Gold-Catalyzed Formal Cycloadditions of Alkynes for Azaheterocycle Syntheses

Presented by:

Zhongyi Zeng

from Hunan, China

A dissertation submitted to the

Combined Faculty of Natural Sciences and Mathematics

Heidelberg University, Germany

for the degree of

Doctor of Natural Sciences (Dr. rer. nat.)

June 2018

Dissertation

Submitted to the

Combined Faculty of Natural Sciences and Mathematics

Heidelberg University, Germany

for the degree of

Doctor of Natural Sciences (Dr. rer. nat.)

Presented by:

Zhongyi Zeng

from Hunan, China

Oral examination: September 11th, 2018

Gold-Catalyzed Formal Cycloadditions of Alkynes for Azaheterocycle Syntheses

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

Prof. Dr. Uwe H. F. Bunz

Oral examination: September 11th, 2018

Acknowledgements

Undoubtedly, my doctoral study in Heidelberg is an extremely significant and impressive part of my life. Having the chance to experience a distinct culture, lifestyle, and foreign language enhanced my understanding of life. On the occasion of graduation, I would like to take this opportunity to express my great and sincere gratitude to all the people I met during this fantastic journey.

First and foremost, my utmost and heartfelt appreciation goes to my doctoral advisor, Prof. Dr. A. Stephen K. Hashmi, the Vice President for Research and Transfer of Heidelberg University. He is not only a great chemist with much enthusiasm for chemistry, but also a good mentor with his great patience, constant support, inspired guidance, and encouragement to me during these periods.

I would extend my whole-hearted gratitude towards Prof. Dr. Uwe H. F. Bunz to be my second Gutachter without any hesitation. Also thanks for his comments on this dissertation.

My sincere thanks to Dr. Matthias Rudolph for his precious and constructive suggestions at different stages of my projects. Discussion with him always benefits me a lot.

I also thank Prof. Dr. Günter Helmchen for his instruction and support. His passion and enthusiasm for chemistry have impressed me and will encourage me all the time.

In addition, I would like to thank Frau Petra Krämer for her kind assistance with the analytical measurements and proper management in the coffee room. My gratitude to Herr Alexander Flatow due to his chemical supplies and equipment maintenance. Many thanks are also extended to Frau Christiane Eckert for her patience in daily administration. Special thanks to Hongming Jin (for countless assistance and discussion), Dr. Jin Xie (for his valuable revision of manuscripts), Dr. Kohei Sekine

(for the discussion and measurement of conjugated π-systems), Benhua Wang and Wei Huang (both for taking photographs of samples), Christoph Hendrich (for the translation of the abstracts into German).

I convey many thanks to my teammate of AK Hashmi for the happiness and delicious food we shared. Knowing and working with these guys has been one of the highlights of my time in Heidelberg. They are: Jintao Yu, Janina Bucher, Long Huang, Fei Chen, Jiatao Yu, Svetlana Tsupova, Thomas Wurm, Xinlong Song, Bing Tian, Anton Makarov, Tsuyoshi Yamada, Ruokun Feng, Kai Cheng, Simon Clemens, David Zahner, Florian Mulks, Poorya Zargaran, Jürgen Schulmeister, Vanessa Weingand, Danilo Machado Lustosa, Marc Zimmer, Jasmin Schießl, Alexander Ahrens, Sebastian Arndt, Qian Wang, Tapas Adak, Sina Witzel, Yufeng Wu, Xianhai Tian, Ximei Zhao, Yangyang Yang, Svenja Taschinski, Daniel Eppel, Lumin Zhang, Sara Tavakkolifard, Xiaojia Si, Vanessa Vethacke, Kirsten Emler, Fabian Stuck, Alejandro Cervantes Reyes, Shaista Tahir, Alexandra Mackenroth, Patrick Antoni, Robin Heckershoff, Lina Song, Chao Hu, Long Hu, Yun Xu, Jhonatan Fiorio, Rahele Pourkaveh, Fabian Jester, Christopher Hüßler, Leon Martin, Leonhard Karger, Philipp Reischenbach, Christina Bauer, Philipp Theobald, Mandeta Dupa, Michael Mulligan, etc.

I also appreciate all the staff of our Institute for the technical and analytical support, such as NMR, X-ray, HRMS and chemical store.

By this chance, I acknowledgement the Guangzhou Elite Scholarship Council for the financial support. Otherwise, this wonderful journey is impossible.

Finally, my deepest gratitude to my parents, my wife, my friends and my whole family for their unconditional understanding, support, and love.

Again, my warmest thanks to all the people who helped and inspired me during my doctoral study. God bless all of you.

Table of Contents

Academic Contributions

Publications

[1] **Zhongyi Zeng**,[+] Hongming Jin,[+] Kohei Sekine, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi. "Gold-catalyzed regiospecific C–H annulation of *o*-ethynylbiaryls with anthranils: π-extension by ring-expansion en route to *N*-doped PAHs". *Angew. Chem. Int. Ed.* **2018**, *57*, 6935−6939; *Angew. Chem.* **2018**, *130*, 7051–7056. ([+] equal contribution)

[2] **Zhongyi Zeng**,[+] Hongming Jin,[+] Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi. "Gold(III)-catalyzed site-selective and divergent synthesis of 2-aminopyrroles and quinoline-embedded polyazaheterocycles". ([+] equal contribution; under review)

[3] **Zhongyi Zeng**, Hongming Jin, Jin Xie, Bing Tian, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi. "α-Imino gold carbenes from 1,2,4-oxadiazoles: concise and atom-economical access to fully substituted 4-aminoimidazoles". *Org. Lett.* **2017**, *19*, 1020−1023.

[4] **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.

[5] Ximei Zhao, Xinlong Song, Hongming Jin, **Zhongyi Zeng**, Qian Wang, Matthias Rudolph, Frank Rominger, A. Stephen K. Hashmi. "Gold-catalyzed intermolecular [4+2] annulation of 2-ethynylanilines with ynamides: an access to substituted 2-aminoquinolines". *Adv. Synth. Catal.* **2018**, DOI: 10.1002/adsc.201800341.

Oral Presentation (underlined is the speaker)

[1] **Zhongyi Zeng**, A. Stephen K. Hashmi. "Gold-catalyzed intermolecular annulation of ynamides with bench-stable 1,3,5-triazinanes". *Gold 2018*, Paris, France: July 15−18th, **2018**.

[2] **Zhongyi Zeng**, Hongming Jin, A. Stephen K. Hashmi. "α-Iminocarbene gold(I) intermediates from nitrogen heterocycles". *Gold 2018*, Paris, France: July 15−18th, **2018**.

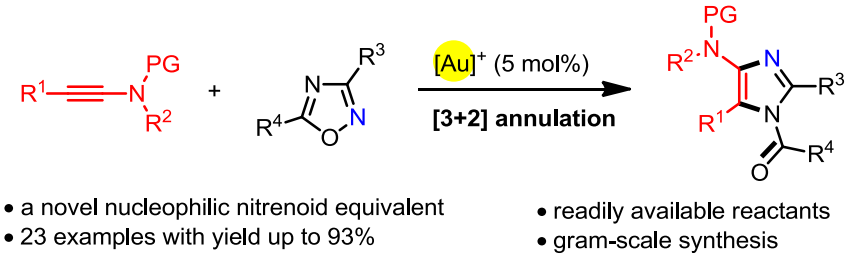
List of Abbreviations

Ac	acetyl
Ar	aryl
ATR	attenuated total refraction
Bn	benzyl
Bu	butyl
Bz	benzoyl
Bs	4-bromobenzenesulfonyl
calcd.	calculated
Cy	cyclohexyl
1,2-DCE	1,2-dichloroethane
DART	direct analysis in real time
DG	donating group
EA	ethyl acetate
EDG	electron-donating group
EI	electron ionization
equiv.	equivalent(s)
ESI	electrospray Ionization
Et	ethyl
h	hour
Hex	hexyl
HRMS	high resolution mass spectrometry
Hz	hertz
IR	infrared
m-	*meta*-
m.p.	melting point
m/z	mass per charge
Me	methyl

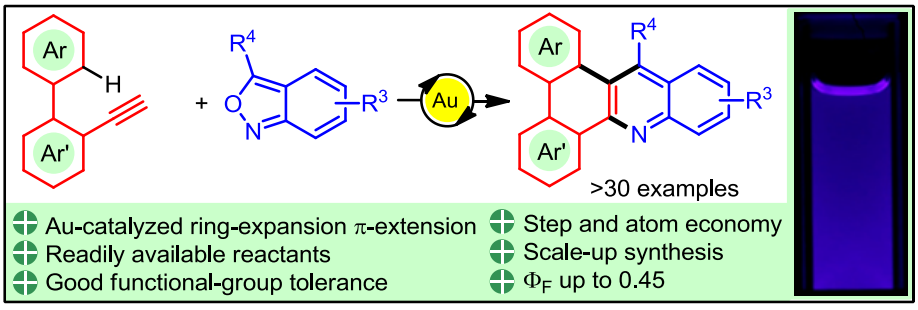
MHz	megahertz
min	minutes
Ms	mesyl
MS	mass spectrometry
NBS	*N*-bromo succinimide
NHC	*N*-heterocyclic carbene
NMR	nuclear magnetic resonance
Ns	4-nitrobenzenesulfonyl
o-	*ortho*-
p-	*para*-
PAH	polycyclic aromatic hydrocarbon
PE	petroleum ether
PG	protecting group
Ph	phenyl
Pr	propyl
rt	room temperature
R_f	ratio of fronts
t	*tert*
Tf	triflate
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethyl silyl
Ts	4-toluenesulfonyl
UV-vis	ultraviolet-visible

Abstract

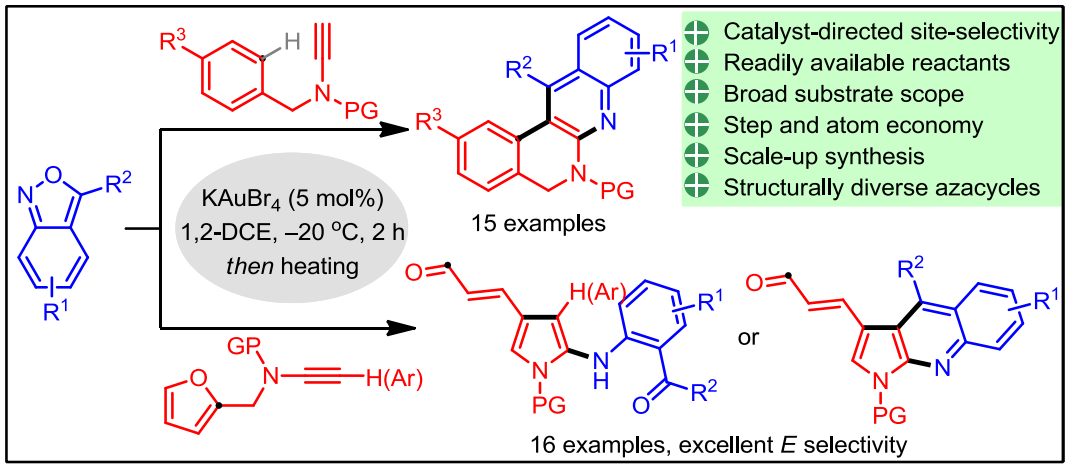
In chapter 2, a novel and atom-economical synthesis of fully substituted 4-aminoimidazoles via gold-catalyzed selective [3+2] annulation of 1,2,4-oxadiazoles with ynamides is achieved. This protocol represents a new strategy to access α-imino gold carbenes, which corresponds to an unprecedented intermolecular transfer of *N*-acylimino nitrenes to ynamides. Moreover, the reaction proceeds with 100% atom economy, exhibits good functional group tolerance, and can be conducted in gram scale.



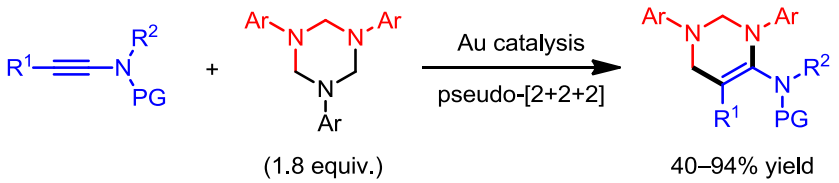
Chapter 3 describes a novel, short, and flexible approach to diverse *N*-doped polycyclic aromatic hydrocarbons (PAHs) through gold-catalyzed π-extension of anthranils with *o*-ethynylbiaryls as reagents. This strategy uses easily accessible starting materials, is simple due to high step and atom economy, and shows good functionalgroup compatibility as well as scale-up potential. Mechanistically, the tandem reaction is proposed to involve a nucleophilic addition/ring opening/regiospecific C–H annulation/protodeauration sequence terminated by a Friedel-Crafts-type cyclization. Photophysical studies of the products indicated violetblue fluorescence emission with quantum yields up to 0.45.



In chapter 4, a facile, site-selective and divergent approach to construct 2-aminopyrroles and quinoline-fused polyazaheterocycles is enabled by a simple gold(III) catalyst from ynamides and anthranils under mild reaction condition. This one-pot strategy uses readily available starting materials, proceeds in a highly step- and atom-economical manner, with broad substrate scope and scale-up potential. Notably, the key element of success in the present tandem reaction is a catalyst-directed preferable quenching of the in-situ generated gold carbene intermediates by a nucleophilic benzyl/2-furanylmethyl moiety on the ynamides as an alternative to the known C–H annulation leading to indoles.

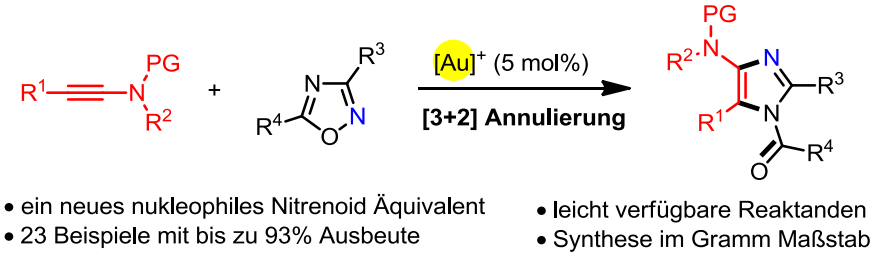


In chapter 5, a gold-catalyzed regioselective cyclocarboamination of ynamides with 1,3,5-triazinanes provides facile and modular access to valuable 5-aminotetrahydropyrimidines in good to excellent yields. It constitutes an unprecedented yet challenging annulation of ynamides with unstrained saturated heterocycles. This new protocol is distinguished by easy operation, readily available starting materials, stable four-atom building units, good functional-group compatibility and scaling-up potential. The preliminary mechanistic studies indicate that the present intermolecular cyclocarboamination arises from a pseudo-three-component [2+2+2] cycloaddition.

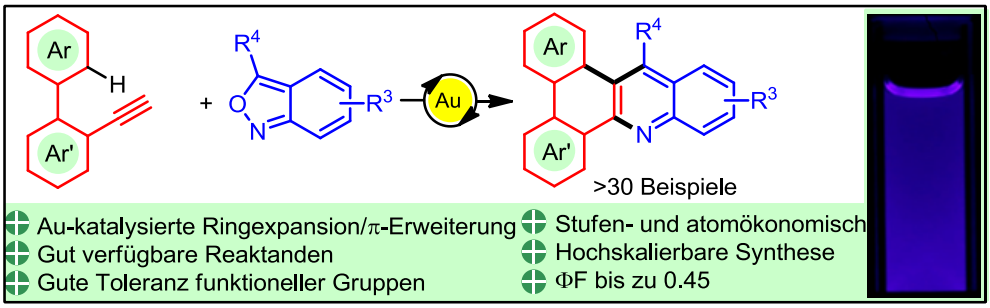


Kurzzusammenfassung

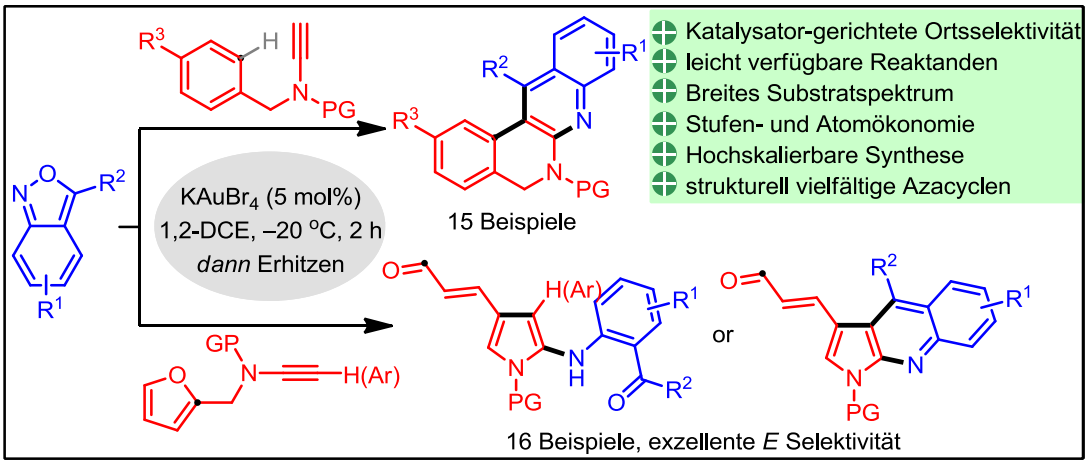
In Kapitel 2 wurde eine neue und atomökonomische Synthese von voll substituierten 4-Aminoimidazolen über eine goldkatalysierte selektive [3+2] Annulierung von 1,2,4-Oxadiazolen mit Inamiden erzielt. Dieses Protokoll repräsentiert eine neue Strategie, α-imino Goldcarbene durch einen noch nicht da gewesenen Transfer von N-Acylimino Nitrenen auf Inamide herzustellen. Die Reaktion verläuft außerdem mit 100% Atomökonomie, weist eine hohe Toleranz bezüglich funktioneller Gruppen auf und kann im Gramm Maßstab durchgeführt werden.



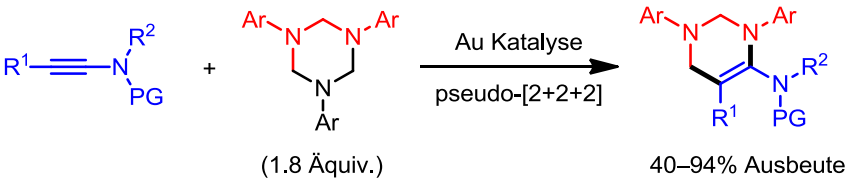
Kapitel 3 beschreibt einen neuen, kurzen und flexiblen Weg zu verschiedenen *N*-haltigen polycyclischen aromatischen Kohlenwasserstoffen (PAK) über eine goldkatalysierte π-Erweiterungsreaktion von Anthranilen mit *o*-Ethinylbiarylen als Reagenzien. Diese Strategie nutzt leicht zugängliche Edukte, ist aufgrund einer hohen Stufen- und Atomökonomie einfach und zeigt eine gute Toleranz gegenüber funktionellen Gruppen, ein Hochskalieren ist ebenfalls möglich. Der mechanistische Vorschlag für die Tandemreaktion beinhaltet eine nukleophile Addition/Ringöffnung/regiospezifische C-H-Anellierung/Protodesaurierung und abschließend eine Friedel-Crafts-artige Cyclisierung. Photophysikalische Studien der Produkte zeigen eine violett-blaue Fluoreszenz mit einer Quantenausbeute von bis zu 0.45.



In Kapitel 4 wird ein einfacher, ortsselektiver und divergenter Zugang zum Aufbau von 2-Aminopyrrolen und Chinolin-verknüpften Polyazaheterocyclen durch einen einfachen Gold(III)-Katalysator aus Inamiden und Anthranilen unter milden Reaktionsbedingungen ermöglicht. Diese Eintopf-Strategie benutzt leicht verfügbare Startmaterialien, verläuft hoch stufen- und atomökonomisch, mit breitem Substratspektrum und hat scale-up Potenzial. Auffallend ist, dass das Schlüsselelement der erfolgreichen Tandemreaktion ein Katalysator-gerichtetes bevorzugtes Quenching des in-situ gebildeten Gold Carben Intermediats durch eine nukleophile Benzyl/2-Furanylmethyl Einheit am Inamid ist, als Alternative zur bekannten C-H Annulierung, welche zu Indolen führt.



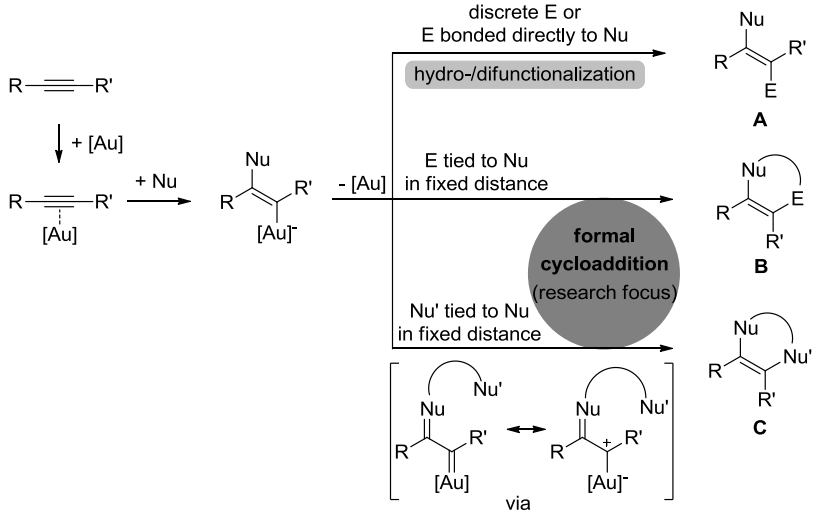
In Kapitel 5 liefert eine goldkatalysierte regioselektive Cyclocarboaminierung von Inamiden mit 1,3,5-Triaziranen einen leichten und modularen Zugang zu nützlichen 5-Aminotetrahydropyrimidinen in guten bis exzellenten Ausbeuten. Er stellt eine beispiellose aber anspruchsvolle Annulierung von Inamiden mit ungespannten gesättigten Heterocyclen dar. Diese neue Strategie unterscheidet sich durch einfache Durchführung, leicht zugänglichen Startmaterialien, stabile vier-Atom Baueinheiten, gute Verträglichkeit gegenüber funktionellen Gruppen und scale-up Potenzial. Die vorläufigen Mechanistischen Studien deuten darauf hin, dass die vorgestellte intermoleculare Cyclocarboaminierung aus einer pseudo-drei Komponenten [2+2+2] Cycloaddition entsteht.



Chapter 1: General Introduction

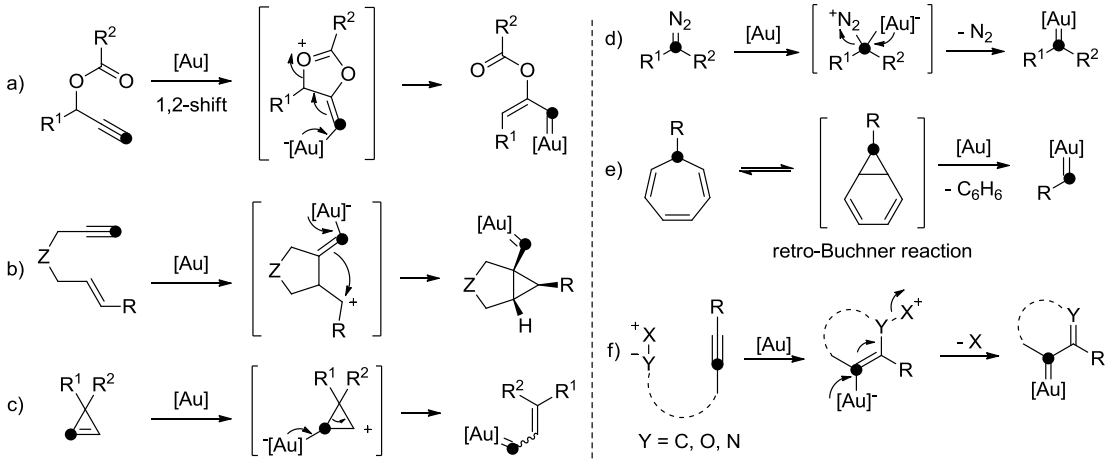
1.1 Homogeneous Gold Catalysis

In the last decades, there has been a revolution in gold chemistry. Until Thomas[1] disclosed the first examples of homogeneous gold-catalyzed organic synthesis, gold had long been regarded inert and unreactive in catalytic transformations. Thereafter, homogeneous gold catalysis has gradually emerged to an efficient and frequently used tool in organic synthesis.[2] Owing to the preferable carbophilicity of gold catalysts, most reactions typically commence with the attack of a nucleophile onto the gold-coordinated alkynes, thus leading to a vinyl gold species. This intermediate often undergoes deauration by an electrophile (either discrete or bonded directly to the Nu) to complete a hydro/difunctionalization process. If the electrophile is tethered to the nucleophilic site in some distance, a cyclic product **B** is afforded. Alternatively, another cyclic compound **C** can be obtained through the generation of gold carbene species. This intermediate is then quenched by another nucleophilic moiety Nu' (which could be either preinstalled or derived from the substrate) tied to the original nucleophilic site Nu by a suitable tether. The last two processes are known as formal cycloadditions, which are the research focus of this thesis.



Scheme 1. Profile of gold-catalyzed intermolecular transformations with alkynes.

The first reaction involving gold carbene intermediates was the cycloisomerization of furan-ynes in the Hashmi phenol synthesis.[3a] This reaction is mechanistically related to the gold-catalyzed cycloisomerization of enynes, but in that case the furan ring serves as an electron-rich alkene.[3,4] In subsequent investigations, such an intermediate is often involved in homogeneous gold catalysis, although the nature of a given gold carbene species remains somewhat uncertain.[5] However, the isolation and full characterization of some electronically stabilized gold carbene complexes have provided new insight into their bonding situation.[6] Furthermore, the character of gold carbenes, carbocations or carbenoids were fully elaborated by Hashmi,[7a,b] Echavarren,[7c,d] and Fürstner[7e,f]. In 2009, Toste and Goddard proposed that the carbon-gold bond in a given gold-stabilized intermediate generally consists of varying degrees of both σ- and π-bonding based on theoretical and experimental analyses.[8] The proportions of each bonding are largely dependent upon the ancillary ligand and the carbene substituent. It is because: a) the 6s vacant valence orbital on gold can accept a pair of electrons from the ligand and carbene substrate, respectively, thus forming a three-center four-electron σ-hyperbond according to Pauli exclusion principle; b) two π-coordination bonds also exist at the gold center due to its backdonation from two filled 5d-orbitals into empty π-acceptors on the ligand and carbene substrate. In this thesis, the term *gold carbene* is used to describe the gold-coordinated carbene species, regardless of the dominant carbene or carbocation form. Typical strategies to access gold carbene intermediates are outlined in Scheme 2: a) 1,2-acyloxy migration of propargylic carboxylates;[9] b) cycloisomerization of 1,6-enynes;[4] c) ring opening of cyclopropenes;[10] d) decomposition of diazo compounds;[11] e) the retro-Buchner reaction of cycloheptatrienes;[12] f) carbon-, oxygen-, or nitrogen-transfer onto alkynes.[13] In this chapter, gold-catalyzed formal cycloadditions of alkynes to access azaheterocycles will be summarized, with the α-imino gold carbene pathway underlined.



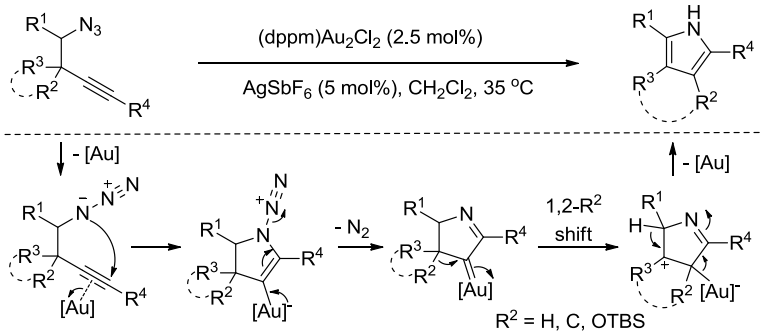
Scheme 2. Most common approaches to access gold carbenes.

1.2 Recent Advances in α-Imino Gold Carbene Chemistry for Azaheterocycle Syntheses

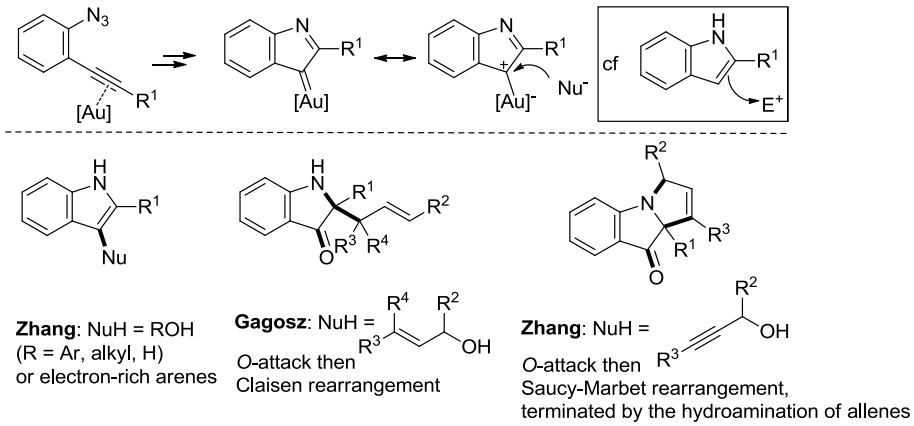
1.2.1 Intramolecular Generation

The first introduction of an α-imino gold carbene came from the Toste group in 2005 via an intramolecular acetylenic Schmidt reaction of homopropargyl azides for the synthesis of pyrroles.[14] This success benefits from the π-acidity and the electron-donating nature of gold complexes. A plausible mechanism was proposed initialized by the addition of the proximal nitrogen of azides to the gold-activated alkyne (Scheme 3). The electron donating property of the gold center promoted the release of dinitrogen. The ensuing α-imino gold carbene species underwent a 1,2-hydride/alkyl/siloxy migration terminated by tautomerization, furnishing the pyrrole product under liberation of the cationic gold catalyst. Inspired by this pioneering work, the intra-/intermolecular nucleophilic capture of gold carbene intermediates was achieved by several groups.[15] For instance, the treatment of 2-alkynylaryl azides under gold catalysis was reported by Zhang's and Gagosz's groups, respectively (Scheme 4).[15b,c,h] Both groups exploited the Umpolung strategy to access valuable and versatile indole derivatives by means of the nucleophilic quenching to the C3 position of indoles. Recently, a sequential annulation of

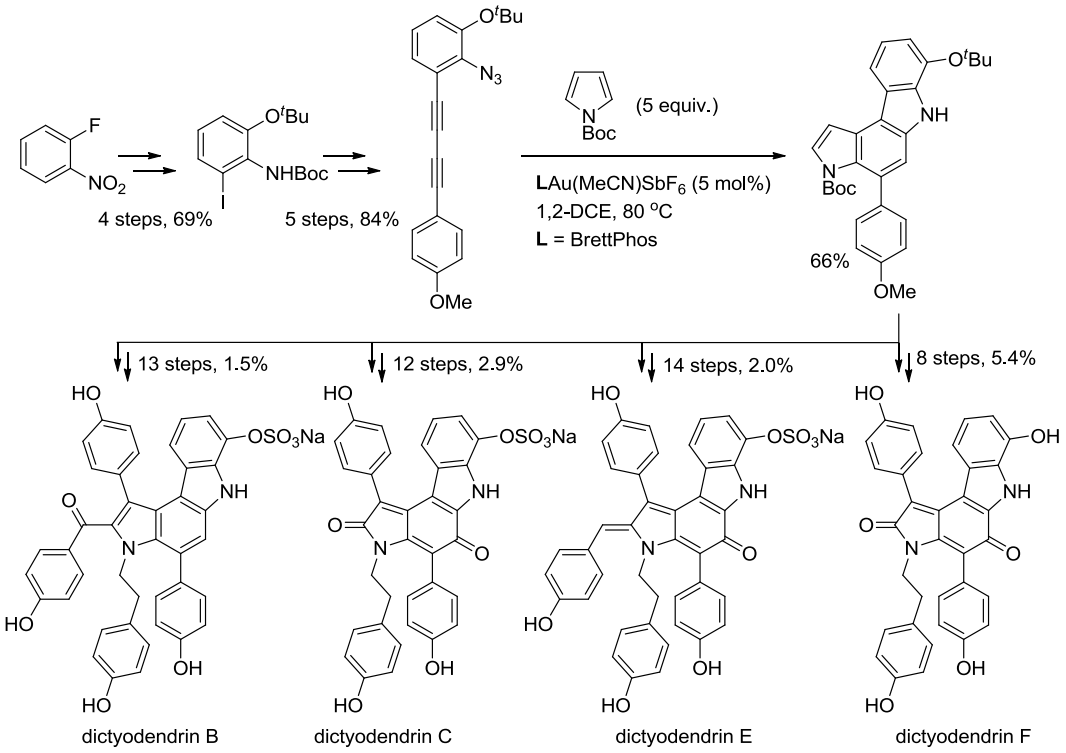
conjugated azido-diynes with pyrroles involving α-imino gold carbene intermediates was reported.[15l] It allowed for the rapid assembly of the pyrrolo[2,3-*c*]carbazole skeleton, a key intermediate in a diversity-oriented and total synthesis of dictyodendrin derivatives (Scheme 5).



Scheme 3. Pyrrole synthesis from homopropargyl azides.

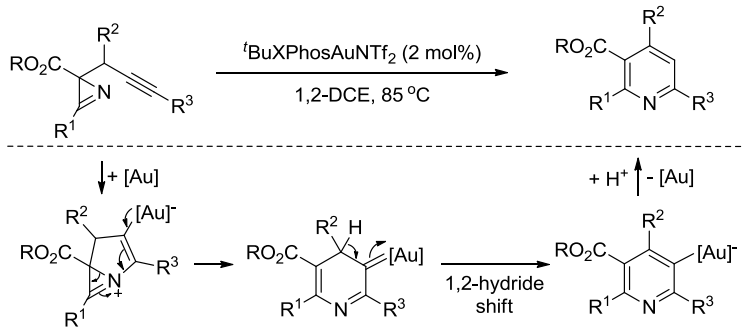


Scheme 4. Umpolung reactivity at the C3 position of indoles.



Scheme 5. Gold-carbene route towards pyrrolo[2,3-*c*]carbazole framework and application in the total synthesis of dictyodendrins.

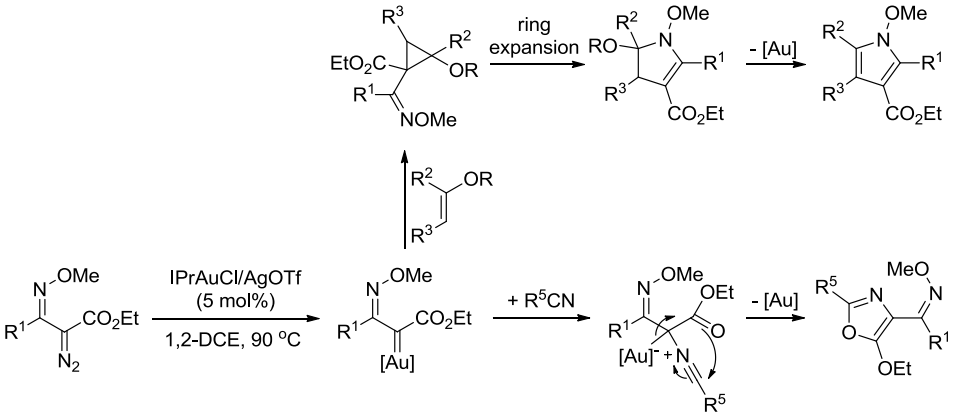
In 2014, a new method towards α-imino gold carbene intermediates was introduced by Gagosz and co-workers through a gold-promoted intramolecular transfer of alkenyl nitrenes to alkynes.[16] In this work, azirines, a strained three-membered ring could be opened via the initial nucleophilic adduct. The resulting gold carbene enabled 1,2-hydride migration, affording a set of polysubstituted pyridines after protodeauration.



Scheme 6. Azirine as alkenyl nitrene precursor via intramolecular transfer to alkynes.

In 2016, Park *et al.* disclosed a divergent synthesis of pyrroles and oxazoles from

α-diazo oxime ethers, a precursor to the α-imino gold carbenes.[17] The latter was then trapped by an external nucleophile, such as enol ethers or nitriles, terminated by a ring expansion or cyclization to yield pyrroles or oxazoles, respectively (Scheme 7).

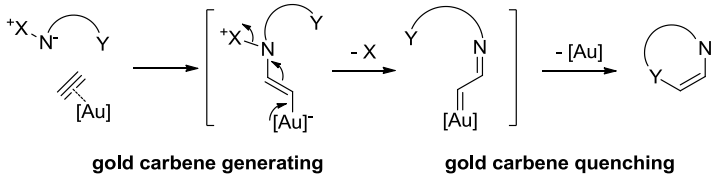


Scheme 7. α-Diazo compounds as a precursor of gold carbenes.

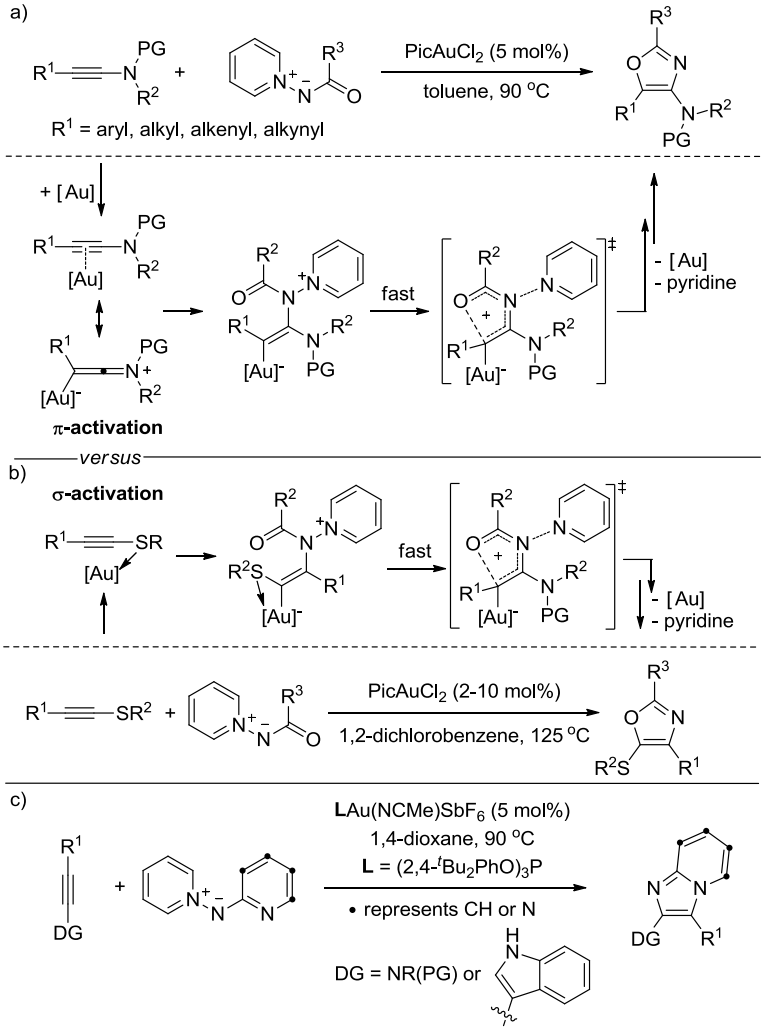
1.2.2 Intermolecular Generation

Despite the aforementioned intramolecular entry to α-imino gold carbene for azaheterocycle syntheses, intermolecular protocols would provide an alternative and particularly appealing approach towards such kind of intermediates, thus allowing for more facile and flexible synthesis from readily accessible starting materials. Davies *et al.* envisioned that an intermolecular nitrene-transfer reaction from a nucleophilic nitrenoid to gold-activated alkynes could also lead to α-imino gold carbenes.[18] It would be quenched by a preinstalled nucleophilic functionality adjacent to the electrophilic organogold center, thus completing the formal cycloaddition. (Scheme 8) In 2011, this concept was first realized via nitrene transfer of pyridine-*N*-aminides onto ynamides assisted by gold(III) complexes, producing a wide array of oxazoles (Scheme 9a).[18a] Noteworthy is the absence of competing 1,2-hydride shift with aliphatic ynamides, which is indicative of the faster formation of C–O than N–N bond fission. Besides ynamides, internal alkynes with conjugation from a remote nitrogen atom turned out to be competent although higher reaction temperatures were required alongside the switch from a gold(III) complex to a cationic phosphite gold(I) catalyst.[19] Importantly, the utilization of alkynyl thioethers led to an inverse regioselectivity, likely due to σ-activation mode complementary to the general

π-activation pattern in ynamides (Scheme 9b versus 9a).[18,20] Furthermore, pyridinium *N*-(heteroaryl)aminides were able to act as a robust nucleophilic 1,3-*N*,*N*-dipole equivalent in a formal [3+2] cycloaddition onto electron-rich internal alkynes enabled by gold catalysis (Scheme 9c).[21]



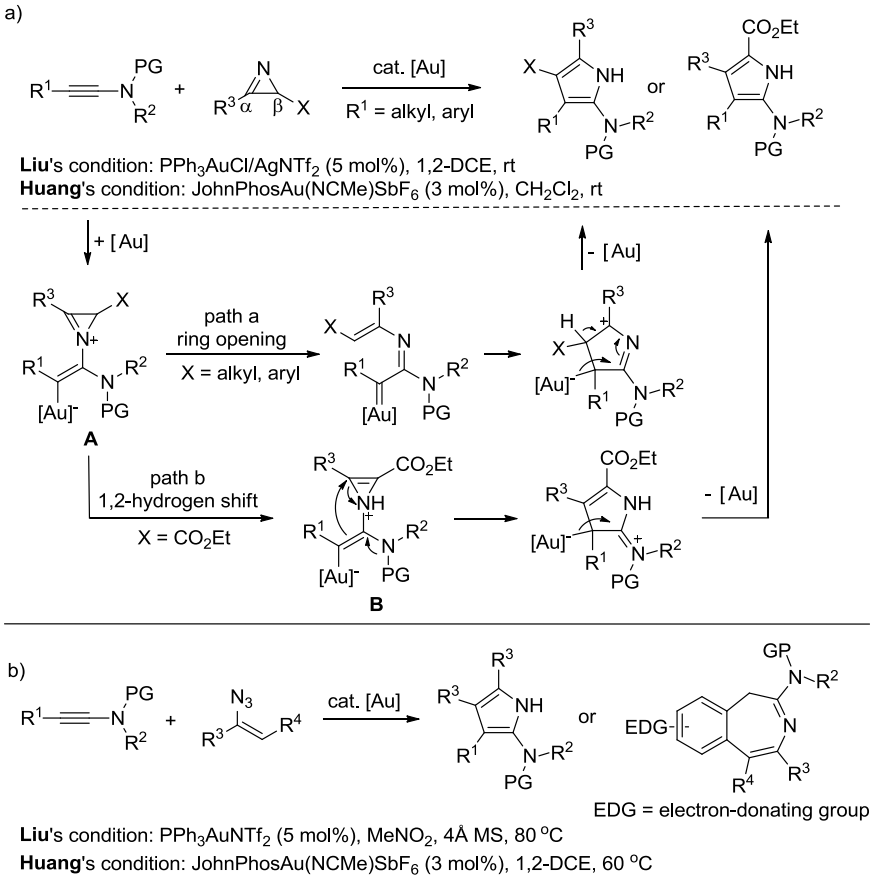
Scheme 8. Schematic of intermolecular formal cycloaddition involving α-imino gold carbenes



Scheme 9. Pyridinium ylides as nucleophilic nitrenoid equivalents.

In 2015, Huang and Liu groups independently revealed intermolecular [3+2]

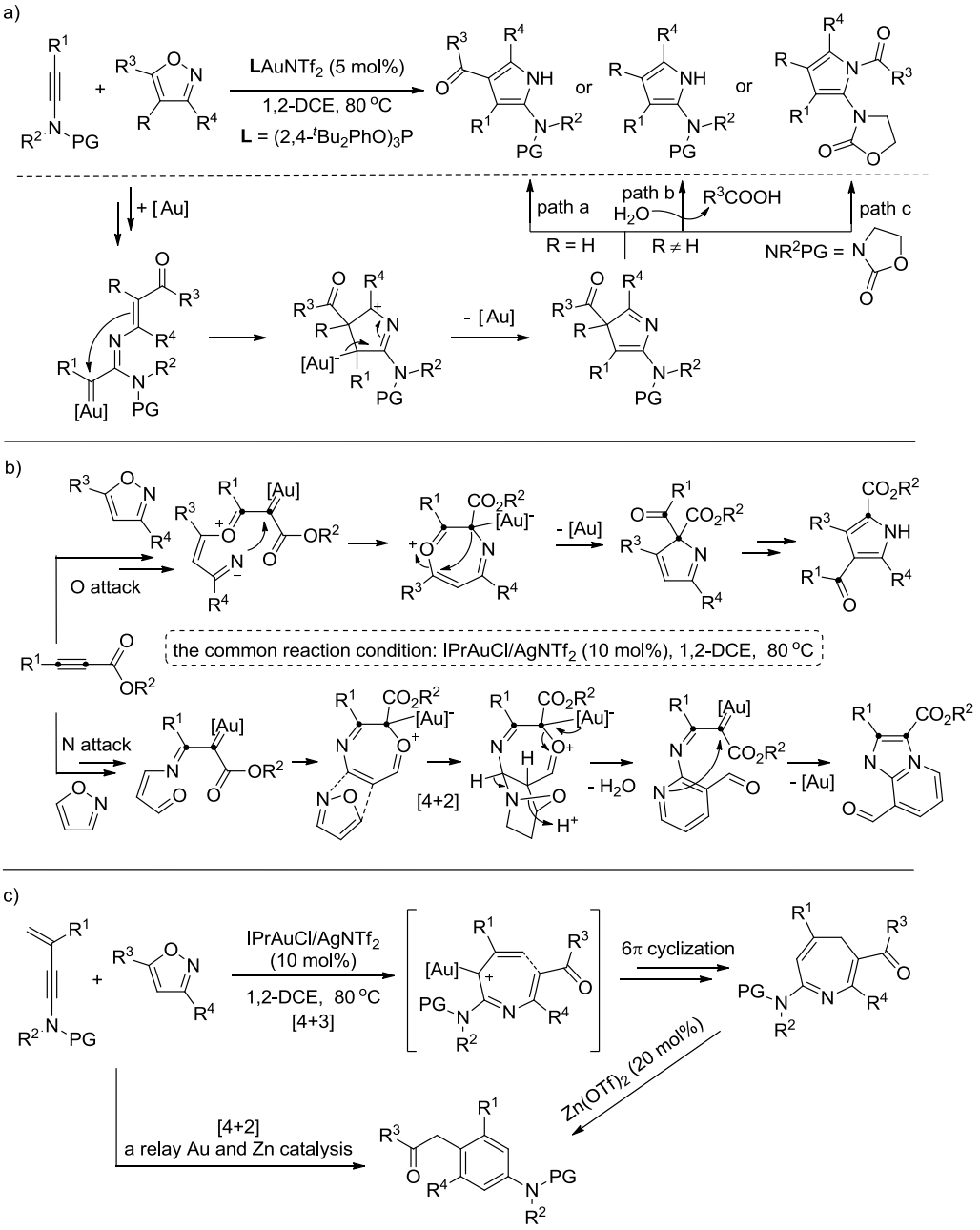
annulations of 2*H*-azirines with ynamides, en route to polysubstituted 2-aminopyrroles (Scheme 10a).[22a,b] Interestingly, the nature of Cβ-substituent (X) on 2*H*-aziridines directs the regioselectivity via distinct pathways. For 2*H*-aziridines with aromatic or aliphatic Cβ-substituents, the intermediacy of gold carbene was proposed by Huang *et al.* (path a). In the case of 2*H*-aziridines with an ester moiety, the common intermediate **A** preferred to undergo a 1,2-hydrogen shift followed by a Michael-type reaction, further giving the pyrrole product (path b, Liu's work). In addition, both groups found vinyl azides as a precursor of 2*H*-aziridines, also reacting with ynamides to furnish [3+2] formal cycloadducts under gold catalysis (Scheme 10b).[22b,c] The choice of ynamides with electron-rich (hetero)aromatic groups on *C*-terminus provided access to 1*H*-benzo[*d*]azepine products via [4+3] annulation.



Scheme 10. 2*H*-Azirines and their equivalents vinyl azides as nucleophilic nitrenoids.

Meanwhile, Ye et al. reported an alternative method for pyrrole synthesis via gold-assisted [3+2] annulation of ynamides and isoxazoles (Scheme 11a).[23] Herein

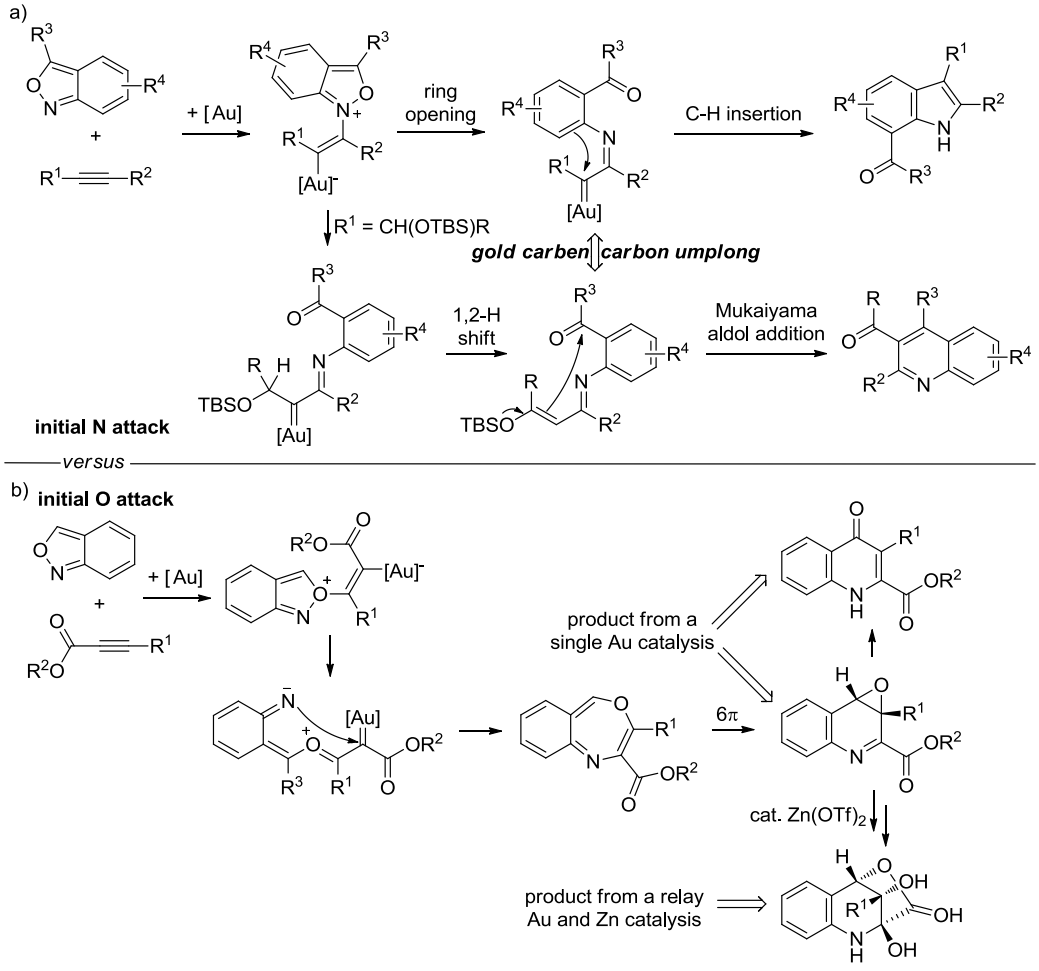
the latter was employed as a nitrene-transfer precursor via sequential nucleophilic addition onto ynamides and ring opening by N–O cleavage to generate the α-imino gold carbene. Due to its high electrophilicity, ensuing 1,5-cyclization readily took place to afford 3*H*-pyrroles after deauration. As a result of varied substrate substitution, different product outcomes could be explained through a hydride shift pathway (path a), water-assisted deacylation (path b), or intermolecular *C*-to-*N* acyl shift facilitated by the more electron-rich oxazolidinone moiety than the related sulfonyl groups (path c). Inspired by those work, Liu and co-workers recently developed two novel annulations of isoxazoles with propiolates under gold catalysis (Scheme 11b).[24] Notably, most isoxazoles follow a weaker nucleophilic *O*-attack pathway to enable the cleavage of carbon-carbon triple bonds, leading to pyrroles via [4+1] annulations, whereas the unsubstituted isoxazole underwent an initial *N* attack step to furnish imidazo[1,2-*a*]pyridines by a sequential [2+2+1]/[4+2] cycloaddition. Both initial *O* and *N* additions gave two key seven-membered ring intermediates, between which a reversible equilibrium existed. A ring contraction and subsequent rearrangement provided the pyrrole product (upper part of Scheme 11b). Alternatively, another discrete unsubstituted isoxazole acted as a potent heterodiene for the [4+2] cycloaddition with its corresponding seven-membered ring intermediate, finally providing imidazo[1,2-*a*]pyridines instead (lower part of Scheme 11b). Very recently, the same group further realized a gold-catalyzed [4+3] annulation of 3-en-1-ynamides with isoxazoles, furnishing 4*H*-azepines enabled by a 6π-electrocyclization of the gold-stabilized 3-azaheptatrienyl cation (Scheme 11c).[25] With the aid of catalytic $Zn(OTf)_2$, the obtained 4*H*-azepine could undergo a ring-contraction rearrangement to yield a pyridine skeleton. In addition, an one-pot synthesis of pyridines was also feasible by a relay Au(I)/Zn(II) catalysis.



Scheme 11. Amination or oxidation of activated alkynes enabled by isoxazoles.

