Site-Selective C-H Functionalization of Indoles: Studies towards C-C and C-N Bond Formation

A Thesis Submitted

in Partial Fulfilment of the Requirements

for the Degree of

Doctor of Philosophy in Chemistry

By

Ms. Sonbidya Banerjee

Roll No. 176122109

Department of Chemistry
Indian Institute of Technology Guwahati
Guwahati 781039

Dedicated To

My Loving Mother

Mrs. Soma Banerjee

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati, India under the supervision of Prof. Tharmalingam Punniyamurthy.

In accordance with the established protocol for reporting scientific observations, proper acknowledgments have been provided whenever the work described relies on the discoveries made by other researchers

Guwahati
November 2023

Sonbidya Banerjee

INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI

Department of Chemistry

CERTIFICATE

This is to certify that Ms. Sonbidya Banerjee has been working under my supervision since January 2018. I am forwarding her thesis entitled "*Site-Selective C-H Functionalization of Indoles: Studies towards C-C and C-N Bond Formation*" being submitted for the Ph.D. degree of this institute. I certify that she has fulfilled all the requirements according to the rules of this institute, and regarding the investigations embodied in her thesis and this work has not been submitted elsewhere for a degree.

Guwahati	Prof. Tharmalingam Punniyamurthy
November 2023	Supervisor

ACKNOWLEDGEMENT

I am at a loss for words to express my gratitude to my mentor and supervisor, **Prof. Tharmalingam Punniyamurthy**, for introducing me to the captivating realm of synthetic chemistry and affording me the privilege and freedom to undertake this research. I am immensely indebted to him for his profound interest, invaluable guidance, unwavering motivation, continual support, and encouragement. Thank you, Sir, for consistently pushing and assisting me in attaining this goal. I will forever cherish the opportunities you've provided and the doors you've opened for me. Besides my supervisor, I would like to acknowledge my doctoral committee members, **Prof. G. Krishnamoorthy**, **Prof. A. S. Achalkumar**, Department of Chemistry and **Prof. Vijay. S. Moholkar,** Department of Chemical Engineering for their valuable suggestions and comments during all assessments in the entire period of my doctoral thesis.

I am genuinely thrilled to express my gratitude to my dear labmates Dr. Subhasish Roy, Dr. Sandeep Kumar, Dr. S. Vivek Kumar, Dr. Tariq. A. Shah, Dr. Dinesh Kumar Nayak, Dr. R. Arunachalam, Dr. Vanaparthi Satheesh, Dr. Raghunath Bag, Dr. Vijay Murugan, Dr. Pinaki Bhusan De, Dr. Sourav Pradhan, Dr. Bijay Ketan Das, Dr. Tanumay Sarkar, Mr. Kangkan Talukdar, Mr. Manmath Mishra, Mr. Pallab Karjee, Mr. Shubhajit Basak, Ms. Tripti Paul, Ms. Subhradeep Kar, Mr. Bijoy Debnath, Mr. Prabhat Kumar Maharana, Mr. Santu Mondal, Mr. Hemanga Bhattacharyya, Mr. Kshitiz Verma, Mr. Shajait Saha, Ms. Swati Samantaray, Mr. Maniya V N, Mr. Madhab Barman, Ms. Anita Sahoo, Mr. Sajal Roy, and Ms. Priya Patra for their moral support and invaluable encouragement whenever I approached them and for friendly relationship.

I would like to express my sincerest appreciation to all the faculty members, Department of Chemistry, staff of Central Instruments Facility and the non-teaching staff of Department of Chemistry for their valuable support during my Ph.D. tenure.

I take immense pleasure in expressing my heartfelt gratitude to IIT Guwahati for their generous financial support and for granting me access to all the facilities essential for my research. Additionally, I extend my thanks to the Central Instrument Facility (CIF), IIT Guwahati, for their invaluable instrument resources, and to DST for providing the X-ray facility.

To my wonderful friends at IIT Guwahati: It gives me an immense pleasure to express my affable gesture to my Ph.D. batch mates (January, 2018), research scholars in the chemistry department and B.Sc., M.Sc. friends for their support and joyful moments shared with them.

I was incredibly fortunate to have the support of wonderful friends, including Ms. Manideepa Dhar, Ms. Manideepa Paul, Ms. Nikita Chakraborty, Mr. Amit Shikari, and Mr. Subhamoy Biswas, as well as esteemed seniors Dr. Pratik Pal and Dr. Rita Dasmahapatra. Their unwavering moral support sustained me during my challenging times, right from the very beginning.

Finally, I profoundly render my deep regards to my beloved mother **Mrs. Soma Banerjee** for her boundless patience, countless sacrifices, genuine encouragement and unwavering inspiration. Throughout my life, my mother has been my steadfast support, shielding me from worldly troubles and allowing me to concentrate solely on my research endeavors. Thank you for believing in my vision and providing me the wings of freedom and opportunity to chase my dreams. Without her blessings and moral support, finishing my thesis work would have been nearly impossible.

Finally, I must acknowledge that my words fall short in conveying my immense gratitude to the Almighty God. I humbly surrender myself to Him, deeply thankful for His blessings that empowered me to successfully complete this thesis work.

Sonbidya Banerjee

List of Abbreviations

acac	acetylacetone
Å	angstrom (10^{-8} cm)
Bn	benzyl
Boc	*tert*-butoxycarbonyl
BQ	benzoquinone
Bz	benzoyl
Cp*	1,2,3,4,5-pentamethylcyclopentadiene
CCDC	Cambridge crystallographic data center
p-cymene	4-isopropyltoluene
DG	directing group
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMSO	dimethylsulfoxide
DMF	*N*,*N*-dimethylformamide
dtbpy	4,4′-di-*tert*-butyl-2,2′-bipyridyl
EDG	electron donating group
eq	equation
equiv	equivalent
ESI	electrospray ionization
EWG	electron wthdrawing group
FT-IR	Fourier transform infrared spectroscopy
FG	functional group
HFIP	hexafluoroisopropanol
het	heterocyclic
HRMS	high-resolution mass spectrometry
Hz	hertz
LG	leaving group
m/z	mass to charge ratio
mp	melting point
mA	milliampere

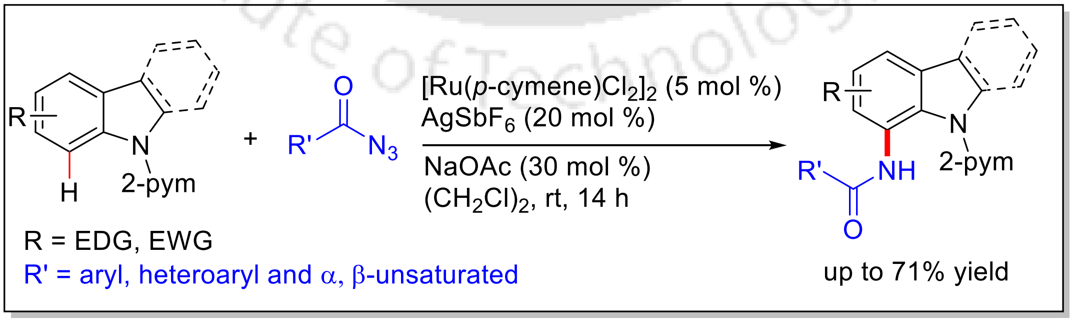
MesCOOH	2,4,6-trimethylbenzoic acid
MsOH	methanesulfonic acid
MHz	megahertz
NMR	nuclear magnetic resonance
NMP	*N*-methyl-2-pyrrolidone
NMO	*N*-methylmorpholine-N-oxide
NHPI	*N*-Hydroxyphthalimide
ORTEP	oak ridge thermal ellipsoid plot
R_f	retardation factor
rt	room temperature
PIDA	(Diacetoxyiodo)benzene
Piv	pivaloyl
py	pyridine
pym	pyrimidine
1, 10-Phen	1, 10-phenanthroline
PivOH	pivalic acid
SET	single-electron transfer
TBN	*tert*-Butyl nitrite
TCP	1,2,3-Trichloropropane
TFE	2,2,2-trifluoroethanol
TMEDA	tetramethylethylenediamine
TLC	thin layer chromatography
TsOH	*p*-toluenesulfonic acid
TMS	trimethylsilyl
TM	transition metal
μL	microliter

Abstract

The thesis is structured into four chapters. The first chapter describes a Ru-catalyzed regioselective C-N bond formation of indolines and carbazole with acyl azides *via* C7(sp^2)-H activation followed by an intramolecular C-N bond formation for the construction of 7-aminoindoline and 1-aminocarbazole scaffolds. The second chapter deals with Cu-catalyzed C7-selective C-H/N-H cross-dehydrogenative coupling of indolines and azaindoles with sulfoximines. The third chapter demonstrates a Rh-catalyzed site-selective C7 and C6 dual C-H functionalization of indolines expending 7-azabenzonorbornaiene for the formation of functionalized pyrrolocarbazoles. The fourth chapter focuses on Pd-catalyzed weak-coordination facilitated C4-selective redox-neutral nitration of indoles with *tert*-butyl nitrite under aerobic oxidation catalysis.

Chapter I. Ru-Catalyzed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides

Indole derivatives are essential for natural product synthesis and drug development. The 7-amino indole core is crucial for many bioactive compounds. Functionalizing indole at the C7 position is challenging, particularly for C-N bond formation, due to the less favored electrophilic nature of the nitrogen atom. Amidation of indoline at C7 is relatively unexplored using acyl azide which usually serve as synthons for the introduction of an amine functional group. The present chapter describes a room temperature Ru-catalyzed pyrimidine directed C7 amidation of carbazole with aryl, heteroaryl and α, β-unsaturated acyl azides with broad substrate scope and functional group diversity (Scheme 1). The reaction can be extended in the case of C1-amidation of carbazoles.

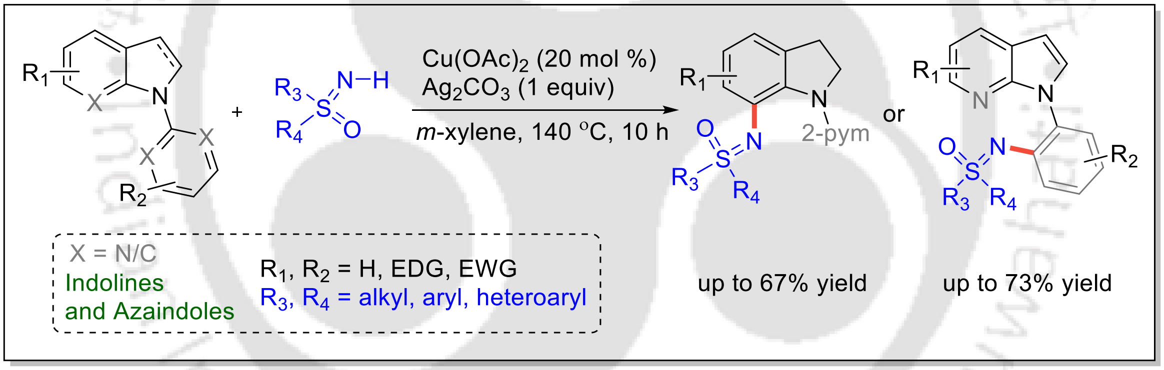


Eur. J. Org. Chem. **2019**, 1677.

Scheme 1. Ru(II)-Catalyzed C7-Amidation of Indolines with Acyl Azides

Chapter II. Cu(II)-Catalyzed C7-Selective C–H/N–H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines

Sulfoximines features as important scaffold that are significant in biological, medicinal, and synthetic sciences. Therefore, considerable efforts are focused on developing efficient methods for synthesizing functionalized sulfoximines. The rapid development of cross-dehydrogenative coupling (CDC) has revolutionized carbon-heteroatom bond formation, offering a step- and atom-economical alternative. Utilizing CDC between sulfoximines and key heterocyclic structures provides versatile aminated scaffolds. In this chapter, we have established copper-mediated regioselective C7-amination of indolines through cross-dehydrogenative coupling utilizing sulfoximines as aminating coupling partners (Scheme 2), which can be oxidized to the indole structural scaffolds in quantitative yields. Remarkably, this method can also be applied to successfully couple substituted *N*-aryl azaindoles, yielding valuable indole derivatives in good yields.

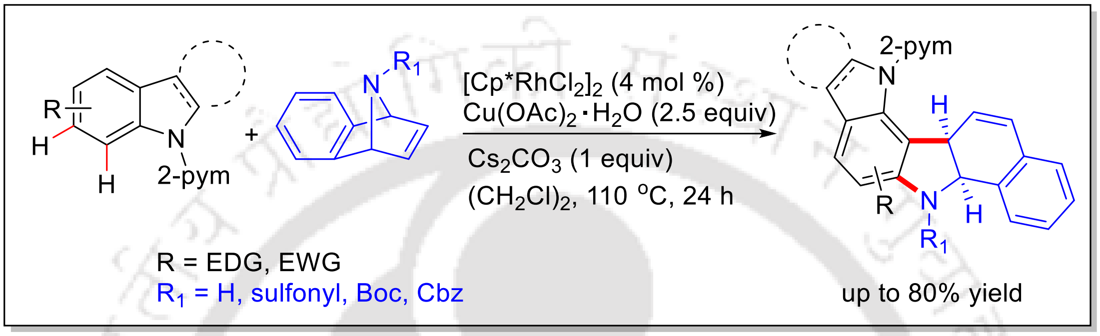


Org. Lett. **2022**, *24*, 7997**.**

Scheme 2. Cu(II)-Catalyzed C7-Amination of Indolines with Sulfoximine

Chapter III. Site-Selective Rh(III)-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles

Transition metal-catalyzed direct C-H functionalization has transformed simple compounds into intricate molecules, promoting structural diversity and atom efficiency. Indole and its analogues are prevalent in natural products and pharmaceuticals. Among them, pyrrolo-/indolocarbazoles represent vital structural patterns with intriguing medicinal and material properties. Functionalization of C-2, C-3, C-4 and C-7 C-H bonds of indole/indoline have thus been considerably investigated. In contrast, the C-6 functionalization remains underdeveloped. In this context, a dual C-H functionalization of indolines holds significant promise, enabling simultaneous formation of C-C and carbon-heteroatom bonds to construct complex structural scaffolds. In this line, azabenzonorbornadienes are realized as versatile building blocks. This chapter elucidates a method for dual C-7 and C-6 C-H functionalization of indolines with azabenzonorbornadienes using Rh-catalysis, to furnish pyrrolocarbazoles (Scheme 3). The site-selectivity, broad substrate scope and functional group diversities are important practical features.

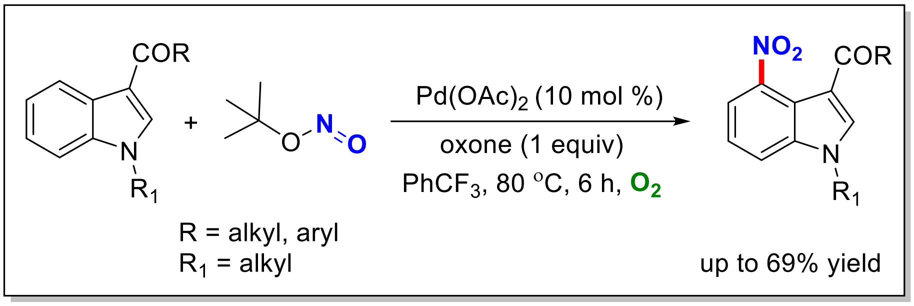


J. Org. Chem. **2020**, *85*, 2793.

Scheme 3. Rh(III)-Catalyzed C7 and C6 Dual C-H Functionalization of Indoles

Chapter IV. Regioselective Direct C4-Nitration of Indoles via Benzenoid C-H Activation under Aerobic Oxidation Catalysis: A Formal Access to Aminated Indoles

Among various nitrogen-containing heterocyclic scaffolds, the indole stands out as most recurring subunits in natural products, and is the fourth-most frequently used heteroatomic motif in marketed pharmaceuticals. Thus, significant efforts have been made for the transition metal-catalyzed direct functionalization at the C2 and C3 positions due to its innate reactivity of the pyrrole type ring. On our contrary, the site-selective functionalization of remote, less activated C–H bonds in the benzenoid core of indole derivatives remains a challenge. Thus, selective C–H functionalization at the poor nucleophilic C4 position of the indole has seen limited attention in previous studies. This chapter outlines a weak coordination facilitated Pd(II)-catalyzed C4-selective redox-neutral nitration of indoles with *tert*-butyl nitrite (Scheme 4). Indoles with versatile functional groups are well tolerated to give the target products in good yields and late-stage modification of the natural products has also been accomplished.



Org. Lett. **2024**, *26*, 988**.**

Scheme 4. Pd(II)-Catalyzed C4-Nitration of Indoles with TBN

Contents

Chapter I. Ru-Catalyzed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides

Chapter II. Cu(II)-Catalyzed C7-Selective C-H/N-H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines

Chapter III. Site-Selective Rh(III)-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles

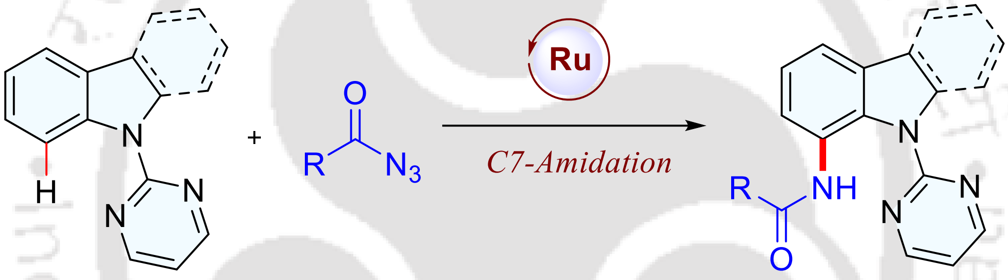
3.1 Literature Study

Chapter IV. Regioselective Direct C4-Nitration of Indoles via Benzenoid C-H Activation under Aerobic Oxidation Catalysis: A Formal Access to Aminated Indoles

4.1 Literature Study

Chapter I

Ru(II)-Catalyzed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides



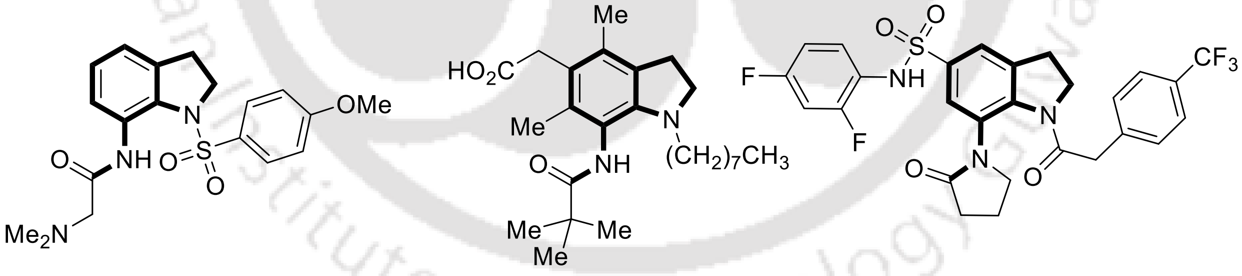
● Regioselective Amidation ● Broad Substrate Scope

● No External Oxidant

Eur. J. Org. Chem. **2019**, 1677.

Ru(II)-Catalyzed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides

Indoles are the important structural units and found in numerous biologically active compounds and natural products.[1] Considerable efforts are thus made for their synthesis and functionalization. The C2[2] and C3[3] C-H bond functionalization have made a considerable progress. Recently, attention is devoted for the C7 C-H bond functionalization.[4] Among them, the C-H amidation[5] is attractive as this motif is present in many compounds that are important in medicinal science (Figure 1). So far the use of tosyl azides has been considerably demonstrated as the nitrogen source for the construction of tosyl amides in the presence of Ru and Ir-catalysis. In contrast, the formation of acyl amide with indoline using C-H functionalization is limited, which may be due to the competitive Curtius rearrangement with acyl azides that can lead to *C-C* bond formation.[6] As acyl azides can be readily prepared, their broad utilization with less expensive catalysts for the selective amidation would thus be valuable. We here report a room temperature Ru-catalysed pyrimidine directed C7 C-H amidation of indolines with aryl, heteroaryl and α,β-unsatrated acyl azides with broad substrate scope and functional group diversity. The reaction can be extended to C1-amidation of carbazole.



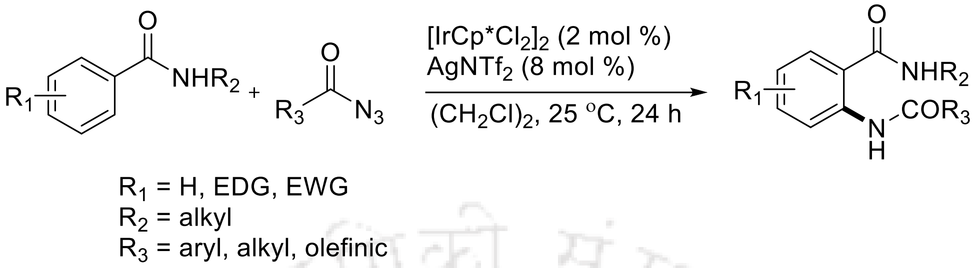
Tubulin polymerization inhibitor MDAT2 Inhibitor hMGMAT2 Inhibitor

Figure 1. Examples of Biologically Active Indoline 7-amide Derivatives.

1.1 Literature Study

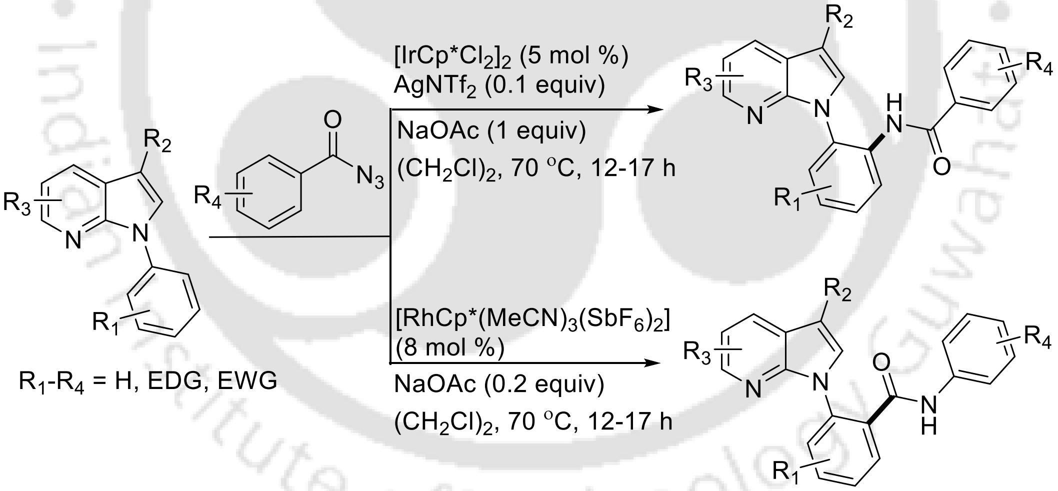
1.1.1 Ir-Catalyzed C-H Amidation of Arenes

Chang and co-workers reported a Ir(III)-catalyzed direct C-H amidation of arenes using acyl azides as the nitrogen source, in the absence of any external oxidants and producing molecular nitrogen as a single byproduct (Scheme 1).[7] This method was extended to the olefinic C-H amidation of alkenes to obtain *Z*-enamides.



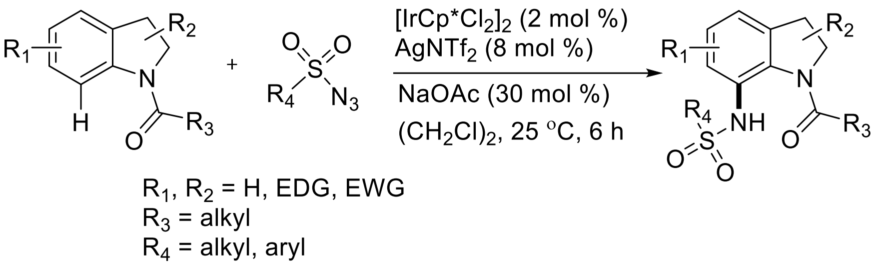
Scheme 1. Ir(III)-Catalyzed Mild C-H Amidation of Arenes and Alkenes with Acyl Azides

Dong and co-workers described that acyl azides can be utilized both as an amino source and a carbon donor, could be coupled with 7-azaindoles, leading to a diverse array of C-C or C-N amidated 7-azaindole derivatives (Scheme 2).[8] The dual reactivity of acyl azides could be precisely controlled suing a specific catalyst system.



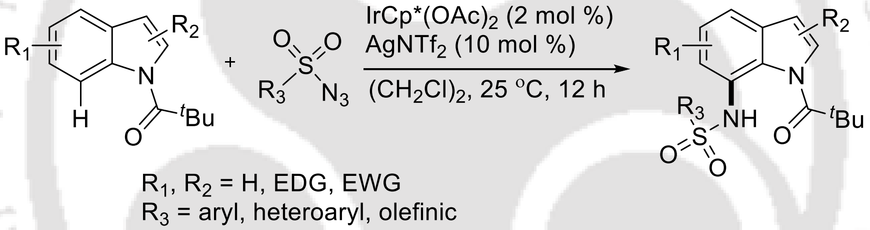
Scheme 2. Ir-Catalyzed C-N Amidation of 7-Azaindoles with Acyl Azides

A Ir-catalyzed regioselective C-7 amination of indolines with organic azides as a facile nitrogen source was reported by Chang and co-workers (Scheme 3).[9] This methodology is tolerated with various types of organic azides (sulfonyl, aryl, and alkyl) and broad range of indoline substrates with high catalytic activity.



Scheme 3. Ir-Catalyzed Direct C-7 Amination of Indolines with Organic Azides

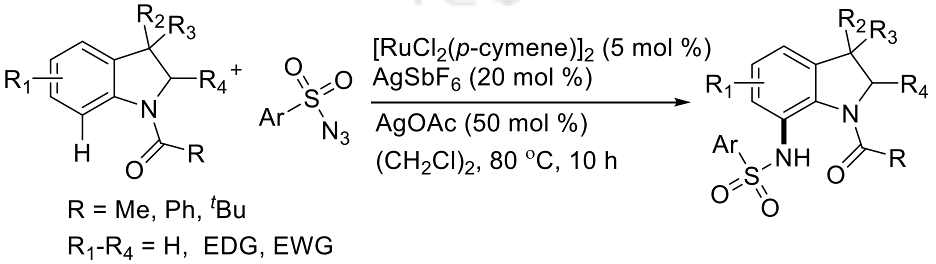
Chang and co-workers disclosed a method for synthesizing 7-aminoindoles through the regioselective direct C-7 amidation of indoles utilizing Ir(III) catalyst in combination with organic azides (Scheme 4).[10] *N*-Pivaloylindoles proved to be highly effective in undergoing the desired amidation at room temperature across a wide variety of substrates. Furthermore, this reaction demonstrated excellent scalability, and the deprotection of the chelation group was also easily achieved.



Scheme 4. Ir-Catalyzed Mild C-HAmidation of *N*-Pivaloylindoles with Organic Azides

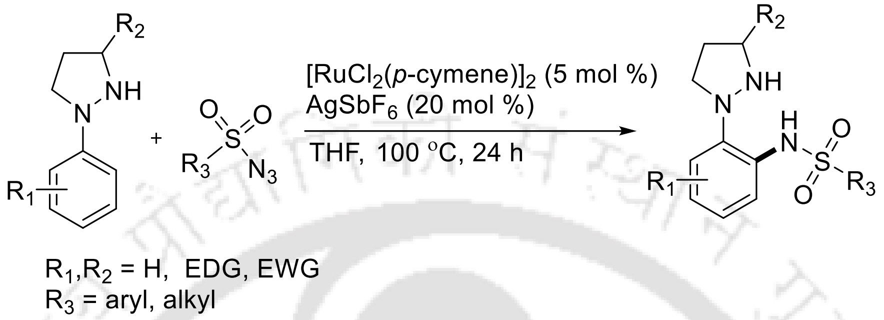
1.1.2 Ru-Catalyzed C-H Amidation of Arenes

Zhu and co-workers accomplished a Ru-catalyzed direct C7 amidation of indoline C-H bonds with sulfonyl azides (Scheme 5).[11] This strategy led to the synthesis of 7-amino substituted indolines, a key scaffold found in numerous biologically relevant compounds.



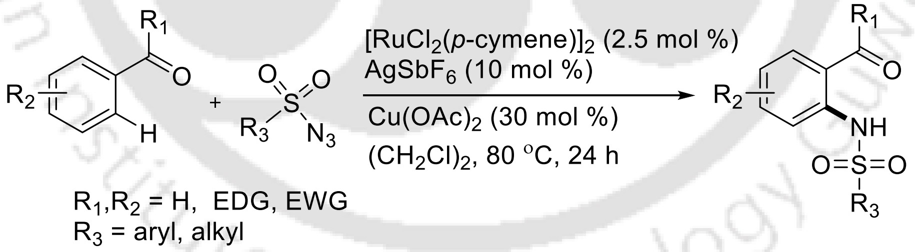
Scheme 5. Ru(II)-Catalyzed C7 Amidation of Indoline C-H Bonds with Sulfonyl Azides

Ackermann and co-workers reported a facile method for Ru-catalyzed C-H amidation of heteroaryl-substituted arenes and heteroarenes with a variety of sulfonyl azides (Scheme 6).[12] The methodology lays forth a straightforward route allowed nitrogenations of both electron-rich and electron-deficient arenes with ample substrate scope.



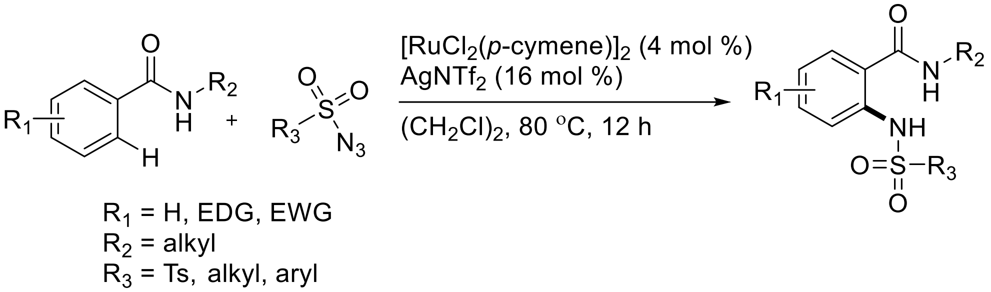
Scheme 6. Ru-Catalyzed C-H Amidation of Heretoaryl Arenes with Sulfonyl Azides

A highly efficient Ru(II)-catalyzed intermolecular amidation of weakly coordinating ketones with sulfonyl azides through C-H bond activation is reported by Jiao and co-workers (Scheme 7).[13] This methodology exhibits remarkable tolerance towards various functional groups, offering a novel and practical method for ketone-directed intermolecular C-N amidation without the need for an additional oxidant.



Scheme 7. Ru-Catalyzed Intermolecular C-H Amidation of Weakly Coordinating Ketones with Sulfonyl Azides

Chang and co-workers described inexpensive Ru-catalyzed direct C-H amidation of arenes by using sulfonyl azides (Scheme 8).[14] Therefore, substrates having weak coordinating ability can be amidated under this ruthenium catalyst system, which enhances the synthetic and practical utility of this strategy.



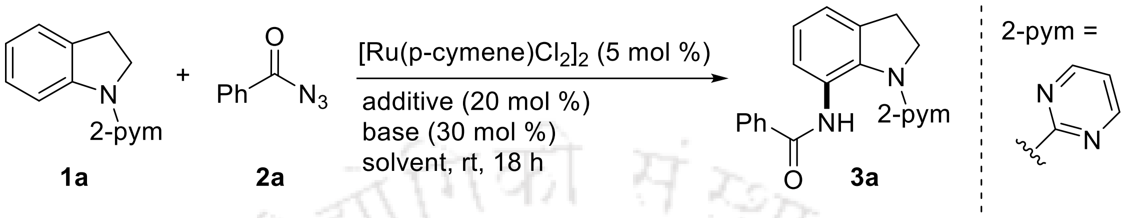
Scheme 8. Ru-Catalyzed C-H Amidation of Arenes with Sulfonyl Azides

1.2 Present Study

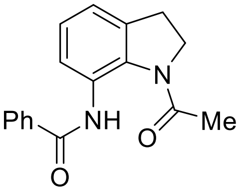
Herein, a Ru(II)-catalyzed C7-selective amidation of *N*-pyrimidylindolines with acyl azides is described utilizing 2-pyrimidine as a directing group auxiliary. We initiated the optimization studies using *N*-pyrimidylindoline **1a** with benzoyl azide **2a** as the model substrates with a series of catalysts, additives, bases and solvents (Table 1). To our delight, the reaction occurred to give **3a** in 69% yield when the substrates were stirred with 5 mol % [Ru(*p*-cymene)Cl_2]$_2$, 20 mol % $AgSbF_6$ and 30 mol % NaOAc in $(CH_2Cl)_2$ at room temperature for 18 h. Screening of the additives revealed that $AgSbF_6$ in combination with NaOAc increases the amidation efficacy compared to others (entries 1-4). In a set of bases studied, NaOAc, KOAc and CsOAc, the former gave the best results (entries 5-6). Solvents such as toluene, CH_2Cl_2, 1,4-dioxane, DMSO and THF yielded inferior results (entries 7-11). Lowering the amount of base (10 mol %) or catalyst (2.5 mol %) led to drop the yield to 41% (entries 12-13). Control experiments confirmed that the combination of [Ru(*p*-cymene)Cl_2]$_2$, $AgSbF_6$ and NaOAc is essential to produce **3a** (entries 14-16). Further, in contrast to Ir-catalysis, the directing groups such as acetyl **A**, pivaloyl **B**, *N*, *N*-dimethylcarbamoyl **C** and Boc **D** are not effective for this transformation. The combination of $AgSbF_6$ and NaOAc enhances the amidation efficacy. $AgSbF_6$ generates the monomeric Ru active species **A** from the coordinatively saturated Ru dimer. NaOAc serves as an internal base, facilitating the concerted metalation-deprotonation (CMD) pathway and promoting C-H activation.

Having optimized the condition, the substrate scope was studied employing a series of substituted acyl azides with **1a** as a standard substrate (Table 2). The reaction of *ortho*-substituted acyl azides **2b-c** with chloro and methyl groups was unsuccessful to give **3b-c** that may be due to the steric effect of the substituents. However, *meta*-substituted acyl azides with chloro **2d** and methoxy **2e** groups underwent reaction to furnish **3d** and **3e** in 71 and 68% yields, respectively. Similar results were observed with the *para*-substituted substrates with bromo **2f**, chloro **2g**, fluoro **2h**, iodo **2i** and methyl **2j** groups, affording **3f-j** in 53-74% yields. Acyl azides having strong electron withdr-

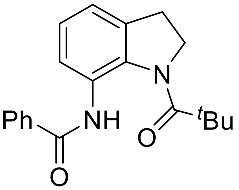
Table 1. Optimization of Reaction Conditions[a]



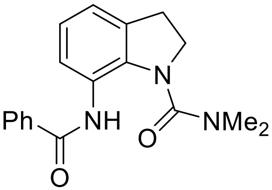
Entry	Additive	Base	Solvent	Yield (%)[b]
1	**AgSbF$_6$**	**NaOAc**	**(CH$_2$Cl)$_2$**	**69**
2	AgBF$_4$	NaOAc	(CH$_2$Cl)$_2$	25
3	AgOTf	NaOAc	(CH$_2$Cl)$_2$	63
4	KPF$_6$	NaOAc	(CH$_2$Cl)$_2$	14
5	AgSbF$_6$	KOAc	(CH$_2$Cl)$_2$	58
6	AgSbF$_6$	CsOAc	(CH$_2$Cl)$_2$	37
7	AgSbF$_6$	NaOAc	toluene	54
8	AgSbF$_6$	NaOAc	(CH$_2$Cl)$_2$	33
9	AgSbF$_6$	NaOAc	1,4-dioxane	29
10	AgSbF$_6$	NaOAc	DMSO	12
11	AgSbF$_6$	NaOAc	THF	n.d.
12[c]	AgSbF$_6$	NaOAc	(CH$_2$Cl)$_2$	26
13[d]	AgSbF$_6$	NaOAc	(CH$_2$Cl)$_2$	41
14	AgSbF$_6$	-	(CH$_2$Cl)$_2$	trace
15[e]	AgSbF$_6$	NaOAc	(CH$_2$Cl)$_2$	n.d.
16	-	NaOAc	(CH$_2$Cl)$_2$	n.d.



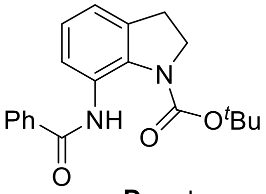
A, n.d.



B, n.d.



C, n.d.

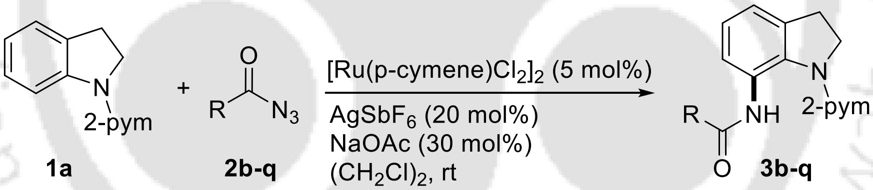


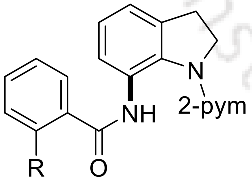
D, n.d.

[a]Reaction condition: **1a** (0.2 mmol), **2a** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5 mol %), $AgSbF_6$ (20 mol %), NaOAc (30 mol %), $(CH_2Cl)_2$ (2 mL), 18 h. [b]Isolated yield. [c]10 mol % NaOAc used. [d]2.5 mol% [Ru(*p*-cymene)Cl_2]$_2$. [e]without catalyst. n.d. = not detected

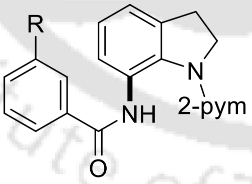
awing 4-CF_3 **2k** and 4-nitro **2l** groups, underwent reaction to provide **3k** and **3l** in 69 and 65% yields, respectively. In addition, naphthyl **2m**, 3,4-dimethylbenzoyl **2n** and cinnamoyl **2o** azides could be coupled to furnish **3m-o** in 52-59% yields. Furthermore, heterocyclic azides, 2-furyl **2p** and 2-thienyl **2q** azides underwent reaction to give **3p** and **3q** in 69 and 71% yields, respectively. Recrystallization of **3g** in a mixture of methanol and acetone gave the single crystals, whose structure was determined using X-ray analysis (Figure 2).

Table 2. Substrate Scope of Acyl Azides with **1a**[a,b]

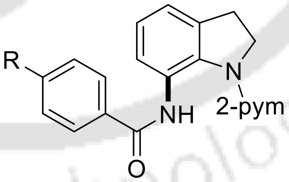




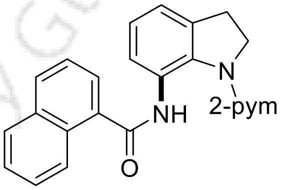
R = Cl, **3b**, n.d., 24 h
Me, **3c**, n.d., 24 h



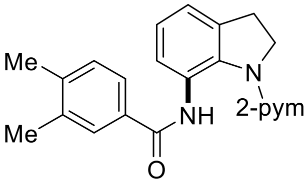
R = Cl, **3d**, 71%, 12 h
OMe, **3e**, 68%, 13 h



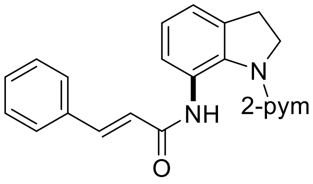
R = Br, **3f**, 53%, 15 h
Cl, **3g**, 74%, 12 h
F, **3h**, 69%, 13 h
I, **3i**, 63%, 15 h
Me, **3j**, 67%, 12 h
CF_3, **3k**, 69%, 12 h
NO_2, **3l**, 65%, 14 h



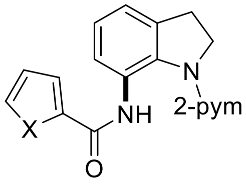
3m, 52%, 15 h



3n, 59%, 14 h



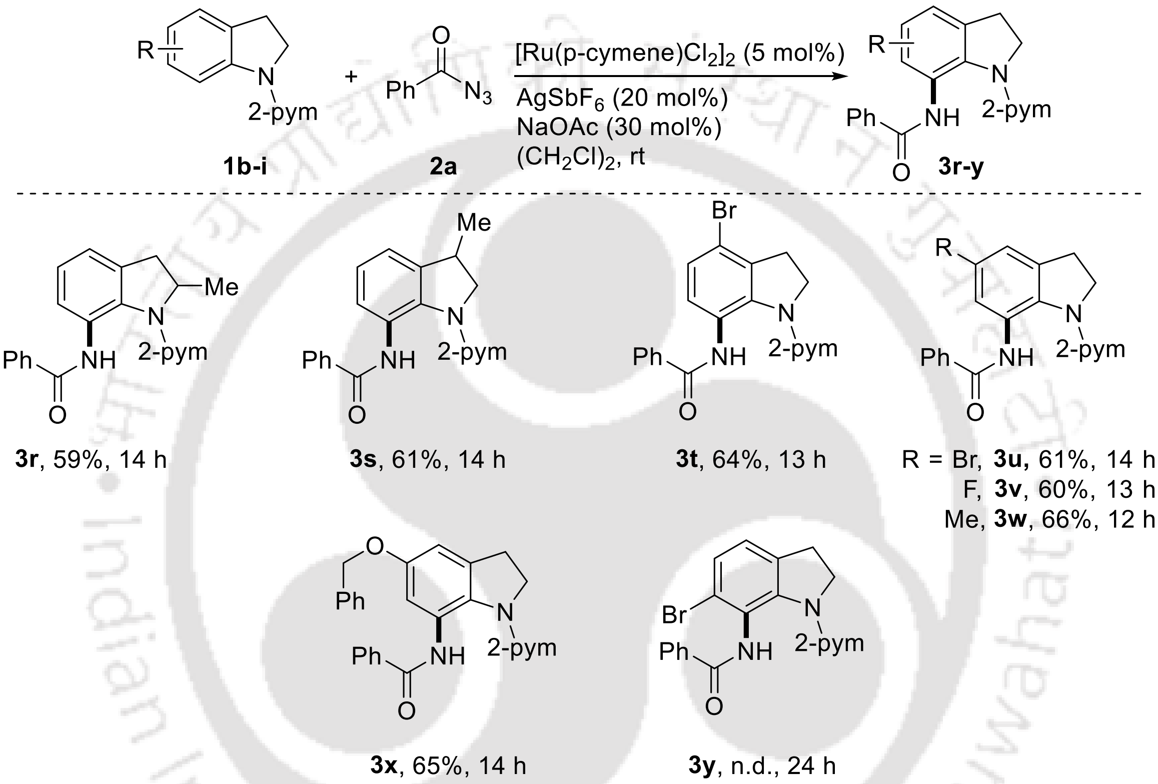
3o, 55%, 15 h



X = O, **3p**, 69%, 14 h
S, **3q**, 71%, 14 h

[a]Reaction conditions: **1a** (0.2 mmol), **2b-q** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5 mol %), $AgSbF_6$ (20 mol %), NaOAc (30 mol %), $(CH_2Cl)_2$ (2 mL). n.d. = not detected. [b]Isolated yield.

Table 3. Substrate Scope of Substituted Indolines with Benzoyl Azide **2a**[a,b]



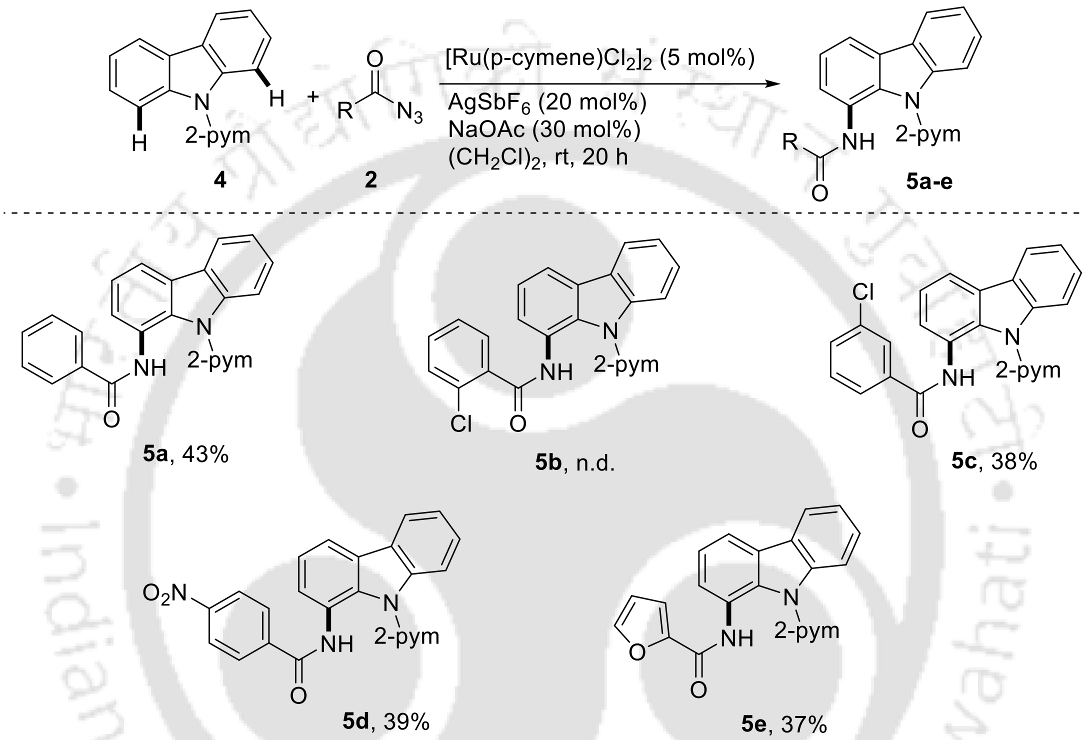
[a]Reaction conditions: **1b-i** (0.2 mmol), **2a** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5 mol %), $AgSbF_6$ (20 mol %), NaOAc (30 mol %), $(CH_2Cl)_2$ (2 mL). n.d. = not detected, [b]Isolated yield.

We extended the scope of the procedure for the coupling of indolines **1b-i** with benzoyl azide **2a** as a standard substrate (Table 3). Indolines bearing 2-methyl **1b**, 3-methyl **1c** and 4-bromo **1d** groups underwent reaction to give **3r-t** in 59-64% yields. Similar results were observed with the indolines containing 5-bromo **1e**, 5-fluoro **1f**, 5-methyl **1g**, and 5-benzyloxy **1h** groups, affording **3u-x** in 60-66% yields. However, indolines **1i** with 6-bromo group was an unsuccessful substrate, which may be attributed to the steric hindrance to the C-H functionalization site.

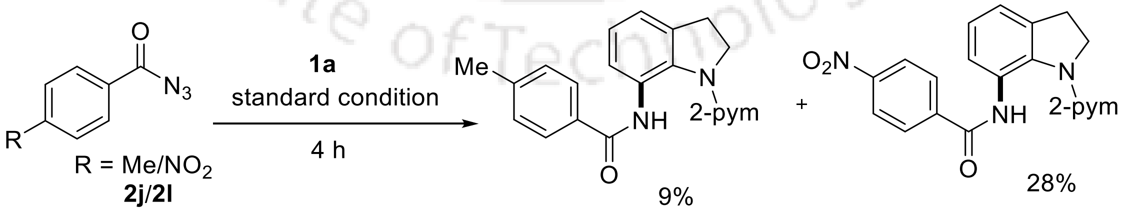
The utility of the procedure was further evaluated for the coupling of carbazole **4** with acyl azides (Table 4). Benzoyl azide **2a** underwent coupling to give **5a** in 43% yield, whereas **2b** bearing 2-

chloro group showed no reaction, which may be due to the steric hindrance. However, acyl azides having 3-chloro **2d**, 4-nitro **2l** and 2-furyl **2p** substituents underwent reaction to deliver **5c-e** in 37-39% yields. The amidation occurred at the C1 position of the carbazole.

Table 4. Substrate Scope of Benzoyl Azides with Carbazole[a,b]

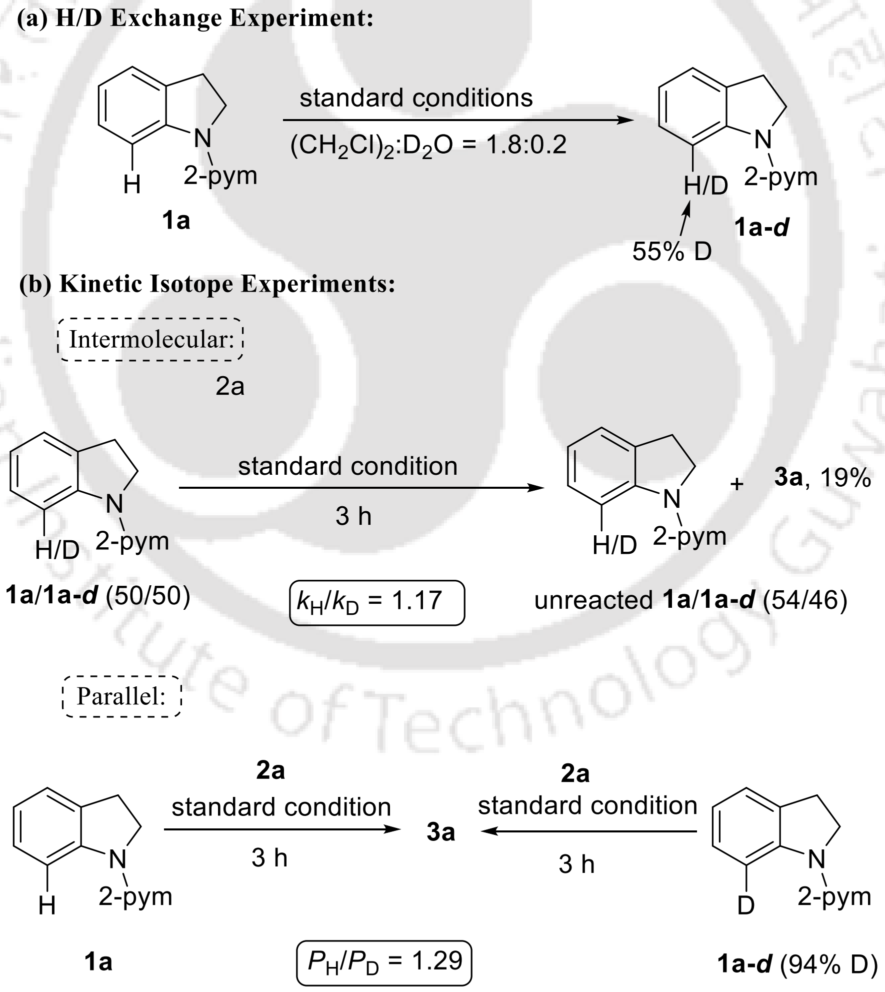


[a]Reaction conditions: **4** (0.2 mmol), **2** (0.3 mmol), [Ru(*p*-cymene)Cl_2]$_2$ (5 mol %), $AgSbF_6$ (20 mol%), NaOAc (30 mol %), $(CH_2Cl)_2$ (2 mL), 20 h, n.d. = not detected, [b]Isolated yield.



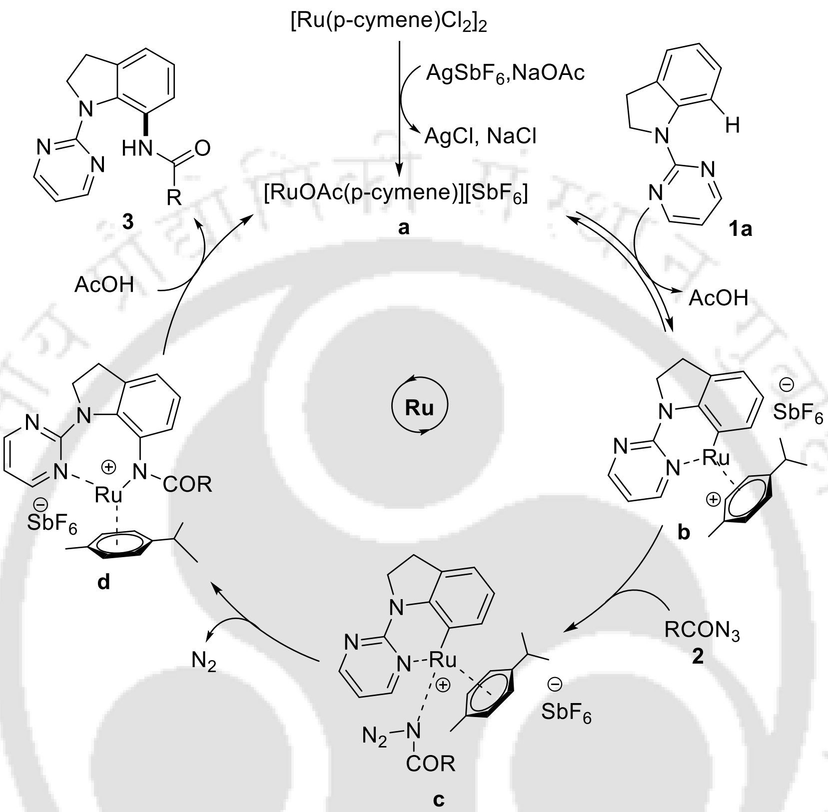
Scheme 9. Intermolecular Competitive Experiment

To gain insight into catalytic cycle, we performed the competitive experiments with electronically varied 4-methyl **2j** and 4-nitrobenzoyl **2l** azides using **1a** as a representative example. The reaction of the electron-deficient **2l** exhibited greater reactivity compared to **2j**, which may due to the greater stability of the electron poor azide (Scheme 9). Further, the H/D exchange experiment using D_2O as a co-solvent showed 55% deuterium incorporation, which implies that the C-H activation may be reversible (Scheme 10a). In addition, the kinetic isotopic experiments in one-pot (k_H/k_D = 1.17) and parallel (P_H/P_D = 1.29) suggest that the C-H bond cleavage may not be involved in the rate-determining step (Scheme 10b).[15a] Thus, the reaction of [Ru(*p*-cymene)Cl_2]$_2$ with $AgSbF_6$ may generate the cationic Ru(II) species ***a***, which can undergo reaction with **1** to give the six-membered ruthenacycle ***b*** (Scheme 11).[15] Coordination of the acyl azide **2** with ***b*** can lead to the formation of [Ru] complex ***c***, which can convert into the seven membered metallacycle ***d*** *via* the removal of N_2. Proto-demetalation of ***d*** can deliver **3** to complete the catalytic cycle.

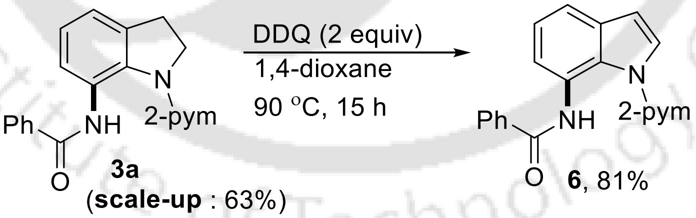


Scheme 10. Mechanistic Investigations

To reveal the scale-up, we studied the coupling of 5 mmol of **1a** with 7.5 mmol of **2a** as the representative substrate. The reaction occurred to produce **3a** in 63% yield, which can be readily oxidized using DDQ to produce indole scaffold **6** in 81% yield (Scheme 12).



Scheme 11. Plausible Catalytic Cycle



Scheme 12. Post-synthetic Utility

In summary, we have presented the direct coupling of the C7 C-H bond of indolines with acyl azides using Ru-catalysis at room temperature. The substrate scope is the important practical feature. The procedure can be extended to the C1-amidation of carbazole.

1.3 Experimental Section

General Information. 2-Chloropyrimidine (95%), [Ru(*p*-cymene)Cl_2]$_2$, $AgSbF_6$ (98%), KPF_6 (≥99%), $AgBF_4$ (98%), AgOTf (≥99.95%) and DDQ (98%) were purchased from Aldrich and used as received. *N*-Pyrimidyl indolines, acyl azides and 1-(pyrimidin-2-yl)indoline-7-*d* were synthesized according to the literature. Merck silica gel G/GF 254 plates were utilized for analytical TLC. Rankem silica gel (100-200 mesh) was employed for column chromatography. DRX-400 Varian and Bruker Avance III 600, 400 and 300 MHz spectrometers were used for recording NMR (^{1}H and ^{13}C) spectra utilizing $CDCl_3$ as the solvent and TMS as an internal standard. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in ppm and in Hz, respectively, and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, and br s = broad singlet. Melting points were determined using a Büchi B-540 apparatus and are uncorrected. FT-IR spectra were collected on Perkin Elmer IR spectrometer. Q-Tof ESI-MS instrument (model HAB 273) was used for mass spectra. Single crystal X-ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/Kα radiation and the structure was solved by direct method using SHELXL-16 (Göttingen, Germany).

General Procedure for Ru(II)-Catalyzed C7-Amidation of Indolines. To a stirred solution of 1-(pyrimidin-2-yl)indoline (0.2 mmol) **1**, [Ru(*p*-cymene)Cl_2]$_2$ (5 mol %, 0.01 mmol, 6.1 mg), $AgSbF_6$ (20 mol%, 0.04 mmol, 13.7 mg) and NaOAc (30 mol %, 0.06 mmol, 4.9 mg) in $(CH_2Cl)_2$ (2 mL), acyl azide **2** (0.3 mmol) was added. The resultant mixture was stirred at 25 °C under air. The progress of the reaction was monitored by TLC using ethyl acetate and hexane as an eluent. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and passed through a short pad of celite. Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford C7-amidated indolines.

Competition Experiment using Acyl Azides 2j and 2l. 1-(Pyrimidin-2-yl)indoline **1a** (19.7 mg, 0.1 mmol), **2j** (16.6 mg, 0.1 mmol), **2l** (19.2 mg, 0.1 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (3.0 mg, 5.0 mol %), $AgSbF_6$ (7.0 mg, 20 mol %) and NaOAc (2.4 mg, 30 mol %) in $(CH_2Cl)_2$ (1.0 mL) were stirred at room temperature (25 °C) for 4 h and **3j** and **3l** were formed in 9 and 28 % yields, respectively.

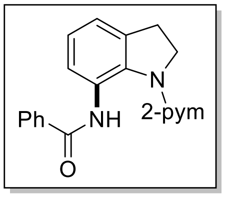
H/D Exchange with D_2O. 1-(Pyrimidin-2-yl)indoline **1a** (19.7 mg, 0.1 mmol), [$RuCl_2$(*p*-cymene)$]_2$] (3.0 mg, 5.0 mol %), $AgSbF_6$ (7 mg, 20 mol %) and NaOAc (2 mg, 30 mol %) were stirred at room temperature (25 ^oC) for 12 h in $(CH_2Cl)_2$:D_2O (1.8:0.2) under air. The reaction mixture was diluted with CH_2Cl_2 (10 mL), and passed through a short pad of celite. Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified using column chromatography on silica gel to give **1a-*d*** in 83% (16.4 mg) yield with 55% deuterium incorporation as estimated by 400 MHz ^1H NMR.

Preparation of 1-(pyrimidin-2-yl)indoline-7-*d* (1a–*d*).[16] The title compound was prepared according to the reported procedure as a pale yellow liquid. The deuterium incorporation was determined using 300 MHz ^1H NMR as 94%.

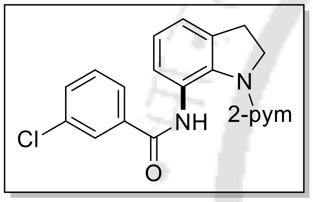
Intermolecular Kinetic Isotope Study.[16] Benzoyl azide **2a** (0.15 mmol, 22.1 mg) was reacted with 1-(pyrimidin-2-yl)indoline **1a** (0.1 mmol, 19.7 mg) and 1-(pyrimidin-2-yl)indoline-7-*d* **1a-*d*** (0.1 mmol, 19.8 mg) for 3 h under standard reaction condition. The reaction mixture was diluted with CH_2Cl_2 (10 mL), and passed through a short pad of celite. Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford **3a** in 19% yield and a mixture of unreacted **1a** and **1a**-*d* as a yellowish liquid. The intermolecular P_H/P_D was found to be 1.17 based on 300 MHz ^1H NMR of the recovered substrates **1a** and **1a**-*d*.

Parallel Kinetic Isotope Effect Study.[16] In a set of two experiments: in first set, benzoyl azide **2a** (0.15 mmol, 22.1 mg) was reacted with 1-(pyrimidin-2-yl)indoline **1a** (0.1 mmol, 19.7 mg) under standard condition. Whereas in another set, 1-(pyrimidin-2-yl)indoline-7-*d* **1a**-*d* (0.1 mmol, 19.8 mg, 94% D) was used instead of **1a** in the reaction with benzoyl azide **2a** (0.18 mmol, 26.5 mg) under the standard condition. The two reactions were allowed to stir at room temperature (25 ^oC) for 3 h. For both cases, the resulting solution was then diluted with CH_2Cl_2 (10 mL) and passed through a short pad of celite. Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford **3a.** The yield of **3a** was obtained as 14 and 17% yields, respectively. The KIE value of 1.29 was determined by the ratio of obtained yield of **3a** (KIE = 17%/14%/94% = 1.29).

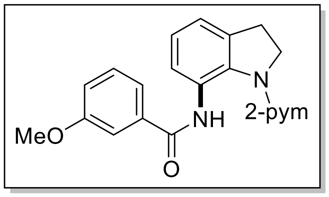
1.4 Characterization Data of Products



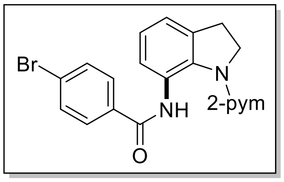
***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)benzamide 3a.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R$_f$ = 0.28; yellow liquid; yield 69% (43.6 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.43 (s, 1H), 8.44 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 165.9, 159.4, 157.9, 136.18, 136.15, 134.7, 131.5, 128.6, 127.4, 127.1, 124.7, 123.9, 121.4, 111.6, 52.0, 28.9; FT-IR (neat) 3448, 2924, 1635, 1552, 1419, 1110 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for C$_{19}$H$_{17}$N$_4$O: 317.1397, found: 317.1404.



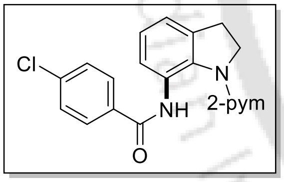
3-Chloro-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3d. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R$_f$ = 0.27; colorless solid; mp 138-139 °C; yield 71% (49.7 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.64 (s, 1H), 8.47 (d, *J* = 4.8 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.81 (s, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 4.8 Hz, 1H), 4.47 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 164.4, 159.3, 158.0, 138.0, 136.2, 134.6, 134.5, 131.5, 130.0, 127.5, 126.8, 125.9, 124.7, 123.7, 121.6, 111.7, 52.0, 28.8; FT-IR (KBr) 3447, 2922, 1670, 1588, 1458, 1373 cm^{-1}; HRMS (ESI) m/z [M+H]$^+$ calcd for C$_{19}$H$_{16}$N$_4$OCl: 351.1007, found: 351.1028.



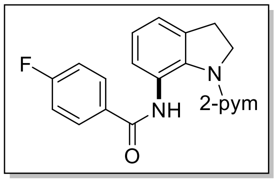
3-Methoxy-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3e. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R$_f$ = 0.28; colorless solid; mp 121-122 °C; yield 68% (47 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.43 (s, 1H), 8.44 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.42 (s, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 7.03-7.01 (m, 1H), 6.70 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.82 (s, 3H), 3.10 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.7, 159.9, 159.4, 158.0, 137.7, 136.1, 134.7, 129.5, 127.2, 124.7, 123.8, 121.3, 119.2, 117.5, 113.0, 111.6, 55.6, 52.0, 28.9; FT-IR (KBr) 3453, 2922, 1667, 1587, 1557, 1461, 1425, 1314, 1104 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}N_4O_2$: 347.1503, found: 347.1513.



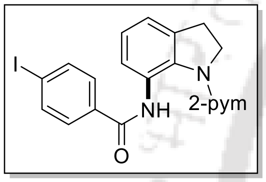
4-Bromo-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3f. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.27; colorless solid; mp 173-174 °C; yield 53% (41.7 mg); ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.52 (s, 1H), 8.43-8.42 (m, 2H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.56-7.54 (m, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.10 (t, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 159.3, 157.9, 136.1, 135.1, 134.7, 131.8, 129.0, 126.9, 126.1, 124.7, 123.8, 121.5, 111.7, 52.0, 28.8; FT-IR (KBr) 3445, 2923, 2853, 1661, 1582, 1452, 1421, 1195, 1107 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}BrN_4O$: 395.0502, found: 395.0508.



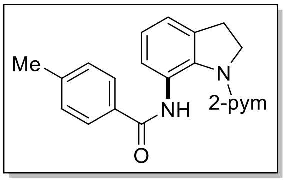
4-Chloro-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3g. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.28; colorless solid; yield 74% (51.8 mg); mp 168-169 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.57 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.9, 159.4, 157.9, 137.7, 136.2, 134.7, 134.6, 128.9, 128.8, 126.9, 124.8, 123.8, 121.5, 111.7, 52.0, 28.9; FT-IR (KBr) 3448, 2923, 1658, 1421, 1109 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{16}N_4OCl$: 351.1007, found: 351.1025.



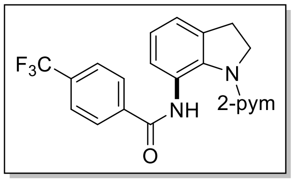
4-Fluoro-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3h. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; yield 69% (46 mg); mp 169-170 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.42 (s, 1H), 8.44 (d, *J* = 4.8 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.86-7.83 (m, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.11 – 7.07 (m, 3H), 6.72 (t, *J* = 4.8 Hz, 1H), 4.47 (t, *J* = 8.4 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.6 ($J_{C\text{-}F}$ = 250.2 Hz), 164.9, 159.4, 157.9, 136.2, 134.7, 132.4 ($J_{C\text{-}F}$ = 3.0 Hz), 129.7 ($J_{C\text{-}F}$ = 8.7 Hz), 127.1, 124.8, 123.9, 121.5, 115.7 ($J_{C\text{-}F}$ = 21.6 Hz), 111.6, 52.0, 28.9; FT-IR (KBr) 3447, 2924, 1634, 1456, 1111 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{16}N_4OF$: 335.1303, found: 335.1314.



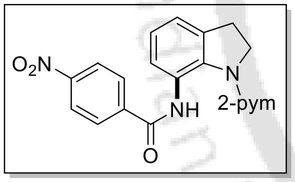
4-Iodo-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3i. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.28; colorless solid; yield 63% (55.6 mg); mp 184-185 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.50 (s, 1H), 8.43 (d, *J* = 5.4 Hz, 2H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.15 (t, *J*= 7.8 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.73 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.1, 159.4, 157.9, 137.8, 136.2, 135.7, 134.7, 129.1, 126.9, 124.8, 123.8, 121.5, 111.7, 98.4, 52.0, 28.9; FT-IR (KBr) 3454, 2924, 1659, 1420, 1108 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{19}H_{16}N_4OI$: 443.0363, found: 443.0377.



