One-Pot Approaches for the Synthesis of Annulated Heteroarenes

A thesis submitted for the partial fulfilment of

the degree of Doctor of Philosophy

by

SEEMA RANI

Department of Chemical Sciences

Indian Institute of Science Education and Research (IISER) Mohali

Sector 81, Knowledge City, S. A. S. Nagar, Manauli PO, Mohali, 140306. Punjab, India.

July 2016

Dedicated to those people who kept me going when I wanted to give up

DECLARATION

The work presented in this thesis titled "***One-Pot Approaches for the Synthesis of Annulated Heteroarenes*****"** has been carried out by me under the supervision of **Dr. Sripada S.V. Rama Sastry** in the Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali.

This work has not been submitted in part or full for a degree, diploma or a fellowship to any other university or institute.

Whenever contributions of others are involved, every effort is made to indicate this clearly with due acknowledgements of collaborative work and discussions. This thesis is a bona fide record of original work done by me and all sources listed within have been detailed in the bibliography.

Seema Rani

Date:

Place:

In my capacity as the supervisor of the candidate's thesis work, I certify that the above statements by the candidate are true to the best of my knowledge.

Dr. Sripada S.V. Rama Sastry
Assistant Professor
Department of Chemical Sciences
Indian Institute of Science Education and Research Mohali

Date:

Place:

CONTENTS

ACKNOWLEDGEMENTS

It gives me immense pleasure to express my profound gratitude to my supervisor **Dr. Sripada S.V. Rama Sastry**, for his inspiring guidance and constant encouragement throughout the course of the present investigations. I cannot quantify the amount of gratitude towards him for believing in me and providing me an opportunity to work in his lab. He goes above and beyond his role as an advisor to be a mentor as well. He showed me the frustrating and enjoyable corners of organic synthesis in a laboratory, and most that determination is the key attitude in a research environment. I enjoyed as a Ph.D. student in his laboratory during my doctoral study. I will always remain thankful to him and consider myself privileged to be associated with him.

Further, I thank my doctoral committee members Dr. S. Arulananda Babu and Dr. R. Vijaya Anand for their valuable suggestions and for spending their valuable time during the yearly assessment of my work.

It is my privilege to thank IISER Mohali director, Professor N. Sathyamurthy, for providing the space and very good infrastructural facilities.

I acknowledge NMR, X-ray and HRMS facilities of IISER Mohali. I would like to specially thank NMR facility committee members Dr. Kavita Dorai, Dr. R. Vijaya Anand, Professor P. Guptasarma for their help. I am very much thankful to Dr. A. R. Choudhury, Professor Sanjay Mandal, Dr. Sanjay Singh for cooperation in recording X-ray analyses of my samples. Next, I sincerely thank HRMS facility committee members, Professor K. S. Viswanathan, Professor P. Guptasarma and Dr. S. A. Babu. I thank head of the department, Professor K. S. Viswanathan, and all other faculty members of the Department of Chemical Sciences for facilitating the use of various departmental instruments and their useful suggestions.

I wish to thank Dr. P. Balanarayan, Dr. Sugumar Venkataramani, Dr. Satya Prakash Singh from IISER Mohali for their useful discussions and valuable suggestions. I sincerely thank Prof. Prasad V Bharatam and Ms. Sheenu from NIPER Mohali for computational support.

I would like to express my heartfelt thanks to my labmembers Messers Rajendra, Bishnu, Bankar, Raghu, Uttam, Sangha, Jopaul, Bara, Ms. Sonu, Manisha, and Dr. Jagdeep for maintaining healthy environment and useful discussions in the lab which helped me in learning and understanding various aspects of research. Further, I thank all summer trainees who worked for short time projects in our lab.

Special thanks to my friends Priya, Divya, Sanjana, Preeti, Meenakshi, Pankaj. I am also thankful to Mr. Triveni, Mr. Balbir for their help on time related to research. Mr. Mangat, Mr. Bahadur, Mr. Satvinder of the chemistry teaching labs are acknowledged for their help. I also wish to thank all my friends in IISER Mohali.

I take this opportunity to thank all the teachers and lecturers who taught me during my career, because of whom I am here today.

I am grateful to IISER Mohali for my fellowship during my doctoral study. I wish to thank to IIT Kanpur and NIPER for providing the HRMS data. Additionally, I also would like to thank to Department of Science and Technology (DST), India and IISER Mohali for funding and enabling me to complete my Ph.D.

Finally, I would like to sincerely thank my parents and my family members for their motivation and support for accomplishing my dream to obtain the highest degree.

SUMMARY

Annulated heteroarenes are ubiquitous in a diverse range of bioactive natural products, pharmaceutically important compounds and organic materials. Among a diverse range of annulated heteroarenes, cyclopenta[*b*]annulated hetroarenes are especially attractive due to their unique biological, physicochemical and opto-electronic properties. Consequently, a myriad of attractive strategies for the cyclopenta[*b*]annulation of heteroarenes have been developed. Despite the availability of several synthetic strategies for cyclopenta[*b*]annulated heteroarenes, the development of general and more efficient one-pot methods starting from readily accessible materials in an inexpensive and atom economical manner remains an area of intense research.

The thesis entitled "*One-Pot Approaches for the Synthesis of Annulated Heteroarenes"* demonstrates the efforts towards the development of new synthetic methodologies for the one-pot annulation of herteroarenes. For the sake of convenience, the content of thesis has been divided into five sections. In all the sections, a brief introduction is provided to keep the presnt work in proper prespective, the compounds are sequentially numbered (bold), and references are marked sequentially as superscript and listed at the end of the thesis.

The first section provides a non-exhaustive introduction to the well-established synthetic approaches toward cyclopentannulation of heteroarenes.

The second section of this thesis discusses the acid promoted ring transformation of furyl/benzofuryl carbinols, and cyclopenta[*b*]annulation of benzothienyl carbinols. The first part talks about the reaction of furyl/benzofuryl carbinols with various nucleophiles under Lewis acid catalysis, and elaboration to some architecturally novel scaffolds. Work in the area of acid catalyzed reaction of furyl/benzofuryl carbinols has also resulted in the discovery of a novel Brønsted acid catalyzed benzofuran ring opening and furan recyclization sequence leading to the formation of tri- and tetrasubstituted furans. Furyl/benzofuryl carbinols and 1,3-dicarbonyls in the presence of a catalytic amount of super acid generates functionalized, polysubstituted furans in good to excellent yields. After the success of furyl carbinols as substrates, an interest in using the benzothienyl carbinols led us to develop the new one-pot protocol for the cyclopentannulation of benzothiophenes. In this new protocol, synthesis of 1,2,3-trisubstituted cyclopenta[*b*]thiophenes has been achieved through a polyphosphoric acid mediated domino process under solvent-free conditions.

Third scetion describes an efficient relay catalytic process involving Au(I)/Brønsted acid to access various di- and trisubstituted cyclopentannulated indoles from easily accessible 1-(2-aminophenyl)prop-2-ynols and readily available 1,3-dicarbonyls. The generality and synthetic utility of this method was further demonstrated *via* the synthesis of pyrrolo[1,2-*a*]indoles.

A continued interest in developing methodologies for the cyclopentannulation of indoles led us to examine 1-(2-aminophenyl)pent-4-en-2-ynols (enynols) as the reactive subunits. Fourth section will discuss an expedient relay gold(I) and Brønsted acid catalyzed intramolecular hydroamination/Nazarov-type cyclization cascade of enynols for the synthesis of various functionalized 1,2-disubstituted cyclopenta[*b*]indoles. An attractive feature of this method lies in its ability to generate natural product-like complex pentacyclic structures and indole steroidal conjugates. Further synthetic utility of this methodology has been successfully demonstrated *via* the enantioselective synthesis of the core carbon skeleton of the *nor*-polyveolinone.

Having developed one-pot relay processes for the construction of complex indole derivatives, we planned to extend these strategies for the synthesis of other annulated indoles. Among them, *β*-carbolines attracted our attention owing to their widespread occurrence in several bioactive natural products and medicinally interesting molecules. Towards this, fifth section discuses the one-pot triple relay catalytic approach, which constitutes sequential employment of silver, bismuth and palladium catalysts for the synthesis of *β*-carbolines through a one-pot cascade involving an intramolecular hydroamination, Friedel-Crafts-type dehydrative azidation, and an unprecedented pyridine annulation of the ε,ω-unsaturated azides. In addition, a one-pot bimetallic relay catalytic approach has been developed to access novel 3-substituted-4-hydroxy-*β*-carbolines in good to excellent yields. Further, we elaborated this to efficiently access other significant [*c*]-fused pyridines such as 1,3-disubstituted and 1,3,4-trisubstituted benzofuro[2,3-*c*]pyridines, benzothieno[2,3-*c*]pyridines and isoquinolines.

LIST OF ABBREVIATIONS

Ac	:	acetyl
AIBN	:	azobisisobutyronitrile
aq	:	aqueous
atm	:	atmospheric
BINAP	:	2,2'-bis(diphenylphosphino)-1,1' binaphthyl
Bn	:	benzyl
Boc	:	*tert*-butyloxycarbonyl
BOX	:	bis(oxazoline)
brd	:	broad doublet
brs	:	broad singlet
calcd	:	calculated
cbz	:	carboxybenzyl
CFL	:	compact fluorescent lamp
COD	:	cyclooctadiene
Cp^*	:	1,2,3,4,5-pentamethylcyclopentadienyl
d	:	doublet
DBU	:	1,8-diazabicyclo[5.4.0]undec-7-ene
dba	:	dibenzylideneacetone
DCE	:	dichloro ethane
DCM	:	dichloro methane
dd	:	doublet of a doublet
ddd	:	doublet of a doublet of doublet
DMAP	:	4-dimethylaminopyridine
DMA	:	dimethylacetamide
DME	:	dimethoxyethane
DMF	:	*N,N'*-dimethyl formamide
DMSO	:	dimethyl sulfoxide
DPP	:	diphenylphosphine acid

dppb	:	1,4-bis(diphenylphosphino)butane
dq	:	doublet of quartet
dr	:	diasteriomeric ratio
dt	:	doublet of a triplet
ee	:	enantiomeric excess
equiv	:	equivalents
ESI	:	electron spray ionization
FT-IR	:	Fourier transform infrared spectroscopy
h	:	hour(s)
HFIP	:	hexafluoroisopropanol
HMDS	:	hexamethyldisilazane
HRMS	:	high resolution mass spectrum
Hz	:	Hertz
ppm	:	parts per million
IBX	:	2-iodoxybenzoic acid
J	:	coupling constant
m	:	multiplet
Mes	:	mesityl
mg	:	milli gram(s)
MHz	:	mega hertz
min	:	minute(s)
mL	:	milliliter(s)
mmol	:	milli mole(s)
m.p.	:	melting point
MS	:	molecular sieves
m/z	:	mass/charge
NBS	:	*N*-bromosuccinimide
NIS	:	*N*-iodosuccinimide
Phen	:	1,10-phenanthroline
PMB	:	4-methoxy benzyl
PPA	:	polyphosphoric acid

PPTS	:	pyridinium *p*-toluenesulfonate
PTSA	:	*p*-toluenesulfonic acid
q	:	quartet
qd	:	quartet of doublet
RT	:	room temperature
s	:	singlet
SEM	:	[2-(trimethylsilyl)ethoxy]methyl
sept	:	septet
t	:	triplet
^{t}Bu	:	*tert*-butyl
TBAF	:	tetrabutylammonium fluoride
TBAB	:	tetrabutylammonium bromide
TBS	:	*tert*-butyldimethylsilyl
TEMPO	:	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
Tf	:	trifluoromethanesulfonate
TFAA	:	trifluoroacetic anhydride
TMEDA	:	tetramethylethylenediamine
TFE	:	trifluroethanol
TMS	:	trimethylsilyl
td	:	triplet of a doublet
tert	:	tertiary
THF	:	tetrahydrofuran
TMS	:	tetramethylsilane
TLC	:	thin layer chromatography

Section 1

General introduction about cyclopenta[b]annulated heteroarenes

Heterocyclic chemistry is one of the most complex and intriguing branches of organic chemistry, and heterocyclic compounds constitute the largest and most varied family of organic compounds. Heteroarenes are an essential part of nature and mankind. They play an active role in the metabolism of all living cells and widely found in nature, particularly, nucleic acids, vitamins, proteins, hormones, amino acids, plant alkaloids, anthocyanins, and flavones, *etc*. The designer heteroaromatic compounds manifest the wide applications in optics, electronics, and materials science such as dyestuff, fluorescent sensors, brightening agents, information storage devices, and analytical reagents. In addition, they have enormous potential to be the lead structures for the design of new drugs. Heterocyclic compounds possess various pharmacological activities such as antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV,

antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal, to mention a few.

Heteroaromatic chemistry has been a topic of significant research interest and continues to be the one of the most active areas of organic chemistry.[1] Especially, oxygen, nitrogen, and sulphur containing heteroaromatic compounds such as benzofuran, indole and benzothiophene have maintained the curiosity of researchers through years of historical progress of organic synthesis. Almost unlimited derivatives of these heteroaromatic compounds can be designed which can exhibit fascinating chemical and biological properties.

Among various heteroaromatics, novel polycyclic frameworks with the most diverse physical, chemical and biological properties are especially important. The fusions of several rings lead to geometrically well-defined rigid polycyclic structures and thus hold the promise of a high functional specialization resulting from the ability to orient substituents in three-dimensional space. Polycyclic heteroaromatic compounds with fused five-, six-, seven- or eight-membered rings are well known in literature with many of them also being biologically active. Among various annulated heteroaromatic compounds, cyclopenta[*b*]heteroaryls are especially attractive due to their unique biological, physicochemical and optico-electronic properties. An overview of the pentannulated heterocyclic structures present in a diverse range of bioactive compounds, including natural products and their synthetic derivatives is presented in Fig. 1.[2]

During past few decades, there has been much consideration towards the synthesis of cyclopentannulated heteroarenes and screening of their different pharmacological activities. It has been recently shown that the introduction of cyclopenta-fused heteroaromatic core in the backbone could improve their properties as organic semiconductors.[3]

The presence of complex molecular architectures coupled with impressive pharmacological properties has attracted the attention of several researchers to develop new processes for the construction of cyclopentannulated derivatives. Toward this, various methods such as Nazarov reaction, [3+2] cycloaddition, Fischer indolization, Pauson–Khand reaction, intramolecular Friedel–Crafts reaction and metal catalyzed cyclization have been reported. Few important methods leading to the synthesis of cyclopentannulated heteroarens is discussed in the next few subsections.

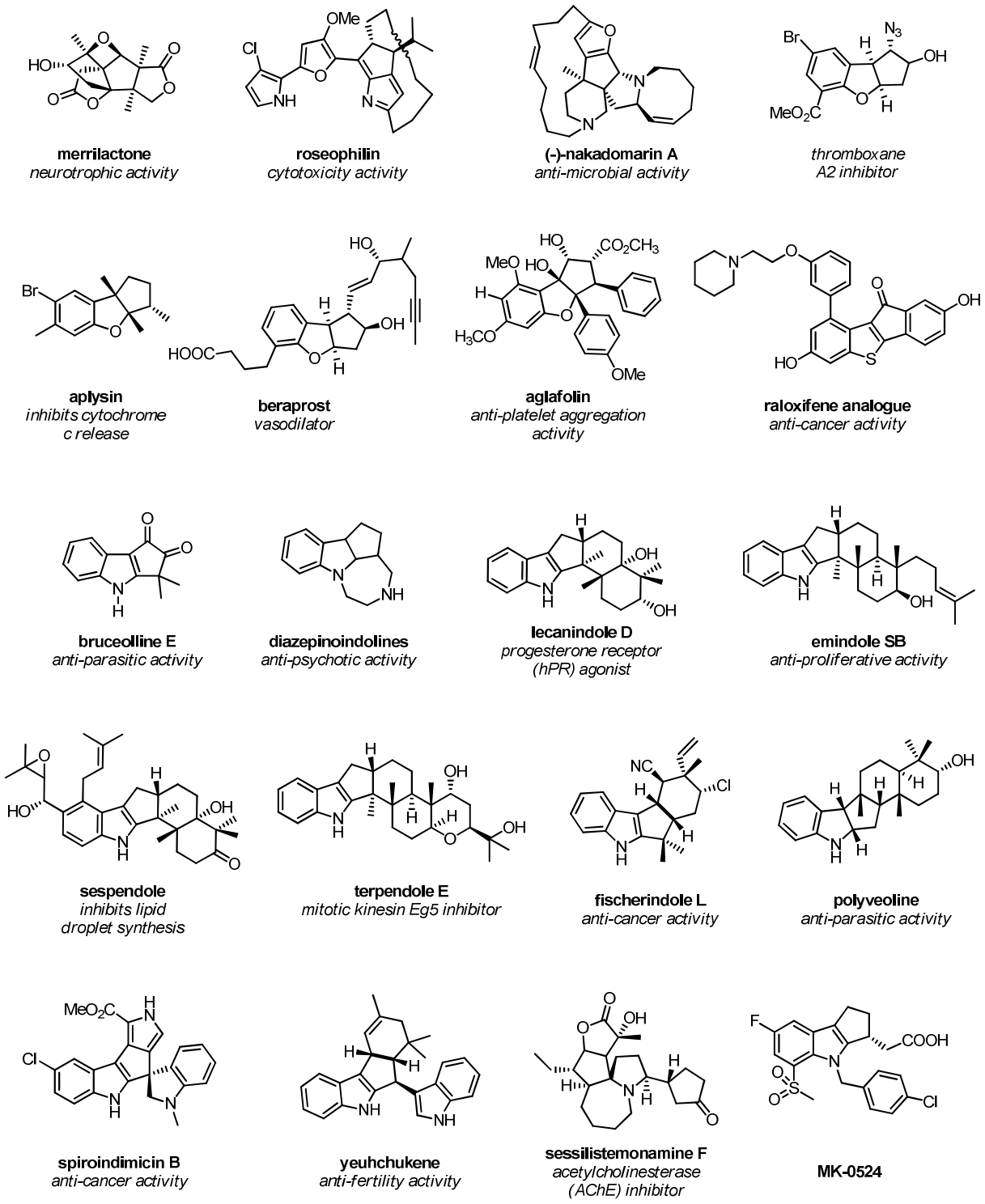
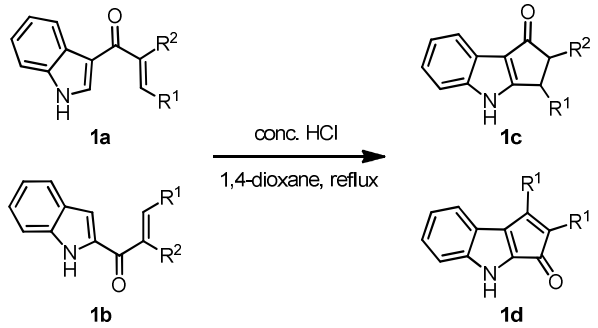


Figure 1: Representative examples of bioactive cyclopenta-fused heteroaromatic compounds.

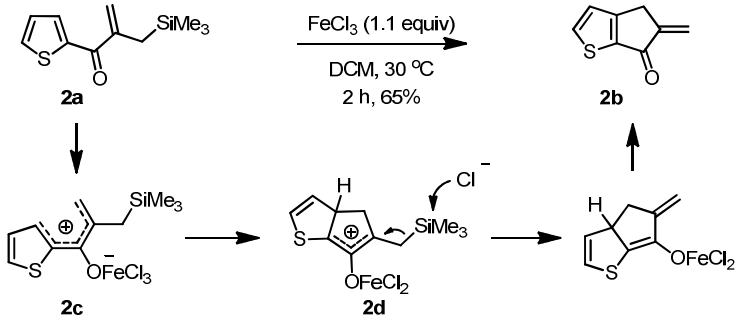
1.1: Nazarov cyclization based approaches

In 1990, Bergman *et al.*[4] reported intramolecular ring closure of *α,β*-unsaturated acylindoles (**1a** and **1b**) for the synthesis of cyclopent[*b*]indol-l-ones **1c** and cyclopent[*b*]indol-3-ones **1d**, Scheme 1.



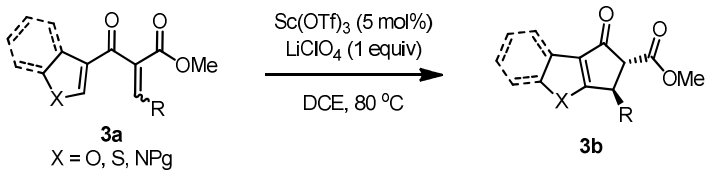
Scheme 1: Cyclization of acyl indoles.

In 1992, Kang *et al.*[5] reported the $FeCl_3$ mediated Nazarov cyclization of thienyl vinyl ketone **2a** to afford the cyclopentannulated thiophene **2b** in good yield, Scheme 2. The $FeCl_3$ complexed, pentadienylic cation **2c** undergoes a ring closure to generate a cyclopentenylic cation **2d**, which, by the rapid loss of the trimethylsilyl group and further bond reorganization provides the cyclopentannualted thiophene **2b**.



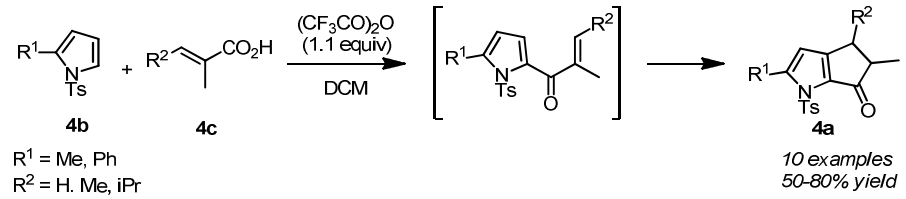
Scheme 2: Nazarov cyclization of thienyl vinyl ketone.

In 2006, Frontier *et al.*[6] developed a general and efficient Lewis acid catalyzed Nazarov cyclization of systems containing heteroaromatic components (**3a**), Scheme 3. This method provided access to a range of cyclopentanone-fused heteroarenes (**3b**) in moderate to good yields.



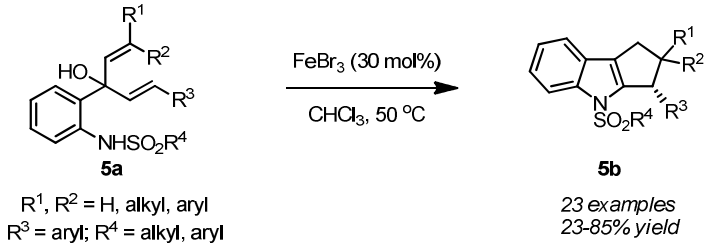
Scheme 3: Nazarov cyclization of heteroaromatic compounds.

In 2006, Knight *et al.*[7] reported an efficient method for the construction of cyclopenta[*b*]pyrroles **4a**. Reaction between N-tosyl pyrroles **4b** and unsaturated carboxylic acids **4c** in the presence of trifluoroacetic anhydride resulted in the smooth acylation of pyrroles, which followed by 4π-electrocyclization generated the respective cyclopenta[*b*]pyrroles **4a** in good yields, Scheme 4.



Scheme 4: One-pot Nazarov cyclization of pyrroles for the synthesis of cyclopenta[*b*]pyrroles.

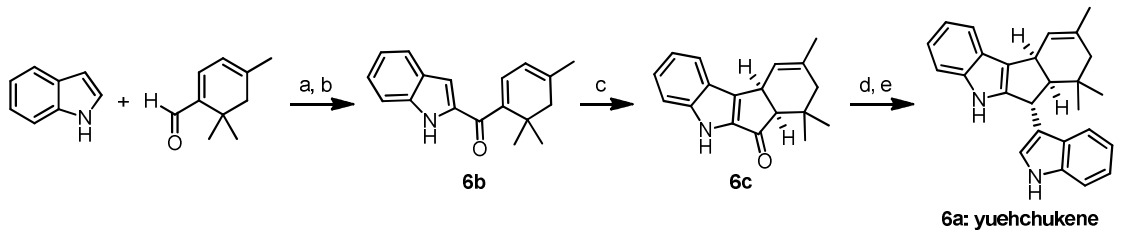
In 2016, Kwon *et al.*[8] described the first Lewis acid-catalyzed intramolecular interrupted Nazarov cyclization of 1,4-pentadien-3-ols **5a** for the construction of substituted cyclopenta[*b*]indoles **5b**. The Nazarov cyclization, nucleophilic amination, and isomerization sequence provided the respective cyclopentannulated indoles **5b** in high diastereo- and regioselectivities and good yields, Scheme 5.



Scheme 5: Nazarov cyclization of 1,4-pentadien-3-ols for the synthesis of cyclopenta[*b*]indoles.

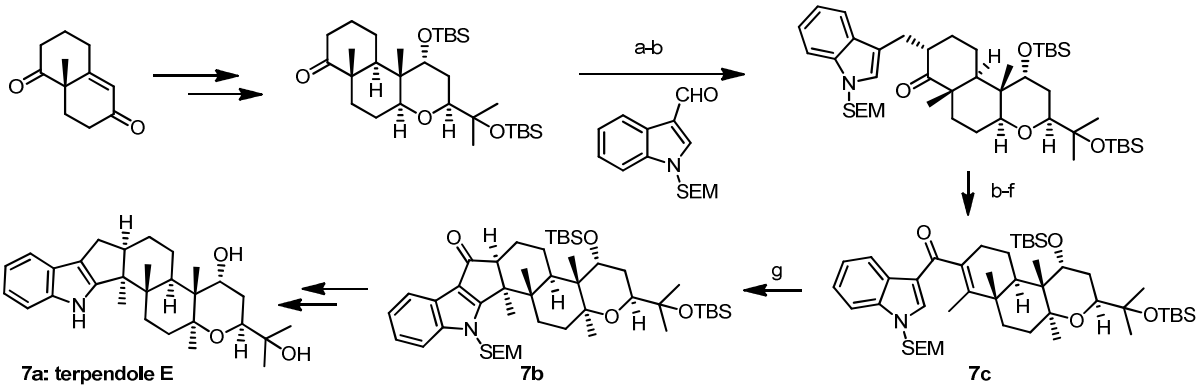
1.1.1: Application of Nazarov reaction in the synthesis of natural products

In 1988, Bergman *et al.*[9] reported the synthesis of yuehchukene **6a** from readily available starting materials with complete regio- and stereocontrol by employing Nazarov cyclization as the key step, Scheme 6. The 4π-electrocyclization of **6b** afforded the advanced intermediate **6c** which upon subsequent transformations furnished yuehchukene **6a**.



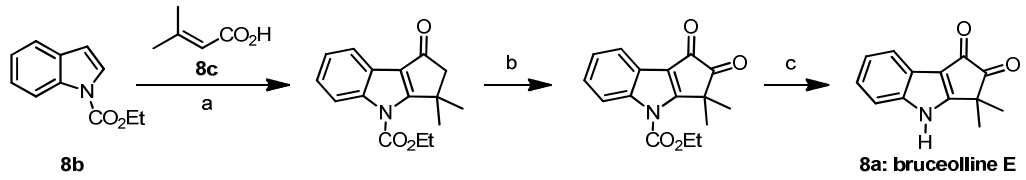
Scheme 6: Synthesis of yuehchukene **6a** by employing Nazarov cyclization as key step. Reagents and conditions: (a) (i) *n*-BuLi (ii) CO_2, ^{t}BuLi (iii) -78 °C, 2 h, 61% yield over three steps. (b) MnO_2, DCM, RT, 3 h, 82%. (c) TFA, DCM, reflux, 6 h, 70%. (d) $LiEt_3BH$, THF, RT, 3 h, 73%. (e) indole, HCl, MeOH-DCM, RT, 0.75 h, 67%.

In 2010, Giannis *et al.*[10] described the application of the photo-Nazarov cyclization as a mild and efficient method to access 16-*epi*-terpendole E **7a**. The construction of the indole diterpene skeleton **7b** was accomplished based on photo-Nazarov cyclization of the enone intermediate **7c**. Further synthetic transformations of **7b** provided an efficient access to **7a**, Scheme 7.



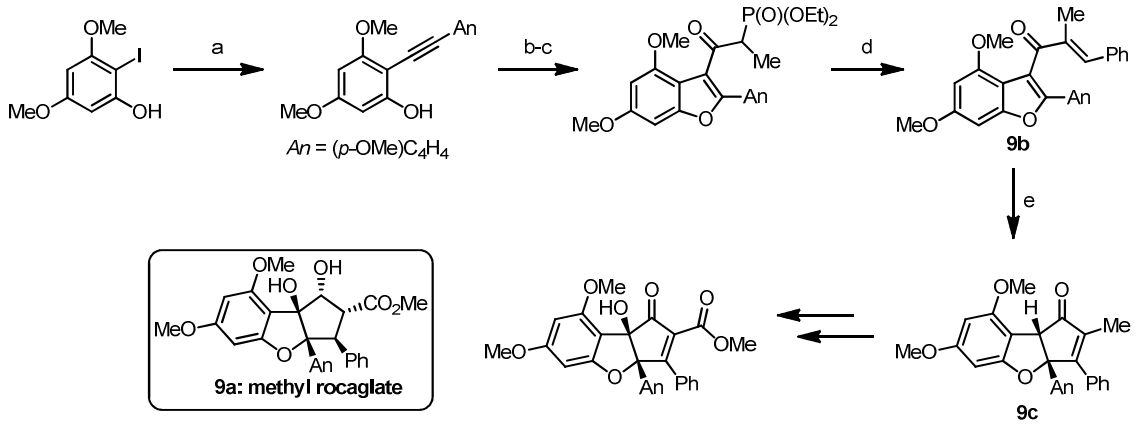
Scheme 7: A novel approach to indoloditerpenes by photo-Nazarov cyclization. Reagents and conditions: (a) KO^{t}Bu, benzene, RT to reflux, 4 h. (b) H_2, Pd/C, EtOAc, RT, 2 h, 68% yield over two steps. (c) MeLi, THF, -78 °C, 20 min. (d) DDQ, THF, 0 °C, 0.5 h, 88% over two steps. (e) Burgess reagent, toluene, 90 °C, 1.5 h. (f) ^{t}BuOH, KO^{t}Bu, 75 °C, 2 h, 51% yield over two steps. (g) *hv*, 350 nm, CH_3CN, RT, 5.5 h, 80%.

In 2011, Badenock *et al.*[11] presented an efficient synthesis of bruceolline E **8a** in three steps from the known ethyl indole-1-carboxylate **8b** *via* the tandem acylation/Nazarov cyclization with 3,3-dimethyl acrylic acid **8c**, followed by selenium dioxide oxidation to install the α-diketone functionality, Scheme 8.