In 2015, our group described a gold-catalyzed C–H annulation of anthranils with alkynes for 7-acylindolyl synthesis taking advantage of the potential binucleophilicity of anthranil (Scheme 12a, upper).[26a] Remarkably, some non-polarized alkynes also worked well for this reaction. If a propargylic ether was introduced, the *in situ* generated α-imino gold carbene species was then quenched by a 1,2-hydride shift/deauration sequence to give an enolether, which allowed for a Mukaiyama aldol

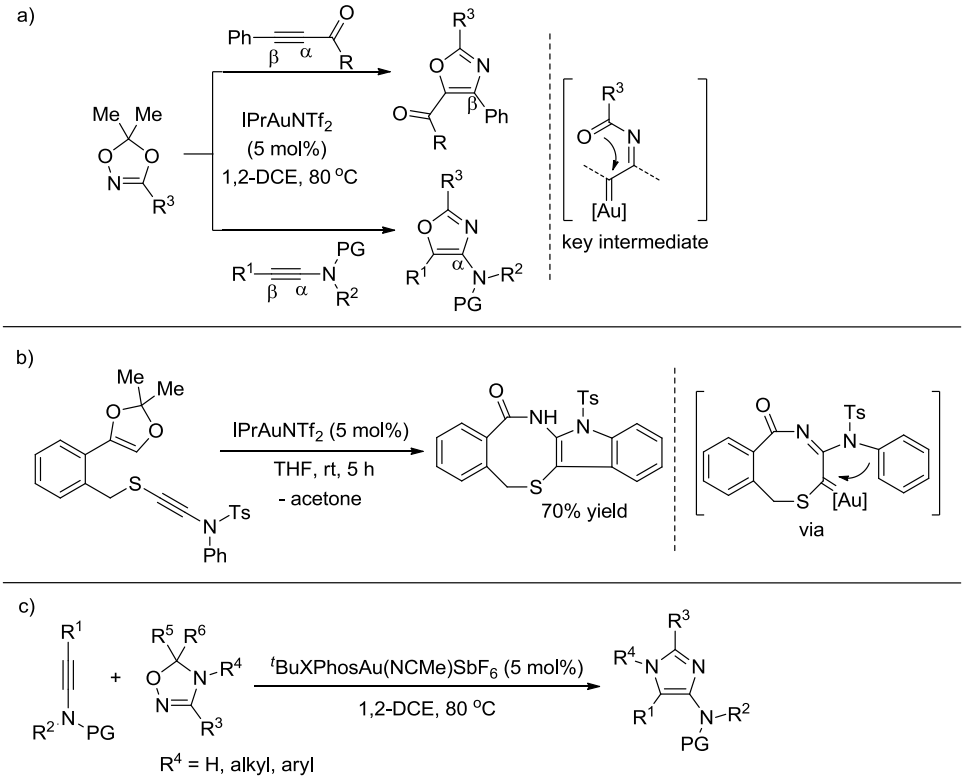
cyclization with the electrophilic carbonyl moiety derived from the anthranil substrate. This Umpolung concept was later realized by the gold-catalyzed reactions of propargyl silyl ethers and anthranils, providing access to various quinolines (Scheme 12a, lower).[26b] Very recently, Liu group contributed a gold-catalyzed reaction of anthranils with propiolates, affording various dihydroquinolines, where anthranils underwent an initial *O*-attack complementary to our proposed *N* attack step.[26c] In addition, a gold(I) and Zn(II) relay catalysis led to highly oxygenated tetrahydroquinolines.



Scheme 12. Amination or oxidation of alkynes enabled by anthranils.

In 2016, Liu and co-workers revealed that 1,4,2-dioxazoles could be also utilized as a robust *N*-acyl nitrenoid precursor in the gold-aided nitrene transfer reaction onto activated alkynes (Scheme 13a).[27a] This reaction engaged the key α-imino gold carbene intermediate in a 4π-cyclization/deauration sequence. The regioselectivity of

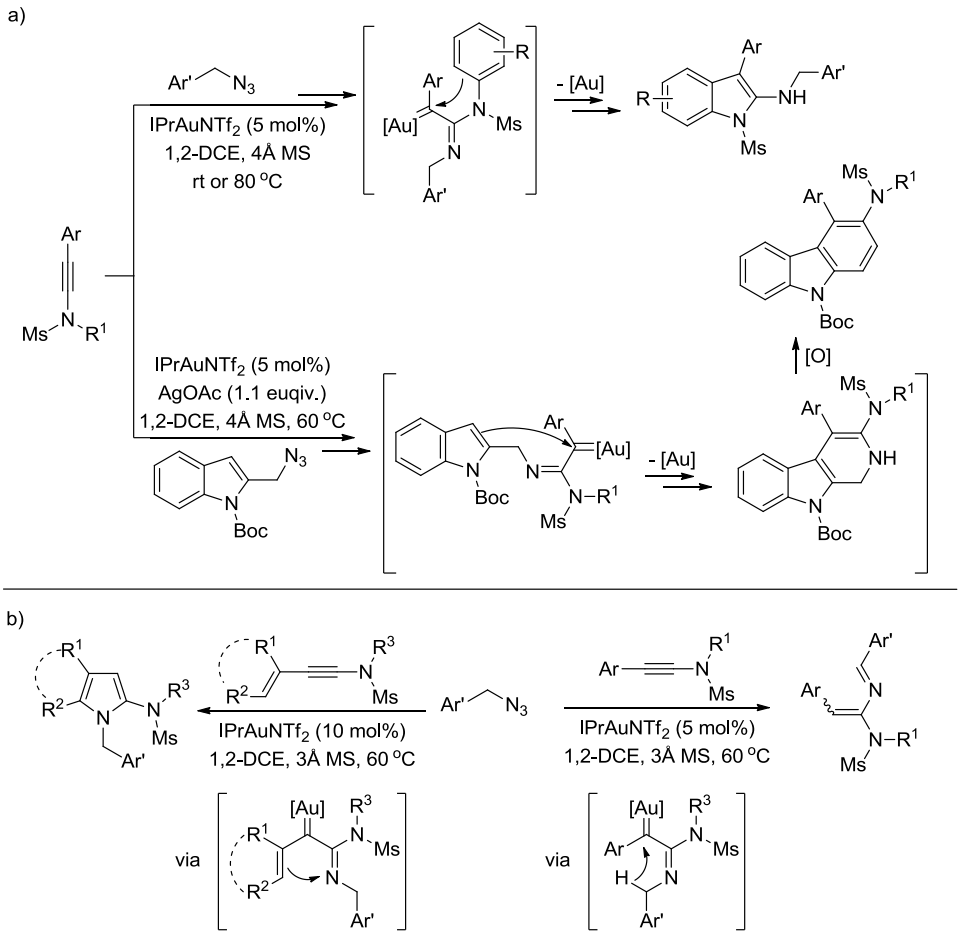
oxazole products was directed by the substituent pattern of alkynes. Electron-rich ynamides favored the nitrene transfer to α-C-terminus position while electron-deficient alkynes (alkynyl esters or alkynyl ketones) reversed the selective attack. It is noteworthy that such a gold-carbene mechanism could be supported by the intramolecular cyclization of dioxazole-ynamide, where the C(sp^2)–H insertion instead of C–O bond formation occurred to give the tetracyclic compound (Scheme 13b). Later, this group found 1,2,4-oxadiazoles as an efficient *N*-imino nitrene equivalent, applied for imidazole synthesis via gold-assisted [3+2] annulations with ynamides (Scheme 13c).[27b]



Scheme 13. 1,4,2-Dioxazoles and its analogue 1,2,4-oxadiazoles as nitrene equivalents.

Despite the intramolecular nitrene transfer of azide moieties onto alkynes to access α-imino gold carbene intermediates, such an intermolecular protocol has not been realized until 2015 by Ye group.[28] Likewise, the interaction of ynamides and azides also led to the gold carbene species.[28a] It could be quenched either by an aryl group on ynamides or by a more nucleophilic indolyl part fixed on the azides. The former

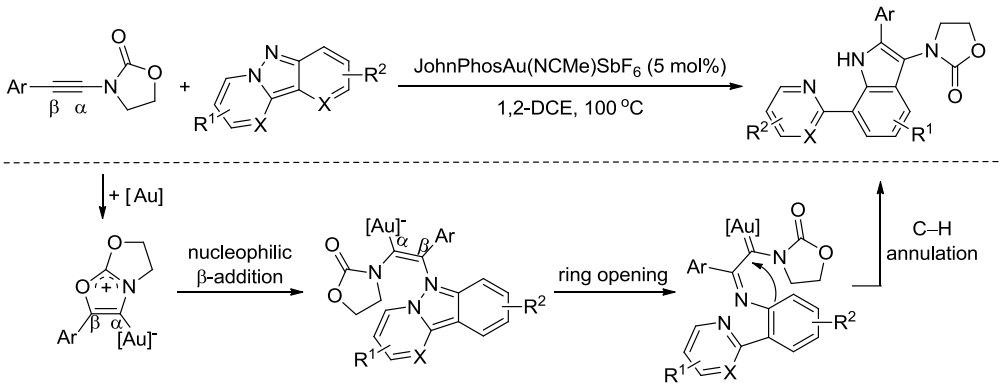
constituted a gold-catalyzed formal [4+2] cycloaddition, en route to indoles; the latter gave carbolines after dehydrogenative oxidation (Scheme 14a, upper verse lower). Later, this group further developed other tandem reactions enabled by such gold carbene intermediates, including an aza-Nazarov cyclization for pyrrole synthesis and a 1,4-hydride shift to access 2-aza-1,3-butadienes (Scheme 14b).[28b,c]



Scheme 14. Intermolecular nitrene transfer of azides to ynamides.

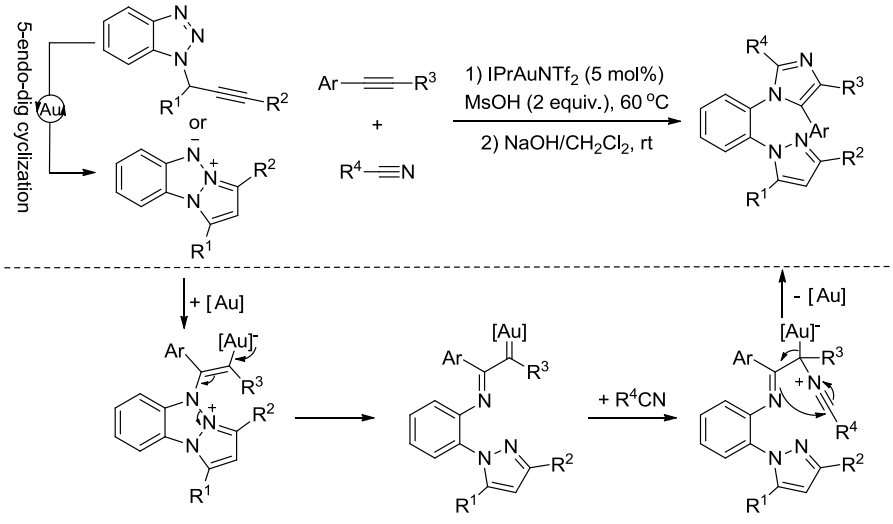
Noteworthy is the initial α-site-regioselective addition onto ynamides in the above cases. In 2016, Huang and co-workers discovered a complementary β-site regioselective [3+2] annulation of pyrido[1,2-*b*]indazoles with ynamides under gold catalysis, leading to a variety of 3-aminoindoles (Scheme 15).[29] Mechanistic studies indicated the reaction pathway initially involves a transient five-membered ring, directing the β-addition of the nucleophilic nitrenoid. After a ring opening, the α-imino gold carbene was formed, which in turn enabled the ensuing C(sp^2)−H

insertion of the phenyl ring to give the final product.



Scheme 15. Pyrido[1,2-*b*]indazoles as nucleophilic nitrenoids.

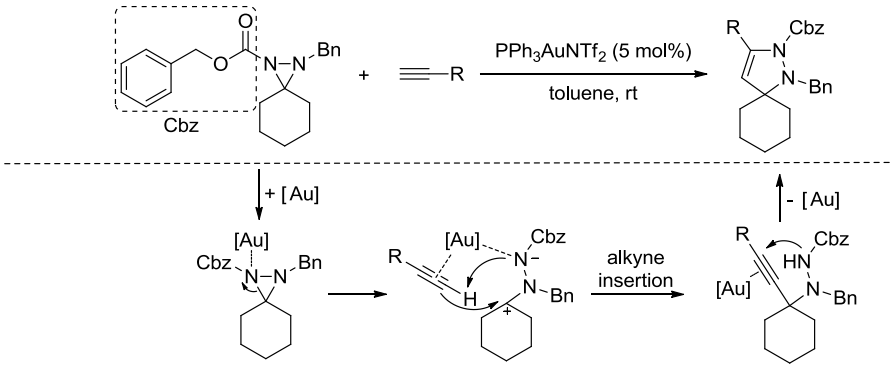
In 2016, Ballesteros group contributed a gold-catalyzed tandem reaction containing three components: triazapentalenes (or its precursor propargylic benzotriazoles), alkynes and nitriles (Scheme 16).[30] Notably, this protocol, in addition to our previous report, are the only two routes involving an intermolecular nitrene transfer to non-polarized alkynes to access the α-imino gold carbene species. This highly electrophilic intermediate was captured by an external nitrile, terminated by a cyclization to construct a new imidazole ring.



Scheme 16. Triazapentalenes as a nucleophilic nitrenoid.

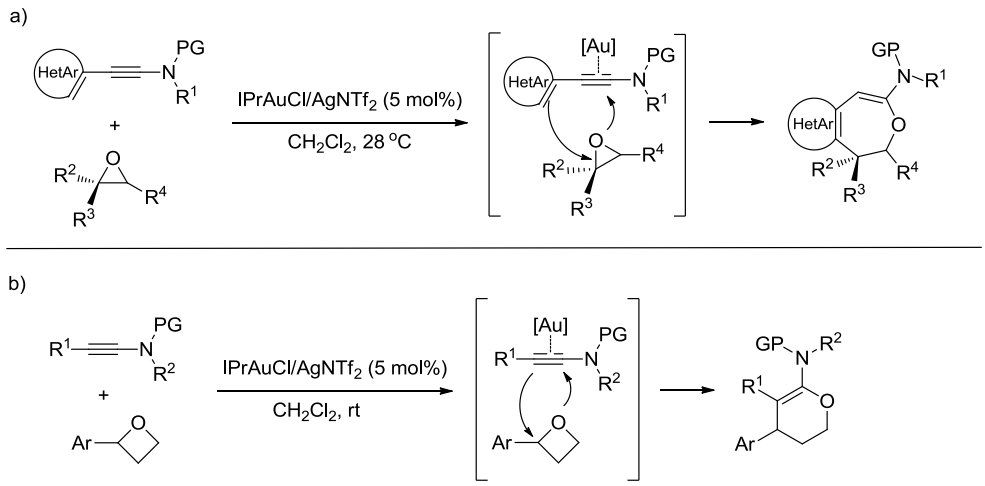
1.3 Recent Advances in Gold-Catalyzed Intermolecular Annulations of Alkynes with Saturated Heterocycles

Gold-catalyzed intermolecular annulations of alkynes with saturated heterocycles provided an efficient and powerful strategy to build a wide range of heterocyclic scaffolds.[31] For instance, in 2011, He and co-workers showcased that diaziridines were valuable three-atom synthons for the synthesis of pyrazolines under gold catalysis (Scheme 17).[32a] Mechanistic investigations supported an initial gold-aided ring opening of the diazridine and subsequent alkyne insertion, terminated by an intramolecular hydroamination to yield the product.



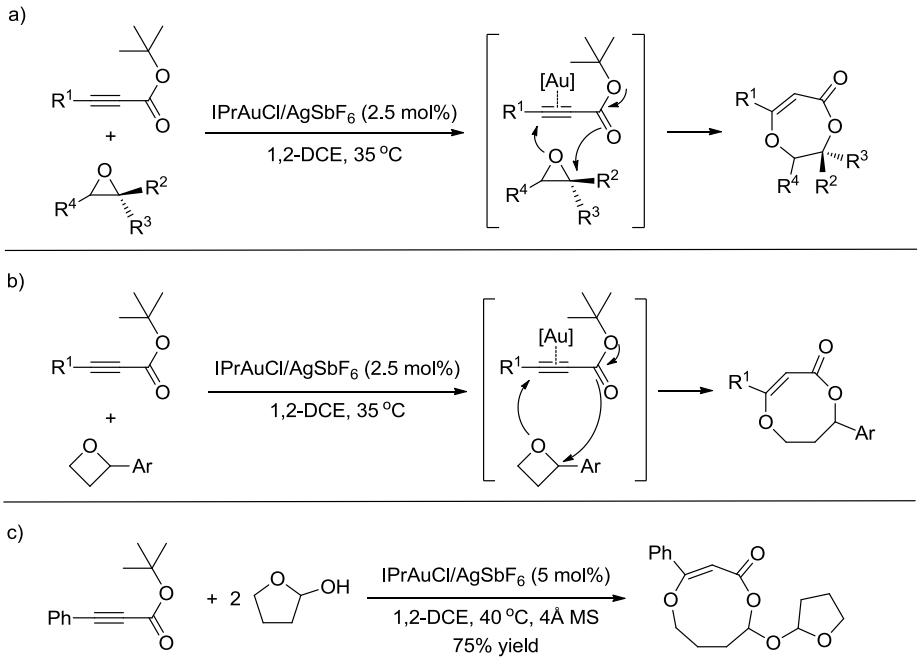
Scheme 17. [3+2] Annulation of diazridines with alkynes

In 2012, Liu *et al.* employed epoxides as the three-atom building blocks for a gold-catalyzed intermolecular formal [4+3] cycloaddition with ynamides (Scheme 18a).[32b] This group later used relatively less ring-strained oxetanes as four-atom units for efficient [4+2] annulations of ynamides (Scheme 18b).[32c]



Scheme 18. Epoxides and oxetanes applied for annulation with ynamides.

Recently, this group further applied the epoxides and oxetanes for gold-catalyzed [4+n] annulations (n = 3, 4) with *tert*-butyl propiolates, yielding various seven- and eight-membered oxaheterocyclic products (Scheme 19a, 19b).[32d] Even a nine-membered ring was also accessible via a formal [4+5] cycloaddition between *tert*-butyl propiolate and γ-lactol (Scheme 19c).



Scheme 19. Epoxides and oxetanes used for annulation with *tert*-butyl propiolates.

1.4 Research Objectives and Thesis Outline

The research interests in this thesis center on the novel and facile synthesis of azaheterocycles via gold-catalyzed formal cycloadditions of alkynes. Herein most synthetic approaches are enabled by α-imino gold carbene intermediates.

In chapter 2, a novel, concise, and atom-economical synthesis of fully substituted 4-aminoimidazoles through a gold-catalyzed selective [3+2] annulation of 1,2,4-oxadiazoles with ynamides is realized. Chapter 3 describes a novel, short, and flexible approach to diverse *N*-doped polycyclic aromatic hydrocarbons via gold-catalyzed ring-expansion/π-extension of anthranils with *o*-ethynylbiaryls. In chapter 4, a facile, site-selective and divergent route is provided to access 2-aminopyrroles and quinoline-fused polyazaheterocycles directed by a simple gold catalyst from ynamides and anthranils. In chapter 5, a gold-catalyzed regioselective cyclocarboamination of ynamides with 1,3,5-triazinanes leads to the valuable 5-aminotetrahydropyrimidines in good and excellent yields.

1.5 References

[1] a) R. O. C. Norman, W. J. E. Parr, C. B. Thomas, *J. Chem. Soc. Perkin Trans. 1*, **1976**, *0*, 811–817; b) R. O. C. Norman, W. J. E. Parr, C. B. Thomas, *J. Chem. Soc. Perkin Trans. 1*, **1976**, *0*, 1983–1987.

[2] For selected reviews, see: a) A. S. K. Hashmi, *Gold. Bull*. **2003**, *36*, 3–9; b) A. S. K. Hashmi, *Gold Bull.* **2004**, *37*, 51–65; c) A. S. K. Hashmi, G. Hutchings, *Angew. Chem. Int. Ed.* **2006**, *45*, 7896–7936; *Angew. Chem*. **2006**, *118*, 8064–8105; d) A. S. K. Hashmi, *Chem. Rev.* **2007**, *107*, 3180–3211; e) A. Fürstner, P. W. Davies, *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; *Angew. Chem*. **2007**, *119*, 3478–3519; f) E. Jiménez-Núñeza, A. M. Echavarren, *Chem. Commun*. **2007**, 333–346; g) D. J. Gorin, F. D. Toste, *Nature* **2007**, *446*, 395–403; h) Z. Li, C. Brouwer, C. He, *Chem. Rev*. **2008**, *108*, 3239–3265; i) D. J. Gorin, B. D. Sherry, F. D. Toste, *Chem. Rev.* **2008**, *108*,

3351–3378; j) A. S. K. Hashmi, M. Rudolph, *Chem. Soc. Rev*. **2008**, *37*, 1766–1775; k) A. Arcadi, *Chem. Rev.* **2008**, *108*, 3266–3325; l) A. Corma, A. Leyva-Pérez, M. J. Sabater, *Chem. Rev*. **2011**, *111*, 1657–1712; m) J. Xiao, X. Li, *Angew. Chem. Int. Ed*. **2011**, *50*, 7226–7236; *Angew. Chem*. **2011**, *123*, 7364-7375; n) M. Rudolph, A. S. K. Hashmi, *Chem. Soc. Rev*. **2012**, *41*, 2448–2462; o) L.-P. Liu, G. B. Hammond, *Chem. Soc. Rev.* **2012**, *41*, 3129; p) R. Dorel, A. M. Echavarren, *Chem. Rev.* **2015**, *115*, 9028–9072.

[3] a) A. S. K. Hashmi, T. M. Frost, J. W. Bats, *J. Am. Chem. Soc*. **2000**, *122*, 11553–11554; b) A. S. K. Hashmi, M. Rudolph, J. P. Weyrauch, M. Wclfle, W. Frey, J. W. Bats, *Angew. Chem. Int. Ed.* **2005**, *44*, 2798–2801; *Angew. Chem.* **2005**, *117*, 2858–2861; c)A. S. K. Hashmi, M. Rudolph, J. W. Bats, W. Frey, F. Rominger, T. Oeser, *Chem. Eur. J.* **2008**, *14*, 6672–6678; d) A. S. K. Hashmi, M. Rudolph, H.-U. Siehl, M. Tanaka, Jan W. Bats, W. Frey, *Chem. Eur. J.* **2008**, *14*, 3703–3708.

[4] For selected reviews, see: E. Jiménez-Núñez, A. M. Echavarren, *Chem. Rev.* **2008**, *108*, 3326–3350; b) C. Obradors, A. M. Echavarren, *Acc. Chem. Res.* **2014**, *47*, 902−912; c) R. Dorel, A. M. Echavarren, *J. Org. Chem.* **2015**, *80*, 7321−7332; d) R. J. Harris, R. A. Widenhoefer, *Chem. Soc. Rev.* **2016**, *45*, 4533−4551.

[5] For selected reviews, see: a) "Gold Carbenes": L. Zhang, in C*ontemporary Carbene Chemistry* (Eds. R. A. Moss, M. P. Doyle), Wiley, Hoboken, **2013**, 526–551. b) D. Qian, J. Zhang, *Chem. Soc. Rev.* **2015**, *44*, 677−698.

[6] Selected examples, see: a) M. Fañanás-Mastral, F. Aznar, *Organometallics* **2009**, *28*, 666–668; b) R. E. M. Brooner, R. A. Widenhoefer, *Chem. Commun.* **2014**, *50*, 2420–2423; c) R. J. Harris, R. A. Widenhoefer, *Angew. Chem. Int. Ed.* **2014**, *53*, 9369–9371; *Angew. Chem.* **2014**, *126*, 9523–9525; d) M. W. Hussong, F. Rominger, P. Krämer, B. F. Straub, *Angew. Chem. Int. Ed.* **2014**, *53*, 9372–9375; *Angew. Chem.* **2014**, 126, 9526–9529; e) G. Seidel, A. Fürstner, *Angew. Chem. Int. Ed*. **2014**, *53*, 4807–4811; *Angew. Chem.* **2014**, *126*, 4907–4911; f) A. Pujol, M. Lafage, F. Rekhroukh, N. Saffon-Merceron, A. Amgoune, D. Bourissou, N. Nebra, M. Boutignon, N. Mézailles, *Angew. Chem. Int. Ed.* **2017**, *56*, 12264–12267; *Angew. Chem.* **2017**, *129*, 12432–12435; g) A. Zeineddine, F. Rekhroukh, E. D. S. Carrizo, S.

Mallet-Ladeira, K. Miqueu, A. Amgoune, D. Bourissou, *Angew. Chem. Int. Ed.* **2018**, *57*, 1306–1310; *Angew. Chem.* **2018**, *130*, 1320–1324.

[7] For selected reviews, see: a) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2008**, *47*, 6754–6756; *Angew. Chem.* **2008**, *120*, 6856–6858; b) A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2010**, 49, 5232–5241; *Angew. Chem.* **2010**, *122*, 5360–5369; c) C. Nieto-Oberhuber, S. López, M. P. Muñoz, D. J. Cárdenas, E. Buñuel, C. Nevado, A. M. Echavarren, *Angew. Chem. Int. Ed.* **2005**, *44*, 6146–6148; *Angew. Chem.* **2005**, *117*, 6302–6304; d) Y. Wang, M. E. Muratore, A. M. Echavarren, *Chem. Eur. J.* **2015**, *21*, 7332–7339; e) A. Fürstner, L. Morency, *Angew. Chem. Int. Ed.* **2008**, *47*, 5030–5033; *Angew. Chem.* **2008**, *120*, 5108–5111; f) G. Seidel, R. Mynott, A. Fürstner, *Angew. Chem. Int. Ed.* **2009**, *48*, 2510–2513; *Angew. Chem.* **2009**, *121*, 2548–2551.

[8] D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Goddard, F. D. Toste, *Nat. Chem.* **2009**, *1*, 482–486.

[9] For selected reviews, see: a) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350–1357; b) S. Wang, G. Zhang, L. Zhang, *Synlett* **2010**, 692–706; c) R. K. Shiroodi, V. Gevorgyan, *Chem. Soc. Rev.* **2013**, *42*, 4991–5001; d) D. P. Day, P. W. H. Chan, *Adv. Synth. Catal.* **2016**, *358*, 1368–1384.

[10] For a review, see: F. Miege, C. Meyer, J. Cossy, *Beilstein J. Org. Chem.* **2011**, *7*, 717–734.

[11] For selected reviews, see: a) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506–516; b) M. R. Fructos, M. M. Díaz-Requejo, P. J. Pérez, *Chem. Commun.* **2016**, *52*, 7326–7335.

[12] For a review, see: M. Jia, S. Ma, *Angew. Chem. Int. Ed.* **2016**, *55*, 9134–9166; *Angew. Chem.* **2016**, *128*, 9280–9313.

[13] For selected original work on carbon transfer, see: a) S. Kramer, T. Skrydstrup, *Angew. Chem. Int. Ed.* **2012**, *51*, 4681–4684; *Angew. Chem.* **2012**, *124*, 4759–4762; b) X. Huang, B. Peng, M. Luparia, L. F. R. Gomes, L. F. Veiros, N. Maulide, *Angew. Chem. Int. Ed.* **2012**, *51*, 8886–8890; *Angew. Chem.* **2012**, *124*, 9016–9020. Selected reviews on oxygen transfer onto alkynes, see: c) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877–888; d) H.-S. Yeom, S. Shin, *Acc. Chem. Res.* **2014**, *47*, 966–977. Reviews on

nitrogen transfer, see: e) P. W. Davies, M. Garzón, *Asian J. Org. Chem.* **2015**, *4*, 694–708; f) L. Li, T.-D. Tan, Y.-Q. Zhang, X. L. L.-W. Ye, *Org. Biomol. Chem.* **2017**, *15*, 8483–8492.

[14] D. J. Gorin, N. R. Davis, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 11260–11261.

[15] Selected examples, see: a) Z. Huo, Y. Yamamoto, *Tetrahedron Lett.* **2009**, *50*, 3651–3653; b) B. Lu, Y. Luo, L. Liu, L. Ye, Y. Wang, L. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 8358–8362; *Angew. Chem.* **2011**, *123*, 8508–8512; c) A. Wetzel, F. Gagosz, *Angew. Chem. Int. Ed.* **2011**, *50*, 7354–7358; *Angew. Chem.* **2011**, *123*, 7492–7496; d) Z.-Y. Yan, Y. Xiao, L. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 8624–8627; *Angew. Chem.* **2012**, *124*, 8752–8755; e) Y. Xiao, L. Zhang, *Org. Lett.* **2012**, *14*, 4662–4665; f) C. Gronnier, G. Boissonnat, F. Gagosz, *Org. Lett.* **2013**, *15*, 4234–4237; g) S. Zhu, L. Wu, X. Huang, *J. Org. Chem.* **2013**, *78*, 9120–9126; h) N. Li, T.-Y. Wang, L.-Z. Gong, L. Zhang, *Chem. Eur. J.* **2015**, *21*, 3585–3588; i) C.-H. Shen, Y. Pan, Y.-F. Yu, Z.-S. Wang,W. He, T. Li, L.-W. Ye, *J. Organomet. Chem.* **2015**, *795*, 63–67; j) Y. Pan, G.-W. Chen, C.-H. Shen, W. He, L.-W. Ye, *Org. Chem. Front.* **2016**, *3*, 491–495; k) N. Li, X.-L. Lian, Y.-H. Li, T.-Y. Wang, Z.-Y. Han, L. Zhang, L.-Z. Gong, *Org. Lett.* **2016**, *18*, 4178−4181; l) J. Matsuoka, Y. Matsuda, Y. Kawada, S. Oishi, H. Ohno, *Angew. Chem. Int. Ed.* **2017**, *56*, 7444–7448; *Angew. Chem.* **2017**, *129*, 7552–7556; m) W.-B. Shen, Q. Sun, L. Li, X.in Liu, B. Zhou, J.-Z. Yan, X. Lu, L.-W. Ye. *Nat. Commun.* **2018**, *8*, 1748; n) J. Cai, B. Wu, G. Rong, C. Zhang, L. Qiu, X. Xu, *Org. Lett.* **2018**, *20*, 2733–2736.

[16] A. Prechter, G. Henrion, P. FaudotditBel, F. Gagosz, *Angew. Chem. Int. Ed.* **2014**, *53*, 4959–4963; *Angew. Chem.* **2014**, *126*, 5059–5063.

[17] N. S. Y. Loy, S. Choi, S. Kim, C.-M. Park, *Chem. Commun.* **2016**, *52*, 7336–7339.

[18] a) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935; *Angew. Chem.* **2011**, *123*, 9093–9097; b) A. D. Gillie, R. J. Redd, P. W. Davies, *Adv. Synth. Catal.* **2016**, *358*, 226–239.

[19] E. Chatzopoulou, P. W. Davies, *Chem. Commun.* **2013**, *49*, 8617–8619.

[20] R. J. Reddy, M. P. Ball-Jones, P. W. Davies, *Angew. Chem. Int. Ed*. **2017**, *56*, 13310–13313; *Angew. Chem*. **2017**, *129*, 13495–13498.

[21] M. Garzón, P. W. Davies, *Org. Lett.* **2014**, *16*, 4850−4853.

[22] a) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33; b) S. K. Pawar, R. L. Sahani, R.-S. Liu, *Chem. Eur. J.* **2015**, *21*, 10843–10850; c) Y. Wu, L. Zhu, Y. Yu, X. Luo, X. Huang, *J. Org. Chem*. **2015**, *80*, 11407–11416.

[23] a) A.-H. Zhou, Q. He, C. Shu, Y.-F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu, L.-W. Ye, *Chem. Sci.* **2015**, *6*, 1265–1271; b) X.-Y. Xiao, A.-H. Zhou, C. Shu, F. Pan, T. Li, L.-W. Ye, *Chem. Asian J*. **2015**, *10*, 1854–1858.

[24] R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 1026–1030; *Angew. Chem*. **2017**, *129*, 1046–1050.

[25] S. S. Giri, R.-S. Liu, *Chem. Sci.* **2018**, 9, 2991–2995.

[26] a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K.Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; *Angew. Chem.* **2016**, *128*, 804–808; b) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Angew. Chem. Int. Ed*. **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *128*, 12880–12884; c) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 12736–12740; *Angew. Chem.* **2017**, *129*, 12910–12914.

[27] a) M. Chen, N. Sun, H. Chen, Y. Liu, *Chem. Commun.* **2016**, *52*, 6324–6327; b) W. Xu, G. Wang, N. Sun, Y. Liu, *Org. Lett.* **2017**, *19*, 3307–3310.

[28] a) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567–9570; b) C. Shu, C.-H. Shen, Y.-H. Wang, L. Li , T. Li, X. Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 4630–4633; c) C. Shu, Y.-H. Wang, C.-H. Shen, P.-P. Ruan, Xin Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 3254–3257; d) P.-P. Ruan, H.-Hao Li, X. Liu, T. Zhang, S.-X. Zuo, C. Zhu, L.-W. Ye, *J. Org. Chem.* **2017**, *82*, 9119–9125; e) B. Zhou, Y.-Q. Zhang, X. Liu, L.-W. Ye, *Sci. Bull.* **2017**, *62*, 1201–1206.

[29] Y. Yu, G. Chen, L. Zhu, Y. Liao, Y. Wu, X. Huang, *J. Org. Chem.* **2016**, *81*, 8142–8154.

[30] J. González, J. Santamaría, Á. L. Suárez-Sobrino, A. Ballesteros, *Adv. Synth.*

Catal. **2016**, *358*, 1398–1403.

[31] For selected reviews, see: a) A. K. Yudin in *Aziridines and Epoxides in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; b) K. V. Gothelf, K. A. Jørgensen, *Chem. Rev.* **1998**, *98*, 863–910; c) W. Carruthers in *Cycloaddition in Organic Synthesis*, Pergamon, Oxford, **1990**, 1.

[32] a) D. A. Capretto, C. Brouwer, C. B. Poor, C. He, *Org. Lett*. **2011**, *13*, 5842–5845; b) S. N. Karad, S. Bhunia, R.-S. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 8722–8725; *Angew. Chem.* **2012**, *124*, 8852–8856; c) S. K. Pawar, D. Vasu, R.-S. Liu, *Adv. Synth. Catal*. **2014**, *356*, 2411–2416; d) R. L. Sahani, R.-S. Liu, *Chem. Commun.* **2016**, *52*, 7482–4785.

Chapter 2: α-Imino Gold Carbenes from 1,2,4-Oxadiazoles: Concise and Atom-Economical Access to Fully Substituted 4-Aminoimidazoles

2.1 Introduction

As one fundamental framework, imidazole motifs frequently exist in a large number of natural products,[1] pharmaceuticals,[2] ionic liquids,[3] and precursors of *N*-heterocyclic carbenes.[4] In this family, fully substituted 4-aminoimidazole derivatives are core structures of some bioactive compounds and also serve as versatile building blocks (Figure 1).[5] However, in contrast with the wealth of imidazole synthesis, few routes can allow direct access to fully substituted 4-aminoimidazoles.[6] Hence, the development of general and practical methods for the construction of highly functionalized 4-aminoimidazole scaffolds is meaningful to synthetic and medicinal chemistry. Recently, we and other groups verified that highly reactive α-imino gold carbenes generated in situ from various nucleophilic nitrenoid equivalents, such as azides,[7] *N*-iminopyridiumylides,[8] 2*H*-azirines,[9] and very recently developed isoxazoles,[10] anthranils,[11] triazapentalenes[12] and dioxazoles,[13] pyrido[1,2-*b*]indazoles,[14] provided a powerful platform to construct an array of structurally diverse aza-heterocycles.[15] Notwithstanding the recent advance attained, the exploration of α-imino gold carbene chemistry with less sensitive nitrene-transfer reagents, especially in an atom-economical and selective manner, is highly desirable.

1,2,4-Oxadiazole is an appealing candidate due to its stability, structural diversity and easy operation. To date, the further transformations of 1,2,4-oxadiazoles were still surprisingly scarce.[16,17] One representative work is the photo-induced rearrangement of 1,2,4-oxadiazoles to form *N*-acylimino nitrene intermediates which subsequently trapped by different nucleophiles (Scheme 1a).[17] Inspired by our previous work on gold carbenes,[11,18] we considered the possibility of using 1,2,4-oxadiazoles as

nucleophilic nitrene equivalents to form α-imino gold carbene intermediates via regioselective addition to gold-activated ynamides. Based on their high electrophilicity, subsequent intramolecular chemoselective trapping completed a [3+2] annulation, affording fully substituted 4-aminoimidazoles (Scheme 1b). If successful, this process would open a new window for the reaction pattern of 1,2,4-oxadiazoles, and also complement the existing strategies for the synthesis of polysubstituted 4-aminoimidazole derivatives. Herein, we disclose a new route to α-imino gold carbenes from 1,2,4-oxadiazoles and ynamides, enabling the convergent, concise, and atom-economical synthesis of fully substituted 4-aminoimidazoles.

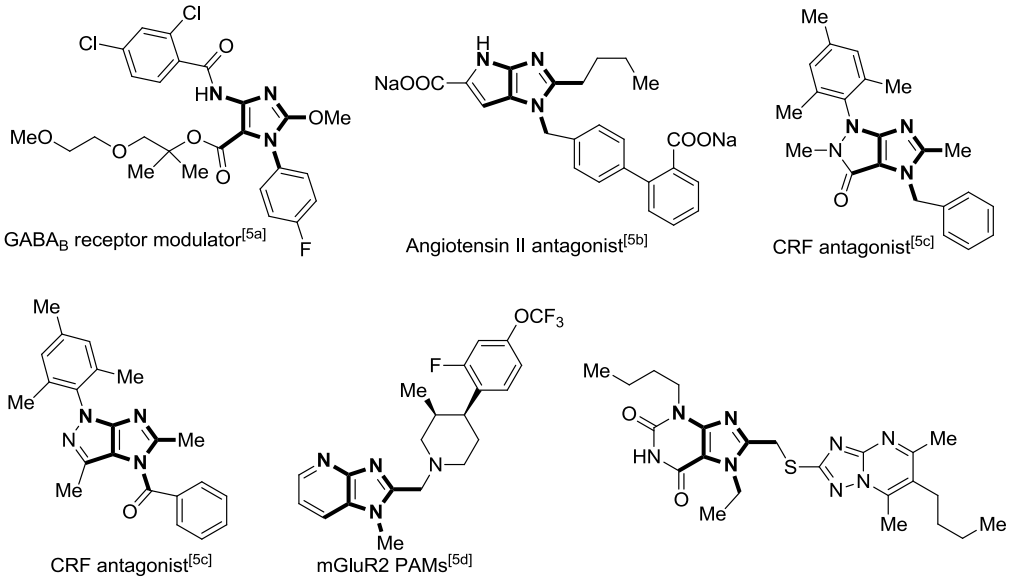
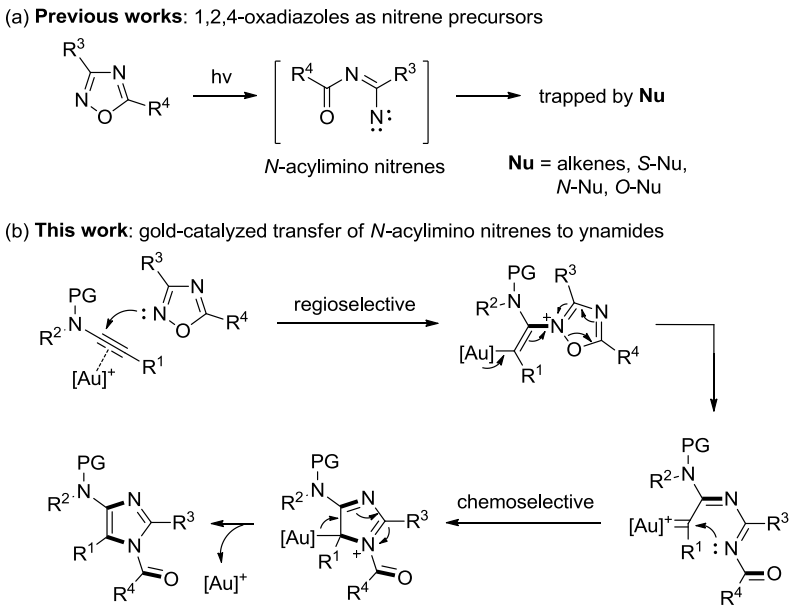


Figure 1. Representative bioactive compounds with fully substituted 4-aminoimidazole frameworks



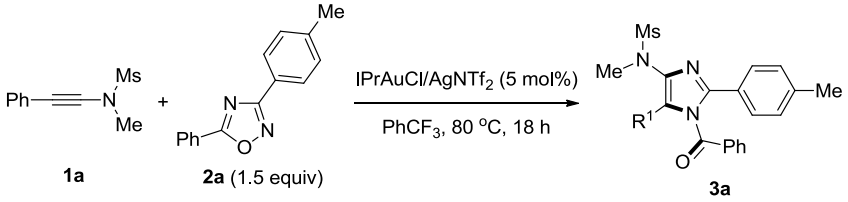
Scheme 1. Previous works and our design

2.2 Results and Discussion

2.2.1 Optimization of Reaction Condition

To evaluate the feasibility, ynamide **1a** and 1,2,4-oxadiazole **2a** were initially chosen as the model reaction (Table 1). Gratifyingly, employing 5 mol% of IPrAuCl/$AgNTf_2$ as a catalyst at 80 °C can afford the desired product **3a** in 95% NMR yield (entry 1). Control experiments without any catalyst or silver salt alone showed no conversion (entries 2 and 3). Other gold catalysts, PPh_3AuNTf_2, $(2,4\text{-}^tBu_2PhO)_3PAuCl/AgNTf_2$, $SPhosAuNTf_2$, $KAuBr_4$, were much less efficient, leading to **3a** in lower yields (entries 4–7). Switching counter anion from NTf_2 to OTf lead to a significantly decreased yield (95% versus 67%, entries 1 and 8). In addition, other solvents such as 1,2-DCE and toluene could not improve the reaction efficiency (entries 9 and 10). Decreasing reaction temperature from 90 °C to 60 °C delivered **3a** in moderate yield (entry 11).

Table 1: Screening for optimal reaction conditions[a]



entry	deviation from "standard" conditions	yield[b]
1	none	95% (90%)
2	no catalyst	n.d.
3	$AgNTf_2$	trace
4	PPh_3AuNTf_2	52%
5	$(2,4\text{-}^tBu_2PhO)_3PAuCl/AgNTf_2$	30%
6	$SPhosAuNTf_2$	48%
7	$KAuBr_4$	39%
8	IPrAuCl/AgOTf	67%
9	1,2-DCE, instead of $PhCF_3$	72%
10	toluene, instead of $PhCF_3$	57%
11	60 °C	54%

[a] "Standard" conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), IPrAuCl/$AgNTf_2$ (5 mol%) reacted in $PhCF_3$ (0.5 mL) for 18 h at 80 °C. [b] Measured by ^1H NMR with 1,3,5-trimethoxybenzene as the internal standard. Yield of isolated product given in parentheses. n.d. = not detected.

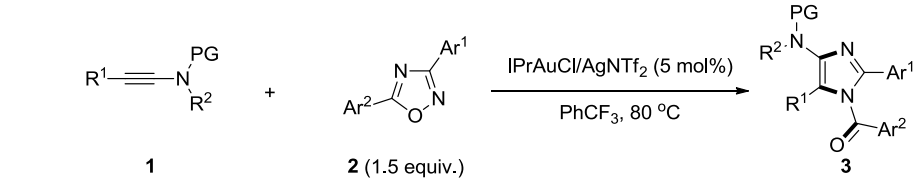
2.2.2 Scope with regard to the Substrate

Under the optimized reaction conditions, the scope of this novel transformation was investigated (Table 2). First, with 1,2,4-oxadiazole **2a** as the reaction partner, diverse ynamides bearing different protecting groups (Ms, Ts, and Bs) and substituents on nitrogen tolerated the reaction conditions well, furnishing **3a**–**f** in satisfying yields. We then examined the influence of R^1 group on the alkyne terminus. Aryl substituted ynamides with various substituents on the phenyl ring uniformly afford the desired

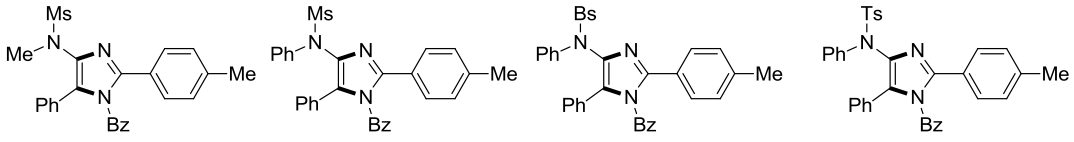
products **3g**–**m** in 71–91% yields, regardless of their electronic and positional properties. An array of functional groups, including chloride, bromide, fluoride, ether, and ester remain intact, offering opportunities for further modification at these positions (**3h**–**m**, **3p**, **3w**). When thiophenyl substituted ynamide was subjected to standard conditions, imidazole **3n** was obtained in high yield. Concerning the scope with regard to the 3,5-diaryl-1,2,4-oxadiazoles, it was found that electron-donating, electron-withdrawing and neutral substituents on the aromatic ring were all compatible (**3e, 3o**–**r**).

Encouraged by these results, we further broaden the scope of this reaction by using a series of 1,2,4-oxadiazoles bearing one alkyl group on the parent ring (Table 3). However, the use of 5 equiv. of 1,2,4-oxadiazoles **2** was necessary to obtain the desired products in acceptable yields, probably due to their reduced nucleophilicity. In this case, the 4-aminoimidazole products were afforded in moderate yields. Of note, the ester group was tolerated in this transformation, providing **3w** in 41% yield. To further confirm the 4-aminoimidazole framework, X-ray crystallography of **3v** was conducted (Table 3).[19]

Table 2: Reaction scope for ynamides and 3,5-diaryl-1,2,4-oxadiazoles.[a,b]



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

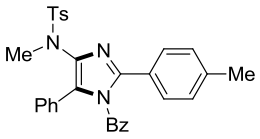


3a, 18 h, 90%

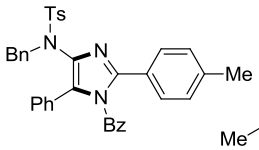
3b, 24 h, 78%

3c, 24 h, 93%

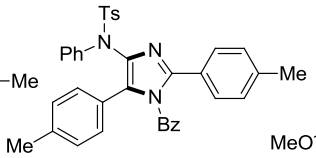
3d, 24 h, 78%



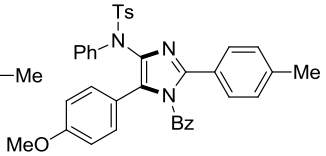
3e, 24 h, 66%



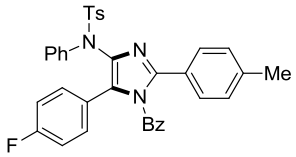
3f, 24 h, 64%



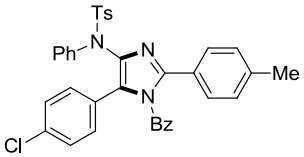
3g, 24 h, 83%



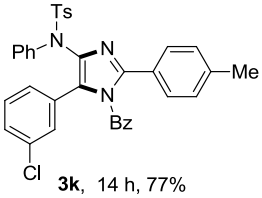
3h, 24 h, 71%



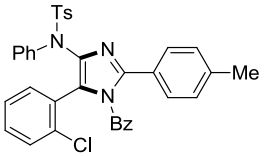
3i, 20 h, 91%



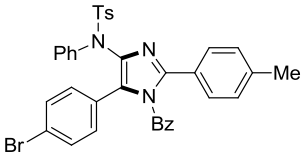
3j, 24 h, 85%



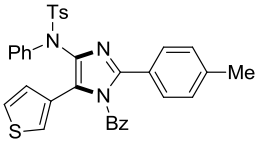
3k, 14 h, 77%



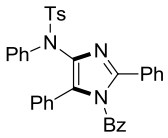
3l, 18 h, 88%



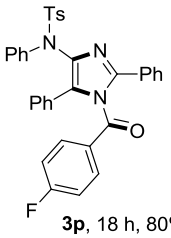
3m, 14 h, 78%



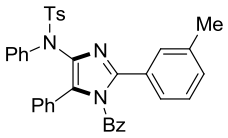
3n, 14 h, 82%



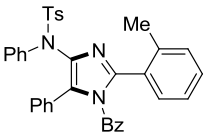
3o, 18 h, 86%



3p, 18 h, 80%



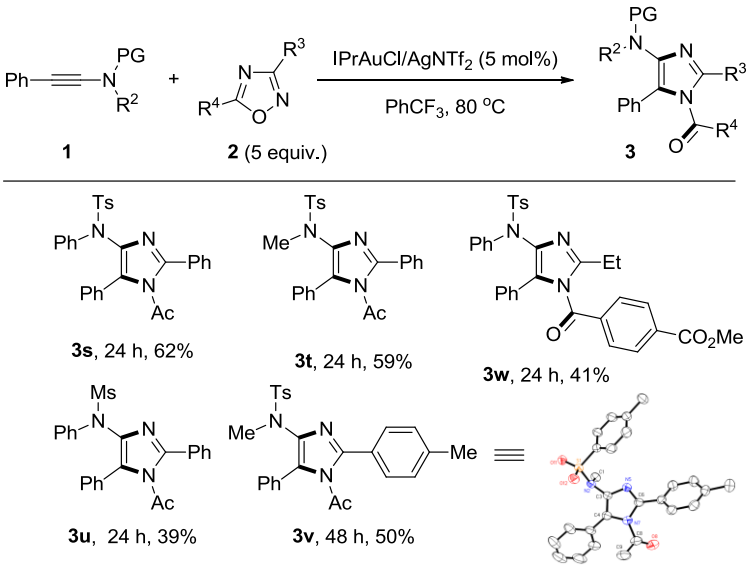
3q, 20 h, 84%



3r, 48 h, 73%

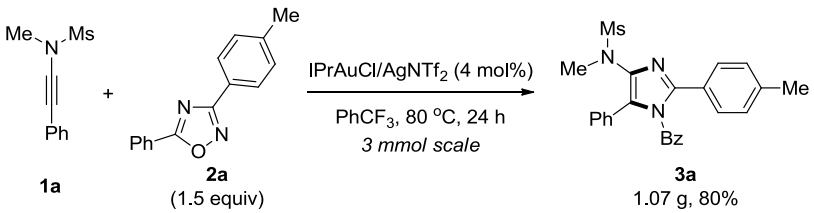
[a] Reaction conditions: **1** (0.2 mmol), **2** (0.3 mmol), IPrAuCl/$AgNTf_2$ (5 mol%), $PhCF_3$ (1 mL), 80 °C.
[b] Isolated yield.

Table 3: Reaction scope for 3,5-disubstituted 1,2,4-oxadiazoles.[a,b]

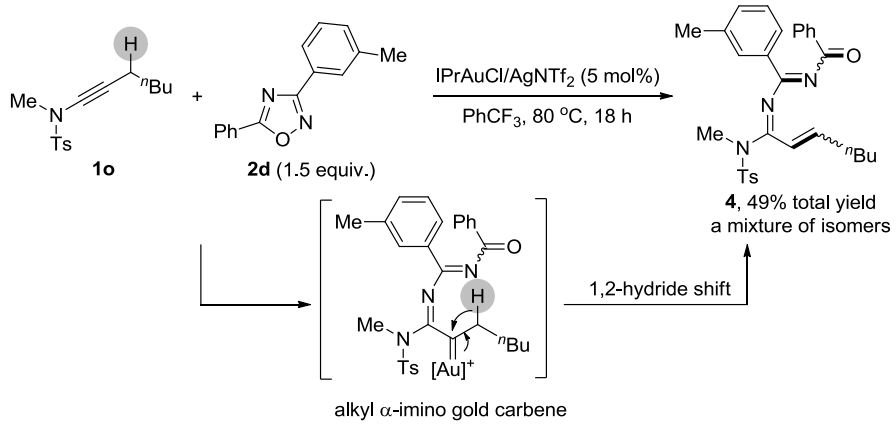


[a] Reaction conditions: **1** (0.2 mmol), **2** (1.0 mmol), IPrAuCl/$AgNTf_2$ (5 mol%), $PhCF_3$ (1 mL), 80 °C. [b] Isolated yield.

To further probe the practicality of this methodology, a 1.07 gram-scale synthesis with a slightly lower catalyst loading (4 mol%) was conducted. It delivered 4-aminoimidazole **3a** in a good yield of 80% (Scheme 2). Finally, we prepared alkyl-substituted ynamide **1o** and then reacted with 1,2,4-oxadiazole **2d** under the standard condition. As expected, α,β-unsaturated imine **4** was isolated in 49% total yield without detection of the desired imidazole (Scheme 3). The successful 1,2-hydride shift leading to alkenes indicates α-imino gold carbenoid intermediate is very likely.[8a,20]



Scheme 2. Gram-scale synthesis



Scheme 3. Reaction of alkyl-substituted ynamide with 1,2,4-oxadiazole

2.3 Conclusion

In conclusion, we have demonstrated 1,2,4-oxadiazoles could serve as novel nucleophilic nitrenoid equivalents for the generation of α-imino gold carbenes, corresponding to an intermolecular transfer of *N*-acyliminonitrenes to ynamides. This protocol offers a new reaction pattern of 1,2,4-oxadiazoles and opens up a novel, concise, and atom-economical strategy for the synthesis of valuable fully substituted 4-aminoimidazoles. The present reaction proceeds with 100% atom economy, displayed good functional-group compatibility, and can be conducted in gram-scale synthesis. Further applications of 1,2,4-oxadiazoles in other organic synthesis are still ongoing in our group.

2.4 Notes and References

[1] a) S. M. Weinreb, *Nat. Prod. Rep.* **2007**, *24*, 931–948; b) Z. Jin, *Nat. Prod. Rep.* **2011**, *28*, 1143–1191; c) L. L. De, *Curr. Med. Chem.* **2006**, *13*, 1–23.

[2] a) N. Xi, Q. Huang, L. Liu, in: *Comprehensive Heterocyclic Chemistry III*, Vol. 4, (Eds.: A. R. Katrirzky, C. W. Rees), Elsevier, Amsterdam **2008**, pp 143–364; b) J. Revuelta, F. Machetti, S. Cicchi, in: *Modern HeterocyclicChemistry*, Vol. 2, (Eds.: J. Álvarez-Builla, J. J. Vaquero, J. Barluenga), Wiley-VCH, Weinheim, **2011**, pp 809–923; c) J. Heeres, L. J. J. Backx, J. H. Mostmans, J. V. Custen, *J. Med. Chem.*

1979, *22*, 1003–1005; d) R. J. C. Lee, P. C. Timmermans, T. F. Gallaghr, S. Kumar, D. McNully, M. Blumenthal, J. R. Heys, *Nature* **1994**, *372*, 739–746; e) M. Antolini, A. Bozzoli, C. Ghiron, G. Kennedy, T. Rossi, A. Ursini, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 1023–1028; f) S. E. De Laszlo, C. Hacker, B. Li, D. Kim, M. MacCoss, N. Mantalo, J. V. Pivnichny, L. Colwell, G. E. Koch, M. A. Cascieri, W. K. Hagmenn, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 641–646; g) L. Wang, K. W. Woods, Q. Li, K. J. Barr, R. W. McCroskey, S. M. Hannick, L. Gherke, R. B. Credo, Y. Hui, K. Marsh, R. Warner, J. Y. Lee, N. Zielinsky-Mozng, D. Frost, S. H. Rosenberg, H. L. Sham, *J. Med.Chem.* **2002**, *45*, 1697–1711; h) H. J. Cho, H. G. Gee, K.-H. Baek, S.-K. Ko, J.-M. Park, H. Lee, N.-D. Kim, M. G. Lee, I. Shin, *J. Am. Chem. Soc.* **2011**, *133*, 20267–20276.

[3] J. Dupont, R. F. de Souza, P. A. Z. Suarez, *Chem. Rev.* **2002**, *102*, 3667–3692.