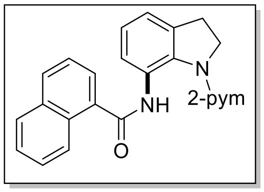
4-Methyl-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3j. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.27; colorless solid; yield 67% (44.2 mg); mp 192-193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.31 (s, 1H), 8.45 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 2H), 7.26-7.23 (m, 2H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 4.45 (t, *J* = 8.1 Hz, 2H), 3.10 (t, *J* = 7.8 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8, 159.4, 157.9, 141.9, 136.0, 134.7, 133.3, 129.2, 127.4, 124.7, 123.9, 121.2, 111.6, 100.1, 52.0, 28.9, 21.6; FT-IR (KBr) 3447, 2922, 1658, 1579, 1524, 1459, 1423, 1280, 1114 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}N_4O$: 331.1553, found: 331.1563.



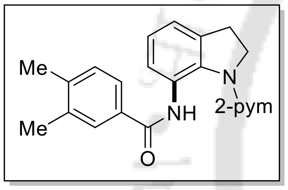
***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)-4-(trifluoromethyl)benzamide 3k.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; yield 69% (52.9 mg); mp 159-160 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.67 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.74 (t, *J* = 4.8 Hz, 1H), 4.47 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.5, 159.3, 157.9, 139.5, 136.2, 134.7, 133.1(q, J_{C-F} = 32.55 Hz), 127.9, 126.7, 125.6 (q, J_{C-F} = 3.6 Hz), 124.8, 123.9 (q, J_{C-F} = 270.75 Hz), 123.8, 121.7, 111.7, 52.0, 28.8; FT-IR (KBr) 3445, 2924, 2853, 1669, 1583, 1556, 1453, 1327, 1161, 1123 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{20}H_{16}N_4OF_3$: 385.1271, found: 385.1278.



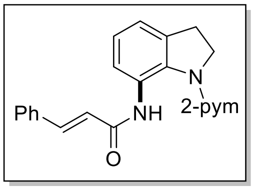
4-Nitro-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3l. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.28; yellow solid; yield 65% (46.9 mg); mp 199-200 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.87 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 2H), 8.29 (d, *J* = 9.0 Hz, 2H), 8.00 (d, *J*= 8.4 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 6.75 (t, *J* = 4.8 Hz, 1H), 4.48 (t, *J* = 8.4 Hz, 2H), 3.12 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.8, 159.3, 157.9, 149.6, 142.0, 136.3, 134.7, 128.6, 126.5, 124.9, 123.9, 123.7, 122.0, 111.8, 52.0, 28.8; FT-IR (KBr) 3445, 2924, 2853, 1662, 1518, 1450, 1421, 1347, 1116 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{16}N_5O_3$: 362.1248, found: 362.1256.



***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)-1-naphthamide 3m.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; colorless solid; yield 52% (38 mg); mp 199-200 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.61 (s, 1H), 8.46 (d, *J* = 4.8 Hz, 2H), 8.32 (s, 1H), 7.99 (d, *J* = 7.8 Hz, 1H), 7.94-7.92 (m, 1H), 7.90-7.86 (m, 3H), 7.58-7.53 (m, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J*=8.4 Hz, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 4.48 (t, *J* = 8.4 Hz, 2H), 3.13 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 159.4, 158.0, 136.1, 134.9, 134.7, 133.5, 132.8, 128.9, 128.5, 128.0, 127.7, 127.3, 126.9, 124.8, 124.3, 123.9, 121.4, 111.6, 52.1, 28.9; FT-IR (KBr) 3449, 2923, 1655, 1582, 1454, 1379, 1130 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{23}H_{19}N_4O$: 367.1553, found: 367.1559.

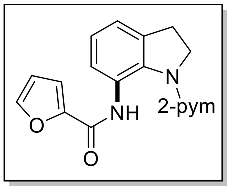


3,4-Dimethyl-*N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3n. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; yield 59% (40.5 mg); mp 174-175 ^{o}C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.21 (s, 1H), 8.45 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.60 (s, 1H), 7.57 (d, *J* = 9.0 Hz, 1H), 7.18-7.14 (m, 2H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.10 (t, *J* = 7.8 Hz, 2H), 2.29 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 159.5, 158.0, 140.6, 136.89, 136.8, 136.1, 134.7, 133.6, 129.8, 128.7, 127.4, 124.9, 124.7, 123.9, 121.2, 111.5, 52.1, 29.0, 20.0; FT-IR (KBr) 3449, 2923, 1656, 1422, 1109 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{21}H_{21}N_4O$: 345.1710, found: 345.1722.

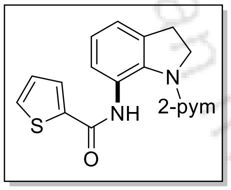


***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)cinnamamide 3o.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; colorless solid; yield 55% (37.6 mg); mp 130-131 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.07 (s, 1H), 8.53 (d, *J* = 4.8 Hz, 2H), 7.96 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 15.6 Hz, 1H), 7.49-7.47 (m, 2H), 7.37-7.36 (m, 3H), 7.14 (t, *J* = 7.5 Hz, 1H), 7.06-

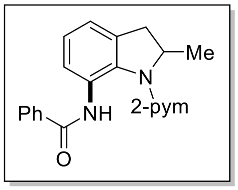
7.04 (m, 1H), 6.79 (t, *J* = 4.8 Hz, 1H), 6.43 (d, *J* = 15.6 Hz, 1H), 4.46 (t, *J* = 8.1 Hz, 2H), 3.10 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 159.4, 157.8, 140.8, 136.0, 135.1, 129.8, 129.0, 127.9, 127.2, 124.7, 123.5, 122.59, 122.55, 121.2, 111.8, 52.0, 28.9; FT-IR (KBr) 3448, 2925, 1672, 1630, 1582, 1558, 1446, 1421, 1374, 1336, 1282, 1154, 992 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for: $C_{21}H_{19}N_4O$: 343.1553, found: 343.1561.



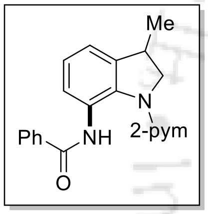
***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)furan-2-carboxamide 3p.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; mp 119-120 °C; yield 69% (42.2 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.70 (s, 1H), 8.54 (d, *J* = 4.8 Hz, 2H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.413-7.411 (m, 1H), 7.15 (d, *J* = 3.0 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 1H), 6.77 (t, *J* = 4.8 Hz, 1H), 6.50-6.49 (m, 1H), 4.45 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.3, 158.0, 156.4, 149.2, 143.7, 136.0, 134.6, 126.3, 124.5, 123.7, 121.4, 114.7, 112.4, 111.6, 51.9, 28.9; FT-IR (KBr) 3455, 2324, 1665, 1643, 1555, 1508, 1420, 1379,1111, 1005 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{17}H_{15}N_4O_2$: 307.1190, found: 307.1195.



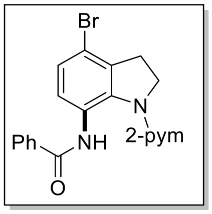
***N*-(1-(Pyrimidin-2-yl)indolin-7-yl)thiophene-2-carboxamide 3q**. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; yield 71% (45.7 mg); mp 158-159 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.15 (s, 1H), 8.53 (d, *J* = 4.8 Hz, 2H), 7.84 (d, *J* = 7.8 Hz, 1H), 7.56 (dd, *J* = 4.2, 1.2 Hz, 1H), 7.46 (dd, *J* = 5.4, 1.2 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.07-7.06 (m, 2H), 6.76 (d, *J* = 4.8 Hz, 1H), 4.48 (t, *J* = 7.8 Hz, 2H), 3.10 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.0, 159.6, 158.1, 140.2, 136.1, 134.9, 129.9 128.8, 127.7, 126.8, 124.8, 124.2, 121.5, 111.6, 51.9, 28.9; FT-IR (KBr) 3448, 2924, 1628, 1581, 1458, 1422, 1103 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{15}N_4OS$: 323.0961, found: 323.0976.



***N*-(2-Methyl-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3r.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.28; yellow solid, mp 160-161 °C; yield 59% (38.9 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.39 (s, 1H), 8.45 (d, *J* = 4.8 Hz, 2H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 5.24-5.19 (m, 1H), 3.45 (dd, *J* = 15.0, 8.4 Hz, 1H), 2.59 (d, *J* = 15.6 Hz, 1H), 1.33 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.8, 159.1, 158.0, 136.2, 134.8, 133.1, 131.5, 128.6, 127.7, 127.4, 124.8, 123.6 , 121.8, 111.6, 59.3, 36.1, 20.5; FT-IR (KBr) 3448, 2924, 2853, 1660, 1550, 1462, 1261, 1112 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}N_4O$: 331.1553, found: 331.1563.

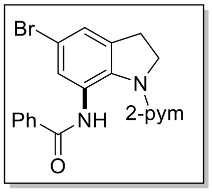


***N*-(3-Methyl-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3s.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.28; yellow solid; mp 115-116 °C; yield 61% (40.2mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.42 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 2H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.04 (d, *J* = 7.2 Hz, 1H), 6.70 (t, *J* = 4.8 Hz, 1H), 4.72 (dd, *J* = 11.4, 8.4 Hz, 1H), 3.90 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.41 (m, 1H), 1.33 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.9, 159.4, 158.0, 141.2, 136.1, 134.4, 131.5, 128.6, 127.4, 127.1, 124.9, 123.9, 120.0, 111.6, 59.6, 35.2, 18.8; FT-IR (KBr) 3450, 2925, 1663, 1597, 1583, 1551, 1442, 1420, 905 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{19}N_4O$: 331.1553, found: 331.1566.

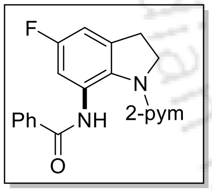


***N*-(4-Bromo-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3t.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.27; colorless solid; mp 140-141 °C; yield 64% (50.5

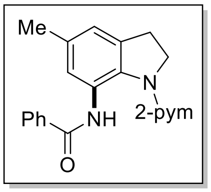
mg); ^{1}H NMR (300 MHz, CDCl$_3$) δ 11.43 (s, 1H), 8.46 (d, *J* = 4.8 Hz, 2H), 7.83 (d, *J* = 6.6 Hz, 3H), 7.50-7.40 (m, 3H), 7.29 (d, *J* = 9.0 Hz, 1H), 6.75 (t, *J* = 4.5 Hz, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.11 (t, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 165.9, 159.3, 158.0, 136.2, 135.8, 131.7, 128.7, 127.4, 126.1, 125.6, 123.0, 119.8, 115.0, 112.1, 51.3, 30.4; FT-IR (KBr) 3447, 2924, 1636, 1466, 1112 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{19}H_{16}BrN_4O$: 395.0502, found: 395.0505.



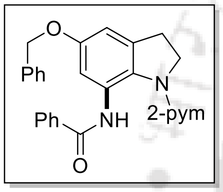
***N*-(5-Bromo-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3u.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R$_f$ = 0.26; colorless solid; mp 188-189 °C; yield 61% (48 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 11.58 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 2H), 8.15 (s, 1H), 7.82 (d, *J* = 7.2 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.17 (s, 1H), 6.73 (t, *J* = 4.8 Hz, 1H), 4.45 (t, *J* = 7.8 Hz, 2H), 3.08 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 165.9, 159.2, 158.0, 137.9, 135.8, 133.9, 131.7, 128.6, 128.2 ,127.4, 126.2, 124.2, 117.0, 111.9, 52.0, 28.7; FT-IR (KBr) 3449, 2924, 1667, 1584, 1463, 1407, 1372, 1121 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{19}H_{16}BrN_4O$: 395.0502, found: 395.0509.



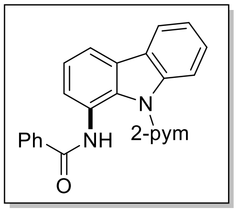
***N*-(5-Fluoro-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3v.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R$_f$ = 0.27; colorless solid; yield 60% (40 mg); mp 193-194 °C; ^{1}H NMR (600 MHz,CDCl$_3$) δ 11.63 (s, 1H), 8.42 (d, *J* = 4.8 Hz, 2H), 7.83 (d, *J* = 7.8 Hz, 2H), 7.80 (dd, *J* = 10.8, 2.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H), 6.80 – 6.78 (m, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 4.48 (t, *J* = 7.8 Hz, 2H), 3.08 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$)δ 165.9, 160.6 ($J_{C\text{-}F}$ = 240.75 Hz), 159.4, 158.0, 137.7 ($J_{C\text{-}F}$ = 9.75 Hz), 135.9, 131.7, 130.7 ($J_{C\text{-}F}$ = 2.55 Hz), 128.6, 128.2 ($J_{C\text{-}F}$ = 11.55 Hz), 127.4, 111.6, 110.0 ($J_{C\text{-}F}$ = 27.0 Hz), 108.7 ($J_{C\text{-}F}$ = 7.95 Hz), 52.1, 29.2; FT-IR (KBr) 3440, 3162, 2916, 1664, 1614, 1582, 1545, 1460, 1423, 1381, 1336, 1266, 1137 cm^{-1}; HRMS (ESI) m/z [M+H]$^+$ calcd for $C_{19}H_{16}FN_4O$: 335.1303, found: 335.1314.



***N*-(5-Methyl-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3w.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane $R_f = 0.28$; colorless solid; mp 172-173 °C; yield 66% (43.5 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 11.44 (s, 1H), 8.42 (d, *J* = 4.8 Hz, 2H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.75 (s, 1H), 7.48 (t, *J* = 7.2 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 6.89 (s, 1H), 6.67 (t, *J* = 4.8 Hz, 1H), 4.44 (t, *J* = 8.4 Hz, 2H), 3.06 (t, *J* = 7.8 Hz, 2H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.8, 159.4, 157.9, 136.2, 136.1, 134.7, 132.3, 131.5, 128.6, 127.4, 126.8, 124.0, 122.3, 111.3, 52.0, 28.9, 21.2; FT-IR (KBr) 3444, 2923, 2854, 1667, 1585, 1548, 1467, 1414, 1378, 1267, 1192 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$calcd for $C_{20}H_{19}N_4O$: 331.1553, found: 331.1563.

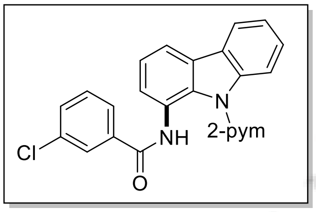


***N*-(5-(Benzyloxy)-1-(pyrimidin-2-yl)indolin-7-yl)benzamide 3x.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane $R_f = 0.25$; colorless liquid; yield 65% (54.8 mg); ^{1}H NMR (600 MHz,$CDCl_3$) δ 11.65 (s, 1H), 8.40 (d, *J* = 4.8 Hz, 2H), 7.86 (d, *J* = 7.2 Hz, 2H), 7.73 (s, 1H), 7.51-7.42 (m, 5H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 7.8 Hz, 1H), 6.746-6.742 (m, 1H), 6.66 (t, *J* = 4.8 Hz, 1H), 5.11 (s, 2H), 4.44 (t, *J* = 7.8 Hz, 2H), 3.06 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.0, 159.3, 157.9, 156.3, 137.4, 137.2, 136.2, 131.6, 128.7, 128.6, 128.2, 128.0, 127.9, 127.8, 127.5, 111.1, 109.6, 108.1, 70.6, 51.9, 29.3; FT-IR (neat) 3450, 2923, 1665, 1586, 1550, 1462, 1422, 1380, 1267, 1222, 1077 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{26}H_{23}N_4O_2$: 423.1821, found: 423.1821.

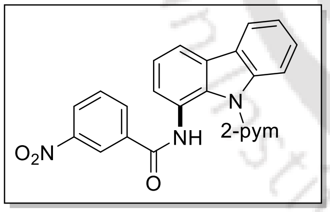


***N*-(9-(Pyrimidin-2-yl)-9*H*-carbazol-1-yl)benzamide 5a.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane $R_f = 0.24$; yellow sticky liquid; yield 43% (31 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.74 (d, *J* = 4.8 Hz, 2H), 8.50 (d, *J* = 8.4 Hz, 1H), 8.14 (d, *J* = 7.2 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.75-7.42

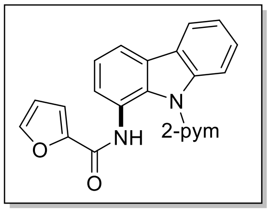
(m, 5H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.09 (t, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 158.6, 158.3, 140.8, 136.2, 131.7, 131.0, 128.7, 128.6, 127.4, 127.1, 126.2, 125.6, 123.6, 123.4, 123.2, 119.8, 116.9, 116.8, 115.5; FT-IR (neat) 3457, 2924, 2853, 2077, 1639, 1453, 1418, 1384, 1341, 1260, 1113 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{23}H_{17}N_4O$: 365.1397, found: 365.1399.



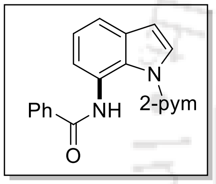
3-Chloro-*N*-(9-(pyrimidin-2-yl)-9*H*-carbazol-1-yl)benzamide 5c. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.25; yellow sticky liquid; yield 38% (30.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.71 (s, 1H), 8.80 (d, *J* = 4.8 Hz, 2H), 8.53 (d, 8.4 Hz, 1H), 8.14 (d, *J* = 7.6 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.73-7.69 (m, 2H), 7.50-7.44 (m, 3H), 7.42-7.37 (m, 2H), 7.16 (t, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 158.6, 158.4, 140.8, 137.9, 134.7, 131.7, 130.9, 130.2, 128.7, 127.3, 127.2, 126.1, 126.0, 125.3, 123.5, 123.4, 123.3, 119.8, 117.1, 116.9, 115.6; FT-IR (neat) 3436, 2925, 2854, 2080, 1637, 1452, 1417, 1113 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{23}H_{16}ClN_4O$: 399.1007, found: 399.1009.



4-Nitro-*N*-(9-(pyrimidin-2-yl)-9*H*-carbazol-1-yl)benzamide 5d. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.24; yellow solid; yield 39% (31.9 mg); mp 256-257 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.00 (s, 1H), 8.75 (d, *J* = 4.8 Hz, 2H), 8.56 (d, *J* = 8.4 Hz, 1H), 8.31 (d, *J* = 8.0 Hz, 2H), 4.14 (d, *J* = 6.8 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.98-7.93 (m, 3H), 7.51-7.45 (m, 2H), 7.42-7.38 (m, 1H), 7.15 (t, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ163.9, 158.7, 158.3, 149.8, 140.8, 129.1, 128.9, 128.5, 127.3, 126.2, 125.1, 124.0, 123.7, 123.5, 119.8, 117.5, 116.9, 115.9; FT-IR (KBr) 3445, 2924, 2860, 2071, 1638, 1452, 1417, 1384, 1345, 1111 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{23}H_{16}N_5O_3$: 410.1248, found: 410.1253.



***N*-(9-(Pyrimidin-2-yl)-9*H*-carbazol-1-yl)furan-2-carboxamide 5e.** Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.24; colorless solid; yield 37% (26.1 mg); mp 152-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ10.60 (s, 1H), 8.93 (d, *J* = 4.8 Hz, 2H), 8.58 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.07 (d, *J* = 7.6 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.48-7.36 (m, 4H), 7.22 (t, *J* = 4.8 Hz, 1H), 7.17 (d, *J* = 3.2 Hz, 1H), 6.53 (d, *J* = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 158.5, 156.3, 149.0, 143.5, 140.8, 131.0, 128.6, 127.1, 126.1, 124.6, 123.7, 123.4, 123.2, 119.8, 117.0, 116.6, 115.4, 115.2, 112.7; FT-IR (KBr) 3446, 2923, 2848, 2073, 1637, 1452, 1415, 1114 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{21}H_{15}N_4O_2$: 355.1190, found: 355.1190.



***N*-(1-(Pyrimidin-2-yl)-1*H*-indol-7-yl)benzamide 6.** To a stirred solution of *N*-(1-(pyrimidin-2-yl)indolin-7-yl)benzamide **3a** (0.2 mmol, 63 mg) in 1,4-dioxane (2 mL), DDQ (0.4 mmol, 91 mg) was added. The resulting mixture was stirred at 90 °C for 15 h. The reaction mixture was then diluted with CH_2Cl_2 (20 mL) and washed with brine (10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford C7 amidated indole **E**. Analytical TLC on silica gel, 1:9 ethyl acetate/hexane R_f = 0.26; colorless solid; yield 81% (50.8 mg); mp 144-145 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.00 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 2H), 8.38-8.27 (m,2H), 7.94 (d, *J* = 6.9 Hz, 2H), 7.57-7.47 (m, 3H), 7.39-7.29(m, 2H), 6.97 (t, *J* = 4.8 Hz, 1H), 6.71 (d, *J*= 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6, 158.2, 157.1, 137.2, 134.4, 131.6, 128.9, 128.7, 127.6, 126.4, 126.2, 123.7, 118.5, 117.6, 116.4, 108.6; FT-IR (KBr) 3449, 2923, 1634, 1571, 1422, 1112 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{19}H_{15}N_4O$: 315.1240, found: 315.1250.

Crystal Data and Structure Refinement for 3g

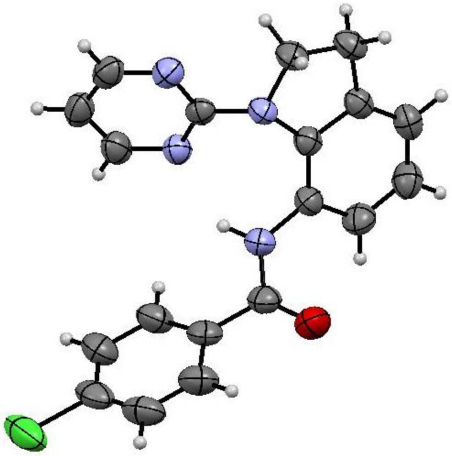


Figure 2. ORTEP diagram of **3g** (CCDC 1856213).

Identification code	**3g**
Empirical formula	$C_{19}H_{15}N_4OCl$
Formula weight	350.80
Crystal habit, color	Needle / colorless
Crystal size, mm^3	0.29 x 0.24 x 0.18
Temperature, T/K	273 (2)
Wavelength, λ/Å	0.71073
Crystal system	monoclinic
Space group	'C 2/c'
Unit cell dimensions	a = 28.915 (5)Å b = 7.2981 (12)Å c = 20.587 (3)Å $\alpha = \gamma$ = 90.00°, β = 128.147 (2)
Volume, V/Å^3	3416.5 (10)
Z	8
Calculated density, Mg·m^{-3}	1.403
Absorption coefficient, μ/mm^{-1}	0.240
F(000)	1536
θ range for data collection	1.79 to 24.99°

Limiting indices	$-34 \le h \le 34, -8 \le k \le 8, -24 \le l \le 24$
Reflection collected / unique	3018/ 2589
Completeness to θ	100 % (θ = 24.99°)
Absorption correction	Multi-scan
Max. and min. transmission	0.958 and 0.933
Refinement method	SHELXL-2016/6
Data / restraints / parameters	3018/0/ 230
Goodness–of–fit on F^2	1.134
Final R indices [I>2sigma(I)]	$R1 = 0.0475$, $wR2 = 0.1469$
R indices (all data)	$R1 = 0.0413$, $wR2 = 0.1375$

1.5 References

1. (a) Kochanowska-Karamyan, A. J.; Hamann, M. T. *Chem. Rev.* **2010**, *110*, 4489; (b) Lee, W.-H.; Liu, H. E.; Chang, J.-Y.; Liou, J.-P.; Huang, H.-M. *Pharmacology*. **2013**, *92*, 90; (c) Lee, H.-Y.; Wang, L.-T.; Li, Y.-H.; Pan, S.-L.; Chen, Y.-L.; Teng, C.-M.; Liou, J.-P. *Org. Biomol. Chem.* **2014**, *12*, 8966.
2. (a) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem. Int. Ed.* **2012**, *51*, 6993. (b) Zhu, X.; Su, J.-H.; Du, C.; Wang, Z.-L.; Ren, C.-J.; Niu, J.-L.; Song, M.-P. *Org. Lett.* **2017**, *19*, 596. (c) Lu, Q.; Cembellín, S.; Greßies, S.; Singha, S.; Daniliuc, C. G.; Glorius, F. *Angew. Chem. Int. Edl.* **2018**, *57*, 1399.
3. (a) Ding, S.; Jiao, N. *J. Am. Chem. Soc.* **2011**, *133*, 12374. (b) Kim, J.; Kim, H.; Chang, S. *Org. Lett.* **2012**, *14*, 3924. (c) Cabrero-Antonino, J. R.; Adam, R.; Junge, K.; Beller, M. *Chem. Sci.* **2017**, *8*, 6439.
4. (a) Kim, M.; Kumar Mishra, N.; Park, J.; Han, S.; Shin, Y.; Sharma, S.; Lee, Y.; Lee, E.-K.; Kwak, J. H.; Kim, I. S. *Chem. Commun.* **2014**, *50*, 14249. (b) Yang, X.-F.; Hu, X.-H.; Loh, T.-P. *Org. Lett.* **2015**, *17*, 1481. (c) Yang, Y.; Qiu, X.; Zhao, Y.; Mu, Y.; Shi, Z. *J. Am. Chem. Soc.* **2016**, *138*, 495. (d) Gandeepan, P.; Koeller, J.; Ackermann, L. *ACS Catal.* **2017**, *7*, 1030. (e) Borah, A. J.; Shi, Z. *J. Am. Chem. Soc.* **2018**, *140*, 6062.

5. For reviews, (a) Thirunavukkarasu, V. S.; Kozhushkov, S. I.; Ackermann, L. *Chem. Commun.* **2014**, *50*, 29. (b) Jiao, J.; Murakami, K.; Itami, K. *ACS Catal.* **2016**, *6* (2), 610. (c) Park, Y.; Kim, Y.; Chang, S. *Chem. Rev.* **2017**, *117*, 9247.

6. Curtius, T.; Dtsch, Ber. *Chem. Ges.* **1890**, *23*, 3023.

7. Ryu, J.; Kwak, J.; Shin, K.; Lee, D.; Chang, S. *J. Am. Chem. Soc.* **2013**, *135*, 12861.

8. Li, W.-H.; Dong, L. *Adv. Synth. Catal.* **2018**, *360*, 1104.

9. Shin, K.; Chang, S. *J. Org. Chem.* **2014**, *79*, 12197.

10. Kim, Y.; Park, J.; Chang, S. *Org. Lett.* **2016**, *18*, 1892.

11. Pan, C.; Abdukader, A.; Han, J.; Cheng, Y.; Zhu, C. *Chem. Eur. J.* **2014**, *20*, 3606.

12. Thirunavukkarasu, V. S.; Raghuvanshi, K.; Ackermann, L. *Org. Lett.* **2013**, *15*, 3286.

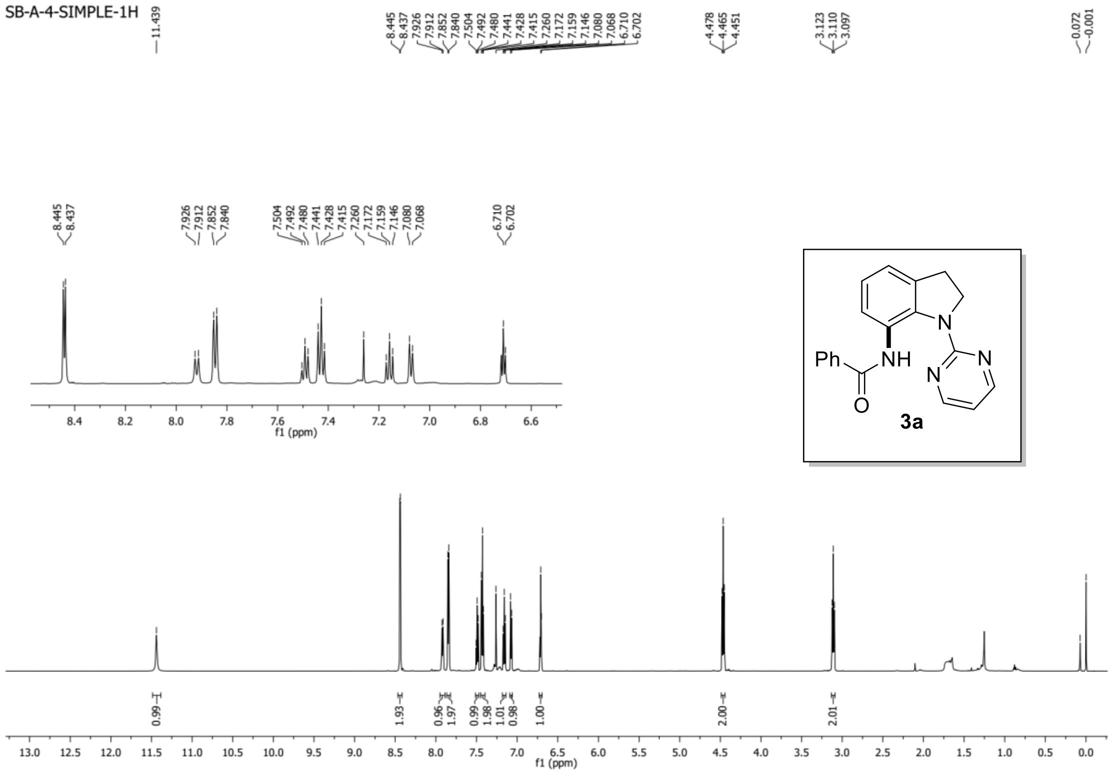
13. Zheng, Q.-Z.; Liang, Y.-F.; Qin, C.; Jiao, N. *Chem. Commun.* **2013**, *49*, 5654.

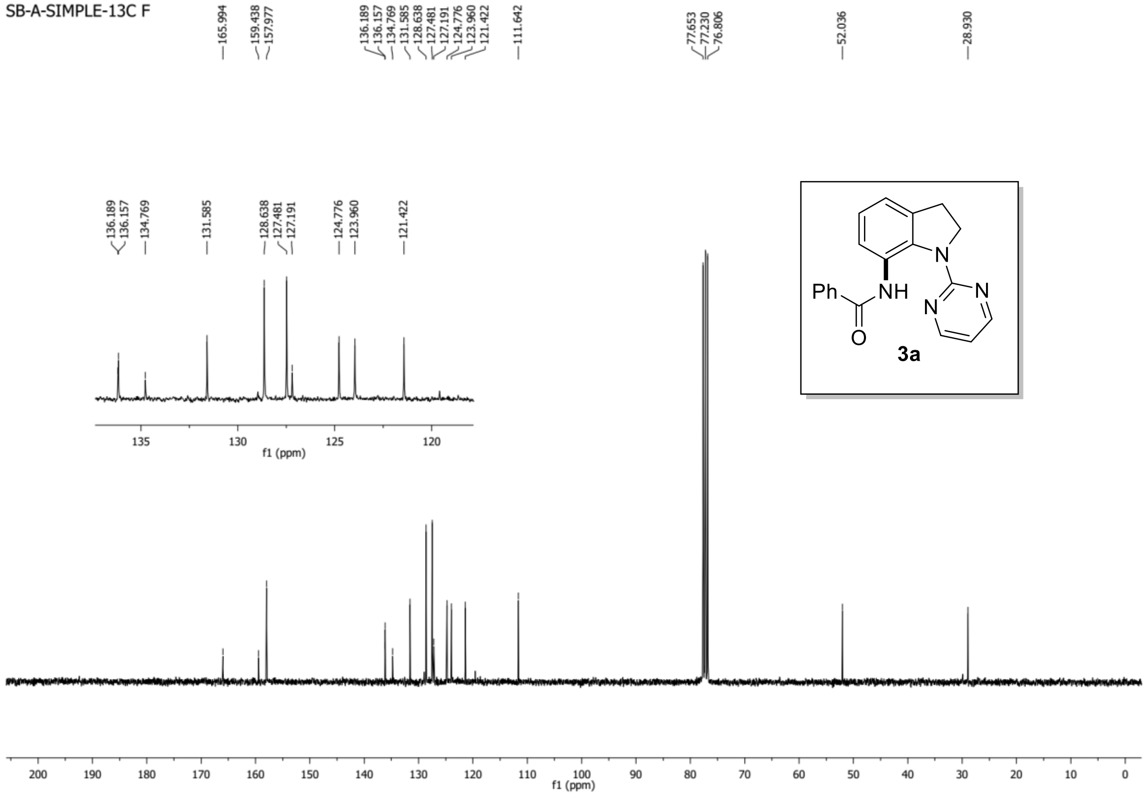
14. Kim, J.; Kim, J.; Chang, S. *Chem. Eur. J.* **2013**, *19*, 7328.

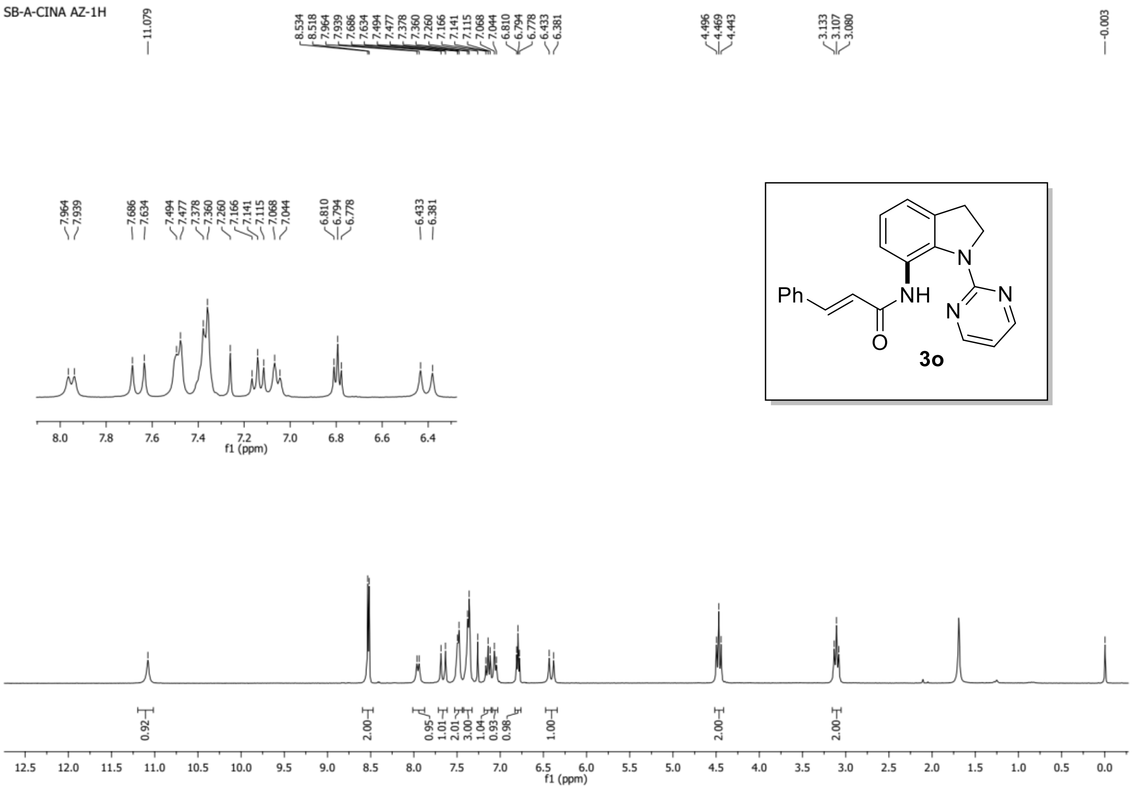
15. (a) Simmons, E. M.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2012**, *51*, 3066. (b) Kim, J.; Kim, J.; Chang, S. *Chem. Eur. J.* **2013**, 19, 7328.

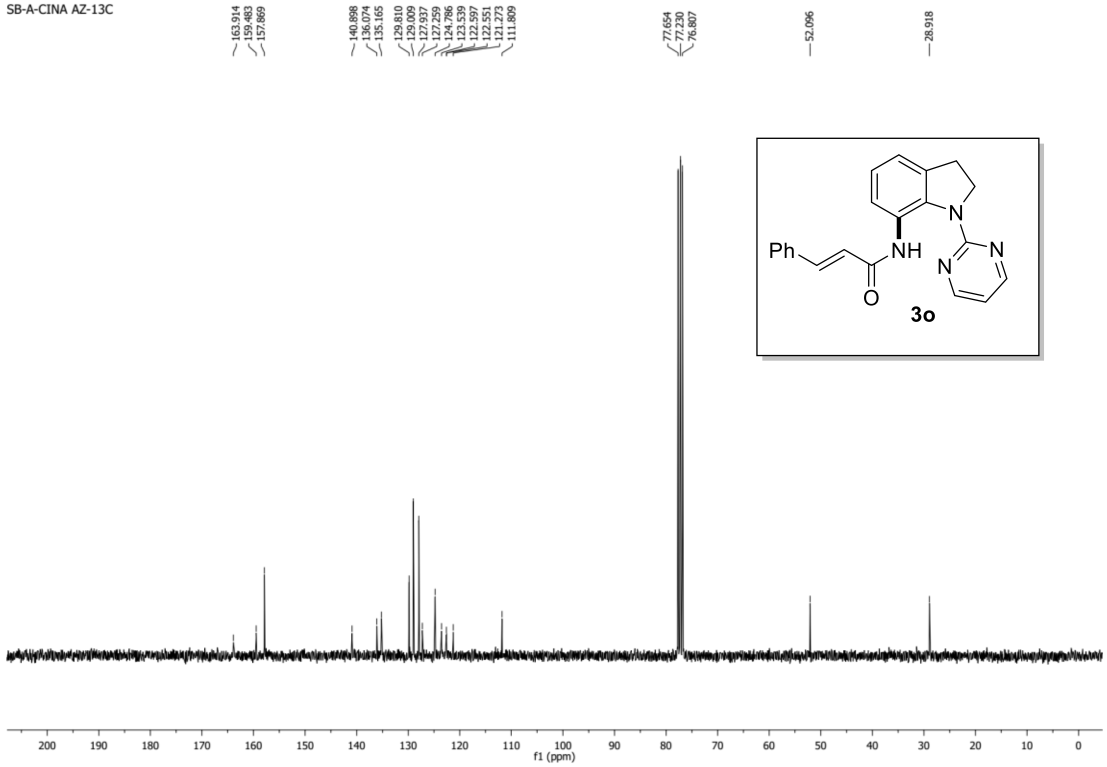
16. De, P. B.; Pradhan, S.; Banerjee, S.; Punniyamurthy, T. *Chem. Commun.* **2018**, *54*, 2494.

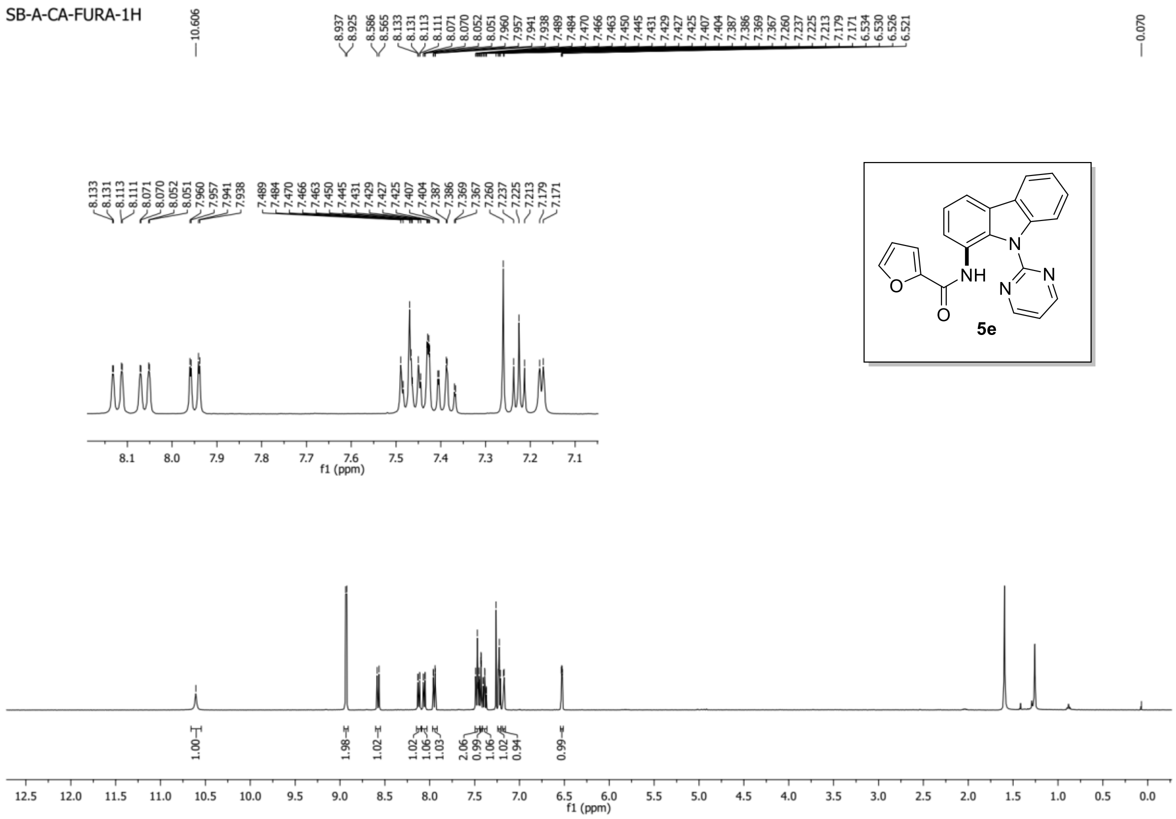
1.6 Selected NMR Spectra

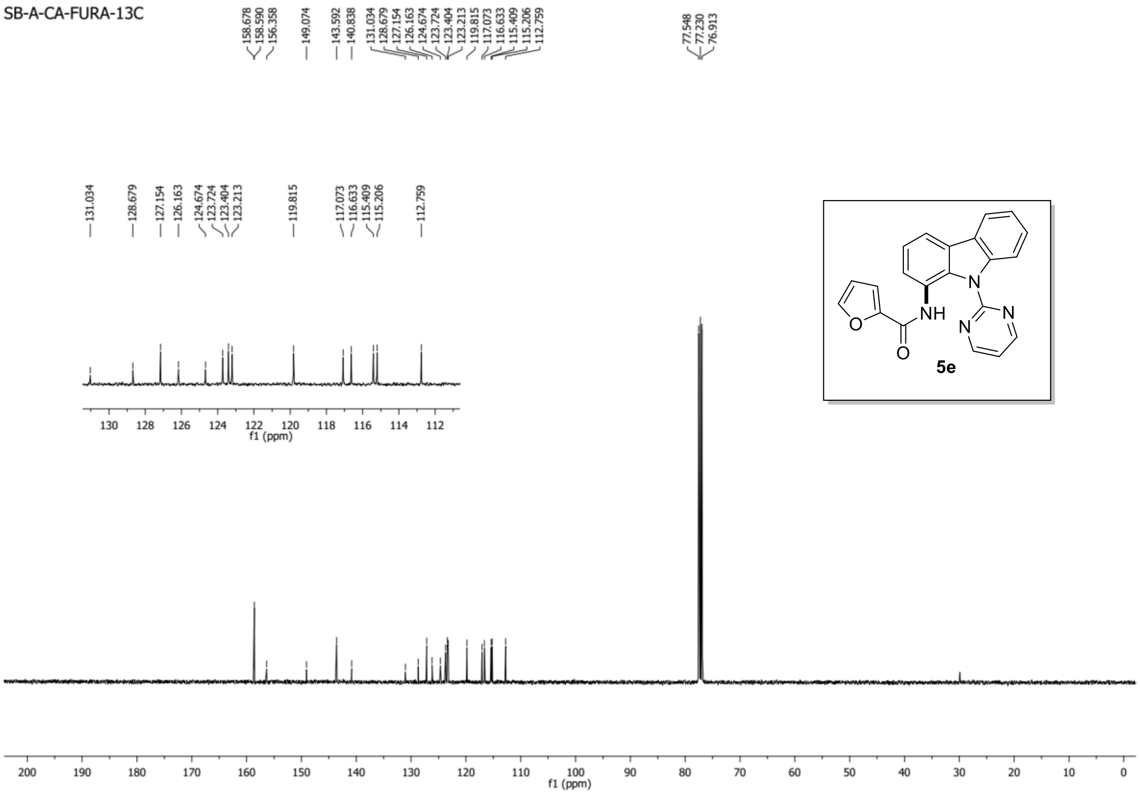





SB-A-CINA AZ-1H
11.079
8.534
8.518
7.964
7.939
7.686
7.634
7.494
7.477
7.378
7.360
7.260
7.166
7.141
7.115
7.068
7.044
6.810
6.794
6.778
6.433
6.381
4.496
4.469
4.443
3.133
3.107
3.080
-0.003
Ph
NH
N
N
N
O
3o
0.92
2.00
0.95
1.01
2.01
3.00
1.04
0.93
0.98
1.00
2.00
2.00
f1 (ppm)

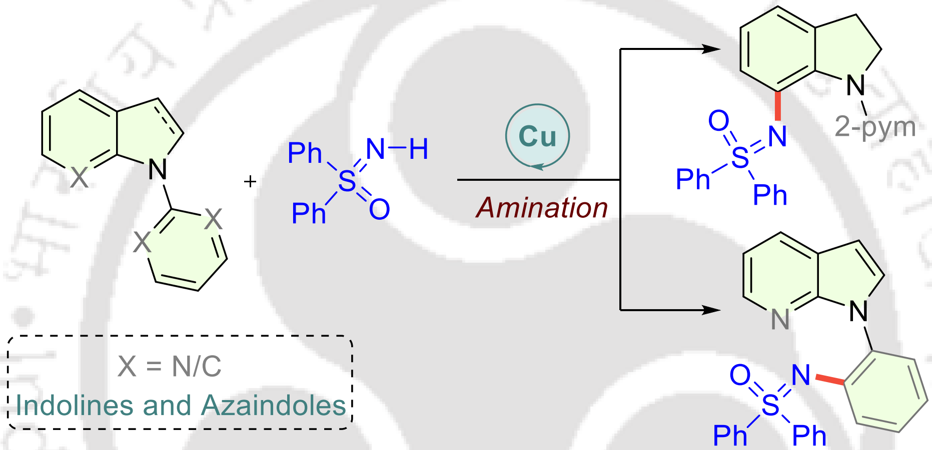

SB-A-CINA AZ-13C
163.914
159.483
157.869
140.898
136.074
135.165
129.810
129.009
127.937
127.259
124.786
123.539
122.597
122.551
121.273
111.809
77.654
77.230
76.807
52.096
28.918
Ph
NH
N
N
N
O
3o
f1 (ppm)


SB-A-CA-FURA-1H
10.606
8.937
8.925
8.586
8.565
8.133
8.131
8.113
8.111
8.071
8.070
8.052
8.051
7.960
7.957
7.941
7.938
7.489
7.484
7.470
7.466
7.463
7.450
7.445
7.431
7.429
7.427
7.425
7.407
7.404
7.387
7.386
7.369
7.367
7.260
7.237
7.225
7.213
7.179
7.171
6.534
6.530
6.526
6.521
0.070
1.00
1.98
1.02
1.02
1.06
1.03
2.06
0.99
1.06
1.02
0.94
0.99
f1 (ppm)
NH
O
N
5e


SB-A-CA-FURA-13C
158.678
158.590
156.358
149.074
143.592
140.838
131.034
128.679
127.154
126.163
124.674
123.724
123.404
123.213
119.815
117.073
116.633
115.409
115.206
112.759
77.548
77.230
76.913
f1 (ppm)
NH
O
N
5e

Chapter II

Cu-Catalyzed C7-Selective C-H/N-H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines

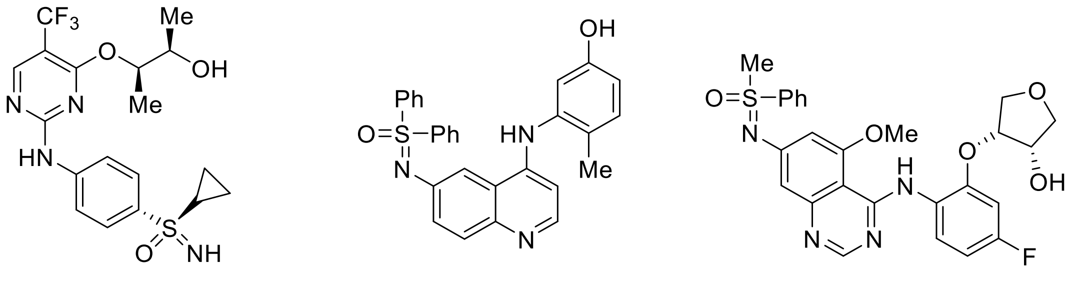


🛑 1st-row TM: Cu Catalysis 🛑 Broad Substrate Scope 🛑 Late-stage Functionalization

Org. Lett., **2022**, *24*, 7997.

Copper-Catalyzed C7-Selective C-H/N-H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines

Sulfoximines feature as pivotal structural motifs of numerous compounds that are important in biological, medicinal and synthetic sciences.[1] Efforts are thus made on the development of effective synthetic approaches for the construction of functionalized sulfoximines. Considerable progress has been made using the transition-metal-catalyzed C-N bond formation of sulfoximines with aryl halides and boronic acids as the aryl source. Recently, the rapid ascent of the cross-dehydrogenative coupling (CDC) has offered an effective synthetic tool to construct carbon-heteroatom bonds, obviating the requirement of prefunctionalized substrate precursors, thus enabling a step- and atom-economical alternative. To this end, harnessing the CDC strategy between sulfoximines with a class of imperative heterocycle structural frameworks would provide versatile aminated scaffolds.[2] In this regard, the functionalization of indole has attracted a great deal of attention, as they are prevalent substructures of plentiful drug candidates and natural products.[3] Among the available six C-H sites, the selective editing of the C7 C-H bond imposes a significant synthetic challenge.[4] By virtue of the reduced indoline intermediate, the C7 C-H bond functionalization can be accomplished using a suitable directing group with transition-metal-catalysis.[5] Thereby, engaging sulfoximines as an aminating coupling partner to afford the C7-amination of indolines in a cross-dehydrogenative manner would thus be valuable. Herein, we report an efficient Cu-catalyzed C7-sulfoximination of indolines via C-H and N-H dehydrogenative strategy using the removable pyrimidyl directing group (Scheme 1C). A broad range of sulfoximines covering (hetero)aryl and alkyl derivatives can be successfully coupled to deliver the aminated indoline scaffolds, which can be oxidized to the indole structural scaffolds in quantitative yields. Further, the late-stage functionalization of naturally occurring alcohol derivatives has been showcased to display the practical synthetic potential. Interestingly, the method can be extended to the coupling of substituted *N*-aryl azaindoles in good yields, which encompasses an important class of valuable indole moieties. These transformations highlight the use of abundant first-row Cu-catalysis with broad substrate scope and functional group compatibility.



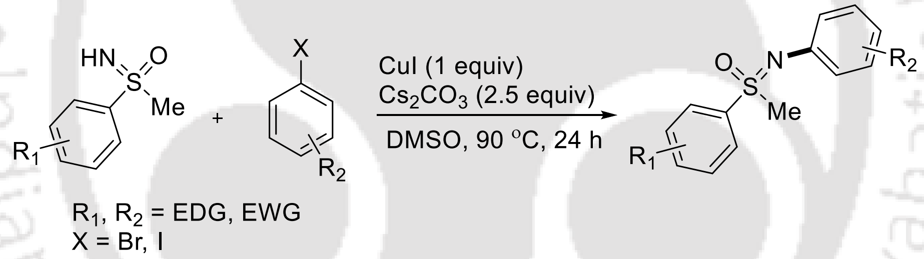
Roniciclib EphB4 Receptor Inhibitor MNK Kinase Inhibitor

Figure 1. Biologically Active Sulfoximine Derivatives

2.1 Literature Study

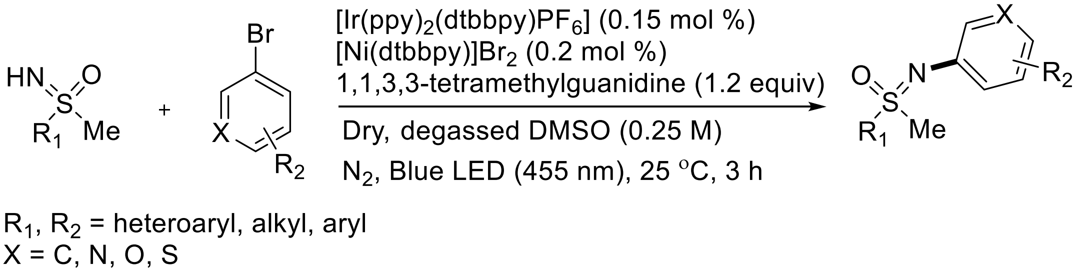
2.1.1 Cross-Coupling Reactions of Sulfoximines with Aryl Halides

Bolm and co-workers reported ligand-free Cu-mediated cross-coupling reactions of sulfoximines with aryl iodides and aryl bromides provide *N*-arylated sulfoximines in high yields (Scheme 1).[6] Shorter reaction times, higher reactivity, and economical practicality are important features of this methodology.



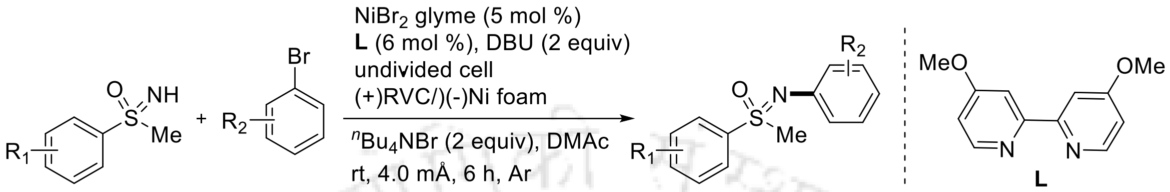
Scheme 1. Cu-Mediated *N*-Arylation of Sulfoximines

König and co-workers demonstrated that NH-sulfoximines can be *N*-arylated with brominated arenes and heteroarenes as coupling partners, by using a dual nickel photocatalyzed strategy (Scheme 2).[7] This method can be extended for other sulfoximidoyl derivatives like sulfonimidamides and sulfinamides proceed smoothly under the developed reaction conditions.



Scheme 2. *N*-Arylation of Sulfoximines via Dual Nickel Photocatalysis

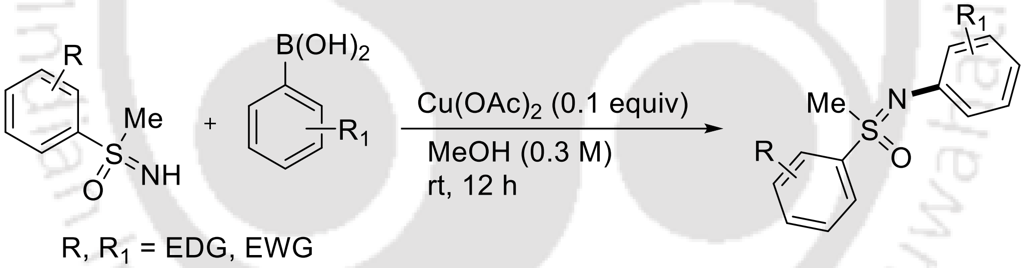
Mei and co-workers developed Ni-catalyzed electrochemical *N*-arylation of NH-sulfoximines with aryl bromides and chlorides in an undivided cell at room temperature, affording sulfoximidoyl derivatives with good to excellent yield (Scheme 3).[8] Mild reaction conditions, wide substrate scope, excellent functional group tolerance are important practical features of this strategy.



Scheme 3. Ni-Catalyzed *N*-Arylation of Sulfoximines via Paired Electrolysis

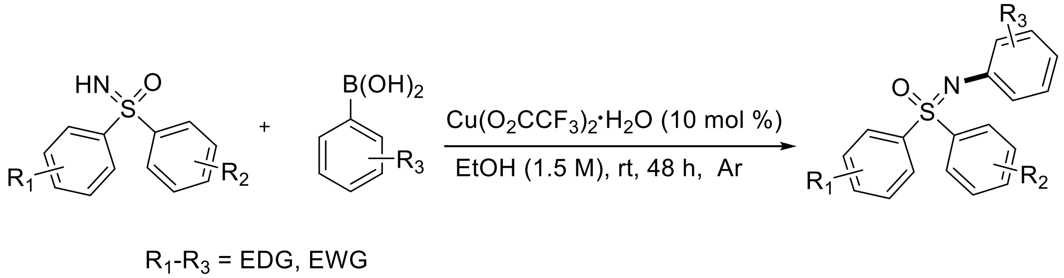
2.1.2 Cu-Catalyzed Cross-Coupling Reaction of Sulfoximines with Aryl Boronic Acids

A novel copper-catalyzed *N*-arylation of sulfoximines using boronic acids as arylating agents was reported by Bolm and co-workers (Scheme 4).[9] The cross-couplings proceed under mild reaction conditions at room temperature without additional external base. This procedure tolerated with a wide range of boronic acids derivatives substrates and various sulfoximines.



Scheme 4. Cu-Catalyzed *N*-Arylation of Sulfoximines

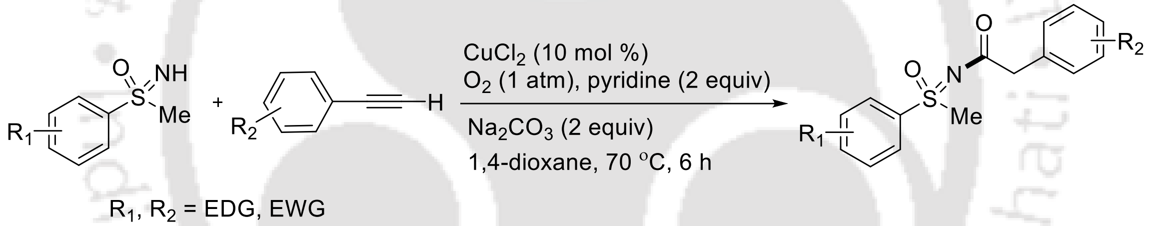
A photoredox copper-catalyzed dehydrogenative Chan-Lam coupling of free diaryl sulfoximines and arylboronic acids has been introduced by Jia and co-workers (Scheme 5).[10] This innovative approach accommodates a variety of functional groups, including heteroaryl boronic acids and free heteroaryl sulfoximines. This methodology not only provides greater substrate versatility but also eliminates the formation of byproducts from oxidants.



Scheme 5. Photoredox Chan-Lam Coupling of Sulfoximines

2.1.3 Cu-Catalyzed Cross-Coupling Reaction of Sulfoximines with Alkynes

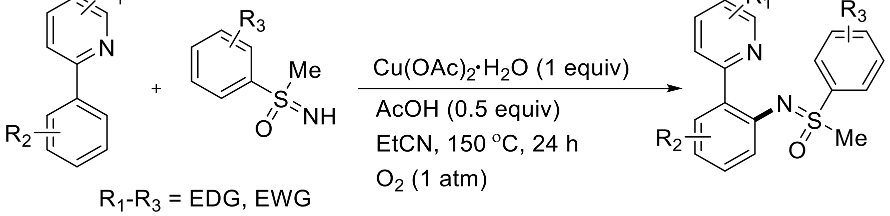
Bolm and co-workers developed a synthetically useful protocol for the preparation of yne sulfoximines through copper-catalyzed oxidative couplings of sulfoximines and terminal alkynes (Scheme 6).[11] Under mild reaction conditions, a cost-effective catalyst and molecular oxygen serve as the oxidant in this process. This methodology allows for the generation of various yne sulfoximines from their corresponding sulfoximines, with good tolerance for both electron-rich and electron-deficient terminal alkynes.



Scheme 6. Cu-Catalyzed Oxidative Cross-Coupling of Sulfoximines

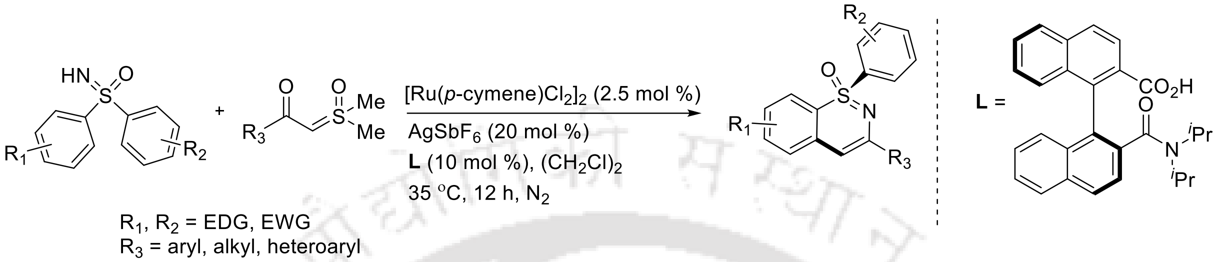
2.1.4 C-H Functionalization of Sulfoximines

Later, the same group described a new approach to *N*-arylation of sulfoximines using dual C-H/N-H activation, wherein pyridine nitrogens act as directing elements, enabling the derivatization of remote positions in connected arenes (Scheme 7).[12] The resulting products can function as *N*,*N′*-chelating ligands, holding potential for applications in catalysis, materials science, and bio-related areas.



Scheme 7. Copper-Mediated Dual N-H/C-H Activation of 2-Arylpyridines

Shi and co-workers reported the Ru(II)-catalyzedenantioselective C-H activation/annulation of sulfoximines with α-carbonyl sulfoxonium ylides enabled by a novel class of chiral binaphthyl monocarboxylic acids (Scheme 8).[13] Moreover, the resolution products can be readily converted into chiral sulfoxides and key intermediates for kinase inhibitors.

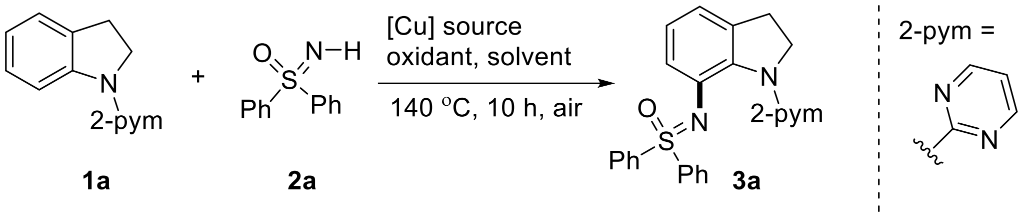


Scheme 8. Ru(II)-Catalyzed Enantioselective C-H Functionalization of Sulfoximines

2.2 Present Study

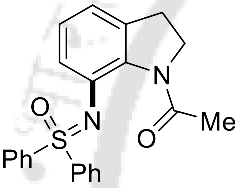
Herein a Cu(II)-catalyzed C7-selective C-H/N-H cross-dehydrogenative coupling of indolines and azaindoles with versatile sulfoximines has been accomplished. Initially, we commenced the optimization studies using 1-(pyrimidin-2-yl)indoline **1a** and sulfoximine **2a** as the model substrates using different solvents, oxidants and copper salts at varied temperature (Table 1). To our delight, the reaction occurred to produce **3a** in 67% yield when the substrates were stirred with $Cu(OAc)_2$ (20 mol %) and Ag_2CO_3 (1 equiv) at 140 °C under air. In a set of solvents examined, *m*-xylene produced the best outcome, whereas the 1,4-dioxane, DMSO, toluene, mesitylene, PhCl and DMF yielded inferior results. The reaction using Ag_2CO_3 as an oxidant was found to be superior to that of Ag_2O, AgOAc and $K_2S_2O_8$. Of the Cu-sources screened, Cu(OAc), $Cu(OAc)_2$, $Cu(OAc)_2{\cdot}H_2O$, CuO, Cu_2O, CuI, $CuCl_2$, and $CuBr_2$, $Cu(OAc)_2$ provided the best results. The reaction using N_2 instead of air led to the drop in the yield to 50% (entry 18). Control experiment in the absence of silver salt (Ag_2CO_3) produced detrimental yield. These results confide the crucial role of Ag(I) as an oxidant in this transformation. In addition, the screening of the directing groups confirmed that pyrimidyl and pyridyl directing groups are superior to the weak chelating carbonyl directing groups, such as acetyl, pivaloyl and carbamoyl, which elucidate the vital role of *N*-chelation in the transformation.

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

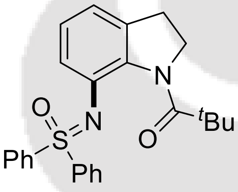


Entry	[Cu] source	Oxidant	Additive	Solvent	Yield (%)[b]
1.	$Cu(OAc)_2$	Ag_2CO_3	-	1,4-dioxane	n.d.
2.	$Cu(OAc)_2$	Ag_2CO_3	-	DMSO	n.d.
3.	$Cu(OAc)_2$	Ag_2CO_3	-	toluene	10
4.	$Cu(OAc)_2$	Ag_2CO_3	-	mesitylene	14
5.	$\mathbf{Cu(OAc)_2}$	$\mathbf{Ag_2CO_3}$	-	***m*-xylene**	**67**
6.	$Cu(OAc)_2$	Ag_2CO_3	-	PhCl	16
7.	$Cu(OAc)_2$	Ag_2CO_3	-	DMF	n.d.
8.	$Cu(OAc)_2$	Ag_2O	-	*m*-xylene	31
9.	$Cu(OAc)_2$	$K_2S_2O_8$	-	*m*-xylene	33
10.	$Cu(OAc)_2$	AgOAc	-	*m*-xylene	51
11.	CuOAc	Ag_2CO_3	-	*m*-xylene	n.d.
12.	$Cu(OAc)_2{\cdot}H_2O$	Ag_2CO_3	-	*m*-xylene	n.d.
13.	CuO	Ag_2CO_3	-	*m*-xylene	n.d.
14.	Cu_2O	Ag_2CO_3	-	*m*-xylene	n.d.
15.	CuI	Ag_2CO_3	-	*m*-xylene	n.d.
16.	$CuCl_2$	Ag_2CO_3	-	*m*-xylene	n.d.
17.	$CuBr_2$	Ag_2CO_3	-	*m*-xylene	n.d.
18.[c]	$Cu(OAc)_2$	Ag_2CO_3	-	*m*-xylene	50
19.	$Cu(OAc)_2$	-	-	*m*-xylene	21
20.	-	Ag_2CO_3	-	*m*-xylene	n.d.
21.	$Cu(OAc)_2$	Ag_2CO_3	K_2CO_3	*m*-xylene	22

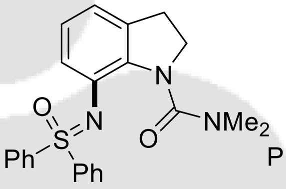
22.	$Cu(OAc)_2$	Ag_2CO_3	Cs_2CO_3	*m*-xylene	n.d.
23.	$Cu(OAc)_2$	Ag_2CO_3	Na_2CO_3	*m*-xylene	25
24.	$Cu(OAc)_2$	Ag_2CO_3	K_3PO_4	*m*-xylene	34
25.	$Cu(OAc)_2$	Ag_2CO_3	PivOH	*m*-xylene	38
26.	$Cu(OAc)_2$	Ag_2CO_3	AcOH	*m*-xylene	65
27.[d]	$Cu(OAc)_2$	Ag_2CO_3	-	*m*-xylene	12
28.[e]	$Cu(OAc)_2$	Ag_2CO_3	-	*m*-xylene	26
29.[f]	$Cu(OAc)_2$	Ag_2CO_3	-	*m*-xylene	70
30.[g]	$Cu(OAc)_2$	Ag_2CO_3	-	*m*-xylene	49



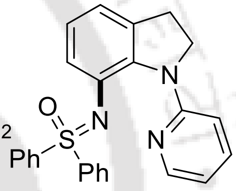
A', n.d.