Scheme 8: Synthesis of bruceolline E **8a**. Reagents and conditions: (a) TFAA, DCE, reflux, 72 h, 66%. (b) SeO_2, aq 1,4-dioxane, 70 ^oC, 16 h, 95%. (c) TBAF, THF, 2 h, 97%.

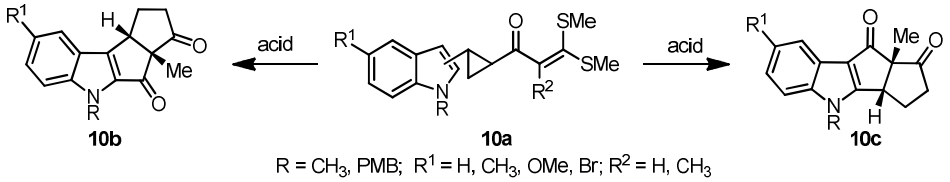
In 2012, Magnus *et al.*[12] reported a formal synthesis of methyl rocaglate **9a**, using an unprecedented acetyl bromide mediated Nazarov cyclization of **9b** to afford the key intermediate **9c**, Scheme 9.



Scheme 9: Formal synthesis of methyl rocaglate **9a** by employing Nazarov cyclization as the key step. Reagents and conditions: (a) AnCCH, EtMgBr, $Pd(PPh_3)_2Cl_2$, THF, 60 °C, 99%. (b) $Pd(OAc)_2$, CO atm, CBr_4, $NaHCO_3$, MeOH, 25 °C, 75%. (c) $EtP(O)(OEt)_2$, *n*-BuLi, THF, 90%. (d) PhCHO, LiCl, DBU, MeCN, 82 °C, 74%. (e) AcBr, DCE, 60 °C, 6 h, 81%.

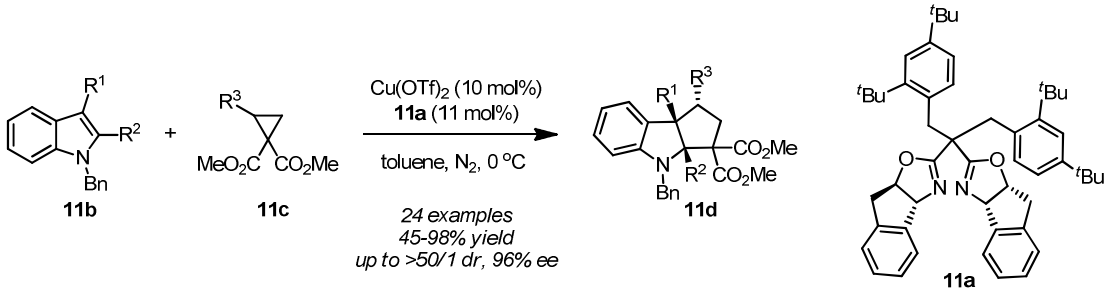
1.2: [3+2] cycloaddition based approaches for cyclopentannulations

In 2006, Ila *et al.*[13] reported a domino carbocationic rearrangement of a number of 2- and 3-indolylcyclopropyl ketones **10a** in the presence of various Brønsted and Lewis acids for the generation of cyclopentannulated indoles **10b** and **10c**, Scheme 10.



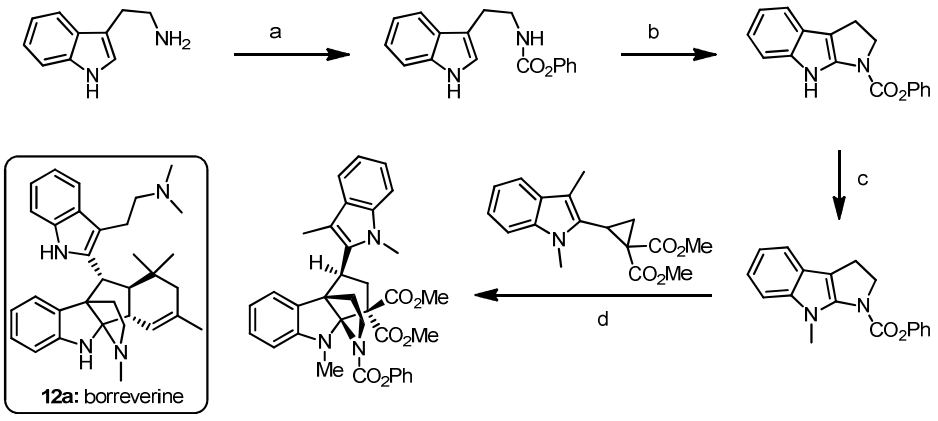
Scheme 10: Domino carbocationic rearrangement of α-[bis(methylthio)methylene]alkyl-2-(3/2-indolyl) cyclopropyl ketones.

In 2013, Tang *et al.*[14] presented a highly diastereo- and enantioselective BOX/Cu(II) **11a** catalyzed C2, C3-cyclopentannulation of indoles **11b** with donor–acceptor cyclopropanes **11c** on the basis of asymmetric formal [3+2] cycloaddition of indoles, Scheme 11. This reaction provides rapid and facile access to a series of enantioenriched cyclopentafused indolines **11d**.



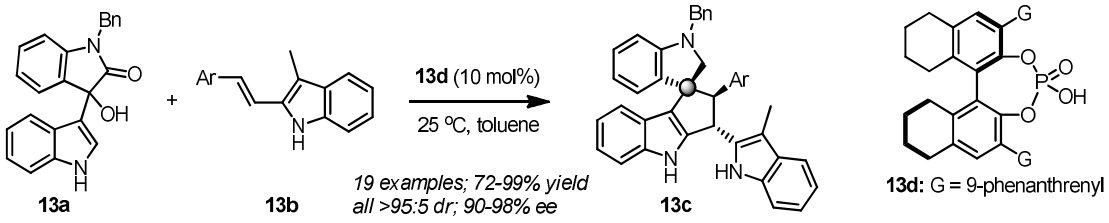
Scheme 11: Copper-catalyzed highly enantioselective cyclopentannulation of indoles.

The synthetic utility of the above-described methodology was further demonstrated by synthesis of the core structure of borreverine **12a** natural product, Scheme 12.



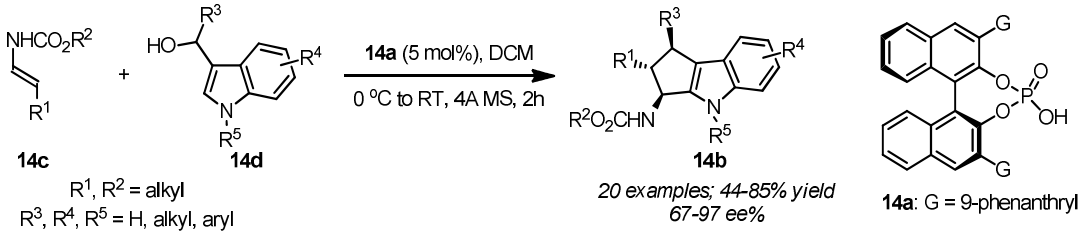
Scheme 12: Synthesis of the core of borreverine **12a**. Reagents and conditions: (a) $ClCO_2Ph$, K_2CO_3, EtOAc/H_2O 0 °C-RT, 99%. (b) ^{t}BuOCl, Et_3N, DCM, N_2, 0 °C-RT, 45%. (c) NaH, MeI, DMF, 0 °C-RT, 54%. (d) $Cu(OTf)_2$, 11a (10 mol%), toluene, -40 °C, 96%, 95% ee.

In 2014, Shi *et al.*[15] described an organocatalytic asymmetric formal [3+2] cycloaddition of isatin-derived 3-indolylmethanol **13a** with 3-methyl-2-vinylindole **13b** for the highly stereoselective construction of spiro[cyclopenta[*b*]indole-1,3'-oxindole] **13c** with the concomitant creation of three contiguous stereogenic centers, Scheme 13.



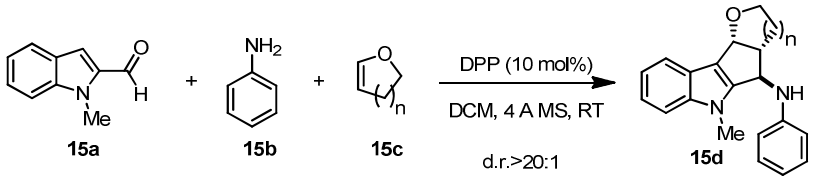
Scheme 13: Organocatalytic asymmetric formal [3+2] cycloaddition of **13a** and **13b**.

In 2015, Masson *et al.*[16] reported highly enantio- and diastereoselective chiral phosphoric acid **14a** catalyzed synthesis of 3-aminocyclopenta[*b*]indoles **14b** *via* formal [3+2] cycloaddition of enecarbamates **14c** and 3-indolylmethanols **14d**, Scheme 14. The chiral phosphoric acid **14a** plays a dual role for the simultaneous activation of both partners of the cycloaddition.



Scheme 14: Catalytic enantioselective synthesis of 3-aminocyclopenta[*b*]indoles **14b**.

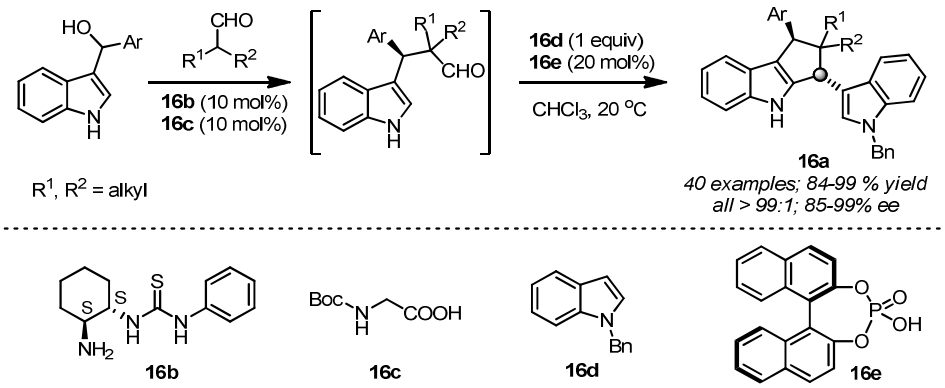
In 2015, Rodriguez *et al.*[17] presented the Brønsted acid catalyzed unprecedented stereoselective [3+2] carbocyclization reaction of indole-2-carboxaldehydes **15a**, anilines **15b**, and electron-rich alkenes **15c** to obtain cyclopenta[*b*]indoles **15d**, Scheme 15. This anti-Povarov reaction involves a stepwise Mannich/Friedel–Crafts cascade sequence for the generation of cyclopentane fused indoles.



Scheme 15: Anti-Povarov reaction for the cyclopenta[*b*]indoles.

1.3: Friedel–Crafts alkylation strategy for cyclopentannulations

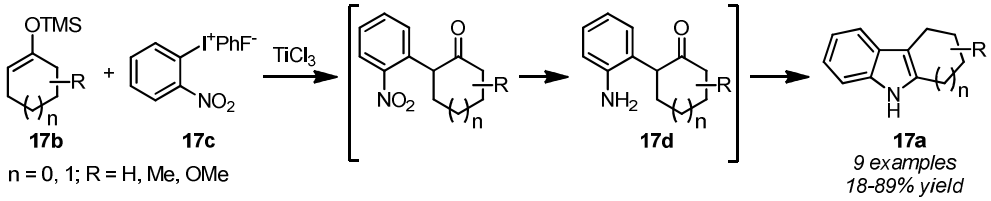
In 2012, Guo *et al.*[18] described a highly efficient diastereoselective and enantioselective one-pot multistep reaction for the construction of cyclopenta[*b*]indoles **16a**, Scheme 16. This process involves consecutive α-alkylation catalyzed by a thiourea catalyst **16b**, and Brønsted acid **16e** catalyzed Friedel–Crafts alkylation reactions. Structurally diverse cyclopenta[*b*]indoles (**16a)** obtained in high yields, with excellent diastereoselectivities and enantioselectivities, under mild reaction conditions.



Scheme 16: Multistep one-pot synthesis of polysubstituted cyclopenta[*b*]indoles.

1.4: Fischer indole synthesis based approaches for cyclopentannulations

In 1999, Rawal *et al.*[19] presented a regiocontrolled synthesis of carbocycle-fused indoles **17a**. The two-step sequence involves the regiospecific arylation of silyl enol ethers **17b** with *o*-nitrophenylphenyliodonium fluoride **17c**. Reduction of the aromatic nitro group with $TiCl_3$ followed by spontaneous condensation of the aniline **17d** afforded indoles **17a**, Scheme 17.

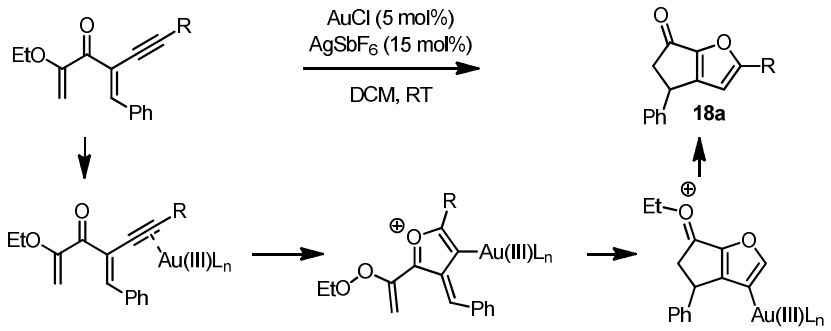


Scheme 17: Regiocontrolled synthesis of carbocycle-fused indoles *via* arylation of silyl enol ethers with *o*-nitrophenylphenyliodonium fluoride.

1.5: Metal catalyzed cyclopentannulation of heteroaryls

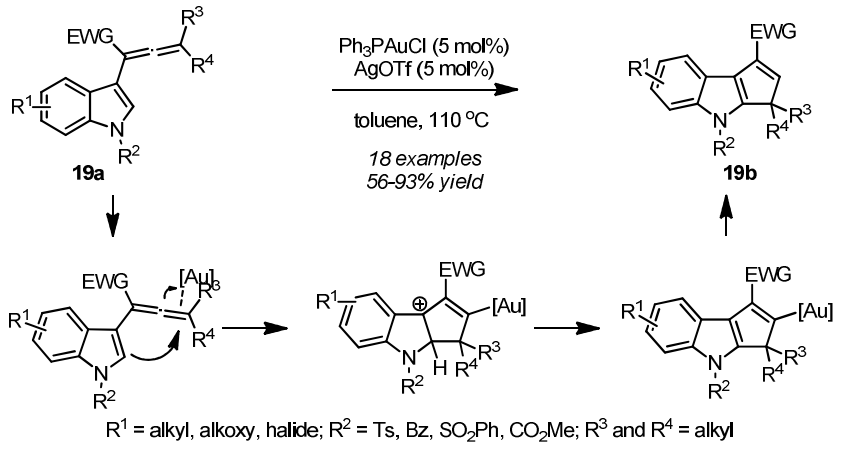
1.5.1: Au-catalyzed

In 2011, Krafft *et al.*[20] reported a one-pot tandem Au(III)-catalyzed heterocyclization/Nazarov cyclization sequence for accessing substituted carbocycle fused furans **18a**, Scheme 18. It was observed that reaction rate depends on substitution pattern; substrates with electron-donating substituents on the alkyne ring underwent fast cyclization while electron poor or bulky groups slowed down the cyclization.



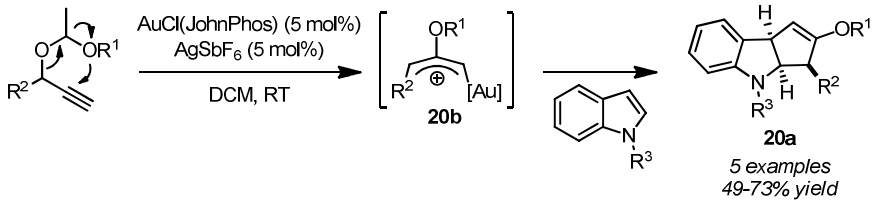
Scheme 18: Au(III)-catalyzed heterocycliztion/Nazarov reaction.

In 2012, Chen *et al.*[21] presented gold-catalyzed cyclization reaction of 3-allenyl indoles **19a** for the formation of cyclopenta[*b*]indole derivatives **19b** in moderate to excellent yields *via* C-2 functionalization of the indole unit, Scheme 19. The presence of the electron-withdrawing groups on the allene is crucial for this transformation.



Scheme 19: Au(I) catalyzed cyclization of 3-allenyl indoles.

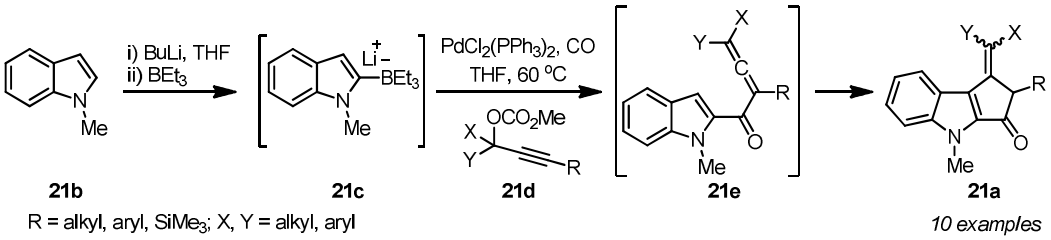
In 2013, Fiksdahl *et al.*[22] presented a gold catalyzed diastereoselective synthesis of cyclopentene-fused dihydroindole **20a**, *via* the formation of highly reactive cationic gold intermediate **20b** by 1,2-alkoxy shift followed a formal [2+3] cycloaddition of indoles, Scheme 20.



Scheme 20: Gold catalyzed synthesis of dihydroindole derivatives.

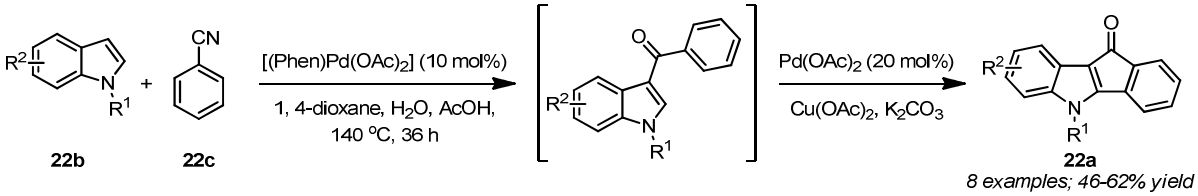
1.5.2: Pd-catalyzed

In 1996, Agata *et al.*[23] developed a new one-pot procedure for the generation of cyclopenta[*b*]indoles **21a** starting from **21b**. The Pd-catalyzed carbonylative cross-coupling reaction of borate **21c** and prop-2-ynyl carbonates **21d** generated **21e**, which upon subsequent cyclization provided access to the substituted cyclopentane fused indoles **21a**, Scheme 21.



Scheme 21: Palladium catalyzed the carbonylative cross-coupling reaction.

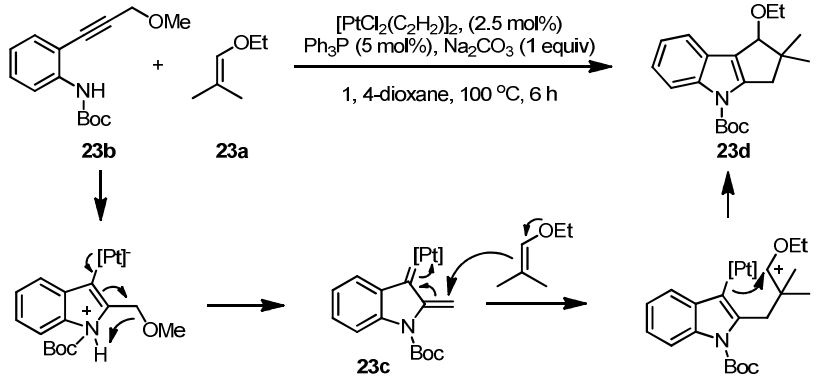
In 2013, Song *et al.*[24] reported an efficient, atom-economical, and operationally simple two step-one pot strategy for the synthesis of indenoindolones **22a**, Scheme 22. A Pd-catalyzed addition of N-alkylated indoles **22b** to nitriles **22c**, followed by Pd-catalyzed intramolecular oxidative C-H/C-H coupling furnished diverse indenoindolones **22a** in good yields.



Scheme 22: Palladium catalyzed one-pot synthesis of indenoindolones **22a**.

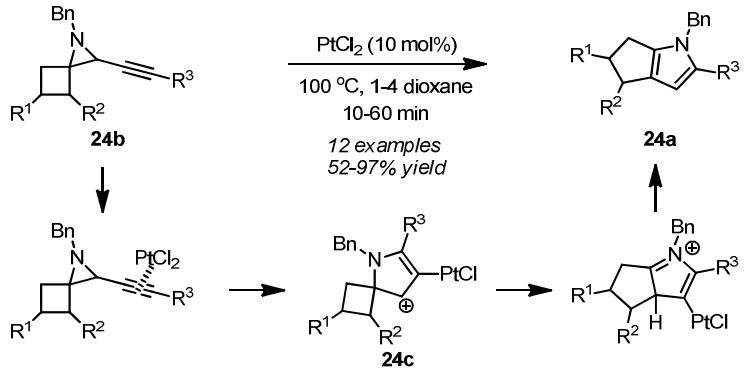
1.5.3: Pt-catalyzed

In 2011, Iwasawa *et al.*[25] reported Pt(II)-catalyzed generation of unsaturated carbene intermediates from various propargyl ether derivatives **23a** *via* electrophilic activation of alkynes **23b**, Scheme 23. *In situ* generated unsaturated carbene complexes **23c** undergo [3+2] cycloaddition reaction with various vinyl ethers **23a**, leading to the efficient formation of indoles **23d** fused with a five-membered ring in high yields.



Scheme 23: Pt(II)-catalyzed synthesis of cyclopentannulated indole **23d**.

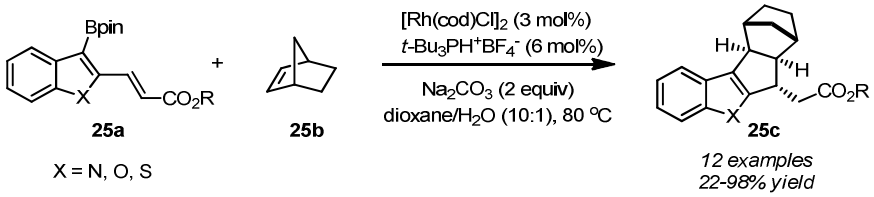
In 2011, Yoshida *et al.*[26] developed a method for the synthesis of cyclopenta[*b*]pyrroles **24a** by Pt-catalyzed cascade cyclization/ring expansion of 2-alkynyl-1-azaspiro[2.3]hexanes **24b**, Scheme 24. The reaction afforded a variety of substituted cyclopenta[*b*]pyrroles in an efficient manner. The coordination of Pt to the triple bond, followed by a regioselective 1,2-migration/ring expansion generated the pyrrolylplatinum species **24c** which after proto-demetallation furnished the cyclopenta[*b*]pyrrole **24a**.



Scheme 24: Pt (II)-catalyzed synthesis of cyclopentannulated pyrroles **24a**.

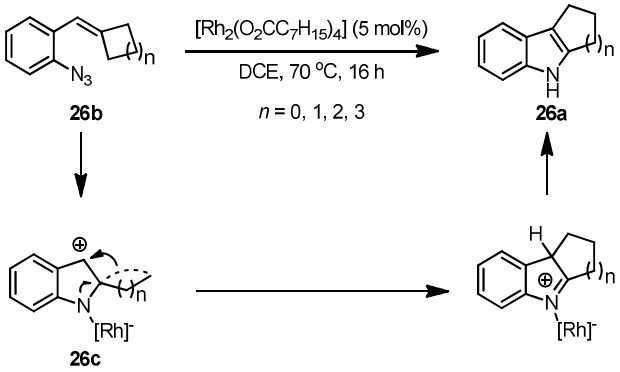
1.5.4: Rh-catalyzed

In 2008, Lautens *et al.*[27] developed a cascade Rh-catalyzed addition/cyclization reaction of bifunctional heteroaromatic boronate esters **25a** and strained bicyclic alkenes **25b** to generate a variety of polycyclic heteroaromatic molecules containing benzothiophene, benzofuran, and indole moieties (**25c**), Scheme 25.



Scheme 25: Rhodium-catalyzed addition/cyclization reaction sequence.

In 2011, Driver *et al.*[28] developed a one-pot synthesis of annulated indoles **26a** from azides **26b**, in high yields, *via* Rh(II)-catalyzed C-N bond formation followed by ring expansion, Scheme 26. The catalytic cycle was initiated by the formation of rhodium nitrene **26c** *via* the coordination of rhodium carboxylate to the azide followed by the extrusion of N_2.



Scheme 26: Rhodium-catalyzed synthesis of annulated indoles **26a**.

The aforementioned methods have motivated us to conceive new advancements in the synthesis of cyclopenatnnulated heteroarenes with broad substrate scope. Accordingly, we initiated research work in this direction and the results are presented in the next few sections of the thesis.

Section 2

Acid promoted ring transformation of furyl/benzofuryl carbinols, and cyclopentannulation of benzothienyl carbinols

Organic compounds possessing five-membered heterocycles are quite frequently encountered in nature. Among five-membered heteroarenes, furans constitute a significant class which are often associated with several important biological properties such as anti-fungal, anti-cancer, anti-bacterial, antiarrhythmic, antiulcer, anti-HIV, etc.[29] The furan subunit is incorporated in various natural products such as furanoflavonoids, furanolactones, furanocoumarins and many natural terpenoids.[30] In addition, furans are primary structural motifs in several macromolecules (such as porphyrins and calixarenes), functional polymers and pharmaceuticals.[31] During the past few decades, there has been much consideration towards the synthesis of furan derivatives and screening of their different pharmacological activities, Fig. 2. One such example, furan-containing bestselling drug, ranitidine **27a**, which was introduced in 1981 as a brand name Zantac.[32] It is used for the treatment of peptic ulcer and gastroesophageal

reflux diseases as its way of activity is an antagonist of histamine H_2 receptors and thereby inhibiting the stomach acid production.

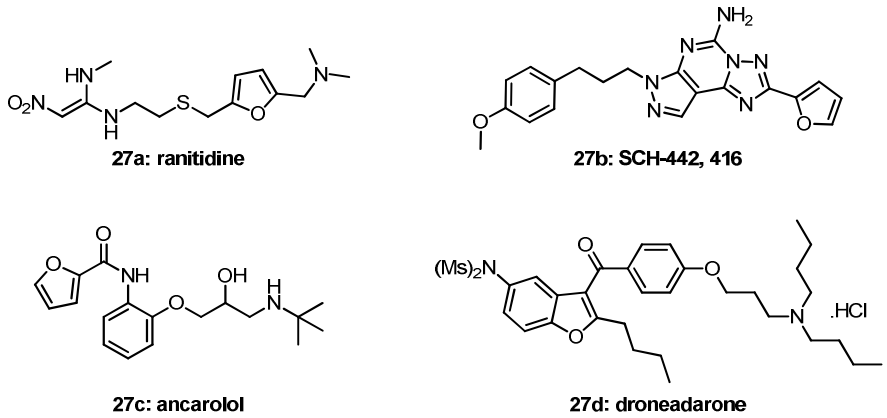
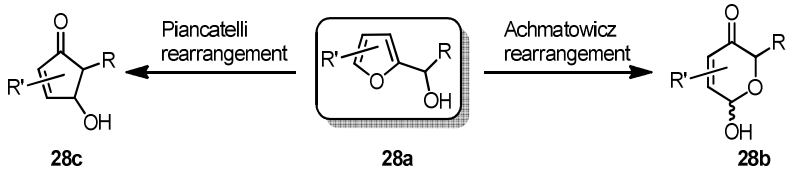


Figure 2: Representative examples of furan-containing drugs.

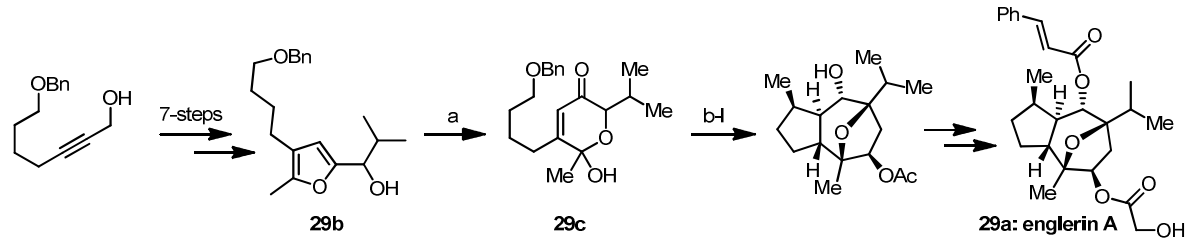
The low Dewar resonance energy of 4.3 kcal/mol and the presence of masked functionalities of 1,4-dicarbonyl, enol ether, diene and olefin in the furan ring, makes it a versatile building block for the synthesis of more complex carbocycles and heterocycles.[33] Advantages of furan-based stratergies for synthesis are the ready availability of starting materials, ease of manipulation, and high degree of synthetic flexibility. Substituted furfuryl alcohols are amongst the most versatile starting materials used in contemporary synthesis, as illustrated recently by Schreiber *et al*., in the context of diversity orientated synthesis.[34] Furfuryl alcohols occupy the distinction of generating some of the most sought after cores in organic synthesis; Achmatowicz rearrangement[35] and Piancatelli rearrangement[36] are the classic examples where furyl carbinols **28a** are oxidatively converted to functionalized pyrans **28b** and under acidic conditions to hydroxy cyclopentenones **28c**, respectively, Scheme 27.



Scheme 27: General representation of Achmatowicz and Piancatelli rearrangement reactions.

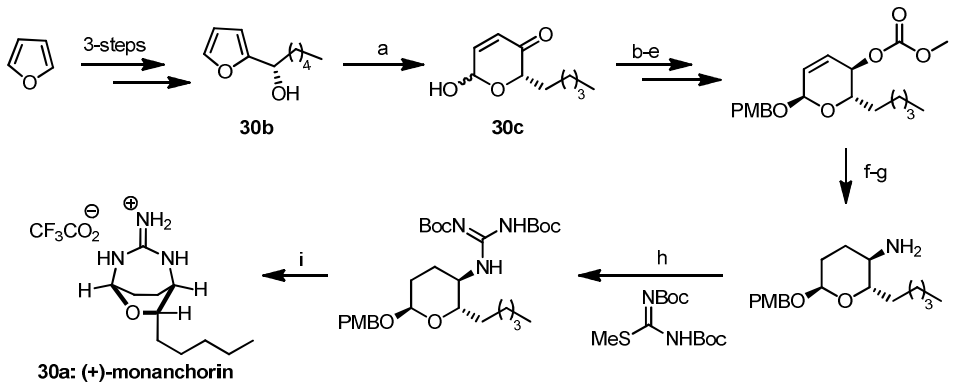
During the past two decades, there has been an immense interest in the Achmatowicz and Piancatelli rearrangement reactions; particularly exploiting this protocol in the synthesis of several biologically relevant compounds.[37] Some of the advancements are briefly discussed here.

