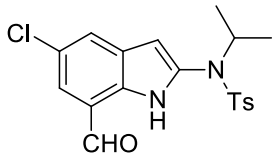


Compound **3n**: Yield 81 %, colourless solid, mp: 152-154 ^{o}C; R_f = 0.50 (PE/EA = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.33 (brs, 1 H), 9.78 (s, 1 H), 7.45-7.42 (m, 2 H), 7.40-7.37 (m, 1 H), 7.31-7.29 (m, 1 H), 7.17-7.13 (m, 2 H), 5.87 (d, *J* = 2.5 Hz, 1 H), 3.47 (t, *J* = 7.5 Hz, 2 H), 2.31 (s, 3 H), 2.27 (s, 3 H), 1.50-1.43 (m, 2 H), 1.33-1.23 (m, 2 H), 0.80 (t, *J* = 7.5 Hz, 3 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.1 (d), 170.3 (s), 144.3 (s), 143.9 (s), 137.3 (s), 134.0 (s), 129.7 (d, 2 C), 129.3 (s), 128.7 (s), 127.5 (d, 2 C), 121.4 (d), 119.9 (s), 119.8 (d), 94.8 (d), 50.3 (t), 29.9 (t), 21.6 (q), 21.1 (q), 19.7 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3425, 3344, 3066, 2959, 2932, 2872, 2733, 1763, 1675, 1613, 1597, 1542, 1480, 1415, 1355, 1202, 1163, 1130, 1083, 1013, 971, 909, 855, 813, 733, 706, 668 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{24}N_2O_5S$: 428.1406; found: 428.1429.

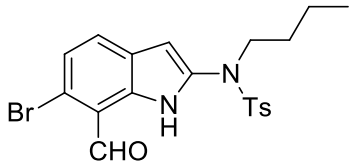


Compound **3o**: Yield 75 %, light yellow solid, mp: 206-208 ^{o}C; R_f = 0.48 (PE/EA =

2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.01 (brs, 1 H), 9.78 (s, 1 H), 7.63-7.59 (m, 2 H), 7.25-7.20 (m, 2 H), 7.17-7.14 (m, 1 H), 6.07 (d, *J* = 2.5 Hz, 1 H), 6.06 (s, 2 H), 4.50 (m, 1 H), 2.37 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 6 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.2 (d), 145.2 (s), 143.9 (s), 140.7 (s), 137.1 (s), 132.4 (s), 131.7 (s), 129.8 (d, 2 C), 127.5 (d, 2 C), 113.2 (s), 112.0 (s), 110.1 (d), 102.1 (t), 98.1 (d), 52.1 (d), 21.9 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3323, 2982, 2922, 2885 2814, 2722, 1661, 1640, 1593, 1544, 1502, 1489, 1425, 1389, 1354, 1343, 1282, 1244, 1210, 1183, 1164, 1128, 1091, 1084, 1045, 1028, 999, 974, 938, 913 890, 863, 842, 818 795, 784, 748, 742, 709, 672 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{20}N_2O_5S$: 400.1093; found: 400.1083.

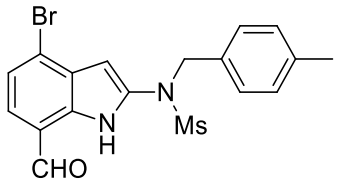


Compound **3p**: Yield 61 %, colourless solid, mp: 135-136 ^{o}C; R_f = 0.33 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.97 (s, 1 H), 9.90 (brs, 1 H), 7.74-7.70 (m, 1 H), 7.60-7.55 (m, 3 H), 7.24-7.19 (m, 2 H), 6.08 (d, *J* = 2.5 Hz, 1 H), 4.52 (m, 1 H), 2.36 (s, 3H), 1.02 (d, *J* = 6.5 Hz, 6 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.0 (d), 143.9 (s), 136.9 (s), 132.3 (s), 130.1 (s), 129.7 (d, 2 C), 129.1 (s), 128.8 (d), 127.5 (d, 2 C), 127.2 (d), 125.4 (s), 120.7 (s), 102.1 (d), 52.2 (d), 21.9 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3306, 3223, 2975, 2925, 2852, 1681, 1670, 1600, 1548, 1495, 1459, 1369, 1344, 1324, 1291, 1213, 1188, 1158, 1117, 1089, 1064, 1032, 1001, 899, 871, 812, 769, 750, 709, 666 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{19}ClN_2O_3S$: 390.0805; found: 390.0833.

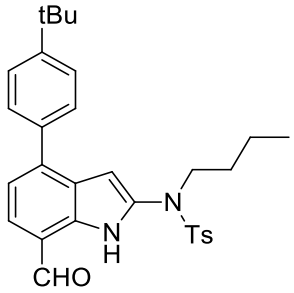


Compound **3q**: Yield 64 %, yellow solid, mp: 152-153 ^{o}C; R_f = 0.72 (PE/EA = 2:1); ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 10.64 (brs, 1 H), 10.42 (s, 1 H), 7.50-7.46 (m, 1 H), 7.43-7.39 (m, 2 H), 7.27-7.23 (m, 1 H), 7.19-7.15 (m, 2 H), 5.84 (d, *J* = 2.5 Hz, 1 H), 3.46 (t, *J* = 6.0 Hz, 2 H), 2.31 (s, 3 H), 1.50-1.42 (m, 2 H), 1.33-1.23 (m, 2 H), 0.80 (t, *J* = 6.0 Hz, 3 H) ppm ; ^{13}C NMR (125 MHz, CD_2Cl_2) δ = 193.9 (d), 144.5 (s), 136.7

(s), 134.0 (s), 133.1 (s), 129.7 (d, 2 C), 127.9 (s), 127.7 (d), 127.4 (d, 2 C), 124.7 (d), 121.7 (s), 117.0 (s), 94.2 (d), 50.2 (t), 29.9 (t), 21.3 (q), 19.7 (t), 13.3 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3413, 3142, 2955, 2934, 2867, 1736, 1659, 1599, 1584, 1535, 1454, 1384, 1350, 1297, 1239, 1163, 1120, 1091, 974, 947, 911, 877, 854, 812, 748, 716, 677, 665, 610 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{21}BrN_2O_3S$ $[M+Na]^+$: 471.0348; found: 471.0361.

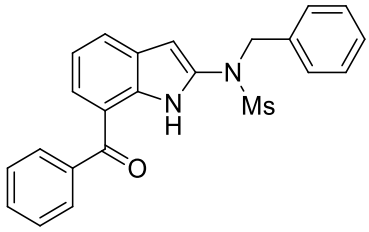


Compound **3r**: Yield 53 %, yellow solid, mp: 155-157 ^oC; R_f = 0.48 (PE/EA = 2:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 10.38 (brs, 1 H), 9.93 (s, 1 H), 7.36-7.29 (m, 2 H), 7.22-7.18 (m, 2 H), 7.06-7.01 (m, 2 H), 6.27 (d, *J* = 2.5 Hz, 1 H), 4.82 (s, 2 H), 2.92 (s, 3 H), 2.22 (s, 3 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.1 (d), 137.1 (s), 135.4 (s), 131.1 (s), 130.1 (s), 128.5 (d, 2 C), 128.1 (s), 127.9 (d), 127.1 (d, 2 C), 122.2 (d), 121.2 (s), 118.2 (s), 93.9 (d), 53.1 (t), 37.1 (q), 20.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3393, 3142, 3023, 2936, 2920, 2853, 1737, 1671, 1603, 1583, 1541, 1481, 1441, 1420, 1344, 1327, 1229, 1198, 1141, 1118, 1061, 1049, 1028, 970, 955, 939, 923, 833, 784, 772, 725, 669, 616, 605 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{17}BrN_2O_3S$: 420.0143; found: 420.0146.

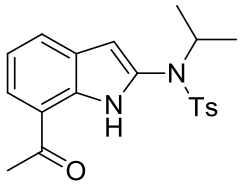


Compound **3s**: Yield 80 %, colourless solid, mp: 178-180 ^oC; R_f = 0.78 (PE/EA = 2:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 10.55 (brs, 1 H), 10.16 (s, 1 H), 7.75-7.71 (m, 1 H), 7.63-7.51 (m, 6 H), 7.37-7.32 (m, 1 H), 7.32-7.26 (m, 2 H), 6.18 (d, *J* = 2.4 Hz, 1 H), 3.59 (t, *J* = 7.2 Hz, 2 H), 2.44 (s, 3 H), 1.65-1.54 (m, 2 H), 1.46-1.35 (m, 11 H), 0.92 (t, *J* = 7.2 Hz, 3 H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 192.6 (d), 151.3 (s), 144.1 (s), 140.8 (s), 136.9 (s), 136.1 (s), 134.3 (s), 132.0 (s), 129.6 (d, 2 C), 129.1 (d), 128.5

(d, 2 C), 127.7 (d, 2 C), 126.2 (s), 125.7 (d, 2 C), 119.9 (d), 118.9 (s), 95.4 (d), 50.5 (t), 34.7 (s), 31.4 (q, 3 C), 30.2 (t), 21.6 (q), 19.7 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3436, 3334, 3032, 2958, 2870, 2730, 2251, 1919, 1737, 1663, 1601, 1543, 1495, 1461, 1408, 1340, 1291, 1269, 1228, 1197, 1167, 1116, 1090, 1052, 1017, 937, 881, 847, 810, 770, 744, 718, 679, 654 cm^{-1}; HRMS (EI) m/z calcd for $C_{30}H_{34}N_2O_3S$: 502.2290; found: 502.2279.

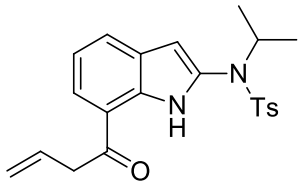


Compound **3t**: Yield 85 %, colourless soild, mp: 154-155 ^{o}C; R_f = 0.46 (PE/EA = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.64 (brs, 1 H), 7.82-7.73 (m, 3 H), 7.64-7.48 (m, 4 H), 7.47-7.40 (m, 2 H), 7.40-7.24 (m, 3 H), 7.18-7.10 (m, 1 H), 6.37 (d, *J* = 2.4 Hz, 1 H), 4.98 (s, 2 H), 3.04 (s, 3 H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.5 (s), 138.8 (s), 135.6 (s), 135.4 (s), 133.6 (s), 131.6 (d), 129.4 (d, 2 C), 128.8 (d, 2 C), 128.5 (s), 128.3 (d, 2 C), 128.2 (d, 3 C), 128.0 (d), 126.4 (d), 119.23 (d), 119.21 (s), 95.4 (d), 54.4 (t), 38.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3428, 3063, 3031, 2929, 1733, 1634, 1600, 1588, 1542, 1491, 1444, 1411, 1356, 1275, 1212, 1188, 1154, 1085, 1049, 1024, 955, 909, 893, 855, 807, 749, 720, 699, 677, 647, 628 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{20}N_2O_3S$: 404.1195; found: 404.1189.

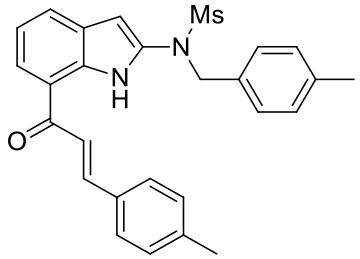


Compound **3u**: Yield 83 %, colourless solid, mp: 132-133 ^{o}C; R_f = 0.34 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.14 (brs, 1 H), 7.76-7.70 (m, 2 H), 7.63-7.59 (m, 2 H), 7.24-7.20 (m, 2 H), 7.13-7.08 (m, 1 H), 6.12 (d, *J* = 2.0 Hz, 1 H), 4.51 (m, 1 H), 2.62 (s, 3H), 2.37 (s, 3 H), 1.02 (d, *J* = 7.0 Hz, 6 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.9 (s), 143.7 (s), 137.3 (s), 132.8 (s), 130.5 (s), 129.6 (d, 2 C), 128.2 (s), 127.5 (d, 2 C), 127.2 (d), 125.7 (d), 120.1 (s), 119.2 (d), 102.6 (d), 51.9 (d), 26.5 (q), 21.9 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3304, 2993, 1737, 1658, 1590,

1542, 1494, 1435, 1392, 1371, 1342, 1305, 1277, 1208, 1184, 1172, 1155, 1131, 1111, 1086, 1027, 997, 892, 834, 821, 803, 779, 749, 710, 681, 663, 623 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{22}N_2O_3S$: 370.1351; found: 370.1357.

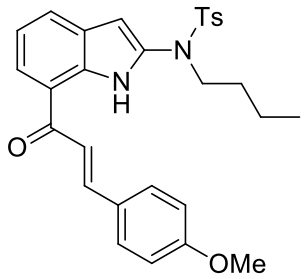


Compound **3v**: Yield 65 %, colourless solid, mp: 122-124 ^oC; R_f = 0.36 (PE/EA = 5:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 10.14 (brs, 1 H), 7.79-7.71 (m, 2 H), 7.62-7.58 (m, 2 H), 7.23-7.19 (m, 2 H), 7.13-7.08 (m, 1 H), 6.13 (d, *J* = 3.0 Hz, 1 H), 6.10-6.01 (m, 1 H), 5.22-5.16 (m, 2 H), 4.50 (m, 1 H), 3.82-3.77 (m, 2 H), 2.36 (s, 3H), 1.02 (d, *J* = 6.5 Hz, 6 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.7 (s), 143.7 (s), 137.3 (s), 133.1 (s), 131.2 (d), 130.5 (s), 129.7 (d, 2 C), 128.3 (s), 127.5 (d, 2 C), 127.3 (d), 125.2 (d), 119.3 (s), 119.2 (d), 118.9 (t), 102.7 (d), 51.9 (d), 43.2 (t), 21.9 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3354, 2979, 2923, 1738, 1670, 1587, 1544, 1494, 1438, 1390, 1379 1353, 1307, 1293, 1249, 1210, 1186, 1173, 1163, 1120, 1087, 1065, 1031, 998, 917, 893, 843, 815, 800, 768, 747, 714, 670, 642, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{24}N_2O_3S$: 396.1508; found: 396.1506.

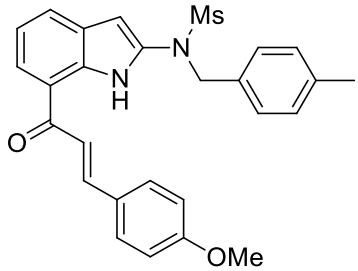


Compound **3w**: Yield 73 %, yellow solid, mp: 193-194 ^oC; R_f = 0.44 (PE/EA = 2:1); ^1H NMR (500 MHz, CD_2Cl_2) δ = 10.75 (brs, 1 H), 7.87-7.82 (m, 1 H), 7.81-7.74 (m, 1 H), 7.71-7.63 (m, 2 H), 7.55-7.49 (m, 2 H), 7.23-7.15 (m, 4 H), 7.14-7.08 (m, 1 H), 7.06-7.01 (m, 2 H), 6.21 (d, *J* = 2.5 Hz, 1 H), 4.81 (s, 2 H), 2.92 (s, 3H), 2.31 (s, 3 H), 2.19 (s, 3 H) ppm ; ^{13}C NMR (125 MHz, CD_2Cl_2) δ = 190.0 (s), 143.7 (d), 141.2 (s), 137.9 (s), 135.5 (s), 133.1 (s), 132.7 (s), 132.3 (s), 129.7 (d, 2 C), 129.3 (d, 2 C), 128.5 (d, 2C), 128.4 (s), 127.9 (d, 2 C), 126.2 (d), 123.9 (d), 120.5 (s), 119.9 (d), 119.5 (d), 94.5 (d), 53.8 (t), 37.6 (q), 21.3 (q), 20.8 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3420, 3001, 2920, 1737, 1644, 1606, 1590, 1581, 1540, 1514, 1493, 1443, 1410, 1356, 1334,

1299, 1279, 1246, 1180, 1148, 1112, 1061, 1040, 1022, 980, 959, 866, 836, 790, 765, 733, 686, 664 cm^{-1}; HRMS (ESI) m/z calcd for $C_{27}H_{26}N_2O_3$ $[M+Na]^+$: 481.1556; found: 481.1569.

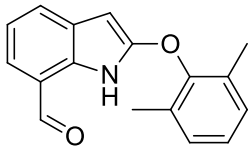


Compound **3x**: Yield 79 %, yellow oil; R_f = 0.62 (PE/EA = 2:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 10.82 (brs, 1 H), 7.88-7.79 (m, 2 H), 7.68-7.64 (m, 1 H), 7.63-7.55 (m, 3 H), 7.50-7.45 (m, 2 H), 7.19-7.08 (m, 3 H), 6.90-6.85 (m, 2 H), 5.92 (d, *J* = 2.5 Hz, 1 H), 3.79 (s, 3 H), 3.49 (t, *J* = 7.5 Hz, 2 H), 2.32 (s, 3 H), 1.53-1.46 (m, 2 H), 1.35-1.26 (m, 2 H), 0.81 (t, *J* = 7.5 Hz, 3 H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 190.1 (s), 161.6 (s), 143.9 (s), 143.7 (d), 135.7 (s), 134.4 (s), 133.3 (s), 130.3 (d, 2 C), 129.6 (d, 2 C), 128.6 (s), 127.8 (s), 127.6 (d, 2C), 126.2 (d), 123.8 (d), 120.7 (s), 119.2 (d), 118.7 (d), 114.4 (d, 2 C), 95.0 (d), 55.5 (q), 50.4 (t), 30.1 (t), 21.6 (q), 19.8 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3427, 2958, 2932, 2872, 1734, 1645, 1602, 1585, 1571, 1537, 1510, 1493, 1441, 1422, 1409, 1358, 1321, 1289, 1244, 1172, 1160, 1105, 1090, 1067, 1031, 982, 951, 871, 830, 802, 745, 671 cm^{-1}; HRMS (EI) m/z calcd for $C_{29}H_{30}N_2O_4S$: 502.1926; found: 502.1908.

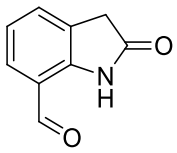


Compound **3y**: Yield 65 %, yellow solid, mp: 204-205 ^oC; R_f = 0.34 (PE/EA = 2:1); ^1H NMR (500 MHz, CD_2Cl_2) δ = 10.76 (brs, 1 H), 7.86-7.83 (m, 1 H), 7.80-7.75 (m, 1 H), 7.70-7.66 (m, 1 H), 7.62-7.57 (m, 3 H), 7.22-7.18 (m, 2 H), 7.14-7.09 (m, 1 H), 7.06-7.02 (m, 2 H), 6.91-6.87 (m, 2 H), 6.22 (d, *J* = 2.5 Hz, 1 H), 4.81 (s, 2 H), 3.78 (s, 3 H), 2.92 (s, 3H), 2.20 (s, 3 H) ppm ; ^{13}C NMR (125 MHz, CD_2Cl_2) δ = 189.9 (s), 161.7 (s), 143.4 (d), 133.1 (s), 137.9 (s), 135.4 (s), 132.7 (s), 130.2 (d, 2 C), 129.3 (d,

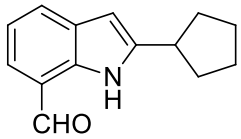
2 C), 128.5 (s), 128.0 (d, 2C), 127.7 (s), 126.1 (d), 123.8 (d), 120.6 (s), 119.4 (d), 118.6 (d), 114.4 (d, 2 C), 94.5 (d), 55.4 (q), 53.8 (t), 37.6 (q), 20.8 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3406, 3031, 3001, 2921,2843, 2309, 1909, 1699, 1643, 1605, 1570, 1541, 1516, 1493, 1442, 1421, 1339, 1287, 1239, 1186, 1147, 1115, 1065, 1036, 976, 958, 933, 904, 885, 867, 830, 791, 765, 742, 722, 689, 665, 639, 622 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{26}N_2O_4S$: 474.1613; found: 474.1612.



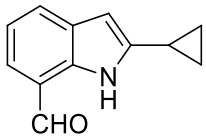
Compound **5a**: Yield 63 %, yellow solid, mp: 93-95 ^oC; R_f = 0.68 (PE/EA = 5:1); ^1H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.87 (brs, 1 H), 7.56-7.48 (m, 1 H), 7.44-7.41 (m, 1 H), 7.12-7.07 (m, 1 H), 7.04-7.00 (m, 3 H), 5.13 (d, *J* = 1.5 Hz, 1 H), 2.14(s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.6 (d), 152.8 (s), 151.3 (s), 130.8 (s, 2C), 129.4 (s), 129.3 (s), 129.2 (d, 2C), 125.9 (d, 2C), 125.8 (d), 119.8 (d), 119.3 (s), 78.9 (d), 16.2 (q, 2C) ppm; IR (reflection): $\tilde{\nu}$ = 3445, 2924, 2817, 1733, 1670, 1613, 1591, 1551, 1455, 1422, 1354, 1291, 1265, 1232, 1190, 1089, 1045, 787, 738, 687 cm^{-1}; HRMS (EI) m/z calcd for $C_{17}H_{15}NO_2$: 265.1103; found: 265.1116.



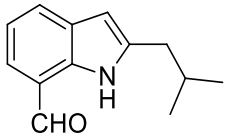
Compound **5a'**: Yield 85 %, colourless soild, mp: 147-148 ^oC; R_f = 0.30 (CH_2Cl_2/EA = 10:1); ^1H NMR (500 MHz, $CDCl_3$) δ = 9.91 (s, 1 H), 9.26 (brs, 1 H), 7.55 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 7.0 Hz, 1 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 3.46 (s, 2 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.5 (d), 176.5 (s), 143.8 (s), 131.4 (d), 130.0 (d), 126.6 (s), 122.0 (d), 118.4 (s), 34.7 (t) ppm; IR (reflection): $\tilde{\nu}$ = 3260, 2924, 2853, 2730, 2357, 1724, 1710, 1677, 1605, 1460, 1395, 1327, 1305, 1254, 1202, 1160, 106, 1014, 96, 945, 894, 859, 774, 732, 670, 615 cm^{-1}; HRMS (EI) m/z calcd for $C_9H_7NO_2$: 161.0477; found: 161.0471.



Compound **7a**: Yield 68 %, colourless solid, mp: 64-65 ^{o}C; R_f = 0.72 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.78 (brs, 1 H), 7.76-7.70 (m, 1 H), 7.50-7.45 (m, 1 H), 7.19-7.09 (m, 1 H), 6.26-6.22 (m, 1 H), 3.22-3.09 (m, 1 H), 2.13-2.00 (m, 2 H), 1.83-1.57 (m, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.7 (d), 146.3 (s), 133.9 (s), 129.9 (s), 127.6 (d), 127.1 (d), 119.8 (s), 119.2 (d), 97.9 (d), 38.9 (d), 32.9 (t, 2C), 25.3 (t, 2C) ppm; IR (reflection): $\tilde{\nu}$ = 3446, 3367, 2954, 2867, 2812, 2730, 1672, 1607, 1593, 1552, 1489, 1454, 1352, 1320, 1292, 1229, 1177, 1145, 1062, 1049, 961, 895, 799, 745, 707, 625 cm^{-1}; HRMS (EI) m/z calcd for $C_{14}H_{15}NO$: 213.1154; found: 213.1138.

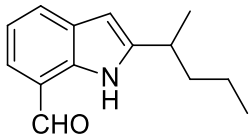


Compound **7b**: Yield 68 %, colourless solid, mp: 66-68 ^{o}C; R_f = 0.56 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.00 (s, 1 H), 9.85 (brs, 1 H), 7.73-7.66 (m, 1 H), 7.50-7.44 (m, 1 H), 7.15-7.07 (m, 1 H), 6.15-6.11 (m, 1 H), 1.99-1.89 (m, 1 H), 0.98-0.90 (m, 2 H), 0.78-0.71 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7 (d), 144.1 (s), 133.7 (s), 129.9 (s), 127.6 (d), 127.0 (d), 119.6 (s), 119.3 (d), 97.5 (d), 8.95 (d), 7.78 (t, 2C) ppm; IR (reflection): $\tilde{\nu}$ = 3444, 3374, 3086, 3057, 3007, 2813, 2731, 1914, 1784, 1673, 1604, 1593, 1560, 1490, 1453, 1427, 1380, 1341, 1301, 1230, 1198, 1174, 1143, 1049, 1024, 973, 900, 879, 798, 744, 681, 657 cm^{-1}; HRMS (EI) m/z calcd for $C_{12}H_{11}NO$: 185.0841; found: 185.0836.

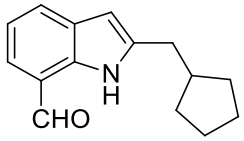


Compound **7c**: Yield 65 %, colourless solid, mp: 69-70 ^{o}C; R_f = 0.66 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.02 (s, 1 H), 9.76 (brs, 1 H), 7.77-7.72 (m, 1 H), 7.52-7.47 (m, 1 H), 7.17-7.10 (m, 1 H), 6.25-6.21 (m, 1 H), 2.61 (d, *J* = 7.2 Hz, 2 H), 2.03-1.89 (m, 1 H), 0.92 (d, *J* = 6.6 Hz, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7 (d), 141.1 (s), 133.8 (s), 130.1 (s), 127.6 (d), 127.0 (d), 119.8 (s), 119.2 (d),

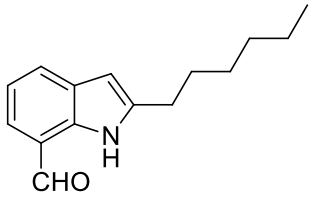
100.4 (d), 37.6 (t), 28.9 (d), 22.5 (q, 2C) ppm; IR (reflection): $\tilde{\nu}$ = 3342, 2957, 2925, 2903, 2868, 2813, 2736, 1674, 1608, 1593, 1556, 1490, 1465, 1434, 1383, 1354, 1292, 1241, 1221, 1200, 1175, 1146, 1063, 1050, 986, 955, 823, 804, 779, 748, 707, 684, 643 cm^{-1}; HRMS (EI) m/z calcd for $C_{13}H_{15}NO$: 201.1154; found: 201.1161.



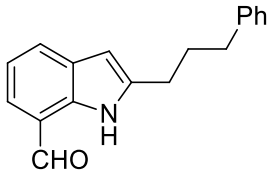
Compound **7d**: Yield 72 %, light yellow oil; R_f = 0.75 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.79 (brs, 1 H), 7.75-7.70 (m, 1 H), 7.49-7.44 (m, 1 H), 7.15-7.08 (m, 1 H), 6.25-6.20 (m, 1 H), 2.95-2.82 (m, 1 H), 1.71-1.46 (m, 2 H), 1.35-1.16 (m, 5 H), 0.83 (t, *J* = 7.2 Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.7 (d), 147.3 (s), 133.7 (s), 129.9 (s), 127.6 (d), 127.1 (d), 119.8 (s), 119.2 (d), 98.1 (d), 39.2 (t), 33.1 (d), 20.53 (t), 20.51 (q), 14.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3448, 3373, 3058, 2959, 2930, 2871, 2811, 2731, 1670, 1605, 1593, 1549, 1489, 1454, 1383, 1350, 1293, 1233, 1192, 1176, 1128, 1049, 966, 879, 800, 745, 696, 661 cm^{-1}; HRMS (EI) m/z calcd for $C_{14}H_{17}NO$: 215.1310; found: 215.1313.



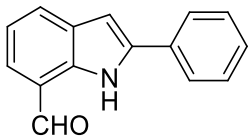
Compound **7e**: Yield 56 %, colourless solid, mp: 68-69 ^{o}C; R_f = 0.70 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.80 (brs, 1 H), 7.76-7.70 (m, 1 H), 7.50-7.45 (m, 1 H), 7.16-7.09 (m, 1 H), 6.25-6.20 (m, 1 H), 2.72 (d, *J* = 8.4 Hz, 2 H), 2.23-2.12 (m, 1 H), 1.79-1.70 (m, 2 H), 1.63-1.44 (m, 4 H), 1.23-1.14 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7 (d), 141.8 (s), 133.8 (s), 130.1 (s), 127.6 (d), 127.1 (d), 119.8 (s), 119.2 (d), 99.9 (d), 39.9 (d), 34.5 (t), 32.7 (t, 2C), 25.1 (t, 2C) ppm; IR (reflection): $\tilde{\nu}$ = 3372, 3057, 2944, 2861, 2816, 2737, 1903, 1738, 1673, 1607, 1593, 1553, 1489, 1454, 1382, 1356, 1288, 1229, 1188, 1175, 1135, 1062, 1048, 987, 956, 902, 798, 779, 743, 704, 671 cm^{-1}; HRMS (EI) m/z calcd for $C_{15}H_{17}NO$: 227.1310; found: 227.1313.



Compound **7f**: Yield 67 %, light yellow oil; R_f = 0.72 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.01 (s, 1 H), 9.79 (brs, 1 H), 7.76-7.71 (m, 1 H), 7.51-7.45 (m, 1 H), 7.16-7.08 (m, 1 H), 6.25-6.21 (m, 1 H), 2.72 (t, *J* = 7.5 Hz, 2 H), 1.73-1.60 (m, 2 H), 1.40-1.17 (m, 6 H), 0.82 (t, *J* = 6.9 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7 (d), 142.3 (s), 133.8 (s), 130.1 (s), 127.6 (d), 127.0 (d), 119.7 (s), 119.2 (d), 99.4 (d), 31.6 (t), 29.1 (t), 29.0 (t), 28.3 (t), 22.6 (t), 14.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3446, 3381, 3057, 2954, 2928, 2856, 2731, 1670, 1606, 1593, 1556, 1489, 1454, 1410, 1351, 1290, 1233, 1196, 1175, 1141, 1109, 1048, 969, 908, 798, 744, 670 cm^{-1}; HRMS (EI) m/z calcd for $C_{15}H_{19}NO$: 229.1467; found: 229.1450

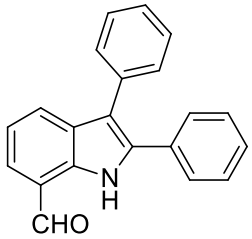


Compound **7g**: Yield 63 %, light yellow solid, mp: 67-68 ^{o}C; R_f = 0.62 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.99 (s, 1 H), 9.80 (brs, 1 H), 7.76-7.69 (m, 1 H), 7.50-7.44 (m, 1 H), 7.26-7.17 (m, 2 H), 7.16-7.07 (m, 4 H), 6.27-6.21 (m, 1 H), 2.74 (t, *J* = 7.5 Hz, 2 H), 2.63 (t, *J* = 7.5 Hz, 2 H), 2.0 (m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.7 (d), 141.65 (s), 141.63 (s), 133.8 (s), 130.1 (s), 128.5 (d, 2C), 128.4 (d, 2C), 127.7 (d), 127.1 (d), 126.0 (d), 119.8 (s), 119.3 (d), 99.6 (d), 35.3 (t), 30.6 (t), 27.6 (t) ppm; IR (reflection): $\tilde{\nu}$ = 3364, 3060, 3028, 2954, 2930, 2863, 2818, 2740, 1670, 1607, 1592, 1556, 1493, 1453, 1440, 1384, 1349, 1325, 1286, 1237, 1206, 1176, 1158, 1140, 1050, 1028, 1009, 980, 961, 825, 797, 745, 698, 670, 651, 624, 610 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{17}NO$: 263.1310; found: 263.1306.

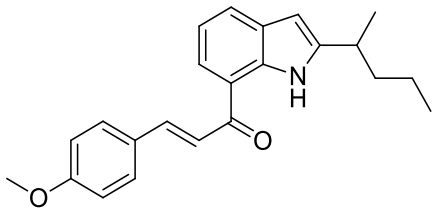


Compound **7h**: Yield 61 %, yellow solid, mp: 118-120 ^{o}C; R_f = 0.56 (PE/EA = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.28 (brs, 1 H), 10.06 (s, 1 H), 7.85-7.81 (m, 1 H),

7.69-7.63 (m, 2 H), 7.58-7.53 (m, 1 H), 7.43-7.35 (m, 2 H), 7.32-7.26 (m, 1 H), 7.20-7.14 (m, 1 H), 6.82-6.78 (m, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.7 (d), 139.9 (s), 134.7 (s), 131.6 (s), 130.4 (s), 129.1 (d, 2C), 128.7 (d), 128.3 (d), 127.8 (d), 125.5 (d, 2C), 120.3 (s), 119.9 (d), 99.5 (d) ppm; IR (reflection): $\tilde{\nu}$ = 3353, 3052, 2836, 2811, 2730, 1790, 1679, 1607, 1593, 1547, 1486, 1452, 1384, 1362, 1340, 1306, 1249, 1226, 1196, 1171, 1063, 1050, 1030, 931, 912, 879, 809, 775, 758, 743, 692, 673, 621, 610 cm^{-1}; HRMS (EI) m/z calcd for $C_{15}H_{11}NO$: 221.0841; found: 221.0833.

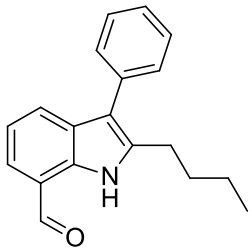


Compound **7i**: Yield 50 %, yellow solid; mp: 138-139 ^{o}C; R_f = 0.58 (PE/EA = 5:1); ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 10.18 (brs, 1 H), 10.05 (s, 1 H), 7.84-7.80 (m, 1 H), 7.62-7.58 (m, 1 H), 7.41-7.35 (m, 2 H), 7.33-7.16 (m, 9 H) ppm; ^{13}C NMR (125 MHz, CD_2Cl_2) δ = 193.4 (d), 135.8 (s), 134.4 (s), 133.6 (s), 132.0 (s), 130.2 (d, 2 C), 130.0 (s), 129.1 (d), 128.7 (d, 2 C), 128.6 (d, 2 C), 128.4 (d, 2 C), 128.1 (d), 126.7 (d), 126.6 (d), 120.4 (s), 120.0 (d), 114.8 (s) ppm; IR (reflection): $\tilde{\nu}$ = 2922, 2852, 1674, 1603, 1461, 1377, 1261, 1026, 954, 801, 743, 698, 664, 612 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{15}NO$: 297.1154; found: 297.1144.

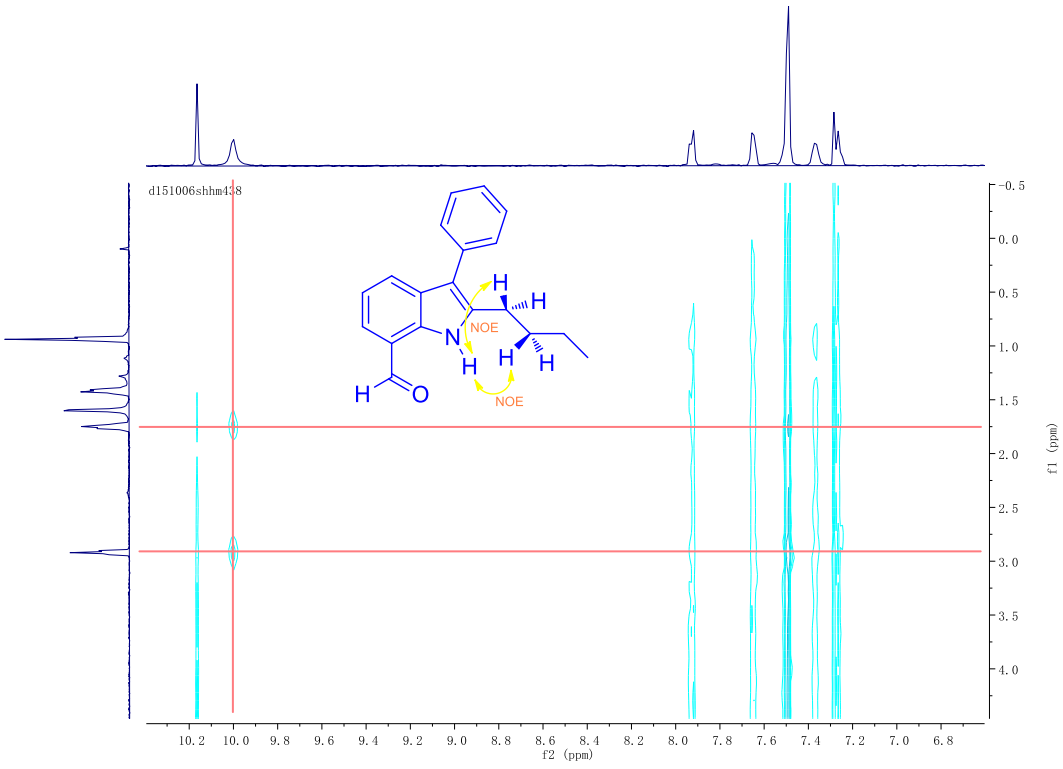


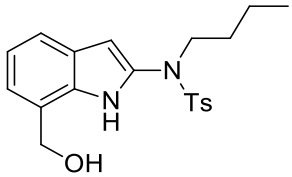
Compound 7j: Yield 66 %, yellow oil; R_f = 0.54 (PE/EA = 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.37 (brs, 1 H), 7.82-7.75 (m, 2 H), 7.74-7.70 (m, 1 H), 7.66-7.61 (m, 1 H), 7.60-7.54 (m, 2 H), 7.11-7.06 (m, 1 H), 6.90-6.85 (m, 2 H), 6.22 (d, *J* = 2.5 Hz, 1 H), 3.78 (s, 3 H), 2.95-2.87 (m, 1 H), 1.74-1.60 (m, 1 H), 1.59-1.50 (m, 1 H), 1.34-1.22 (m, 5 H), 0.84 (t, *J* = 7.0 Hz, 3 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 190.8 (s), 161.6 (s), 147.0 (s), 143.2 (d), 135.6 (s), 130.3 (s), 130.2 (d, 2 C), 127.9 (s), 126.2 (d), 122.9 (d), 120.2 (s), 119.1 (d), 118.6 (d), 114.4 (d, 2 C), 97.9 (d), 55.5 (q), 39.3 (t), 33.1 (d), 20.6 (t), 20.5 (q), 14.1 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3430, 3367,

2959, 2929, 2871, 1644, 1600, 1570, 1543, 1510, 1491, 1458, 1441, 1422, 1350, 1285, 1241, 1172, 1102, 1031, 981, 950, 829, 801, 742, 701 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{25}NO_2$: 347.1885; found: 347.1878.

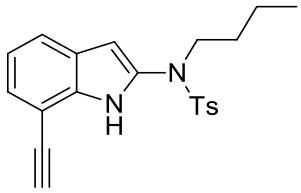


Compound 7k: Yield 27 %; yellow soild, mp: 97-98 ^{o}C; R_f = 0.44 (PE/EA = 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.05 (s, 1 H), 9.91 (brs, 1 H), 7.84-7.79 (m, 1 H), 7.56-7.51 (m, 1 H), 7.42-7.35 (m, 4 H), 7.29-7.22 (m, 1 H), 7.18-7.11 (m, 1 H), 2.81 (t, *J* = 7.5 Hz, 2 H), 1.69-1.60 (m, 2 H), 1.36-1.25 (m, 2 H), 0.83 (t, *J* = 7.5 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 193.8 (d), 138.2 (s), 134.7 (s), 133.2 (s), 129.7 (d, 2 C), 129.3 (s), 128.6 (d, 2 C), 128.2 (d), 126.3 (d, 2 C), 119.8 (s), 119.5 (d), 114.5 (s), 32.0 (t), 26.1 (t), 22.6 (t), 13.9 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3348, 3058, 2954, 2929, 2869, 2734, 1668, 1601, 1572, 1553, 1495, 1459, 1444, 1422, 1371, 1341, 1225, 1197, 1088, 1056, 1006, 790, 758, 744, 705, 659, 617 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{19}NO$: 277.1467; found: 277.1441.





Compound 3g': Yield 95 %, colourless soild, mp: 142-143 ^{o}C; R_f = 0.34 (PE/EA = 2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.34 (brs, 1 H), 7.45-7.41 (m, 2 H), 7.37-7.33 (m, 1 H), 7.16-7.12 (m, 2 H), 6.98-6.93 (m, 2 H), 5.80 (d, *J* = 2.0 Hz, 1 H), 4.93 (s, 2 H), 3.43 (t, *J* = 7.5 Hz, 2 H), 2.32 (s, 3 H), 2.13 (brs, 1 H), 1.50-1.42 (m, 2 H), 1.32-1.22 (m, 2 H), 0.79 (t, *J* = 7.5 Hz, 3 H) ppm ; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.9 (s), 134.3 (s), 134.0 (s), 132.3 (s), 129.5 (d, 2 C), 127.7 (d, 2C), 127.5 (s), 123.3 (s), 120.3 (d), 119.9 (d), 119.7 (d), 95.2 (d), 64.0 (t), 50.5 (t), 30.0 (t), 21.6 (q), 19.8 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3337, 3057, 2961, 2929, 2873, 1737, 1617, 1598, 1562, 1498, 1437, 1408, 1345, 1302, 1183, 1158, 1118, 1088, 1044, 995, 880, 856, 808, 745, 722, 711, 688, 666, 636, 608 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{24}N_2O_3S$: 372.1508; found: 372.1509.



Compound 3g'': Yield 85 %, colourless soild, mp: 102-103 ^{o}C; R_f = 0.73 (PE/EA = 2:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.90 (brs, 1 H), 7.45-7.34 (m, 3 H), 7.30-7.22 (m, 1 H), 7.18-7.09 (m, 2 H), 7.00-6.91 (m, 1 H), 5.78 (d, *J* = 2.4 Hz, 1 H), 3.44 (t, *J* = 6.9 Hz, 2 H), 3.32 (s, 1 H), 2.31 (s, 3 H), 1.55-1.40 (m, 2 H), 1.36-1.20 (m, 2 H), 0.80 (t, *J* = 7.2 Hz, 3 H) ppm ; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.1 (s), 134.9 (s), 134.7 (s), 133.8 (s), 129.6 (d, 2 C), 127.5 (d, 2C), 126.6 (s), 126.0 (d), 121.3 (d), 120.0 (d), 104.8 (s), 95.3 (d), 81.8 (d), 79.8 (s), 50.3 (t), 30.0 (t), 21.6 (q), 19.8 (t), 13.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3324, 2958, 2927, 2868, 1601, 1557, 1492, 1452, 1430, 1407, 1337, 1298, 1242, 1213, 1160, 1112, 1089, 1070, 1038, 1006, 975, 943, 886, 842, 812, 778, 741, 707, 681, 644, 617 cm^{-1}; HRMS (ESI) m/z calcd for $C_{21}H_{22}N_2O_2S$ $[M+Na]^+$: 389.1294; found: 389.1295.

[1] L. V. Graux, H. Clavier, G. Buono, *ChemCatChem.* **2014**, *6*, 2544-2548.

[2] H. Clavier, A. Lepronier, N. B.-Mintsa, D. Gatineau, H. Pellissier, L. Giordano, A. Tenaglia, G. Buono, *Adv. Synth. Catal.* **2013**, *355*, 403-408.

[3] Y. Komine, K. Tanaka, *Org. Lett*. **2010**, *12*, 1312-1315.

[4] K. Graf, C. L. Rühl, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 12727-12731; *Angew. Chem*. **2013**, *125*, 12960-12964.

[5] J. Chauhana, S. Fletcher, *Tetrahedron Lett*. **2012**, *53*, 4951-4954.