B', n.d.



C', n.d

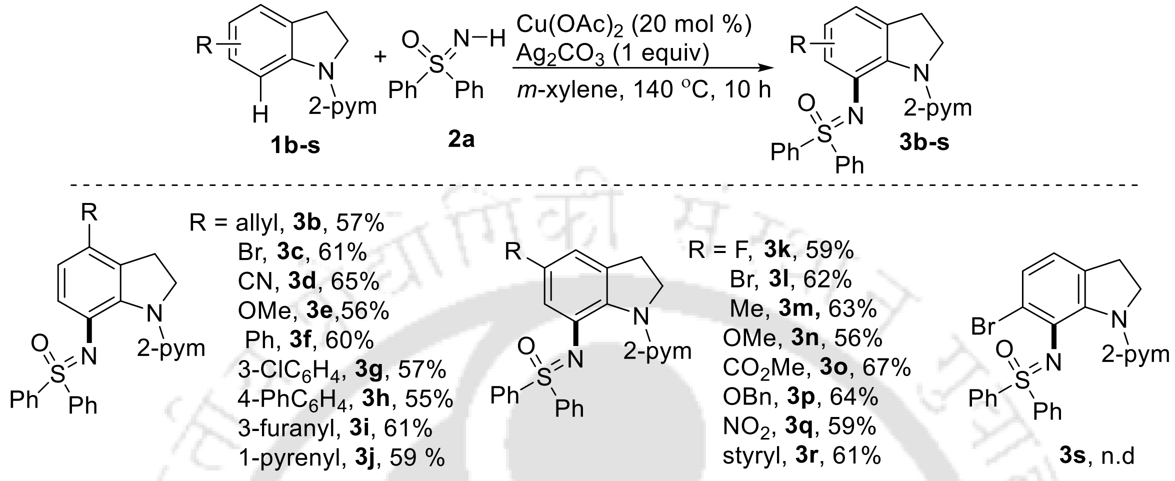


D', 59 %[b]

[a]Reaction conditions: **1a** (0.1 mmol), **2a** (0.15 mmol), $Cu(OAc)_2$ (20 mol %), oxidant (1 equiv), additive (50 mol %), solvent (0.5 mL), 140 °C, 10 h, air. [b]Isolated yield. [c]Under N_2 atmosphere [d]Reaction at 100 °C. [e]Reaction at 120 °C. [f]Using 50 mol % $Cu(OAc)_2$. [g]Using 10 mol % $Cu(OAc)_2$. n.d. = not detected.

Having established the optimal reaction conditions, we explored the scope of the procedure for a series of substituted indolines **1b-s** with sulfoximine **2a** as a standard substrate (Table 2). Substrates bearing allyl **1b**, bromo **1c**, cyano **1d**, methoxy **1e**, phenyl **1f**, substituted aryl **1g-h**, 3-furanyl **1i** and 1-pyrenyl **1j** substituents at the C4 position successfully participated in giving the aminated indolines **3b-j** in 55-65% yields. The reaction of the substrates having fluoro **1k**, bromo **1l**, methyl **1m**, methoxy **1n**, ester **1o**, benzyloxy **1p**, nitro **1q** and styryl **1r** substituents at the C5 position occurred efficiently to deliver the target products **3k-r** in 56-67% yields. The compound **3n** produced single crystal whose structure was determined using the X-ray analysis (Figure 2). In contrast, indoline **1s** bearing bromo substituent at the C6 position showed no reaction and the starting material was recovered intact, which may be due to steric hindrance of the bromo group near the coupling site.

Table 2. Substrate Scope of Indolines[a,b]

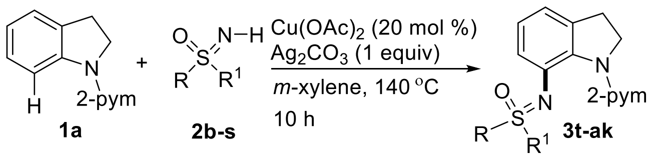


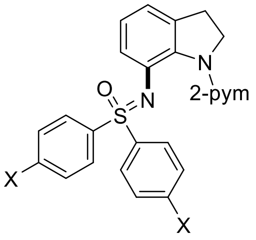
[a]Reaction conditions: **1b-s** (0.2 mmol), **2a** (0.3 mmol), $Cu(OAc)_2$ (20 mol %), Ag_2CO_3 (0.2 mmol), *m*-xylene (1 mL), 140 °C, 10 h, air. [b]Isolated yield. n.d. = not detected.

The reaction conditions were extended to the coupling of a broad range of sulfoximines **2b-s** with indoline **1a** as a standard substrate (Table 3). Symmetric biaryl sulfoximine substrates conveyed the target products **3t-3v** in 52-63% yields. Further, unsymmetrical biaryl derivatives having functional group in one of the aryl rings, 2-isopropyl **3w**, 3-chloro **3x**, 4-bromo **3y**, 4-fluoro **3z**, 4-methoxy **3aa**, 4-nitro **3ab**, 4-*tert* butyl **3ac** and 4-trifluoromethyl **3ad** groups were amenable in delivering the aminated products in good yields. In addition, 3-chloro and 4-bromo groups containing substrate **2m** underwent reaction to furnish **3ae** in 60% yield. Moreover, 3,5-dimethyl **2n**, 2-/1-naphthyl **2o-p** analogues were coupled to deliver **3af-ah** in 59-63% yields. Further, 2-pyridyl and morpholinyl derivatives were proven competent, furnishing **3ai** and **3aj** in 57 and 51% yields, respectively. A dialkyl congener **2s** gave **3ak** in 55% yield. These results indicated the significant functional group tolerance of the current amination procedure.

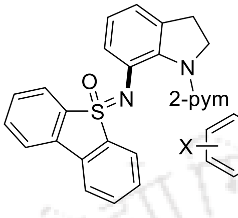
The scope of the procedure was further examined for the coupling of substituted azaindoles **4a-j** with **2a** as the representative substrate (Table 4). The reaction of **4a** efficiently took place to produce **5a** in 73% yield. In addition, the substrates bearing 3-iodo **4b** and 5-bromo **4c** substituents

Table 3. Substrate Scope of Sulfoximines[a,b]

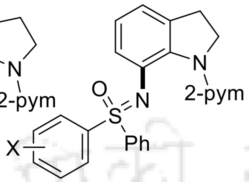




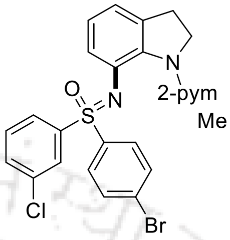
X = Me, **3t**, 63%
NO$_2$, **3u**, 52%



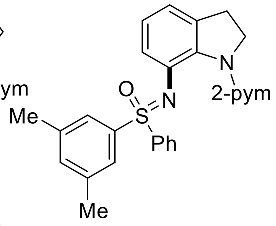
3v, 58%



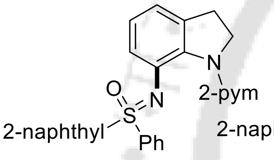
X = 2-iPr, **3w**, 58%
3-Cl, **3x**, 62%
4-Br, **3y**, 65%
4-F, **3z**, 64%
4-OMe, **3aa**, 54%
4-NO$_2$, **3ab**, 56%
4-^{t}Bu, **3ac**, 61%
4-CF$_3$, **3ad**, 53%



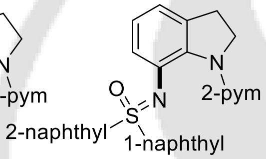
3ae, 60%



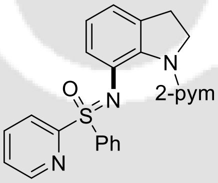
3af, 63%



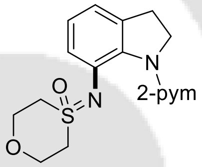
3ag, 62%



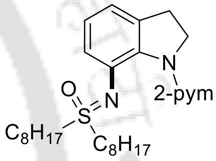
3ah, 59%



3ai, 57%



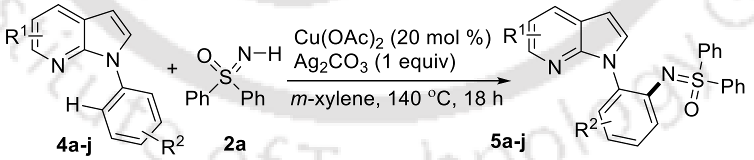
3aj, 51%

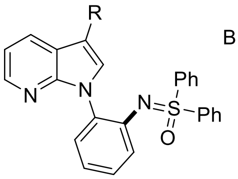


3ak, 55%

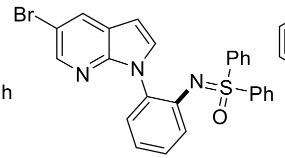
[a]Reaction conditions: **1a** (0.2 mmol), **2b-s** (0.3 mmol), Cu(OAc)$_2$ (20 mol %), Ag$_2$CO$_3$ (0.2 mmol), *m*-xylene (1 mL), air, 140 °C, 10 h. [b]Isolated yield.

Table 4. Substrate Scope of Azaindoles[a,b]

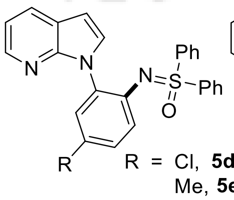




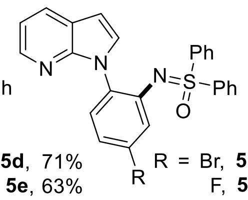
R = H, **5a**, 73%
I, **5b**, 53%



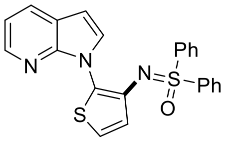
5c, 66%



R = Cl, **5d**, 71%
Me, **5e**, 63%
OMe, **5f**, 68%



R = Br, **5g**, 70%
F, **5h**, 68%
NO$_2$, **5i**, 61%

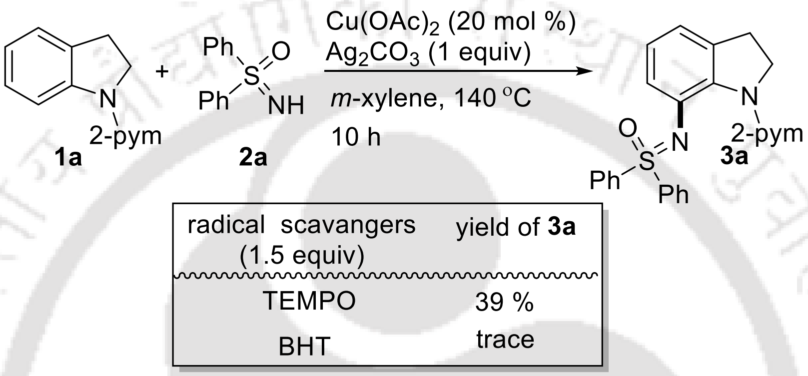


5j, 59%

[a]Reaction conditions: **4a-j** (0.2 mmol), **2a** (0.3 mmol), Cu(OAc)$_2$ (20 mol %), Ag$_2$CO$_3$ (1 equiv), *m*-xylene (1 mL), air, 140 °C, 18 h. [b]Isolated yield.

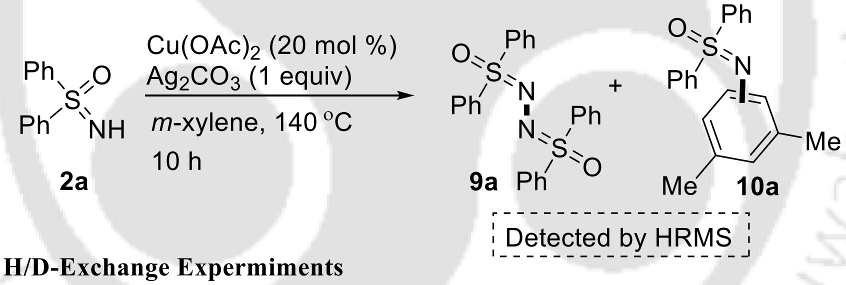
successfully underwent the coupling to give **5a** and **5b** in 73% and 53% yields, respectively. Moreover, the substrates bearing 3-chloro **4d**, 3-methyl **4e**, 3-methoxy **4f**, 4-bromo **4g**, 4-fluoro **4h** and 4-nitro **4i** groups in the *N*-aryl ring were smoothly reacted to give **5d-5i** in good yields. Crystallization of **5h** yielded single crystals whose structure was determined using the X-ray analysis (Figure 3). Further, the substrate having *N*-heteroaryl congener with 2-thienyl group **4j** can be reacted to furnish **5j** in 59% yield.

(a) Radical Scavanger Experiment

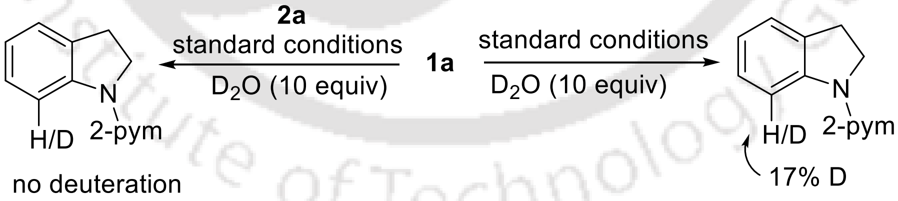


radical scavangers (1.5 equiv)	yield of **3a**
TEMPO	39 %
BHT	trace

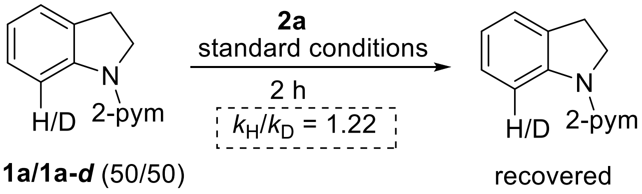
(b) Detection of Dimer 9a and Arene-adduct 10



(c) H/D-Exchange Expermiments

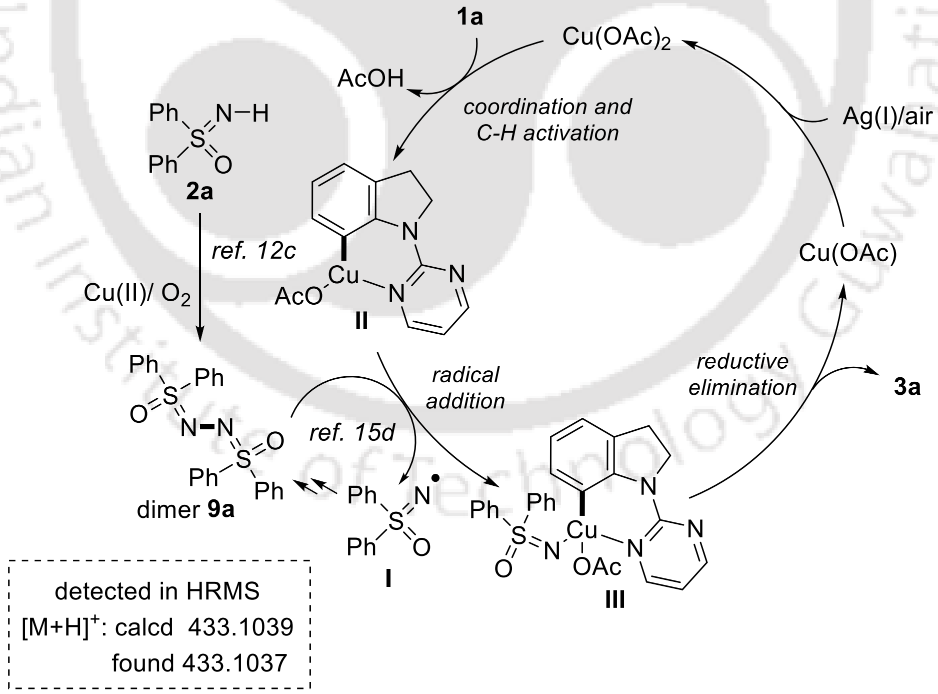


(d) Kinetic Isotope Experiment



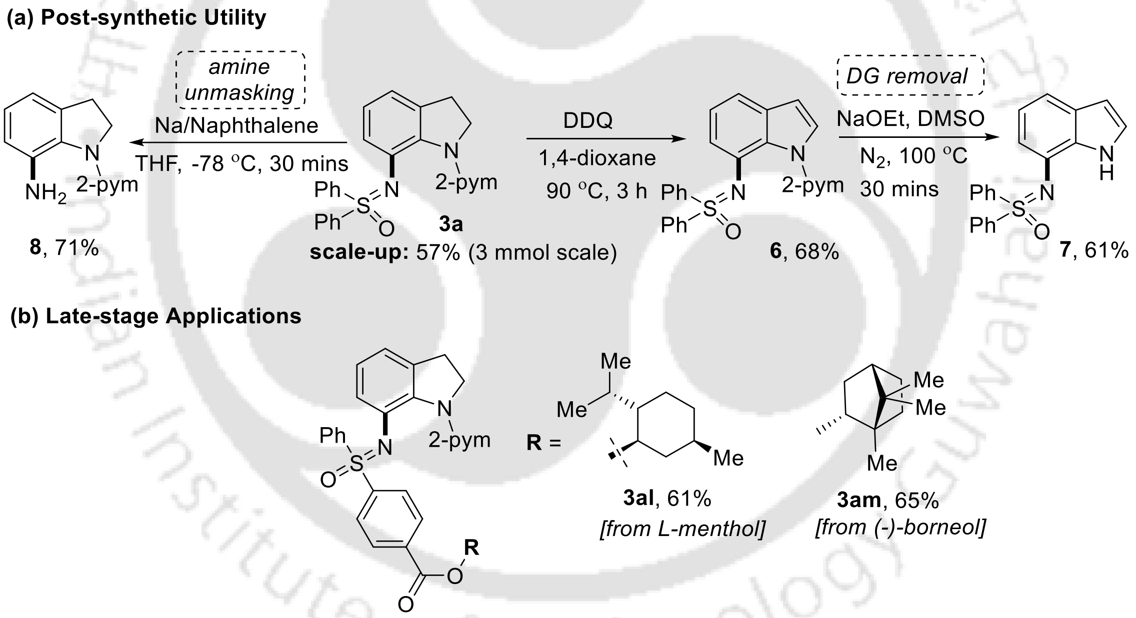
Scheme 9: Preliminary Mechanistic Investigations

To gain insight into the reaction pathway, we carried out the reaction of **1a** and **2a** independently in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) as radical scavengers (Scheme 9a). The reaction slowed dropping the yield to <39%. Further, the reaction of **2a** in the absence of **1a** produced the dimer **9a** and the arene adduct **10a** (Scheme 9b), which suggest that the reaction involves radical intermediate. Further, H/D-scrambling experiments in the presence and absence of **2a** using D_2O, implied that C-H activation step might not be reversible (Scheme 9c). In addition, the intermolecular kinetic isotope experiment yielded a k_H/k_D 1.22 (Scheme 9d), indicating C-H activation might not be the rate-determining.[14] These experimental results and literature precedents[15] suggest that chelation followed by C-H activation of **1a** with $Cu(OAc)_2$ can produce the intermediate **II**, while the sulfoximine with Cu(II)/O_2 can produce dimer **9a**, which may undergo homolytic cleavage to give *N*-center radical **I**. The coupling of the Cu(II)-species **II** with **I** can produce the Cu(III) species **III** that can undergo reductive elimination to furnish the target C7-aminated **3a** and Cu(I), which can be oxidized to $Cu(OAc)_2$ to complete the catalytic cycle (Scheme 10).



Scheme 10: Plausible Catalytic Cycle

Finally, the scale-up of the procedure was investigated using 3 mmol of **1a** with **2a** as the representative substrate (Scheme 11). The reaction took place to produce **3a** in 54%. In addition, oxidation of **3a** using 2,3-dichloro-5,6-dicyano-1,4-benzoquin-none (DDQ) can be accomplished to afford **6**, which can be reacted with base (NaOEt) to furnish the aminated indole **7** in 61% yield. Further, amine unmasking of **3a** can be carried out using Na/naphthalene to afford primary amine derivative **8** in 71% yield, which can serve as a versatile functional handle for downstream modifications at C7 site of indole. Further, effort was made to the removal of the pyrimidyl directing group from **3a** using NaO^tBu/DMSO,[17] however, the reaction was unsuccessful, producing **8** in 49% yield. Later, the late-stage application of the procedure has been studied using sulfoximines derived from naturally-occurring alcohols, *L*-menthol and (-)-borneol to produce **3al** and **3am** in 61 and 65% yields, respectively.



Scheme 11: Post-synthetic Applications

In summary, we have developed a Cu(II)-catalyzed dehydrogenative amination for the C-H and N-H coupling of indole derivatives and versatile sulfoximines. The broad diversity of sulfoximines and indole derivatives were coupled efficiently to build the C7-aminated indoles. We hope that the present method will open up new avenues to utilize sulfoximines for potential amination transformations.

2.3 Experimental Section

General Information. $Cu(OAc)_2$ (98%), $Cu(OAc)_2{\cdot}H_2O$ (>98%), Cu_2O (≥99.99%), Ag_2CO_3 (99%), Ag_2O (99%), AgOTf (≥98.0%), AgOAc (≥99.99%), Cs_2CO_3 (99%), K_3PO_4 ((≥98.0%), $K_2S_2O_8$ (≥99.9%) and K_2CO_3 ((≥99.0%) were purchased from Aldrich and used as received. The solvents were dried prior to use according to the standard procedure. Merck silica gel G/GF254 plates were utilized for analytical thin-layer chromatography (TLC) with a mixture of *n*-hexane and EtOAc as the eluent. Rankem silica gel (60-120 mesh) was employed for column chromatography. Melting point of the products was measured on Büchi melting point apparatus, MPB-540. Open capillary tubes were used for the measurements and are uncorrected. NMR (^1H, ^{13}C and ^{19}F) spectra were recorded on Bruker 400, 500 and 600 MHz NMR instruments utilizing tetramethylsilane (Me_4Si) as an internal standard and $CDCl_3$ as a solvent. Mestrenova software was used throughout the spectral analysis. Chemical shifts (δ) and spin-spin coupling constant (J) are reported in parts per million and hertz (Hz), respectively, and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet and br s = broad singlet. Quadrupole time-of-flight electrospray ionization (ESI) mass spectrometer (model HAB 273) was used for mass spectra. Fourier transform infrared attenuated total reflectance spectra (FTIR-ATR) was recorded using Perkin Elmer instrument. Single crystal X-ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/-Kα radiation and the structure was solved by direct method using SHELXL-16 (Göttingen, Germany).

General Procedure for the Cu(II)-Catalyzed C7-Amination of Indolines. A mixture of 1-(pyrimidin-2-yl)indoline **1** (0.2 mmol), iminodiphenyl-λ^6-sulfanone **2** (0.3 mmol), $Cu(OAc)_2$ (20 mol %, 0.04 mmol, 7.2 mg) and Ag_2CO_3 (0.2 mmol, 55.2 mg) was stirred in *m*-xylene (1 mL) at 140 ^oC in a preheated oil bath for 10 h under**.** After completion, as judged by the TLC, the reaction mixture was cooled to room temperature and filtered through a short pad of celite using EtOAc (2 x 10 mL). The organic phase was washed successively with brine (1 x 10 mL) and extracted with EtOAc (3 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified by silica gel column chromatography (*n*-hexane: EtOAc = 3:1) to afford C7-aminated indolines **3**.

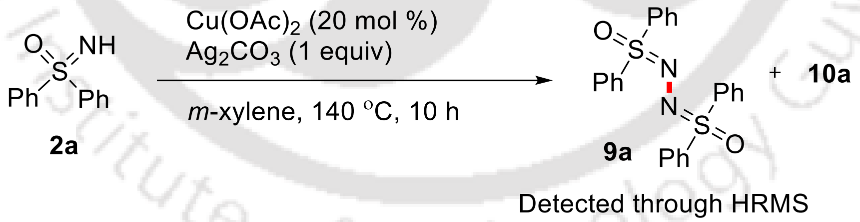
General Procedure for the Cu(II)-Catalyzed *ortho* C-H Amination of *N*-Aryl-7-Azaindoles. A mixture of 1-phenyl-1*H*-pyrrolo[2,3-*b*]pyridine **4** (0.2 mmol), iminodiphenyl-λ^6-sulfanone **2**

(0.3 mmol), $Cu(OAc)_2$ (20 mol %, 0.04 mmol, 7.2 mg) and Ag_2CO_3 (0.2 mmol, 55.2 mg) was stirred in *m*-xylene (1 mL) at 140 °C in a preheated oil bath for 18 h**.** After completion, as judged by the TLC, the reaction mixture was cooled to room temperature and filtered through a short pad of celite using EtOAc (2 x 10 mL). The organic phase was washed successively with brine (1 x 10 mL) and extracted with EtOAc (3 x 10 mL). Drying (Na_2SO_4) and evaporation of the organic layer gave a residue that was purified by silica gel column chromatography (*n*-hexane: EtOAc = 6:1) to obtain ortho-aminated *N*-aryl-7-azaindoles **5**.

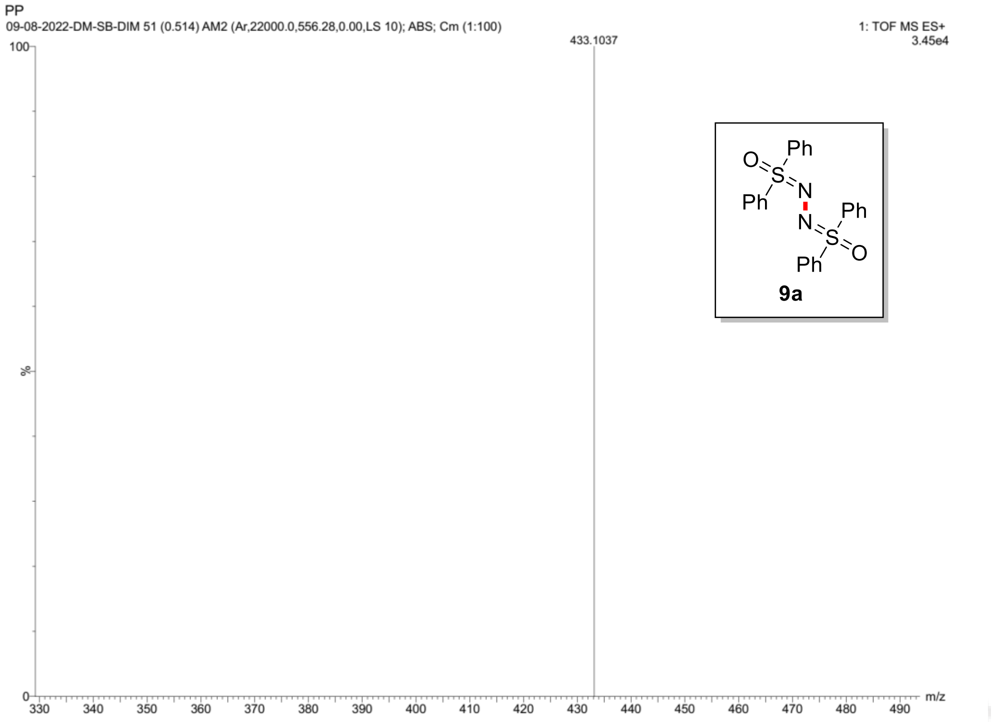
Scale-up Synthesis of 3a. A mixture of 1-(pyrimidin-2-yl)indoline **1a** (3 mmol, 591 mg), iminodiphenyl-λ^6-sulfanone **2a** (4.5 mmol, 976.5 mg), $Cu(OAc)_2$ (20 mol %, 0.6 mmol, 109.2 mg), Ag_2CO_3 (3 mmol, 828 mg) was stirred in *m*-xylene (20 mL) at 140 °C in a preheated oil bath for 10 h**.** Progress of the reaction was monitored by TLC using *n*-hexane and EtOAc as an eluent. Then the work up procedure was followed as described in the general procedure. Purification using *n*-hexane and EtOAc (3:1) as an eluent, gave **3a** in 54% (667.4 mg) yield.

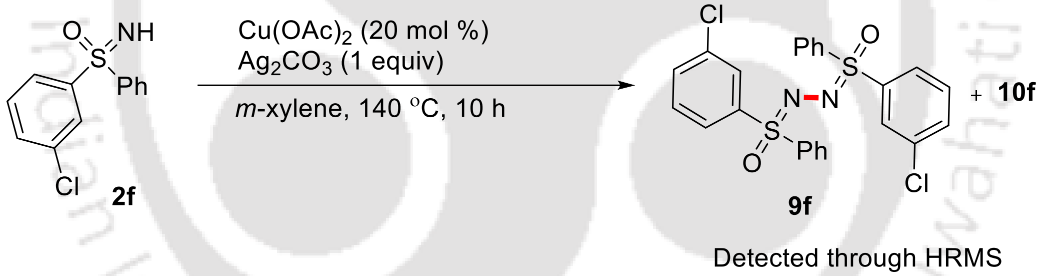
1-(Pyrimidin-2-yl)indolines, *N*-substituted indoline directing groups, 1-phenyl-1*H*-pyrrolo[2,3-*b*]pyridines and iminodiphenyl-λ^6-sulfanone were synthesized as per reported procedures.

Detection of Dimer 9 in the reaction.[17] A mixture of iminodiphenyl-λ^6-sulfanone **2a** (0.2 mmol, 43.4 mg), $Cu(OAc)_2$ (20 mol %, 7.3 mg) and Ag_2CO_3 (0.2 mmol, 55.2 mg) was stirred in *m*-xylene (1 mL) at 140 °C in a preheated oil bath for 10 h. After completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and passed through a short pad of celite. The solvent was evaporated under reduced pressure and the residue was submitted for HRMS in CH_3CN from which formation of dimer **9a** was detected.

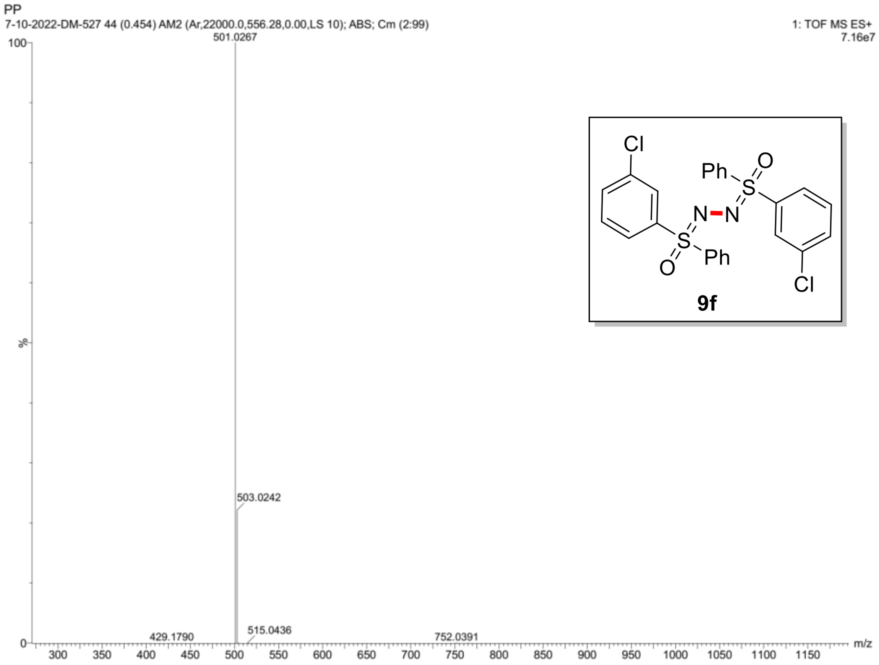


HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{21}N_2O_2S_2^+$: 433.1039, found: 433.1037.



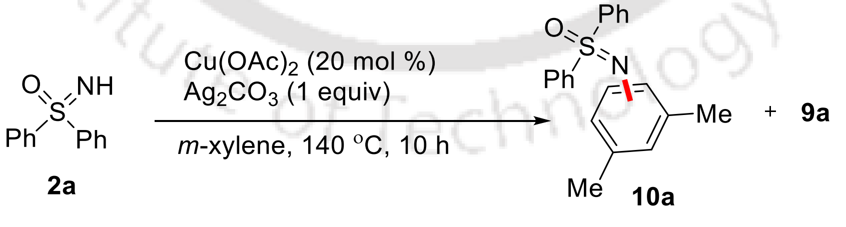


HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}Cl_2N_2O_2S_2^+$: 501.0260, found: 501.0267.

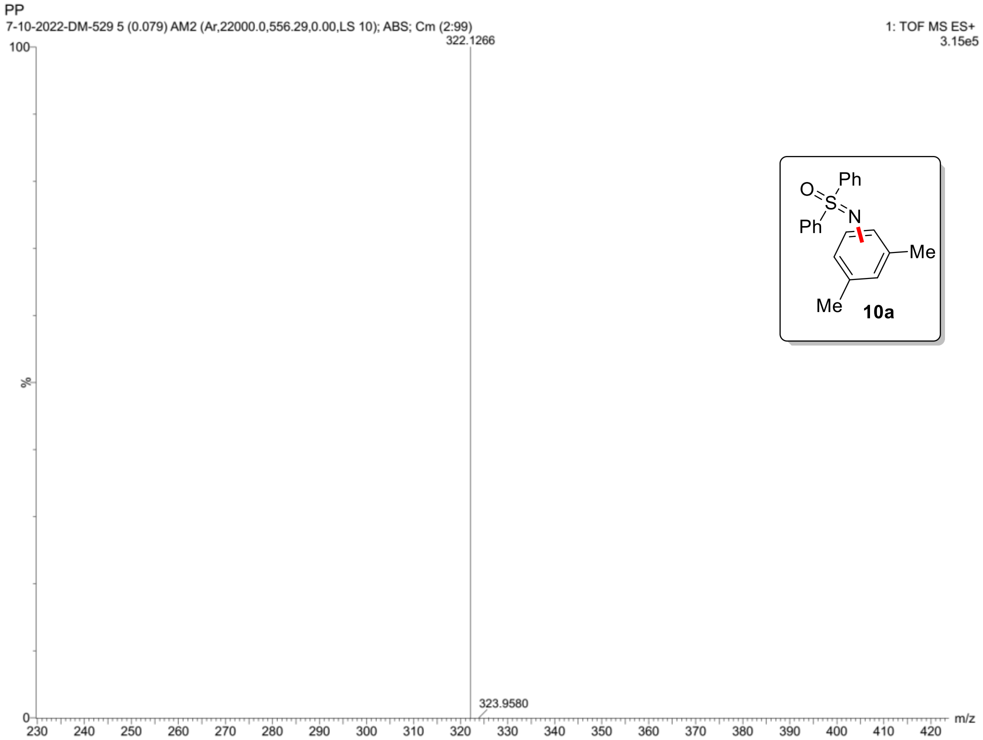


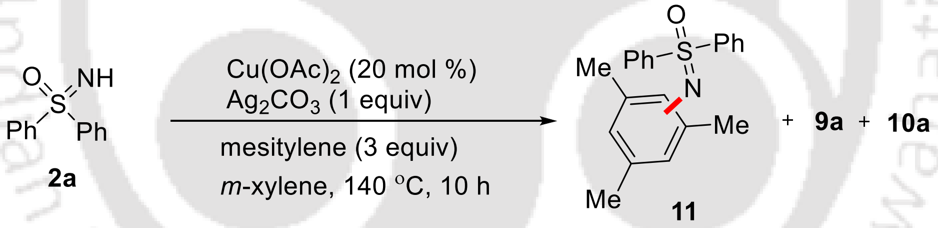
Detection of Arene Adducts. A mixture of iminodiphenyl-λ^6-sulfanone **2a** (0.1 mmol, 21.7 mg), $Cu(OAc)_2$ (20 mol %, 3.6 mg) and Ag_2CO_3 (0.1 mmol, 27.6 mg) was stirred in *m*-xylene (1 mL) at 140 ^{o}C in a preheated oil bath for 10 h. After completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and passed through a short pad of celite. The solvent was evaporated under reduced pressure and the residue was submitted for HRMS in CH_3CN from which formation of xylene-adduct **10** was detected.

HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{20}NOS^+$: 332.1260, found: 332.1266.



Detected through HRMS

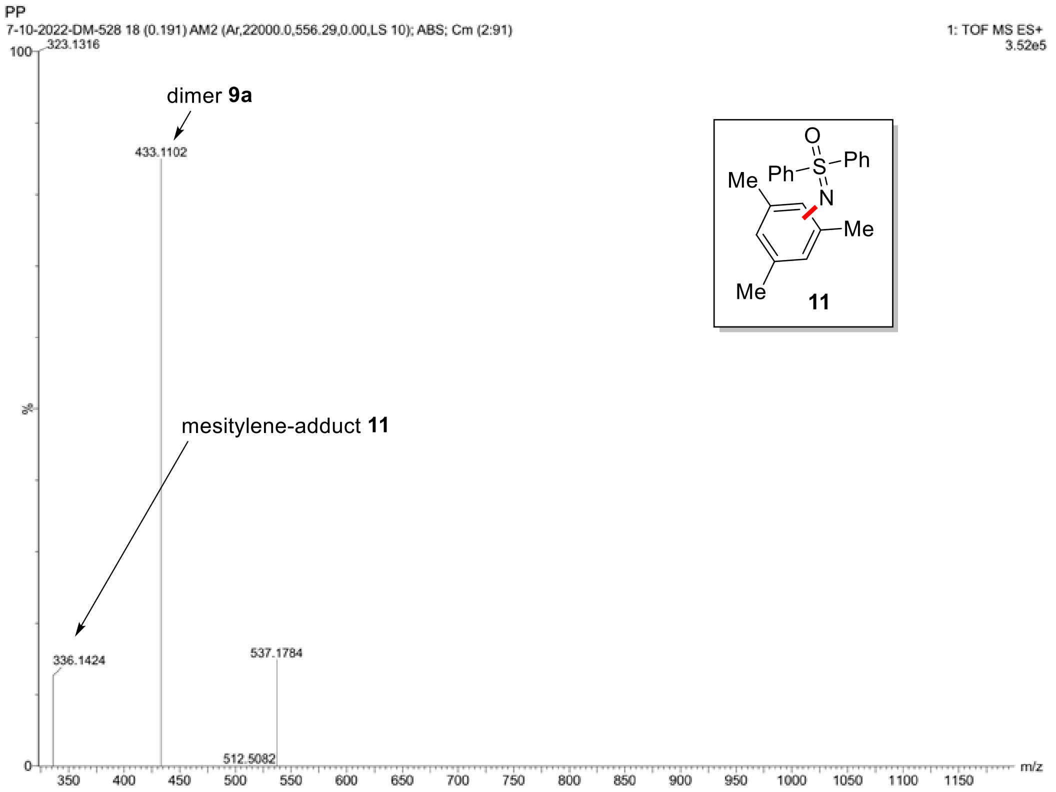




Detected through HRMS

A mixture of iminodiphenyl-λ^6-sulfanone **2a** (0.1 mmol, 21.7 mg), $Cu(OAc)_2$ (20 mol %, 3.6 mg), Ag_2CO_3 (0.1 mmol, 27.6 mg) and mesitylene (0.3 mmol, 3 equiv, 41.7µL) was stirred in *m*-xylene (1 mL) at 140 °C in a preheated oil bath for 10 h. After completion, the reaction mixture was cooled to room temperature and diluted with EtOAc and passed through a short pad of celite. The solvent was evaporated under reduced pressure and the residue was submitted for HRMS in CH_3CN from which formation of mesitylene-adduct **11** was detected.

HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{21}H_{22}NOS^+$: 336.1417, found: 336.1424.



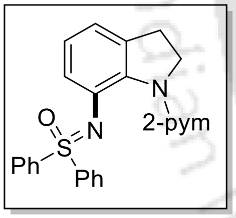
H/D Exchange Experiment with D_2O in the Absence of 2a. To a stirred solution of 1-(pyrimidin-2-yl)indoline **1a** (0.1 mmol, 19.7 mg), $Cu(OAc)_2$ (0.02 mmol, 3.6 mg) and Ag_2CO_3 (0.1 mmol, 27.6 mg) in *m*-xylene (1 mL), D_2O (1 mmol, 0.2 mL) was added. The reaction mixture was stirred at 140 ^{o}C in a preheated oil bath under air for 10 h under air. The reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL), and passed through a short pad of celite using EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified upon silica gel column chromatography using 9:1 mixture of *n*-hexane and EtOAc as an eluent. The ^{1}H NMR analysis showed 17% deuterium incorporation at C7 position.

H/D Exchange Experiment with D_2O in the Presence of 2a. To a stirred solution of 1-(pyrimidin-2-yl)indoline **1a** (0.1 mmol, 19.7 mg), iminodiphenyl-λ^6-sulfanone **2a** (0.15 mmol, 32.6 mg), $Cu(OAc)_2$ (0.02 mmol, 3.6 mg) and Ag_2CO_3 (0.1 mmol, 27.6 mg) in *m*-xylene (1 mL), D_2O (1 mmol, 0.2 mL) was added. The reaction mixture was stirred at 140 ^{o}C in a preheated oil bath under air for 10 h under air. The reaction mixture was cooled to room temperature, diluted with EtOAc (10 mL), and passed through a short pad of celite using EtOAc (2 x 10 mL). The reaction mixture was concentrated under reduced pressure and the ^{1}H NMR analysis showed no deuterium incorporation at C7 and 26% **3a** formation (using 1,2-dibromoethane as an internal standard).

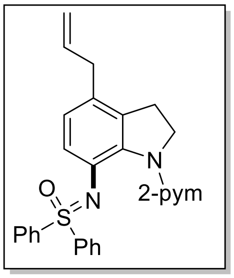
Preparation of 1-(Pyrimidin-2-yl)indoline-7-*d* (1a-*d*).[18] The titled compound was prepared according to the reported procedure as a pale yellow liquid. The deuterium incorporation was determined using 500 MHz ^{1}H NMR as 92%.

Kinetic Isotope Effect Experiment. A mixture of 1-(pyrimidin-2-yl)indoline **1a** (0.1 mmol, 19.7 mg) and 1-(pyrimidin-2-yl)indoline-7-*d* **1a-*d*** (0.1 mmol, 19.8 mg) was reacted with diphenyl sulfoximine **2a** (0.15 mmol, 32.6 mg) for 2 hrs under standard reaction conditions. The resulting mixture was diluted with EtOAc (10 mL) and passed through a short pad of celite using EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and EtOAc as an eluent to afford **3a** in 14% yield and a mixture of unreacted **1a** and **1a-*d*** as a colorless liquid. The intermolecular k_H/k_D was found to be 1.219 based on 500 MHz ^{1}H NMR of the recovered substrates **1a** and **1a-*d***.

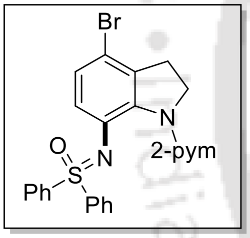
2.4 Characterization Data of Products



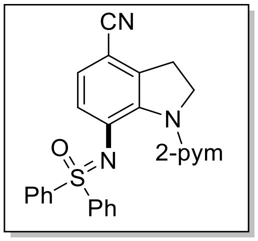
Diphenyl((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3a. Colorless solid; mp 146-147 °C; yield 67% (55.2 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 5.0 Hz, 2H), 7.91 (d, *J* = 7.5 Hz, 4H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 4H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.83-6.77 (m, 2H), 6.75 (t, *J* = 5.0 Hz, 1H), 4.42 (t, *J* = 8.0 Hz, 2H), 3.1 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 157.6, 141.3, 138.1, 135.9, 135.0, 132.5, 129.2, 128.6, 124.6 122.4, 118.1, 112.1, 54.2, 30.5; FT-IR (neat) 2924, 2851, 1577, 1549, 1473, 1463, 1428, 1291, 1258, 1214, 1093, 1062 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{21}N_4OS^+$: 413.1431, found: 413.1436.



((4-Allyl-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3b. Colorless solid; mp 141-142 °C; yield 57% (51.5 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.53 (d, *J* = 4.8 Hz, 2H), 7.90 (d, *J* = 7.2 Hz, 4H), 7.43 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 4H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.75 (t, *J* = 4.8 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 5.90-5.83 (m, 1H), 5.00-4.95 (m, 2H), 4.42 (t, *J* = 7.8 Hz, 2H), 3.23 (d, *J* = 6.0 Hz, 2H), 3.00 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.7, 157.6, 141.4, 137.8, 136.8, 132.9, 134.5, 129.2, 129.1, 128.6, 125.1, 122.61, 122.56, 115.5, 112.0, 54.1, 37.4, 28.9; FT-IR (neat) 2924, 2854, 1574, 1549, 1493, 1457, 1412, 1324, 1292, 1216, 1113, 1093 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{27}H_{25}N_4OS^+$: 453.1744, found: 453.1748.

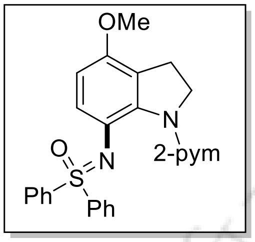


((4-Bromo-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3c. Brown solid; mp 174-175 °C; yield 61% (59.8 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.54 (d, *J* = 4.8 Hz, 2H), 7.86 (d, *J* = 7.2 Hz, 4H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.8 Hz, 4H), 6.90-6.86 (m, 2H), 6.79 (t, *J* = 4.8 Hz, 1H), 4.43 (t, *J* = 7.8 Hz, 2H), 3.09 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.6, 157.6, 141.0, 139.2, 136.0, 134.1, 132.8, 129.3, 128.5, 127.1, 124.0, 112.6, 111.4, 53.5, 31.9; FT-IR (neat) 2924, 2853, 1579, 1552, 1453, 1325, 1293, 1216, 1093 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{24}H_{20}BrN_4OS^+$: 491.0536, found: 491.0538.

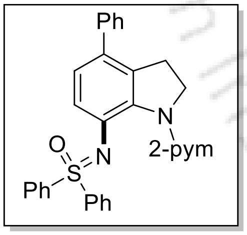


7-((Oxodiphenyl-λ^6-sulfaneylidene)amino)-1-(pyrimidin-2-yl)indoline-4-carbonitrile 3d. Colorless solid; mp 212-214 °C; yield 65% (56.8 mg); ^{1}H NMR (400 MHz,

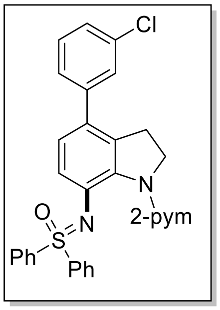
$CDCl_3$) δ 8.54 (d, *J* = 4.8 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 4H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.380 (t, *J* = 7.6 Hz, 4H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 1H), 6.82 (t, *J* = 4.8 Hz, 1H), 4.50 (t, *J* = 8.0 Hz, 2H), 3.26 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.1, 157.6, 140.5, 140.4, 139.8, 133.1, 129.5, 128.3, 128.0, 122.5, 112.9, 54.0, 30.1; FT-IR (neat) 2954, 2924, 2856, 2216, 1594, 1583, 1552, 1490, 1454, 1412, 1329, 1294, 1224, 1096 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{20}N_5OS^+$: 438.1383, found: 438.1392.



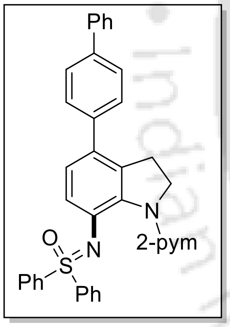
((4-Methoxy-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3e. Colorless solid; mp 167-168 ^{o}C; yield 56% (49.5 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.5 Hz, 2H), 7.86 (d, *J* = 8.5 Hz, 4H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 4H), 6.98 (d, *J* = 8.5 Hz, 1H), 6.76 (t, *J* = 5.0 Hz, 1H), 6.39 (d, *J* = 8.5 Hz, 1H), 4.40 (t, *J* = 7.5 Hz, 2H), 3.73 (s, 3H), 3.01 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 141.5, 132.4, 129.1, 128.7, 123.3, 112.3, 107.2, 55.7, 54.5, 27.3.; FT-IR (neat) 2999, 2958, 2851, 1574, 1549, 1495, 1460, 1445, 1417, 1320, 1264, 1219, 1096 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{23}N_4O_2S^+$: 443.1536, found: 443.1542.



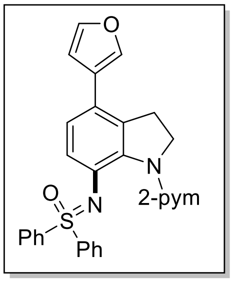
Diphenyl((4-phenyl-1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3f. Colorless solid; mp 195-196 ^{o}C; yield 60% (58.6 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.8 Hz, 2H), 7.93 (d, *J* = 7.8 Hz, 4H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.38-7.34 (m, 7H), 7.28 (d, *J* = 9.6 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 4.8 Hz, 1H), 4.42 (t, *J* = 7.8 Hz, 2H), 3.16 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.7, 141.4, 132.6, 129.3, 128.6, 128.4, 128.4, 126.7, 125.3, 122.7, 112.1, 54.4, 30.6; FT-IR (neat) 2919, 2848, 1579, 1548, 1478, 1459, 1406, 1325, 1294, 1219, 1111 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{30}H_{25}N_4OS^+$: 489.1744, found: 489.1750.



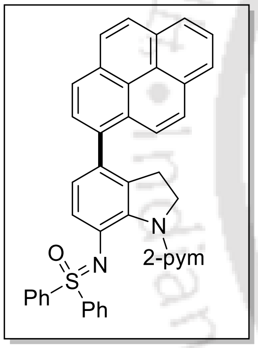
((4-(3-chlorophenyl)-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^{6}-sulfanone 3g. Brown liquid; yield 57% (59.5 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.56 (d, *J* = 5.0 Hz, 2H), 7.92 (d, *J* = 7.5 Hz, 4H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.38-7.35 (m, 4H), 7.28 (t, *J* = 7.5 Hz, 1H) 7.26-7.23 (m, 2H), 7.05 (d, J = 8.5 Hz, 1H), 6.87 (d, J = 8.5 Hz, 1H), 6.78 (t, J = 5.0 Hz, 1H), 4.43 (t, J = 7.5 Hz, 2H), 3.14 (t, J = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.7, 157.7, 142.5, 141.1, 138.4, 135.0, 134.2, 133.7, 132.7, 130.5, 129.6, 129.3, 128.5, 128.4, 126.7, 126.5, 125.1, 122.7, 112.2, 54.4, 30.5; FT-IR (neat) 2923, 2854, 1580, 1548, 1501, 1466, 1325, 1291, 1219, 1110, 1093 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{30}H_{24}ClN_4OS^+$: 523.1354, found: 523.1344.



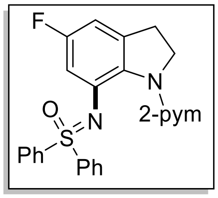
((4-([1, 1'-Biphenyl]-4-yl)-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphen-yl-λ^{6}-sulfanone 3h. Colorless solid; mp 178-179 °C; yield 55% (62 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.56 (d, *J* = 5.0 Hz, 2H), 7.94 (d, *J* = 7.5 Hz, 4H), 7.61 (t, *J* = 7.5 Hz, 4H), 7.45 (t, *J* = 7.5 Hz, 6H), 7.37 (t, *J* = 8.0 Hz, 5H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 1H), 6.78 (t, *J* = 5.0 Hz, 1H), 4.44 (t, *J* = 7.5 Hz, 2H), 3.21 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.8, 157.7, 141.4, 141.0, 139.7, 139.4, 138.4, 134.6, 133.7, 132.6, 131.5, 129.3, 128.9, 128.8, 128.6, 127.3, 127.2, 127.1, 125.2, 122.7, 112.1, 54.4, 30.7; FT-IR (neat) 2923, 2851, 1581, 1548, 1478, 1463, 1414, 1325, 1291, 1218, 1109, 1093 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{36}H_{29}N_4OS^+$: 565.2057, found: 565.2054.



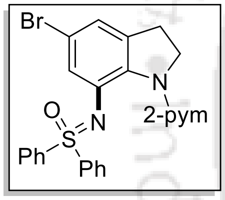
((4-(Furan-3-yl)-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3i. Colorless solid; mp 165-166 °C; yield 61% (58.3 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.55 (d, *J* = 4.8 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 4H), 7.51 (s, 1H), 7.44 (t, *J* = 7.8 Hz, 3H), 7.35 (t, *J* = 7.8 Hz, 4H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.78 (t, *J* = 4.8 Hz, 1H), 6.59 (s, 1H), 4.46 (t, *J* = 7.8 Hz, 2H), 3.17 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 168.8, 157.6, 143.0, 141.3, 139.1, 138.5, 134.1, 133.0, 132.6, 129.3, 128.6, 125.1, 123.6, 122.8, 122.7, 112.2, 110.0, 54.0, 30.9; FT-IR (neat) 2923, 2853, 1730, 1580, 1461, 1215, 1093 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{23}N_4O_2S^+$: 479.1536, found: 479.1541.



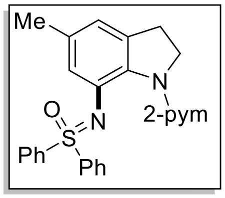
Diphenyl((4-(pyren-1-yl)-1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3j. Brown solid; mp 184-185 °C; yield 59% (72.2 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.59 (d, *J* = 4.5 Hz, 2H), 8.18-8.14 (m, 3H), 8.07 (s, 2H), 8.03 (d, *J* = 7.5 Hz, 2H), 8.00-7.92 (m, 5H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.44-7.40 (m, 4H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 5.0 Hz, 1H), 4.45-4.36 (m, 2H), 2.88-2.76 (m, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.6, 157.7, 141.5, 141.3, 137.9, 136.3, 135.6, 134.3, 132.7, 132.6, 131.5, 131.14, 131.05, 129.4, 129.3, 128.8, 128.7, 128.5, 127.6, 127.5, 127.4, 127.3, 127.0, 126.1, 126.0, 125.1, 125.01 124.96, 124.9, 124.6, 122.5, 112.1, 54.2, 30.1; FT-IR (neat) 2924, 2854, 1601, 1579, 1549, 1454, 1406, 1322, 1293, 1217, 1107, 1093, 1023 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{40}H_{29}N_4OS^+$: 613.2057, found: 613.2062.



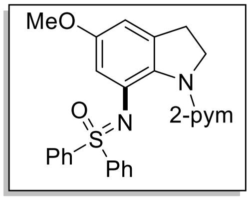
((5-Fluoro-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^{6-}sulfanone 3k. Colorless solid; mp 224-225 °C; yield 59% (50.7 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.2 Hz, 2H), 7.91 (d, *J* = 7.2 Hz, 4H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.36 (t, *J* = 7.8 Hz, 4H), 6.76 (t, *J* = 4.8 Hz, 1H), 6.71 (d, *J* = 13.2 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 4.44 (t, *J* = 7.8 Hz, 2H), 3.04 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 160.0 (d, $J_{C\text{-}F}$ = 241.7 Hz), 157.6, 141.0, 136.9 (d, $J_{C\text{-}F}$ = 10.4 Hz), 135.9 (d, $J_{C\text{-}F}$ = 10.5 Hz), 134.5 (d, $J_{C\text{-}F}$ = 2.3 Hz), 132.8, 129.3, 128.5, 112.1, 108.9 (d, $J_{C\text{-}F}$ = 24.8 Hz), 105.3 (d, *J* = 24.2 Hz), 54.5, 30.8 (d, $J_{C\text{-}F}$ = 2.3 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -118.7; FT-IR (neat) 2923, 2854, 1606, 1578, 1549, 1475, 1448, 1419, 1377, 1341, 1304, 1218, 1142 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}FN_4OS^+$: 431.1336, found: 431.1343.



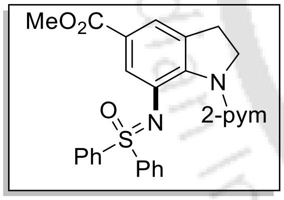
((5-Bromo-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3l. Brown solid; mp 215-216 °C; yield 62% (60.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$ δ 8.52 (d, *J* = 5.0 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 4H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.36 (t, *J* = 8.0 Hz, 4H), 7.11 (s, 1H), 6.94 (s, 1H), 6.77 (t, *J* = 5.0 Hz, 1H), 4.40 (t, *J* = 8.0 Hz, 2H), 3.05 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 157.6, 141.0, 137.7, 137.5, 136.1, 132.8, 129.3, 128.5, 124.8, 121.2, 116.6, 112.4, 53.3, 30.3; FT-IR (neat) 2922, 2854, 1708, 1597, 1549, 1474, 1445, 1409, 1322, 1294, 1220, 1115, 1093, 1070 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}BrN_4OS^+$: 491.0536, found: 491.0560.



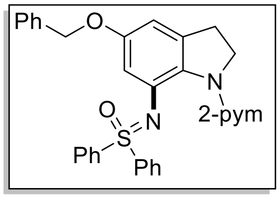
((5-Methyl-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3m. Colorless solid; mp 232-233 °C; yield 63% (53.7 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.8 Hz, 2H), 7.94 (d, *J* = 7.8 Hz, 4H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 4H), 6.81(s, 1H), 6.76 (t, *J* = 4.8 Hz, 1H), 6.67 (s, 1H), 4.43 (t, *J* = 7.8 Hz, 2H), 3.05 (t, *J* = 7.8 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.9, 157.6, 141.5, 135.9, 135.8, 134.7, 134.5, 132.5, 129.2, 128.6, 122.9, 119.1, 111.9, 54.3, 30.5, 21.3; FT-IR (neat) 2923, 2854, 1643, 1580, 1548, 1466, 1448, 1286, 1249, 1218, 1095 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{23}N_4OS^+$: 427.1587, found: 427.1593.



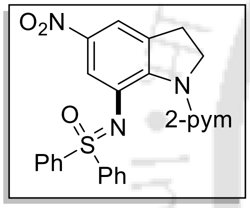
((5-methoxy-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3n. Colorless solid; mp 186-187 °C; yield 56% (49.5 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 5.0 Hz, 2H), 7.93(d, *J* = 7.5 Hz, 4H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 4H), 6.72 (t, *J* = 5.0 Hz, 1H), 6.57 (d, *J* = 2.0 Hz, 1H), 6.43 (d, *J* = 2.0 Hz, 1H), 4.41 (t, *J* = 7.5 Hz, 2H), 3.63 (s, 3H), 3.02 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.0, 157.6, 157.2, 141.2, 136.8, 135.6, 132.6, 132.0, 129.2, 128.6, 111.7, 107.8, 104.7, 55.7, 54.4, 30.9; FT-IR (neat) 2925, 1596, 1579, 1548, 1479, 1451, 1425, 1339, 1192, 1163 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{23}N_4O_2S^+$: 443.1536, found: 443.1537.



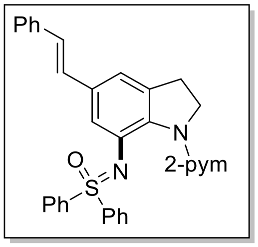
Methyl 7-((oxodiphenyl-λ^6-sulfaneylidene)amino)-1-(pyrimidin-2-yl) indoline-5-carboxylate 3o. Brown solid; mp 194-195 °C; yield 67% (62.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 5.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 4H), 7.69 (s, 1H), 7.50 (s, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.34 (t, *J* = 8.0 Hz, 4H), 6.80 (t, *J* = 5.0 Hz, 1H), 4.41 (t, *J* = 8.0 Hz, 2H), 3.79 (s, 3H), 3.11 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.2, 161.2, 157.6, 142.5, 141.0, 135.6, 134.1, 132.7, 129.2, 128.5, 126.0, 124.4, 119.8, 112.9, 54.3, 52.0, 29.9; FT-IR (neat) 2958, 2923, 2848, 1709, 1575, 1552, 1433, 1414, 1255, 1223, 1120, 1092, 1022 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{23}N_4O_3S^+$: 471.1485, found: 471.1489.



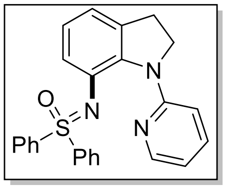
((5-(Benzyloxy)-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3p. Colorless solid; mp 201-202 °C; yield 64% (66.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, *J* = 5.0 Hz, 2H), 7.91(d, *J* = 8.0 Hz, 4H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.36-7.33 (m, 8H), 7.29-7.27 (m, 1H), 6.72(t, *J* = 5.0 Hz, 1H), 6.68 (d, *J* = 2.5 Hz, 1H), 6.50 (d, *J* = 2.0 Hz, 1H), 4.88 (s, 2H), 4.41 (t, *J* = 7.5 Hz, 2H), 3.02 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 157.6, 156.4, 141.3, 137.5, 136.7, 135.6, 132.6, 132.2, 129.2, 128.6, 128.5, 127.8, 127.6, 111.7, 108.8, 105.9, 70.5, 54.3, 30.9; FT-IR (neat) 3060, 3030, 2926, 2890, 1593, 1579, 1548, 1478, 1454, 1423, 1377, 1338, 1299, 1220, 1163, 1110, 1092 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{31}H_{27}N_4O_2S^+$: 519.1849, found: 519.1850.



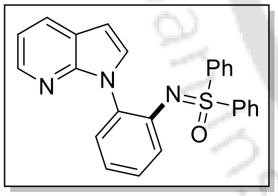
((5-Nitro-1-(pyrimidin-2-yl)indolin-7-yl)imino)diphenyl-λ^6-sulfanone 3q. Yellow solid; mp 218-219 °C; yield 59% (53.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.5 Hz, 2H), 7.87 (d, *J* = 2.0 Hz, 1H), 7.82-7.81 (m, 4H), 7.70-7.69 (m, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 8.0 Hz, 4H), 6.86 (t, *J* = 5.0 Hz, 1H), 4.47 (t, *J* = 8.0 Hz, 2H), 3.17 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.9, 157.6, 144.3, 144.1, 140.4, 135.9, 134.1, 133.1, 129.4, 128.4, 118.2, 114.0, 113.6, 54.5, 29.7; FT-IR (neat) 2924, 2854, 1571, 1557, 1512, 1470, 1442, 1417, 1321, 1219, 1123, 1090, 1068 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}N_5O_3S^+$: 458.1281, found: 458.1283.



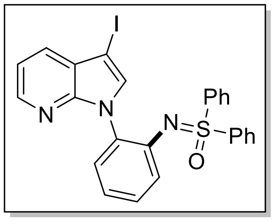
(*E*)-Diphenyl((1-(pyrimidin-2-yl)-5-styrylindolin-7-yl)imino)-λ^6-sulfanone 3r. Colorless solid; mp 244-245 °C; yield 61% (62.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 5.0 Hz, 2H), 7.91 (d, *J* = 7.5 Hz, 4H), 7.45-7.42 (m, 4H), 7.36 (t, *J* = 8.0 Hz, 4H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.11 (s, 1H), 7.06 (s, 1H), 6.95 (d, *J* = 16.5 Hz, 1H), 6.85 (d, *J* = 16.5 Hz, 1H), 6.77 (t, *J* = 5.0 Hz, 1H), 4.43(t, *J* = 8.0 Hz, 2H), 3.10 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 157.6, 141.3, 138.0, 137.9, 136.3, 134.8, 134.2, 132.6, 129.3, 129.1, 128.7, 128.6, 127.2, 126.9, 126.4, 121.7, 116.0, 112.2, 54.2, 30.3; FT-IR (neat) 2922, 2851, 1577, 1549, 1473, 1448, 1417, 1347, 1220, 1160, 1108 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{32}H_{27}N_4OS^+$: 515.1900, found: 515.1900.



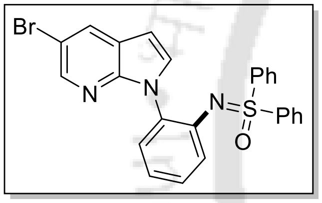
Diphenyl((1-(pyridin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone D'. Colorless solid; mp 130-132 °C; yield 59% (48.5 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40-8.38 (m, 1H), 7.66-7.65 (m, 4H), 7.49-7.46 (m, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.28 (t, *J* = 8.4 Hz, 4H), 7.05 (t, *J* = 8.4 Hz, 2H), 6.84-6.81 (m, 2H), 6.73 (t, *J* = 7.8 Hz, 1H), 4.39 (t, *J* = 8.4 Hz, 2H), 3.06 (t, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.5, 147.3, 140.9, 139.3, 136.2, 135.6, 132.8, 132.6, 129.1, 128.6, 123.2, 123.1, 119.1, 115.1, 114.6, 54.4, 30.1; FT-IR (neat) 3060, 2924, 2854, 1588, 1475, 1448, 1433, 1372, 1333, 1295, 1219, 1160, 1109, 1093 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{22}N_3OS^+$: 412.1478, found: 412.1483.



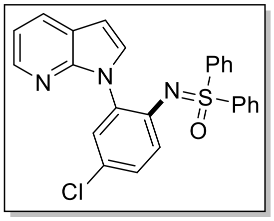
((2-(1*H*-Pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5a. Brown solid; mp 137-138 °C; yield 73% (59.7 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 (d, *J* = 4.8 Hz, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 3.6 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 4H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.2 Hz, 1H), 7.33 (t, *J* = 7.8 Hz, 4H), 7.26-7.24 (m, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.80 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 143.3, 141.6, 140.6, 132.6, 132.3, 131.3, 129.2, 128.9, 128.8, 128.7, 128.6, 123.8, 122.3, 121.0, 116.2, 99.9; FT-IR (neat) 3061, 1593, 1512, 1493, 1447, 1423, 1357, 1319, 1291, 1229, 1204, 1090, 1014 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{20}N_3OS^+$: 410.1322, found: 410.1324.



((2-(3-Iodo-1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5b. Colorless solid; mp 141-142 °C; yield 53% (56.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.4 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.82 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 4H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.28 (t, *J* = 9.2 Hz, 5H), 7.24 (t, *J* = 4.4 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.4, 146.0, 144.6, 141.2, 140.5, 135.4, 132.8, 131.4, 129.39, 129.35, 129.2, 128.49, 128.46, 123.9, 123.4, 122.4, 117.2; FT-IR (neat) 3058, 2954, 2922, 2854, 1590, 1510, 1490, 1448, 1411, 1315, 1291, 1260, 1218, 1112, 1093, 1015 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}IN_3OS^+$: 536.0288, found: 536.0286.