In 2010, Nicolaou *et al.*[38] reported a first total synthesis of englerin A **29a**, Scheme 28. The Achmatowicz reaction of **29b** was employed as the key step for the synthesis of **29c**. Further synthetic transformations of **29c** efficiently furnished englerin A **29a**.



Scheme 28: Nicolaou's total synthesis of englerin A **29a**. Reagents and conditions: (a) *m*-CPBA, DCM, 0 ^{o}C, 84%. (b) ethyl acrylate, MsCl, *i*Pr_2NEt, toluene, 46%. (c) PtO_2, H_2, benzene, RT, 88%. (d) Pd/C, H_2, RT, 91%. (e) ArSeCN, *n*-Bu_3P, THF, *m*-CPBA, DCM, DBU, 86%. (f) $PdCl_2$, CuCl, DMF:H_2O (9:1), O_2, RT, 86%. (g) KHMDS, THF, -10 ^{o}C, 77%. (h) $NaBH_4$, $CeCl_3.7H_2O$, MeOH, 93%. (i) Crabtree catalyst, H_2, DCM, RT, 91%. (j) *i*-PrMgCl, MeNH(OMe).HCl, THF, -15 ^{o}C, 90%. (k) MeLi, THF:Et_2O (1:1), -78 ^{o}C, 73%. (l) *m*-CPBA, DCE, 80 ^{o}C, 65%.

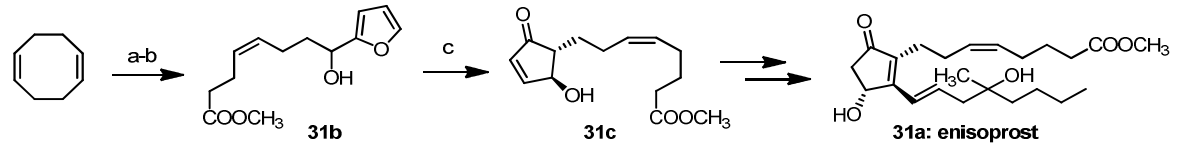
In 2015, O'Doherty *et al.*[39] reported a *de novo* asymmetric total synthesis of the guanidine alkaloid natural product (+)-monanchorin **30a** by employing Achmatowicz rearrangement as the key step, Scheme 29. Oxidative rearrangement of furfuryl alcohol **30b** to the pyranone alcohol **30c** and subsequent transformations provided an efficient access to (+)-monanchorin **30a**.



Scheme 29: O'Doherty's synthesis of monanchorin **30a** employing Achmatowicz rearrangement as the key step. Reagents and conditions: (a) NBS, NaOAc, $NaHCO_3$, THF/H_2O, 88%. (b) $(Boc)_2O$, DMAP, DCM, 76% (4:1 α/β). (c) PMBOH, $Pd(PPh_3)_2$, DCM, 87%. (d) $NaBH_4$, 0.4 M $CeCl_3$ in MeOH, DCM, 99% (dr > 98%). (e) CH_3OCOCl, DMAP, DCM, 92%. (f) $TMSN_3$, Allyl$(PdCl)_2$, Dppb, THF, 70%. (g) H_2, Pd/C, THF/MeOH, 92%. (h) Et_3N, $AgNO_3$, DMF, 85%. (i) CF_3COOH, DCM, 98%.

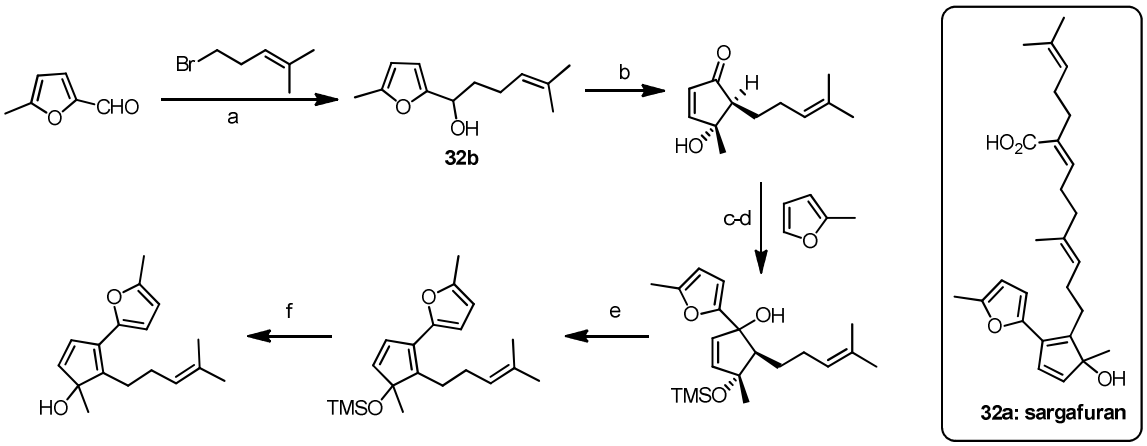
On the other hand, Piancatelli reaction also has received significant attention due to the versatility of the resulting products. One of the most important applications of the Piancatelli rearrangement is in the synthesis of prostaglandins and their derivatives.[40]

In 1990, Dygos *et al.*[41] reported an efficient synthesis of the antisecretory prostaglandin enisoprost **31a** starting from (*Z*,*Z*)-1,5-cyclooctadene by employing Piancatelli reaction as the key step, Scheme 30. The Lewis acid catalyzed Piancatelli rearrangement of furanylcarbinol **31b** furnished the cyclopentenone **31c** and subsequent transformations provided efficient access to enisoprost **31a**.



Scheme 30: Dygos's synthesis of antisecretory prostaglandin enisoprost **31a**. Reagents and conditions: (a) O_3, $NaHCO_3$, MeOH:DCM (1:10), -40 ^oC, Ac_2O, Et_3N, 50 %. (b) 2-furyl magnesiumchloride, THF, 0 ^oC. (c) $ZnCl_2$, aq. Dioxane, reflux.

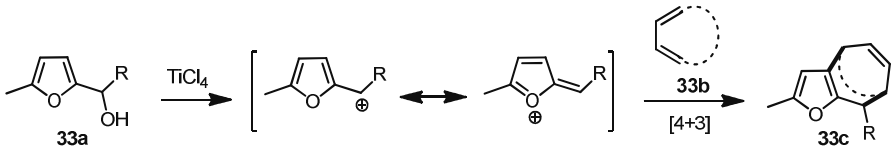
In 2013, Katsuta *et al.*[42] accomplished the synthesis of core framework of the proposed structure of sargafuran **32a** *via* the $MgCl_2$-promoted Piancatelli rearrangement of the intermediate **32b**, Scheme 31.



Scheme 31: Katsuta's synthesis of the core framework of sargafuran **32a**. Reagents and conditions: (a) Mg, Et_2O, 0 ^oC, 93%. (b) $MgCl_2$, H_2O, 1,4-dioxane, reflux, 58%. (c) TMSCl, DMAP, imidazole, DCM, 95%. (d) *n*-BuLi, THF, -78 0 ^oC. (e) PPTS, DCM, 58% over two steps. (f) 0.5 N HCl, THF, 0 ^oC, 99%.

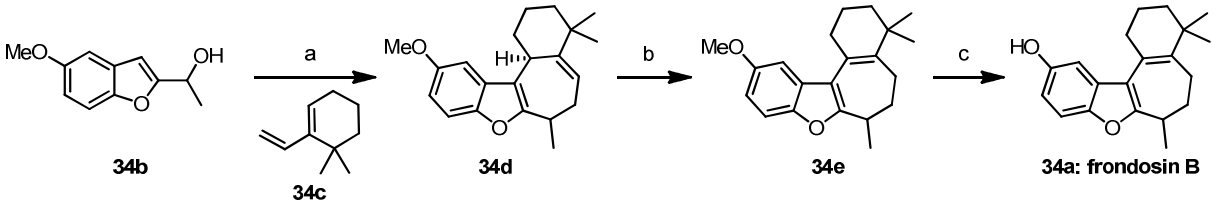
Furfuryl alcohols also have been widely employed in the [4+3] cycloaddition reactions. For example, in 2011, Winne *et al.*[43] have documented [4+3] cycloaddition reactions between a

variety of furfuryl alcohols **33a** and 1,3-dienes **33b** promoted by $TiCl_4$, Scheme 32. The [4+3] cycloaddition reaction between conjugated dienes and furanoxonium ions provide a convenient and straightforward method for the synthesis of novel cycloheptene fused furans **33c**. DFT calculations further supported a stepwise process for this reaction, instead of a concerted [4+3] process, Scheme 32.



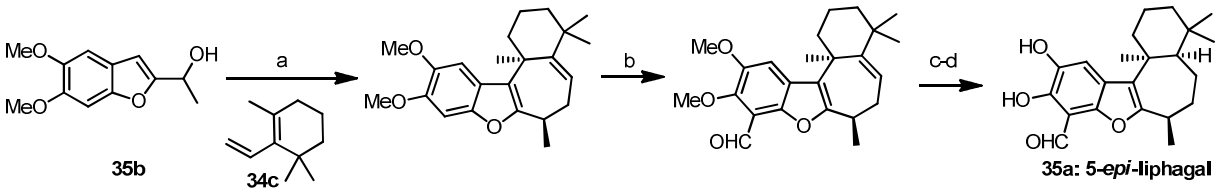
Scheme 32: Intermolecular [4+3] cycloaddition reactions between furanoxonium ions and 1,3-dienes.

Later on, Zhang[44] and Winne[45] groups extended this key step for the synthesis of cycloheptene based natural products, frondosin B **34a**. Zhang *et al*. showed that the treatment of benzofuryl carbinol **34b** and 1,3-diene **34c** in the presence of catalytic amounts of camphorsulfonic acid (CSA) gave a 1:1 diastereoisomeric mixture of the adduct **34d** in 52% yield. A subsequent isomerization of the trisubstituted double bond with PTSA provided the conjugated diene **34e**, which upon demethylation with BBr_3 delivered the racemic frondosin B **34a**, Scheme 33.



Scheme 33: Zhang's synthesis of frondosin B **34a** through [4+3] cycloaddition reaction. Reagents and conditions: (a) CSA, $MeNO_2$, 35-40 °C, 52%. (b) TsOH, Benzene, reflux. (c) BBr_3, DCM, −78 to 0 °C, 64% over 2 steps.

Winne *et al*. extended [4+3] cycloaddition based approach for the synthesis of racemic 5-*epi*-Liphagal **35a**, employing the [4+3] cycloaddition reaction between benzofuryl carbinol **35b** and 1,3-diene **34c** as a key step, Scheme 34.[45]

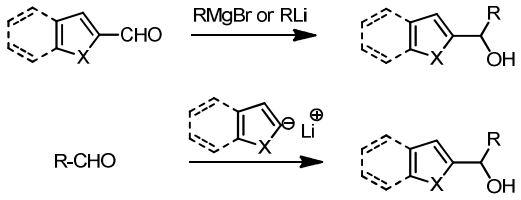


Scheme 34: Winne's synthesis of 5-*epi*-Liphagal **35a**. Reagents and conditions: (a) TFA, DCM, -78 to -25 ^{o}C, 35%, dr = 6:1. (b) TMEDA, *n*-BuLi, DMF, 71%, dr = 10:1. (c) H_2-Pd/C, RT, TFE, 80%, dr = 1:1. (d) BBr_3, DCM, -55 to 0 ^{o}C, 81%.

As showcased above, furfuryl cation equivalents were employed as reactive intermediates in order to generate complex scaffolds and natural products. But a brief literature survey revealed that only a handful of reports actually dealt with the generation of furfuryl cations from the respective furfuryl alcohol precursors and subsequent elaborations.[46] Brønsted or Lewis acid-catalyzed generation of respective cationic species from benzyl alcohols, allyl alcohols and doubly activated systems like bisbenzyl, bis-allyl, benzyl–allyl, benzyl-propargyl alcohols and their reactivity with wide range of substrates is well-documented.[47] However, a systematic study of generating furfuryl cations from the respective α- or β-furylcarbinols and subsequent exploitation of the cationic center was never realized, despite having huge potential for the synthesis of a diverse range of natural products and medicinally important compounds. Consequently, we initiated our efforts towards the generation of furfuryl cation equivalents from respective furfuryl alcohols under Lewis acid catalysis, their reactions with various nucleophiles and elaboration to some architecturally novel scaffolds.

2.1: Lewis acid catalyzed reactions of furfuryl alcohols with various nucleophiles for the synthesis of privileged structures and novel scaffolds.

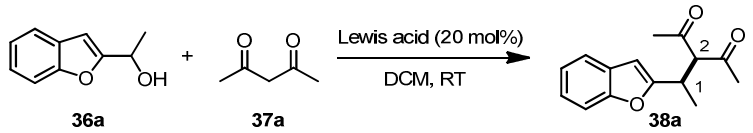
Furyl and thienyl carbinols employed in this study were prepared based on literature procedures, Scheme 35.[43]



Scheme 35: Synthesis of furyl and thienyl carbinols.

At the outset, optimization studies were carried out for the generation of furfurylic cation equivalents from furfuryl alcohol **36a** and reaction with acetylacetone **37a**. The results are compiled in Table 1. From these experiments $FeCl_3$, $BiCl_3$ and $Bi(OTf)_3$ have emerged as effective catalysts to afford **38a** in terms of reaction time and yield (Table 1, entries 6-8). However, when prolonged beyond 0.5 h, the reaction catalyzed by $FeCl_3$ was found to be yielding undesired products. Thus, $BiCl_3$ was identified as the catalyst of choice for subsequent study as it is environmentally friendly, cost-effective, and less toxic.[48] Lowering the $BiCl_3$ loading prolonged the reaction times with marginal drop in the yields (Table 1, entries 9 and 10). Control experiments verified that the reaction did not proceed in the absence of a Bi source (Table 1, entry 11). Presence of two absorption band at 1724 and 1700 cm^{-1} due to the two acetyl group in the IR spectrum indicated the formation of product **38a**. In the ^1H NMR spectrum presence of a characteristic doublet at δ 4.10 due to the C-2 methine proton, a doublet of quartet at 3.77 due to C-1 methine proton, two singlets at 2.15 and 1.96 due to the acetyl methyls and in the ^{13}C NMR spectrum (Fig 4), presence of two quaternary carbons at δ 202.8 and 202.6 due to the two carbonyl group of acetyl acetone, confirmed the structure of the compound **38a.**

Table 1: Optimization of Lewis acid for the conversion of **36a** to **38a**.



36a **37a** **38a**

Entry	Lewis acid (20 mol%)	Time (h)	Yield[a] (%)
1	$BF_3.OEt_2$	12	78
2	$InCl_3$	1	75
3	$ZnCl_2$	3	38
4	$Sc(OTf)_3$	1	69
5	CuOTf	16	49
6	$FeCl_3$	0.5	81
7	$Bi(OTf)_3$	0.5	84
8	**$BiCl_3$**	**1**	**85**
9[b]	$BiCl_3$	2	82
10[c]	$BiCl_3$	4	80
11[d]	-	250	-

[a]Isolated yields after silica gel column chromatography. [b]10 mol% catalyst was used. [c]5 mol% catalyst was used. [d]No catalyst was used, no trace of product was observed by crude ^1H-NMR.

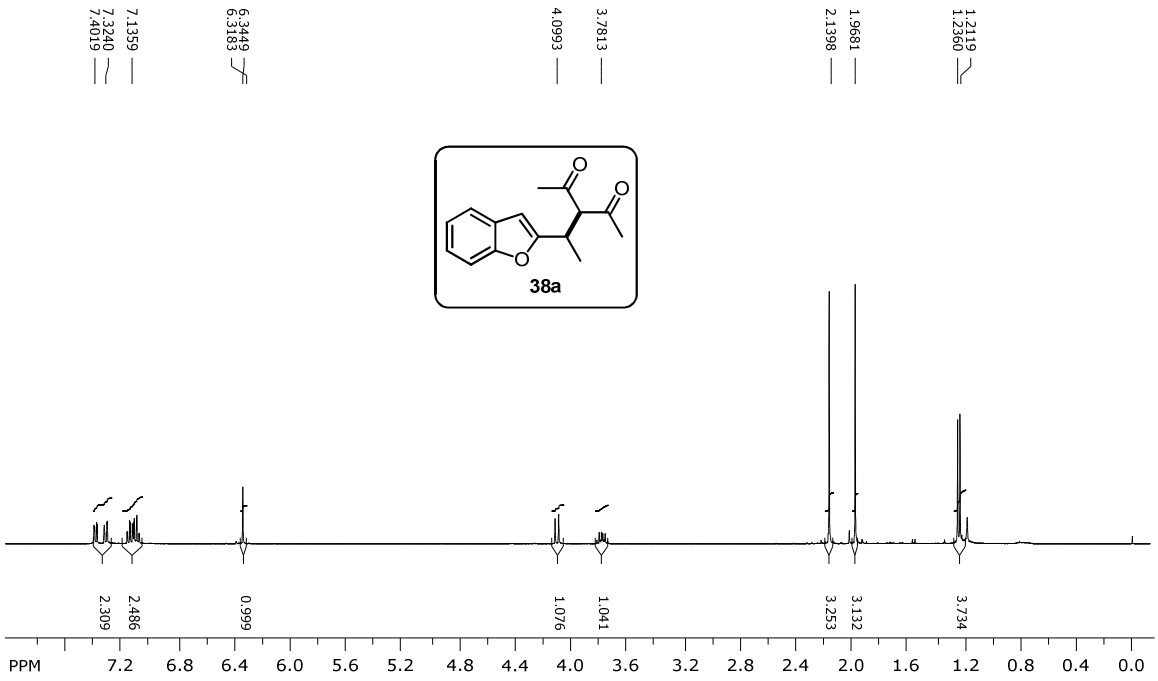


Figure 3: ^{1}H NMR spectrum of **38a**.

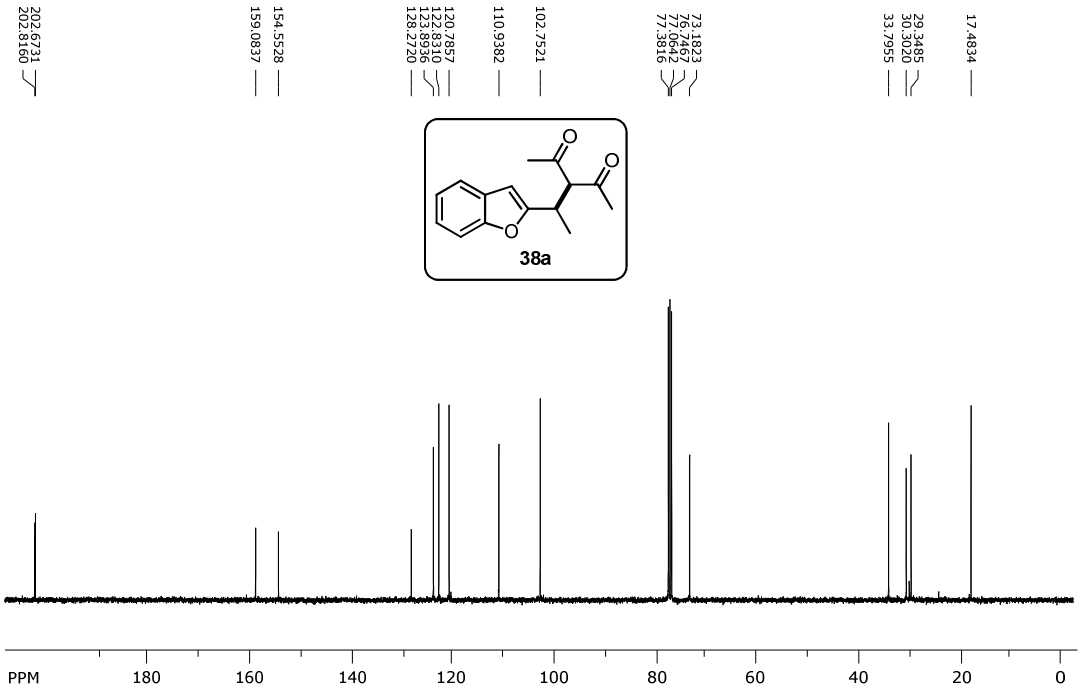
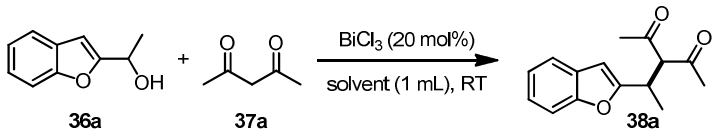


Figure 4: ^{13}C NMR spectrum of **38a**.

A brief solvent screening was performed to further improve the yield. Among them, $MeNO_2$ was found to be optimal for the reaction in terms of time and yield (Table 2, entry 3). This result prompted us to replace DCM with $MeNO_2$. Our efforts to develop aqueous conditions or solvent-free conditions were not encouraging (Table 2, entries 7 and 8). Thus, we identified the optimized conditions to be 20 mol% $BiCl_3$ in $MeNO_2$ at room temperature.

Table 2: Optimization of solvent for the conversion of the alcohol **36a** to the acetylacetone adduct **38a**.



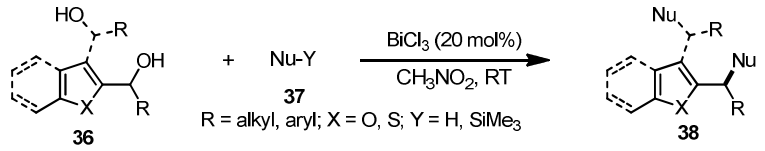
36a **37a** **38a**

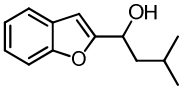
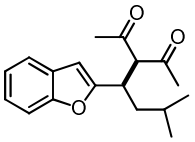
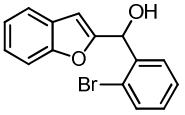
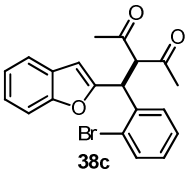
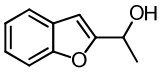
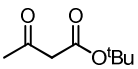
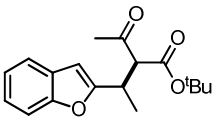
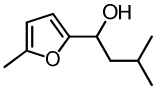
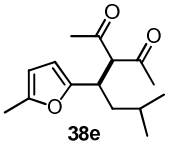
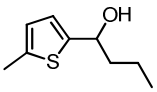
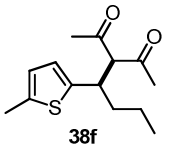
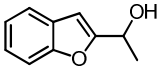
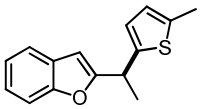
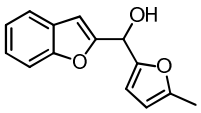
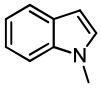
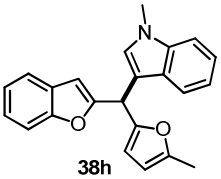
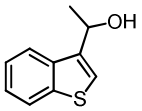
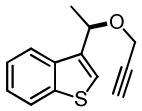
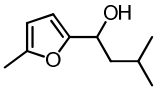
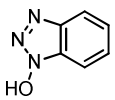
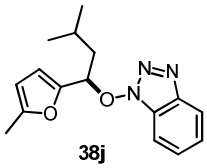
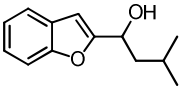
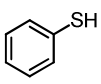
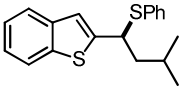
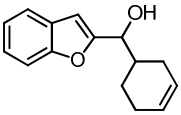
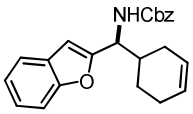
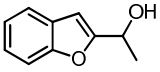
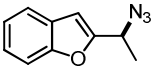
Entry	Solvent	Time (h)	Yield (%)
1	Toluene	4	66
2	Xylene	2	57
3	**CH_3NO_2**	**1**	**85**
4	Water-CH_3NO_2 (1:1)	24	-
5	Acetone	75	<5
6	Acetonitrile	72	54
7[a]	Water	36	-
8[b]	Water	60	-
9	--	6	75

[a]In 0.5 mL water, stirred in the presence of 20 mol% sodium dodecyl sulfate (SDS) for 24 h, added an additional 20 mol% and stirred for 12 h, further added an additional 60 mol% and stirred for 24 h more. [b]In 0.5 mL water, stirred in the presence of 20 mol% Triton® X-100 for 24 h, added an additional 20 mol% and stirred for 12 h, further added an additional 60 mol% and stirred for 24 h more.

With the optimized conditions in hand, we investigated the substrate scope with various furyl and thienyl carbinols, and different nucleophiles. The results of this study are presented in Table 3. The reaction of various aliphatic and aromatic benzofuranyl carbinols **36a**-**36c** with 1,3-dicarbonyls (**37a** and **37b**) furnished respective products (**38b-38d**) in excellent yields (Table 3, entries 1-3). Surprisingly, in the case of *tert*-butyl acetoacetate **37b** as the reactant under the optimized conditions *tert*-butyl ester group survives despite being acid sensitive group.

Table 3: $BiCl_3$ catalyzed reactions of furyl and thienyl carbinols with different nucleophiles.



Entry	Substrates	Nucleophiles	Products
1	 **36b**	**37a**	 **38b** 1 h, 84%
2	 **36c**	**37a**	 **38c** 1 h, 83%
3	 **36a**	 **37b**	 **38d** 0.5 h, 75% (dr = ~1:1)
4	 **36d**	**37a**	 **38e** 0.5 h, 62%
5	 **36e**	**37a**	 **38f** 1 h, 85%
6	 **36a**	 **37c**	 **38g** 1 h, 84%
7	 **36f**	 **37d**	 **38h** 45 min, 83%
8	 **36g**	 **37e**	 **38i** 1.5 h, 90%
9	 **36d**	 **37f**	 **38j** 1 h, 78%
10	 **36b**	 **37g**	 **38k** 1 h, 92%
11	 **36h**	NH_2Cbz **37h**	 **38l** 1 h, 80%
12	 **36a**	$TMSN_3$ **37i**	 **38m** 0.5 h, 81%

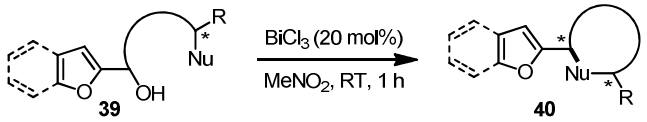
Evidently, 5-methyl furfuryl alcohol **36d** and 5-methyl thienyl alcohol **36e** were found to be excellent substrates under the optimized conditions (Table 3, entries 4 and 5). After successfully employing 1,3-dicarbonyls as nucleophiles, heteroaromatic compounds were also studied as nucleophiles and obtained the respective Friedel-Crafts-type alkylation products (**38g** and **38h**) in very good yields (Table 3, entries 6 and 7). Of significance, compound **38h**, belongs to the class of unsymmetrical trisubstituted methane derivatives (TRSMs). TRSMs possess non-steroidal aromatase inhibitory activity, anti-proliferative, antitubercular activities.[49] Reaction with alcohols **37e** and **37f** and thiol **37g** as nucleophiles under optimized conditions generated respective ethers in excellent yields (Table 3, entries 8-10). Amination of furfuryl alcohols was also achieved in an easy and efficient manner by treating benzofuranyl carbinols **36h** and **36a** with $CbzNH_2$ (**37h**) and trimethylsilyl azide (**37i**), and the respective products **38l** and **38m** were obtained in excellent yields (Table 3, entries 10 and 11).

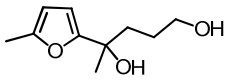
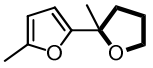
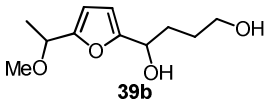
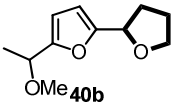
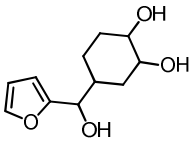
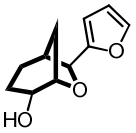
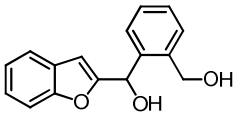
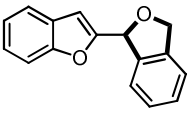
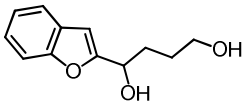
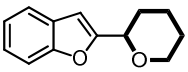
After successfully demonstrating the generality of $BiCl_3$-catalyzed intermolecular furfurylation reactions, we turned our attention to investigate the entropically advantageous intramolecular version. The required starting compounds **39a**-**39e** were prepared based on literature procedures,[50] and were subjected to the optimized conditions.

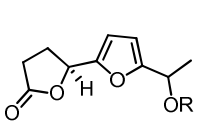
The representative results are showcased in Table 4. Diverse furan containing natural product-like tetrahydrofurans, tetrahydropyrans, and pyrrolidines can be accessed by this method. For example, the cyclic ether **40b** is an advanced precursor for the synthesis of the monoterpene natural product **41a**, a secondary metabolite isolated from an extract of sun-cured Greek tobacco leaves.[51] Strained bicyclic ether **40c** can be obtained in 75% yield by subjecting the triol **39c** under the optimized conditions (Table 4, entry 3). Similarly, the designer substrate **39d** generates an unusual isobenzofuran variant **40d** in excellent yield (Table 4, entry 4). Even the 2-benzofuranyl tetrahydropyran **40e** can be accessed conveniently *via* this methodology (Table 4, entry 5).

In summary, we have developed an efficient Lewis acid catalyzed inter- and intramolecular furfurylation reactions which provide an easy and straightforward access to structurally unique furan derivatives and pharmaceutically relevant compounds.

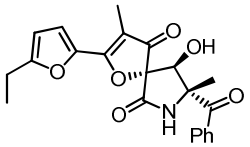
Table 4: $BiCl_3$-catalyzed intramolecular cyclization reactions.