[4] W. A. Herrmann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1290–1309; *Angew. Chem.* **2002**, *114*, 1342–1363.

[5] a) U. Bauer, W. Brailstord, L. Cheng, M. Jonforsen, F. Raubacher, P. Schell, T. Svensson, WO2008130313, **2008**; b) M. M. Akhavan, J. S. Mojarrad, A. Rouzrokh, S. A. Ebrahimi, M. Mahmoudian, A. Shafiee, *Il Farmaco* **2003**, 58, 1193–1199; c) J. P. Beck, P. J. Gilligan, (Du Pont Pharm CO). WO9910350, **1999**; d) L. Zhang, M. A. Brodney, J. Candler, A. C. Doran, A. J. Duplantier, I. V. Efremov, E. Evrard, K. Kraus, A. H. Ganong, J. A. Haas, A. N. Hanks, K. Jenza, J. T. Lazzaro, N. Maklad, S. A. McCarthy, W. Qian, B. N. Rogers, M. D. Rottas, C. J. Schmidt, J. A. Siuciak, F. D. Tingley III, A. Q. Zhang, *J. Med. Chem.* **2011**, *54*, 1724–1739; e) B. Raux, Y. Voitovich, C. Derviaux, A. Lugari, E. Rebuffet, S. Milhas, S. Priet, T. Roux, E. Trinquet, J.-C. Guillemot, S. Knapp, J.-M. Brunel, A. Y. Fedorov, Y. Collette, P. Roche, S. Betzi, S. Combes, X. Morelli, *J. Med. Chem.* **2016**, *59*, 1634–1641.

[6] a) E. Rossi, E. Pini, *Tetrahedron* **1996**, *52*, 7939–7946; b) A. Rolfs, J. Liebscher, *J. Org. Chem.* **1997**, *62*, 3480–3487; c) A. Marwaha, P. Singh, M. P. Mahajan, D. Velumurugan, *Tetrahedron Lett.* **2004**, *45*, 8945–8947.

[7] *Intra*molecular formation of α-imino gold carbenes, see: a) D. J. Gorin, N. R. Davis, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 11260–11261; b) A. Wetzel, F.

Gagosz, *Angew. Chem. Int. Ed.* **2011**, *50*, 7354–7358; *Angew. Chem.* **2011**, *123*, 7492–7496; c) B. Lu, Y. Luo, L. Liu, L. Ye, Y. Wang, L. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 8358–8362; *Angew. Chem.* **2011**, *123*, 8508–8512; d) Z.-Y. Yan, Y. Xiao, L. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 8624–8627; *Angew. Chem.* **2012**, *124*, 8752–8755; e) C. Gronnier, G. Boissonnat, F. Gagosz, *Org. Lett.* **2013**, *15*, 4234–4237; f) Y. Tokimizu, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2014**, *16*, 3138–3141; g) N. Li, T.-Y. Wang, L.-Z. Gong, L. Zhang, *Chem. Eur. J.* **2015**, *21*, 3585–3588; h) C.-H. Shen, Y. Pan, Y.-F. Yu, Z.-S. Wang, W. He, T. Li, L.-W. Ye, *J. Organomet. Chem.* **2015**, *795*, 63–67; i) Y. Xiao, L. Zhang, *Org. Lett.* **2012**, *14*, 4662–4665; j) X. Zhang, X. Sun, H. Fan, C. Lyu, P. Li, H. Zhao, W. Rao, *RSC Adv.* **2016**, *6*, 56319–56322; k) G. H. Lonca, C. Tejo, H. L. Chan, S. Chiba, F. Gagosz, *Chem. Commun.* **2017**, *53*, 736–739. *Inter*molecular versions, see: l) Y. Wu, L. Zhu, Y. Yu, X. Luo, X. Huang, *J. Org. Chem.* **2015**, *80*, 11407–11416; m) S. K. Pawar, R. L. Sahani, R.-S. Liu, *Chem. Eur. J.* **2015**, *21*, 10843–10850; n) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567–9570; o) C. Shu, Y.-H. Wang, C.-H. Shen, P.-P. Ruan, Xin Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 3254–3257; p) C. Shu, C.-H. Shen, Y.-H. Wang, L. Li , T. Li, X. Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 4630–4633.

[8] a) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738–1741; b) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935; *Angew. Chem.* **2011**, *123*, 9093–9097; c) E. Chatzopoulou, P. W. Davies, *Chem. Commun.* **2013**, *49*, 8617–8619; d) H.-H. Hung, Y.-C. Liao, R.-S. Liu, *J. Org. Chem.* **2013**, *78*, 7970–7976; e) A. D. Gillie, R. J. Redd, P. W. Davies, *Adv. Synth. Catal.* **2016**, *358*, 226–239.

[9] a) A. Prechter, G. Henrion, P. FaudotditBel, F. Gagosz, *Angew. Chem. Int. Ed.* **2014**, *53*, 4959–4963; *Angew. Chem.* **2014**, *126*, 5059–5063; b) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33.

[10] a) A.-H. Zhou, Q. He, C. Shu, Y.-F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu, L.-W. Ye, *Chem. Sci.* **2015**, *6*, 1265–1271; b) X.-Y. Xiao, A.-H. Zhou, C. Shu, F. Pan, T. Li, L.-W. Ye, *Chem. Asian J.* **2015**, *10*, 1854–1858; c) W.-B. Shen, X.-Y. Xiao, Q. Sun,

B. Zhou, X.-Q. Zhu, J.-Z. Yan, X, Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2017**, *56*, 605–609; *Angew. Chem.* **2017**, *129*, 620–624; d) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 1026–1030; *Angew. Chem.* **2017**, *129*, 1046–1050.

[11] a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K.Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; *Angew. Chem.* **2016**, *128*, 804–808; b) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *128*,12880–12884.

[12] J. González, J. Santamaría, Á. L. Suárez-Sobrino, A. Ballesteros, *Adv. Synth. Catal.* **2016**, *358*, 1398–1403.

[13] M. Chen, N. Sun, H. Chen, Y. Liu, *Chem. Commun.* **2016**, *52*, 6324–6327.

[14] Y. Yu, G. Chen, L. Zhu, Y. Liao, Y. Wu, X. Huang, *J. Org. Chem.* **2016**, *81*, 8142–8154.

[15] Selected reviews on aza-heterocycles from α-imino gold carbenes, see: a) P. W. Davies, M. Garzón, *Asian J. Org. Chem.* **2015**, *4*, 694–708; b) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506–516.

[16] a) D. Korbonits, I. Kanzel-Stvoboda, K. Horváth, *J. Chem. Soc., Perkin Trans. 1* **1982**, 759–766; b) S. Buscemi, M. G. Cicero, N. Vivona, T. Caronna, *J. Chem. Soc., Perkin Trans. 1* **1988**, 1313–1315; c) A. P. Piccionello, A. Pace, P. Pierro, I. Pibiri, S. Buscemi, N. Vivona, *Tetrahedron* **2009**, *65*, 119–127.

[17] a) S. Buscemi, N. Vivona, *J. Org. Chem.* **1996**, *61*, 8397–8401; b) N. Vivona, S. Buscemi, S. Asta, *Tetrahedron* **1997**, *53*, 12629–12636; c) A. P. Piccionello, I. Pibiri, A. Pace, R. A. Raccuglia, S. Buscemi, N. Vivona, G. Giorgi, *Heterocycles* **2007**, *71*, 1529–1537.

[18] a) A. S. K. Hashmi, T. Wang, S. Shi, M. Rudolph, *J. Org. Chem.* **2012**, *77*, 7761–7767; b) W. Yang, T. Wang, Y. Yu, S. Shi, T. Zhang, A. S. K. Hashmi, *Adv. Synth. Catal.* **2013**, *355*, 1523–1528; c) E. Rettenmeier, A. M. Schuster, M. Rudolph, F. Rominger, C. A. Gade, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 5880–5884; *Angew. Chem.* **2013**, *125*, 5993–5997; d) Y. Yu, W. Yang, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 7586–7589; *Angew. Chem.* **2013**, *125*, 7735–7738; e) P. Nösel, L. Nunes dos S. Comprido, T. Lauterbach, M. Rudolph,

F. Rominger, A. S. K. Hashmi, *J. Am. Chem. Soc.* **2013**, *135*, 15662–15666; f) T. Lauterbach, M. Ganschow, M. W. Hussong, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Adv. Synth. Catal.* **2014**, *356*, 680–686; g) Wang, T. Shi, S. Rudolph, M. A. S. K. Hashmi, *Adv. Synth. Catal.* **2014**, *356*, 2337–2342; h) T. Wang, S. Shi, M. M. Hansmann, E. Rettenmeier, M. Rudolph, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2014**, *53*, 3715–3719; *Angew. Chem.* **2014**, *126*, 3789–3793; i) T. Wang, L. Huang, S. Shi, M. Rudolph, A. S. K. Hashmi, *Chem. Eur. J.* **2014**, *20*, 14868–14871; j) J. Bucher, T. Stößer, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2015**, *54*, 1666–1670; *Angew. Chem.* **2015**, *127*, 1686–1690; k) T. Lauterbach, T. Higuchi, M. W. Hussong, M. Rudolph, F. Rominger, K. Mashima, A. S. K. Hashmi, *Adv. Synth. Catal.* **2015**, *357*, 775–781.

[19] CCDC 1523663 (**3v**) contain the supplementary crystallographic data for this paper, which can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[20] a) P. W. Davies, A. Cremonesi, N. Martin, *Chem. Commun.* **2011**, *47*, 379–381; b) B. Lu, C. Li, L. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 14070–14072.

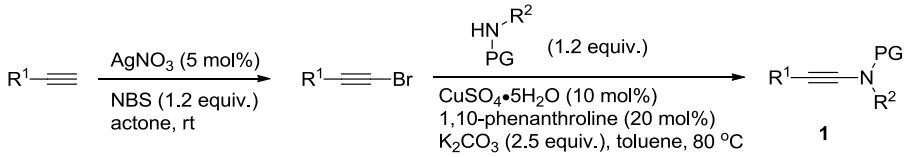
2.5 Experimental Section

General Remarks: Chemicals were purchased from commercial suppliers and used without further purification. Reagents **1** and **2** were easily prepared according to the previous literatures.[1,2] Dry solvents were dispensed from the solvent purification system MB SPS-800. Deuterated solvents were bought from Euriso-Top. NMR spectra were recorded at room temperature on the following spectrometers: Bruker Avance-III-300, Bruker Avance DRX-300 or Bruker Avance 500. Chemical shifts were referenced to residual solvent protons and reported in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). 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. HRMS were determined at the chemistry department of the University of Heidelberg. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For DART-spectra a Bruker ICR Apex-Qe spectrometer was applied. IR spectra were recorded on a Bruker Vector 22, and the absorption maxima were given in wavelength in cm^{-1} units. 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. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Thin-layer chromatography (TLC) was performed on precoated polyester sheets (POLYGRAM SIL G/UV254), and components were visualized by observation under UV light. Melting points were uncorrected.

Experiment Procedures

General Procedure 1: Synthesis of ynamides 1[2]



To a solution of terminal alkynes (3.0 mmol) in acetone (10 mL) were added NBS (3.6 mmol) and $AgNO_3$ (0.15 mmol), the resulting mixture was stirred under N_2 at room temperature for 3 hours. After removing excess acetone, the reaction was quenched with saturated NH_4Cl solution, and the organic layer was extracted with petroleum ether (10 mL × 2), dried over anhydrous $NaSO_4$, filtered and concentrated under reduced pressure to give bromoalkynes.

To a dried flask were added sulfonamides (2.4 mmol), $CuSO_4•5H_2O$ (0.2 mmol), 1,10-phenanthroline (0.4 mmol) and K_2CO_3 (5.0 mmol). The resulting mixture was subsequently treated with anhydrous toluene (10 mL) and bromoalkynes (2.0 mmol), and stirred at 80 °C overnight under N_2. When the reaction is complete, the crude mixture was cooled to room temperature, filtered through Celite, and concentrated in

vacuo. The resulting residue was purified by chromatography on silica gel (eluent: PE/EA) to afford ynamides **1**.

General Procedure 2: Gold-catalyzed formal [3+2] cycloaddition of ynamides with 1,2,4-oxadiazoles

A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (5 mol%, 6.2 mg), $AgNTf_2$ (5 mol%, 3.9 mg), and $PhCF_3$ (0.5 mL). The mixture was stirred for 5 minutes at room temperature. Ynamides (0.2 mmol) and 1,2,4-oxadiazoles (0.3 mmol or 1.0 mmol) were added followed by 0.5 mL $PhCF_3$. The reaction mixture was then stirred at 80 ^oC and the progress of the reaction was monitored by TLC. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the desired product **3**.

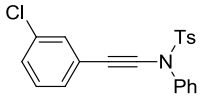
Gram-scale reaction: A round bottom flask equipped with a magnetic stirrer bar was charged with IPrAuCl (4 mol%, 74.4 mg), $AgNTf_2$ (4 mol%, 46.6 mg), and $PhCF_3$ (10 mL). The mixture was stirred for 5 minutes at room temperature. The ynamide **1a** (3.0 mmol) and the 1,2,4-oxadiazole **2a** (4.5 mmol) were added followed by 5 mL $PhCF_3$. The reaction mixture was then stirred at 80 ^oC and the progress of the reaction was monitored by TLC. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the desired product **3a** in 80% yield (1.07 g).

[1] K. K. D. Amarasinghe, M. B. Maier, A. Srivastavab, J. L. Graya, *Tetrahedron Lett.* **2006**, *47*, 3629–3631.

[2] L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33.

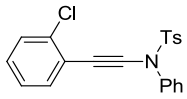
Characterization

1k: *N*-((3-chlorophenyl)ethynyl)-4-methyl-*N*-phenylbenzenesulfonamide

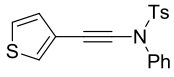


382.1 mg (50% yield), yellow oil; R_f = 0.42 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.56–7.53 (m, 2H), 7.29–7.15 (m, 11H), 2.37 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.2 (s), 138.7 (s), 134.1 (s), 133.0 (s), 131.1 (d), 129.6 (d), 129.5 (d), 129.4 (d), 129.2 (d), 128.4 (d), 128.3 (d), 128.1 (d), 126.3 (d), 124.5 (s), 84.2 (s), 69.4 (s), 21.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3067, 3039, 2923, 2239, 1707, 1593, 1560, 1490, 1477, 1455, 1409, 1373, 1334, 1295, 1258, 1201, 1173, 1089, 1027, 1004, 923, 890, 832, 813, 784, 757, 706, 690, 671, 653 cm^{-1}; **HRMS** (DART) calcd for $[C_{21}H_{17}NO_2SCl]^+$ $(M)^+$: 382.0663; found: 382.0664.

1l: *N*-((2-chlorophenyl)ethynyl)-4-methyl-*N*-phenylbenzenesulfonamide



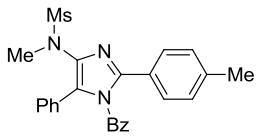
573.1 mg (75% yield), light yellow solid, m.p.: 79–80 °C; R_f = 0.55 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.3 Hz, 2H), 7.37–7.10 (m, 11H), 2.35 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 145.1 (s), 138.8 (s), 135.7 (s), 133.0 (d), 134.0 (s), 129.6 (d), 129.2 (d), 129.1 (d), 128.9 (d), 128.4 (d), 128.3 (d), 126.5 (d), 126.3 (d), 122.8 (s), 87.8 (s), 67.8 (s), 21.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3066, 2241, 1919, 1595, 1492, 1479, 1455, 1438, 1377, 1343, 1307, 1294, 1254, 1202, 1187, 1174, 1089, 1043, 1029, 922, 892, 813, 793, 755, 705, 692, 670, 654 cm^{-1}; **HRMS** (DART) calcd for $[C_{21}H_{17}NO_2SCl]^+$ $(M)^+$: 382.0663; found: 382.0664.



1n: 4-methyl-*N*-phenyl-*N*-(thiophen-3-ylethynyl)benzenesulfonamide

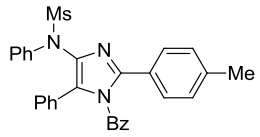
317.7 mg (75% yield), yellow solid, m.p.: 115–116 °C; R_f = 0.40 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 8.0 Hz, 2H), 7.31–7.15 (m, 9H), 6.98 (d, *J* = 4.8 Hz, 1H), 2.35 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.1 (s), 138.9 (s), 133.0 (s), 130.2 (d), 129.6 (d), 129.2 (d), 129.0 (d), 128.3 (d), 126.3 (d), 125.3 (d), 121.3 (s), 82.3 (s), 65.6 (s), 21.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3113, 3052, 2232, 1737, 1714, 1590, 1489, 1421, 1367, 1299, 1218, 1186, 1164, 1088, 1027, 938, 903, 870, 802, 783, 766, 710, 702, 691, 655, 626 cm^{-1}; **HRMS** (EI) calcd for

$[C_{19}H_{15}NO_2S_2]^+$ $(M)^+$: 353.0539; found: 353.0544.



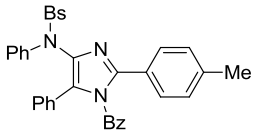
3a: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-*N*-methylmethanesulfonamide

80.1 mg (90% yield), white solid, m.p.: 179–180 °C; R_f = 0.28 (PE/EA = 2:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59–7.52 (m, 6H), 7.44 (d, *J* = 7.4 Hz, 1H), 7.31–7.21 (m, 5H), 7.15 (d, *J* = 8.0 Hz, 2H), 3.30 (s, 3H), 3.25 (s, 3H), 2.33 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7 (s), 145.9 (s), 139.6 (s), 136.8 (s), 135.0 (d), 132.4 (s), 130.8 (d), 130.3 (s), 129.4 (d), 129.3 (d), 128.9 (d), 128.6 (d), 128.4 (d), 127.4 (s), 126.8 (s), 38.8 (d), 37.4 (d), 21.3 (d) ppm; **IR** (ATR): $\tilde{\nu}$ 3067, 3024, 2934, 1714, 1597, 1587, 1493, 1454, 1415, 1338, 1293, 1278, 1218, 1188, 1149, 1103, 1078, 1031, 998, 971, 908, 869, 835, 812, 772, 732, 697, 665, 629 cm^{-1}; **HRMS** (DART) calcd for $[C_{25}H_{24}N_3O_3S]^+$ $(M+H)^+$: 446.1533 ; found: 446.1531.



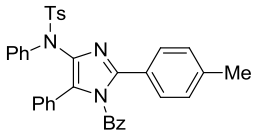
3b: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-*N*-phenylmethanesulfonamide

79.1 mg (78% yield), yellow solid, m.p.: 188–189 °C; R_f = 0.26 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.59–7.53 (m, 6H), 7.48–7.41 (m, 3H), 7.34–7.15 (m, 10H), 3.42 (s, 3H), 2.35 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7 (s), 145.7 (s), 140.8 (s), 139.6 (s), 136.3 (s), 135.0 (d), 132.4 (s), 131.0 (s), 130.8 (d), 129.4 (d), 129.3 (d), 129.1 (d), 128.9 (d), 128.6 (d), 128.5 (d), 128.3 (d), 127.53 (d), 127.48 (d), 127.3 (s), 126.9 (s), 39.0 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3062, 3033, 2967, 2928, 2868, 1721, 1595, 1583, 1561, 1489, 1447, 1410, 1347, 1299, 1277, 1260, 1226, 1155, 1116, 1077, 1020, 1001, 965, 914, 889, 837, 764, 737, 720, 697, 627, 609 cm^{-1}; **HRMS** (DART) calcd for $[C_{30}H_{26}N_3O_3S]^+$ $(M+H)^+$: 508.1689; found: 508.1692.



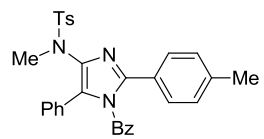
3c: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-bromo-*N*-phenylbenzenesulfonamide

120.4 mg (93% yield), yellow solid, m.p.: 173–174 °C; R_f = 0.23 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82–7.80 (m, 2H), 7.60 (dd, *J* = 12.9, 8.3 Hz, 4H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.45–7.42 (m, 3H), 7.31–7.19 (m, 10H), 7.14 (d, *J* = 7.9 Hz, 2H), 2.33 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7 (s), 145.5 (s), 140.2 (s), 139.5 (s), 138.1 (s), 136.2 (s), 135.0 (d), 132.5 (s), 131.6 (d), 130.8 (d), 130.7 (d), 129.5 (d), 129.3 (d), 128.94 (d), 128.89 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.0 (d), 127.9 (s), 127.6 (d), 127.4 (s), 127.0 (s), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3070, 1721, 1597, 1574, 1488, 1450, 1389, 1358, 1298, 1274, 1219, 1169, 1089, 1069, 1012, 910, 821, 769, 738, 696, 662 cm^{-1}; **HRMS** (DART) calcd for $[C_{35}H_{27}N_3O_3SBr]^+$ $(M+H)^+$: 648.0951; found: 648.0949.



3d: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

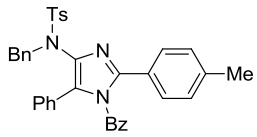
91.0 mg (78% yield), yellow solid, m.p.: 186–187 °C; R_f = 0.34 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.7 Hz, 2H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 7.5 Hz, 2H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.34–7.27 (m, 8H), 7.25–7.19 (m, 4H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.9 (s), 145.5 (s), 143.6 (s), 140.5 (s), 139.4 (s), 136.4 (s), 136.2 (s), 134.9 (d), 132.5 (s), 131.7 (s), 130.8 (d), 129.5 (d), 129.2 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.8 (d), 128.6 (d), 128.5 (d), 128.3 (d), 128.0 (d), 127.6 (s), 127.3 (d), 127.1 (s), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3072, 3029, 2954, 2923, 2853, 1917, 1720, 1597, 1585, 1565, 1488, 1452, 1412, 1351, 1300, 1276, 1223, 1184, 1159, 1089, 1019, 947, 922, 887, 816, 769, 739, 728, 708, 696, 668, 647, 611 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{30}N_3O_3S]^+$ $(M+H)^+$: 584.2002; found: 584.2004.



3e: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-*N*,4-dimethylbenzenesulfonamide

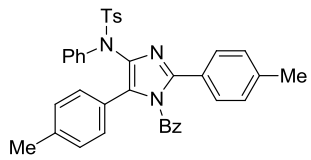
68.8 mg (66% yield), yellow solid, m.p.: 211–212 °C; R_f = 0.26 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 2H), 7.59–7.51 (m,

4H), 7.48–7.43 (m, 3H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.32–7.22 (m, 5H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.12 (s, 3H), 2.48 (s, 3H), 2.32 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.8 (s), 145.7 (s), 143.6 (s), 139.5 (s), 136.9 (s), 135.3 (s), 134.9 (d), 132.6 (s), 130.8 (s), 130.7 (d), 129.5 (d), 129.3 (d), 129.2 (d), 128.9 (d), 128.6 (d), 128.44 (d), 128.41 (d), 127.8 (s), 126.9 (s), 38.1 (q), 21.6 (q), 21.3 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2967, 2925, 2855, 1713, 1597, 1582, 1491, 1452, 1343, 1304, 1277, 1190, 1176, 1159, 1110, 1088, 1032, 995, 921, 862, 809, 770, 725, 691, 665, 644, 626 cm^{-1}; **HRMS** (DART) calcd for $[C_{31}H_{28}N_3O_3S]^+$ $(M+H)^+$: 522.1846; found: 522.1848.



3f: *N*-(1-benzoyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-*N*-benzyl-4-methylbenzenesulfonamide

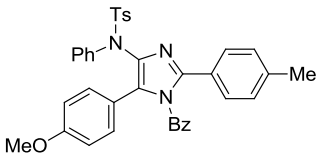
76.4 mg (64% yield), yellow solid, m.p.: 172–173 °C; R_f = 0.26 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.3 Hz, 2H), 7.49–7.37 (m, 7H), 7.28–7.22 (m, 2H), 7.20–7.02 (m, 12H), 4.59 (s, 2H), 2.50 (s, 3H), 2.33 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.7 (s), 145.5 (s), 143.6 (s), 139.4 (s), 136.2 (s), 135.2 (s), 134.7 (d), 134.3 (s), 133.0 (s), 132.6 (s), 130.6 (d), 129.7 (d), 129.5 (d), 129.4 (d), 129.2 (d), 128.9 (d), 128.7 (d), 128.5 (d), 128.2 (d), 128.0 (d), 127.9 (d), 127.6 (d), 127.5 (s), 127.0 (s), 54.2 (t), 21.7 (q), 21.3 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3067, 3031, 2962, 2926, 1719, 1596, 1493, 1449, 1350, 1335, 1273, 1264, 1217, 1184, 1162, 1088, 1028, 912, 885, 851, 818, 807, 764, 731, 695, 666, 651 cm^{-1}; **HRMS** (DART) calcd for $[C_{37}H_{32}N_3O_3S]^+$ $(M+H)^+$: 598.2159; found: 598.2161.



3g: *N*-(1-benzoyl-2,5-di-*p*-tolyl-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

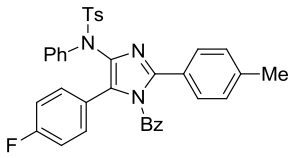
99.1 mg (83% yield), yellow solid, m.p.: 180–181 °C; R_f = 0.33 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.1 Hz, 2H), 7.47 (d, *J* = 7.7 Hz, 2H), 7.41 (d, *J* = 7.9 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.27–7.15 (m, 8H), 7.09–7.06 (m, 3H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 7.9 Hz, 2H), 2.32 (s, 3H), 2.20 (s, 3H), 2.16 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.0 (s), 145.2 (s), 143.5 (s), 140.6 (s), 139.3 (s), 138.4 (s), 136.3 (s), 136.2 (s), 134.9 (d), 132.6 (s),

131.9 (s), 130.8 (d), 129.4 (d), 129.2 (d), 129.11 (d), 129.10 (s), 129.0 (d), 128.9 (d), 128.8 (d), 128.5 (d), 127.9 (d), 127.24 (d), 127.21 (s), 124.6 (s), 21.7 (q), 21.36 (q), 21.35 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3064, 3032, 1718, 1597, 1508, 1489, 1451, 1412, 1350, 1297, 1271, 1165, 1092, 1032, 910, 817, 758, 730, 693, 655 cm^{-1}; **HRMS** (DART) calcd for $[C_{37}H_{32}N_3O_3S]^+$ $(M+H)^+$: 598.2159; found: 598.2169.



3h: *N*-(1-benzoyl-5-(4-methoxyphenyl)-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

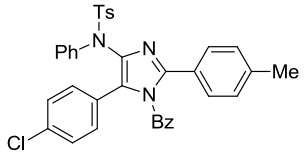
87.1 mg (71% yield), light yellow solid, m.p.: 150–151 °C; R_f = 0.18 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 2H), 7.44 (dd, *J* = 15.8, 7.7 Hz, 4H), 7.35–7.31 (m, 3H), 7.22–7.14 (m, 6H), 7.11–7.00 (m, 5H), 6.69 (d, *J* = 8.8 Hz, 2H), 3.64 (s, 3H), 2.32 (s, 3H), 2.20 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.1 (s), 159.7 (s), 145.0 (s), 143.5 (s), 140.6 (s), 139.3 (s), 136.3 (s), 136.1 (s), 134.9 (d), 132.6 (s), 131.7 (s), 131.0 (d), 130.8 (d), 129.2 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.8 (d), 128.5 (d), 127.9 (d), 127.24 (s), 127.23 (d), 119.9 (s), 113.8 (d), 55.2 (q), 21.7 (q), 21.3 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2933, 1718, 1615, 1597, 1508, 1489, 1452, 1417, 1352, 1301, 1278, 1253, 1167, 1093, 1039, 1026, 946, 911, 837, 824, 735, 696, 656 cm^{-1}; **HRMS** (DART) calcd for $[C_{37}H_{32}N_3O_4S]^+$ $(M+H)^+$: 614.2119; found: 614.2108.



3i: *N*-(1-benzoyl-5-(4-fluorophenyl)-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

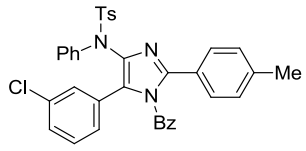
109.4 mg (91% yield), light yellow solid, m.p.: 91–92 °C; R_f = 0.44 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.9 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.53–7.48 (m, 5H), 7.31–7.26 (m, 6H), 7.20–7.18 (m, 3H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.97 (t, *J* = 8.7 Hz, 2H), 2.43 (s, 3H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8 (s), 162.7 (s, d: $J_{C\text{-}F}$ = 249.0 Hz), 145.6 (s), 143.7 (s), 140.4 (s), 139.5 (s), 136.7 (s), 136.0 (s), 135.1 (d), 132.4 (s), 131.6 (d, d: $J_{C\text{-}F}$ = 8.4 Hz), 130.8 (d), 130.7 (s), 129.3 (d), 129.1 (d, d: $J_{C\text{-}F}$ = 3.1 Hz), 129.0 (d), 128.9 (d), 128.5 (d), 128.0 (d), 127.4 (d), 127.0 (s), 123.7 (s, d: $J_{C\text{-}F}$ = 3.2 Hz), 115.5 (d, d: $J_{C\text{-}F}$ = 21.7 Hz),

21.7 (q), 21.4 (q) ppm; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -112.06– -112.07 (m) ppm; **IR** (ATR): $\tilde{\nu}$ 3024, 2933, 1718, 1596, 1505, 1488, 1451, 1411, 1351, 1296, 1270, 1227, 1164, 1092, 1028, 908, 842, 817, 759, 731, 693, 653 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{29}FN_3O_3S]^+$ $(M+H)^+$: 602.1908; found: 602.1911.



3j: *N*-(1-benzoyl-5-(4-chlorophenyl)-2-(*p*-tolyl)-1*H*-imidaz ol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

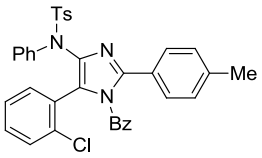
104.9 mg (85% yield), yellow solid, m.p.: 176–177 °C; R_f = 0.39 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.46–7.44 (m, 3H), 7.33–7.24 (m, 8H), 7.21–7.17 (m, 3H), 7.13 (d, *J* = 8.2 Hz, 2H), 2.42 (s, 3H), 2.31 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8 (s), 145.8 (s), 143.7 (s), 140.3 (s), 139.6 (s), 136.8 (s), 136.0 (s), 135.2 (d), 134.7 (s), 132.3 (s), 130.9 (d), 130.8 (d), 130.5 (s), 129.3 (d), 129.12 (d), 129.09 (d), 129.05 (d), 128.9 (d), 128.7 (d), 128.6 (d), 128.0 (d), 127.5 (d), 126.9 (s), 126.1 (s), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2960, 2924, 2853, 1719, 1596, 1559, 1489, 1451, 1403, 1352, 1294, 1264, 1165, 1091, 1012, 909, 815, 759, 731, 693, 655, 619 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{28}N_3O_3SCl]^+$ $(M)^+$: 617.1534; found: 617.1545.



3k: N-(1-benzoyl-5-(3-chlorophenyl)-2-(*p*-tolyl)-1H-imidaz ol-4-yl)-4-methyl-N-phenylbenzenesulfonamide

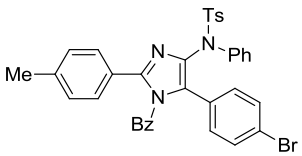
95.0 mg (77% yield), light yellow solid, m.p.: 178–179 °C; R_f = 0.40 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 7.3 Hz, 2H), 7.55–7.21 (m, 16H), 7.16 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.6 (s), 146.0 (s), 143.7 (s), 140.4 (s), 139.6 (s), 137.1 (s), 136.0 (s), 135.1 (d), 134.1 (s), 132.4 (s), 130.7 (d), 130.1 (s), 129.7 (d), 129.5 (d), 129.4 (s), 129.2 (d), 129.10 (d), 129.05 (d), 129.0 (d), 128.9 (d), 128.63 (d), 128.58 (d), 128.0 (d), 127.7 (d), 127.5 (d), 126.9 (s), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3068, 2964, 2923, 1719, 1597, 1576, 1487, 1477, 1451, 1410, 1352, 1296, 1262, 1206, 1165, 1091, 1037, 910, 814, 792, 756, 727, 691, 663, 612 cm^{-1};

HRMS (DART) calcd for $[C_{36}H_{29}N_3O_3SCl]^+$ $(M+H)^+$: 618.1613; found: 618.1609.



3l: *N*-(1-benzoyl-5-(2-chlorophenyl)-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

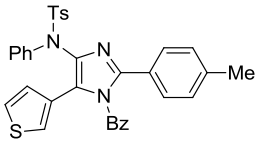
108.8 mg (88% yield), light yellow solid, m.p.: 56–57 °C; R_f = 0.20 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.52–7.50 (m, 2H), 7.41–7.38 (m, 3H), 7.27–7.18 (m, 11H), 7.07 (d, *J* = 7.8 Hz, 2H), 2.43 (s, 3H), 2.30 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.5 (s), 146.5 (s), 143.5 (s), 140.2 (s), 139.3 (s), 138.0 (s), 136.1 (s), 134.8 (s), 134.2 (d), 133.7 (d), 132.2 (s), 131.0 (d), 130.5 (d), 130.1 (d), 130.0 (d), 129.1 (d), 129.04 (d), 129.02 (d), 128.7 (d), 128.6 (d), 128.34 (d), 128.29 (d), 127.5 (s), 127.4 (s), 127.3 (d), 126.6 (d), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3068, 2922, 1716, 1598, 1488, 1451, 1410, 1352, 1296, 1277, 1223, 1165, 1119, 1092, 1073, 1035, 948, 927, 907, 890, 814, 760, 731, 693, 658, 613 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{29}N_3O_3SCl]^+$ $(M)^+$: 618.1613; found: 618.1615.



3m: *N*-(1-benzoyl-5-(4-bromophenyl)-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

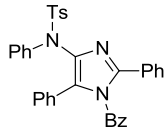
103.1 mg (78% yield), yellow solid, m.p.: 194–195 °C; R_f = 0.43 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85–7.83 (m, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.55–7.53 (m, 2H), 7.50–7.40 (m, 5H), 7.36–7.28 (m, 6H), 7.24–7.21 (m, 3H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8 (s), 145.8 (s), 143.7 (s), 140.3 (s), 139.6 (s), 136.8 (s), 135.9 (s), 135.2 (d), 132.3 (s), 131.7 (d), 131.1 (d), 130.8 (d), 130.6 (s), 129.3 (d), 129.11 (d), 129.09 (d), 129.06 (d), 128.9 (d), 128.5 (d), 128.0 (d), 127.5 (d), 126.9 (s), 126.6 (s), 123.0 (s), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2920, 1718, 1596, 1556, 1486, 1451, 1352, 1293, 1264, 1165, 1091, 1073, 1028, 1008, 909, 821, 759, 731, 693, 673, 614 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{29}N_3O_3SBr]^+$ $(M+H)^+$: 662.1108; found: 662.1124.

3n: *N*-(1-benzoyl-5-(thiophen-3-yl)-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenyl



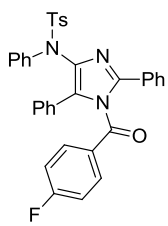
benzenesulfonamide

96.6 mg (82% yield), light yellow solid, m.p.: 72–73 °C; R_f = 0.38 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 7.7 Hz, 3H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.40–7.38 (m, 2H), 7.35–7.28 (m, 5H), 7.23–7.20 (m, 4H), 7.15 (d, *J* = 7.9 Hz, 2H), 2.45 (s, 3H), 2.33 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.2 (s), 145.2 (s), 143.7 (s), 140.4 (s), 139.5 (s), 136.23 (s), 136.15 (s), 135.1 (d), 132.4 (s), 130.8 (d), 129.3 (d), 129.12 (d), 129.06 (d), 129.0 (d), 128.9 (d), 128.4 (d), 128.1 (d), 127.8 (d), 127.5 (s), 127.34 (d), 127.27 (s), 127.1 (s), 125.82 (d), 125.75 (d), 21.7 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3066, 2920, 2851, 1718, 1596, 1555, 1486, 1451, 1352, 1293, 1265, 1165, 1091, 1074, 1008, 909, 820, 759, 731, 693, 673, 617 cm^{-1}; **HRMS** (DART) calcd for $[C_{34}H_{28}N_3O_3S_2]^+$ $(M+H)^+$: 590.1567; found: 590.1562.



3o: *N*-(1-benzoyl-2,5-diphenyl-1*H*-imidazol-4-yl)-4-methyl-*N*-phenyl benzenesulfonamide

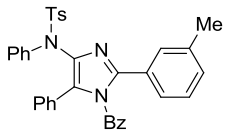
97.9 mg (86% yield), yellow solid, m.p.: 64–65 °C; R_f = 0.20 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.71–7.63 (m, 4H), 7.56–7.22 (m, 18H), 2.47 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 169.8 (s), 145.3 (s), 143.6 (s), 140.5 (s), 136.6 (s), 136.2 (s), 135.0 (d), 132.5 (s), 132.0 (s), 130.8 (d), 130.0 (s), 129.6 (d), 129.3 (d), 129.10 (d), 129.09 (d), 128.9 (d), 128.8 (d), 128.7 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.0 (d), 127.6 (s), 127.4 (d), 21.7 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3065, 1717, 1597, 1491, 1475, 1447, 1348, 1295, 1274, 1207, 1165, 1091, 1028, 1001, 908, 813, 767, 738, 721, 693, 669, 616 cm^{-1}; **HRMS** (DART) calcd for $[C_{35}H_{28}N_3O_3S]^+$ $(M + H^+)$: 570.1832; found: 570.1842.



3p: *N*-(1-(4-fluorobenzoyl)-2,5-diphenyl-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

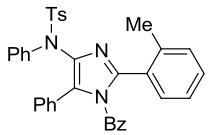
93.9 mg (80% yield), yellow solid, m.p.: 154–155 °C; R_f = 0.25 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.2 Hz,

2H), 7.64–7.60 (m, 4H), 7.49 (d, *J* = 6.9 Hz, 2H), 7.36–7.34 (m, 3H), 7.31–7.26 (m, 7H), 7.19–7.18 (m, 3H), 6.96 (t, *J* = 8.5 Hz, 2H), 2.44 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.5 (s), 166.6 (s, d: $J_{C\text{-}F}$ = 259.3 Hz), 145.3 (s), 143.7 (s), 140.3 (s), 136.6 (s), 136.1 (s), 133.7 (d, d: $J_{C\text{-}F}$ = 9.9 Hz), 131.9 (s), 129.8 (s), 129.5 (d), 129.4 (d), 129.1 (d, d: $J_{C\text{-}F}$ = 3.1 Hz), 128.9 (s), 128.8 (d), 128.74 (d), 128.65 (d), 128.6 (d), 128.5 (d), 128.0 (d), 127.40 (d), 127.39 (s), 116.4 (d, d: $J_{C\text{-}F}$ = 22.4 Hz), 21.7 (q) ppm; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -100.45 ppm; **IR** (ATR): $\tilde{\nu}$ 3067, 2924, 1719, 1598, 1506, 1491, 1475, 1446, 1413, 1348, 1296, 1274, 1243, 1206, 1185, 1166, 1156, 1092, 1028, 1016, 947, 910, 855, 814, 791, 762, 695, 669, 619 cm^{-1}; **HRMS** (DART) calcd for $[C_{35}H_{27}FN_3O_3S_2]^+$ $(M+H)^+$: 588.1752.; found: 588.1748.



3q: *N*-(1-benzoyl-5-phenyl-2-(*m*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

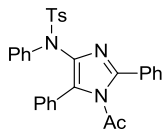
98.0 mg (84% yield), light yellow solid, m.p.: 140–141 °C; R_f = 0.37 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.3 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.48–7.47 (m, 3H), 7.41–7.32 (m, 4H), 7.26–7.16 (m, 11H), 7.10 (d, *J* = 7.6 Hz, 1H), 2.40 (s, 3H), 2.31 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.8 (s), 145.5 (s), 143.6 (s), 140.6 (s), 138.2 (s), 136.5 (s), 136.2 (s), 135.0 (d), 132.6 (s), 131.9 (s), 130.8 (d), 130.2 (d), 129.8 (s), 129.6 (d), 129.5 (d), 129.12 (d), 129.09 (d), 128.9 (d), 128.8 (d), 128.6 (d), 128.38 (d), 128.36 (d), 128.0 (d), 127.6 (s), 127.4 (d), 125.7 (d), 21.7 (q), 21.5 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3066, 2968, 2925, 2855, 1720, 1595, 1583, 1562, 1486, 1451, 1347, 1295, 1274, 1227, 1167, 1154, 1088, 1024, 1000, 934, 889, 817, 797, 769, 742, 726, 715, 696, 671, 646, 634, 613 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{30}N_3O_3S]^+$ $(M+H)^+$: 584.2002; found: 584.2022.



3r: *N*-(1-benzoyl-5-phenyl-2-(*o*-tolyl)-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

85.1 mg (73% yield), yellow solid, m.p.: 171–172 °C; R_f = 0.37 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 2H), 7.56 (dd, *J* = 13.9, 7.8 Hz, 4H), 7.44–7.40 (m, 3H), 7.33–7.21 (m, 13H), 7.14–7.11 (m, 1H), 2.52 (s,

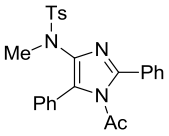
3H), 2.42 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 168.9 (s), 145.0 (s), 143.6 (d), 140.5 (s), 138.1 (s), 136.1 (s), 136.0 (s), 134.6 (s), 132.7 (s), 131.2 (s), 130.8 (d), 130.53 (d), 130.47 (d), 129.6 (d), 129.5 (s), 129.4 (d), 129.1 (d), 128.9 (d), 128.6 (d), 128.5 (d), 128.4 (d), 128.1 (d), 127.8 (s), 127.4 (d), 125.4 (d), 21.7 (q), 20.6 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3470, 3063, 2959, 2926, 2872, 2855, 1720, 1598, 1491, 1451, 1352, 1299, 1275, 1209, 1167, 1093, 1029, 1015, 948, 927, 911, 814, 766, 726, 696, 670 cm^{-1}; **HRMS** (DART) calcd for $[C_{36}H_{30}N_3O_3S]^+$ $(M+H)^+$: 584.2002; found: 584.2032



3s: *N*-(1-acetyl-2,5-diphenyl-1*H*-imidazol-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide

62.9 mg (62% yield), light yellow solid, m.p.: 176–177 °C; R_f = 0.60 (PE/EA = 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.2 Hz, 2H), 7.61–7.58(m, 2H), 7.51–7.45 (m, 8H), 7.23–7.14 (m, 7H), 2.40 (s, 3H), 2.12 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.6 (s), 145.0 (s), 143.6 (s), 140.3 (s), 137.3 (s), 136.0 (s), 130.5 (s), 130.1 (s), 129.9 (d), 129.6 (d), 129.3 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.8 (d), 128.7 (d), 128.4 (d), 128.3 (d), 128.1 (s), 127.5 (d), 28.3 (q), 21.6 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3067, 2962, 2925, 2848, 2258, 1750, 1596, 1491, 1475, 1446, 1353, 1291, 1270, 1219, 1167, 1092, 1029, 948, 912, 814, 769, 731, 698, 675, 650, 618 cm^{-1}; **HRMS** (DART) calcd for $[C_{30}H_{26}N_3O_3S]^+$ $(M+H)^+$: 508.1689; found: 508.1690.

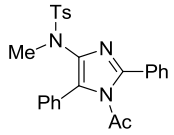
3t: *N*-(1-acetyl-2,5-diphenyl-1*H*-imidazol-4-yl)-*N*,4-dimethylbenzenesulfonamide



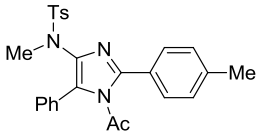
52.5 mg (59% yield), yellow solid, m.p.: 154–155 °C; R_f = 0.33 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 6.9 Hz, 2H), 7.55 (dd, *J* = 6.5, 3.0 Hz, 2H), 7.50–7.42 (m, 6H), 7.31 (d, *J* = 8.1 Hz, 2H), 3.02 (s, 3H), 2.43 (s, 3H), 2.13 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.7 (s), 145.3 (s), 143.7 (s), 137.7 (s), 135.1 (s), 130.3 (s), 129.71 (d), 129.68 (d), 129.4 (d), 129.33 (d), 129.26 (s), 129.1 (d), 128.8 (d), 128.7 (d), 128.5 (d), 128.3 (s), 38.0 (q), 28.4 (q), 21.6 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3057, 2924, 2853, 1748, 1597, 1583, 1569, 1493, 1480, 1463, 1445, 1368, 1340, 1285, 1263, 1196, 1176, 1154, 1087, 1032, 1002, 970, 925, 865, 806, 782, 769, 757, 721,

700, 682, 666, 638, 607 cm^{-1}; **HRMS** (DART) calcd for $[C_{25}H_{24}N_3O_3S]^+$ $(M+H)^+$: 446.1533; found: 446.1534.

3u: *N*-(1-acetyl-2,5-diphenyl-1*H*-imidazol-4-yl)-*N*-phenylmethanesulfonamide



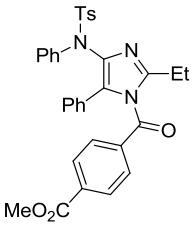
33.6 mg (39% yield), white solid, m.p.: 110–111 ºC; R_f = 0.40 (PE/EA = 2:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65–7.62 (m, 2H), 749–7.43 (m, 3H), 7.42–7.41 (m, 7H), 7.27–7.25 (m, 3H), 3.30 (s, 3H), 2.11 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.5 (s), 145.2 (s), 140.6 (s), 137.1 (s), 130.3 (s), 129.8 (d), 129.7 (d), 129.4 (s), 129.3 (d), 129.14 (d), 129.10 (d), 128.7 (d), 128.5 (d), 127.8 (s), 127.71 (d), 127.69 (d), 39.0 (q), 28.3 (q); **IR** (ATR): $\tilde{\nu}$ 3067, 3029, 2923, 2851, 1752, 1592, 1583, 1567, 1490, 1473, 1446, 1417, 1366, 1339, 1296, 1275, 1253, 1216, 1151, 1077, 1054, 1028, 973, 922, 857, 767, 730, 698, 652, 631 cm^{-1}; **HRMS** (DART) calcd for $[C_{24}H_{22}N_3O_3S]^+$ $(M+H)^+$: 432.1376; found: 432.1376.



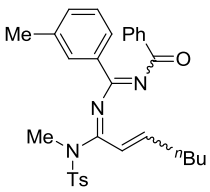
3v: *N*-(1-acetyl-5-phenyl-2-(*p*-tolyl)-1*H*-imidazol-4-yl)-*N*,4-dimethylbenzenesulfonamide

45.9 mg (50% yield), yellow solid, m.p.: 174–175 ºC; R_f = 0.32 (PE/EA = 5:1); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.59–7.57 (m, 2H), 7.48–7.42 (m, 5H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 3.01 (s, 3H), 2.43 (s, 3H), 2.40 (s, 3H), 2.12 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.8 (s), 145.4 (s), 143.6 (s), 139.8 (s), 137.6 (s), 135.2 (s), 129.7 (d), 129.3 (d), 129.22 (d), 129.15 (d), 129.1 (s), 129.0 (d), 128.8 (d), 128.7 (d), 128.4 (s), 127.5 (s), 38.0 (q), 28.4 (q), 21.6 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3058, 2932, 2851, 1751, 1615, 1598, 1492, 1461, 1447, 1365, 1340, 1297, 1268, 1256, 1194, 1158, 1114, 1091, 1034, 997, 930, 879, 818, 782, 732, 716, 699, 672, 650, 635, 610 cm^{-1}; **HRMS** (DART) calcd for $[C_{26}H_{26}N_3O_3S]^+$ $(M+H)^+$: 460.1689; found: 460.1693.

3w: methyl 4-(2-ethyl-4-(4-methyl-*N*-phenylphenylsulfonamido)-5-phenyl-1*H*-imidazole-1-carbonyl)benzoate



47.5 mg (41% yield), white solid, m.p.: 150–151 ºC; R_f = 0.19 (PE/EA = 5:1); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.3 Hz, 2H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.33–7.04 (m, 12H), 3.88 (s, 3H), 2.89 (q, *J* = 7.5 Hz, 2H), 2.43 (s, 3H), 1.34 (t, *J* = 7.5 Hz, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.7 (s), 165.6 (s), 149.2 (s), 143.5 (s), 140.2 (s), 136.2 (s), 135.9 (s), 135.4 (s), 134.5 (s), 130.3 (d), 129.8 (s), 129.5 (d), 129.0 (d), 128.9 (d), 128.8 (d), 128.7 (d), 128.3 (d), 128.1 (d), 128.0 (s), 127.7 (d), 127.2 (d), 52.5 (q), 21.9 (t), 21.6 (q), 12.2 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2925, 2852, 1721, 1597, 1573, 1528, 1491, 1446, 1408, 1355, 1279, 1209, 1166, 1108, 1092, 1019, 940, 916, 813, 772, 730, 698, 669, 611 cm^{-1}; **HRMS** (DART) calcd for $[C_{33}H_{30}N_3O_5S]^+$ $(M+H)^+$: 580.1901; found: 580.1902.



4: *N*-(1-(*N*,4-dimethylphenylsulfonamido)hept-2-en-1-ylidene)amino(*m*-tolyl)methylene)benzamide

50.5 mg (49% yield), yellow solid, m.p.: 48–49 ºC; isomers of compound **4** cannot be separated by column chromatography. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.68 (d, *J* = 8.2 Hz, 1.6H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.19–7.15 (m, 4H), 7.12–7.05 (m, 4.4H), 7.02–6.96 (m, 6H), 6.94–6.83 (m, 4.6H), 5.66 (d, *J* = 6.2 Hz, 1H), 5.11 (q, *J* = 6.0 Hz, 0.8H), 4.97 (q, *J* = 6.9 Hz, 1H), 3.17 (s, 3H), 3.11 (d, *J* = 4.9 Hz, 2.4H), 2.34 (s, 3H), 2.20 (s, 2.4H), 2.12 (s, 2.4H), 2.08 (s, 3H), 1.64–1.05 (m, 15.4H), 0.84 (t, *J* = 7.2 Hz, 3.4H), 0.79 (t, *J* = 7.3 Hz, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.7 (s), 171.4 (s), 159.7 (s), 154.1 (s), 152.5 (s), 143.4 (s), 142.9 (s), 142.0 (s), 141.8 (s), 138.1 (s), 137.7 (s), 136.5 (s), 136.2 (s), 136.1 (s), 135.8 (s), 135.7 (s), 132.8 (d), 131.4 (d), 131.2 (d), 129.8 (d), 129.5 (d), 129.4 (d), 129.0 (d), 128.4 (d), 128.3 (d), 128.01 (d), 128.00 (d), 127.95 (d), 127.9 (d), 126.6 (d), 125.6 (d), 111.1 (d), 86.7 (s), 53.2 (q), 52.7 (q), 36.3 (q), 34.3 (t), 32.5 (t), 28.9 (q), 27.6 (t), 26.8 (t), 22.6 (t), 22.55 (t), 21.58 (q), 21.4 (q), 21.14 (q), 21.06 (q), 14.0 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3381, 3062, 3029, 2956, 2929, 2870, 2859, 1674, 1603, 1557, 1449, 1381, 1348, 1271, 1208, 1178, 1161, 1133, 1087, 1061, 1001, 972, 930, 898, 813, 791, 754, 720, 695, 677, 659 cm^{-1}; **HRMS** (DART) calcd for $[C_{30}H_{34}N_3O_3S]^+$ $(M+H)^+$: 516.2315; found: 516.2317.

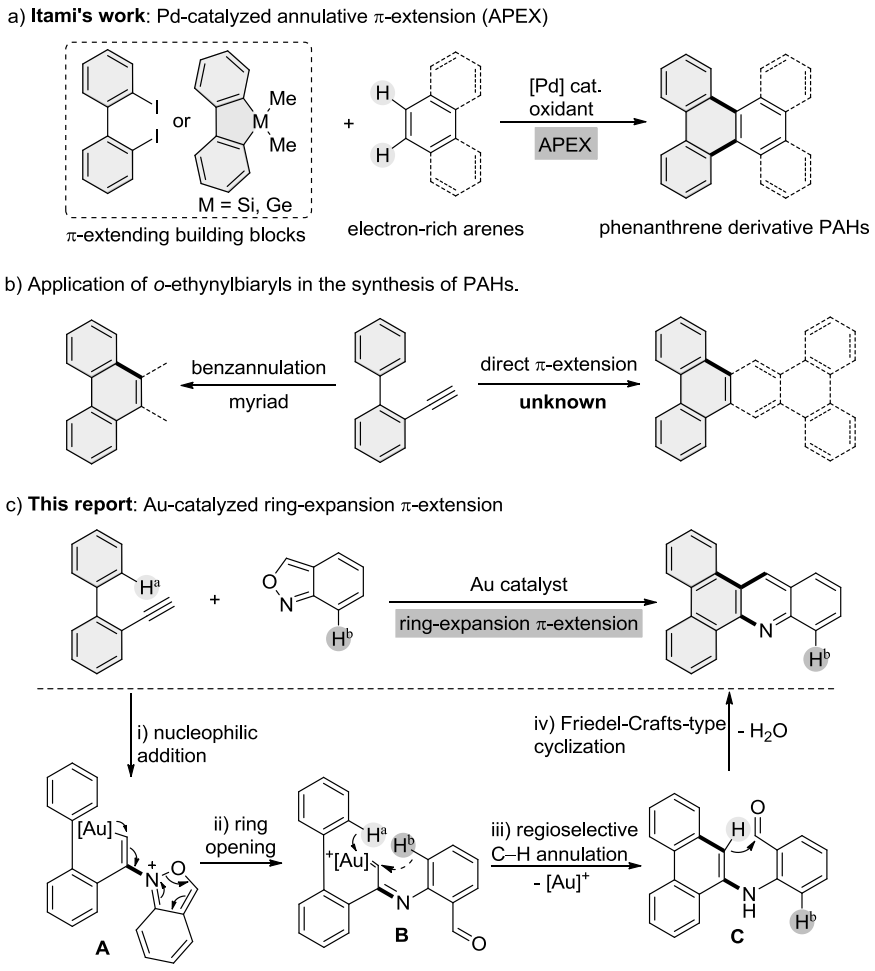
Chapter 3: Gold-Catalyzed Regiospecific C–H Annulation of *o*-Ethynylbiaryls with Anthranils: π-Extension by Ring-Expansion en route to *N*-Doped PAHs

3.1 Introduction

π-Conjugated polycyclic aromatic hydrocarbons (PAHs) attract increasing attention from the synthetic community due to their use in pharmaceuticals and materials[1] as well as their potential for the bottom-up construction of structurally uniform graphenes.[2] Recently, direct C–H functionalization to access π-extended PAHs constitutes a rapid, facile and efficient synthetic strategy.[3,4] Among these, Itami and co-workers developed a palladium-catalyzed dual C–H annulative π-extension (APEX) of readily accessible electron-rich (hetero)arenes towards PAH derivatives, and even nanographenes.[4] A variety of π-extending building blocks, such as dibenzosiloles, dibenzogermoles and diiodobiaryls, have been employed to unite larger π-conjugated systems via the formation of a phenanthrene framework (Scheme 1a). *o*-Ethynylbiaryls were also considered as an important synthetic precursor to phenanthrene-fused PAHs.[5] For instance, a two-dimensional monolayer graphene was facilely prepared by the poly(*o*-ethynylbiphenyl) benzannulation.[5i] Despite these spectacular achievements, the direct π-extending synthesis of PAHs from *o*-ethynylbiaryls is still a challenge (Scheme 1b). Hence, exploring a convergent assembly protocol of *o*-ethynylbiaryls for π-expanding PAHs synthesis remains highly desirable and significant.