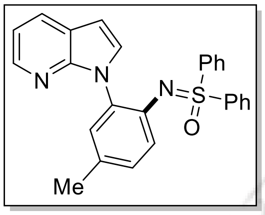


((2-(5-Bromo-1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl -λ^6-sulfanone 5c. Brown solid; mp 165-166 °C; yield 66% (64.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.4 Hz, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 7.64 (d, *J* = 3.6 Hz, 1H), 7.61 (d, *J* = 8.0 Hz, 4H), 7.50 (d, *J* = 7.6, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 9.6 Hz, 5H), 7.17 (t, *J* = 8.0 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.68 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.2, 143.8, 141.6, 140.6, 132.9, 132.8, 131.8, 130.9, 129.3, 129.2, 128.6, 128.5, 123.7, 122.6, 122.3, 112.1, 99.5; FT-IR (neat) 3064, 2920, 2854, 1594, 1511, 1492, 1448, 1402, 1314, 1296, 1227, 1207, 1113, 1091, 1015 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{19}BrN_3OS^+$: 488.0427, found: 488.0431.

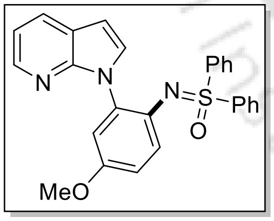


((4-Chloro-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5d. Brown solid; mp 182-183 °C; yield 71% (62.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ

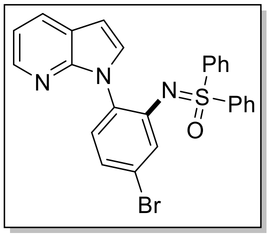
8.45 (d, *J* = 4.5 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.5 Hz, 5H), 7.57 (d, *J* = 2.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 8.0 Hz, 4H), 7.24 (t, *J* = 7.0 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 1H), 6.77 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 148.7, 143.5, 140.43, 140.36, 133.1, 132.9, 130.9, 129.3, 129.0, 128.91, 128.87, 128.5, 126.8, 124.4, 121.0, 116.5, 100.5; FT-IR (neat) 2920, 2851, 1585, 1512, 1491, 1437, 1316, 1294, 1214, 1087, 1015 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}ClN_3OS^+$: 444.0932, found: 444.0937.



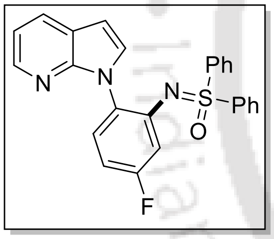
((4-Methyl-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5e. Brown solid; mp 188-189 °C; yield 63% (53.3 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.39 (d, *J* = 4.4 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 7.603 (d, *J* = 3.6 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 4H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.31 (d, *J* = 1.2 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 4H), 7.17 (t, *J* = 4.0 Hz, 1H), 7.15 (s, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 3.6 Hz, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 143.3, 140.8, 138.8, 132.6, 132.0, 131.9, 131.4, 129.7, 129.5, 129.3, 129.2, 128.9, 128.6, 123.6, 121.0, 116.1, 99.9, 20.9; FT-IR (neat) 3058, 2921, 2854, 1594, 1574, 1513, 1478, 1442, 1353, 1322, 1293, 1233, 1211, 1092, 1017 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{26}H_{22}N_3OS^+$: 424.1478, found: 424.1479.



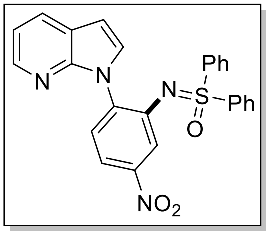
((4-Methoxy-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5f. Brown solid; mp 175-176 °C; yield 68% (59.7 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.39 (d, *J* = 4.8 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 3.6 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 4H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.23 (t, *J* = 7.2 Hz, 5H), 7.18-7.16 (m, 1H), 7.09 (d, *J* = 3.0 Hz, 1H), 6.74-6.72 (m, 1H), 6.71 (d, *J* = 3.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 154.9, 148.7, 143.4, 140.7, 134.3, 132.7, 132.6, 131.2, 129.2, 128.9, 128.6, 124.6, 120.9, 116.3, 114.5, 114.3, 100.0, 55.6; FT-IR (neat) 3060, 2928, 2834, 1615, 1590, 1575, 1512, 1498, 1447, 1413, 1356, 1311, 1280, 1234, 1206, 1180, 1149, 1096, 1043 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{26}H_{22}N_3O_2S^+$: 440.1427, found: 440.1432.



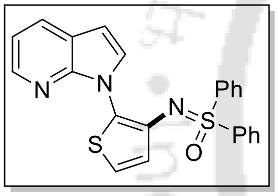
((5-Bromo-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5g. Colorless solid; mp 205-206 °C; yield 70% (68.2 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38 (d, *J* = 4.2 Hz, 1H), 8.09 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 3.6 Hz, 1H), 7.57 (d, *J* = 7.2 Hz, 4H), 7.44 (d, *J* = 1.8 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 8.4 Hz, 4H), 7.19-7.17 (m, 2H), 6.72 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.8, 143.5, 143.0, 140.2, 132.9, 131.0, 129.8, 129.34, 129.32, 129.0, 128.5, 126.4, 125.4, 122.1, 121.0, 116.4, 100.3; FT-IR (neat) 2923, 2854, 1585, 1513, 1489, 1426, 1400, 1358, 1322, 1283, 1213, 1092, 1016 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}BrN_3OS^+$: 488.0427, found: 488.0429.



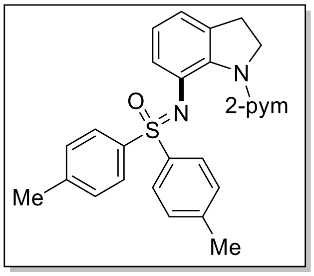
((5-Fluoro-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5h. Colorless solid; mp 158-159 °C; yield 68% (58.1 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.39 (d, *J* = 3.6 Hz, 1H), 8.09 (d, *J* = 7.2 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 3H), 7.55 (d, *J* = 3.6 Hz, 2H), 7.46-7.44 (m, 1H), 7.41 (t, *J* = 7.2 Hz, 2H), 7.27 (t, *J* = 8.4 Hz, 4H), 7.18-7.16 (m, 1H), 6.99-6.97 (m, 1H), 6.76-6.73 (m, 1H), 6.71 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 162.4 (d, J_{C-F} = 247.2 Hz), 149.0, 143.44, 143.42 (d, J_{C-F} = 10.0 Hz), 140.2, 132.9, 131.3, 129.6 (d, J_{C-F} = 10.4 Hz), 129.3, 128.9, 128.53, 128.50, 120.9, 116.3, 110.4 (d, J_{C-F} = 24.0 Hz), 108.9 (d, J_{C-F} = 22.9 Hz), 100.1; ^{19}F NMR (470 MHz, $CDCl_3$) δ -112.4; FT-IR (neat) 3062, 2924, 2854, 1607, 1514, 1498, 1425, 1358, 1328, 1296, 1230, 1209, 1175, 1110, 1020 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}FN_3OS^+$: 428.1227, found: 428.1229.



((5-Nitro-2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)phenyl)imino)diphenyl-λ^6-sulfanone 5i. Yellow solid; mp 184-185 °C; yield 61% (55.4 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.38 (d, *J* = 4.2 Hz, 1H), 8.12 (d, *J* = 1.8 Hz, 1H), 8.10 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 4.2 Hz, 1H), 7.72 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 4H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 7.8 Hz, 4H), 7.23-7.21 (m, 1H), 6.76 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 148.6, 147.2, 143.7, 142.2, 139.8, 137.7, 133.3, 130.5, 129.5, 129.2, 128.8, 128.4, 121.2, 118.3, 117.2, 117.0, 101.1; FT-IR (neat) 2932, 2853, 1576, 1519, 1496, 1424, 1342, 1325, 1279, 1230, 1211, 1105, 1034 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{19}N_4O_3S^+$: 455.1172, found: 455.1175.

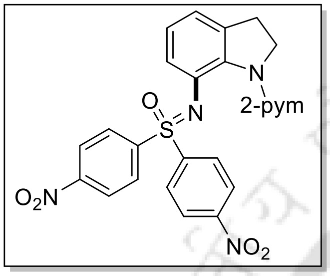


((2-(1*H*-pyrrolo[2,3-*b*]pyridin-1-yl)thiophen-3-yl)imino)diphenyl-λ^6-sulfanone 5j. Brown solid; mp 145-146 °C; yield 59% (48.9 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.40 (d, *J* = 5.5 Hz, 1H), 8.01 (d, *J* = 9.0 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 4H), 7.74 (d, *J* = 4.0 Hz, 1H), 7.41 (t, *J* = 7.0 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 5H), 7.17-7.15 (m, 1H), 7.01(d, *J* = 5.4 Hz, 1H), 6.90 (d, *J* = 6.0 Hz, 1H), 6.670 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 149.0, 143.6, 140.7, 136.1, 132.8, 131.2, 129.3, 128.9, 128.5, 124.9, 124.2, 123.6, 120.9, 116.7, 101.2; FT-IR (neat) 3061, 2924, 2856, 1590, 1561, 1508, 1475, 1447, 1387, 1355, 1311, 1272, 1213, 1142, 1119, 1091, 1066 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{23}H_{18}N_3OS_2^+$: 416.0886, found: 416.0889.

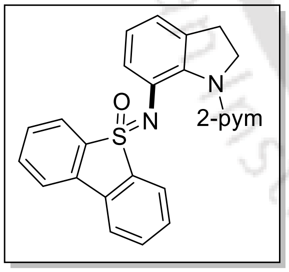


((1-(Pyrimidin-2-yl)indolin-7-yl)imino)di-*p*-tolyl-λ^6-sulfanone 3t. Colorless solid; mp 167-168 °C; yield 63% (55.4 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.52 (d, *J* =

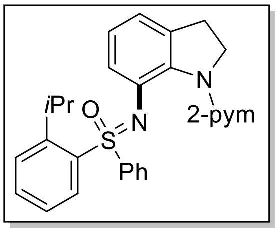
4.5 Hz, 2H), 7.76 (d, *J* = 8.5 Hz, 4H), 7.13 (d, *J* = 8.0 Hz, 4H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 7.0 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 6.75 (t, *J* = 5.0 Hz, 1H), 4.42 (t, *J* = 7.5 Hz, 2H), 3.07 (t, *J* = 8.0 Hz, 2H), 2.31 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.7, 157.6, 143.2, 138.7, 138.0, 135.8, 135.3, 129.9, 128.5, 124.5, 122.4, 117.9, 112.0, 54.2, 30.5, 21.6; FT-IR (neat) 2923, 2851, 1592, 1576, 1549, 1477, 1460, 1430, 1293, 1217, 1179, 1110, 1068 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{25}N_4OS^+$: 441.1744, found: 441.1742.



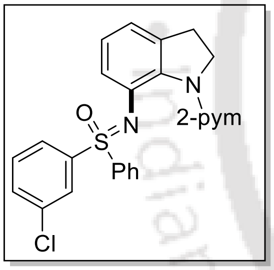
Bis(4-nitrophenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3u. Red solid; mp 134-135 °C; yield 52% (52.2 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.8 Hz, 2H), 8.22 (d, *J* = 9.0 Hz, 4H), 8.14 (d, *J* = 9.0 Hz, 4H), 6.92-6.91 (m, 2H), 6.85 (d, *J* = 4.8 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 4.45 (t, *J* = 7.8 Hz, 2H), 3.10 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.7, 157.8, 150.6, 146.0, 138.3, 136.6, 133.1, 130.4, 125.0, 124.7, 122.4, 119.6, 112.5, 54.4, 30.4; FT-IR (neat) 3020, 1576, 1531, 1476, 1462, 1429, 1260, 1214, 1088, 1009 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}N_6O_5S^+$: 503.1132, found: 503.1136.



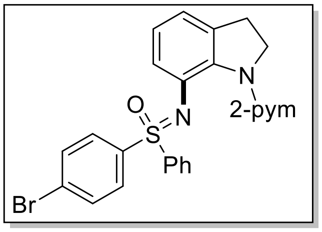
5-((1-(Pyrimidin-2-yl)indolin-7-yl)imino)-5*H*-5λ^4-dibenzo[*b,d*]thiophene 5-oxide 3v. Colorless solid; mp 187-188 °C; yield 58% (47.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 4.8 Hz, 2H), 7.74-7.68 (m, 4H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 3H), 6.97 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 6.8 Hz, 1H), 6.28 (t, *J* = 4.8 Hz, 1H), 4.11 (t, *J* = 8.0 Hz, 2H), 2.99 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 160.2, 156.4, 139.3, 138.5, 135.9, 133.2, 132.7, 131.5, 130.1, 124.1, 122.6, 121.2, 119.6, 111.6, 53.2, 29.9; FT-IR (neat) 2923, 2851, 1575, 1549, 1474, 1462, 1428, 1290, 1217, 1128, 1093 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}N_4OS^+$: 411.1274, found: 411.1279.



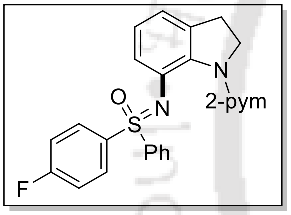
(2-Isopropylphenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3w. Brown solid; mp 145-146 °C; yield 58% (52.6 mg); ^{1}H NMR (500 MHz, $CDCl_3$ δ 8.50 (d, *J* = 5.0 Hz, 2H), 8.32 (d, *J* = 7.0 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 2H), 7.46-7.40 (m, 2H), 7.31 (t, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 8.5 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.79 (d, *J* = 6.0 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.71 (t, *J* = 5.0 Hz, 1H), 4.37-4.27 (m, 2H), 3.82-3.77 (m, 1H), 3.10-2.98 (m, 2H), 0.80 (d, *J* = 6.5 Hz, 3H), 0.73 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.5, 157.5, 149.5, 142.2, 138.0, 137.8, 135.6, 134.9, 133.2, 132.3, 130.7, 128.8, 128.3, 128.2, 126.0, 124.3, 121.9, 118.0, 112.0, 54.0, 30.4, 28.4, 23.9, 23.5; FT-IR (neat) 2922, 2851, 1589, 1575, 1541, 1469, 1451, 1428, 1295, 1218, 1108, 1065 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{27}H_{27}N_4OS^+$: 455.1900, found: 455.1902.



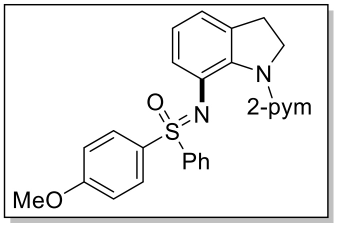
(3-Chlorophenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3x. Colorless solid; mp 194-195 °C; yield 62% (55.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$ δ 8.54 (d, *J* = 4.5 Hz, 2H), 7.92 (s, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.40-7.35 (m, 3H), 7.30 (t, *J* = 8.0 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.81 (d, *J* = 7.5 Hz, 1H), 6.77 (t, *J* = 5.0 Hz, 1H), 4.43 (t, *J* = 9.5 Hz, 2H), 3.08 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 157.6, 143.3, 140.8, 138.3, 136.1, 135.3, 134.6, 132.9, 132.8, 130.4, 129.4, 128.8, 128.7, 126.8, 124.6, 122.5, 118.4, 112.4, 54.3, 30.5; FT-IR (neat) 2921, 2851, 1577, 1550, 1476, 1460, 1431, 1322, 1310, 1221, 1165, 1108 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}ClN_4OS^+$: 447.1047, found: 447.1047.



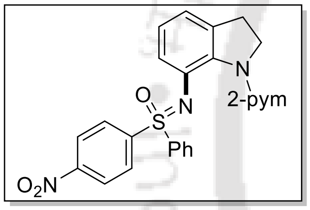
(4-Bromophenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3y. Colorless solid; mp 168-169 °C; yield 65% (63.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 5.0 Hz, 2H), 7.86 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 7.0 Hz, 1H), 7.35 (t, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 5.0 Hz, 1H), 4.42 (t, *J* = 8.0 Hz, 2H), 3.08 (t, *J* = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 157.6, 141.0, 140.6, 138.2, 136.0, 134.7, 132.8, 132.5, 130.3, 129.3, 128.6, 127.9, 124.6, 122.5, 118.4, 112.1, 54.3, 30.5; FT-IR (neat) 3024, 2924, 2848, 1576, 1551, 1478, 1462, 1428, 1294, 1214 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}BrN_4OS^+$: 491.0536, found: 491.0543.



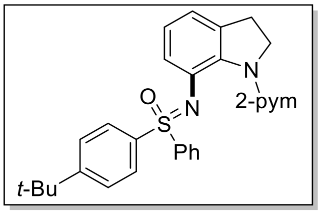
(4-Fluorophenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3z. Colorless solid; mp 210-211 °C; yield 64% (55 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (d, *J* = 4.5 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 2H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.44 (t, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 8.5 Hz, 2H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.0 Hz, 1H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 5.0 Hz, 1H), 4.42 (t, *J* = 8.0 Hz, 2H), 3.08 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 165.2 (d, $J_{C\text{-}F}$ = 254.9 Hz), 161.8, 157.6, 141.2, 138.1, 137.2 (d, $J_{C\text{-}F}$ = 2.9 Hz), 136.0, 134.8, 132.7, 131.4 (d, $J_{C\text{-}F}$ = 9.4 Hz), 129.3, 128.5, 124.6, 122.4, 118.3, 116.5 (d, $J_{C\text{-}F}$ = 22.3 Hz), 112.1, 54.3, 30.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -105.9; FT-IR (neat) 2924, 2852, 1587, 1577, 1549, 1477, 1460, 1429, 1322, 1295, 1221, 1158, 1112, 1093 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{20}FN_4OS^+$: 431.1336, found: 431.1341.



(4-Methoxyphenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3aa. Colorless solid; mp 165-166 °C; yield 54% (47.7 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.53 (d, *J* = 4.8 Hz, 2H), 7.85 (t, *J* = 9.0 Hz, 4H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.801 (d, *J* = 7.8 Hz, 3H), 6.77 (t, *J* = 7.8 Hz, 1H), 6.75 (t, *J* = 4.8 Hz, 1H), 4.42 (t, *J* = 7.8 Hz, 2H), 3.78 (s, 3H), 3.07 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 163.0, 161.8, 157.6, 142.0, 138.0, 135.9, 135.2, 132.5, 132.3, 130.8, 129.1, 128.3, 124.6, 122.4, 118.0, 114.5, 112.0, 55.7, 54.2, 30.5; FT-IR (neat) 3024, 2923, 2851, 1591, 1576, 1550, 1477, 1459, 1428, 1294, 1259, 1214, 1110, 1026 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{25}H_{23}N_4O_2S^+$: 443.1536, found: 443.1540.

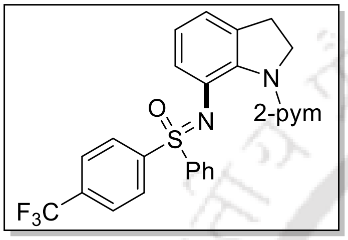


(4-Nitrophenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ab. Red solid; mp 182-183 °C; yield 56% (51.2 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.54 (d, *J* = 4.8 Hz, 2H), 8.18 (d, *J* = 8.4 Hz, 2H), 8.13 (d, *J* = 8.4 Hz, 2H), 7.90 (d, *J* = 7.8 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 5.4 Hz, 1H), 4.43 (t, *J* = 7.8 Hz, 2H), 3.09 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.8, 157.7, 150.1, 147.5, 139.9, 138.2, 136.2, 134.0, 133.4, 130.0, 129.6, 128.9, 124.8, 124.4, 122.4, 118.9, 112.3, 54.3, 30.5; FT-IR (neat) 2922, 2851, 1576, 1551, 1529, 1476, 1461, 1431, 1345, 1221, 1113 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{24}H_{20}N_5O_3S^+$: 458.1281, found: 458.1285.

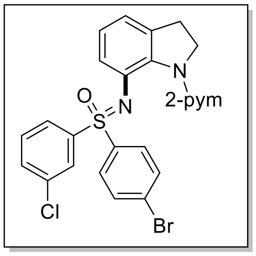


(4-(*tert*-Butyl)phenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ac. Brown liquid; yield 61% (57.1 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.54

(d, *J* = 4.5 Hz, 2H), 7.91 (d, *J* = 7.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* = 7.5 Hz, 3H), 7.33 (d, *J* = 9.5 Hz, 1H), 6.97 (d, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 7.0 Hz, 1H), 6.80 (d, *J* = 7.5 Hz, 1H), 6.76 (t, *J* = 5.0 Hz, 1H), 4.43 (t, *J* = 8.0 Hz, 2H), 3.07 (t, *J* = 7.5 Hz, 2H), 1.26 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.8, 157.6, 156.3, 141.7, 138.2, 138.0, 135.9, 135.3, 132.4, 129.2, 128.5, 128.4, 126.3, 124.6, 122.3, 117.9, 112.0, 54.2, 35.2, 31.2; FT-IR (neat) 2960, 2921, 2854, 1590, 1576, 1548, 1478, 1462, 1428, 1293, 1219, 1090 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{29}N_4OS^+$: 469.2057, found: 469.2060.

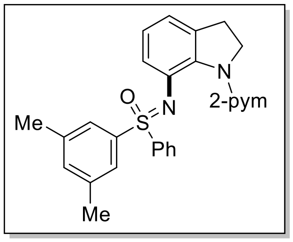


Phenyl((1-(pyrimidin-2-yl)indolin-7-yl)imino)(4-(trifluoromethyl) phenyl)-λ^6-sulfanone 3ad. Brown solid; mp 186-187 °C; yield 53% (50.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.5 Hz, 2H), 8.07 (d, *J* = 8.0 Hz, 2H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 7.0 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.78 (t, *J* = 4.5 Hz, 1H), 4.43 (t, *J* = 7.5 Hz, 2H), 3.08 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.8, 157.7, 145.2, 140.4, 138.2, 136.1, 134.6 (q, J_{C-F} = 32.6 Hz), 134.4, 133.1, 129.5, 129.2, 128.8, 126.4 (q, J_{C-F} = 3.8 Hz), 126.1 (q, J_{C-F} = 271.5 Hz), 124.7, 122.4, 118.6, 112.2, 54.3, 30.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -63.1; FT-IR (neat) 2922, 2851, 1577, 1550, 1478, 1459, 1431, 1322, 1294, 1222, 1172, 1133, 1109, 1062 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{20}F_3N_4OS^+$: 481.1304, found: 481.1304.

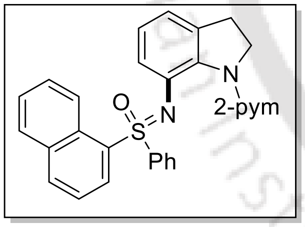


(4-Bromophenyl)(3-chlorophenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino) -λ^6-sulfanone 3ae. Brown liquid; yield 60% (60.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (d, *J* = 4.5 Hz, 2H), 7.88 (s, 1H), 7.78 (t, *J* = 8.5 Hz, 3H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.42 (d, *J* = 8.5 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.87(d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.79 (t, *J* = 5.0 Hz, 1H), 4.44 (t, *J* = 7.5 Hz, 2H), 3.08 (t, *J* = 7.5 Hz, 2H); ^{13}C NMR (150

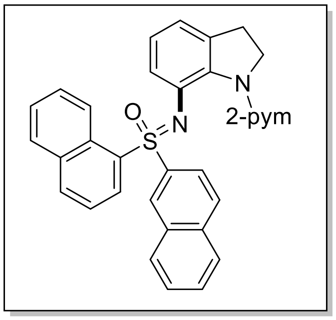
MHz, $CDCl_3$) δ 161.8, 157.6, 142.8, 139.8, 138.2, 136.2, 135.4, 134.2, 133.0, 132.7, 130.6, 130.4, 128.7, 128.3, 126.7, 124.7, 122.4, 118.7, 112.5, 54.3, 30.5; FT-IR (neat) 3019, 2922, 2851, 1575, 1549, 1476, 1461, 1430, 1383, 1305, 1215, 1111, 1067, 1008 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}BrClN_4OS^+$:525.0146, found: 525.0150.



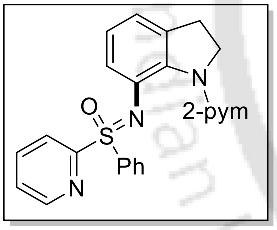
(3,5-Dimethylphenyl)(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino) -λ^6-sulfanone 3af. Colorless solid; mp 219-220 °C; yield 63% (55.4 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.5 Hz, 2H), 7.99 (d, *J* = 7.5 Hz, 2H), 7.44 (s, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.03 (s, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 6.0 Hz, 1H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.75 (t, *J* = 5.0 Hz, 1H), 4.49-4.36 (m, 1H) 3.13-3.01 (m, 1H), 2.22 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 157.5, 141.6, 141.2, 139.0, 138.1, 135.8, 135.3, 134.4, 132.4, 129.2, 128.8, 126.0, 124.6, 122.5, 118.0, 112.1, 54.2, 30.5, 21.4; FT-IR (neat) 2923, 2851, 1592, 1576, 1549, 1477, 1460, 1430, 1293, 1217, 1179, 1110, 1068 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{25}N_4OS^+$: 441.1744, found: 441.1747.



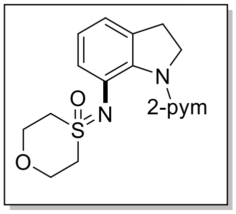
Naphthalen-1-yl(phenyl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ag. Brown solid; mp 198-199 °C; yield 62% (52.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 8.5 Hz, 1H), 8.69 (d, *J* = 6.5 Hz, 1H), 8.55 (d, *J* = 4.5 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 3H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 4.0 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 7.5 Hz, 1H), 6.77-6.72 (m, 3H), 4.39-4.35 (m, 1H), 4.31-4.25 (m, 1H), 3.08-3.02 (m, 1H), 3.00-2.94 (m, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 157.6, 141.6, 138.0, 135.8, 135.7, 134.9, 134.6, 134.5, 132.4, 131.5, 129.1, 128.90, 128.86, 128.09, 128.08, 128.0, 126.6, 124.7, 124.6, 124.4, 122.2, 118.2, 112.0, 54.0, 30.4; FT-IR (neat) 2924, 2848, 1587, 1575, 1549, 1477, 1462, 1429, 1319, 1294, 1217, 1107, 1070 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{23}N_4OS^+$: 463.1587, found: 463.1587.



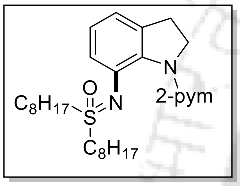
Naphthalen-1-yl(naphthalen-2-yl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ah. Brown solid; mp 178-179 °C; yield 59% (60.4 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, *J* = 8.0 Hz, 1H), 8.76 (d, *J* = 7.5 Hz, 1H), 8.61 (d, *J* = 4.5 Hz, 2H), 8.49 (s, 1H), 7.98 (d, *J* = 8.5 Hz, 1H), 7.79-7.74 (m, 3H), 7.72-7.67 (m, 2H), 7.55-7.49 (m, 3H), 7.46-7.40 (m, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.79 (t, *J* = 5.0 Hz, 1H), 6.78-6.72 (m, 2H), 4.40-4.27 (m, 2H), 3.08-2.95 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.6, 157.7, 138.5, 138.0, 135.8, 135.7, 135.0, 134.74, 134.66, 134.5, 132.2, 131.6, 129.6, 129.5, 129.14, 129.07, 128.9, 128.8, 128.1, 127.9, 127.3, 126.6, 124.7, 124.5, 123.3, 122.2, 118.2, 112.1, 54.0, 30.5; FT-IR (neat) 3058, 2922, 2851, 1590, 1576, 1549, 1501, 1477, 1462, 1431, 1322, 1298, 1089 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{32}H_{25}N_4OS^+$: 513.1744, found: 513.1749.



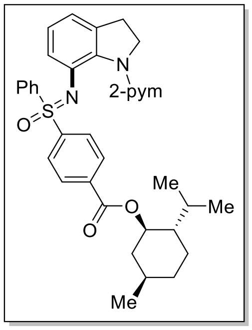
Phenyl(pyridin-2-yl)((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ai. Colorless solid; mp 199-200 °C; yield 57% (47.1 mg); ^{1}H NMR (500 MHz, $CDCl_3$ δ 8.59 (d, *J* = 4.5 Hz, 1H), 8.47 (d, *J* = 4.5 Hz, 2H), 8.09 (d, *J* = 7.5 Hz, 2H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.65-7.62 (m, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.33-7.30 (m, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.79 (t, *J* = 7.5 Hz, 1H), 6.69 (t, *J* = 5.0 Hz, 1H), 4.46-4.36 (m, 2H), 3.15-3.02 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.5, 158.6, 157.5, 150.4, 138.5, 137.8, 135.9, 134.5, 133.1, 129.9, 129.3, 126.3, 125.1, 124.6, 123.3, 122.3, 118.2, 111.9, 54.1, 30.5; FT-IR (neat) 3053, 2922, 2853, 1577, 1549, 1476, 1464, 1429, 1322, 1302, 1222, 1104, 1069 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{20}N_5OS^+$: 414.1383, found: 414.1376.



4-((1-(Pyrimidin-2-yl)indolin-7-yl)imino)-1,4λ^6-oxathiane 4-oxide 3aj. Colorless solid; mp 158-157 °C; yield 51% (33.6 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.49 (d, *J* = 4.2 Hz, 2H), 7.14-7.13 (m, 1H), 6.952 (t, *J* = 7.2 Hz, 2H), 6.71 (t, *J* = 4.8 Hz, 1H), 4.39 (t, *J* = 7.8 Hz, 2H), 4.02-3.99 (m, 2H), 3.88-3.84 (m, 2H), 3.27-3.17 (m, 4H), 3.08 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 161.4, 157.4, 138.1, 136.3, 134.5, 124.8, 122.9, 119.0, 112.3, 65.6, 54.2, 51.8, 30.3; FT-IR (neat) 2922, 2854, 1591, 1577, 1548, 1476, 1461, 1428, 1297, 1219, 1107, 1082 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{16}H_{19}N_4O_2S^+$: 331.1223, found: 331.1225.

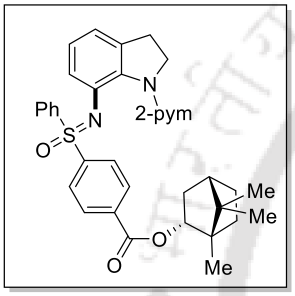


Dioctyl((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone 3ak. Brown liquid; yield 55% (53.2 mg); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.42 (d, *J* = 4.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 7.2 Hz, 1H), 6.65 (t, *J* = 4.8 Hz, 1H), 4.35 (t, *J* = 7.8 Hz, 2H), 3.09 (d, *J* = 6.0 Hz, 1H), 3.05 (t, *J* = 8.4 Hz, 3H), 2.98-2.93 (m, 2H), 1.65-1.57 (m, 4H), 1.28-1.25 (m, 10H), 1.22 (s, 11H), 0.88 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 161.6, 157.2, 137.9, 135.9, 135.8, 124.7, 122.4, 118.2, 112.0, 54.1, 52.1, 31.8, 30.4, 29.2, 29.1, 28.6, 23.5, 22.7, 14.2; FT-IR (neat) 2924, 2854, 1591, 1576, 1548, 1477, 1466, 1428, 1298, 1203, 1104 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{28}H_{45}N_4OS^+$: 485.3309, found: 485.3305.

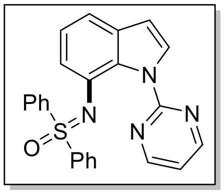


(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 4-(*N*-(1-(pyrimidin-2-yl)indolin-7-yl)phenylsulfonimidoyl)benzoate 3al. Yellow liquid; yield 61% (72.4 mg); ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.54 (d, *J* = 5.0 Hz, 2H), 8.01 (d, *J* = 13.0 Hz, 4H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.45

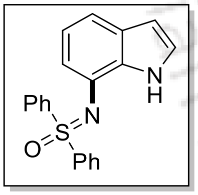
(t, *J* = 7.0 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.79 (t, *J* = 8.0 Hz, 2H), 4.92-4.87 (m, 1H), 4.43 (t, *J* = 7.5 Hz, 2H), 3.08 (t, *J* = 7.5 Hz, 2H), 2.05 (s, 1H), 1.86 (t, *J* = 3.0 Hz, 1H), 1.73 (d, *J* = 12.0 Hz, 2H), 1.51 (t, *J* = 12.0 Hz, 2H), 1.11-1.03 (m, 2H), 0.90-0.87 (m, 6H), 0.74 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.87, 164.86, 161.79, 161.77, 157.6, 145.3, 145.2, 140.75, 140.72, 138.2, 138.1, 136.1, 136.0, 134.64, 134.6, 134.4, 132.9, 130.41, 130.36, 129.3, 128.70, 128.69, 128.68, 128.67, 128.5 124.7, 124.6, 122.5, 122.3, 118.5, 118.4, 112.2, 106.6, 75.8, 54.3, 47.3, 41.0, 34.3, 31.6, 30.5, 26.59, 26.56, 23.7, 23.6, 22.1, 20.9, 16.6, 16.5; FT-IR (neat) 2958, 2869, 1756, 1714, 1578, 1549, 1475, 1434, 1278, 1214, 1107 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{35}H_{39}N_4O_3S^+$: 595.2737, found: 595.2744.



(1*S*,2*R*,4*S*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-yl 4-(*N*-(1-(pyrimidin-2-yl)indolin-7-yl)phenylsulfonimidoyl)benzoate 3am. Yellow liquid; yield 65% (76.9 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, *J* = 5.0 Hz, 2H), 8.02 (t, *J* = 9.5 Hz, 4H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.34 (t, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 7.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 4.5 Hz, 1H), 5.08-5.06 (m, 1H), 4.48-4.39 (m, 2H), 3.13-3.04 (m, 2H), 2.47-2.41 (m, 1H), 2.04-1.99 (m, 1H), 1.81-1.77 (m, 1H), 1.73 (d, *J* = 2.0 Hz, 1H), 1.43-1.36 (m, 1H), 1.32-1.28 (m, 2H), 1.08-1.02 (m, 1H), 0.94 (s, 3H), 0.90 (s, 3H), 0.87 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 161.8, 157.6, 145.4, 140.8, 138.2, 136.1, 134.6, 134.5, 132.9, 130.4, 129.3, 128.8, 128.7, 124.6, 122.4, 118.4, 112.2, 85.5, 54.3, 49.3, 48.1, 45.1, 37.0, 30.5, 28.2, 27.5, 19.8, 19.0, 13.72, 13.70; FT-IR (neat) 2956, 2886, 1719, 1577, 1549, 1476, 1462, 1429, 1394, 1280, 1222, 1110, 1016 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{35}H_{37}N_4O_3S^+$: 593.2581, found: 593.2584.

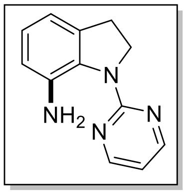


Diphenyl((1-(pyrimidin-2-yl)-1*H*-indol-7-yl)imino)-λ^6-sulfanone 6.[19] To a stirred solution of diphenyl((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone **3a** (0.2 mmol, 82.4 mg) in 1,4-dioxane (2 mL), DDQ (0.4 mmol, 90.8 mg) was added at room temperature and stirred at 90 °C for 3 h. After completion, as monitored by TLC, the reaction mixture was cooled to room temperature and diluted with EtOAc (2 × 10 mL). The reaction mixture was then washed with brine (2 × 5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent using a rotary evaporator gave a residue that was purified by silica gel column chromatography (*n*-hexane: EtOAc = 3:1) to give **6** as a brown solid in 68% yield (55.8 mg); mp 167-168 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.5 Hz, 2H), 7.70 (d, *J* = 7.0 Hz, 4H), 7.63 (d, *J* = 3.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 8.0 Hz, 4H), 7.21 (d, *J* = 8.0 Hz, 1H), 7.09 (t, *J* = 5.0 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.66 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 158.9, 158.1, 140.9, 132.6, 132.5, 132.4, 130.7, 129.8, 129.1, 128.3, 122.6, 117.5, 117.2, 114.7, 106.5; FT-IR (neat) 3058, 2924, 2856, 1566, 1479, 1433, 1350, 1289, 1248, 1216, 1177, 1145, 1111, 1092 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{24}H_{19}N_4OS^+$: 411.1274, found: 411.1271.



((1*H*-indol-7-yl)imino)diphenyl-λ^6-sulfanone 7.[20] Indole **6** (0.1 mmol, 41.1 mg) was dissolved in DMSO (1 mL) and freshly prepared NaOEt (5 equiv) in EtOH (0.2 mL) was added to the mixture and stirred at 100 °C for 30 min. After completion, the reaction mixture was cooled to room temperature and diluted with EtOAc (2 × 10 mL). The mixture was washed with 2 N HCl (1 × 5 mL), brine (2 × 5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent provided a residue that was purified by silica gel column chromatography (CH_2Cl_2: *n*-hexane = 9:1) to furnish **7** as a brown solid in 61% yield (20.3 mg); mp 164-165 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.34 (s, 1H), 8.07-8.05 (m, 4H), 7.54-7.47 (m, 7H), 7.23 (t, *J* = 3.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.81 (d, *J* = 7.2 Hz, 1H), 6.56 (t, *J* = 3.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.5, 133.2, 132.4, 129.6, 128.5, 128.0, 127.3, 124.3, 119.8, 119.7, 116.9, 101.5; FT-IR (neat)

3391, 2924, 2853, 1612, 1574, 1512, 14823, 1442, 1414, 1350, 1334, 1294, 1264, 1215, 1171, 1097, 1066 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{20}H_{17}N_2OS^+$: 333.1056, found: 333.1053.



1-(Pyrimidin-2-yl)indolin-7-amine 8.[21] To a stirred solution of diphenyl((1-(pyrimidin-2-yl)indolin-7-yl)imino)-λ^6-sulfanone **3a** (0.2 mmol, 82.4 mg) in THF was added Na/naphthalene (4.0 mL, 2.0 mmol, 0.5 M in THF) dropwise vigorously stirring at -78 °C under nitrogen atm. The reaction mixture was stirred at -78 °C for 30 min and quenched with MeOH. After completion, as judged by the TLC, 1(N) HCl was added dropwise until pH 7 and extracted with EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography (EtOAc: *n*-hexane = 2 : 1) to afford **8** as dark brown liquid in 71% (30.1 mg) yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.427 (d, *J* = 4.8 Hz, 2H), 6.93 (t, *J* = 7.8 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.64 (d, *J* = 4.8 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 4.77 (br s, 2H), 4.42 (t, *J* = 7.8 Hz, 2H), 3.05 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.6, 1579, 136.7, 136.0, 130.6, 125.2, 117.3, 115.5, 110.8, 52.2, 29.5; FT-IR (neat) 2953, 2922, 2851, 1581, 1548, 1478, 1445, 1381, 1340, 1285, 1218, 1059 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{12}H_{13}N_4^+$: 213.1135, found: 213.1132.

Crystal Data and Structure Refinement for 3n

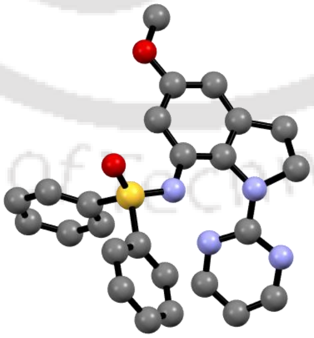


Figure 2. ORTEP diagram of **3n** (**CCDC 2129119**). H-Atoms omitted for clarity.

Identification code	**3n**
CCDC No.	2129119
Empirical formula	$C_{25}H_{22}N_4O_2S$
Formula weight	442.53
Crystal habit, colour	block /yellow
Temperature, *T*/K	273 K
Wavelength, λ/Å	0.71073
Crystal system	triclinic
Space group	'P -1'
Unit cell dimensions	a = 8.5052(9)Å b = 9.1789(10)Å c = 14.5417(16)Å α = 88.724(3), β = 88.629(3) γ = 74.372(3)
Volume, *V*/Å^3	1092.8(2)
Z	2
Calculated density, Mg·m^{-3}	1.345
Absorption coefficient, μ/mm^{-1}	0.179
F(000)	464
θ range for data collection	2.30 to 26.98°
Limiting indices	$-10 \leq h \leq 10$, $-10 \leq k \leq 10$, $-17 \leq l \leq 17$
Reflection collected / unique	3846/3211
Completeness to θ	99.4% (θ = 25.043°)
Absorption correction	none
Refinement method	'SHELXL-2014 (Sheldrick 2014)'
Data / restraints / parameters	3846/0/290
Goodness–of–fit on F^2	1.041
Final *R* indices [*I*>2sigma(*I*)]	R1 = 0.0549, wR2 = 0.1487
R indices (all data)	R1 = 0.0708, wR2 = 0.1770

Crystal Data and Structure Refinement for 5h

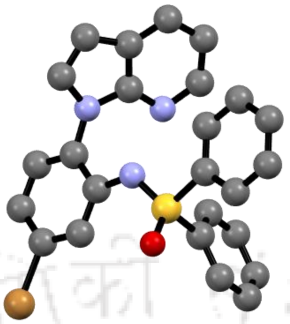


Figure 3. ORTEP diagram of **5h** (**CCDC** 2129126). H-Atoms omitted for clarity.

Identification code	**5h**
CCDC No.	2129126
Empirical formula	$C_{25}H_{18}BrN_3OS$
Formula weight	488.38
Crystal habit, colour	block /Colorless
Temperature, *T*/K	296 K
Wavelength, λ/Å	0.71073
Crystal system	triclinic
Space group	'P -1'
Unit cell dimensions	a = 15.8930(12)Å
	b = 19.2800(12)Å
	c = 14.3730(12)Å
	α = 90, β = 90
	γ = 90
Volume, *V*/Å^3	4404(6)
Z	8
Calculated density, Mg·m^{-3}	1.473
Absorption coefficient, μ/mm^{-1}	1.984
F(000)	1984
θ range for data collection	2.54 to 23.42°

Limiting indices	$-18 \leq h \leq 18$, $-22 \leq k \leq 22$, $-17 \leq l \leq 17$
Reflection collected / unique	3876/3079
Completeness to θ	100% ($\theta = 24.99°$)
Absorption correction	none
Refinement method	'SHELXL-97 (Sheldrick, 1997)'
Data / restraints / parameters	3876/0/280
Goodness–of–fit on F^2	1.065
Final *R* indices [$I > 2\sigma(I)$]	R1 = 0.0408, wR2 = 0.1004
R indices (all data)	R1 = 0.0561, wR2 = 0.1106

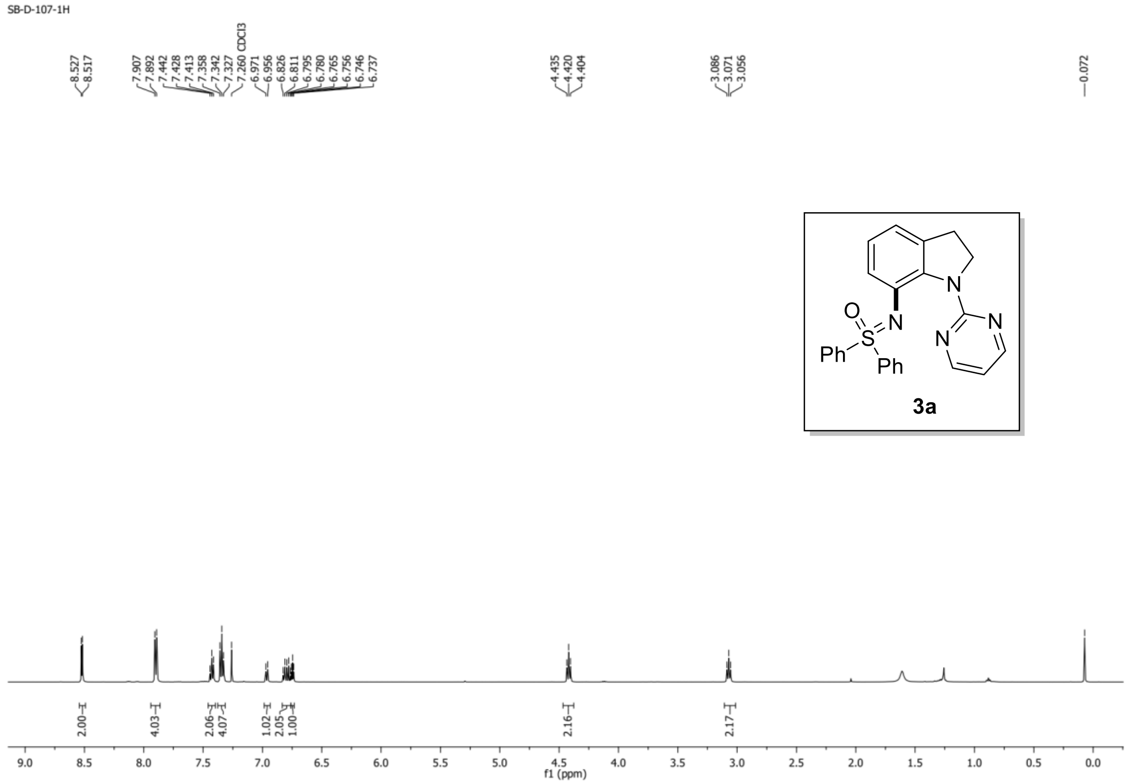
2.5 References

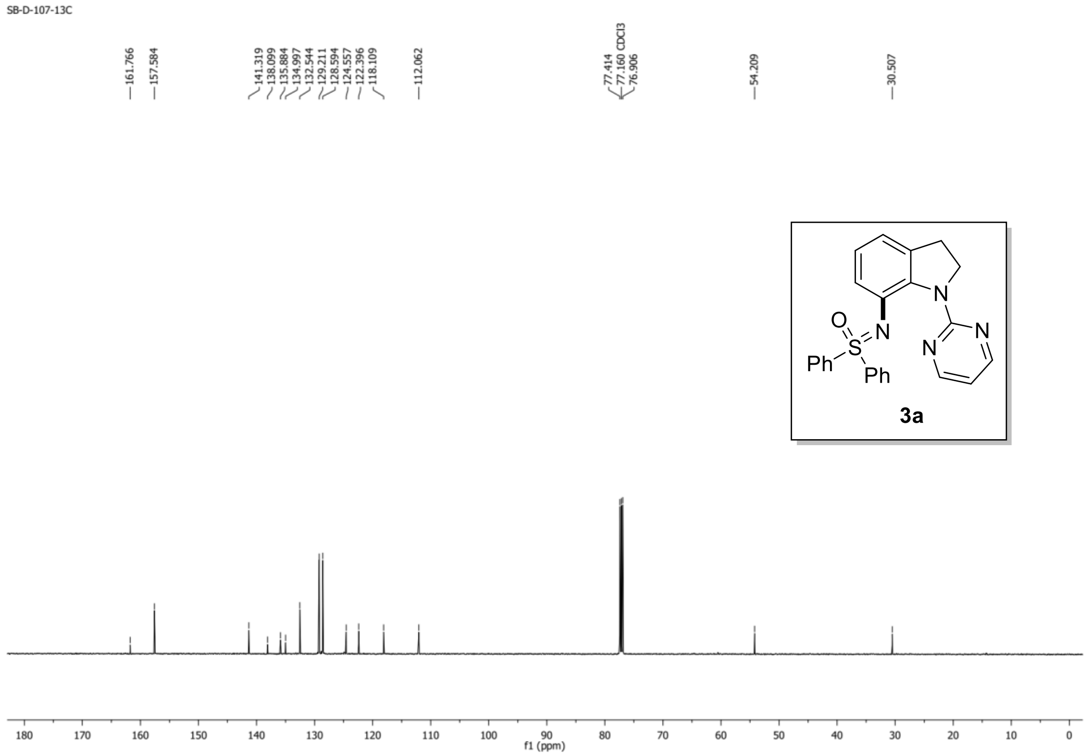
1. (a) Lücking, U. *Angew. Chem. Int. Ed.* **2013**, *52*, 9399. (b) Frings, M.; Bolm, C.; Blum, A.; Gnamm, C. *Eur. J. Med. Chem.* **2017**, *126*, 225. (c) Mäder, P.; Kattner, L. *J. Med. Chem.* **2020**, *63*, 14243. (d) Andresini, M.; Tota, A.; Degennaro, L.; Bull, J. A.; Luisi, R. *Chem. Eur. J.* **2021**, *27*, 17293.
2. (a) Li, Z.; Yu, H.; Bolm, C. *Angew. Chem. Int. Ed.* **2017**, *56*, 9532. (b) Zhang, Y.-F.; Dong, X.-Y.; Cheng, J.-T.; Yang, N.-Y.; Wang, L.-L.; Wang, F.-L.; Luan, C.; Liu, J.; Li, Z.-L.; Gu, Q.-S.; Liu, X.-Y. *J. Am. Chem. Soc.* **2021**, *143*, 15413.
3. (a) Zhang, M.-Z.; Chen, Q.; Yang, G.-F. *Eur. J. Med. Chem.* **2015**, *89*, 421. (b) Lepri, S.; Buonerba, F.; Goracci, L.; Velilla, I.; Ruzziconi, R.; Schindler, B. D.; Seo, S. M.; Kaatz, S.; Cruciani, G. *J. Med. Chem.* **2016**, *59*, 867.
4. (a) Yang, Y.; Qiu, X.; Zhao, Y.; Mu, Y.; Shi, Z. *J. Am. Chem. Soc.* **2016**, *138*, 495. (b) Leitch, J. A.; Bhonoah, Y.; Frost, C. G. *ACS Catal*. **2017**, *7*, 5618. (c) Qiu, X.; Wang, P.; Wang, D.; Wang, M.; Yuan, Y.; Shi, Z. *Angew. Chem., Int. Ed*. **2019**, *58*, 1504. (d) Choi, I.; Messinis, A. M.; Ackermann, L. *Angew. Chem., Int. Ed*. **2020**, *59*, 12534. (e) Wang, D.; Chen, X.; Wong, J. J.; Jin, L.; Li, M.; Zhao, Y.; Houk, K. N.; Shi, Z. *Nat. Commun*. **2021**, *12*, 524
5. (a) Yan, Q.; Huang, H.; Zhang, H.; Li, M.-H.; Yang, D.; Song, M.-P.; Niu, J.-L. *J. Org. Chem*., **2020**, *85*, 11190. (b) Suzuki, H.; Sasamori, F.; Matsuda, T. *Org. Lett*. **2022**, *24*,

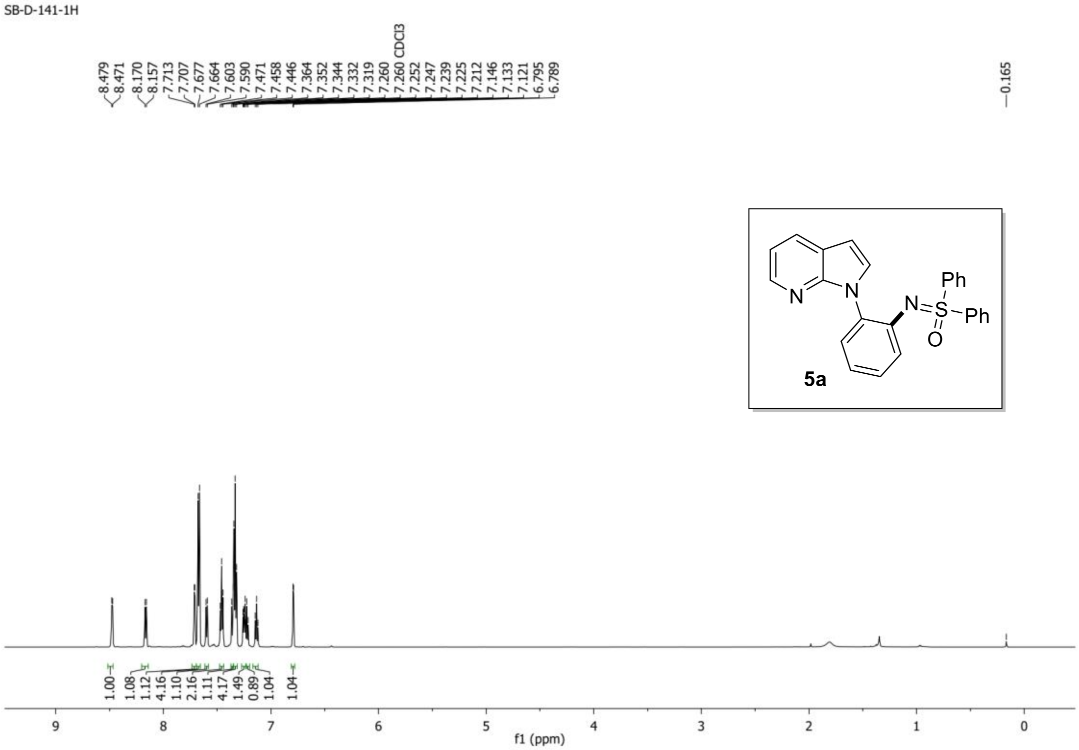
1141. (c) Pahl, J.; Noone, E.; Uzelac, M.; Yuan, K.; Ingleson, M. J. *Angew. Chem. Int. Ed.* **2022**, 61, e202206230.

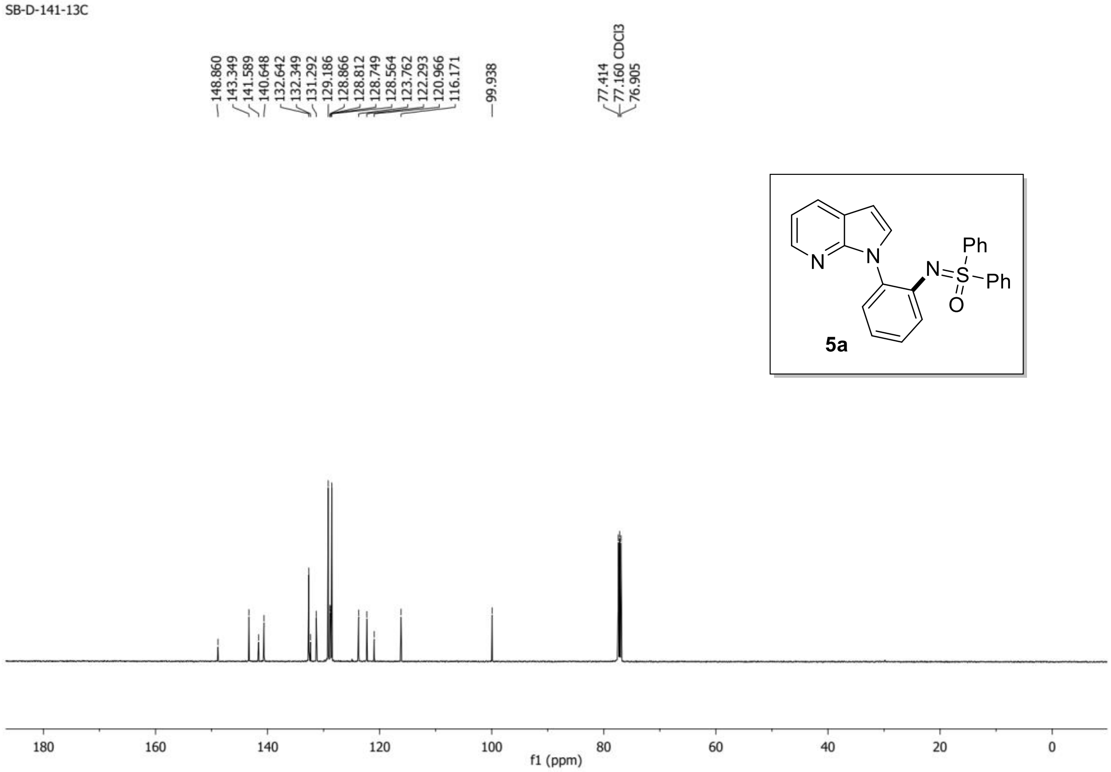
6. Cho, G. Y.; Re´my, P.; Jansson, J.; Moessner, C.; Bolm, C. *Org. Lett*. **2004**, *6*, 3293.
7. Wimmer, A.; König, B. *Org. Lett*. **2019**, *21*, 2740.
8. Liu, D.; Liu, Z.- R.; Ma, C.; Jiao, K.-J.; Sun, B.; Wei, L.; Lefranc, J.; Herbert, S.; Mei, T.-S. *Angew. Chem. Int. Ed.* **2021**, *60*, 9444.
9. Moessner, C.; Bolm, C. *Org. Lett*. **2005**, *7*, 2667.
10. Wang, C.; Zhang, H.; Wells, L. A.; Liu, T.; Meng, T.; Liu, Q.; Walsh, P. J.; Kozlowski, M. C.; Jia, T. *Nat. Commun.* **2021**, *12*, 932.
11. Wang, L.; Huang, H.; Priebbenow, D. L.; Pan, F.-F.; Bolm, C. *Angew. Chem. Int. Ed*. **2013**, *52*, 3478.
12. Wang, L.; Priebbenow, D. L.; Dong, W.; Bolm, C. *Org.Lett*. **2014**, *16*, 2661.
13. Zhou, T.; Qian, P.-F.; Li, J.-Y.; Zhou,Y.-B.; Li, H.-C.; Chen, H.-Y.; Shi, B.-F. *J. Am. Chem. Soc*. **2021**, *143*, 6810.
14. (a) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q. *J. Am. Chem. Soc.* **2006**, *128*, 6790. (b) Simmons, E. M.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2012**, *51*, 3066. (c) Wimmer, A.; König, B. *Adv. Synth. Catal.* **2018**, *360*, 3277.
15. (a) Suess, A. M.; Ertem, M. Z.; Cramer, C. J.; Stahl, S. S. *J. Am. Chem. Soc.* **2013**, *135*, 9797. (b) Gandeepan, P.; Koeller, J.; Ackermann, L. *ACS Catal*. **2017**, *7*, 1030. (c) Ryan, M. C.; Martinelli, J. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2018**, *140*, 9074. (d) Takamatsu, K.; Hayashi, Y.; Kawauchi, S.; Hirano, K.; Miura, M. *ACS Catal.* **2019**, *9*, 5336.
16. Yan, Q.; Huang, H.; Zhang, H.; Li, M.-H.; Yang, D.; Song, M.-P.; Niu, J.-L. *J. Org. Chem.*, **2020**, *85*, 11190.
17. Ryan, M. C.; Martinelli, J. R.; Stahl, S. S. *J. Am. Chem. Soc*. **2018**, *140*, 9074.
18. Xie, W.; Li, B.; Wang, B. *J. Org. Chem*. **2016**, *81*, 396
19. Gandeepan, P.; Koeller, J.; Ackermann, L. *ACS Catal*. **2017**, *7*, 1030.
20. Ackermann, L.; Lygin, A. V. *Org. Lett*. **2012**, *14*, 764.
21. Zhang, Y.-F.; Dong, X.-Y.; Cheng, J.-T.; Yang, N.-Y.; Wang, L.-L.; Wang, F.-L.; Luan, C.; Liu, J.; Li, Z.-L.; Gu, Q.-S.; Liu, X.-Y. *J. Am. Chem. Soc*. **2021**, *143*, 15413.

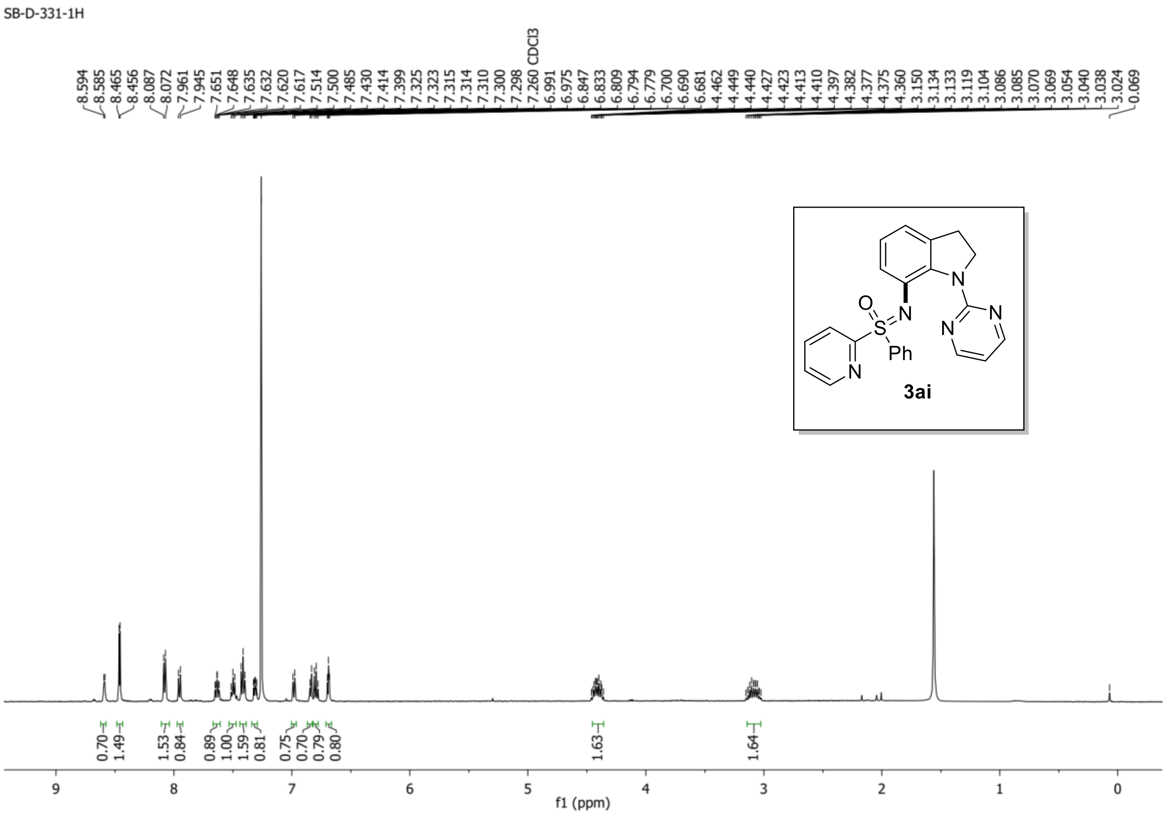
2.6 Selected NMR Spectra

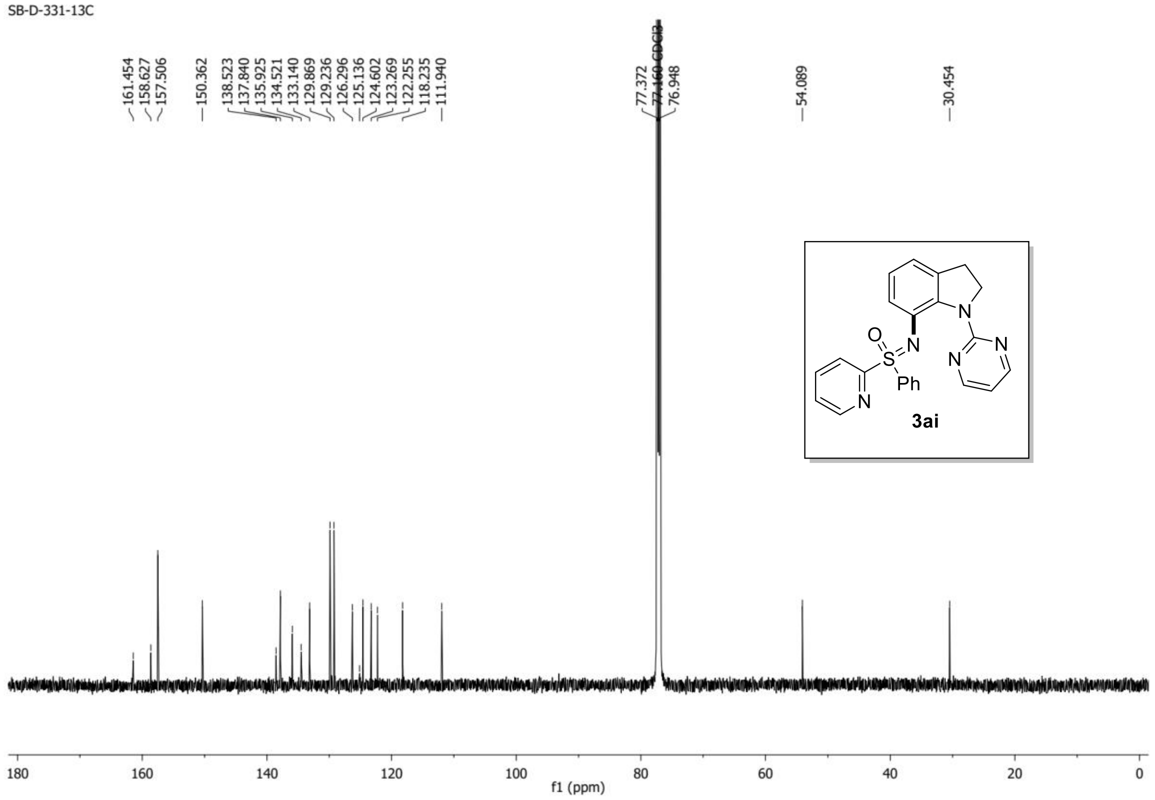





SB-D-141-1H
8.479
8.471
8.170
8.157
7.713
7.707
7.677
7.664
7.603
7.590
7.471
7.458
7.446
7.364
7.352
7.344
7.332
7.319
7.260
7.260 CDCl3
7.252
7.247
7.239
7.225
7.212
7.146
7.133
7.121
6.795
6.789
0.165
N
N
N
S
Ph
Ph
O
5a
1.00
1.08
1.12
4.16
1.10
2.16
1.11
4.17
1.49
0.89
1.04
1.04
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

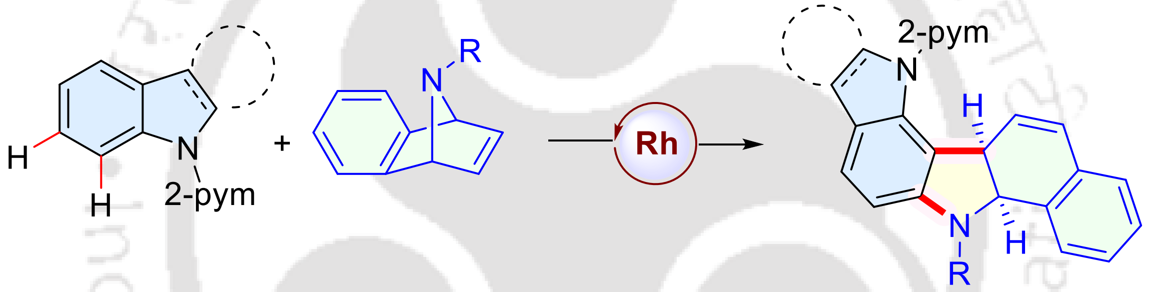

SB-D-141-13C
148.860
143.349
141.589
140.648
132.642
132.349
131.292
129.186
128.866
128.812
128.749
128.564
123.762
122.293
120.966
116.171
99.938
77.414
77.160 CDCl3
76.905
N
N
N
S
Ph
Ph
O
5a
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


SB-D-331-1H
8.594
8.585
8.465
8.456
8.087
8.072
7.961
7.945
7.651
7.648
7.635
7.632
7.620
7.617
7.514
7.500
7.485
7.430
7.414
7.399
7.325
7.323
7.315
7.314
7.310
7.300
7.298
7.260 CDCl3
6.991
6.975
6.847
6.833
6.809
6.794
6.779
6.700
6.690
6.681
4.462
4.449
4.440
4.427
4.423
4.413
4.410
4.397
4.382
4.377
4.375
4.360
3.150
3.134
3.133
3.119
3.104
3.086
3.085
3.070
3.069
3.054
3.040
3.038
3.024
0.069
O
S
N
N
N
N
Ph
N
3ai
0.70
1.49
1.53
0.84
0.89
1.00
1.59
0.81
0.75
0.70
0.79
0.80
1.63
1.64
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


SB-D-331-13C
161.454
158.627
157.506
150.362
138.523
137.840
135.925
134.521
133.140
129.869
129.236
126.296
125.136
124.602
123.269
122.255
118.235
111.940
77.372
77.160 CDCl3
76.948
54.089
30.454
O
S
N
N
N
N
Ph
N
3ai
180
160
140
120
100
80
60
40
20
0
f1 (ppm)

Chapter III

Site-Selective Rh-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles



☽ Dual C-H Activation ☽ Site-Selectivity ☽ Broad Substrate Scope

J. Org. Chem. **2020**, *85*, 2793.

Site-Selective Rh(III)-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles

Transition-metal-catalyzed direct C-H functionalization revolutionizes the transformation of simple substrates into complex molecules with structural diversity and atom economy.[1] Indole and its analogue are ubiquitous in natural products and pharmaceuticals.[2] Particularly, pyrrolo-/indolocarbazoles represents an imperative class of structural motifs[3] that exhibit interesting medicinal[4] and material properties (Figure 1).[5] Functionalization of C-2,[6] C-3,[6] C-4[7] and C-7[8] C-H bonds of indole/indoline have thus been considerably investigated.[9] In contrast, the C-6 functionalization remains underdeveloped.[10] Contextually, a dual C-H functionalization of indolines would be valuable as it can lead to tandem C-C and carbon-heteroatom bond formation for the construction of complex structural scaffolds. In this line, azabenzonorbornadienes are realized as versatile building blocks. Herein, we report a dual C-7 and C-6 C-H functionalization of indolines with azabenzonorbornadienes using a Rh-catalysis to furnish pyrrolocarbazoles. The site-selectivity, substrate scope and functional group diversities are important practical features.