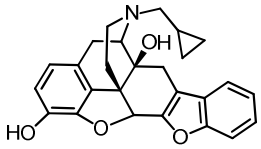
Entry	Substratre	Time,yield	Product
1	 **39a**	1 h, 83%	 **40a**
2	 **39b**	1 h, 82%	 **40b**
3	 **39c**	1 h, 75%	 **40c**
4	 **39d**	1 h, 86%	 **40d**
5	 **39e**	1 h, 86%	 **40e**



41a: R = H
41b: R = Me



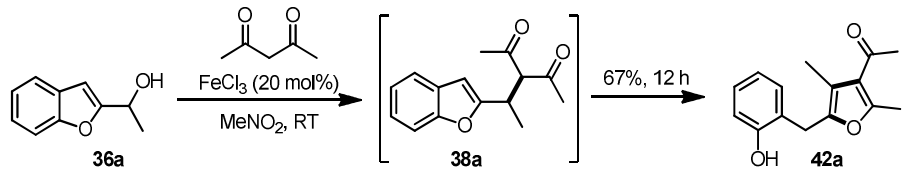
41c: FD-838



41d: naltriben

As part of optimization studies towards the furfurylation of 1,3-dicarbonyls, under the $FeCl_3$ catalysis, we observed that the concentration of the acetylacetone adduct **38a** started diminishing while the accumulation of an unknown compound was observed on TLC. The structure of the newly formed compound **42a** was deduced from ^1H and ^{13}C NMR data and characterized as the tetrasubstituted furan **42a**, Scheme 36. Presence of an absorption band at 1643 cm^{-1} in the IR spectrum indicated the presence of the conjugated carbonyl group. In the ^1H NMR spectrum, presence of a doublet of triplet at δ 7.02, a doublet at 7.07, a multiplet at 6.80-6.73 due to the aromatic protons, a broad singlet at 6.19 due to the phenolic OH, a singlet at 3.92

due to the benzylic protons, a methyl at 2.59 due to the acetyl methyl, a singlet at 2.45 due to the aromatic methyl group, and in the ^{13}C NMR spectrum, presence of one quaternary carbon at δ 195.8 due to the carbonyl group, a methylene carbon at 30.8 due to the benzylic carbon, two signals at 26.3 and 15.4 due to the acetyl methyl and furyl methyl confirmed the structure of the compound **42a**. In high resolution mass spectrum, presence of sodiated molecular ion at 281.1153 (M+Na) further established the structure of **42a**. Subsequent details including the efforts towards the development of one-pot Brønsted acid catalyzed ring transformation of benzofurans to tri- and tetrasubstituted furans are discussed in the next sub-section.



Scheme 36: Serendipitous formation of tetrasubstituted furan under $FeCl_3$ catalysis.

2.2: One-pot Brønsted acid catalyzed ring transformation of benzofurans to tri- and tetrasubstituted furans

Majority of the important discoveries in chemical science occurred out of accident or serendipity. This phenomenon was responsible, for example, for the development of fundamental synthetic transformations such as Friedel-Crafts reaction, Wittig olefination, and several rearrangement reactions.[52]

On the other hand, domino reactions[53] have attracted wide attention from synthetic community as they display high atom economy, efficiently build complex molecular architectures in a single step while skipping the need for several workup and time-consuming purification operations, thus allowing savings of both solvents and reagents. In this regard, we describe a serendipitous outcome of a one-pot domino process that generates tetrasubstituted furans from readily available precursors under operationally simple conditions. In an unprecedented event, a rigid benzofuran core sacrifices itself to facilitate the formation of a polysubstituted furan.

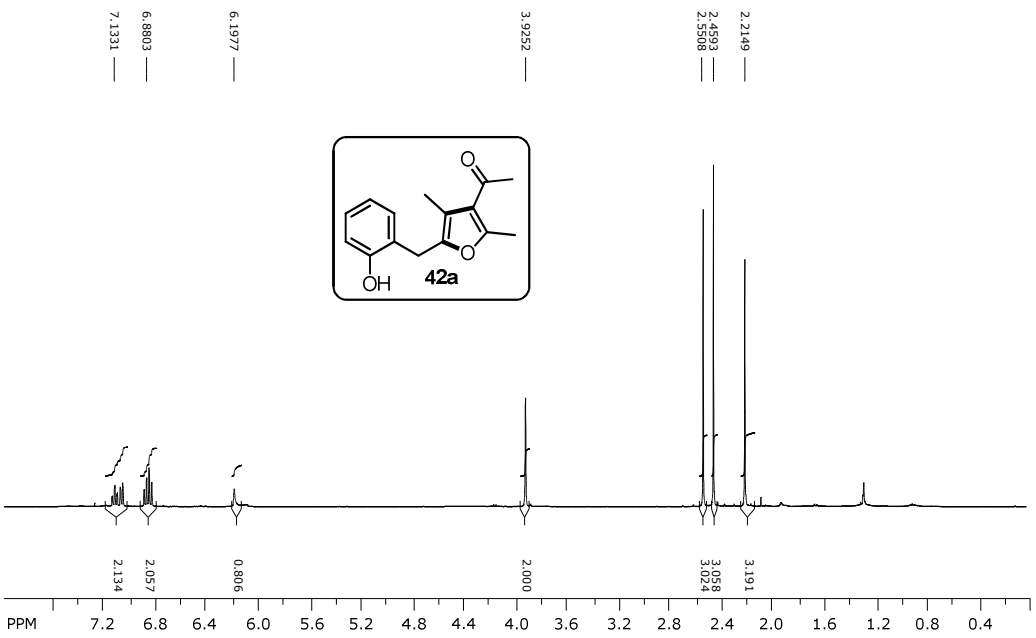


Figure 5: ^{1}H NMR spectrum of **42a**.

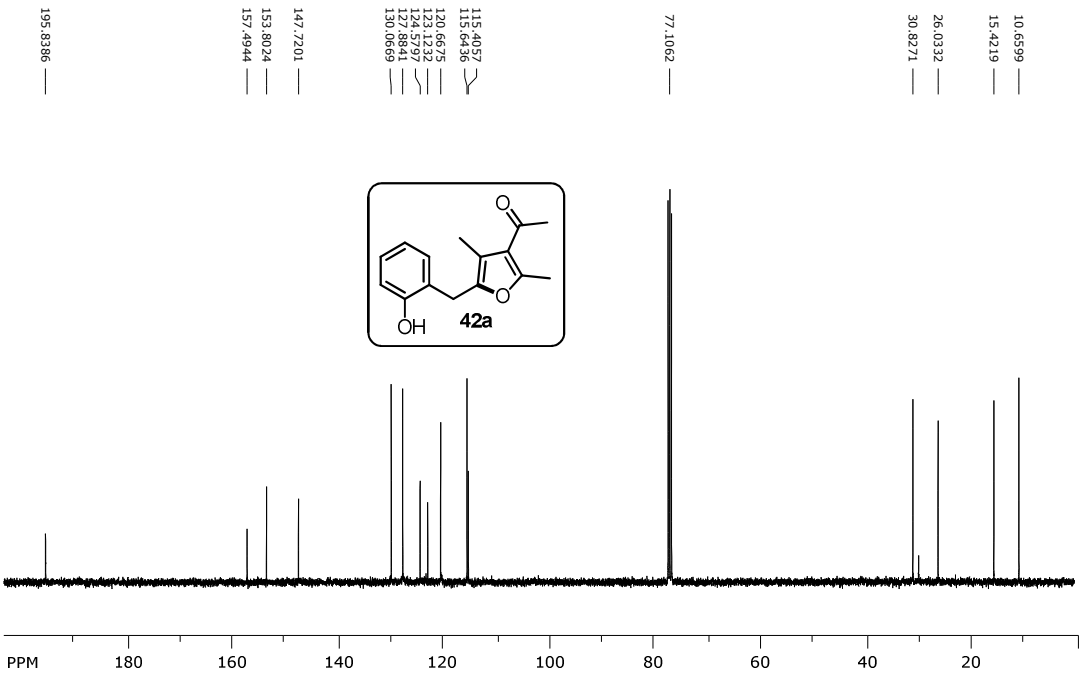


Figure 6: ^{13}C NMR spectrum of **42a**.

Furans represent an important class of five membered heterocycles which are components of many bioactive natural products as well as primary structural motifs in several pharmaceutics, molecular electronics and functional polymers.[54] While most frequently used methods for furan synthesis include the versatile Paal–Knorr synthesis[55] and the classical Feist–Benary synthesis,[56] Kanematsu's famous Furan Ring Transfer (FRT) reactions of furanyl propargyl ethers,[57] Butin's versatile furan ring opening-ring closures,[58] novel propargylation-cycloisomerization strategy[59] and Yin's recent attractive approaches to furans.[60] These approaches represent some of the excellent alternatives to the synthesis of polysubstituted furans which garnered great attention from synthetic community. However, the design, execution and outcome some of these approaches are rather predictive and several limitations surround these approaches, *viz.,* i) lack of selectivity, ii) not flexible regarding their substitution pattern, iii) not economical and scalable, iv) difficulty in accessing starting materials, v) environmentally unfriendly, vi) harsh reaction conditions that lack functional group tolerance. For these reasons, development of general and more efficient methods for the synthesis of functionalized and polysubstituted furans under inexpensive, atom-economical, mild and readily accessible methods still remains an area of intense research.

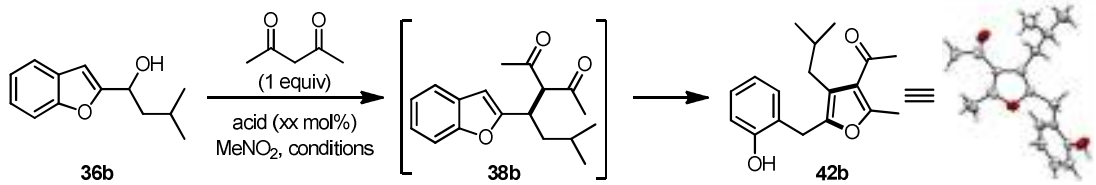
2.2.1: Results and discussion

We commenced to study the transformation of benzofuranyl carbinol **36b** into the tetrasubstituted furan **38b** under different Lewis and Brønsted acidic conditions, and some noteworthy results are shown in Table 5.

From Table 5, it can be realized that there was no product formation in the absence of an acid (Table 5, entry 1). Interestingly, catalytic amounts of Lewis acids such as $BF_3.OEt_2$, $Zn(OTf)_2$, $Sc(OTf)_3$, $BiCl_3$, $Cu(OTf)_2$ and Brønsted acids such as *p*-toluenesulfonic acid (PTSA) and phosphoric acid (H_3PO_4) generated only the acetylacetone adduct **38b** (Table 5, entries 2-10). Product formation was observed with Lewis acids such as $InCl_3$, $FeCl_3$, $In(OTf)_3$, TMSOTf, $Bi(OTf)_3$ and Brønsted acids such as H_2SO_4 (Table 5, entries 11-16). No significant improvement in the yield of **42b** was observed by increasing the acid loading; in fact, a marginal drop in yield was realized (Table 5, entries 12 and 15). Further, among several Lewis acids and Brønsted acids, triflic acid catalyzed reaction in nitromethane at room temperature found to be the best yielding condition (Table 5, entry 17).The structure of the polysubstituted furan **42b** was

deduced from ^{1}H and ^{13}C NMR data and was further confirmed by the single-crystal X-ray diffraction analysis.

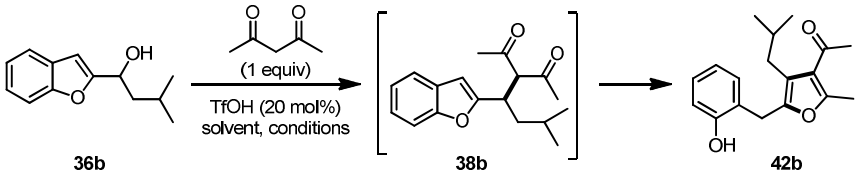
Table 5: Optimization of acid for the conversion of the alcohol **36b** to the tetrasubstituted furan **42b**.



Entry	Acid	% Yield /time (h) for **42b**[a]	% Yield /time (h) for **42b**[b]	% Yield /time (h) for **42b**[c]	% Yield /time (h) for **42b**[d]
1	-	-	-	-	-
2	BF_3OEt_2	-	-	-	-
3	$Zn(OTf)_2$	-	-	<5 (48)	-
4	$Sc(OTf)_3$	-	-	-	-
5	$Cu(OTf)_2$	-	-	-	-
6	$BiCl_3$	-	-	-	-
7	PTSA	<5 (48)	-	-	<5 (48)
8	Amberlyst-15	NP (48)[f]	-	46 (7)[g]	-
9	TFA	NP (72)	-	NP (48)	-
10	H_3PO_4	NP (70)	-	-	-
11	$InCl_3$	<5 (48)	-	-	-
12	$FeCl_3$	56 (72)	-	53 (8)	-
13	$In(OTf)_3$	30 (70)	-	57 (2)	-
14	TMSOTf	56 (10)	-	66 (3)	-
15	$Bi(OTf)_3$	60 (12)	64 (6)	57 (2)	56 (0.5)
16	H_2SO_4	51 (9)	-	42 (3)	-
17[e]	**TfOH**	**74 (6)**	**71 (1.5)**	**72 (1)**	**66 (0.5)**

[a]20 mol% of acid was employed. [b]50 mol% of acid was employed. [c]1 equiv of acid was employed. [d]5 equiv of acid was employed. [e]With 10 mol% TfOH, only about 80% conversion was observed, even after 72 h. [f]20 wt% of Amberlyst-15 was employed. [g]At 100 °C, 1 wt equiv of Amberlyst-15 was employed.

Table 6: Optimization of solvent for the conversion of the alcohol **36b** to **42b**.



Entry	Solvent	Time (h)	Yield (%)
1	Dichloromethane	18	42
2	Toluene	48	32
3	Dichloroethane	10	43
4	Acetonitrile	48	NR
5	Nitroethane	1	56
6	Nitropropane	4	62
7[a]	Water	72	NR

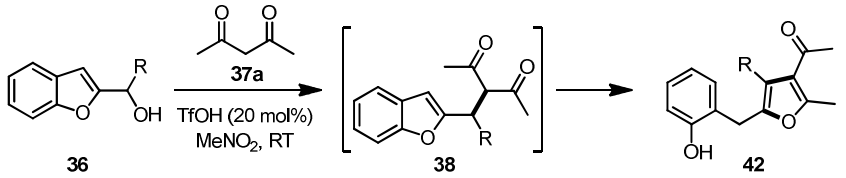
[a]20 mol% of sodium dodecyl sulfate (SDS) was employed.

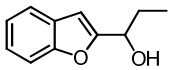
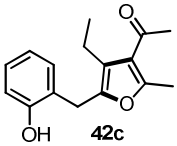
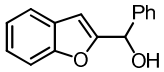
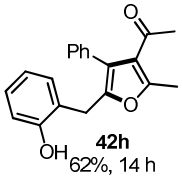
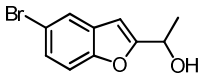
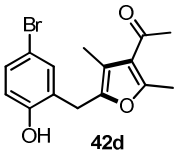
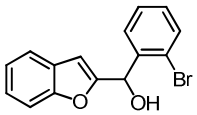
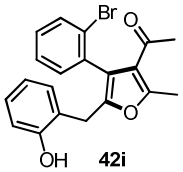
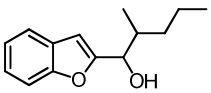
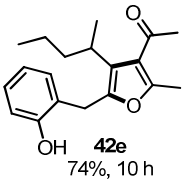
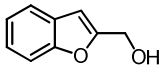
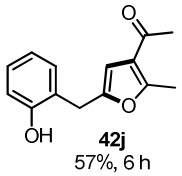
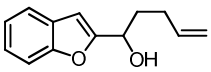
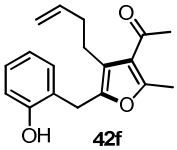
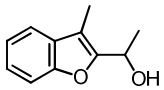
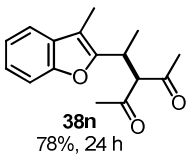
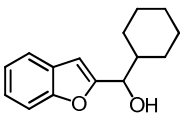
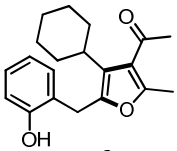
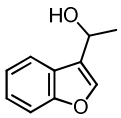
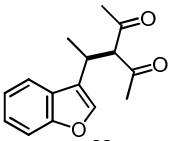
In an attempt to improve the yield, a brief solvent screening was undertaken, Table 6. However, no significant enhancement in the yield or reaction time was observed. Our efforts towards the development of aqueous conditions were unsuccessful (Table 6, entry 7). Thus, we, identified through the screening that triflic acid (20 mol%) in $MeNO_2$ at room temperature efficiently transformed **36b** to **42b**.

With the optimized reaction conditions in hand, the scope of the one-pot domino reactions for the synthesis of polysubstituted furans was investigated with a range of benzofuranyl carbinols. Initially, a series of aliphatic and aromatic benzofuranyl carbinols (**36i-36n** and **36c**) were reacted with acetylacetone **37a** under the optimized conditions, and obtained the respective tetrasubstituted furans in good yields (Table 7, entries 1-7). Among them, the structure of **42c** was unambiguously confirmed by x-ray diffraction analysis, Fig. 7. Interestingly, the reaction of primary benzofuranyl carbinol **36o** with acetylacetone, under optimized conditions furnished the trisubstituted furan **42j**, though in moderate yield (Table 7, entry 8). Despite several efforts, surprisingly, the benzofuranyl carbinol **36p** bearing a methyl group at C-3 failed to furnish the expected rearranged product, generated only the acetylacetone

adduct **38n** (Table 7, entry 9). To further elaborate the scope of one-pot domino reaction, 3-benzofuranyl carbinol **36q** was reacted with acetylacetone under the optimized conditions; however, only the acetylacetone adduct was isolated **38o** (Table 7, entry 10).

Table 7: Reaction of benzofuranyl carbinols and acetylacetone for the synthesis of polysubstituted furans.



Entry	Alcohol	Product	Entry	Alcohol	Product
1	 **36i**	 **42c** 76%, 8 h	6	 **36n**	 **42h** 62%, 14 h
2	 **36j**	 **42d** 77%, 16 h	7	 **36c**	 **42i** 64%, 15 h
3	 **36k**	 **42e** 74%, 10 h	8	 **36o**	 **42j** 57%, 6 h
4	 **36l**	 **42f** 64%, 29 h	9	 **36p**	 **38n** 78%, 24 h
5	 **36m**	 **42g** 68%, 18 h	10	 **36q**	 **38o** 74%, 24 h

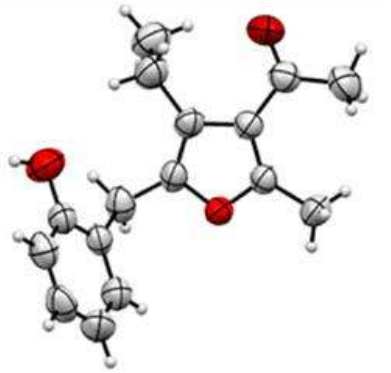
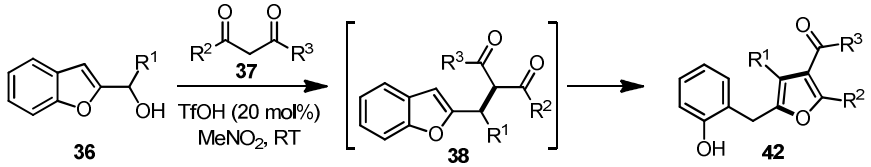


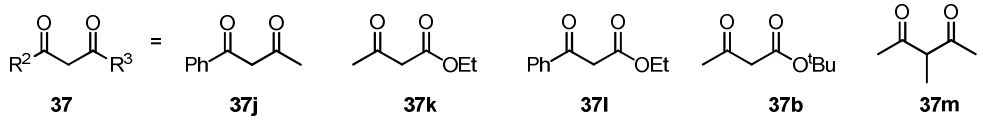
Figure 7: ORTEP diagram of tetrasubstituted furan **42c**.

With an interest in expanding the scope of the protocol, we subsequently investigated the reactions of benzofuryl-2-carbinols with various 1,3-dicarbonyls under the optimized conditions, Table 8. The one-pot cascade reactions with 1-phenylbutane-1,3-dione **37j** and benzofuryl carbinols **36a** and **36o** furnished the 3-phenacylcarbonyl furan derivatives **42k** and **42l**, respectively, in good yields (Table 8, entries 1 and 2). On the other hand, the reaction of β-keto esters **37k** and **37l** with benzofuranyl carbinols **(36i, 36b** and **36a)** generated the 3-alkoxycarbonyl furan derivatives **42m-42o** (Table 8, entries 3-5). Surprisingly, in the case of *tert*-butyl acetoacetate **37b** as the reactant, the acid treatment leads to an *in situ* decarboxylation leading to the formation of *β*-branched 4-(2-benzofuranyl)-2-butanone furans **38p** and **38q**, which are otherwise difficult to access (Table 8, entries 6-7). On the other hand, the reaction of 3-methyl acetylacetone **37m** failed to furnish the desired domino product; rather, furfurylation product **38r** was obtained in 73% yield after 12 h (Table 8, entry 8).

Having established successfully a general methodology for the synthesis of tri- and tetrasubstituted furans from benzofuranyl carbinols, we turned our attention to the curious case of furyl and thienyl carbinols. Accordingly, the alcohols **36d** and **36r-36u** were subjected to the optimized reaction conditions. The results are summarized in Table 9. Reaction of furyl carbinols **36d** and **36r-36t** with 1,3-dicarbonyls **37a** and **37k** furnished 4-(3,5-alkyl/aryl-4-acetyl-2-furanyl)butanones **42p-42t** in moderate yields (Table 9, entries 1-5). Thienyl carbinol **36u** generated initially the respective acetylacetone adducts, which during the course of the reaction, transformed into a complex mixture of products (Table 9, entries 6).

Table 8: Scope of benzofuranyl carbinols and 1,3-dicarbonyls.





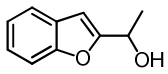
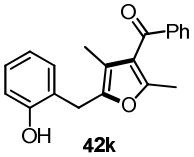
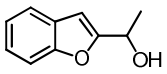
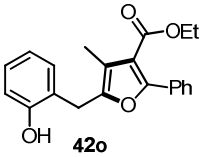
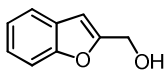
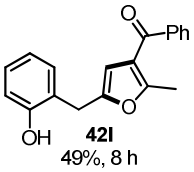
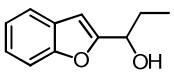
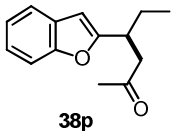
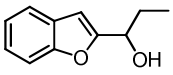
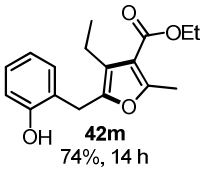
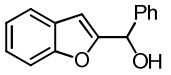
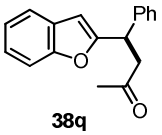
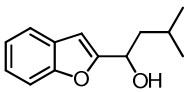
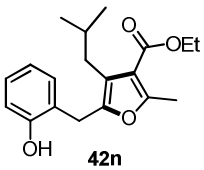
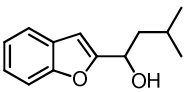
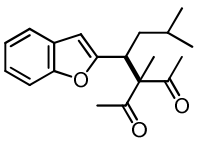
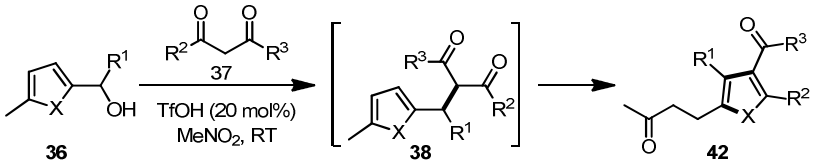
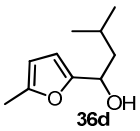
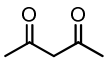
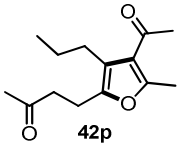
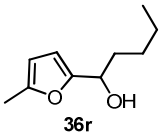
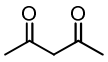
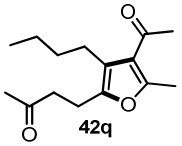
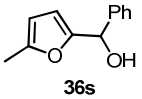
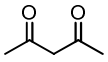
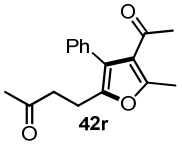
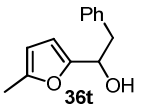
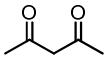
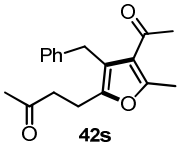
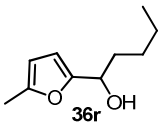
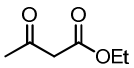
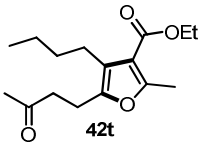
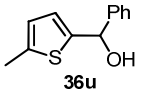
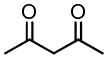
Entry	Alcohol	1,3-dicarbonyl	Product	Entry	Alcohol	1,3-dicarbonyl	Product
1	 **36a**	**37j**	 **42k** 71%, 18 h	5	 **36a**	**37l**	 **42o** 69%, 15 h
2	 **36o**	**37j**	 **42l** 49%, 8 h	6	 **36i**	**37b**	 **38p** 73%, 1 h
3	 **36i**	**37k**	 **42m** 74%, 14 h	7	 **36n**	**37b**	 **38q** 72%, 13 h
4	 **36b**	**37k**	 **42n** 72%, 16 h	8	 **36b**	**37m**	 **38r** 73%, 12 h

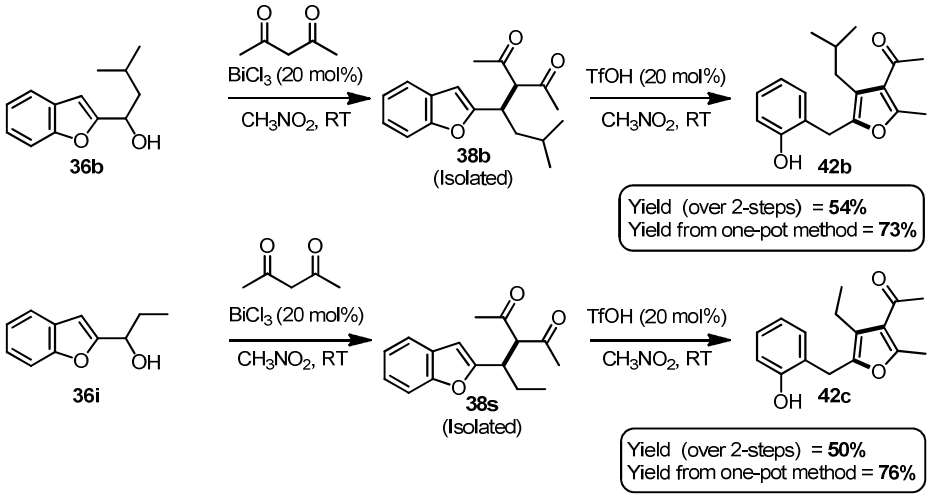
Table 9: Substrate scope with furyl and thienyl carbinols.



36 38 42

Entry	Furyl/thienyl carbinol	1,3-Dicarbonyl	Time (h)	Yield (%)	Product
1	 **36d**	 **37a**	2	34	 **42p**
2	 **36r**	 **37a**	2	33	 **42q**
3	 **36s**	 **37a**	2	37	 **42r**
4	 **36t**	 **37a**	2	51	 **42s**
5	 **36r**	 **37k**	2	46	 **42t**
6	 **36u**	 **37a**	9	-	Complex mixture

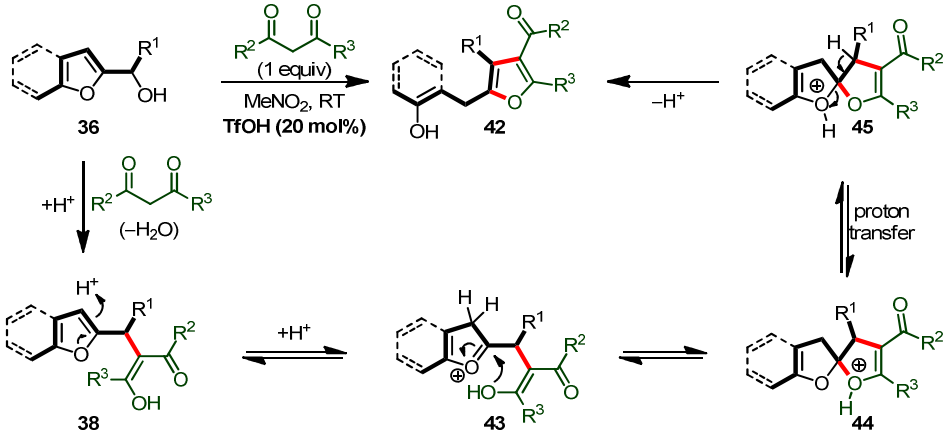
The efficiency of the one-pot process was further evaluated over the step-wise process. In a separate reaction, acetylacetone adducts **38b** and **38s** were prepared *via* $BiCl_3$ catalysis from benzofuranyl carbinols **36b** and **36i**, respectively, Scheme 37. Isolated acetylacetone adducts (**38b** and **38s**) were individually subjected to TfOH catalysis and the respective furans **42b** and **42c** were obtained in 54% and 50% overall yields. However, under the one-pot cascade process, the same products were obtained in 73% and 76% yields from alcohols **36b** and **36i**, respectively, highlighting the advantage of the one-pot domino process over the step-wise process.



Scheme 37: A comparison between the efficiency of one-pot process and two step approach to synthesize the same end-product.

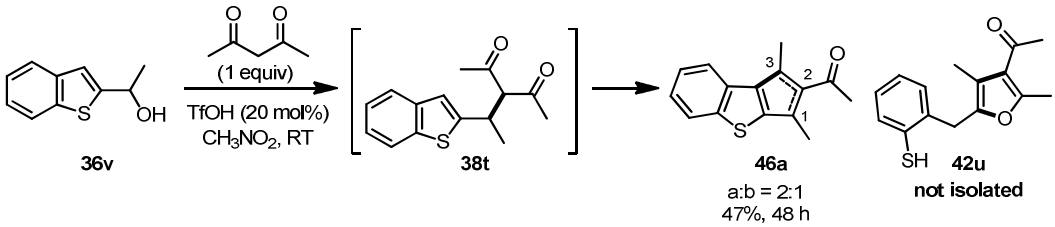
2.2.2: Mechanistic details

The proposed mechanism for the acid catalyzed ring transformation of benzofuryl and furyl carbinols to tri- and tetrasubstituted furans reaction is illustrated in Scheme 38. The reaction commences with the acid catalyzed furfurylation of 1,3-dicarbonyls generating 1,3-dicarbonyl adduct **38**. The reversible protonation of the benzofuran/furan ring at C-3, generates a highly reactive oxonium ion **43**. The reversible attack of the enol oxygen of 1,3-dicarbonyl at the positively charged C-2, generates the unstable spiro intermediate **44**. Subsequent proton transfer and furan ring opening provides the polysubstituted furans **42**.