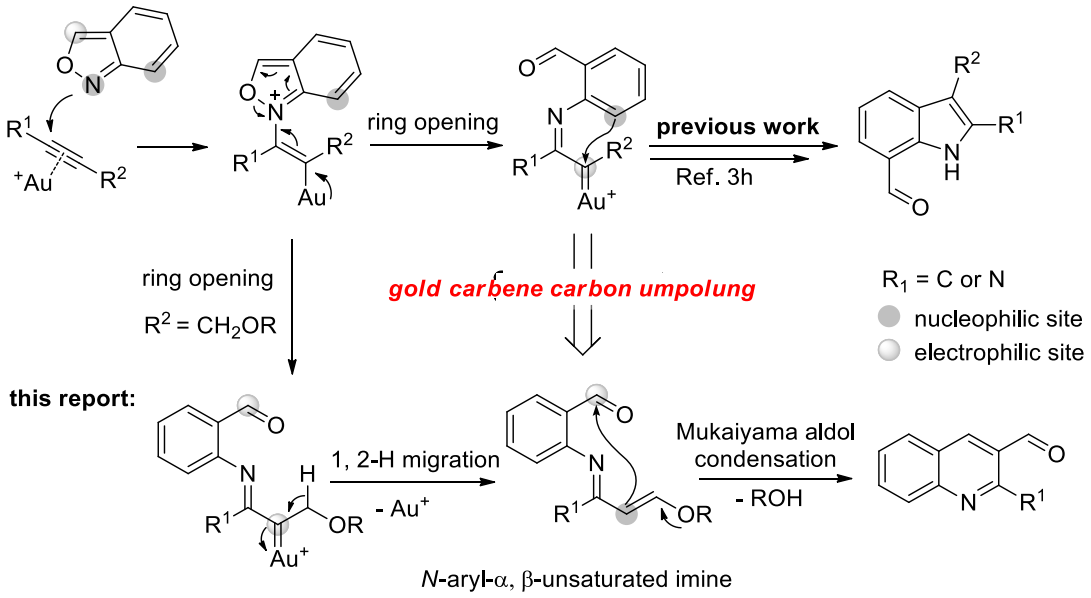
Chapter 3: Gold-Catalyzed Synthesis of Quinolines from Propargyl Silyl Ethers and Anthranils through the Umpolung of a Gold Carbene Carbon

3.1 Introduction

The recent rapid development of gold-catalyzed tandem transformations[1] has afforded atom- and step-economical synthetic approaches to complex heterocyclic scaffolds that are not easily accessible by traditional methods. Following this principle, gold-catalyzed intramolecular nitrene transfers to proximal triple bonds have enabled efficient access to pyrroles,[2a,b] indoles,[2c-g] imidazoles,[2h] pyridines,[2i] isoquinolines, [2j,k] and quinolines.[2l,m] In addition, gold-catalyzed formal [3+2] annulations of nitrenoids with alkynes have attracted attention since these offer more flexible routes to aza-heterocyclic frameworks.[3] For instance, Davies and co-workers disclosed a gold-catalyzed intermolecular reaction of iminopyridinium ylides and ynamides,[3a] delivering polysubstituted oxazoles in high efficiency. The gold-catalyzed syntheses of 2-aminopyrroles using isoxazoles or 2*H*-azirines as nitrene precursors have been achieved by Ye, [3c] Liu[3d] and Huang[3e,f] et al respectively. Recently, we contributed a gold-catalyzed C-H annulation of anthranils with alkynes for the expedient assembly of 7-acylindolyl skeletons[3h] by using the potential of anthranil to act as a binucleophile (Scheme 1, upper part). It is worth noting that all of the above studies rely on α-imino gold carbenes as key electrophilic intermediates en route to the aza-heterocycles.[1k] If internal alkynes with adjacent methylene moieties are involved in these reactions, the presumed α-imino gold carbene intermediate is usually quenched by a 1,2-hydride shift/deauration sequence that rapidly delivers α, β-unsaturated imines.[3g,h] As far as we know, although a related migration process has been described by Zhang et al.,[4] gold-catalyzed construction of aza-heterocycles triggered by a 1,2-H shift[2a] onto the α-imino gold carbene species is no reported.

The quinoline motif is important, it is embedded in numerous natural products,[5a-c] pharmaceutical relevant molecules,[5d] and functional materials.[5e,f] In particular, 2-amino-quinolines exhibit diverse biological activities[6] and have been identified as

a beta-site amyloid precursor protein cleaving enzyme 1 (BACE1) inhibitors for Alzheimer's disease therapeutics.[7] But compared to the enormous methods for the preparation of quinolines,[8] direct access routes to 2-aminoquinolines from readily available substrates are scarce.[9] The prevalent route still focuses on the C2-amination of quinolines, which usually requires harsh conditions and specific amination reagents.[10] Thus a facile, general, and environmentally benign access to 2-aminoquinolines is still desirable. In continuation of our previous work on gold catalysis,[3h,11] herein we report an unprecedented gold-catalyzed cascade annulation of anthranils[11e] and propargylic silyl ethers, which enables the regiospecific and convergent synthesis of 2-aminoquinolines and quinoline derivatives under mild conditions (Scheme 1, lower part). This reactivity pattern exploits the nucleophilicity of the in situ generated *N*-aryl-α, β-unsaturated imine (achieved through Umpolung of the electrophilic carbene carbon that reacts in the case of indol formation[3h]). In the presence of a propargylic oxygen atom, a Mukaiyama aldol-type reaction of the enol/enolether with the electrophilic aldehyde moiety derived from the ring opening of the anthranil becomes feasible.



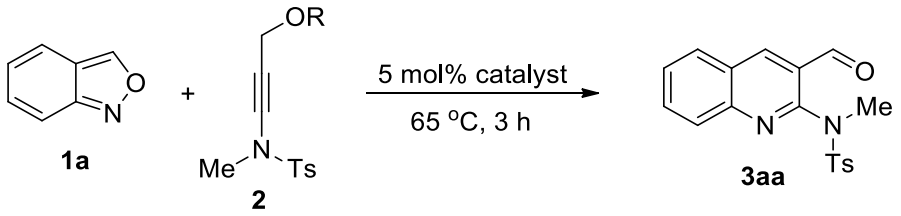
Scheme 1. Upper part: Our previous work on the gold-assisted synthesis of 7-acylindoles through the generation of a-imino gold carbenes from anthranils. Lower part: The new reaction of anthranils with propargylic ethers.

3.2 Results and Discussion

3.2.1 Optimization of the Reaction Conditions

Firstly the effect of the substituent at the propargylic oxygen in ynamides **2** was investigated (Table 1). Only 16% of the product **3aa** was obtained from the reaction of **1a** with **2a** bearing a propargylic alcohol with 5 mol% IPrAuCl/$AgNTf_2$ in 1,2-DCE at 65 ^oC for 3 h (entry 1). The yield was significantly increased to 80% by using a ynamide propargylic methyl ether under the same conditions (entry 2). Benzyl and phenyl ethers also afforded moderate yields (entries 3, 4). In order to initiate a Mukaiyama-type aldol reaction,[12] anthranil was reacted with various propargylic silyl ethers (entries 5, 6). The use of tert-butyldimethylsilyl raised the yield to 88% (entry 6). Based on these results, the transformation of anthranil **1a** and ynamide propargyl silyl ether **2a** (R=TBS) was selected as a model reaction for optimization of the catalysts and solvents (entry 7–13). IPrAuCl/$AgNTf_2$ turned out to be the best catalyst system. $(ArO)_3PAuCl/AgNTf_2$ (Ar = 2, 4-di-*tert*-butylphenyl) also performed outstandingly, with a 87 % yield (entry 7), while only moderate yields were furnished by phosphane ligands. 1,2-DCE gave the best result among the screened solvents. The control experiment without a catalyst showed no conversion (entry 14).

Table 1: Optimization of the reaction conditions[a]



Entry	catalyst	R	Solvent	Yield %[b]
1	IPrAuCl/$AgNTf_2$	H	$ClCH_2CH_2Cl$	16
2	IPrAuCl/$AgNTf_2$	Me	$ClCH_2CH_2Cl$	80
3	IPrAuCl/$AgNTf_2$	Bn	$ClCH_2CH_2Cl$	74
4	IPrAuCl/$AgNTf_2$	Ph	$ClCH_2CH_2Cl$	40
5	IPrAuCl/$AgNTf_2$	TMS[c]	$ClCH_2CH_2Cl$	86
6	**IPrAuCl/$AgNTf_2$**	**TBS[c]**	**$ClCH_2CH_2Cl$**	**88**

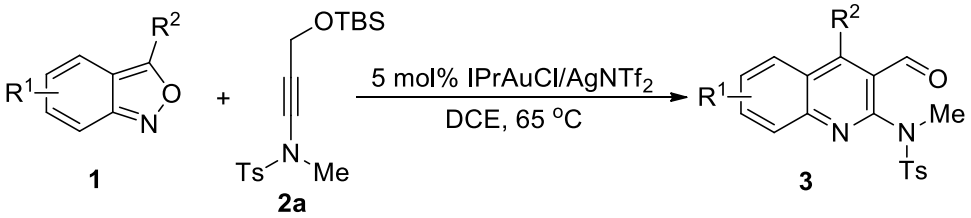
7	$(ArO)_3PAuCl$ /$AgNTf_2$	TBS	$ClCH_2CH_2Cl$	87
8	$Ph_3PAuCl/AgNTf_2$	TBS	$ClCH_2CH_2Cl$	40
9	JohnPhosAuCl/$AgNTf_2$	TBS	$ClCH_2CH_2Cl$	61
10	IPrAuCl/$AgNTf_2$	TBS	$CHCl_3$	73
11	IPrAuCl/$AgNTf_2$	TBS	CH_2Cl_2 [d]	70
12	IPrAuCl/$AgNTf_2$	TBS	$PhCF_3$	84
13	IPrAuCl/$AgNTf_2$	TBS	PhMe	80
14	None	TBS	$ClCH_2CH_2Cl$	0

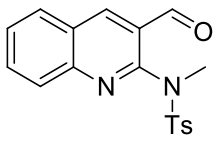
[a] Reaction conditions: **1a** (0.24 mmol) and **2** (0.2 mmol) were reacted in 1 ml solvent at 65 ^oC for 3 h. [b] Isolated yield. [c] TMS = trimethylsilyl, TBS = *tert*-butyldimethylsilyl, Ar = 2, 4-di-*tert*-butylphenyl. [d] Sealed tube.

3.2.2 Scope and Limitation

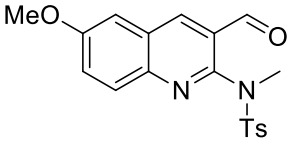
Under the optimized reaction conditions, we started to survey the scope of the reaction with respect to the anthranil. The transformation of differently substituted anthranils with ynamide **2a** proceeded smoothly to afford various 3-formyl-2-aminoquinoline derivatives in moderate to excellent yields (Table 2). A broad range of functional groups, including ethers (**3ba**, **3oa**, **3ta**), esters (**3ca**), acetals (**3ga**), amines (**3ka**), bromides (**3fa**, **3ja**), fluorides (**3da**), trifluoromethyl (**3la**), and unsaturated systems (**3ua**, **3va**), was well compatible under the mild conditions. In general, substituents with electron-donating properties at the anthranil led to higher yields, while anthranils bearing electron-withdrawing groups usually led moderate yields or even disabled the reaction (**3sa**). This facile access, which allows substituents at each position of the 2-aminoquinoline framework, illustrates the great generality and flexibility of this approach. A fused quinoline (**3ha**) that can serve as an important substrate in C-H functionalization[13] was smoothly obtained in 72% yield. The connectivity was unambiguously determined by X-ray crystal structure analysis of **3aa**.[14] An isoxazole was examined too, but the corresponding 2-aminopyridine was not formed, which might result from decomposition of the unstable *N*-alkenyl-α, β-unsaturated imine intermediate.[15]

Table 2: Scope with respect to the anthranils[a, b]

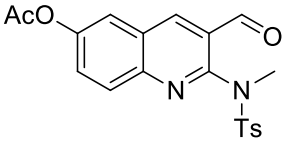




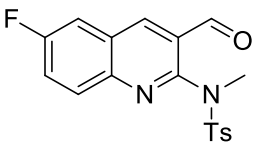
3aa, 88 %



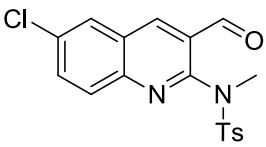
3ba, 93 %



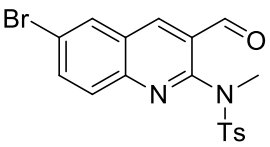
3ca, 94 %



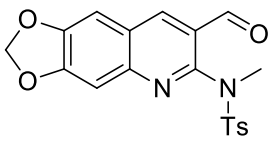
3da, 77 %



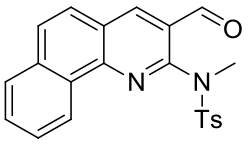
3ea, 87 %



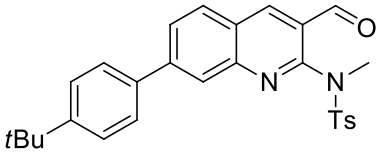
3fa, 87 %



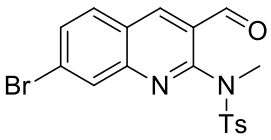
3ga, 92 %



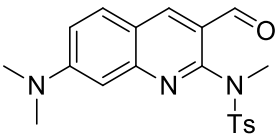
3ha, 72 %



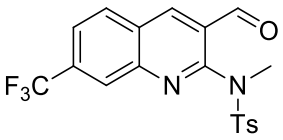
3ia, 78 %



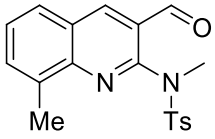
3ja, 74 %



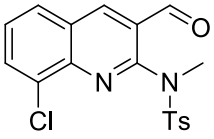
3ka, 80 %



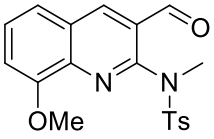
3la, 68 %



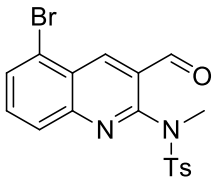
3ma, 71 %

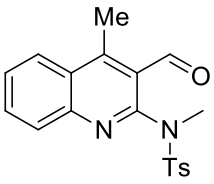


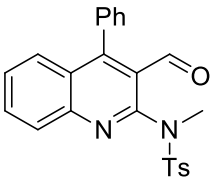
3na, 69 %



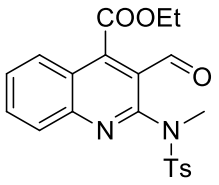
3oa, 86 %



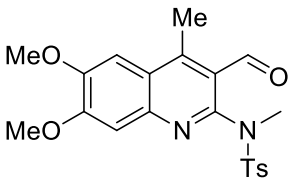




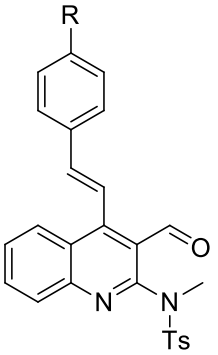
3pa, 79 %



3qa, 71 %



3ra, 66 %



3sa, 0 %

3ta, 53 %

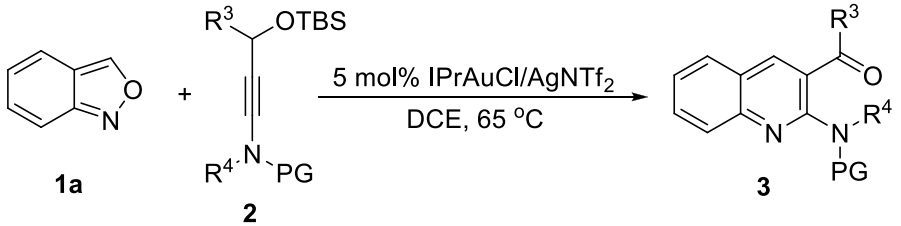
3ua, R = Me, 58 %

3va, R = MeO, 53 %

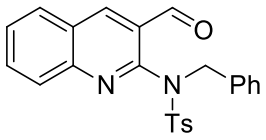
[a] Reaction conditions: **1** (0.24 mmol), **2a** (0.2 mmol), and 5 mol% IPrAuCl/$AgNTf_2$ at 65 ^oC for 3 h in 1 mL dry 1,2-DCE. [b] Yield of isolated product.

Next, we applied a series of ynamide propargyl ethers **2** in the reaction with anthranil **1a** (Table 3). Mesyl (**3ac**), nosyl (**3af**), and oxazolidinone (**3ad**) substituents at the ynamide nitrogen were all well tolerated. Various substituents on the sulfonamide moiety such as a *p*-methoxylbenzyl group (**3ac**) and an ester (**3ah**) turned out to be compatible, delivering good to excellent yields. An *N*-alkynyl indole provided 2-(indol-1-yl) quinoline (**3ae**) in 95% yield. Silyl ethers bearing a secondary carbon in the propargylic position gave rise to diversely functionalized ketones (**3ai**–**3an**). Ynamide substrates bearing 1^o- and 2^o-alkyl substitution patterns still afforded moderate yields. Some substituents derived from natural resources, like citronellal (**3ak**) and lily aldehyde (**3am**), were successfully introduced by this method. An electron-deficient perfluorinated aryl substituent gave 68% yield (**3ao**). An X-ray structure analysis of **3aj** was conducted to confirm the structural assignment.[14]

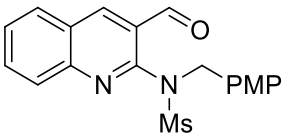
Table 3: Scope with respect to the ynamides[a, b]



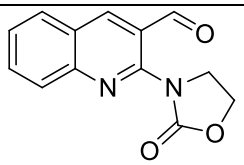
1a **2** **3**



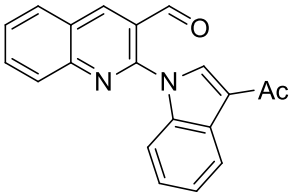
3ab, 93 %



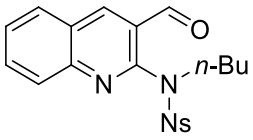
3ac, 84 %



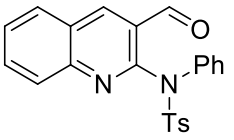
3ad, 81 %



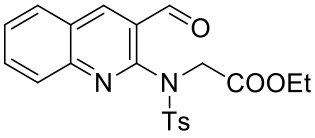
3ae, 95 %



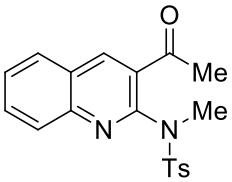
3af, 78 %



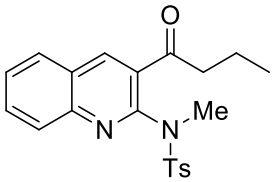
3ag, 90 %



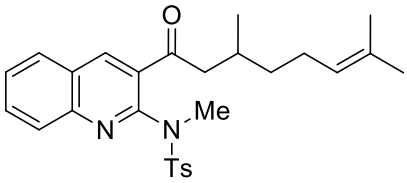
3ah, 85 %



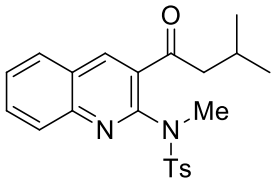
3ai, 66 %



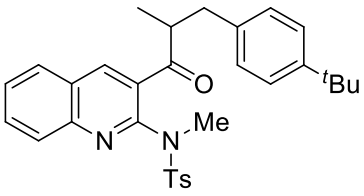
3aj, 71 %



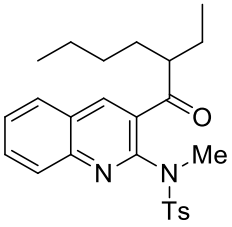
3ak, 52 %



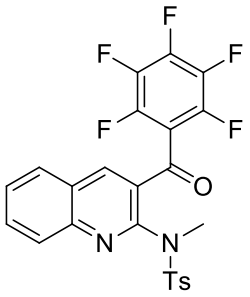
3al, 71 %



3am, 58 %



3an, 50 %



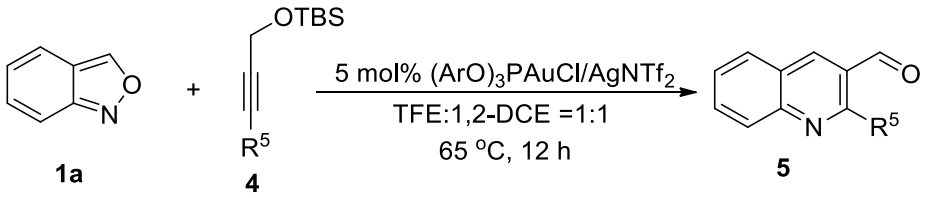
3ao, 68 %

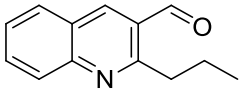
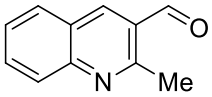
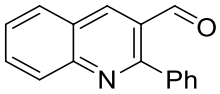
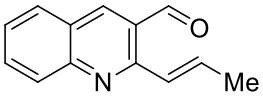
[a] Reaction conditions: **1** (0.24 mmol), **2a** (0.2 mmol), and 5 mol% IPrAuCl/$AgNTf_2$ at 65 ^{o}C for 3 h in 1 mL dry 1,2-DCE. [b] Yield of isolated product.

An extension of the synthesis of other C2-substituted quinolines was possible. The less-polarized alkyne **4a** (R^5 = *n*-propyl) and anthranil **1a** provided **5a**, albeit in only 40% yield. A screening of catalysts and solvents was conducted (Table 4), 70% yield of **5a** could be achieved in TFE/1,2-DCE (1:1) using 5 mol% $(ArO)_3PAuCl$/ $AgNTf_2$ (Ar=2,4-di-*tert*-butylphenyl). Alkyl, aryl, and alkenyl groups were all compatible under the adjusted conditions (**5a**-**5d**). The high regioselectivity can be explained by

the inductive effect of the etheral oxygen facilitating the reaction of the distal carbon of the triple bond with the oxygen atom.[16] This highly selective synthesis of 2,3-disubstituted quinolines complements the traditional Friedlnder synthesis.[8a]

Table 4: Reaction scope with less-polarized alkynes[a, b, c]

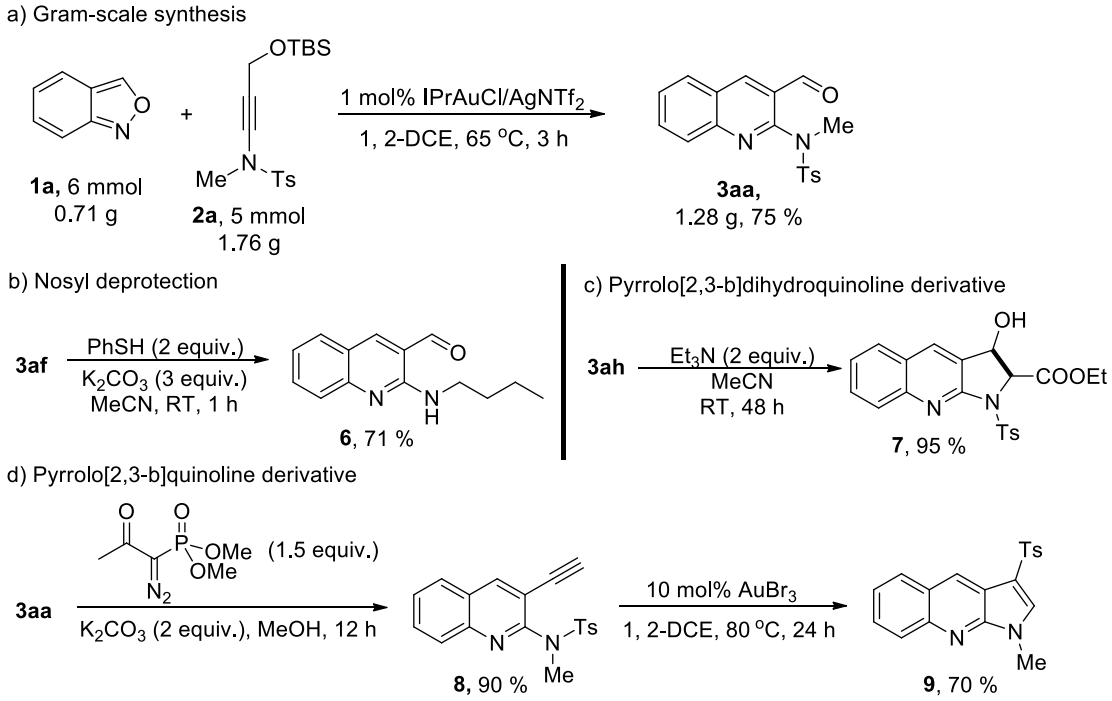


	entry	variation from standard conditions	Yield of **5a**
	1	without TFE	40 %
	2	without 1,2-DCE	20 %
5a, 70 %	3	IPrAuCl as gold catalyst	58 %
			
5b, 67 %	**5c**, 66 %	**5d**, 48 %	

[a] Reaction conditions: **1a** (0.4 mmol), **4** (0.2 mmol), 5 mol % $(ArO)_3PAuCl/AgNTf_2$ (Ar = 2, 4-di-*tert*-butylphenyl) in 1 ml TFE/1,2-DCE (1:1) at 65 ^oC for 12 h. [b] Isolated yield. [c] TFE = CF_3CH_2OH; 1,2-DCE = $ClCH_2CH_2Cl$.

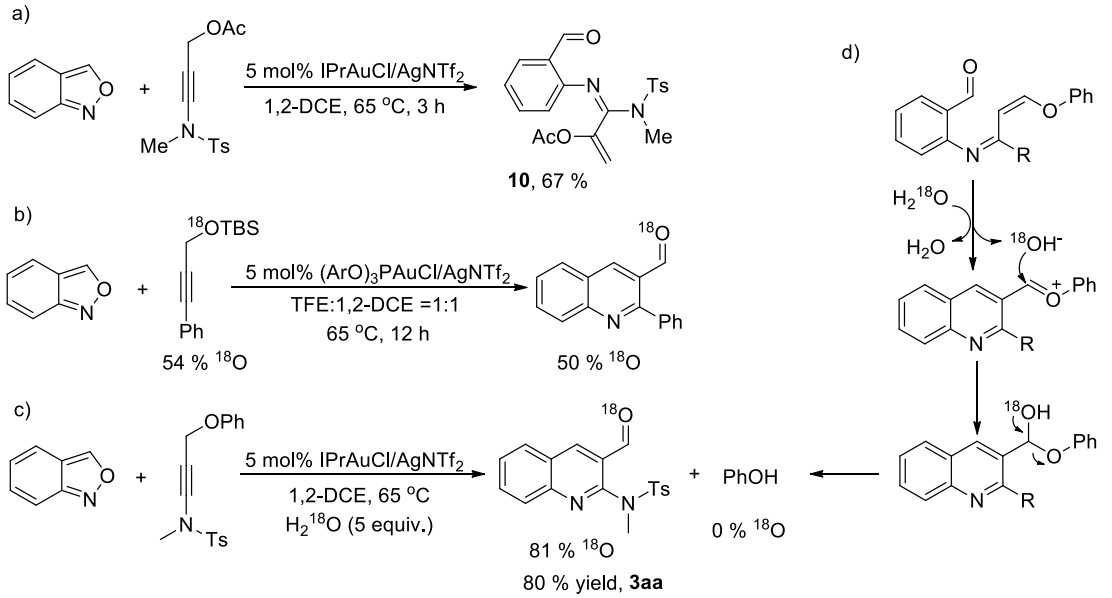
3.2.3 Further Applications

A gram-scale synthesis was carried out with a lower catalyst loading (Scheme 2a), to access **3aa** in 75% yield. The high potential of the obtained 3-formyl-2-amino-quinolines for further conversions was proved by deprotection of the nosyl group of **3af** to the secondary amine **6** (Scheme 2b) and the intramolecular aldol cyclization of **3ah** to deliver the pyrrolo[2,3-b]dihydroquinoline framework, which possesses anti-inflammatory, anticonvulsant and antihypertensive properties[17] (Scheme 2c). In addition, the pyrrolo[2,3-b]quinoline derivative **9** could be easily prepared from **3aa** in only two steps[18] (Scheme 2d).



Scheme 2. Gram-scale synthesis and subsequent conversions.

3.2.4 Mechanistic investigation



Scheme 3. Mechanistic investigation.

Preliminary mechanistic studies were also conducted. The reaction of anthranil and a propargylic ester afforded the 1,2-acyloxy migration product[19], which suggests a gold carbene intermediate formed through ring opening of the anthranil, which is

trapped in a subsequent step by the adjacent acetoxy group (Scheme 3a). The cyclization process of the silyl propargyl ether substrate follows a Mukaiyama-type process, which was verified by a ^{18}O-labelling experiment (Scheme 3b). In contrast, the reaction of a phenyl propargyl ether could be promoted by isotope-labeled water and 81% ^{18}O was found on product **3aa** (Scheme 3c), which indicates that instead the C-O bond is cleaved rather than the O-Si bond in the upper case (Scheme 3d).

3.3 Conclusion

In conclusion, the new reaction allows very interesting ring expansions which has a widly range of substates and the excellent tolerance to various functional groups. The mechanistic investigation represents two dinct progresses with respect to the substituent.

3.4 References

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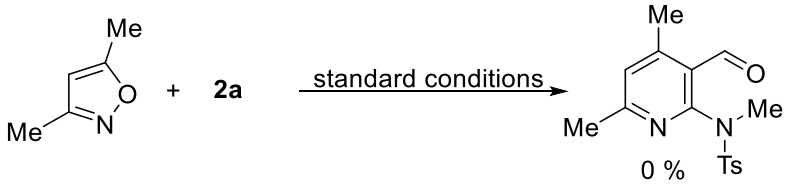
[14] CCDC 1481674 (**3aa**), and 1481675 (**3aj**) contain the supplementary crystallographic data. These data can be obtained free of charge from the cambridge crystallographic data centre.

[15] 

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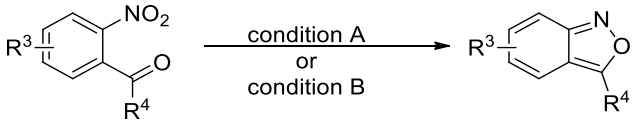
3.5 Experimental Section

General information: Chemicals were purchased from commercial suppliers and

used as delivered. The reagents **2**, **4** have been prepared according to the literature[1-3]. Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance DRX-300, Bruker-Avance DRX-500 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) and m (multiplet) as well as combinations of them. 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 and HSQC 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^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-K_α-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Heavy atom diffractions were solved by direct methods and refined against F2 with full matrix least square algorithm. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Gas Chromatography / Mass Spectrometry (GC/MS) spectra were measured on two different hardware systems: 1. HP 5972 Mass Selective Detector, coupled with a HP 5890 SERIES II plus gas chromatograph. 2. Agilent 5975C Mass Selective Detector, coupled with an Agilent 7890A gas chromatograph. In both cases, as a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and helium was used as the carrier gas. Gas Chromatography (GC) was carried out on a HP 5890 SERIES II plus gas

chromatograph. As a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and nitrogen was used as the carrier gas. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not corrected. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400 mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and diethylether (Et_2O) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)), molybdatophosphoric acid (5 % in ethanol), vanillin/H_2SO_4 (in ethanol) or anisaldehyde/HOAc (in ethanol). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

Experimental Procedure 1: Synthesis of substituted anthranils



Condition A[5]: A round bottom flask equipped with a magnetic stirrer bar was charged with the substituted 2-nitroacylbenzene (3.00 mmol) in EtOAc–MeOH (1:1; 20 mL). $SnCl_2 \cdot H_2O$ (9.00 mmol) was added and the reaction was stirred at room temperature for 24 h. The reaction was quenched by saturated $NaHCO_3$ (20 ml), and filtered. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the organic portions were combined, washed with H_2O (20 mL), saturated aqueous NaCl (20 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization data of unknown compounds has been listed in part 3.

Condition B[6]: A round bottom flask equipped with a magnetic stirrer bar was charged with the substituted 2-nitroacylbenzene (1.00 mmol) in conc. HCl (3 ml). $SnCl_2 \cdot H_2O$ (4 mmol) was added and the reaction was stirred at 10 ^oC for 30 mins. The reaction was quenched with saturated $NaHCO_3$ (20 ml), and filtered. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the organic portions were combined,

washed with H_2O (20 mL), saturated aqueous NaCl (20 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization data of unknown compounds has been listed in part 3.

Experimental Procedure 2: Gold-catalyzed transformation of anthranils with ynamide propargylic ethers

A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (5 mol%, 6.2 mg), $AgNTf_2$ (5 mol%, 4 mg), and solvent (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the ynamide propargylic ethers (0.2 mmol) and anthranil (0.24 mmol) were added. The reaction was heated at 65 ^oC for 3 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization data of the products are listed in part 3.

Gram-scale reaction: A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (1 mol%, 31 mg), $AgNTf_2$ (1 mol%, 20 mg), and solvent (20 ml). The mixture was stirred for 10 minutes at room temperature. Then the ynamide propargylic ethers (5 mmol, 1.76 g) and anthranil (6 mmol, 0.71 g) were added. The reaction was heated at 65 ^oC for 3 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc = 8:1) to provide the product in 75 % yield (1.28 g).

Experimental Procedure 3: Gold-catalyzed transformation of non-polarized propargylic ethers with anthranils

A round bottom flask equipped with a magnetic stirrer bar was charged with $(ArO)_3PAuCl$ (5 mol%, 8.8 mg) (Ar = 2, 4- di-*tert*-butylphenyl), $AgNTf_2$ (5 mol%, 4 mg) in 1 ml TFE/1,2-DCE co-solvent (ratio 1:1). The mixture was stirred for 5 minutes at room temperature. Then the anthranil (0.4 mmol) and the alkyne (0.2 mmol) were added. The reaction was stirred at 65 ^oC for 12 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by

column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization data of the products has been listed in part 3.

Experimental Procedure 4: Removal of the nosyl group of 3af

To the solution of **3af** (0.2 mmol) and K_2CO_3 (0.6 mmol) in MeCN (1 ml) PhSH (0.4 mmol) was added. The reaction was stirred at room temperature until complete consumption of the starting material, monitored by TLC (about 1 h). The reaction was washed with H_2O (15 mL), extracted with EtOAc (3 × 5 mL) and the organic portions were combined, dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound **6**. The characterization data of the obtained product is listed in part 3.

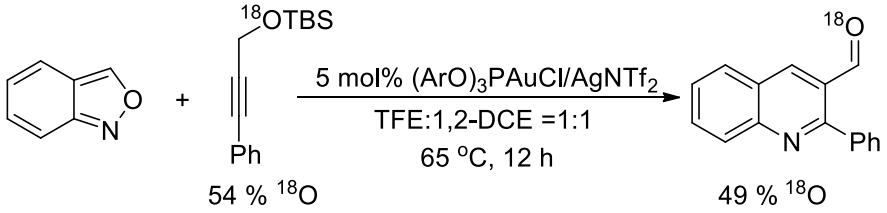
Experiment Procedure 5: The synthesis of 7 from 3ah

The mixture of **3ah** (0.2 mmol), MeCN (1 ml) and Et_3N (0.4 mmol) was stirred 48 h at room temperature. The mixture was washed with H_2O (10 mL), and extracted with EtOAc (3 × 5 mL). The organic portions were combined and washed with saturated aqueous NaCl (10 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexane/EtOAc) to provide the title compound **7**. The characterization data of the product is listed in part 3.

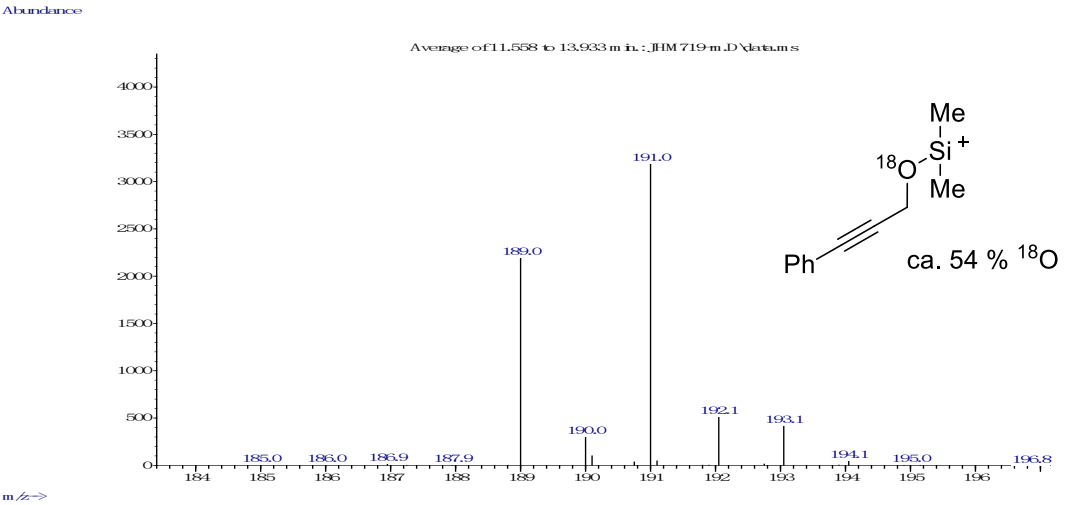
Experimental Procedure 6: The synthesis of 9 from 3aa

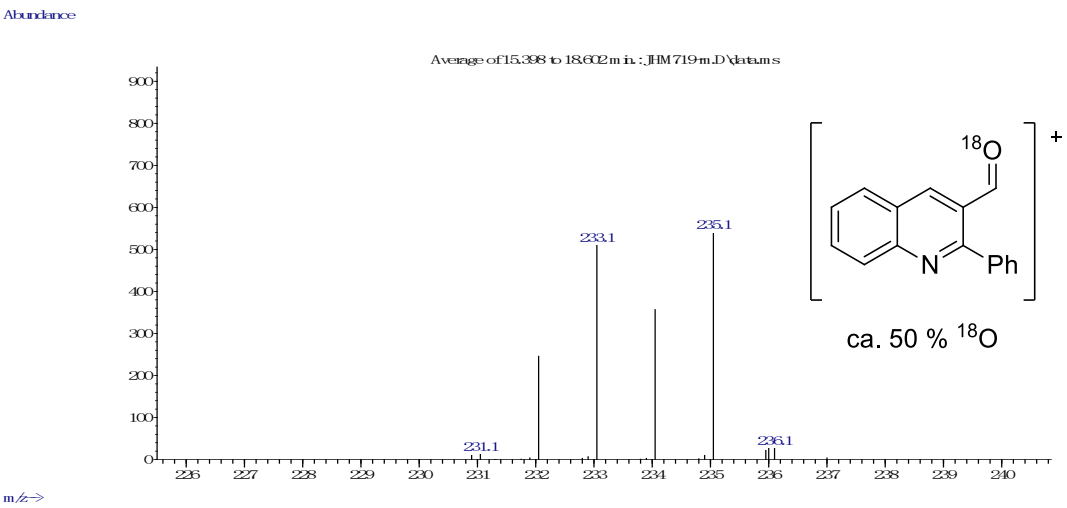
To a mixture of **3aa** (0.5 mmol), K_2CO_3 (1 mmol) in MeOH (2 ml) was added the Bestman-Ohira reagent and the reaction was stirred for 12 h at room temperature to afford the product **8**. Then, the compound **8** was heated at 80 ^oC for 24 h catalyzed by 10 mol% $AuBr_3$ in 1 ml DCE under argon protection. The mixture was washed with H_2O (10 mL), and extracted with EtOAc (3 × 5 mL). The organic portions were combined and washed with saturated aqueous NaCl (10 mL), dried over $NaSO_4$, filtered and reduced in vacuo. The residue was purified by column chromatography (SiO_2, hexane/EtOAc) to provide the product **9**. The characterization of product has been listed in part 3.

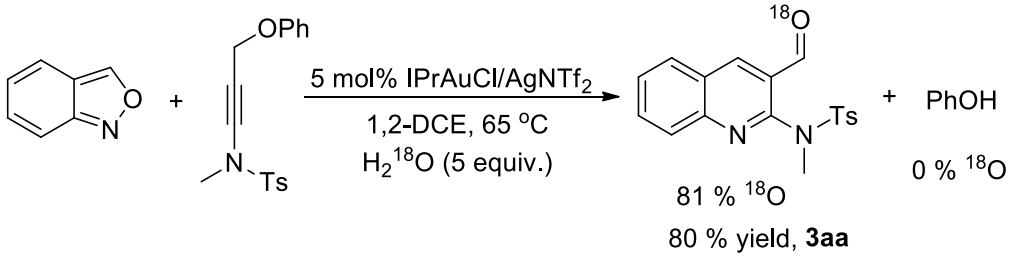
Mechanistic Investigation



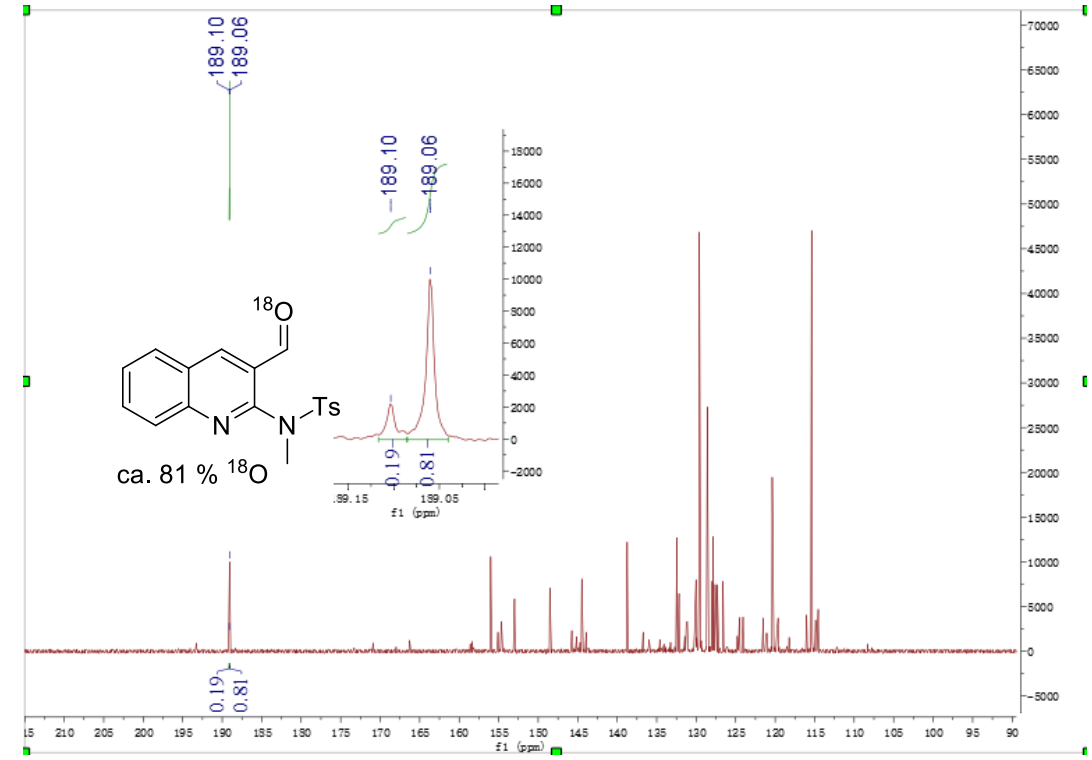
Conditions according to procedure 3. The result was monitored by GC/MS without isolation.

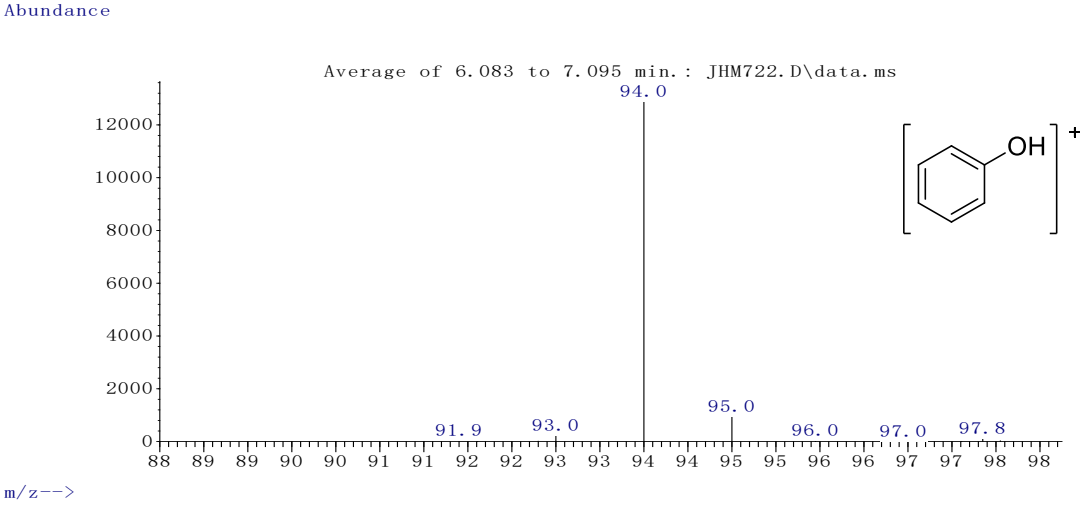




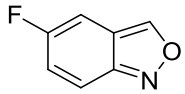


The operation was the same as procedure 2, in addition 5 equiv. $H_2{}^{18}O$ were added to the reaction mixture before heating. The result was detected by NMR and GC/MS without isolation.