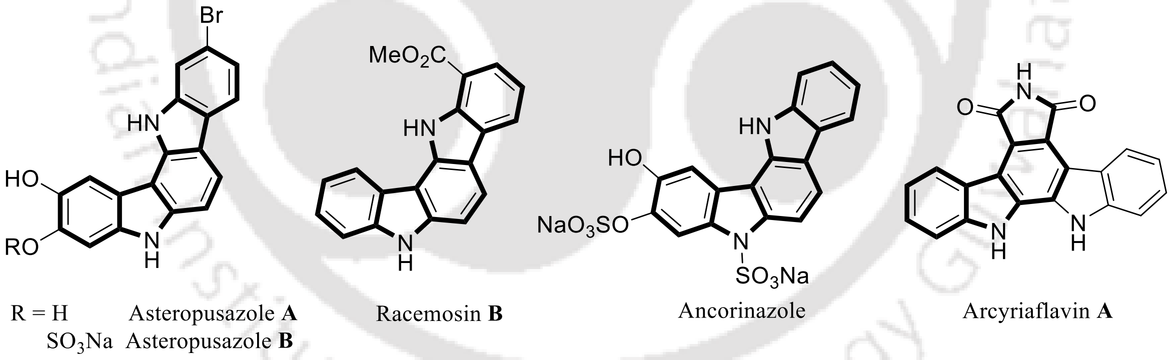
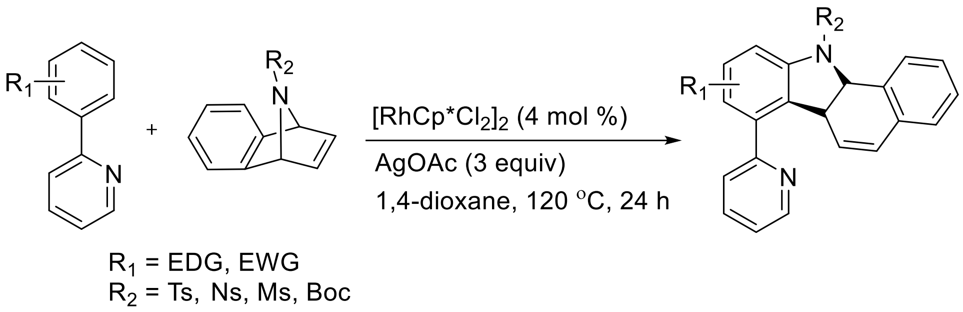


Figure 1. Some Examples of Medicinally Important Pyrrolo-/Indolocarbazole Natural Products

3.1 Literature Study

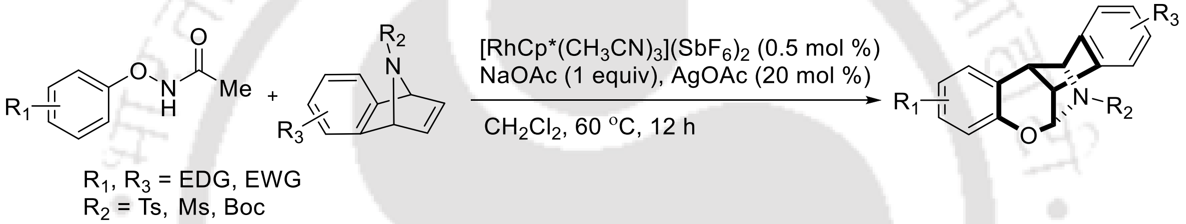
3.1.1 Rh-Catalyzed C-H Activation with Oxa/azabicyclic Olefins

Li and co-workers reported a Rh(III)-catalyzed dual C-H activation of arenes and (hetero)arenes with 7-azabenzonorbornadienes under oxidative conditions to furnish dihydrocarbazoles (Scheme 1).[11] High activity of Rh-catalyst, high-selectivity, wide substrate scope, and functional-group tolerance are the practical findings of this strategy.



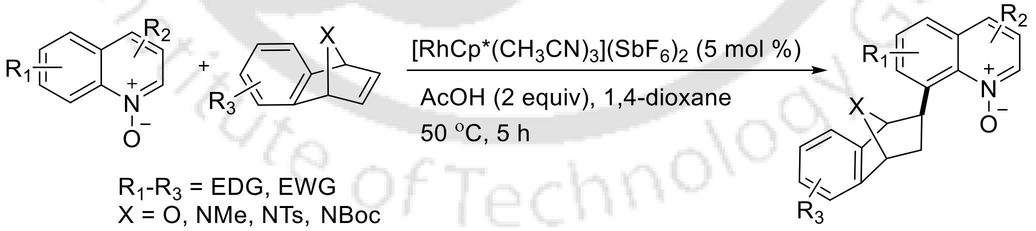
Scheme 1. Rh-Catalyzed Coupling of Arenes with 7-Azabenzonorbornadienes

Glorius and co-workers developed an efficient Rh(III)-catalyzed combined C-H activation/ Wagner-Meerwein-type rearrangement under mild conditions. The Rh-catalyst demonstrates high efficiency in the coupling of *N*-phenoxyacetamide with 7-azabenzonorbornadiene, leading to the formation of bridged polycyclic molecules. (Scheme 2).[12]



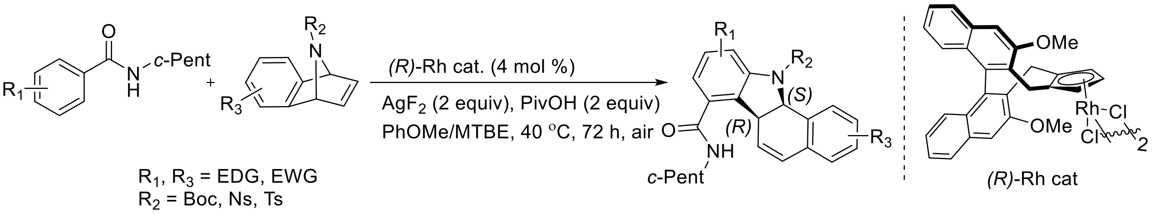
Scheme 2. Rh-Catalyzed C-H Activation *N*-phenoxyacetamide with 7-azabenzonorbornadiene

Liu and co-workers demonstrated the heterocyclic core retained hydroarylation of oxa/azabenzonorbornadienes with quinoline *N*-oxides using rhodium as a catalyst under mild conditions (Scheme 3),[13] furnishing quinoline *N*-oxide substituted heterobicyclic structures with excellent regioselectivity and good yields.



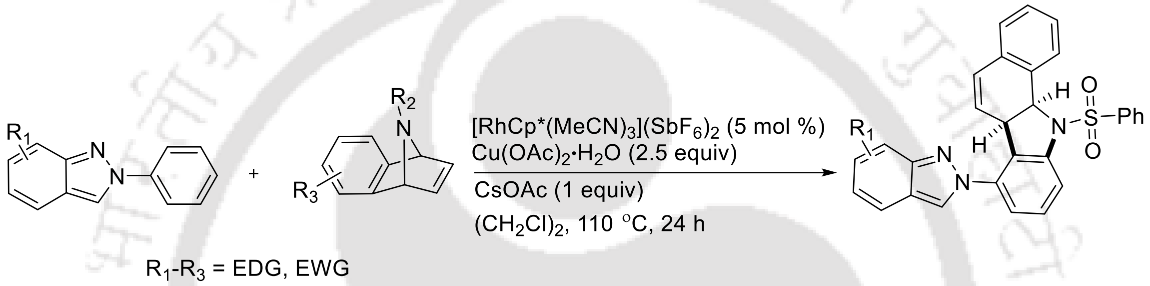
Scheme 3. Rh-Catalyzed C-H Activation of Quinoline-N-Oxide with 7-Azabenzonorbornadiene

Rh(III)-catalyzed asymmetric [3+2] trans-annulation of arenes with 7-azabenzonorbornadienes by employing a flexible chelating group and a strong oxidant, was described by Li and co-workers (Scheme 4).[14] Herein, two distinct classes of arenes have been identified as substrates, and the coupling proceeded with high enantioselectivity and excellent diastereoselectivity through sequential activation of ortho and meta C-H bonds.



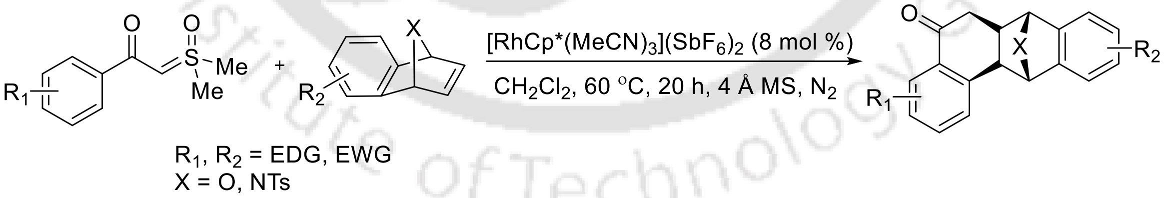
Scheme 4. Rh-Catalyzed Two-fold C-H Activation of Arenes and Azabicyclic Olefins

Our group reported Rh-Catalyzed tandem site-selective C–H activation and ring opening/cyclization of 7-azabenzonorbornadienes with aryl-2*H*-indazoles, furnishing indazolyl-benzocarbazoles (Scheme 5).[15] The use of an air stable cationic Rh-catalyst and site-selectivity, and substrate scope are the important practical features.



Scheme 5. Rh-Catalyzed Site-selective C-H Activation of Indazoles with 7-azabenzonorbornadienes

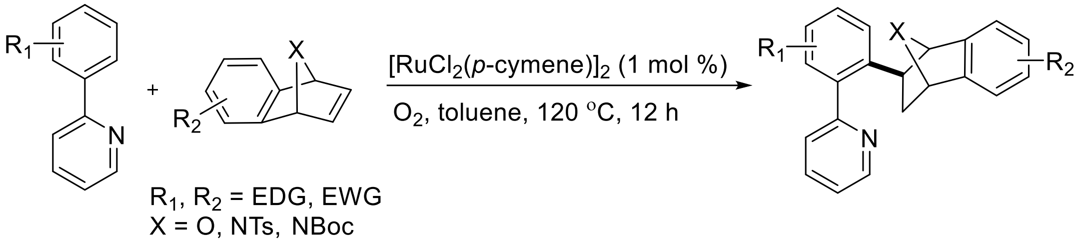
Li and co-workers described Rh(III)-catalyzed chemo-divergent coupling of sulfoxonium ylides with 7-oxa/azabenzonorbornadiene (Scheme 6).[16] Herein, sulfoxonium ylide functions as a traceless oxidizing directing group. This annulation proceeded under redox-neutral conditions with decent substrate scope.



Scheme 6. Rh-Catalyzed Annulation of Sulfoxonium Ylides with 7-Oxa/Azabenzonorbornadienes

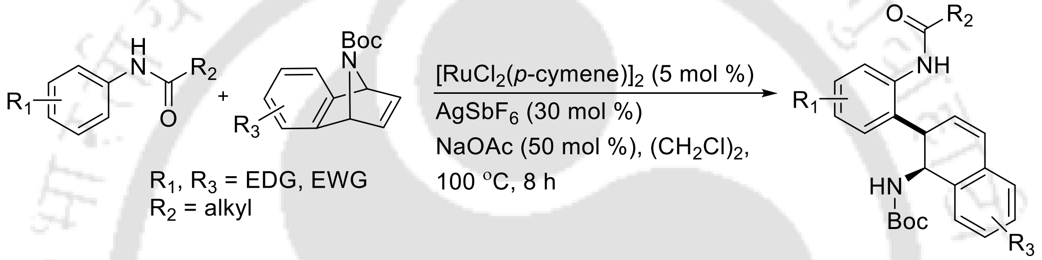
3.1.2 Ru-Catalyzed C-H Activation with Oxa/azabicyclic Olefins

A Ru-catalyzed arylation reaction of oxa- and azabicyclic alkenes with (hetero)arenes by C-H bond activation has been discovered by Bolm and co-workers (Scheme 7).[17] Broad substrate scope, absence of any additives and role of oxygen are the practical features of this methodology.



Scheme 7. Ru(II)-Catalyzed Hydroarylation of Arenes with 7-Oxa/Azanorbornadiene

Zhang and co-workers developed Ru(II)-catalyzed direct ring-opening reaction of 7-azabenzonorbornadienes with anilides via C-H activation to access hydronaphthylamines (Scheme 8).[18] The transformation proceeds with a high stereoselectivity to yield *cis*-configuration products under redox-neutral conditions.

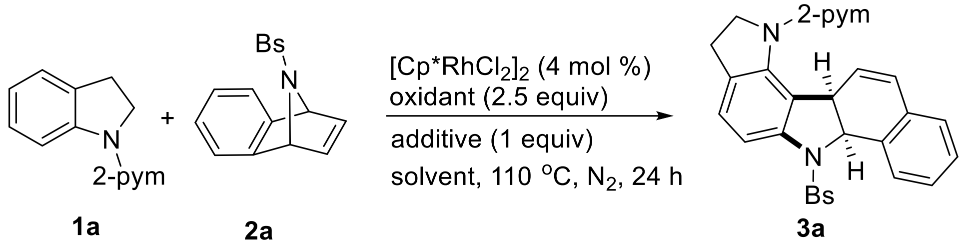


Scheme 8. Ru-Catalyzed Ring-Opening Addition of Anilides to 7-Azabenzonorbornadienes

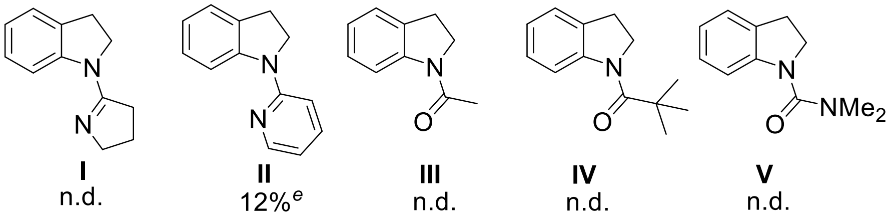
3.2 Present Study

This chapter outlines a Rh(III)-catalyzed site-selective C7 and C6 dual C-H functionalization of indolines expending 7-azabenzonorbornaiene for the formation of functionalized pyrrolocarbazoles. Our optimization studies commenced employing 1-(pyrimidin-2-yl)indoline **1a** and azabenzonorbornadiene **2a** as the model substrates (Table 1). Delightfully, the reaction occurred to furnish pyrrolocarbazole **3a** in 48% yield when the substrates reacted using 4 mol % $[Cp^*RhCl_2]_2$, 2.5 equiv $Cu(OAc)_2 \cdot H_2O$ and 1 equiv K_2CO_3 for 24 h at 110 °C in DCE. Subsequent screening of the additives led to an enhance in the yield to 72% utilizing Cs_2CO_3, whereas KOAc, CsOPiv and CsOAc produced moderate results. The reaction utilizing $AgSbF_6$ inhibited the formation of **3a**, indicating cationic Rh(III) catalysis might not be involved. Further, screening of the oxidants revealed that $Cu(OAc)_2 \cdot H_2O$ is the optimal oxidant. DCE was found to be the solvent of choice. Control experiments confirmed that the combination of the Rh-catalyst, oxidant and additive is crucial to produce **3a**. Moreover, the directing groups, 3,4-dihydro-2*H*-pyrrole **I**, pyridinyl **II**, acetyl **III**, pivaloyl **IV** and *N*,*N*-dimethylcarbonyl **V**, were ineffective and the starting materials were recovered.

Table 1. Optimization of Reaction Conditions[a]

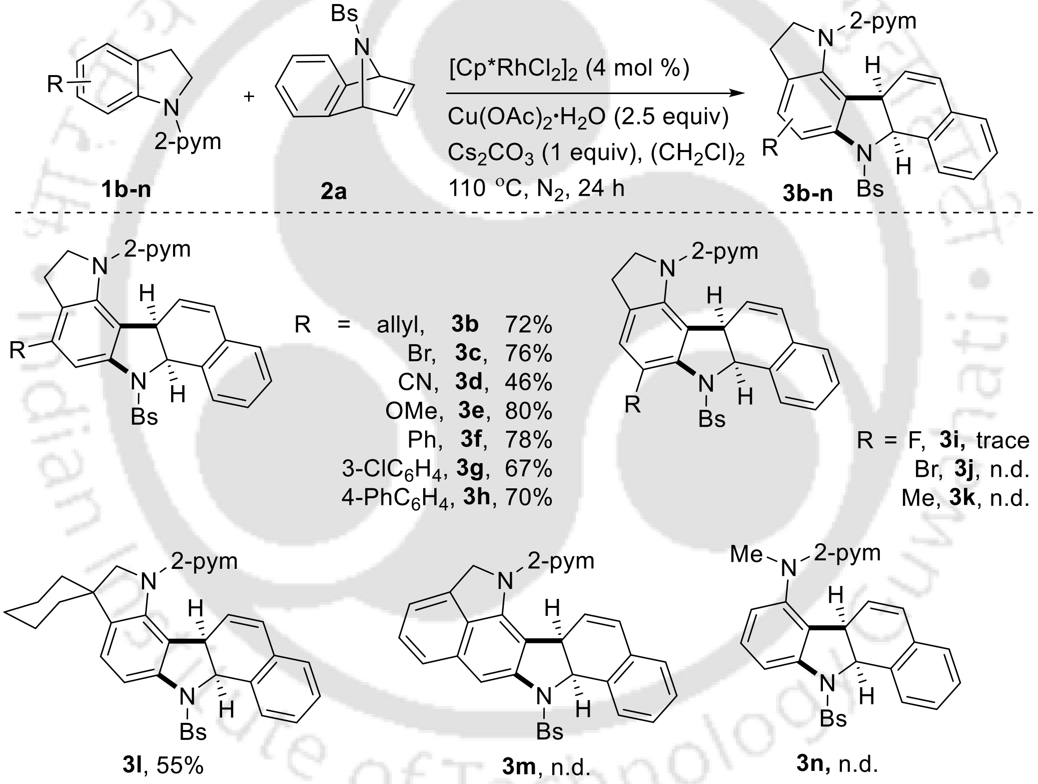


Entry	Oxidant	Additive	Solvent	Yield (%)[b]
1	$Cu(OAc)_2{\cdot}H_2O$	K_2CO_3	$(CH_2Cl)_2$	48
2	$Cu(OAc)_2{\cdot}H_2O$	KOAc	$(CH_2Cl)_2$	46
3	$Cu(OAc)_2{\cdot}H_2O$	CsOPiv	$(CH_2Cl)_2$	53
4	$Cu(OAc)_2{\cdot}H_2O$	CsOAc	$(CH_2Cl)_2$	56
5	**$Cu(OAc)_2{\cdot}H_2O$**	**Cs_2CO_3**	**$(CH_2Cl)_2$**	**72**
6[c]	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	$(CH_2Cl)_2$	n.d.
7	$Cu(OPiv)_2$	Cs_2CO_3	$(CH_2Cl)_2$	47
8	AgOAc	Cs_2CO_3	$(CH_2Cl)_2$	32
9	Ag_2CO_3	Cs_2CO_3	$(CH_2Cl)_2$	n.d.
10	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	THF	42
11	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	CH_3CN	16
12	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	1,4-dioxane	54
13	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	toluene	n.d.
14	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	PhCl	trace
15	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	$PhCF_3$	12
16	$Cu(OAc)_2{\cdot}H_2O$	-	$(CH_2Cl)_2$	trace
17	-	Cs_2CO_3	$(CH_2Cl)_2$	n.d.
18[d]	$Cu(OAc)_2{\cdot}H_2O$	Cs_2CO_3	$(CH_2Cl)_2$	n.d.



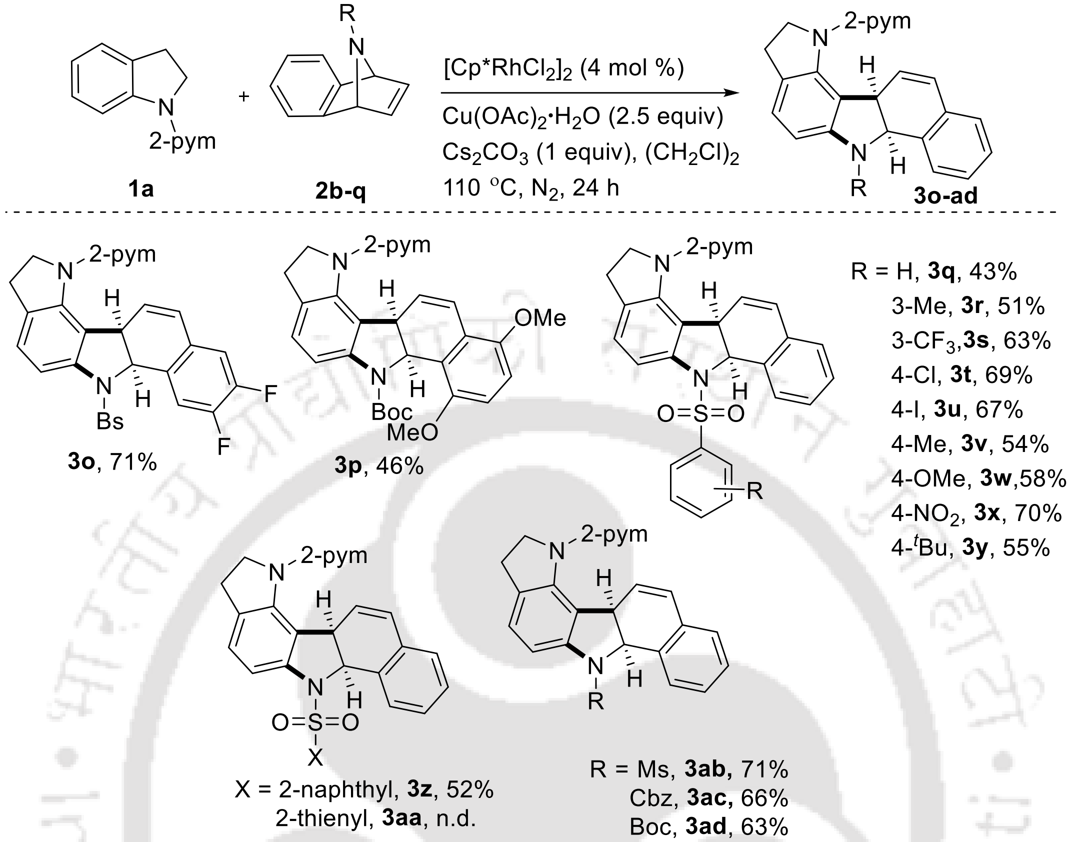
[a]Reaction conditions: **1a** (0.25 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (4 mol %), oxidant (0.63 mmol), additive (0.25 mmol), solvent (2 mL), 110 °C, 24 h, N_2. [b]Isolated yield. [c]20 mol % $AgSbF_6$ used. [d]No Rh catalyst. [e]NMR yield. n.d. = not detected. 2-pym = 2-pyrimidine. Bs = brosyl.

Table 2. Substrate Scope of Indolines[a,b]



[a]Reaction conditions: **1b-n** (0.25 mmol), **2a** (0.3 mmol), $[Cp^*RhCl_2]_2$ (4 mol %), $Cu(OAc)_2{\cdot}H_2O$ (0.63 mmol), Cs_2CO_3 (0.25 mmol), $(CH_2Cl)_2$ (2 mL), 110 °C, 24 h, N_2. [b]Isolated yield. n.d. = not detected.

Table 3. Substrate Scope of Azabenzonorbornadienes[a,b]



3o, 71%

3p, 46%

R = H, **3q**, 43%
3-Me, **3r**, 51%
3-CF$_3$,**3s**, 63%
4-Cl, **3t**, 69%
4-I, **3u**, 67%
4-Me, **3v**, 54%
4-OMe, **3w**,58%
4-NO$_2$, **3x**, 70%
4-^{t}Bu, **3y**, 55%

X = 2-naphthyl, **3z**, 52%
2-thienyl, **3aa**, n.d.

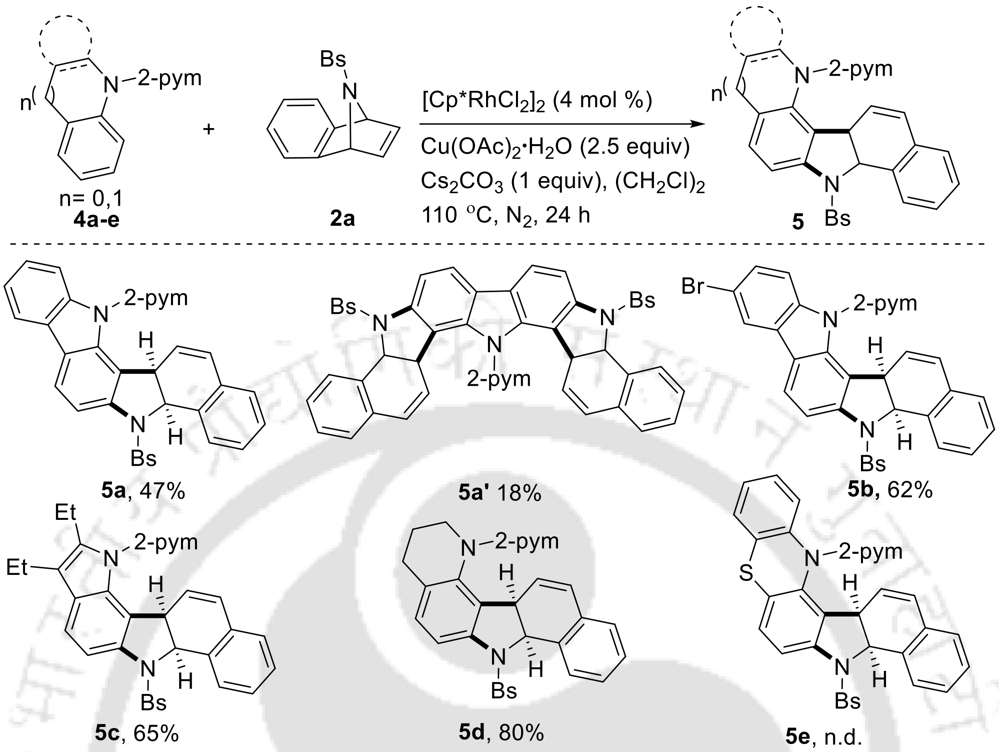
R = Ms, **3ab,** 71%
Cbz, **3ac,** 66%
Boc, **3ad**, 63%

[a]Reaction conditions: **1a** (0.25 mmol), **2b-q** (0.3 mmol), [Cp*RhCl$_2$]$_2$ (4 mol %), Cu(OAc)$_2$·H$_2$O (0.63 mmol), Cs$_2$CO$_3$ (0.25 mmol), (CH$_2$Cl)$_2$ (2 mL), 110 °C, 24 h, N$_2$. [b]Isolated yield. n.d. = not detected.

Having optimized the reaction conditions, the scope of the procedure was investigated for substituted indolines **1** utilizing **2a** as a standard substrate (Table 2). The substrates having substitution at the 4-position of indoline, with allyl **1b**, bromo **1c**, cyano **1d**, methoxy **1e** and phenyl **1f**, 3-chlorophenyl **1g** and 4-biphenyl **1h** groups underwent reaction to produce **3b-h** in 46-80% yields. In contrast, 5-substituted indolines **1i-k** were unsuccessful, which might be due to steric hindrance near the C6-site. However, a spiroindoline **1l** gave **3l** in 55% yield. Analogous 1-(pyrimidin-2-yl)-1,2-dihydrobenzoindole **1m** and *N*-methyl-*N*-phenylpyrimidin-2-amine **1n** substrates were found incompatible

The scope of the method was extended for diverse azabenzonorbornadienes **2** with indoline **1a** as a standard substrate (Table 3). Substrates with 6,7-difluoro **2b** and 5,8-dimethoxy **2c** groups in the aryl ring **A** reacted to give **3o** and **3p** in 71 and 46% yields, respectively. The reaction of **2d** having

Table 4. Scope of Carbazoles and Related Frameworks **4**[a,b]

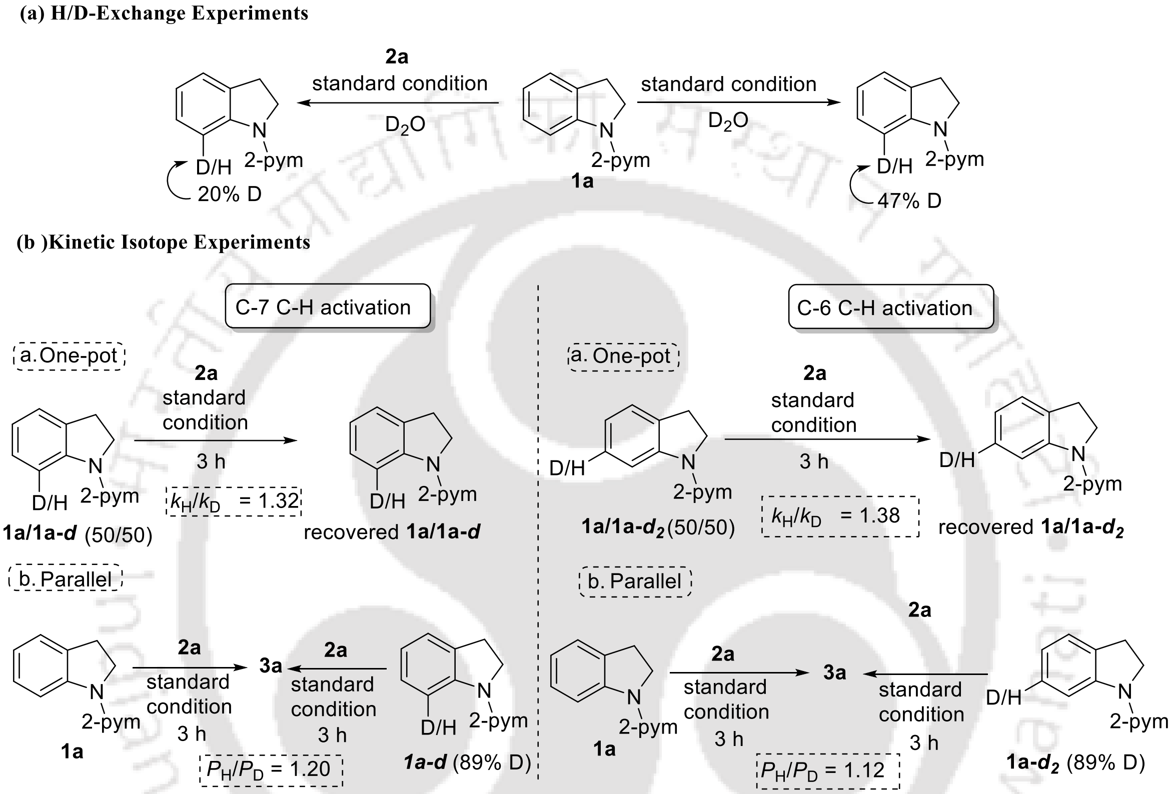


[a]Reaction conditions: **4a-e** (0.25 mmol), **2a** (0.3 mmol), [Cp*RhCl$_2$]$_2$ (4 mol %), Cu(OAc)$_2$·H$_2$O (0.63 mmol), CsOAc (0.25 mmol), (CH$_2$Cl)$_2$ (2 mL), 110 °C, 24 h, N$_2$. [b]Isolated yield. n.d. = not detected.

9-phenylsulfonyl substituent afforded **3q** in 43% yield. In addition, the substrates containing 3-methyl **2e** and 3-trifluoromethyl **2f** groups in the 9-arylsulfonyl ring reacted to provide **3r** and **3s** in 51 and 63% yields, respectively. Further, the reaction of the substrates bearing substitution at the 4-position of the 9-arylsulfonyl ring *viz*; chloro **2g**, iodo **2h**, methyl **2i**, methoxy **2j**, nitro **2k** and *tert*-butyl **2l** groups, produced **3t-y** in 54-70% yields. Likewise, 9-naphthylsulfonyl substituted **2m** furnished **3z** in 52% yield, whereas **2n** bearing 2-thiophene group was an unsuccessful substrate, which might be due to the chelation to the Rh-catalyst. The substrates with 9-mesyl **2o**, 9-Cbz **2p** and 9-Boc **2q** protecting groups readily reacted to deliver **3ab-ad** in 63-71% yields. Notably, the products were obtained as a single diastereoisomer and stereochemistry was assigned by single-crystal X-ray of **3t** as a representative example (Figure 2).

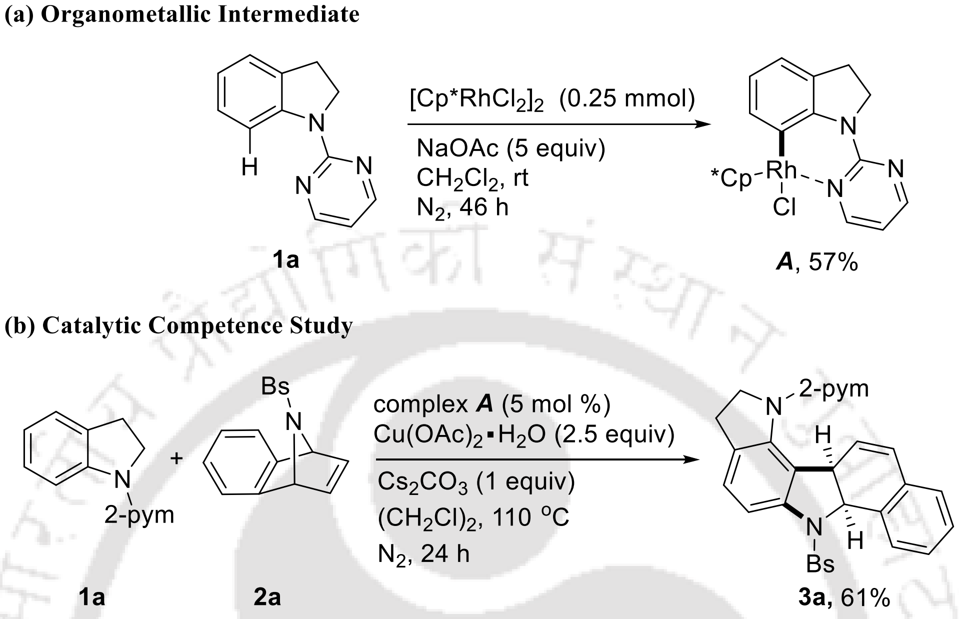
The method was explored with carbazoles and related frameworks (Table 4). Thus, 9-(pyrimidin-2-yl)-9*H*-carbazole **4a** reacted to afford **5a** and **5a′** in 47 and 18% yields, respectively. The reaction of 3-bromo-9-(pyrimidin-2-yl)-9*H*-carbazole **4b** afforded **5b** in 62% yield. Interestingly, 2,3-

diethyl-1-(pyrimidin-2-yl)-1*H*-indole **4c** and 1-(pyrimidin-2-yl)-1,2,3,4-tetrahydroquinoline **4d**, conveyed **5c** and **5d** in 65 and 80% yields, respectively. However, 10-(pyrimidin-2-yl)-10*H*-phenothiazine **4e** failed to furnish **5e**, which might be due to the chelation of the thioether moiety to the Rh-catalyst.



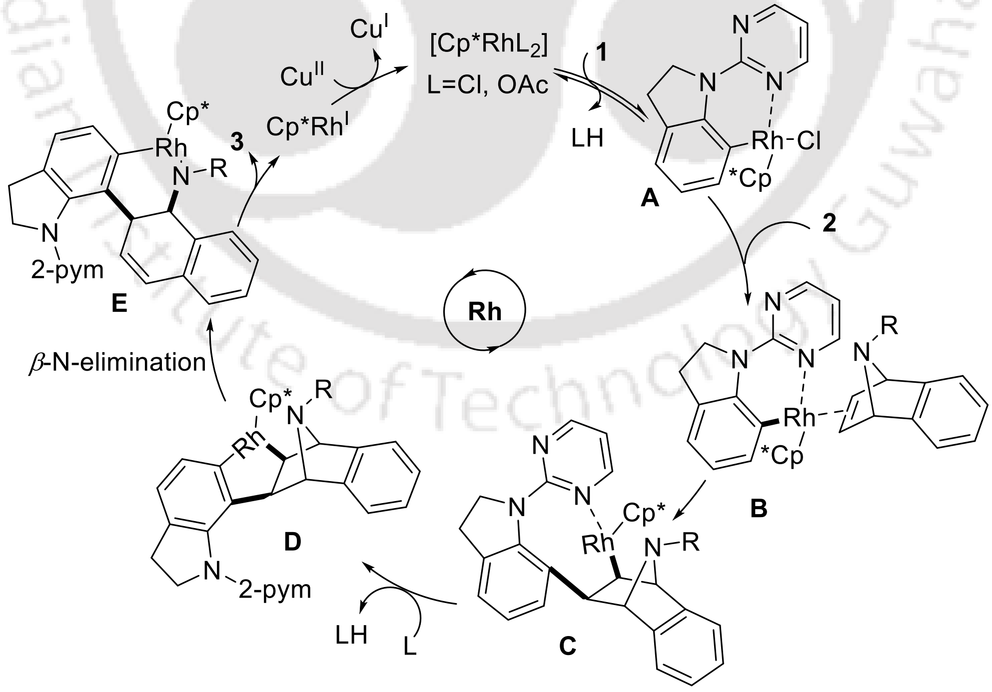
Scheme 9. Mechanistic Investigations

To get insight into the mechanism, H-D scrambling experiment was performed using **1a** in the presence of D_2O as a co-solvent, and 47% D incorporation was observed, while as using **1a** and **2a** in the presence of D_2O produced 20% D incorporation (Scheme 9a). These results suggest that the migratory insertion of alkene is faster than H/D exchange and the initial C-H activation is reversible. In addition, the kinetic isotope experiments for the C(7)-H activation exhibited k_H/k_D = 1.32 (one-pot) and $[P_H]/[P_D]$ = 1.20 (parallel). Similarly, for the C(6)-H activation, yielded k_H/k_D = 1.38 (one-pot) and $[P_H]/[P_D]$ = 1.12 (parallel) (Scheme 9b). These results confide that the C-H bond cleavage might not be involved in the rate-determining step. Further, the stoichiometric reaction of $[Cp^*RhCl_2]_2$ with **1a** produced the rhodacycle **A** in 57% yield (Scheme 6a), whose structure was determined using the single-crystal X-ray analysis (Figure 3). The complex **A** was catalytically competent to afford **3a** in 61% yield (Scheme 6b), suggesting an involvement of a rhodacycle as the active species in the catalytic cycle.

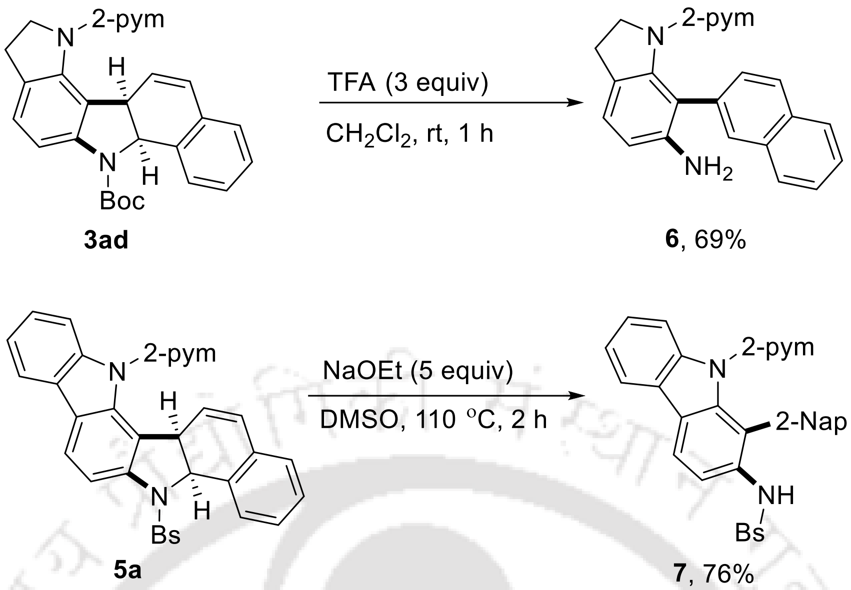

(a) Organometallic Intermediate

(b) Catalytic Competence Study

Scheme 10. Isolation of the Rhodacycle **A** and Catalysis



Scheme 11. Plausible Catalytic Cycle



Scheme 12. Post-synthetic Modifications

Preliminary mechanistic results and literature[1-8] suggest that the 2-pyrimidine directed reversible fast C(7)-H activation can lead to the formation of a rhodacycle **A (**Scheme 10). Coordination of **A** with **2a** can give the Rh-species **B**, which can lead to the migratory insertion to yield **C**. Concomitant activation of the C(6)-H bond can deliver **D**, which can undergo *β*-*N*-elimination to furnish **E** that may, in turn, undergo reductive elimination to deliver **3** and Rh^{I} species. Oxidation of Rh^{I} using Cu^{II} can regenerate the active Rh^{III} to complete the catalytic cycle (Scheme 11).

The products can be further transformed into diverse scaffolds (Scheme 12). For example, **3ad** could be converted to **6** in 69% yield employing TFA *via* Boc deprotection and acid-mediated elimination. Similarly, **5a** could be transformed to **7** in 76% yield using base mediated elimination and the structure was determined using X-ray analysis (Figure 4).

In summary, we have developed a Rh-catalyzed two-fold C-7 and C-6 functionalization of indolines with 7-azabenzonorbornadienes to produce pyrrolocarbazoles. The site-selectivity, substrate scope and functional group diversity are important practical features.

3.3 Experimental Section

General Information. $Cu(OAc)_2.H_2O$ (>98%), Cs_2CO_3 (99%), $[Cp^*RhCl_2]_2$, AgOAc (99.99%) and Ag_2CO_3 (99%) were purchased from aldrich and used as receivd. Silica gel-G plates (Merck) were used for TLC analysis with a mixture of hexane and ethyl acetate as the eluent. Melting point of the products was measured on Büchi melting point apparatus, MPB-540. Open capillary tubes were used for the measurements and are uncorrected. NMR (^{1}H, ^{13}C and ^{19}F) spectra were recorded on Bruker 400 MHz and 600 MHz NMR instruments using TMS as an internal standard and $CDCl_3$ as a solvent. Mestrenova software was used throughout the spectral analysis. Chemical shifts are given in parts per million (δ-scale) and the coupling constants are given in Hertz. Q-Tof ESI-MS instrument (model HAB273) was used for recording HRMS data. Infrared spectra were recorded on Perkin Elmer FT-IR instrument using KBr disc. Single crystal X-ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/-Kα radiation and the structure was solved by direct method using SHELXL-16 (Göttingen, Germany).

1-(Pyrimidin-2-yl)indolines and 7-Azabenzonorbornadienes were synthesized as per reported procedure.

General Procedure for Synthesis of Pyrrolocarbazoles. 1-(Pyrimidin-2-yl)indoline **1** (0.25 mmol), 9-((aryl)sulfonyl)-1,4-dihydro-1,4-epiminonaphthalene **2** (0.3 mmol), $[Cp^*RhCl_2]_2$ (4 mol %, 0.01 mmol, 6.2 mg), $Cu(OAc)_2 \cdot H_2O$ (0.625 mmol, 124.4 mg) and Cs_2CO_3 (0.25 mmol, 81.5 mg) were stirred at 110 °C in a preheated oil bath for 24 h in $(CH_2Cl)_2$ (2 mL) under nitrogen atmosphere. Progress of the reaction was monitored using TLC with ethyl acetate and hexane as the eluent. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (20 mL) and passed through a short pad of celite. Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford analytically pure functionalized pyrrolocarbazoles.

H/D Exchange Studies in $(CH_2Cl)_2$:D_2O (Scheme S2). 1-(Pyrimidin-2-yl)indoline **1a** (0.25 mmol, 49.3 mg), $Cu(OAc)_2 \cdot H_2O$ (0.62 mmol, 124 mg), Cs_2CO_3 (0.25 mmol, 81.5 mg), D_2O (1 mmol, 18 μL) and $[Cp^*RhCl_2]_2$ (4 mol %, 6.2 mg) were stirred in $(CH_2Cl)_2$ under nitrogen at 110 °C in a preheated oil bath for 6 h. The reaction mixture was cooled to room temperature and extracted with dichloromethane (15 mL). The combined organic layer was washed with water (5 mL) and dried over Na_2SO_4. Evaporation of the solvent gave a residue which was purified on silica gel column chromatography using a 1:9 mixture of ethyl acetate and hexanes. The ^{1}H NMR analysis showed 47% D incorporation at C-7.

H/D Exchange Studies $(CH_2Cl)_2$:D_2O with 2a (Scheme S2). 1-(Pyrimidin-2-yl)indoline **1a** (0.25 mmol, 49.3 mg), 9-((4-bromophenyl)sulfonyl)-1,4-dihydro-1,4-epiminonaphthalene **2a** (0.30, 108.7 mg), $Cu(OAc)_2 \cdot H_2O$ (0.62 mmol, 124 mg), Cs_2CO_3 (0.25 mmol, 81.5 mg), D_2O (1 mmol, 18 μL) and $[Cp^*RhCl_2]_2$ (4 mol %, 6.2 mg) were stirred in $(CH_2Cl)_2$ under nitrogen at 110 °C in a preheated oil bath for 12 h. The reaction mixture was cooled to room temperature and extracted with CH_2Cl_2 (15 mL). The combined organic layer was washed with water (5 mL) and dried over Na_2SO_4. Evaporation of the solvents gave a residue that was purified on silica gel column chromatography using a 1:9 mixture of ethyl acetate and hexanes. The ^1H NMR analysis showed 20% D incorporation at C-7.

Preparation of 1-(pyrimidin-2-yl)indoline-7-*d*. The titled compound was prepared according to the reported procedure as a pale yellow liquid. The deuterium incorporation was determined using 400 MHz ^1H NMR as 89%.

Synthesis of 1-(pyrimidin-2-yl)indoline-4,6-*d*$_2$. The titled compound was prepared using the following procedure.

Step-1. **2-Nitrobenzen-4,6-*d*$_2$-amine**: Trifluoroacetic anhydride (1.40 mL, 10 mmol) was added slowly to D_2O (4 mL) in a screw-capped pressure tube at 0 °C. Then, 2-nitroaniline (1.380 g, 10 mmol) was added in portion wise. The tube was sealed and heated at 120 °C for 24 h. The reaction mixture was cooled to room temperature and then 2 M NaOH solution (20 mL) was added. The resulting mixture was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic layer was dried over Na_2SO_4. Evaporation of the solvent afforded 2-nitrobenzen-4,6-d_2-amine in 98% (1.40 g) yield as a yellow solid that was used for step-2 without further purification. ^1H NMR showed 89% D incorporation. ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.27 (s, 1H).

Step-2. **1-Iodo-2-nitrobenzene-4,6-*d*$_2$**: To a solution of 2-nitrobenzen-4,6-d_2-amine (5 mmol, 691 mg) in water (25 mL), concentrated HCl (10 mL) was added and the resultant solution was cooled to 0 °C. Then, $NaNO_2$ (6 mmol, 414 mg) in water (10 mL) was added dropwise over 30 min and the stirring continued for additional 1 h. The resultant diazonium salt solution was treated with NaI (15 mmol, 2.25 g) and the stirring was continued for an additional 1 h. Sodium thiosulfate was added to quench the excess iodine present, and the product was extracted using ethyl acetate (3 × 15 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using 2% ethyl acetate in hexane to afford the 1-iodo-2-nitrobenzene-4,6-d_2 in 84% (1.05 g) yield as a yellow solid. ^1H NMR showed 89% D incorporation. ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 1.6 Hz, 1H), 7.20 (d, J = 3.5 Hz, 1H).

Step-3. **2-Iodobenzen-3,5-*d*$_2$-amine**. To a stirring solution of 1-iodo-2-nitrobenzene-4,6-d_2 (4 mmol), $FeCl_3$ (1.5 mol %, 9.7 mg) and activated charcoal (20 mol %, 9.6 mg) at 70 °C in methanol, hydrazine hydrate (8 mmol, 256 mg) was added and the striring was continued for an additional 2 h. The reaction mixture was then passed through a pad of celite and the solvent was evaproated. The residue was diluted with ethyl acetate (15 mL) and washed with water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using a 1:4 mixture of ethyl acetate and hexane to provide 2-iodobenzen-3,5-d_2-amine in 92% (813 mg) yield as yellow oil. ^{1}H NMR showed 89% D incorporation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (d, J = 1.3 Hz, 1H), 6.54-6.42 (m, 1H), 3.52 (br s, 2H).

Step-4. **2-Ethynylbenzen-3,5-d_2-amine**: To a solution of 2-iodobenzen-3,5-d_2-amine (3.5 mmol, 721 mg), $PdCl_2(PPh_3)_2$ (5 mol %, 123 mg), CuI (5 mol %, 33 mg), trimethylamine (15 mL) and trimethylsilylacetylene (5.25 mmol, 500 μL) were added under nitrogen atmosphere. The mixture was stirred at room temperature for 24 h, and then concentrated to give a residue, which was diluted with dichloromethane (10 mL). The solution was washed with water (5 mL) and the aqueous phase was extracted with CH_2Cl_2 (20 mL). Drying (Na_2SO_4) and evaporation of the solvent gave brown oil that was dissolved in a 1:1 mixture of methanol and CH_2Cl_2, treated with K_2CO_3 (10.5 mmol, 1.45 g) and stirred for 2 h at room temperature. The mixture was then concentrated in vacuo, and the residue was extracted using ethyl acetate (20 mL) and washed with water (5 mL). Drying (Na_2SO_4) and evaporation of the sovlent provided a residue that was purified on silica gel chromatography using a 3:7 mixture of ethyl acetate and hexane to provide 2-ethynylbenzen-3,5-d_2-amine in 93% (387 mg) yield as a brown oil. ^{1}H NMR showed that 89% D incorporation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.55 (d, J=5.3 Hz, 2H), 4.11 (br s, 2H), 3.25 (s, 1H).

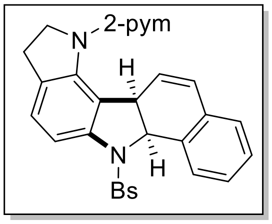
Step-5. **1*H*-Indole-4,6-d_2**: To a mixture of 2-ethynylbenzen-3,5-d_2-amine (250 mg, 2.1 mmol), triethylamine (3.5 mmol, 0.5 mL,) and DMAP (0.21 mmol, 26 mg,) in dichloromethane (10 mL) was added acetyl chloride (3.23 mmol, 230 μL) at 0 °C. The resultant mixture was warmed to room temperature and stirred for 24 h. The reaction was quenched using water and extracted with CH_2Cl_2 (15 mL). Drying (Na_2SO_4) and evaporation of the solvent furnished as brown solid, which was used for the next step without further purification. The resultant *N*-(2-ethynylphenyl-3,5-d_2)acetamide (2.1 mmol) was dissolved with toluene (5 mL) and treated with Cs_2CO_3 (2 equiv, 1.40 g) in a screw capped pressure tube. The tube was sealed and stirred at 150 °C for 12 h. The reaction mixture was diluted with water (5 mL) and extracted with ethyl acetate (20 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography to provide 1*H*-indole-4,6-*d*$_2$ in 76% (190 mg) yield as brown solid. ^{1}H NMR showed 89% D incorporation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.40 (s, 1H), 7.21 (t, *J* = 2.8 Hz, 1H), 7.15 (s, 1H), 6.58 (t, *J* = 1.6 Hz, 1H).

Step-6. Finally, the 1-(pyrimidin-2-yl)indoline-4,6-*d*$_2$ was prepared from 1*H*-indole-4,6-*d*$_2$ as per literature.[13] ^{1}H NMR showed 89% D incorporation. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 4.8 Hz, 2H), 8.40 (s, 1H), 6.94 (s, 1H), 6.69 (t, *J* = 4.8 Hz, 1H). 4.25 (dd, *J* = 9.2, 8.1 Hz, 2H), 3.21 (dd, *J* = 9.3, 8.1 Hz, 2H).

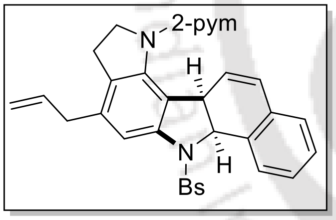
Preparation of Cyclometalted Rh-complex A. 1-(Pyrimidin-2-yl)indoline **1a** (1 mmol, 197 mg), $[Cp^*RhCl_2]_2$ (0.25 mmol, 154.5 mg) and NaOAc (5.0 mmol, 410 mg) were stirred in CH_2Cl_2 (3 mL) for 46 h at room temperature under N_2. The solution was passed through a short pad of celite and the solvent was evaporated under reduced pressure. The residue was washed with diethyl ether (10 mL) to afford a residue that was recrystalized using a mixture of diethyl ether and CH_2Cl_2 to afford analytically pure red crystals in 57% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (dd, *J* = 5.6, 2.4 Hz, 1H), 8.29 (dd, *J* = 4.5, 2.4 Hz, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.71 (dd, *J* = 7.2, 1.2 Hz, 1H), 6.60 (dd, *J* = 5.6, 4.5 Hz, 1H), 4.21 (ddd, *J* = 11.8, 10.1, 6.5 Hz, 1H), 3.94 (ddd, *J* = 11.8, 10.2, 7.0 Hz, 1H), 3.13 (td, *J* = 9.6, 6.5 Hz, 2H), 1.35 (s, 15H).

Catalytic Studies with Rhodacycle A. 1-(Pyrimidin-2-yl)indoline **1a** (0.25 mmol, 49.3 mg), 9-((4-bromophenyl)sulfonyl)-1,4-dihydro-1,4-epiminonaphthalene **2a** (0.30 mmol, 108.7 mg) $Cu(OAc)_2{\cdot}H_2O$ (0.62 mmol, 124 mg), Cs_2CO_3 (0.25 mmol, 81.5 mg) and rhodacycle **A** (5 mol %, 7.7 mg) in $(CH_2Cl)_2$ (5 mL) stirred at 110 °C in a preheated oil bath for 24 h under nitrogen. The resultant mixture was treated with dichloromethane (10 mL) and washed with water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent afforded a residue that was purified on silica gel column chromatography using a 1:4 mixture of ethyl acetate and hexane to furnish the target product in 61% yield.

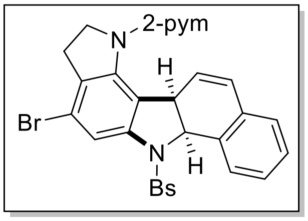
3.4 Characterization Data



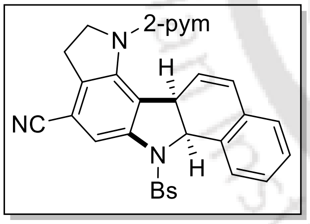
6-((4-Bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*] pyrrolo-[2,3-*g*]carbazole 3a. Brown solid; yield 72% (100 mg); mp 213-214 °C; R_f = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.57-7.55 (m, 2H), 7.47-7.45 (m, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 5.09 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.67-4.61 (m, 1H), 4.03 (q, *J* = 10.0 Hz, 1H), 3.66 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.29-3.20 (m, 1H), 2.88-2.80 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.6, 157.9, 140.9, 140.0, 136.5, 133.0, 132.5, 131.8, 131.6, 129.0, 128.6, 128.5, 128.2, 127.9, 127.2, 126.6, 126.4, 123.4, 123.0, 116.2, 112.7, 63.6, 51.8, 42.0, 29.0; FT-IR (KBr) 3128, 1630, 1576, 1550, 1400, 1166, 1088, 1014 cm^{-1}; HRMS (ESI) calcd for $[C_{24}H_{21}BrN_4O_2S+H]^+$ 557.0641, found 557.0661.



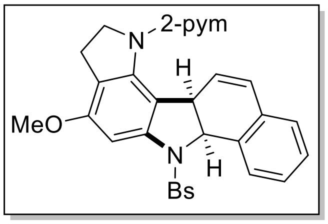
4-Allyl-6-((4-bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6, 6a,12a-hexahydrobenzo [*a*]-pyrrolo[2,3-*g*]carbazole 3b. Colorless solid; yield 72% (107 mg); mp 168-169 °C; R_f = 0.29 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.28-7.24 (m, 1H), 7.18 (s, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 5.95-5.85 (m, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 5.10-5.03 (m, 3H), 4.67-4.61 (m, 1H), 4.02 (q, *J* = 10.4 Hz, 1H), 3.66 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.31 (d, *J* = 6.4 Hz, 2H), 3.18-3.09 (m, 1H), 2.84-2.77 (m, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.7, 157.8, 141.2, 139.7, 136.7, 135.8, 135.0, 132.4, 131.8, 131.7, 131.5, 129.0, 128.6, 128.5, 128.1, 127.9, 127.1, 126.6, 124.3, 123.2, 116.5, 116.4, 112.6, 63.7, 51.5, 41.9, 37.9, 27.6; FT-IR (KBr) 3130, 1631, 1575, 1400, 1167, 1085, 1066 cm^{-1}. HRMS (ESI) calcd for [$C_{31}H_{25}BrN_4O_2S+H$]$^+$ 597.0954, found 597.0950.



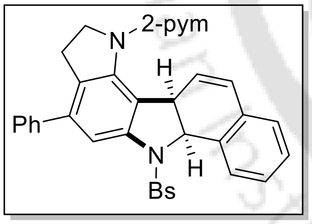
4-Bromo-6-((4-bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydro- benzo-[*a*]pyrrolo[2,3-*g*]carbazole 3c. Brown solid; yield 76% (120 mg); mp 237-238 °C; R$_f$ = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.31 (d, *J* = 4.4 Hz, 2H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.47 (s, 1H), 7.28-7.25 (m, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.77 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 5.02 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.61 (t, *J* = 10.0 Hz, 1H), 4.13-4.03 (m, 1H), 3.59 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.22-3.13 (m, 1H), 2.88 (dd, *J* = 16.4, 8.4 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 160.4, 157.8, 142.2, 140.5, 136.4, 133.2, 132.5, 131.6, 131.2, 128.9, 128.6, 128.5, 128.3, 128.1, 127.5, 126.7, 125.4, 122.4, 118.7, 117.3, 113.2, 63.8, 50.9, 41.7, 30.5; FT-IR (KBr) 3132, 1736, 1574, 1452, 1401, 1360, 1285, 1231, 1168, 1086 cm^{-1}; HRMS (ESI) calcd for [$C_{28}H_{20}Br_2N_4O_2S+H$]$^+$ 634.9746, found 634.9746.



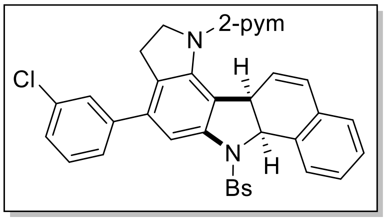
6-((4-Bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]- pyrrolo-[2,3-*g*]carbazole-4-carbonitrile 3d. Yellow solid; yield 46% (67 mg); mp 214-215 °C; R$_f$ = 0.26 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.32 (d, *J* = 4.8 Hz, 2H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.62-7.60 (m, 2H), 7.53 (s, 1H), 7.50-7.48 (m, 2H), 7.31-7.27 (m, 1H), 7.19-7.15 (m, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.82 (t, *J* = 4.8 Hz, 1H), 6.13 (d, *J* = 10.0 Hz, 1H), 5.61 (d, *J* = 10.4 Hz, 1H), 5.00 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.73-4.67 (m, 1H), 4.13 (q, *J* = 10.0 Hz, 1H), 3.74-3.70 (m, 1H), 3.43-3.34 (m, 1H), 3.12-3.05 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 160.3, 158.0, 142.1, 141.2, 137.9, 136.3, 132.7, 131.5, 130.9, 130.8, 128.94, 128.90, 128.62, 128.57, 128.4, 128.3, 126.9, 121.3, 118.1, 116.9, 113.7, 107.8, 63.7, 51.5, 42.3, 28.7. FT-IR (KBr) 3129, 2225, 1574, 1400, 1288, 1168, 1067 cm^{-1}; HRMS (ESI) calcd for [$C_{29}H_{20}BrN_5O_2S$+H]$^+$ 582.0594, found 582.0589.



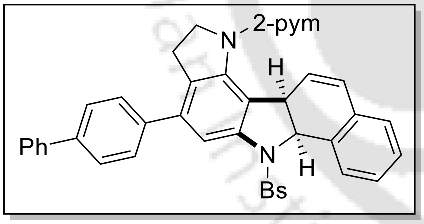
6-((4-Bromophenyl)sulfonyl)-4-methoxy-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydro- benzo-[*a*]pyrrolo[2,3-*g*]carbazole 3e. Colorless solid; yield 80% (117 mg); mp 229-230 °C; R_f = 0.25 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.58 (d, *J* = 8.8 Hz, 2H), 7.49-7.47 (m, 2H), 7.29-7.25 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.94 (s, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.71 (t, *J* = 4.8 Hz, 1H), 6.07 (d, *J* = 10.0 Hz, 1H), 5.55 (d, *J* = 10.0 Hz, 1H), 5.07 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.64-4.58 m, 1H), 4.03 (q, *J* = 10.8 Hz, 1H), 3.86 (s, 3H), 3.59 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.13-3.04 (m, 1H), 2.87-2.80 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.7, 157.8, 155.1, 142.1, 140.5, 136.5, 132.4, 131.8, 131.7, 129.0, 128.6, 128.4, 128.1, 127.9, 126.9, 126.6, 123.6, 119.8, 119.0, 112.6, 100.1, 64.0, 55.9, 51.9, 41.5, 26.0; FT-IR (KBr) 3125, 3011, 1630, 1575, 1400, 1169 cm^{-1}; HRMS (ESI) calcd for [$C_{29}H_{23}BrN_4O_3S$+H]$^+$ 587.0747, found 587.0751.



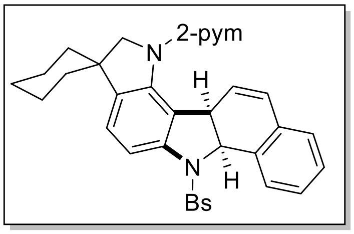
6-((4-Bromophenyl)sulfonyl)-4-phenyl-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydro- benzo-[*a*]pyrrolo[2,3-*g*]carbazole 3f. Colorless solid; yield 78% (123 mg); mp 245-246 °C; R_f = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 4.8 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.41 (q, *J* = 6.4 Hz, 5H), 7.35-7.28 (m, 2H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 7.2 Hz, 1H), 6.75 (t, *J* = 4.8 Hz, 1H), 6.13 (d, *J* = 10.0 Hz, 1H), 5.63 (d, *J* = 10.0 Hz, 1H), 5.12 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.68 (t, *J* = 9.6 Hz, 1H), 3.99 (q, *J* = 9.2 Hz, 1H), 3.72 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.43-3.34 (m, 1H), 2.80 (dd, *J* = 15.6, 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 157.9, 141.4, 140.1, 140.0, 137.7, 136.6, 132.5, 131.7, 131.6, 130.8, 129.0, 128.7, 128.5, 128.2, 127.9, 127.5, 127.3, 126.6, 125.3, 122.9, 116.7, 112.6, 63.7, 51.7, 41.9, 29.1; FT-IR (KBr) 3130, 1616, 1574, 1550, 1400, 1168, 1085 cm^{-1}; HRMS (ESI) calcd for $[C_{34}H_{25}BrN_4O_2S+H]^+$ 633.0954, found 633.0959.



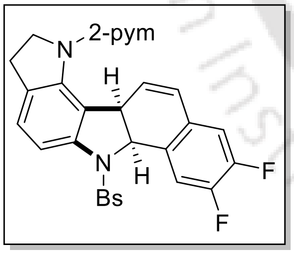
6-((4-Bromophenyl)sulfonyl)-4-(3-chlorophenyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexa-hydrobenzo[*a*]pyrrolo[2,3-*g*]carbazole 3g. Colorless solid; yield 67% (112 mg); mp 252-253 °C; $R_f = 0.27$ (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, $J = 4.8$ Hz, 2H), 7.85 (d, $J = 8.0$ Hz, 1H), 7.52-7.50 (m, 2H), 7.43-7.40 (m, 2H), 7.31 (s, 1H), 7.26-7.18 (m, 5H), 7.07 (t, $J = 7.6$ Hz, 1H), 6.78 (d, $J = 6.8$ Hz, 1H), 6.65 (t, $J = 4.8$ Hz, 1H), 6.03 (d, $J = 10.0$ Hz, 1H), 5.51 (d, $J = 10.0$ Hz, 1H), 4.99 (dd, $J = 9.8, 5.6$ Hz, 1H), 4.61-4.55 (m, 1H), 3.93-3.85 (m, 1H), 3.61-3.57 (m, 1H), 3.32-3.23 (m, 1H), 2.72-2.65 (m, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.6, 157.9, 141.8, 141.7, 140.4, 136.7, 136.3, 134.5, 132.5, 131.8, 131.6, 130.8, 129.0, 128.7, 128.6, 128.3, 128.2, 128.0, 127.6, 127.4, 126.8, 126.7, 125.9, 122.7, 116.5, 112.8, 63.8, 51.7, 41.9, 29.0; FT-IR (KBr) 3129, 1634, 1574, 1400, 1167, 1087 cm^{-1}; HRMS (ESI) calcd for $[C_{34}H_{24}BrClN_4O_2S+H]^+$ 667.0565, found 667.0562.