Scheme 38: Proposed mechanism for the one-pot domino process transformation.

After successful establishment of a general methodology for the synthesis of tri- and tetrasubstituted furans from benzofuryl and furyl carbinols, we have attempted to employ benzothienyl carbinols as substrates under the optimized conditions. Reaction of the benzothienyl carbinol **36v** with acetylacetone under TfOH catalysis furnished 1,2,3-trisubstituted cyclopenta[*b*]benzothiophene **46a** against the predicted tetrasubstituted furan **42u**, in 47% yield after 48 h at RT, in a regioisomeric ratio of approximately 2:1, the structures of which were confirmed spectroscopically, Scheme 39.



Scheme 39: Reaction of benzothienyl carbinol with acetylacetone.

Presence of the absorption band at 1638 cm^{-1} due to the *α,β*-unsaturated carbonyl stretch in the IR spectrum indicated the formation of cyclopenta[*b*]annulated benzothiophene **46a**. In ^{1}H NMR spectrum, presence of a quartet at δ 3.96 (*J* = 2.0 Hz) due to the methine proton present on the phenyl connected carbon (C-1), shows a long range coupling with olefinic methyl, supported by the presence of a doublet at 2.85 (*J* = 2.0 Hz) due to the olefinic methyl, and a singlet at 2.51 ppm due to the acetyl methyl confirmed the formation of **46a**. In ^{13}C NMR spectrum, presence of a quaternary carbon at δ 194.6 due the *α,β*-unsaturated carbonyl carbon, a methine carbon at 44.9 due to the phenyl connected carbon (C-1), presence of two methyl carbons at 30.6 and 18.2 ppm due to the olefinic methyl (C-3) and acetyl methyl (C-2), respectively, further established the structure of **46a**.

The serendipitous formation of cyclopenta[*b*]benzothiophene provided an opportunity to develop a new approach for the cyclopentannulation of benzothiophenes. Efforts towards the one-pot synthesis of cyclopenta[*b*]annulated benzothiophenes from 2-benzothienyl carbinols are illustratred in the next sub-scetion.

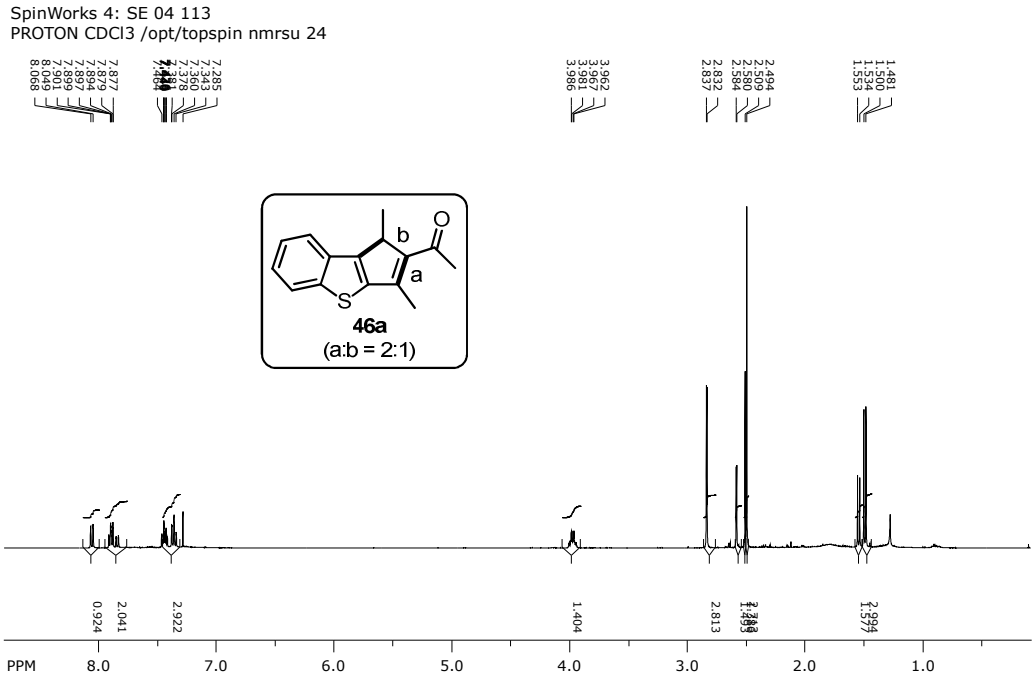


Figure 8: ^{1}H NMR spectrum of **46a**.

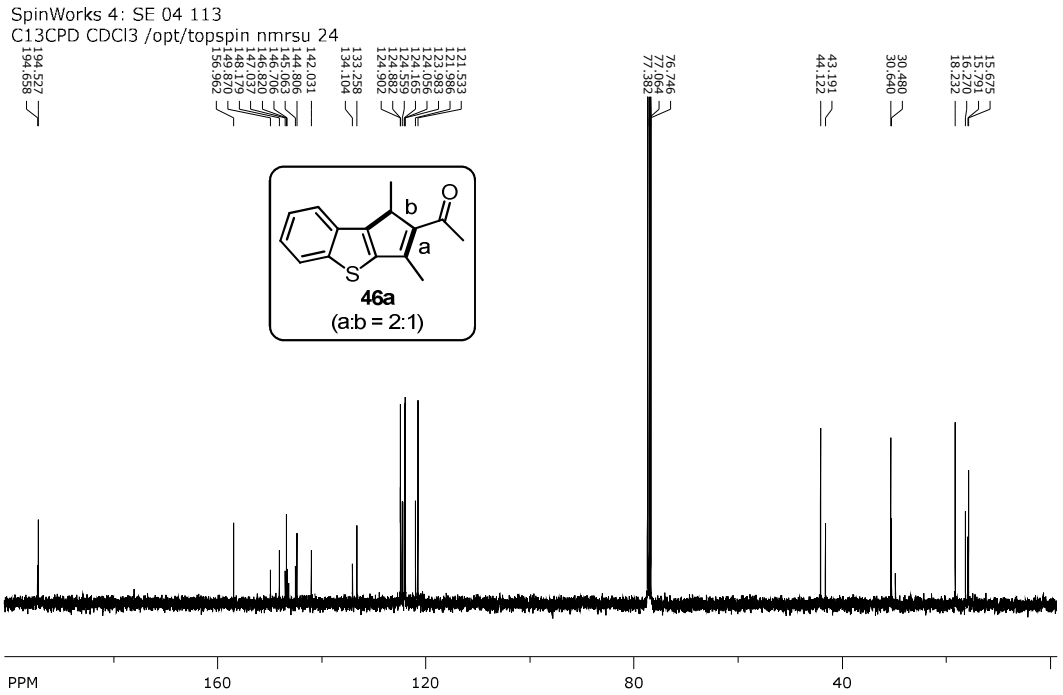


Figure 9: ^{13}C NMR spectrum of **46a**.

2.3: Synthesis of 1,2,3-trisubstituted cyclopentannulated benzothiophenes through a Brønsted acid-mediated, solvent-free, one-pot domino process

Cyclopenta[*b*]thiophenes are well known organic semiconducting materials, often used as organic field-effect transistors (OFETs).[61] OFETs find wide applications in the manufacturing of electronic papers, radio frequency identification (RFID) tags, and chemo-/bio-sensors, etc. Despite their wide applications, only a few methods are known for the cyclopentannulation of benzothiophenes. Commonly employed methods include the Nazarov cyclization and [3+2] cycloaddition based approaches. However, the existing methods suffer from limitations such as the difficulty in accessing starting materials and expensive reagents. Consequently, development of general and more efficient methods for the synthesis of functionalized cyclopenta[*b*]benzothiophenes by inexpensive, atom-economical, and readily accessible methods is desired.

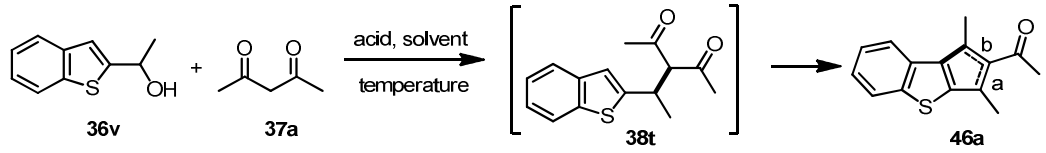
Among the various strategies to rapidly assemble complex molecular architectures, domino processes have received much attention in recent years.[53] They display high atom economy while skipping the need for several workup and time-consuming purification steps, thereby minimizing the waste and the consumption of solvents. Solvent-free thermal processes are especially appealing because of enhanced reaction rates and, specifically, from a green chemistry point of view. Thus, development of a solvent-free domino process for the cyclopentannulation of benzothiophenes can be an attractive alternative.

2.3.1: Results and discussion

In an attempt to identify the best yielding conditions for the transformation of **36v** to **46a** (Scheme 39), we initiated optimization of various parameters such as acids, solvents, temperature, etc., with benzothiophen-2-yl(methyl)methanol **36v** and acetylacetone **37a** as model substrates, Table 10. We were initially interested to evaluate the influence of various Lewis and Brønsted acids on the transformation of benzothienyl carbinol **36v** to the cyclopentannulated benzothiophene **46a**. Brønsted acids such as trifluoroacetic acid, H_2SO_4, $HClO_4$, H_3PO_4, p-toluenesulfonic acid and Amberlyst-15, and Lewis acids such as $Cu(OTf)_2$, $Yb(OTf)_3$, $Ln(OTf)_3$, AgOTf and $Zn(OTf)_2$ generated either the acetylacetone adduct **38t** or failed to generate **46a** in nitromethane solvent. In contrast, the use of polyphosphoric acid (PPA) resulted in the formation of enones **46a** in moderate yield under solvent-free conditions (Table 10, entry 2), whereas the

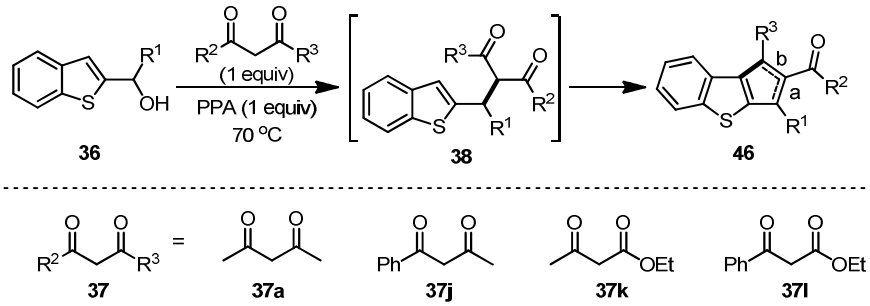
solvent-free reaction with TfOH resulted in a lower yield of the product (Table 10, entries 3 and 4). No significant improvement in the yield of **46a** was observed by increasing the loading of PPA; in fact, a marginal decrease in the yield was realized (Table 10, entries 5–7). Gratifyingly, performing the reaction with PPA at an elevated temperature delivered the product in good yield in a regioisomeric ratio of approximately 1:1(Table 10, entry 8). Attempts to develop an aqueous version were unsuccessful (Table 10, entry 9). Lewis acids such as the triflates of Bi, Sc, and In successfully generated the desired product **46a**, albeit in moderate yields (Table 10, entries 10–14).

Table 10: Optimization of the reaction conditions.



Entry	Solvent	Acid	Temperature (^{o}C)	Time (h)	Yield (%)
1	$MeNO_2$	TfOH (1 equiv)	30	4	66
2	-	PPA (1 equiv)	30	48	55
3	-	TfOH (1 equiv)	30	10	45
4	-	TfOH (1 equiv)	55	5	51
5	-	PPA (1 equiv)	45	30	70
6	-	PPA (2 equiv)	45	28	67
7	-	PPA (5 equiv)	45	25	62
8	**-**	**PPA (1 equiv)**	**70**	**13**	**74**
9	water	PPA (1 equiv)	45	120	-
10	$MeNO_2$	$Bi(OTf)_3$ (10 mol%)	100	24	40
11	$MeNO_2$	$Bi(OTf)_3$ (30 mol%)	80	18	47
12	$MeNO_2$	$Bi(OTf)_3$ (50 mol%)	100	5	59
13	$MeNO_2$	$Sc(OTf)_3$ (20 mol%)	80	5	58
14	$MeNO_2$	$In(OTf)_3$ (20 mol%)	80	24	35

Table 11: Scope of benzothienyl carbinols and 1,3-dicarbonyls.



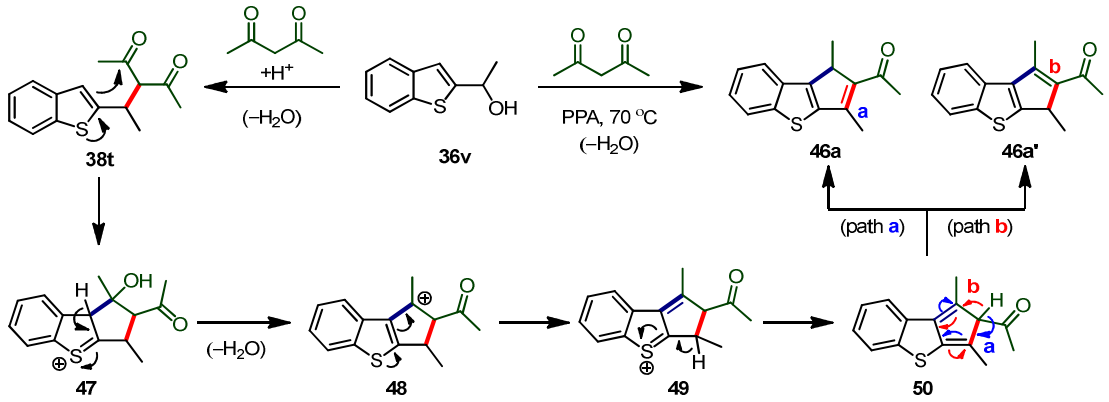
Entry	Alcohol	1,3-dicarbonyl	product	Entry	Alcohol	1,3-dicarbonyl	product
1	36w	36a	46b 74%, 14 h; a/b = 1:2	5	36v	37k	46f 61%, 4 h; a/b = 1.5:1
2	36x	36a	46c 68%, 24 h	6	36y	37k	46g 52%, 10 h; a/b = 1:1.7
3	36y	37j	46d 64%, 10 h; a/b = 1:2	7	36z	37k	46h 54%, 4 h; a/b = 1:1.4
4	36z	37j	46e 50%, 4 h	8	36aa	37l	46i 52%, 8 h; a/b = 2:1

With the optimized conditions in hand, a diverse set of 2-benzothienyl carbinols and 1,3-dicarbonyls were examined to determine the reaction scope and limitations, Table 11. Benzothienyl-2-carbinols **36w-36aa** with aliphatic, aromatic and heteroaromatic substituents (R^1) were found to be efficient substrates under the reaction conditions, and they delivered the respective pentannulated benzothiophenes **46b-46i** in moderate to good yields. Reaction of benzothienyl carbinols **36w-36z** with 1,3-diketones **37a** and **37j** furnished 4-acetyl/phenacyl cyclopent[*b*]benzothiophenes respectively in good to moderate yields (Table 11, entries 1-4) .

Reaction of benzothienyl carbinols with *β*-ketoesters 3**7k** and **37l** under the optimized conditions generated 4-acetoxy cyclopenta[*b*]benzothiophenes (Table 10, entries 5-8). Except in a few cases (Table 11, entries 2 and 4), the formation of double-bond regioisomers (indicated by 'a' and 'b') were observed in most instances.

2.3.2: Mechanistic details

A general and straightforward mechanism was proposed that rationalizes the transformation of benzothienyl carbinols into cyclopentannulated benzothiophenes under acidic conditions, Scheme 40. The reaction commences with benzothienylation of acetylacetone followed by an intramolecular aldol-type reaction, which is accompanied by alcohol protonation and water elimination to lead to the formation of tertiary carbocationic intermediate **48**. Upon losing the original carbinol proton, **49** generates neutral but unstable intermediate **50**. [1,5] sigmatropic hydrogen shift by "path a" generates enone **46a**, whereas [1,5] sigmatropic hydrogen shift by "path b" generates enone **46a'**.



Scheme 40: Proposed mechanism for the synthesis of polysubstituted cyclopenta[*b*]benzothiophenes.

In summary, we have developed an unprecedented super acid catalyzed benzofuran ring opening and furan ring recyclization to afford polysubstituted furans. In addition, generality of this method was further demonstrated by employing furanyl carbinols as the substrate for the synthesis of tetrasubstituted furans. This method was further extended to the generation of cyclopentannulated benzothiophenes from benzothienyl carbinols and this methodology provides a direct and facile access to the preparation of synthetically useful and medicinally important cylopenta[*b*]benzothiophenes. This approach possesses great potential and further can be

elaborated for the construction of other cyclopentannulated heteroaryls such as cylopenta[*b*]indoles.

In order to extend this method for the construction of cyclopent[*b*]annulated indoles, we made efforts for the synthesis of the required starting compounds, 2-indolyl carbinols. All our attempts to obtain 2-indolyl carbinols were unsuccessful owing to their inherent instability. Thus at this stage we envisioned the development of an alternate approach that involves the generation of 2-indolyl cation equivalents, their subsequent reaction with 1,3-dicarbonyls, and eventual cyclization for cyclopenta[*b*]indoles. Our ventures towards the development of a one-pot approach for cyclopentannulated indoles are presented in next section.

Section 3

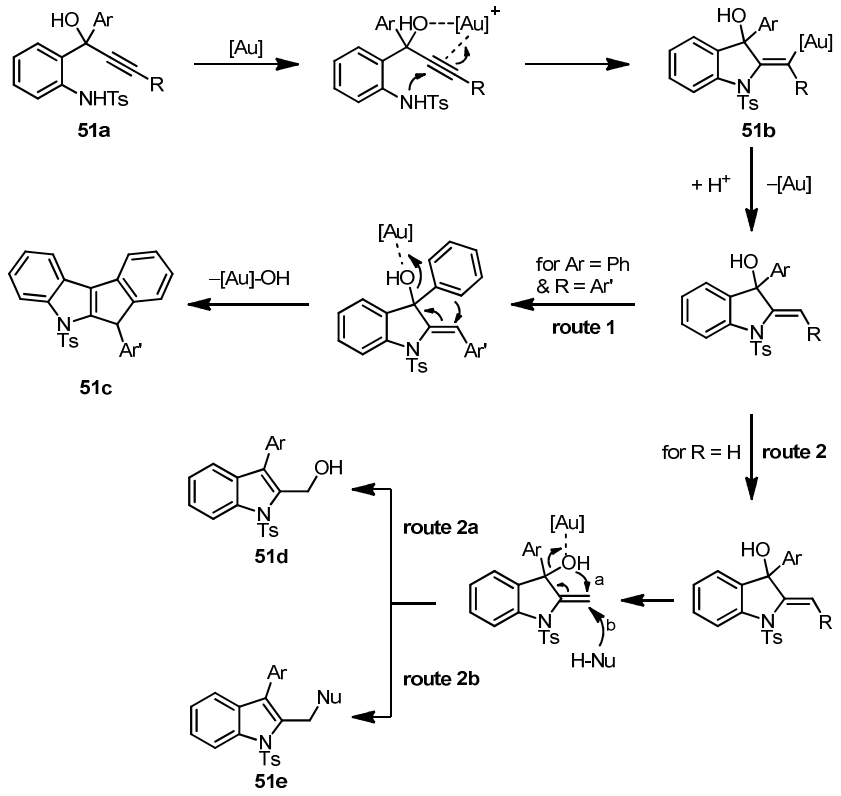
Synthesis of 1,2,3-trisubstituted cyclopenta[b]indoles via one-pot gold(I)/Brønsted acid relay catalysis

In the last few decades, there has been an immense focus on the practice of green and sustainable chemistry. The study of "green chemistry" and "sustainable chemistry" examines the idea of increasing efficiency and decreasing waste in synthetic sequences.[62] One way of improving the productivity of a synthetic sequence is to utilize reactions which achieve multiple bond-forming events under one-pot. Hayashi defines a one-pot synthesis as "a strategy to improve the efficiency of a chemical reaction, whereby a reactant is subjected to successive chemical reactions in just one reactor".[63] Such methods for carrying out multiple reactions are usually superior to stepwise approaches since no isolation of intermediates is required. To further increase the efficiency of these processes, recent attention has been focused on developing one-

pot sequences featuring multiple catalytic reactions. The use of multiple catalysts in one-pot transformations can be problematic for many reasons. Oftentimes, different catalysts can react differently with similar reactive functional groups, presenting selectivity issues in a one-pot process. In addition, compatibility between two or more different catalysts can further hamper the evolution of these methods. Regardless of these intricacies, a number of successful applications of this concept are present in the literature.[64]

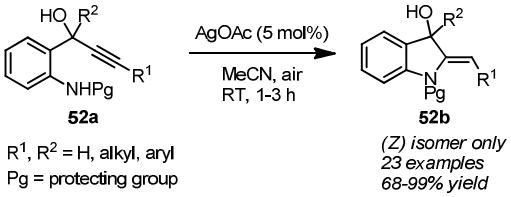
In recent years, gold catalysis received significant attention, due to its remarkable inherent property of activating the π-systems of alkynes and alkenes for the synthesis of a wide range of natural products and complex molecules in an efficient and predictable manner.[65] The combination of gold catalysis with other catalytic processes opens up various powerful avenues for the construction of complex natural product-like molecules. Within several one-pot gold relay catalytic processes, particularly gold/acid relay catalysis holds wider applications in creating intricate molecular architectures. Consequently, a myriad of impressive methodologies have been developed which manifest the above concept judiciously for composing complex scaffolds from simple starting materials in concise and efficient manner.[66]

Among several gold promoted relay processes, Chan's work on the synthesis of complex indole derivatives by employing a one-pot gold/acid catalyzed intramolecular tandem heterocyclization and Friedel–Crafts alkylation reaction sequence attracted our attention, Scheme 41.[67] This strategy is especially attractive owing to the ease of synthesis of starting materials, 1-(2-aminophenyl)prop-2-ynols **51a**, and furthermore, this reaction generates some of the most sought-after cores in organic synthesis. Gold(I)-mediated intramolecular cyclization of **51a** in selective 5-*exo*-*dig* manner furnished the vinyl gold species **51b**, which followed by protodeauration and acid mediated intramolecular Friedel–Crafts alkylation (when R = Ar, Route 1, Scheme 41), afforded the indenyl-fused indoles **51c**. On the other hand, when R = H, a more reactive primary vinyl gold species was generated, which upon rapid protodeauration and 1,3-allylic alcohol isomerization (1,3-AAI) furnished primary indolyl carbinol **51d** (Route 2a, Scheme 41). However in the presence of a strong nucleophile, the reaction followed a different pathway. Preferential S_N2' substitution with nucleophiles such as methanol and electron rich arenes furnished the respective 2-alkyl-1*H*-indoles **51e**, (Route 2b, Scheme 41).



Scheme 41: Chan's gold-catalyzed cycloisomerization approach for indenyl-fused indole synthesis.

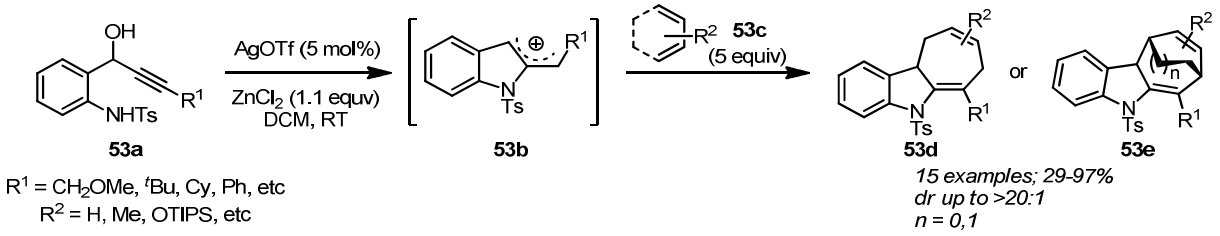
In 2012,[68] Chan's group further demonstrated a silver(I)-catalyzed chemo- and stereoselective hydroamination reaction of 1-(2-(sulfonylamino)phenyl)-prop-2-yn-1-ols **52a** yielding (*Z*)-2-methyleneindolines **52b**, Scheme 42.



Scheme 42: Chan's Ag(I) catalyzed hydroamination of 1-(2(sulfonylamino)phenyl)prop-2-yn-1-ols.

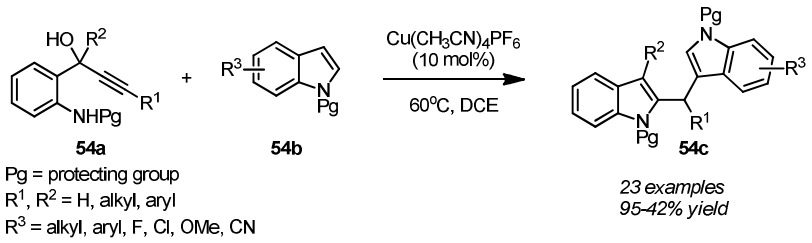
Subsequent to Chan's work, few other reports employing 1-(2-aminophenyl)prop-2-ynols as starting materials appeared in the literature. Some of the important studies are discussed herein.

In 2014, Xue and Li *et al.*[69] utilized silver-catalyzed hydroamination of 1-(2-(sulfonylamino)-phenyl)prop-2-yn-1-ols **53a** as the key step during the tandem hydroamination/[4+3] cycloaddition reaction sequence, Scheme 43. This strategy provided access to multitudinal indole-containing 5,7,6-tricyclic skeletons. In a one-pot cascade event, silver catalyzed intramolecular hydroamination followed by $ZnCl_2$ mediated 1,3-allylic isomerization generated 2-indolyl cation equivalents **53b** which facilitated cycloaddition between **53b** and dienes **53c**, resulting in the formation of cyclohepta[*b*]indoles **53d** or **53e**.



Scheme 43: One pot hydroamination/[4+3] cycloaddition sequence for the synthesis of cyclohepta[*b*]indoles.

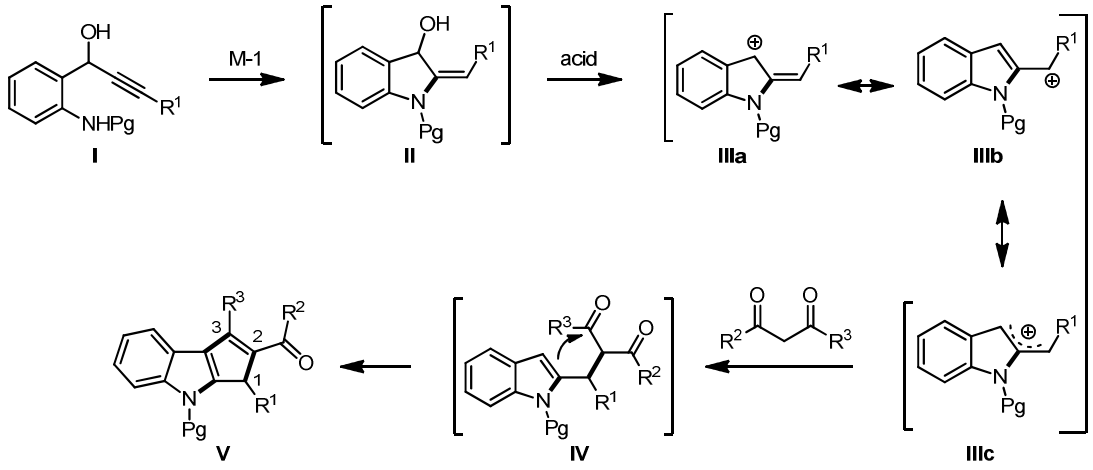
In 2014, Tang *et al.* [70] expanded the silver catalyzed hydroamination methodology for the synthesis of diverse 2,3'-diindolylmethanes from propargylic *tert*-alcohols **54a** and indoles **54b**, Scheme 44. During the optimization studies, copper (I) was realized to be optimal in promoting the intramolecular hydroamination and arylation cascade. In a one-pot synthetic sequence, Cu(I)-catalyzed 5-*exo*-*dig*-cyclization, 1,3-allylic isomerization followed by dehydrative nucleophilc arylation of various indoles afforded bisindolylmethanes **54c**. The generality of the reaction was further demonstrated by the employment of several other electron-rich arenes and alcohols as nucleophiles.



Scheme 44: Copper catalyzed tandem hydroamination and arylation sequence for the synthesis of bisindolylmethanes.

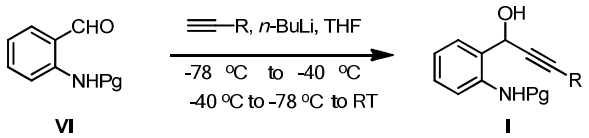
3.1: Results and discussion

As showcased above, the prevailing 2-indolylmethyl cation intermediate was routinely trapped by nucleophiles such as alcohols, aryls, heteroaryls, etc.[71] However, to our surprise, no attempt was ever made to employ readily available 1,3-dicarbonyl compounds as nucleophiles. Motivated by the pioneering studies of Chan for the synthesis of indole derivatives starting from, 1-(2-aminophenyl)prop-2-ynols and with our experience in the chemistry of heteroaryl carbinols,[50,72] we intended to extend the polyphosphoric acid (PPA) mediated solvent-free domino process (described in Section 2)[73] for the synthesis of cyclopenta[*b*]indoles. We envisioned that an intramolecular hydroamination of alkynols **I** promoted by an appropriate metal catalyst M-1 could provide the indolines **II** and subsequent acid-catalyzed 1,3-allylic alcohol isomerization (1,3-AAI) of indolines **II** followed by ene reaction with 1,3-dicarbonyls could generate the acetylacetone adduct **IV**. It was further hypothesized that intramolecular Friedel–Crafts-type reaction in 1,3-dicarbonyl adduct **IV** could afford 1,2,3-trisubstituted cyclopenta[*b*]indole **V**, Scheme 45.



Scheme 45: Proposed approach for the synthesis of cyclopentannulated indoles.

Since modular access to ynols **I** can be readily achieved from the amino benzaldehydes **VI** in a single step (Scheme 46),[67] this method thus serves as an efficient alternative to the existing approaches for the synthesis of cyclopenta[*b*]indoles.

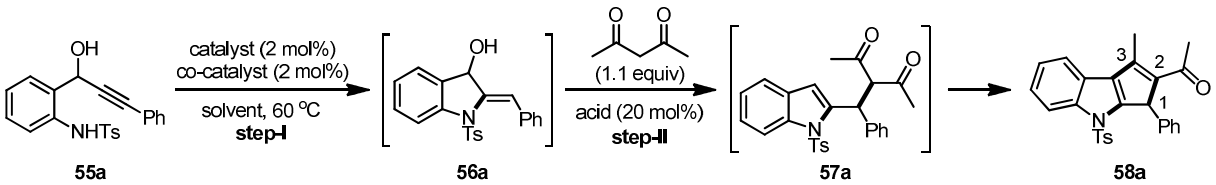


Scheme 46: Schematic representation of the synthesis of 1-(2-aminophenyl)prop-2-ynols.