The recent rapid advances in gold-catalyzed intermolecular formal cycloaddition of alkynes with nucleophilic nitrenoids have afforded efficient methodologies for the construction of aza-heterocyclic skeletons.[6] However, these transformations mostly rely on polarized alkynes,[7,8] especially ynamides,[7] which limits the generality of these reactions. Very recently, a gold-catalyzed [3+2] annulation of anthranils with

ynamides, delivering a set of 7-acylindole products, was disclosed by our group.[7n] Remarkably, some non-polarized alkynes were also suitable for this reaction. In continuation of this work, we herein report an unprecedented gold-catalyzed ring-expansion/π-extension of anthranils by taking advantage of *o*-ethynylbiaryls as modular building blocks (Scheme 1c). We envisioned that the *in situ*-generated α-imino gold carbene species **B** could be trapped by the C–H^a bond of *o*-ethynylbiphenyl as alternative to the C–H^b insertion known from the indole synthesis.[7n] Finally, the desired pyridine-embedded PAHs could be furnished by a Friedel-Crafts-type cyclization of intermediate **C**.



Scheme 1. Different π-extension approaches towards phenanthrene-embedded extended π-systems.

3.2 Results and Discussion

3.2.1 Optimization of Reaction Condition

Initially, we performed the reaction between *o*-ethynylbiphenyl (**1a**) and anthranil **2a** with the precatalyst IPrAuCl (10 mol%) and $AgNTf_2$ (20 mol%) as chloride scavenger in $PhCF_3$ at 80 °C for 12 h, which delivered 50% of an 1:1 mixture of *N*-doped PAH **3aa** and the undesired indole product **4aa** (Table 1, entry 1). The selectivity could be controlled by a phosphite ligand $(ArO)_3P$ (Ar = 2,4-di-*tert*-butylphenyl) and the yield of **3aa** increased to 40% while no **4aa** was formed (entry 2). The choice of anthranil **2b** instead of **2a** afforded the corresponding *N*-doped PAH **3ab** in an increased yield of 70%. On the basis of these results, the reaction of terminal alkyne **1a** with anthranil **2b** was chosen as the model one for a further optimization (see SI for details). Precatalysts with a phosphite ligand showed higher catalytic activity than those with NHC and phosphane ligands (entries 3–7). $(ArO)_3PAuCl/AgNTf_2$ turned out to be the preferred catalytic system. The use of 1,2-DCE as reaction medium could not improve the efficiency (entry 8). The addition of water was not beneficial (entry 9). In contrast to our recent work,[7n] catalytic MsOH as an additive gave poor result, which is probably attributed to the faster intramolecular cyclization of *o*-ethynylbiphenyl (entry 10). The addition of 4 Å MS also failed to improve the conversion (entry 11). The 10 mol% $(ArO)_3PAuCl$/10 mol% $AgNTf_2$ afforded *N*-doped PAH **3ab** in moderate yield (entry 12). Control experiments in the presence of only silver or other transition metal catalysts showed no conversion (entry 13). The structural assignment of compound **3ab** was further verified by X-ray diffraction (Figure 1).[9]

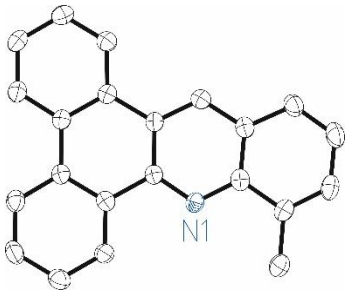
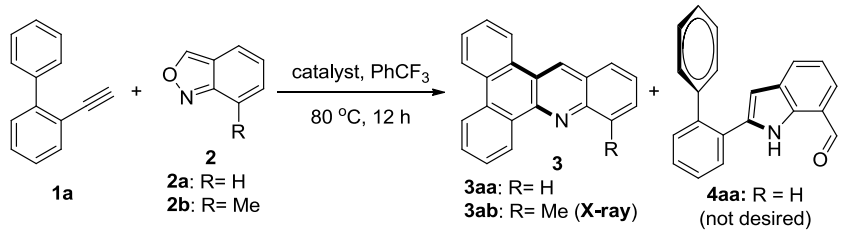


Figure 1. Solid-state molecular structure of **3ab** (hydrogen atoms omitted).

Table 1: Representative examples from the optimization of the reaction conditions.[a]



entry	**2**	catalyst (mol%)	solvent	yield [%][b]
1	**2a**	IPrAuCl/$AgNTf_2$ (10:20)	$PhCF_3$	25 (25)
2	**2a**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	$PhCF_3$	40 (trace)
3	**2b**	**$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)**	**$PhCF_3$**	**70**
4	**2b**	$(Ar'O)_3PAuCl$[d]/$AgNTf_2$ (10:20)	$PhCF_3$	58
5	**2b**	IPrAuCl/$AgNTf_2$ (10:20)	$PhCF_3$	45
6	**2b**	PPh_3AuCl/$AgNTf_2$ (10:20)	$PhCF_3$	54
7	**2b**	^{t}BuXPhosAuCl/$AgNTf_2$ (10:20)	$PhCF_3$	50
8	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	1,2-DCE	50
9	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	$PhCF_3/H_2O$ (10:1)	44
10[e]	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	$PhCF_3$	17
11[f]	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	$PhCF_3$	63
12	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:10)	$PhCF_3$	40
13	**2b**	$AgNTf_2$ (20)	$PhCF_3$	trace
14	**2b**	$PtCl_2$, or $Cu(OTf)_2$ (20)	$PhCF_3$	-

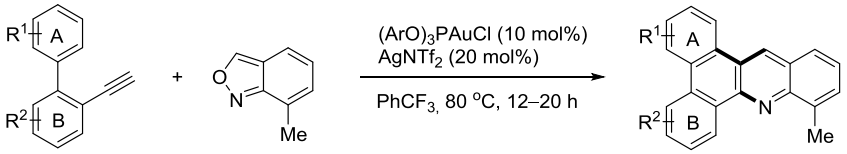
[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.2 mmol) were reacted in 0.5 mL $PhCF_3$ at 80 °C for 12 h. [b] Isolated yield of **3**; yield of product **4aa** given in parentheses. [c] Ar = 2,4-di-*tert*-butylphenyl. [d] Ar' = 2-(*tert*-butyl)-4-(trifluoromethyl)phenyl. [e] 10 mol% MsOH was added. [f] 10 mg of 4Å MS was added.

3.2.2 Scope and Limitation with regard to the Substrate

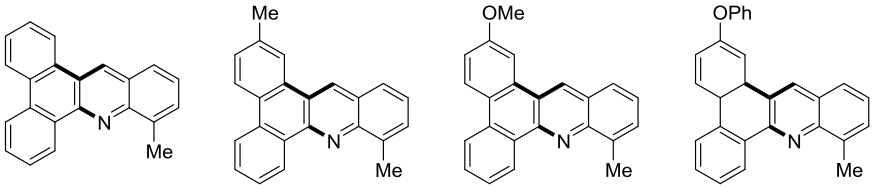
Under the optimized conditions, first a diverse set of *o*-ethynylbiaryls were tested by varying the aromatic rings A and B (Table 2). The unsubstituted precursor gave the corresponding *N*-doped PAH **3ab** in 70% yield.[10] A scale-up (1 mmol) conversion

gave a 60% yield. *o*-Ethynylbiaryls with either electron-donating (**3bb**–**3gb**) or electron-withdrawing **(3hb)** substituents attached to the *para* position of the phenyl ring A proceeded smoothly to provide the desired products in moderate to good yield (33–68%). Fluorine and trifluoromethoxy groups were also compatible.[11] A vinyl group (**3fb**) remained intact. A trimethylsilyl(TMS)-prefunctionalized *N*-doped PAH **3gb**, a common precursor for Hiyama cross-coupling reaction,[12] was prepared in a good yield of 68%. If a methoxy group was tethered at the *meta* position of the A ring, a pair of inseparable regioisomers **3ib** and **3ib'** was isolated in a 3:2 ratio. **1j** failed to undergo the desired π-extension reaction. A 3,5-disubstituted *o*-ethynylbiphenyl still gave the target product **3kb** in moderate yield. Besides substituted phenyl moieties, naphthyl (**3lb**, **3mb**), heterocyclic rings such as 2- (**3ob**) or 3-thienyl (**3nb/3nb'**, ratio 3:2) and 2-benzothienyl (**3pb**) could also be introduced, affording the desired product in moderate to good yields. The effect of the substitution pattern on the B ring of substrate **1** was also examined. The corresponding *N*-doped PAHs **3qb**–**3sb** with fluorine groups emerging at position 5, 6, or 7 were obtained in good yields. The electronic nature of the substituent played no detrimental influence on the efficiency of the conversion (**3sb** versus **3tb**). In addition, the phenyl ring B could also be replaced by a naphthyl (**3ub**) moiety.

Table 2: Scope with regard to *o*-ethynylbiaryls.[a]



1 **2b** (2 equiv.) **3**

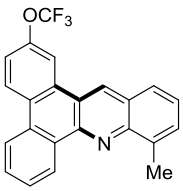


3ab, 70% (60%)[b]

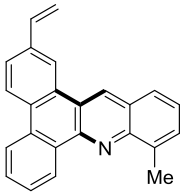
3bb, 54%

3cb, 33%

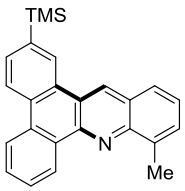
3db, 42%



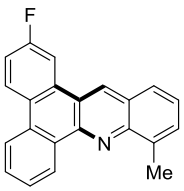
3eb, 53%



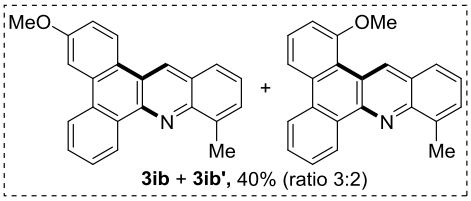
3fb, 47%



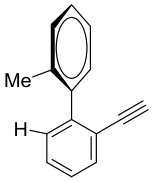
3gb, 68%



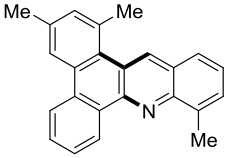
3hb, 59%



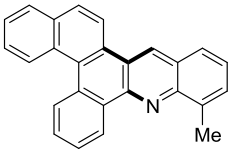
3ib + **3ib'**, 40% (ratio 3:2)



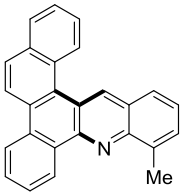
1j, no reaction



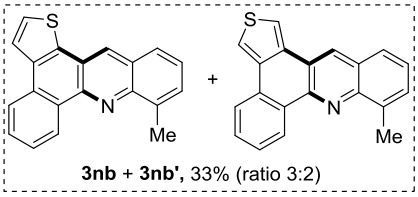
3kb, 40%



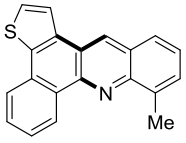
3lb, 41%



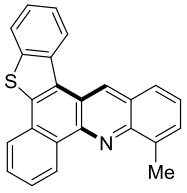
3mb, 48%



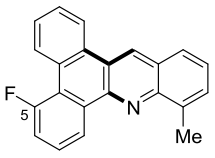
3nb + **3nb'**, 33% (ratio 3:2)



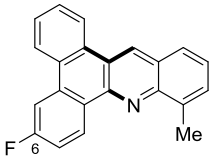
3ob, 61%



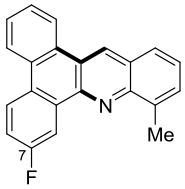
3pb, 20%



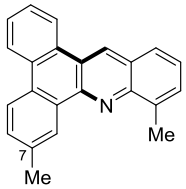
3qb, 57%



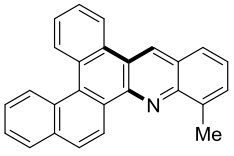
3rb, 53%



3sb, 47%



3tb, 50%

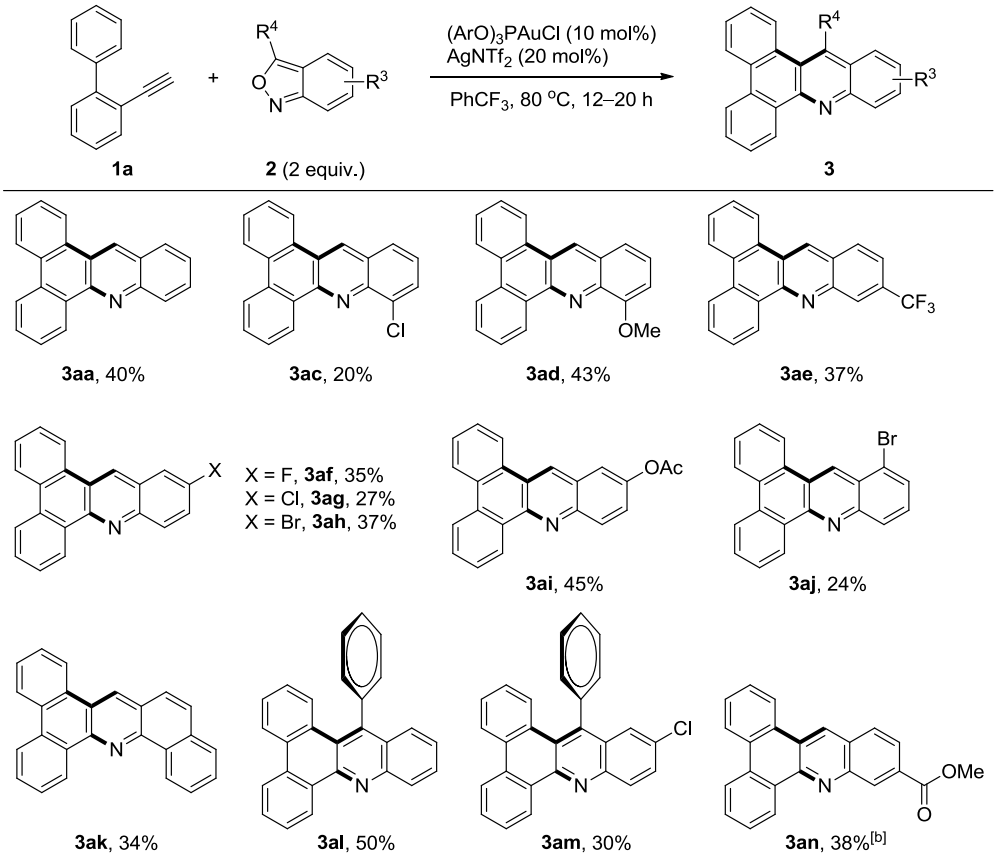


3ub, 41%

[a] Reaction conditions: **1** (0.2 mmol), **2b** (0.4 mmol), 10 mol% $(ArO)_3PAuCl$/20 mol% $AgNTf_2$, $PhCF_3$ (1 mL), 80 °C, 12–20 h; yield of isolated product. [b] 1 mmol scale.

Next, the substrate scope of the reaction with respect to the anthranil was investigated (Table 3). The conversion of differently substituted anthranils **2** with *o*-ethynylbiphenyl (**1a**) proceeded regioselectively to afford diverse *N*-doped PAHs in moderate to good yields. A variety of functional groups, including fluoride (**3af**), chloride (**3ac**, **3ag**, **3am**), bromide (**3ah**, **3aj**), methoxy (**3ad**), ester (**3ai, 3an**) and trifluoromethyl (**3ae**) were well tolerated, allowing further derivatization at the relevant positions. Substituents could be attached to each position of the anthranil, showcasing the great flexibility and generality of this synthetic strategy. π-Extended system **3ak** could also be readily constructed by virtue of this strategy. Even the sterically bulky *N*-doped PAHs **3al** and **3am** were obtained in 50% and 30% yields, respectively.

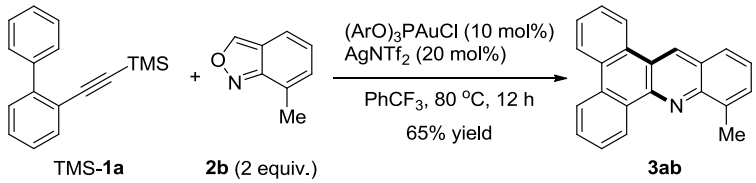
Table 3: Substrate scope with respect to anthranils.[a]



[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), 10 mol% $(ArO)_3PAuCl$/20 mol% $AgNTf_2$, $PhCF_3$ (1 mL), 80 °C for 12–20 h; yield of isolated product. [b] 15 mol% $(ArO)_3PAuCl$/30 mol% $AgNTf_2$ was used.

3.2.3 Alternative Synthesis and Applications

Intriguingly, treatment of TMS-protected *o*-ethynylbiphenyl (TMS-**1a**) with anthranil **2b** also provided *N*-doped PAH **3ab** in comparable yield (65%), which further improved the step economy as no additional deprotection step is necessary (Scheme 2). After construction of these *N*-doped PAHs, we then moved to investigate the optical properties of representative analogues **3ab**, **3lb**, **3ob**, **3ub**, and **3ak** in dilute CH_2Cl_2 solution (Figure 2). UV-Vis spectroscopy indicated that the λ_{max} of tested *N*-doped PAHs appeared in the range of 278–302 nm. In addition, they emitted violet-blue fluorescence (e.g., **3ak**: Φ_F = 0.45) with large Stokes shift (107–138 nm).



Scheme 2. In situ TMS removal on the way to *N*-doped PAH.

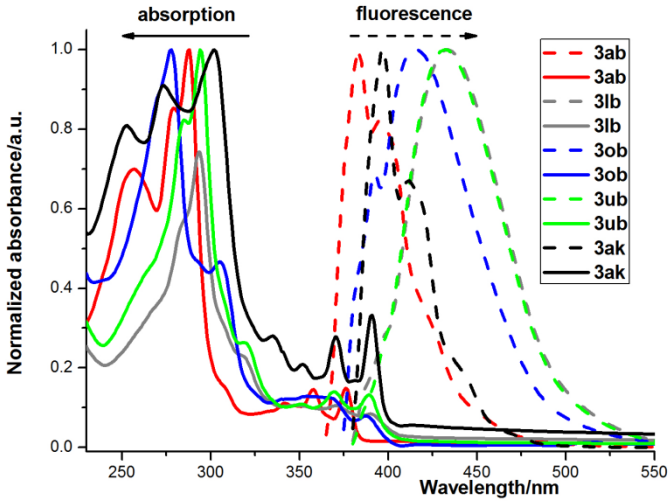


Figure 2. UV/Vis absorption (solid lines) and emission spectra (dotted ones) in dilute CH_2Cl_2.

3.3 Conclusion

In conclusion, a rapid, concise, and facile route to *N*-doped PAHs enabled by the gold-catalyzed ring-expansion π-extension reaction of anthranils using

o-ethynylbiaryls as a π-extending agent has been developed. A ligand-controlled pseudo-intramolecular regioselective C–H annulation allows this π-extension technology. Unlike previous synthetic methods, our complementary strategy features a one-step operation, high atom economy, as well as a broad substrate scope. Preliminary photochemical studies suggest these compounds emit violet-blue fluorescence, and the investigation on application in material science is ongoing.

3.4 Notes and References

[1] For selected reviews, see: a) R. G. Harvey, *Polycyclic Aromatic Hydrocarbons*, Wiley-VCH, New York, **1997**, pp. 43–128; b) M. M. Boorum, L. T. Scott, *Modern Arene Chemistry* (Ed.: D. Astruc), Wiley-VCH, Weinheim, **2002**, pp. 20–31; c) M. D. Watson, A. Fechtenkötter, K. Müllen, *Chem. Rev.* **2001**, *101*, 1267–1300; d) J. E. Anthony, *Chem. Rev.* **2006**, *106*, 5028–5048; e) J. Wu, W. Pisula, K. Müllen, *Chem. Rev.* **2007**, *107*, 718–747; f) K. Itami, *Pure Appl. Chem.* **2012**, *84*, 907–916; g) V. Georgakilas, J. A. Perman, J. Tucek, R. Zboril, *Chem. Rev.* **2015**, *115*, 4744–4822; h) Y. Segawa, H. Ito, K. Itami, *Nat. Rev. Mater.* **2016**, *1*, 15002.

[2] a) D. Wei, Y. Liu, *Adv. Mater.* **2010**, *22*, 3225–3241; b) T. N. Hoheisel, S. Schrettl, R. Szilluweit, H. Frauenrath, *Angew. Chem. Int. Ed.* **2010**, *49*, 6496–6515; c) X. Feng, W. Pisula, K. Müllen, *Pure Appl. Chem.* **2009**, *81*, 2203–2224.

[3] a) Y. Segawa, T. Maekawa, K. Itami, *Angew. Chem. Int. Ed.* **2015**, *54*, 66–81; *Angew. Chem.* **2015**, *127*, 68–83; b) Y. Huang, D. Wu, J. Huang, Q. Guo, J. Li, J. You, *Angew. Chem. Int. Ed.* **2014**, *53*, 12158–12162; *Angew. Chem.* **2014**, *126*, 12354–12358; c) J. Dong, Z. Long, F. Song, N. Wu, Q. Guo, J. Lan, J. You, *Angew. Chem. Int. Ed.* **2013**, *52*, 580–584; *Angew. Chem.* **2013**, *125*, 608–612; d) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, 5, 369–375; e) J. H. Kim, T. Gensch, D. Zhao, L. Stegemann, C. A. Strassert, F. Glorius, *Angew. Chem. Int. Ed.* **2015**, *54*, 10975–10979; *Angew. Chem.* **2015**, *127*, 11126–11130; f) K. Kim, D. Vasu, H. Im, S. Hong, *Angew. Chem. Int. Ed.* **2016**, *55*, 8652–8655; *Angew. Chem.* **2016**, *128*, 8794–8797; g) J. Yin, M. Tan, D. Wu, R. Jiang, C. Li, J. You, *Angew. Chem. Int. Ed.*

2017, *56*, 13094–13098; *Angew. Chem.* **2017**, *129*, 13274–13278; h) K. Xu, Y. Fu, Y. Zhou, F. Hennersdorf, P. Machata, I. Vincon, J. J. Weigand, A. A. Popov, R. Berger, X. Feng, *Angew. Chem. Int. Ed.* **2017**, *56*, 15876–15881; *Angew. Chem.* **2017**, *129*, 16092–16097.

[4] a) K. Ozaki, K. Kawasumi, M. Shibata, H. Ito, K. Itami, *Nat. Commun.* **2015**, *6*, 6251; b) Y. Yano, H. Ito, Y. Segawa, K. Itami, *Synlett* **2016**, *27*, 2081–2084; c) K. Kato, Y. Segawa, K. Itami, *Can. J. Chem.* **2017**, *95*, 329–333; d) K. Ozaki, H. Zhang, H. Ito, A. Lei, K. Itami, *Chem. Sci.* **2013**, *4*, 3416–3420; e) K. Ozaki, W. Matsuoka, H. Ito, K. Itami, *Org. Lett.* **2017**, *19*, 1930–1933; f) K. Ozaki, K. Murai, W. Matsuoka, K. Kawasumi, H. Ito, K. Itami, *Angew. Chem. Int. Ed.* **2017**, *56*, 1361–1364; *Angew. Chem.* **2017**, *129*, 1381–1384; g) W. Matsuoka, H. Ito, K. Itami, *Angew. Chem. Int. Ed.* **2017**, *56*, 12224–12228; *Angew. Chem.* **2017**, 129, 12392–12396. For a review on APEX reactions, see: h) H. Ito, K. Ozaki, K. Itami, *Angew. Chem. Int. Ed.* **2017**, *56*, 11144–11164; *Angew. Chem.* **2017**, *129*, 11296–11317.

[5] a) A. Fürstner, V. Mamane, *J. Org. Chem.* **2002**, *67*, 6264–6267; b) V. Mamane, P. Hannen, A. Fürstner, *Chem. Eur. J.* **2004**, *10*, 4556–4575; c) H.-C. Shen, J.-M. Tang, H.-K. Chang, C.-W. Yang, R.-S. Liu, *J. Org. Chem.* **2005**, *70*, 10113–10116; d) M. L. Hossain, F. Ye, Z. Liu, Y. Xia, Y. Shi, L. Zhou, Y. Zhang, J. Wang, *J. Org. Chem.* **2014**, *79*, 8689−8699; e) B. Seo, W. H. Jeon, J. Kim, S. Kim, P. H. Lee, *J. Org. Chem.* **2015**, *80*, 722−732; f) Y. Yamamoto, K. Matsui, M. Shibuya, *Chem. Eur. J.* **2015**, *21*, 7245–7255; g) T. Matsuda, K. Kato, T. Goya, S. Shimada, M. Murakami, *Chem. Eur. J.* **2016**, *22*, 1941–1943; h) D. Lu, Y.Wan, L. Kong, G. Zhu, *Chem. Commun.* **2016**, *52*, 13971–13974; i) W. Yang, A. Lucotti, M. Tommasini, W. A. Chalifoux, *J. Am. Chem. Soc.* **2016**, *138*, 9137–9144; j) H.-B. Ling, Z.-S. Chen, F. Yang, B. Xu, J.-M. Gao, K. Ji, *J. Org. Chem.* **2017**, *82*, 7070−7076;

[6] Selected reviews on aza-heterocycle synthesis from α-imino gold carbenes, see: a) P. W. Davies, M. Garzón, *Asian J. Org. Chem.* **2015**, *4*, 694–708; b) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506–516; c) L. Li, T.-D. Tan, Y.-Q. Zhang, X. Liu, L.-W. Ye, *Org. Biomol. Chem.* **2017**, *15*, 8483–8492.

[7] Intermolecular versions invloving ynamides, see: a) Y. Wu, L. Zhu, Y. Yu, X. Luo, X. Huang, *J. Org. Chem.* **2015**, *80*, 11407–11416; b) S. K. Pawar, R. L. Sahani, R.-S. Liu, *Chem. Eur. J.* **2015**, *21*, 10843–10850; c) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567–9570; d) C. Shu, C.-H. Shen, Y.-H. Wang, L. Li , T. Li, X. Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 4630–4633; e) C. Shu, Y.-H. Wang, C.-H. Shen, P.-P. Ruan, X. Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 3254–3257; f) P.-P. Ruan, H.-Hao Li, X. Liu, T. Zhang, S.-X. Zuo, C. Zhu, L.-W. Ye, *J. Org. Chem.* **2017**, *82*, 9119–9125; g) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738–1741; h) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935; *Angew. Chem.* **2011**, *123*, 9093–9097; i) A. D. Gillie, R. J. Redd, P. W. Davies, *Adv. Synth. Catal.* **2016**, *358*, 226–239; j) I. Costa, M. Marín-Luna, M. González Comesaña, O. N. Faza, C. S. López, *ChemCatChem* **2016**, *8*, 2387–2392; k) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33; l) A.-H. Zhou, Q. He, C. Shu, Y.-F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu, L.-W. Ye, *Chem. Sci.* **2015**, *6*, 1265–1271; m) X.-Y. Xiao, A.-H. Zhou, C. Shu, F. Pan, T. Li, L.-W. Ye, *Chem. Asian J.* **2015**, *10*, 1854–1858; n) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; *Angew. Chem.* **2016**, *128*, 804–808; o) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *128*,12880–12884; p) Z. Zeng, H. Jin, J. Xie, B. Tian, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Org. Lett.* **2017**, *19*, 1020–1023; q) Z. Zeng, H. Jin, X. Song, Q. Wang, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Chem. Commun.* **2017**, *53*, 4304–4307; r) M. Chen, N. Sun, H. Chen, Y. Liu, *Chem. Commun.* **2016**, *52*, 6324–6327; s) W. Xu, G. Wang, N. Sun, Y. Liu, *Org. Lett.*, **2017**, *19*, 3307–3310; t) W.-B. Shen, X.-Y. Xiao, Q. Sun, B. Zhou, X.-Q. Zhu, J.-Z. Yan, X. Lu, L.-W. Ye, *Angew. Chem. Int. Ed.* **2017**, *56*, 605–609; *Angew. Chem.* **2017**, *129*, 620–624.

[8] Intermolecular versions other polarized alkynes, see: a) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 1026–1030; *Angew. Chem.* **2017**, *129*, 1046–1050; b) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 12736–12740; *Angew. Chem.* **2017**, *129*, 12910–12914; c) E. Chatzopoulou, P. W. Davies, *Chem. Commun.* **2013**,

49, 8617–8619; d) R. J. Reddy, M. P. Ball-Jones, P. W. Davies, *Angew. Chem. Int. Ed.* **2017**, *56* ,13310–13313; *Angew. Chem.* **2017**, *129*, 13495–13498. For few reactions involving unfunctionalized alkynes, see: e) H.-H. Hung, Y.-C. Liao, R.-S. Liu, *J. Org. Chem.* **2013**, *78*, 7970–7976; f) J. González, J. Santamaría, Á. L. Suárez-Sobrino, A. Ballesteros, *Adv. Synth. Catal.* **2016**, 358, 1398–1403.

[9] CCDC 1811350 (**3ab**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[10] For a possible derivation into valuable N^N^C pincer ligands, see: Q. Mahmood, E. Yue, W. Zhang, G. A. Solan, T. Liang, W.-H. Sun, *Org. Chem. Front.* **2016**, *3*, 1668–1679.

[11] a) C. Huang, T. Liang, S. Harada, E. Lee, T. Ritter, *J. Am. Chem. Soc.* **2011**, *133*, 13308–13310; b) K. N. Hojczyk, P. Feng, C. Zhan, M.-Y. Ngai, *Angew. Chem. Int. Ed.* **2014**, *53*, 14559–14563; *Angew. Chem.* **2014**, *126*, 14787–14791.

[12] Selected reviews, see: a) A. F. Littke, G. C. Fu, *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211; *Angew. Chem.* **2002**, *114*, 4350–4386; b) A. C. Frisch, M. Beller, *Angew. Chem. Int. Ed.* **2005**, *44*, 674–688; *Angew. Chem.* **2005**, *117*, 680–695; c) A. Rudolph, M. Lautens, *Angew. Chem. Int. Ed.* **2009**, *48*, 2656–2670; *Angew. Chem.* **2009**, *121*, 2694–2708; d) S. E. Denmark, J. H.-C. Liu, *Angew. Chem. Int. Ed.* **2010**, *49*, 2978–2986; *Angew. Chem.* **2010**, *122*, 3040–3049; e) C. C. C. J. Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.* **2012**, *51*, 5062–5085; *Angew. Chem.* **2012**, *124*, 5150–5174.

3.5 Experimental Section

General Remarks: Chemicals were purchased from commercial suppliers and used without further purification. Reagents **1**[1] and **2**[2] were easily prepared according to our previous literatures. Dry solvents were dispensed from the solvent purification system MB SPS-800. Deuterated solvents were bought from Euriso-Top. Unless otherwise stated, NMR spectra were recorded at room temperature on the following

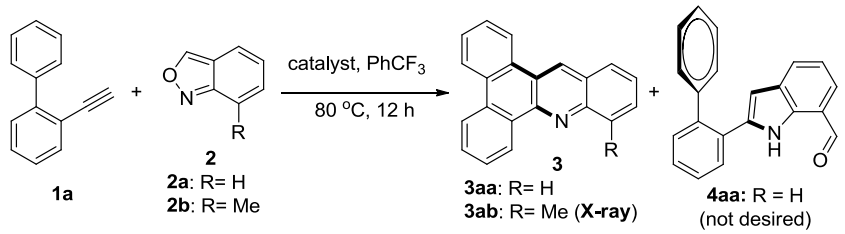
spectrometers: Bruker Avance 300, 400, 500 or 600. Chemical shifts were referenced to residual solvent protons and reported in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). 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. HRMS were determined at the chemistry department of the University of Heidelberg. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For DART-spectra a Bruker ICR Apex-Qe spectrometer was applied. IR spectra were recorded on a Bruker Vector 22, and the absorption maxima were given in wavelength in cm^{-1} units. 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. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Thin-layer chromatography (TLC) was performed on precoated polyester sheets (POLYGRAM SIL G/UV254), and components were visualized by observation under UV light. Melting points were uncorrected.

[1] a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K.Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; *Angew. Chem.* **2016**, *128*, 804–808; b) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *128*, 12880–12884.

[2] a) A. Fürstner, V. Mamane, *J. Org. Chem.* **2002**, *67*, 6264–6267; b) J. Carreras, G. Gopakumar, L. Gu, A. Gimeno, P. Linowski, J. Petuškova, W. Thiel, M. Alcarazo, *J. Am. Chem. Soc.* **2013**, *135*, 18815–18823; c) D. Lu, Y. Wan, L. Kong, G. Zhu, *Chem. Commun.* **2016**, *52*, 13971–13974.

Detailed Optimization of Reaction Condition

Table S1: Detailed Optimization



entry	**2**	catalyst (mol%)	additive, solvent	yield [%][b]
1	**2a**	IPrAuCl/$AgNTf_2$ (10:20)	--, $PhCF_3$	25 (25)
2	**2a**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, $PhCF_3$	40 (trace)
3	**2b**	**$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)**	**--, $PhCF_3$**	**70**
4	**2b**	$(Ar'O)_3PAuCl$[d]/$AgNTf_2$ (10:20)	--, $PhCF_3$	58
5	**2b**	IPrAuCl/$AgNTf_2$ (10:20)	--, $PhCF_3$	45
6	**2b**	PPh_3AuCl/$AgNTf_2$ (10:20)	--, $PhCF_3$	54
7	**2b**	^{t}BuXPhosAuCl/$AgNTf_2$ (10:20)	--, $PhCF_3$	50
8	**2b**	$PicAuCl_2$ (10)	--, $PhCF_3$	trace
9	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	10 mol% MsOH, $PhCF_3$	17
10	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	10mol% $In(OTf)_3$, $PhCF_3$	39
11	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	10 mg of 4Å MS, $PhCF_3$	63
12	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	10 mol% $(ArO)_3P$, $PhCF_3$	63
13	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, 1,2-DCE	50
14	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, $PhCF_3$/TFE (1:1)	24
15	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, $PhCF_3/H_2O$ (10:1)	44
16[e]	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, $PhCF_3$	62
17[f]	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:20)	--, $PhCF_3$	44
18	**2b**	$(ArO)_3PAuNTf_2$[c]/$AgNTf_2$ (10:10)	--, $PhCF_3$	51
19	**2b**	$(ArO)_3PAuCl$[c]/$AgNTf_2$ (10:10)	--, $PhCF_3$	40
20	**2b**	$AgNTf_2$, $PtCl_2$, or $M(OTf)_2$[g] (20)	--, $PhCF_3$	< 5

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.2 mmol) were reacted in 0.5 mL solvent at 80 °C for 12 h. [b] Isolated yield of **3**; yield of product **4aa** given in parentheses. [c] Ar = 2,4-di-*tert*-butylphenyl. [d] Ar' = 2-(*tert*-butyl)-4-(trifluoromethyl)phenyl. [e] 3 equiv. of **2b** was used. [f] Run at 100 °C. [g] M = Cu, Zn.

Experiment Procedure: Gold-catalyzed ring-expansion π-extension to access *N*-doped PAHs

A round bottom flask equipped with a magnetic stirrer bar was charged with $(ArO)_3PAuCl$ (10 mol%, 17.6 mg), $AgNTf_2$ (20 mol%, 15.5 mg), and $PhCF_3$ (0.5 mL). The mixture was stirred for 5 minutes at room temperature. Biarylacetylenes **1** or TMS-**1a** (0.2 mmol) and anthranils **2** (0.4 mmol) were added followed by 0.5 mL $PhCF_3$. The reaction mixture was then stirred at 80 ^oC and the progress of the reaction was monitored by TLC. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the desired product **3**.

Scale-up reaction: A round bottom flask equipped with a magnetic stirrer bar was charged with $(ArO)_3PAuCl$ (10 mol%, 70.4 mg), $AgNTf_2$ (20 mol%, 62.1 mg), and $PhCF_3$ (2.5 mL). The mixture was stirred for 5 minutes at room temperature. Biphenylacetylene **1a** (1.0 mmol) and anthranil **2b** (2.0 mmol) were added followed by 2.5 mL $PhCF_3$. The reaction mixture was then stirred at 80 ^oC for 14 h. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the desired product **3ab** in 60% yield (176.0 mg).

Optical and Photophysical Properties

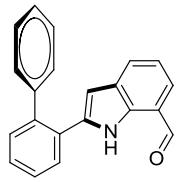
All properties were examined in CH_2CH_2 solution (0.27–0.32 mg/L) and in quartz cuvettes providing a layer thickness of 1 cm. UV-vis absorption spectra were recorded on a Jasco V-670 device. Fluorescence spectra were measured on a Jasco FP6500 device. Photographs were taken under UV light irradiation (λ = 365 nm) using a Canon EOS 7D digital camera (objective: EF-S60mm f/2.8 Macro USM).

Table S2: Photophysical data of representative *N*-doped PAHs.

	λ_{abs} [nm] (log ε)	λ_{em}[a] [nm] (Φ_F[b])	Stokes shift (nm)
3ab	288 (4.84)	395 (0.11)	107
3lb	293 (4.94)	433 (0.20)	140
3ob	278 (4.71)	416 (0.40)	138
3ub	294 (4.91)	432 (0.22)	138
3ak	302 (4.71)	411 (0.45)	109

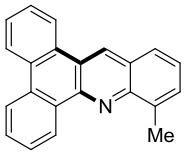
[a] Excited at λ_{abs}. [b] Fluorescence quantum yields (Φ_F) in CH_2Cl_2 at 298 K.

Characterization



4aa: 2-([1,1'-biphenyl]-2-yl)-1*H*-indole-7-carbaldehyde

light yellow solid, m.p.: 145–146 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 9.62 (s, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.76–7.74 (m, 1H), 7.54 (dd, *J* = 7.3, 0.8 Hz, 1H), 7.49–7.42 (m, 3H), 7.37–7.35 (m, 3H), 7.33–7.31 (m, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 2.3 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.0 (d), 141.0 (s), 140.4 (s), 139.7 (s), 134.0 (s), 131.1 (d), 130.5 (s), 129.61 (d), 129.60 (s), 129.2 (d, 2C), 128.6 (d, 2C), 128.30 (d), 128.27 (d), 127.8 (d), 127.5 (d, 2C), 120.0 (s), 119.4 (d), 102.0 (d) ppm; **IR** (reflection): $\tilde{\nu}$ 3442, 3058, 2819, 2742, 1663, 1604, 1590, 1568, 1548, 1496, 1465, 1452, 1435, 1381, 1352, 1336, 1296, 1251, 1231, 1211, 1170, 1113, 1065, 1047, 1008, 961, 948, 936, 915, 879, 811, 786, 776, 761, 745, 717, 700, 683, 666, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{21}H_{15}NO]^+$ $(M)^+$: 297.1148; found: 297.1154.

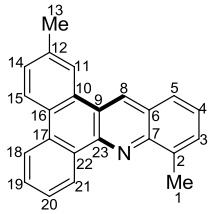


3ab: 10-methyldibenzo[*a*,*c*]acridine

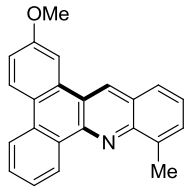
41.1 mg (70% yield), yellow solid, m.p.: 184–185 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.56–9.54 (m, 1H), 9.16 (s, 1H), 8.64–8.62 (m, 1H), 8.57–8.55 (m, 1H), 8.52–8.51 (m, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.75–7.71 (m, 2H), 7.67–7.63 (m, 3H), 7.48 (t, *J* = 7.5 Hz, 1H), 3.03 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.6 (s), 146.3 (s), 137.4 (s), 131.9 (s), 131.6 (s), 130.2 (d), 129.8 (s), 129.5 (d), 129.3 (d), 129.2 (s), 128.0 (d), 127.6 (d), 127.5 (d), 127.0 (s), 126.3 (d), 126.02 (d), 126.00 (d), 123.6 (d), 123.5 (d), 123.0 (s), 122.6 (d), 18.1 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3071, 3040, 2955, 2919, 2850, 1919, 1728, 1615, 1599, 1574, 1553, 1505, 1493, 1461, 1446, 1402, 1383, 1372, 1351, 1295, 1250, 1176, 1155, 1131, 1081, 1050, 1033, 972, 961, 944, 910, 890, 857, 805, 788, 762, 721, 701, 679, 617 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{15}N]^+$ $(M)^+$: 293.1199; found: 293.1210.

3bb: 2,10-dimethyldibenzo[*a*,*c*]acridine

Note: The numbers in the structure are gave in random, thus not consistent with those in chemical nomenclature.



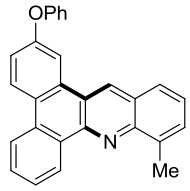
33.2 mg (54% yield), light yellow solid, m.p.: 158–159 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.55–9.51 (m, C21-H), 9.14 (s, C8-H), 8.49–8.45 (m, C18-H), 8.42 (d, *J* = 8.3 Hz, C15-H), 8.39 (s, C11-H), 7.86 (d, *J* = 8.2 Hz, C5-H), 7.74–7.67 (m, C19-H and C20-H), 7.63 (d, *J* = 6.8 Hz, C3-H), 7.46 (ddd, *J* = 8.2, 7.1, 4.1 Hz, C4-H and C14-H), 3.04 (s, C1-H_3), 2.61 (s, C13-H_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.6 (s), 146.5 (s), 137.4 (s), 137.2 (s), 132.1 (s), 131.3 (s), 130.1 (d, C8), 129.4 (d, C3), 129.30 (d, C19), 129.27 (d, C14), 129.2 (s), 127.5 (s), 127.1 (d, C20), 127.0 (s), 126.2 (d, C21), 126.0 (d, C5), 125.9 (d, C4), 123.7 (d, C11), 123.4 (d, C15), 123.0 (s), 122.4 (d, C18), 21.7 (q, C13), 18.1 (q, C1) ppm; **IR** (reflection): $\tilde{\nu}$ 3030, 2968, 2952, 2916, 2855, 1737, 1614, 1600, 1575, 1548, 1514, 1486, 1466, 1447, 1427, 1397, 1376, 1352, 1304, 1233, 1192, 1158, 1113, 1080, 1055, 1039, 964, 952, 907, 889, 859, 812, 803, 782, 756, 720, 712, 703, 666, 616 cm^{-1}; **HRMS** (DART) calcd for $[C_{23}H_{18}N]^+$ $(M+H)^+$: 308.1434; found: 308.1431.



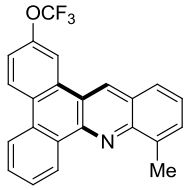
3cb: 2-methoxy-10-methyldibenzo[*a*,*c*]acridine

21.3 mg (33% yield), light red solid, m.p.: 176–177 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.53 (dd, *J* = 7.9, 1.4 Hz, 1H), 9.13 (s, 1H), 8.49 (d, *J* = 9.0 Hz, 1H), 8.43 (d, *J* = 7.9 Hz, 1H), 8.06 (d, *J* = 2.6 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.73–7.64 (m, 3H), 7.49 (dd, *J* = 8.1, 7.0 Hz, 1H), 7.28–7.25 (m, 2H), 4.06 (s, 3H), 3.05 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.2 (s), 146.72 (s), 146.67 (s), 137.4 (s), 132.1 (s), 130.73 (s), 130.65 (s), 130.3 (d), 129.6 (d), 129.4 (d), 126.9 (s), 126.7 (d), 126.3 (d), 126.02 (d), 125.97 (d), 125.1 (d), 123.7 (s), 122.8 (s), 122.1 (d), 116.0 (d), 106.7 (d), 55.6 (q), 18.1 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2998, 2958, 2916, 2832, 1608, 1548, 1512, 1487, 1465, 1455, 1428, 1398, 1137, 1359, 1326, 1292, 1249, 1238, 1222, 1208, 1183, 1156, 1130, 1114, 1078, 1043, 999, 981, 959, 901, 881, 849, 840, 826, 782, 767, 758, 717, 709, 662 cm^{-1}; **HRMS** (DART) calcd for $[C_{23}H_{18}NO]^+$ $(M+H)^+$: 324.1383; found: 324.1380.

3db: 10-methyl-2-phenoxydibenzo[*a*,*c*]acridine



32.4 mg (42% yield), light yellow solid, m.p.: 191–192 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.54–9.51 (m, 1H), 8.98 (s, 1H), 8.51 (d, *J* = 9.0 Hz, 1H), 8.44–8.41 (m, 1H), 8.24 (d, *J* = 2.5 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.74–7.67 (m, 2H), 7.63 (d, *J* = 6.8 Hz, 1H), 7.48–7.41 (m, 3H), 7.33 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.22–7.16 (m, 3H), 3.03 (s, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.3 (s), 156.7 (s), 146.8 (s), 146.4 (s), 137.4 (s), 131.7 (s), 131.1 (s, 2C), 130.5 (d), 130.0 (d, 2C), 129.7 (d), 129.4 (d), 127.2 (d), 126.9 (s), 126.3 (d), 126.1 (d), 126.0 (d), 125.7 (s), 125.3 (d), 123.6 (d), 122.5 (s), 122.4 (d), 119.5 (d), 119.0 (d, 2C), 112.9 (d), 18.1 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3050, 2919, 1741, 1613, 1587, 1552, 1484, 1444, 1397, 1372, 1357, 1323, 1292, 1261, 1224, 1181, 1161, 1132, 1071, 1036, 1021, 986, 964, 906, 883, 852, 840, 820, 800, 758, 745, 719, 695, 666 cm^{-1}; **HRMS** (EI) calcd for $[C_{28}H_{19}NO]^+$ $(M)^+$: 385.1461; found: 385.1470.

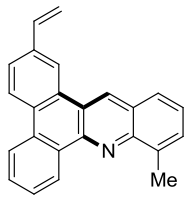


3eb: 10-methyl-2-(trifluoromethoxy)dibenzo[*a*,*c*]acridine

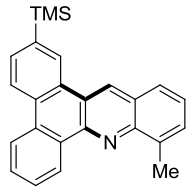
40.0 mg (53% yield), light yellow solid, m.p.: 204–205 °C; **^{1}H NMR** (600 MHz, $CDCl_3$, 50 °C) δ 9.49 (dd, *J* = 6.4, 3.0 Hz, 1H), 9.01 (s, 1H), 8.52 (d, *J* = 8.9 Hz, 1H), 8.41–8.39 (m, 1H), 8.37 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.73–7.70 (m, 2H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.50–7.48 (m, 2H), 3.01 (s, 3H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$, 50 °C) δ 148.98 (s), 148.97 (s), 147.3 (s), 146.5 (s), 137.8 (s), 131.9 (s), 131.2 (s, d: $J_{C\text{-}F}$ = 7.1 Hz), 130.7 (d), 130.2 (d), 129.7 (d), 128.7 (s), 128.2 (d), 127.2 (s), 126.7 (d), 126.6 (d), 126.2 (d), 125.6 (d), 122.8 (d), 122.2 (s), 121.0 (s, q: $J_{C\text{-}F}$ = 257.5 Hz), 120.7 (d), 115.6 (d), 18.1 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -57.42 ppm; **IR** (reflection): $\tilde{\nu}$ 3073, 2951, 2916, 1600, 1553, 1511, 1490, 1463, 1448, 1378, 1352, 1260, 1203, 1184, 1150, 1078, 1039, 1002, 969, 909, 890, 858, 843, 827, 785, 762, 720, 709, 671, 632 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{14}NOF_3]^+$ $(M)^+$: 377.1022; found: 377.1017.

3fb: 10-methyl-2-vinyldibenzo[*a*,*c*]acridine

30.0 mg (47% yield), light yellow solid, m.p.: 185–186 °C; **^{1}H NMR** (500 MHz,



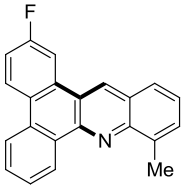
$CDCl_3$) δ 9.52 (s, 1H), 9.17 (dd, *J* = 7.7, 5.3 Hz, 1H), 8.52 (dd, *J* = 35.7, 6.8 Hz, 3H), 7.89 (d, *J* = 5.4 Hz, 1H), 7.75–7.71 (m, 3H), 7.64 (d, *J* = 6.5 Hz, 1H), 7.49 (t, *J* = 7.4 Hz, 1H), 6.98 (dd, *J* = 17.4, 11.0 Hz, 1H), 6.01 (d, *J* = 17.5 Hz, 1H), 5.45 (d, *J* = 10.8 Hz, 1H), 3.03 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.6 (s), 146.4 (s), 137.4 (s), 136.7 (d), 136.6 (s), 131.8 (s), 131.6 (s), 130.2 (d), 129.5 (d), 129.39 (s), 129.35 (d), 129.3 (s), 127.6 (d), 127.0 (s), 126.3 (d), 126.1 (d), 126.0 (d), 125.3 (d), 123.8 (d), 122.9 (s), 122.6 (d), 121.8 (d), 114.8 (t), 18.1 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3042, 2914, 1599, 1543, 1512, 1485, 1450, 1373, 1234, 1196, 1157, 1115, 1080, 1032, 987, 960, 903, 882, 858, 835, 803, 786, 760, 726, 711, 682, 666 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{17}N]^+$ $(M)^+$: 319.1356; found: 319.1365.



3gb: 10-methyl-2-(trimethylsilyl)dibenzo[*a*,*c*]acridine

41.7 mg (68% yield), yellow solid, m.p.: 214–215 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.57 (dd, *J* = 6.2, 3.2 Hz, 1H), 9.26 (s, 1H), 8.83 (s, 1H), 8.57–8.54 (m, 2H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.82 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.76–7.72 (m, 2H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.51 (dd, *J* = 8.0, 7.1 Hz, 1H), 3.05 (s, 3H), 0.47 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5 (s), 147.3 (s), 140.5 (s), 138.3 (s), 133.7 (d), 132.9 (s), 132.7 (s), 131.1 (s), 130.9 (d), 130.4 (d), 130.3 (d), 129.5 (d), 129.2 (s), 128.6 (d), 128.0 (s), 127.2 (d), 127.0 (d), 126.9 (d), 124.0 (s), 123.6 (d), 123.5 (d), 19.0 (q), 0.0 (q, 3C) ppm; **IR** (reflection): $\tilde{\nu}$ 3061, 3038, 2953, 2914, 1600, 1567, 1509, 1482, 1462, 1420, 1364, 1259, 1246, 1214, 1157, 1124, 1080, 1054, 1036, 978, 945, 903, 884, 836, 806, 787, 771, 756, 723, 705, 649, 622 cm^{-1}; **HRMS** (EI) calcd for $[C_{25}H_{23}NSi]^+$ $(M)^+$: 365.1594; found: 365.1583.

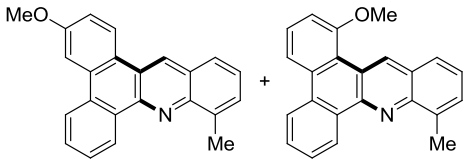
3hb: 2-fluoro-10-methyldibenzo[*a*,*c*]acridine



36.7 mg (59% yield), light yellow solid, m.p.: 213–214 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.56 (d, *J* = 6.9 Hz, 1H), 9.11 (s, 1H), 8.58–8.55 (m, 1H), 8.46 (d, *J* = 7.3 Hz, 1H), 8.29 (d, *J* = 10.0 Hz, 1H), 7.90 (d, *J*

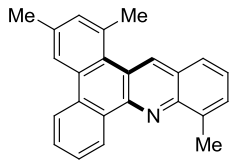
= 8.3 Hz, 1H), 7.76–7.67 (m, 3H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.39 (t, *J* = 7.3 Hz, 1H), 3.05 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.9 (s, d: $J_{C\text{-}F}$ = 247.5 Hz, s), 146.7 (s), 145.7 (s, d: $J_{C\text{-}F}$ = 0.9 Hz), 137.3 (s), 134.0 (s, d: $J_{C\text{-}F}$ = 8.4 Hz), 130.4 (d), 129.71 (s), 129.67 (d), 128.98 (s, d: $J_{C\text{-}F}$ = 0.4 Hz), 128.96 (d), 128.9 (d), 128.10 (d), 128.08 (s), 128.05 (d), 126.9 (s), 126.04 (d), 126.02 (d), 123.7 (d, d: $J_{C\text{-}F}$ = 6.6 Hz), 122.5 (s), 115.6 (d, d: $J_{C\text{-}F}$ = 22.5 Hz), 108.4 (d, d: $J_{C\text{-}F}$ = 23.0 Hz), 18.1 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -111.39 ppm; **IR** (reflection): $\tilde{\nu}$ 3068, 3051, 3036, 2957, 2922, 1930, 1730, 1614, 1597, 1554, 1510, 1488, 1465, 1448, 1396, 1377, 1352, 1289, 1260, 1214, 1192, 1160, 1114, 1076, 1035, 1003, 984, 964, 945, 912, 892, 855, 822, 803, 782, 762, 720, 707 cm^{-1}; **HRMS** (DART) calcd for $[C_{22}H_{15}FN]^+$ $(M+H)^+$: 312.1183; found: 312.1180.

3ib + **3ib'**: 3-methoxy and 1-methoxy-10-methyldibenzo[*a*,*c*]acridine



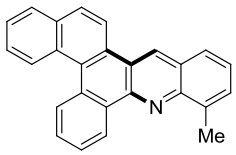
Inseparable regioisomers, 25.9 mg (40% combined yield), yellow solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.28 (s, 1H), 9.62–9.60 (m, 1H), 9.57–9.55 (m, 0.7H), 9.05 (s, 0.7H), 8.53–8.51 (m, 1.7H), 8.45–8.44 (m, 0.7H), 8.27 (d, *J* = 8.1 Hz, 1H), 7.97 (s, 0.7H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.84 (d, *J* = 8.1 Hz, 0.7H), 7.73 (dd, *J* = 8.5, 4.5 Hz, 3.4H), 7.65–7.62 (m, 1.7H), 7.61–7.58 (m, 1H), 7.49–7.44 (m, 1.7H), 7.22 (t, *J* = 9.6 Hz, 1.7H), 4.17 (s, 3H), 4.02 (s, 2.1H), 3.05 (s, 3H), 3.04 (s, 2.1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.57 (s), 159.55 (s), 146.48 (s), 146.12 (s), 145.75 (s), 145.41 (s), 137.38 (s), 136.93 (s), 136.80 (d), 132.24 (s), 132.17 (s), 131.97 (s), 131.68 (s), 131.32 (s), 129.40 (s), 129.38 (d), 129.24 (d), 129.21 (d), 129.06 (d), 127.90 (d), 127.73 (d), 127.18 (s), 127.01 (s), 126.80 (d), 126.42 (d), 126.35 (d), 125.98 (d), 125.83 (d), 125.54 (d), 125.20 (d), 123.27 (d), 123.15 (s), 122.84 (s), 122.82 (s), 122.63 (d), 119.19 (d), 117.80 (s), 116.17 (s), 115.57 (d), 110.00 (d), 109.99 (s), 106.54 (d), 55.86 (q), 55.53 (q), 18.12 (q), 17.90 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2915, 2833, 1726, 1614, 1575, 1556, 1505, 1463, 1435, 1402, 1381, 1359, 1322, 1253, 1238, 1213, 1181, 1159, 1133, 1093, 1069, 1055, 1021, 960, 920, 885, 866, 843, 819, 799, 760, 722, 702, 686, 656, 618 cm^{-1}; **HRMS**

(DART) calcd for $[C_{23}H_{18}NO]^+$ $(M+H)^+$: 324.1383; found: 324.1380.