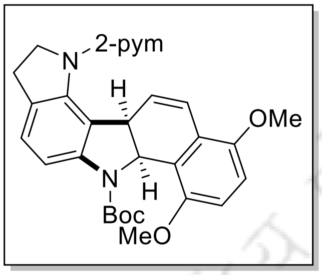
4-([1,1'-Biphenyl]-4-yl)-6-((4-bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]pyrrolo[2,3-*g*]carbazole 3h. Colorless solid; yield 70% (124 mg); mp 241-242 °C; $R_f = 0.28$ (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, $J = 4.8$ Hz, 2H), 7.98 (d, $J = 7.6$ Hz, 1H), 7.65-7.60 (m, 6H), 7.54-7.44 (m, 7H), 7.36 (t, $J = 7.2$ Hz, 1H), 7.33-7.29 (m, 1H), 7.17 (t, $J = 7.6$ Hz, 1H), 6.88 (d, $J = 7.2$ Hz, 1H), 6.75 (t, $J = 4.8$ Hz, 1H), 6.14 (d, $J = 10.0$ Hz, 1H), 5.63 (d, $J = 10.4$ Hz, 1H), 5.12 (dd, $J = 9.6, 5.6$ Hz, 1H), 4.70 (t, $J = 9.6$ Hz, 1H), 4.00 (q, $J = 9.2$ Hz, 1H), 3.72 (dd, $J = 10.0, 6.0$ Hz, 1H), 3.48-3.40 (m, 1H), 2.87 (q, $J = 8.0, 7.8$ Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.7, 157.9, 141.5, 140.8, 140.3, 140.3, 139.0, 137.3, 136.7, 132.5, 131.8, 131.7, 130.8, 129.01, 128.95, 128.7, 128.6, 128.2, 128.0, 127.5, 127.3, 127.24, 127.20, 126.7, 125.4, 122.9, 116.6, 112.7, 63.8, 51.8, 41.9, 29.3; FT-IR (KBr) 3128, 1633, 1569, 1550, 1400, 1168, 1072 cm^{-1}; HRMS (ESI) calcd for $[C_{40}H_{29}BrN_4O_2S+H]^+$ 709.1267, found 709.1288.



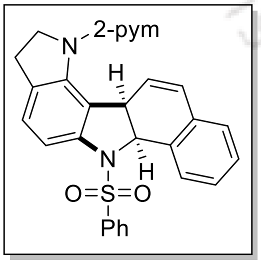
6-((4-Bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,6,6a,12a-tetrahydro-2H-spiro[benzo- [*a*]-pyrrolo[2,3-*g*]carbazole-3,1'-cyclohexane] 3l. Colorless solid; yield 55% (86 mg) mp 243-244 °C; R_f = 0.27 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.29-7.25 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 6.8 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 9.6 Hz, 1H), 5.56 (d, *J* = 10.0 Hz, 1H), 5.08 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.68 (d, *J* = 11.2 Hz, 1H), 3.70-3.63 (m, 2H), 1.81-1.74 (m, 3H), 1.64 (t, *J* = 11.6 Hz, 2H), 1.46 (t, *J* = 11.2 Hz, 2H), 1.35-1.26 (m, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.9, 157.9, 142.5, 141.0, 139.1, 136.4, 132.3, 131.8, 131.7, 129.0, 128.7, 128.5, 128.2, 127.9, 127.1, 126.6, 126.3, 123.1, 121.2, 116.4, 112.6, 63.5, 61.5, 45.3, 42.0, 37.1, 36.0, 25.7, 23.5, 23.0; FT-IR (KBr) 3128, 1631, 1576, 1548, 1400, 1167, 1088, 1068, 1019 cm^{-1}; HRMS (ESI) calcd for $[C_{33}H_{29}BrN_4O_2S+H]^+$ 625.1267, found 625.1282.



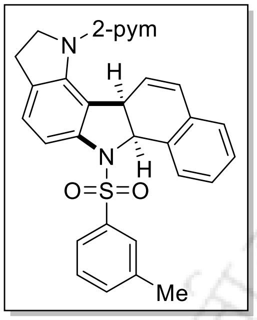
6-((4-Bromophenyl)sulfonyl)-8,9-difluoro-1-(pyrimidin-2-yl)-1,2,3,6, 6a,12a-hexahydro-benzo[*a*]pyrrolo[2,3-*g*]carbazole 3o. Colorless solid; yield 71% (105 mg); mp 253-254 °C; R_f = 0.24 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 4.8 Hz, 2H), 7.74 (dd, *J* = 10.8, 8.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 4.8 Hz, 1H), 6.64 (dd, *J* = 10.8, 7.8 Hz, 1H), 5.97 (d, *J* = 10.2 Hz, 1H), 5.46 (d, *J* = 10.2 Hz, 1H), 5.12 (dd, *J* = 9.6, 5.4 Hz, 1H), 4.67-4.63 (m, 1H), 4.05 (q, *J* = 11.4 Hz, 1H), 3.64 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.29-3.23 (m, 1H), 2.87 (dd, *J* = 15.6, 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.5, 157.9, 150.8 (dd, *J* = 12.6, 10.0 Hz), 149.2 (dd, *J* = 21.0, 9.4 Hz), 140.5, 140.0, 136.1, 133.2, 132.5, 128.9, 128.7 (dd, *J* = 6.3, 3.6 Hz), 128.5 (t, *J* = 4.1 Hz), 128.1, 125.7, 125.3, 123.9, 123.7, 118.0 (d, *J* = 19.1 Hz), 116.1, 115.0 (d, *J* = 17.8 Hz), 112.8, 62.9, 51.7, 41.5, 28.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -137.2, -137.3, -139.5, -139.6; FT-IR (KBr) 3130, 1576, 1548, 1400, 1310, 1167, 1085 cm^{-1}; HRMS (ESI) calcd for $[C_{28}H_{19}BrF_2N_4O_2S+H]^+$ 593.0453, found 593.0453.



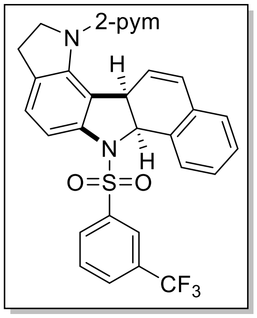
***tert*-Butyl-7,10-dimethoxy-1-(pyrimidin-2-yl)-2,3,6a,12a-tetrahydrobenzo[*a*]pyrrolo[2,3-*g*]carbazole-6(1*H*)-carboxylate 3p.** Thick liquid; yield 46% (57 mg); R_f = 0.23 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 4.8 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 6.72 (d, *J* = 9.2 Hz, 2H), 6.66 (t, *J* = 4.8 Hz, 1H), 5.71 (d, *J* = 7.6 Hz, 1H), 5.52 (dd, *J* = 10.0, 3.2 Hz, 1H), 4.60 (dd, *J* = 5.2, 2.4 Hz, 1H), 4.55-4.49 (m, 1H), 4.19 (q, *J* = 9.6 Hz, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 3.22-3.13 (m, 1H), 2.98-2.91 (m, 1H), 1.32 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 159.7, 157.7, 153.4, 149.3, 144.2, 139.5, 129.0, 127.0, 123.7, 123.0, 121.2, 121.1, 120.1, 112.2, 112.1, 111.3, 111.0, 80.2, 57.3, 56.4, 56.3, 52.2, 43.1, 29.8, 28.6, 28.4; FT-IR (KBr) 3131, 1690, 1633, 1579, 1552, 1460, 1400, 1328, 1259, 1158 cm^{-1}; HRMS (ESI) calcd for $[C_{29}H_{30}N_4O_4+H]^+$ 499.2340, found 499.2356.



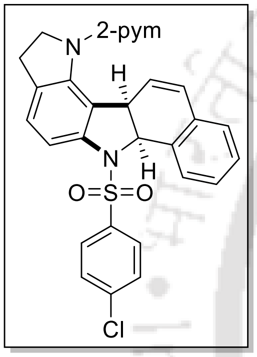
6-(Phenylsulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]pyrrolo[2,3-*g*]carb-azole 3q. Brown solid; yield 43% (51 mg); mp 196-197 °C; R_f = 0.25 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 4.8 Hz, 2H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.65-7.59 (m, 3H), 7.42 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.29-7.27 (m, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.84 (d, *J* = 6.4 Hz, 1H), 6.67 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 9.6 Hz, 1H), 5.61 (d, *J* = 10.4 Hz, 1H), 5.07 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.65-4.60 (m, 1H), 4.06-3.98 (m, 1H), 3.67 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.29-3.20 (m, 2H), 2.88-2.81 (m, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.6, 157.7, 141.1, 139.9, 137.8, 132.6, 131.9, 131.8, 129.2, 128.7, 128.5, 128.1, 127.5, 127.2, 126.6, 126.5, 126.4, 123.3, 123.2, 116.1, 112.5, 63.5, 51.7, 42.0, 29.0; FT-IR (KBr) 3129, 1633, 1400, 1163, 1091 cm^{-1}. HRMS (ESI) calcd for $[C_{29}H_{23}N_3O_2S+H]^+$ 479.1536, found 479.1551.



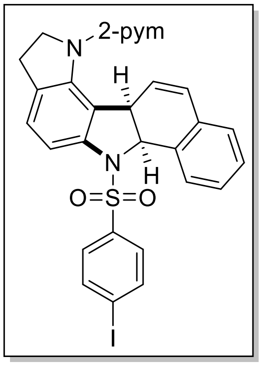
1-(Pyrimidin-2-yl)-6-(m-tolylsulfonyl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*] pyrrolo[2,3-*g*]-carbazole 3r. Yellow solid; yield 51% (63 mg); mp 228-229 °C; R_f = 0.28 (1: 9 ethyl acetate/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, *J* = 4.8 Hz, 2H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 11.6 Hz, 1H), 7.32 (dd, *J* = 8.0, 3.2 Hz, 2H), 7.28-7.24 (m, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 5.6 Hz, 1H), 6.68 (t, *J* = 4.8 Hz, 1H), 6.08 (d, *J* = 9.6 Hz, 1H), 5.57 (d, *J* = 10.4 Hz, 1H), 5.08 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.67-4.61 (m, 1H), 4.07-3.99 (m, 1H), 3.66 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.28-3.19 (m, 1H), 2.88-2.82 (m, 1H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.7, 157.6, 141.4, 139.8, 139.3, 137.7, 133.4, 132.5, 132.1, 131.8, 129.0, 128.8, 128.5, 128.0, 128.0, 127.2, 126.5, 126.5, 124.7, 123.3, 116.1, 112.5, 63.5, 51.8, 42.1, 29.0, 21.5; FT-IR (KBr) 3129, 1631, 1400, 1159 cm^{-1}; HRMS (ESI) calcd for $[C_{29}H_{24}N_4O_2S+H]^+$ 493.1693, found 493.1705.



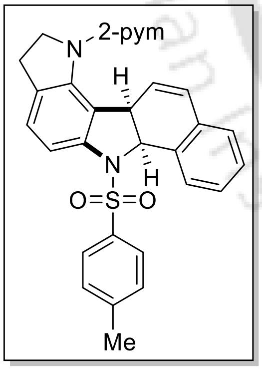
1-(Pyrimidin-2-yl)-6-((3-(trifluoromethyl)phenyl)sulfonyl)-1,2,3,6,6a,12a -hexahydro- benzo-[*a*]pyrrolo[2,3-*g*]carbazole 3s. Colorless solid; yield 63% (86 mg); mp 220-221 °C; R_f = 0.26 (1:9 ethyl acetate/hexane); ^1H NMR (400 MHz, $CDCl_3$)) δ 8.19 (d, *J* = 4.8 Hz, 2H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.81 (t, *J* = 8.4 Hz, 3H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.30-7.28 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.2 Hz, 1H), 6.68 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 10.4 Hz, 1H), 5.67 (d, *J* = 10.0 Hz, 1H), 5.07 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.66-4.60 (m, 1H), 4.07-4.00 (m, 1H), 3.70 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.27-3.18 (m, 1H), 2.88-2.82 (m, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.4, 157.6, 140.6, 140.0, 138.6, 133.2, 131.7, 131.4, 130.7, 129.8, 129.2 (q, *J* = 3.4 Hz), 128.7, 128.5, 128.2, 127.1, 126.6, 125.9, 124.5 (q, *J* = 3.7 Hz), 123.5, 123.0, 115.8, 112.6, 63.7, 51.8, 42.0, 28.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.87. FT-IR (KBr) 3129, 1609, 1578, 1553, 1462, 1400, 1326, 1168, 1133, 1104 cm^{-1}; HRMS (ESI) calcd for $[C_{29}H_{21}F_3N_4O_2S+H]^+$ 547.1410, found 547.1419.



6-((4-Chlorophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]-pyrrolo-[2,3-*g*]carbazole 3t. Colorless solid; yield 69% (59 mg); mp 240-241 °C; R_f = 0.28 (1: 9 ethyl acetate/hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.29-7.25 (m, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.72 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 9.6 Hz, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 5.09 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.67-4.61 (m, 1H), 4.04 (q, *J* = 9.6 Hz, 1H), 3.65 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.29-3.20 (m, 1H), 2.88-2.82 (m, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.6, 157.8, 141.0, 140.0, 139.5, 136.1, 133.0, 131.8, 131.7, 129.5, 129.0, 128.7, 128.6, 128.2, 127.3, 126.7, 126.4, 123.5, 123.0, 116.3, 112.7, 63.6, 51.8, 42.1, 29.0; FT-IR (KBr) 3125, 1719, 1631, 1577, 1400, 1166, 1088 cm^{-1}; HRMS (ESI) calcd for $[C_{28}H_{21}ClN_4O_2S+H]^+$ 513.1147, found 513.1161.

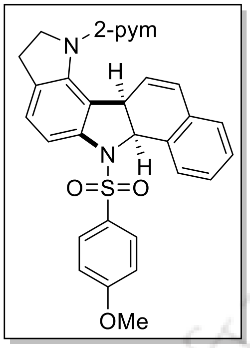


6-((4-Iodophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydro-benzo[*a*]pyrrolo-[2,3-*g*]carbazole 3u. Colorless solid; yield 67% (101 mg); mp 246-247 °C; R_f = 0.29 (1: 9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.30 (d, *J* = 4.8 Hz, 2H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.30 (t, *J* = 8.4 Hz, 3H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.74 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 10.2 Hz, 1H), 5.56 (d, *J* = 10.2 Hz, 1H), 5.09 (dd, *J* = 9.6, 5.4 Hz, 1H), 4.64 (t, *J* = 9.6 Hz, 1H), 4.04 (q, *J* = 10.2 Hz, 1H), 3.67 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.28-3.22 (m, 1H), 2.85 (dd, *J* = 15.6, 9.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.6, 157.9, 140.9, 140.0, 138.4, 137.3, 132.9, 131.7, 131.6, 128.8, 128.6, 128.5, 128.1, 127.2, 126.6, 126.3, 123.4, 123.0, 116.1, 112.6, 100.3, 63.5, 51.7, 42.0, 28.9; FT-IR (KBr) 3129, 1573, 1546, 1400, 1163, 1087 cm^{-1}; HRMS (ESI) calcd for $[C_{28}H_{21}IN_4O_2S+H]^+$ 605.0503, found 605.0513.

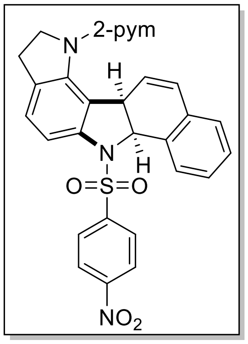


1-(Pyrimidin-2-yl)-6-tosyl-1,2,3,6,6a,12a-hexahydrobenzo[*a*]pyrrolo[2,3 -*g*]carbazole 3v. Yellow solid; yield 54% (66 mg); mp 230-231 °C; R_f = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (d, *J* = 4.2 Hz, 2H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 9.6 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.83 (d, *J* = 7.2 Hz, 1H), 6.68 (t, *J* = 4.8 Hz, 1H), 6.08 (d, *J* = 10.2 Hz, 1H), 5.60 (d, *J* = 10.2 Hz, 1H), 5.08 (dd, *J* = 10.2, 6.0 Hz, 1H), 4.65-4.61 (m, 1H), 4.02 (q, *J* = 10.2 Hz, 1H), 3.74 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.27-3.21 (m, 1H), 2.84 (dd, *J* =

15.0, 9.0 Hz, 1H), 2.42 (s, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.7, 157.6, 143.4, 141.3, 139.8, 135.1, 132.5, 132.1, 131.8, 129.7, 128.8, 128.5, 128.0, 127.6, 127.2, 126.5, 126.4, 123.4, 123.3, 116.2, 112.4, 63.4, 51.7, 42.1, 28.9, 21.8; FT-IR (KBr) 3129, 1631, 1571, 1544, 1400, 1163, 1091 cm^{-1}; HRMS (ESI) calcd for $[C_{29}H_{24}N_4O_2S+H]^+$ 493.1693, found 493.1703.

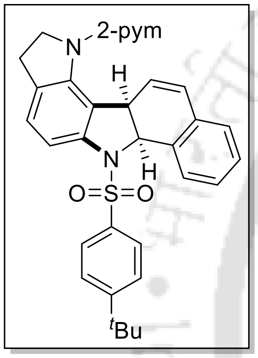


6-((4-Methoxyphenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*] pyrrolo[2,3-*g*]carbazole 3w. Colorless solid; yield 58% (74 mg); mp 233-234 °C; R_f = 0.26 (1:9 ethyl acetate/hexane); ^1H NMR (600 MHz, $CDCl_3$) δ 8.22 (d, *J* = 4.8 Hz, 2H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 5.4 Hz, 1H), 7.12 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 7.2 Hz, 1H), 6.69 (t, *J* = 4.8 Hz, 1H), 6.08 (d, *J* = 10.2 Hz, 1H), 5.56 (d, *J* = 10.2 Hz, 1H), 5.09 (dd, *J* = 9.6, 5.4 Hz, 1H), 4.65-4.61 (m, 1H), 4.02 (q, *J* = 10.8 Hz, 1H), 3.82 (s, 3H), 3.68 (dd, *J* = 10.2, 6.0 Hz, 1H), 3.27-3.21 (m, 1H), 2.84 (dd, *J* = 15.6, 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 163.2, 160.6, 157.7, 141.4, 139.8, 132.5, 132.1, 131.7, 129.5, 129.3, 128.7, 128.5, 128.0, 127.1, 126.6, 126.5, 123.2, 123.2, 116.4, 114.4, 112.5, 63.3, 55.7, 51.7, 42.0, 29.0; FT-IR (KBr) 3130, 1632, 1595, 1400, 1260, 1155, 1091, 1021 cm^{-1}; HRMS (ESI) calcd for $[C_{29}H_{24}N_4O_3S+H]^+$ 509.1642, found 509.1648.

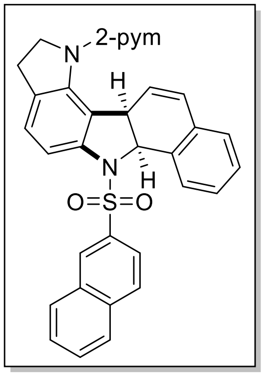


6-((4-Nitrophenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]- pyrrolo-[2,3-*g*]carbazole 3x. Yellow solid; yield 70% (91 mg); mp 237-238 °C; R_f =

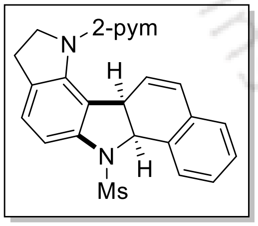
0.24 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.25-8.23 (m, 2H), 8.15 (d, *J* = 4.8 Hz, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.81-7.79 (m, 2H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.30-7.26 (m, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.68 (t, *J* = 4.8 Hz, 1H), 6.10 (d, *J* = 10.0 Hz, 1H), 5.65 (d, *J* = 10.0 Hz, 1H), 5.06 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.67-4.61 (m, 1H), 4.04 (q, *J* = 11.2 Hz, 1H), 3.70 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.30-3.21 (m, 1H), 2.90-2.83 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$) δ 160.5, 157.6, 150.4, 143.4, 140.4, 140.1, 131.7, 131.2, 128.7, 128.62, 128.61, 128.4, 127.3, 126.7, 125.8, 124.2, 123.6, 122.7, 115.8, 112.8, 63.8, 51.8, 42.0, 28.9; FT-IR (KBr) 3129, 1632, 1573, 1528, 1400, 1167, 1087 cm^{-1}; HRMS (ESI) calcd for $[C_{28}H_{21}N_5O_4S+H]^+$ 524.1387, found 524.1391.



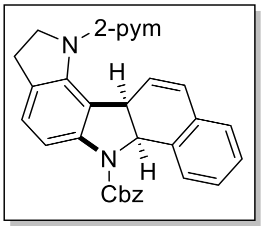
6-((4-(*tert*-Butyl)phenyl)sulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]-pyrrolo[2,3-*g*]carbazole 3y. Colorless solid; yield 55% (73 mg); mp 251-252 °C; R$_f$ = 0.27 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.21 (d, *J* = 4.2 Hz, 2H), 7.99 (d, *J* = 7.2 Hz, 1H), 7.59 (d, *J* = 9.0 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.28-7.25 (m, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.64 (t, *J* = 4.8 Hz, 1H), 6.09 (d, *J* = 10.2 Hz, 1H), 5.63 (d, *J* = 10.2 Hz, 1H), 5.10 (dd, *J* = 10.0, 5.4 Hz, 1H), 4.65-4.62 (m, 1H), 4.03 (q, *J* = 10.8 Hz, 1H), 3.92 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.28-3.22 (m, 1H), 2.85 (dd, *J* = 15.6, 9.0 Hz, 1H), 1.32 (s, 9H); ^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$) δ 160.5, 157.6, 156.6, 141.3, 139.8, 135.4, 132.4, 132.1, 131.8, 128.8, 128.5, 128.0, 127.4, 127.2, 126.4, 126.1, 126.0, 123.4, 123.3, 115.9, 112.3, 63.2, 51.6, 42.2, 35.3, 31.4, 28.9; FT-IR (KBr) 3129, 1577, 1551, 1400, 1166, 1113, 1084 cm^{-1}; HRMS (ESI) calcd for $[C_{32}H_{30}N_4O_2S+H]^+$ 535.2162, found 535.2177.



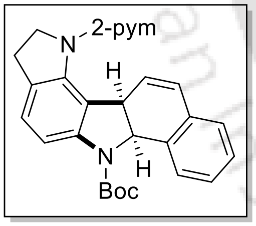
6-(Naphthalen-2-ylsulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]-pyrrolo-[2,3-*g*]carbazole 3z. Brown solid; yield 52% (69 mg); mp 174-175 °C; R_f = 0.27 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.26 (d, *J* = 4.8 Hz, 2H), 8.0 (d, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.64 (t, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.51 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.82 (d, *J* = 7.2 Hz, 1H), 6.44 (t, *J* = 4.8 Hz, 1H), 6.04 (d, *J* = 10.2 Hz, 1H), 5.68 (d, *J* = 9.6 Hz, 1H), 4.96 (dd, *J* = 10.2, 6.0 Hz, 1H), 4.60-4.56 (m, 1H), 3.99 (q, *J* = 10.8 Hz, 1H), 3.52 (dd, *J* = 9.6, 5.4 Hz, 1H), 3.27-3.21 (m, 1H), 2.84 (dd, *J* = 15.6, 9.0 Hz, 1H); ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 160.4, 157.4, 141.2, 139.9, 135.0, 134.9, 132.6, 132.4, 131.9, 131.7, 129.7, 129.1, 128.9, 128.71, 128.67, 128.5, 128.0, 127.8, 127.4, 127.0, 126.5, 126.4, 123.3, 123.1, 122.9, 116.2, 112.2, 63.5, 51.6, 41.9, 28.9; FT-IR (KBr) 3129, 1624, 1576, 1552, 1400, 1161, 1134, 1073 cm^{-1}; HRMS (ESI) calcd for $[C_{32}H_{24}N_4O_2S+H]^+$ 529.1693, found 529.1705.



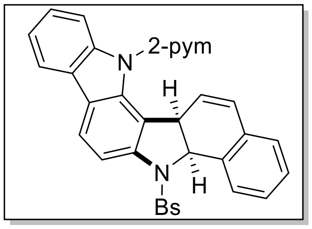
6-(Methylsulfonyl)-1-(pyrimidin-2-yl)-1,2,3,6,6a,12a-hexahydrobenzo[*a*]pyrrolo[2,3-*g*]-carbazole 3ab. Colorless solid; yield 71% (74 mg); mp 249-250 °C; R_f = 0.26 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, *J* = 4.8 Hz, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.28-7.25 (m, 1H), 7.21-7.15 (m, 2H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.81 (t, *J* = 4.4 Hz, 1H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.84 (d, *J* = 10.4 Hz, 1H), 5.36 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.92 (dd, *J* = 10.4, 5.6 Hz, 1H), 4.75-4.70 (m, 1H), 4.17-4.10 (m, 1H), 3.30-3.21 (m, 1H), 2.95 (s, 3H), 2.93-2.87 (m, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.6, 158.0, 140.8, 140.1, 132.6, 132.0, 131.7, 129.0, 128.5, 128.2, 127.4, 126.5, 124.5, 123.7, 123.1, 114.6, 112.8, 63.7, 52.1, 42.7, 36.3, 28.9; FT-IR (KBr) 3126, 2927, 2855, 1637, 1577, 1553, 1400, 1263, 1156 cm^{-1}; HRMS (ESI) calcd for $[C_{23}H_{20}N_4O_2S+H]^+$ 417.1380, found 417.1382.



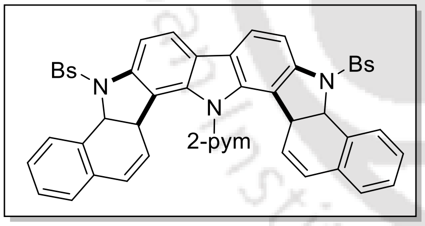
Benzyl-1-(pyrimidin-2-yl)-2,3,6a,12a-tetrahydrobenzo[*a*]pyrrolo[2,3-*g*]carbazol-6(1*H*)-yl)-sulfonyl)methanoate 3ac. Yellow solid; yield 66% (78 mg); mp 196-197 °C; R_f = 0.26 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.50 (d, *J* = 4.8 Hz, 2H), 7.47 (d, *J* = 7.2 Hz, 2H), 7.43 (d, *J* = 1.8 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 14.6 Hz, 1H), 7.30 (d, *J* = 4.2 Hz, 1H), 7.12 (t, *J* = 6.0 Hz, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 6.88 (t, *J* = 4.8 Hz, 1H), 6.76 (t, *J* = 4.8 Hz, 1H), 6.19 (d, *J* = 10.2 Hz, 1H), 6.05 (d, *J* = 10.8 Hz, 1H), 5.41-5.33 (m, 3H), 4.74 (dd, *J* = 10.2, 5.4 Hz, 1H), 4.67 (t, *J* = 9.6 Hz, 1H), 4.07 (q, *J* = 10.8 Hz, 1H), 3.23-3.17 (m, 1H), 2.82 (dd, *J* = 15.6, 9.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.9, 158.0, 139.6, 136.3, 133.1, 132.2, 130.3, 128.7, 128.5, 128.4, 128.2, 127.9, 127.5, 127.5, 126.6, 124.0, 123.1, 113.0, 112.5, 67.8, 60.9, 52.2, 42.0, 28.9; FT-IR (KBr) 3130, 1702, 1616, 1577, 1551, 1400, 1288, 1215, 1138 cm^{-1}; HRMS (ESI) calcd for $[C_{30}H_{24}N_4O_2+H]^+$ 473.1972, found 473.1980.



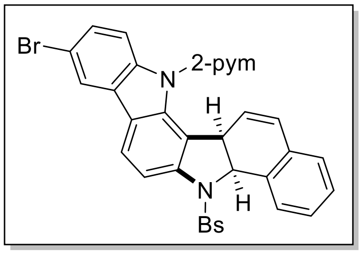
***tert*-Butyl-1-(pyrimidin-2-yl)-2,3,6a,12a-tetrahydrobenzo[*a*]pyrrolo[2,3-*g*]carbazole-6(1*H*)-carboxylate 3ad.** Brown solid; yield 63% (69 mg); mp 137-138 °C; R_f = 0.27 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 4.8 Hz, 2H), 7.50 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 7.19-7.15 (m, 1H), 7.11 (t, *J* = 6.8 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.88-6.86 (m, 1H), 6.76 (t, *J* = 4.8 Hz, 1H), 6.19 (d, *J* = 10.0 Hz, 1H), 5.99 (d, *J* = 10.4 Hz, 1H), 5.35 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.73 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.70-4.65 (m, 1H), 4.11-4.03 (m, 1H), 3.24-3.15 (m, 1H), 2.81 (dd, *J* = 15.6, 8.8 Hz, 1H), 1.63 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.9, 158.0, 153.7, 141.9, 139.6, 133.8, 132.3, 129.8, 128.2, 127.7, 127.5, 127.4, 126.6, 124.1, 123.3, 122.9, 113.2, 112.5, 81.3, 60.5, 52.3, 41.9, 29.0, 28.7. FT-IR (neat) 3130, 1694, 1616, 1577, 1551, 1460, 1400, 1302, 1257, 1148 cm^{-1}; HRMS (ESI) calcd for $[C_{27}H_{26}N_4O_2+H]^+$ 439.2129, found 439.2141.



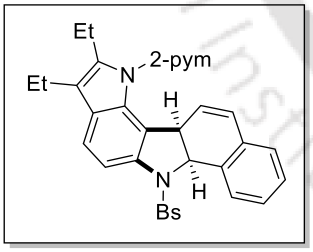
5-((4-Bromophenyl)sulfonyl)-12-(pyrimidin-2-yl)-4b,5,12,12c-tetrahydrobenzo[*a*]indolo-[2,3-*g*]carbazole 5a. Brown solid; yield 47% (71 mg); mp 154-155 °C; R_f = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 4.8 Hz, 2H), 8.51 (d, *J* = 8.4 Hz, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.95 (t, *J* = 6.4 Hz, 2H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.46-7.42 (m, 3H), 7.35-7.27 (m, 2H), 7.15 (t, *J* = 4.8 Hz, 1H), 7.10 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 6.06 (d, *J* = 10.0 Hz, 1H), 5.70 (d, *J* = 10.0 Hz, 1H), 4.51 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.64 (dd, *J* = 9.6, 5.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.3, 158.3, 141.1, 140.5, 135.9, 135.4, 132.3, 131.4, 131.1, 128.9, 128.6, 128.12, 128.05, 127.9, 126.9, 126.6, 126.1, 125.7, 123.7, 122.9, 121.5, 119.6, 119.2, 117.4, 116.2, 114.0, 63.5, 41.5; FT-IR (KBr) 3128, 1572, 1400, 1208, 1170, 1087 cm^{-1}. HRMS (ESI) calcd for $[C_{32}H_{21}BrN_4O_2S+H]^+$ 605.0641, found 605.0656.



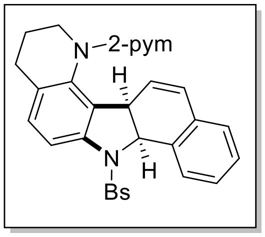
Bis-5,5'-((4-bromophenyl)sulfonyl)-8-(pyrimidine-2-yl)-4b,4'b,8c,8'c-tetrahydrobenzo[*a*]-indolo-[2,3-*g*]dicarbazole 5a'. Colorless solid; yield 18% (43 mg); mp 205-206 °C; R_f = 0.25 (1:9 ethyl acetate/hexane); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 4.8 Hz, 2H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 4H), 7.48 (d, *J* = 8.4 Hz, 4H), 7.25 (d, *J* = 7.8 Hz, 2H), 7.11 (t, *J* = 7.8 Hz, 2H), 7.01 (t, *J* = 4.8 Hz, 1H), 6.82 (d, *J* = 7.2 Hz, 2H), 6.18 (d, *J* = 10.2 Hz, 2H), 5.69 (dd, *J* = 10.2, 6.0 Hz, 2H), 5.65 (d, *J* = 10.2 Hz, 2H), 4.04 (dd, *J* = 9.6, 5.4 Hz, 2H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 160.9, 157.6, 140.8, 139.7, 136.7, 132.4, 131.6, 131.0, 129.1, 128.7, 128.6, 128.3, 128.0, 127.99, 127.93, 127.6, 126.7, 122.6, 118.8, 118.1, 115.8, 63.7, 43.0, 29.9; FT-IR (KBr) 3129, 1641, 1572, 1400, 1261, 1168, 1087 cm^{-1}; HRMS (ESI) calcd for $[C_{48}H_{31}Br_2N_5O_4S_2+H]^+$ 964.0257, found 964.0256.



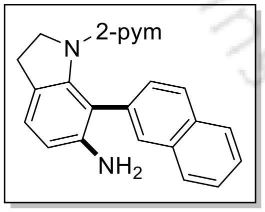
10-Bromo-5-((4-bromophenyl)sulfonyl)-12-(pyrimidin-2-yl)-4b, 5,12,12c-tetrahydro- benzo-[*a*]indolo[2,3-*g*]carbazole 5b. Colorless solid; yield 62% (106 mg); mp 178-179 °C; R_f = 0.29 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.8 Hz, 2H), 8.36 (d, *J* = 8.8 Hz, 1H), 8.08 (d, *J* = 2.0 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 1H), 7.90-7.87 (m, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.50 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 2H), 7.30-7.28 (m, 1H), 7.21 (t, *J* = 4.8 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.2 Hz, 1H), 6.05 (d, *J* = 10.0 Hz, 1H), 5.64 (d, *J* = 10.0 Hz, 1H), 4.43 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.58 (dd, *J* = 10.0, 5.6 Hz, 1H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 158.5, 158.2, 141.3, 139.9, 136.0, 135.8, 132.5, 131.3, 131.1, 129.6, 129.0, 128.9, 128.7, 128.4, 128.3, 128.0, 127.8, 126.7, 125.0, 124.0, 122.5, 121.2, 119.6, 117.7, 116.8, 116.1, 115.8, 63.6, 41.6, 29.8; FT-IR (KBr) 3129, 1622, 1567, 1400, 1210, 1169, 1086 cm^{-1}; HRMS (ESI) calcd for $[C_{32}H_{20}Br_2N_4O_2S+H]^+$ 682.9746, found 682.9746.



6-((4-Bromophenyl)sulfonyl)-2,3-diethyl-1-(pyrimidin-2-yl)-1,6,6a, 12a-tetrahydrobenzo [*a*]-pyrrolo[2,3-*g*]carbazole 5c. Yellow solid; yield 65% (99 mg); mp 147-148 °C; R_f = 0.29 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.8 Hz, 2H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.58-7.55 (m, 2H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H), 7.38-7.35 (m, 2H), 7.23 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.20 (t, *J* = 4.8 Hz, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 6.75 (d, *J* = 7.2 Hz, 1H), 5.99 (d, *J* = 10.0 Hz, 1H), 5.50 (d, *J* = 9.6 Hz, 1H), 3.95 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.23 (dd, *J* = 9.6, 5.6 Hz, 1H), 3.16-3.06 (m, 1H), 2.74-2.64 (m, 3H), 1.23 (t, *J* = 7.6 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 158.7, 140.3, 137.3, 136.2, 132.5, 132.4, 131.6, 131.3, 130.2, 129.0, 128.7, 128.6, 128.2, 128.1, 127.7, 126.5, 121.5, 118.17, 118.15, 117.7, 115.2, 63.5, 41.0, 19.0, 17.8, 15.5, 15.3; FT-IR (KBr) 3129, 1628, 1565, 1400, 1288, 1261, 1169, 1091, 1026 cm^{-1}; HRMS (ESI) calcd for [$C_{32}H_{27}BrN_4O_2S$+H]$^+$ 611.1111, found 611.1119.

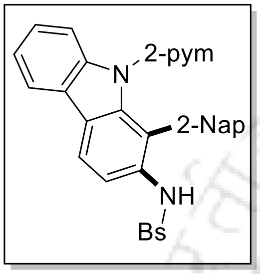


7-((4-Bromophenyl)sulfonyl)-1-(pyrimidin-2-yl)-2,3,4,7,7a,13a-hexahydro-1*H*-benzo[*a*]-pyrido[2,3-*g*]carbazole 5d. Yellow solid; yield 80% (114 mg); mp 167-168 °C; R$_f$ = 0.28 (1:9 ethyl acetate/hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 2H), 7. 94 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.28-7.24 (m, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.64 (t, *J* = 4.4 Hz, 1H), 6.14 (d, *J* = 10.0 Hz, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 5.05 (dd, *J* = 9.6, 5.6 Hz, 1H), 4.58-4.52 (m, 1H), 3.33 (dd, *J* = 10.0, 5.6 Hz, 1H), 3.27-3.20 (m, 1H), 2.76-2.61 (m 2H), 2.12-2.03 (m, 1H), 1.79-1.69 (m, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 160.4, 158.0, 139.5, 137.2, 136.5, 132.5, 132.38, 132.35, 131.83, 131.81, 128.9, 128.4, 128.3, 128.2, 127.8, 127.7, 127.0, 126.5, 122.4, 116.7, 111.9, 63.7, 45.0, 41.8, 27.0, 24.1; FT-IR (KBr) 3129, 1577, 1552, 1471, 1400, 1355, 1298, 1165, 1086 cm^{-1}; HRMS (ESI) calcd for [$C_{29}H_{23}BrN_4O_2S$+H]$^+$ 571.0798, found 571.0809.



7-(Naphthalen-2-yl)-1-(pyrimidin-2-yl)indolin-6-amine 6. To a stirred solution of *tert*-butyl-1-(pyrimidin-2-yl)-2,3,6a,12a-tetrahydrobenzo[*a*]pyrrolo[2,3-*g*]carbazole-6(1*H*) carbox -ylate **3ab** (0.25 mmol, 109.5 mg) in CH_2Cl_2, trifluoroacetic acid (0.75 mmol, 57 μL) was added at 0 °C. The resultant solution was stirred at room temperature for 1 h. After completion, as indicated by TLC, the reaction mixture was diluted with CH_2Cl_2 (15 mL). The mixture was successively washed with brine (2 x 5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford 7-(naphthalen-2-yl)-1-(pyrimidin-2-

yl)indolin-6-amine **6** as a brown solid. R$_f$ = 0.24 (1:9 ethyl acetate/hexane); yield 69% (58 mg); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.77 (d, *J* = 4.8 Hz, 2H), 7.74-7.68 (m, 4H), 7.50 (dd, *J* = 8.8, 1.6 Hz, 1H), 7.41-7.35 (m, 2H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.08 (t, *J* = 4.8 Hz, 1H), 4.39 (t, *J* = 8.0 Hz, 2H), 3.56 (br s, 2H), 3.07 (t, *J* = 8.0 Hz, 2H); ^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$) δ 159.2, 156.4, 143.7, 142.8, 135.9, 133.7, 132.2, 128.1, 128.0, 127.7, 127.6, 127.5, 125.7, 125.7, 124.8, 124.6, 116.8, 111.6, 110.9, 53.4, 29.3; FT-IR (KBr) 3128, 1617, 1576, 1550, 1401, 1278 cm^{-1}; HRMS (ESI) calcd for [$C_{22}H_{18}N_4$+H]$^+$ 339.1604, found 339.1606.



4-Bromo-*N*-(1-(naphthalen-2-yl)-9-(pyrimidin-2-yl)-9*H*-carbazol-2-yl) benzenesulfon- amide 7. To a stirred solution of **5a** (0.25 mmol, 151 mg) in DMSO (3 ml), NaOEt (1.5 mmol) in EtOH (0.2 mL) was added. The mixture was warmed up to 110 °C in a preheated oil bath and stirred for 2 h. The reaction mixture was cooled to room temperature and diluted with ethyl acetate (15 mL). The resultant mixture was washed with 2 N HCl (1 x 5 mL), brine (2 x 5 mL) and water (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford 4-bromo-*N*-(1-(naphthalen-2-yl)-9-(pyrimidin-2-yl)-9*H*-carbazol-2-yl)benzene sulfonamide **7** as a brown solid. R$_f$ = 0.32 (1:9 ethyl acetate/hexane); yield 76% (115 mg); mp 139-140 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.17 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 7.2 Hz, 1H), 7.99 (d, *J* = 4.8 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.74 (dd, *J* = 13.8, 7.8 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.51-7.48 (m, 1H), 7.47-7.43 (m, 2H), 7.42-7.39 (m, 1H), 7.37-7.35 (m, 1H), 7.16 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 3H), 6.96 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.80 (s, 1H), 6.33 (t, *J* = 4.8 Hz, 1H); ^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$) δ 157.4, 157.0, 141.1, 138.0, 137.8, 133.1, 132.10, 132.06, 131.93, 131.9, 128.6, 128.44, 128.40, 127.9, 127.8, 127.6, 126.7, 126.8, 126.6, 124.6, 124.0, 122.2, 120.7, 120.5, 120.2, 118.2, 117.0, 111.5; FT-IR (KBr) 3128, 2800, 1913, 1566, 1454, 1401, 1329, 1267, 1216, 1160, 1088, 1046 cm^{-1}; HRMS (ESI) calcd for [$C_{32}H_{21}BrN_4O_2S$+H]$^+$ 605.0641, found 605.0656.

Crystal Structure of 3t

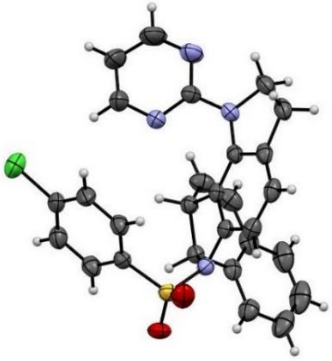


Figure 2. ORTEP diagram of **3t** (CCDC 1948984). H-Atoms omitted for clarity**.**

CCDC No.	1948984	
Identification code	**3t**	
Empirical formula	$C_{28} H_{22} Cl N_4 O_2 S$	
Formula weight	514.00	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 13.267(2) Å	a= 90°.
	b = 11.8390(19) Å	b= 110.301 (5)°.
	c = 16.549(3) Å	g = 90°.
Volume	2437.9(7) Å^3	
Z	4	
Density (calculated)	1.400 Mg/m^3	
Absorption coefficient	0.277 mm^{-1}	

F(000)	1068
Crystal size	0.164 x 0.07 x 0.04 mm^3
Theta range for data collection	1.637 to 24.99°.
Reflections collected	82680
Independent reflections	4267 [R(int) = 0.0926]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4267 / 0 / 325
Goodness-of-fit on F^2	1.098
Final R indices [I>2sigma(I)]	R1 = 0.0493, wR2 = 0.1047
R indices (all data)	R1 = 0.0687, wR2 = 0.1218

Crystal Structure of Rhodacycle Complex A

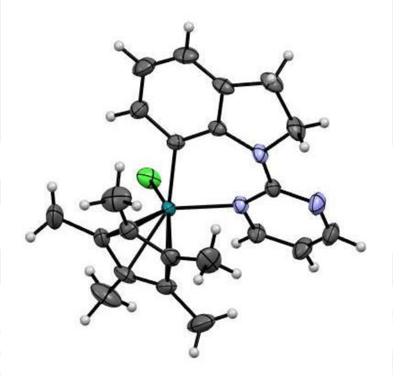


Figure 3. ORTEP diagram of **A** (CCDC 1948961).

CCDC No.	1948961
Identification code	**A**
Empirical formula	C_{22} H_{25} Cl N_3 Rh
Formula weight	469.81

Temperature	296 K	
Wavelength	0.71073Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.314(2) Å	a= 94.821(6)°.
	b = 10.671(3) Å	b= 91.645(6)°.
	c = 11.777(3) Å	g = 106.762(5)°.
Volume	995.4(4) Å^3	
Z	2	
Density (calculated)	1.567 Mg/m^3	
Absorption coefficient	1.004 mm^{-1}	
F(000)	480	
Crystal size	0.30 x 0.25 x 0.15 mm^3	
Theta range for data collection	1.738 to 28.809°.	
Reflections collected	45688	
Independent reflections	5099 [R(int) = 0.0430]	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5099 / 0 / 249	
Goodness-of-fit on F^2	0.872	
Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0970	
R indices (all data)	R1 = 0.0423, wR2 = 0.1084	

Crystal Structure of 7

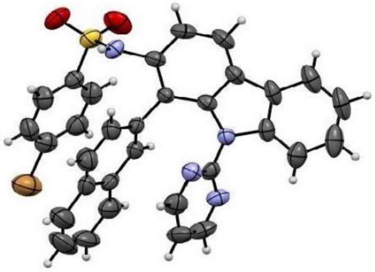


Figure 4. ORTEP diagram of **7** (CCDC 1951990).

CCDC No.	1951990	
Identification code	**7**	
Empirical formula	C_{32} H_{21} Br N_4 O_2 S	
Formula weight	605.49	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 2ac 2ab	
Unit cell dimensions	a = 11.0736(9) Å	a= 90°.
	b = 14.0744(11) Å	b= 90°.
	c = 17.6490(13) Å	g = 90°.
Volume	2750.7(4) $Å^3$	
Z	4	
Density (calculated)	1.462 Mg/m^3	
Absorption coefficient	1.608 mm^{-1}	

F(000)	1232
Crystal size	0.30 x 0.25 x 0.15 mm^3
Theta range for data collection	1.851 to 25.040°.
Reflections collected	113515
Independent reflections	4863 [R(int) = 0.2318]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4863 / 0 / 361
Goodness-of-fit on F^2	0.835
Final R indices [I>2sigma(I)]	R1 = 0.0416, wR2 = 0.0828
R indices (all data)	R1 = 0.1132, wR2 = 0.0984

3.5 References

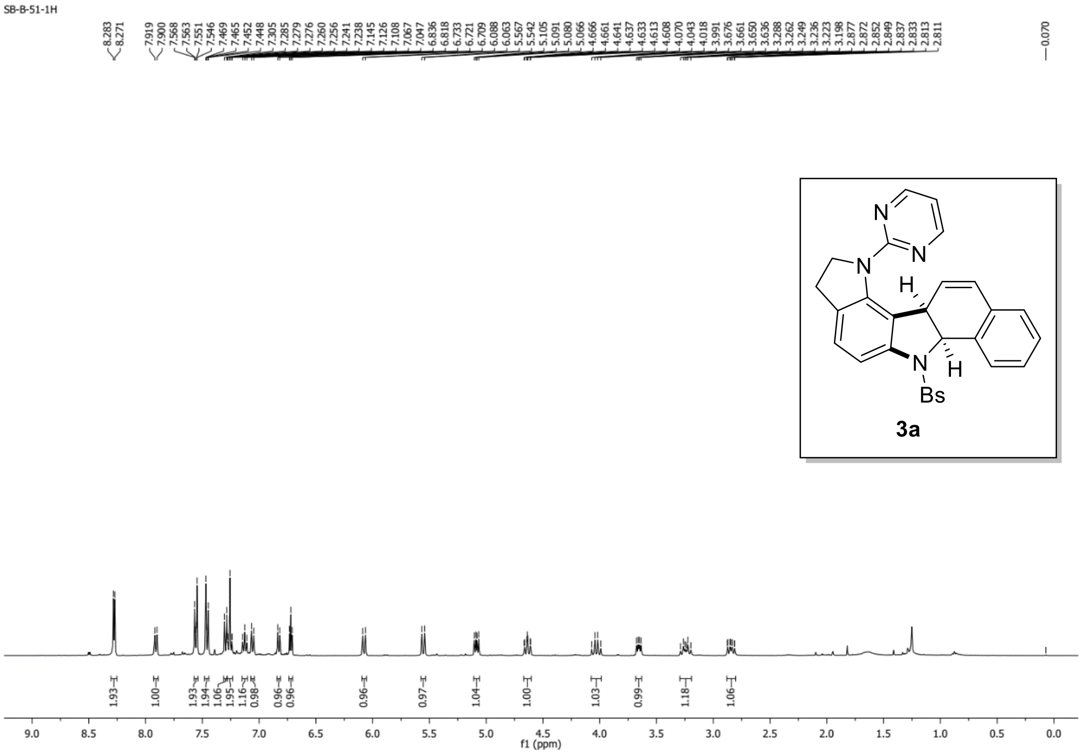
1. (a) Rej, S.; Chatani, N. *Angew. Chem. Int. Ed.* **2019**, *58*, 8304. (b) Xia, G.; Weng, J.; Liu, L.; Verma, P.; Li, Z.; Yu, J.-Q. *Nat. Chem.* **2019**, *11*, 571. (c) Lu, Q.; Mondal, S.; Cembellín, S.; Greßies, S.; Glorius, F. *Chem. Sci.* **2019**, *10*, 6560. (d) Zhang, J.; Jung, H.; Kim, D.; Park, S.; Chang, S. *Angew. Chem. Int. Ed.* **2019**, *58*, 7361. (e) Phipps, E. J. T.; Rovis, T. *J. Am. Chem. Soc.* **2019**, *141*, 6807. (f) Wen, J.; Wang, D.; Qian, J.; Wang, D.; Zhu, C.; Zhao, Y.; Shi, Z. *Angew. Chem. Int. Ed.* **2019**, *58*, 2078.
2. (a) Kaushik, N. K.; Kaushik, N.; Attri, P.; Kumar, N.; Kim, C. H.; Verma, A. K.; Choi, E. H. *Molecules* **2013**, *18*, 6620. (b) Lepri, S.; Buonerba, F.; Goracci, L.; Velilla, I.; Ruzziconi, R.; Schindler, B. D.; Seo, S. M.; Kaatz, G. W.; Cruciani, G. *J. Med. Chem.* **2016**, *59*, 867. (c) Singh, T. P.; Singh, O. M. *Mini-Rev. Med. Chem.* **2017**, *18*, 9.
3. (a) Steglich, W.; Steffan, B.; Kopanski, L.; Eckhardt, G. *Angew. Chem., Int. Ed.* **1980**, *19*, 459. (b) Meragelman, K. M.; West, L. M.; Northcote, P. T.; Pannell, L. K.; McKee, T. C.; Boyd, M. R. *J. Org. Chem.* **2002**, *67*, 6671. (c) Warabi, K.; Matsunaga, S.; van Soest, R. W. M.; Fusetani, N. *J. Org. Chem.* **2003**, *68*, 2765. (d) Russell, F.; Harmody, D.; McCarthy, P. J.; Pomponi, S. A.; Wright, A. E. *Asteropus. J. Nat. Prod.* **2013**, *76*, 1989.

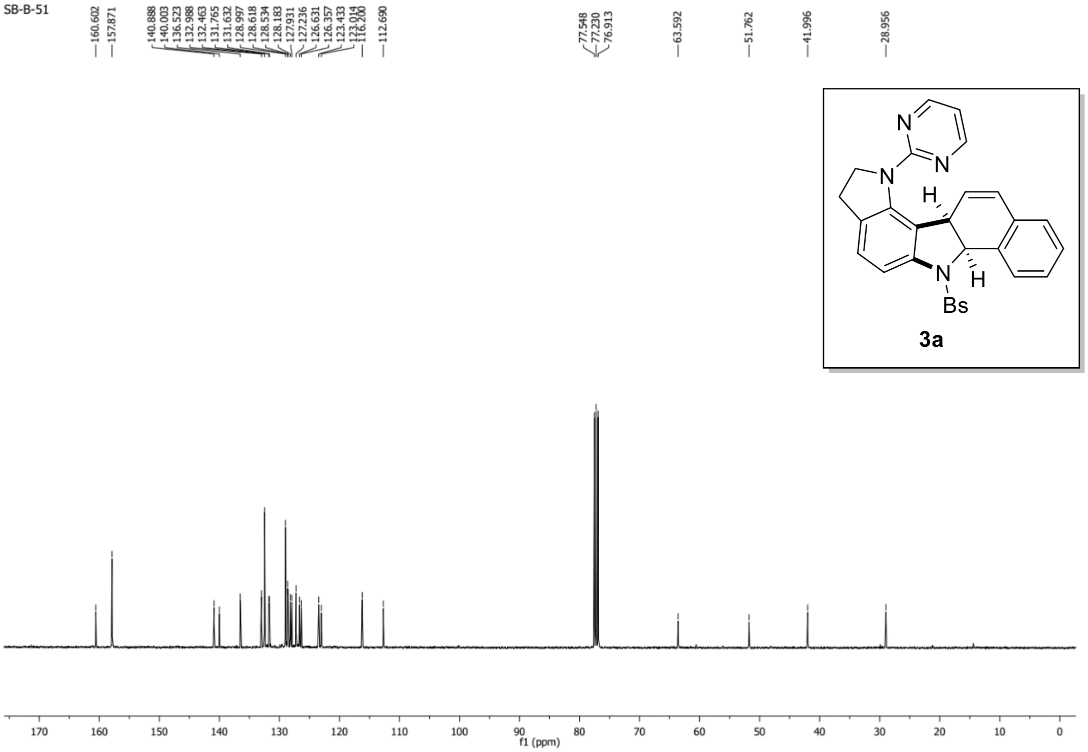
(e) Liu, D.-Q.; Mao, S.-C.; Zhang, H.-Y.; Yu, X.-Q.; Feng, M.-T.; Wang, B.; Feng, L.-H.; Guo, Y.-W. *Fitoterapia* **2013**, *91*, 15.

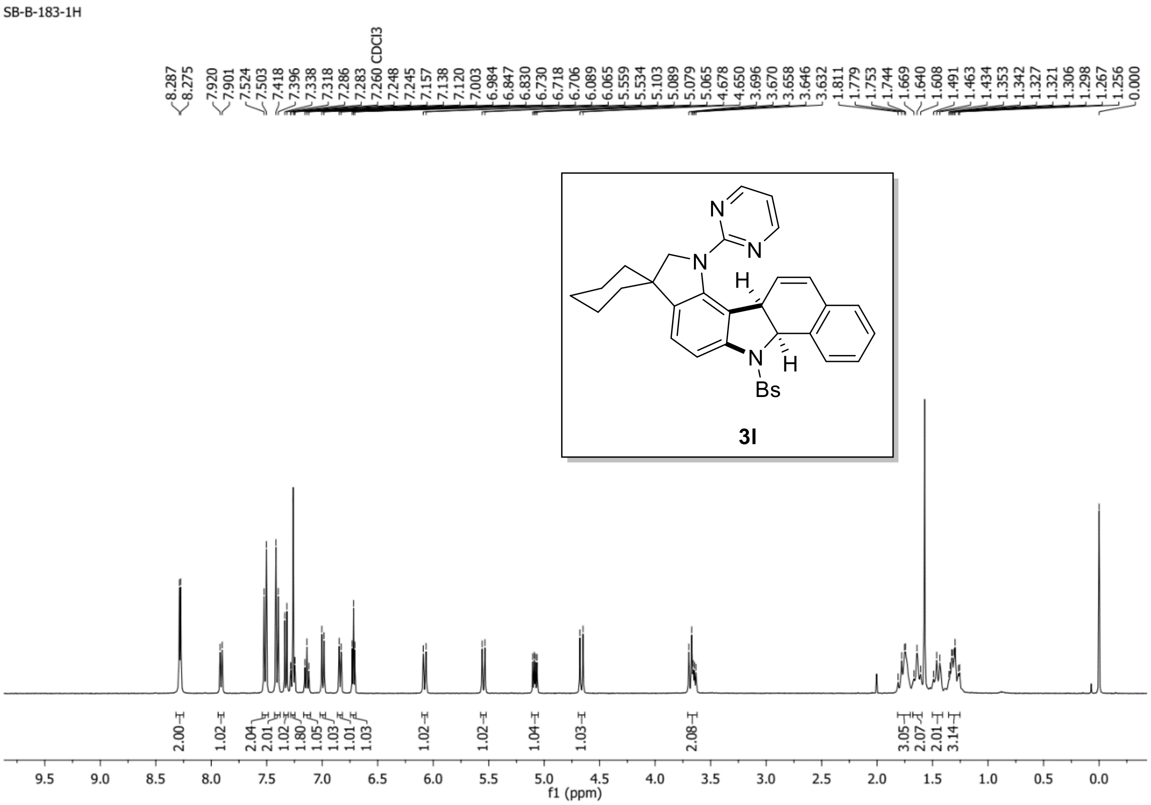
4. (a) Sánchez, C.; Méndez, C.; Salas, J. A. *Nat. Prod. Rep.* **2006**, *23*, 1007. (b) Fousteris, M. A.; Papakyriakou, A.; Koutsourea, A.; Manioudaki, M.; Lampropoulou, E.; Papadimitriou, E.; Spyroulias, G. A.; Nikolaropoulos, S. S. *J. Med. Chem.* **2008**, *51*, 1048. (c) Nakano, H.; Ōmura, S. *J. Antibiot.* **2009**, *62*, 17. (d) Lampropoulou, E.; Manioudaki, M.; Fousteris, M.; Koutsourea, A.; Nikolaropoulos, S.; Papadimitriou, E. *Pharmacother.* **2011**, *65*, 142. (e) Giraud, F.; Akué-Gédu, R.; Nauton, L.; Candelon, N.; Debiton, E.; Théry, V.; Anizon, F.; Moreau, P. *Eur. J. Med. Chem.* **2012**, *56*, 225.
5. 5. (a) Belletête, M.; Blouin, N.; Boudreault, P.-L. T.; Leclerc, M.; Durocher, G. *J. Phys. Chem. A* **2006**, *110*, 13696. (b) Lai, C.-C.; Huang, M.-J.; Chou, H.-H.; Liao, C.-Y.; Rajamalli, P.; Cheng, C.-H. *Adv. Funct. Mater.* **2015**, *25*, 5548. (c) Ohisa, S.; Takahashi, T.; Igarashi, M.; Fukuda, H.; Hikichi, T.; Komatsu, R.; Ueki, E.; Pu, Y.-J.; Chiba, T.; Kido, J. *Adv. Funct. Mater*. **2019**, *29*, 1808022.
6. (a) Tayu, M.; Nomura, K.; Kawachi, K.; Higuchi, K.; Saito, N.; Kawasaki, T. *Chemistry* **2017**, *23*, 10925. (b) Cabrero-Antonino, J. R.; Adam, R.; Junge, K.; Beller, M. *Chem. Sci.* **2017**, *8*, 6439. (c) Lu, Q.; Cembellín, S.; Greßies, S.; Singha, S.; Daniliuc, C. G.; Glorius, F. *Angew. Chem. Int. Ed.* **2018**, *57*, 1399
7. (a) Yang, Y.; Gao, P.; Zhao, Y.; Shi, Z. *Angew. Chem. Int. Ed.* **2017**, *56*, 3966. (b) Kalepu, J.; Gandeepan, P.; Ackermann, L.; Pilarski, L. T. *Chem. Sci*. **2018**, *9*, 4203. (c) Lv, J.; Wang, B.; Yuan, K.; Wang, Y.; Jia, Y. *Org. Lett.* **2017**, *19*, 3664.
8. (a) Qiu, X.; Deng, H.; Zhao, Y.; Shi, Z. *Sci. Adv*. **2018**, *4*, eaau6468. (b) Borah, A. J.; Shi, Z. *J. Am. Chem. Soc.* **2018**, *140*, 6062. (c) Shah, T. A.; De, P. B.; Pradhan, S.; Punniyamurthy, T. *Chem. Commun.* **2019**, *55*, 572. (d) Qiu, X.; Wang, P.; Wang, D.; Wang, M.; Yuan, Y.; Shi, Z. *Angew. Chem. Int. Edl.* **2019**, *58*, 1504. (e) Lv, J.; Chen, X.; Xue, X.-S.; Zhao, B.; Liang, Y.; Wang, M.; Jin, L.; Yuan, Y.; Han, Y.; Zhao, Y.; Lu, Y.; Zhao, J.; Sun, W.-Y.; Houk, K. N.; Shi, Z. *Nature* **2019**, *575*, 336.
9. (a) Bandini, M.; Eichholzer, A. *Angew. Chem. Int. Ed.* **2009**, *48*, 9608. (b) Sandtorv, A. H. *Adv. Synth. Catal.* **2015**, *357*, 2403. (c) Leitch, J. A.; Bhonoah, Y.; Frost, C. G. *ACS Catal.* **2017**, *7*, 5618. (d) Yang, Y.; Shi, Z. *Chem. Commun.* **2018**, *54*, 1676.

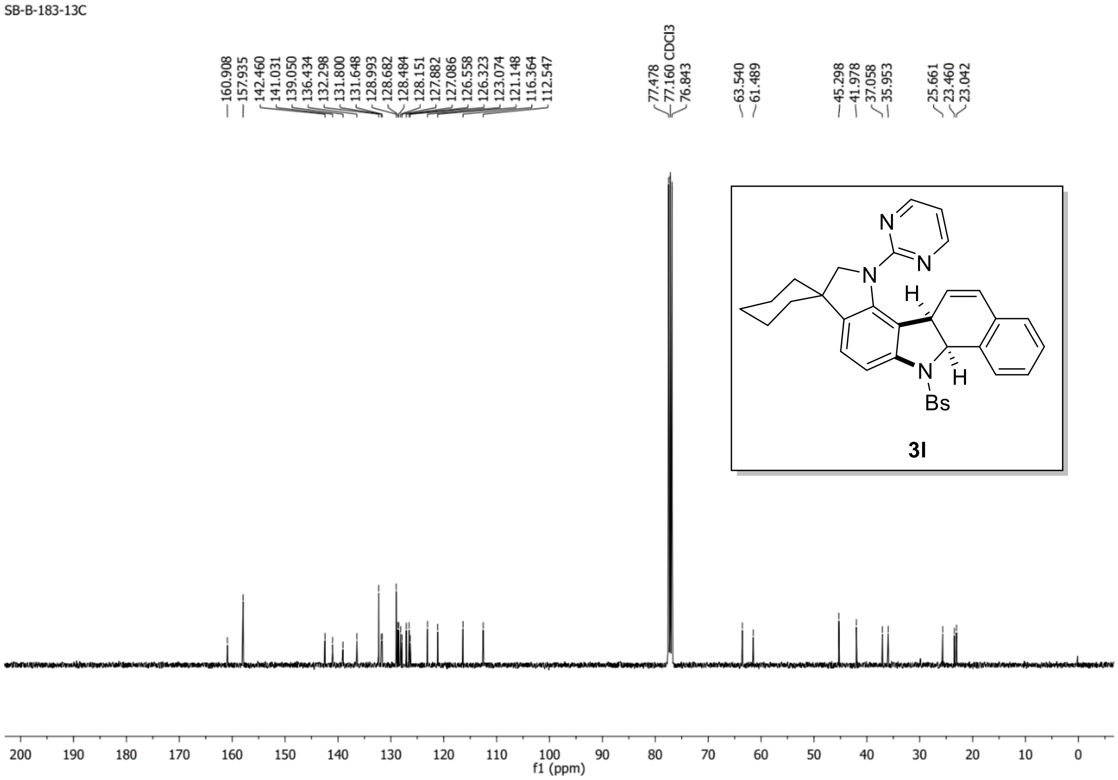
10. (a) Yang, G.; Lindovska, P.; Zhu, D.; Kim, J.; Wang, P.; Tang, R.-Y.; Movassaghi, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2014**, *136*, 10807. (b) Feng, Y.; Holte, D.; Zoller, J.; Umemiya, S.; Simke, L. R.; Baran, P. S. *J. Am. Chem. Soc.* **2015**, *137*, 10160. (c) Yang, Y.; Li, R.; Zhao, Y.; Zhao, D.; Shi, Z. *J. Am. Chem. Soc.* **2016**, *138*, 8734. (d) Leitch, J. A.; McMullin, C. L.; Mahon, M. F.; Bhonoah, Y.; Frost, C. G. *ACS Catal.* **2017**, *7*, 2616.
11. Qi, Z.; Li, X. *Angew. Chem. Int. Ed.* **2013**, *52*, 8995.
12. Wang, X.; Lerchen, A.; Gensch, T.; Knecht, T.; Daniliuc, C. G.; Glorius, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 1381.
13. Li, D.-Y.; Huang, Z.-L.; Liu, P.-N. *Org. Lett.* **2018**, *20*, 2028.
14. Mi, R.; Zheng, G.; Qi, Z.; Li, X. *Angew. Chem. Int. Ed.* **2019**, *58*, 17666.
15. Vivek Kumar, S.; Banerjee, S.; Punniyamurthy, T. *Org. Chem. Front.* **2019**, *6*, 3885.
16. Wang, P.; Xu, Y.; Sun, J.; Li, X. *Org. Lett.* **2019**, *21*, 8459.
17. Cheng, H.; Dong, W.; Dannenberg, C. A.; Dong, S.; Guo, Q.; Bolm, C. *ACS Catal.* **2015**, *5*, 2770.
18. Yan, Q.; Xiong, C.; Chu, S.; Liu, Z.; Zhang, Y. *J. Org. Chem.* **2018**, *83*, 5598.