We initiated studies by screening various conditions for the cyclization of amino alcohol **55a** to indoline **56a**, Table 12. The reaction of **55a** in the presence of Au(I) alone failed to deliver indoline **56a** (Table 12, entries 1 and 2). Under a combination of Au(I) and silver based Lewis acids, amino alcohol **55a** was found to be unstable and gave a complex mixture (Table 12, entries 3 and 4). Interestingly, the cyclization of amino alcohol **55a** to the indoline **56a** was achieved by employing a combination of Au(I) and base, but the subsequent transformation of indoline **56a** to cyclopentannulated indole **58a** was not observed (Table 12, entry 5). In order to achieve the cation-ene reaction and subsequent cyclization for the synthesis of cyclopentannulated indole **58a**, influence of various acids was studied. Lewis acids such as $Sc(OTf)_3$, $In(OTf)_3$, AgOTf failed to deliver required product, only acetylacetone adduct **57a** was isolated (Table 12, entries 6-8). Upon further screening, $Bi(OTf)_3$ in $MeNO_2$ and TMSOTf in DCE gratifyingly generated the cyclopentannulated indole **58a** in good yields (Table 12, entries 9 and10).

The structure of the cyclopenta[*b*]annulated indole **58a** was confirmed from its spectral data. Presence of an absorption band at 1630 cm^{-1} due to the *α,β*-unsaturated carbonyl stretch in the IR spectrum indicated the formation of cyclopenta[*b*]annulated indole **58a**. In ^1H NMR spectrum, presence of a quartet at δ 5.27 (*J* = 2.0 Hz) due to the methine (C-1), which shows a long range coupling with olefinic methyl, supported by the presence of a doublet at 2.84 (*J* = 2.0 Hz) due to the olefinic methyl, and a singlet at 2.29 ppm due to the acetyl methyl confirmed the formation of **58a**. In ^{13}C NMR spectrum, presence of quaternary carbon at δ 194.7 due to the *α,β*-unsaturated carbonyl carbon, a signal at 52.8 due to the phenyl connected carbon (C-1), presence of two methyl carbons at 30.4 and 21.5 ppm due to the olefinic methyl (C-3) and acetyl methyl (C-2), respectively, further established the structure of **58a**.

Table 12: Optimization of reaction parameters.



55a **56a** **57a** **58a**

Entry	Catalyst	Co-catalyst	Acid	Solvent	Time (h)	Yield (%)[a]
1	AuCl	–	–	DCE	48	–
2	PPh_3AuCl	–	–	DCE	48	–
3	AuCl	AgOTf	–	DCE	48	–
4	PPh_3AuCl	AgOTf	–	DCE	48	–
5	AuCl	K_2CO_3	–	DCE	40	–
6	AuCl	K_2CO_3	$Sc(OTf)_3$	$MeNO_2$	48	–
7	AuCl	K_2CO_3	$In(OTf)_3$	$MeNO_2$	48	–
8	AuCl	K_2CO_3	AgOTf	$MeNO_2$	48	–
9	AuCl	K_2CO_3	$Bi(OTf)_3$	$MeNO_2$	26	74
10	AuCl	K_2CO_3	TMSOTf	DCE	20	82
11	AuCl	K_2CO_3	TFA	DCE	13	–
12	AuCl	K_2CO_3	H_3PO_4	DCE	16	51
13	AuCl	K_2CO_3	$HClO_4$	DCE	15	72
14	AuCl	K_2CO_3	H_2SO_4	DCE	18	70
15	AuCl	K_2CO_3	TfOH	DCE	13	83
16	AuCl	K_2CO_3	TfOH	$MeNO_2$	24	74
17	AuCl	K_2CO_3	TfOH	Toluene	13	80
18	AuCl	Na_2CO_3	TfOH	DCE	35	53
19	AuCl	Et_3N	TfOH	DEC	27	72
20[b]	**AuCl**	**K_2CO_3**	**TfOH**	**DCE**	**18**	**90**
21[b]	PPh_3AuCl	K_2CO_3	TfOH	DCE	42	76
22[b]	AuCl	K_2CO_3	TMSOTf	DCE	36	85

[a]Isolated yields after silica gel column chromatography. [b]10 mol% acid was employed.

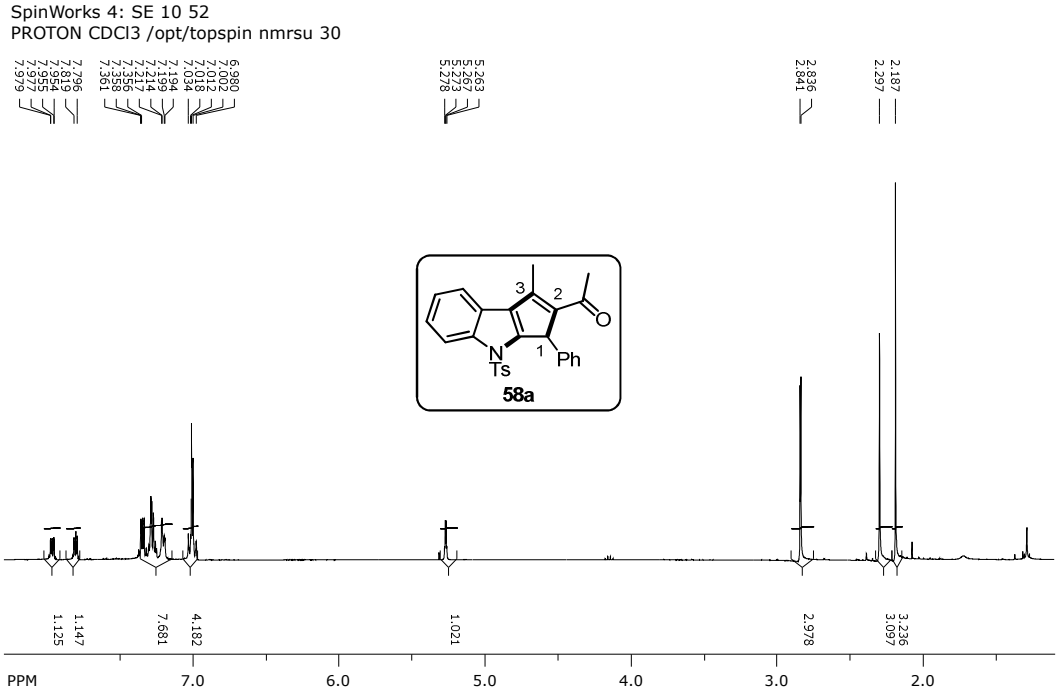


Figure 10: ^{1}H NMR spectrum of **58a**.

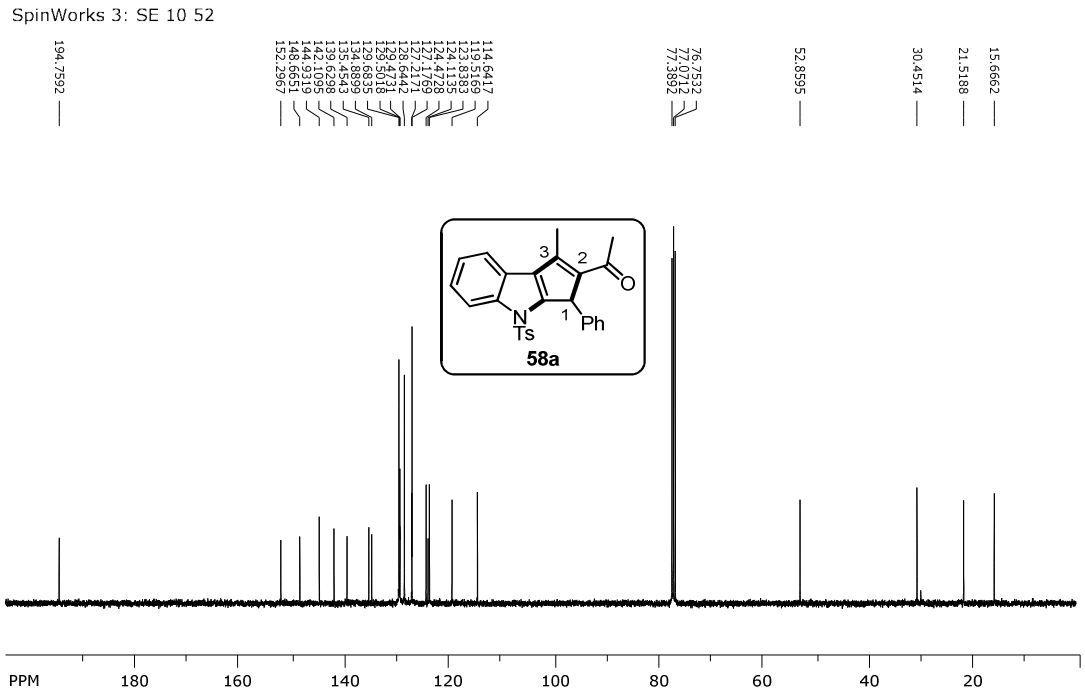
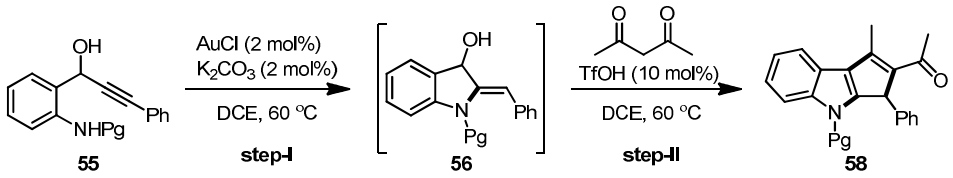


Figure 11: ^{13}C NMR spectrum of **58a**.

In order to further improve the efficiency of the reaction, we opted to investigate the influence of Brønsted acids in place of Lewis acids in step-II. Among several Brønsted acids explored, H_3PO_4, $HClO_4$, and H_2SO_4 generated the cyclopenta[*b*]annulated indole **58a** in moderate yields (Table 12, entries 11-14). To our delight, triflic acid mediated reaction in DCE delivered the cyclopentannulated indole **58a** in very good yield (Table 12, entry 15). A brief solvent screening was performed; however, no significant increase in yield was observed (Table 12, entries 16 and 17). Further, effect of different inorganic and organic bases as co-catalysts (in step-I) was studied. While no desired product was observed when sodium bicarbonate was employed as the co-catalyst, sodium carbonate and an organic base such as triethylamine furnished **58a** only in moderate yields (Table 12, entries 18 and 19). Gratifyingly, further enhancement in the yield was observed, when acid loading was decreased from 20 mol% to 10 mol% (Table 12, entry 20). Further attempts to enhance the yield were not encouraging (Table 12, entries 21 and 22).

Having optimized conditions in hand, effect of different protecting groups (Pg) on the relay Au(I)/Brønsted acid catalyzed domino process was studied. From the Table 13, it is evident that N-sulfonyl protecting groups are efficient and generated respective cyclopentannulated indoles (**58a** and **58b**). However, the N-acetate or N-Boc group-containing propargyl alcohols (**55c** and **55d**) failed to generate even the respective step-I products.

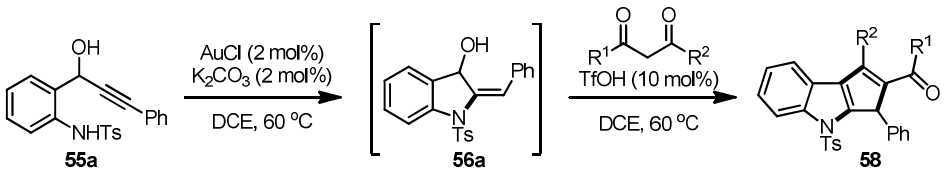
Table 13: Scope of different protecting group.

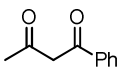
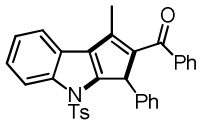
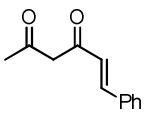
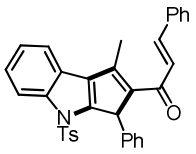
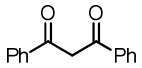
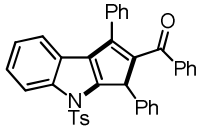
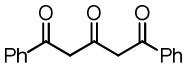
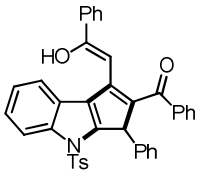
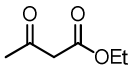
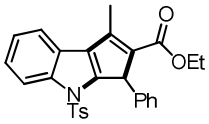
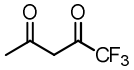
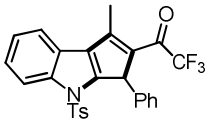
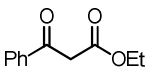
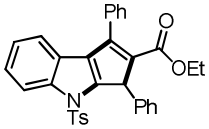
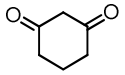
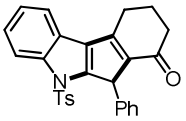
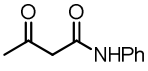
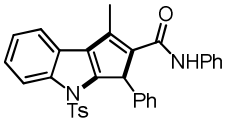
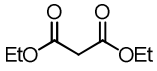
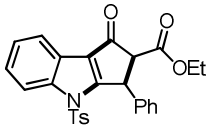


Entry	N-Protecting group	Time (h)	Yield (%)
1	Ts (**55a**)	18	90 (**58a**)
2	Ms (**55b**)	24	83 (**58b**)
3	Ac (**55c**)	48	NP (**58c**)
4	Boc (**55d**)	48	NP (**58d**)

NP = no product

Table 14: Scope of various 1,3-dicarbonyls.



Entry	1,3-dicarbonyl	Time/Yield	Product	Entry	1,3-dicarbonyl	Time/Yield	Product
1		24 h, 86%		6		16 h, 63%	
	37j		**58e**		**37p**		**58j**
2		24 h, 87%		7		18 h, 83%	
	37n		**58f**		**37q**		**58k**
3		13 h, 76%		8		48 h, 0%	
	37k		**58g**		**37r**		**58l**
4		12 h, 74%		9		48 h, 0%	
	37l		**58h**		**37s**		**58m**
5		24 h, 86%		10		48 h, 0%	
	37o		**58i**		**37t**		**58n**

In order to validate the generality of the unprecedented method for the synthesis of 1,2,3-trisubstituted cyclopenta[*b*]indoles, initially, the reaction of 1-(2-aminophenyl)prop-2-ynol **55a** with a variety of 1,3-dicarbonyls was investigated. Reaction of the amino alcohol **55a** with 1,3-diketones **37j** and **37n** generated the respective 1,2,3-trisubstituted cyclopenta[*b*]annulated indoles **58e** and **58f** in excellent yields (Table 14, entries 1-2). As it is evident from the Table 14, not only 1,3-diketones, even *β*-ketoesters and *β*-ketoamides were also found to be excellent for the cyclopentannulation of indoles. For example, the reaction of *β*-ketoesters **37k** and **37l** with

55a provided highly functionalized cyclopenta[*b*]annulated indoles **58g** and **58h**, respectively, in good yields (Table 14, entries 3 and 4). Similarly, *β*-ketoamide **37o** delivered 1,2,3-trisubstituted cyclopenta[*b*]annulated indole **58i** in excellent yield (Table 14, entry 5). In addition, Nazarov-diketone **37p** and 1,3,5-triketone **37q** upon reaction with **55a** under the optimized condition furnished fully conjugated cyclopetannulated indoles **58j** and **58k**, which can exhibit interesting photo physical properties (Table 14, entries 6 and 7). Single crystal X-ray diffraction analysis unambiguously confirmed the structure of the cyclopentannulated indole **58j**, Fig. 12. However, our attempts with diketone **37r**, cyclic diketones **37s** and malonates **37t** were unsuccessful (Table 14, entries 8-10).

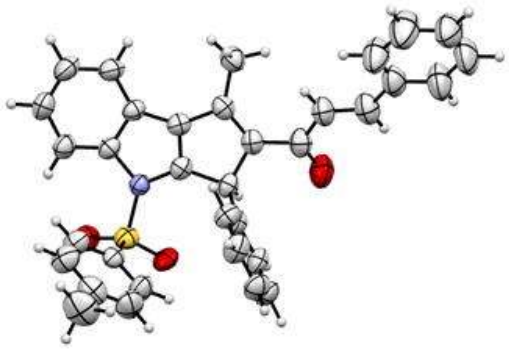
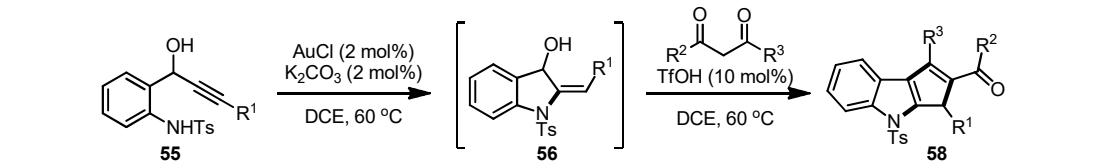
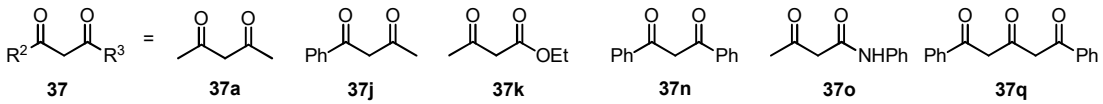


Figure 12: ORTEP diagram of cyclopentannulated indole **58j**.

After screening various 1,3-dicarbonyls for the cyclopentannulation of indoles, with an interest to expand the scope of the protocol, electronically diverse 1-(2-aminophenyl)prop-2-ynols **55e**-**55j** were chosen as substrates, Table 15. The reaction displays significant tolerance towards various alkynols bearing electron-donating as well as electron-withdrawing aryl groups. Alkynol having a tolyl group on the acetylenic carbon center (**55e**), upon reaction with *β*-ketoester **37k**, *β*-ketoamide **37o** and 1,3,5-triketone **37p** furnished the respective cyclopenta[*b*]annulated indoles in good yields (Table 15, entries 1-3). Ynol **55f** bearing a mild electron-withdrawing aryl group such as *p*-fluorophenyl was found to be the excellent substrate in terms of yield and reaction time (Table 15, entry 4). Presence of heteroaryls such as thienyl group on the alkyne was well-tolerated under the optimized reaction conditions and generated respective cyclopentannulated indoles **58s** and **58t** in good yields (Table 15, entries 5 and 6). Complex indole derivatives bearing electron-withdrawing (-OTs or -CF_3) as well as electron-donating (-OMe) substituents on the indole moiety could also be accessed easily in high yields (Table 15, entries 6-8).

Table 15: Substrate scope for the synthesis of cyclopenta[*b*]annulated indoles.





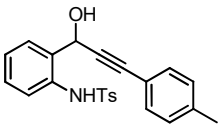
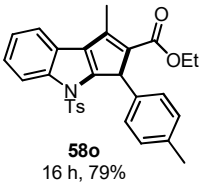
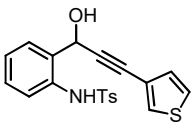
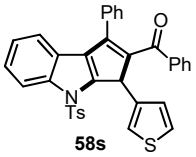
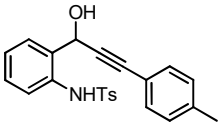
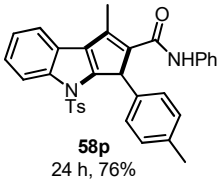
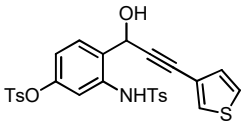
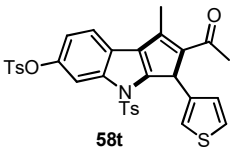
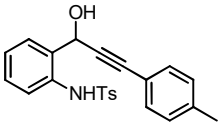
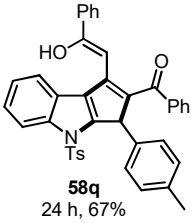
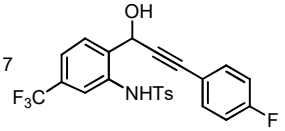
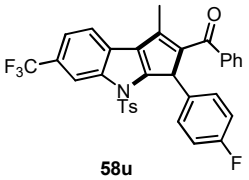
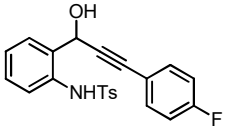
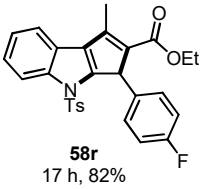
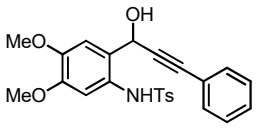
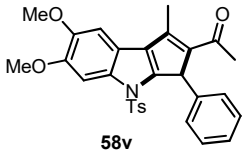
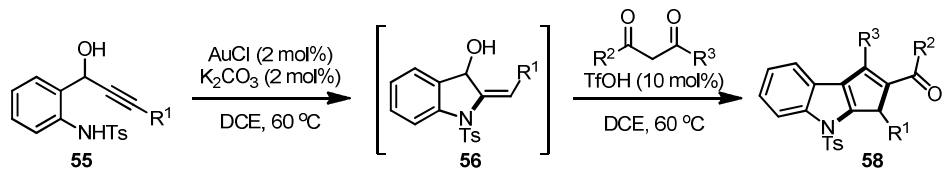
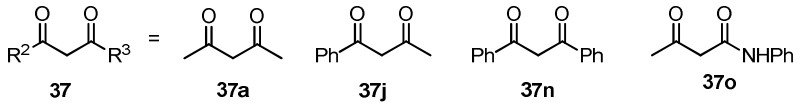
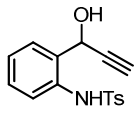
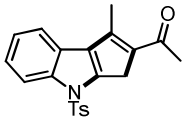
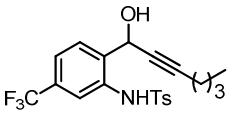
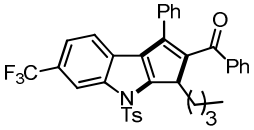
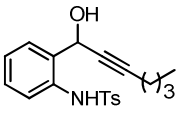
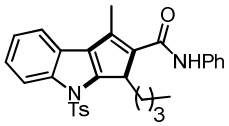
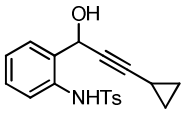
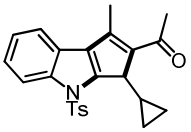
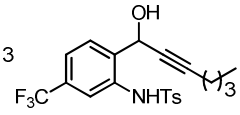
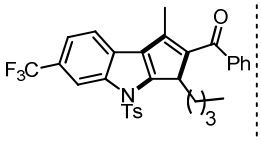
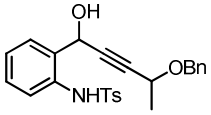
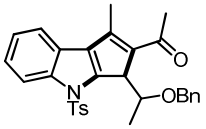
Entry	Substrate	1,3-dicarbonyls	Products	Entry	Substrate	1,3-dicarbonyls	Products
1	 **55e**	**37k**	 **58o** 16 h, 79%	5	 **55g**	**37n**	 **58s** 24 h, 82%
2	 **55e**	**37o**	 **58p** 24 h, 76%	6	 **55h**	**37a**	 **58t** 24 h, 75%
3	 **55e**	**37q**	 **58q** 24 h, 67%	7	 **55i**	**37j**	 **58u** 24 h, 78%
4	 **55f**	**37k**	 **58r** 17 h, 82%	8	 **55j**	**37a**	 **58v** 24 h, 78%

Table 16: Substrate scope for the synthesis of cyclopenta[*b*]annulated indoles.

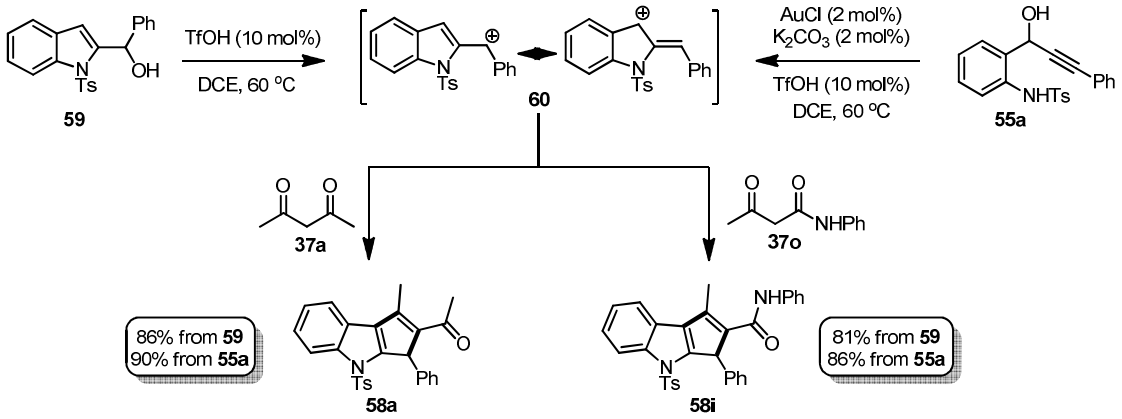




Entry	Substrate	1,3-dicarbonyls	Products	Entry	Substrate	1,3-dicarbonyls	Products
1	 **55k**	**37a**	 **58w** 36 h, 67%	4	 **55m**	**37n**	 **58z** 18 h, 69%
2	 **55l**	**37o**	 **58x** 23 h, 51%	5	 **55n**	**37a**	 **58aa** 13 h, 0%
3	 **55m**	**37j**	 **58y** 19 h, 74%	6	 **55o**	**37a**	 **58ab** 13 h, 0%

Interestingly, the reaction of unsubstituted alkynol **55k** with acetylacetone **37a** efficiently generated the 1,2-disubstituted cyclopentannulated indole **58w** (Table 16, entry 1) in good yield, but enhanced the scope of this method. In addition, reaction of **55l**, having a pendent alkyl group on the acetylenic carbon center, with diketone **37o** also furnished the respective annulated indole **58x** in moderate yield (Table 16, entry 2). Cyclopentannulated indoles having trifluormethyl group on indole moiety were obtained in excellent yields by the reaction of **55m** with **37j** and **37n** under the optimized conditions (Table 16, entries 3 and 4). However, contrary to our expectation, the amino alcohols **55n** and **55o** failed to deliver the desired products under the reaction conditions. Presumably, the presence of acid sensitive cyclopropyl and –OBn groups would have triggered some unwanted side reactions (Table 16, entry 5 and 6).

Since alcohol **59** and cationic intermediate **60** are believed to be the intermediates in the transformation of **55a** to **58a** and **58i**, we planned to undertake a comparative study between the reactions of amino alcohol **55a** and 2-indolyl carbinol **59** under the optimized conditions, Scheme 47. It can be noted that the reaction of amino alcohol **55a** with **37a** or **37o** is found to be efficient in generating **58a** or **58i**, respectively, when compared to the reaction of alcohol **59** in forming **58a** and **55i**, thereby clearly demonstrating the advantage of the one-pot tandem process. It is worth mentioning that the direct Friedel–Crafts-type alkylation of unmodified 2-indolyl carbinols and 1,3-dicarbonyls as such is unprecedented and of course the subsequent cyclization cascade as well.



Scheme 47: Comparison between the efficiency of amino alcohol **55a** and indolyl carbinol **59** in forming the same end product. First demonstration of a direct reaction between 2-indolyl carbinols and 1,3-dicarbonyls.

3.2: Elaboration towards the synthesis of pyrrolo[1,2-a]indole

Synthesis of natural product-like complex structures and medicinally important compounds from simple substrates in an efficient manner, always remains an area of great interest for synthetic chemists. Pyrrolo[1,2-*a*]indole **61a** ring system occurs in many bioactive natural products and synthetic drugs (Fig. 13), and can serve as important intermediate in organic synthesis. For example, filnderole A **61b** is an indole alkaloid isolated from *Flindersia acuminate* which shows micromolar activity against the *Plasmodium falciparum.*[74] Similarly, dimethylisoborreverine **61c** also displays antimalarial activity by inhibiting the parasitic hemoglobin metabolism pathway.[75] Mitomycin C **61d** is very well- well-known antitumor agent isolated from *Streptomyces caespitosus* or *Streptomyces lavendulae* and currently used extensively in cancer treatment.[76] Given that the pyrrolo[1,2-*a*]indole-containing natural

products have diverse bioactivity profiles, new methodologies to access them are of great importance.

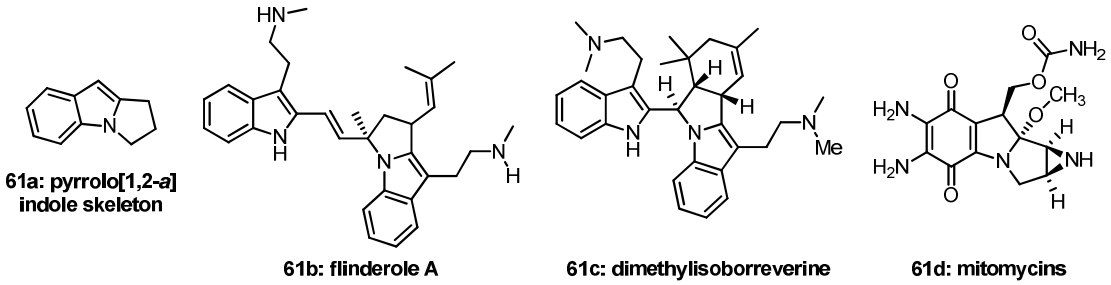
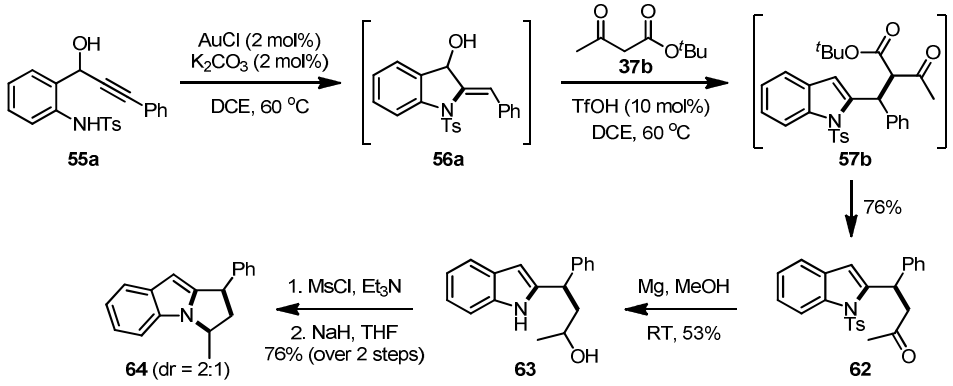


Figure 13: Representative examples of pyrrolo[1,2-*a*]indole-containing natural products.