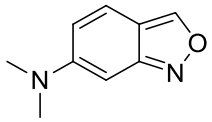




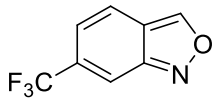
Characterization



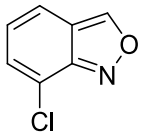
Compound **1d**: Yield 80 %, colourless soild, mp: 46-47 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.09 (s, 1 H), 7.67-7.60 (m, 1 H), 7.18-7.08 (m, 2 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 158.9 (*J* = 245.4 Hz, s), 154.5 (*J* = 10.8 Hz, d), 154.3 (s), 124.2 (*J* = 31.2 Hz, d), 117.8 (*J* = 9.3 Hz, d), 117.4 (*J* = 11.5 Hz, s), 100.8 (*J* = 24.9Hz, d) ppm; IR (ATR): $\tilde{\nu}$ = 3127, 1651, 1575, 1552, 1524, 1469, 1410, 1358, 1326, 1270, 1227, 1155, 1131, 1114, 955, 922, 885, 851, 812, 742 cm^{-1}; HRMS (EI) m/z calcd for C_7H_4FNO: 137.0277; found: 137.0276.



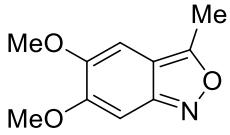
Compound **1k**: Yield 43 %, yellow green soild, mp: 50-51 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.83 (s, 1 H), 7.41-7.38 (m, 1 H), 6.88-6.84 (m, 1 H), 6.36 (s, 1 H), 3.04 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 157.9 (s), 153.0 (d), 151.4 (s), 119.8 (d), 118.7 (d), 114.1 (s), 87.4 (d), 40.6 (q, 2 C) ppm; IR (ATR): $\tilde{\nu}$ = 3446, 3092, 2919, 2854, 2821, 2489, 2359, 2215, 2071, 1910, 1868, 1646, 1574, 1509, 1483, 1443, 1396, 1356, 1303, 1261, 1225, 1151, 1114, 1063, 958, 917, 849, 793, 735, 715, 639 cm^{-1}; HRMS (EI) m/z calcd for $C_9H_{10}N_2O$: 162.0793; found: 162.0785.



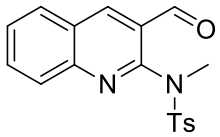
Compound **1l**: Yield 78 %, light yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.26 (s, 1 H), 8.01 (s, 1 H), 7.74 (d, *J* = 9.0 Hz, 1 H), 7.17 (d, *J* = 9.0 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 155.6 (d), 154.8 (s), 133.0 (*J* = 32.1 Hz, s), 123.3 (*J* = 271 Hz, s), 121.7 (d), 120.3 (*J* = 2.5 Hz, d), 118.5 (s), 114.2 (*J* = 5 Hz, d) ppm; IR (ATR): $\tilde{\nu}$ = 3142, 3122, 2928, 2362, 1914, 1754, 1651, 1627, 1568, 1521, 1464, 1417, 1389, 1347, 1285, 1255, 1240, 1191, 1155, 1105, 936, 925, 884, 827, 787, 746, 661 cm^{-1}; HRMS (EI) m/z calcd for $C_8H_4F_3NO$: 187.0245; found: 187.0218.



Compound **1n**: Yield 90 %, light yellow soild, mp: 46-47 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.22 (s, 1 H), 7.51 (d, *J* = 9.0 Hz, 1 H), 7.34 (d, *J* = 7.0 Hz, 1 H), 6.97 (dd, *J* = 7.0 Hz and 9.0 Hz, 1 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156.0 (d), 154.7 (s), 130.0 (d), 124.8 (d), 121.3 (s), 119.4 (s), 118.5 (d) ppm; IR (ATR): $\tilde{\nu}$ = 3120, 2925, 2854, 1750, 1635, 1610, 1581, 1552, 1512, 1463, 1385, 1318, 1248, 1212, 1155, 1120, 1024, 978, 922, 879, 830, 775, 741, 678, 622 cm^{-1}; HRMS (EI) m/z calcd for C_7H_4ClNO: 152.9981; found: 152.9987.

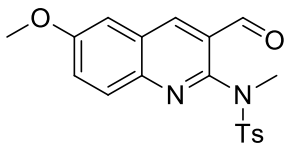


Compound **1t**: Yield 60 %, light yellow soild, mp: 131-132 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 6.68 (s, 1 H), 6.48 (s, 1 H), 3.94 (s, 3 H), 3.90 (s, 3 H), 2.68 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.5 (s), 155.24 (s), 155.2 (s), 148.8 (s), 111.0 (s), 94.4 (d), 91.1 (d), 56.2 (q), 55.9 (q), 11.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3082, 3009, 2970, 2841, 1737, 1656, 1583, 1533, 1502, 1465, 1451, 1434, 1376, 1317, 1243, 1224, 1204, 1173, 1072, 1030, 1008, 978, 841, 820, 737, 724 cm^{-1}; HRMS (EI) m/z calcd for $C_{10}H_{11}NO_3$: 193.0739; found: 193.0735.

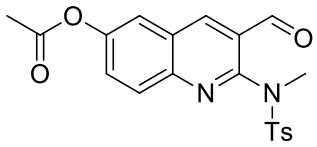


Compound **3aa**: Yield 88 %, colourless soild, mp: 152-154 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.58 (s, 1 H), 8.84 (s, 1 H), 8.03-8.00 (m, 1 H), 7.86-7.74 (m, 2 H), 7.67-7.57 (m, 1 H), 7.36 (d, *J* = 8.1 Hz, 2 H), 7.21 (d, *J* = 7.8 Hz, 2 H), 3.32 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 188.9 (d), 153.0 (s), 148.5 (s), 144.4 (s), 138.6 (d), 132.32 (s), 132.31 (d), 129.5 (d, 2 C), 129.4 (d), 128.7 (d), 128.6 (d, 2 C), 127.8 (d), 127.7 (s), 126.6 (s), 36.7 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2968, 2926, 2883, 1717, 1688, 1615, 1584, 1494, 1459, 1409, 1386, 1372, 1345, 1304, 1294, 1266, 1185, 1159, 1115, 1087, 1049, 1016, 1005, 970, 940, 920, 890, 869, 817, 806, 792, 779, 759, 751, 706, 670, 622 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{16}N_2O_3S$:

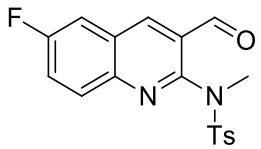
340.0882; found: 340.0854.



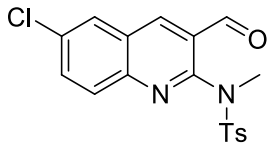
Compound **3ba**: Yield 93 %, colourless soild, mp: 170-171 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.57 (s, 1 H), 8.71 (s, 1 H), 7.73-7.66 (m, 1 H), 7.46-7.31 (m, 3 H), 7.25-7.16 (m, 3 H), 3.95 (s, 3 H), 3.29 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.2 (d), 158.7 (s), 151.0 (s), 144.7 (s), 144.2 (s), 137.0 (d), 132.4 (s), 130.0 (d), 129.4 (d, 2 C), 128.6 (d, 2 C), 127.9 (s), 127.7 (s), 125.5 (d), 106.2 (d), 55.8 (q), 36.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3086, 3056, 2998, 2966, 2948, 2935, 2875, 1698, 1620, 1589, 1500, 1451, 1423, 1394, 1375, 1352, 1342, 1307, 1263, 1226, 1186, 1158, 1138, 1117, 1087, 1036, 1025, 958, 943, 904, 864, 834, 819, 801, 783, 772, 730, 666, 625, 611 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_4S$: 370.0987; found: 370.0971.



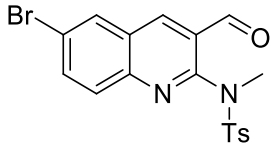
Compound **3ca**: Yield 94 %, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.56 (s, 1 H), 8.78 (s, 1 H), 7.86-7.80 (m, 1 H), 7.73-7.69 (m, 1 H), 7.56-7.50 (m, 1 H), 7.34 (d, *J* = 8.4 Hz, 2 H), 7.21 (d, *J* = 8.1 Hz, 2 H), 3.30 (s, 3 H), 2.41 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.6 (d), 169.3 (s), 152.9 (s), 149.4 (s), 146.4 (s), 144.5 (s), 138.2 (d), 132.2 (s), 130.2 (d), 129.5 (d, 2 C), 128.6 (d, 2 C), 128.0 (s), 127.7 (d), 126.9 (s), 119.8 (d), 36.6 (q), 21.6 (q), 21.1 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3066, 2944, 2874, 2256, 1766, 1698, 1622, 1592, 1571, 1497, 1449, 1419, 1370, 1353, 1306, 1260, 1241, 1188, 1150, 1120, 1088, 1046, 1012, 969, 934, 898, 841, 813, 785, 774, 734, 706, 682, 658, 625 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{18}N_2O_5S$: 398.0936; found: 398.0918.



Compound **3da**: Yield 77 %, colourless soild, mp: 184-185 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.56 (s, 1 H), 8.76 (s, 1 H), 7.85-7.80 (m, 1 H), 7.64-7.57 (m, 1 H), 7.57-7.50 (m, 1 H), 7.33 (d, *J* = 8.5 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 3.30 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 188.6 (d), 161.0 (*J* = 249.6 Hz, s), 152.5 (*J* = 3 Hz, s), 145.6 (s), 144.5 (s), 137.9 (*J* = 5.5 Hz, d), 132.1 (s), 131.2 (*J* = 8.3 Hz, d), 129.5 (d, 2 C), 128.6 (d, 2 C), 128.1 (s), 127.3 (*J* = 10.5 Hz, s), 122.6 (*J* = 25.7 Hz, d), 112.3 (*J* = 21.7 Hz, d), 36.6 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3082, 2884, 1692, 1626, 1588, 1569, 1498, 1464, 1419, 1386, 1372, 1346, 1306, 1294, 1262, 1214, 1187, 1163, 1151, 1134, 1120, 1087, 1051, 1018, 1005, 966, 944, 897, 875, 838, 817, 804, 786, 772, 738, 722, 665, 623 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}FN_2O_3S$: 358.0787; found: 358.0797.

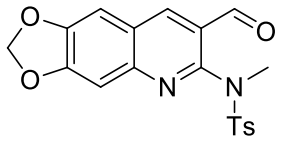


Compound **3ea**: Yield 87 %, colourless soild, mp: 186-188 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.54 (s, 1 H), 8.73 (s, 1 H), 7.98-7.94 (m, 1 H), 7.79-7.66 (m, 2 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 3.30 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.4 (d), 153.2 (s), 146.8 (s), 144.5 (s), 137.6 (d), 133.6 (s), 133.2 (d), 132.1 (s), 130.2 (d), 129.5 (d, 2 C), 128.5 (d, 2 C), 128.3 (s), 127.8 (d), 127.2 (s), 36.6 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3069, 2883, 1693, 1609, 1581, 1486, 1465, 1413, 1384, 1369, 1349, 1296, 1249, 1178, 1160, 1122, 1076, 1044, 1003, 937, 885, 832, 814, 801, 786, 770, 729, 707, 685, 656, 624 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}ClN_2O_3S$: 374.0492; found: 374.0496.

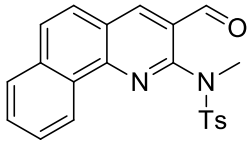


Compound **3fa**: Yield 87 %, colourless soild, mp: 186-187 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.54 (s, 1 H), 8.72 (s, 1 H), 8.17-8.10 (m, 1 H), 7.86-7.78 (m, 1 H), 7.74-7.64 (m, 1 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 3.30 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.3 (d), 153.2 (s), 147.0 (s), 144.5 (s), 137.5 (d), 135.7 (d), 132.1 (s), 131.2 (d), 130.3 (d), 129.5 (d, 2 C), 128.5 (d,

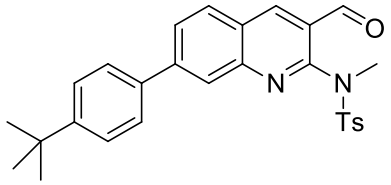
2 C), 128.3 (s), 127.7 (s), 121.6 (s), 36.6 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3067, 2962, 2927, 2883, 1692, 1581, 1482, 1464, 1411, 1384, 1368, 1348, 1294, 1249, 1178, 1160, 1122, 1085, 1061, 1042, 938, 927, 885, 831, 814, 785, 768, 706, 677, 647, 624 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}BrN_2O_3S$: 417.9987; found: 418.9989.



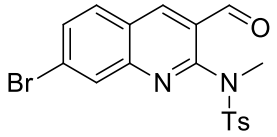
Compound **3ga**: Yield 92 %, colourless soild, mp: 139-140 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.51 (s, 1 H), 8.57 (s, 1 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.15 (s, 1 H), 7.05 (s, 1 H), 6.13 (s, 2 H), 3.25 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.2 (d), 153.3 (s), 151.8 (s), 149.0 (s), 147.7 (s), 144.2 (s), 136.5 (d), 132.5 (s), 129.4 (d, 2 C), 128.6 (d, 2 C), 125.8 (s), 123.9 (s), 105.2 (d), 103.8 (d), 102.5 (t), 36.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3063, 2919, 2872, 2782, 1693, 1643, 1613, 1589, 1490, 1463, 1394, 1369, 1349, 1307, 1283, 1260, 1234, 1187, 1163, 1136, 1088, 1037, 945, 908, 846, 816, 771, 740, 707, 697, 684, 662, 626 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{16}N_2O_5S$: 384.0780; found: 384.0766.



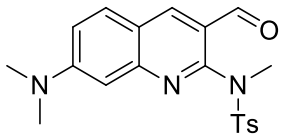
Compound **3ha**: Yield 72 %, colourless soild, mp: 140-141 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.67 (s, 1 H), 8.82 (s, 1 H), 8.64-8.57 (m, 1 H), 7.95-7.77 (m, 3 H), 7.77-7.68 (m, 1 H), 7.65-7.56 (m, 1 H), 7.40 (d, *J* = 8.4 Hz, 2 H), 7.18 (d, *J* = 8.1 Hz, 2 H), 3.42 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.2 (d), 152.7 (s), 147.6 (s), 144.2 (s), 137.6 (d), 134.7 (s), 132.4 (s), 130.4 (s), 129.7 (d), 129.4 (d, 2 C), 129.1 (d), 128.7 (d, 2 C), 128.0 (d), 127.8 (s), 127.3 (d), 125.4 (d), 125.2 (s), 125.0 (d), 37.1 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2948, 2879, 1693, 1586, 1509, 1486, 1444, 1405, 1372, 1344, 1309, 1291, 1264, 1230, 1181, 1159, 1132, 1088, 1046, 996, 939, 898, 876, 856, 819, 802, 794, 759, 729, 715, 686, 667, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{18}N_2O_3S$: 390.1038; found: 390.1019.



Compound **3ia**: Yield 78 %, colourless soild, mp: 207-208 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.60 (s, 1 H), 8.85 (s, 1 H), 8.08-8.01 (m, 2 H), 7.94-7.87 (m, 1 H), 7.69 (d, *J* = 8.4 Hz, 2 H), 7.54 (d, *J* = 8.4 Hz, 2 H), 7.40 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.4 Hz, 2 H), 3.35 (s, 3 H), 2.41 (s, 3 H), 1.39 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.9 (d), 153.5 (s), 151.9 (s), 149.0 (s), 144.9 (s), 144.4 (s), 138.3 (d), 136.5 (s), 132.4 (s), 129.8 (d), 129.5 (d, 2 C), 128.6 (d, 2 C), 127.41 (s), 127.37 (d), 127.23 (d, 2 C), 126.1 (d, 2 C), 125.8 (d), 125.6 (s), 36.7 (q), 34.7 (s), 31.3 (q, 3 C), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2965, 2872, 1693, 1620, 1587, 1490, 1462, 1430, 1411, 1371, 1349, 1309, 1269, 1242, 1181, 1156, 1119, 1087, 1049, 972, 936, 890, 809, 765, 736, 727, 706, 677, 657, 632, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{28}H_{28}N_2O_3S$: 472.1821; found: 472.1811.

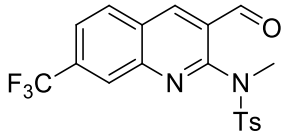


Compound **3ja**: Yield 74 %, colourless soild, mp: 145-146 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.53 (s, 1 H), 8.79 (s, 1 H), 8.03 (s, 1 H), 7.90-7.82 (m, 1 H), 7.73-7.65 (m, 1 H), 7.33 (d, *J* = 8.1 Hz, 2 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 3.29 (s, 3 H), 2.42 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.3 (d), 153.9 (s), 148.8 (s), 144.6 (s), 138.5 (d), 132.1 (s), 131.4 (d), 131.0 (d), 130.5 (d), 129.6 (d, 2 C), 128.5 (d, 2 C), 127.9 (s), 127.1 (s), 125.2 (s), 36.6 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3084, 3063, 2936, 2877, 1698, 1605, 1585, 1561, 1482, 1429, 1406, 1385, 1373, 1353, 1304, 1251, 1188, 1158, 1122, 1089, 1046, 934, 895, 873, 819, 808, 780, 757, 724, 708, 674, 655, 631, 619 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}BrN_2O_3S$: 417.9987; found: 417.9995.

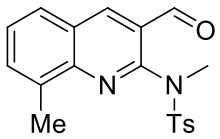


Compound **3ka**: Yield 80 %, colourless oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.47 (s, 1 H), 8.59 (s, 1 H), 7.77-7.73 (m, 1 H), 7.46-7.42 (m, 2 H), 7.24-7.20 (m, 2 H),

7.17-7.13 (m, 1 H), 6.76-6.74 (m, 1 H), 3.26 (s, 3 H), 3.12 (s, 6 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 189.2 (d), 154.1 (s), 153.1 (s), 150.9 (s), 144.0 (s), 137.8 (d), 132.9 (s), 130.5 (d), 129.4 (d, 2 C), 128.7 (d, 2 C), 123.7 (s), 119.0 (s), 116.8 (d), 105.2 (d), 40.3 (q, 2 C), 36.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2925, 2876, 1682, 1621, 1585, 1553, 1505, 1449, 1432, 1389, 1360, 1345, 1257, 1233, 1189, 1157, 1126, 1087, 1047, 967, 926, 895, 830, 807, 775, 760, 727, 707, 696, 666, 645, 618 cm^{-1}; HRMS (ESI) m/z calcd for $C_{20}H_{21}N_3O_3S$ $[M+Na]^+$: 406.1196; found: 406.1198.

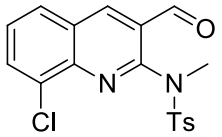


Compound **3la**: Yield 68 %, colourless solid, mp: 154-155 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.57 (s, 1 H), 8.89 (s, 1 H), 8.17-8.12 (m, 2 H), 7.82-7.77 (m, 1 H), 7.36-7.31 (m, 2 H), 7.26-7.21 (m, 2 H), 3.28 (s, 3 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 188.1 (d), 154.1 (s), 147.5 (s), 144.8 (s), 138.4 (d), 133.6 (*J* = 32.7 Hz, s), 131.9 (s), 130.6 (d), 129.6 (d, 2 C), 129.2 (s), 128.5 (d, 2 C), 127.9 (s), 126.3 (*J* = 4.1 Hz, d), 123.5 (J = 271.2 Hz, s), 123.3 (*J* = 3.1 Hz, d), 36.5 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3057, 2873, 1692, 1618, 1586, 1569, 1497, 1457, 1420, 1375, 1365, 1350, 1304, 1259, 1233, 1197, 1185, 1162, 1139, 1114, 1089, 1039, 1029, 967, 909, 884, 837, 814, 798, 780, 748, 696, 672, 628 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{15}F_3N_2O_3S$: 408.0755; found: 408.0749.

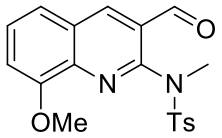


Compound **3ma**: Yield 71 %, colourless soild, mp: 157-158 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.63 (s, 1 H), 8.79 (s, 1 H), 7.84-7.81 (m, 1 H), 7.63-7.60 (m, 1 H), 7.52-7.47 (m, 1 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 7.20 (d, *J* = 8.5 Hz, 2 H), 3.31 (s, 3 H), 2.40 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 189.3 (d), 152.0 (s), 147.4 (s), 144.2 (s), 138.8 (d), 137.1 (s), 132.4 (d), 132.2 (s), 129.2 (d, 2 C), 128.7 (d, 2 C), 127.7 (d), 127.3 (d), 127.2 (s), 126.6 (s), 36.9 (q), 21.6 (q), 17.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2920, 2872, 1693, 1613, 1589, 1492, 1468, 1421, 1402, 1373, 1348, 1307, 1248, 1180, 1158, 1136, 1089, 1064, 1028, 940, 898, 843, 819, 803, 778, 759, 737, 710, 671, 623 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_3S$: 354.1038; found:

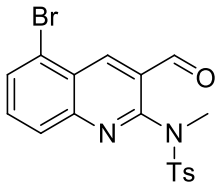
354.1021.



Compound **3na**: Yield 69 %, colourless soild, mp: 171-172 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.60 (s, 1 H), 8.84 (s, 1 H), 7.95-7.83 (m, 2 H), 7.58-7.49 (m, 1 H), 7.40 (d, *J* = 8.1 Hz, 2 H), 7.22 (d, *J* = 8.1 Hz, 2 H), 3.34 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.5 (d), 153.5 (s), 144.6 (s), 144.5 (s), 139.1 (d), 133.4 (s), 132.2 (d), 132.1 (s), 129.4 (d, 2 C), 128.6 (d, 2 C), 128.3 (d), 128.2 (s), 127.8 (d), 127.7 (s), 36.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2881, 1698, 1609, 1592, 1485, 1447, 1425, 1407, 1386, 1369, 1345, 1308, 1261, 1179, 1159, 1122, 1088, 1034, 1010, 963, 934, 912, 899, 816, 806, 774, 758, 738, 707, 676, 636, 622 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}ClN_2O_3S$: 374.0492; found: 374.0494.

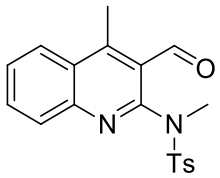


Compound **3oa**: Yield 86 %, colourless soild, mp: 162-163 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.57 (s, 1 H), 8.77 (s, 1 H), 7.58-7.40 (m, 4 H), 7.25-7.19 (m, 2 H), 7.17-7.12 (m, 1 H), 3.91 (s, 3 H), 3.34 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.0 (d), 155.2 (s), 151.9 (s), 144.1 (s), 140.4 (s), 138.6 (d), 132.9 (s), 129.4 (d, 2 C), 128.8 (d, 2 C), 128.1 (d), 127.9 (s), 127.6 (s), 121.2 (d), 111.8 (d), 56.6 (q), 37.0 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3066, 2955, 1697, 1612, 1593, 1571, 1495, 1471, 1420, 1389, 1374, 1345, 1306, 1273, 1259, 1207, 1176, 1157, 1093, 1038, 1007, 964, 932, 898, 842, 816, 806, 758, 741, 716, 705, 671, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_4S$: 370.0987; found: 370.0961.

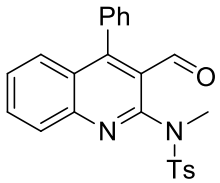


Compound **3pa**: Yield 79 %, colourless soild, mp: 177-178 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.56 (s, 1 H), 9.15 (s, 1 H), 7.90-7.82 (m, 1 H), 7.81-7.73 (m, 1 H),

7.66-7.56 (m, 1 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.20 (d, *J* = 8.1 Hz, 2 H), 3.31 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 188.2 (d), 153.6 (s), 149.1 (s), 144.6 (s), 138.5 (d), 132.4 (d), 132.1 (s), 131.4 (d), 129.5 (d, 2 C), 128.5 (d, 2 C), 128.4 (d), 128.3 (s), 126.4 (s), 123.6 (s), 36.6 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2871, 2254, 1696, 1604, 1584, 1549, 1484, 1451, 1418, 1378, 1346, 1306, 1265, 1208, 1183, 1156, 1116, 1086, 1040, 939, 916, 894, 814, 766, 757, 733, 705, 667, 616 cm^{-1}; HRMS (EI) m/z calcd for $C_{18}H_{15}BrN_2O_3S$: 417.9987; found: 417.9941.

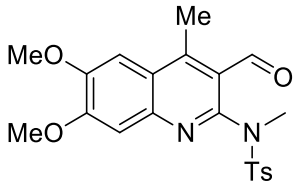


Compound **3qa**: Yield 71 %, colourless soild, mp: 122-123 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.75 (s, 1 H), 8.25-8.18 (m, 1 H), 7.81-7.70 (m, 2 H), 7.68-7.59 (m, 1 H), 7.42 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.1 Hz, 2 H), 3.28 (s, 3 H), 3.06 (s, 3 H), 2.42 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 192.1 (d), 153.8 (s), 150.2 (s), 147.3 (s), 144.2 (s), 132.7 (s), 131.6 (d), 129.4 (d), 129.3 (d, 2 C), 128.8 (d, 2 C), 127.6 (d and s, 2 C), 126.0 (s), 125.4 (d), 37.1 (q), 21.6 (q), 14.9 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3067, 3033, 2944, 2927, 2871, 1920, 1733, 1699, 1614, 1598, 1565, 1500, 1446, 1418, 1386, 1354, 1291, 1239, 1187, 1163, 1113, 1089, 1019, 967, 913, 882, 814, 765, 734, 706, 691, 671, 619 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_3S$: 354.1038; found: 354.1048.

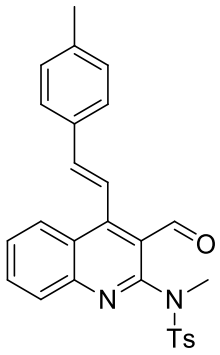


Compound **3ra**: Yield 66 %, colourless soild, mp: 200-201 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.32 (s, 1 H), 7.92-7.86 (m, 1 H), 7.80-7.72 (m, 1 H), 7.64-7.46 (m, 7 H), 7.40-7.32 (m, 2 H), 7.31-7.24 (m, 2 H), 3.33 (s, 3 H), 2.45 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 190.7 (d), 152.2 (s), 151.8 (s), 147.6 (s), 144.1 (s), 134.2 (s), 133.7 (s), 131.6 (d), 129.7 (d, 2 C), 129.4 (d, 2 C), 128.9 (d), 128.8 (d), 128.7 (d, 2 C), 128.4 (d, 2 C), 127.6 (d), 127.4 (d), 126.8 (s), 126.5 (s), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1699, 1610, 1598, 1567, 1550, 1488, 1441, 1423, 1387, 1348, 1308, 1287, 1236, 1193, 1163, 1151, 1117, 1086, 1071, 1052, 1026, 999, 952, 922, 878, 847, 800, 784,

770, 701, 667, 638, 621 cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{20}N_2O_3S$: 416.1195; found: 416.1173.

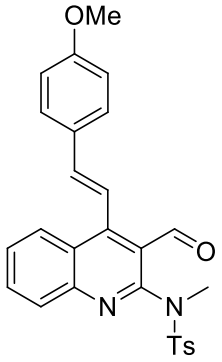


Compound **3ta**: Yield 73 %, colourless soild, mp: 166-167 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ = 10.71 (s, 1 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.34 (s, 1 H), 7.23 (d, *J* = 8.1 Hz, 2 H), 7.07 (s, 1 H), 4.06 (s, 3 H), 3.99 (s, 3 H), 3.26 (s, 3 H), 301 (s, 3 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 192.3 (d), 154.2 (s), 152.8 (s), 150.5 (s), 147.9 (s), 145.0 (s), 144.0 (s), 133.0 (s), 129.3 (d, 2 C), 128.8 (d, 2 C), 124.4 (s), 123.1 (s), 107.8 (d), 102.8 (d), 56.4 (q), 56.2 (q), 37.1 (q), 21.6 (q), 15.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2949, 1692, 1618, 1597, 1556, 1504, 1472, 1431, 1411, 1345, 1311, 1272, 1252, 1216, 1188, 1164, 1140, 1101, 1086, 1061, 1026, 1003, 955, 910, 861, 831, 821, 805, 741, 708, 672, 648 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{22}N_2O_5S$: 414.1249; found: 414.1246.

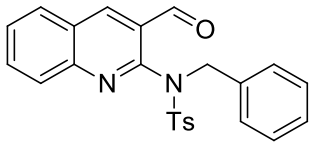


Compound **3ua**: Yield 58 %, yellow soild, mp: 203-204 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 10.69 (s, 1 H), 8.40-8.35 (m, 1 H), 7.95 (d, *J* = 16.5 Hz, 1 H), 7.84-7.74 (m, 2 H), 7.62-7.58 (m, 1 H), 7.55 (d, *J* = 8.0 Hz, 2 H), 7.48 (d, *J* = 8.0 Hz, 2 H), 7.27-7.22 (m, 4 H), 6.83 (d, *J* = 16.5 Hz, 1 H), 3.31 (s, 3 H), 2.44 (s, 3 H), 2.41 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.2 (d), 153.3 (s), 149.7 (s), 148.3 (s), 144.1 (s), 139.7 (d), 139.1 (s), 133.6 (s), 133.0 (s), 131.7 (d), 129.6 (d, 2 C), 129.4 (d, 2 C), 129.1 (d), 128.8 (d, 2 C), 127.5 (d), 127.4 (d), 127.2 (d, 2 C), 126.0 (s), 124.5 (s), 122.0 (d), 37.0 (q), 21.7 (q), 21.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2963, 2926, 2863, 191, 1687, 1631, 1607, 1566, 1536, 1511, 1493, 1445, 1416, 1384, 1340, 1304, 1234, 1184,

1157, 1115, 1086, 1014, 972, 937, 898, 855, 811, 780, 733, 706, 667, 619 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{24}N_2O_3S$: 456.1508; found: 456.1518.

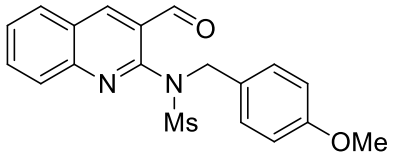


Compound **3va**: Yield 53 %, yellow soild, mp: 202-204 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.48 (s, 1 H), 8.20-8.13 (m, 1 H), 7.68 (d, *J* = 16.5 Hz, 1 H), 7.63-7.50 (m, 2 H), 7.43-7.34 (m, 3 H), 7.27 (d, *J* = 8.4 Hz, 2 H), 7.03 (d, *J* = 8.1 Hz, 2 H), 6.75 (d, *J* = 8.7 Hz,2 H), 6.60 (d, *J* = 16.5 Hz, 1 H), 3.65 (s, 3 H), 3.09 (s, 3 H), 2.22 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.3 (d), 160.4 (s), 153.3 (s), 149.8 (s), 148.3 (s), 144.1 (s), 139.6 (d), 133.1 (s), 131.7 (d), 129.4 (d, 2 C), 129.2 (s), 129.1 (d), 128.75 (d, 2 C), 128.69 (d, 2 C), 127.5 (d), 127.4 (d), 126.0 (s), 124.4 (s), 120.6 (d), 114.4 (d, 2 C), 55.5 (q), 37.0 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2969, 1686, 1602, 1566, 1537, 1512, 1493, 1462, 1421, 1385, 1340, 1306, 1251, 1177, 1158, 1113, 1087, 1029, 1014, 973, 940, 899, 853, 828, 813, 800, 786, 766, 732, 705, 670, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{24}N_2O_4S$: 472.1457; found: 472.1466.

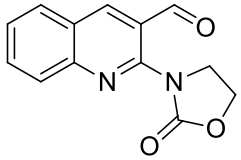


Compound **3ab**: Yield 93 %, colourless soild, mp: 152-153 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.45 (s, 1 H), 8.65 (s, 1 H), 7.92-7.81 (m, 2 H), 7.80-7.71 (m, 1 H), 7.60-7.52 (m, 1 H), 7.50-7.43 (m, 2 H), 7.27-7.19 (m, 4 H), 7.16-7.03 (m, 3 H), 4.93 (s, 2 H), 2.42 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.0 (d), 151.5 (s), 148.6 (s), 144.4 (s), 138.5 (d), 135.4 (s), 134.1 (s), 132.3 (d), 129.6 (d, 2 C), 129.5 (d), 129.0 (d, 2 C), 128.7 (d), 128.6 (s), 128.5 (d, 2 C), 128.4 (d, 2 C), 127.9 (d, 2 C), 126.7 (s), 52.8 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3089, 2873, 1741, 1693, 1618, 1586, 1570, 1497, 1457, 1420, 1375, 1365, 1348, 1304, 1294, 1259, 1233, 1197, 1185, 1162, 1139, 1114, 1089, 1039, 1029, 1014, 967, 909, 885, 814, 798, 780, 747, 696, 672, 628

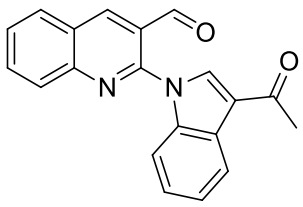
cm^{-1}; HRMS (EI) m/z calcd for $C_{24}H_{20}N_2O_3S$: 416.1195; found: 416.1226.



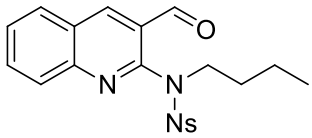
Compound **3ac**: Yield 83 %, colourless solid, mp: 144-145 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.26 (s, 1 H), 8.66 (s, 1 H), 8.14-8.08 (m, 1 H), 7.98-7.83 (m, 2 H), 7.68-7.58 (m, 1 H), 7.18-7.10 (m, 2 H), 6.70-6.63 (m, 2 H), 5.09 (s, 2 H), 3.68 (s, 3 H), 3.14 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.1 (d), 159.4 (s), 152.1 (s), 148.9 (s), 139.0 (d), 132.6 (d), 130.5 (d, 2 C), 129.6 (d), 128.8 (d), 128.3 (s), 128.2 (d), 127.1 (s), 126.8 (s), 114.1 (d, 2 C), 55.1 (q), 53.6 (t), 37.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3050, 3013, 2902, 2836, 1693, 1614, 1580, 1513, 1494, 1456, 1421, 1389, 1374, 1345, 1324, 1305, 1263, 1243, 1192, 1154, 1108, 1053, 1033, 1007, 959, 944, 917, 890, 849, 811, 791, 770, 744, 725, 649, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_4S$: 370.0987; found: 370.0991.



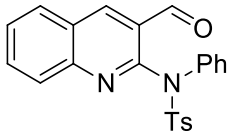
Compound **3ad**: Yield 81 %, colourless soild, mp: 168-169 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.09 (s, 1 H), 8.73 (s, 1 H), 8.00-7.88 (m, 2 H), 7.84-7.75 (m, 1 H), 7.60-7.52 (m, 1 H), 4.65 (t, *J* = 7.5 Hz, 2 H), 4.52 (t, *J* = 7.5 Hz, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 187.1 (d), 157.4 (s), 148.6 (s), 148.0 (s), 139.9 (d), 132.6 (d), 129.4 (d), 128.2 (d), 126.9 (d), 126.0 (s), 123.3 (s), 63.4 (t), 44.9 (t) ppm; IR (ATR): $\tilde{\nu}$ = 2910, 1745, 1686, 1618, 1590, 1497, 1468, 1425, 1384, 1340, 1298, 1266, 1248, 1211, 1197, 1155, 1144, 1133, 1102, 1030, 1002, 967, 913, 864, 819, 784, 768, 752, 735, 699, 644, 622 cm^{-1}; HRMS (EI) m/z calcd for $C_{13}H_{10}N_2O_3$: 242.0691; found: 242.0687.



Compound **3ae**: Yield 95 %, yellow soild, mp: 213-214 ^{o}C; ^{1}H NMR (300 MHz, d^{6}-DMSO) δ = 9.94 (s, 1 H), 9.27 (s, 1 H), 8.86 (s, 1 H), 8.43-8.30 (m, 2 H), 8.18-8.12 (m, 1 H), 8.09-8.01 (m, 1 H), 7.87-7.81 (m, 1 H), 7.62-7.56 (m, 1 H), 7.36-7.28 (m, 2 H), 2.55 (s, 3 H) ppm; ^{13}C NMR (125 MHz, d^{6}-DMSO) δ = 193.9 (s), 189.2 (d), 148.7 (s), 148.5 (s), 143.6 (d), 138.2 (d), 137.8 (s), 134.3 (d), 130.5 (d), 128.8 (d, 2 C), 127.2 (s), 126.5 (s), 124.8 (s), 124.6 (d), 123.7 (d), 122.3 (d), 118.9 (s), 112.5 (d), 28.0 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3108, 3053, 2884, 1691, 1645, 1617, 1584, 1526, 1496, 1451, 1432, 1402, 1375, 1332, 1295, 1263, 1232, 1197, 1160, 1118, 1101, 1029, 1015, 964, 927, 914, 857, 822, 785, 751, 739, 716, 703, 656, 642, 623 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{14}N_2O_2$: 314.1055; found: 314.1057.

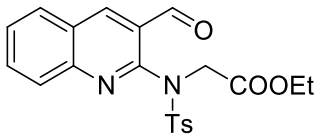


Compound **3af**: Yield 78 %, colourless soild, mp: 155-156 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.64 (s, 1 H), 8.91 (s, 1 H), 8.29 (d, *J* = 9.0 Hz, 2 H), 8.08-8.03 (m, 1 H), 7.87-7.78 (m, 2 H), 7.75 (d, *J* = 9.0 Hz, 2 H), 7.71-7.66 (m, 1 H), 3.82 (d, *J* = 7.5 Hz, 2 H), 1.49-1.40 (m, 2 H), 1.37-1.28 (m, 2 H), 0.85 (t, *J* = 7.5 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 188.7 (d), 151.2 (s), 150.4 (s), 148.7 (s), 142.6 (s), 139.2 (d), 132.9 (d), 129.7 (d, 2 C), 129.6 (d), 128.7 (s), 128.6 (d), 128.5 (d), 126.9 (s), 123.9 (d, 2 C), 49.7 (t), 30.2 (t), 20.0 (t), 13.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3112, 3061, 2933, 2875, 1693, 1618, 1583, 1529, 1496, 1461, 1447, 1423, 1349, 1311, 1256, 1229, 1196, 1167, 1158, 1105, 1086, 1066, 1037, 1010, 970, 920, 901, 871, 856, 796, 757, 735, 683, 648, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{20}H_{19}N_2O_5S$: 413.1045; found: 413.1044.

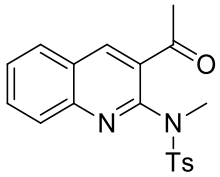


Compound **3ag**: Yield 90 %, colourless soild, mp: 176-177 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.52 (s, 1 H), 8.57 (s, 1 H), 7.80-7.75 (m, 2 H), 7.68-7.63 (m, 1 H), 7.48-7.42 (m, 3 H), 7.30-7.25 (m, 2 H), 7.13-7.06 (m, 5 H), 2.27 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 189.2 (d), 152.9 (s), 148.8 (s), 144.1 (s), 139.9 (d), 139.7 (s), 135.6 (s), 132.7 (d), 129.5 (d), 129.4 (d, 2 C), 129.3 (d, 2 C), 129.04 (d), 129.02 (d, 2 C), 128.9 (d, 2 C), 128.4 (d), 128.2 (d), 127.0 (s), 126.9 (s), 21.7 (q) ppm;

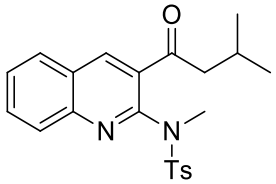
IR (ATR): $\tilde{\nu}$ = 3066, 2968, 2926, 2869, 1738, 1694, 1617, 1585, 1493, 1455, 1420, 1354, 1261, 1214, 1185, 1163, 1104, 1090, 1030, 966, 936, 910, 813, 796, 756, 696, 675, 627, 612 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{18}N_2O_3S$: 402.1038; found: 402.1039.



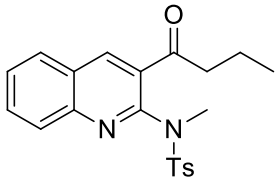
Compound **3ah**: Yield 85 %, colorless oil, mp: 116-117 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.75 (s, 1 H), 8.87 (s, 1 H), 8.04-7.98 (m, 1 H), 7.82-7.74 (m, 2 H), 7.66-7.60 (m, 1 H), 7.37 (d, *J* = 8.5 Hz, 2 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 4.64 (s, 2 H), 4.04 (q, *J* = 7.0 Hz, 2 H), 2.42 (s, 3 H), 1.11 (t, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 189.7 (d), 168.0 (s), 151.9 (s), 148.3 (s), 144.7 (s), 138.6 (d), 133.4 (s), 132.2 (d), 129.7 (d, 2 C), 129.5 (d), 128.6 (d), 128.5 (s), 128.2 (d, 2 C), 127.9 (d), 126.9 (s), 61.6 (t), 50.2 (t), 21.7 (q), 14.0 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2968, 2926, 1751, 1732, 1690, 1618, 1587, 1496, 1458, 1423, 1374, 1346, 1308, 1270, 1196, 1162, 1119, 1089, 1029, 965, 935, 919, 884, 808, 783, 759, 740, 706, 675, 624 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{20}N_2O_5S$: 412.1093; found: 412.1097.



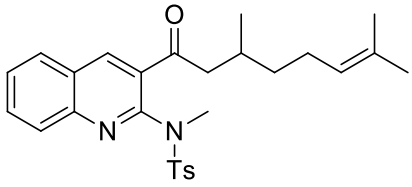
Compound **3ai**: Yield 65 %, colourless solid, mp: 137-138 ^{o}C;; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.53 (s, 1 H), 7.95-7.91 (m, 1 H), 7.82-7.78 (m, 1 H), 7.76-7.71 (m, 1 H), 7.61-7.56 (m, 1 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 8.0 Hz, 2 H), 3.33 (s, 3 H), 2.83 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 199.2 (s), 150.2 (s), 147.3 (s), 144.1 (s), 138.8 (d), 133.1 (s), 132.8 (s), 131.4 (d), 129.4 (d, 2 C), 128.6 (d), 128.5 (d), 128.4 (d, 2 C), 127.5 (d), 126.5 (s), 36.5 (q), 29.6 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3062, 2942, 2874, 1737, 1694, 1619, 1586, 1531, 1492, 1456, 1427, 1402, 1376, 1349, 1264, 1202, 1159, 1130, 1088, 1020, 962, 922, 848, 814, 793, 761, 738, 707, 685, 660, 620 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{18}rN_2O_3S$: 354.1038; found: 354.1028.



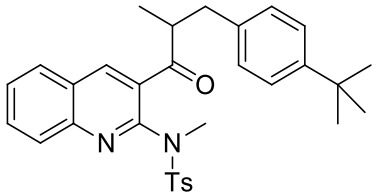
Compound **3aj**: Yield 71 %, colorless oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.45 (s, 1 H), 7.94-7.87 (m, 1 H), 7.83-7.77 (m, 1 H), 7.76-7.67 (m, 1 H), 7.62-7.54 (m, 1 H), 7.37 (d, *J* = 8.4 Hz, 2 H), 7.18 (d, *J* = 8.1 Hz, 2 H), 3.32 (s, 3 H), 3.12 (d, *J* = 6.9 Hz, 2 H), 2.38 (s, 3 H), 2.33-2.19 (m, 1 H), 1.00 (t, *J* = 6.9 Hz, 6 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 201.9 (s), 150.2 (s), 147.1 (s), 144.0 (s), 138.5 (d), 133.7 (s), 133.1 (s), 131.2 (d), 129.3 (d, 2 C), 128.47 (d, 3 C), 128.45 (d), 127.5 (d), 126.6 (s), 50.6 (t), 36.7 (q), 25.2 (d), 22.7 (q, 2 C), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3063, 2959, 2931, 2872, 1690, 1618, 1584, 1564, 1490, 1456, 1424, 1401, 1376, 1353, 1306, 1263, 1186, 1159, 1121, 1087, 1057, 985, 920, 865, 812, 778, 760, 706, 676, 639, 609 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{24}N_2O_3S$: 396.1508; found: 396.1500.