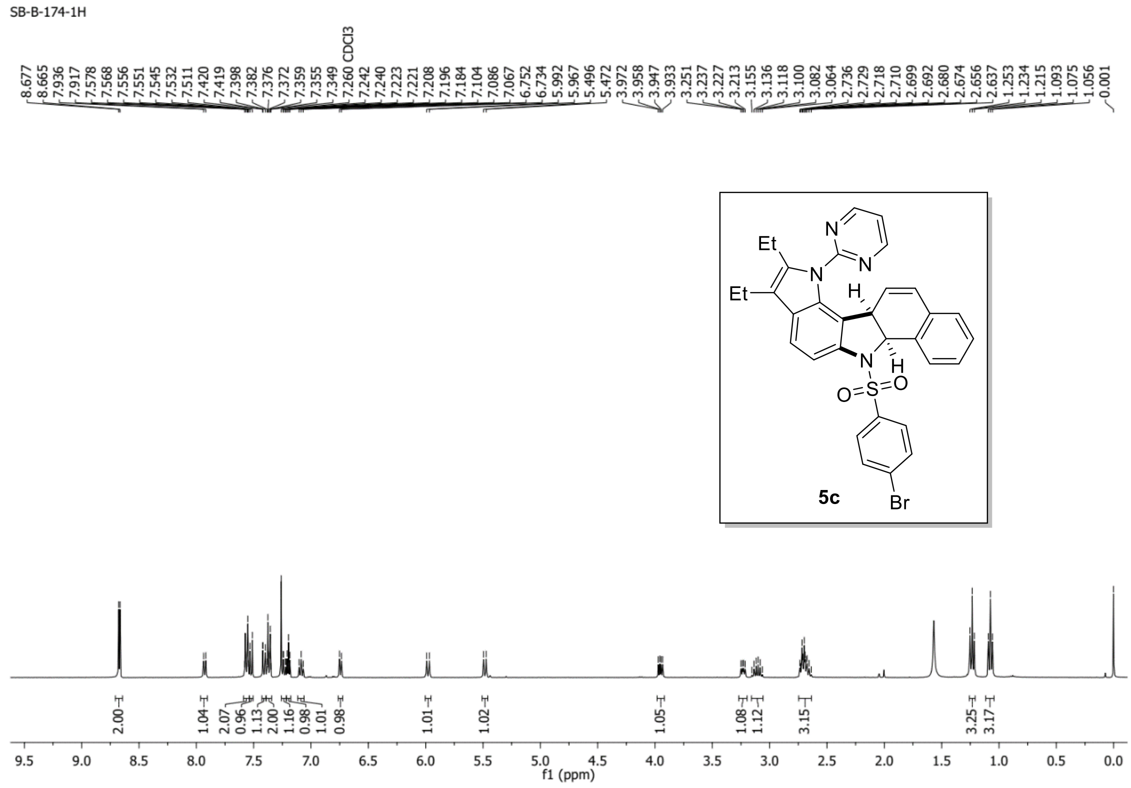
3.6 Selected NMR Spectra

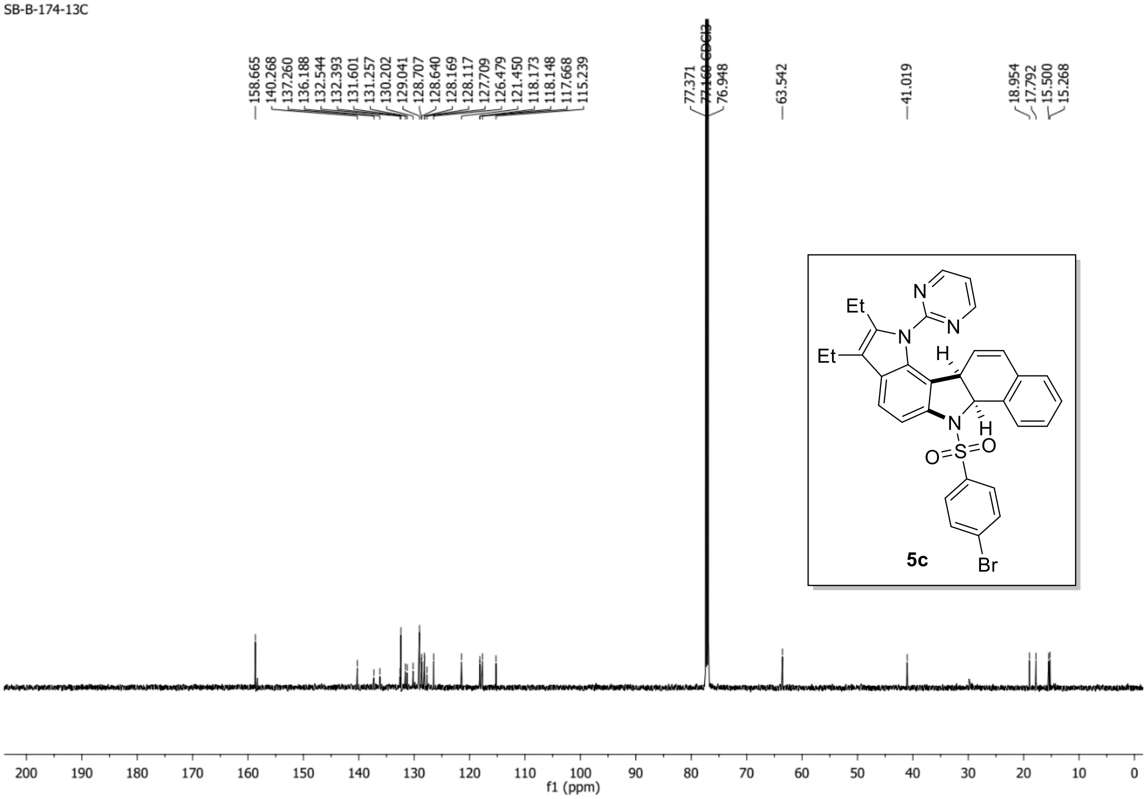





SB-B-183-1H
8.287
8.275
7.920
7.901
7.524
7.503
7.418
7.396
7.338
7.318
7.286
7.283
7.260 CDCl3
7.248
7.245
7.157
7.138
7.120
7.003
6.984
6.847
6.830
6.730
6.718
6.706
6.089
6.065
5.559
5.534
5.103
5.089
5.079
5.065
4.678
4.650
3.696
3.670
3.658
3.646
3.632
1.811
1.779
1.753
1.744
1.669
1.640
1.608
1.491
1.463
1.434
1.353
1.342
1.327
1.321
1.306
1.298
1.267
1.256
0.000
N
N
N
H
N
H
Bs
3l
2.00
1.02
2.04
2.01
1.02
1.80
1.05
1.03
1.01
1.03
1.02
1.02
1.04
1.03
2.08
3.05
2.07
2.01
3.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

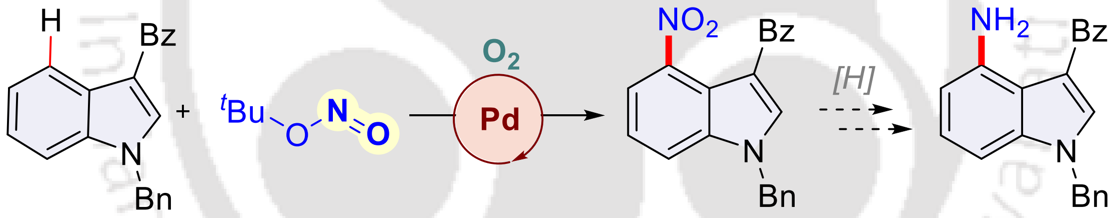

SB-B-183-13C
160.908
157.935
142.460
141.031
139.050
136.434
132.298
131.800
131.648
128.993
128.682
128.484
128.151
127.882
127.086
126.558
126.323
123.074
121.148
116.364
112.547
77.478
77.160 CDCl3
76.843
63.540
61.489
45.298
41.978
37.058
35.953
25.661
23.460
23.042
N
N
N
H
N
H
Bs
3l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


SB-B-174-1H
8.677
8.665
7.936
7.917
7.578
7.568
7.556
7.551
7.545
7.532
7.511
7.420
7.419
7.398
7.382
7.376
7.372
7.359
7.355
7.349
7.260 CDCl3
7.242
7.240
7.223
7.221
7.208
7.196
7.184
7.104
7.086
7.067
6.752
6.734
5.992
5.967
5.496
5.472
3.972
3.958
3.947
3.933
3.251
3.237
3.227
3.213
3.155
3.136
3.118
3.100
3.082
3.064
2.736
2.729
2.718
2.710
2.699
2.692
2.680
2.674
2.656
2.637
1.253
1.234
1.215
1.093
1.075
1.056
0.001
Et
Et
N
N
N
H
N
H
O
S
O
Br
5c
2.00
1.04
2.07
0.96
1.13
2.00
1.16
0.98
1.01
0.98
1.01
1.02
1.05
1.08
1.12
3.15
3.25
3.17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SB-B-174-13C
158.665
140.268
137.260
136.188
132.544
132.393
131.601
131.257
130.202
129.041
128.707
128.640
128.169
128.117
127.709
126.479
121.450
118.173
118.148
117.668
115.239
77.371
77.160 CDCl3
76.948
63.542
41.019
18.954
17.792
15.500
15.268
Et
Et
N
N
N
H
N
H
O
S
O
Br
5c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

Chapter IV

Regioselective Direct C4-Nitration of Indoles via Benzenoid C-H Activation under Aerobic Oxidation Catalysis: A Formal Access to Aminated Indoles



★ C4-Selectivity ★ Aerobic Radical Oxidation ★ Late-Stage Functionalization

Org. Lett. ***2024***, *26*, 988.

Regioselective Direct C4-Nitration of Indoles via Benzenoid C-H Activation under Aerobic Oxidation Catalysis: A Formal Access to Aminated Indoles

Indole, as a nitrogen containing heteroaromatic framework, is pervasive among a multitude of bioactive natural products, functional materials and is reckoned to be the fourth most dominant building subunit among currently marketed pharmaceuticals.[1] Among others, C4-aminated indoles exhibit a widespread application ranging from bioactive compounds to pesticides[2] and also serve as a starting precursor for teleocidins B-1−B-4.[2e] In this regard, selective C4 C-H activation of benzenoid nucleus of the indole moiety has attracted substantial research efforts among the available six C-H sites on the indole backbone.[3] Taking advantage of the innate nucleophilic nature of the pyrrolic type core extensive development of C2/C3 functionalization[4] has been witnessed in past years. In contrary, direct and selective activation of the inherently poor nucleophilic C4-site continues to be underdeveloped. Moreover, selective C4 activation in the presence of a bare C2 site imposes significant challenge in transition metal-catalysis. To mention, attaching a suitable directing group at the C3 site, a five-membered metallacycle at the C2 site is supposed to be more favorable as compared to the corresponding six-membered metallacycle at the C4 site. Keeping the associated challenges in mind direct C4 functionalization of indoles has been investigated by several groups to achieve mostly C-C coupling reactions,[5] whereas C-N bond coupling[6] reactions are scarcely reported. Driven by the potential implications of the C4-aminated indole derivatives it is desirable to develop a robust and efficient method that can enable versatile access to the aminated indoles. Nitro groups are multipurpose organic synthons in organic synthesis and can easily be modified into amino groups by virtue of simple organic transformations.[7] In recent years, *tert*-butyl nitrite (TBN) has been demonstrated as active radical reactants under aerobic Pd(II)/Pd(IV) catalysis to accomplish regioselective nitration of arenes.[8] In continuation of our efforts to encompass C4-selective activation of indoles, herein we report direct C4-selctive nitration of indoles harnessing a weakly coordinating benzoyl directing group[9] using simple and readily available *tert*-butyl nitrite as the radical precursor under oxygen atmosphere. The nitration is believed to proceed likely via oxidative oxidation of TBN to enable a Pd(II)/Pd(IV) catalysis under aerobic conditions. The nitro indoles can be efficiently transformed into invaluable amino indole scaffolds in high yields which may find broad utility in medicinal chemistry. The current method shows broad substrate scope with functional group diversity of different indoles, easy conversion to aminated indoles and diverse post-synthetic applications are the significant practical features.

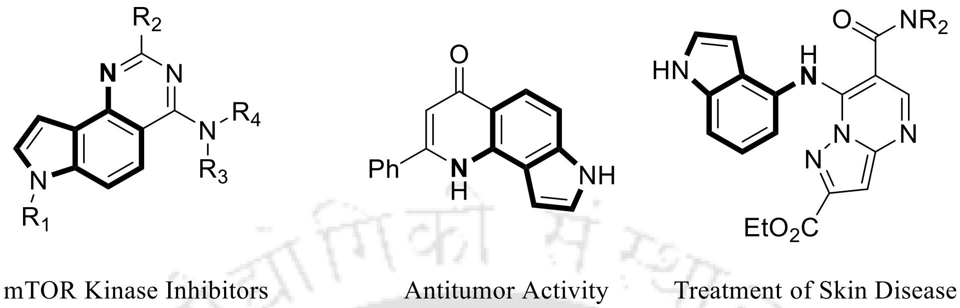
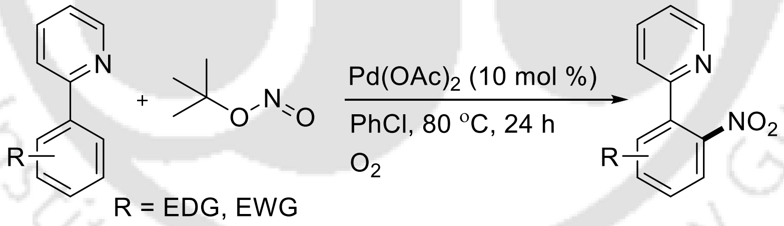


Figure 1. Examples of Biologically Active Aminated Indole Scaffolds.

4.1 Literature Study

4.1.1 Metal-Catalyzed Nitration with *tert*-Butyl Nitrite

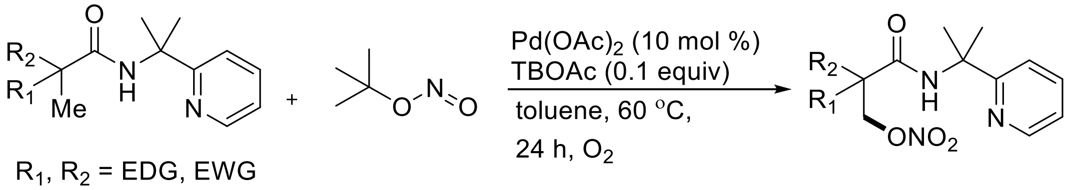
Jiao and co-workers reported Pd-catalyzed aerobic oxidative direct regioselective C-H nitration and acylation reactions with simple, inexpensive, and readily available *tert*-butyl nitrite (TBN) and toluene as the radical precursors (Scheme 1).[10] This nitration protocol exhibits excellent tolerance towards various directing groups, including pyridine, pyrimidine, pyrazole, pyridol, pyridylketone, oxime, and azo.



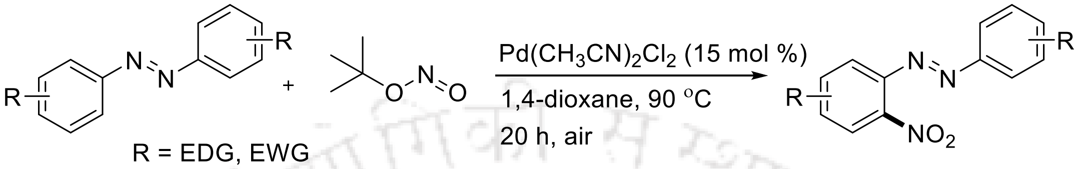
Scheme 1. Pd-Catalyzed Nitration of 2-Arylpyridines with TBN

Shi and co-workers described a Pd(II)-catalyzed nitrooxylation of unactivated C(sp^3)-H bonds using commercial available *tert*-butyl nitrite (TBN) as ONO_2 radical precursor (Scheme 2).[11] Environmentally benign oxygen is utilized as the terminal oxidant to initiate the generation of active radical reactants.

Ranu and co-workers developed an efficient procedure for the highly regioselective *ortho*-nitration of azoarenes by *tert*-butyl nitrite with a Pd-catalyzed directed C-H activation (Scheme 3).[12] Mild reaction condition, applicability to a wide range of diversely substituted azoarenes and excellent regioselectivity are the significant features of this protocol.

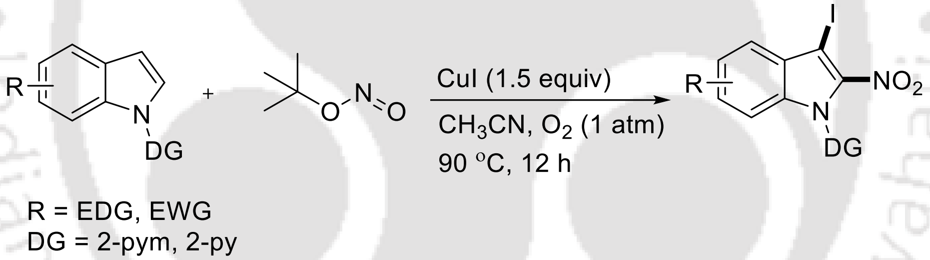


Scheme 2. Pd-Catalyzed C(sp^3)-H Nitrooxylation of Aliphatic Carboxamides with TBN



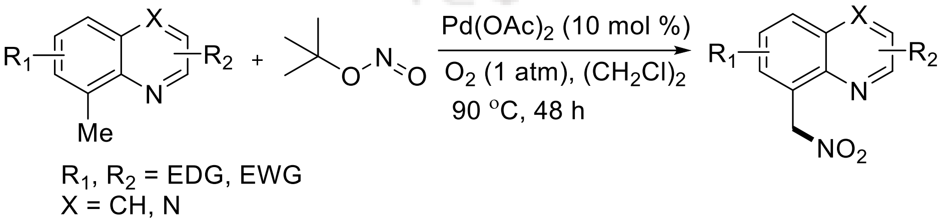
Scheme 3. Pd-catalyzed *ortho*-directed C-H nitration of azoarenes with TBN

Jiang and co-workers presented Cu-mediated aerobic oxidative C-H iodination and nitration of indoles through dual C-H functionalization which proceeds smoothly and regioselectively to give 3-iodo-2-nitroindoles (Scheme 4).[13] High regioselectivity, broad substrate scope, use of earth-abundant copper reagents, readily available nitro sources and aerobic oxidative conditions are the important findings of this strategy.



Scheme 4. Cu-Mediated Domino C-H Iodination and Nitration of Indoles with TBN

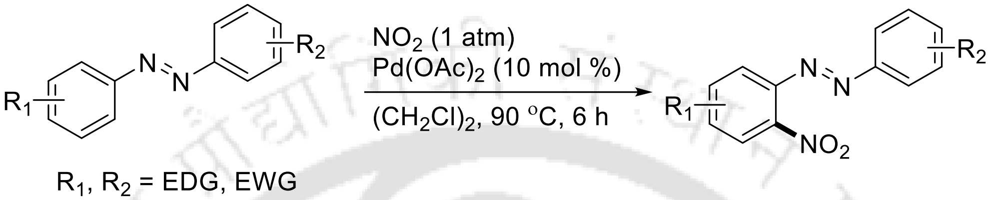
Liu and co-workers reported a Pd-catalyzed efficient and mild nitration of 8-methylquinolines with *t*-BuONO to give 8-(nitromethyl)quinolines in moderate to excellent yields, which involves sp^3 C-H bond activation (Scheme 5).[14] A wide range of functional groups with diverse electronic properties were found to be well tolerated.



Scheme 5. Palladium-Catalyzed sp^3 C-H Nitration with TBN

4.1.2 Pd-Catalyzed Nitration with NO_2 as Nitro Source

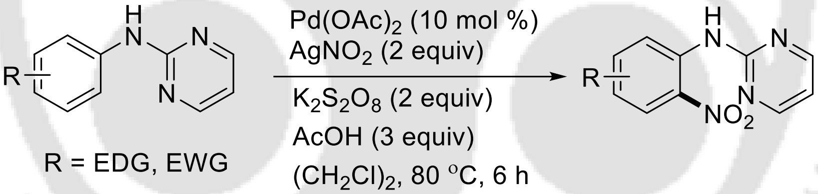
A palladium-catalyzed direct *ortho*-nitration reaction of azoarenes was developed by Sun and co-workers in which NO_2 was used as both nitro source and oxidant (Scheme 6).[15] The nitration products were converted into *o*-amino azoarenes or benzotriazole derivatives by a simple reduction and this protocol provided a convenient and atom-economic route for the syntheses of 2-nitroazoarenes and related compounds.



Scheme 6. Pd-Catalyzed Direct *ortho*-Nitration Using NO_2 as Nitro Source

4.1.3 Pd-Catalyzed Nitration with $AgNO_2$

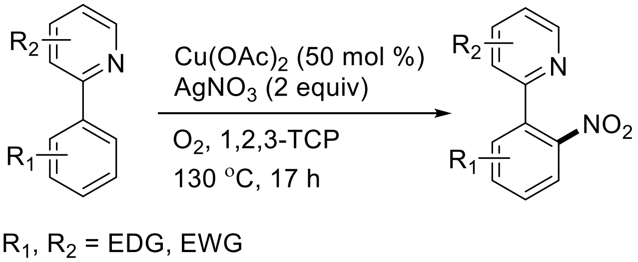
Kapur and co-workers described an efficient Pd- catalyzed direct C-H nitration of anilines with high levels of chemo- and regioselectivity by utilizing pyrimidine as a removable directing group (Scheme 7).[16] This methodology exhibits excellent tolerance to a wide range of functional groups, enabling the synthesis of diverse 2-nitroaniline derivatives in good to excellent yields.



Scheme 7. Pd(II)-Catalyzed Regioselective Nitration with $AgNO_2$

4.1.4 Cu-Catalyzed Nitration with $AgNO_3$

Liu and co-workers demonstrated copper-mediated chelation-assisted *ortho* C-H bond nitration of (hetero)-arenes using oxygen as a terminal oxidant, leading to the synthesis of nitroaromatics with excellent regioselectivity and in good yields (Scheme 8).[17]

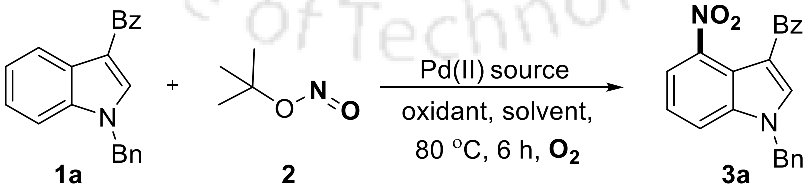


Scheme 8. Cu-Mediated Chelation-Assisted *ortho*-Nitration with $AgNO_3$

4.2 Present Study

Herein, a Pd(II)-catalyzed C4-selective nitration of indoles was developed leveraging weakly coordinating benzoyl directing group using *tert*-butyl nitrite with broad scope and functional group diversity. We initiated the optimization studies using (3-benzyl-1*H*-indol-1-yl)(phenyl)methanone **1a** and TBN as the nitration source, using various Pd sources, oxidants, and solvents at varied temperature (Table 1). To our delight, the C4-nitration product **3a** was obtained in 10% yield when the substrates were reacted in presence of $Pd(OAc)_2$ (10 mol %) and 1 equiv of $K_2S_2O_8$ in toluene at 80 °C for 6 h under oxygen atmosphere. Further solvent screening resulted in the improvement of yield of **3a** (48%) using $PhCF_3$, whereas, PhCl, CH_3CN, 1,2-DCE, MeOH and 1,4-dioxane yielded inferior yields of the desired product. This efficacy of $PhCF_3$ resides in its ability to dissolve a diverse array of organic compounds and its fluorinated nature might provide stability to the radical.[18] Subsequent examination of different oxidants led to produce the target product **3a** in 73% yield utilizing oxone (1 equiv). In contrast, oxidants such as hypervalent iodine reagents and Ag(I) sources delivered insufficient results. $Pd(OAc)_2$ was proven efficient in producing effective yields in comparison with other Pd-sources, such as, $PdCl_2$, $Pd(PPh_3)_2Cl_2$ and $Pd(CH_3CN)_2Cl_2$. In addition, substituting TBN with other nitro sources ($NaNO_3$, $AgNO_2$, $AgNO_3$, or isopentyl nitrite) significantly deteriorated the yield of nitration product. Moreover, addition of external additives (AcOH, PivOH and TFA) did not provide beneficial results. A control experiment was carried out under air, providing slightly diminished yield to **3a** (61%), while as one performed under an argon atmosphere yielded drastic results (22%), proving the essential role of aerobic (O_2) atmosphere. Likewise, in the absence of an oxidant or a Pd(II) catalyst either poor yield or no product formation was detected, respectively.

Table 1. Optimization of the Reaction Conditions*ᵃ*



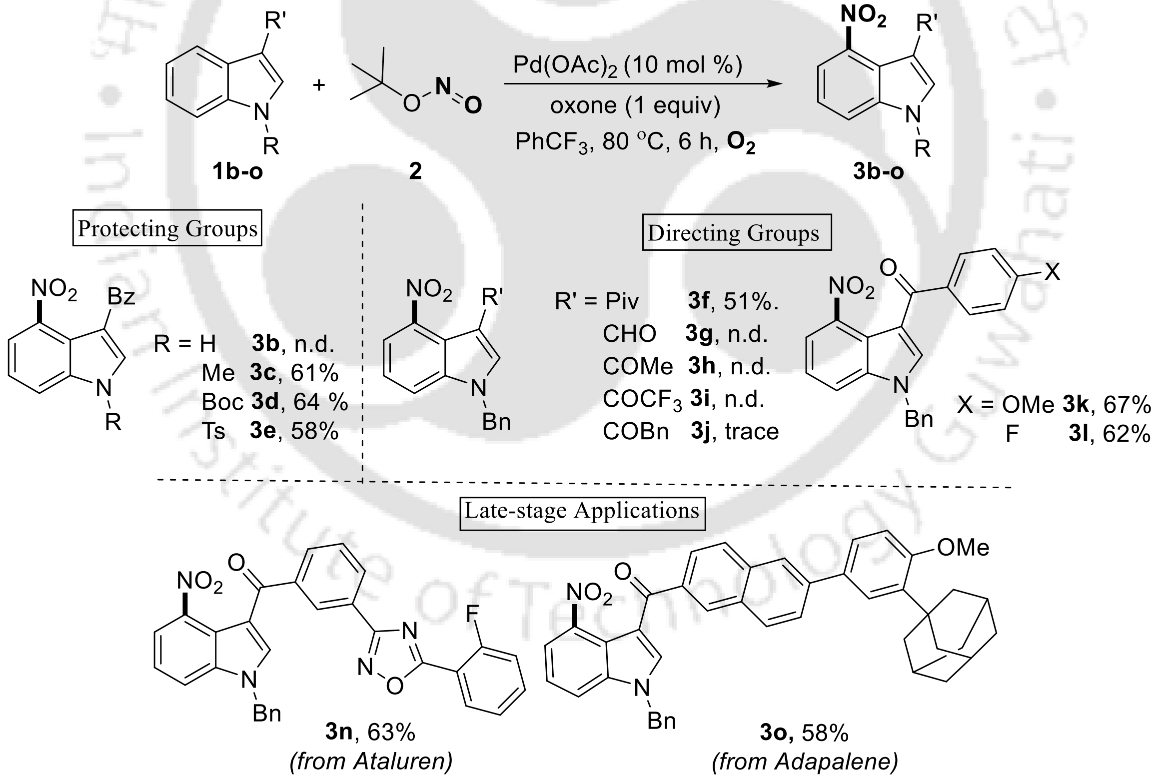
Entry	[Pd] source (10 mol %)	Oxidant	Additive	Nitro source	Solvent	Yield (%)^b
1.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	toluene	20

2.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	PhCl	trace
3.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	$PhCF_3$	58
4.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	CH_3CN	n.d.
5.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	$(CH_2Cl)_2$	n.d.
6.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	dioxane	n.d.
7.	$Pd(OAc)_2$	$K_2S_2O_8$	-	-	MeOH	41
8.	**$Pd(OAc)_2$**	**oxone**	-	-	**$PhCF_3$**	**73**
9.	$Pd(OAc)_2$	$PhI(OAc)_2$	-	-	$PhCF_3$	n.d.
10.	$Pd(OAc)_2$	$PhI(OCOCF_3)_2$	-	-	$PhCF_3$	n.d.
11.	$Pd(OAc)_2$	Ag_2CO_3	-	-	$PhCF_3$	49
12.	$Pd(OAc)_2$	AgOAc	-	-	$PhCF_3$	n.d.
13.	$PdCl_2$	oxone	-	-	$PhCF_3$	trace
14.	$Pd(PPh_3)_2Cl_2$	oxone	-	-	$PhCF_3$	trace
15.	$Pd(CH_3CN)_2Cl_2$	oxone	-	-	$PhCF_3$	n.d.
16..	$Pd(OAc)_2$	oxone	-	$NaNO_3$	$PhCF_3$	n.d.
17.	$Pd(OAc)_2$	oxone	-	$AgNO_2$	$PhCF_3$	24
18.	$Pd(OAc)_2$	oxone	-	$AgNO_3$	$PhCF_3$	n.d.
19.	$Pd(OAc)_2$	oxone	-	isopentyl nitrite	$PhCF_3$	n.d
20.	$Pd(OAc)_2$	oxone	AcOH	-	$PhCF_3$	n.d.
21.	$Pd(OAc)_2$	oxone	PivOH	-	$PhCF_3$	59
22.	$Pd(OAc)_2$	oxone	TFA	-	$PhCF_3$	n.d.

23.[c]	$Pd(OAc)_2$	oxone	-	-	$PhCF_3$	61
24.[d]	$Pd(OAc)_2$	oxone	-	-	$PhCF_3$	22
25.	-	oxone	-	-	$PhCF_3$	n.d.
26.	$Pd(OAc)_2$	-	-	-	$PhCF_3$	37
27.[e]	$Pd(OAc)_2$	oxone	-	-	$PhCF_3$	53
28.[f]	$Pd(OAc)_2$	oxone	-	-	$PhCF_3$	63

[a]Reaction Conditions: **1a** (0.1 mmol), **2** (0.12 mmol), $Pd(OAc)_2$ (10 mol %), oxidant (0.1 mmol), additive (50 mol %), solvent (1 mL), 80 °C, 6 h, O_2. [b]Isolated yield. [c]Under Air. [d]Under Ar atmosphere [e]Reaction at 60 °C. [f]Reaction at 120 °C. n.d.= not detected. Bz = benzoyl.

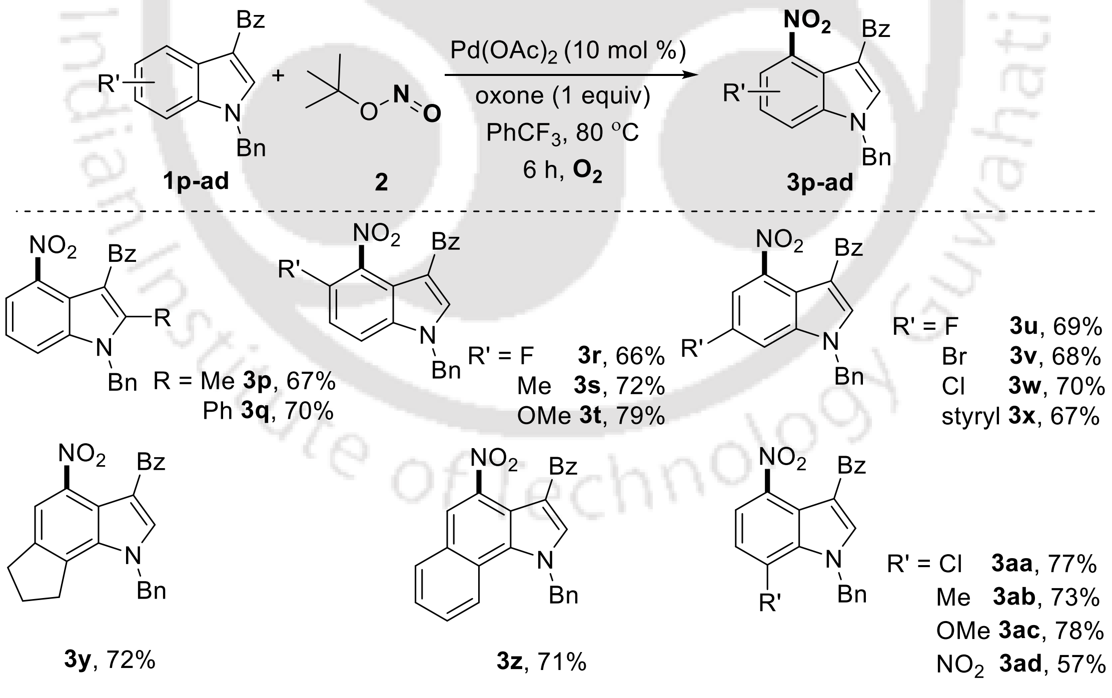
Table 2. Effect of *N*-Protecting and Directing Groups[a,b]



[a]Reaction conditions: **1b-o** (0.2 mmol), **2** (0.24 mmol), $Pd(OAc)_2$ (10 mol %), oxone (0.2 mmol), $PhCF_3$ (2 mL), 80 °C, 6 h, O_2. [b]Isolated yield. n.d. = not detected. Bz = benzoyl.

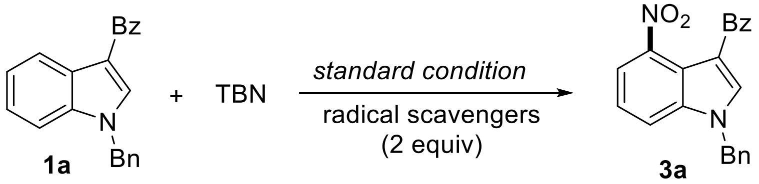
Having identified the optimized reaction conditions for selective C4-nitration we first examined the effect of few synthetically useful *N*-protecting and C3-attached directing groups (Table 2). Nitration of the unprotected indole substrate **1b** was unsuccessful which may be due to unwanted chelation of the NH group with Pd catalyst. On the other, substrates bearing Me (**1c**), Boc (**1d**) and tosyl (**1e**) protecting groups underwent reaction to afford nitrated products **3c-e**, in 58-64% yields, respectively. Directing groups, such as, pivaloyl (**1f**) conveyed moderate reactivity, whereas formyl **1g**, acetyl **1h,** trifluoroacetyl **1i** and benzylcarbonyl **1j** exhibited no nitration. These results showed that chelating effects of C3-carbonyl groups is critical for effective nitration. To highlight the benzoyl directing effect, substrates bearing 4-methyl and 4-fluro benzoyl groups at C3-site produced similar results as that of **1a**, giving **3k** and **3l** in 67% and 62 % yields, respectively and the latter produced a single crystal, whose structure was determined using X-ray analysis (Figure 2). To demonstrate late-stage synthetic utility of our method, selective C4-nitration of indoles derived from bio-active acids ataluren and adapalene **1n-o** was achieved to furnish **3n** and **3o** in 63% and 58% yields, respectively.

Table 3. Substrate Scope of Indoles[a,b]



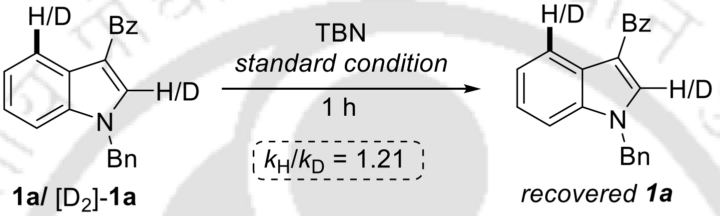
[a]Reaction conditions: **1p-ad** (0.2 mmol), **2** (0.24 mmol), Pd(OAc)$_2$ (10 mol %), oxone (0.2 mmol), PhCF$_3$ (2 mL), 80 °C, 6 h, O$_2$. [b]Isolated yield. Bz = benzoyl.

(a) Radical Scavenger Experiments

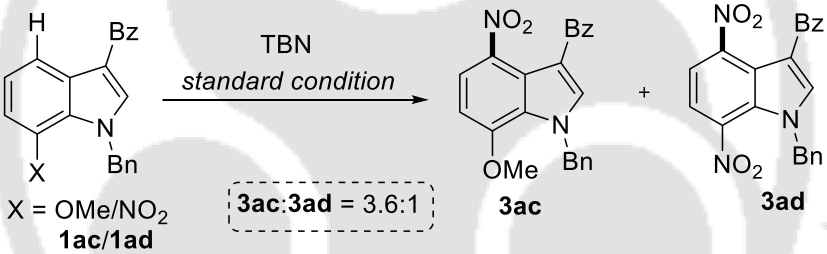


radical scavengers	yield of **3a**
TEMPO	n.d.
BHT	n.d.

(b) Kinetic Isotope Experiment

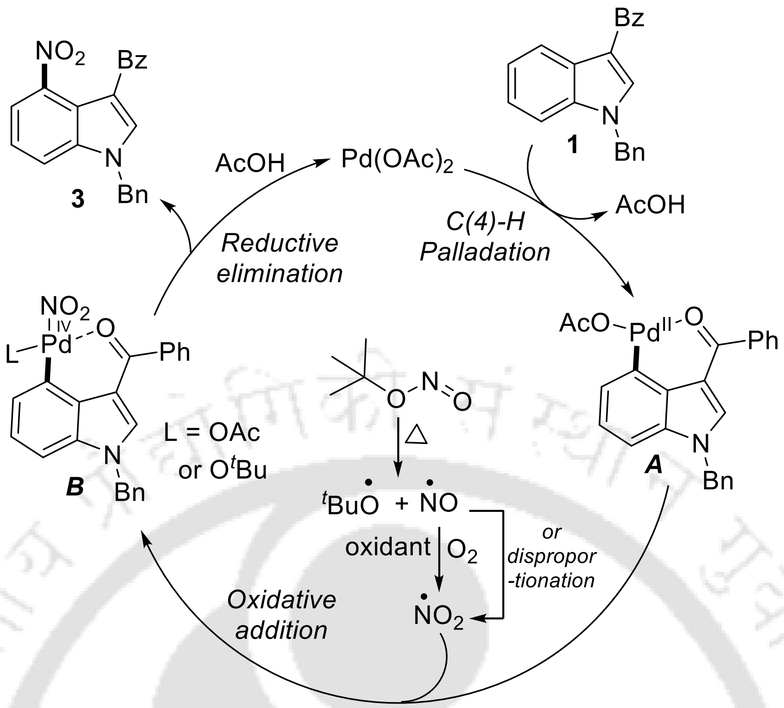


(c) Intermolecular Competitive Experiment



Scheme 9. Preliminary Mechanistic Investigations

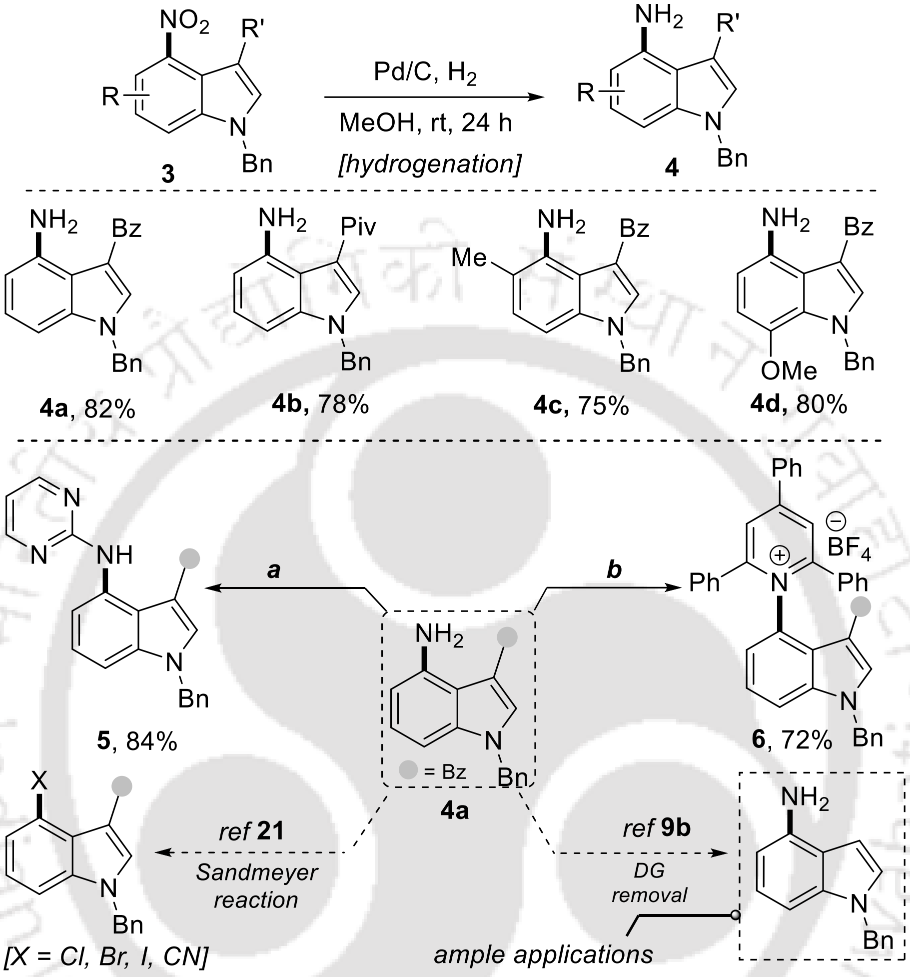
Next, we set out to extend the substrate scope of nitration using a series of substituted indoles **1p-ad** with TBN under optimal reaction conditions (Table 3). Substrates bearing methyl (**1p**) and phenyl (**1q**) substituents at the position C2 successfully afforded nitrated indoles **3p-q**, respectively, in 67-70% yields. However, the reaction of 5-fluoro (**1r**), 5-methyl (**1s**) and 5-methoxy (1t) substituted indole occurred to furnish 3r-t in 66-72% yields. The substrates bearing substitution at the C6-position with fluoro (**1u**), bromo (**1v**), chloro (**1w**) and styryl (**1x**) groups coupled to afford **3u-x** in 67-70% yields, whereas the fused indoles **1y** and **1z** were amenable, affording **3y** and **3z** in 72% and 71% yields, respectively. Further, indole containing substitution at the C7-position chloro (**1aa**), methyl (**1ab**), methoxy (**1ac**) and nitro (**1ad**) underwent nitration to provide **3aa-ad** in 57-77% yields.



Scheme 10. Proposed Catalytic Cycle

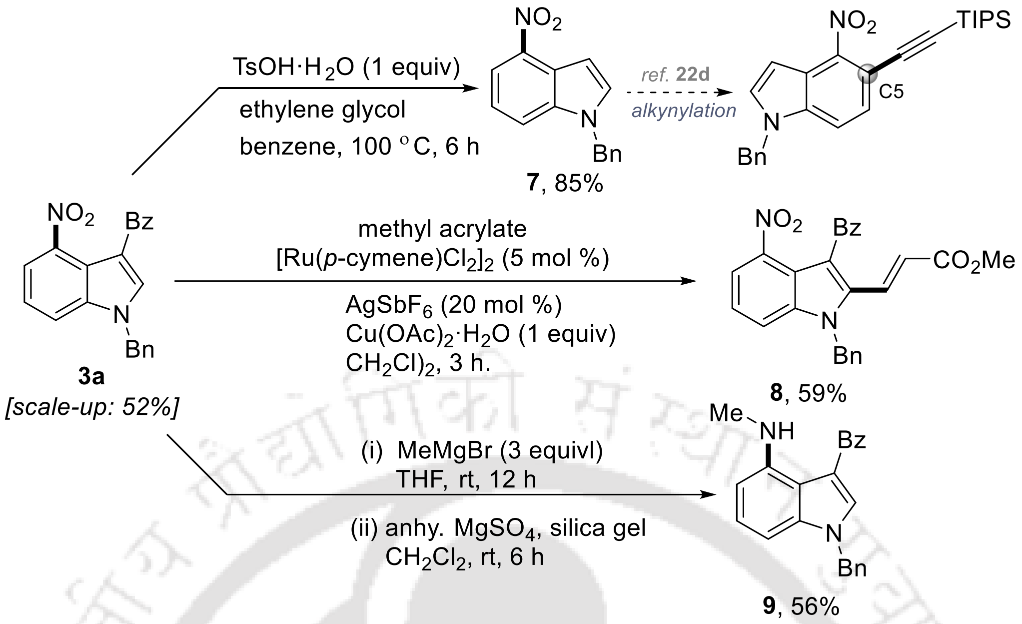
To gain insight into the reaction pathway, we performed the reaction of **1a** and **2** independently in the presence of 2,2,6,6-tetramethylpiperidine1-oxyl (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) as radical scavengers (Scheme 9a). The product formation was completely inhibited which suggested that radical process might be involved in this transformation. The H/D exchange experiments using either D_2O, CD_3COOD or CD_3OD as co-solvents indicated no H/D scrambling at C4 or C2 position of **1a**, revealing that the initial C-H bond cleavage step is irreversible in nature.[9b] Furthermore, the intermolecular kinetic isotope reactions using **1a** and [D_2]-**1a** under standard conditions produced a k_H/k_D of 1.21, implying that the C−H bond cleavage might not be involved in the rate-determining step (Scheme 9b). In addition, competitive experiments between electronically differentiated indoles bearing 7- methoxy **1ac** and 7-nitro **1ad** groups produced **3ac** and **3ad** in a ratio of 3.6:1, which indicates that the substrates containing an electron-donating group exhibited greater reactivity compared to that having an electron-withdrawing group thus an electrophilic C(4)-H palladation might be feasible under optimal conditions (Scheme 9c).

Table 4. Efficient Access to Aminoindoles and their Applications[a,b]



[a]Reaction conditions: **3** (0.1 mmol), Pd/C, MeOH (1 mL), H_2, rt, 24 h. (***a***) **4a** (0.075 mmol), 2-chloropyrimidine (0.05 mmol), AcOH (50 μL), 1,4-dioxane (150 μL), 110 °C, 10 h. (***b***) **4a** (0.12 mmol), 2,4,6-Triphenylpyrylium tetrafluoroborate (0.1 mmol), EtOH (1 mL), 90 °C, 4 h [b]Isolated yield. Bz = benzoyl.

In accordance with the experimental mechanistic studies and literature precedents[8,10,11] a plausible mechanistic pathway is depicted in scheme 5. Initial, directed C(sp^2)-H activation at C4- site of **1** may take place *via* the formation of six-membered palladacycle intermediate ***A*** via electrophilic metallation. TBN may undergo a homolytic cleavage upon heating, producing ^{t}BuO and NO radicals. Consequent oxidation of NO radical may take place either in presence of aerobic O_2 or external oxidant or a disproportionation may also take place in presence of O_2 to furnish active



Scheme 11. Post-synthetic Utility of Nitroindoles

NO_2 radical intermediate.[10] The imminent NO_2 and ^{t}BuO radicals can participate in radical oxidative addition to furnish Pd^{IV} intermediate ***B***.[10] Further, reductive elimination can lead to the formation of the target nitration product **3** along with the regeneration of active Pd^{II} catalyst to complete the catalytic cycle (Scheme 10).

After establishing the generality of the developed C4-selective nitration of indoles we were interested to convert them into their more valuable C4-amino analogues in an efficient way. To our delight, simple hydrogenation in the presence of Pd/C provided aminated indoles in high yields (Table 4). To mention, hydrogenation of nitro indoles **3a, 3f, 3s, 3ac** was performed under Pd/C in MeOH at room temperature to furnish amino indoles **4a-d** in good yields. One of the amino indoles, **4a** was further engaged in reaction with 2-chloropyrimidine to give **5** in excellent yield, such analogues are representative of biologically relevant indole-based scaffolds.[19] Likewise, treatment of **4a** with 2,4,6-triphenylpyrylium tetrafluoroborate produced a redox-active pyridinium salt **6**, that may find broad application in SET based (hetero)arylation reactions.[20] It is also notable to mention that, amino group can be further converted to other useful functional groups (e.g., Cl, Br, I, CN etc.) via Sandmeyer reaction.[21] After removal of the benzoyl DG, C4-aminated indoles may serve as invaluable building blocks in medicinal chemistry perceptive due to the facile transformation of the amino group into a diverse array of versatile functional moieties.[2]

To display practical utility of our nitration approach, we conducted a scale-up experiment employing 4 mmol of **1a** with TBN as the representative substrate (Scheme 11), yielding the target nitro product **3a** in 52% yield. Moreover, the benzoyl directing group could be efficiently removed using TsOH and ethylene glycol to provide **7** in 85% yield. In addition, Ru-catalyzed C2-alkenylation of **3a** was performed with methyl acrylate giving **8** in 59% yield. Moreover, sequential treatment of **3a** with MeMgBr followed $MgSO_4$/silica under mild reaction conditions provided amino alkylated indole **9** in 56% yield.[22a-c] Notably, the nitro group can also serve as a directing group, enabling C5-alkynylation through the utilization of Cp*Rh(III) catalyst and bromo-alkyne.[22d] These results demonstrate that diverse functional groups can be introduced across the different C-H sites of indole fragment.

In summary, we have developed a Pd-catalyzed site-selective C4-nitration of indoles, leveraging weakly coordinating benzoyl chelation using TBN as active radical reactant under aerobic conditions. The notable features of our findings include exclusive C4 site-selectivity, compatibility with various functional group, facile access to invaluable aminated indole scaffolds and late-stage natural product modifications.

4.3 Experimental Section

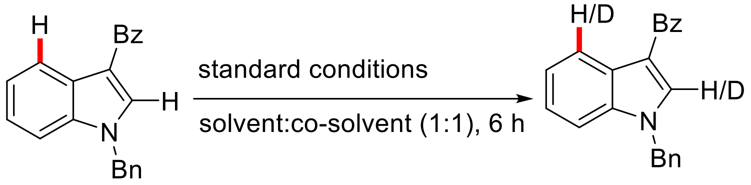
General Information. Indole (>99.0%), $[Pd(OAc)_2]_3$ (98%), $Pd(PPh_3)_2Cl_2$ (98%), $PdCl_2$ (>98%), OXONE®, monopersulfate compound, Ag_2CO_3 (99%), AgOAc (≥99.99%), $Na_2S_2O_8$ (≥98.0%), $AgNO_2$ (99%), $AgNO_3$ (≥99.0%), $NaNO_2$ (≥99.0%), $NaNO_3$ (≥99.0%), isopentyl nitrite (96%), $PhI(OAc)_2$ (98%), $PhI(OCOCF_3)_2$ (97%), $K_2S_2O_8$ (≥99.9%), HFIP (>99.0%) and α,α,α-trifluorotoluene (anhydrous, ≥99%) were purchased from Aldrich and TCI chemicals used as received. The solvents were dried prior to use according to the standard procedure. Merck silica gel G/GF254 plates were utilized for analytical thin-layer chromatography (TLC) with a mixture of *n*-hexane and EtOAc as the eluent. Rankem silica gel (60-120 mesh) was employed for column chromatography. Melting point of the products was measured on Büchi melting point apparatus, MPB-540. Open capillary tubes were used for the measurements and are uncorrected. NMR (^1H, ^{13}C and ^{19}F) spectra were recorded on Bruker 400, 500 and 600 MHz NMR instruments utilizing tetramethylsilane (Me_4Si) as an internal standard and $CDCl_3$ as a solvent. Mestrenova software was used throughout the spectral analysis. Chemical shifts (δ) and spin-spin coupling constant (*J*) are reported in parts per million and hertz (Hz), respectively, and other data are reported as follows: s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet and br s = broad singlet. Quadrupole time-of-flight electrospray ionization mass spectrometer (Agilent 6546) and Xevo XS mass spectrometer were used for recording HRMS. Fourier transform infrared attenuated total reflectance spectra (FTIR-ATR) was recorded using Perkin Elmer instrument. Single crystal X-ray data were collected on a Bruker SMART APEX equipped with a CCD area detector using Mo/-Kα radiation and the structure was solved by direct method using SHELXL-16 (Göttingen, Germany).

Substrates of indoles are prepared according to the reported procedure and *tert*-butyl nitrite (90%) of Sigma-Aldrich was utilized for the reactions as received.

General Procedure for Pd(II)-Catalyzed C4-Nitration of Indoles. A mixture of indole ***1*** (0.2 mmol), *tert*-butyl nitrite ***2*** (0.24 mmol, 1.2 equiv, 24.7 mg), $Pd(OAc)_2$ (10 mol %, 0.02 mmol, 4.5 mg) and oxone (0.2 mmol, 1 equiv, 61.4 mg) were stirred in α,α,α-trifluorotoluene (2 mL) at 80 °C in a preheated oil bath for 6 h under oxygen atmosphere. The progress of the reaction was monitored using TLC. After completion, the reaction mixture was cooled to room temperature and filtered through a short pad of celite using EtOAc (2 x 10 mL). Evaporation of the solvent gave a residue that was purified by silica gel column chromatography (*n*-hexane: EtOAc = 6:1) to afford C4-nitroindoles **3** in good to moderate yield.

Scale-up synthesis of 3a. A mixture of (1-Benzyl-1*H*-indol-3-yl)(phenyl)methanone **1a** (4 mmol, 1 equiv, 1245.5 mg), *tert*-Butyl nitrite **2** (4.8 mmol, 1.2 equiv, 495.0 mg), $Pd(OAc)_2$ (10 mol %, 0.4 mmol, 89.8 mg) and oxone (4 mmol, 1 equiv, 1229.2 mg) was stirred α,α,α-trifluorotoluene (25 mL) at 80 °C in a preheated oil bath for 6 h under oxygen atmosphere. Progress of the reaction was monitored by TLC using *n*-hexane and EtOAc as an eluent. The work up and purification were followed as described in the general procedure to give **3a** in 62% (882.9 mg) yield.

H/D-Exchange Experiments. To a stirred solution of (1-benzyl-1*H*-indol-3-yl)(phenyl)methanone *1a* (0.1 mmol, 31 mg), *tert*-butyl nitrite ***2*** (0.12 mmol, 1.2 equiv, 12.4 mg), $Pd(OAc)_2$ (10 mol %, 0.01 mmol, 2.3 mg), oxone (0.1 mmol, 1 equiv, 30.5 mg) were stirred in α,α,α-trifluorotoluene (0.5 mL) and deuterated solvent (D_2O, CD_3COOD or CD_3OD, 0.5 mL) were added. The reaction mixture was stirred at 90 °C in a preheated oil bath for 6 h under oxygen atmosphere. The resulting reaction mixture was cooled to room temperature and the purification was carried out according to the general procedure as described above. No deuterium incorporation was observed either at C4



Co-solvent	C2-H deuteration	C4-H deuteration
D_2O	no deuteration	no deuteration
CD_3COOD		
CD_3OD		

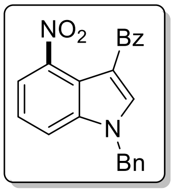
and C2 position of recovered **1a**, based on 400 MHz ^{1}H NMR spectrum.

Preparation of (1-benzyl-1*H*-indol-3-yl-2,4-d$_2$)(phenyl)methanone [D$_2$]-**1a**.[9b] The titled compound was prepared according to the reported procedure as a pale yellow solid in 85% yield (26.4 mg). The deuterium incorporation was determined using 400 MHz ^{1}H NMR as 91% at C4-H.

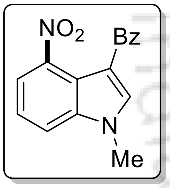
Kinetic Isotope Experiment. A mixture of of (1-benzyl-1*H*-indol-3yl)(phenyl)meth- anone *1a* (0.1 mmol, 1 equiv, 31.1 mg) and (1-benzyl-1*H*-indol-3-yl)(phenyl)methanone [D$_2$]-*1a* (0.1 mmol, 1 equiv, 31.5 mg) was reacted with *tert*-butyl nitrite ***2*** (0.24 mmol, 1.2 equiv, 24.7 mg) for 1 h under standard reaction conditions. The resulting mixture was diluted with EtOAc (10 mL) and passed through a short pad of celite using EtOAc (2 x 10 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and EtOAc as an eluent to afford [D$_1$]-**3a** and a mixture of unreacted **1a** and [D$_2$]-**1a** as a colorless solid. The intermolecular k_H/k_D was found to be 1.206 based on 400 MHz ^{1}H NMR of the recovered substrates **1a** and [D$_2$]-**1a**.

Intermolecular Competition Experiment Using Indoles 1ac and 1ad. (1-Benzyl-7-methoxy-1*H*-indol-3-yl)(phenyl)methanone **1ac** (0.1 mmol, 34.1 mg), (1-benzyl-7-nitro-1*H*-indol-3-yl)(phenyl)methanone **1ad** (0.1 mmol, 35.6 mg), *tert*-butyl nitrite ***2*** (0.24 mmol, 24.7 mg), $Pd(OAc)_2$ (10 mol %, 0.02 mmol, 4.5 mg) and oxone (0.2 mmol, 1 equiv, 61.4 mg) were stirred in α,α,α-trifluorotoluene (2 mL) at 90 °C in a preheated oil bath for 6 h under oxygen atmosphere. The reaction mixture was cooled to room temperature and filtered through a short pad of celite using EtOAc (2 x 10 mL). Evaporation of the solvent gave a residue that was purified by silica gel column chromatography (*n*-hexane: EtOAc = 6:1) to afford **3ac** and **3ad** in 3.6:1 ratio.

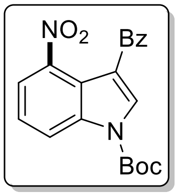
4.4 Characterization Data



(1-Benzyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3a. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.45$; brown solid; mp 119-120 °C; yield 73% (51.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 6.8 Hz, 2H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.68 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.35-7.30 (m, 4H), 7.15 (d, *J* = 6.0 Hz, 2H), 5.43 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 143.8, 139.0, 138.8, 137.4, 135.2, 132.6, 129.5, 129.3, 128.63, 128.56, 126.9, 122.8, 119.0, 118.4, 116.0, 115.7, 51.3; FT-IR (KBr) 2925, 1637, 1600, 1521, 1451, 1379, 1333, 1244, 1176, 1077 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{17}N_2O_3^+$: 357.1234, found: 357.1246.

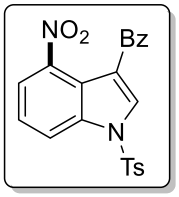


(1-Methyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3c. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.63$; yellow solid; mp 141-142 °C; yield 61% (34.2 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.61 (s, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.47-7.39 (m, 3H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.3, 143.8, 139.4, 139.3, 137.9, 132.5, 129.5, 128.6, 122.7, 118.8, 118.3, 115.8, 115.1, 34.0; FT-IR (KBr) 2925, 1713, 1635, 1521, 1455, 1372, 1334, 1240, 1144 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{16}H_{13}N_2O_3^+$: 281.0921, found: 281.0924.

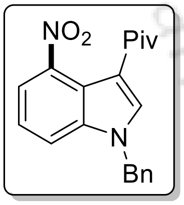


***tert*-Butyl 3-benzoyl-4-nitro-1*H*-indole-1-carboxylate 3d.** Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.41$; brown solid ; mp 174-175 °C; yield 64% (46.8 mg); ^{1}H

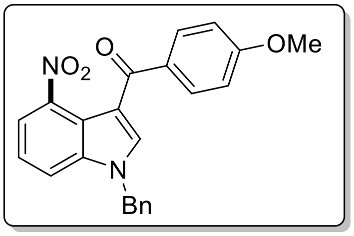
NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 8.0 Hz, 1H), 8.06 (s, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.0 Hz, 2H), 7.59 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 8.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 3H), 1.69 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.7, 148.6, 142.9, 138.1, 137.2, 133.4, 132.6, 129.5, 128.8, 125.1, 120.9, 120.1, 119.7, 86.2, 28.2; FT-IR (KBr) 2981, 2927, 1749, 1656, 1529, 1436, 1369, 1274, 1259, 1150, 1099 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{22}H_{19}N_2O_5^+$: 367.1288, found: 367.1286.



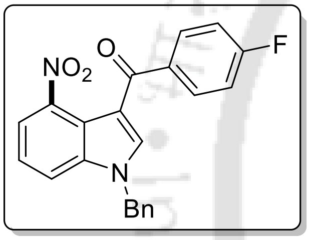
(4-Nitro-1-tosyl-1*H*-indol-3-yl)(phenyl)methanone 3e. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.52; yellow solid; mp 135-136 °C; yield 58% (48.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 8.0 Hz, 1H), 8.05 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 7.5 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H), 7.63 (t, J = 7.5 Hz, 1H), 7.54-7.48 (m, 3H), 7.32 (d, J = 8.5 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 146.8, 143.3, 137.6, 136.5, 134.1, 133.7, 132.7, 130.7, 129.7, 128.9, 127.4, 125.5, 121.3, 120.6, 120.5, 118.7, 21.8; FT-IR (KBr) 2925, 1766, 1655, 1596, 1528, 1447, 1338, 1217, 1191, 1174, 1146, 1086, 1032 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{22}H_{17}N_2O_5S^+$: 421.0853, found: 421.0851.



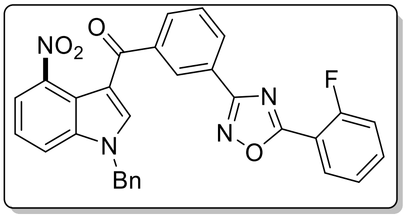
1-(1-Benzyl-4-nitro-1*H*-indol-3-yl)-2,2-dimethylpropan-1-one 3f. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.53; brown solid; mp 152-153 °C; yield 51% (34.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 7.6 Hz, 1H), 7.60 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.38-7.32 (m, 3H), 7.30 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 5.41 (s, 2H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.8, 143.2, 138.1, 135.5, 131.8, 129.3, 128.6, 126.8, 122.3, 119.5 118.2, 115.7, 115.6, 51.0, 44.9, 27.7; FT-IR (KBr) 2970, 1760, 1656, 1620, 1523, 1455, 1361, 1259, 1212, 1183, 1183 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{20}H_{21}N_2O_3^+$: 337.1547, found: 337.1549.



(1-Benzyl-4-nitro-1*H*-indol-3-yl)(4-methoxyphenyl)methanone 3k. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.4$; yellow solid; mp 109-110 °C; yield 67% (51.7 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.8 Hz, 2H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.67 (s, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.36-7.32 (m, 4H), 7.16 (d, *J* = 5.6 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 5.43 (s, 2H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 163.3, 143.7, 138.8, 136.4, 135.3, 132.0, 131.7, 129.4, 128.7, 127.0, 122.7, 119.3, 118.4, 116.3, 115.7, 113.9, 55.6, 51.3; FT-IR (KBr) 3020, 1636, 1599, 1521, 1452, 1376, 1248, 1214, 1165, 1025 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_4^+$: 387.1339, found: 387.1342.

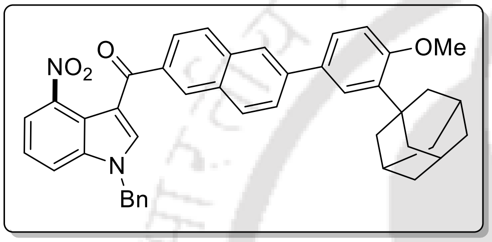


(1-Benzyl-4-nitro-1*H*-indol-3-yl)(4-fluorophenyl)methanone 3l. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.43$; yellow solid; mp 155-156 °C; yield 62% (46.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92-7.89 (m, 2H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.67 (s, 1H), 7.63 (d, *J* = 8.4 Hz, 1H), 7.37-7.33 (m, 4H), 7.17 (d, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 8.4 Hz, 2H), 5.44 (s, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.9, 165.5 (d, $J_{C\text{-}F}$ = 252.2 Hz), 143.6, 138.8, 136.8, 135.5 (d, $J_{C\text{-}F}$ = 2.9 Hz), 135.1, 131.9 (d, $J_{C\text{-}F}$ = 9.0 Hz), 129.4, 128.8, 127.0, 122.9, 119.1, 118.6, 115.91, 115.86, 115.7 (d, $J_{C\text{-}F}$ = 21.8 Hz), 51.3; ^{19}F NMR (470 MHz, $CDCl_3$) δ -106.2; FT-IR (KBr) 3022, 1641, 1597, 1522, 1450 1372, 1344, 1215, 1155 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}FN_2O_3^+$: 375.1139, found: 375.1142.

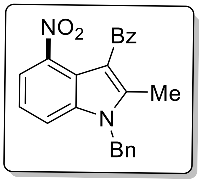


(1-Benzyl-4-nitro-1*H*-indol-3-yl)(3-(5-(2-fluorophenyl)-1,2,4-oxadiazol-3-yl)phenyl)methanone 3n. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f =

0.42; pale yellow solid ; mp 186-187 °C; yield 63% (65.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.38 (d, *J* = 8.0 Hz, 1H), 8.20 (t, *J* = 7.5 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.76 (s, 1H), 7.64-7.59 (m, 3H), 7.39-7.32 (m, 5H), 7.31-7.29 (m, 1H), 7.19 (d, *J* = 7.5 Hz, 2H), 5.46 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 173.2 (d, $J_{C\text{-}F}$ = 4.3 Hz), 168.32, 168.28, 160.9 (d, $J_{C\text{-}F}$ = 259.0 Hz), 144.0, 139.8, 139.0, 137.5, 135.0, 134.9 (d, $J_{C\text{-}F}$ = 8.6 Hz), 132.1, 131.5, 131.1, 129.4, 128.8, 127.30, 127.28, 127.1, 124.9 (d, $J_{C\text{-}F}$ = 3.8 Hz), 123.1, 119.1, 118.6, 117.3 (d, $J_{C\text{-}F}$ = 20.6 Hz), 115.9, 115.7, 112.9 (d, $J_{C\text{-}F}$ = 11.3.0 Hz), 51.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -108.2; FT-IR (KBr) 2926, 1620, 1519, 1452, 1380, 1341, 1219, 1176 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{30}H_{20}FN_4O_4^+$: 519.1463, found: 519.1459.

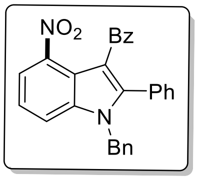


(6-(3-(Adamantan-1-yl)-4-methoxyphenyl)naphthalen-2-yl)(1-benzyl-4-nitro-1*H*-indol-3-yl)methanone 3o. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.4; pale yellow solid; mp 242-243 °C; yield 58% (74.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.14 (d, *J* = 9.2, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 9.2 Hz, 1H), 7.74 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.42-7.30 (m, 7H), 7.20 (d, *J* = 7.6 Hz, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.47 (s, 2H), 3.89 (s, 3H), 2.11 (s, 6H), 2.08 (s, 3H), 1.78 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 159.7, 146.9, 143.8, 139.3, 138.9, 137.5, 137.2, 134.9, 134.2, 131.9, 131.7, 130.4, 129.5, 129.0, 128.9, 128.3, 128.1, 127.2, 127.1, 126.8, 126.6, 123.2, 122.4, 119.1, 118.8, 116.0, 115.9, 112.1, 55.2, 51.5, 40.6, 37.4, 37.2, 29.2; FT-IR (KBr) 2919, 2854, 1729, 1605, 1527, 1463, 1369, 1333, 1238, 1178 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{43}H_{39}N_2O_4^+$: 647.2904, found: 647.2899.

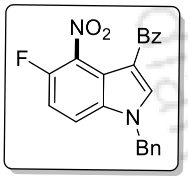


(1-Benzyl-2-methyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3p. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.45; yellow solid; mp 77-78 °C; yield 67% (49.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J*

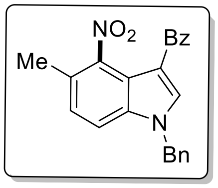
= 8.4 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 7.36-7.30 (m, 3H), 7.27-7.23 (m, 1H), 7.03 (d, J = 6.8 Hz, 2H), 5.46 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.7, 143.8, 141.4 140.1, 138.4, 135.7, 132.8, 129.4, 128.9, 128.7, 128.3, 125.9, 121.3, 119.6, 118.6, 115.8, 113.4, 47.3, 11.9; FT-IR (KBr) 2963, 1644, 1518, 1450, 1413, 1338, 1243 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_3^+$: 371.1390, found: 371.1388.



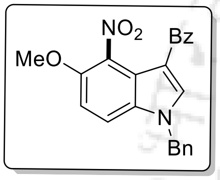
(1-Benzyl-4-nitro-2-phenyl-1*H*-indol-3-yl)(phenyl)methanone 3q. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.43; yellow solid; mp 161-162 °C; yield 70% (60.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.73 (d, J = 7.2 Hz, 2H), 7.59 (d, J = 8.4 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.32-7.25 (m, 11H), 6.99 (d, J = 6.0 Hz, 2H), 5.37 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.4, 145.9, 141.8, 139.4, 138.5, 136.4, 132.6, 130.5, 129.7, 129.4, 129.3, 129.2, 128.6, 128.3, 128.1, 126.0, 122.1, 119.6, 118.9, 117.1, 114.7, 48.4; FT-IR (KBr) 3022, 1657, 1517, 1478, 1442, 1408, 1344, 1212, 1168 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{28}H_{21}N_2O_3^+$: 433.1547, found: 433.1542.