Realizing the significance of pyrrolo[1,2-*a*]indoles we elaborated the aforementioned one-pot relay gold(I)/Brønsted acid relay catalytic approach for their synthesis, Scheme 48. Reaction of **55a** with *β*-ketoester **37b** under the optimized conditions furnished the adduct **57b**, which underwent smooth *in situ* decarboxylation to form *β*-branched 4-(2-indolyl)-2-butanone **62**, synthesis of which otherwise would require a multistep sequence. Indole **62** upon reaction with excess Mg in methanol generated alcohol **63** by undergoing simultaneous tosyl deprotection and ketone reduction. Selective O-mesylation and subsequent intramolecular N-alkylation of **63** conveniently produced 1,3-disubstituted dihydropyrroloindole **64**, in 76 % yield, Scheme 48.[77]



Scheme 48: Elaboration to pyrrolo[1,2-*a*]indole scaffold.

In conclusion, we have developed a general and efficient relay Au(I)/Brønsted acid catalyzed one-pot tandem process for the synthesis of medicinally significant 1,2-di- and 1,2,3-trisubstituted cyclopentannulated indoles from 1-(2-aminophenyl)prop-2-ynols and 1,3-dicarbonyls. This method was further elaborated to the synthesis of pyrrolo[1,2-*a*]indoles starting from 1-(2-aminophenyl)prop-2-ynols.

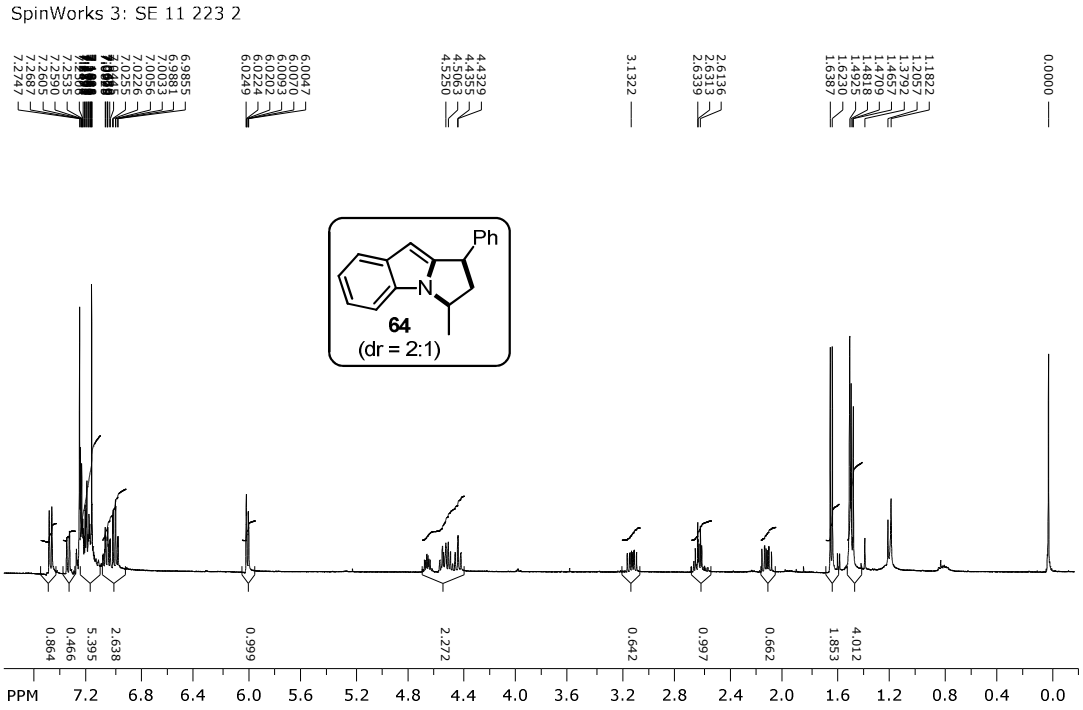


Figure 14: ^{1}H NMR spectrum of **64**.

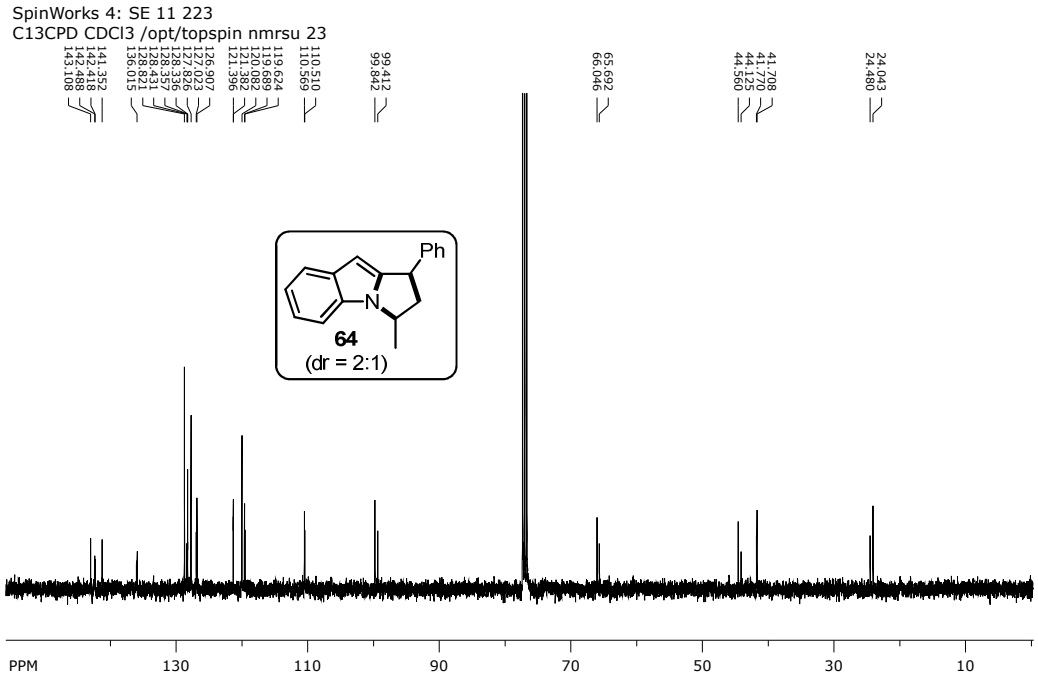
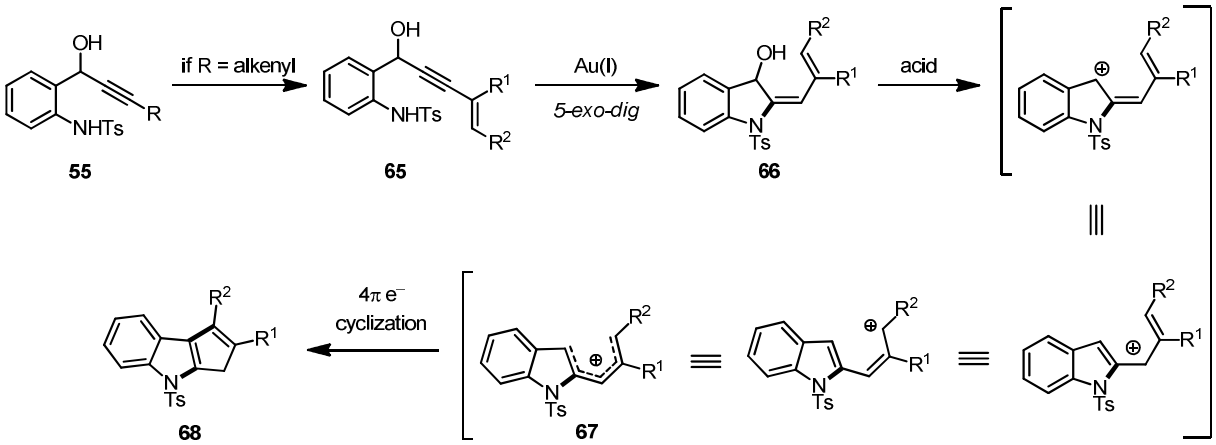


Figure 15: ^{13}C NMR spectrum of **64**.

Section 4

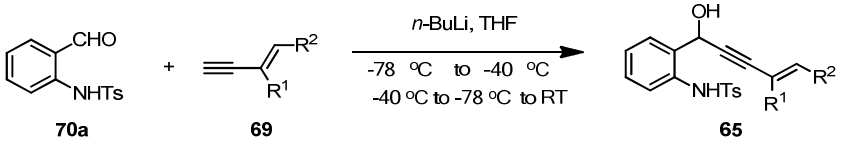
One-pot gold(I)/Brønsted acid relay catalytic approach for the synthesis of 1,2-disubstituted cyclopenta[b]indoles

After the successful development of an efficient approach for the synthesis of 1,2,3-trisubstituted cyclopenta[*b*]indoles (as describe in Section 3),[78] we envisioned that a mere replacement of R in **55** by an alkenyl group would lead to the underexplored substrates **65**, Scheme 49. It was hypothesized that Au (I) catalyzed 5-*exo-dig* cyclzation of 1-(2-aminophenyl)pent-4-en-2-ynols **65** could generate 2-allylidene indolinols **66**. Further, under acidic conditions, indolinols **66** could generate the pentadienyl cations **67** (4π-electron system or divinyl cationic equivalent), which can potentially undergo a Nazarov-type cyclization leading to the formation of 1,2-disubstituted cyclopenta[*b*]indoles **68**.



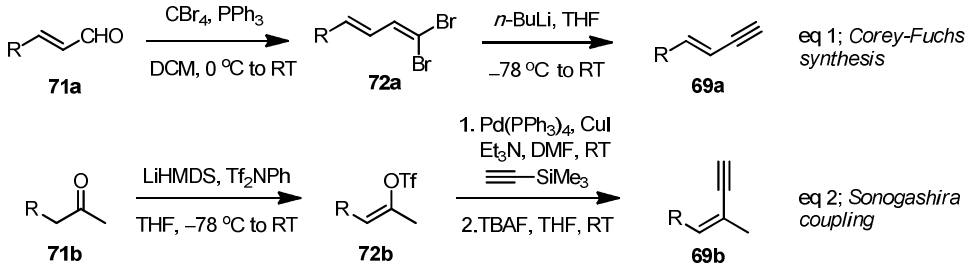
Scheme 49: Hypothesis for the cyclopentannulation of indoles *via* Nazarov-type cyclization of pentadienyl cations.

1-(2-Aminophenyl)pent-4-en-2-ynols **65** can be easily prepared in one step from readily available starting materials, Scheme 50.[78] *n*-Butyllithium mediated addition of enynes **69** to amino benzaldehydes **70a** can provide access to enynols **65**. Since modular access to enynols **65** can be easily achieved in a single step, this method thus can serve as an efficient alternative to the existing approaches for the synthesis of cyclopenta[*b*]indoles.



Scheme 50: Proposed approach for the synthesis of 1-(2-aminophenyl)pent-4-en-2-ynols **65**.

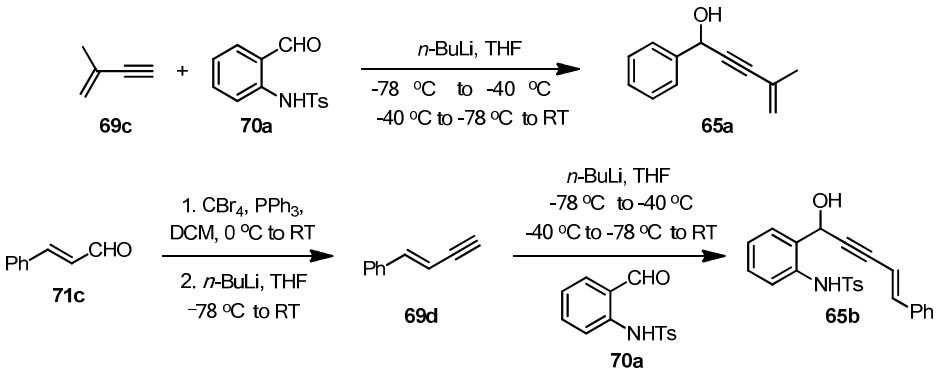
Enynes are valuable synthons for the synthesis of various enynols which play a major role in generating diversity and complexity in the respective products. Enynes can be easily accessed by different synthetic routes depending upon the starting material.[79] Enynes (**69a** and **69b**) can be efficiently obtained from enals **71a** by employing classical Corey-Fuchs synthesis (Scheme 51, eq 1),[80] or from ketones **71b** by Sonogashira coupling of respective vinyl triflates **72b** and ethynyltrimethylsilane (Scheme 51, eq 2).[81] Vinyl triflates can be prepared from a Buchwald protocol using LiHMDS and Tf_2NPh.[82]



Scheme 51: Methods for the synthesis of enynes.

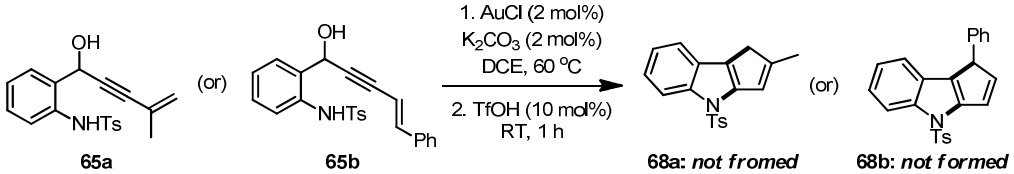
4.1: Results and discussion

In order to validate the mechanistic hypothesis proposed in Scheme 49, the enynols **65a** and **65b** having monosubstituted olefin frameworks were prepared as shown in Scheme 52. The enyne **69c** was procured from commercial sources and enyne **67d** was prepared from cinnamaldehyde **71c** by following the Corey-Fuchs synthesis.



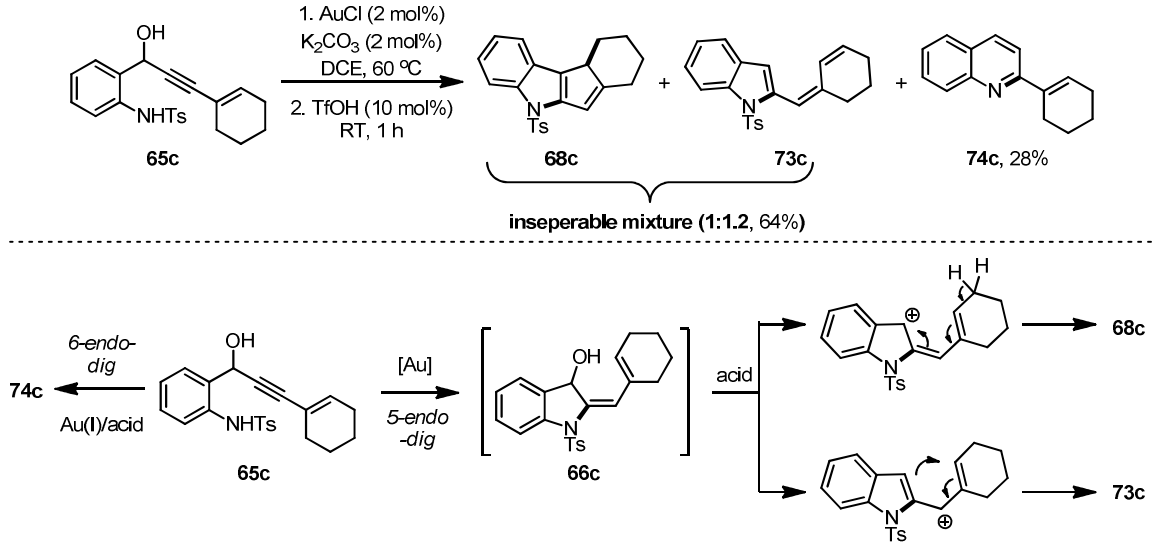
Scheme 52: Synthesis of enynols **65a** and **65b**.

Prompted by our earlier success with Au(I)-TfOH relay catalytic system for the cyclopentannulation of heteroaryls, we have chosen this catalyst system in the preliminary evaluation.[78] Reaction of the monosubstituted enynols **65a** or **65b** under these conditions, however, generated no desired product; only a complex mixture was observed despite numerous efforts, Scheme 53.



Scheme 53: Reaction of monosubstituted enynols **65a** and **65b**.

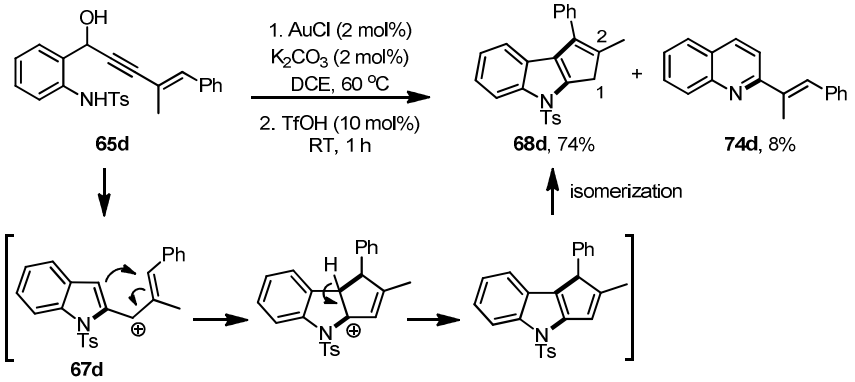
On the other hand, reaction of the enynol **65c** having disubstituted olefin under the prototypical conditions furnished an inseparable mixture of the desired product **68c**, and elimination product **73c** along with quinoline **74c**, Scheme 54.[67] Au(I)-catalyzed 6-*endo-dig* cyclization of **65c** and subsequent aromatization during acid treatment generated the quinoline **74c**.[83] Despite isolating **68c** contaminated with **73c**, this result indicated that the pentadienyl cation prevailed under the acidic conditions underwent Nazarov-type cyclization, leading to the formation of **68c**.



Scheme 54: Reaction of the disubstituted enynol **65c**.

The preliminary results indicated a remarkable substituent dependence on the product distribution and also necessitated a modified design of the substrate so as to make it suitable for the selective and high yielding conversion to the anticipated product.[84] Accordingly, the enynol **65d** was synthesized, which now possesses disubstituted olefin and also lacks allylic protons. Reaction of **65d** under the prototypical conditions furnished, as expected the cyclopenta[*b*]annulated indole **68d** in 74% yield along with an easily separable quinoline **74d** in 8% yield (Scheme 55). Careful analysis of the spectroscopic data of **68d** not only confirmed its structure, but further revealed the regioisomeric nature of the double bond in the cyclopentene ring. In the ^{1}H NMR spectrum, the presence of a characteristic singlet at δ 3.75 ppm due to the C-1 protons, a singlet at 2.36 due to the olefinic methyl, and in ^{13}C NMR spectrum, presence of a methylene at 40.1 due to the C-1 carbon, a methyl at 14.8 ppm due to the C-2 olefinic methyl established the structure of the cyclopentannulated indole **68d**. The presence of the sodiated

molecular ion m/z 422.1192 in high resolution mass spectrum further confirmed the structure of **68d**. Exclusive formation of **68d** can be explained by the intermediacy of **67d** in a Nazarov-type reaction followed by double bond isomerization leading to the formation of thermodynamically preferred product **68d**.

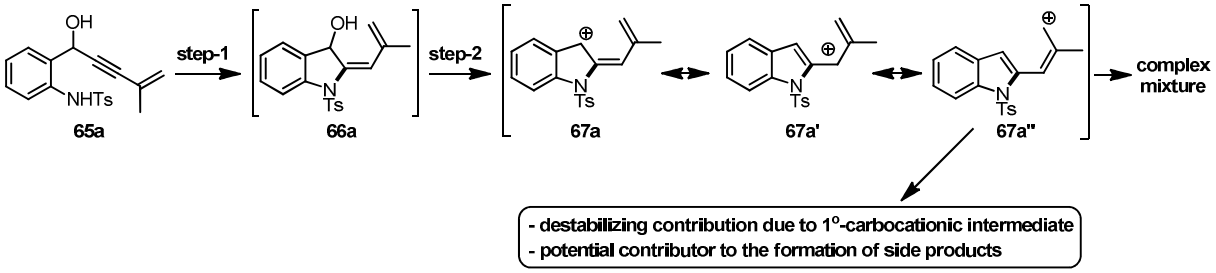


Scheme 55: Reaction of the disubstituted enynol **65d**.

In order to explain the remarkable substituent dependence on the product formation, following mechanistic hypothesis is proposed on the basis of experimental observations.

4.2: Proposed hypothesis for the non-formation of expected product with the enynol 65a

In case of monosubstituted enynol **65a**, the initially formed cationic intermediate **67a** can exist in the resonating forms **67a'** and **67a''**. Among them, **67a''** contributes to the destabilization of the transition state and thus disfavours the formation of the expected product **68a**, Scheme 56.



Scheme 56: Plausible explanation for the enynol **65a**.

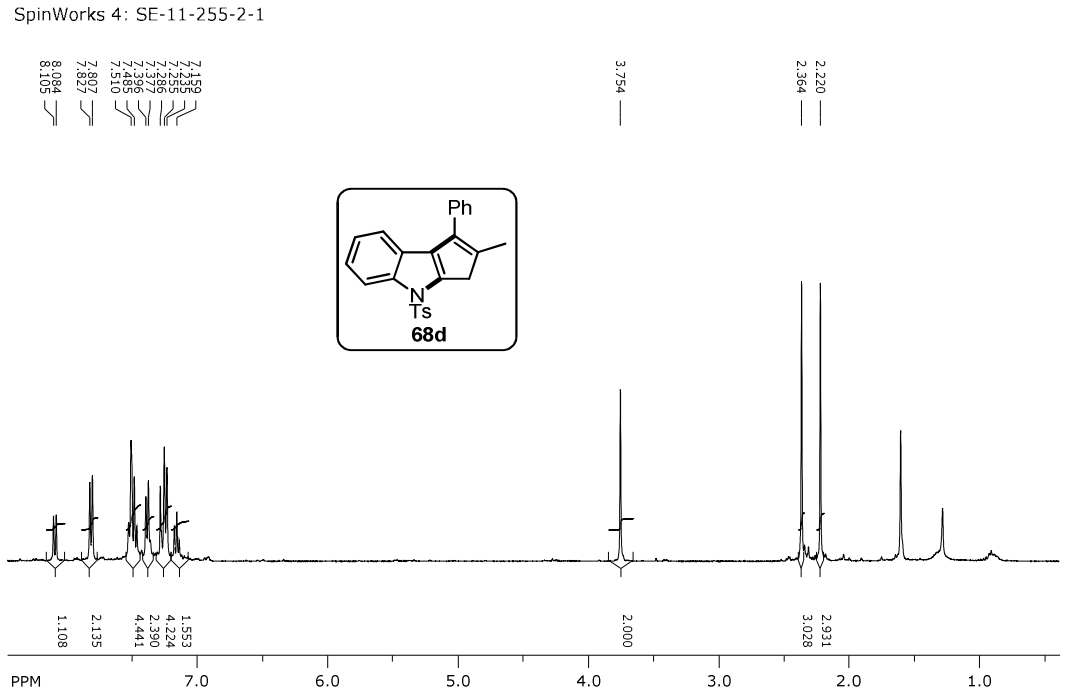


Figure 16: ^{1}H NMR spectrum of **68d**.

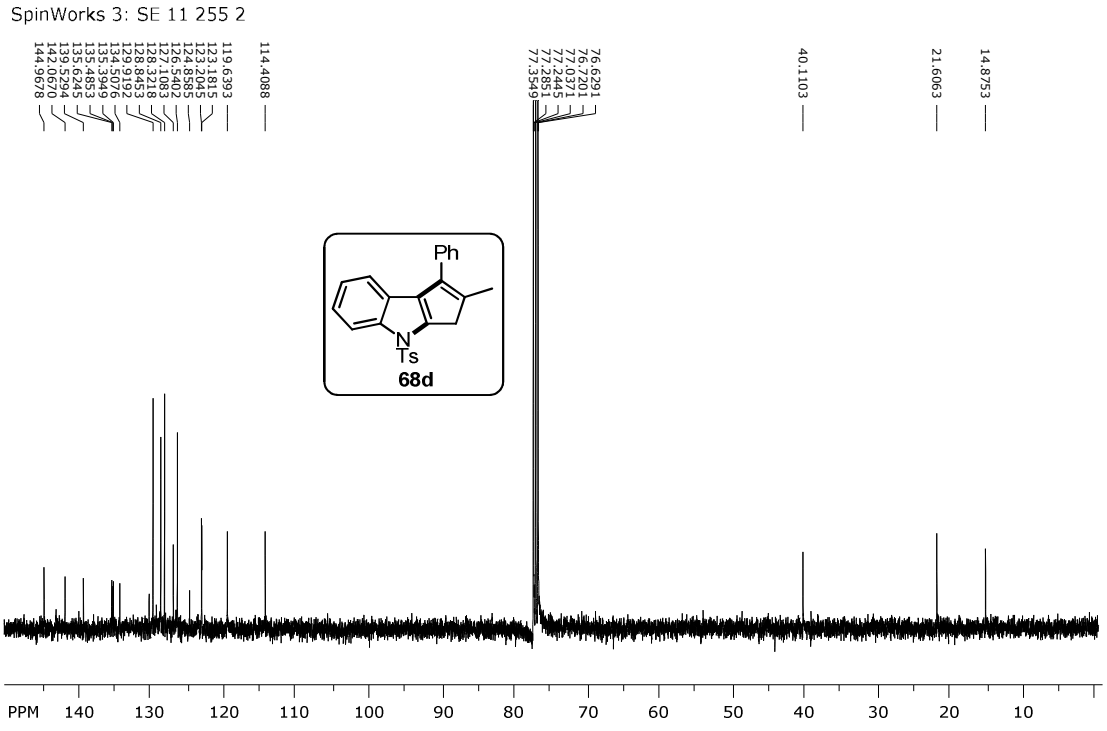
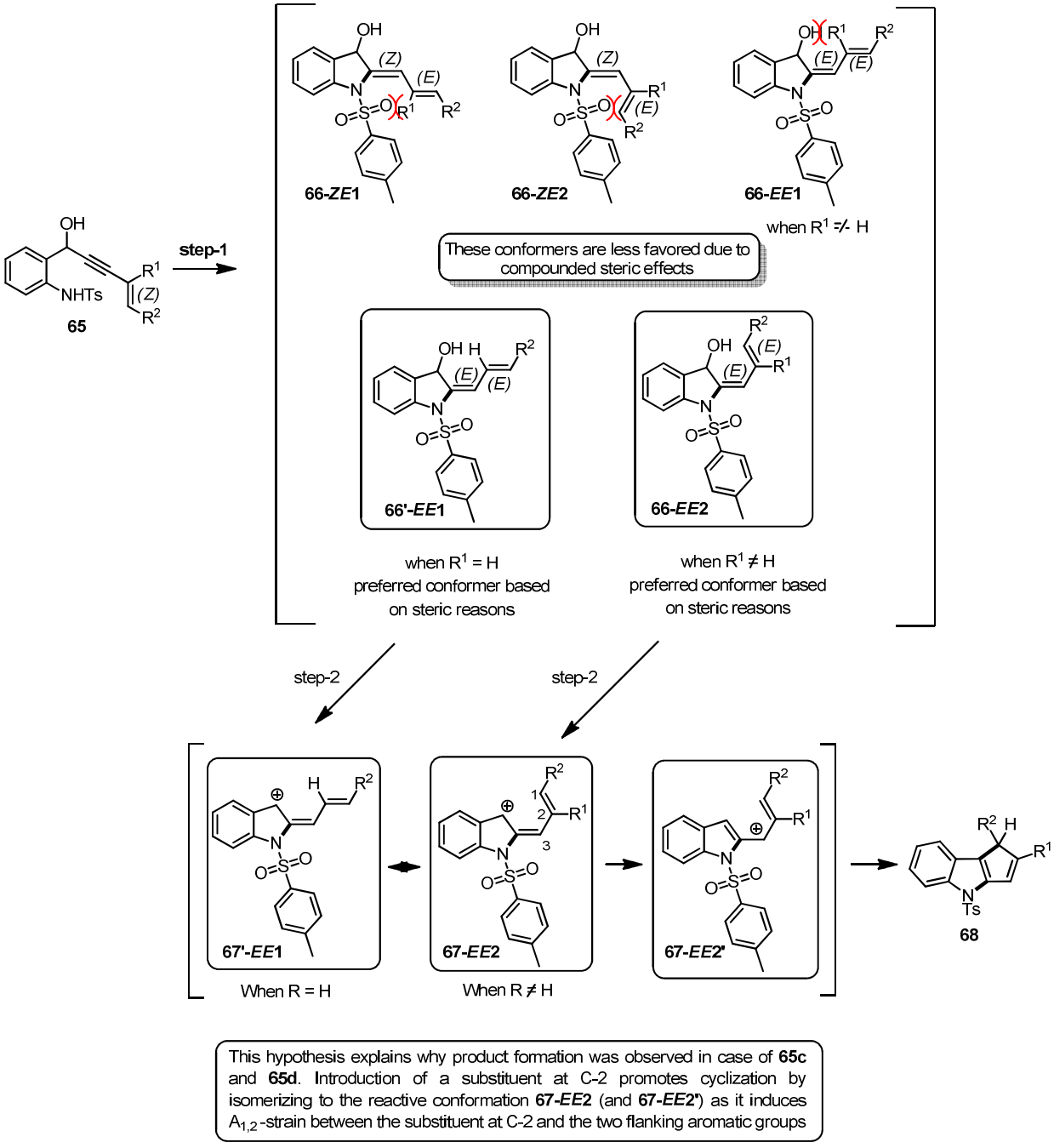


Figure 17: ^{13}C NMR spectrum of **68d**.