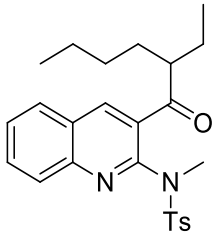
Compound **3ak**: Yield 71 %, colourless solid, mp: 88-89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.45 (s, 1 H), 7.94-7.90 (m, 1 H), 7.83-7.78 (m, 1 H), 7.75-7.70 (m, 1 H), 7.62-7.56 (m, 1 H), 7.38 (d, *J* = 8.0 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 3.32 (s, 3 H), 3.19 (t, *J* = 7.0 Hz, 2 H), 2.40 (s, 3 H), 1.85-1.75 (m, 2 H), 1.02 (t, *J* = 7 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 202.3 (s), 150.1 (s), 147.1 (s), 144.0 (s), 138.5 (d), 133.5 (s), 133.0 (s), 131.2 (d), 129.3 (d, 2 C), 128.5 (d), 128.47 (d, 2 C), 128.45 (d), 127.5 (d), 126.6 (s), 43.6 (t), 36.7 (q), 21.6 (q), 18.0 (t), 13.9 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3057, 2981, 2956, 2928, 2872, 1738, 1690, 1618, 1586, 1567, 1491, 1454, 1421, 1400, 1377, 1342, 1305, 1290, 1258, 1186, 1157, 1125, 1086, 1060, 991, 944, 917, 900, 838, 816, 796, 768, 742, 707, 673, 642, 615 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{22}N_2O_3S$: 382.1351; found: 382.1292.



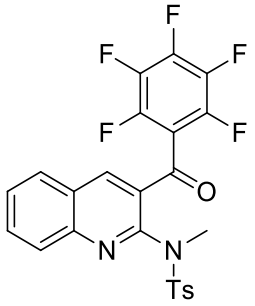
Compound **3al**: Yield 52 %, colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.45 (s, 1 H), 7.95-7.90 (m, 1 H), 7.82-7.78 (m, 1 H), 7.75-7.70 (m, 1 H), 7.61-7.56 (m, 1 H), 7.36 (d, *J* = 8.0 Hz, 2 H), 7.18 (d, *J* = 8.5 Hz, 2 H), 5.07-5.01 (m, 1 H), 3.31-3.23 (m, 4 H), 3.09-3.01 (m, 1 H), 2.39 (s, 3 H), 2.14-2.05 (m, 1 H), 2.03-1.94 (m, 2 H), 1.61 (s, 3 H), 1.56 (s, 3 H), 1.46-1.36 (m, 1 H), 1.30-1.21 (m, 1 H), 0.97 (d, *J* = 6.5 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 202.1 (s), 150.2 (s), 147.1 (s), 144.0 (s), 138.7 (d), 133.7 (s), 132.9 (s), 131.5 (s), 131.2 (d), 129.3 (d, 2 C), 128.5 (d, 4 C), 127.5 (d), 126.6 (s), 124.4 (d), 49.2 (t), 37.1 (t), 36.7 (q), 29.5 (q), 25.7 (d), 25.5 (t), 21.6 (q), 19.8 (q), 17.7 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3063, 2959, 2925, 2873, 2855, 1918, 1692, 1618, 1585, 1566, 1491, 1454, 1427, 1402, 1376, 1355, 1307, 1264, 1188, 1161, 1123, 1088, 1060, 1019, 996, 921, 846, 814, 793, 778, 760, 706, 678, 611 cm^{-1}; HRMS (EI) m/z calcd for $C_{27}H_{32}N_2O_3S$: 464.2134; found: 464.2145.



Compound **3am**: Yield 58 %, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.22 (s, 1 H), 7.85-7.80 (m, 1 H), 7.77-7.65 (m, 2 H), 7.57-7.51 (m, 1 H), 7.38-7.32 (m, 2 H), 7.20-7.05 (m, 6 H), 4.18-4.09 (m, 1 H), 3.30 (s, 3 H), 3.10-3.00 (m, 1 H), 2.81-2.71 (m, 1 H), 2.38 (s, 3 H), 1.33 (d, *J* = 6.6 Hz, 3 H), 1.15 (s, 9 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 206.2 (s), 149.9 (s), 148.8 (s), 147.0 (s), 144.0 (s), 139.6 (d), 136.6 (s), 133.0 (s), 132.8 (s), 131.1 (d), 129.3 (d, 2 C), 128.8 (d, 2 C), 128.48 (s), 128.47 (d, 2 C), 128.4 (d), 127.3 (d), 126.5 (s), 125.0 (d, 2 C), 46.1 (d), 40.1(t), 36.7 (q), 34.2 (s), 31.2 (q, 3 C), 21.6 (q), 17.0 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3059, 3026, 2963, 2870, 1800, 1692, 1618, 1585, 1563, 1510, 1491, 1460, 1424, 1401, 1376, 1354, 1306, 1267, 1187, 1159, 1120, 1088, 1053, 969, 921, 814, 797, 777, 760, 736, 706, 678, 638, 609 cm^{-1}; HRMS (EI) m/z calcd for $C_{31}H_{34}N_2O_3S$: 514.2290; found: 514.2297.

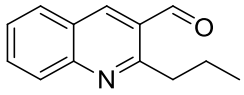


Compound **3an**: Yield 50 %, colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.45 (s, 1 H), 7.95-7.91 (m, 1 H), 7.81-7.77 (m, 1 H), 7.75-7.70 (m, 1 H), 7.62-7.56 (m, 1 H), 7.40 (d, *J* = 8.5 Hz, 2 H), 7.20 (d, *J* = 8.5 Hz, 2 H), 3.77-3.71 (m, 1 H), 3.30 (s, 3 H), 2.41 (s, 3 H), 1.87-1.76 (m, 2 H), 1.59-1.44 (m, 2 H), 1.36-1.23 (m, 4 H), 0.94 (t, *J* = 7.5 Hz, 3 H), 0.86 (t, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.4 (s), 150.2 (s), 147.1 (s), 143.9 (s), 139.5 (d), 133.5 (s), 133.1 (s), 131.2 (d), 129.3 (d, 2 C), 128.7 (d, 2 C), 128.5 (d), 128.4 (d), 127.5 (d), 126.8 (s), 50.4 (d), 37.1 (q), 30.0 (t), 29.3 (t), 23.7 (t), 22.9 (t), 21.6 (q), 14.0 (q), 11.4 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3063, 2959, 2931, 2872, 1691, 1618, 1597, 1584, 1564, 1491, 1457, 1424, 1401, 1376, 1354, 1307, 1264, 1186, 1160, 1121, 1088, 1057, 1018, 985, 962, 920, 865, 812, 778, 760, 706, 677, 693, 609 cm^{-1}; HRMS (EI) m/z calcd for $C_{25}H_{30}N_2O_3S$: 438.1977; found: 438.1966.

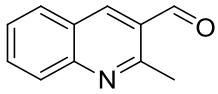


Compound **3ao**: Yield 68 %, yellow soild, mp: 191-192 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.84 (s, 1 H), 8.05-8.02 (m, 1 H), 7.87-7.84 (m, 1 H), 7.84-7.78 (m, 1 H), 7.67-7.63 (m, 1 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 7.16 (d, *J* = 8.5 Hz, 2 H), 3.09 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 183.0 (s), 150.3 (s), 147.9 (s), 145.6 (dm, J_f = 253.7 Hz, s, 2 C), 144.5 (s), 143.1 (dm, J_f = 255.0 Hz, s), 141.3 (d), 137.7 (dm, J_f = 231.6 Hz, s, 2 C), 132.4 (d), 131.9 (s), 130.8 (s), 129.5 (d, 2 C), 129.1 (d), 128.6 (d), 128.3 (d, 2C), 127.8 (d), 126.5 (s), 114.7(s), 35.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3422, 3336, 3065, 2947, 2930, 1680, 1652, 1618, 1586, 1523, 1498, 1457, 1427, 1404, 1377, 1353, 1310, 1266, 1194, 1160, 1131, 1106, 1088, 1056, 994, 921, 860, 815, 792, 781, 759, 737, 706, 672, 615 cm^{-1}; HRMS (ESI) m/z calcd for

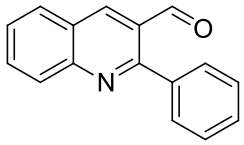
$C_{24}H_{15}F_5N_2O_3S$ $[M+Na]^+$: 529.0616; found: 529.0621.



Compound **5a**: Yield 70 %, yellow soild, mp: 63-64 ^oC; ^1H NMR (300 MHz,$CDCl_3$) δ = 10.37 (s, 1 H), 8.58 (s, 1 H), 8.11-8.03 (m, 1 H), 7.94-7.87 (m, 1 H), 7.85-7.76 (m, 1 H), 7.60-7.50 (m, 1 H), 3.37-3.26 (m, 2 H), 1.91-1.73 (m, 2 H), 1.05 (t, *J* = 7.2 Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.1 (d), 162.2 (s), 149.3 (s), 142.1 (d), 132.6 (d), 129.1 (d), 128.9 (d), 127.6 (s), 126.9 (d), 126.1 (s), 38.2 (t), 23.6 (t), 14.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2957, 2930, 2899, 2873, 2741, 1694, 1619, 1597, 1558, 1491, 1467, 1455, 1428, 1415, 1375, 1341, 1217, 1185, 1154, 1110, 961, 916, 869, 842,784, 762, 751 cm^{-1}; HRMS (EI) m/z calcd for $C_{13}H_{13}NO$: 199.0997; found: 199.0992.

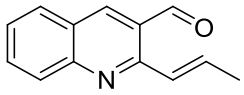


Compound **5b**: Yield 67 %, yellow soild, mp: 78-79 ^oC; ^1H NMR (500 MHz,$CDCl_3$) δ = 10.38 (s, 1 H), 8.61 (s, 1 H), 8.14-8.06 (m, 1 H), 7.98-7.92 (m, 1 H), 7.88-7.82 (m, 1 H), 7.63-7.56 (m, 1 H), 3.05 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.3 (d), 158.3 (s), 149.2 (s), 142.5 (d), 132.7 (d), 129.0 (d), 128.7 (d), 128.0 (s), 127.0 (d), 126.1 (s), 23.9 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 2853, 2755, 1698, 1647, 1619, 1593, 1560, 1492, 1421, 1372, 1340, 1282, 1253, 1232, 1157, 1111, 1032, 1006, 970, 929, 904, 876, 811, 788, 759, 670, 625 cm^{-1}; HRMS (EI) m/z calcd for $C_{11}H_9NO$: 171.0684; found: 171.0680.

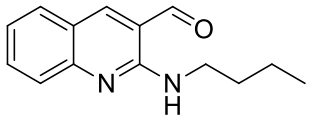


Compound **5c**: Yield 66 %, yellow soild, mp: 117-118 ^oC; ^1H NMR (500 MHz,$CDCl_3$) δ = 10.17 (s, 1 H), 8.84 (s, 1 H), 8.25-8.19 (m, 1 H), 8.03-7.98 (m, 1 H), 7.90-7.84 (m, 1 H), 7.72-7.66 (m, 2 H), 7.65-7.60 (m, 1 H), 7.59-7.50 (m, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 191.5 (d), 160.3 (s), 149.5 (s), 138.3 (d), 137.7 (s), 132.7 (d), 130.3 (d, 2 C), 129.6 (d), 129.51 (d), 129.49 (d), 128.8 (d, 2 C), 127.7 (s), 127.6 (d), 126.4 (s) ppm; IR (ATR): $\tilde{\nu}$ = 3054, 2864, 1692, 1615, 1584, 1555, 1486, 1455, 1444, 1423,

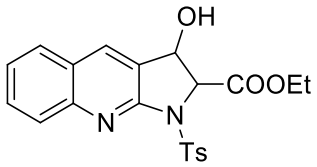
1371, 1270, 1200, 1157, 1123, 1076, 1038, 1019, 1009, 964, 934, 916, 868, 822, 796, 774, 753, 711, 679, 614 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{11}NO$: 233.0841; found: 233.0828.



Compound **5d**: Yield 48 %, yellow soild, mp: 60-61 ^{o}C; ^{1}H NMR (500 MHz,$CDCl_3$) δ = 10.40 (s, 1 H), 8.58 (s, 1 H), 8.12-8.05 (m, 1 H), 7.93-7.88 (m, 1 H), 7.85-7.78 (m, 1 H), 7.58-7.52 (m, 1 H), 7.51-7.44 (m, 1 H), 7.19-7.09 (m, 1 H), 2.10-2.03 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 191.4 (d), 155.1 (s), 149.5 (s), 142.3 (d), 137.3 (d), 132.7 (d), 129.2 (d), 129.0 (d), 127.1 (d), 126.9 (d), 126.6 (s), 126.2 (s), 19.0 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2911, 1771, 1694, 1652, 1617, 1588, 1553, 1491, 1426, 1403, 1370, 1326, 1249, 1186, 1153, 1108, 1019, 959, 911, 871, 854, 779, 756, 697, 634, 615 cm^{-1}; HRMS (EI) m/z calcd for $C_{13}H_{11}NO$: 197.0841; found: 197.0842.

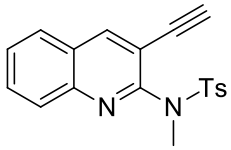


Compound **6**: Yield 71 %, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.95 (s, 1 H), 8.18 (s, 1 H), 7.99 (brs, 1 H), 7.71-7.58 (m, 3 H), 7.23-7.14 (m, 1 H), 3.70-3.60 (m, 2 H), 1.77-1.63 (m, 2 H), 1.56-1.41 (m, 2 H), 0.99 (t, *J* = 7.2 Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.1 (d), 154.9 (s), 151.3 (s), 148.6 (d), 133.5 (d), 129.2 (d), 126.5 (d), 122.3 (d), 121.8 (s), 117.4 (s), 40.4 (t), 31.5 (t), 20.4 (t), 13.9 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3364, 3057, 2957, 2929, 2871, 2860, 2724, 1673, 1622, 1604, 1571, 1538, 1467, 1399, 1374, 1355, 1323, 1271, 1222, 1162, 1143, 1124, 1077, 952, 915, 856, 754, 728 cm^{-1}; HRMS (EI) m/z calcd for $C_{14}H_{16}N_2O$: 228.1263; found: 228.1257.

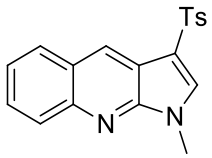


Compound **7**: Yield 95 %, colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.13-8.04 (m, 2 H), 7.83-7.73 (m, 2 H), 7.54-7.40 (m, 2 H), 7.27-7.11 (m, 3 H), 5.15 (s, 1 H), 4.98-4.93 (m, 1 H), 4.19-4.04 (m, 2 H), 3.99-3.85 (m, 1 H), 2.24 (s, 3 H), 1.15 (t, *J* =

7.2 Hz, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.7 (s), 153.6 (s), 147.9 (s), 144.6 (s), 135.6 (s), 134.6 (d), 130.1 (d), 129.1 (d, 2 C), 129.0 (d, 2 C), 128.2 (d), 128.1 (d), 125.2 (s), 124.8 (d), 124.3 (s), 71.6 (d), 70.3 (d), 62.2 (t), 21.6 (q), 14.0 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3486, 3066, 2983, 2927, 2254, 1748, 1633, 1597, 1584, 1511, 1494, 1470, 1413, 1354, 1322, 1198, 1169, 1121, 1094, 1054, 1024, 960, 915, 865, 831, 813, 798, 757, 731, 703, 666, 621 cm^{-1}; HRMS (EI) m/z calcd for $C_{21}H_{20}N_2O_5S$: 412.1093; found: 412.1080.

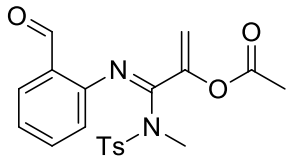


Compound **8**: Yield 90 %, yellow solid; mp: 124-125 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.40 (s, 1 H), 7.89-7.76 (m, 4 H), 7.74-7.66 (m, 1 H), 7.60-7.52 (m, 1 H), 7.36-7.28 (m, 2 H), 3.47 (s, 1 H), 3.26 (s, 3 H), 2.46 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.9 (s), 145.9 (s), 143.7 (s), 143.1 (d), 135.0 (s), 130.7 (d), 129.2 (d, 2 C), 129.0 (d, 2 C), 128.8 (d), 127.7 (d), 127.2 (d), 126.6 (s), 116.6 (s), 83.4 (d), 79.4 (s), 37.2 (q), 21.7 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3266, 2925, 1618, 1599, 1586, 1564, 1489, 1458, 1445, 1422, 1401, 1370, 1348, 1302, 1264, 1186, 1162, 1152, 1121, 1088, 1048, 958, 917, 864, 808, 793, 778, 753, 706, 692, 664, 631, 619 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{16}N_2O_2S$: 336.0932; found: 336.0918.



Compound **9**: Yield 70 %, yellow solid; mp: 148-149 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.71 (s, 1 H), 8.12-8.07 (m, 2 H), 8.03-7.92 (m, 3 H), 7.74-7.66 (m, 1 H), 7.53-7.46 (m, 1 H), 7.31-7.24 (m, 2 H), 4.01 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 148.9 (s), 145.6 (s), 143.7 (s), 140.2 (s), 137.8 (d), 129.8 (d, 2 C), 129.2 (d), 128.6 (d), 128.1 (d), 127.7 (d), 126.7 (d, 2 C), 125.3 (s), 124.4 (d), 117.3 (s), 113.4 (s), 32.2 (q), 21.6 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3121, 3068, 2952, 2924, 2855, 1620, 1596, 1572, 1528, 1500, 1478, 1433, 1389, 1363, 1337, 1301, 1290, 1261, 1177, 1137, 1120, 1083, 1052, 1021, 938, 903, 871, 843, 813, 787, 768, 737, 706, 669, 648 cm^{-1}; HRMS (EI) m/z calcd for $C_{19}H_{16}N_2O_2S$: 336.0932; found:

336.0928.



Compound **10**: Yield 67 %, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.65 (s, 1 H), 7.94-7.70 (m, 3 H), 7.50-7.40 (m, 1 H), 7.37-7.27 (m, 2 H), 7.21-7.10 (m, 1 H), 6.85-6.76 (m, 1 H), 5.46-5.30 (m, 2 H), 3.22 (s, 3 H), 2.44 (s, 3 H), 1.75 (s, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 190.6 (d), 168.2 (s), 150.2 (s), 144.6 (s), 135.0 (d), 134.7 (s), 129.5 (d, 3 C), 128.4 (d), 127.7 (d, 2 C), 126.1 (s), 124.2 (d), 119.6 (d, 2 C), 112.5 (t), 36.3 (q), 21.6 (q), 20.0 (q) ppm; IR (reflection): $\tilde{\nu}$ = 3267, 3066, 3031, 2926, 2855, 2750, 1761, 1687, 1665, 1625, 1592, 1524, 1495, 1453, 1401, 1358, 1320, 1275, 1203, 1170, 1120, 1091, 1063, 1021, 971, 923, 816, 777, 706, 671, 610 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{20}H_{20}N_2O_5S+H]^+$: 401.1166; found: 401.1165.

[1] T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833-835.

[2] K. A. DeKorver, R. P. Hsung, A. G. Lohse, Y. Zhang, *Org. Lett.* **2010**, *12*, 1840-1843

[3] D. A. Rooke, E. M. Ferreira, *Angew. Chem. Int. Ed.* **2012**, *51*, 3225-3230; *Angew. Chem*. **2012**, 124, 3279-3284.

[4] K. Graf, C. L. Rühl, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 12727-12731; *Angew. Chem*. **2013**, *125*, 12960-12964.

[5] J. Chauhana, S. Fletcher, *Tetrahedron Lett*. **2012**, *53*, 4951-4954.

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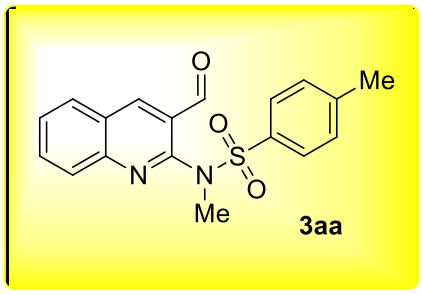
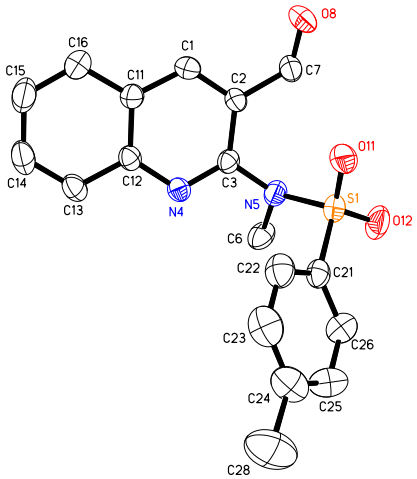
X-Ray Crystal Structure Analyses

The crystallographic data (CCDC) can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.





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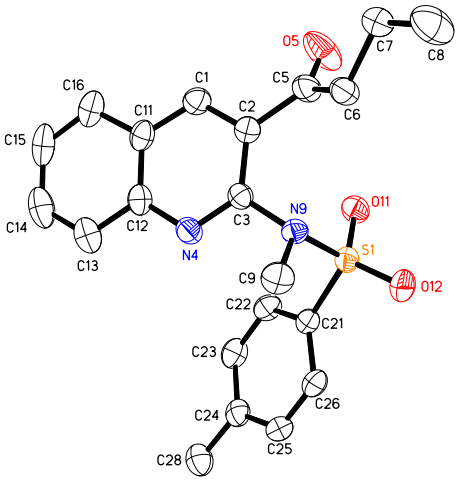

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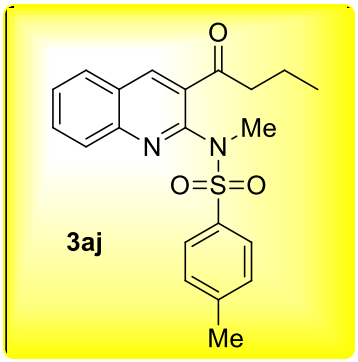


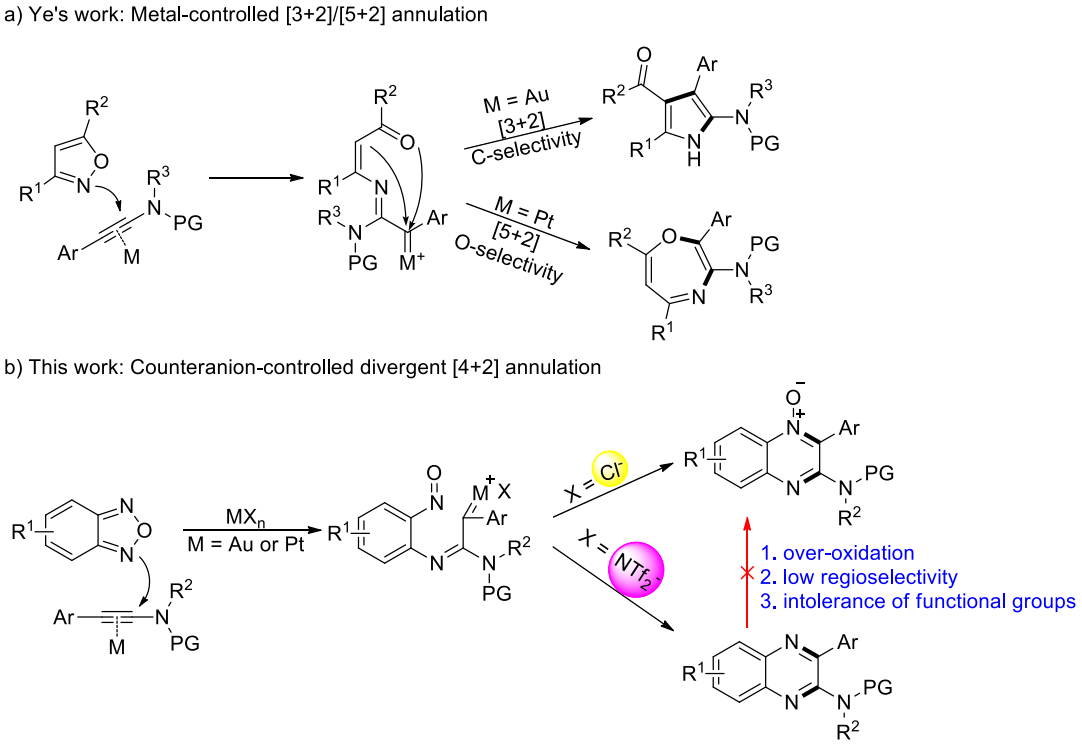
Chapter 4: Counteranion-Directed Divergent [4+2] Annulation of Benzofurazans with Ynamides by Gold and Platinum Catalysis: Switchable Access to Quinoxaline *N*-Oxides/ Quinoxalines

4.1 Introduction

Quinoxaline *N*-oxides and quinoxalines are of great significance owning to their important biological properties, including antiinflammatory, antimicrobial and antitumoral activities. This created increasing attentions from the synthetic community.[1] The condensation of o-phenylenediamine with aldehydes/ketones is the prevalent entry to quinoxalines, despite regioselectivity frustration.[2] Various oxidation approaches toward quinoxaline *N*-oxides from the corresponding quinoxalines also exist.[3] However, the specific synthesis of quinoxaline mono-*N*-oxide is still a challenge due to easy over-oxidations, low regioselectivity between both nitrogen atoms and limited tolerance of functional groups. Moreover, these linear synthetic strategies are usually accompanied with low atom-economy and low yields. Thus, the exploration of versatile protocols for the convergent assembly of functionalized quinoxaline mono-*N*-oxides[4a] and quinoxalines[4b-e] remains highly desirable.

Catalytic alkyne activation by π acids, especially gold and platinum, had immense impact on synthetic chemistry, greatly promoting the facile and flexible construction of intricate heterocyclic scaffolds.[5] In recent years, α-imino gold carbene-mediated intramolecular transfer of nitrene to alkynes enabled novel and atom-economical accesses to diverse aza-heterocycles.[6-11] For instance, our group contributed gold-catalyzed formal [3+2] and [4+2] cycloadditions of alkynes with anthranils toward the 7-acylindole and 2-aminoquinoline skeleton respectively.[10] A concise route to 2-aminopyroles through gold-catalyzed [3+2] annulation of ynamides with isoxazoles as nitrene equivalent was reported by Ye and co-workers.[11a] Divergent to gold catalysis, α-imino platinum carbenoids turned out to be more oxophilic giving rise to a [5+2] annulation strategy (Scheme 1, a).[12]

In most gold and platinum-catalyzed transformations, the counteranion is generally considered as an accelerating factor and the counteranion effect on the reaction selectivity or the catalyst structure is less focused.[13] Herein we presented Au/Pt-catalyzed counteranion-directed selective syntheses of quinoxaline *N*-oxides and quinoxalines. Benzofurazan was selected as a new nucleophilic "nitrenoid" as potential α-imino metal carbenoid precursor. Despite its commercial availability and wide existence in medical molecules,[14] the chemistry of this compound is rare. In contrast to isoxazole as reactant, both gold and platinum carbenes, generated from the reaction of ynamide with benzofurazan, triggered the same [4+2] annulation without a chemoselective divergence. Nevertheless, the choice of the counteranion had the crucial influence on switching access to different products. While the deoxidized product quinoxaline resulted from the bulky NTf_2^- anion, chloride as counterion led to quinoxaline mono-*N*-oxide as the major product (Scheme 1, b). Further, counteranion-induced alternative cyclization processes were indicated by mechanistic investigations.



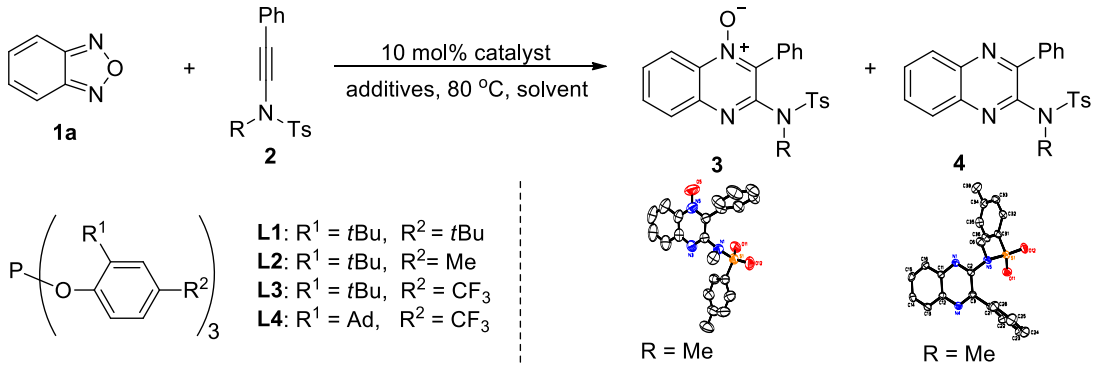
Scheme 1. Switchable access to aza-heterocyclic compounds.

4.2 Results and Discussion

4.2.1 Optimization of the Reaction Conditions

We initially surveyed the reaction of 2 equiv. benzofurazan **1a** and ynamide **2a** (R = Me) with 10 mol % $PtCl_2$ in PhMe at 80 ^oC for 24 h (Table 1, entry 1). The products **3a** and **4a** were obtained in 30 % and 13 % respectively. Both solid state molecular structures were determined by single-crystal X-ray diffraction.[15a] In order to increase the selectivity, various ligands and anions were examined (entry 2-9). $PtCl_2$ in combination with highly hindered phosphite ligand **L4** gave the best result with 80 % yield of **3a** and 12 % yield of **4a** (entry 8), whereas PtI_2 delivered low yield and selectivity (entry 9). To our delight, the transformation of benzofurazan **1a** with ynamide **2b** (R = Bn) specifically produced **3a** in 83 % yield with **L4** as ligand (entry 10). Taking advantage of AuCl/**L4** or $AuCl_3$ also afforded the excellent selectivity, albeit in lower yield (entry 11, 13). The yield of **3a** could be raised to 79 % by AuCl without any ligand (entry 12). In contrast, 10 mol% $AgNTf_2$ as additive reversed the product selectivity, favoring the quinoxaline product. Under these conditions 1,2-DCE performed better in yield than toluene (entry 14). Based on this result, we chose the reaction of 4 equiv. benzofurazan **1a** and ynamide **2a** in 1,2-DCE as model system to optimize the catalyst (entry 15-22). Among gold and platinum catalysts, **L1**AuCl/$AgNTf_2$ showed higher catalytic activity and selectivity, delivering **4a** in 67 % yield (entry 18). Besides of NTf_2^-, the other bulky anion SbF_6^- also offered good selectivity of **4a** although with moderate yield (entry 19). The control experiment demonstrated the catalytic capacity of gold and platinum (entry 23). Moreover, the absence of silver salt has a slightly negative impact on the selectivity (entry 24). Finally, $PtCl_2$/**L4** qualified for the syntheses of quinoxaline *N*-oxides, while quinoxalines were favorably prepared with the **L1**AuCl/$AgNTf_2$ catalyst system.

Table 1. Reaction optimization[a, b, c]



Entry	10 mol% Catalyst	R	Additive	Yield of 3	Yield of 4
1[a]	$PtCl_2$	Me	—	30 %	13 %
2[a]	$Pt(COD)Cl_2$	Me	—	40 %	23 %
3[a]	$PtCl_2$	Me	1 atm. CO	45 %	28 %
4[a]	$PtCl_2$	Me	10 mol% $P(C_6F_5)_3$	38 %	25 %
5[a]	$PtCl_2$	Me	10 mol% L1	50 %	13 %
6[a]	$PtCl_2$	Me	10 mol% L2	55 %	15 %
7[a]	$PtCl_2$	Me	10 mol% L3	70 %	18 %
8[a]	$PtCl_2$	Me	10 mol% L4	80 %	12 %
9[a]	PtI_2	Me	10 mol% L4	35 %	10 %
10[a]	$PtCl_2$	Bn	10 mol% L4	83 %	< 5 %
11[a]	AuCl	Bn	10 mol% L4	48 %	< 5 %
12[a]	AuCl	Bn	—	79 %	13 %
13[a]	$AuCl_3$	Bn	—	50 %	<5 %
14[a]	AuCl	Bn	10 mol% $AgNTf_2$	8 % (10 %)[b]	34 % (41 %)[b]
15[b]	IPrAuCl	Me	10 mol% $AgNTf_2$	12 %	43 %
16[b]	*t*BuXPhosAuCl	Me	10 mol% $AgNTf_2$	10 %	54 %
17[b]	**L4**AuCl	Me	10 mol% $AgNTf_2$	< 5 %	51 %
18[b]	**L1**AuCl	Me	10 mol% $AgNTf_2$	< 5 %	67 %
19[b]	**L1**AuCl	Me	10 mol% $AgSbF_6$	8 %	43 %
20[b]	$PtCl_2$	Me	20 mol% $AgNTf_2$	< 5 %	41 %
21[b]	$Pt(COD)Cl_2$	Me	20 mol% $AgNTf_2$	< 5 %	38 %
22[b]	$Pt(\mathbf{L1})_2Cl_2$	Me	20 mol% $AgNTf_2$	< 5 %	49 %

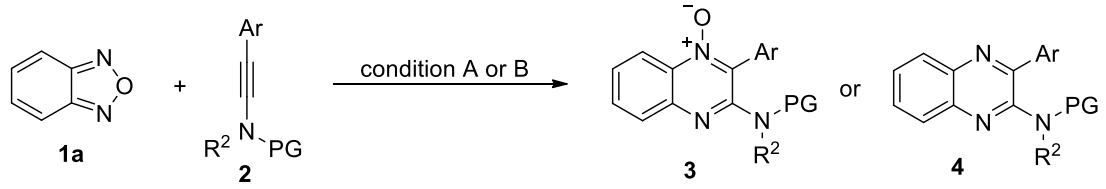
23[b]	$AgNTf_2$	Me	—	< 5 %	23 %
24[b]	**L1**$AuNTf_2$	Me	—	12 %	51 %

[a] **1a** (0.2 mmol) and **2** (0.1 mmol) in toluene at 80 ^oC for 24 h. [b] **1a** (0.4 mmol) and **2** (0.1 mmol) in 1,2-DCE at 80 ^oC for 24 h. [c] isolated yield.

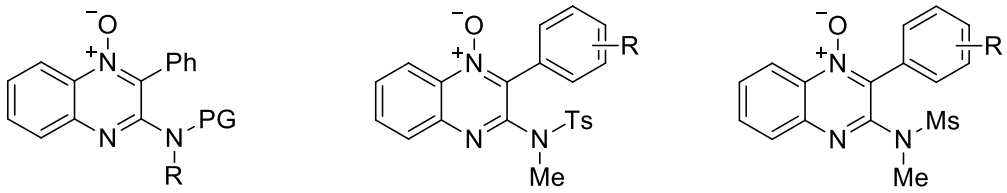
4.2.2 Scope and Limitation

Under the optimized reaction conditions, we began to evaluate the scope of ynamides (Table 2). First the treatment of diverse ynamides with benzofurazan **1a** was conducted under condition A. A broad set of protecting groups and substituents at the R^2-position were checked (**3a-f**). Ms, Bs and the easily removable nosyl group were well tolerated. Benzyl substituted ynamides provided higher yield than methyl. Then, our attention was turned to variations on the aryl moiety of the ynamide. A wide range of functional groups, including trifluoromethyl (**3i**), fluoride (**3h**, **3s**), bromide (**3l**, **3n**), ester (**3m**) and methoxyl moieties (**3o**, **3q**), were all compatible, delivering the corresponding functionalized quinoxaline *N*-oxides in good to excellent yields. Naphthyl, heterocyclic and even alkenyl substituted ynamides also proceeded smoothly (**3r**, **3t-v**). Subsequently, the generality of ynamides was also examined under condition B (**4a-m**). A range of substituted quinoxalines was also successfully prepared in moderate to good yields with fine tolerance of functional groups.

Table 2. Scope of ynamides[a, b]

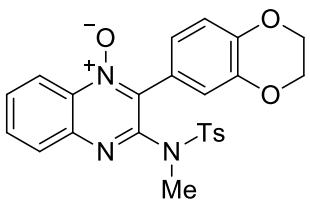


Condition A ($PtCl_2$/**L4**):

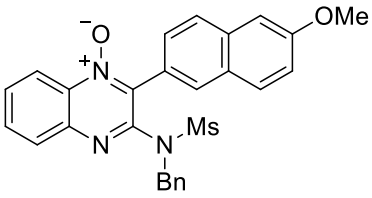


3a, PG = Ts, R = Me, 80 % **3g**, R = 4-Me, 70 %

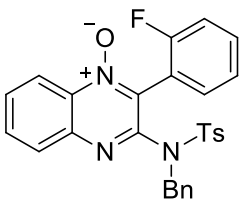
3b, PG = Ts, R = Bn, 83 %
3c, PG = Ms, R = Me, 70 %
3d, PG = Ms, R = PMB, 95 %
3e, PG = Bs, R = PMB, 80 %
3f, PG = Ns, R = *n*-Bu, 94 %
3h, R = 4-F, 78 %
3i, R = 4-CF_3, 50 %
3j, R = 4-*t*Bu, 78 %
3k, R = 3-Cl, 59 %
3l, R = 2-Br, 42 %
3m, R = 4-COOMe, 54 %
3n, R = 4-Br, 70 %
3o, R = 4-MeO, 50 %
3p, R = 4-Ph, 65 %



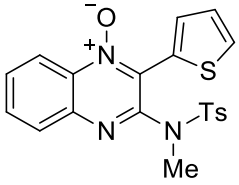
3q, 63 %



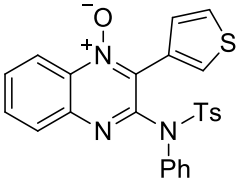
3r, 97 %



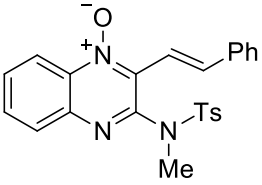
3s, 70 %



3t, 50 %

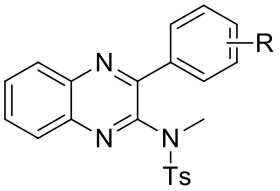


3u, 74 %

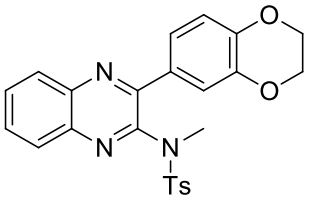


3v, 33 %

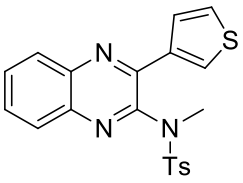
Condition B (**L1**AuCl/$AgNTf_2$):



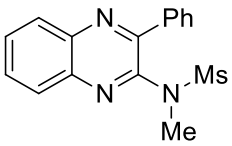
4a, R = H, 67 %
4b, R = 4-Me, 70 %
4c, R = 4-MeO, 63 %
4d, R = 4-F, 51 %
4e, R = 4-CF_3, 49 %
4f, R = 4-*t*Bu, 71 %
4g, R = 3-Cl, 53 %
4h, R =3-Me, 50 %



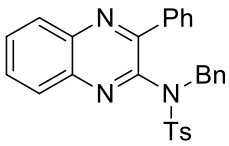
4i, 69 %



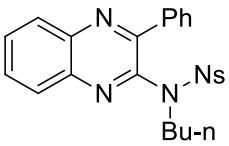
4j, 58 %



4k, 57 %



4l, 62 %

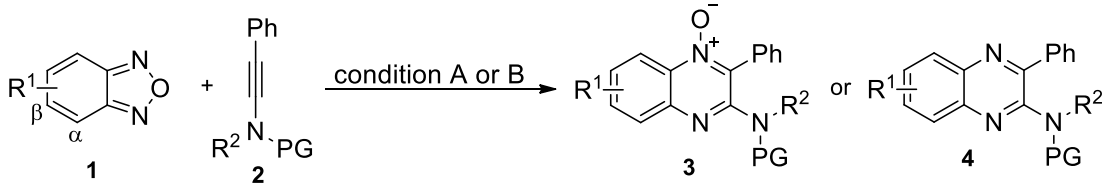


4m, 53 %

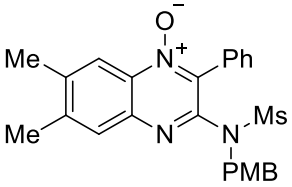
[a] Condition A: **1a** (0.2mmol), **2** (0.1 mmol), and 10 mol% $PtCl_2$/**L4** at 80 ^oC for 24 h in toluene. Condition B: **1a** (0.4 mmol), **2** (0.1 mmol), and 10 mol% **L1**AuCl/$AgNTf_2$ at 80 ^oC for 24 h in 1,2-DCE. [b] Isolated yields.