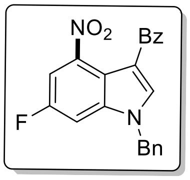
(1-Benzyl-5-fluoro-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3r. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.42; pale yellow solid; mp 117-118 °C; yield 66% (49.4 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, J = 8.0 Hz, 2H), 7.70 (s, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 7.43-7.40 (m, 1H), 7.73-7.33 (m, 3H), 7.16 (t, J = 9.5 Hz, 1H), 7.12 (d, J = 7.0 Hz, 2H), 5.41 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.4, 151.0 (d, $J_{C\text{-}F}$ = 250.3 Hz), 138.9, 138.8, 134.8, 134.6, 132.5, 129.6, 129.5 (d, $J_{C\text{-}F}$ = 14.6 Hz), 128.9, 128.6, 127.7, 126.8, 119.7, 115.8 (d, $J_{C\text{-}F}$ = 4.0 Hz), 114.5 (d, $J_{C\text{-}F}$ = 9.3 Hz), 112.8 (d, $J_{C\text{-}F}$ = 23.9 Hz), 51.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -130.1; FT-IR (KBr) 3021, 2926, 1638, 1539, 1455, 1390, 1266, 1214 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}FN2O_3^+$: 375.1139, found: 375.1138.



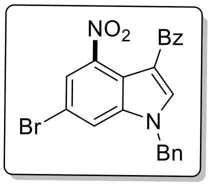
(1-Benzyl-5-methyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3s. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.45; yellow solid; mp 126-127 °C; yield 72% (53.3 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.2 Hz, 2H), 7.60 (s, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.36-7.32 (m, 4H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 5.38 (s, 2H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 144.3, 139.2, 138.1, 137.4, 135.3, 132.2, 129.7, 129.3, 128.6, 128.5, 126.8, 124.8, 118.9, 115.1, 113.1, 51.2, 17.9; FT-IR (KBr) 2929, 1636, 1526, 1454, 1382, 1253, 1214 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_3^+$: 371.1390, found: 371.1392.



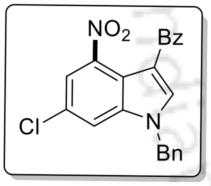
(1-Benzyl-5-methoxy-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3t. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.4; pale yellow solid; mp 154-155 °C; yield 79% (60.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.64 (s, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.37-7.32 (m, 4H), 7.12 (d, *J* = 7.2 Hz, 2H), 7.06 (d, *J* = 9.2 Hz, 1H), 5.37 (s, 2H), 3.93 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.7, 147.9, 139.3, 138.9, 135.2, 133.2, 132.1, 129.6, 129.4, 128.7, 128.5, 126.8, 119.8, 114.9, 113.6, 110.6, 57.9, 51.4; FT-IR (KBr) 2924, 2849, 1633, 1527, 1455, 1390, 1349, 1269, 1209, 1178, 1059, 1023 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_4^+$: 387.1339, found: 387.1341.



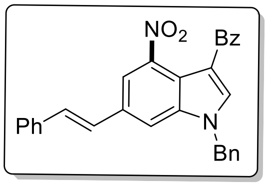
(1-Benzyl-6-fluoro-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3u. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.41; pale yellow solid; mp 105-106 °C; yield 69% (51.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 2H), 7.68 (s, 1H), 7.63-7.60 (m, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.38-7.35 (m, 3H), 7.31-7.28 (m, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.38 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9, 158.5 (d, J_{C-F} = 243.3 Hz), 138.9, 138.8, 137.6 (d, J_{C-F} = 2.6 Hz), 134.6, 132.8, 129.5 (d, J_{C-F} = 3.5 Hz), 129.4, 128.9, 128.7, 126.97, 126.92, 116.3, 116.0 (d, $J_{C\text{-}F}$ = 1.4 Hz), 107.6 (d, $J_{C\text{-}F}$ = 28.7 Hz), 102.4 (d, $J_{C\text{-}F}$ = 25.9 Hz), 51.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -115.8; FT-IR (KBr) 3102, 1636, 1529, 1455, 1380, 1351, 1315, 1263, 1219, 1168 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}N_2O_3^+$: 375.1139, found: 375.1134.



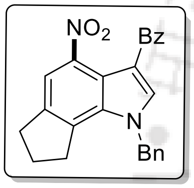
(1-Benzyl-6-bromo-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3v. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.45; brown solid; mp 162-163 °C; yield 68% (62.0 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.949-7.947 (m, 1H), 7.87 (d, *J* = 7.5 Hz, 2H), 7.748-7.746 (m, 1H), 7.65 (s, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.39-7.35 (m, *J* =), 7.15 (d, *J* = 6.5 Hz, 2H), 5.39 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 143.9, 139.6, 138.8, 137.5, 134.6, 132.9, 129.53, 129.49, 128.9, 128.7, 126.9, 121.5, 118.3, 118.2, 116.4, 115.4, 51.4; FT-IR (KBr) 2923, 1640, 1526, 1455, 1376, 1245, 1215, 1175 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{15}BrN_2NaO_3^+$: 457.0158, found: 457.0161.



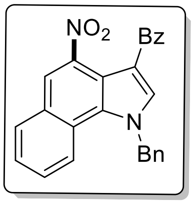
(1-Benzyl-6-chloro-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3w. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.43; pale yellow solid; mp 154-155 °C; yield 70% (54.6 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 7.2 Hz, 2H), 7.830-7.826 (m, 1H), 7.67 (s, 1H), 7.593-7.589 (m, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 2H), 7.40-7.35 (m, 3H), 7.16 (d, *J* = 8.0 Hz, 2H), 5.39 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.0, 143.8, 139.2, 138.8, 137.6, 134.6, 132.8, 129.54, 129.50, 129.0, 128.74, 128.69, 127.0, 119.0, 117.9, 116.4, 115.4, 51.4; FT-IR (KBr) 2926, 1641, 1527, 1457, 1378, 1300, 1247, 1175 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}ClN_2O_3^+$: 391.0844, found: 391.0843.



(*E*)-(1-Benzyl-4-nitro-6-styryl-1*H*-indol-3-yl)(phenyl)methanone 3x. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.39; pale yellow solid; mp 151-152 °C; yield 67% (61.4 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.0 Hz, 1H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.70 (s, 1H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.46-7.41 (m, 6H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.34-7.30 (m, 2H), 7.20 (d, *J* = 6.8 Hz, 2H), 6.94 (s, 1H), 5.34 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.8, 150.0, 140.6, 138.6, 137.3, 135.4, 131.63, 131.59, 130.1, 129.34, 129.26, 128.9, 128.7, 128.6, 128.5, 127.24, 127.20, 125.6, 123.9, 123.5, 122.3, 116.4, 109.7, 51.3; FT-IR (KBr) 2925, 1619, 1522, 1452, 1381, 1206, 1173 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{30}H_{23}N_2O_3^+$: 459.1703, found: 459.1702.

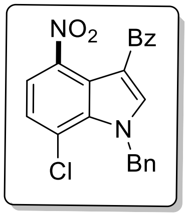


(1-Benzyl-4-nitro-1,6,7,8-tetrahydrocyclopenta[*g*]indol-3-yl)(phenyl)methanone 3y. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.41; pale yellow solid; mp 112-113°C; yield 72% (57.0 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 6.8 Hz, 2H), 7.75 (s, 1H), 7.55-7.51 (m, 2H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.36-7.30 (m, 3H), 7.00 (d, *J* = 6.8 Hz, 2H), 5.55 (s, 2H), 3.16 (t, *J* = 7.6 Hz, 2H), 3.04 (t, *J* = 7.6 Hz, 2H), 2.21-2.14 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.5, 142.7, 140.9, 139.3, 137.4, 137.0, 135.8, 132.5, 132.2, 129.5, 129.4, 128.5, 128.4, 125.8, 118.7, 116.6, 115.7, 52.1, 32.5, 31.7, 25.5; FT-IR (KBr) 3022, 2919, 1641, 1523, 1450, 1375, 1351, 1250, 1214 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{25}H_{21}N_2O_3^+$: 397.1547, found: 397.1548.

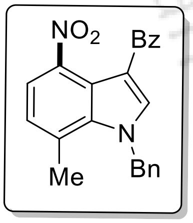


(1-Benzyl-4-nitro-1*H*-benzo[*g*]indol-3-yl)(phenyl)methanone 3z. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.41; pale yellow solid; mp 161-162 °C; yield 71% (57.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.5

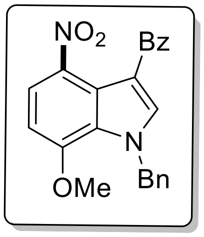
Hz, 1H), 7.84 (d, *J* = 7.0 Hz, 2H), 7.67 (s, 1H), 7.59-7.54 (m, 2H), 7.50-7.45 (m, 3H), 7.36-7.30 (m, 3H), 7.09 (d, *J* = 7.5 Hz, 2H), 5.88 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.6, 144.1, 139.8, 139.1, 135.4, 133.3, 132.1, 129.6, 128.9, 128.7, 128.5, 127.3, 126.9, 125.9, 124.5, 123.7, 122.7, 122.1, 121.5, 120.8, 117.7, 54.9; FT-IR (KBr) 2921, 2837, 1711, 1631, 1600, 1534, 1452, 1400, 1372, 1325, 1261, 1217, 1173 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{26}H_{19}N_2O_3^+$: 407.1390, found: 407.1388.



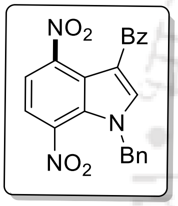
(1-Benzyl-7-chloro-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3aa. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.45; yellow solid; mp 124-125 °C; yield 77% (60.1 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.2 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 1H), 7.63 (s, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.36-7.31 (m, 4H), 7.05 (d, *J* = 6.4 Hz, 2H), 5.86; (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 142.5, 139.4, 138.6, 136.7, 134.0, 132.9, 129.6, 129.3, 128.7, 128.4, 126.3, 124.7, 122.9, 121.9, 119.2, 116.4, 53.0; FT-IR (KBr) 2926, 2849, 1765, 1644, 1527, 1452, 1375, 1341, 1245, 1214, 1178 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{22}H_{16}ClN_2O_3^+$: 391.0844, found: 391.0843.



(1-Benzyl-7-methyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3ab. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane R_f = 0.43; yellow solid; mp 132-133 °C; yield 73% (54.0 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.60 (s, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.35-7.30 (m, 3H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 7.0 Hz, 2H), 5.66 (s, 2H), 2.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.4, 142.4, 139.1, 138.9, 137.3, 132.6, 129.53, 129.47, 128.6, 128.34, 128.26, 125.8, 125.4, 120.2, 118.9, 116.2, 53.3, 19.9; FT-IR (KBr) 2921, 2854, 1646, 1602, 1522, 1452, 1382, 1331, 1253, 1216 cm^{-1}; HRMS (ESI) *m/z* [M+H]$^+$ calcd for $C_{23}H_{19}N_2O_3^+$: 371.1390, found: 371.1384.

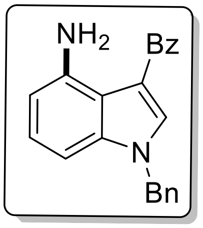


(1-Benzyl-7-methoxy-4-nitro-1*H*-indol-3-yl)(phenyl)methanone 3ac. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.4$; pale yellow solid; mp 112-113 °C; yield 78% (63.6 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 2H), 7.54-7.51 (m, 2H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.34-7.28 (m, 3H), 7.11 (d, *J* = 7.5 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 1H), 5.67 (s, 2H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 151.9, 139.3, 137.5, 137.0, 136.9, 132.6, 129.4, 129.0, 128.5, 128.1, 127.2, 126.7, 121.7, 121.3, 116.7, 103.1, 56.3, 53.6; FT-IR (KBr) 2928, 2850, 1642, 1573, 1512, 1452, 1383, 1329, 1270, 1174 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{18}N_2NaO_4^+$: 409.1159, found: 409.1161.

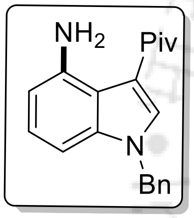


(1-Benzyl-4,7-dinitro-1*H*-indol-3-yl)(phenyl)methanone 3ad. Analytical TLC on silica gel, 1:6 EtOAc/*n*-hexane $R_f = 0.32$; yellow solid; mp 167-168 °C; yield 57% (45.7 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.84-7.81 (m, 3H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.30-7.29 (m, 4H), 6.91 (d, *J* = 4.5 Hz, 2H), 5.56 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.1, 154.4, 144.1, 137.6, 133.8, 133.4, 131.6, 129.9, 129.5, 129.24, 129.18, 129.13, 129.08, 127.2, 123.1, 121.4, 118.9, 55.9; FT-IR (KBr) 2929, 1600, 1530, 1455, 1390, 1318, 1217, 1185 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}N_3O_5^+$: 402.1084, found: 402.1085.

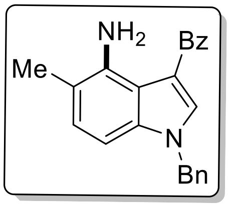
General Procedure for the Preparation of C4-aminoindoles 4. To a stirred solution of (1-Benzyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone **3** (0.1 mmol) in MeOH (1 mL), palladium on activated charcoal was added. The resulting mixture was stirred at room temperature for 24 h under H_2 atmosphere and then filtered. The filtrate was concentrated and was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford C4-aminoindoles **4** in good yields.



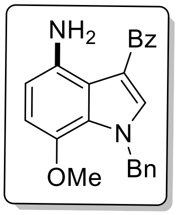
(4-Amino-1-benzyl-1*H*-indol-3-yl)(phenyl)methanone 4a. Analytical TLC on silica gel, 1:4 EtOAc/*n*-hexane R_f = 0.52; brown solid; mp 95-96 °C; yield 82% (53.5 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.40 (s, 1H), 7.32-7.27 (m, 3H), 7.11-7.07 (m, 3H), 6.62 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 7.5 Hz, 1H), 5.80 (br s, 2H), 5.26 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 143.4, 139.67, 140.9, 139.7, 139.0, 135.9, 131.3, 129.2, 129.1, 128.3, 128.2, 126.9, 125.9, 117.8, 114.7, 107.1, 99.3, 50.9; FT-IR (KBr) 3441, 3305, 2924, 1595, 1516, 1494, 1449, 1377, 1306, 1236, 1172, 1078 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{22}H_{19}N_2O^+$: 327.1492, found: 327.1496.



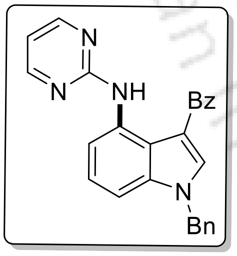
1-(4-Amino-1-benzyl-1*H*-indol-3-yl)-2,2-dimethylpropan-1-one 4b. Analytical TLC on silica gel, 1:4 EtOAc/*n*-hexane R_f = 0.62; brown solid; mp 149-150 °C; yield 78% (23.9 mg); ^{1}H NMR (400 MHz, $CDCl_3$, *2Hs were not observed due to line broadening*) δ 7.77 (s, 1H), 7.36-7.30 (m, 3H), 7.14 (d, *J* = 6.8 Hz, 2H), 7.03 (t, *J* = 8.0 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 6.43 (d, *J* = 7.6 Hz, 1H), 5.28 (s, 2H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7, 143.2, 138.4, 136.0, 133.9, 129.0, 128.1, 126.9, 125.2, 115.14, 115.07, 107.3, 98.9, 50.7, 44.4, 29.6; FT-IR (KBr) 3454, 3335, 2944, 1566, 1465, 1449, 1387, 1366, 1286, 1135, 1055 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{23}N_2O^+$: 307.1805, found: 307.1806.



(4-Amino-1-benzyl-5-methyl-1*H*-indol-3-yl)(phenyl)methanone 4c. Analytical TLC on silica gel, 1:4 EtOAc/*n*-hexane R_f = 0.54; brown solid; mp 119-120 °C; yield 75% (25.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$, *2Hs were not observed due to line broadening*) δ 7.78 (d, *J* = 6.8 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.38 (s, 1H), 7.32-7.27 (m, 3H), 7.10 (d, *J* = 6.4 Hz, 2H), 7.02 (d, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.24 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.9, 141.0, 140.7, 139.3, 138.3, 135.9, 131.1, 129.1, 128.9, 128.1, 128.0, 127.6, 126.7, 117.3, 114.7, 113.8, 98.7, 50.8, 17.4; FT-IR (KBr) 3488, 3355, 2934, 1575, 1577, 1454, 1347, 1326, 1188, 1099 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{21}N_2O^+$: 341.1648, found: 341.1650.

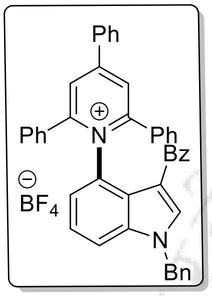


(4-Amino-1-benzyl-7-methoxy-1*H*-indol-3-yl)(phenyl)methanone 4d. Analytical TLC on silica gel, 1:4 EtOAc/*n*-hexane R_f = 0.46; brown solid; mp 112-113 °C; yield 80% (28.5 mg); ^{1}H NMR (400 MHz, $CDCl_3$, *2Hs were not observed due to line broadening*) δ 7.80 (d, *J* = 6.8 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.31 (s, 1H), 7.28-7.23 (m, 3H), 7.06 (d, *J* = 6.8 Hz, 2H), 6.64 (d, *J* = 8.4 Hz, 1H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.59 (s, 2H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7, 140.9, 140.3, 139.8, 138.2, 136.8, 131.4, 129.4, 128.81, 128.80, 128.3, 127.7, 126.5, 117.7, 117.5, 108.1, 107.1, 56.5, 53.5; FT-IR (KBr) 3488, 3355, 2977, 1590, 1495, 1454, 1366, 1316, 1277, 1188, 1078 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{21}N_2O_2^+$: 357.1598, found: 357.1601.

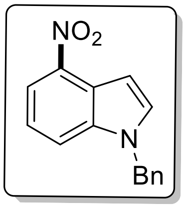


(1-Benzyl-4-(pyrimidin-2-ylamino)-1*H*-indol-3-yl)(phenyl)methanone 5. To a solution of (4-amino-1-benzyl-1*H*-indol-3-yl)(phenyl)methanone **4a** (0.075 mmol, 1.5 equiv, 24.5 mg) in 1,4-dioxane (150 µL), AcOH (50 µL) and 2-chloropyrimidine (0.05 mmol, 1 equiv, 5.7 mg) were added in sealed tube. The mixture was heated at reflux in a preheated oil bath at 110 °C for 10 h. The mixture was then cool to room temperature and extracted using CH_2Cl_2 (3 x 10 mL), washed with H_2O (5 mL) and saturated $NaHCO_3$ solution (5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford **6**. Analytical TLC on silica gel, 1:12 EtOAc/*n*-hexane R_f = 0.49; brown solid; mp 135-136 °C; yield 84% (24.8 mg); ^{1}H NMR (400

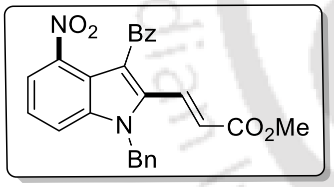
MHz, $CDCl_3$) δ 11.85 (s, 1H), 8.55 (d, *J* = 8.4 Hz, 1H), 8.49 (d, *J* = 4.8 Hz, 2H), 7.83-7.81 (m, 2H), 7.56- 7.52 (m, 2H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.36 -7.29 (m, 4H), 7.13-7.11 (m, 2H), 6.94 (d, *J* = 8.4 Hz, 1H), 6.68 (t, *J* = 4.8 Hz, 1H), 5.33 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.6, 160.7, 158.0, 140.6, 140.1, 139.1, 136.0, 135.6, 131.6, 129.6, 129.2, 128.4, 128.2, 126.9, 125.7, 117.7, 117.4, 112.3, 111.6, 103.8, 51.1; FT-IR (KBr) 3422, 3355, 2944, 1576, 1506, 1474, 1429, 1355, 1316, 1224, 1188, 1008 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{21}N_4O^+$: 405.1710, found: 405.1718.



1-(3-Benzoyl-1-benzyl-1*H*-indol-4-yl)-2,4,6-triphenylpyridin-1-iumtetrafluoroborate 6. To a suspension of 2,4,6-triphenylpyrylium tetrafluoroborate (0.1 mmol, 1.0 equiv, 39.6 mg) in EtOH (1 mL), (4-amino-1-benzyl-1*H*-indol-3-yl)(phenyl)methanone **4a** (0.12 mmol, 1.2 equiv, 39.1 mg) was added in a Schlenk tube. The mixture was heated at reflux in a preheated oil bath at 90 ºC for 4 h. The mixture was then cool to room temperature. The solid was filtered, washed with EtOH (3 × 10 mL) then Et_2O (3 × 10 mL), and dried under high vacuum. The solution was diluted with Et_2O (10 mL) and vigorously stirred for 1 h to induce trituration. The resulting solid pyridinium salt was filtered and washed with Et_2O (3 × 10 mL). It was then purified on silica gel column chromatography using CH_2Cl_2 and acetone as an eluent to afford **6**. Analytical TLC on silica gel, 1:10 acetone/CH_2Cl_2 R_f = 0.32; brown solid; mp 129-130ºC; yield 72% (44.3 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (s, 2H), 7.90 (d, *J* = 7.5 Hz, 2H), 7.59-7.47 (m, 10H), 7.30-7.25 (m, 9H), 7.17-7.11 (m, 5H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 7.0 Hz, 2H), 5.31 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 156.9, 140.60, 140.58, 139.4, 138.0, 135.4, 134.7, 133.4, 132.3, 132.0, 131.9, 130.01, 129.7, 129.6, 129.5, 129.0, 128.7, 128.4, 128.3, 128.1, 126.1, 125.54, 125.47, 125.4, 123.9, 123.1, 115.5, 113.5, 50.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -153.1; FT-IR (KBr) 3032, 2926, 1621, 1569, 1556, 1520, 1495, 1450, 1393, 1376, 1218, 1176 cm^{-1}; HRMS (ESI) *m/z* $[M^+]$ calcd for $C_{45}H_{33}N_2O^+$: 617.2587, found: 617.2583.

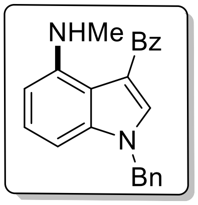


1-Benzyl-4-nitro-1*H*-indole 7. (1-Benzyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone **3a** (0.1 mmol, 35.6 mg), ethylene glycol (0.1 mL) and *p*-toluenesulfonic acid monohydrate (0.1 mmol, 1 equiv, 21 mg) were stirred for 6 h in benzene (2 mL) under reflux. After the completion (monitored by TLC), the reaction mixture was cooled to room temperature and extracted using EtOAc (3 x 10 mL) and washed with saturated $NaHCO_3$ (2 x 5 mL) and water (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford **7.** Analytical TLC on silica gel, 1:10 EtOAc/*n*-hexane $R_f = 0.53$; yellow solid; mp 113-114 ^{o}C; yield 85% (21.4 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 3.0 Hz, 1H), 7.34-7.28 (m, 4H), 7.23 (t, *J* = 8.5 Hz, 1H), 7.11 (d, *J* = 6.5 Hz, 2H), 5.40 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.7, 138.5, 136.4, 132., 129.1, 128.3, 126.8, 123.0, 120.8, 117.7, 116.7, 102.5, 50.8; FT-IR (KBr) 2925, 1724, 1565, 1504, 1448, 1357, 1317, 1281, 1201, 1110 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{15}H_{13}N_2O_2^+$: 253.0972, found: 253.0968.



Methyl (*E*)-3-(3-benzoyl-1-benzyl-4-nitro-1*H*-indol-2-yl)acrylate 8. (1-Benzyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone **3a** (0.1 mmol, 35.6 mg), $[Ru(p\text{-cymene})Cl_2]_2$ (0.005 mmol, 5 mol %, 3 mg), $AgSbF_6$ (0.02 mmol, 20 mol %, 6.8 mg), $Cu(OAc)_2{\cdot}H_2O$ (0.1 mmol, 1 equiv, 20 mg) and methyl acrylate (0.12 mmol, 1.2 equiv, 10.3 mg) were stirred at 100 ^{o}C in in 1,2-dichloroethane (2 mL) under air for 3 h. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (10 mL) and passed through a short pad of celite using CH_2Cl_2 (2 x 10 mL). Evaporation of the solvent gave a residue that was purified on silica gel column chromatography using *n*-hexane and ethyl acetate as an eluent to afford **8.** Analytical TLC on silica gel, 1:7 EtOAc/*n*-hexane $R_f = 0.52$; brown solid; mp 98-99 ^{o}C; yield 59% (25.9 mg); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, *J* = 16.2 Hz, 1H), 7.79 (d, *J* = 7.2 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 1H), 7.59-7.55 (m, 3H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.36-7.31 (m, 4H), 7.12 (d, *J*

= 6.6 Hz, 2H), 6.38 (d, *J* = 15.6 Hz, 1H), 5.40 (s, 2H), 3.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.4, 167.1, 144.5, 143.2, 140.1, 139.1, 138.7, 134.9, 134.8, 131.3, 129.9, 129.4, 129.3, 128.7, 127.8, 126.9, 123.3, 120.4, 118.6, 118.5, 117.8, 115.53, 51.8, 51.4; FT-IR (KBr) 2925, 2856, 1712, 1636, 1522, 1451, 1380, 1351, 1320, 1279, 1176 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{26}H_{21}N_2O_5^+$: 441.1445, found: 441.1444.



1-Benzyl-5-methyl-4-nitro-3-(1-phenylvinyl)-1*H*-indole 9. To a solution of (1-Benzyl-4-nitro-1*H*-indol-3-yl)(phenyl)methanone **3a** (0.1 mmol, 35.6 mg) in dry THF (1 mL) at 0 °C was added methylmagnesium bromide solution (0.1 mL, 3.0 M in diethyl ether, 3 equiv) dropwise. The reaction mixture was warmed to room temperature overnight. Upon completion, the reaction mixture was cooled to 0 °C. A saturated aqueous NH_4Cl solution (3 mL) was added dropwise. The organic layer was separated. The aqueous layer was extracted with Et_2O (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and dried under high vacuum. The residue was dissolved in CH_2Cl_2 (1 mL), to which was added anhydrous $MgSO_4$ (50 mg, 0.5 g per mmol of substrate) followed by silica gel (230-400 mesh particle size, 50 mg, 0.5 g per mmol of substrate). The mixture was then stirred at room temperature for 6 h, and the reaction progress was monitored by thin layer chromatography. The reaction mixture was filtered and washed with Et_2O. The filtrate was concentrated and the residue was purified by silica gel chromatography using *n*-hexane and ethyl acetate as an eluent to afford **9**. Analytical TLC on silica gel, 1:7 EtOAc/*n*-hexane R_f = 0.50; brown solid; mp 134-135 °C; yield 56% (19.0 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (br s, 1H), 7.76 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 8.0 Hz, 2H), 7.37 (s, 1H), 7.32-7.26 (m, 5H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 7.0 Hz, 2H), 6.57 (d, *J* = 8.5 Hz, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.26 (s, 2H), 2.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.3, 141.1, 139.3, 138.8, 136.0, 131.3, 129.2, 129.1, 128.3, 128.2, 126.8, 126.5, 118.1, 114.5, 101.2, 98.1, 51.0, 29.8; FT-IR (KBr) 3022, 2924, 1600, 1509, 1445, 1382, 1305, 1214, 1170 cm^{-1}; HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{23}H_{21}N_2O^+$: 341.1648, found: 341.1651.

Crystal Data and Structure Refinement for 3l

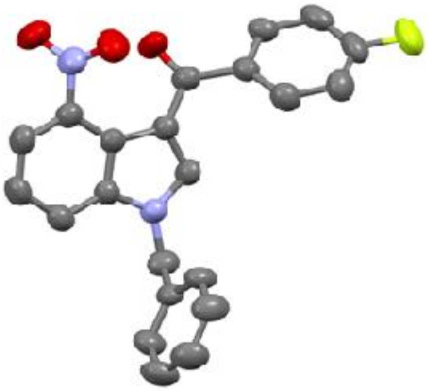


Figure1. ORTEP diagram of **3l** (CCDC 2286958). H-Atoms omitted for clarity**.**

Identification code	**3l**
CCDC No.	2286958
Empirical formula	$C_{22}H_{15}FN_2O_3$
Formula weight	374.36
Crystal habit, colour	needle /colorless
Temperature, *T*/K	298 K
Wavelength, λ/Å	0.71073
Crystal system	triclinic
Space group	'P -1'
Unit cell dimensions	a = 9.000(4)Å
	b = 10.227(5)Å
	c = 11.230(5)Å
	α = 98.808(16), β = 112.612(14)
	γ = 99.194(16)
Volume, *V*/Å^3	915.5(7)
Z	2
Calculated density, Mg·m^{-3}	1.358
Absorption coefficient, μ/mm^{-1}	0.179
F(000)	388

θ range for data collection	2.49 to 26.21°
Limiting indices	$-10 \leq h \leq 10, -12 \leq k \leq 12, -13 \leq l \leq 13$
Reflection collected / unique	3233/2782
Completeness to θ	100% (θ = 24.999°)
Absorption correction	none
Refinement method	'SHELXL-2014 (Sheldrick 2014)'
Data / restraints / parameters	3233/0/253
Goodness−of−fit on F^2	1.186
Final *R* indices [*I*>2sigma(*I*)]	R1 = 0.0572, wR2 = 0.1402
R indices (all data)	R1 = 0.0630, wR2 = 0.1439

Crystal Data and Structure Refinement for 3ab

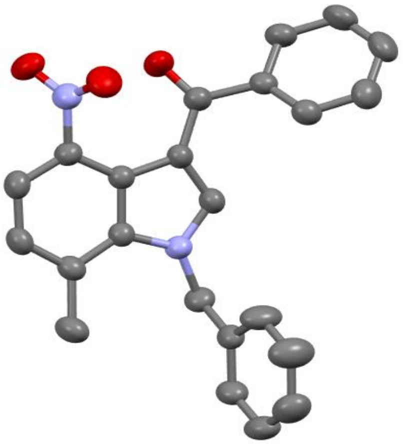


Figure 3. ORTEP diagram of **3ab** (CCDC 2286959). H-Atoms omitted for clarity**.**

Identification code	**3ab**
CCDC No.	2286959
Empirical formula	$C_{23}H_{18}N_2O_3$
Formula weight	370.39
Crystal habit, colour	needle /colorless
Temperature, *T*/K	297 K

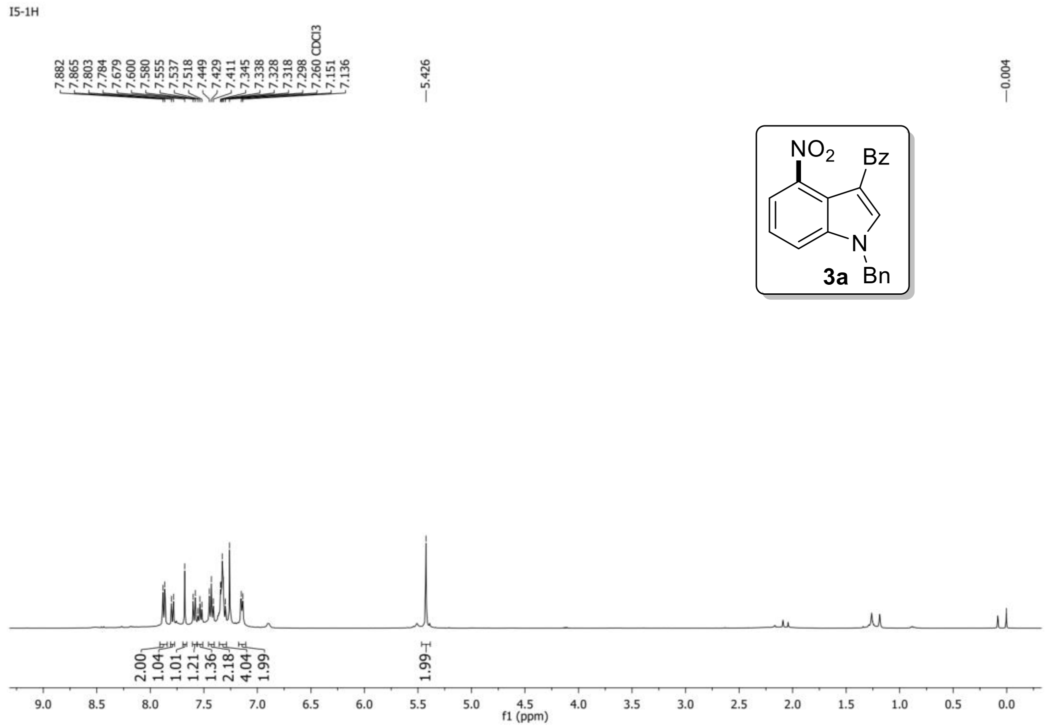
Wavelength, λ/Å	0.71073
Crystal system	triclinic
Space group	'P -1'
Unit cell dimensions	a = 9.5609(5)Å
	b = 10.8520(5)Å
	c = 10.8694(5)Å
	α = 107.849(1), β = 102.814(1)
	γ = 110.688(1)
Volume, V/Å^3	933.59(8)
Z	2
Calculated density, Mg·m^{-3}	1.318
Absorption coefficient, μ/mm^{-1}	0.088
F(000)	388
θ range for data collection	2.21 to 25.08°
Limiting indices	$-11 \leq h \leq 11$, $-12 \leq k \leq 12$, $-12 \leq l \leq 12$
Reflection collected / unique	3271/2725
Completeness to θ	99.4% (θ = 25.045°)
Absorption correction	none
Refinement method	'SHELXL-2014 (Sheldrick 2014)'
Data / restraints / parameters	3271/0/254
Goodness–of–fit on F^2	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0458, wR2 = 0.0960
R indices (all data)	R1 = 0.0586, wR2 = 0.1061

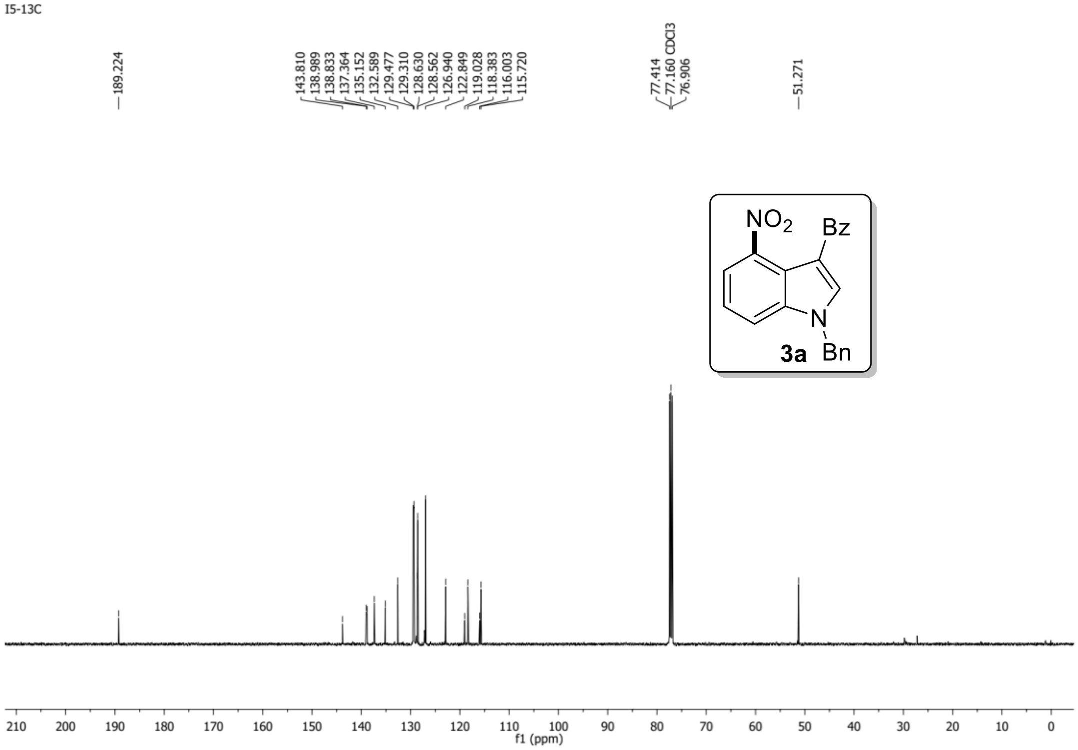
4.5 References

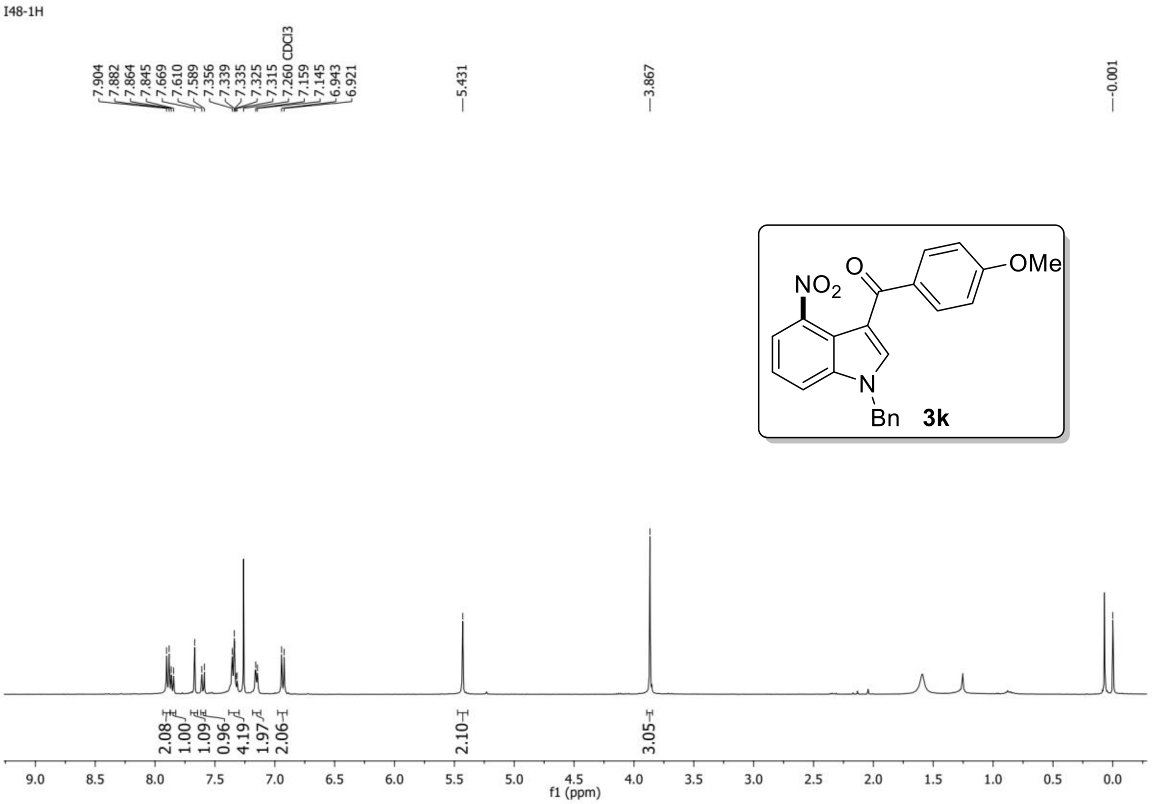
1. (a) Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. *J. Med. Chem.* **2014**, *57*, 5845. (b) Cho, I.; Park, S. K.; Kang, B.; Chung, J. W.; Kim, J. H.; Cho, K.; Park, S. Y. *Adv. Funct. Mater.* **2016**, *26*, 2966. (c) Suliphuldevara Mathada, B.; Gunavanthrao Yernale, N.; Basha, J. N. *ChemistrySelect* **2023**, *8*, e202204181.
2. (a) Gamage, S. A.; Spicer, J. A.; Rewcastle, G. W.; Milton, J.; Sohal, S.; Dangerfield, W.; Mistry, P.; Vicker, N.; Charlton, P. A.; Denny, W. A. *J. Med. Chem.* **2002**, *45*, 740. (b) Ferlin, M. G.; Chiarelotto, G.; Gasparotto, V.; Dalla Via, L.; Pezzi, V.; Barzon, L.; Palù, G.; Castagliuolo, I. *J. Med. Chem.* **2005**, *48*, 3417. (c) Wang, X.; Xu, F.; Xu, Q.; Mahmud, H.; Houze, J.; Zhu, L.; Akerman, M.; Tonn, G.; Tang, L.; McMaster, B. E.; Dairaghi, D. J.; Schall, T. J.; Collins, T. L.; Medina, J. C. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2800. (d) Venkatesan, A. M.; Chen, Z.; Dos S., O.; Brooijmans, N.; Gopalsamy, A. WO2009111547, **2009**. (e) Nakamura, H.; Yasui, K.; Kanda, Y.; Baran, P. S. *J. Am. Chem. Soc.* **2019**, *141*, 1494.
3. (a) Kalepu, J.; Gandeepan, P.; Ackermann, L.; Pilarski, L. T. *Chem. Sci.* **2018**, *9*, 4203. (b) Pradhan, S.; De, P. B.; Shah, T. A.; Punniyamurthy, T. *Chem. Asian J.* **2020**, *15*, 4184. (c) Wen, J.; Shi, Z. *Acc. Chem. Res.* **2021**, *54*, 1723. (c) Prabagar, B.; Yang, Y.; Shi, Z. *Chem. Soc. Rev.* **2021**, *50*, 11249.
4. (a) Toutov, A. A.; Liu, W.-B.; Betz, K. N.; Fedorov, A.; Stoltz, B. M.; Grubbs, R. H. *Nature* **2015**, *518*, 80. (b) Lu, Q.; Greßies, S.; Klauck, F. J. R.; Glorius, F. *Angew. Chem. Int. Ed.* **2017**, *56*, 6660. (c) Jacob, N.; Zaid, Y.; Oliveira, J. C. A.; Ackermann, L.; Wencel-Delord, J. *J. Am. Chem. Soc.* 2022, *144*, 798.
5. (a) Pradhan, S.; Mishra, M.; De, P. B.; Banerjee, S.; Punniyamurthy, T. *Org. Lett.* 2020, *22*, 1720. (b) Cheng, Y.; Yu, S.; He, Y.; An, G.; Li, G.; Yang, Z. *Chem. Sci.* 2021, *12*, 3216. (c) Basak, S.; Paul, T.; Punniyamurthy, T. *Chem. Commun.* 2023, *59*, 11568.
6. (a) Chen, S.; Feng, B.; Zheng, X.; Yin, J.; Yang, S.; You, J. *Org. Lett.* **2017**, *19*, 2502. (b) Tang, S.-B.; Fu, X.-P.; Wu, G.-R.; Zhang, L.-L.; Deng, K.-Z.; Yang, J.-Y.; Xia, C.-C.; Ji, Y.-F. *Org. Biomol. Chem.* **2020**, *18*, 7922.
7. Fan, Z.; Ni, J.; Zhang, A. *J. Am. Chem. Soc.* **2016**, *138*, 8470.

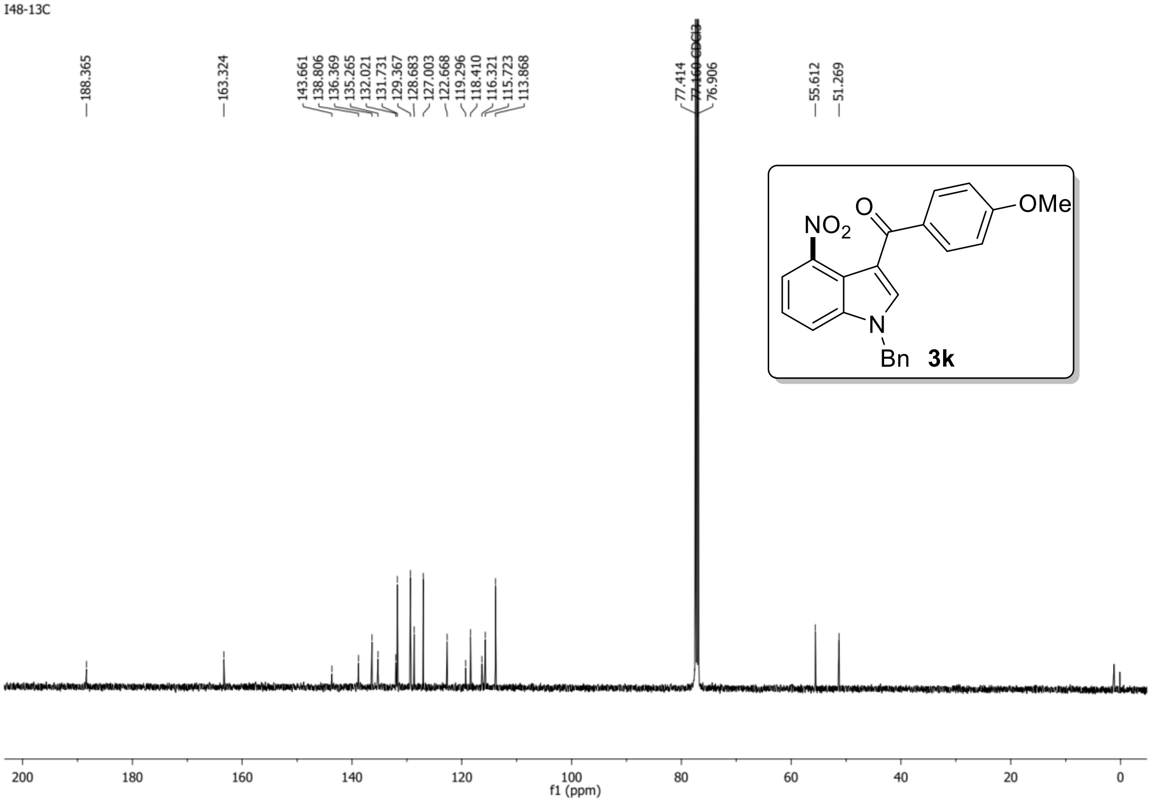
8. (a) Stowers, K. J.; Kubota, A.; Sanford, M. S. *Chem. Sci.* **2012**, *3*, 3192. (b) Weinstein, A. B.; Stahl, S. S. *Catal. Sci. Technol.* **2014**, *4*, 4301.
9. (a) Zhang, J.; Wu, M.; Fan, J.; Xu, Q.; Xie, M. *Chem. Commun.* **2019**, *55*, 8102. (b) Basak, S.; Paul, T.; Punniyamurthy, T. *Org. Lett.* **2022**, *24*, 554.
10. Liang, Y.-F.; Li, X.; Wang, X.; Yan, Y.; Feng, P.; Jiao, N. *ACS Catal.* **2015**, *5*, 1956.
11. Li, B.; Han, Y.-Q.; Yang, X.; Shi, B.-F. *Org. Lett.* **2020**, *22*, 9719.
12. Majhi, B.; Kundu, D.; Ahammed, S.; Ranu, B. C. *Chem. Eur. J.* **2014**, *20*, 9862.
13. Tu, D.; Luo, J.; Jiang, C. *Chem. Commun.* **2018**, *54*, 2514.
14. Zhang, W.; Ren, S.; Zhang, J.; Liu, Y. *J. Org. Chem.* **2015**, *80*, 5973.
15. Dong, J.; Jin, B.; Sun, P. *Org. Lett.* **2014**, *16*, 4540.
16. Pawar, G. G.; Brahmanandan, A.; Kapur, M. *Org. Lett.* **2016**, *18*, 448.
17. Zhang, L.; Liu, Z.; Li, H.; Fang, G.; Barry, B.-D.; Belay, T. A.; Bi, X.; Liu, Q. *Org. Lett.* **2011**, *13*, 6536.
18. (a) Ogawa, A.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 450. (b) Wencel-Delord, J.; Colobert, F. *Org. Chem. Front.* **2016**, *3*, 394.
19. (a) Garcia-echeverria, C.; Kanazawa, T.; Kawahara, E.; Masuya, K.; Matsuura, N. WO2005016894A1, **2005**. (b) Reddy, M. V. R.; Akula, B.; Cosenza, S. C.; Athuluridivakar, S.; Mallireddigari, M. R.; Pallela, V. R.; Billa, V. K.; Subbaiah, D. R. C. V.; Bharathi, E. V.; Vasquez-Del Carpio, R.; Padgaonkar, A.; Baker, S. J.; Reddy, E. P. *J. Med. Chem.* **2014**, *57*, 578.
20. (a) Fortage, J.; Tuyèras, F.; Ochsenbein, P.; Puntoriero, F.; Nastasi, F.; Campagna, S.; Griveau, S.; Bedioui, F.; Ciofini, I.; Lainé, P. P. *Chem. Eur. J.* **2010**, *16*, 11047. (b) Xu, C.-H.; Li, J.-H.; Xiang, J.-N.; Deng, W. *Org. Lett.* **2021**, *23*, 3696.
21. Subject Index. *March's Advanced Organic Chemistry*. Wiley December 27, 2006, pp 2190.
22. (a) Sapountzis, I.; Knochel, P. *J. Am. Chem. Soc.* **2002**, *124*, 9390. (b) Ricci, A.; Fochi, M. *Angew. Chem. Int. Ed.* **2003**, *42*, 1444. (c) Liu, K.-M.; Zhang, F.; Duan, X.-F. *Eur J. Org. Chem.* **2013**, *2013*, 6152. (d) Tan, E.; Montesinos-Magraner, M.; García-Morales, C.; Mayans, J. G.; Echavarren, A. M. *Chem. Sci.* **2021**, *12*, 14731.

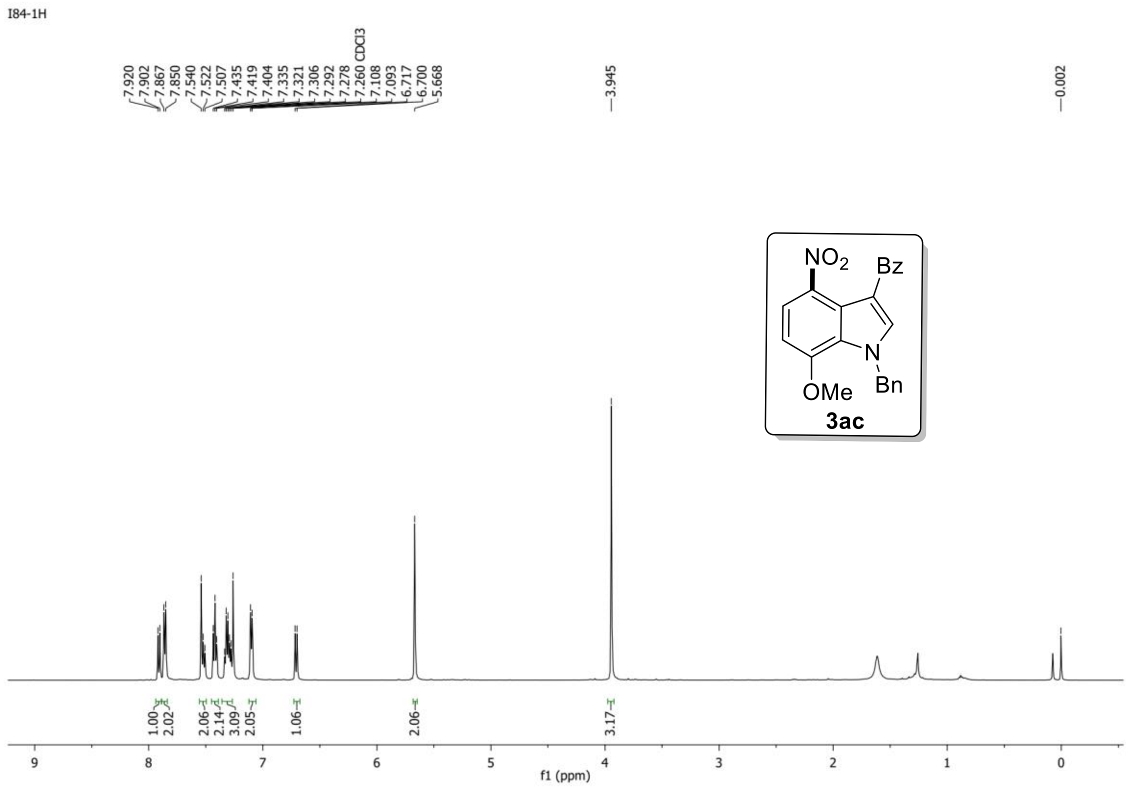
4.6 Selected NMR Spectra

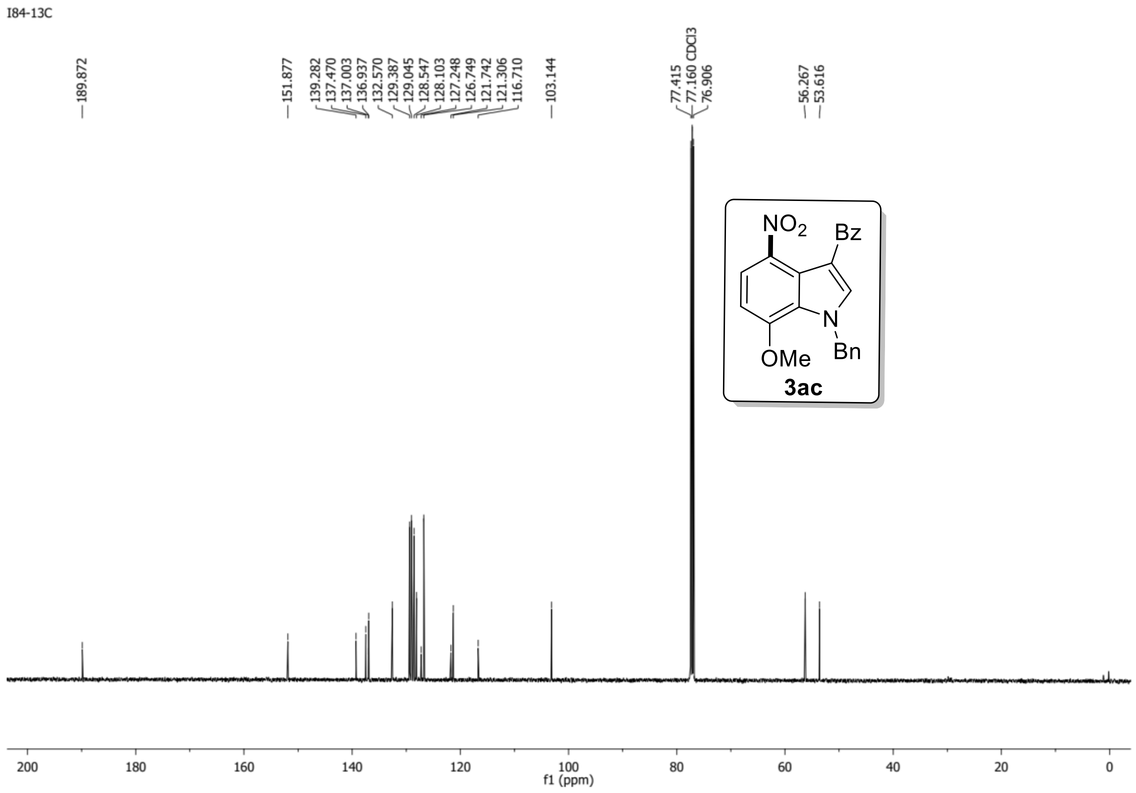


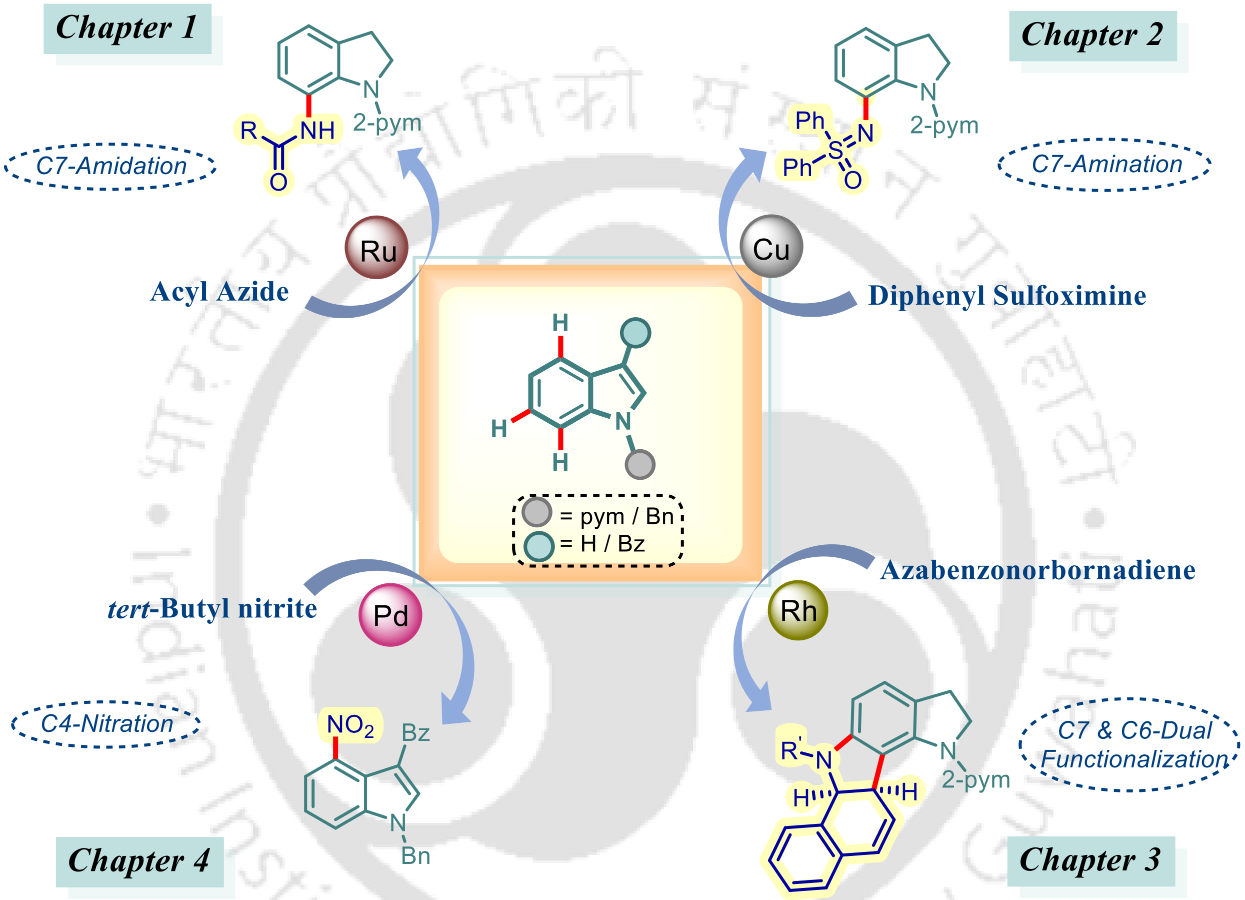



I48-1H
7.904
7.882
7.864
7.845
7.669
7.610
7.589
7.356
7.339
7.335
7.325
7.315
7.260 CDCl3
7.159
7.145
6.943
6.921
5.431
3.867
-0.001
NO2
O
OMe
N
Bn
3k
2.08
1.00
1.09
0.96
4.19
1.97
2.06
2.10
3.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


I48-13C
188.365
163.324
143.661
138.806
136.369
135.265
132.021
131.731
129.367
128.683
127.003
122.668
119.296
118.410
116.321
115.723
113.868
77.414
77.160 CDCl3
76.906
55.612
51.269
NO2
O
OMe
N
Bn
3k
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


I84-1H
7.920
7.902
7.867
7.850
7.540
7.522
7.507
7.435
7.419
7.404
7.335
7.321
7.306
7.292
7.278
7.260 CDCl3
7.108
7.093
6.717
6.700
5.668
3.945
0.002
NO2
Bz
N
Bn
OMe
3ac
1.00
2.02
2.06
2.14
3.09
2.05
1.06
2.06
3.17
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


I84-13C
189.872
151.877
139.282
137.470
137.003
136.937
132.570
129.387
129.045
128.547
128.103
127.248
126.749
121.742
121.306
116.710
103.144
77.415
77.160 CDCl3
76.906
56.267
53.616
NO2
Bz
N
Bn
OMe
3ac
200
180
160
140
120
100
80
60
40
20
0
f1 (ppm)


Chapter 1
C7-Amidation
R
NH
O
N
2-pym
Ru
Acyl Azide
Chapter 2
Ph
Ph
S
N
O
N
2-pym
C7-Amination
Cu
Diphenyl Sulfoximine
H
H
H
N
= pym / Bn
= H / Bz
tert-Butyl nitrite
Pd
C4-Nitration
NO2
Bz
N
Bn
Chapter 4
Azabenzonorbornadiene
Rh
R'
N
H
H
N
2-pym
C7 & C6-Dual Functionalization
Chapter 3

In chapter I, we have presented a Ru(II)-catalyzed regioselective C-N bond formation of indolines with acyl azides through C7(sp^2)-H activation strategy to construct synthetically useful 7-aminoindoline, which easily transformed into 7-aminoindole upon oxidation. The reaction proceeds via an intramolecular C-N bond formation. Furthermore, this methodology was successfully expanded to the coupling of carbazole with acyl azides, yielding a valuable 1-amidocarbazole scaffold.

In chapter II, a Cu(II)-mediated regioselective C-H/N-H dehydrogenative cross-coupling of indoline, 7-azaindole derivatives with versatile sulfoximines was developed, utilizing 2-pyrimidyl as a directing group. This innovative reaction pathway provides a prospective route to construct C7-aminated indoles and leverge sulfoximines for potential amination transformations.

In chapter III, we have demonstrated a Rh(III)-catalyzed site-selective C7 and C6 dual C-H functionalization of indolines expending 7-azabenzonorbornaienes. Indolines bearing diverse functional groups are well endured to give the target functionalized pyrrolocarbazoles. This method was further extended to the coupling of carbazole and related frameworks. The remarkable site-selectivity, wide substrate scope and functional group diversity are significant practical findings.

In chapter IV, a weak carbonyl coordination guided Pd(II)-catalyzed oxidative C4-nitration of indoles was achieved utilizing *tert*-butyl nitrite. Indoles with diverse functional groups are well tolerated to furnish intended C4-nitroindoles. The elegant features of our findings comprise of exclusive C4-selectivity, functional group tolerance and late-stage modification of the natural products.

List of Publications

1. Pinaki Bhusan De, Sourav Pradhan, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Expedient Cobalt(II)-Catalyzed Site-Selective C7-Arylation of Indolines with Arylboronic Acids, *Chem. Commun*. **2018**, *54*, 2494.
2. Pinaki Bhusan De, **Sonbidya Banerjee**, Sourav Pradhan and Tharmalingam Punniyamurthy, Ru(II)-Catalyzed C7-Acyloxylation of Indolines with Carboxylic Acids, *Org. Biomol. Chem.* **2018**, *16*, 5889.
3. **Sonbidya Banerjee**, Pinaki Bhusan De, Sourav Pradhan, Tariq A. Shah and Tharmalingam Punniyamurthy, Ru(II)-Catalysed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides, *Eur. J. Org. Chem*. **2019**, 1677.
4. Tariq A. Shah, Pinaki Bhusan De, Sourav Pradhan, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Exploiting Strained Rings in Chelation Guided C-H Functionalization: Integration of C-H Activation with Ring Cleavage, *Chem. Asian J.* **2019**, *14*, 4520.
5. Sundaravel Vivek Kumar, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Rh-Catalyzed C-C/C-N Bond Formation via C-H Activation: Synthesis of 2*H*-indazol-2-yl-benzo[*a*]carbazoles, *Org. Chem. Front*. **2019**, *6*, 3885.
6. Tariq. A. Shah, Pinaki Bhusan De, Sourav Pradhan, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Cp*Co(III)-Catalyzed Regioselective C2-Amidation of Indoles Using Acyl Azides, *J. Org. Chem*. **2019**, *84*, 16278.
7. **Sonbidya Banerjee**, Sundaravel Vivek Kumar and Tharmalingam Punniyamurthy, Site-Selective Rh-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles, *J. Org. Chem*. **2020**, *85*, 2793.
8. Sourav Pradhan, Manmath Mishra, Pinaki Bhusan De, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Weak Coordination Enabled Switchable C4-Alkenylation and Alkylation of Indoles with Allyl Alcohols, *Org. Lett.* **2020**, *22*, 1720.
9. Pinaki Bhusan De, Sayan Atta, Sourav Pradhan, **Sonbidya Banerjee**, Tariq A. Shah and Tharmalingam Punniyamurthy, Cp*Co(III)-Catalyzed C-7 C-C Coupling of Indolines with Aziridines: Merging C-H Activation and Ring Opening, *J. Org. Chem*. **2020**, *85*, 4785.
10. Sourav Pradhan, Subhasish Roy, **Sonbidya Banerjee**, Pinaki Bhusan De and Tharmalingam Punniyamurthy, Oxidative C-H/N-H Annulation of Aromatic Amides with

Dialkyl Malonates: Access to Isoindolinones and Dihydrobenzoindoles, *J. Org. Chem*. **2020**, *85*, 5741.

11. Sundaravel Vivek Kumar, **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Transition-Metal-Catalyzed Coupling of Heterocyclic Alkenes via C-H Functionalization: Recent Trends and Applications, *Org. Chem. Front*. **2020**, *7*, 1527.
12. **Sonbidya Banerjee**, Manmath Mishra and Tharmalingam Punniyamurthy, Copper-Catalyzed C7-Selective C–H/N–H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines, *Org. Lett*. **2022**, *24*, 7997.
13. **Sonbidya Banerjee** and Tharmalingam Punniyamurthy, Regioselective Direct C4-Nitration of Indoles via Benzenoid C-H Activation under Aerobic Oxidation Catalysis: A Formal Access to Aminated Indoles *Org. Lett*. **2024**, *26*, 988.
14. Manmath Mishra, Kshitiz Verma, **Sonbidya Banerjee** and T. Punniyamurthy, Fe(III)-Catalyzed Regioselective C-C/C-O Bond Formation of D-A Cyclopropanes with 2,4-Dienals *Chem.Commun*. **2024**, *60*, 2788.

Conference Attended

Participant:

NOST-OCC, Udaipur, Rajasthan, December 4-7, 2019.

Poster Presentation:

1. **Sonbidya Banerjee**, Pinaki Bhusan De, Sourav Pradhan, Tariq A. Shah and Tharmalingam Punniyamurthy, "Ru(II)-Catalysed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides" OrganiX-2018, Tezpur University.
2. **Sonbidya Banerjee**, Pinaki Bhusan De, Sourav Pradhan, Tariq A. Shah and Tharmalingam Punniyamurthy, "Ru(II)-Catalysed Regioselective C-N Bond Formation of Indolines and Carbazole with Acyl Azides" Research Conclave-19, IIT Guwahati.
3. **Sonbidya Banerjee**, Sundaravel Vivek Kumar and Tharmalingam Punniyamurthy, "Site-Selective Rh-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles" XVI J-NOST, Indian Institute of Science, Bangalore, Oct 31-Nov 1, 2020. (Virtual Conference)
4. **Sonbidya Banerjee**, Sundaravel Vivek Kumar and Tharmalingam Punniyamurthy, "Site-Selective Rh-Catalyzed C-7 and C-6 Dual C-H Functionalization of Indolines: Synthesis of Functionalized Pyrrolocarbazoles" CRSI-RSC-15, IIT Guwahati
5. **Sonbidya Banerjee**, Manmath Mishra and Tharmalingam Punniyamurthy, "Copper-Catalyzed C7-Selective C–H/N–H Cross-Dehydrogenative Coupling of Indolines with Sulfoximines" Frontiers in Chemical Sciences-2022, IIT Guwahati