3kb: 1,3,10-trimethyldibenzo[*a*,*c*]acridine

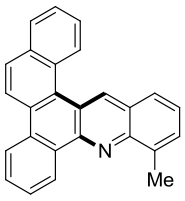
25.7 mg (40% yield), light yellow solid, m.p.: 147–148 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.56–9.54 (m, 1H), 9.27 (s, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.32 (s, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.72–7.68 (m, 2H), 7.64 (d, *J* = 6.7 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.36 (s, 1H), 3.09 (s, 3H), 3.05 (s, 3H), 2.58 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.3 (s), 145.3 (s), 137.0 (s), 136.8 (s), 136.3 (s), 134.9 (d), 133.4 (d), 132.5 (s), 131.9 (s), 131.4 (s), 129.37 (d), 129.36 (d), 127.5 d), 126.8 (s), 126.3 (d), 126.1 (d), 126.0 (s), 125.8 (d), 124.3 (s), 123.0 (d), 122.0 (d), 26.6 (q), 21.5 (q), 17.9 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2911, 1736, 1615, 1498, 1459, 1403, 1382, 1307, 1178, 1154, 1079, 1030, 902, 884, 850, 805, 787, 766, 754, 731, 701, 639 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{19}N]^+$ $(M)^+$: 321.1512; found: 321.1510.



3lb: 10-methylbenzo[*c*]naphtho[2,1-*a*]acridine

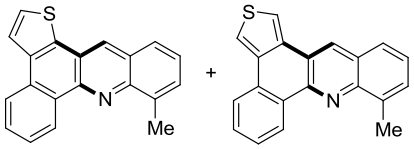
28.2 mg (41% yield), yellow solid, m.p.: 169–170 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.64 (d, *J* = 7.7 Hz, 1H), 9.23 (s, 1H), 8.97 (d, *J* = 8.3 Hz, 1H), 8.81 (d, *J* = 7.8 Hz, 1H), 8.62 (d, *J* = 8.6 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.79–7.73 (m, 2H), 7.67–7.59 (m, 3H), 7.50 (t, *J* = 7.5 Hz, 1H), 3.08 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.7 (s), 146.3 (s), 137.4 (s), 134.0 (s), 132.6 (s), 131.7 (s), 130.8 (d), 130.4 (s), 129.6 (d), 128.8 (d), 128.4 (d), 128.19 (d), 128.16 (d), 128.1 (d), 127.5 (s), 127.4 (s), 127.2 (s), 127.1 (d), 126.33 (d), 126.30 (d), 126.1 (d, 2C), 126.0 (d), 123.1 (s), 120.6 (d), 18.2 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3067, 3046, 2972, 2944, 2911, 1925, 1755, 1589, 1545, 1483, 1458, 1431, 1406, 1375, 1361, 1331, 1270, 1246, 1211, 1159, 1124, 1087, 1049, 979, 946, 900, 875, 861, 837, 816, 797, 789, 774, 761, 741, 706, 685, 666, 629, 611 cm^{-1}; **HRMS** (DART) calcd for $[C_{26}H_{18}N]^+$ $(M+H)^+$: 344.1434; found: 344.1434.

3mb: 12-methylbenzo[*c*]naphtho[1,2-*a*]acridine



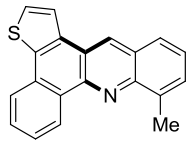
33.0 mg (48% yield), yellow solid, m.p.: 187–188 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.65–9.54 (m, 1H), 9.54 (s, 1H), 8.92 (d, *J* = 8.4 Hz, 1H), 8.61–8.57 (m, 2H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.83–7.76 (m, 2H), 7.71–7.67 (m, 2H), 7.65–7.61 (m, 1H), 7.52 (dd, *J* = 8.0, 7.1 Hz, 1H), 3.10 (s, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.0 (s), 146.0 (s), 137.3 (s), 136.2 (d), 133.7 (s), 131.9 (s), 131.8 (s), 130.6 (d), 129.6 (s), 129.5 (d), 128.5 (d), 128.4 (d, 2C), 127.63 (d), 127.59 (d), 126.8 (d), 126.5 (s), 126.2 (s), 126.1 (d), 126.04 (d), 126.00 (d), 125.9 (d), 123.2 (d), 122.5 (s), 120.9 (d), 18.0 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3072, 3057, 2977, 2953, 2916, 2851, 1921, 1779, 1600, 1568, 1545, 1489, 1464, 1426, 1407, 1374, 1347, 1329, 1220, 1165, 1127, 1075, 1041, 1011, 953, 921, 893, 858, 816, 790, 750, 715, 706, 665, 630 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{17}N]^+$ $(M)^+$: 343.1356; found: 343.1357.

3nb + **3nb'**: 9-methylbenzo[*c*]thieno[2,3-*a*]acridine and 9-methylbenzo[*c*]thieno[3,4-*a*]acridine



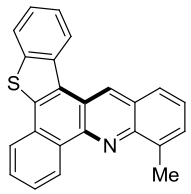
Inseparable regioisomers, 19.8 mg (33% combined yield), yellow solid; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.55–9.53 (m, 1H), 9.31–9.29 (m, 0.7H), 8.75 (s, 0.7H), 8.74 (s, 1H), 8.20 (d, *J* = 7.4 Hz, 1H), 8.12–8.10 (m, 1.4H), 8.01 (d, *J* = 2.9 Hz, 0.7H), 7.92 (d, *J* = 5.3 Hz, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.78–7.70 (m, 2.8H), 7.64–7.58 (m, 4H), 7.50–7.43 (m, 1.7H), 3.05 (s, 3H), 2.99 (s, 2.1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.99 (s), 146.33 (s), 146.32 (s), 145.40 (s), 137.71 (s), 137.62 (s), 135.24 (s), 134.91 (s), 134.76 (s), 134.10 (s), 130.89 (s), 130.73 (s), 130.63 (s), 130.24 (d), 130.22 (s), 129.93 (d), 129.55 (d), 129.28 (d), 129.23 (d), 129.17 (d), 127.38 (d), 127.17 (s), 126.84 (s), 126.61 (d), 126.55 (d), 126.40 (d), 126.26 (d), 126.21 (d), 125.67 (d), 125.52 (d), 125.49 (d), 123.63 (d), 123.56 (d), 123.42 (d), 121.72 (s), 121.70 (s), 118.46 (d), 117.71 (d), 18.22 (q), 18.07 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3102, 3041, 2912, 1603, 1561, 1527, 1498, 1475, 1457, 1405, 1373, 1349, 1301, 1250, 1214, 1193, 1156, 1134, 1109, 1093, 1079, 1038, 989, 960, 906, 889, 865, 813, 780, 762, 715, 659, 630 cm^{-1}; **HRMS** (DART) calcd for $[C_{20}H_{14}NS]^+$

$(M+H)^+$: 300.0841; found: 300.0838.



3ob: 9-methylbenzo[*c*]thieno[3,2-*a*]acridine

36.5 mg (61% yield), light yellow solid, m.p.: 150–151 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.56–9.52 (m, 1H), 8.90 (s, 1H), 8.07–8.05 (m, 1H), 8.00 (d, *J* = 5.3 Hz, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.73–7.69 (m, 2H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.58 (d, *J* = 5.3 Hz, 1H), 7.50 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.06 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.1 (s), 146.0 (s), 137.7 (s), 136.6 (s), 133.8 (s), 130.4 (d), 130.3 (s), 130.2 (s), 129.4 (d), 129.1 (d), 126.9 (s), 126.8 (d), 126.4 (d), 126.1 (d), 125.7 (d), 125.3 (d), 123.6 (d), 123.4 (d), 122.0 (s), 18.2 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3026, 2957, 2916, 1908, 1738, 1602, 1561, 1529, 1496, 1462, 1432, 1413, 1374, 1333, 1298, 1283, 1264, 1238, 1217, 1191, 1160, 1095, 1056, 1034, 994, 974, 956, 904, 879, 854, 807, 784, 753, 728, 706, 681, 647 cm^{-1}; **HRMS** (EI) calcd for $[C_{20}H_{13}NS]^+$ $(M)^+$: 299.0763; found: 299.0768.

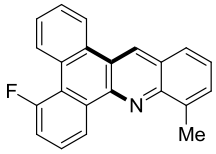


3pb: 11-methylbenzo[*c*]benzo[4,5]thieno[3,2-*a*]acridine

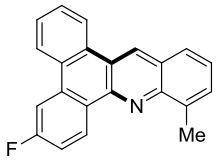
14.0 mg (20% yield), light yellow solid, m.p.: 230–231 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.63–9.60 (m, 2H), 8.80 (d, *J* = 8.3 Hz, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 7.9 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.80–7.76 (m, 2H), 7.70–7.64 (m, 2H), 7.47 (dt, *J* = 14.7, 7.4 Hz, 2H), 3.09 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.2 (s), 145.4 (s), 139.3 (s), 138.7 (s), 137.8 (s), 137.5 (s), 131.2 (s), 130.2 (d), 129.9 (s), 129.5 (d), 129.3 (d), 127.8 (d), 126.7 (s), 126.49 (s), 126.46 (d), 126.3 (d), 126.0 (d), 125.3 (d), 125.2 (d), 124.4 (d), 124.1 (d), 123.5 (d), 123.1 (s), 18.03 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3053, 2920, 2852, 1926, 1721, 1608, 1563, 1521, 1493, 1459, 1406, 1393, 1378, 1322, 1252, 1227, 1200, 1162, 1062, 1040, 1010, 983, 894, 872, 858, 833, 820, 761, 745, 718, 653, 631 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{15}NS]^+$ $(M)^+$: 349.0920; found: 349.0933.

3qb: 5-fluoro-10-methyldibenzo[*a*,*c*]acridine

35.5 mg (57% yield), yellow solid, m.p.: 177–178 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ



9.45 (d, *J* = 7.9 Hz, 1H), 9.19 (s, 1H), 9.06–9.04 (m, 1H), 8.68–8.67 (m, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.69–7.64 (m, 4H), 7.51–7.43 (m, 2H), 3.02 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 161.3 (s, d: $J_{C\text{-}F}$ = 251.7 Hz), 146.7 (s), 145.5 (s, d: $J_{C\text{-}F}$ = 3.7 Hz), 137.4 (s), 134.4 (s), 134.3 (s), 130.3 (d), 129.7 (d), 129.5 (s), 128.7 (d, d: $J_{C\text{-}F}$ = 27.4 Hz), 128.3 (d, d: $J_{C\text{-}F}$ = 2.6 Hz), 127.71 (d, d: $J_{C\text{-}F}$ = 7.6 Hz), 127.66 (d), 127.3 (s), 126.4 (d), 126.0 (d), 123.3 (d), 123.1 (s), 122.2 (d, d: $J_{C\text{-}F}$ = 3.4 Hz), 120.9 (s, d: $J_{C\text{-}F}$ = 7.9 Hz), 116.8 (d, d: $J_{C\text{-}F}$ = 25.7 Hz), 18.1 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -109.97 ppm; **IR** (reflection): $\tilde{\nu}$ 3053, 3028, 2971, 2951, 2916, 1943, 1684, 1612, 1575, 1552, 1505, 1485, 1462, 1445, 1405, 1387, 1377, 1352, 1310, 1286, 1234, 1217, 1156, 1125, 1076, 1042, 983, 958, 908, 891, 859, 835, 816, 793, 770, 718, 704, 683, 664 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{14}NF]^+$ $(M)^+$: 311.1105; found: 311.1110.

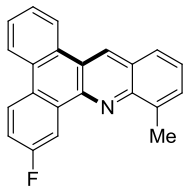


3rb: 6-fluoro-10-methyldibenzo[*a*,*c*]acridine

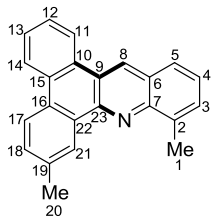
33.0 mg (53% yield), light yellow solid, m.p.: 190–191 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.20 (s, 1H), 9.16 (dd, *J* = 10.5, 1.8 Hz, 1H), 8.65 (d, *J* = 7.1 Hz, 1H), 8.51–8.49 (m, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.68–7.65 (m, 3H), 7.52–7.49 (m, 1H), 7.44 (td, *J* = 8.5, 2.8 Hz, 1H), 3.03 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 162.5 (s, d: $J_{C\text{-}F}$ = 246.2 Hz), 146.6 (s), 145.4 (s, d: $J_{C\text{-}F}$ = 3.4 Hz), 137.5 (s), 133.9 (s, d: $J_{C\text{-}F}$ = 8.3 Hz), 130.4 (d), 129.7 (d), 129.3 (s), 128.7 (s, d: $J_{C\text{-}F}$ = 0.9 Hz), 128.4 (s, d: $J_{C\text{-}F}$ = 2.3 Hz), 128.2 (d), 127.4 (d), 127.3 (s), 126.4 (d), 126.0 (d), 125.0 (d, d: $J_{C\text{-}F}$ = 8.3 Hz), 123.6 (d), 123.4 (d), 123.2 (s), 117.4 (d, d: $J_{C\text{-}F}$ = 23.4 Hz), 111.6 (d, d: $J_{C\text{-}F}$ = 22.9 Hz), 18.1 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -113.59 ppm; **IR** (reflection): $\tilde{\nu}$ 3038, 2917, 2388, 2285, 1609, 1578, 1555, 1508, 1489, 1449, 1398, 1376, 1338, 1280, 1241, 1179, 1157, 1081, 1038, 944, 890, 861, 842, 825, 801, 783, 764, 745, 728, 717, 701 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{14}NF]^+$ $(M)^+$: 311.1105; found: 311.1107.

3sb: 7-fluoro-10-methyldibenzo[*a*,*c*]acridine

29.3 mg (47% yield), light yellow solid, m.p.: 200–201 °C; **^{1}H NMR** (500 MHz,



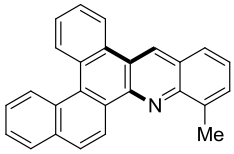
$CDCl_3$) δ 9.49–9.46 (m, 1H), 9.10 (s, 1H), 8.59–8.58 (m, 1H), 8.39–8.37 (m, 1H), 8.07 (dd, *J* = 11.0, 2.3 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.68–7.62 (m, 3H), 7.49–7.46 (m, 1H), 7.39 (td, *J* = 8.8, 2.4 Hz, 1H), 2.98 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.9 (s, d: $J_{C\text{-}F}$ = 247.5 Hz, s), 146.7 (s), 145.7 (s, d: $J_{C\text{-}F}$ = 0.9 Hz), 137.3 (s), 134.0 (s, d: $J_{C\text{-}F}$ = 8.4 Hz), 130.4 (d), 129.71 (s), 129.67 (d), 128.98 (s, d: $J_{C\text{-}F}$ = 0.4 Hz), 128.96 (d), 128.9 (d), 128.10 (d), 128.08 (s), 128.05 (d), 126.9 (s), 126.04 (d), 126.02 (d), 123.7 (d, d: $J_{C\text{-}F}$ = 6.6 Hz), 122.5 (s), 115.6 (d, d: $J_{C\text{-}F}$ = 22.5 Hz), 108.4 (d, d: $J_{C\text{-}F}$ = 23.0 Hz), 18.1 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -111.39 ppm; **IR** (reflection): $\tilde{\nu}$ 3038, 2392, 1920, 1617, 1600, 1576, 1542, 1498, 1453, 1421, 1402, 1382, 1348, 1315, 1263, 1231, 1216, 1185, 1171, 1156, 1127, 1107, 1081, 1030, 977, 961, 948, 910, 898, 890, 868, 834, 798, 782, 766, 734, 698, 650, 634, 607 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{14}NF]^+$ $(M)^+$: 311.1105; found: 311.1115.



3tb: 7,10-dimethyldibenzo[*a*,*c*]acridine

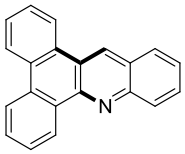
Note: The numbers in the structure are gave in random, thus not consistent with those in chemical nomenclature.

30.7 mg (50% yield), light yellow solid, m.p.: 188–189 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.27 (s, C21-H), 9.10 (s, C8-H), 8.57 (dd, *J* = 6.8, 2.5 Hz, C11-H), 8.49 (dd, *J* = 6.9, 2.5 Hz, C14-H), 8.36 (d, *J* = 8.3 Hz, C17-H), 7.82 (d, *J* = 8.2 Hz, C5-H), 7.64–7.57 (m, C3-H, C13-H and C12-H), 7.52 (dd, *J* = 8.3, 1.7 Hz, C18-H), 7.46 (dd, *J* = 8.1, 7.0 Hz, C4-H), 3.04 (s, C1-H_3), 2.65 (s, C20-H_3) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.5 (s), 146.3 (s), 137.4 (s, 2C), 131.5 (s), 130.7 (d, C18), 130.1 (d, C8), 130.0 (s), 129.6 (s), 129.4 (d, C13), 128.8 (s), 127.9 (d, C3), 126.99 (d, C12), 126.95 (s), 126.1 (d, C21), 126.0 (d, C5), 125.9 (d, C4), 123.5 (d, C11), 123.2 (d, C14), 123.1 (s), 122.6 (d, C17), 21.8 (q, C20), 18.1 (q, C1) ppm; **IR** (reflection): $\tilde{\nu}$ 3038, 2915, 1613, 1599, 1572, 1551, 1510, 1491, 1422, 1400, 1377, 1352, 1263, 1236, 1187, 1154, 1081, 1039, 900, 885, 858, 817, 803, 757, 727, 702, 663 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{17}N]^+$ $(M)^+$: 307.1356; found: 307.1346.



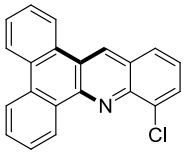
3ub: 13-methylbenzo[*a*]naphtho[1,2-*c*]acridine

28.2 mg (41% yield), yellow solid, m.p.: 168–169 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.59 (d, *J* = 8.6 Hz, 1H), 9.29 (s, 1H), 8.97 (d, *J* = 7.5 Hz, 1H), 8.88 (d, *J* = 7.8 Hz, 1H), 8.76 (d, *J* = 7.4 Hz, 1H), 8.09–8.05 (m, 2H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.72–7.61 (m, 5H), 7.51 (t, *J* = 7.5 Hz, 1H), 3.08 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.0 (s), 146.2 (s), 137.5 (s), 135.1 (s), 130.4 (s), 130.3 (s), 129.97 (d), 129.95 (s), 129.9 (s), 129.7 (s), 129.6 (d), 129.5 (d), 128.6 (d), 128.1 (d), 128.0 (d), 127.0 (d, 2C), 126.9 (d), 126.4 (d), 126.1 (d), 126.02 (d), 125.98 (d), 123.9 (d), 123.2 (s), 123.0 (d), 18.2 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3072, 3044, 2953, 2918, 1916, 1765, 1618, 1595, 1546, 1495, 1478, 1440, 1401, 1382, 1299, 1275, 1247, 1214, 1192, 1155, 1144, 1126, 1113, 1079, 1053, 1031, 937, 899, 883, 858, 826, 794, 769, 746, 714, 659, 632, 608 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{17}N]^+$ $(M)^+$: 343.1356; found: 343.1345.



3aa: dibenzo[*a*,*c*]acridine

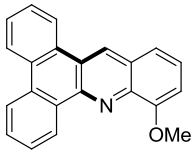
22.3 mg (40% yield), yellow solid, m.p.: 194–195 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.25 (s, 1H), 8.92–8.31 (m, 4H), 7.98 (d, *J* = 7.5 Hz, 1H), 7.91–7.46 (m, 6H) ppm; **^{13}C NMR** (75 MHz, $Cl_2CDCDCl_2$, 80 °C) δ 145.8 (s), 144.3 (s), 133.7 (d), 133.7 (d), 133.0 (d), 132.9 (s), 132.0 (s), 131.4 (d), 129.8 (s), 129.1 (d), 128.3 (d), 128.2 (d), 127.9 (s), 127.7 (d), 127.4 (d), 127.0 (s), 126.9 (d), 123.9 (s), 123.8 (d), 123.7 (d), 123.1 (d) ppm; **IR** (reflection): $\tilde{\nu}$ 3067, 3030, 2801, 1634, 1611, 1526, 1501, 1475, 1458, 1444, 1380, 1344, 1265, 1252, 1227, 1183, 1159, 1094, 1036, 966, 925, 893, 877, 802, 754, 715, 699, 681, 617 cm^{-1}; **HRMS** (DART) calcd for $[C_{21}H_{14}N]^+$ $(M+H)^+$: 280.1121; found: 280.1118.



3ac: 10-chlorodibenzo[*a*,*c*]acridine

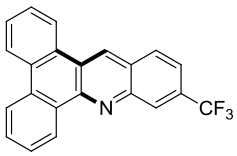
15.6 mg (20% yield), light yellow solid, m.p.: 216–217 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.65–9.63 (m, 1H), 9.28 (s, 1H), 8.67 (d, *J* = 7.4 Hz, 1H), 8.61 (d, *J* = 7.4 Hz, 1H), 8.56–8.54 (m, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 1H), 7.80–7.75 (m, 2H), 7.73–7.67 (m, 2H), 7.51 (t, *J* = 7.8 Hz, 1H) ppm;

^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0 (s), 143.5 (s), 133.8 (s), 132.2 (s), 131.1 (s), 130.6 (d), 130.2 (s), 130.0 (d), 129.6 (d), 128.7 (s), 128.6 (d), 128.2 (s), 128.0 (d), 127.7 (d), 127.1 (d), 126.9 (d), 125.9 (d), 124.1 (s), 123.8 (d), 123.7 (d), 122.6 (d) ppm; **IR** (reflection): $\tilde{\nu}$ 3073, 2923, 2854, 1738, 1611, 1599, 1541, 1492, 1450, 1406, 1378, 1346, 1263, 1228, 1205, 1192, 1161, 1128, 1049, 1036, 989, 970, 962, 942, 913, 891, 853, 805, 790, 759, 722, 700, 689, 669, 617 cm^{-1}; **HRMS** (DART) calcd for $[C_{21}H_{13}ClN]^+$ $(M+H)^+$: 314.0731; found: 314.0729.



3ad: 10-methoxydibenzo[*a*,*c*]acridine

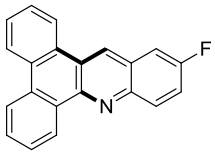
26.6 mg (43% yield), yellow solid, m.p.: 220–221 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.58 (dd, *J* = 6.1, 3.2 Hz, 1H), 9.29 (s, 1H), 8.71–8.69 (m, 1H), 8.63–8.61 (m, 1H), 8.57–8.55 (m, 1H), 7.77–7.75 (m, 2H), 7.72–7.65 (m, 3H), 7.53 (t, *J* = 7.9 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 1H), 4.21 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.4 (s), 146.6 (s), 139.9 (s), 131.9 (s), 131.2 (s), 130.3 (d), 130.1 (s), 129.6 (d), 129.0 (s, 2C), 128.3 (d), 127.8 (d), 127.6 (d), 126.7 (d), 126.4 (d), 123.8 (s), 123.7 (d), 123.6 (d), 122.6 (d), 120.0 (d), 107.6 (d), 56.4 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2917, 2849, 1737, 1619, 1550, 1493, 1462, 1409, 1387, 1356, 1265, 1255, 1239, 1135, 1111, 1000, 957, 908, 862, 794, 762, 724 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{15}NO]^+$ $(M)^+$: 309.1148; found: 309.1140.



3ae: 11-(trifluoromethyl)dibenzo[*a*,*c*]acridine

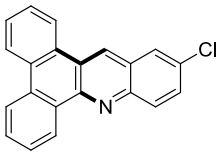
25.7 mg (37% yield), light yellow solid, m.p.: 165–166 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.48 (dd, *J* = 7.7, 1.6 Hz, 1H), 9.25 (s, 1H), 8.65–8.52 (m, 4H), 8.13 (d, *J* = 8.6 Hz, 1H), 7.80–7.66 (m, 5H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.8 (s), 146.2 (s), 132.2 (s), 131.3 (s, q: $J_{C\text{-}F}$ = 32.5 Hz), 130.7 (s), 130.23 (s), 130.16 (d), 129.9 (d), 129.2 (d), 128.8 (d), 128.6 (s), 128.1 (s), 127.9 (d), 127.8 (d), 127.4 (d, q: $J_{C\text{-}F}$ = 4.5 Hz), 126.4 (d), 124.9 (s), 124.15 (s, q: $J_{C\text{-}F}$ = 272.5 Hz), 123.9 (d), 123.7 (d), 122.7 (d), 121.5 (d, q: $J_{C\text{-}F}$ = 3.0 Hz) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -62.64 ppm; **IR** (reflection): $\tilde{\nu}$ 3071, 3032, 2923, 1738, 1637, 1598, 1494, 1479, 1454, 1435, 1421, 1386, 1333, 1301, 1283, 1256, 1212, 1195, 1168,

1143, 1101, 1054, 1036, 965, 927, 901, 891, 825, 798, 777, 752, 718, 700, 656, 617 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{12}NF_3]^+$ $(M)^+$: 347.0916; found: 347.0910.



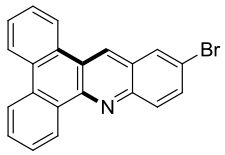
3af: 12-fluorodibenzo[*a*,*c*]acridine

20.8 mg (35% yield), light yellow solid, m.p.: 191–192 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 9.16 (s, 1H), 8.63–8.52 (m, 3H), 8.30 (dd, *J* = 9.2, 5.4 Hz, 1H), 7.77–7.56 (m, 6H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.3 (s, d: $J_{C\text{-}F}$ = 248.5 Hz), 147.1 (s, d: $J_{C\text{-}F}$ = 2.6 Hz), 144.7 (s), 132.1 (d), 132.0 (d), 131.9 (s), 131.0 (s), 130.1 (s), 129.7 (d), 129.4 (d, d: $J_{C\text{-}F}$ = 6.2 Hz), 128.7 (s), 128.5 (d), 127.8 (d), 127.7 (d), 127.4 (s, d: $J_{C\text{-}F}$ = 10.2 Hz), 126.1 (d), 123.9 (s), 123.7 (d, d: $J_{C\text{-}F}$ = 16.2 Hz), 122.7 (d), 120.6 (d, d: $J_{C\text{-}F}$ = 26.6 Hz), 110.3 (d, d: $J_{C\text{-}F}$ = 21.6 Hz) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -113.44 ppm; **IR** (reflection): $\tilde{\nu}$ 3071, 2923, 1911, 1703, 1630, 1605, 1548, 1504, 1493, 1474, 1437, 1380, 1346, 1302, 1263, 1230, 1205, 1173, 1150, 1119, 1051, 1037, 973, 950, 897, 852, 825, 775, 747, 717, 700, 679, 624 cm^{-1}; **HRMS** (EI) calcd for $[C_{21}H_{12}NF]^+$ $(M)^+$: 297.0948; found: 297.0956.



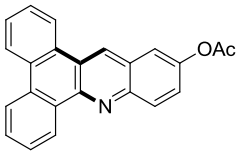
3ag: 12-chlorodibenzo[*a*,*c*]acridine

16.9 mg (27% yield), light yellow solid, m.p.: 228–229 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.49–9.47 (m, 1H), 9.17 (s, 1H), 8.60 (ddd, *J* = 31.3, 16.5, 7.5 Hz, 3H), 8.26 (d, *J* = 9.0 Hz, 1H), 8.02 (d, *J* = 2.1 Hz, 1H), 7.79–7.66 (m, 5H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.8 (s), 145.8 (s), 132.1 (s), 131.9 (s), 131.1 (d), 130.8 (d), 130.1 (s), 129.9 (d), 129.2 (d), 128.7 (s), 128.6 (d), 127.9 (d), 127.8 (d), 127.5 (s, 2C), 126.4 (d), 126.3 (d), 124.1 (s), 123.7 (d), 123.6 (d), 122.8 (d) ppm; **IR** (reflection): $\tilde{\nu}$ 1702, 1598, 1576, 1542, 1499, 1489, 1463, 1427, 1378, 1342, 1302, 1259, 1231, 1189, 1128, 1068, 1049, 1035, 960, 917, 906, 875, 861, 822, 797, 781, 761, 721, 698, 653, 619 cm^{-1}; **HRMS** (EI) calcd for $[C_{21}H_{12}NCl]^+$ $(M)^+$: 313.0653; found: 313.0656.



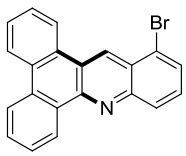
3ah: 12-bromodibenzo[*a*,*c*]acridine

26.5 mg (37% yield), light yellow solid, m.p.: 237–238 °C; **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 9.45 (d, *J* = 7.9 Hz, 1H), 9.21 (s, 1H), 8.67 (dd, *J* = 6.4, 2.8 Hz, 1H), 8.62–8.60 (m, 1H), 8.57 (d, *J* = 7.9 Hz, 1H), 8.25 (d, *J* = 1.9 Hz, 1H), 8.16 (d, *J* = 9.0 Hz, 1H), 7.86 (dd, *J* = 9.0, 2.1 Hz, 1H), 7.80–7.68 (m, 4H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 147.9 (s), 146.0 (s), 133.2 (d), 132.2 (s), 131.1 (d), 130.9 (s), 123.0 (s), 129.91 (d), 129.90 (d), 129.2 (d), 128.8 (s), 128.6 (d), 128.1 (s), 127.83 (d), 127.81 (d), 126.1 (d), 124.0 (s), 123.8 (d), 123.6 (d), 122.8 (d), 119.9 (s) ppm; **IR** (reflection): $\tilde{\nu}$ 1707, 1597, 1575, 1489, 1458, 1421, 1378, 1342, 1302, 1259, 1231, 1189, 1167, 1129, 1055, 1034, 983, 960, 907, 878, 863, 826, 798, 781, 762, 722, 697, 639, 617 cm^{-1}; **HRMS** (EI) calcd for $[C_{21}H_{12}NBr]^+$ $(M)^+$: 357.0148; found: 357.0145.



3ai: dibenzo[*a*,*c*]acridin-12-yl acetate

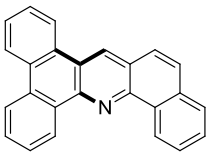
30.4 mg (45% yield), light yellow solid, m.p.: 213–214 °C; **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 9.45 (dd, *J* = 7.8, 1.3 Hz, 1H), 9.24 (s, 1H), 8.66–8.64 (m, 1H), 8.60–8.58 (m, 1H), 8.55 (d, *J* = 7.8 Hz, 1H), 8.28 (d, *J* = 9.1 Hz, 1H), 7.79–7.66 (m, 5H), 7.55 (dd, *J* = 9.1, 2.5 Hz, 1H), 2.38 (s, 3H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 169.5 (s), 148.5 (s), 147.4 (s), 145.5 (s), 132.0 (s), 131.0 (s), 130.8 (d), 129.90 (s), 129.85 (d), 129.7 (d), 128.9 (s), 128.4 (d), 127.74 (d), 127.72 (d), 127.2 (s), 126.0 (d), 125.6 (d), 123.73 (d), 123.70 (s), 123.5 (d), 122.7 (d), 118.2 (d), 21.0 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3070, 2924, 1920, 1742, 1632, 1601, 1548, 1504, 1493, 1474, 1437, 1384, 1370, 1343, 1295, 1261, 1217, 1150, 1133, 1036, 1015, 969, 959, 947, 915, 902, 865, 847, 831, 784, 744, 716, 701, 655, 627 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{15}NO_2]^+$ $(M)^+$: 337.1097; found: 337.1102.



3aj: 13-bromodibenzo[*a*,*c*]acridine

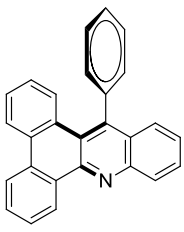
17.1 mg (24% yield), light yellow solid, m.p.: 264–265 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.52 (d, *J* = 7.9 Hz, 1H), 8.80–8.78 (m, 1H), 8.63–8.61 (m, 1H), 8.58 (d, *J* = 7.9 Hz, 1H), 8.32 (d, *J* = 8.3 Hz,

1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.81–7.72 (m, 4H), 7.66 (t, *J* = 7.9 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 148.2 (s), 147.9 (s), 132.4 (s), 130.5 (s), 130.1 (s), 130.11 (d), 130.05 (s), 130.0 (d), 129.8 (d), 129.4 (d), 128.9 (d), 128.7 (d), 127.88 (d), 127.87 (d), 126.6 (d), 126.5 (s), 124.4 (s), 124.1 (d), 123.6 (d), 122.8 (d), 122.1 (s) ppm; **IR** (reflection): $\tilde{\nu}$ 3068, 2922, 2852, 1738, 1602, 1563, 1536, 1490, 1456, 1393, 1371, 1330, 1295, 1261, 1231, 1207, 1177, 1129, 1032, 969, 897, 861, 837, 809, 794, 778, 758, 718, 698, 684, 658, 611 cm^{-1}; **HRMS** (EI) calcd for $[C_{21}H_{12}NBr]^+$ $(M)^+$: 357.0148; found: 357.0155.



3ak: tribenzo[*a*,*c*,*h*]acridine

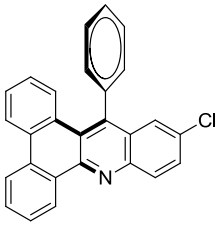
22.4 mg (34% yield), light yellow solid, m.p.: 205–206 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.73 (d, *J* = 7.0 Hz, 1H), 9.65 (d, *J* = 7.8 Hz, 1H), 9.19 (s, 1H), 8.62 (dd, *J* = 34.1, 15.7 Hz, 3H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.85–7.69 (m, 8H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.72 (s), 145.70 (s), 133.9 (s), 131.8 (s), 131.7 (s), 131.5 (s), 129.9 (s), 129.8 (d), 129.2 (d), 129.1 (s), 128.5 (d), 127.93 (d), 127.89 (d), 127.7 (d), 127.6 (d), 127.5 (d), 127.1 (d), 126.2 (d), 125.7 (d), 125.4 (s, 2C), 125.0 (d), 123.53 (d), 123.52 (d), 122.7 (d) ppm; **IR** (reflection): $\tilde{\nu}$ 3067, 3033, 1594, 1571, 1550, 1502, 1485, 1465, 1442, 1404, 1391, 1315, 1237, 1198, 1170, 1151, 1127, 1110, 1066, 1047, 1029, 1016, 955, 904, 876, 859, 817, 803, 760, 747, 722, 700, 672, 625, 617 cm^{-1}; **HRMS** (DART) calcd for $[C_{25}H_{16}N]^+$ $(M+H)^+$: 330.1277; found: 330.1274.



3al: 14-phenyldibenzo[*a*,*c*]acridine

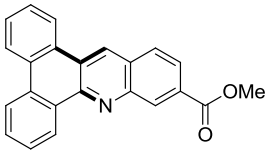
35.5 mg (50% yield), yellow solid, m.p.: 245–246 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.53–9.51 (m, 1H), 8.51 (t, *J* = 7.0 Hz, 2H), 8.32 (d, *J* = 8.4 Hz, 1H), 7.80–7.71 (m, 3H), 7.67–7.55 (m, 5H), 7.48–7.41 (m, 4H), 7.04 (t, *J* = 7.7 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 148.1 (s), 146.7 (s), 145.5 (s), 139.9 (s), 132.2 (s), 131.5 (s), 131.3 (s), 129.98 (d), 129.97 (d, 2C), 129.8 (s), 129.7 (d), 129.5 (d, 2C), 129.4 (d), 129.3 (d), 128.2 (d), 127.7 (d), 127.4 (d), 127.1 (s), 126.64 (d), 126.57 (d), 126.0 (d), 125.9 (d), 123.4 (d), 122.5 (d), 121.5 (s)

ppm; **IR** (reflection): $\tilde{\nu}$ 3062, 2923, 1953, 1739, 1606, 1587, 1565, 1539, 1502, 1489, 1471, 1454, 1442, 1397, 1369, 1354, 1255, 1237, 1176, 1126, 1107, 1073, 1044, 1027, 976, 960, 865, 850, 812, 782, 758, 723, 703, 685, 642, 613 cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{18}N]^+$ $(M+H)^+$: 356.1434; found: 356.1430.



3am: 12-chloro-14-phenyldibenzo[*a*,*c*]acridine

23.4 mg (57% yield), light yellow solid, m.p.: 222–223 °C; **^{1}H NMR** (600 MHz, CD_2Cl_2) δ 9.48 (dd, *J* = 7.9, 1.4 Hz, 1H), 8.51 (t, *J* = 8.2 Hz, 2H), 8.27 (d, *J* = 8.9 Hz, 1H), 7.76–7.70 (m, 3H), 7.65–7.60 (m, 4H), 7.52 (d, *J* = 8.4 Hz, 1H), 7.49–7.46 (m, 1H), 7.40–7.39 (m, 2H), 7.05–7.02 (m, 1H) ppm; **^{13}C NMR** (150 MHz, CD_2Cl_2) δ 148.7 (s), 145.3 (s), 145.0 (s), 139.6 (s), 132.6 (s), 132.0 (s), 131.8 (s), 131.6 (s), 131.4 (d), 130.6 (d), 130.4 (d), 130.2 (d), 130.1 (d, 2C), 130.0 (d, 2C), 129.7 (s), 128.8 (d), 128.12 (d), 128.06 (s), 128.0 (d), 126.8 (d), 126.3 (d), 125.5 (d), 123.7 (d), 122.8 (d), 122.5 (s) ppm; **IR** (reflection): $\tilde{\nu}$ 3062, 2924, 2853, 1734, 1606, 1566, 1538, 1497, 1465, 1442, 1419, 1398, 1353, 1339, 1262, 1230, 1197, 1182, 1125, 1106, 1078, 1041, 1028, 978, 957, 923, 874, 828, 805, 781, 763, 742, 723, 705, 681, 657, 626, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{27}H_{16}NCl]^+$ $(M)^+$: 389.0966; found: 389.0962.



3an: methyl dibenzo[*a*,*c*]acridine-11-carboxylate

25.6 mg (38% yield), light yellow solid, m.p.: 230–231 °C; **^{1}H NMR** (500 MHz, $Cl_2CDCDCl_2$) δ 9.42 (d, *J* = 7.0 Hz, 1H), 9.17 (s, 1H), 8.93 (s, 1H), 8.59–8.48 (m, 3H), 8.07 (dd, *J* = 38.5, 7.7 Hz, 2H), 7.77–7.65 (m, 4H), 4.02 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $Cl_2CDCDCl_2$) δ 167.1 (s), 148.4 (s), 146.4 (s), 132.2 (d), 132.1 (s), 131.0 (s), 130.6 (s), 130.3 (d), 130.1 (s), 130.0 (d), 129.2 (s), 129.0 (d), 128.6 (s), 128.5 (d), 128.1 (d), 128.0 (d), 126.4 (d), 125.4 (d), 124.8 (s), 124.1 (d), 123.7 (d), 122.9 (d), 52.8 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3072, 3028, 2952, 2841, 1712, 1601, 1567, 1491, 1477, 1453, 1435, 1387, 1316, 1297, 1270, 1250, 1210, 1191, 1139, 1094, 1078, 1036, 978, 960, 903, 806, 756, 721, 707, 618 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{15}NO_2]^+$ $(M)^+$: 337.1097; found: 337.1082.

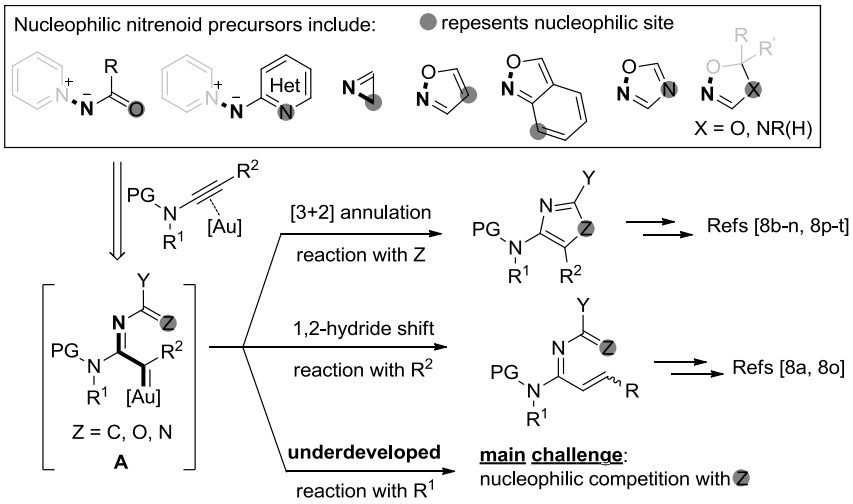
Chapter 4: Gold(III)-Catalyzed Site-Selective and Divergent Synthesis of 2-Aminopyrroles and Quinoline-Embedded Polyazaheterocycles

4.1 Introduction

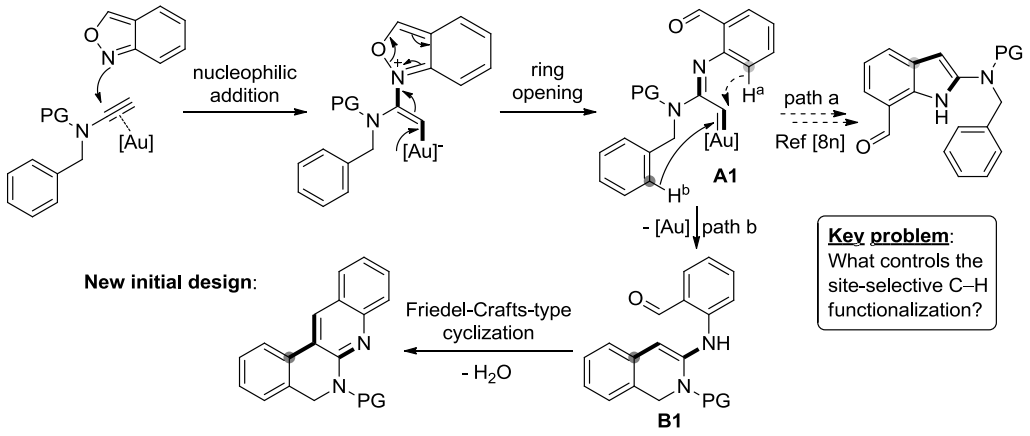
The efficient and rapid synthesis of azaheterocycles is of significance for synthetic and medicinal chemistry.[1] 2-Aminopyrroles[2] as well as quinoline-fused polyazaheterocycles, such as pyrrolo[2,3-*b*]quinoline[3] and dihydrodibenzo[*b,f*][1,8]naphthyridine derivatives,[4,5f] are fundamental motifs in numerous pharmaceuticals, natural products, and organic functional materials. Several synthetic routes towards these quinoline-fused polyazaheterocycles have been developed.[5] However, most methods involve multiple-step synthesis from the relevant quinoline precursors, and suffer from low functional group tolerance.[5] More importantly, the installation of a propenal side chain to the parent pyrrole ring is also a challenge, making it difficult to construct the pyrrolo[2,3-*b*]quinolines with such a valuable grip.[5a-d] To this end, the development of a novel, general, and environmentally benign method towards these polyazaheterocycles in a selective and divergent fashion from easily accessible starting materials is still highly desired.

Recent rapid advances in gold carbene-promoted reactions have provided efficient and powerful strategies to access complex and diverse carbon- and azaheterocycles.[6] In this context, gold-catalyzed intra-/intermolecular nitrene transfers of azide moieties onto carbon-carbon triple bonds were used to prepare different azaheterocycles, including pyrroles,[7a-c] indoles,[7d-h] imidazoles,[7i] (iso)quinolines,[7j-m] and others.[7n-o] The azide moieties were generally introduced from sodium azide, a toxic and potentially explosive reagent. Intermolecular protocols to access α-imino gold carbene intermediates from non-toxic, safe and easily available nitrenoid precursors, are more practical and flexible. In line with this principle, various nitrenoid equivalents have been realized for intermolecular nitrene-transfer processes to ynamides, generating

highly electrophilic gold carbene intermediates **A**.[8] Typically, a nucleophilic functionality tethered on the nitrene-transfer reagent traps the gold carbene, leading to formal [3+2] cycloadducts (Scheme 1, upper);[8] or a new C–C double bond is formed via a 1,2-hydride shift if the α-hydrogens exist (middle).[8a,8o] The site-selective trapping by the R^1 substituent at the ynamide is more challenging, as the competing nucleophilic site Z can induce undesired side reactions. Recently, we disclosed a gold(I)-catalyzed synthesis of 7-acylindoles via the C–H^a annulation between alkynes and anthranils by exploiting the potential binucleophilicity of anthranils (Scheme 2, path a).[8n] We envisioned that the *in-situ* generated α-imino gold carbene species **A1** could be quenched by the C–H^b bond of *N*-benzyl ynamides as alternative to the C–H^a insertion known from the indole synthesis.[8n] Finally, the desired quinoline-embedded polyazaheterocycles would be formed via a Friedel-Crafts-type cyclization of intermediate **B1**.



Scheme 1. Different site-selective reaction patterns of α-amino gold carbene intermediates.



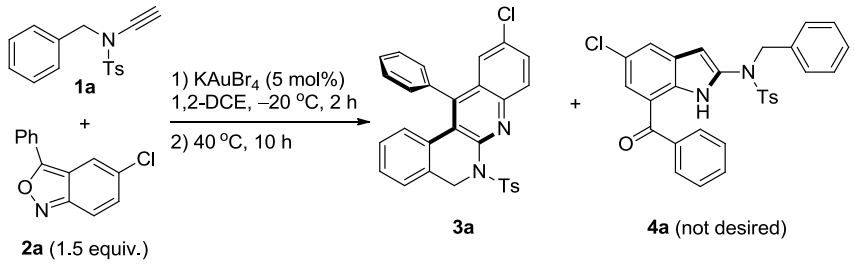
Scheme 2. Site-selective C–H functionalization of gold carbene intermediates. path a: our previous work; path b: present new initial design.

4.2 Results and Discussion

4.2.1 Optimization of Reaction Condition

To evaluate the feasibility, *N*-benzyl ynamide **1a** and anthranil **2a** were initially chosen as the model reaction (Table 1). After various screenings, a "standard condition" (5 mol% $KAuBr_4$ in 1,2-DCE at –20 ^oC for 2 h; then heating to 40 ^oC for 10 h) was obtained, which delivered product **3a** in 50% isolated yield accompanied by a small amount of the undesired indole product **4a** (Table 1, entry 1). Other tested gold(III) catalysts gave a similar proportion between **3a** and **4a** (entries 2–5). Switching to the cationic gold(I) complex favored the formation of indole product while the unactivated catalyst delivered messy conversion (entries 6–7). Unexpectedly, neutral ligand-free AuCl also worked in a selective manner, affording **3a** in 43% yield (about 5:1 **3a**:**4a**; entry 8). $PhCF_3$ as reaction medium did not improve the efficiency (entry 9). The control experiment in the absence of catalyst showed no conversion (entry 10).

Table 1: Representative examples from the optimization of the reaction conditions.[a]



entry	deviation from "standard" conditions	yield of **3a**[b]	yield of **4a**[b]
1	none	54% (50%)	9
2	$NaAuBr_4$ as catalyst	50	14
3	$HAuBr_4$ as catalyst	49	15
4	$AuBr_3$ as catalyst	45	17
5	$PicAuCl_2$ as catalyst	47	14
6	$IPrAuCl/AgNTf_2$ as catalyst	27	37
7	IPrAuCl as catalyst	trace	trace
8	10 mol % AuCl as catalyst	43	8
9	$PhCF_3$ instead of 1,2-DCE	48	12
10	no $KAuBr_4$	-	-

[a] "Standard" conditions: a solution of **1a** (0.1 mmol) in 1,2-DCE (0.5 mL) was added over 5 mins to a mixture of **2a** (0.15 mmol), $KAuBr_4$ (5 mol%) in 1,2-DCE (0.5 mL) at –20 °C and after 2 h the reaction mixture was heated to 40 °C for 10 h. [b] Measured by ^1H NMR with 1,3,5-trimethoxybenzene as the internal standard. Yield of isolated product given in parentheses.

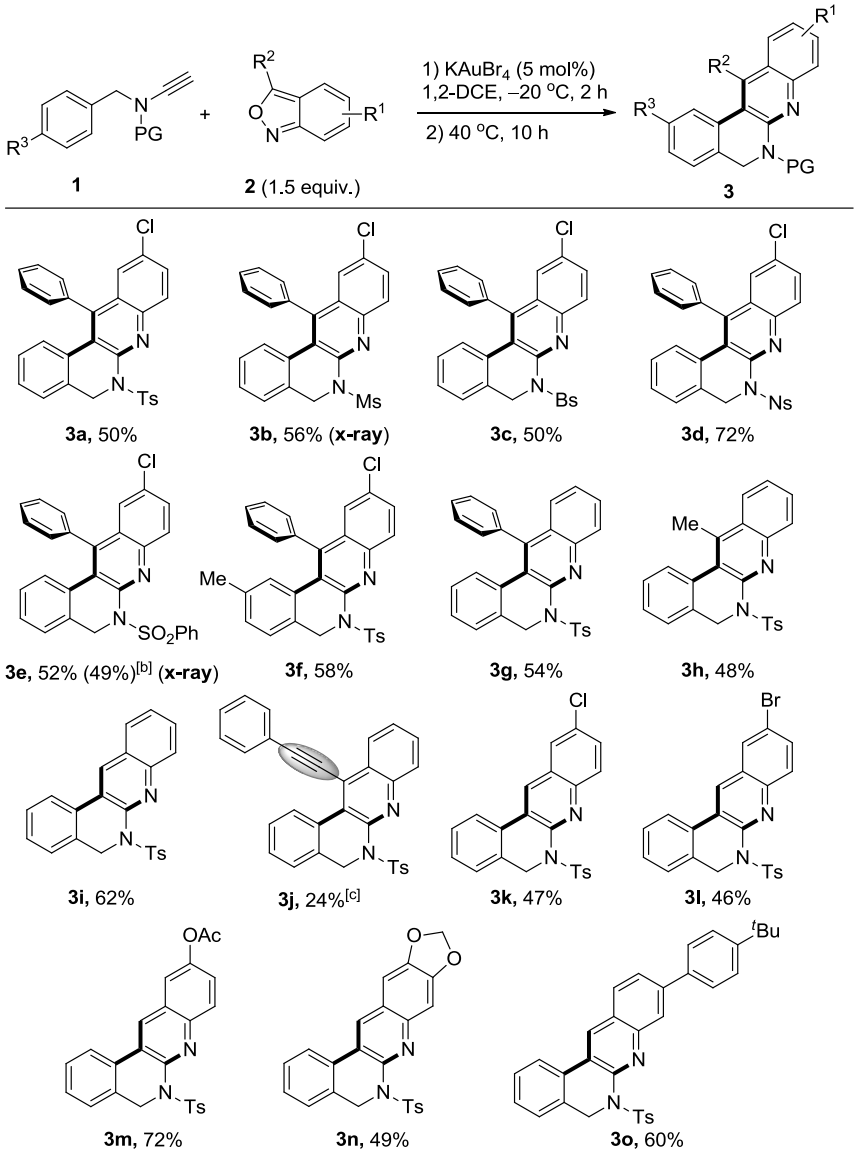
4.2.2 Scope with regard to the Substrate

Under the optimized conditions, a diverse set of *N*-benzyl ynamides with different anthranils were first tested (Table 2). Ynamides bearing different protecting groups (Ms, Ts, Bs, Ns, SO_2Ph) on nitrogen reacted quite well with anthranil **2a**, giving **3a–e** in satisfying yields. A scale-up (1 mmol) synthesis of **3e** provided a slightly lower yield. A tolyl group in **3f** delivered 58% yield. Various substituted anthranils were

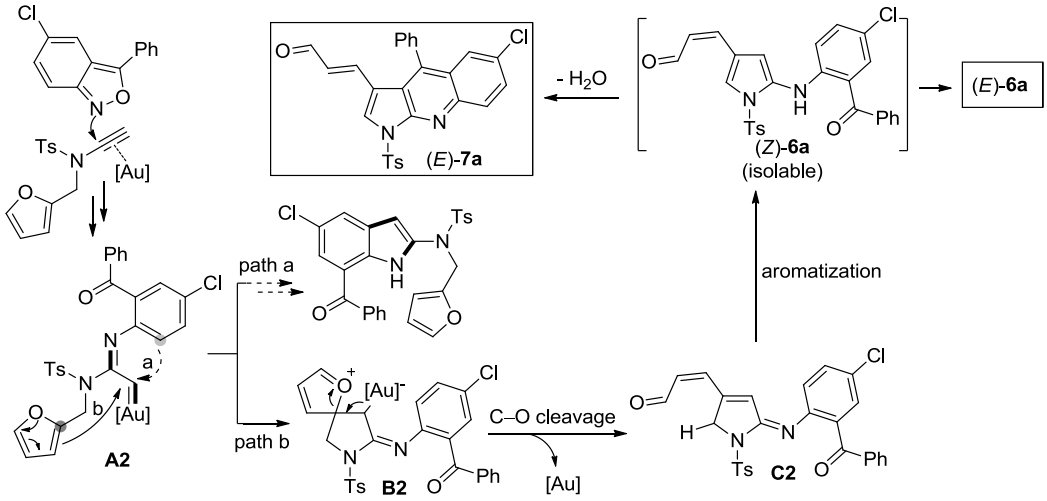
then examined. Besides the phenyl group (**3g**), methyl or hydrogen at the R^2 position afforded the desired products **3h** or **3i** in 48% and 62% yields, respectively. A less-polar carbon-carbon triple bond, that was also reactive in our previous work, remained intact.[8n] The obtained product **3j** emitted violet-blue fluorescence (Φ_F = 0.21), somewhat showcasing the importance of the compatibility with such a triple bond.[9] Besides, some other functional groups including chloride (**3k**), bromide (**3l**), ester (**3m**) and acetal (**3n**) were well tolerant, thus allowing for further derivatization. If an aryl group was introduced at the C6 position of anthranils, **3o** was obtained in 60% yield. For the structural assignments of these products, single-crystal X-ray structure analyses of **3b** and **3e** were conducted.[9]

Ynamides with an electron-rich heteroaromatic system which has the potential to serve as an alternative nucleophilic site to trap the gold carbene intermediate were also tested. Under the above optimum condition, it was found that the treatment of *N*-furanylmethyl ynamide **5a** and anthranil **2a** proceeded well. However, the above expected tetracyclic *N*-heterocycles derived by C3–H insertion into the gold carbene were not obtained; instead pyrrole (*E*)-**6a** was isolated in 69% yield. Despite being thermodynamically less stable than its *E* isomer, the isolation of (*Z*)-**6a** was also viable by just omitting the subsequent warming, which suggests the latter was likely to be generated first via a ring opening of furan by the regioselective attack of the C2-position to the gold carbene (Scheme 3). The primary product can be further transformed to the thermodynamically stable (*E*)-isomer **6a** or to tricyclic azaheterocycles (*E*)-**7a** via a Friedel-Crafts-type cyclization driven by heating or/and Lewis acid.