In addition to benzofurazan, a variety of substituted derivatives were also explored to suit the reaction with ynamides under condition A and B (Table 3). Gratifyingly, methoxy (**3x**, **3ab-c**, **4p-q**), bromide (**3y**, **4o**) and amide (**3aa**) were all tolerated delivering versatile scaffolds for further decoration. For common approaches to quinoxalines, the control of regioselectivity remains a challenge.[2, 4d-e] Hence, a few attempts were made on the regiospecific synthesis of quinoxalines *N*-oxides and quinoxalines following this method. In the case of **3ab** and **4p**, the conjugative effect of the β-methoxy group enhances the nucleophilicity of the adjacent nitrogen which induces good regioselectivity. An analogous substituent effect attributes to the formation of product **3aa**. An excellent regioselectivity was obtained by the reaction of α-substituted benzofurazans, in which one of the nitrogen was shielded by an additional substituent (**3ac-d**, **4q-r**). To underline the correct structural assignments the major isomers of **3ab**, **4p** and **4r** were determined by single-crystal X-ray analysis.[15b]

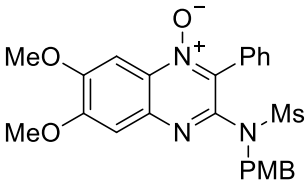
Table 3. Scope of benzofurazans and investigation on regioselectivity[a, b]



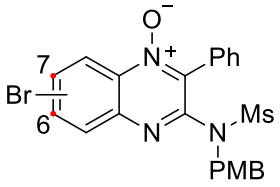
Condition A ($PtCl_2$/**L4**):



3w, 90 %

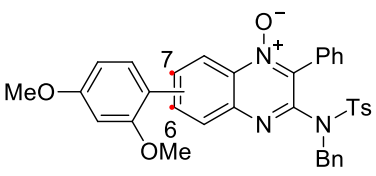


3x, 86 %

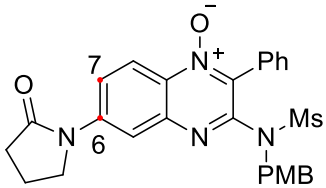


3y, 75 %[d]

isomeric ratio: 5:4

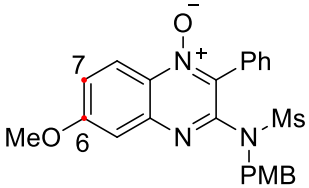


3z, 84 %[d] isomeric ratio: 2:1



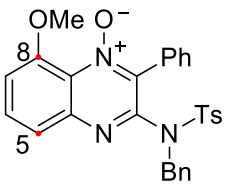
3aa, 96 %[d]

(C6:C7 = 5:1)

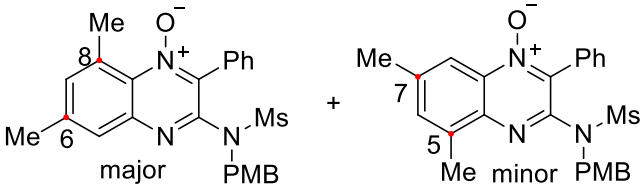


3ab, 97 %[d]

(C6:C7 = 7:1)

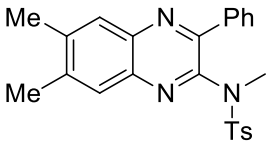


3ac, 55 %[d] (C8:C5 > 20:1)

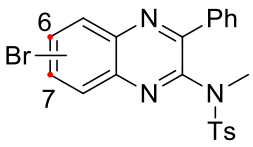


3ad, 76 %[d] (isomeric ratio > 20:1)

Condition B (**L1**AuCl/$AgNTf_2$):

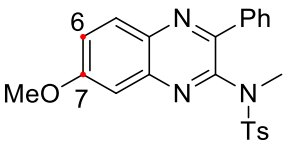


4n, 65 %



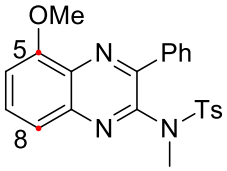
4o, 51 %[d]

(isomeric ratio: 5:2)



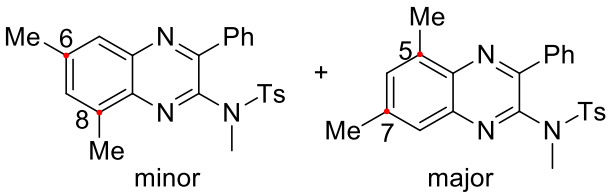
4p, 65 %[d]

(C7:C6 = 7:1)

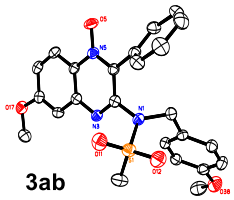


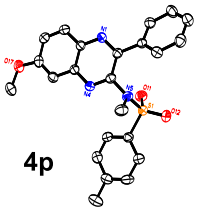
4q, 52 %[d]

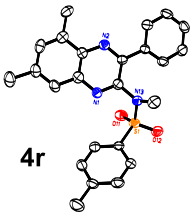
(C5:C8 = 8:1)



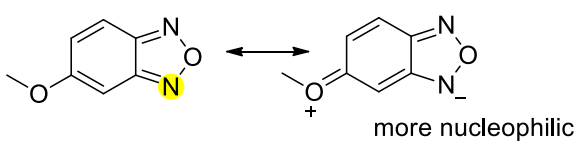
4r, 61 %[d] (isomeric ratio: 18:1)

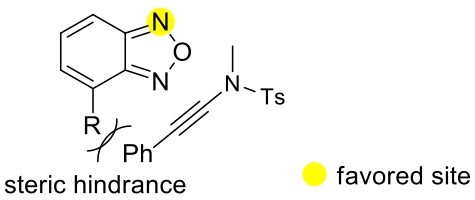






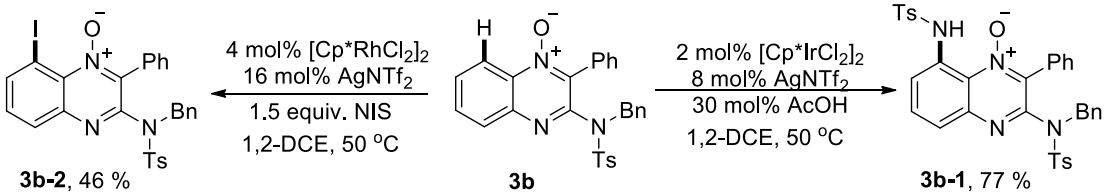
[a] Condition A: **1** (0.2 mmol), **2** (0.1 mmol), and 10 mol% $PtCl_2$/**L4** at 80 °C for 24 h in toluene. Condition B: **1** (0.4 mmol), **2** (0.1 mmol), and 10 mol% **L1**AuCl/$AgNTf_2$ at 80 °C for 24 h in 1,2-DCE. [b] Isolated yields. [c] Isomeric ratios were determined by ^{1}H NMR of the crude product mixture. [d] Total yield.





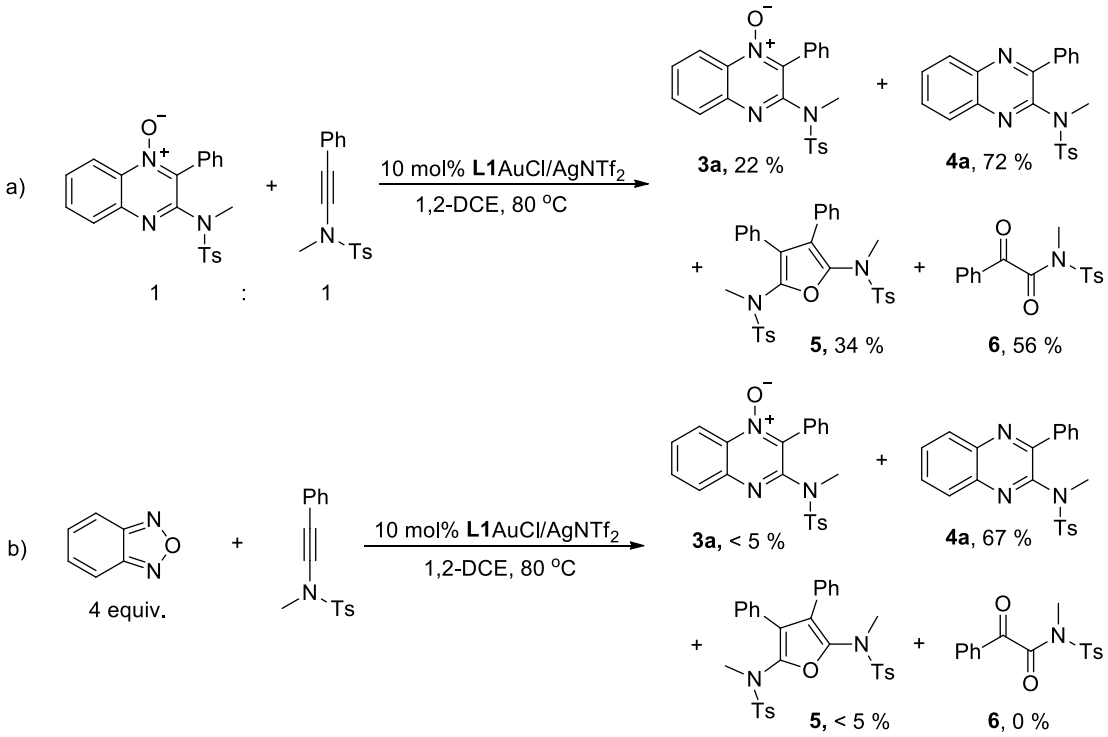
4.2.3 Further Applications

Quinoxaline *N*-oxides are considered as significant intermediates in organic synthesis. By taking the advantage of *N*-oxides as directing group, the further decoration could be facilely accomplished by direct C-H functionalization (Scheme 2).[16] As example, the quinoxaline *N*-oxide **3b** was suitable for iridium-catalyzed selective C8-amination (**3b-1**). The iodinated product **3b-2** was also prepared from **3a** with *N*-iodosuccinimide *via* a similar strategy.



Scheme 2. C-H functionalization of quinoxaline *N*-oxide.

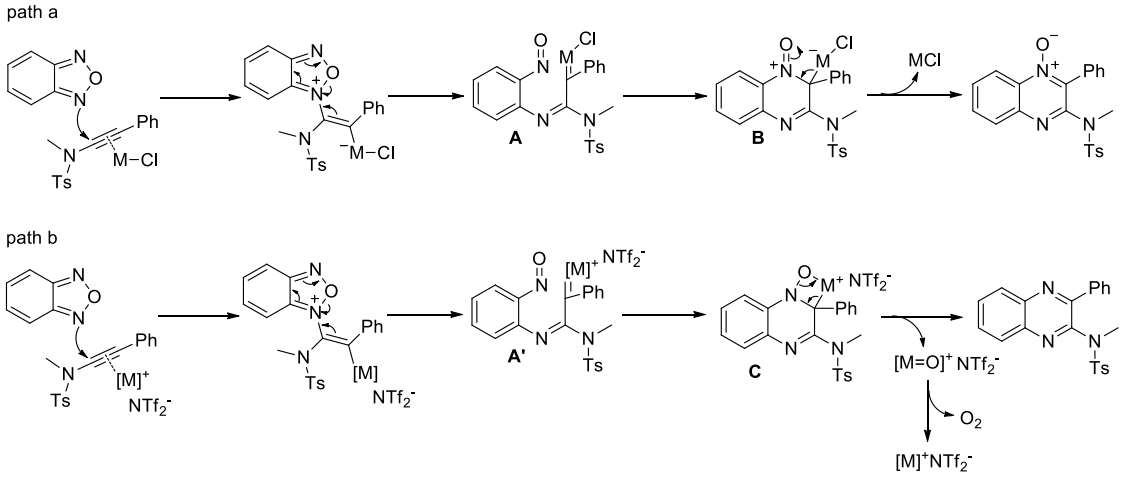
4.2.3 Mechanistic Investigation



Scheme 3. Mechanistic investigation.

Preliminary mechanistic investigations on the counteranion-mediated selectivity

switch were investigated next. The treatment of quinoxaline *N*-oxide and ynamide with **L1**AuCL/$AgNTf_2$ offered the quinoxaline accompanied by oxidized by-products (Scheme 3, a). However, under the same condition only few oxidized by-products were observed for the transformation of benzofurazan with the same ynamide (Scheme 3, b). This result suggests that the quinoxaline is not formed by the deoxidization of its corresponding quinoxaline *N*-oxide. On the basis of above studies, a probable reaction mechanism is shown in Scheme 4. The benzofurazan initially reacts with the metal-activated ynamide to generate a α-imino metal carbene **A/A'** with the *in-situ* formation of a nitrosyl group. Then, the resulting carbene intermediate can follow different pathways. In the case of a chloride ion, the metal carbene **A** is attacked by the nitrosyl group furnishing metal-ligated cyclized intermediate **B**, which subsequently produces quinoxaline *N*-oxide after metal elimination (path a). On the other hand, when the bulky ion NTf_2^- is involved, due to the higher electrophilicity of exposed metal core a [2+2] cycloaddition of nitrosyl group and metal carbene **A'** is preferred.[17] The quinoxaline is generated by a metathesis process losing the metallic oxide, which might decompose to regenerate the active metal catalyst (path b).



Scheme 4. Plausible mechanism.

4.3 Summary

In summary, we described gold and platinum-catalyzed counteranion-controlled divergent [4+2] cycloaddition of benzofurazans and ynamides. The tunable protocol provided convenient and regioselective syntheses of quinoxaline mono-*N*-oxides and quinoxalines from common starting materials. A wide range of functional groups were

well tolerated. Mechanistic studies disclosed the counteranion effect on the selectivity of the products *via* alternative cyclization pathways.

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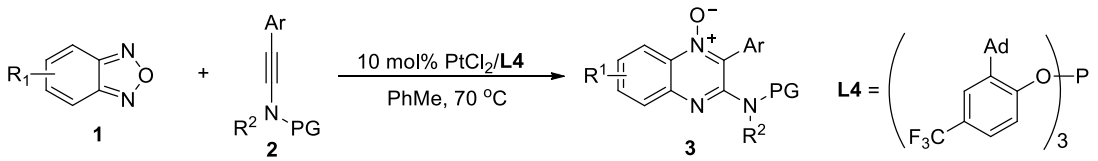
[17] a) V. V. Pagar, A. M. Jadhav, R.-S. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 20728-20731; b) D. B. Huple, S. Ghorpade, R.-S. Liu, *Adv. Synth. Catal*. **2016**, *358*, 1348-1367.

4.5 Experimental Section

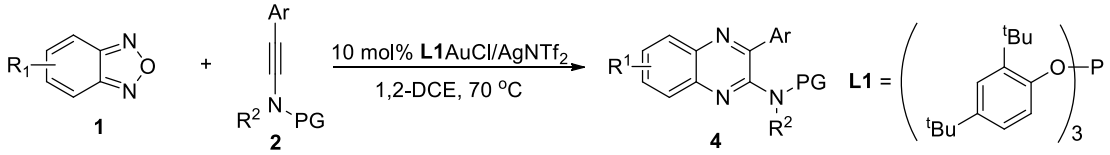
General information: Chemicals were purchased from commercial suppliers and used as delivered. The benzofurazan is bought from SigmaAldrich. Substrates **1** and **2** were prepared according to related literatures.[1-5] Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance DRX-300, Bruker-Avance DRX-500 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) and m (multiplet) as well as combinations of them. 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 and HSQC 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^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-K_α-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Heavy atom diffractions were solved by direct methods and refined against F2 with full matrix least square algorithm. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Gas Chromatography / Mass Spectrometry (GC/MS) spectra were measured on two different hardware systems: 1. HP 5972 Mass Selective Detector, coupled with a HP 5890 SERIES II plus gas

chromatograph. 2. Agilent 5975C Mass Selective Detector, coupled with an Agilent 7890A gas chromatograph. In both cases, as a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and helium was used as the carrier gas. Gas Chromatography (GC) was carried out on a HP 5890 SERIES II plus gas chromatograph. As a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and nitrogen was used as the carrier gas. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not corrected. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400 mesh ASTM) purchased from Macherey-Nagel or Aluminium oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and diethylether (Et_2O) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)), molybdatophosphoric acid (5 % in ethanol), vanillin/H_2SO_4 (in ethanol) or anisaldehyde/HOAc (in ethanol). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

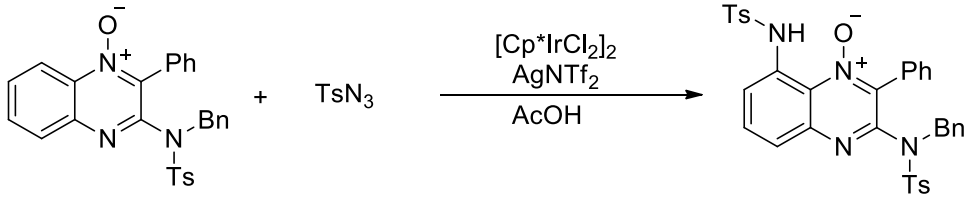
Experimental Procedures



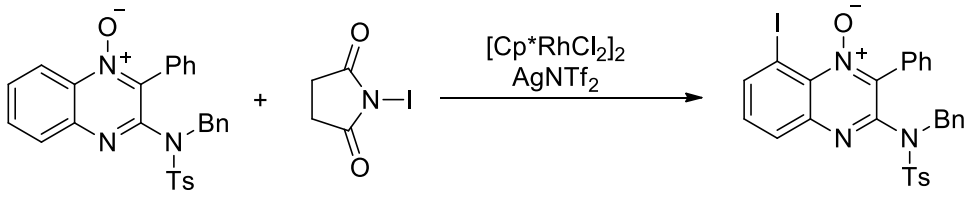
A round bottom flask equipped with a magnetic stirrer bar was added 10 mol% $PtCl_2$ (2.6 mg), 10 mol% **L4** (9.2 mg), **1** (0.2 mmol), **2** (0.1 mmol) and toluene (1 ml). The reaction was heated at 70 °C for 24 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound. The characterization data of the products are listed in part 3.



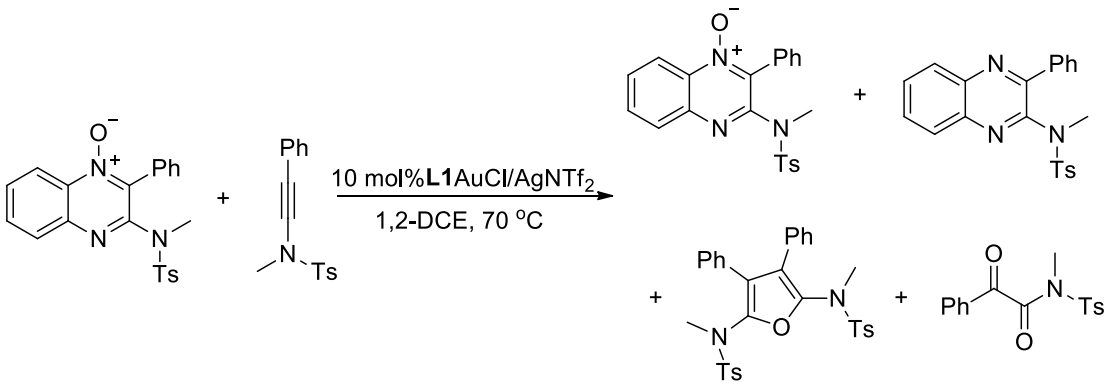
A round bottom flask equipped with a magnetic stirrer bar was charged with **L1**AuCl (10 mol%, 6.5 mg), $AgNTf_2$ (10 mol%, 4 mg), and 1,2-DCE (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the benzofurazan **1** (0.4 mmol) were added. The ynamides **2** (0.1 mmol) dissolved in 1 ml 1,2-DCE was dropwisely added into above mixture over 10 h at 70 ^{o}C by syringe pump. The reaction continued to heat for 12 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound.



A round bottom flask equipped with a magnetic stirrer bar was charged with $[Cp^*IrCl_2]_2$ (2 mol%, 3.2 mg), $AgNTf_2$ (8 mol%, 3.2 mg), quinoxaline N-oxide (0.1 mmol), TsN_3 (0.15 mmol) and 1,2-dichloroethane (0.5 ml). The mixture heated at 50 ^{o}C for 12 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound.

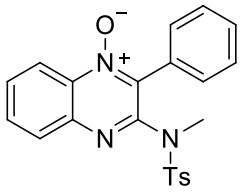


A round bottom flask equipped with a magnetic stirrer bar was charged with $[Cp^*RhCl_2]_2$ (4 mol%, 2.5 mg), $AgNTf_2$ (16 mol%, 6.4 mg), quinoxaline N-oxide (0.1 mmol), NIS (0.15 mmol) and 1,2-dichloroethane (0.5 ml) under nitrogen atmosphere. The mixture was heated at 50 ^{o}C for 12 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound.

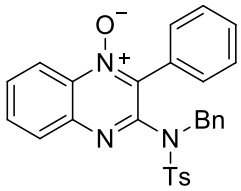


A round bottom flask equipped with a magnetic stirrer bar was charged with **L1**AuCl (10 mol%, 6.5 mg), $AgNTf_2$ (10 mol%, 4 mg), and 1,2-DCE (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the ynamide (0.1 mmol) and quinoxaline N-oxide (0.1 mmol) were added. The mixture was heated for 1 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the title compound.

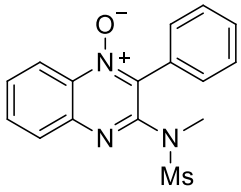
Characterization



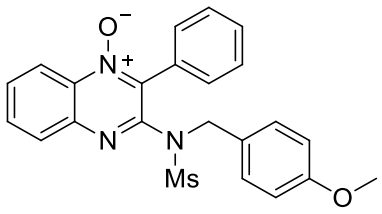
Compound 3a: Yield 80 %, R_f = 0.25 (PE/EA = 4:1), colourless soild, mp: 195-196 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.64-8.58 (m, 1 H), 8.01-7.95 (m, 1 H), 7.87-7.82 (m, 1 H), 7.82-7.56 (m, 1 H), 7.74-7.67 (m, 4 H), 7.63-7.53 (m, 3 H), 7.35-7.30 (m, 2 H), 2.94 (s, 3 H), 2.49 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.1 (s), 144.1 (s), 142.0 (s), 140.8 (s), 136.8 (s), 135.1 (s), 131.8 (d), 130.6 (d), 130.4 (d), 129.8 (d), 129.5 (d), 129.4 (d), 129.0 (s), 128.9 (d), 128.6 (d), 119.5 (d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3064, 2957, 1717, 1597, 1575, 1537, 1497, 1481, 1453, 1397, 1344, 1297, 1237, 1162, 1117, 1084, 1032, 1018, 995, 902, 867, 814, 767, 728, 699, 666, 618 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 406.1220; found: 406.1223.



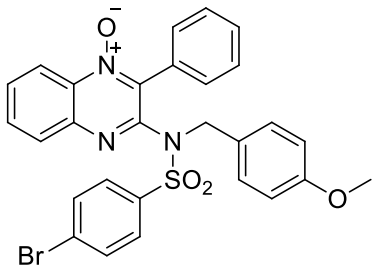
Compound 3b: Yield 83 %, R_f = 0.24 (PE/EA = 4:1), colourless soild, mp: 194-195 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.47-8.42 (m, 1 H), 7.98-7.94 (m, 1 H), 7.79-7.72 (m, 1 H), 7.70-7.64 (m, 1 H), 7.45-7.35 (m, 3 H), 7.35-7.29 (m, 2 H), 7.22-7.15 (m, 2 H), 7.14-7.07 (m, 1 H), 7.05-6.93 (m, 4 H), 6.78-6.67 (m, 2 H), 4.48 (s, 2 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 149.6 (s), 144.3 (s), 142.7 (s), 141.9 (s), 136.8 (s), 135.3 (s), 134.0 (s), 131.8 (d), 130.7 (d), 130.6 (d), 129.8 (d), 129.5 (d), 129.4 (d), 129.0 (d), 128.9 (s), 128.5 (d), 128.2 (d), 128.1 (d), 119.6 (d), 53.7 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3067, 2931, 1911, 1599, 1578, 1530, 1495, 1479, 1454, 1402, 1375, 1344, 1300, 1225, 1184, 1152, 1117, 1088, 1049, 1019, 993, 963, 915, 892, 866, 810, 769, 722, 700, 677, 663, 653, 630, 617 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 482.1533; found: 482.1532



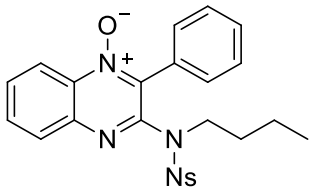
Compound 3c: Yield 70 %, R_f = 0.1 (PE/EA = 4:1), colourless soild, mp: 198-199 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.53-8.47 (m, 1 H), 7.99-7.94 (m, 1 H), 7.79-7.73 (m, 1 H), 7.72-7.66 (m, 1 H), 7.63-7.57 (m, 2 H), 7.52-7.40 (m, 3 H), 3.12 (s, 3 H), 2.90 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.3 (s), 141.9 (s), 139.8 (s), 136.9 (s), 131.9 (d), 130.6 (d), 130.2 (d), 130.0 (d), 129.5 (d), 128.7 (d), 128.5 (s), 119.6 (d), 39.5 (q), 37.0 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2959, 2903, 2867, 1716, 1600, 1578, 1509, 1484, 1454, 1394, 1362, 1346, 1300, 1240, 1202, 1187, 1161, 1131, 1108, 1084, 1017, 1004, 896, 875, 831, 810, 788, 773, 758, 731, 717, 704, 675, 660, 635, 624, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 330.0907; found: 330.0907.



Compound 3d: Yield 95 %, R_f = 0.12 (PE/EA = 4:1), colourless soild, mp: 189-191 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.49-8.44 (m, 1 H), 8.01-7.95 (m, 1 H), 7.79-7.73 (m, 1 H), 7.71-7.65 (m, 1 H), 7.42-7.36 (m, 3 H), 7.35-7.28 (m, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.64 (d, *J* = 8.5 Hz, 2 H), 4.41 (s, 2 H), 3.67 (s, 3 H), 2.89 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.6 (s), 150.4 (s), 141.9 (s), 140.9 (s), 136.8 (s), 131.9 (d), 130.8 (d), 130.6 (d), 130.5 (d), 129.8 (d), 129.6 (d), 128.5 (s), 128.4 (d), 126.2 (s), 119.6 (d), 114.1 (d), 55.3 (q), 53.8 (t), 41.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2933, 2837, 1723, 1612, 1576, 1513, 1483, 1454, 1402, 1337, 1247, 1177, 1150, 1112, 1028, 953, 893, 865, 808, 784, 765, 722, 698, 665, 651, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 436.1326; found: 436.1323.

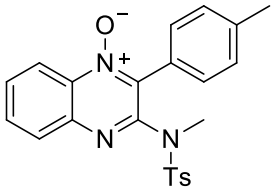


Compound 3e: Yield 80 %, R_f = 0.2 (PE/EA = 4:1), colourless soild, mp: 194-195 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.49-8.45 (m, 1 H), 7.96-7.92 (m, 1 H), 7.81-7.75 (m, 1 H), 7.73-7.67 (m, 1 H), 7.56-7.51 (m, 2 H), 7.45-7.39 (m, 3 H), 7.39-7.33 (m, 2 H), 7.13-7.02 (m, 2 H), 6.66 (d, *J* = 8.5 Hz, 2 H), 6.64 (d, *J* = 9.0 Hz, 2 H), 4.40 (s, 2 H), 3.65 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.6 (s), 149.5 (s), 142.5 (s), 141.9 (s), 137.6 (s), 136.9 (s), 131.95 (d), 131.92 (d), 131.0 (d), 130.8 (d), 130.5 (d), 130.4 (d), 129.5 (d), 129.4 (d), 128.7 (s), 128.4 (s), 128.2 (d), 125.6 (s), 119.7 (d), 113.9 (d), 55.2 (q), 53.6 (t) ppm; IR (ATR): $\tilde{\nu}$ = 3064, 2934, 2836, 1738, 1612, 1573, 1513, 1500, 1482, 1452, 1401, 1390, 1349, 1293, 1279, 1247, 1162, 1087, 1068, 1009, 963, 894, 865, 822, 803, 782, 754, 737, 698, 670, 633 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 576.0587; found: 576.0597.

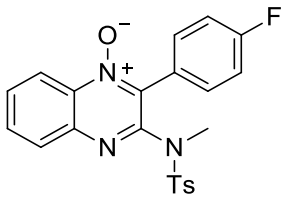


Compound 3f: Yield 80 %, R_f = 0.3 (PE/EA = 4:1), colourless soild, mp: 192-193 ^oC;

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.54-8.50 (m, 1 H), 8.31 (d, *J* = 8.5 Hz, 2 H), 8.04 (d, *J* = 9.0 Hz, 2 H), 7.86-7.82 (m, 1 H), 7.81-7.76 (m, 1 H), 7.75-7.69 (m, 1 H), 7.65-7.60 (m, 2 H), 7.54-7.46 (m, 3 H), 3.20 (t, *J* = 7. 5 Hz, 2 H), 1.11-1.02 (m, 2 H), 0.96-0.86 (m, 2 H), 0.60 (t, *J* = 7.5 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.3 (s), 149.2 (s), 145.1 (s), 141.9 (s), 141.6 (s), 137.1 (s), 132.2 (d), 131.0 (d), 130.4 (d), 130.2 (d), 130.1 (d), 129.4 (d), 128.7 (d), 128.5 (s), 123.8 (d), 119.7 (d), 50.4 (t), 29.7 (t), 19.8 (t), 13.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3109, 2959, 2930, 2911, 2872, 2850, 1736, 1606, 1575, 1524, 1499, 1480, 1463, 1446, 1404, 1347, 1312, 1293, 1240, 1227, 1160, 1130, 1110, 1077, 1034, 1024, 978, 949, 884, 859, 778, 769, 746, 734, 719, 700, 683, 666, 636 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 479.1384; found: 479.1381.

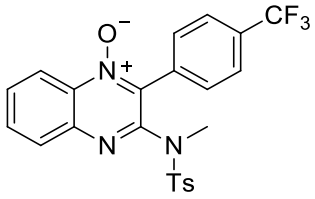


Compound 3g: Yield 70 %, R_f = 0.3 (PE/EA = 4:1), colourless soild, mp: 189-190 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.47 (m, 1 H), 7.87-7.83 (m, 1 H), 7.74-7.69 (m, 1 H), 7.69-7.61 (m, 3 H), 7.52 (d, *J* = 8.0 Hz, 2 H), 7.30 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 2.84 (s, 3 H), 2.39 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.2 (s), 144.0 (s), 141.9 (s), 140.8 (s), 140.0 (s), 136.9 (s), 135.3 (s), 131.6 (d), 130.4 (d), 130.2 (d), 129.4 (d), 129.3 (d), 129.2 (d), 128.9 (d), 125.8 (s), 119.5 (d), 35.8 (q), 20.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2934, 1738, 1595, 1576, 1510, 1485, 1460, 1425, 1395, 1355, 1329, 1296, 1232, 1186, 1161, 1115, 1085, 1019, 987, 898, 866, 816, 784, 767, 733, 716, 703, 675, 646, 616 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 420.1376; found: 420.1379.

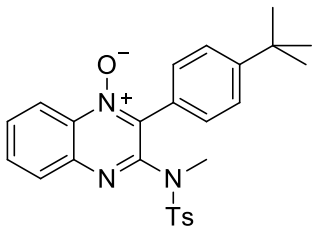


Compound 3h: Yield 78 %, R_f = 0.2 (PE/EA = 4:1), colourless soild, mp: 185-186 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.47 (m, 1 H), 7.87-7.84 (m, 1 H), 7.77-7.72 (m, 1 H), 7.71-7.66 (m, 1 H), 7.66-7.59 (m, 4 H), 7.27-7.22 (m, 2 H), 7.22-7.15 (m, 2 H),

2.86 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.4 (*J* = 249 Hz, s), 151.1 (s), 144.2 (s), 142.0 (s), 140.0 (s), 136.9 (s), 134.9 (s), 132.6 (*J* = 8.7 Hz, d), 131.9 (d), 130.7 (d), 129.5 (d), 129.4 (d), 129.0 (d), 124.8 (*J* = 3.8 Hz, s), 119.5 (d), 115.8 (*J* = 21.8 Hz, d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 1600, 1577, 1535, 1510, 1483, 1451, 1428, 1395, 1345, 1295, 1231, 1186, 1161, 1117, 1084, 1019, 1003, 903, 874, 834, 812, 771, 732, 706, 666, 643, 616 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 424.1126; found: 424.1125.

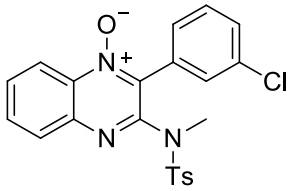


Compound 3i: Yield 50 %, R_f = 0.13 (PE/EA = 4:1), colourless soild, mp: 209-210 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.53-8.48 (m, 1 H), 7.91-7.87 (m, 1 H), 7.80-7.68 (m, 6 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 2.91 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.7 (s), 144.4 (s), 142.3 (s), 139.7 (s), 136.8 (s), 134.5 (s), 132.9 (*J* = 1.3 Hz, s), 132.2 (d), 131.6 (J = 31.8 Hz, s), 131.1 (d), 130.8 (d), 129.6 (d), 129.4 (d), 128.8 (d), 128.5 (J = 283 Hz, s), 125.4 (*J* = 3.7 Hz, d), 119.5 (d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3066, 2363, 1664, 1617, 1597, 1574, 1518, 1484, 1450, 1408, 1397, 1352, 1321, 1236, 1187, 1164, 1124, 1091, 1075, 1063, 1019, 990, 901, 871, 827, 816, 770, 741, 732, 698, 674, 656, 646, 622 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 474.1094; found: 474.1093.

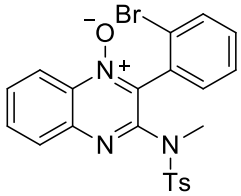


Compound 3j: Yield 78 %, R_f = 0.24 (PE/EA = 4:1), colourless soild, mp: 192-193 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.47 (m, 1 H), 7.88-7.84 (m, 1 H), 7.75-7.69 (m, 1 H), 7.69-7.60 (m, 3 H), 7.59-7.54 (m, 2 H), 7.53-7.48 (m, 2 H), 7.25-7.20 (m, 2 H), 2.83 (s, 3 H), 2.38 (s, 3 H), 1.32 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.9 (s), 151.2 (s), 144.0 (s), 141.8 (s), 140.7 (s), 136.9 (s), 135.3 (s), 131.6 (d), 130.4 (d), 130.0 (d), 129.4 (d), 129.3 (d), 129.0 (d), 125.7 (s), 125.5 (d),

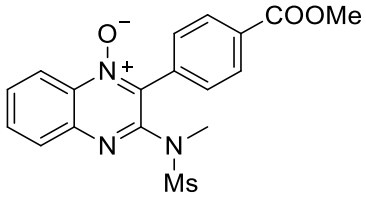
119.5 (d), 36.9 (q), 34.9 (s), 31.3 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2958, 1734, 1599, 1577, 1540, 1509, 1484, 1453, 1393, 1362, 1346, 1300, 1240, 1202, 1187, 1160, 1131, 1108, 1084, 1016, 1003, 896, 875, 831, 810, 788, 773, 758, 730, 717, 704, 675, 660, 635, 624, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 462.1846; found: 462.1846.



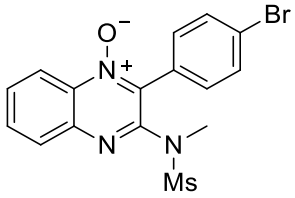
Compound 3k: Yield 59 %, R_f = 0.2 (PE/EA = 4:1), colourless soild, mp: 179-181 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.48 (m, 1 H), 7.89-7.85 (m, 1 H), 7.78-7.73 (m, 1 H), 7.73-7.67 (m, 1 H), 7.62-7.56 (m, 3 H), 7.55-7.50 (m, 1 H), 7.45-7.40 (m, 2 H), 7.26-7.21 (m, 2 H), 2.89 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.9 (s), 144.2 (s), 142.1 (s), 139.7 (s), 136.9 (s), 134.7 (s), 134.3 (s), 132.1 (d), 130.8 (d), 130.7 (s), 130.4 (d), 130.0 (d), 129.9 (d), 129.6 (d), 129.4 (d), 128.9 (d), 128.8 (d), 119.5 (d), 37.0 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3068, 2929, 1724, 1597, 1576, 1534, 1490, 1450, 1397, 1346, 1292, 1263, 1236, 1187, 1161, 1117, 1085, 999, 873, 806, 774, 752, 728, 691, 667, 617 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 440.0830; found: 440.0827.



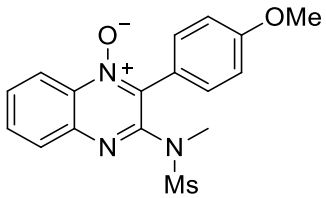
Compound 3l: Yield 42 %, R_f = 0.24 (PE/EA = 4:1), colourless soild, mp: 210-211 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.55-8.50 (m, 1 H), 7.92-7.88 (m, 1 H), 7.81-7.74 (m, 1 H), 7.73-7.59 (m, 5 H), 7.53-7.47 (m, 1 H), 7.39-7.33 (m, 1 H), 7.26-7.22 (m, 2 H), 2.94 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.1 (s), 144.2 (s), 142.5 (s), 140.8 (s), 136.8 (s), 134.8 (s), 133.3 (d), 132.6 (d), 132.1 (d), 131.3 (d), 130.9 (s), 130.6 (d), 129.6 (d), 129.4 (d), 129.0 (d), 127.9 (d), 123.8 (s), 119.6 (d), 37.0 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2923, 2854, 1713, 1661, 1596, 1575, 1536, 1492, 1466, 1449, 1399, 1353, 1333, 1303, 1260, 1236, 1157, 1119, 1084, 1047, 1019, 1001, 966, 867, 812, 762, 719, 704, 665, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 484.0325; found: 484.0321.



Compound 3m: Yield 54 %, R_f = 0.08 (PE/EA = 5:2), colourless soild, mp: 208-209 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.47 (m, 1 H), 8.17-8.13 (m, 2 H), 8.01-7.96 (m, 1 H), 7.81-7.77 (m, 1 H), 7.75-7.66 (m, 3 H), 3.89 (s, 3 H), 3.15 (s, 3 H), 2.91 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 166.5 (s), 150.9 (s), 142.1 (s), 139.2 (s), 136.9 (s), 133.1 (s), 132.3 (d), 131.3 (s), 130.8 (d), 130.5 (d), 129.8 (d), 129.6 (d), 119.5 (d), 52.4 (q), 39.2 (q), 37.1 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2931, 1720, 1611, 1578, 1537, 1511, 1484, 1452, 1435, 1395, 1340, 1276, 1193, 1157, 1110, 1085, 1021, 1005, 963, 907, 878, 853, 825, 799, 767, 747, 723, 701, 666, 651, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 338.0962; found: 338.0959.

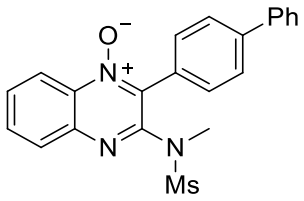


Compound 3n: Yield 70 %, R_f = 0.08 (PE/EA = 4:1), colourless soild, mp: 210-211 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.51-8.46 (m, 1 H), 7.98-7.94 (m, 1 H), 7.80-7.75 (m, 1 H), 7.73-7.68 (m, 1 H), 7.62 (d, *J* = 8.5 Hz, 2 H), 7.51 (d, *J* = 8.5 Hz, 2 H), 3.19 (s, 3 H), 2.91 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.0 (s), 142.0 (s), 139.0 (s), 136.9 (s), 132.2 (d), 132.0 (d), 131.9 (d), 130.8 (d), 129.5 (d), 127.3 (s), 124.6 (s), 119.5 (d), 39.3 (q), 37.1 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2930, 1717, 1578, 1537, 1495, 1481, 1454, 1405, 1390, 1338, 1294, 1242, 1200, 1156, 1115, 1085, 1070, 1014, 1002, 963, 904, 871, 822, 798, 766, 748, 728, 707, 665, 651, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 408.0012; found: 408.0010.

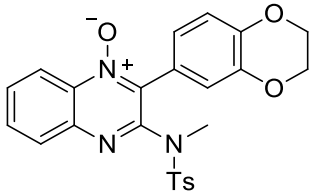


Compound 3o: Yield 50 %, R_f = 0.08 (PE/EA = 4:1), colourless soild, mp: 203-204 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.52-8.48 (m, 1 H), 7.96-7.92 (m, 1 H),

7.77-7.72 (m, 1 H), 7.71-7.65 (m, 1 H), 7.61 (d, *J* = 8.5 Hz, 2 H), 7.00 (d, *J* = 9.0 Hz, 2 H), 3.81 (s, 3 H), 3.20 (s, 3 H), 2.88 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 160.8 (s), 151.4 (s), 141.6 (s), 139.5 (s), 136.9 (s), 131.8 (d), 131.7 (d), 130.5 (d), 129.4 (d), 120.1 (s), 119.5 (d), 114.2 (d), 55.4 (q), 39.7 (q), 36.9 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2932, 2840, 1716, 1607, 1578, 1483, 1455, 1396, 1337, 1303, 1291, 1250, 1178, 1155, 1113, 1085, 1023, 1001, 964, 906, 873, 831, 804, 767, 747, 667, 645, 631, 616 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 360.1013; found: 360.1012.

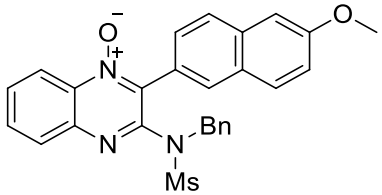


Compound 3p: Yield 65 %, R_f = 0.08 (PE/EA = 4:1), colourless soild, mp: 200-201 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.54-8.49 (m, 1 H), 7.99-7.93 (m, 1 H), 7.79-7.74 (m, 1 H), 7.73-7.66 (m, 5 H), 7.62-7.57 (m, 2 H), 7.43-7.37 (m, 2 H), 7.34-7.28 (m, 1 H), 3.18 (s, 3 H), 2.93 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.3 (s), 142.7 (s), 141.9 (s), 140.3 (s), 139.6 (s), 137.0 (s), 132.0 (d), 130.7 (d), 130.6 (d), 129.5 (d), 128.9 (d), 127.9 (d), 127.3 (d), 127.27 (d), 127.22 (s), 119.6 (d), 39.6 (q), 37.1 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 1725, 1602, 1579, 1519, 1483, 1450, 1397, 1335, 1299, 1236, 1200, 1157, 1144, 1114, 1084, 1027, 1005, 965, 909, 875, 837, 765, 747, 731, 695, 663, 649, 637, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 406.1220; found: 406.1221.

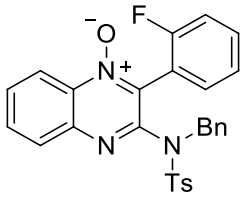


Compound 3q: Yield 63 %, R_f = 0.06 (PE/EA = 4:1), colourless soild, mp: 208-209 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.51-8.47 (m, 1 H), 7.86-7.82 (m, 1 H), 7.74-7.63 (m, 4 H), 7.27-7.23 (m, 2 H), 7.17-7.10 (m, 2 H), 6.99-6.96 (m, 1 H), 4.31-4.21 (m, 4 H), 2.87 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.2 (s), 145.0 (s), 144.0 (s), 143.6 (s), 141.8 (s), 140.2 (s), 136.9 (s), 135.4 (s), 131.6 (d), 130.4 (d), 129.4 (d), 129.3 (d), 128.9 (d), 123.8 (d), 121.5 (s), 119.6 (d), 119.5 (d), 117.6 (d), 37.0 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2975, 2872, 1717, 1599,

1577, 1540, 1508, 1483, 1459, 1448, 1430, 1398, 1367, 1343, 1304, 1281, 1249, 1186, 1158, 1139, 1126, 1116, 1087, 1062, 1003, 937, 915, 885, 836, 810, 767, 748, 720, 705, 687, 663, 618 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 464.1275; found: 464.1271.

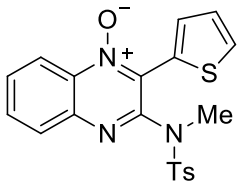


Compound 3r: Yield 97 %, R_f = 0.1 (PE/EA = 4:1), colourless soild, mp: 191-193 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.50-8.45 (m, 1 H), 8.01-7.98 (m, 1 H), 7.79-7.71 (m, 2 H), 7.71-7.64 (m, 1 H), 7.64-7.58 (m, 2 H), 7.48-7.41 (m, 1 H), 7.19-7.13 (m, 1 H), 7.12-7.04 (m, 4 H), 6.96-6.90 (m, 2 H), 4.47 (s, 2 H), 3.87 (s, 3 H), 2.88 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.9 (s), 150.5 (s), 141.8 (s), 141.0 (s), 136.9 (s), 135.1 (s), 134.4 (s), 131.9 (d), 130.6 (d), 130.4 (d), 130.3 (d), 129.6 (d), 129.5 (d), 128.7 (d), 128.4 (d), 128.3 (s), 127.8 (d), 126.8 (d), 123.4 (s), 119.5 (d), 119.1 (d), 105.8 (d), 55.4 (q), 54.1 (t), 41.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3034, 2929, 1738, 1632, 1650, 1573, 1492, 1479, 1451, 1411, 1342, 1287, 1272, 1209, 1155, 1140, 1110, 1060, 1022, 950, 919, 895, 856, 835, 810, 772, 758, 740, 721, 697, 680, 668, 644, 628 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 486.1482; found: 486.1480.

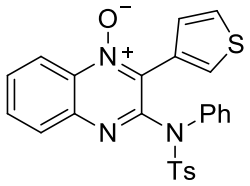


Compound 3s: Yield 70 %, R_f = 0.26 (PE/EA = 4:1), colourless soild, mp: 186-187 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.50-8.45 (m, 1 H), 7.94-7.89 (m, 1 H), 7.79-7.73 (m, 1 H), 7.71-7.65 (m, 1 H), 7.52 (d, *J* = 8.5 Hz, 2 H), 7.45-7.38 (m, 1 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.14-7.07 (m, 2 H), 7.06-6.91 (m, 4 H), 6.87-6.81 (m, 2 H), 4.64 (d, *J* = 8.5 Hz, 1 H), 4.41 (d, *J* = 9.0 Hz, 1 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 161.3 (*J* = 251 Hz, s), 150.1 (s), 144.3 (s), 142.2 (s), 139.2 (s), 136.7 (s), 135.1 (s), 134.0 (s), 132.1 (d), 131.8 (*J* = 2.7 Hz, d), 131.7 (*J* = 8.7 Hz, d), 130.7 (d), 129.6 (d), 129.5 (d), 129.4 (d), 129.0 (d), 128.5 (d), 128.2 (d), 123.8 (*J* = 3.7 Hz, d), 119.7 (d), 117.5 (J = 15 Hz, s), 115.5 (*J* = 21.6 Hz, d), 54.0 (q), 21.7 (q)

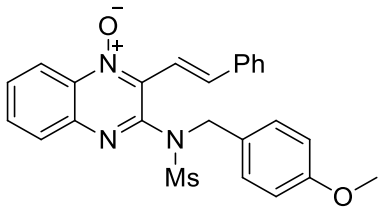
ppm; IR (ATR): $\tilde{\nu}$ = 3065, 2927, 1734, 1618, 1598, 1577, 1533, 1498, 1481, 1455, 1404, 1354, 1304, 1264, 1230, 1186, 1162, 1118, 1089, 1028, 965, 916, 872, 814, 759, 731, 701, 664, 651, 626 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 500.1439; found: 500.1436.