Table 2: Substrate scope of *N*-benzyl ynamides and anthranils.[a]



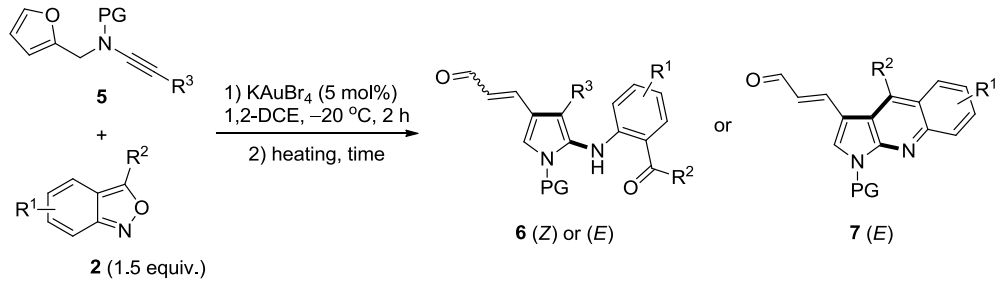
[a] Reaction conditions: a solution of **1** (0.12 mmol) in 1,2-DCE (1.2 mL) was added over 6 mins to a mixture of **2** (0.18 mmol), $KAuBr_4$ (5 mol%) in 1,2-DCE (1.2 mL) at –20 °C and after 2 h the reaction mixture was heated to 40 °C for 10 h; yield of isolated product. [b] 1 mmol scale. [c] heating to 80 °C for 10 h.



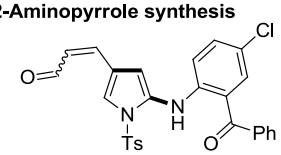
Scheme 3. Proposed mechanism towards 2-aminopyrroles and related derivatives

This synthetic strategy features the ability to deliver 2-aminopyrroles **6** with a propenal side chain at C4 position. The location of such a versatile handle at this position is not so easy to be introduced, thus distinguishing this method for pyrrole synthesis.[10] Besides, a myriad of potential derivatization for the enal moiety could be anticipated, such as cycloaddition and some textbook transformations (oxidation, reduction and Michael addition).[11] With this in mind, various 2-aminopyrroles **6** were first investigated from anthranils and *N*-furanylmethyl ynamide **5a** under the adjusted reaction temperature. Aromatic (**6b**), aliphatic (**6c** and **6d**) and electron-neutral (**6f**–**i**) substituents could be attached to the R^2 position, providing the desired products in moderate to good yield. Again, a carbon-carbon triple bond was possible to be pre-installed on the anthranil substrate (**6e**). Other functional groups such as chloride (**6a**), methoxy (**6d** and **6f**), ester (**6g**), acetal (**6h**) were well tolerated. While internal *N*-benzyl ynamides were unsuccessful for the synthesis of **3**, the corresponding internal *N*-furanylmethyl derivative was converted into trisubstituted pyrrole **6j**. At a relatively higher reaction temperature, some pyrrole-fused compounds **7** were also accessible in 35–59% yields via a one-pot process. A 45% yield of **7a** was acquired on a 1 mmol scale and its constitutional isomerism was further verified by X-ray diffraction.[9]

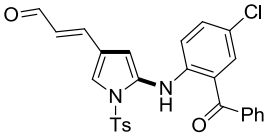
Table 3: Reaction scope between *N*-furanylmethyl ynamides and anthranils.[a]



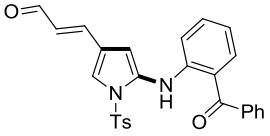
2-Aminopyrrole synthesis



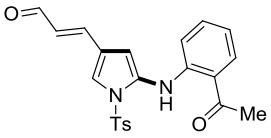
6a, 75% (*Z*/*E* 17:1)
(without heating)



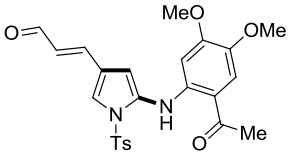
(*E*)-**6a,** 69%
(40 °C, 2 h)



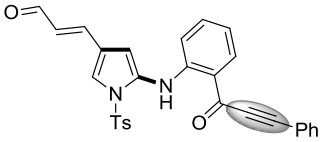
6b, 51%
(rt, 2 h)



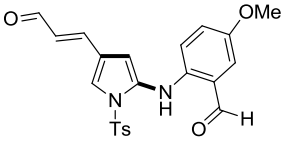
6c, 64%
(40 °C, 2 h)



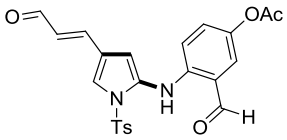
6d, 50%
(40 °C, 2 h)



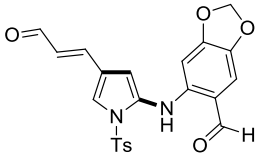
6e, 69%
(40 °C, 2 h)



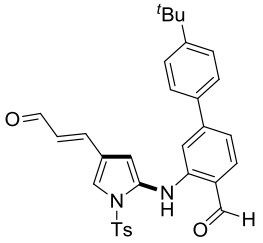
6f, 43%
(40 °C, 1 h)



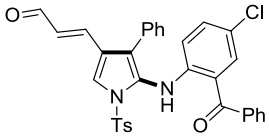
6g, 22%
(40 °C, 2 h)



6h, 60%
(40 °C, 2 h)

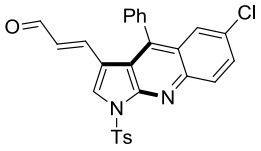


6i, 58%
(rt, 3 h)

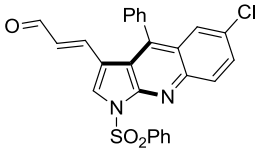


6j, 64%
(40 °C, 2 h)

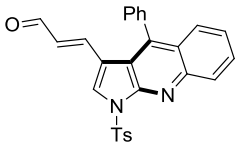
Pyrrolo[2,3-*b*]quinoline synthesis



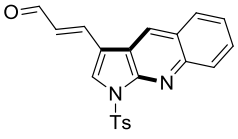
7a, 52% (45%)[b]
(**x-ray**) (60 °C, 4 h)



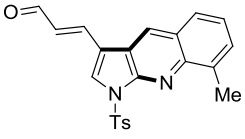
7b, 52%
(80 °C, 10 h)



7c, 59%
(60 °C, 10 h)



7d, 50%
(40 °C, 2 h)



7e, 35%
(40 °C, 10 h)

[a] Reaction conditions: a solution of **5** (0.12 mmol) in 1,2-DCE (1.2 mL) was added over 6 mins to a mixture of **2** (0.18 mmol), $KAuBr_4$ (5 mol%) in 1,2-DCE (1.2 mL) at –20 °C, and after 2 h the reaction mixture was heated for the given time; yield of isolated product. [b] 1 mmol scale.

4.3 Conclusion

In conclusion, an atom-economical, site-selective, divergent assembly of valuable and versatile 2-aminopyrroles and quinoline-fused polyazaheterocycles has been achieved. This protocol was enabled by a simple gold(III) catalyst leading to a preferable quenching of gold carbene intermediate by a nucleophilic functionality on the ynamides, complementary to the C–H annulation known from the indole synthesis. This will also open up a new window for the challenging intramolecular site-selective C–H functionalization. Unlike previous synthetic methods, our strategy features a one-step operation, easily accessible starting materials, good functional-group tolerance, and scale-up potential accompanied by a broad substrate scope. Further application of anthranils for the synthesis of (π-extended) *N*-doped polycyclic aromatics is ongoing in our lab.

4.4 Notes and References

[1] Selected examples: a) K. Moonen, I. Laureyn, C. V. Stevens, *Chem. Rev.* **2004**, *104*, 6177–6216; b) G. J. Tanoury, *Synthesis* **2016**, *48*, 2009–2025; c) J. Dolfen, N. N. Yadav, N. D. Kimpe, M. D'hooghe, H.-J. Ha, *Adv. Synth. Catal.* **2016**, *358*, 3485–3511; d) Z. Zeng, H. Jin, X. Song, Q. Wang, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Chem. Commun.* **2017**, *53*, 4304–4307.

[2] For selected examples, see: a) S. M. Bennett, N. Nguyen-Ba, K. K. Ogilvie, *J. Med. Chem.* **1990**, *33*, 2162–2173; b) M. T. Cocco, C. Congiu, V. Onnis, *Bioorg. Med. Chem.* **2003**, *11*, 495–503; c) M. T. Migawa, J. C. Drach, L. B. Townsend, *J. Med. Chem.* **2005**, *48*, 3840–3851; d) A. Lauria, M. Bruno, P. Diana, P. Barraja, A. Montalbano, G. Cirrincione, G. Dattolo, A. M. Almerico, *Bioorg. Med. Chem.* **2005**, *13*, 1545–1553; e) H. Oda, T. Hanami, T. Iwashita, M. Kojima, M. Itoh, Y. Hayashizaki, *Tetrahedron* **2007**, *63*, 12747–1275338; f) V. Onnis, A. De Log, M. T. Cocco, R. Fadda, R. Meleddu, C. Congiu, *Eur. J. Med. Chem.* **2009**, *44*, 1288–1295; g) M. B. Wallace, M. E. Adams, T. Kanouni, C. D. Mol, D. R. Dougan, V. A. Feher, S.

M. O'Connell, L. Shi, P. Halkowycz, Q. Dong, *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4156–4158.

[3] For a review, see: M. A. Khan, J. F. da Rocha, *Heterocycles* **1977**, *6*, 1229–1246 and references cited therein.

[4] Selected examples, see: a) H. Misbahi, P. Brouant, A. Hever, A. M. Molnar, K. Wolfard, G. Spengler, H. Mefetah, J. Molnar, J. Barbe, *Anticancer Res.* **2002**, *22*, 2097; b) L. Fu, X. Feng, J.-J. Wang, Z. Xun, J.-J. Zhang, Y.-W. Zhao, Z.-B. Huang, D.-Q. Shi, *ACS Comb. Sci.* **2015**, *17*, 24; c) W. Tian, R. Yougnia, S. Depauw, A. Lansiaux, M. H. D. Cordonnier, B. Pfeiffer, L. K. Berthier, S. Leonce, A. Pierre, H. Dufat, S. Michel, *J. Med. Chem.* **2014**, *57*, 10329.

[5] For pyrrolo[2,3-*b*]quinoline synthesis, see: a) W. H. Perkin, jun., R. Robinson, *J. Chem. Soc., Trans.* **1913**, *103*, 1973–1985; b) M. Murugesan, N. Soundararajan, K. Ramasamy, P. Shanmugam, *Synthesis* **1979**, *5*, 352–354; c) M. L. Davis, B. J. Wakefield, J. A. Wardellt, *Tetrahedron* **1992**, *48*, 939–952; d) P. Molina, J. Alcántara, C. López-Leonardo, *Tetrahedron* **1997**, *53*, 3281–3286. For the synthesis of dibenzo[*b*,*f*][1,8]naphthyridine skeleton, see: e) L. M. Potikha, R. M. Gutsul, A. S. Plaskon, V. A. Kovtunenko, A. A. Tolmachev, *Chem. Heterocycl. Compd.* **2011**, *47*, 342–354; f) V. M. Sviripa, R. Burikhanov, J. M. Obiero, Y. Yuan, J. R. Nickell, L. P. Dwoskin, C.-G. Zhan, C. Liu, O. V. Tsodikov, V. M. Rangnekar, D. S. Watt, *Org. Biomol. Chem.* **2016**,*14*, 74–84; g) B. K. Villuri, A. Konala, V. Kavala, T. Kotipalli, C.-W. Kuo, C.-F. Yao, *Adv. Synth. Catal.* **2017**, *359*, 3142–3153.

[6] For selected reviews, see: a) I. Braun, A. M. Asiri, A. S. K. Hashmi, *ACS Catal.* **2013**, *3*, 1902–1907; b) L. Zhang, *Acc. Chem. Res.* **2014**, *47*, 877–888; c) P. W. Davies, M. Garzón, *Asian J. Org. Chem.* **2015**, *4*, 694–708; d) L. Liu, J. Zhang, *Chem. Soc. Rev.* **2016**, *45*, 506–516; e) L. Li, T.-D. Tan, Y.-Q. Zhang, X. L. L.-W. Ye, *Org. Biomol. Chem.* **2017**, *15*, 8483–8492.

[7] D. J. Gorin, N. R. Davis, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 11260–11261; b) Z.-Y. Yan, Y. Xiao, L. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 8624–8627; *Angew. Chem.* **2012**, *124*, 8752–8755; c) C. Shu, Y.-H. Wang, C.-H. Shen, P.-P. Ruan, Xin Lu, L.-W. Ye, *Org. Lett.* **2016**, *18*, 3254–3257; d) A. Wetzel, F. Gagosz, *Angew.*

Chem. Int. Ed. **2011**, *50*, 7354–7358; *Angew. Chem.* **2011**, *123*, 7492–7496; e) B. Lu, Y. Luo, L. Liu, L. Ye, Y. Wang, L. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 8358–8362; *Angew. Chem.* **2011**, *123*, 8508–8512; f) N. Li, T.-Y. Wang, L.-Z. Gong, L. Zhang, *Chem. Eur. J.* **2015**, *21*, 3585–3588; g) C.-H. Shen,Y. Pan, Y.-F. Yu, Z.-S. Wang, W. He, T. Li, L.-W. Ye, *J. Organomet. Chem.* **2015**, *795*, 63–67; h) C. Shu, Y.-H. Wang, B. Zhou, X.-L. Li, Y.-F. Ping, X. Lu, L.-W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567–9570; i) Y. Xiao, L. Zhang, *Org. Lett.* **2012**, *14*, 4662–4665; j) Z. Huo, Y. Yamamoto, *Tetrahedron Lett.* **2009**, *50*, 3651–3653; k) C. Gronnier, G. Boissonnat, F. Gagosz, *Org. Lett.* **2013**, *15*, 4234–4237; l) Y. Pan, G.-W. Chen, C.-H. Shen, W. He, L.-W. Ye, *Org. Chem. Front.* **2016**, *3*, 491–495; m) S. Zhu, L. Wu, X. Huang, *J. Org. Chem.* **2013**, *78*, 9120–9126; n) P.-P. Ruan, H.-Hao Li, X. Liu, T. Zhang, S.-X. Zuo, C. Zhu, L.-W. Ye, *J. Org. Chem.* **2017**, *82*, 9119–9125; o) W.-B. Shen, Q. Sun, L. Li, X. Liu, B. Zhou, J.-Z. Yan, X. Lu, L.-W. Ye. *Nat. Commun.* **2018**, *8*, 1748.

[8] For *N*-iminopyridiumylides, see: a) C. Li, L. Zhang, *Org. Lett.* **2011**, *13*, 1738–1741; b) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935; *Angew. Chem.* **2011**, *123*, 9093–9097; c) E. Chatzopoulou, P. W. Davies, *Chem. Commun.* **2013**, *49*, 8617–8619; d) H.-H. Hung, Y.-C. Liao, R.-S. Liu, *J. Org. Chem.* **2013**, *78*, 7970–7976; e) A. D. Gillie, R. J. Redd, P. W. Davies, *Adv. Synth. Catal.* **2016**, *358*, 226–239; f) R. J. Reddy, M. P. Ball-Jones, P. W. Davies, *Angew. Chem. Int. Ed.* **2017**, *56* ,13310–13313; *Angew. Chem.* **2017**, *129*, 13495–13498. For 2*H*-azirines, see: g) Y. Wu, L. Zhu, Y. Yu, X. Luo, X. Huang, *J. Org. Chem.* **2015**, *80*, 11407–11416; h) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33; i) S. K. Pawar, R. L. Sahani, R.-S. Liu, *Chem. Eur. J.* **2015**, *21*, 10843–10850. For isoxazoles, see: j) A.-H. Zhou, Q. He, C. Shu, Y.-F. Yu, S. Liu, T. Zhao, W. Zhang, X. Lu, L.-W. Ye, *Chem. Sci.* **2015**, *6*, 1265–1271; k) X.-Y. Xiao, A.-H. Zhou, C. Shu, F. Pan, T. Li, L.-W. Ye, *Chem. Asian J.* **2015**, *10*, 1854–1858; l) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 1026–1030; *Angew. Chem.* **2017**, *129*, 1046–1050; m) S. S. Giri, R.-S. Liu, *Chem. Sci.* **2018**, 9, 2991–2995. For anthranils, see: n) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; *Angew. Chem.* **2016**, *128*,

804–808; o) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *128*, 12880–12884; p) R. L. Sahani, R.-S. Liu, *Angew. Chem. Int. Ed.* **2017**, *56*, 12736–12740; *Angew. Chem.* **2017**, *129*, 12910–12914; q) Z. Zeng, H. Jin, K. Sekine, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2018**, *57*, 6935–6939; *Angew. Chem.* **2018**, *130*, 7051–7056. For 1,2,4-oxadiazoles, see: r) Z. Zeng, H. Jin, J. Xie, B. Tian, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Org. Lett.* **2017**, *19*, 1020–1023; For 1,4,2-dioxazoles and 4,5-dihydro-1,2,4-oxadiazoles, see: s) M. Chen, N. Sun, H. Chen, Y. Liu, *Chem. Commun.* **2016**, *52*, 6324–6327; t) W. Xu, G. Wang, N. Sun, Y. Liu, *Org. Lett.* **2017**, *19*, 3307–3310.

[9] CCDC 1840932 (**3b**), CCDC 1840933 (**3e**), and CCDC 1840931 (**7a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre. For the X-ray crystal structures and photophysical studies, see Supporting Information for details.

[10] For selected reviews, see: a) E. Baltazzi, L. I. Krimen, *Chem. Rev.* **1963**, *63*, 511–556; b) V. Est évez, M. Villacampa, J. C. Men éndez, *Chem. Soc. Rev.* **2010**, *39*, 4402–4421; c) V. Est évez, M. Villacampa, J. C. Men éndez, *Chem. Soc. Rev.* **2014**, *43*, 4633–4657; d) A. Sharma, P. Piplani, *J. Heterocyclic Chem.* **2017**, *54*, 27–34.

[11] For selected reviews, see: a) E. Marsault, A. Tor ó, P. Nowak, P. Deslongchamps, *Tetrahedron*, **2001**, *57*, 4243–4260; b) Z. Zeng, D. Yang, *Chin. J. Org. Chem.* **2013**, *33*, 2131–2142; c)V. Marcos, J. Alem án, *Chem. Soc. Rev.* **2016**, *45*, 6812–6832.

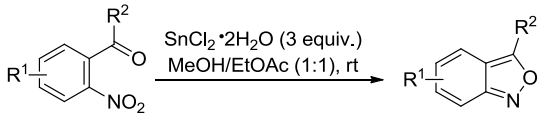
4.5 Experimental Section

General Remarks: Chemicals were purchased from commercial suppliers and used without further purification. Ynamide substrates **1** and **5** were easily prepared according to the previous literatures.[1] Dry solvents were dispensed from the solvent purification system MB SPS-800. Deuterated solvents were bought from Euriso-Top. Unless otherwise stated, NMR spectra were recorded at room temperature on the following spectrometers: Bruker Avance 400, 500 or 600. Chemical shifts were

referenced to residual solvent protons and reported in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). 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. HRMS were determined at the chemistry department of the University of Heidelberg. EI^+-spectra were measured on a JOEL JMS-700 spectrometer. For DART-spectra a Bruker ICR Apex-Qe spectrometer was applied. IR spectra were recorded on a Bruker Vector 22, and the absorption maxima were given in wavelength in cm^{-1} units. 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. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Thin-layer chromatography (TLC) was performed on precoated polyester sheets (POLYGRAM SIL G/UV254), and components were visualized by observation under UV light. Melting points were uncorrected.

Experiment Procedures

General Procedure 1: Synthesis of substituted anthranils 2[2]



S1 2

A round bottom flask equipped with a magnetic stirrer bar was charged with the corresponding substituted 2-nitroacylbenzene (3.0 mmol) in EtOAc–MeOH (1:1, v/v; 20 mL). $SnCl_2 \cdot 2H_2O$ (9.0 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 to provide the title compound.

General Procedure 2: Gold(III)-catalyzed site-selective reaction of ynamides and anthranils

A round bottom flask equipped with a magnetic stirrer bar was charged with $KAuBr_4$ (5 mol%, 3.3 mg) and anthranils **2** (1.8 equiv.) in 1,2-DCE (1.2 mL). The reaction was cooled to –20 ^oC and ynamides **1** or **5** (0.12 mmol, 1.0 equiv.) dissolved in 1,2-DCE (1.2 mL) was added dropwise over 6 minutes and maintained at –20 ^oC for 1h. Then the reaction mixture was heating at the relevant temperature and the progress of the reaction was monitored by TLC. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EtOAc) to afford the desired products **3**, **6**, and **7**.

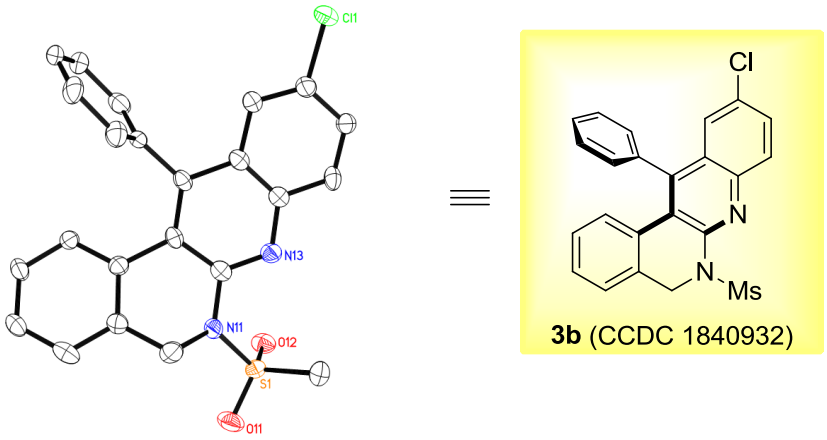
Scale-up reaction: A round bottom flask equipped with a magnetic stirrer bar was charged with $KAuBr_4$ (5 mol%, 27.8 mg) and anthranil **2a** (1.5 mmol, 345.0 mg) in 1,2-DCE (10.0 mL). The reaction was cooled to –20 ^oC and ynamides **1** or **5** (1.0 mmol) dissolved in 1,2-DCE (10.0 mL) was added dropwise over 6 minutes and maintained at –20 ^oC for 1 h. Then the reaction mixture was heating at the relevant temperature and the progress of the reaction was monitored by TLC. Upon completion, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EtOAc) to afford the desired products **3e** and **7a**.

[1] a) L. Zhu, Y. Yu, Z. Mao, X. Huang, *Org. Lett.* **2015**, *17*, 30–33; b) Z. Zeng, H. Jin, J. Xie, B. Tian, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Org. Lett.* **2017**, *19*, 1020–1023.

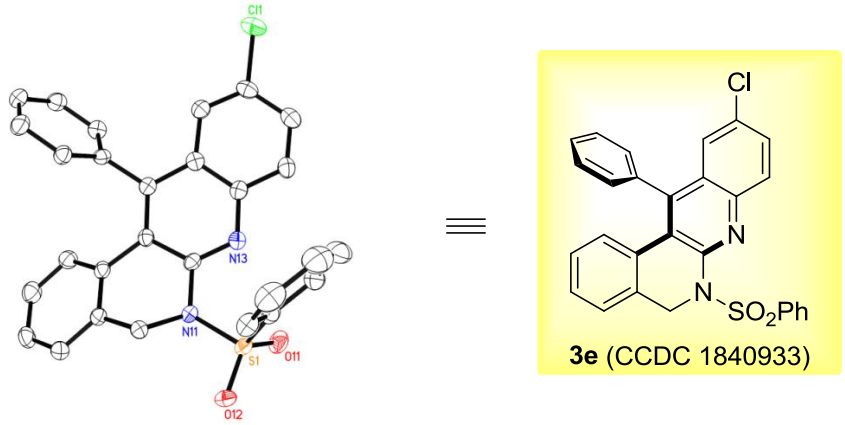
[2] a) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 794–797; b) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K, Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692.

X-Ray Single Crystal Structure Analyses

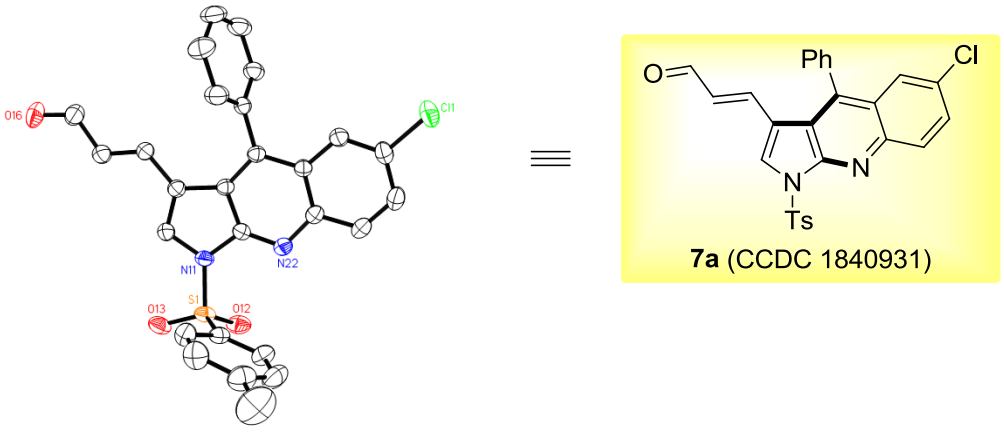
The crystallographic data of compounds **3b**, **3e**, and **7a** can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



3b (CCDC 1840932)



3e (CCDC 1840933)



7a (CCDC 1840931)

Photophysical Properties

All properties were examined in CH_2CH_2 solution (9.6 mg/L) and in quartz cuvettes providing a layer thickness of 1 cm. UV-vis absorption spectra were recorded on a Jasco V-670 device. Fluorescence spectra were measured on a Jasco FP6500 device. Photographs were taken under UV light irradiation (λ = 365 nm) using a Canon EOS 7D digital camera (objective: EF-S60mm f/2.8 Macro USM).

Table S1. Photophysical data of compound **3j**.

	λ_{abs} [nm] (log ε)	λ_{em}[a] [nm] (Φ_F[b])	Stokes shift (nm)
3j	280 (4.52)	542 (21.3%)	162

[a] Excited at λ_{abs}. [b] Fluorescence quantum yields (Φ_F) in CH_2Cl_2 at 298 K.

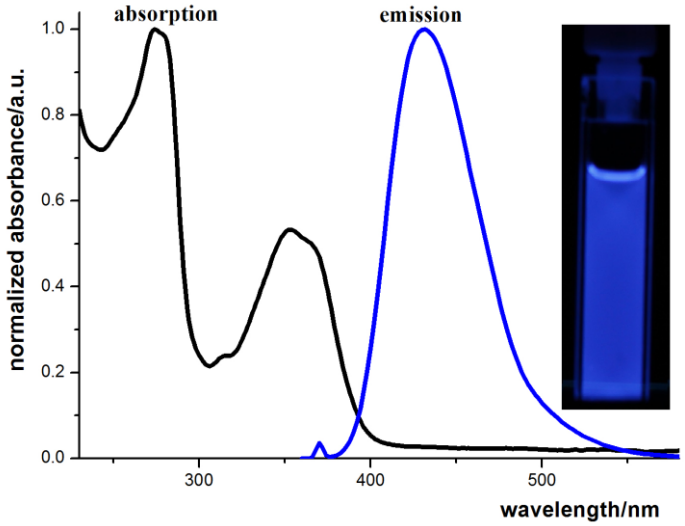
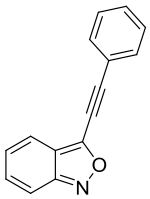


Figure S1. UV/Vis absorption (black lines), emission spectra (blue) and picture in dilute CH_2Cl_2 of compound **3j**.

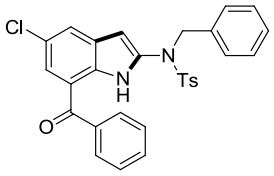
Characterization



2e: 3-(phenylethynyl)benzo[*c*]isoxazole

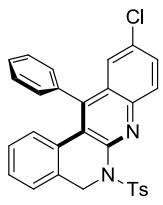
60% yield, light yellow solid, m.p.: 56–57 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65–7.63 (m, 4H), 7.47–7.41 (m, 3H), 7.35–7.32 (m, 1H), 7.11–7.08 (m, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.2 (s), 149.3 (s), 131.9 (d, 2C), 131.1 (d), 130.1 (d), 128.7 (d, 2C), 125.2 (d), 121.0 (s), 120.3 (s), 119.8 (d), 115.7 (d), 103.5 (s), 75.8 (s) ppm; **IR** (reflection): $\tilde{v}$ 3058, 2207, 1638, 1634, 1557, 1552, 1493, 1447, 1304, 1232, 1148, 1132, 1066, 924, 903, 847, 859, 694, 658, 640 cm^{-1}; **HRMS** (EI) calcd for $[C_{15}H_9NO]^+$ $(M)^+$: 219.0679; found: 219.0682.

4a: *N*-(7-benzoyl-5-chloro-1*H*-indol-2-yl)-*N*-benzyl-4-methylbenzenesulfonamide



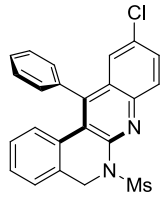
yellow solid, m.p.: 67–68 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.66 (s, 1H), 7.77–7.75 (m, 2H), 7.63–7.60 (m, 4H), 7.55–7.51 (m, 2H), 7.49 (d, *J* = 1.9 Hz,1H), 7.35 (d, *J* = 7.1 Hz, 2H), 7.31–7.27 (m, 4H), 7.24–7.21 (m, 1H), 5.91 (d, *J* = 2.3 Hz, 1H), 4.77 (s, 2H), 2.43 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 196.3 (s), 144.5 (s), 138.1 (s), 137.0 (s), 135.2 (s), 134.2 (s), 132.0 (d), 131.9 (s), 129.9 (d, 2C), 129.5 (s), 129.4 (d, 2C), 128.7 (d, 2C), 128.5 (d, 2C), 128.0 (d), 127.9 (d, 2C), 127.6 (d, 2C), 126.9 (d), 125.3 (d), 124.5 (s), 119.7 (s), 94.2 (d), 54.0 (t), 21.7 (q) ppm; **IR** (reflection): $\tilde{v}$ 3420, 2962, 2924, 1738, 1638, 1598, 1581, 1537, 1496, 1459, 1406, 1357, 1331, 1253, 1211, 1160, 1089, 1055, 1025, 963, 916, 856, 807, 774, 744, 715, 697, 664 cm^{-1}; **HRMS** (EI) calcd for $[C_{29}H_{23}N_2O_3SCl]^+$ $(M)^+$: 514.1112; found: 514.1096.

3a: 10-chloro-12-phenyl-6-tosyl-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine



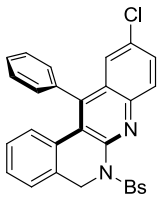
34.0 mg (57% yield), white solid, m.p.: 264–265 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.8 Hz, 2H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.57–7.47 (m, 5H), 7.32 (d, *J* = 6.8 Hz, 3H), 7.26 (s, 2H), 7.18 (t, *J* = 7.3 Hz, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 4.99 (s, 2H), 2.41 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.4 (s), 145.2 (s), 144.0 (s), 143.8 (s), 137.4 (s), 136.7 (s), 135.4 (s), 131.3 (s), 130.5 (d), 130.2 (d, 2C), 130.1 (s),

129.5 (d), 129.4 (d, 2C), 129.2 (d), 129.1 (d, 2C), 129.0 (d, 2C), 128.8 (d), 128.1 (d), 127.3 (d), 126.8 (s), 126.1 (d), 125.4 (d), 120.3 (s), 49.0 (t), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1395, 1380, 1353, 1323, 1275, 1168, 1134, 1099, 1083, 1027, 936, 918, 906, 814, 784, 762, 734, 705, 661, 634 cm^{-1}; **HRMS** (DART) calcd for $[C_{29}H_{22}N_2O_2SCl]^+$ $(M+H)^+$: 497.1085; found: 497.1073.



3b: 10-chloro-6-(methylsulfonyl)-12-phenyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine

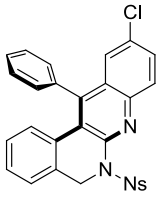
28.3 mg (56% yield), white solid, m.p.: 250–251 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.9 Hz, 1H), 7.60 (dd, *J* = 8.9, 2.3 Hz, 1H), 7.55–7.53 (m, 4H), 7.34–7.32 (m, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 6.90 (t, *J* = 7.7 Hz, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 4.92 (s, 2H), 3.68 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ151.1 (s), 145.6 (s), 144.0 (s), 136.7 (s), 135.5 (s), 131.5 (s), 130.7 (d), 130.1 (d, 2C), 130.0 (s), 129.7 (d), 129.4 (d, 2C), 129.2 (d), 128.9 (d), 128.2 (d), 127.3 (d), 126.9 (s), 126.0 (d), 125.4 (d), 120.5 (s), 48.2 (t), 42.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2259, 1601, 1566, 1480, 1442, 1420, 1396, 1331, 1285, 1255, 1226, 1161, 1138, 1117, 1102, 1083, 1053, 1031, 992, 971, 963, 937, 913, 877, 831, 797, 763, 728, 703, 660, 648, 630 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{17}N_2O_2SCl]^+$ $(M)^+$: 420.0694; found: 420.0684.



3c: 6-((4-bromophenyl)sulfonyl)-10-chloro-12-phenyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine

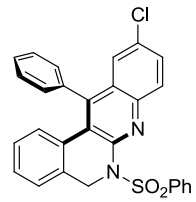
33.7 mg (50% yield), white solid, m.p.: 288–289 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.84 (d, *J* = 8.9 Hz, 1H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.58 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.52–7.49 (m, 4H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.28–7.26 (m, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.14 (d, *J* = 156.5 Hz, 2H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.1 (s), 145.5 (s), 143.9 (s), 139.4 (s), 136.6 (s), 135.1 (s), 131.7 (d, 2C), 131.5 (s), 130.7 (d), 130.4 (d, 2C), 130.1 (d, 2C), 130.0 (s), 129.4 (d, 3C), 129.2 (d), 128.9 (d), 128.2 (d), 128.1 (s), 127.4 (d), 126.9 (s), 126.1 (d), 125.4 (d), 120.3 (s), 49.0 (t) ppm;

IR (reflection): $\tilde{\nu}$ 1572, 1472, 1394, 1350, 1329, 1278, 1164, 1137, 1120, 1100, 1085, 1070, 1049, 1031, 1008, 949, 937, 904, 867, 830, 820, 790, 761, 743, 728, 700, 660, 641 cm^{-1}; **HRMS** (EI) calcd for $[C_{28}H_{18}N_2O_2SClBr]^+$ $(M)^+$: 559.9955; found: 559.9953.



3d: 10-chloro-6-((4-nitrophenyl)sulfonyl)-12-phenyl-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine

45.6 mg (72% yield), light yellow solid, m.p.: 255–256 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 35.9, 8.5 Hz, 4H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.59 (dd, *J* = 8.6, 1.4 Hz, 1H), 7.51 (dd, *J* = 11.3, 2.9 Hz, 4H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.27–7.26 (m, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 5.03 (s, 2H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.1 (s), 149.7 (s), 146.4 (s), 145.8 (s), 143.8 (s), 136.4 (s), 134.8 (s), 131.9 (s), 131.0 (d), 130.04 (d, 2C), 129.99 (d, 2C), 129.9 (s), 129.5 (d, 2C), 129.3 (d, 2C), 129.0 (d), 128.3 (d), 127.6 (d), 127.1 (s), 126.2 (d), 125.5 (d), 123.7 (d, 2C), 120.4 (s), 49.3 (t) ppm; **IR** (reflection): $\tilde{\nu}$ 3115, 3069, 2926, 2858, 1603, 1567, 1528, 1477, 1444, 1351, 1327, 1288, 1209, 1170, 1136, 1117, 1100, 1081, 1050, 1030, 954, 936, 918, 854, 828, 811, 789, 768, 736, 715, 700, 681, 660, 640 cm^{-1}; **HRMS** (EI) calcd for $[C_{28}H_{18}N_3O_4SCl]^+$ $(M)^+$: 527.0701; found: 527.0721.

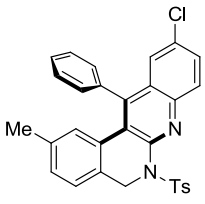


3e: 10-chloro-12-phenyl-6-(phenylsulfonyl)-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine

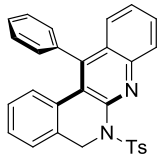
30.1 mg (52% yield), white solid, m.p.: 273–274 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.25 (d, *J* = 7.5 Hz, 2H), 7.85 (d, *J* = 8.9 Hz, 1H), 7.58–7.47 (m, 8H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.27–7.25 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 1H), 6.89 (t, *J* = 7.7 Hz, 1H), 6.68 (d, *J* = 8.1 Hz, 1H), 5.02 (s, 2H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.3 (s), 145.3 (s), 144.0 (s), 140.5 (s), 136.7 (s), 135.3 (s), 132.9 (d), 131.4 (s), 130.6 (d), 130.1 (d, 2C), 130.0 (s), 129.5 (d), 129.4 (d, 2C), 129.2 (d), 128.8 (d), 128.7 (d, 2C), 128.4 (d, 2C), 128.1 (d), 127.3 (d), 126.9 (s), 126.1 (d), 125.4 (d), 120.3 (s), 49.0 (t) ppm; **IR** (reflection): $\tilde{\nu}$ 3066, 2853, 1568, 1480, 1446,

1396, 1380, 1350, 1325, 1275, 1210, 1171, 1159, 1130, 1084, 1026, 936, 910, 882, 850, 829, 790, 772, 759, 736, 720, 705, 689, 636, 605 cm^{-1}; **HRMS** (EI) calcd for $[C_{28}H_{19}N_2O_2SCl]^+$ $(M)^+$: 482.0850; found: 482.0857.

3f: 10-chloro-2-methyl-12-phenyl-6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine



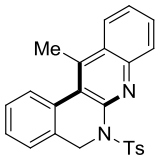
35.6 mg (58% yield), light yellow solid, m.p.: 246–247 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 2H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.56 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.52–7.49 (m, 4H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.27–7.25 (m, 2H), 7.19 (d, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.42 (s, 1H), 4.96 (s, 2H), 2.41 (s, 3H), 1.93 (s, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.5 (s), 145.0 (s), 143.9 (s), 143.7 (s), 137.5 (s), 136.9 (s), 136.7 (s), 132.5 (s), 131.2 (s), 130.4 (d), 130.2 (d, 2C), 130.0 (d), 129.8 (s), 129.5 (d), 129.2 (d, 2C), 129.0 (d, 2C), 128.9 (d, 2C), 128.7 (d), 128.6 (d), 126.8 (s), 125.8 (d), 125.3 (d), 120.4 (s), 48.7 (t), 21.6 (q), 21.1 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2922, 1738, 1605, 1561, 1478, 1443, 1421, 1389, 1353, 1323, 1281, 1227, 1209, 1165, 1083, 1051, 1001, 950, 923, 892, 877, 829, 812, 794, 759, 736, 700, 662, 633 cm^{-1}; **HRMS** (EI) calcd for $[C_{30}H_{23}N_2O_2SCl]^+$ $(M)^+$: 510.1163; found: 510.1165.



3g: 12-phenyl-6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine

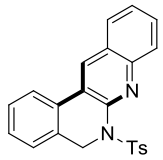
30.0 mg (54% yield), light yellow solid, m.p.: 266–267 °C; **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 8.12 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.3 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.51–7.47 (m, 4H), 7.32–7.31 (m, 4H), 7.27 (dd, *J* = 6.2, 2.8 Hz, 2H), 7.16 (t, *J* = 7.4 Hz, 1H), 6.87 (t, *J* = 7.7 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.95 (s, 2H), 2.38 (s, 3H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 150.3 (s), 146.2 (s), 145.4 (s), 144.0 (s), 137.5 (s), 137.3 (s), 135.6 (s), 130.5 (s), 130.2 (d, 2C), 129.8 (d), 129.1 (d), 129.03 (d, 2C), 129.01 (d, 2C), 128.8 (d, 2C), 128.5 (d), 127.7 (d), 127.6 (d), 127.1 (d), 126.7 (d), 126.0 (s), 125.9 (d), 125.5 (d), 119.5 (s), 49.1 (t), 21.3 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2840, 1738, 1582, 1566, 1483, 1445, 1396, 1352, 1335, 1290, 1276, 1255, 1235, 1207, 1185, 1164, 1132, 1112, 1088, 1048, 1033, 1018, 949, 926, 896, 864, 816, 785, 757, 735, 715, 701, 672, 655, 635 cm^{-1}; **HRMS** (EI) calcd for

$[C_{29}H_{22}N_2O_2S]^+$ $(M)^+$: 462.1397; found: 462.1382.



3h: 12-methyl-6-tosyl-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine

23.0 mg (48% yield), white solid, m.p.: 243–244 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.1 Hz, 2H), 7.98 (d, *J* = 8.3 Hz, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.58 (d, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.44–7.35 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.92 (s, 2H), 2.92 (s, 3H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.2 (s), 145.1 (s), 143.5 (s), 141.5 (s), 137.4 (s), 135.8 (s), 131.0 (s), 129.5 (d), 129.3 (d), 128.9 (d, 2C), 128.8 (d, 2C), 128.7 (d), 128.0 (d), 127.6 (d), 126.9 (s), 126.2 (d), 125.5 (d), 124.3 (d), 121.1 (s), 49.3 (t), 21.6 (q), 17.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3079, 3028, 1738, 1587, 1489, 1440, 1398, 1353, 1343, 1290, 1252, 1206, 1187, 1163, 1118, 1088, 1070, 1040, 994, 969, 865, 808, 762, 745, 716, 704, 672, 651, 618 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{20}N_2O_2S]^+$ $(M)^+$: 400.1240; found: 400.1239.

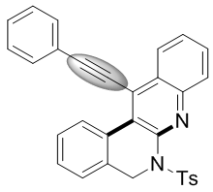


3i: 6-tosyl-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine

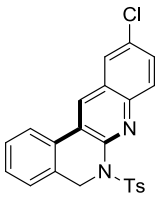
28.8 mg (62% yield), white solid, m.p.: 214–215 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.16 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.44–7.32 (m, 4H), 7.29 (d, *J* = 8.1 Hz, 2H), 5.12 (s, 2H), 2.39 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.2 (s), 146.0 (s), 143.8 (s), 137.3 (s), 132.8 (s), 131.0 (d), 130.1 (s), 129.9 (d), 129.02 (d, 2C), 128.98 (d, 2C), 128.8 (d), 128.6 (d), 127.9 (d), 127.7 (d), 126.4 (d), 126.1 (s), 125.7 (d), 123.7 (d), 121.3 (s), 48.6 (t), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2926, 2838, 2738, 1668, 1626, 1585, 1506, 1466, 1368, 1339, 1262, 1190, 1157, 1121, 1087, 1062, 1038, 1008, 980, 939, 908, 810, 784, 750, 722, 702, 670, 644, 622, 612 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{18}N_2O_2S]^+$ $(M)^+$: 386.1084; found: 386.1085.

3j: 12-(phenylethynyl)-6-tosyl-5,6-dihydrodibenzo[*b,f*][1,8]naphthyridine

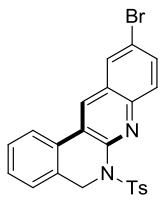
14.0 mg (24% yield), light yellow solid, m.p.: 218–219 °C; **^{1}H NMR** (600 MHz,



$CDCl_3$) δ 9.10 (d, *J* = 7.5 Hz, 1H), 8.71 (d, *J* = 8.1 Hz, 1H), 8.41 (d, *J* = 7.8 Hz, 2H), 8.25 (d, *J* = 8.0 Hz, 1H), 8.00 (t, *J* = 7.3 Hz, 1H), 7.95 (d, *J* = 4.5 Hz, 2H), 7.86 (t, *J* = 7.3 Hz, 1H), 7.77–7.73 (m, 5H), 7.59–7.57 (m, 3H), 5.32 (s, 2H), 2.70 (s, 3H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 150.2 (s), 145.5 (s), 144.0 (s), 137.5 (s), 135.5 (s), 132.2 (d, 2C), 130.6 (s), 130.4 (d), 129.9 (d), 129.4 (d), 129.3 (d, 2C), 129.2 (d, 2C), 129.0 (d, 2C), 128.6 (d), 128.3 (d), 127.9 (d), 126.72 (s), 126.69 (d), 126.6 (d), 126.4 (d), 125.8 (s), 122.8 (s), 122.6 (s), 102.7 (s), 86.1 (s), 49.2 (t), 21.9 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3068, 2204, 1738, 1599, 1561, 1492, 1444, 1396, 1355, 1338, 1307, 1290, 1259, 1243, 1202, 1186, 1168, 1116, 1089, 1039, 969, 899, 884, 866, 841, 813, 758, 733, 715, 674, 657, 628 cm^{-1}; **HRMS** (DART) calcd for $[C_{31}H_{23}N_2O_2S]^+$ (M + H)$^+$: 487.1475; found: 487.1464.

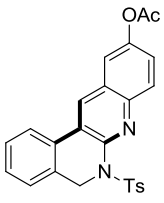


3k: 10-chloro-6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine 23.7 mg (47% yield), white solid, m.p.: 242–243 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.13 (d, *J* = 8.3 Hz, 2H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.73 (d, *J* = 1.9 Hz, 1H), 7.54 (dd, *J* = 8.9, 2.1 Hz, 1H), 7.44–7.34 (m, 3H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.12 (s, 2H), 2.40 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.4 (s), 144.3 (s), 144.0 (s), 137.1 (s), 132.8 (s), 131.2 (s), 130.6 (d), 129.8 (d), 129.6 (s), 129.4 (d), 129.2 (d), 129.04 (d, 2C), 128.96 (d, 2C), 128.7 (d), 126.7 (s), 126.5 (d), 126.3 (d), 123.8 (d), 122.1 (s), 48.5 (t), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2923, 1738, 1604, 1486, 1452, 1431, 1408, 1352, 1293, 1274, 1203, 1161, 1135, 1087, 1075, 1019, 982, 949, 916, 906, 865, 813, 778, 758, 729, 702, 662, 634, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{17}N_2O_2SCl]^+$ (M)$^+$: 420.0694; found: 420.0700.



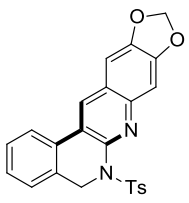
3l: 10-bromo-6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine 25.7 mg (46% yield), white solid, m.p.: 196–197 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.14 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 1.9

Hz, 1H), 7.79 (d, *J* = 7.5 Hz, 1H), 7.73 (d, *J* = 8.9 Hz, 1H), 7.66 (dd, *J* = 8.9, 2.0 Hz, 1H), 7.43–7.29 (m, 5H), 5.12 (s, 2H), 2.40 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.4 (s), 144.5 (s), 144.0 (s), 137.1 (s), 133.1 (d), 132.8 (s), 129.7 (d), 129.6 (d), 129.51 (s), 129.46 (d), 129.3 (d), 129.1 (d, 2C), 129.0 (d, 2C), 128.7 (d), 127.2 (s), 126.5 (d), 123.8 (d), 122.0 (s), 119.1 (s), 48.5 (t), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1738, 1716, 1600, 1483, 1429, 1406, 1352, 1294, 1273, 1186, 1162, 1087, 1061, 1008, 914, 816, 778, 757, 727, 702, 688, 658, 631, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{23}H_{17}N_2O_2SBr]^+$ $(M)^+$: 464.0189; found: 464.0179.



3m: 6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridin-10-yl acetate 38.4 mg (72% yield), light yellow solid, m.p.: 232–233 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.11 (d, *J* = 8.1 Hz, 2H), 7.89 (d, *J* = 8.9 Hz, 1H), 7.79 (d, *J* = 6.9 Hz, 1H), 7.50 (s, 1H), 7.43–7.34 (m, 4H), 7.28–7.26 (m, 2H), 5.13 (s, 2H), 2.39 (s, 3H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5 (s), 149.1 (s), 147.9 (s), 143.93 (s), 143.90 (s), 137.1 (s), 132.8 (s), 130.6 (d), 129.7 (s), 129.3 (d), 129.1 (d), 129.0 (d, 2C), 128.9 (d, 2C), 128.6 (d), 126.5 (d), 126.2 (s), 124.9 (d), 123.8 (d), 121.8 (s), 118.5 (d), 48.5 (t), 21.6 (q), 21.3 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1759, 1611, 1496, 1443, 1410, 1358, 1297, 1275, 1201, 1163, 1088, 1044, 1012, 962, 912, 826, 780, 756, 728, 705, 681, 662, 640, 621 cm^{-1}; **HRMS** (EI) calcd for $[C_{25}H_{20}N_2O_4S]^+$ $(M)^+$: 444.1138; found: 444.1148.

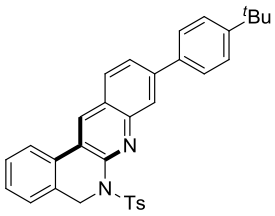
3n: 6-tosyl-5,6-dihydro-[1,3]dioxolo[4',5':4,5]benzo[1,2-*b*]benzo[*f*][1,8]naphthyridine



25.3 mg (49% yield), light yellow solid, m.p.: 250–251 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 8.03 (d, *J* = 7.8 Hz, 2H), 7.72 (d, *J* = 6.4 Hz, 1H), 7.39–7.30 (m, 3H), 7.26–7.20 (m, 3H), 7.01 (s, 1H), 6.08 (s, 2H), 5.07 (s, 2H), 2.38 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) 151.1 (s), 147.7 (s), 147.3 (s), 144.3 (s), 143.6 (s), 137.4 (s), 132.4 (s), 130.3 (s), 130.1 (d), 129.0 (d, 2C), 128.7 (d, 2C), 128.42 (d), 128.41 (d), 126.3 (d), 123.3 (d), 122.9 (s), 119.5 (s), 105.0 (d), 103.0 (d), 101.8 (t), 48.8 (t), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2897, 2779, 1620, 1493, 1451, 1399, 1375, 1322, 1281, 1265, 1241,

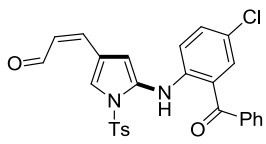
1186, 1156, 1121, 1093, 1083, 1035, 1020, 1011, 983, 949, 907, 858, 847, 815, 775, 755, 716, 700, 681, 657, 638, 623, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{18}N_2O_4S]^+$ $(M)^+$: 430.0982; found: 430.0996.

3o: 9-(4-(*tert*-butyl)phenyl)-6-tosyl-5,6-dihydrodibenzo[*b*,*f*][1,8]naphthyridine



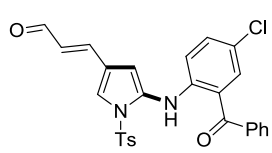
37.3 mg (60% yield), light yellow solid, m.p.: 243–244 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 0.7 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 2H), 8.10 (s, 1H), 7.83 (s, 2H), 7.71 (d, *J* = 7.8 Hz, 3H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.43–7.34 (m, 3H), 7.29 (d, *J* = 7.8 Hz, 2H), 5.13 (s, 2H), 2.38 (s, 3H), 1.41 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 151.1 (s), 149.6 (s), 146.4 (s), 143.8 (s), 142.5 (s), 137.5 (s), 137.1 (s), 132.7 (s), 130.9 (d), 130.2 (s), 129.1 (d, 2C), 129.0 (d, 2C), 128.8 (d), 128.6 (d), 128.2 (d), 127.2 (d, 2C), 126.4 (d), 126.0 (d, 2C), 125.5 (d), 125.3 (d), 125.1 (s), 123.7 (d), 121.0 (s), 48.6 (t), 34.7 (s), 31.4 (q, 3C), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2959, 2867, 2260, 1736, 1610, 1500, 1485, 1449, 1403, 1360, 1336, 1272, 1194, 1168, 1090, 1010, 982, 933, 904, 834, 809, 779, 761, 728, 704, 688, 659, 619 cm^{-1}; **HRMS** (EI) calcd for $[C_{33}H_{30}N_2O_2S]^+$ $(M)^+$: 518.2023; found: 518.2036.

(*Z*)-**6a**: (*Z*)-3-(5-((2-benzoyl-4-chlorophenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde



45.4 mg (*Z*/*E* = 17:1, 75% combined yield,), light yellow solid; **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 10.16 (d, *J* = 7.9 Hz, 1H), 9.77 (s, 1H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.55–7.47 (m, 3H), 7.47 (d, *J* = 2.4 Hz, 1H), 7.14 (dd, *J* = 17.6, 9.9 Hz, 3H), 7.06 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.59 (d, *J* = 9.0 Hz, 1H), 6.30 (s, 1H), 5.98 (dd, *J* = 11.7, 7.9 Hz, 1H), 2.31 (s, 3H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 197.8 (s), 190.8 (d), 146.2 (s), 146.1 (s), 139.1 (d), 138.6 (s), 134.1 (s), 133.9 (d), 133.0 (d), 132.2 (d), 131.4 (s), 129.9 (d, 2C), 129.5 (d, 2C), 128.4 (d, 2C), 127.8 (d, 3C), 122.1 (s), 121.8 (d), 120.7 (s), 120.4 (s), 115.9 (d), 107.5 (d), 21.3 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1672, 1629, 1595, 1572, 1493, 1447, 1402, 1370, 1288, 1238, 1190, 1174, 1119, 1088, 1061, 949, 810, 701, 666, 647

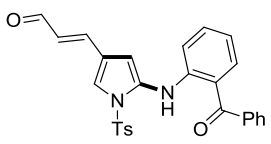
cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{22}N_2O_4SCl]^+$ $(M + H)^+$: 505.0983; found: 505.0995.