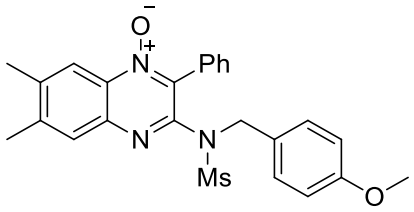
Compound 3t: Yield 50 %, R_f = 0.24 (PE/EA = 4:1), yellow soild, mp: 188-189 ^oC; ^1H NMR (500 MHz, CD_2Cl_2) δ = 8.73-8.71 (m, 1 H), 8.52-8.48 (m, 1 H), 7.28-7.61 (m, 6 H), 7.33-7.26 (m, 3 H), 3.11 (s, 3 H), 2.42 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 149.2 (s), 144.4 (s), 138.9 (s), 135.8 (s), 135.1 (s), 134.4 (s), 132.9 (d), 131.03 (d), 131.00 (d), 130.9 (d), 129.4 (d), 129.3 (d), 128.9 (d), 128.4 (s), 127.1 (d), 119.3 (d), 37.0 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3077, 2909, 1738, 1597, 1583, 1524, 1504, 1482, 1451, 1415, 1393, 1363, 1344, 1333, 1304, 1281, 1244, 1223, 1185, 1166, 1114, 1088, 1075, 1046, 1017, 956, 903, 863, 841, 812, 781, 759, 747, 719, 704, 668, 651, 617 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 412.0784; found: 412.0790.



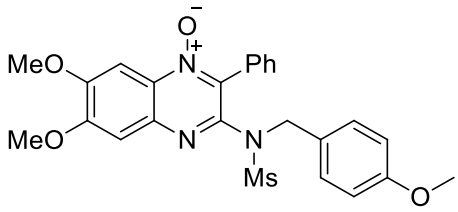
Compound 3u: Yield 74 %, R_f = 0.26 (PE/EA = 4:1), yellow soild, mp: 190-192 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.47-8.42 (m, 1 H), 7.90-7.85 (m, 1 H), 7.82-7.78 (m, 1 H), 7.76-7.70 (m, 1 H), 7.68-7.61 (m, 3 H), 7.33-7.29 (m, 1 H), 7.28-7.24 (m, 1 H), 7.23-7.18 (m, 2 H), 7.10-7.05 (m, 1 H), 7.02-6.96 (m, 2 H), 6.79-6.72 (m, 2 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.9 (s), 144.0 (s), 141.3 (s), 138.2 (s), 136.7 (s), 136.6 (s), 136.2 (s), 131.7 (d), 130.4 (d), 129.8 (d), 129.4 (d), 128.9 (d), 128.8 (d), 128.7 (d), 128.5 (d), 128.1 (d), 127.4 (s), 125.0 (d), 119.4 (d), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3104, 2959, 2925, 1734, 1596, 1578, 1522, 1484, 1451, 1428, 1346, 1308, 1280, 1237, 1211, 1186, 1165, 1138, 1111, 1089, 1056, 1017, 949, 908, 846, 811, 767, 717, 694, 680, 661, 634, 619, 610 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 474.0941; found: 474.0939.



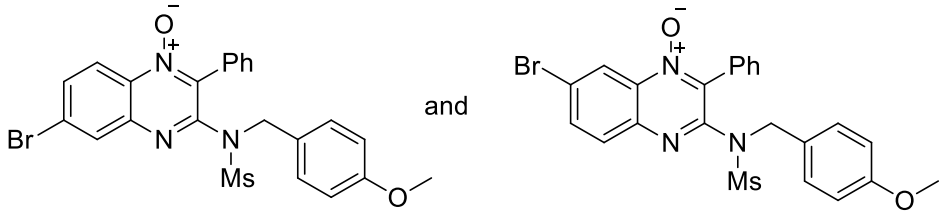
Compound 3v: Yield 33 %, R_f = 0.12 (PE/EA = 4:1), colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.86-8.80 (m, 1 H), 8.51-8.45 (m, 1 H), 7.96-7.91 (m, 1 H), 7.74-7.67 (m, 2 H), 7.51-7.46 (m, 2 H), 7.37-7.25 (m, 4 H), 7.07 (d, *J* = 8.5 Hz, 2 H), 6.58 (d, *J* = 8.5 Hz, 2 H), 4.84 (s, 2 H), 3.55 (s, 3 H), 3.15 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.6 (s), 150.5 (s), 139.9 (d), 138.7 (s), 137.5 (s), 137.3 (s), 131.0 (d), 130.97 (s), 130.95 (d), 130.8 (d), 129.4 (d), 129.3 (d), 128.8 (d), 127.9 (d), 126.0 (s), 119.0 (d), 115.8 (d), 114.1 (d), 55.1 (q), 54.8 (t), 38.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2955, 1612, 1576, 1513, 1441, 1409, 1396, 1342, 1248, 1177, 1154, 1113, 1032, 965, 947, 901, 864, 813, 756, 689, 652, 627 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 462.1482; found: 462.1480.



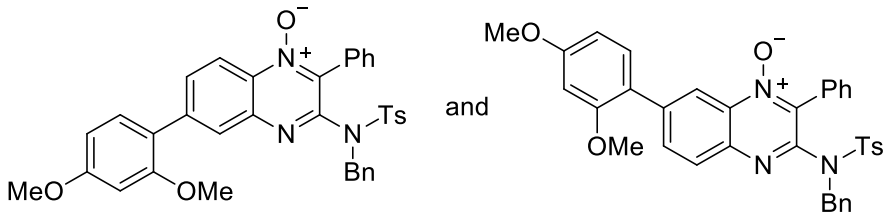
Compound 3w: Yield 90 %, R_f = 0.14 (PE/EA = 4:1), colourless soild, mp: 191-192 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.21 (s, 1 H), 7.73 (s, 1 H), 7.40-7.33 (m, 3 H), 7.32-7.25 (m, 2 H), 6.85 (d, *J* = 8.5 Hz, 2 H), 6.62 (d, *J* = 8.5 Hz, 2 H), 4.38 (s, 2 H), 3.67 (s, 3 H), 2.91 (s, 3 H), 2.43 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.5 (s), 149.3 (s), 142.7 (s), 141.8 (s), 140.7 (s), 140.3 (s), 135.1 (s), 130.8 (d), 130.5 (d), 129.5 (d), 128.8 (d), 128.7 (s), 128.2 (d), 126.3 (s), 118.6 (d), 114.0 (d), 55.3 (q), 53.8 (t), 41.1 (q), 20.6 (q), 20.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2994, 2919, 2835, 1698, 1613, 1570, 1513, 1484, 1462, 1423, 1399, 1353, 1337, 1320, 1267, 1248, 1231, 1150, 1097, 1075, 1026, 1011, 976, 952, 937, 888, 865, 854, 827, 776, 767, 755, 744, 691, 678, 666, 651, 622 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 464.1639; found: 464.1640.



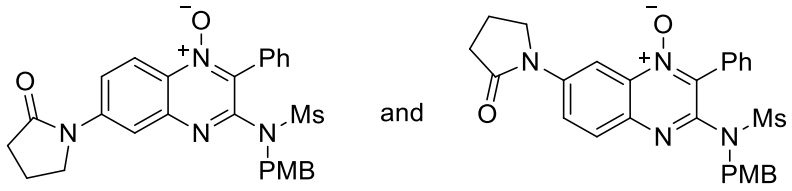
Compound 3x: Yield 86 %, R_f = 0.75 (pure EA), colourless soild, mp: 198-200 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.79 (s, 1 H), 7.39-7.33 (m, 3 H), 7.30-7.22 (m, 3 H), 6.85 (d, *J* = 9.0 Hz, 2 H), 6.63 (d, *J* = 8.5 Hz, 2 H), 4.40 (s, 2 H), 4.02 (s, 3 H), 3.98 (s, 3 H), 3.68 (s, 3 H), 2.90 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.5 (s), 154.2 (s), 153.7 (s), 148.0 (s), 139.7 (s), 139.0 (s), 132.6 (s), 130.8 (d), 130.5 (d), 129.4 (d), 128.8 (s), 128.2 (d), 126.3 (s), 114.0 (d), 107.3 (d), 98.0 (d), 56.8 (q), 56.7 (q), 55.3 (q), 53.7 (t), 41.0 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2942, 2836, 1716, 1613, 1581, 1499, 1456, 1434, 1387, 1322, 1285, 1237, 1212, 1174, 1150, 1112, 1069, 1028, 1001, 955, 903, 831, 771, 748, 701, 669, 654, 612 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 496.1537; found: 496.1536.



Compound 3y: R_f = 0.24 (PE/EA = 4:1), total yield 75 % (mixture ratio = 5:4), yellow soild; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.64 (s, 0.41 H), 8.36-8.30 (m, 0.52 H), 8.18 (s, 0.50 H), 7.84 (s, 1 H), 7.77-7.71 (m, 0.56 H), 7.44-7.37 (m, 3 H), 7.37-7.27 (m, 2 H), 6.91-6.84 (m, 2 H), 6.69-6.60 (m, 2 H), 4.44-4.33 (m, 2 H), 3.71-3.62 (m, 3 H), 2.91-2.80 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.6 (s), 151.5 (s), 150.7 (s), 142.5 (s), 141.3 (s), 141.0 (s), 140.6 (s), 137.3 (s), 135.8 (s), 135.6 (d), 133.8 (d), 131.7 (d), 130.84 (d), 130.80 (d), 130.7 (d), 130.43 (d), 130.41 (d), 130.0 (d), 128.7 (s), 128.48 (d), 128.47 (d), 128.1 (s), 128.0 (s), 126.4 (s), 126.1 (s), 125.0 (s), 122.3 (d), 121.1 (d), 114.1 (d), 114.0 (d), 55.3 (q), 53.7 (t), 41.6 (q), 41.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2933, 1612, 1567, 1513, 1476, 1459, 1401, 1340, 1247, 1216, 1178, 1150, 1117, 1028, 954, 912, 874, 822, 779, 757, 723, 697, 662, 639 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 514.0431; found: 514.0429.

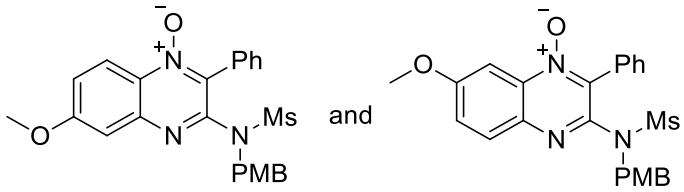


Compound 3z: R_f = 0.14 (PE/EA = 4:1), total yield 84 % (mixture ratio = 2:1), yellow soild; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.56 (s, 0.33 H), 8.44-8.40 (m, 0.65 H), 8.04 (s, 0.69 H), 8.00-7.96 (m, 0.36 H), 7.94-7.86 (m, 1 H), 7.47-7.41 (m, 2 H), 7.40-7.27 (m, 4 H), 7.22-7.15 (m, 2 H), 7.14-7.08 (m, 1 H), 7.06-6.92 (m, 4 H), 6.77-6.70 (m, 2 H), 6.61-6.50 (m, 2 H), 4.49 (s, 2 H), 3.84-3.74 (m, 6 H), 2.41-2.35 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 161.5 (s), 161.4 (s), 157.76 (s), 157.71 (s), 149.4 (s), 148.7 (s), 144.2 (s), 142.7 (s), 142.6 (s), 142.3 (s), 142.2 (s), 141.7 (s), 140.8 (s), 136.8 (s), 135.4 (s), 135.39 (s), 135.37 (s), 134.1 (s), 134.0 (d), 133.1 (d), 131.7 (d), 131.6 (d), 130.7 (d), 130.6 (d), 129.9 (d), 129.8 (d), 129.4 (d), 129.23 (d), 129.21 (d), 129.17 (s), 129.12 (s), 129.08 (d), 128.8 (d), 128.6 (d), 128.5 (d), 128.2 (d), 128.1 (d), 128.0 (d), 121.3 (s), 121.1 (s), 118.8 (d), 118.7 (d), 105.22 (d), 105.20 (d), 99.2 (d), 99.1 (d), 55.7 (q), 55.6 (q), 55.5 (q), 53.8 (t), 53.7 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2938, 1678, 1608, 1578, 1511, 1496, 1461, 1411, 1347, 1302, 1265, 1209, 1185, 1160, 1120, 1090, 1028, 965, 938, 867, 807, 779, 762, 732, 698, 663, 624 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 618.2057; found: 618.2055.

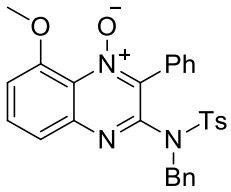


Compound 3aa: R_f = 0.5 (pure EA), total yield 96 % (C7: C6 = 5:1), colourless soild; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.85-8.80 (m, 0.17 H), 8.45-8.40 (m, 0.84 H), 8.26-8.21 (m, 0.85 H), 8.09-8.03 (m, 1 H), 7.99-7.94 (m, 0.18 H), 7.42-7.24 (m, 5 H), 6.91-6.82 (m, 2 H), 6.67-6.60 (m, 2 H),4.43-4.35 (m, 2 H), 4.00-3.88 (m, 2 H), 3.67 (s, 3 H), 2.95-2.85 (m, 3 H), 2.68-2.59 (m, 2 H), 2.24-2.12 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 175.0 (s), 159.7 (s), 150.9 (s), 149.0 (s), 142.6 (s), 142.4 (s), 142.2 (s), 139.9 (s), 138.7 (s), 136.8 (s), 133.2 (s), 130.85 (d), 130.81 (d), 130.5 (d), 130.4 (d), 130.0 (d), 129.7 (d), 128.5 (s), 128.4 (s), 128.3 (d), 128.2 (d), 126.2 (s), 126.1 (s), 125.3 (d), 123.1 (d), 120.1 (d), 116.7 (d), 114.1 (d), 114.0 (d), 105.9 (d), 55.3 (q), 53.8

(t), 53.7 (t), 48.8 (t), 48.7 (t), 41.5 (q), 41.1 (q), 33.0 (t), 32.9 (t), 17.9 (t), 17.7 (t) ppm; IR (ATR): $\tilde{\nu}$ = 2960, 1703, 1612, 1578, 1513, 1471, 1379, 1332, 1276, 1248, 1214, 1178, 1150, 1123, 1028, 954, 868, 825, 779, 756, 731, 699, 669, 625 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 503.1748; found: 503.1744.

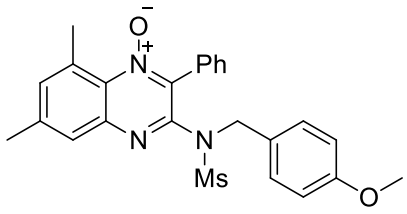


Compound 3ab: R_f = 0.08 (PE/EA = 4:1), total yield 97 % (C7: C6 = 7:1), colourless soild; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.38-8.33 (m, 0.89 H), 7.89-7.85 (m, 0.12 H), 7.80-7.78 (m, 0.10 H), 7.40-7.21 (m, 7 H), 6.91-6.82 (m, 2 H), 6.77-6.59 (m, 2 H), 4.40 (s, 2 H), 3.95-3.87 (m, 3 H), 3.68 (s, 3 H), 2.93-2.83 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.4 (s), 159.6 (s), 150.6 (s), 143.9 (s), 139.2 (s), 132.0 (s), 130.8 (d), 130.6 (d), 129.6 (d), 128.6 (s), 128.3 (d), 126.3 (s), 123.1 (d), 120.8 (d), 114.0 (d), 107.4 (d), 56.1 (q), 55.3 (q), 53.7 (t), 41.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2966, 2930, 1611, 1581, 1514, 1470, 1414, 1380, 1350, 1336, 1316, 1257, 1216, 1178, 1147, 1105, 1047, 1024, 956, 866, 850, 828, 771, 754, 738, 720, 699, 659, 634, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 450.1482; found: 450.1481.

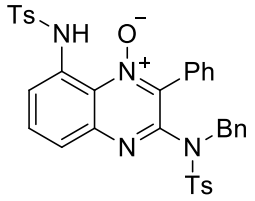


Compound 3ac: Yield 55 %, R_f = 0.14 (PE/EA = 4:1), colourless soild, mp: 198-199 ^oC;; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.64-7.56 (m, 1 H), 7.54-7.48 (m, 1 H), 7.45-7.39 (m, 2 H), 7.39-7.33 (m, 1 H), 7.32-7.25 (m, 2 H), 7.21-7.16 (m, 2 H), 7.13-7.08 (m, 1 H), 7.04-6.98 (m, 3 H), 6.98-6.90 (m, 2 H), 6.74-6.67 (m, 2 H), 4.44 (s, 2 H), 3.89 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.5 (s), 149.3 (s), 144.7 (s), 144.2 (s), 144.1 (s), 135.5 (s), 134.1 (s), 131.3 (d), 130.7 (d), 129.8 (d), 129.6 (s), 129.3 (d), 129.04 (d), 129.02 (d), 128.9 (s), 128.4 (d), 128.1 (d), 127.9 (d), 121.7 (d), 110.8 (d), 57.1 (q), 53.4 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3062, 2930, 1716, 1595, 1500, 1455, 1364, 1334, 1266, 1236, 1168, 1087, 1035, 1023, 972, 944, 869, 843, 813, 770, 737, 697, 665 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$:

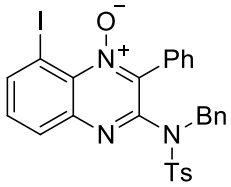
512.1639; found: 512.1636.



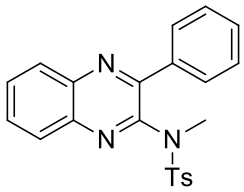
Compound 3ad: Yield 76 %, R_f = 0.14 (PE/EA = 4:1), colourless soild, mp: 194-195 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.58 (s, 1 H), 7.38-7.32 (m, 3 H), 7.26-7.16 (m, 3 H), 6.89 (d, *J* = 8.5 Hz, 2 H), 6.66 (d, *J* = 8.5 Hz, 2 H), 4.40 (s, 2 H), 3.68 (s, 3 H), 2.91 (s, 3 H), 2.85 (s, 3 H), 2.43 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.5 (s), 149.6 (s), 144.0 (s), 141.7 (s), 141.1 (s), 135.4 (d), 134.8 (s), 133.1 (s), 130.8 (d), 130.4 (d), 129.4 (d), 129.0 (s), 128.4 (d), 127.1 (d), 126.4 (s), 114.0 (d), 55.3 (q), 53.6 (t), 41.1 (q), 24.2 (q), 21.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2932, 2838, 1714, 1612, 1581, 1513, 1461, 1342, 1284, 1248, 1152, 1113, 1075, 1031, 947, 926, 839, 765, 699, 656, 640, 618 cm^{-1}; HRMS (ESI) m/z calcd for $[M+H]^+$: 464.1639; found: 464.1639.



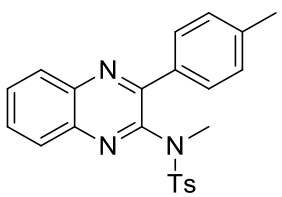
Compound 3b-1: Yield 77 %, R_f = 0.18 (PE/EA = 4:1), yellow soild, mp: 215-216 ^oC;; ^1H NMR (500 MHz, $CDCl_3$) δ = 12.4 (s, 1 H), 7.80-7.76 (m, 1 H), 7.70-7.65 (m, 2 H), 7.62-7.55 (m, 1 H), 7.55-7.50 (m, 1 H), 7.45-7.40 (m, 1 H), 7.37-7.30 (m, 4 H), 7.20-7.11 (m, 5 H), 7.06-7.00 (m, 2 H), 6.94-6.86 (m, 2 H), 6.73-6.66 (m, 2 H), 4.41 (s, 2 H), 2.38 (s, 3 H), 2.28 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 149.4 (s), 144.6 (s), 144.2 (s), 143.5 (s), 142.9 (s), 136.2 (s), 134.9 (s), 133.7 (s), 133.1 (s), 131.9 (d), 130.4 (d), 129.8 (d), 129.7 (d), 129.4 (d), 128.9 (d), 128.5 (d), 128.3 (d), 128.2 (d), 128.0 (s), 127.4 (d), 126.4 (s), 123.6 (d), 118.2 (d), 53.5 (t), 21.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1580, 1532, 1496, 1446, 1410, 1345, 1292, 1185, 1162, 1122, 1088, 1023, 957, 889, 855, 811, 756, 726, 698, 659 cm^{-1}; HRMS (ESI) m/z calcd for $[M+Na]^+$: 673.1550; found:673.1563.



Compound 3b-2: Yield 46 %, R_f = 0.35 (PE/EA = 4:1), yellow soild, mp: 203-204 ^{o}C;; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.33-8.27 (m, 1 H), 7.94-7.88 (m, 1 H), 7.42-7.36 (m, 3 H), 7.35-7.28 (m, 3 H), 7.21-7.16 (m, 2 H), 7.15-7.10 (m, 1 H), 7.06-6.92 (m, 4 H), 6.75-6.69 (m, 2 H), 4.45 (s, 2 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 149.2 (s), 145.4 (d), 144.3 (s), 143.4 (s), 142.5 (s), 135.6 (s), 135.2 (s), 133.9 (s), 132.1 (d), 130.7 (d), 130.6 (d), 129.8 (d), 129.4 (d), 129.3 (d), 128.9 (d), 128.8 (s), 128.5 (d), 128.3 (d), 128.2 (d), 80.6 (s), 53.5 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1596, 1548, 1522, 1497, 1475, 1446, 1417, 1387, 1337, 1266, 1185, 1160, 1088, 1025, 968, 907, 862, 804, 772, 756, 722, 696, 664, 629 cm^{-1}; HRMS (ESI) m/z calcd for $[M+Na]^+$: 630.0319; found: 630.0328.

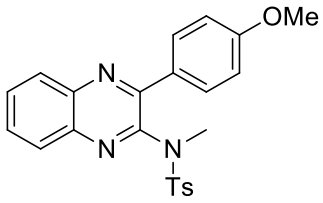


Compound 4a: Yield 67 %, R_f = 0.45 (PE/EA = 4:1), colourless soild, mp: 192-193 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.11-8.05 (m, 1 H), 7.96-7.90 (m, 2 H), 7.85-7.79 (m, 1 H), 7.72-7.60 (m, 4 H), 7.51-7.41 (m, 3 H), 7.25-7.19 (m, 2 H), 2.99 (s, 3 H), 2.37 (s, 3 H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.2 (s), 148.2 (s), 143.9 (s), 141.6 (s), 140.1 (s), 137.4 (s), 135.0 (s), 130.4 (d), 130.1 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.0 (d), 128.6 (d), 128.3 (d), 36.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3058, 3043, 3028, 1597, 1546, 1488, 1468, 1444, 1395, 1351, 1304, 1224, 1185, 1160, 1087, 1067, 1032, 1003, 995, 917, 851, 815, 771, 745, 694, 670, 640, 612 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{19}N_3O_2S$: 389.1198; found: 389.1167.

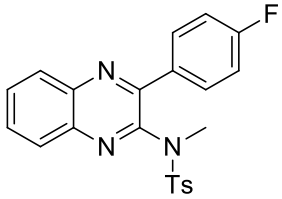


Compound 4b: Yield 70 %, R_f = 0.43 (PE/EA = 4:1), colourless soild, mp: 184-185

^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07-8.04 (m, 1 H), 7.86-7.82 (m, 2 H), 7.81-7.78 (m, 1 H), 7.70-7.60 (m, 4 H), 7.28-7.20 (m, 4 H), 2.98 (s, 3 H), 2.37 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.0 (s), 147.1 (s), 142.8 (s), 140.5 (s), 138.8 (s), 138.5 (s), 133.9 (s), 133.4 (s), 129.3 (d), 128.9 (d), 128.3 (d), 128.2 (d), 128.1 (d), 128.08 (d), 128.07 (d), 127.9 (d), 35.8 (q), 20.6 (q), 20.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3055, 2961, 1693, 1598, 1453, 1392, 1353, 1304, 1259, 1224, 1183, 1162, 1088, 1069, 1024, 998, 916, 853, 825, 814, 802, 769, 751, 705, 676, 648, 629, 611 cm^{-1}; HRMS (EI) m/z calcd for $C_{23}H_{21}N_3O_2S$: 403.1354; found: 403.1329.

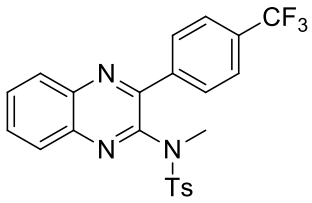


Compound 4c: Yield 63 %, R_f = 0.3 (PE/EA = 4:1), colourless soild, mp: 193-195 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07-8.03 (m, 1 H), 7.99-7.93 (m, 2 H), 7.81-7.76 (m, 1 H), 7.72-7.61 (m, 4 H), 7.27-7.22 (m, 2 H), 7.03-6.97 (m, 2 H), 3.83 (s, 3 H), 3.00 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 160.8 (s), 152.5 (s), 148.1 (s), 143.9 (s), 141.6 (s), 139.8 (s), 135.0 (s), 130.8 (d), 130.4 (d), 129.8 (d), 129.6 (s), 129.3 (d), 129.1 (d), 128.2 (d), 114.2 (d), 55.4 (q), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2962, 2934, 1611, 1579, 1516, 1484, 1465, 1420, 1392, 1348, 1293, 1255, 1224, 1172, 1159, 1111, 1087, 1072, 1031, 995, 915, 853, 830, 812, 802, 774, 755, 706, 674, 646, 624, 611 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{23}H_{21}N_3O_3S+H]^+$: 420.1376; found: 420.1373.

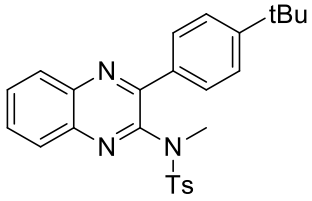


Compound 4d: Yield 51 %, R_f = 0.5 (PE/EA = 4:1), colourless soild, mp: 175-176 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07-8.04 (m, 1 H), 7.98-7.93 (m, 2 H), 7.81-7.77 (m, 1 H), 7.72-7.63 (m, 2 H), 7.59 (d, *J* = 8.0 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.16-7.11 (m, 2 H), 3.01 (s, 3 H), 2.37 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.6 (*J* = 248.2 Hz, s), 152.2 (s), 148.0 (s), 144.1 (s), 141.5 (s), 140.1 (s), 134.6 (s),

133.5 (*J* = 3.4 Hz, s), 131.4 (*J* = 8.5 Hz, d), 130.6 (d), 130.3 (d), 129.3 (d), 129.1 (d), 129.0 (d), 128.4 (d), 115.7 (*J* = 21 Hz, d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3067, 1914, 1693, 1598, 1510, 1482, 1396, 1347, 1303, 1217, 1156, 1131, 1105, 1085, 1001, 918, 866, 841, 808, 772, 752, 719, 705, 679, 650, 624 cm^{-1}; HRMS (EI) m/z calcd for $C_{22}H_{18}FN_3O_2S$: 407.1104; found: 407.1098.

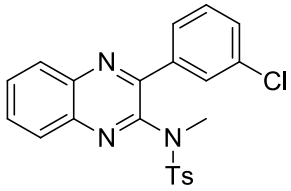


Compound 4e: Yield 49 %, R_f = 0.47 (PE/EA = 4:1), colourless soild, mp: 195-196 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.11-8.08 (m, 1 H), 8.07-8.02 (m, 2 H), 7.85-7.82 (m, 1 H), 7.76-7.68 (m, 4 H), 7.50 (d, *J* = 8.0 Hz, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 3.07 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.1 (s), 147.9 (s), 144.2 (s), 141.5 (s), 141.1 (*J* = 1.0 Hz, s), 140.4 (s), 134.3 (s), 131.1 (*J* = 31.8 Hz, s), 130.8 (d), 130.7 (d), 129.7 (d), 129.4 (d), 129.3 (d), 128.8 (d), 128.4 (d), 126.3 (*J* = 273.2 Hz, s), 125.5 (*J* = 3.8 Hz, d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1598, 1471, 1395, 1345, 1323, 1292, 1245, 1228, 1165, 1118, 1075, 1019, 998, 952, 919, 861, 846, 817, 805, 774, 758, 732, 708, 701, 672, 648, 630, 617 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{23}H_{18}F_3N_3O_2S+Na]^+$: 480.0964; found: 480.0985.

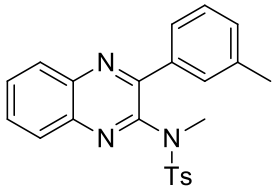


Compound 4f: Yield 71 %, R_f = 0.52 (PE/EA = 4:1), colourless soild, mp: 190-192 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.07-8.03 (m, 1 H), 7.88 (d, *J* = 8.5 Hz, 2 H), 7.82-7.78 (m, 1 H), 7.68-7.59 (m, 4 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 2.98 (s, 3 H), 2.36 (s, 3 H), 1.31 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.0 (s), 152.6 (s), 148.1 (s), 143.9 (s), 141.6 (s), 139.9 (s), 135.1 (s), 134.4 (s), 130.3 (d), 129.9 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.9 (d), 128.3 (d), 125.7 (d), 36.9 (q), 34.8 (s), 31.4 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2961, 2870, 1739, 1694, 1599, 1481, 1463, 1395, 1349, 1307, 1228, 1158, 1112, 1087, 1021, 998, 918, 862, 838, 811,

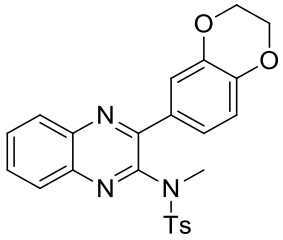
764, 735, 706, 676, 650, 633, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{26}H_{27}N_3O_2S+H]^+$: 446.1897; found: 446.1893.



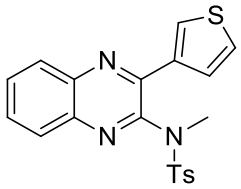
Compound 4g: Yield 53 %, R_f = 0.45 (PE/EA = 4:1), colourless soild, mp: 169-171 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.12-8.08 (m, 1 H), 7.92-7.82 (m, 3 H), 7.76-7.67 (m, 2 H), 7.57 (d, *J* = 8.0 Hz, 2 H), 7.43-7.39 (m, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 3.06 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 151.8 (s), 144.1 (s), 141.5 (s), 140.3 (s), 139.2 (s), 134.6 (s), 134.5 (s), 130.7 (d), 130.5 (d), 129.8 (d), 129.5 (d), 129.4 (d), 129.3 (d), 129.2 (d), 128.9 (d), 128.4 (d), 127.4 (d), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2924, 2854, 1598, 1571, 1486, 1466, 1452, 1440, 1426, 1389, 1352, 1305, 1254, 1223, 1182, 1160, 1136, 1088, 1069, 1038, 1012, 968, 916, 855, 817, 803, 770, 744, 706, 693, 677, 664, 639, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{22}H_{18}ClN_3O_2S+H]^+$: 424.0881; found: 424.0876.



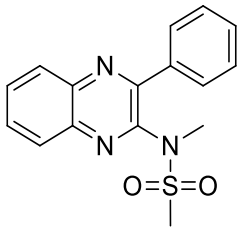
Compound 4h: Yield 50 %, R_f = 0.45 (PE/EA = 4:1), colourless soild, mp: 155-157 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.12-8.06 (m, 1 H), 7.85-7.81 (m, 1 H), 7.75-7.62 (m, 6 H), 7.39-7.33 (m, 1 H), 7.28-7.20 (m, 3 H), 2.99 (s, 3 H), 2.40 (s, 3 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.3 (s), 148.2 (s), 143.9 (s), 141.5 (s), 140.1 (s), 138.4 (s), 137.2 (s), 135.1 (s), 130.4 (d), 130.3 (d), 130.1 (d), 129.8 (d), 129.3 (d), 129.2 (d), 128.9 (d), 128.5 (d), 128.3 (d), 126.2 (d), 36.8 (q), 21.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3053, 3034, 2925, 1599, 1545, 1486, 1454, 1441, 1389, 1351, 1317, 1304, 1249, 1223, 1177, 1158, 1141, 1088, 1071, 1024, 966, 918, 870, 828, 806, 784, 770, 750, 700, 688, 670, 639, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{23}H_{21}N_3O_2S+Na]^+$: 426.1247; found: 426.1249.



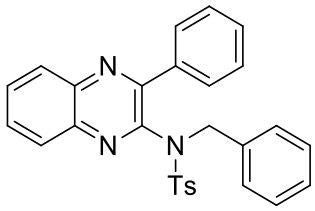
Compound 4i: Yield 69 %, R_f = 0.21 (PE/EA = 4:1), yellow soild, mp: 198-199 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.13-8.09 (m, 1 H), 7.87-7.83 (m, 1 H), 7.77-7.68 (m, 4 H), 7.63-7.57 (m, 2 H), 7.32 (d, *J* = 8.5 Hz, 2 H), 7.04-7.00 (m, 1 H), 4.36-4.30 (m, 4 H), 3.12 (s, 3 H), 2.49 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.2 (s), 148.0 (s), 145.1 (s), 143.9 (s), 143.6 (s), 141.5 (s), 139.8 (s), 135.0 (s), 130.6 (s), 130.3 (d), 129.9 (d), 129.3 (d), 129.1 (d), 129.0 (d), 128.2 (d), 122.7 (d), 118.5 (d), 117.5 (d), 64.6 (t), 64.3 (t), 36.9 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2939, 1586, 1510, 1484, 1464, 1432, 1392, 1344, 1304, 1285, 1255, 1225, 1175, 1156, 1129, 1087, 1063, 1048, 1016, 933, 918, 900, 870, 835, 816, 802, 773, 758, 744, 707, 672, 651, 633, 618, 609 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{24}H_{21}N_3O_4S+Na]^+$: 470.1145; found: 470.1145.



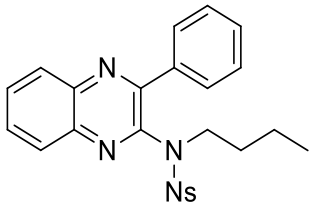
Compound 4j: Yield 58 %, R_f = 0.43 (PE/EA = 4:1), colourless soild, mp: 178-179 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.51-8.46 (m, 1 H), 8.16-8.11 (m, 1 H), 8.08-8.04 (m, 1 H), 7.85-7.76 (m, 4 H), 7.75-7.69 (m, 1 H), 7.50-7.44 (m, 1 H), 7.40-7.34 (m, 2 H), 3.18 (s, 3 H), 2.51 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 148.1 (s), 147.5 (s), 144.1 (s), 141.6 (s), 139.7 (s), 138.0 (s), 134.5 (s), 130.6 (d), 129.8 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.8 (d), 128.5 (d), 128.2 (d), 125.7 (d), 37.1 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3116, 2923, 1598, 1537, 1482, 1463, 1429, 1338, 1254, 1225, 1185, 1166, 1155, 1139, 1072, 1017, 903, 884, 851, 805, 789, 772, 748, 704, 677, 651, 626 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{20}H_{17}N_3O_2S_2+H]^+$: 396.0835; found: 396.0830.



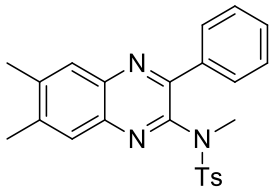
Compound 4k: Yield 57 %, R_f = 0.24 (PE/EA = 4:1), colourless solid, mp: 170-171 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.12-8.04 (m, 1 H), 7.97-7.86 (m, 3 H), 7.75-7.65 (m, 2 H), 7.51-7.37 (m, 3 H), 3.24 (s, 3 H), 3.00 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.2 (s), 148.3 (s), 141.7 (s), 139.9 (s), 136.8 (s), 130.5 (d), 130.4 (d), 129.7 (d), 129.3 (d), 129.1 (d), 128.7 (d), 128.4 (d), 39.4 (q), 37.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3062, 3030, 2931, 1738, 1563, 1544, 1483, 1445, 1395, 1345, 1250, 1227, 1166, 1149, 1088, 1068, 1033, 1004, 964, 915, 857, 793, 767, 738, 698, 634, 613 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{15}N_3O_2S$: 313.0885; found: 313.0875.



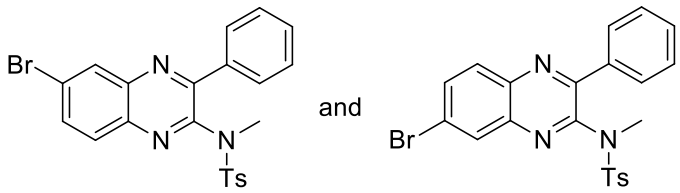
Compound 4l: Yield 62 %, R_f = 0.47 (PE/EA = 4:1), colourless solid, mp: 189-190 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07-8.02 (m, 1 H), 7.91-7.86 (m, 1 H), 7.71-7.65 (m, 2 H), 7.52 (d, *J* = 8.0 Hz, 2 H), 7.50-7.46 (m, 2 H), 7.39-7.30 (m, 3 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 7.05-6.99 (m, 1 H), 6.97-6.92 (m, 2 H), 6.83-6.77 (m, 2 H), 4.60 (s, 2 H), 2.39 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 154.8 (s), 146.9 (s), 144.1 (s), 141.4 (s), 140.2 (s), 137.5 (s), 135.5 (s), 134.2 (s), 130.6 (d), 130.1 (d), 129.7 (d), 129.6 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.9 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.9 (d), 53.9 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3064, 3031, 2952, 2925, 1705, 1598, 1542, 1496, 1482, 1456, 1445, 1399, 1347, 1305, 1195, 1161, 1139, 1089, 1024, 983, 917, 903, 851, 814, 760, 737, 696, 672 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{28}H_{23}N_3O_2S+H]^+$: 466.1584; found: 466.1578.



Compound 4m: Yield 53 %, R_f = 0.6 (PE/EA = 4:1), colourless solid, mp: 163-164 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.32 (d, *J* = 8.5 Hz, 2 H), 8.16-8.11 (m, 1 H), 8.06 (d, *J* = 8.0 Hz, 2 H), 7.98-7.91 (m, 2 H), 7.83-7.69 (m, 3 H), 7.54-7.41 (m, 3 H), 3.37 (t, *J* = 8.0 Hz, 2 H), 1.12-1.04 (m, 2 H), 0.98-0.89 (m, 2 H), 0.57 (t, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 153.8 (s), 150.2 (s), 146.3 (s), 145.2 (s), 141.7 (s), 140.1 (s), 136.9 (s), 131.1 (d), 130.6 (d), 130.3 (d), 129.6 (d), 129.5 (d), 129.4 (d), 128.7 (d), 128.2 (d), 123.8 (d), 50.6 (t), 29.7 (t), 19.9 (t), 13.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3105, 2962, 2930, 2873, 1606, 1528, 1480, 1466, 1444, 1401, 1347, 1314, 1246, 1198, 1166, 1151, 1128, 1112, 1080, 1035, 1014, 983, 913, 886, 857, 811, 786, 763, 746, 736, 700, 682, 649, 627, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{24}H_{22}N_4O_4S+H]^+$: 463.1435; found: 463.1431.

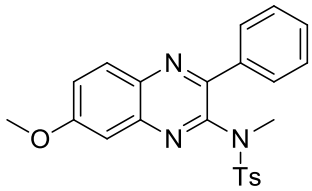


Compound 4n: Yield 65 %, R_f = 0.35 (PE/EA = 4:1), colourless soild, mp: 194-195 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.89 (d, *J* = 7.0 Hz, 1 H), 7.82 (s, 1 H), 7.62 (d, *J* = 7.5 Hz, 2 H), 7.56 (s, 1 H), 7.49-7.37 (m, 3 H), 7.25-7.19 (m, 2 H), 2.97 (s, 3 H), 2.41 (s, 3 H), 2.40 (s, 3 H), 2.37 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 152.2 (s), 147.3 (s), 143.8 (s), 141.1 (s), 140.8 (s), 140.6 (s), 139.1 (s), 137.7 (s), 135.1 (s), 129.3 (d), 129.2 (d), 129.1 (d), 129.0 (d), 128.6 (d), 128.3 (d), 127.4 (d), 36.8 (q), 21.7 (q), 20.5 (q), 20.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2971, 1739, 1598, 1483, 1448, 1401, 1338, 1301, 1272, 1214, 1183, 1153, 1118, 1084, 1022, 1004, 894, 879, 835, 804, 777, 753, 696, 662, 638, 628, 613 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{24}H_{23}N_3O_2S+Na]^+$: 440.1403; found: 440.1406.

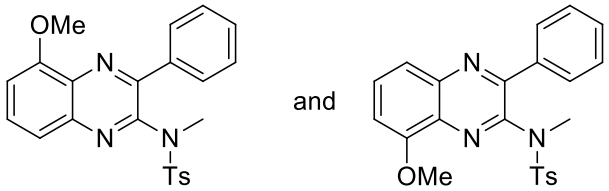


Compound 4o: Yield 51 %, R_f = 0.29 (PE/EA = 4:1), colourless soild; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.27-8.24 (m, 0.26 H), 8.01-7.98 (m, 0.67 H), 7.97-7.88 (m, 2.62 H), 7.80-7.70 (m, 1 H), 7.70-7.65 (m, 0.3 H), 7.64-7.55 (m, 2 H), 7.50-7.39 (m, 3 H),

7.28-7.19 (m, 2 H), 3.03-2.93 (m, 3 H), 2.43-2.33 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 154.0 (s), 153.4 (s), 148.9 (s), 148.4 (s), 144.16 (s), 144.10 (s), 142.0 (s), 140.6 (s), 140.2 (s), 138.8 (s), 137.1 (s), 137.0 (s), 134.7 (s), 133.9 (d), 133.7 (d), 131.5 (d), 130.6 (d), 130.5 (d), 129.8 (d), 129.7 (d), 129.6 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.1 (d), 128.92 (d), 128.91 (d), 128.75 (d), 128.72 (d), 124.4 (s), 124.2 (s), 36.83 (q), 36.80 (q), 21.71 (q), 21.70 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 2854, 1738, 1597, 1540, 1494, 1463, 1447, 1395, 1338, 1290, 1251, 1201, 1175, 1155, 1082, 1033, 1005, 932, 867, 835, 811, 769, 739, 703, 678, 629 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{22}H_{18}BrN_3O_2S+Na]^+$: 490.0195; found: 490.0200.

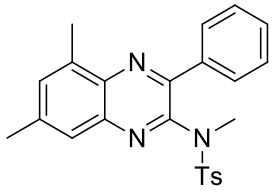


Compound 4p: Yield 65 %, R_f = 0.23 (PE/EA = 4:1), colourless soild, mp: 179-180 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.98-7.94 (m, 1 H), 7.92-7.84 (m, 2 H), 7.60 (d, *J* = 7.5 Hz, 2 H), 7.49-7.37 (m, 3 H), 7.37-7.29 (m, 1 H), 7.22 (d, *J* = 7.0 Hz, 2H), 7.13-7.08 (m, 1 H), 3.89 (s, 3 H), 3.00 (s, 3 H), 2.40 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 161.1 (s), 150.6 (s), 148.2 (s), 143.8 (s), 141.9 (s), 137.8 (s), 137.6 (s), 135.0 (s), 130.2 (d), 129.3 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.6 (d), 123.6 (d), 105.8 (d), 55.9 (q), 36.8 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2925, 1618, 1598, 1535, 1486, 1448, 1413, 1342, 1292, 1238, 1215, 1182, 1167, 1122, 1074, 1017, 997, 963, 875, 848, 826, 814, 801, 752, 729, 704, 688, 668, 647, 624 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{23}H_{21}N_3O_3S+Na]^+$: 442.1196; found: 442.1198.