(*E*)-**6a**: (*E*)-3-(5-((2-benzoyl-4-chlorophenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

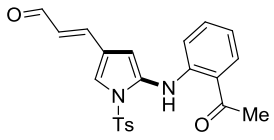
41.8 mg (69% yield), yellow solid, m.p.: 84–85 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.80 (s, 1H), 9.62 (d, *J* = 7.8 Hz, 1H), 7.76–7.71 (m, 4H), 7.64–7.61 (m, 1H), 7.55–7.52 (m, 3H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.32 (d, *J* = 15.7 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.10 (dd, *J* = 9.0, 2.5 Hz, 1H), 6.66 (d, *J* = 9.0 Hz, 1H), 6.37 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.26 (s, 1H), 2.33 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.8 (s), 193.3 (d), 146.0 (s), 145.9 (s), 144.4 (d), 138.4 (s), 134.3 (s), 133.9 (d), 133.0 (d), 132.4 (d), 132.1 (s), 130.0 (d, 2C), 129.7 (d, 2C), 128.5 (d, 2C), 128.0 (d), 127.9 (d, 2C), 122.5 (s), 121.6 (s), 121.3 (d), 120.9 (s), 116.1 (d), 103.2 (d), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1736, 1671, 1630, 1595, 1572, 1492, 1371, 1288, 1239, 1190, 1174, 1156, 1119, 1087, 1061, 949, 809, 701, 666, 647 cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{22}N_2O_4SCl]^+$ $(M + H)^+$: 505.0983; found: 505.0974.

6b: (*E*)-3-(5-((2-benzoylphenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

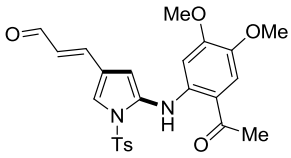


28.8 mg (51% yield), yellow oil, m.p.: 42–43 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 9.62 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.1 Hz, 4H), 7.61–7.49 (m, 5H), 7.32 (d, *J* = 15.7 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.80–6.73 (m, 2H), 6.36 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.26 (s, 1H), 2.31 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.9 (s), 193.4 (d), 147.2 (s), 145.7 (s), 144.6 (d), 139.2 (s), 134.4 (s), 134.3 (d), 134.1 (d), 132.9 (s), 131.9 (d), 123.0 (d, 2C), 129.7 (d, 2C), 128.2 (d, 2C), 127.90 (d), 127.87 (d, 2C), 121.7 (s), 121.0 (d), 120.1 (s), 117.8 (d), 114.6 (d), 102.2 (d), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1674, 1630, 1579, 1513, 1451, 1372, 1308, 1262, 1217, 1192, 1177, 1123, 1092, 1063, 969, 940, 752, 735, 703, 674 cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{23}N_2O_4S]^+$ $(M + H)^+$: 471.1373; found: 471.1379.

6c: (*E*)-3-(5-((2-acetylphenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

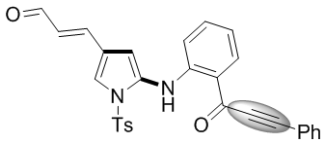


31.4 mg (64% yield), light yellow solid, m.p.: 155–156 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.54 (s, 1H), 9.61 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.51 (d, *J* = 1.5 Hz, 1H), 7.31 (d, *J* = 15.7 Hz, 1H), 7.17–7.11 (m, 3H), 6.77 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 6.35 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.24 (s, 1H), 2.68 (s, 3H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 201.5 (s), 193.4 (d), 147.3 (s), 145.6 (s), 144.6 (d), 134.6 (d), 134.4 (s), 132.4 (s), 132.0 (d), 129.9 (d, 2C), 127.9 (d), 127.8 (d, 2C), 121.6 (s), 121.3 (d), 119.4 (s), 117.9 (d), 114.3 (d), 103.4 (d), 28.1 (q), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1681, 1643, 1628, 1588, 1569, 1503, 1452, 1360, 1244, 1218, 1187, 1161, 1114, 1085, 1053, 964, 804, 755, 667, 639 cm^{-1}; **HRMS** (DART) calcd for $[C_{22}H_{21}N_2O_4S]^+$ $(M + H)^+$: 409.1217; found: 409.1215.



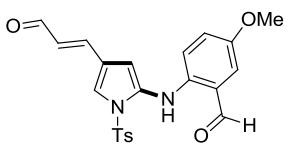
6d: (*E*)-3-(5-((2-acetyl-4,5-dimethoxyphenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

28.1 mg (50% yield), yellow solid, m.p.: 75–76 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.73 (s, 1H), 9.61 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 2H), 7.52 (d, *J* = 1.7 Hz, 1H), 7.31 (d, *J* = 15.7 Hz, 1H), 7.18 (s, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.34 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.22 (s, 1H), 6.09 (s, 1H), 3.87 (s, 3H), 3.61 (s, 3H), 2.62 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 199.1 (s), 193.3 (d), 155.2 (s), 145.7 (s), 144.6 (d), 144.4 (s), 141.2 (s), 134.4 (s), 132.9 (s), 129.9 (d, 2C), 127.9 (d, 2C), 127.8 (d), 121.6 (s), 121.3 (d), 114.0 (d), 111.8 (s), 102.9 (d), 96.9 (d), 56.7 (q), 55.7 (q), 27.9 (q), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1671, 1627, 1577, 1511, 1451, 1407, 1366, 1342, 1257, 1205, 1190, 1166, 1120, 1088, 1058, 999, 957, 812, 729, 671 cm^{-1}; **HRMS** (DART) calcd for $[C_{22}H_{21}N_2O_4S]^+$ $(M + H)^+$: 469.1428; found: 469.1431.



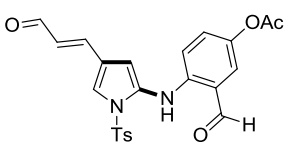
6e: (*E*)-3-(5-((2-(3-phenylpropioloyl)phenyl)amino)-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

40.9 mg (69% yield), yellow solid, m.p.: 78–79 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.31 (s, 1H), 9.62 (d, *J* = 7.8 Hz, 1H), 8.28 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.72–7.67 (m, 4H), 7.56 (d, *J* = 1.8 Hz, 1H), 7.52–7.49 (m, 1H), 7.45 (t, *J* = 7.4 Hz, 2H), 7.33 (d, *J* = 15.7 Hz, 1H), 7.23–7.19 (m, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.38 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.31 (s, 1H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.3 (d), 180.0 (s), 148.5 (s), 145.7 (s), 144.5 (d), 135.5 (d), 134.6 (d), 134.3 (s), 133.0 (d, 2C), 131.4 (s), 130.8 (d), 130.0 (d, 2C), 128.8 (d, 2C), 128.0 (d), 127.9 (d, 2C), 121.7 (d), 121.6 (s), 120.2 (s), 119.9 (s), 118.2 (d), 113.9 (d), 104.9 (d), 93.8 (s), 87.0 (s), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2198, 1672, 1614, 1593, 1573, 1510, 1450, 1370, 1270, 1207, 1191, 1174, 1158, 1119, 1088, 1060, 1009, 995, 750, 669 cm^{-1}; **HRMS** (DART) calcd for $[C_{29}H_{23}N_2O_4S]^+$ $(M + H)^+$: 495.1373; found: 495.1371.



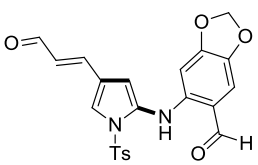
6f: (*E*)-5-methoxy-2-((4-(3-oxoprop-1-en-1-yl)-1-tosyl-1*H*-pyrrol-2-yl)amino)benzaldehyde

21.9 mg (43% yield), light yellow solid, m.p.: 70–71 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.92 (s, 1H), 9.66 (s, 1H), 9.61 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 1.7 Hz, 1H), 7.31 (d, *J* = 15.7 Hz, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 7.07 (d, *J* = 2.9 Hz, 1H), 6.88 (dd, *J* = 9.1, 2.9 Hz, 1H), 6.67 (d, *J* = 9.1 Hz, 1H), 6.35 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.23 (s, 1H), 3.81 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.9 (d), 193.3 (d), 152.3 (s), 145.7 (s), 144.5 (d), 141.3 (s), 134.4 (s), 132.5 (s), 130.0 (d, 2C), 128.0 (d), 127.8 (d, 2C), 123.8 (d), 121.7 (s), 121.2 (d), 119.8 (s), 117.7 (d), 115.3 (d), 102.9 (d), 55.9 (q), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3131, 2927, 2838, 2740, 1667, 1626, 1584, 1505, 1464, 1366, 1340, 1272, 1225, 1190, 1157, 1120, 1088, 1061, 1038, 968, 933, 811, 777, 730, 702, 667 cm^{-1}; **HRMS** (EI) calcd for $[C_{22}H_{20}N_2O_5S]^+$ $(M + H)^+$: 424.1087; found: 424.1072.



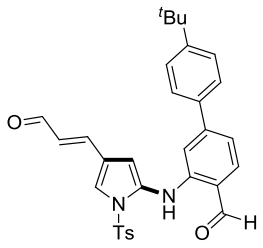
6g: (*E*)-3-formyl-4-((4-(3-oxoprop-1-en-1-yl)-1-tosyl-1*H*-pyrrol-2-yl)amino)phenyl acetate

11.9 mg (22% yield), light yellow solid, m.p.: 71–72 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.90 (s, 1H), 9.82 (s, 1H), 9.62 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 1.3 Hz, 1H), 7.33–7.30 (m, 2H), 7.15 (d, *J* = 8.1 Hz, 2H), 6.93 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.61 (d, *J* = 9.1 Hz, 1H), 6.37 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.30 (s, 1H), 2.34 (s, 3H), 2.30 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.4 (d), 193.3 (d), 169.6 (s), 146.0 (s), 144.9 (s), 144.2 (d), 142.2 (s), 134.2 (s), 131.2 (s), 130.1 (d, 2C), 129.3 (d), 128.1 (d), 127.7 (d, 2C), 127.5 (d), 121.58 (d), 121.56 (s), 119.4 (s), 114.3 (d), 104.5 (d), 21.6 (q), 21.0 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1757, 1667, 1627, 1583, 1510, 1367, 1299, 1191, 1174, 1148, 1121, 1088, 1061, 1013, 963, 907, 810, 785, 702, 670 cm^{-1}; **HRMS** (DART) calcd for $[C_{23}H_{21}N_2O_6S]^+$ $(M + H)^+$: 453.1115; found: 453.1119.



6h: (*E*)-6-((4-(3-oxoprop-1-en-1-yl)-1-tosyl-1*H*-pyrrol-2-yl)amino)benzo[*d*][1,3]dioxole-5-carbaldehyde

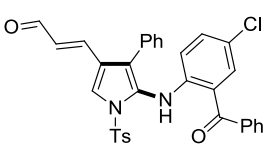
31.6 mg (60% yield), yellow solid, m.p.: 188–189 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.19 (s, 1H), 9.69 (s, 1H), 9.62 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 1.3 Hz, 1H), 7.31 (d, *J* = 15.7 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.91 (s, 1H), 6.36 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.27 (s, 1H), 6.08 (s, 1H), 5.92 (s, 2H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.3 (d), 191.4 (d), 154.2 (s), 146.7 (s), 145.7 (s), 144.3 (d), 140.6 (s), 134.3 (s), 131.3 (s), 130.0 (d, 2C), 128.1 (d), 127.9 (d, 2C), 121.8 (d), 121.6 (s), 112.9 (s), 112.0 (d), 105.1 (d), 101.9 (t), 94.1 (d), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1671, 1651, 1629, 1592, 1515, 1497, 1480, 1371, 1266, 1227, 1170, 1122, 1087, 1041, 1011, 978, 938, 815, 802, 671 cm^{-1}; **HRMS** (DART) calcd for $[C_{22}H_{19}N_2O_6S]^+$ $(M + H)^+$: 439.0958; found: 439.0961.



6i: (*E*)-4'-(*tert*-butyl)-3-((4-(3-oxoprop-1-en-1-yl)-1-tosyl-1*H*-pyrrol-2-yl)amino)-[1,1'-biphenyl]-4-carbaldehyde

36.7 mg (58% yield), light yellow solid, m.p.: 100–101 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 9.94 (s, 1H), 9.63 (d, *J* = 7.8 Hz, 1H), 7.63 (dd, *J* = 15.7, 8.1 Hz, 3H), 7.58 (d, *J* = 1.7 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.31 (dd, *J* = 20.1, 12.0 Hz, 3H), 7.08 (d, *J* =

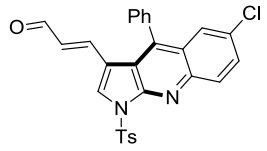
8.0 Hz, 3H), 6.70 (s, 1H), 6.38 (dd, *J* = 15.7, 7.8 Hz, 1H), 6.34 (s, 1H), 2.21 (s, 3H), 1.34 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.8 (d), 193.4 (d), 152.1 (s), 148.2 (s), 147.5 (s), 145.7 (s), 144.5 (d), 136.6 (s), 136.4 (d), 134.3 (s), 131.2 (s), 129.9 (d, 2C), 128.1 (d), 127.8 (d, 2C), 126.8 (d, 2C), 125.9 (d, 2C), 121.7 (d), 121.6 (s), 118.5 (s), 117.5 (d), 111.2 (d), 105.0 (d), 34.7 (s), 31.3 (q, 3C), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 2968, 2741, 1738, 1663, 1615, 1574, 1556, 1510, 1432, 1371, 1304, 1271, 1191, 1175, 1119, 1088, 1060, 1016, 967, 928, 839, 808, 728, 702, 669 cm^{-1}; **HRMS** (EI) calcd for $[C_{31}H_{30}N_2O_4S]^+$ $(M)^+$: 526.1921; found: 526.1925.



6j: (*E*)-3-(5-((2-benzoyl-4-chlorophenyl)amino)-4-phenyl-1-tosyl-1*H*-pyrrol-3-yl)acrylaldehyde

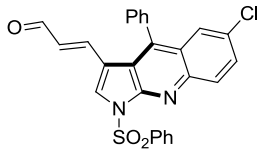
44.6 mg (64% yield), light yellow solid, m.p.: 180–181 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.52 (d, *J* = 7.8 Hz, 1H), 9.38 (s, 1H), 7.81 (s, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.65–7.59 (m, 3H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.28 (d, *J* = 16.2 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 3H), 7.14 (dd, *J* = 7.8, 1.5 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.82 (dd, *J* = 9.0, 2.4 Hz, 1H), 6.43 (dd, *J* = 16.0, 7.8 Hz, 1H), 6.00 (d, *J* = 9.0 Hz, 1H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 198.0 (s), 193.6 (d), 146.9 (s), 146.0 (s), 144.4 (d), 138.6 (s), 134.1 (s), 133.5 (d), 132.6 (d), 132.2 (d), 130.9 (s), 129.9 (d, 2C), 129.5 (d, 2C), 129.2 (d, 2C), 128.7 (d, 2C), 128.5 (d, 2C), 128.23 (d), 128.15 (d, 2C), 127.9 (d), 126.6 (s), 124.0 (s), 121.8 (s), 119.9 (s), 119.84 (d), 119.81 (s), 115.9 (d), 21.6 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1678, 1625, 1596, 1567, 1514, 1495, 1378, 1237, 1189, 1174, 1154, 1123, 1090, 1067, 1011, 949, 746, 700, 665, 645 cm^{-1}; **HRMS** (DART) calcd for $[C_{33}H_{26}N_2O_4SCl]^+$ $(M + H)^+$: 581.1296; found: 581.1300.

7a: (*E*)-3-(6-chloro-4-phenyl-1-tosyl-1*H*-pyrrolo[2,3-*b*]quinolin-3-yl)acrylaldehyde



32.7 mg (56% yield), light yellow solid, m.p.: 230–231 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 7.4 Hz, 1H), 8.30–8.27 (m, 3H), 8.19 (d, *J* = 9.0 Hz, 1H), 7.66 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.64–7.58 (m, 4H), 7.36 (d, *J* = 7.9 Hz, 4H), 6.45 (d, *J* = 16.0 Hz, 1H), 6.37 (dd,

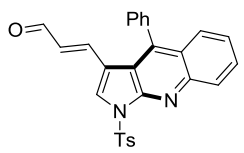
J = 15.9, 7.4 Hz, 1H), 2.40 (s, 4H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.1 (d), 147.3 (s), 146.1 (s), 143.9 (s), 143.0 (d), 141.2 (s), 134.5 (s), 134.4 (s), 131.3 (s), 130.7 (d), 130.2 (d), 129.8 (d, 2C), 129.7 (d, 2C), 129.4 (d), 129.1 (d), 129.00 (d, 2C), 128.98 (d, 2C), 128.3 (d), 125.8 (s), 124.6 (d), 119.7 (s), 115.0 (s), 21.8 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3112, 2926, 2854, 1738, 1672, 1611, 1596, 1532, 1488, 1445, 1402, 1377, 1356, 1310, 1271, 1230, 1212, 1172, 1159, 1122, 1090, 1002, 974, 952, 877, 835, 821, 813, 766, 731, 710, 664, 628, 605 cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{20}N_2O_3SCl]^+$ $(M + H)^+$: 487.0878; found: 487.0879.



7b: (*E*)-3-(6-chloro-4-phenyl-1-(phenylsulfonyl)-1*H*-pyrrolo[2,3-*b*]quinolin-3-yl)acrylaldehyde

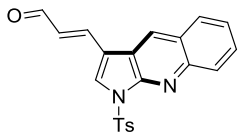
29.5 mg (52% yield), light yellow solid, m.p.: 214–215 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 9.05 (d, *J* = 7.4 Hz, 1H), 8.41 (d, *J* = 8.1 Hz, 2H), 8.27 (s, 1H), 8.18 (d, *J* = 9.0 Hz, 1H), 7.68–7.55 (m, 8H), 7.35 (dd, *J* = 7.8, 1.3 Hz, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.37 (dd, *J* = 15.9, 7.4 Hz, 1H) ppm; **^{13}C NMR** (150 MHz, $CDCl_3$) δ 193.4 (d), 147.6 (s), 144.2 (s), 143.2 (d), 141.6 (s), 137.6 (s), 135.0 (d), 134.7 (s), 131.7 (s), 131.0 (d), 130.6 (d), 130.0 (d, 2C), 129.7 (d), 129.5 (d, 2C), 129.3 (d, 2C), 129.2 (d, 3C), 128.7 (d), 126.1 (s), 125.0 (d), 120.0 (s), 115.5 (s) ppm; **IR** (reflection): $\tilde{\nu}$ 3139, 3059, 2926, 1738, 1675, 1610, 1538, 1487, 1448, 1403, 1378, 1352, 1312, 1272, 1229, 1172, 1158, 1120, 1090, 958, 875, 834, 816, 760, 725, 708, 683, 666, 630 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{17}N_2O_3SCl]^+$ $(M)^+$: 472.0643; found: 472.0649.

7c: (*E*)-3-(4-phenyl-1-tosyl-1*H*-pyrrolo[2,3-*b*]quinolin-3-yl)acrylaldehyde



32.0 mg (59% yield), light green solid, m.p.: 226–227 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.05 (d, *J* = 7.2 Hz, 1H), 8.28 (dd, *J* = 29.5, 7.6 Hz, 4H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.61–7.57 (m, 3H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.36 (dd, *J* = 12.8, 7.7 Hz, 4H), 6.48 (d, *J* = 15.9 Hz, 1H), 6.37 (dd, *J* = 15.8, 7.4 Hz, 1H), 2.39 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.2 (d), 147.3 (s), 145.9 (s), 145.6 (s), 143.5 (d), 142.0 (s),

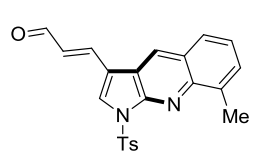
135.2 (s), 134.5 (s), 129.8 (d, 2C), 129.7 (d, 2C), 129.3 (d), 129.2 (d), 129.1 (d), 129.0 (d, 2C), 128.8 (d, 2C), 128.6 (d), 128.1 (d), 126.1 (d), 125.4 (d), 125.2 (s), 119.1 (s), 115.1 (s), 21.8 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1673, 1622, 1594, 1537, 1376, 1357, 1333, 1188, 1172, 1150, 1119, 1089, 955, 814, 760, 735, 703, 681, 663, 650 cm^{-1}; **HRMS** (DART) calcd for $[C_{27}H_{21}N_2O_3S]^+$ $(M + H)^+$: 453.1267; found: 453.1258.



7d: (*E*)-3-(1-tosyl-1*H*-pyrrolo[2,3-*b*]quinolin-3-yl)acrylaldehyde 22.6 mg (50% yield), light yellow solid, m.p.: 216–217 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.71 (d, *J* = 7.6 Hz, 1H), 8.55 (s, 1H), 8.26–8.23 (m, 3H), 8.19 (d, *J* = 8.5 Hz, 1H), 7.93 (d, *J* = 8.1 Hz, 1H), 7.77–7.74 (m, 1H), 7.60–7.53 (m, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 6.89 (dd, *J* = 16.1, 7.6 Hz, 1H), 2.35 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ

193.5 (d), 148.0 (s), 146.0 (s), 145.6 (s), 143.2 (d), 134.3 (s), 133.0 (d), 129.7 (d, 3C), 129.98 (d), 128.95 (d), 128.9 (d, 2C), 128.7 (d), 128.3 (d), 125.8 (s), 125.7 (d), 119.9 (s), 114.6 (s), 21.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1675, 1625, 1596, 1531, 1395, 1366, 1214, 1191, 1169, 1119, 1089, 1065, 957, 940, 897, 821, 753, 702, 678, 648 cm^{-1}; **HRMS** (DART) calcd for $[C_{21}H_{17}N_2O_3S]^+$ $(M + H)^+$: 377.0954; found: 377.0948.

7e: (*E*)-3-(8-methyl-1-tosyl-1*H*-pyrrolo[2,3-*b*]quinolin-3-yl)acrylaldehyde



16.4 mg (35% yield), white solid, m.p.: 244–245 °C; **^{1}H NMR** (500 MHz, CD_2Cl_2) δ 9.69 (d, *J* = 7.4 Hz, 1H), 8.59 (s, 1H), 8.27– 8.21 (m, 3H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.63–7.60 (m, 2H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.87 (dd, *J* = 16.1, 7.5 Hz, 1H), 2.88 (s, 3H), 2.34 (s, 3H) ppm; **^{13}C NMR** (125 MHz, CD_2Cl_2) δ 193.3 (d), 147.2 (s), 146.2 (s), 144.6 (s), 143.1 (d), 136.4 (s), 134.2 (s), 132.9 (d), 129.7 (d), 129.6 (d, 2C), 129.3 (d), 128.9 (d, 2C), 128.6 (d), 126.4 (d), 125.7 (s), 125.3 (d), 119.6 (s), 114.5 (s), 21.4 (q), 18.3 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 1677, 1620, 1531, 1395, 1369, 1235, 1218, 1190, 1163, 1133, 1100, 1036, 972, 922, 815, 799, 765, 706, 672, 651 cm^{-1}; **HRMS** (DART) calcd for $[C_{22}H_{19}N_2O_3S]^+$ $(M + H)^+$: 391.1111; found: 391.1102.

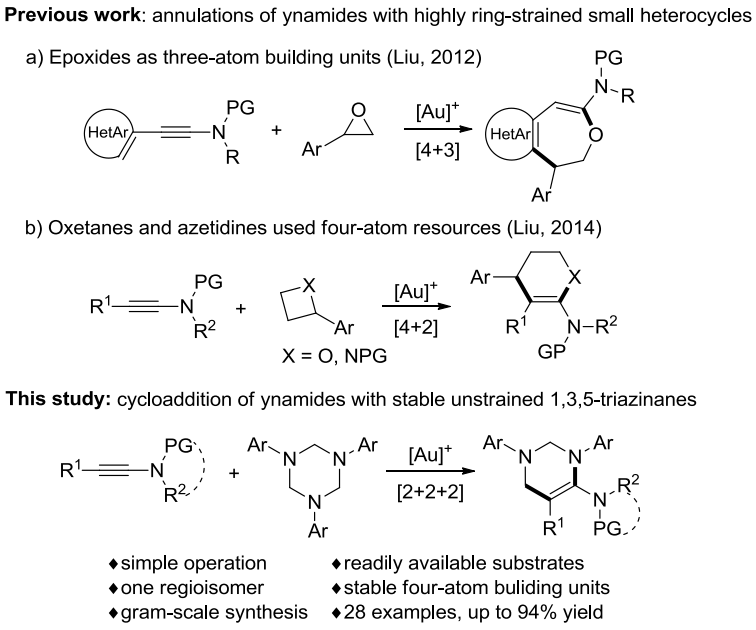
Chapter 5: Gold-Catalyzed Intermolecular Cyclocarboamination of Ynamides with 1,3,5-Triazinanes: En Route to Tetrahydropyrimidines

5.1 Introduction

Ynamides, a subgroup of nitrogen-substituted alkynes, are versatile synthons. They have frequently emerged in contemporary organic synthesis in the past decades.[1] Their catalytic annulations with highly ring-strained saturated heterocycles were deemed as powerful strategies to construct a wide range of heterocyclic scaffolds.[2] For example, in 2012, using epoxides as the three-atom building units, Liu's group disclosed a gold-mediated intermolecular [4+3] annulations with ynamides (Scheme 1a).[2a] Later, the same group employed the less strained oxetanes and azetidines as four-atom building units, and an impressive [4+2] annulation was reported (Scheme 1b).[2b] Despite these splendid advances, gold-catalyzed intermolecular annulation reaction of ynamides with unstrained saturated heterocycles so far remains a challenge.

The 1,3,5-triaryl-1,3,5-triazinanes are attractive building blocks due to their stability, structural diversity as well as easy access and handling.[3] The groups of Krische[4] and Feng[5] have employed triazinanes as hydroaminomethylation reagents in ruthenium-catalyzed transfer hydrogenation and as Mannich reagents in asymmetric Mannich-type reactions, respectively. Sun and co-workers[6] recently achieved elegant gold-catalyzed [4+1]/[4+3] annulations of 1,3,5-triazinanes with diazo esters, where triazinanes reacted directly. Inspired by these seminal works and our continual interests in gold-catalyzed ynamide transformations,[7] we herein describe a gold-catalyzed regioselective cyclocarboamination of ynamides with 1,3,5-triazinanes, which enables the

facile and modular access synthesis of 5-aminotetrahydropyrimidine derivatives in good to excellent yields (Scheme 1, lower part). Importantly, the resulting 5-aminotetrahydropyrimidine skeletons possess diverse biological activities (Figure 1).[8] This method represents the first direct 5-aminotetrahydropyrimidine synthesis from ynamides and unstrained saturated heterocycles, complementing the current tetrahydropyrimidine synthesis strategies,[9] and thus is meaningful for both organic synthesis and medicinal chemistry.



Scheme 1. Transition metal-catalyzed intermolecular reactions of ynamides with saturated heterocycles

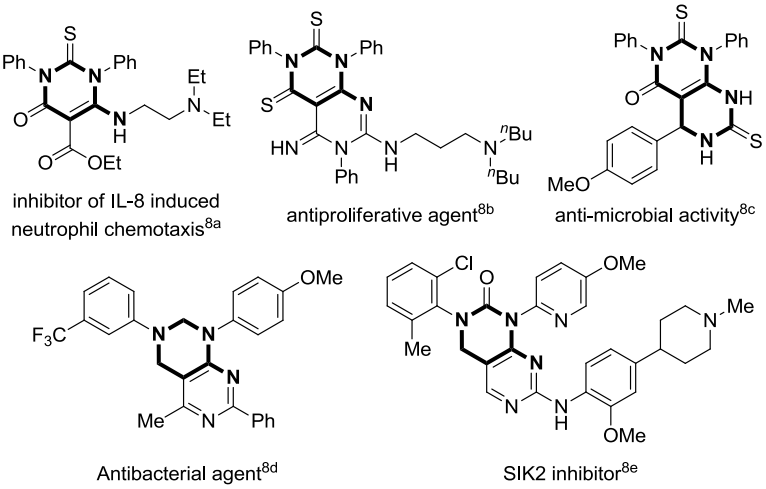


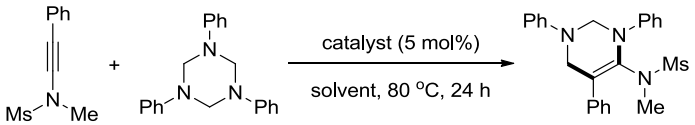
Figure 1. Representative bioactive 5-aminotetrahydropyrimidine frameworks.

5.2 Results and Discussion

5.2.1 Optimization of Reaction Condition

Initially, ynamide **1a** and 1,3,5-triazinane **2a** were set as the model substrates to optimize the reaction conditions (Table 1). The desired product **3a** was obtained in 64% yield with 5 mol% of IPrAuCl/$AgNTf_2$ in 1,2-DCE at 80 ^oC (entry 3). Control experiments with either the silver salt or the gold precatalyst alone showed no conversions (entries 1 and 2). The screened gold precatalysts bearing phosphane ligands were generally more active than those with NHC or phosphate ligands (entries 3–9). With $KAuBr_4$ as the catalyst, product **3a** was not detected (entry 10). Thus, CyJohnPhosAuCl/$AgNTf_2$ turned out to be the optimal catalyst system for this transformation (entry 8). Replacing $AgNTf_2$ with AgOTf, as the activator of the gold precatalyst, decreased the yield from 81% to 70% (entries 8 and 11). A further solvent screen revealed that CH_2Cl_2, toluene, and THF could not improve the reaction efficiency (entries 12–14). Decreasing the reaction temperature to 60 ^oC delivered **3a** in a lower yield (entry 15). Further improvement was achieved by adding the amount of 1,3,5-triazinane **2a** from 1.5 equiv. to 1.8 equiv., and in this case **3a** was isolated in 90% yield with 5 mol% CyJohnPhosAuCl/$AgNTf_2$ as the catalyst in 1,2-DCE at 80 ^oC for 24 h (entry 16).

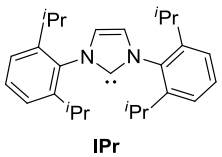
Table 1: Optimization of reaction conditions.[a]



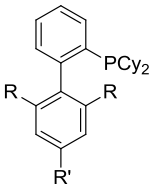
1a **2a** **3aa**

entry	catalyst	solvent	yield (%)[b]
1	$AgNTf_2$	1,2-DCE	0
2	IPrAuCl	1,2-DCE	< 5
3	IPrAuCl/$AgNTf_2$	1,2-DCE	64
4	$PPh_3AuCl/AgNTf_2$	1,2-DCE	17
5	$(2,4\text{-}^tBu_2PhO)_3PAuCl/AgNTf_2$	1,2-DCE	42
6	SPhosAuCl/$AgNTf_2$	1,2-DCE	74
7	JohnPhosAuCl/$AgNTf_2$	1,2-DCE	70
8	CyJohnPhosAuCl/$AgNTf_2$	1,2-DCE	81
9	^{t}BuXPhosAuCl/$AgNTf_2$	1,2-DCE	31
10	$KAuBr_4$	1,2-DCE	< 5
11	CyJohnPhosAuCl/AgOTf	1,2-DCE	70
12	CyJohnPhosAuCl/$AgNTf_2$	CH_2Cl_2	71
13	CyJohnPhosAuCl/$AgNTf_2$	toluene	70
14	CyJohnPhosAuCl/$AgNTf_2$	THF	70
15[c]	CyJohnPhosAuCl/$AgNTf_2$	1,2-DCE	71
16[d]	**CyJohnPhosAuCl/$AgNTf_2$**	**1,2-DCE**	**98 (90)**

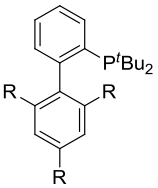
[a] Reaction conditions: **1a** (0.1 mmol) and **2a** (0.15 mmol) reacted in 0.5 mL dry solvent at 80 °C for 24 h. [b] Measured by ^{1}H NMR with 1,3,5-trimethoxybenzene as the internal standard. Yield of isolated product given in parentheses. [c] 60 °C. [c] 1.8 equiv. of **2a**.



IPr



CyJohnPhos: R = R' = H
SPhos: R = OMe, R' = H
XPhos: R = R' = ^{i}Pr



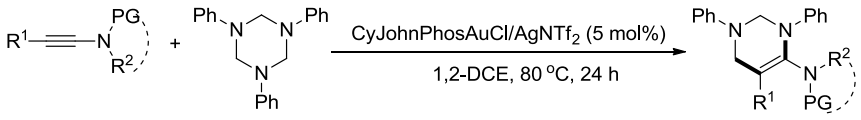
JohnPhos: R = R' = H
^{t}BuXPhos: R = R' = ^{i}Pr

5.2.2 Scope with regard to the Substrate

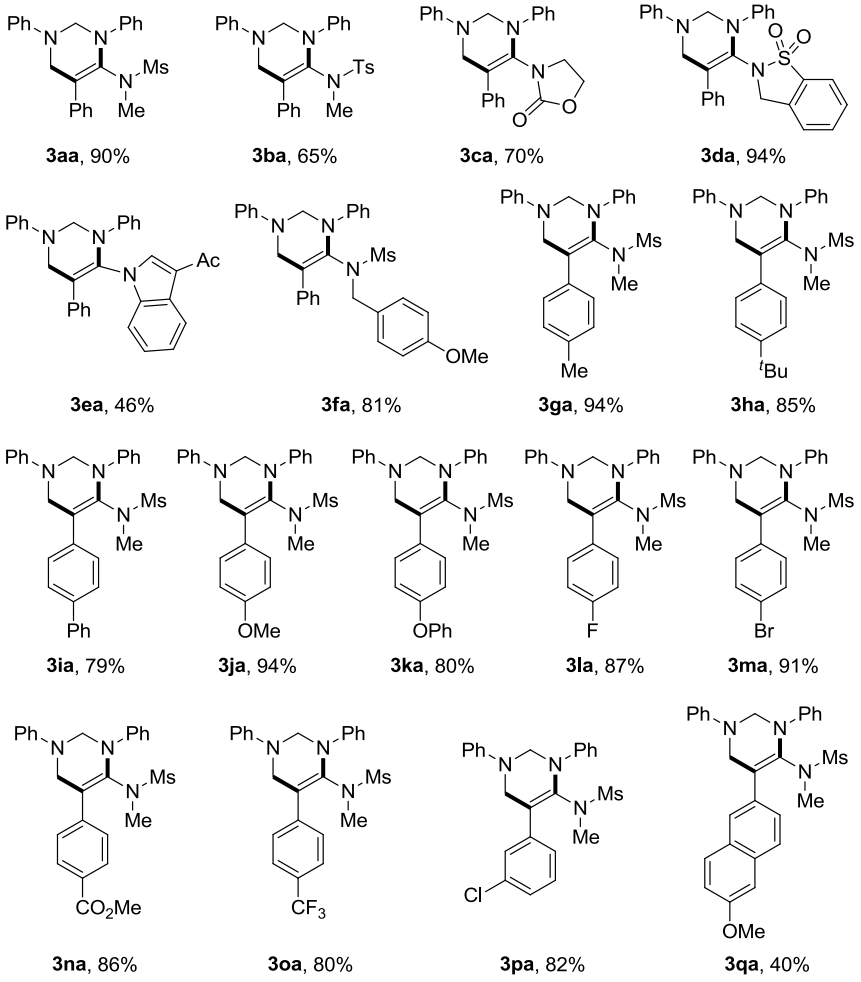
After optimization, we began to explore the substrate scope by varying the ynamide partner (Table 2). Various protecting groups (PG) such as mesyl (**3aa**), tosyl (**3ba**), oxazolidinone (**3ca**), and benzosultam (**3da**) tethered on the ynamide nitrogen were all well compatible, providing good to excellent yields. An indole-derived ynamide led to the corresponding tetrahydropyrimidine **3ea** in 64% yield. A *para*-methoxylbenzyl group at the sulfonamide moiety turned out to be also suitable. Aryl-substituted ynamides, whenever bearing an electronically neutral, an electron-donating or an electron-withdrawing substituent on the aromatic rings, provided products **3ga**–**pa** in 79–94% yields. An array of functional groups, including fluorides (**3la**), chlorides (**3pa**), bromides (**3ma**), ethers (**3ja**, **3ka**), esters (**3na**), and trifluoromethyl (**3oa**) remained intact, giving opportunities for downstream manipulation at such positions. The 6-methoxy-2-naphthalenyl substituted ynamide converted into the product **3qa** in moderate yield.

Next, a series of 1,3,5-triaryl-1,3,5-triazinanes were subjected to the gold-catalyzed cyclocarboamination of ynamide **1a** under the standard reaction conditions (Table 3). In general, both electron-deficient and electron-rich groups attached to the *ortho*-, *meta*-, or *para*-positions of the aromatic rings were tolerated, affording the target products **3ab**–**ak** in satisfactory yields (up to 86%). The reaction of triazinanes with electron-rich substituents usually delivered higher yields (**3ab**–**af** versus **3ag**–**ai**), which is consistent with a step-wise nucleophilic addition mechanism (Scheme 4). A variety of functional groups attached to the aromatic ring of such a substrate, namely fluoro (**3ag**, **3ak**), chloro (**3ah**, **3al**), bromo (**3ai**), and ether (**3ae**, **3af**) moieties, were also compatible. Triazinane substrates bearing disubstituted patterns could furnish **3al** in 81% yield.

Table 2: Reaction scope with respect to ynamides.[a,b]

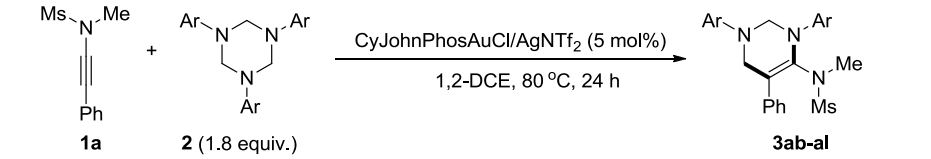


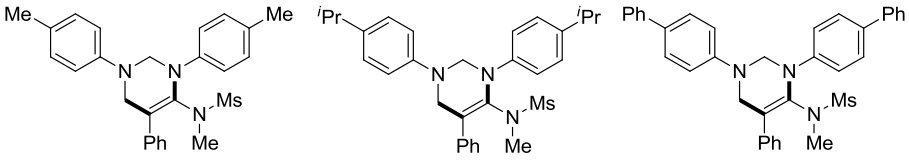
1 **2a** (1.8 equiv.) **3aa-qa**



[a] Reaction conditions: **1** (0.15 mmol), **2a** (0.27 mmol), and CyJohnPhosAuCl/AgNTf$_2$ (5 mol%) at 80 °C in 0.75 mL dry 1,2-DCE for 24 h. [b] Yield of isolated product.

Table 3: Reaction scope with respect to 1,3,5-triazinanes.[a,b]

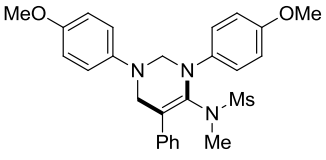




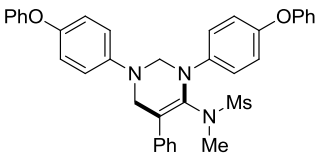
3ab, 86%

3ac, 73%

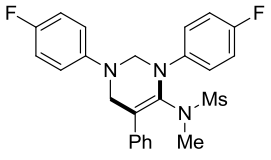
3ad, 70%



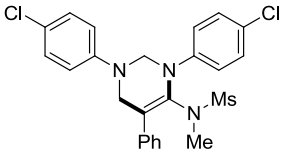
3ae, 76%



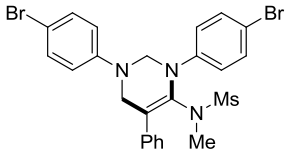
3af, 90%



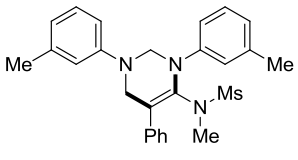
3ag, 83%



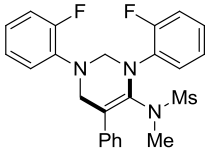
3ah, 55%



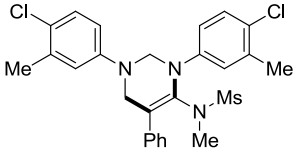
3ai, 53%



3aj, 86%



3ak, 80%



3al, 81%

[a] Reaction conditions: **1a** (0.15 mmol), **2** (0.27 mmol), and CyJohnPhosAuCl/AgNTf$_2$ (5 mol%) at 80 °C in 0.75 mL dry 1,2-DCE for 24 h. [b] Yield of isolated product.

To further verify the structural assignment, an X-ray single crystal structure analysis of **3da** was conducted (Figure 2).[10] The reaction of **1a** with **2a** could be easily run on gram scale with a lower catalyst loading (1 mol%), and **3aa** was still isolated in a good yield of 80% (Scheme 2).

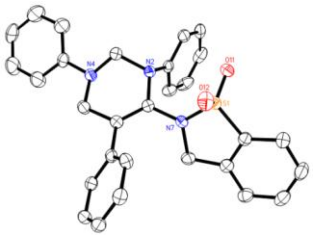
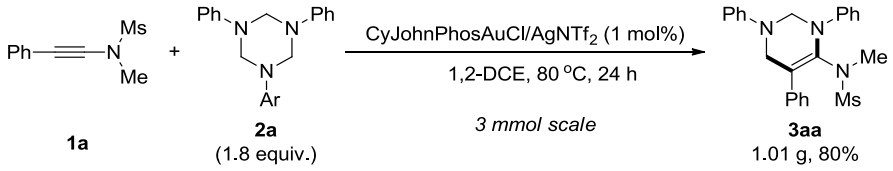


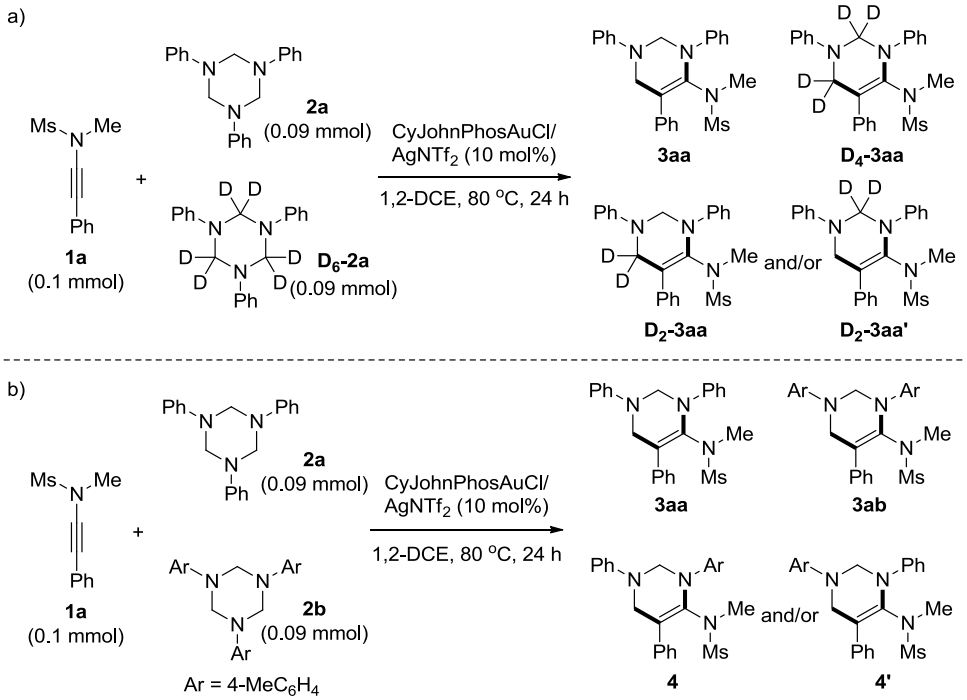
Figure 2. Solid-state molecular structure of **3da**.



Scheme 2. Gram-scale synthesis of **3aa**.

5.2.3 Mechanistic Study

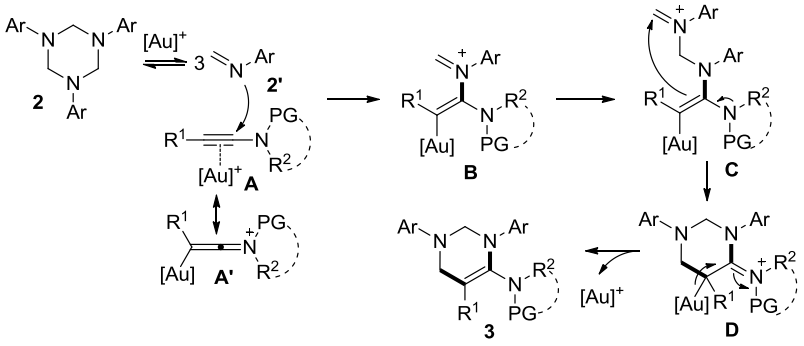
With regard to the reaction mechanism, we performed the experiment with the deuterium-labelled substrate under the standard condition (Scheme 3a). The treatment of **1a** with **2a** and **D$_6$-2a** gave a mixture of **3aa**, **D$_4$-3aa**, **D$_2$-3aa**, and/or **D$_2$-3aa'**, which rules out the direct nucleophilic attacking of triazinanes. To further verify a possible step-wise mechanism, a competition experiment was conducted (Scheme 3b). The HRMS analysis of the roughly isolated products of **1a** with **2a** and **2b** showed the formation of **3aa**, **3ab**, **4** and/or **4'**. These two cross-over experiments reveal that the present cyclocarboamination is probably caused by a three-component [2+2+2] cycloaddition.



Scheme 3. Mechanistic investigation.

A plausible mechanism is depicted in Scheme 4 according to our observations

in combination with previous reports.[4-6] First, formaldimines **2'**, *in situ* generated from 1,3,5-triazinanes **2**, regiospecifically attack the gold-activated ynamides **A** or **A'** to form the iminium intermediates **B.** It is worth noting that in Skrydstrup's previous report, a preferable intramolecular trapping of the iminium species by the aromatic ring (R^1 = Ar) affords dihydroisoquinolines.[11] However, probably due to the smaller steric hindrance, another formaldimine rapidly reacts to give new iminium species **C** in the present reaction. Then an intramolecular cyclization followed by protodeauration takes place to provide the final products **3** and regenerates the active gold catalyst.



Scheme 4. Proposed mechanism for the formation of **3**.

5.3 Conclusion

In conclusion, we have demonstrated a facile and modular synthesis of valuable 5-aminotetrahydropyrimidines through a gold-catalyzed regiocontrolled cyclocarboamination of ynamides with 1,3,5-triazinanes. Easy operation, readily available starting materials, stable four-atom building units, broad functional-group tolerance, and scaling-up potential make this new protocol attractive and practical. Mechanistic studies indicate that the present intermolecular cyclocarboamination results from a pseudo-three-component [2+2+2] cycloaddition.[12]

5.4 Notes and References

[1] For selected reviews, see: a) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840–2859; *Angew. Chem.* **2010**, *122*, 2902–2921; b) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064–5106; c) G. Evano, K. Jouvin, A. Coste, *Synthesis* **2013**, *45*, 17–26; d) X.-N. Wang, H.-S. Yeom, L.-C. Fang, S. He, Z.-X. Ma, B. L. Kedrowski, R. P. Hsung, *Acc. Chem. Res.* **2014**, *47*, 560–578.

[2] a) S. N. Karad, S. Bhunia, R.-S. Liu, *Angew. Chem. Int. Ed.* **2012**, *51*, 8722–8725; *Angew. Chem.* **2012**, *124*, 8852–8856; b) S. K. Pawar, D. Vasu, R.-S. Liu, *Adv. Synth. Catal.* **2014**, *356*, 2411–2416. For normal alkynes and propiolates, see: c) P. A. Wender, D. Strand, *J. Am. Chem. Soc.* **2009**, *131*, 7528–7529; d) D. A. Capretto, C. Brouwer, C. B. Poor, C. He, *Org. Lett.* **2011**, *13*, 5842–5845; e) R. L. Sahani, R.-S. Liu, *Chem. Commun.* **2016**, *52*, 7482–7485.

[3] A. G. Giumanini, G. Verardo, E. Zangrando, L. Lassiani, *J. Prakt. Chem.* **1987**, *329*, 1087–1103.

[4] a) S. Oda, B. Sam, M. J. Krische, *Angew. Chem. Int. Ed.* **2015**, *54*, 8525–8528; *Angew. Chem.* **2015**, *127*, 8645–8648; b) S. Oda, J. Franke, M. J. Krische, *Chem. Sci.* **2016**, *7*, 136–141.

[5] X. Lian, L. Lin, K. Fu, B. Ma, X. Liu, X. Feng, *Chem. Sci.* **2017**, *8*, 1238–1242.

[6] a) C. Zhu, G. Xu, J. Sun, *Angew. Chem. Int. Ed.* **2016**, *55*, 11867–11871; *Angew. Chem.* **2016**, *128*, 12046–12050; b) S. Liu, P. Yang, S. Peng, C. Zhu, S. Cao, J. Li, J. Sun, *Chem. Commun.* **2017**, *53*, 1152–1155.

[7] a) E. Rettenmeier, A. M. Schuster, M. Rudolph, F. Rominger, C. Gade, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 5880–5884; *Angew. Chem.* **2013**, *125*, 5993–5997; b) M. C. B. Jaimes, V. Weingand, F. Rominger, A. S. K. Hashmi, *Chem. Eur. J.* **2013**, *19*, 12504–12511; c) Y. Tokimizu, M. Wieteck, M. Rudolph, S. Oishi, N. Fujii, A. S. K. Hashmi, H. Ohno, *Org. Lett.* **2015**, *17*, 604–607; d) H. Jin, L. Huang, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi,

Angew. Chem. Int. Ed. **2016**, *54*, 794–797; *Angew. Chem.* **2016**, *127*, 804–808 e) H. Jin, B. Tian, X. Song, J. Xie, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2016**, *55*, 12688–12692; *Angew. Chem.* **2016**, *127*, 12880–12884.

[8] a) S. Cesarini, A. Spallarossa, A. Ranise, O. Bruno, N. Arduino, M. Bertolotto, F. Dallegri, M. Tognolini, T. Gobbetti, E. Barocelli, *Bioorg. Med. Chem.* **2009**, *17*, 3580–3587; b) A. Spallarossa, C. Rotolo, C. Sissi, G. Marson, M. L. Greco, A. Ranise, P. L. Colla, B. Busonera, R. Loddo, *Bioorg. Med. Chem.* **2013**, *21*, 6328–6336; c) V. V. Dabholkar, T. D. Ravi, *J. Serb. Chem. Soc.* **2010**, *75*, 1033–1040; d) J. Cieplik, M. Stolarczyk, J. Pluta, O. Gubrynowicz, I. Bryndal, T. Lis, M. Mikulewicz, *Acta Pol Pharm.* **2011**, *68*, 57–65; e) T. B. Sundberg, Y. Liang, H. Wu, H. G. Choi, N. D. Kim, T. Sim, L. Johannessen, A. Petrone, B. Khor, D. B. Graham, I. J. Latorre, A. J. Phillips, S. L. Schreiber, J. Perez, A. F. Shamji, N. S. Gray, R. J. Xavier, *ACS Chem. Biol.* **2016**, *11*, 2105–2111; f) T. Xu, L. Zhang, S. Xu, C.-Y. Yang, J. Luo, F. Ding, X. Lu, Y. Liu, Z. Tu, S. Li, D. Pei, Q. Cai, H. Li, X. Ren, S. Wang, K. Ding, *Angew. Chem. Int. Ed.* **2013**, *52*, 8387–8390; *Angew. Chem.* **2013**, 12*5*, 8545–8548.

[9] a) M. Zhang, H. Jiang, H. Liu, Q. Zhu, *Org. Lett.* **2007**, *9*, 4111–4113; b) H. Cao, X. Wang, H. Jiang, Q. Zhu, M. Zhang, H. Liu, *Chem. Eur. J.* **2008**, *14*, 11623–11633; c) L. Nagarapu, H. R. Vulupala, C. Venkatanarsimhaji, R. Bantu, A. R. Reddy, *Synth. Commun.* **2012**, *42*, 2131–2138; d) S. Myadaraboina, M. Alla, A. Parlapalli, S. Manda, *Res. Chem. Intermed.* **2016**, *42*, 923–937.

[10] CCDC 1525557 (**3da**) contain the supplementary crystallographic data for this paper, which can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[11] Z. Xin, S. Kramer, J. Overgaard, T. Skrydstrup, *Chem. Eur. J.* **2014**, *20*, 7926–7930.

[12] a) S. N. Karad, R.-S. Liu, *Angew. Chem. Int. Ed.* **2014**, *53*, 9072–9076; *Angew. Chem.* **2014**, *126*, 9218–9222; b) Y.-L. Chen, P. Sharma, R.-S. Liu, *Chem. Commun.* **2016**, 52, 3187–3190.

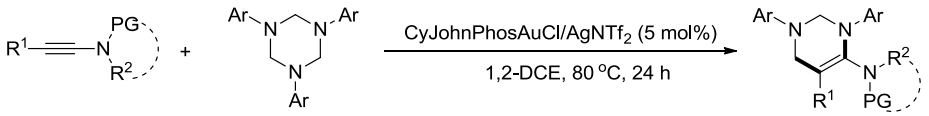
5.5 Experimental Section

General Remarks: Chemicals were purchased from commercial suppliers and used without further purification. Reagents **1** and **2** could be easily prepared according to the previous literatures.[1,2] 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 and Bruker Avance-III-500. Chemical shifts were referenced to residual solvent protons and reported in ppm and coupling constants in Hz. The following abbreviations were used for ^{1}H NMR spectra to indicate the signal multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). 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. 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. IR spectra were recorded on a Bruker Vector 22, and the absorption maxima were given in wavelength in cm^{-1} units. 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. The structures were solved and refined by Dr. F. Rominger using the SHELXTL software package. Thin-layer chromatography (TLC) was performed on precoated polyester sheets (POLYGRAM SIL G/UV254), and components were visualized by observation under UV ligh. Melting points were uncorrected.

[1] L. Zhu, Y. Yu, Z. Mao, and X. Huang, *Org. Lett.* **2015**, *17*, 30–33.

[2] A. G. Giumanini, G. Verardo, E. Zangrando, L. Lassiani, *J. Prakt. Chem.* **1987**, *329*, 1087–1103.

Experiment Procedure: Gold-catalyzed intermolecular cyclocarboamination of ynamides with 1,3,5-triazinanes



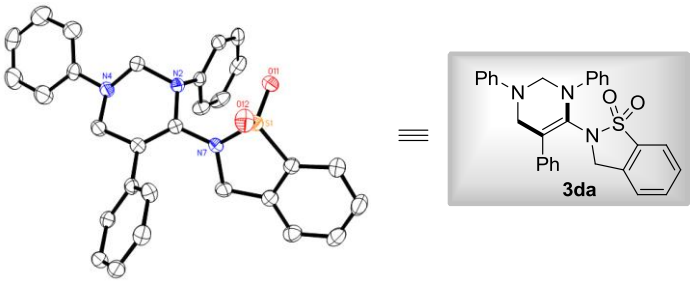
1 **2** **3**

A round bottom flask equipped with a magnetic stirrer bar was charged with CyJohnPhosAuCl (5 mol%, 4.4 mg), $AgNTf_2$ (5 mol%, 2.9 mg), and 1,2-DCE (0.40 mL). The mixture was stirred for 5 minutes at room temperature. Ynamides **1** (0.15 mmol) and 1,3,5-triazinanes **2** (0.27 mmol) were added followed by 0.35 mL 1,2-DCE. The reaction mixture was then stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the desired product **3**.