Compound 4q: R_f = 0.13 (PE/EA = 4:1), Yield 52 %, colourless soild; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.99-7.95 (m, 0.2 H), 7.95-7.90 (m, 1.7 H), 7.65 (d, *J* = 8.5 Hz, 2 H), 7.61-7.54 (m, 1 H), 7.50-7.37 (m, 4 H), 7.27 (d, *J* = 8.0 Hz, 0.2 H), 7.22 (d, *J* = 8.0 Hz, 1.9 H), 7.03-7.00 (m, 1 H), 4.03-3.95 (m, 3 H), 2.96 (s, 2.7 H), 2.83 (s, 0.3 H),

2.41-2.34 (m, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 155.3 (s), 151.5 (s), 148.5 (s), 143.9 (s), 141.2 (s), 137.4 (s), 135.1 (s), 133.6 (s), 130.4 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.0 (d), 128.6 (d), 120.0 (d), 108.6 (d), 56.4 (q), 36.8 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2970, 2936, 1738, 1598, 1571, 1541, 1496, 1478, 1461, 1445, 1347, 1269, 1229, 1157, 1120, 1087, 1033, 1006, 972, 847, 814, 789, 761, 734, 697, 671, 650, 606 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{23}H_{21}N_3O_3S+Na]^+$: 442.1196; found: 442.1198.



Compound 4r: Yield 61 %, R_f = 0.52 (PE/EA = 4:1), colourless soild, mp: 180-181 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.03-7.97 (m, 2 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 7.48-7.37 (m, 4 H), 7.35 (s, 1 H), 7.22 (d, J = 8.5 Hz, 2 H), 2.98 (s, 3 H), 2.69 (s, 3 H), 2.45 (s, 3 H), 2.37 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.4 (s), 147.6 (s), 143.8 (s), 140.5 (s), 140.4 (s), 139.3 (s), 137.8 (s), 137.2 (s), 135.1 (s), 132.7 (d), 129.4 (d), 129.3 (d), 129.2 (d), 129.0 (d), 128.5 (d), 124.9 (d), 36.8 (q), 21.9 (q), 21.7, 17.2 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2925, 1738, 1617, 1596, 1572, 1537, 1477, 1455, 1435, 1374, 1340, 1305, 1278, 1256, 1234, 1208, 1182, 1163, 1148, 1117, 1085, 1065, 1034, 1008, 961, 908, 855, 814, 777, 740, 706, 693, 683, 664, 636, 607 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{24}H_{23}N_3O_2S+Na]^+$: 440.1403; found: 440.1405.

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[2] Y. Kim, R. B. Dateer, S. Chang, *Org. Lett.*, **2017**, *19*, 190–193.

[3] S. Nobuo, S. Hiroaki, M. Shinichi, T. Tohru, *Heterocycles*, **2005**, *65*, 1589-1600.

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[5] L. Dyall, *Aust. J. Chem.*, **1986**, *39*, 89-101.

Chapter 5: Gold-Catalyzed Oxidative [2+2+1] Annulation of Ynamides with Quinoxaline *N*-Oxides toward Fully-Functionalized Furans

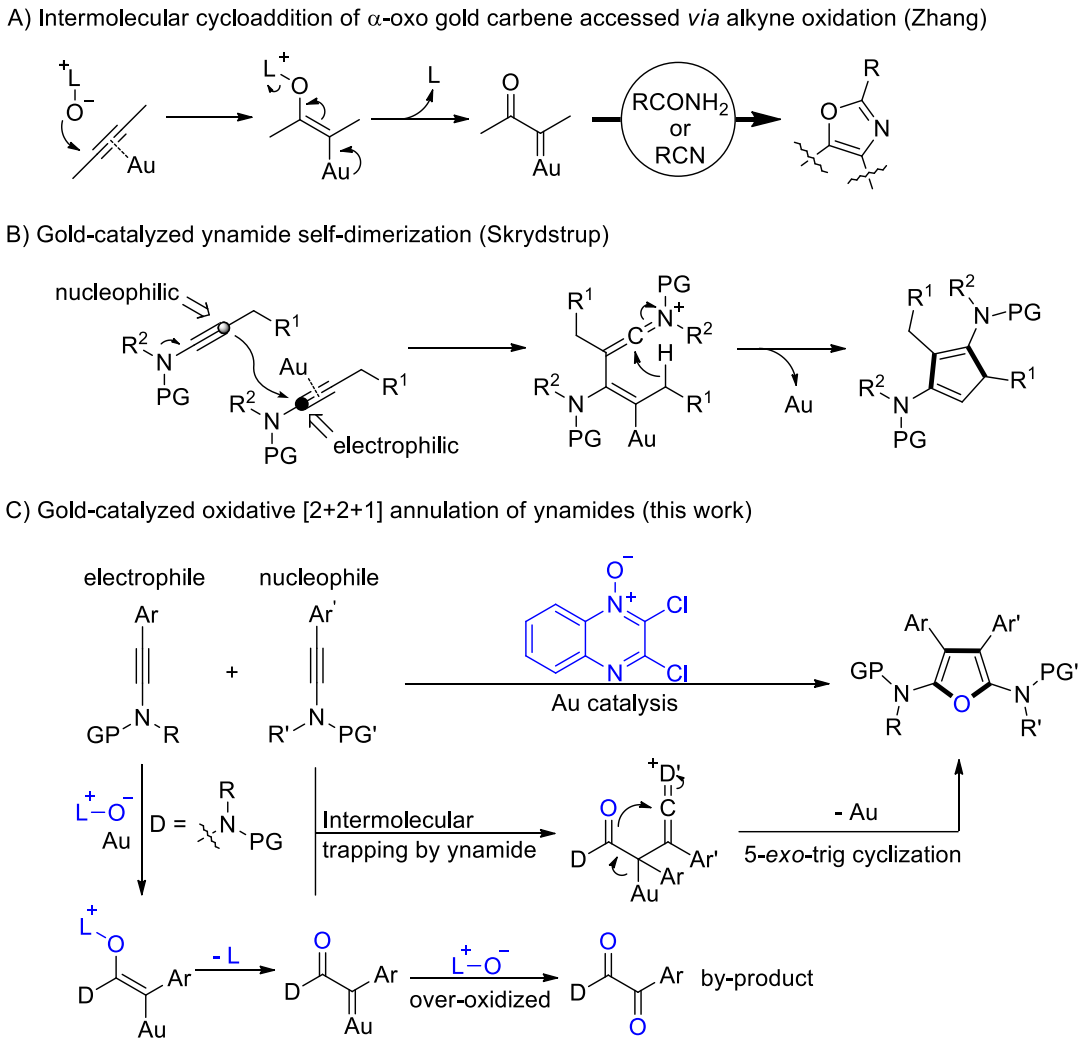
5.1 Introduction

Gold-catalyzed oxidative cyclizations have attracted enormous attention as powerful, flexible and abundant tool for the construction of heterocyclic frameworks.[1] Therein the facile alkyne oxidation by *N*-oxides to access α-oxo gold carbene instead of using hazardous diazo carbonyl compounds as carbenoid precursors significantly expands the substrate generality and the synthetic horizon of gold catalysis.[2,3] However, the published cyclization processes involve mostly intramolecular trappings of α-oxo gold carbenes *via* tethered nucleophiles.[4] Currently, intermolecular cyclization patterns for α-oxo gold carbenes is still limited to the reaction with external nitriles[5a] or amides[5b] leading to oxazole derivatives (Scheme 1 A). For more challenging C-nucleophiles, despite of spectacular achievements on intermolecular oxygenative C-C bond couplings of alkynes with electron-rich arenes *via* *N*-oxides,[6] further tandem cyclizations are no reported. Moreover, the exploitation of new C-nucleophiles in combination with matching *N*-oxides for gold-catalyzed oxygenative reactions with alkynes remains highly desirable.

Ynamides are easily accessible and significant building blocks for synthetic chemists.[7] Due to the polarization of the triple bond, ynamides possess both electrophilic and nucleophilic properties. In recent years, the introduction of ynamides into gold catalysis has greatly promoted the boom of ynamide chemistry.[8] Yet, most of transformations were invoked by only one role of the ynamide, either acting as an electrophile or a nucleophile. A scarce case of a gold-catalyzed ynamide self-dimerization enabled by its amphoteric character was reported by Skrydstrup and co-workers (Scheme 1 B).[9] Inspired by this study and in continuation of our interest on ynamide transformations,[10] we envisaged that a-oxo gold carbene generated via the electrophilic character of the ynamide would be electrophilic enough to be trapped via the nucleophilic character of the other molecule of ynamide. In fact, the major

obstacle for the reaction design was that under the oxidative condition the *in-situ* generated gold carbenes are easily over-oxidized by nucleophilic *N*-oxides, as competing reaction to the presumed trapping with the weakly nucleophilic ynamide.

Herein, we achieved the unique gold-catalyzed oxidative [2+2+1] annulation of two molecules of ynamide with an oxygen atom transferred from 2,3-dichloroquinoxaline *N*-oxide (Scheme 1 C). This give rise to densely substituted furans that are widely embed in functional materials and pharmaceuticals.[11] 2,3-Dichloroquinoxaline *N*-oxide was found to suit for the cascade reaction and successfully restrain the formation of over-oxidized by-product. Symmetric and unsymmetric furans can be prepared by the homo- or cross-coupling of ynamides. Furthermore, we applied this methodology for the intramolecular transformation of di-ynamides resulting in a variety of valuable macrocyclic furan-containing frameworks.



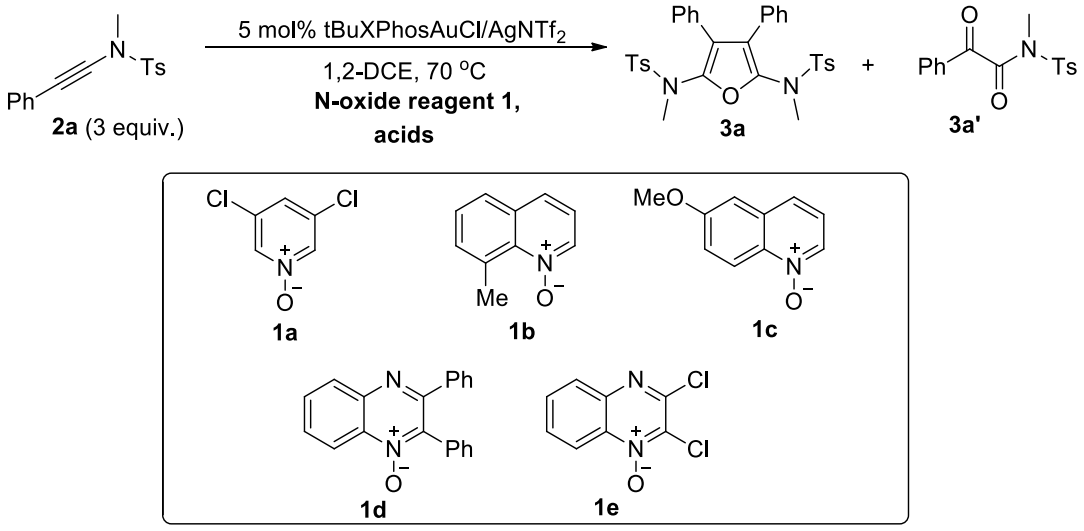
Scheme 1. Gold-catalyzed oxidative cyclization with ynamide starting materials

5.2 Results and Discussion

5.2.1 Optimization of the Reaction Conditions

Initially, we focused on the reaction of ynamide **2a** with different *N*-oxides using 5 mol% of tBuXPhosAuCl/$AgNTf_2$ at 70 °C. As shown in Table 1, pyridine *N*-oxide **1a** or quinoline *N*-oxides **1b** and **1c** delivered no furan product **3a** even if the *N*-oxide reagents were slowly added to the reaction mixture (entry 1-3). To our delight, 2, 3-diphenyl quinoxaline *N*-oxide **1d** produced the furan **3a** in 63 % yield accompanied by 24 % of **3a'** resulting from ynamide over-oxidation (entry 4). This revealed that the less nucleophilic *N*-oxides can prevent from the over-oxidation of ynamides. Following this principle, the chloro-substituted quinoxaline *N*-oxide **1e** was tested, the formation of **3a'** was almost suppressed and **3a** was gained in 84 % yield (entry 5). In order to increase the yield further, some acids were screened. 0.5 equiv. MsOH led to 61 % yield of furan and the by-product of ynamide hydrolysis (entry 6). Anhydrous acids, such as $HBF_4 \cdot Et_2O$ and HCl dioxane solevent gave rise to 89% yield of **3a** (entry 7-8). 0.1 equiv. HCl dioxane solevent affored the furan in 90 % isolated yield (entry 9). Other common gold catalysts in combination with the acid did not improve the reaction (entry 10-12). The controlled experiment presented the reaction could not proceed without gold catalyst (entry 13).

Table 1. Reaction optimization[a, b]

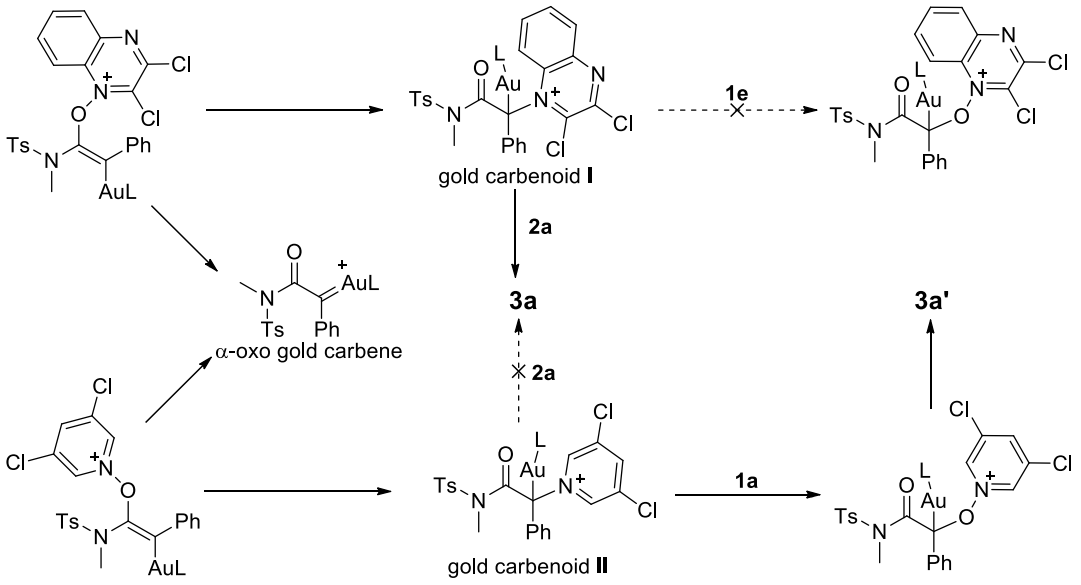


Entry	Catalyst (5 mol%)	*N*-oxide **1**	acids	Yield of **3a**	Yield of **3a'**

1	tBuXPhosAuCl/AgNTf$_2$	**1a**	—	0 %	99 %
2	tBuXPhosAuCl/AgNTf$_2$	**1b**	—	0 %	99 %
3	tBuXPhosAuCl/AgNTf$_2$	**1c**	—	0 %	99 %
4	tBuXPhosAuCl/AgNTf$_2$	**1d**	—	63 %	24 %
5	tBuXPhosAuCl/AgNTf$_2$	**1e**	—	84 %	< 5 %
6	tBuXPhosAuCl/AgNTf$_2$	**1e**	0.5 equiv. MsOH[c]	61 %	< 5 %
7	tBuXPhosAuCl/AgNTf$_2$	**1e**	0.5 equiv. HBF$_4$.Et$_2$O	89 %	< 5 %
8	tBuXPhosAuCl/AgNTf$_2$	**1e**	0.5 equiv. HCl[d]	89 %	< 5 %
9	tBuXPhosAuCl/AgNTf$_2$	**1e**	0.1 equiv. HCl[d]	98 % (90 %)[e]	< 5 %
10	JohnPhosAuCl/AgNTf$_2$	**1e**	0.1 equiv. HCl[d]	85 %[e]	< 5 %
11	Ph$_3$PAuCl/AgNTf$_2$	**1e**	0.1 equiv. HCl[d]	82 %[e]	< 5 %
12	IPrAuCl/AgNTf$_2$	**1e**	0.1 equiv. HCl[d]	75 %[e]	< 5 %
13	—	**1e**	0.1 equiv. HCl[d]	0 %	0 %

[a] Reaction conditions: **2a** (0.3 mmol), *N*-oxide reagent (0.1 mmol), additives and 5 mol% catalyst in 1 ml 1,2-DCE at 70 ^{o}C for 30 mins. [b] Measured by ^{1}H NMR with dibromomethane as the internal standard. [c] Methanesulfonic acid. [d] 4 M HCl in dioxane. [e] Isolated yield.

5.2.2 Mechanism Investigation



Scheme 2. Proposed gold carbenoid intermediate.

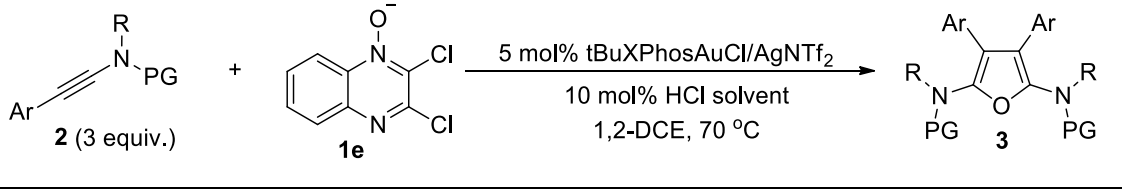
Remarkably, while the presumed α-oxo gold carbene, produced by 2,3-dichloroquinoxaline *N*-oxide, performed the furan in the excellent selectivity, the gold carbene species generated *via* pyridine *N*-oxides could not promote the furan

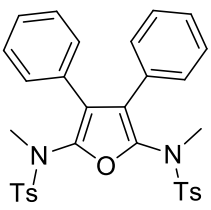
formation with an excess of ynamide. The distinct result suggests that the actual intermediate is not a free carbene species. Instead, the addition of the leaving *N*-heterocycle to the α-oxo gold carbene takes place (Scheme 2).[12] The so formed gold carbenoid **I** with weakly nucleophilic quinoxaline could facilitate the selective formation of furan and disable the reaction with quinoxaline *N*-oxide, whereas the gold carbenoid **II** can not be trapped by the ynamide due to the stronger coordinating pyridine which reduces the reactivity of the carbenoid.

5.2.3 Scope and Limitation

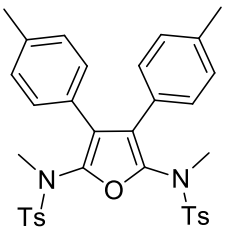
With the optimized condition in hand, a vast range of aryl substituted ynamides was employed to prepare symmetric furans (Table 2). The reaction tolerated various functional groups, including methoxy (**3c**), halogen (**3d**, **3j**, **3m**), trifluoromethyl (**3e**), ester groups (**3h**) and a dioxane moiety (**3n**). Due to the steric effect, low yields were obtained with bulky 3, 5-disubstituted phenyl ynamides (**3k**, **3l**). Alkyl substituted ynamides decomposed under the oxidizing condition. Next we varied the amide moiety of the ynamide. A set of protecting groups and substituents at the R-position were checked (**3r-t**). Both mesyl (**3r**) and an easily removable nosyl group (**3t**) were well compatible. The molecular structure of **3a** was confirmed by single crystal X-ray diffraction.[13]

Table 2. Scope of ynamides[a, b]

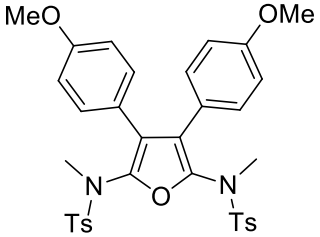




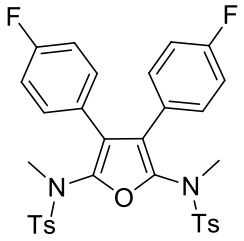
3a, 90 %



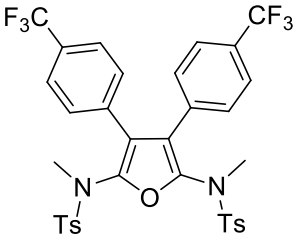
3b, 92 %



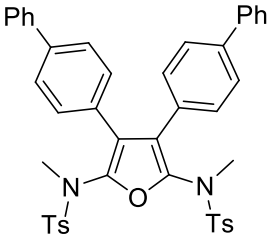
3c, 80 %



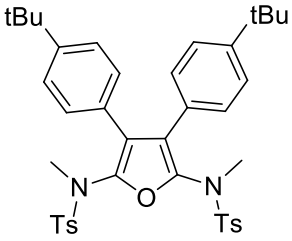
3d, 85 %



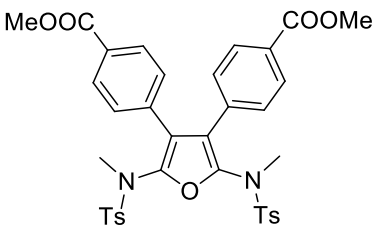
3e, 65 %



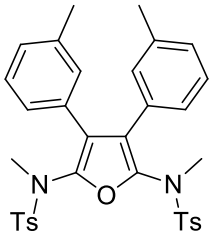
3f, 95 %



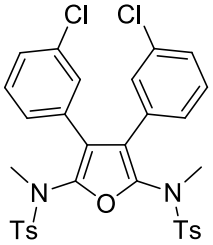
3g, 95 %



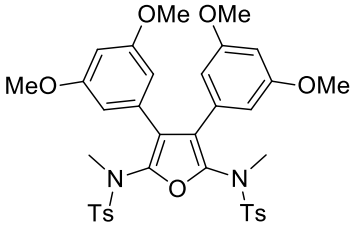
3h, 66 %



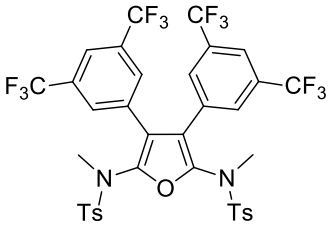
3i, 70 %



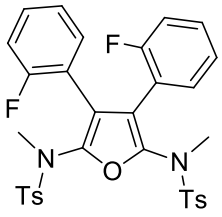
3j, 66 %



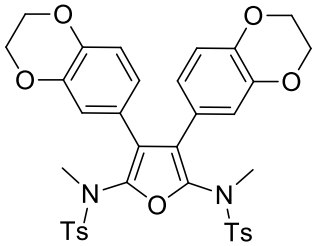
3k, 23 %



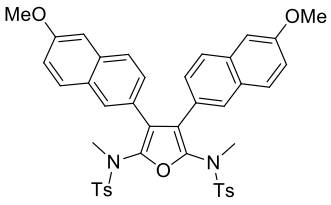
3l, 20 %



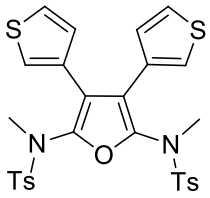
3m, 64 %



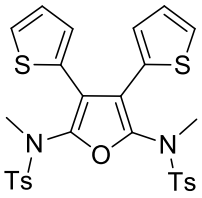
3n, 91 %



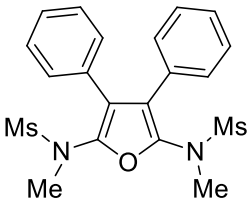
3o, 84 %



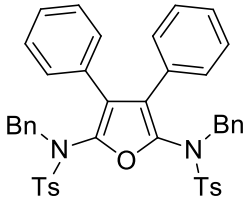
3p, 82 %



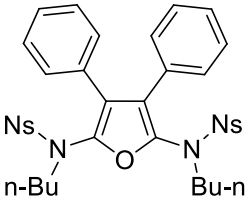
3q, 35 %



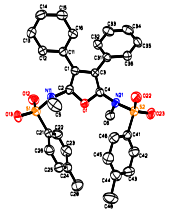
3r, 85 %



3s, 54 %



3t, 83 %

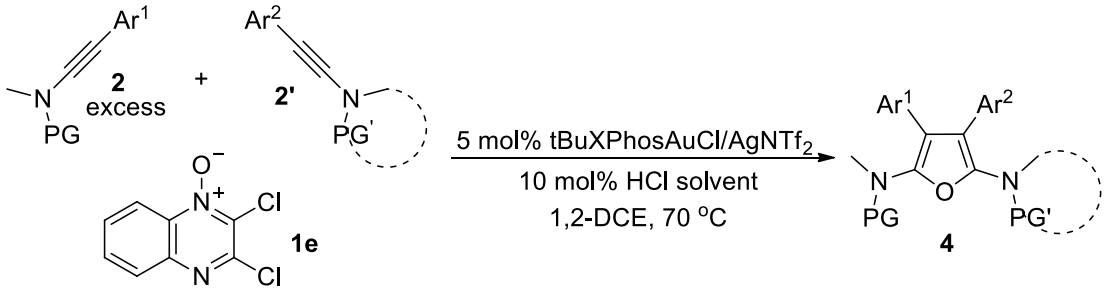


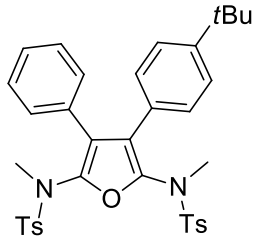
X-ray of 3a

[a] Reaction conditions: **1e** (0.1 mmol), **2** (0.3 mmol), 10 mol% HCl solvent(4 M HCl in dioxane), and 5 mol% *t*BuXPhosAuCl /$AgNTf_2$ at 70 ^oC for 30 mins in 1 ml 1,2-DCE. [b] Isolated yields.

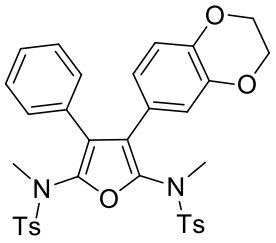
In order to enhance the synthetic utility, our attention was turned to the construction of unsymmetrical furan skeletons as well (Table 3). The reaction of quinoxaline *N*-oxide **1e**, a threefold excess of ynamide **2**, and another more nulecophilic ynamide **2'** under the standard condition could delivered unsymmetrical furans by the cross-coupling of different ynamides. Ynamides containing different aryl substituents and protecting groups were tested together to suit the principle. A whole series of unsymmetrical furans **4** were obtained in moderate to good yields with well tolerance to diverse functional groups (**4a**-**h**). Besides of sulfamides, the transformation of an oxazolidinone-derived ynamide together with ynamide **2a** also afforded the product **4i** in 21 % yield. However, the cross dimerization of aryl substituted ynamide with alkyl substituted ynamides failed to produce the furan.

Table 3. Syntheses of unsymmetrical furans[a, b]

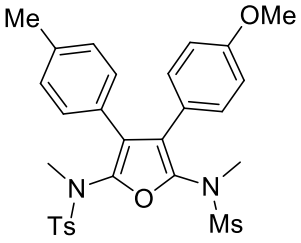




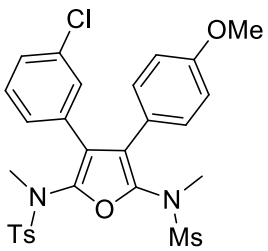
4a, 70 %



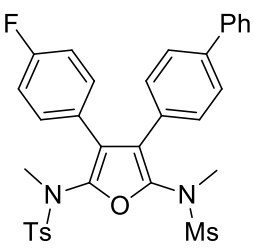
4b, 65 %



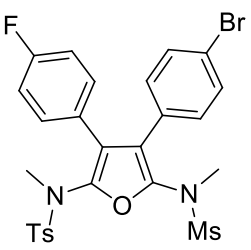
4c, 60 %



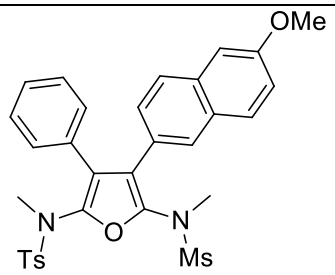
4d[c], 70 %



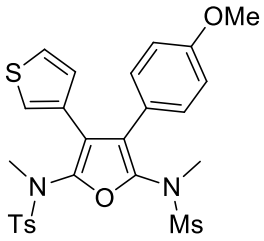
4e, 76 %



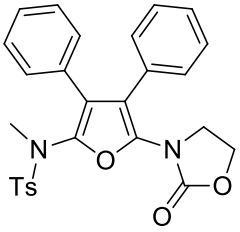
4f, 74 %



4g, 61 %

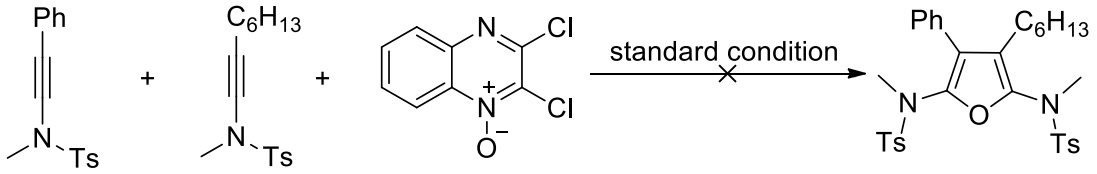


4h, 64 %



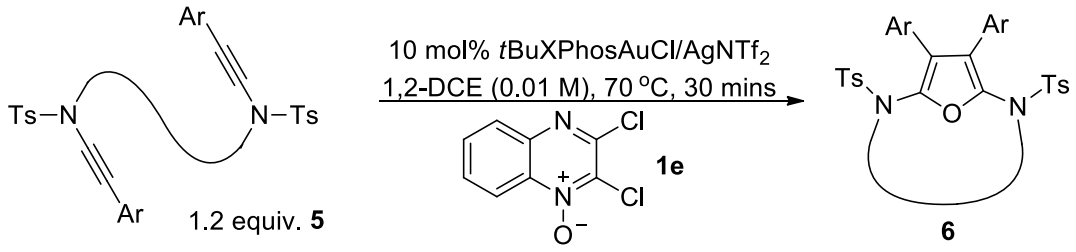
4i, 21 %

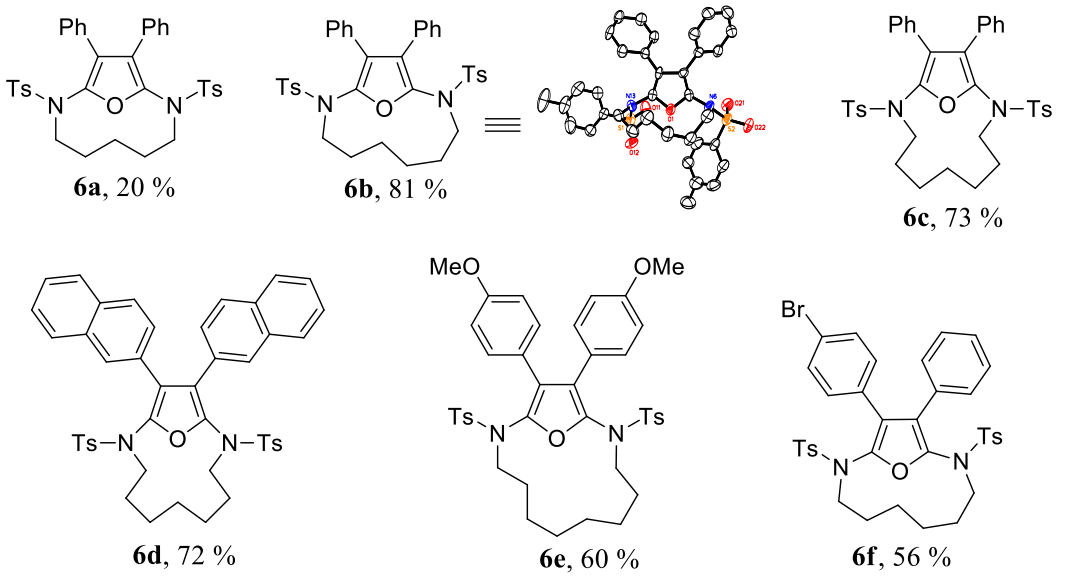
[a] Reaction conditions: **1e** (0.1 mmol), **2** (0.3 mmol), **2'** (0.1 mmol), 10 mol% HCl solvent (4 M HCl in dioxane), and 5 mol% *t*BuXPhosAuCl /$AgNTf_2$ at 70 ^{o}C for 1 h in 1 ml 1,2-DCE. [b] Isolated yields. [c] 4 equiv. **2** was used.



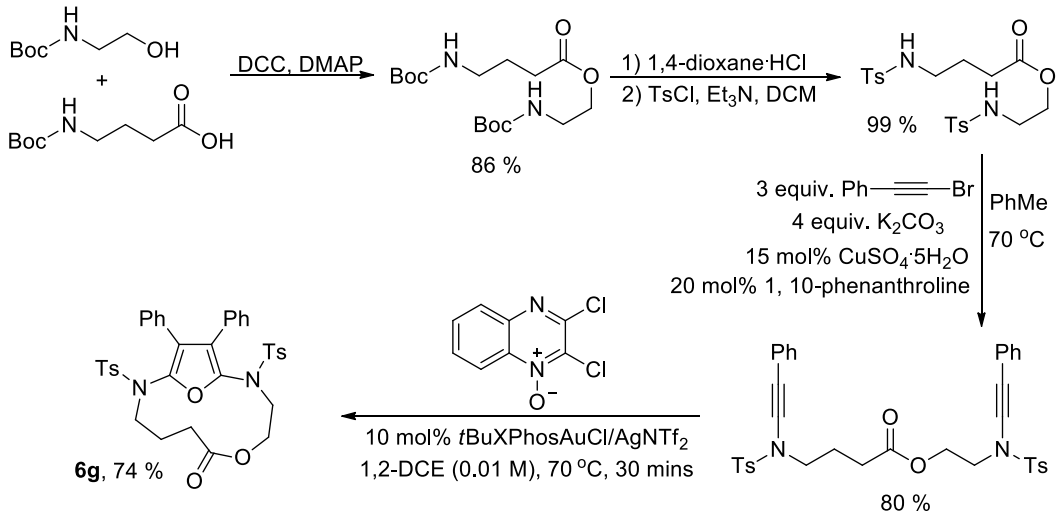
Macrocyclic furan derivatives widely exist in natural products, such as lophotoxin and bipinnatin.[14] The conventional entry to macrocyclic furans mainly focused on the furan synthesis inside of a macrocycle. As a complementary strategy, this methodology was applied in the intramolecular macrocyclization of di-ynamides to construct furan motifs incorporated in macrocyclic systems during the macrocylization step (Table 4). The use of 10 mol% gold catalyst and diluted concentration (0.01 M) led to the strained 10-membered ring **6a** in 20 % yield and 11- to 13-membered rings in good yields (**6b**-**e**). The solid state structure of **6b** was disclosed by X-ray diffraction.[13] The synthesis of unsymmetric macrocyclic furan **6f** was accomplished as well. In addition, the efficient approach to macrolactone **6g** from Boc-protected 2-aminoethanol and 4-aminobutanoic acid was demonstrated (Scheme 3).

Table 4. Intramolecular macrocyclization of di-ynamides.[a, b]





[a] Reaction conditions: **1e** (0.1 mmol), **5** (0.12 mmol), and 10 mol% *t*BuXPhosAuCl /$AgNTf_2$ at 70 °C for 30 mins in 10 ml 1,2-DCE. [b] Isolated yields.



Scheme 3. Application in the synthesis of macrolactone.

5.3 Summary

In summary, gold-catalyzed oxidative [2+2+1] cycloaddition of ynamides with 2, 3-dichloroquinoxaline *N*-oxide has been disclosed. A whole series of densely subtituted symmetric and asymmetric furans was prepared with excellent tolerance to diverse functional groups. The method was further employed to the intramolecular annulation of di-ynamides, enabling the convergent assembly of valuable macrocyclic furan derivatives.

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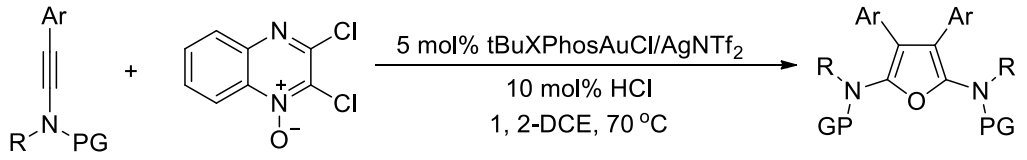
5.5 Experimental Section

General information: Chemicals were purchased from commercial suppliers and used as delivered. The pyridine *N*-oxide **1a** and quinoline *N*-oxides **1b**, **1c** are bought from SigmaAldrich. Quinoxaline *N*-oxides **1d**, **1e** and ynamides were prepared according to related literatures.[1-4] Deuterated solvents were bought from Euriso-Top. NMR spectra were, if not mentioned otherwise, recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance DRX-300, Bruker-Avance DRX-500 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) and m (multiplet) as well as combinations of them. 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 and HSQC 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^+-spectra a Bruker ApexQu FT-ICR-MS spectrometer was applied. Infrared Spectroscopy (IR) was processed on an FT-IR Bruker (IF528), IR Perkin Elmer (283) or FT-IR Bruker Vector 22. The solvent or matrix is denoted in brackets. For the most significant bands the wave number ν (cm^{-1}) is given. X-ray crystal structure analyses were measured at the chemistry department of the University of Heidelberg under the direction of Dr. F. Rominger on a Bruker Smart CCD or Bruker APEX-II CCD instrument using Mo-K_α-radiation. Diffraction intensities were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using SADABS based on the Laue symmetry of reciprocal space. Heavy atom diffractions were solved by direct methods and refined against F2 with full matrix least square algorithm. Hydrogen atoms were either isotropically refined or calculated. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Gas Chromatography / Mass Spectrometry (GC/MS) spectra were measured on two different hardware systems: 1. HP 5972 Mass Selective Detector, coupled with a HP 5890 SERIES II plus gas chromatograph. 2. Agilent 5975C Mass Selective Detector, coupled with an Agilent 7890A gas chromatograph. In both cases, as a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and helium was used as the carrier gas. Gas Chromatography (GC) was carried out on a HP 5890 SERIES II plus gas chromatograph. As a capillary column, an OPTIMA 5 cross-linked Methyl Silicone column (30 m x 0.32 mm, 0.25 µm) was employed and nitrogen was used as the carrier gas. Melting Points were measured in open glass capillaries in a Büchi melting point apparatus (according to Dr. Tottoli) and were not corrected. Flash Column Chromatography was accomplished using Silica gel 60 (0.04 - 0.063 mm / 230 - 400 mesh ASTM) purchased from Macherey-Nagel or Aluminium

oxide (neutral or basic) purchased from Macherey-Nagel. As eluents, mixtures of petroleum ether (PE), ethyl acetate (EA), dichloromethane (DCM) and diethylether (Et_2O) were used. Analytical Thin Layer Chromatography (TLC) was carried out on precoated Macherey-Nagel POLYGRAM® SIL G/UV254 or POLYGRAM® ALOX N/UV254 plastic sheets. Detection was accomplished using UV-light (254 nm), $KMnO_4$ (in 1.5 M Na_2CO_3 (aq.)), molybdatophosphoric acid (5 % in ethanol), vanillin/H_2SO_4 (in ethanol) or anisaldehyde/HOAc (in ethanol). IUPAC names of the compounds described in the experimental section were determined with the program ACDLabs 12.0®.

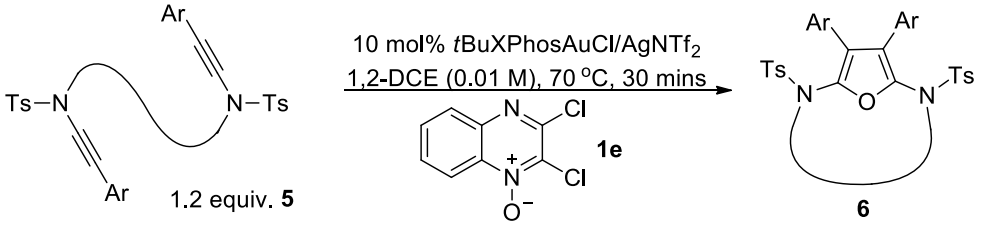
Experimental Procedures



A round bottom flask equipped with a magnetic stirrer bar was charged with tBuXPhosAuCl (5 mol%, 3.2 mg), $AgNTf_2$ (5 mol%, 2 mg), and 1,2-DCE (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the ynamide (0.3 mmol) and 2,3-dichloroquinoxaline *N*-oxide (0.1 mmol, 21.5 mg) and 2.5 mL HCl (4M HCl in dioxane) were added. The reaction was heated at 70 °C for 30 mins. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the symmetric furan product. The characterization data of the products are listed in part 3.

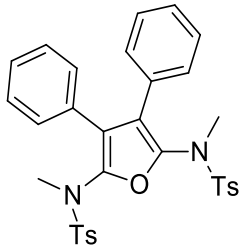
A round bottom flask equipped with a magnetic stirrer bar was charged with tBuXPhosAuCl (5 mol%, 3.2 mg), $AgNTf_2$ (5 mol%, 2 mg), and 1,2-DCE (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the ynamide **2** (0.3 mmol or 0.4 mmol), another ynamide **2'** (0.1 mmol), 2,3-dichloroquinoxaline *N*-oxide (0.1 mmol) and 2.5 mL HCl (4M HCl in dioxane) were added. The reaction was heated at 70 °C for 1 h. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to

provide the unsymmetric furan product. The characterization data of the products are listed in part 3.

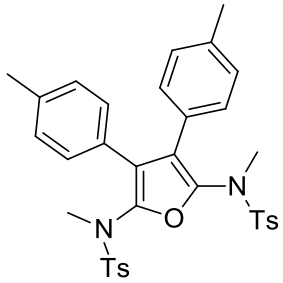


A round bottom flask equipped with a magnetic stirrer bar was charged with tBuXPhosAuCl (10 mol%, 6.4 mg), $AgNTf_2$ (5 mol%, 4 mg), and 1,2-DCE (1 ml). The mixture was stirred for 5 minutes at room temperature. Then the di-ynamide **5** (0.12 mmol) and 2,3-dichloroquinoxaline *N*-oxide (0.1 mmol) in 9 ml 1,2-DCE were added. The reaction was heated at 70 ^{o}C for 30 mins. After cooling to room temperature, the solvent was reduced in vacuo, and the residue was purified by column chromatography (SiO_2, hexanes/EtOAc) to provide the macrocyclic furan compound. The characterization data of the products are listed in part 3.

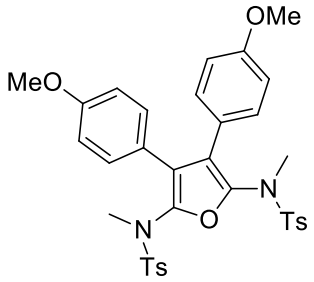
Characterization



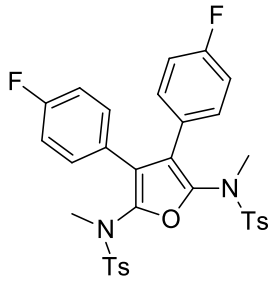
Compound **3a**: Yield 83 %, colourless soild, mp: 185-186 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.56-7.48 (m, 4 H), 7.20-7.06 (m, 14 H), 2.94 (s, 6 H), 2.33 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.8 (s), 140.3 (s), 135.0 (s), 130.3 (s), 129.5 (d), 129.4 (d), 128.21 (d), 128.19 (d), 127.5 (d), 122.9 (s), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3064, 2927, 1614, 1598, 1587, 1495, 1447, 1385, 1350, 1305, 1209, 1168, 1151, 1120, 1088, 1063, 1018, 992, 981, 890, 829, 813, 786, 773, 734, 704, 684, 664, 608cm^{-1}; HRMS (ESI) m/z calcd for $[C_{32}H_{30}N_2O_5S_2+Na]^+$: 609.1488; found: 609.1490.



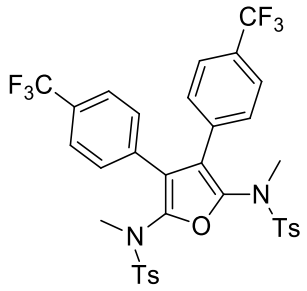
Compound **3b**: Yield 90 %, colourless soild, mp: 204-205 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (d, *J* = 8.0 Hz, 4 H), 7.09 (d, *J* = 8.0 Hz, 4 H), 7.02 (d, *J* = 8.0 Hz, 4 H), 6.96 (d, *J* = 8.0 Hz, 4 H), 2.92 (s, 6 H), 2.32 (s, 6 H), 2.24 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7 (s), 140.0 (s), 137.1 (s), 135.1 (s), 129.4 (d), 129.3 (d), 128.9 (d), 128.2 (d), 127.4 (s), 122.9 (s), 37.7 (q), 21.6 (q), 21.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2925, 1683, 1595, 1515, 1453, 1353, 1306, 1164, 1120, 1087, 981, 891, 815, 737, 706, 668, 628 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{34}H_{34}N_2O_5S_2+Na]^+$: 637.1801; found: 637.1807.



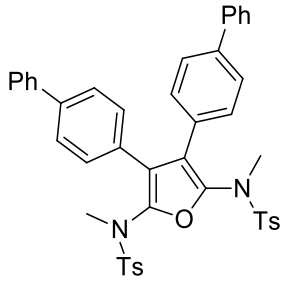
Compound **3c**: Yield 80 %, colourless soild, mp: 209-211 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 8.5 Hz, 4 H), 7.10 (d, *J* = 8.0 Hz, 4 H), 7.07 (d, *J* = 8.5 Hz, 4 H), 6.71 (d, *J* = 8.5 Hz, 4 H), 3.72 (s, 6 H), 2.92 (s, 6 H), 2.33 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.9 (s), 143.7 (s), 139.7 (s), 135.1 (s), 130.6 (d), 129.4 (d), 128.2 (d), 122.6 (s), 122.5 (s), 113.6 (d), 55.2 (q), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2949, 2924, 2832, 1685, 1593, 1513, 1457, 1391, 1349, 1294, 1246, 1212, 1167, 1112, 1087, 1068, 1036, 981, 894, 836, 808, 746, 704, 666, 628 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{34}H_{34}N_2O_7S_2+H]^+$: 647.1880; found: 647.1886.



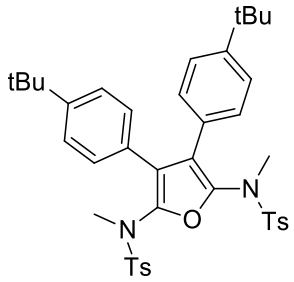
Compound **3d**: Yield 90 %, colourless soild, mp: 207-209 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53-7.48 (m, 4 H), 7.15-7.07 (m, 8 H), 6.90-6.85 (m, 4 H), 2.93 (s, 6 H), 2.34 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.3 (*J* = 245.7 Hz, s), 144.0 (s), 140.3 (s), 134.8 (s), 131.2 (*J* = 7.5 Hz, d), 129.5 (d), 128.1 (d), 126.0 (*J* = 2.8 Hz, s), 122.0 (s), 115.4 (*J* = 21.5 Hz, d), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1585, 1509, 1387, 1360, 1340, 1307, 1218, 1188, 1157, 1091, 1061, 1018, 994, 982, 894, 836, 815, 741, 704, 688, 670, 660, 642, 625 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{32}H_{28}F_2N_2O_5S_2+Na]^+$: 645.1300; found: 645.1313.



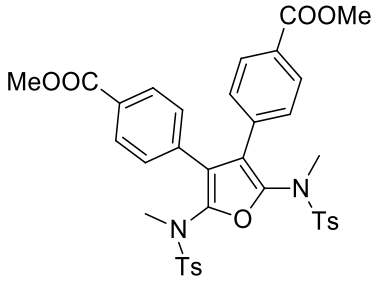
Compound **3e**: Yield 50 %, colourless soild, mp: 209-210 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.48 (d, *J* = 8.0 Hz, 4 H), 7.44 (d, *J* = 8.5 Hz, 4 H), 7.23 (d, *J* = 8.0 Hz, 4 H), 7.54 (d, *J* = 8.5 Hz, 4 H), 2.98 (s, 6 H), 2.33 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.2 (s), 141.3 (s), 134.6 (s), 133.6 (*J* = 0.9 Hz, s), 129.8 (*J* = 32.3 Hz, s), 129.7 (d), 129.5 (d), 128.1 (d), 126.2 (*J* = 270 Hz, s), 125.4 (*J* = 3.7 Hz, d), 121.6 (s), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2928, 1683, 1621, 1598, 1461, 1409, 1357, 1322, 1164, 1123, 1089, 1067, 1019, 986, 895, 831, 814, 776, 758, 733, 705, 691, 667, 635, 615 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{34}H_{28}F_6N_2O_5S_2+Na]^+$: 745.1236; found: 745.1256.



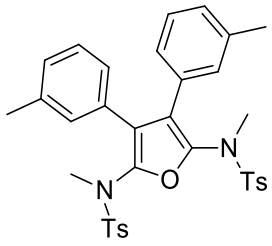
Compound **3f**: Yield 95 %, colourless solid, mp: 190-191 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53-7.48 (m, 8 H), 7.41 (d, *J* = 8.0 Hz, 4 H), 7.36-7.30 (m, 4 H), 7.26-7.21 (m, 6 H), 7.07 (d, *J* = 8.0 Hz, 4 H), 2.98 (s, 6 H), 2.26 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.9 (s), 140.5 (s), 140.1 (s), 135.0 (s), 129.9 (d), 129.5 (d), 129.3 (s), 128.8 (d), 128.2 (d), 127.4 (d), 126.9 (d), 126.8 (d), 122.6 (s), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3031, 2937, 1748, 1684, 1595, 1488, 1449, 1353, 1306, 1165, 1119, 1087, 981, 893, 842, 813, 770, 739, 697, 668, 610 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{44}H_{38}N_2O_5S_2+Na]^+$: 761.2114; found: 761.2119.



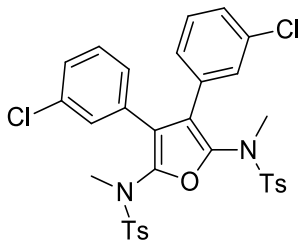
Compound **3g**: Yield 92 %, colourless soild, mp: 199-200 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.51 (d, *J* = 8.0 Hz, 4 H), 7.16 (d, *J* = 8.5 Hz, 4 H), 7.10-7.04 (m, 8 H), 2.92 (s, 6 H), 2.31 (s, 6 H), 1.23 (s, 18 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.2 (s), 143.7 (s), 140.0 (s), 135.0 (s), 129.4 (d), 129.1 (d), 128.3 (d), 127.3 (s), 125.0 (d), 122.9 (s), 37.7 (q), 34.6 (s), 31.4 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2962, 2904, 2867, 1739, 1599, 1582, 1461, 1380, 1359, 1345, 1269, 1169, 1153, 1109, 1090, 1066, 1021, 996, 982, 890, 826, 813, 756, 740, 706, 669, 620 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{40}H_{46}N_2O_5S_2+Na]^+$: 721.2740; found: 721.2738.



Compound **3h**: Yield 60 %, colourless soild, mp: 213-214 ^{o}C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 7.81 (d, *J* = 8.0 Hz, 4 H), 7.45 (d, *J* = 8.0 Hz, 4 H), 7.17 (d, *J* = 8.0 Hz, 4 H), 7.12 (d, *J* = 8.5 Hz, 4 H), 3.80 (s, 6 H), 2.95 (s, 6 H), 2.31 (s, 6 H) ppm; ^{13}C NMR (125 MHz, CD_2Cl_2) δ = 166.5 (s), 144.4 (s), 141.1 (s), 134.8 (s), 134.6 (s), 129.6 (d), 129.5 (d), 129.4 (d), 129.3 (s), 127.9 (d), 121.9 (s), 52.0 (q), 37.7 (s), 21.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2953, 1715, 1614, 1596, 1510, 1438, 1408, 1355, 1276, 1186, 1165, 1111, 1088, 1066, 1020, 983, 891, 860, 816, 779, 737, 706, 668, 634, 617 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{34}N_2O_9S_2N + Na]^+$: 725.1598; found: 725.1599.

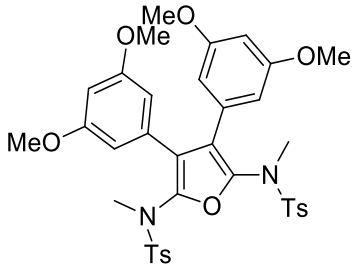


Compound **3i**: Yield 73 %, colourless soild, mp: 161-163 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 8.0 Hz, 4 H), 7.11 (d, *J* = 8.0 Hz, 4 H), 7.05-7.00 (m, 2 H), 6.99-6.91 (m, 4 H), 6.89-6.85 (m, 2 H), 2.94 (s, 6 H), 2.33 (s, 6 H), 2.15 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.8 (s), 140.1 (s), 137.6 (s), 135.1 (s), 130.2 (s), 130.1 (d), 129.4 (d), 128.2 (d), 128.1 (d), 127.9 (d), 126.6 (d), 122.9 (s), 37.7 (q), 21.6 (q), 21.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2924, 1684, 1598, 1453, 1351, 1306, 1224, 1165, 1122, 1088, 1064, 1027, 982, 924, 844, 812, 789, 726, 706, 669, 612 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{34}H_{34}N_2O_5S_2 + Na]^+$: 637.1801; found: 637.1828.

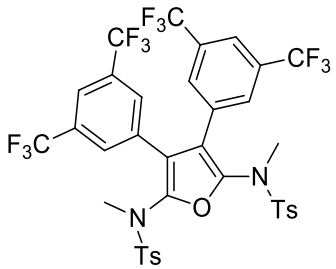


Compound **3j**: Yield 61 %, colourless soild, mp: 158-159 ^{o}C; ^{1}H NMR (500 MHz,

$CDCl_3$) δ = 7.51 (d, *J* = 8.5 Hz, 4 H), 7.18-7.09 (m, 8 H), 7.05-7.03 (m, 2 H), 6.99-6.95 (m, 2 H), 2.97 (s, 3 H), 2.34 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.2 (s), 140.8 (s), 134.6 (s), 134.1 (s), 131.7 (s), 129.63 (d), 129.60 (d), 129.3 (d), 128.1 (d), 127.9 (d), 127.7 (d), 121.5 (s), 37.7 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1768, 1681, 1611, 1597, 1565, 1494, 1475, 1450, 1419, 1351, 1308, 1295, 1170, 1151, 1121, 1087, 1062, 995, 916, 902, 816, 795, 762, 737, 708, 669, 610 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{32}H_{28}Cl_2N_2O_5S_2+H]^+$: 655.0889; found: 655.0893.

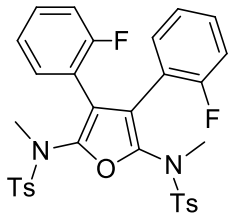


Compound **3k**: Yield 18 %, colourless soild, mp: 190-191 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 8.0 Hz, 4 H), 7.13 (d, *J* = 8.0 Hz, 4 H), 6.38 (d, *J* = 2.5 Hz, 4 H), 6.30 (t, *J* = 2.5 Hz, 2 H), 3.59 (s, 12 H), 2.94 (s, 6 H), 2.34 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 160.3 (s), 143.8 (s), 140.2 (s), 135.1 (s), 131.8 (s), 129.5 (d), 128.1 (d), 122.9 (s), 107.3 (d), 100.7 (d), 55.4 (q), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2932, 2841, 1738, 1684, 1595, 1455, 1424, 1351, 1291, 1205, 1155, 1088, 1065, 1018, 926, 835, 814, 784, 732, 706, 668, 616 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{38}N_2O_9S_2+Na]^+$: 729.1911; found: 729.1932.

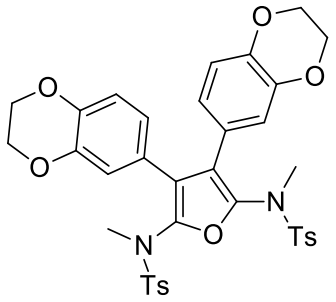


Compound **3l**: Yield 17 %, colourless solid, mp: 199-200 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.72 (s, 2 H), 7.53 (s, 4 H), 7.49 (d, *J* = 8.0 Hz, 4 H), 7.13 (d, *J* = 8.0 Hz, 4 H), 3.04 (s, 6 H), 2.33 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.6 (s), 142.1 (s), 134.3 (s), 132.0 (*J* = 33 Hz, s), 131.6 (s), 129.7 (d), 129.4 (*J* = 4.1 Hz, d), 128.0 (d), 122.8 (*J* = 271 Hz, s), 121.7 (*J* = 3.0 Hz, d), 119.1 (s), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2970, 2929, 1740, 1684, 1597, 1465, 1359, 1343, 1278, 1168,

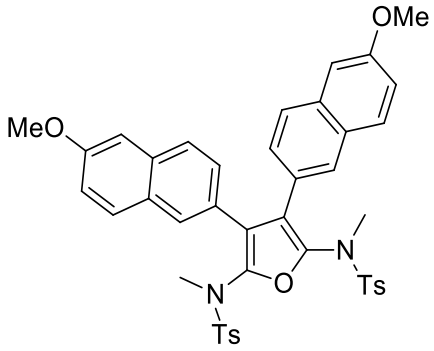
1133, 1064, 1032, 1014, 899, 848, 813, 777, 740, 706, 672, 613 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{26}F_{12}N_2O_5S_2+Na]^+$: 881.0984; found: 881.0998.



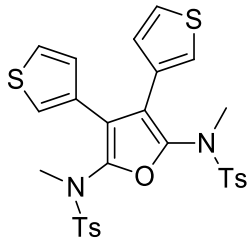
Compound **3m**: Yield 64 %, colourless soild, mp: 168-169 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.45 (d, *J* = 8.5 Hz, 4 H), 7.17-7.12 (m, 2 H), 7.10 (d, *J* = 8.0 Hz, 4 H), 7.08-7.03 (m, 2 H), 6.95-6.90 (m, 2 H), 6.88-6.81 (m, 2 H), 3.00 (s, 6 H), 2.30 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.7 (*J* = 246.7 Hz, s), 143.9 (s), 141.0 (s), 134.9 (s), 131.7 (*J* = 2.8 Hz, d), 129.7 (*J* = 8.5 Hz, d), 129.5 (d), 127.9 (d), 123.9 (*J* = 3.5 Hz, d), 118.4 (*J* = 15.7 Hz, s), 117.9 (s), 115.5 (*J* = 22.1 Hz, d), 37.1 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1596, 1494, 1453, 1351, 1307, 1267, 1229, 1188, 1168, 1152, 1105, 1088, 1066, 985, 896, 814, 761, 706, 668, 610 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{32}H_{28}F_2N_2O_5S_2+H]^+$: 623.1480; found: 623.1483.



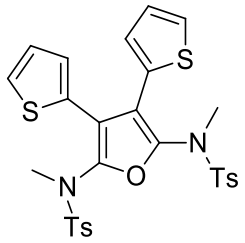
Compound **3n**: Yield 91 %, colourless soild, mp: 210-212 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.52 (d, *J* = 8.0 Hz, 4 H), 7.11 (d, *J* = 8.0 Hz, 4 H), 6.67-6.53 (m, 6 H), 4.20-4.07 (m, 8 H), 2.93 (s, 6 H), 2.33 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7 (s), 143.2 (s), 143.1 (s), 139.8 (s), 135.1 (s), 129.4 (d), 128.2 (d), 123.5 (s), 122.8 (d), 122.4 (s), 118.3 (d), 117.0 (d), 64.4 (t), 64.2 (t), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2927, 2877, 1749, 1685, 1581, 1508, 1458, 1352, 1303, 1283, 1251, 1162, 1125, 1087, 1067, 1000, 932, 918, 891, 870, 813, 756, 734, 706, 667, 625 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{34}N_2O_9S_2+Na]^+$: 725.1598; found: 725.1613.



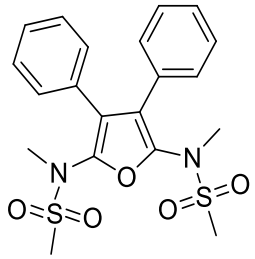
Compound **3o**: Yield 85 %, colourless soild, mp: 192-194 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.62-7.60 (m, 2 H), 7.54-7.43 (m, 8 H), 7.14-7.10 (m, 2 H), 7.03-6.97 (m, 8 H), 3.84 (s, 6 H), 3.01 (s, 6 H), 2.26 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 157.9 (s), 143.8 (s), 140.5 (s), 135.2 (s), 133.8 (s), 129.8 (d), 129.4 (d), 128.7 (s), 128.4 (d), 128.1 (d), 127.9 (d), 126.6 (d), 125.6 (s), 122.9 (s), 118.7 (d), 105.5 (d), 55.4 (q), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2940, 1631, 1606, 1487, 1462, 1390, 1352, 1262, 1216, 1188, 1162, 1087, 1030, 1000, 957, 911, 878, 854, 811, 733, 706, 667, 614 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{42}H_{38}N_2O_7S_2Na]^+$: 769.2013; found: 769.2035.



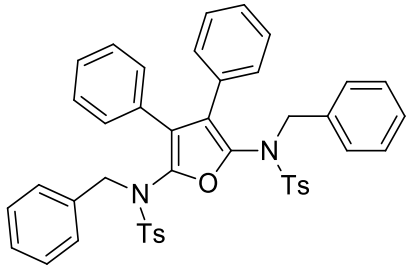
Compound **3p**: Yield 80 %, colourless soild, mp: 204-205 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53 (d, *J* = 8.0 Hz, 4 H), 7.22-7.20 (m, 2 H), 7.18-7.15 (m, 2 H), 7.12 (d, *J* = 8.5 Hz, 4 H), 6.93-6.90 (m, 2 H), 2.91 (s, 3 H), 2.33 (s, 3 H) ppm; ^{13}C NMR (125 MHz, d^6-DMSO) δ = 143.9 (s), 140.0 (s), 134.8 (s), 130.1 (s), 129.5 (d), 128.2 (d), 128.1 (d), 125.1 (d), 124.5 (d), 118.4 (s), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3108, 2946, 1762, 1685, 1597, 1521, 1493, 1450, 1415, 1344, 1304, 1292, 1215, 1164, 1087, 1069, 1018, 999, 923, 891, 861, 849, 813, 789, 730, 707, 669, 630, 609 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{28}H_{26}N_2O_5S_4+H]^+$: 599.0797; found: 599.0799.



Compound **3q**: Yield 30 %, light yellow solid, mp: 193-194 ^{o}C;; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 8.5 Hz, 4 H), 7.24-7.21 (m, 2 H), 7.15 (d, *J* = 8.5 Hz, 4 H), 6.92-6.87 (m, 4 H), 2.98 (s, 3 H), 2.34 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.0 (s), 140.6 (s), 134.8 (s), 130.3 (s), 129.6 (d), 128.3 (d), 128.2 (d), 127.0 (d), 126.6 (d), 116.9 (s), 37.6 (q), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3110, 2871, 2928, 2855, 1688, 1640, 1598, 1520, 1449, 1353, 1342, 1305, 1225, 1156, 1087, 1035, 940, 867, 829, 814, 705, 667 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{28}H_{26}N_2O_5S_4+Na]^+$: 621.0617; found: 621.0627.

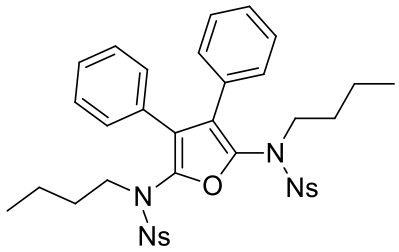


Compound **3r**: Yield 76 %, colourless soild, mp: 190-191 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.35-7.22 (m, 10 H), 3.25 (s, 6 H), 2.89 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 140.3 (s), 130.1 (s), 129.4 (d), 128.5 (d), 127.9 (d), 122.7 (s), 39.1 (q), 38.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2931, 1738, 1605, 1584, 1496, 1463, 1444, 1411, 1386, 1344, 1209, 1147, 1077, 1057, 1031, 963, 890, 832, 776, 756, 730, 702, 671 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{20}H_{22}N_2O_5S_2+H]^+$: 435.1043; found: 435.1045.

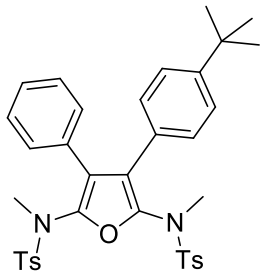


Compound **3s**: Yield 48 %, colourless soild, mp: 184-185 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54 (d, *J* = 8.5 Hz, 4 H), 7.12 (d, *J* = 8.5 Hz, 4 H), 7.08-7.03 (m, 4 H),

7.02-6.95 (m, 8 H), 6.75-6.66 (m, 8 H), 4.23 (s, 4 H), 2.37 (s, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7 (s), 138.2 (s), 136.1 (s), 134.2 (s), 130.0 (s), 129.6 (d), 129.4 (d), 129.2 (d), 128.3 (d), 128.2 (d), 128.0 (d), 127.8 (d), 127.2 (d), 125.0 (s), 54.0 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3064, 3033, 2925, 1598, 1581, 1495, 1456, 1400, 1353, 1306, 1163, 1090, 1012, 965, 915, 843, 813, 768, 731, 697, 663 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{44}H_{38}N_2O_5S_2+H]^+$: 739.2295; found: 739.2283.

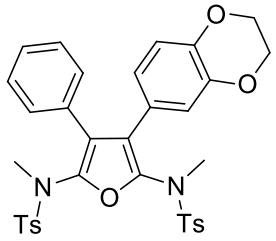


Compound **3t**: Yield 79 %, colourless soild, mp: 157-159 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.08 (d, *J* = 9.0 Hz, 4 H), 7.83 (d, J = 9.0 Hz, 4 H), 7.18-7.12 (m, 2 H), 7.12-7.07 (m, 4 H), 7.02-6.97 (m, 4 H), 3.36 (t, *J* = 7.0 Hz, 4 H), 1.30-1.22 (m, 4 H), 1.11-1.02 (m, 4 H), 0.64 (t, *J* = 6.0 Hz, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.2 (s), 144.5 (s), 138.6 (s), 129.6 (s), 129.3 (d), 129.2 (d), 128.3 (d), 127.9 (d), 125.2 (s), 123.9 (d), 51.5 (t), 30.5 (t), 19.6 (t), 13.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3103, 2961, 2930, 2862, 1608, 1586, 1525, 1485, 1444, 1401, 1351, 1311, 1173, 1146, 1108, 1087, 1073, 1037, 1023, 1007, 996, 977, 901, 855, 803, 775, 737, 701, 685, 616 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{36}N_4O_9S_2+H]^+$: 733.1996; found: 733.1995.

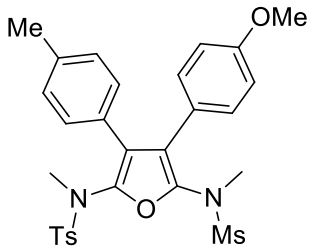


Compound **4a**: Yield 70 %, colourless soild, mp: 180-182 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.55-7.49 (m, 4 H), 7.20-7.13 (m, 7 H), 7.13-7.06 (m, 4 H), 7.05-7.01 (m, 4 H), 2.94 (s, 3 H), 2.93 (s, 3 H), 2.33 (s, 3 H), 2.32 (s, 3 H), 1.22 (s, 9 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 150.3 (s), 143.78 (s), 143.72 (s), 140.2 (s), 140.0 (s), 135.0 (s), 130.5 (s), 129.6 (d), 129.4 (d), 129.3 (d), 129.0 (d), 128.24 (d), 128.21 (d), 128.1 (d), 127.4 (d), 127.1 (s), 125.0 (d), 123.0 (s), 122.9 (s), 37.8 (q), 34.6 (s), 31.3

(q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2961, 2871, 1686, 1598, 1495, 1448, 1353, 1306, 1271, 1164, 1121, 1087, 1020, 982, 889, 836, 813, 774, 731, 703, 667, 621 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{38}N_2O_5S_2+H]^+$: 643.2295; found: 643.2291.

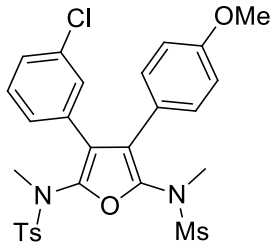


Compound **4b**: Yield 65 %, colourless soild, mp: 187-188 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.55-7.49 (m, 4 H), 7.20-7.15 (m, 3 H), 7.15-7.08 (m, 6 H), 6.64-6.61 (m, 2 H), 6.57-6.53 (m, 1 H), 4.17-4.10 (m, 4 H), 2.95 (s, 3 H), 2.92 (s, 3 H), 2.32 (d, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.8 (s), 143.7 (s), 143.2 (s), 143.1 (s), 140.1 (s), 140.0 (s), 135.1 (s), 135.0 (s), 130.3 (s), 129.5 (d), 129.45 (d), 129.42 (d), 128.2 (d), 127.5 (d), 123.5 (s), 122.88 (s), 122.86 (d), 122.4 (s), 118.3 (d), 116.9 (d), 64.4 (t), 64.2 (t), 37.8 (q), 37.7 (q), 21.63 (q), 21.62 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2935, 2876, 1697, 1581, 1509, 1456, 1351, 1303, 1283, 1251, 1159, 1125, 1067, 1009, 985, 936, 907, 889, 850, 812, 776, 752, 703, 665, 624 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{34}H_{32}N_2O_7S_2+Na]^+$: 667.1543; found: 667.1552.

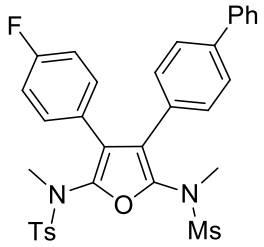


Compound **4c**: Yield 60 %, colourless soild, mp: 102-103 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 9.0 Hz, 2 H), 6.95 (s, 4 H), 6.74 (d, *J* = 8.5 Hz, 2 H), 3.71 (s, 3 H), 3.06 (s, 3 H), 3.01 (s, 3 H), 2.72 (s, 3 H), 2.36 (s, 3 H), 2.24 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.1 (s), 144.0 (s), 140.1 (s), 139.7 (s), 137.3 (s), 135.3 (s), 130.6 (d), 129.5 (d), 129.2 (d), 128.9 (d), 128.1 (d), 127.2 (s), 122.7 (s), 122.5 (s), 122.1 (s), 113.8 (d), 55.1 (q), 38.8 (q), 38.2 (q), 37.8 (q), 21.6 (q), 21.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3030,, 2934, 2839, 1748, 1682, 1641, 1590, 1514, 1456, 1386, 1347, 1293, 1249, 1150, 1086, 1032, 981, 964, 894, 817, 763, 736, 707, 671, 626 cm^{-1}; HRMS (ESI) m/z calcd for

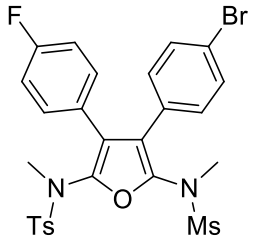
$[C_{28}H_{30}N_2O_6S_2+Na]^+$: 577.1437; found: 577.1453.



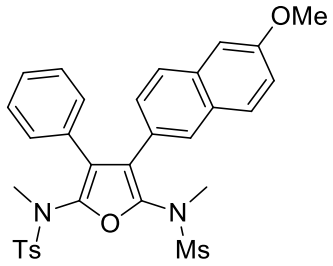
Compound **4d**: Yield 74 %, colourless soild, mp: 110-111 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.57 (d, *J* = 8.0 Hz, 2 H), 7.22-7.17 (m, 2 H), 7.16-7.12 (m, 1 H), 7.10-7.04 (m, 3 H), 6.99-6.97 (m, 1 H), 6.96-6.92 (m, 1 H), 6.75 (d, *J* = 8.5 Hz, 2 H), 3.72 (s, 3 H), 3.06 (s, 3 H), 3.05 (s, 3 H), 2.74 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.2 (s), 144.3 (s), 140.5 (s), 140.1 (s), 134.8 (s), 134.0 (s), 132.2 (s), 130.5 (d), 129.6 (d), 129.5 (d), 129.3 (d), 128.1 (d), 127.74 (d), 127.71 (d), 122.0 (s), 121.8 (s), 121.5 (s), 114.0 (d), 55.2 (q), 38.9 (q), 38.1 (q), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2936, 2840, 1748, 1682, 1600, 1514, 1456, 1347, 1293, 1250, 1211, 1163, 1084, 1032, 986, 964, 899, 834, 815, 792, 772, 732, 705, 672, 628 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{27}H_{27}ClN_2O_6S_2+Na]^+$: 597.0891; found: 597.0902.



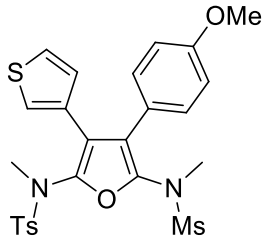
Compound **4e**: Yield 76 %, colourless soild, mp: 98-99 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.61 (d, *J* = 8.0 Hz, 2 H), 7.53-7.48 (m, 2 H), 7.46 (d, *J* = 8.5 Hz, 2 H), 7.37-7.32 (m, 2 H), 7.28-7.24 (m, 1 H), 7.24-7.18 (m, 4 H), 7.12-7.06 (m, 2 H), 6.90-6.83 (m, 2 H), 3.08 (s, 3 H), 3.04 (s, 3 H), 2.74 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.3 (*J* = 246 Hz, s), 144.3 (s), 140.5 (*J* = 2.2 Hz, s), 140.3 (s), 140.2 (s), 135.1 (s), 131.2 (*J* = 8.1 Hz, d), 129.7 (d), 129.6 (d), 128.9 (s), 128.8 (d), 128.2 (d), 127.6 (d), 127.1 (d), 127.0 (s), 126.9 (d), 126.1 (*J* = 3.3 Hz, s), 122.0 (s), 121.9 (s), 115.4 (*J* = 21 Hz, d), 38.9 (q), 38.2 (q), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2935, 1680, 1590, 1510, 1489, 1450, 1348, 1222, 1159, 1087, 982, 963, 895, 838, 813, 770, 738, 700, 671, 629 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{32}H_{29}FN_2O_5S_2+H]^+$: 605.1575; found: 605.1573.



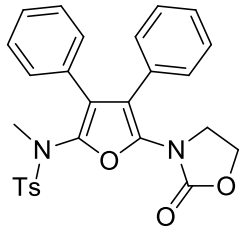
Compound **4f**: Yield 74 %, colourless soild, mp: 121-122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58 (d, *J* = 8.5 Hz, 2 H), 7.37-7.32 (m, 2 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.06-7.00 (m, 4 H), 6.91-6.83 (m, 2 H), 3.04 (s, 3 H), 3.03 (s, 3 H), 2.77 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 162.4 (*J* = 246 Hz, s), 144.3 (s), 140.5 (s), 140.3 (s), 135.0 (s), 131.7 (d), 131.1 (*J* = 7.8 Hz, d), 130.9 (d), 129.6 (d), 128.8 (s), 128.1 (d), 125.8 (*J* = 3.3 Hz, s), 122.2 (s), 121.7 (s), 121.4 (s), 115.5 (*J* = 22 Hz, d), 38.7 (q), 38.1 (q), 37.8 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 1682, 1597, 1581, 1510, 1491, 1456, 1349, 1223, 1160, 1072, 1014, 981, 964, 893, 831, 813, 764, 736, 706, 670, 634 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{26}H_{24}BrFN_2O_5S_2+Na]^+$: 629.0186; found: 629.0200.



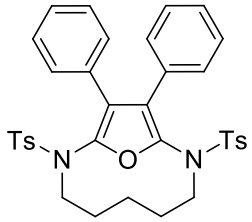
Compound **4g**: Yield 61 %, colourless soild, mp: 117-118 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.64-7.60 (m, 3 H), 7.57-7.52 (m, 2 H), 7.22-7.17 (m, 3 H), 7.17-7.13 (m, 2 H), 7.12-7.06 (m, 3 H), 7.06-7.00 (m, 2 H), 3.83 (s, 3 H), 3.07 (s, 3 H), 3.05 (s, 3 H), 2.72 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.1 (s), 144.1 (s), 140.4 (s), 140.3 (s), 135.1 (s), 133.8 (s), 130.2 (s), 129.8 (d), 129.6 (d), 129.4 (d), 128.7 (s), 128.4 (d), 128.2 (d), 128.1 (d), 127.6 (d), 127.5 (d), 126.8 (d), 125.3 (s), 122.8 (s), 122.4 (s), 119.0 (d), 105.6 (d), 55.4 (q), 38.9 (q), 38.2 (q), 37.9 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2933, 2850, 1748, 1681, 1628, 1600, 1486, 1456, 1350, 1261, 1163, 1085, 1030, 963, 924, 887, 855, 813, 764, 700, 669, 611 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{31}H_{30}N_2O_6S_2+Na]^+$: 613.1437; found: 613.1446.



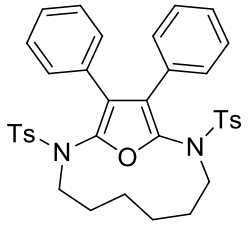
Compound **4h**: Yield 64 %, yellow soild, mp: 112-114 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.65 (d, *J* = 8.5 Hz, 2 H), 7.23 (d, *J* = 8.5 Hz, 2 H), 7.17-7.13 (m, 2 H), 7.12-7.09 (m, 1 H), 7.07-7.05 (m, 1 H), 6.86-6.83 (m, 1 H), 6.82-6.78 (m, 2 H), 3.74 (s, 3 H), 3.04 (s, 3 H), 3.03 (s, 3 H), 2.68 (s, 3 H), 2.36 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.4 (s), 144.2 (s), 140.0 (s), 139.8 (s), 135.0 (s), 130.7 (d), 130.1 (s), 129.6 (d), 128.3 (d), 127.9 (d), 124.9 (d), 124.2 (d), 122.5 (s), 122.0 (s), 118.4 (s), 113.9 (d), 55.2 (q), 38.9 (q), 38.2 (q), 37.6 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3007, 2935, 2839, 1710, 1596, 1514, 1456, 1348, 1291, 1250, 1222, 1156, 1087, 1032, 988, 965, 916, 877, 836, 817, 793, 762, 731, 707, 674, 631 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{25}H_{26}N_2O_6S_3+Na]^+$: 569.0845; found: 569.0852.



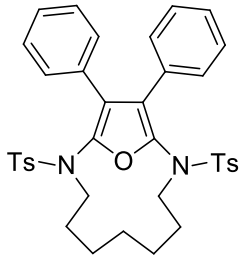
Compound **4i**: Yield 21 %, colourless soild, mp: 92-93 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.68-7.63 (m, 2 H), 7.26-7.13 (m, 12 H), 7.12-7.07 (m, 2 H), 4.33 (t, *J* = 7.5 Hz, 2 H), 3.65 (t, *J* = 8.0 Hz, 2 H), 2.95 (s, 3 H), 2.38 (s, 3 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 156.7 (s), 144.2 (s), 140.5 (s), 136.7 (s), 135.0 (s), 130.2 (s), 130.1 (s), 129.7 (d), 129.4 (d), 129.2 (d), 128.5 (d), 128.3 (d), 128.2 (d), 127.8 (d), 127.6 (d), 123.0 (s), 121.2 (s), 62.9 (t), 46.4 (t), 37.7 (q), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 3061, 2958, 2923, 1766, 1693, 1645, 1613, 1596, 1494, 1479, 1445, 1409, 1352, 1219, 1167, 1123, 1076, 1045, 1002, 983, 937, 856, 815, 773, 759, 701, 660, 608 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{27}H_{24}N_2O_5S+Na]^+$: 511.1298; found: 511.1305.



Compound **6a**: Yield 20 %, colourless soild, mp: 147-148 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.26-7.22 (m, 2 H), 7.20-7.16 (m, 2 H), 7.01-6.62 (m, 14 H), 4.30-3.88 (m, 3 H), 3.28-3.17 (m, 1 H), 2.23 (s, 6 H), 1.92-1.52 (m, 6 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 145.0 (s), 142.7 (s), 137.3 (s), 133.5 (s), 132.4 (s), 132.3 (s), 130.0 (d), 129.9 (s), 129.8 (d), 129.3 (d), 129.2 (d), 128.2 (d), 127.8 (d), 127.5 (d), 127.0 (d), 125.9 (d), 125.2 (d), 120.6 (s), 119.9 (s), 111.8 (s), 54.8 (t), 42.3 (t), 31.2 (t), 27.2 (t), 24.9 (t), 21.6 (q), 21.4 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2962, 1738, 1600, 1542, 1374, 1334, 1259, 1049, 1020, 871, 798, 696, 675, 625 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{35}H_{34}N_2O_5S_2+Na]^+$: 649.1801; found: 649.1817.

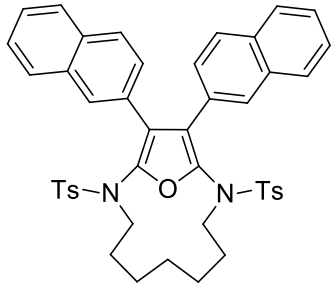


Compound **6b**: Yield 81 %, colourless soild, mp: 150-151 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58-7.48 (m, 4 H), 7.23-7.09 (m, 14 H), 3.33-3.18 (m, 4 H), 2.34 (s, 6 H), 1.31-1.18 (m, 4 H), 0.86-0.74 (m, 4 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.9 (s), 139.2 (s), 135.7 (s), 130.3 (s), 129.6 (d), 129.3 (d), 128.2 (d), 128.1 (d), 127.5 (d), 124.6 (s), 50.0 (t), 23.8 (t), 23.2 (t), 21.7 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 1697, 1598, 1579, 1494, 1444, 1399, 1349, 1306, 1161, 1089, 1048, 1018, 981, 917, 871, 813, 771, 693, 665 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{36}N_2O_5S_2+Na]^+$: 663.1958; found: 663.1974.

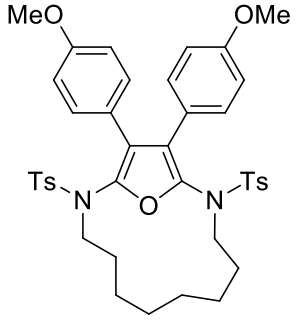


Compound **6c**: Yield 78 %, colourless soild, mp: 151-152 ^{o}C; ^{1}H NMR (500 MHz,

$CDCl_3$) δ = 7.63-7.58 (m, 4 H), 7.17-7.10 (m, 10 H), 7.09-7.03 (m, 4 H), 3.65-3.00 (m, 4 H), 2.32 (s, 6 H), 1.41-0.88 (m, 10 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7 (s), 138.3 (s), 136.1 (s), 130.4 (s), 129.5 (d), 129.2 (d), 128.2 (d), 128.1 (d), 127.4 (d), 124.6 (s), 49.0 (t), 25.8 (t), 25.3 (t), 23.1 (t), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2926, 2862, 1600, 1579, 1495, 1444, 1403, 1352, 1341, 1307, 1188, 1160, 1113, 1074, 1022, 986, 921, 896, 867, 809, 773, 701, 663 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{37}H_{38}N_2O_5S_2+Na]^+$: 677.2114; found: 677.2112.

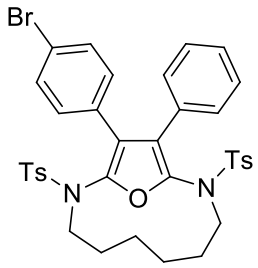


Compound **6d**: Yield 80 %, colourless soild, mp: 167-168 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.70-7.50 (m, 12 H), 7.40-7.30 (m, 4 H), 7.15-7.10 (m, 2 H), 7.03-6.96 (m, 4 H), 3.78-3.03 (m, 4 H), 2.20 (s, 3 H), 1.43-0.93 (m, 10 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.7 (s), 138.8 (s), 136.3 (s), 133.2 (s), 132.6 (s), 129.4 (d), 128.3 (d), 128.2 (d), 128.0 (d), 127.9 (s), 127.7 (d), 127.5 (d), 127.1 (d), 126.1 (d), 125.9 (d), 124.5 (s), 49.2 (t), 26.0 (t), 25.4 (t), 23.2 (t), 21.5 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2928, 2863, 1598, 1495, 1458, 1350, 1186, 1162, 1126, 1089, 1069, 1019, 995, 943, 926, 894, 860, 814, 753, 726, 705, 666 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{45}H_{42}N_2O_5S_2+Na]^+$: 777.2427; found: 777.2438.

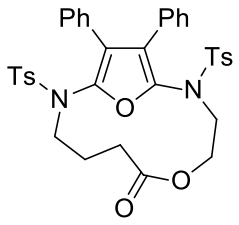


Compound **6e**: Yield 60 %, colourless soild, mp: 165-167 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.62 (d, *J* = 7.5 Hz, 4 H), 7.10 (d, *J* = 8.0 Hz, 4 H), 6.95-6.89 (m, 4 H), 6.67-6.61 (m, 4 H), 3.70 (s, 3 H), 3.67-3.50 (m, 2 H), 3.23-3.07 (m, 2 H), 2.30 (s, 3 H), 1.66-1.06 (m, 8 H), 1.04-0.93 (m, 4 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 158.8

(s), 143.4 (s), 138.5 (s), 136.6 (s), 130.3 (d), 129.3 (d), 128.0 (d), 123.3 (s), 122.8 (s), 113.6 (d), 55.1 (q), 50.4 (t), 27.5 (t), 25.3 (t), 22.5 (t), 21.6 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2931, 2859, 1713, 1577, 1513, 1458, 1397, 1348, 1291, 1247, 1158, 1110, 1089, 1067, 1031, 993, 976, 945, 908, 832, 813, 754, 706, 686, 664, 626 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{40}H_{44}N_2O_7S_2+Na]^+$: 751.2482; found: 751.2486.



Compound **6f**: Yield 56 %, colourless soild, mp: 152-154 °C; ^{1}H NMR (500 MHz, CD_2Cl_2) δ = 7.52-7.46 (m, 4 H), 7.32-7.28 (m, 2 H), 7.22-7.12 (m, 9 H), 7.06-7.01 (m, 2 H), 3.31-3.15 (m, 4 H), 2.35 (s, 3 H), 2.34 (s, 3 H), 1.29-1.18 (m, 4 H), 0.84-0.71 (m, 4 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.4 (s), 144.3 (s), 139.4 (s), 139.3 (s), 135.7 (s), 135.6 (s), 131.3 (d), 131.0 (d), 130.2 (s), 129.7 (s), 129.6 (d), 129.5 (d), 129.3 (d), 128.2 (d), 128.0 (d), 127.9 (d), 127.7 (d), 124.5 (s), 123.4 (s), 121.7 (s), 50.06 (t), 50.02 (t), 23.8 (t), 23.7 (t), 23.2 (t), 23.0 (t), 21.4 (q), 21.3 (q) ppm; IR (ATR): $\tilde{\nu}$ = 2957, 1598, 1576, 1492, 1447, 1350, 1305, 1161, 1090, 1046, 1011, 981, 918, 870, 813, 770, 705, 665 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{35}BrN_2O_5S_2+H]^+$: 719.1244; found: 719.1242.



Compound **6g**: Yield 74 %, colourless soild, mp: 150-151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 (d, *J* = 8.5 Hz, 2 H), 7.42 (d, *J* = 8.5 Hz, 2 H), 7.24-7.14 (m, 12 H), 7.10-7.06 (m, 2 H), 4.49-2.80 (m, 6 H), 2.34 (s, 3 H), 2.32-2.23 (m, 5 H), 2.04-1.91 (m, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.5 (s), 144.2 (s), 144.1 (s), 139.4 (s), 139.3 (s), 136.6 (s), 134.7 (s), 130.7 (s), 130.2 (s), 129.9 (d), 129.7 (d), 129.4 (d), 129.2 (d), 128.4 (d), 128.3 (d), 128.2 (d), 127.8 (d), 127.7 (d), 127.4 (d), 124.0 (s), 122.7 (d), 62.8 (t), 48.7 (t), 46.7 (t), 31.0 (t), 24.1 (t), 21.7 (q), 21.6 (q) ppm; IR

(ATR): $\tilde{\nu}$ = 2955, 1736, 1598, 1494, 1444, 1353, 1251, 1213, 1159, 1088, 988, 904, 847, 813, 769, 693, 665 cm^{-1}; HRMS (ESI) m/z calcd for $[C_{36}H_{34}N_2O_7S_2+Na]^+$: 693.1700; found: 693.1697.

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