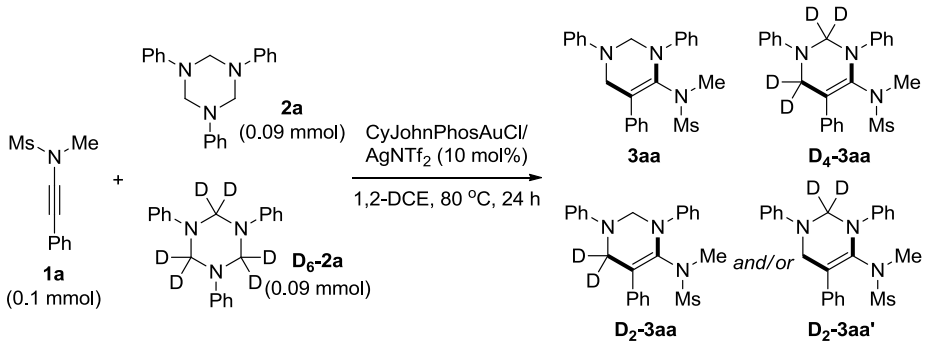
Gram-scale reaction: A round bottom flask equipped with a magnetic stirrer bar was charged with CyJohnPhosAuCl (5 mol%, 87.4 mg), $AgNTf_2$ (5 mol%, 58.2 mg), and 1,2-DCE (8.0 mL). The mixture was stirred for 5 minutes at room temperature. Ynamide **1a** (3 mmol) and 1,3,5-triazinane **2a** (5.4 mmol) were added followed by 7.0 mL 1,2-DCE. The reaction mixture was then stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was concentrated and the residue was purified by chromatography on silica gel (eluent: PE/EA) to afford the product **3aa** in 80% yield (1.01g).

X-Ray crystal structure analysis

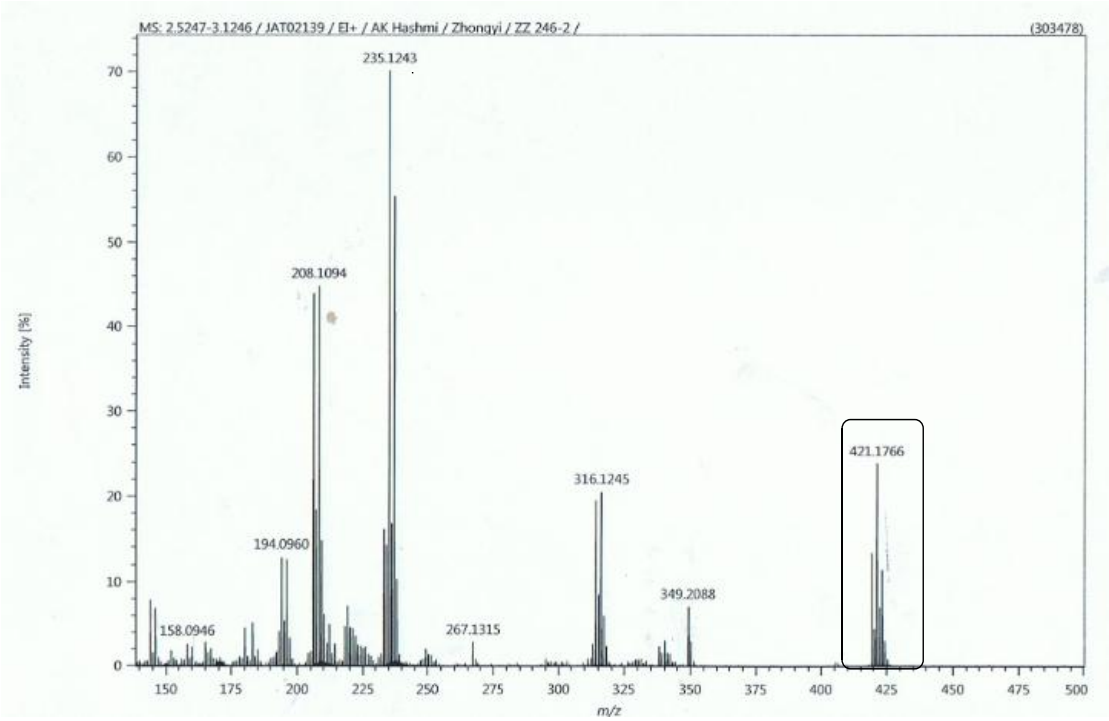
The crystallographic data of compound **3da** (CCDC 1525557) can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



Mechanistic investigations



A round bottom flask equipped with a magnetic stirrer bar was charged with CyJohnPhosAuCl (10 mol%, 5.8 mg), $AgNTf_2$ (10 mol%, 3.9 mg), and 1,2-DCE (0.5 mL). The mixture was stirred for 5 minutes at room temperature. Ynamide **1a** (0.1 mmol, 2 equiv.), 1,3,5-triazinanes **2a** (0.09 mmol, 1.8 equiv.) and **D_6-2a** (0.09 mmol, 1.8 equiv.) were added followed by 0.5 mL 1,2-DCE. The reaction mixture was then stirred at 80 °C for 24 h. After cooling to room temperature, the mixture was concentrated and the residue was purified by flash chromatography on silica gel (PE/EA = 5:1, v/v) to afford the crude product. Then such a crude product was subjected to HRMS analysis. The result showed that the formation of **3aa**, **D_4-3aa**, **D_2-3aa**, and/or **D_2-3aa'**. See the copies of the HRMS spectra below.

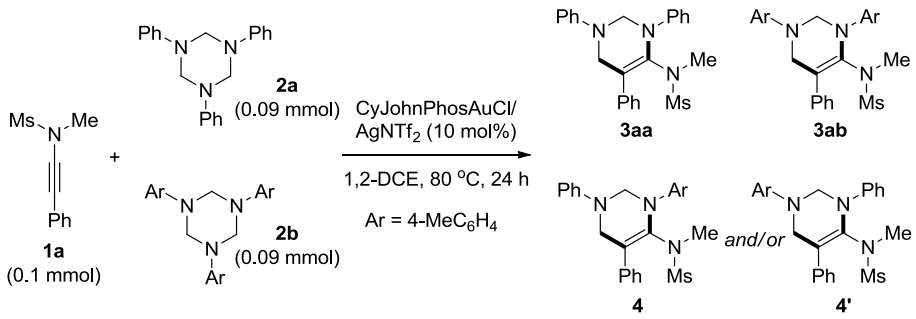


Overall spectrum

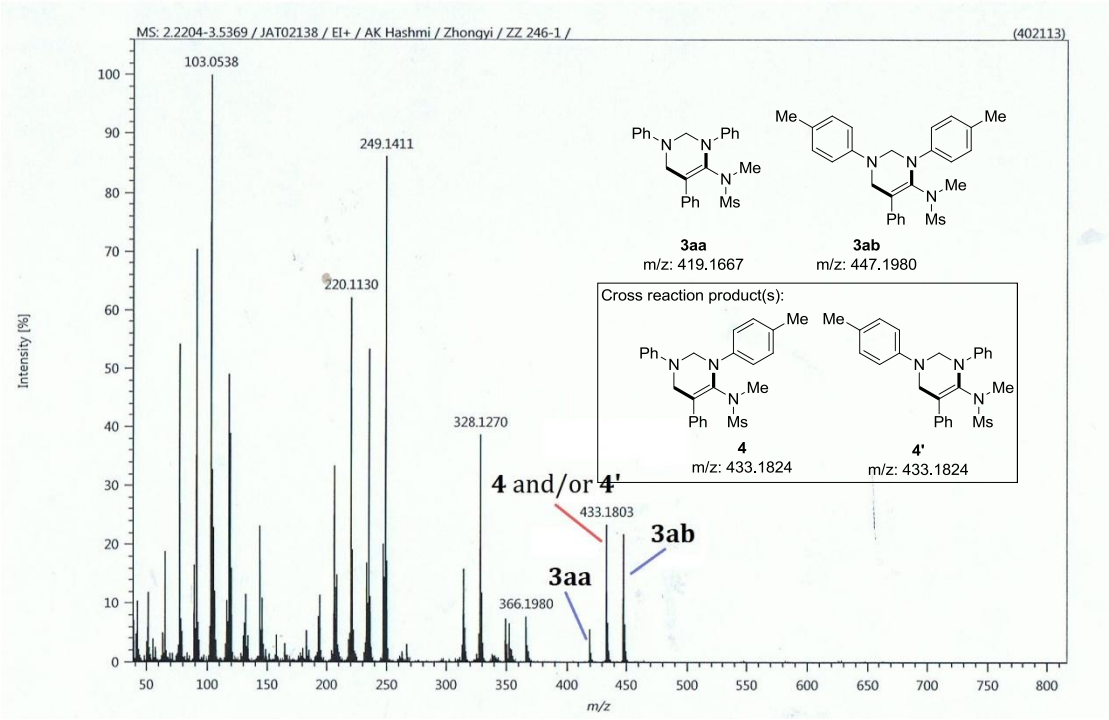
Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]
423.18815	C24 H21 N3 O2 S D4	423.19131	-3.16
	C24 H23 N3 O2 S D3	423.19285	-4.71
	C24 H25 N3 O2 S D2	423.19440	-6.25
	C24 H27 N3 O2 S D	423.19595	-7.80
422.18031	C24 H20 N3 O2 S D4	422.18348	-3.18
	C24 H22 N3 O2 S D3	422.18503	-4.72
	C24 H24 N3 O2 S D2	422.18658	-6.27
	C24 H26 N3 O2 S D	422.18813	-7.82
421.17665	C24 H21 N3 O2 S D3	421.17720	-0.56
	C24 H19 N3 O2 S D4	421.17566	0.99
	C24 H23 N3 O2 S D2	421.17875	-2.11
	C24 H25 N3 O2 S D	421.18030	-3.65
	C24 H27 N3 O2 S	421.18185	-5.20
420.16850	C24 H18 N3 O2 S D4	420.16783	0.67
	C24 H20 N3 O2 S D3	420.16938	-0.87
	C24 H22 N3 O2 S D2	420.17093	-2.42
	C24 H24 N3 O2 S D	420.17248	-3.97
	C24 H26 N3 O2 S	420.17402	-5.52
419.16463	C24 H23 N3 O2 S D	419.16465	-0.02
	C24 H21 N3 O2 S D2	419.16310	1.53
	C24 H25 N3 O2 S	419.16620	-1.57
	C24 H19 N3 O2 S D3	419.16155	3.08
	C24 H17 N3 O2 S D4	419.16001	4.63

Report list



A round bottom flask equipped with a magnetic stirrer bar was charged with CyJohnPhosAuCl (10 mol%, 5.8 mg), $AgNTf_2$ (10 mol%, 3.9 mg), and 1,2-DCE (0.5 mL). The mixture was stirred for 5 minutes at room temperature. Ynamide **1a** (0.1 mmol, 2 equiv.), 1,3,5-triazinanes **2a** (0.09 mmol, 1.8 equiv.) and **2b** (0.09 mmol, 1.8 equiv.) were added followed by 0.5 mL 1,2-DCE. The reaction mixture was then stirred at 80 ^{o}C for 24 h. After cooling to room temperature, the mixture was concentrated and the residue was purified by flash chromatography on silica gel (PE/EA = 5:1, v/v) to afford the crude product. Then such a crude product was subjected to HRMS analysis. The result showed that the formation of **3aa**, **3ab**, **4** and/or **4'**. See the copy of the HRMS spectrum below.



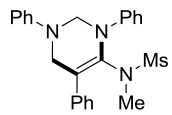
Overall spectrum

Results

Mass	Formula	Calculated Mass	Mass Difference [mDa]	Mass Difference [ppm]
447.19577	C29 H25 N3 O2	447.19413	1.65	3.68
	C26 H29 N3 O2 S	447.19750	-1.72	-3.86
	C34 H25 N	447.19815	-2.38	-5.31
	C31 H29 N S	447.20152	-5.75	-12.85
	C30 H27 N2 S	447.18895	6.83	15.27
433.18029	C25 H27 N3 O2 S	433.18185	-1.56	-3.60
	C28 H23 N3 O2	433.17848	1.81	4.18
	C33 H23 N	433.18250	-2.21	-5.11
	C30 H27 N S	433.18587	-5.58	-12.89
	C29 H25 N2 S	433.17330	6.99	16.14
419.16536	C24 H25 N3 O2 S	419.16620	-0.84	-2.01
	C32 H21 N	419.16685	-1.49	-3.56
	C27 H21 N3 O2	419.16283	2.53	6.03
	C29 H25 N S	419.17022	-4.86	-11.61
	C28 H23 N2 S	419.15765	7.71	18.40

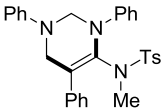
Report list

Characterization



3aa: *N*-methyl-*N*-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)methanesulfonamide

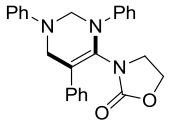
Yield 90%, light yellow solid, m.p.: 59–60 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57–7.55 (m, 2H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.37–7.32 (m, 3H), 7.18–7.13 (m, 5H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.6 Hz, 2H), 5.04 (s, 1H), 4.75 (s, 1H), 4.29 (s, 1H), 4.03 (s, 1H), 2.69 (s, 3H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.6 (s), 146.1 (s), 137.2 (s), 137.1 (s), 129.4 (d), 129.2 (d), 128.8 (d), 128.4 (d), 127.6 (d), 124.7 (d), 124.0 (d), 119.3 (d), 117.7 (s), 115.0 (d), 69.4 (t), 51.0 (t), 39.9 (q), 37.6 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3057, 3028, 2928, 2853, 1685, 1639, 1595, 1494, 1451, 1416, 1340, 1220, 1146, 1078, 1041, 1001, 960, 879, 768, 734, 698, 637, 619 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{25}N_3O_2S]^+$ $(M)^+$: 419.1647; found: 419.1662.



3ba: *N*,4-dimethyl-*N*-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)benzenesulfonamide

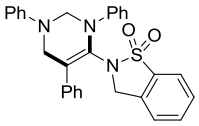
Yield 65%, light yellow solid, m.p.: 89–90 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 8.2 Hz, 2H), 7.13 (t, *J* = 7.9 Hz, 2H), 7.07 (t, *J* = 7.7 Hz, 2H), 6.95 (t, *J* = 8.8 Hz, 3H), 6.75–6.72 (m, 3H), 6.62 (d, *J* = 8.3 Hz, 2H), 4.80 (s, 2H), 4.14 (s, 2H), 2.77 (s, 3H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.6 (s), 145.9 (s), 142.5 (s), 137.9 (s), 137.3 (s), 137.2 (s), 129.2 (d), 128.9 (d), 128.7 (d), 128.5 (d), 128.4 (d), 127.5 (d), 126.7 (d), 123.7 (d), 123.5 (d), 119.0 (d), 118.2 (s), 114.7 (d), 69.2 (t), 51.0 (t), 38.6 (q), 21.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3416, 3058, 3029, 2960, 2926, 2872, 2852, 1638, 1600, 1494, 1448, 1341, 1287, 1215, 1154, 1088, 1078, 1029, 995, 961, 931, 863, 813, 761, 696, 668, 646, 607 cm^{-1}; **HRMS** (EI) calcd for $[C_{30}H_{29}N_3O_2S]^+$ $(M)^+$: 495.1975; found: 495.1978.

3ca: 3-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)oxazolidin-2-one



Yield 70%, light yellow solid, m.p.: 82–83 °C; **^{1}H NMR** (500 MHz,

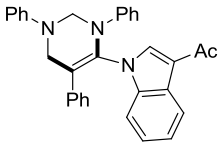
$CDCl_3$) δ 7.42–7.37 (m, 4H), 7.33–7.28 (m, 3H), 7.19–7.11 (m, 5H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 2H), 4.90 (s, 2H), 4.20 (s, 2H), 4.01 (t, *J* = 8.0 Hz, 2H), 3.50 (t, *J* = 8.0 Hz, 2H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.9 (s), 147.7 (s), 145.4 (s), 137.6 (s), 132.0 (s), 129.4 (d), 129.2 (d), 128.7 (d), 127.7 (d), 127.3 (d), 124.8 (d), 123.8 (d), 119.6 (d), 116.3 (s), 115.4 (d), 69.5 (t), 61.9 (t), 50.8 (t), 45.2 (t) ppm; **IR** (ATR): $\tilde{\nu}$ 3059, 3030, 2918, 2850, 1754, 1681, 1596, 1493, 1447, 1401, 1389, 1324, 1206, 1120, 1070, 1034, 992, 973, 933, 910, 804, 749, 696, 650 cm^{-1}; **HRMS** (ESI) calcd for $[C_{25}H_{23}N_3O_2Na]^+$ $(M + Na)^+$: 420.1682; found: 420.1686.



3da: 2-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-2,3-dihydrobenzo[*d*]isothiazole 1,1-dioxide

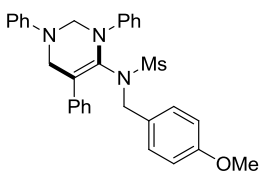
Yield 94%, white solid, m.p.: 168–169 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.56 (d, *J* = 6.6 Hz, 2H), 7.42 (s, 2H), 7.32–7.12 (m, 10H), 6.98 (s, 1H), 6.80 (t, *J* = 6.7 Hz, 1H), 6.70 (d, *J* = 7.5 Hz, 2H), 4.98 (s, 2H), 4.26 (s, 2H), 4.20 (s, 2H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.6 (s), 146.7 (s), 136.8 (s), 134.7 (s), 133.1 (s), 132.9 (s), 132.3 (d), 129.2 (d), 128.9 (d), 128.8 (d), 128.8 (d), 127.6 (d), 125.0 (d), 124.7 (d), 123.8 (d), 121.4 (d), 119.3 (d), 115.3 (s), 114.9 (d), 69.7 (t), 50.8 (t), 50.0 (t) ppm; **IR** (ATR): $\tilde{\nu}$ 3062, 2865, 2783, 1650, 1597, 1505, 1490, 1456, 1372, 1304, 1294, 1277, 1267, 1204, 1169, 1131, 1104, 1066, 1056, 1036, 992, 971, 933, 900, 827, 794, 754, 734, 700, 661, 624, 609 cm^{-1}; **HRMS** (EI) calcd for $[C_{29}H_{25}N_3O_2S]^+$ $(M)^+$: 479.1662; found: 479.1668.

3ea: 1-(1-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-1*H*-indol-3-yl)ethanone



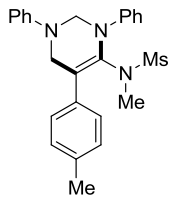
Yield 46%, white solid, m.p.: 96–97 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.19–8.17 (m, 1H), 7.56 (s, 1H), 7.53–7.50 (m, 1H), 7.24–7.21 (m, 2H), 7.17–7.08 (m, 7H), 7.04 (d, *J* = 7.4 Hz, 2H), 7.00–6.98 (m, 2H), 6.95 (t, *J* = 7.2 Hz, 1H), 6.86–6.80 (m, 3H), 5.10 (s, 2H), 4.40 (s, 2H), 2.28 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 193.4 (s), 147.5 (s), 145.0 (s), 136.6 (s), 136.3 (s), 135.4 (d), 133.9 (s), 129.4 (d), 129.2 (d), 128.6 (d), 127.2 (d), 127.2 (d), 1261 (s), 125.0 (d), 123.8 (d), 123.5 (d), 122.9 (d), 122.1 (d), 112.0 (d),

118.9 (s), 115.6 (d), 114.8 (s), 112.2 (d), 70.0 (t), 50.5 (t), 27.5 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3056, 3028, 2922, 1738, 1649, 1597, 1530, 1492, 1454, 1376, 1347, 1310, 1271, 1201, 1154, 1069, 1028, 1016, 996, 973, 932, 909, 748, 695, 637, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{32}H_{27}N_3O]^+$ $(M)^+$: 469.2149; found: 469.2148.



3fa: *N*-(4-methoxybenzyl)-*N*-(1,3,5-triphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)methanesulfonamide

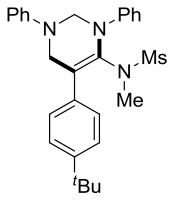
Yield 81%, white solid, m.p.: 73–74 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.41–7.36 (m, 4H), 7.33–7.27 (m, 3H), 7.22 (t, *J* = 6.8 Hz, 1H), 7.16–7.12 (m, 4H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.75 (t, *J* = 7.3 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 2H), 4.93 (d, *J* = 12.0 Hz, 1H), 4.68 (d, *J* = 12.1 Hz, 1H), 4.16 (d, *J* = 14.8 Hz, 2H), 4.06–3.96 (m, 2H), 3.81 (s, 3H), 2.04 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.5 (s), 147.7 (s), 145.8 (s), 137.9 (s), 135.1 (s), 131.4 (d), 129.42 (d), 129.35 (d), 129.2 (d), 128.3 (d), 127.6 (s), 127.4 (d), 125.9 (d), 125.7 (d), 119.7 (s), 119.1 (d), 114.8 (d), 113.7 (d), 69.8 (t), 55.3 (q), 51.9 (t), 51.8 (t), 41.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3058, 3037, 2933, 2350, 2248, 1681, 1628, 1611, 1596, 1512, 1494, 1453, 1338, 1303, 1247, 1216, 1175, 1150, 1073, 1034, 962, 911, 834, 764, 730, 697, 647, 618 cm^{-1}; **HRMS** (EI) calcd for $[C_{31}H_{31}N_3O_3S]^+$ $(M)^+$: 525.2081; found: 525.2067.



3ga: *N*-(1,3-diphenyl-5-(*p*-tolyl)-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

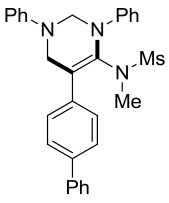
Yield 94%, white solid, m.p.: 69–70 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.9 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.27–7.25 (m, 2H), 7.18–7.12 (m, 5H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 8.5 Hz, 2H), 5.06 (s, 1H), 4.73 (s, 1H), 4.29 (s, 1H), 4.00 (s, 1H), 2.70 (s, 3H), 2.39 (s, 6H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.7 (s), 146.2 (s), 137.3 (s), 136.8 (s), 134.1 (s), 129.5 (d), 129.4 (d), 129.2 (d), 128.2 (d), 124.6 (d), 123.9 (d), 119.2 (d), 117.8 (s), 114.9 (d), 69.4 (t), 51.1 (t), 40.0 (q), 37.7 (q), 21.3 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3056, 3030, 2923, 2856, 2249, 1677, 1637, 1597, 1494, 1456, 1336, 1287, 1271, 1220, 1145, 1080, 1039, 996, 961,

931, 911, 867, 822, 798, 754, 731, 699, 648 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{25}N_3O_2S]^+$ $(M)^+$: 433.1819; found: 433.1817.



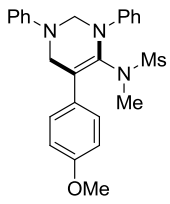
3ha: *N*-(5-(4-(*tert*-butyl)phenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 85%, white solid, m.p.: 176–177 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.48 (q, *J* = 7.8 Hz, 4H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.18–7.12 (m, 5H), 6.77 (t, *J* = 7.2 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.04 (s, 1H), 4.74 (s, 1H), 4.29 (s, 1H), 4.01 (s, 1H), 2.70 (s, 3H), 2.37 (s, 3H), 1.36 (s, 9H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 150.5 (s), 147.7 (s), 146.2 (s), 136.8 (s), 134.1 (s), 129.4 (d), 129.2 (d), 128.0 (d), 125.6 (d), 124.6 (d), 123.9 (d), 119.2 (d), 117.7 (s), 117.5 (s), 114.9 (d), 69.4 (t), 51.0 (t), 40.0 (q), 37.7 (q), 34.7 (s), 31.4 (q); **IR** (ATR): $\tilde{\nu}$ 2951, 2866, 1623, 1599, 1505, 1491, 1455, 1395, 1335, 1273, 1209, 1145, 1084, 1060, 1030, 998, 965, 931, 852, 837, 796, 782, 751, 695, 644 cm^{-1}; **HRMS** (EI) calcd for $[C_{28}H_{33}N_3O_2S]^+$ $(M)^+$: 475.2288; found: 475.2273.



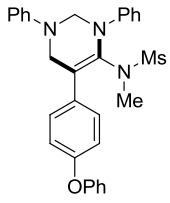
3ia: *N*-(5-([1,1'-biphenyl]-4-yl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 79%, white solid, m.p.: 159–160 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70–7.62 (m, 6H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.38–7.34 (m, 3H), 7.18–7.13 (m, 5H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 2H), 5.07 (s, 1H), 4.74 (s, 1H), 4.35 (s, 1H), 4.04 (s, 1H), 2.74 (s, 3H), 2.40 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.6 (s), 146.1 (s), 140.5 (s), 140.1 (s), 137.3 (s), 136.1 (s), 129.4 (d), 129.2 (d), 128.9 (d), 128.7 (d), 127.4 (d), 127.3 (d), 127.0 (d), 124.7 (d), 123.9 (d), 119.3 (d), 117.1 (s), 115.0 (d), 69.4 (t), 50.9 (t), 40.0 (q), 37.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3060, 3029, 2954, 2924, 2852, 1633, 1598, 1502, 1488, 1454, 1339, 1279, 1212, 1147, 1082, 1032, 1006, 963, 932, 847, 766, 751, 730, 695, 643 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{25}N_3O_2S]^+$ $(M)^+$: 495.1975; found: 495.1945.



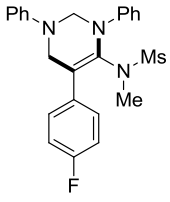
3ja: *N*-(5-(4-methoxyphenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 94%, white solid, m.p.: 145–146 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.6 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.17–7.12 (m, 5H), 6.99 (d, *J* = 8.7 Hz, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 2H), 5.06 (s, 1H), 4.70 (s, 1H), 4.28 (s, 1H), 3.97 (s, 1H), 3.85 (s, 3H), 2.70 (s, 3H), 2.41 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.0 (s), 147.6 (s), 146.3 (s), 136.7 (s), 129.5 (d), 129.4 (d), 129.3 (s), 129.2 (d), 124.6 (d), 123.8 (d), 119.2 (d), 117.5 (s), 114.9 (d), 114.1 (d), 69.4 (t), 55.3 (q), 51.1 (t), 40.1 (q), 37.7 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3030, 2933, 2838, 2254, 1738, 1641, 1598, 1504, 1494, 1460, 1336, 1278, 1246, 1217, 1205, 1179, 1145, 1081, 1032, 995, 961, 931, 911, 867, 835, 799, 755, 732, 702, 649, 615 cm^{-1}; **HRMS** (EI) calcd for $[C_{25}H_{27}N_3O_3S]^+$ $(M)^+$: 449.1768; found: 419.1779.



3ka: *N*-methyl-*N*-(5-(4-phenoxyphenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)methanesulfonamide

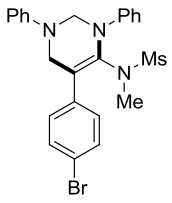
Yield 80%, light yellow solid, m.p.: 60–61 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.55–7.52 (m, 2H), 7.39–7.34 (m, 4H), 7.18–7.13 (m, 6H), 7.10–7.05 (m, 4H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 2H), 5.06 (s, 1H), 4.71 (s, 1H), 4.30 (s, 1H), 4.00 (s, 1H), 2.74 (s, 3H), 2.42 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.9 (s), 156.8 (s), 147.6 (s), 146.2 (s), 137.1 (s), 131.9 (s), 129.9 (d), 129.7 (d), 129.4 (d), 129.2 (d), 124.7 (d), 123.9 (d), 123.6 (d), 119.3 (d), 119.2 (d), 118.8 (d), 117.1 (s), 115.0 (d), 69.4 (t), 51.1 (t), 40.1 (q), 37.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3061, 3036, 2929, 2851, 2363, 2252, 1647, 1597, 1489, 1457, 1336, 1273, 1236, 1169, 1144, 1080, 1033, 995, 961, 932, 910, 868, 800, 750, 732, 694, 650 cm^{-1}; **HRMS** (EI) calcd for $[C_{30}H_{29}N_3O_2S]^+$ $(M)^+$: 511.1924; found: 511.1920.



3la: *N*-(5-(4-fluorophenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

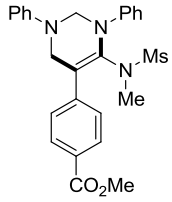
Yield 87%, light yellow solid, m.p.: 64–65 °C; **^{1}H NMR** (500 MHz,

$CDCl_3$) δ 7.55–7.52 (m, 2H), 7.37–7.34 (m, 2H), 7.17–7.12 (m, 7H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.66 (d, *J* = 7.9 Hz, 2H), 5.05 (s, 1H), 4.71 (s, 1H), 4.27 (s, 1H), 3.97 (s, 1H), 2.69 (s, 3H), 2.40 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 162.1 (s, d: $J_{C\text{-}F}$ = 247.1 Hz), 147.5 (s), 146.1 (s), 137.4 (s), 133.0 (s, d: $J_{C\text{-}F}$ = 3.4 Hz), 130.1 (d, d: $J_{C\text{-}F}$ = 8.0 Hz), 129.4 (d), 129.2 (d), 124.8 (d), 123.9 (d), 119.4 (d), 116.8 (s), 115.7 (d, d: $J_{C\text{-}F}$ = 21.3 Hz), 115.0 (d), 69.5 (t), 51.1 (t), 40.0 (q), 37.8 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -114.16 ppm; **IR** (ATR): $\tilde{\nu}$ 3063, 2929, 1681, 1638, 1595, 1494, 1336, 1222, 1157, 1146, 1099, 1080, 1040, 961, 912, 840, 799, 761, 729, 696, 648, 613 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{24}N_3O_2S]^+$ $(M)^+$: 437.1568; found: 437.1557.



3ma: *N*-(5-(4-bromophenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

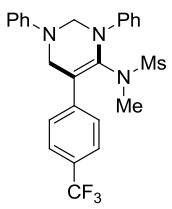
Yield 91%, white solid, m.p.: 165–166 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.18–7.12 (m, 5H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 8.2 Hz, 2H), 5.05 (s, 1H), 4.70 (s, 1H), 4.29 (s, 1H), 3.98 (s, 1H), 2.70 (s, 3H), 2.39 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5 (s), 146.0 (s), 137.6 (s), 136.1 (s), 131.9 (d), 130.0 (d), 129.5 (d), 129.3 (d), 124.9 (d), 124.0 (d), 121.5 (s), 119.5 (d), 116.4 (s), 115.0 (d), 69.4 (t), 50.8 (t), 39.9 (q), 37.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3067, 3035, 2862, 1641, 1599, 1490, 1461, 1424, 1385, 1362, 1329, 1295, 1283, 1199, 1142, 1080, 1041, 1008, 997, 963, 932, 893, 869, 833, 803, 789, 763, 733, 700, 658 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{24}N_3O_2SBr]^+$ $(M)^+$: 497.0767; found: 497.0745.



3na: methyl 4-(6-(*N*-methylmethylsulfonamido)-1,3-diphenyl-1,2,3,4-tetrahydropyrimidin-5-yl)benzoate

Yield 86%, white solid, m.p.: 81–82 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.18–7.12 (m, 5H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.9 Hz, 2H), 5.05 (s, 1H), 4.73 (s, 1H), 4.34 (s, 1H), 4.03 (s, 1H), 3.93 (s, 3H), 2.68 (s, 3H), 2.35 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.9 (s), 147.5 (s), 145.8 (s), 142.1 (s), 138.2

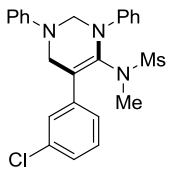
(s), 130.0 (d), 129.5 (d), 129.3 (d), 129.0 (s), 128.3 (d), 125.0 (d), 124.1 (d), 119.5 (d), 116.2 (s), 115.1 (d), 69.3 (t), 52.2 (q), 50.6 (t), 39.8 (q), 37.7 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2951, 1717, 1685, 1637, 1597, 1494, 1456, 1436, 1337, 1278, 1221, 1182, 1146, 1110, 1039, 1020, 960, 933, 862, 828, 772, 697, 647 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{27}N_3O_4S]^+$ $(M)^+$: 477.1717; found: 477.1701.



3oa: *N*-(1,3-diphenyl-5-(4-(trifluoromethyl)phenyl)-1,2,3,6-tetrahydro pyrimidin-4-yl)-*N*-methylmethanesulfonamide

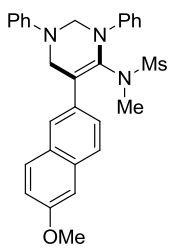
Yield 80%, light yellow solid, m.p.: 139–140 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.71–7.67 (m, 4H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.18–7.12 (m, 5H), 6.79 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.06 (s, 1H), 4.72 (s, 1H), 4.34 (s, 1H), 4.01 (s, 1H), 2.69 (s, 3H), 2.37 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5 (s), 145.8 (s), 141.0 (s, d: $J_{C\text{-}F}$ = 1.1 Hz), 138.3 (s), 129.5 (d), 129.4 (s, q: $J_{C\text{-}F}$ = 32.5 Hz), 129.3 (d), 128.6 (d), 125.7 (d, q: $J_{C\text{-}F}$ = 3.7 Hz), 125.0 (d), 124.15 (s, q: $J_{C\text{-}F}$ = 270.0 Hz), 124.07 (d), 119.6 (d), 116.0 (s), 115.1 (d), 69.4 (t), 50.7 (t), 39.8 (q), 37.9 (q) ppm; **^{19}F NMR** (470 MHz, $CDCl_3$) δ -62.459, -62.464 ppm; **IR** (ATR): $\tilde{\nu}$ 3029, 2924, 2849, 1599, 1493, 1455, 1411, 1337, 1277, 1213, 1148, 1114, 1066, 1033, 1016, 996, 963, 935, 862, 850, 794, 769, 754, 694, 609 cm^{-1}; **HRMS** (EI) calcd for $[C_{25}H_{24}N_3O_2SF_3]^+$ $(M)^+$: 487.1536; found: 487.1522.

3pa: *N*-(5-(3-chlorophenyl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methyl methanesulfonamide



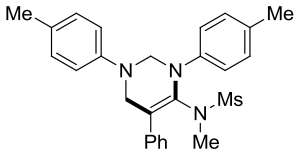
Yield 82%, light yellow solid, m.p.: 78–79 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.39–7.29 (m, 4H), 7.18–7.12 (m, 5H), 6.78 (t, *J* = 7.3 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 2H), 5.03 (s, 1H), 4.71 (s, 1H), 4.27 (s, 1H), 4.00 (s, 1H), 2.71 (s, 3H), 2.37 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.5 (s), 145.9 (s), 139.1 (s), 137.9 (s), 134.4 (s), 130.1 (d), 129.5 (d), 129.2 (d), 128.1 (d), 127.6 (d), 126.9 (d), 124.9 (d), 124.1 (d), 119.5 (d), 116.1 (s), 115.1 (d), 69.4 (t), 50.8 (t), 39.8 (q), 37.7 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3063, 3030, 2929, 2854, 1639, 1594, 1562, 1493, 1411, 1336, 1285, 1205, 1145, 1080, 1033, 996, 962, 866, 787, 752,

721, 695, 611 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{24}N_3O_2SCl]^+$ $(M)^+$: 453.1272; found: 453.1265.



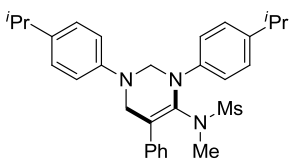
3qa: *N*-(5-(6-methoxynaphthalen-2-yl)-1,3-diphenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 40%, white solid, m.p.: 188–189 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 1.1 Hz, 1H), 7.80 (t, *J* = 9.3 Hz, 2H), 7.71 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.37–7.34 (m, 2H), 7.19–7.12 (m, 7H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.70 (d, *J* = 7.9 Hz, 2H), 5.10 (s, 1H), 4.75 (s, 1H), 4.44 (s, 1H), 4.06 (s, 1H), 3.94 (s, 3H), 2.67 (s, 3H), 2.39 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.9 (s), 147.7 (s), 146.2 (s), 137.3 (s), 133.8 (s), 132.3 (s), 129.6 (d), 129.4 (d), 129.2 (d), 128.9 (s), 127.2 (d), 127.1 (d), 126.6 (d), 124.6 (d), 123.8 (d), 119.3 (d), 119.2 (d), 117.5 (s), 114.9 (d), 105.7 (d), 69.3 (t), 55.4 (q), 51.0 (t), 40.0 (q), 37.8 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2932, 2236, 1627, 1599, 1485, 1392, 1340, 1268, 1214, 1156, 1026, 955, 914, 756, 696 cm^{-1}; **HRMS** (EI) calcd for $[C_{29}H_{29}N_3O_2S]^+$ $(M)^+$: 499.1924; found: 499.1926.



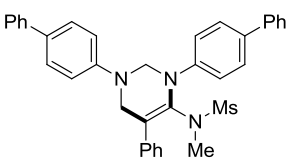
3ab: *N*-methyl-*N*-(5-phenyl-1,3-di-*p*-tolyl-1,2,3,6-tetrahydropyrimidin-4-yl)methanesulfonamide

Yield 86%, white solid, m.p.: 79–80 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 8.1 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.61 (d, *J* = 8.4 Hz, 2H), 4.91 (s, 1H), 4.66 (s, 1H), 4.23 (s, 1H), 3.98 (s, 1H), 2.68 (s, 3H), 2.38 (s, 3H), 2.33 (s, 3H), 2.22 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.5 (s), 143.7 (s), 137.4 (s), 137.2 (s), 134.4 (s), 129.9 (d), 129.7 (d), 128.72 (s), 128.70 (d), 128.5 (s), 127.4 (d), 124.1 (d), 117.4 (s), 115.3 (d), 70.2 (t), 51.3 (t), 40.0 (q), 37.6 (q), 20.9 (q), 20.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3032, 3010, 2926, 2864, 2239, 1680, 1635, 1596, 1513, 1450, 1408, 1381, 1339, 1330, 1273, 1218, 1175, 1040, 961, 914, 876, 819, 769, 729, 703, 645 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{29}N_3O_2S]^+$ $(M)^+$: 447.1975; found: 447.1956.



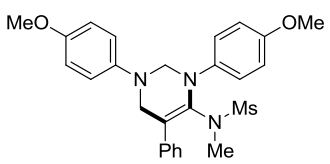
3ac: *N*-(1,3-bis(4-isopropylphenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 73%, light yellow solid, m.p.: 140–141 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.35–7.32 (m, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.06 (t, *J* = 7.7 Hz, 4H), 6.67 (d, *J* = 8.1 Hz, 2H), 4.98 (s, 1H), 4.68 (s, 1H), 4.29 (s, 1H), 3.99 (s, 1H), 2.90 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.80 (dt, *J* = 13.8, 6.9 Hz, 1H), 2.70 (s, 3H), 2.40 (s, 3H), 1.25 (d, *J* = 6.9 Hz, 6H), 1.19 (d, *J* = 6.9 Hz, 6H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.9 (s), 145.3 (s), 143.9 (s), 139.9 (s), 137.4 (s), 137.3 (s), 128.7 (d), 128.4 (d), 127.4 (d), 127.2 (d), 127.1 (d), 124.0 (d), 117.4 (s), 115.3 (d), 70.0 (t), 51.3 (t), 40.0 (q), 37.7 (q), 33.5 (q), 33.2 (q), 24.2 (q), 24.1 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3402, 3053, 3022, 2833, 1738, 1627, 1598, 1509, 1472, 1440, 1386, 1361, 1291, 1264, 1220, 1176, 1145, 1125, 1030, 980, 956, 935, 832, 809, 746, 702, 653, 619 cm^{-1}; **HRMS** (EI) calcd for $[C_{30}H_{37}N_3O_2S]^+$ $(M)^+$: 503.2601; found: 503.2590.



3ad: *N*-(1,3-di([1,1'-biphenyl]-4-yl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

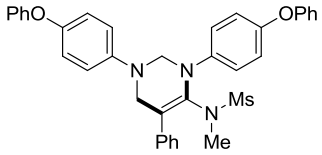
Yield 70%, light yellow solid, m.p.: 150–151 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.61–7.57 (m, 6H), 7.49–7.32 (m, 13H), 7.22 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 5.12 (s, 1H), 4.80 (s, 1H), 4.35 (s, 1H), 4.10 (s, 1H), 2.72 (s, 3H), 2.42 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.9 (s), 145.3 (s), 140.8 (s), 140.1 (s), 137.4 (s), 137.1 (s), 137.0 (s), 132.1 (s), 128.9 (d), 128.8 (d), 128.7 (d), 128.4 (d), 128.0 (d), 127.9 (d), 127.6 (d), 127.3 (d), 126.8 (d), 126.5 (d), 124.0 (d), 117.9 (s), 115.1 (d), 69.1 (t), 51.0 (t), 40.1 (q), 37.7 (q) ppm; **IR** (reflection): $\tilde{\nu}$ 3055, 3030, 2924, 2852, 1681, 1637, 1609, 1523, 1486, 1449, 1337, 1297, 1263, 1215, 1176, 1145, 1077, 1041, 1007, 960, 931, 911, 841, 762, 728, 697, 649 cm^{-1}; **HRMS** (ESI) calcd for $[C_{36}H_{33}N_3O_2SNa]^+$ $(M+Na)^+$: 594.2186; found: 594.2192.



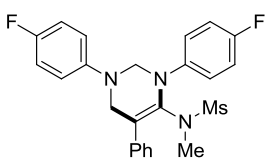
3ae: *N*-(1,3-bis(4-methoxyphenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 76%, light yellow solid, m.p.: 158–159 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54–7.52 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 1H), 7.13–7.10 (m, 2H), 6.89–6.86 (m, 2H), 6.76–6.73 (m, 2H), 6.69–6.66 (m, 2H), 4.73 (s, 1H), 4.62 (s, 1H), 4.13 (s, 1H), 3.99 (s, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 2.68 (s, 3H), 2.33 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.0 (s), 153.6 (s), 142.0 (s), 139.4 (s), 137.6 (s), 137.2 (s), 128.7 (d), 128.6 (d), 127.4 (d), 126.0 (d), 117.6 (d), 117.1 (s), 114.6 (d), 114.4 (d), 71.9 (t), 55.6 (q), 55.4 (q), 52.1 (t), 39.7 (q), 37.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3058, 3039, 2988, 2958, 2914, 2837, 2788, 1654, 1608, 1581, 1508, 1455, 1445, 1479, 1331, 1295, 1240, 1194, 1143, 1107, 1088, 1064, 1032, 963, 933, 876, 837, 828, 770, 747, 699 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{29}N_3O_4S]^+$ $(M)^+$: 479.1873; found: 479.1874.

3af: *N*-(1,3-bis(4-phenoxyphenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide



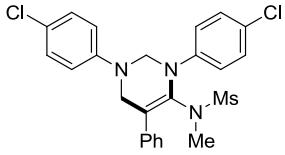
Yield 90%, white solid, m.p.: 75–76 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.1 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.34–7.28 (m, 5H), 7.13–7.08 (m, 3H), 7.04–6.96 (m, 5H), 6.91–6.88 (m, 4H), 6.74–6.72 (m, 2H), 4.88 (s, 1H), 4.75 (s, 1H), 4.22 (s, 1H), 4.07 (s, 1H), 2.69 (s, 3H), 2.36 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 158.4 (s), 157.2 (s), 154.2 (s), 149.8 (s), 144.3 (s), 141.5 (s), 137.3 (s), 136.9 (s), 129.8 (d), 129.6 (d), 128.8 (d), 128.5 (d), 127.6 (d), 125.7 (d), 123.4 (d), 122.4 (d), 120.7 (d), 119.6 (d), 118.7 (d), 117.6 (d), 117.4 (s), 117.2 (d), 70.9 (t), 51.8 (t), 39.8 (q), 37.4 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3059, 3039, 2931, 1643, 1589, 1504, 1487, 1338, 1291, 1234, 1198, 1144, 1105, 1076, 1023, 961, 931, 869, 841, 756, 692 cm^{-1}; **HRMS** (EI) calcd for $[C_{36}H_{33}N_3O_4S]^+$ $(M)^+$: 603.2186; found: 603.2183.



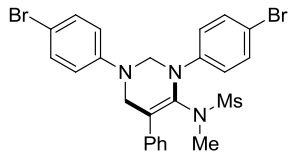
3ag: *N*-(1,3-bis(4-fluorophenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 83%, light yellow solid, m.p.: 154–155 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.1 Hz, 2H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.18–7.14 (m, 2H), 7.03 (t, *J* = 8.5 Hz, 2H), 6.87 (t, *J* = 8.6 Hz, 2H), 6.67–6.62 (m, 2H), 4.74 (s, 2H), 4.09 (s, 2H), 2.69 (s, 13H), 2.26 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 160.1 (s, d: $J_{C\text{-}F}$ = 244.8 Hz), 157.1 (s, d: $J_{C\text{-}F}$ = 239.0 Hz), 144.2 (s, d: $J_{C\text{-}F}$ = 2.2 Hz), 142.1 (s, d: $J_{C\text{-}F}$ = 2.8 Hz), 137.37 (s), 136.72 (s), 128.78 (d), 128.65 (d), 127.64 (d), 126.21 (d, d: $J_{C\text{-}F}$ = 8.2 Hz), 117.53 (s), 117.19 (d, d: $J_{C\text{-}F}$ = 7.6 Hz), 116.11 (d, d: $J_{C\text{-}F}$ = 22.5 Hz), 115.69 (d, d: $J_{C\text{-}F}$ = 22.3 Hz), 71.25 (t), 51.88 (t), 39.58 (q), 37.12 (q); **^{19}F NMR** (282 MHz, CD_3Cl_3) δ -122.45, -129.63 ppm; **IR** (ATR): $\tilde{\nu}$ 3063, 3032, 3012, 2868, 2799, 1648, 1598, 1506, 1462, 1453, 1441, 1425, 1375, 1330, 1293, 1275, 1224, 1197, 1171, 1154, 1141, 1098, 1081, 1065, 1025, 997, 962, 934, 911, 883, 843, 822, 774, 762, 752, 733, 723, 701, 642, 608 cm^{-1}; **HRMS** (ESI) calcd for $[C_{24}H_{23}N_3O_2SF_2Na]^+$ $(M+Na)^+$: 478.1371; found: 478.1376.

3ah: *N*-(1,3-bis(4-chlorophenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

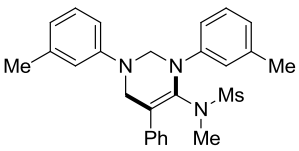


Yield 55%, yellow solid, m.p.: 170–171 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.1 Hz, 12H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.35–7.30 (m, 3H), 7.11–7.09 (m, 4H), 6.58 (d, *J* = 8.9 Hz, 2H), 4.81 (s, 2H), 4.10 (s, 2H), 2.67 (s, 3H), 2.30 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.1 (s), 144.5 (s), 137.0 (s), 136.5 (s), 130.4 (s), 129.6 (d), 129.1 (d), 128.8 (d), 128.5 (d), 127.8 (d), 125.4 (d), 124.4 (s), 118.0 (s), 116.3 (d), 69.5 (t), 51.2 (t), 39.8 (q), 37.2 (q); **IR** (ATR): $\tilde{\nu}$ 3092, 3061, 2932, 2851, 1685, 1635, 1595, 1492, 1451, 1391, 1377, 1358, 1337, 1293, 1273, 1245, 1222, 1205, 1147, 1094, 1077, 1056, 1016, 1001, 961, 927, 910, 854, 836, 816, 800, 780, 766, 756, 731, 701, 661, 632, 621 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{23}N_3O_2SCl_2]^+$ $(M)^+$: 487.0883; found: 487.0877.



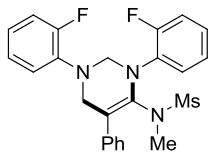
3ai: *N*-(1,3-bis(4-bromophenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 53%, light yellow solid, m.p.: 188–189 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.51–7.42 (m, 6H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.26–7.23 (m, 2H), 7.05–7.03 (m, 2H), 6.53 (d, *J* = 9.0 Hz, 2H), 4.80 (s, 2H), 4.09 (s, 2H), 2.67 (s, 3H), 2.31 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.5 (s), 144.9 (s), 136.9 (s), 136.5 (s), 132.5 (d), 132.0 (d), 128.8 (d), 128.5 (d), 127.8 (d), 125.6 (d), 118.09 (s), 118.08 (s), 116.6 (d), 111.6 (s), 69.2 (t), 51.1 (t), 39.9 (q), 37.2 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3054, 3025, 2924, 2851, 1682, 1637, 1590, 1487, 1336, 1217, 1145, 1074, 1040, 1010, 961, 911, 872, 830, 768, 731, 701 cm^{-1}; **HRMS** (ESI) calcd for $[C_{24}H_{23}N_3O_2S^{79}Br^{81}BrNa]^+$ $(M+Na)^+$: 599.9749; found: 599.9759.



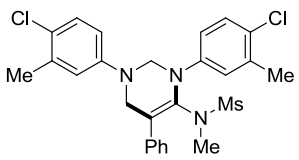
3aj: *N*-methyl-*N*-(5-phenyl-1,3-di-*m*-tolyl-1,2,3,6-tetrahydropyrimidin-4-yl)methanesulfonamide

Yield 86%, light yellow solid, m.p.: 149–150 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.9 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.26–7.22 (m, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.96–6.85 (m, 3H), 6.61 (d, *J* = 7.4 Hz, 1H), 6.52–6.50 (m, 2H), 5.03 (s, 1H), 4.71 (s, 1H), 4.30 (s, 1H), 4.01 (s, 1H), 2.69 (s, 3H), 2.38 (s, 3H), 2.35 (s, 3H), 2.24 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.8 (s), 146.1 (s), 139.2 (s), 139.0 (s), 137.3 (s), 137.1 (s), 129.1 (d), 129.0 (d), 128.7 (d), 128.4 (d), 127.5 (d), 125.4 (d), 124.5 (d), 120.9 (d), 120.1 (d), 117.5 (s), 115.7 (d), 112.2 (d), 69.2 (t), 51.2 (t), 39.9 (q), 37.7 (q), 21.7 (q), 21.5 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 3055, 3034, 3009, 2918, 1682, 1644, 1604, 1490, 1446, 1371, 1333, 1276, 1238, 1174, 1144, 1078, 1045, 1006, 962, 945, 894, 870, 858, 787, 766, 742, 704, 688, 659, 610 cm^{-1}; **HRMS** (ESI) calcd for $[C_{26}H_{29}N_3O_2SNa]^+$ $(M+Na)^+$: 470.1873; found: 470.1876.



3ak: *N*-(1,3-bis(2-fluorophenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 80%, white solid, m.p.: 160–161 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.10–7.08 (m, 3H), 7.04–6.98 (m, 3H), 6.89–6.85 (m, 2H), 4.84 (s, 1H), 4.71 (s, 1H), 4.19 (s, 1H), 4.14 (s, 1H), 2.68 (s, 3H), 2.27 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 157.0 (s, d: $J_{C\text{-}F}$ = 198.9 Hz), 155.1 (s, d: *J* = 197.5 Hz), 137.4 (s), 136.3 (s, d: $J_{C\text{-}F}$ = 8.9 Hz), 136.1 (s), 132.9 (s, d: $J_{C\text{-}F}$ = 9.7 Hz), 128.8 (d), 127.6 (d), 127.2 (d), 126.4 (d, d: $J_{C\text{-}F}$ = 7.8 Hz), 124.4 (d, d: $J_{C\text{-}F}$ = 3.6 Hz), 124.0 (d, d: $J_{C\text{-}F}$ = 3.8 Hz), 122.7 (d, d: $J_{C\text{-}F}$ = 7.8 Hz), 119.6 (d), 119.6 (d), 117.3 (s), 116.2 (d, d: $J_{C\text{-}F}$ = 20.0 Hz), 116.2 (d, d: $J_{C\text{-}F}$ = 20.0 Hz), 72.5–67.8 (t, m), 52.5 (t), 39.5 (q), 37.0 (q) ppm; **^{19}F NMR** (282 MHz, $CDCl_3$) δ -123.46, -124.26 ppm; **IR** (ATR): $\tilde{\nu}$ 3053, 2927, 2187, 1656, 1488, 1416, 1356, 1302, 1259, 1208, 1192, 1154, 1108, 1043, 1017, 980, 938, 883, 828, 793, 732, 714, 675, 612 cm^{-1}; **HRMS** (EI) calcd for $[C_{24}H_{23}N_3O_2SF_2]^+$ $(M)^+$: 455.1474; found: 455.1487.



3al: *N*-(1,3-bis(4-chloro-3-methylphenyl)-5-phenyl-1,2,3,6-tetrahydropyrimidin-4-yl)-*N*-methylmethanesulfonamide

Yield 81%, light yellow solid, m.p.: 121–122 °C; **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.53–7.51 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.36–7.29 (m, 2H), 7.09 (d, *J* = 8.7 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.54 (d, *J* = 2.7 Hz, 1H), 6.45 (dd, *J* = 8.7, 2.8 Hz, 1H), 4.79 (s, 2H), 4.10 (s, 2H), 2.68 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H), 2.25 (s, 3H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.3 (s), 144.4 (s), 137.2 (s), 137.1 (s), 136.5 (s), 130.4 (s), 129.8 (d), 129.4 (d), 128.8 (d), 128.5 (d), 127.7 (d), 126.4 (d), 124.8 (s), 122.6 (d), 117.8 (s), 117.6 (d), 114.1 (d), 69.4 (t), 51.4 (t), 39.9 (q), 37.2 (q), 20.4 (q), 20.3 (q) ppm; **IR** (ATR): $\tilde{\nu}$ 2927, 2856, 1640, 1597, 1482, 1446, 1413, 1336, 1230, 1145, 1089, 1046, 962, 862, 817, 767, 700 cm^{-1}; **HRMS** (EI) calcd for $[C_{26}H_{27}N_3O_2SCl_2]^+$ $(M)^+$: 515.1196; found: 515.1198.

Eidesstattliche Versicherung gemäß § 8 der Promotionsordnung der Naturwissenschaftlich-Mathematischen Gesamtfakultät der Universität Heidelberg

1. Bei der eingereichten Dissertation zu dem Thema

Gold-Catalyzed Formal Cycloadditions of Alkynes for Azaheterocycle Syntheses

handelt es sich um meine eigenständig erbrachte Leistung.

2. Ich habe nur die angegebenen Quellen und Hilfsmittel benutzt und mich keiner unzulässigen Hilfe Dritter bedient. Insbesondere habe ich wörtlich oder sinngemäß aus anderen Werken übernommene Inhalte als solche kenntlich gemacht.

3. Die Arbeit oder Teile davon habe ich wie folgt/bislang nicht1) an einer Hochschule des In- oder Auslands als Bestandteil einer Prüfungs- oder Qualifikationsleistung vorgelegt.

Titel der Arbeit:_____

_____

Hochschule und Jahr:_____

Art der Prüfungs- oder Qualifikationsleistung:_____

4. Die Richtigkeit der vorstehenden Erklärungen bestätige ich.

5. Die Bedeutung der eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unrichtigen oder unvollständigen eidesstattlichen Versicherung sind mir bekannt. Ich versichere an Eides statt, dass ich nach bestem Wissen die reine Wahrheit erklärt und nichts verschwiegen habe.

_____ _____

Ort und Datum Unterschrift

1) Nicht Zutreffendes streichen. Bei Bejahung sind anzugeben: der Titel der andernorts vorgelegten

Arbeit, die Hochschule, das Jahr der Vorlage und die Art der Prüfungs- oder Qualifikationsleistung.