4.3: Proposed hypothesis for enynols 65b, 65c and 65d

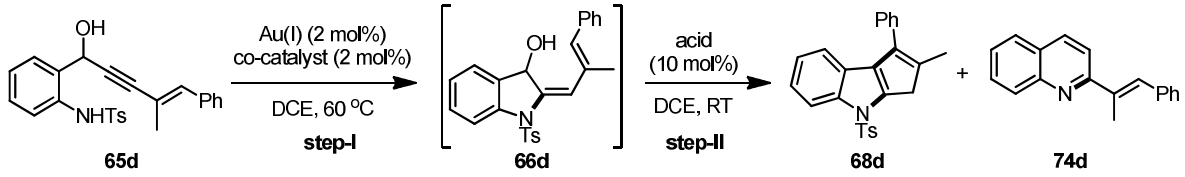
Indoline generated by the gold catalyzed 5-*exo-dig* cyclization of enynols (Scheme 57) can possibly exist in four conformers **66-*ZE*1, 66-*ZE*2, 66-*EE*1**, and **66-*EE*2**. The conformers **66-*ZE*1**, **66-*ZE*2**, and **66-*EE*1** (when $R^1 \neq H$) are less favored due to compounded steric effects as shown in Scheme 57. When $R^1 = H$, the conformer **66'-*EE*1** can be the preferred form, since no steric factors contributing to its destabilization. Among all the four possible conformers, only **66-*EE*2** exists in "S" conformation and is capable of undergoing 4π e^- cyclization. In case when $R^1 = H$, **66-*EE*2** conformer is less preferred over the **66'-*EE*1**. But when $R^1 \neq H$, **66-*EE*2** can be a preferred conformer for the cyclization, based on the steric reasons. The failure of monosubstituted enynol **65b** ($R^1 = H$) to undergo cyclization to cyclopentannulated indole **68b** can be attributed to the difficulty of isomerization of cation **67'-*EE*1** ($R^1 = H$) (generated from the **66'-*EE*1)** into the reactive conformations **67-*EE*2** or **67-*EE*2'** necessary for cyclization. The absence of C-2 substituent in the monosubstituted enynol **65b** does not afford sufficient amount of $A_{1,2}$ strain, required for the isomerization of **67'-*EE*1** to **67-*EE*2** or **67-*EE*2'**, Scheme 57. This $A_{1,2}$ strain would not occur for the unsubstituted case **67'-*EE*1** ($R^1 = H$). Thus introduction of a substituent at the C-2 position promotes cyclization as for the reactions of enynols **65c** and **65d**. In these cases, $A_{1,2}$ strain due to the central 2-substituent would be expected to result in **67-*EE*1**, and facilitate isomerization.[84] This hypothesis thus explains the remarkable substituent dependence on the formation of cyclopenta[*b*]annulated indole **68d** by facilitating reaction through the "S" conformation of the pentadienyl cation.

After identifying the appropriate substrate design to accomplish this transformation, we initiated optimization studies to identify an effective relay catalytic system that delivers the required product **68d** in superior yield while suppressing the formation of the side product **74d**. For this purpose, the amino alcohol **65d** was chosen as the substrate for optimization studies. Various Au(I), base, acid and solvent combinations were investigated and few important results are compiled in Table 17.



Scheme 57: Plausible explanation for the enynols **65b**, **65c**, and **65d**.

Table 17: Optimization of reaction parameters.



Entry	Catalyst	Co-catalyst	Acid	Time (h)	Yield **68d** (%)[a]
1	AuCl	AgOTf	TfOH	48	–
2	PPh_3AuCl	$AgSbF_6$	TfOH	48	–
3	**AuCl**	**K_2CO_3**	**TfOH**	**13**	**74**
4	AuCl	Na_2CO_3	TfOH	13	60
5	AuCl	Et_3N	TfOH	13	38
6[b]	AuCl	K_2CO_3	TfOH	15	57
7[c]	AuCl	K_2CO_3	–	48	–
8[d]	AuCl	K_2CO_3	TfOH	13	–
9	AuCl	K_2CO_3	$HClO_4$	16	64
10	PPh_3AuCl	K_2CO_3	TfOH	26	56
11	AuCl	K_2CO_3	TMSOTf	16	70
12	AuCl	K_2CO_3	$Bi(OTf)_3$	60	43
13	AuCl	K_2CO_3	$In(OTf)_3$	60	49
14	AuCl	K_2CO_3	$BF_3.OEt_2$	13	67
15	AuCl	K_2CO_3	$AgSbF_6$	60	36
16	AgOAc	–	TfOH	14	68

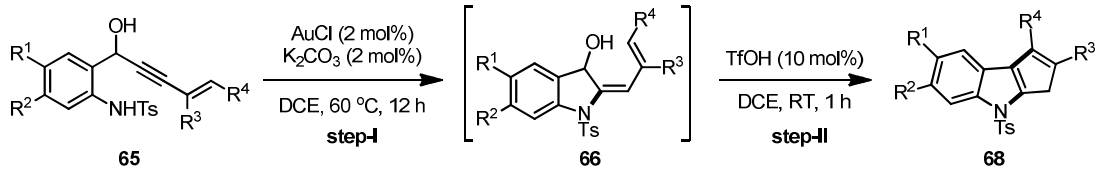
[a]Isolated yield after silica gel column chromatography. [b]Toluene as solvent. [c]THF as solvent, even step-I did not work. [d]Step-II at 60 °C.

No indoline formation was observed with the commonly employed Au(I)/Ag(I) combinations, even otherwise addition of catalytic amount of TfOH generated a complex mixture (Table 17, entries 1 and 2). After having an intial success with Au(I)/base combination (see Section 3), further attempts were made to improve the yield with different inorganic or

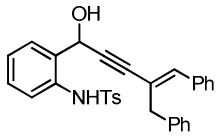
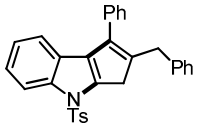
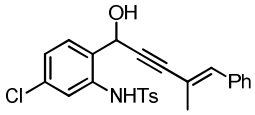
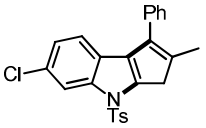
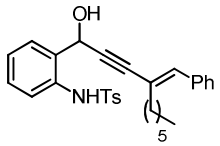
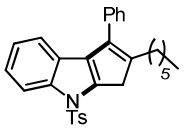
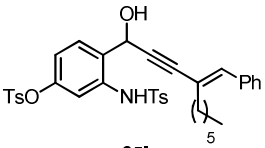
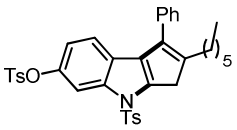
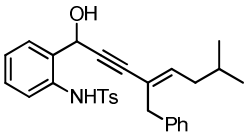
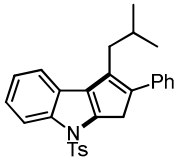
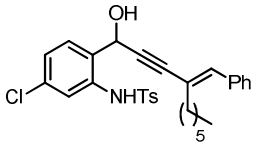
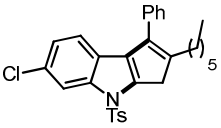
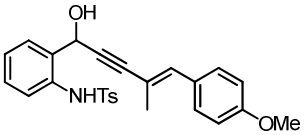
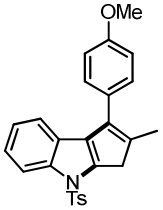
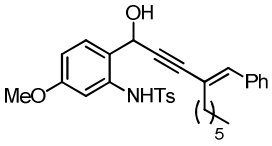
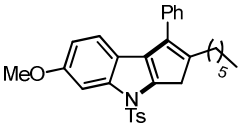
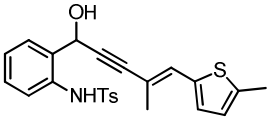
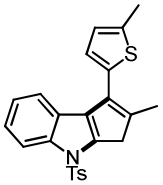
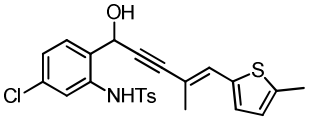
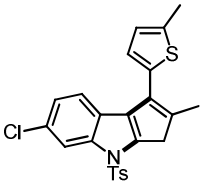
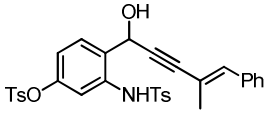
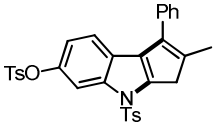
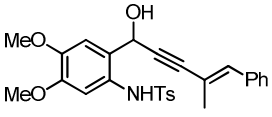
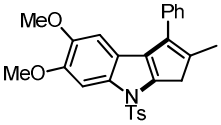
organic bases. However, our efforts in this direction were discouraging (Table 17, entries 4 and 5). A brief solvent screening was performed, but no promising results were obtained (Table 17, entries 6 and 7). Further attempt to increase the yield of **68d** by performing step-II at an elevated temperature was unsuccessful (Table17, entry 8). After realizing the inefficiency of the Brønsted acids other than TfOH in step-II, with the intention to further improve the reaction, we opted to investigate the influence of Lewis acids in place of Brønsted acids. However, among several Lewis acids screened, except TMSOTf and $BF_3.OEt_2$, all others Lewis acids provided **68d** in poor yields (Table 17, entries 11-15). Interestingly, among few Ag(I) salts evaluated, a combination of AgOAc (for step-I) and TfOH (for step-II) provided **68d** in good yield (Table 17, entry 16).

With the optimal conditions in hand, we next focused on investigating the substrate scope. Towards this, a diverse range of 1-(2-aminophenyl)pent-4-en-2-ynols **65e-65p** were prepared and were subjected to the optimized conditions, Table 18. The relay catalytic process was realized to be very general and efficient, and a wide range of cyclopentannulated indoles **68e-68o** could be rapidly assembled in good to excellent yields. In general, consistent reaction times were observed irrespective of the electronic or steric factors involved. In most of the cases, about 5-8% of the respective quinolines were also usually isolated. Regarding the olefin, a variety of alkyl, aryl and heteroaryl substituents (R^3 and R^4) were well-tolerated under the reaction conditions furnished the respective 1,2-substituted cyclopenta[*b*]indoles **68e-68i** (Table 18, entries 1-5). Notably, among several other similar cases studied, as an exception, no elimination product could be observed in case of the enynol **65g** despite possessing allylic protons, otherwise **68g** was obtained in good yield, (Table 18, entry 3). Table 18 further outlines the tolerable substituents across the aryl ring (R^1 and R^2) which can be electron-withdrawing such as –Cl, and –OTs (entries 6-9) as well as electron-donating such as –OMe (entry 10). Enynol **65n** with mono-methoxy substituent conveniently furnished **68n** in good yield (Table 18, entry 10). However, the enynol **65p** having di-methoxy groups on the aryl ring failed to generate the expected product **68p**, even Au(I)-mediated cyclization (step-I) was unsuccessful (Table 18, entry 12), leading to the hypothesis that electron-rich aryls probably render the acidity of –NHTs group unsuitable for the Au(I)-mediated cyclization.

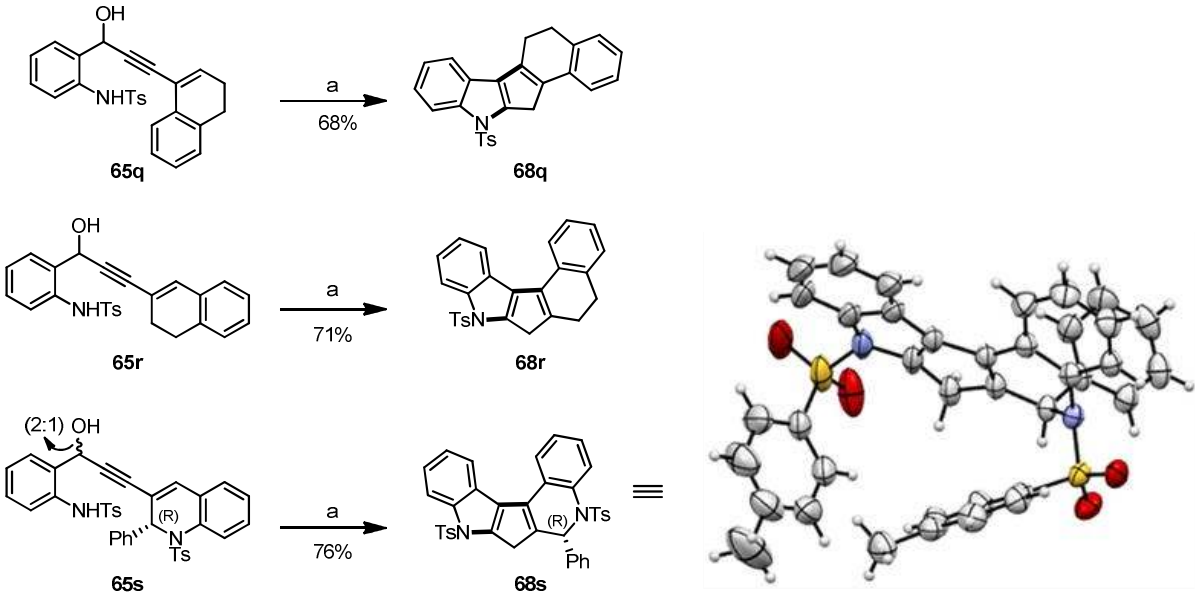
Table 18: Substrate Scope.



65 66 68

Entry	Substrate	Product	Entry	Substrate	Product
1	 **65e**	 **68e**, 80%	7	 **65k**	 **68k**, 71%
2	 **65f**	 **68f**, 75%	8	 **65l**	 **68l**, 63%
3	 **65g**	 **68g**, 72%	9	 **65m**	 **68m**, 72%
4	 **65h**	 **68h**, 71%	10	 **65n**	 **68n**, 68%
5	 **65i**	 **68i**, 63%	11	 **65o**	 **68o**, 68%
6	 **65j**	 **68j**, 64%	12	 **65p**	 **68p**, 0%

In addition, easy synthesis of enynols **65q-65s** from readily available precursors makes this an attractive strategy for the synthesis of natural product-like complex pentacyclic indoles (**68q-68s**, Scheme 58). Furthermore, structure of **68s** was confirmed by single crystal X-ray diffraction analysis. This strategy thus could pave the way for easy synthesis of their complex analogues which may find suitable applications in medicinal chemistry and also in materials science.



Scheme 58: Synthesis of complex pentacyclic indoles. Reagents and conditions: a) i) AuCl (2 mol%), K_2CO_3 (2 mol%), DCE, 60 ^oC, 12 h. ii) TfOH (10 mol%), RT, 1 h.

Steroidal conjugates have found significant applications in medicinal and supramolecular chemistry. Indoles and steroids are well-established privileged scaffolds and therefore synthesis of indole steroidal hybrids can offer potential opportunities to validate their biological properties.[85] Towards this, the cholesteryl enynol **65t** was synthesized by following the four step protocol starting from cholesterol (Scheme 59).[86] Thermodynamic vinyl triflate of 5-cholestan-3-one **72c** was selectively prepared by using KHMDS, which was further converted to **69e** by following Sonogashira coupling protocol. *n*-Butyllithium mediated addition of enynes **69e** to amino benzaldehydes **70a** provided access to enynols **65t**.

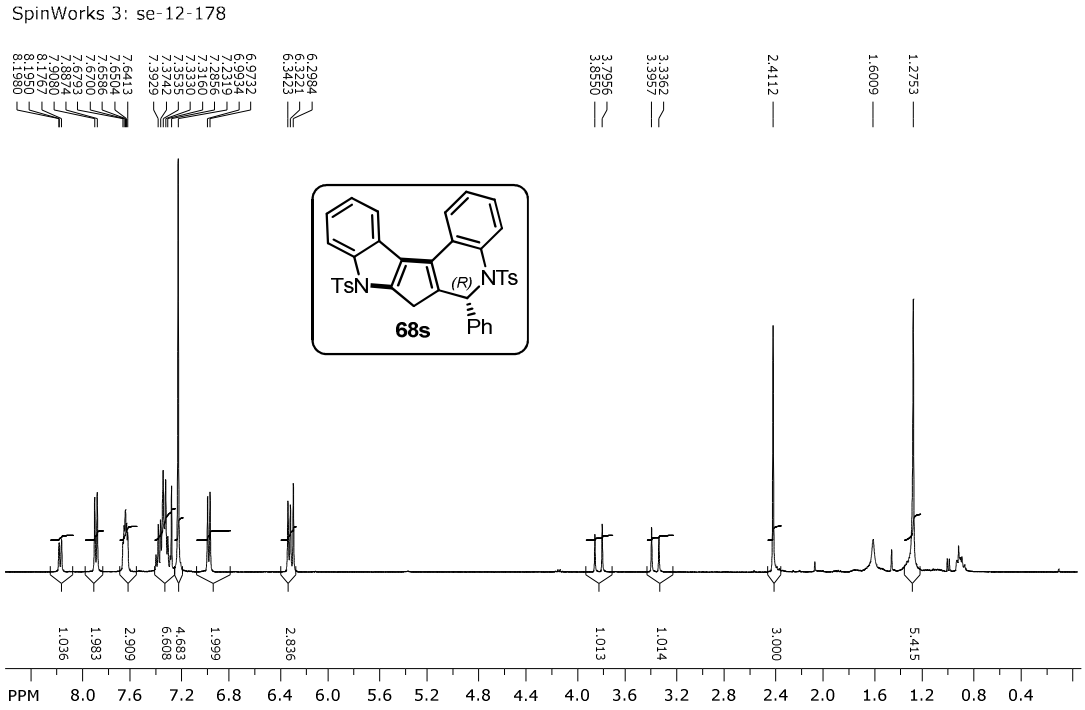


Figure 18: ^{1}H NMR spectrum of **68s**.

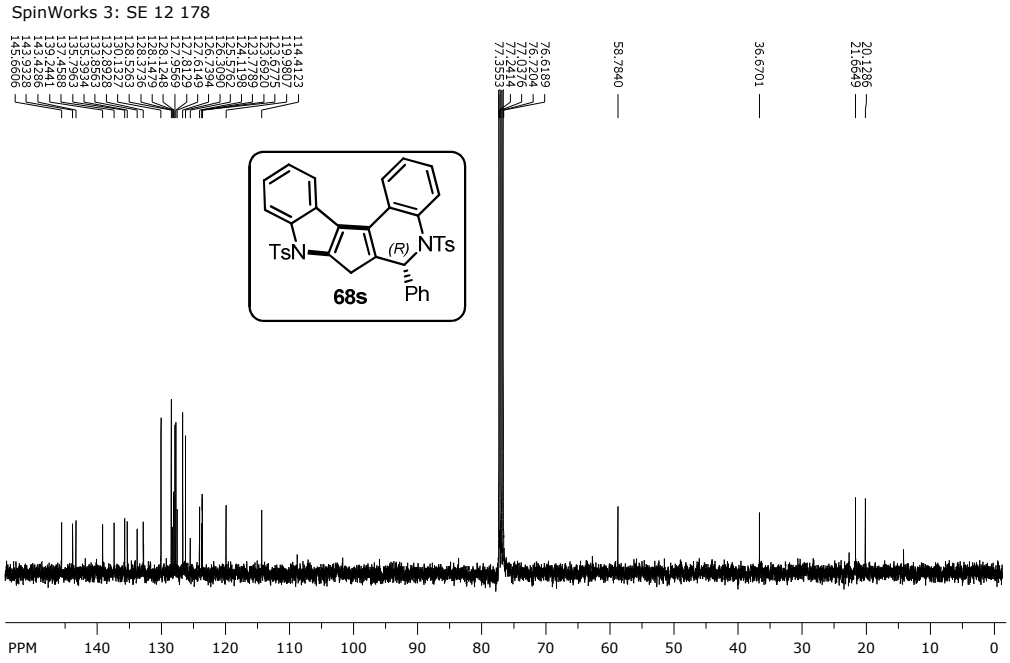
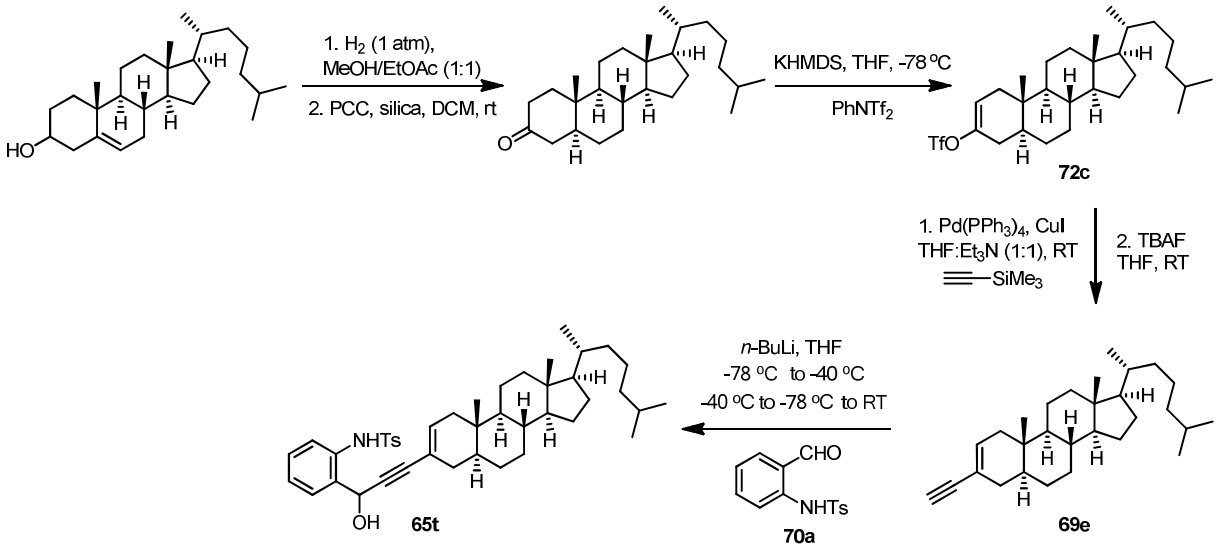
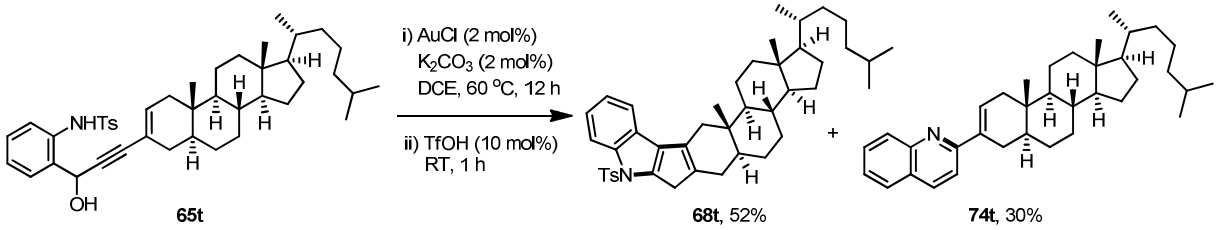


Figure 19: ^{13}C NMR spectrum of **68s**.



Scheme 59: Synthesis of cholesteryl enynol **65t**.

The enynol **65t** was then subjected to the optimized conditions, Scheme 60. Along with the desired product **68t** in 52% yield, respective quinoline **74t** (in 30% yield) was also isolated as expected. Nevertheless, a novel entry for the previously unknown indole steroidal hybrids has been established.



Scheme 60: Synthesis of indole-steroid hybrids.

Although this relay catalytic process is general in its current form, it is not without limitations. While studying the role of substituents on the cyclization processes, we observed that the enynols **65u** having a tetrasubstituted olefin failed to generate the expected product **68u**, however, furnished exclusively the quinoline **74u,** Scheme 61. Similarly, enynol **65v** where the olefin is part of the aromatic system generated only the quinoline **74v**.

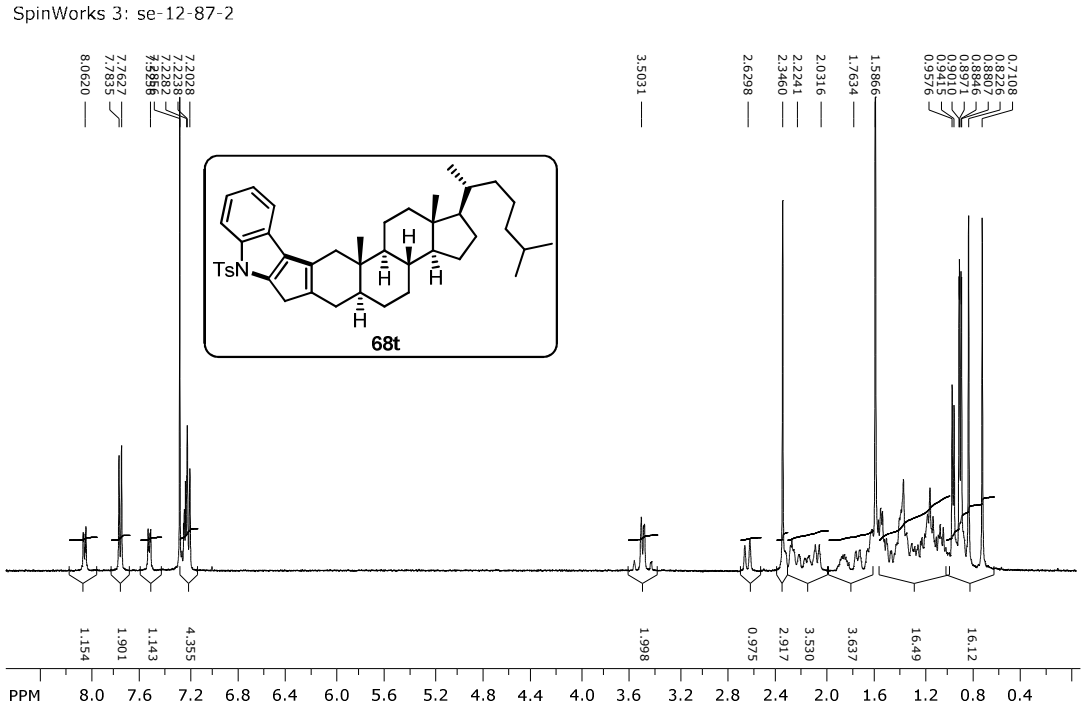


Figure 20: ^{1}H NMR spectrum of **68t**.

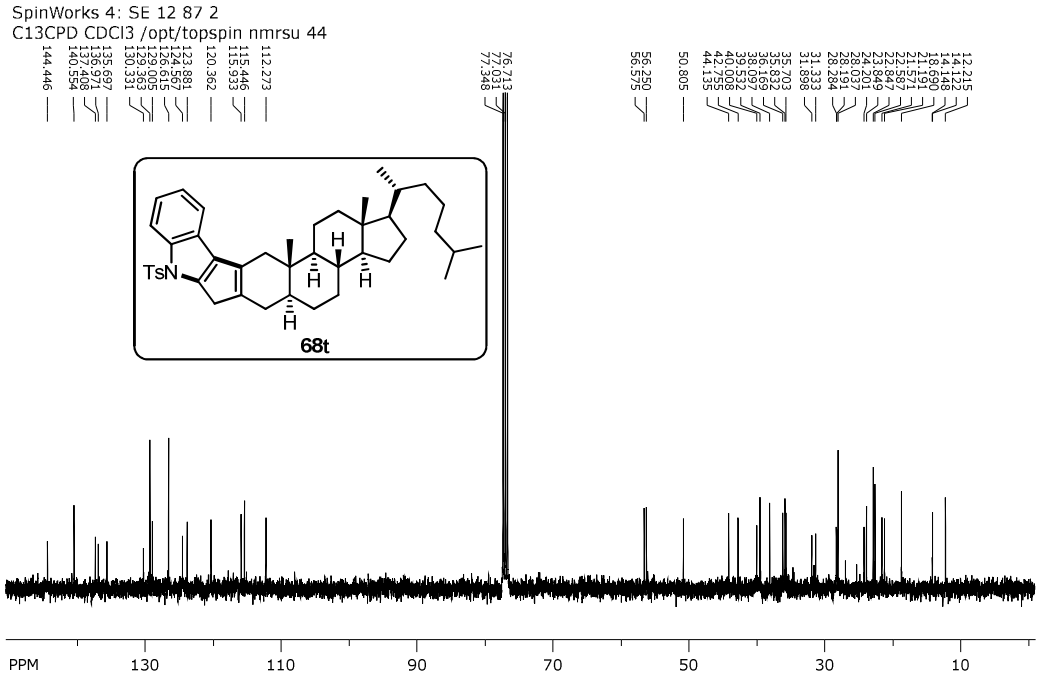
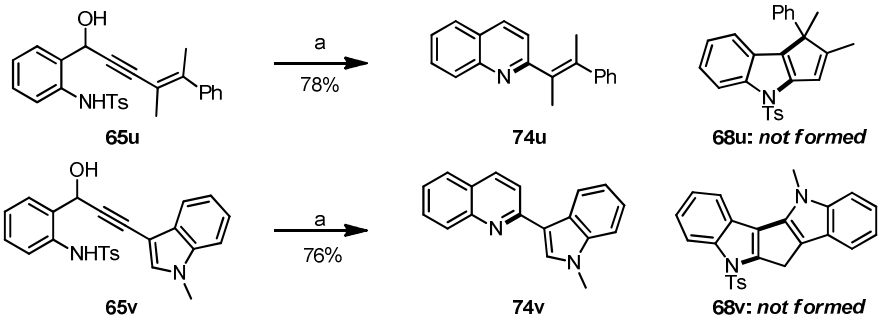
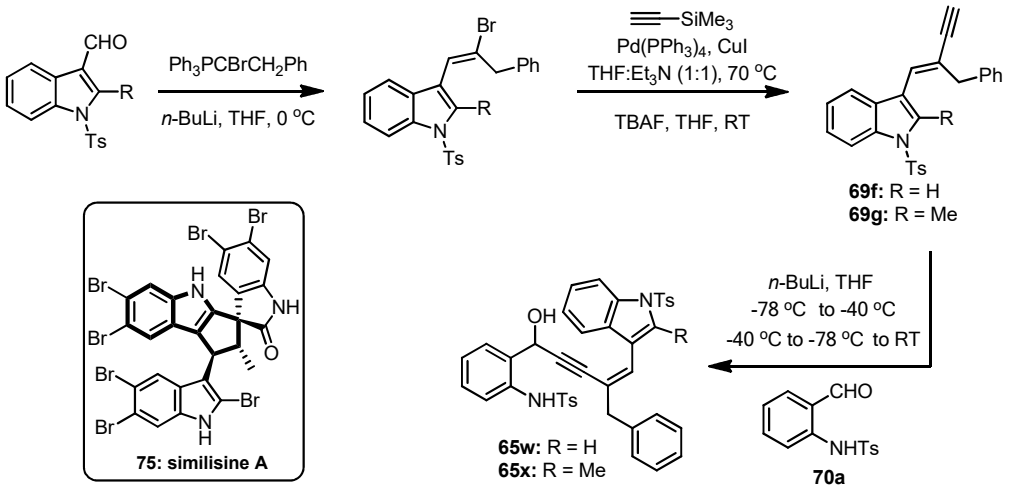


Figure 21: ^{13}C NMR spectrum of **68t**.



Scheme 61: Some of the unsuccessful systems under the optimized conditions. Reagents and conditions: a) i) AuCl (2 mol%), K_2CO_3 (2 mol%), DCE, 60 °C, 12 h. ii) TfOH (10 mol%), RT, 1 h.

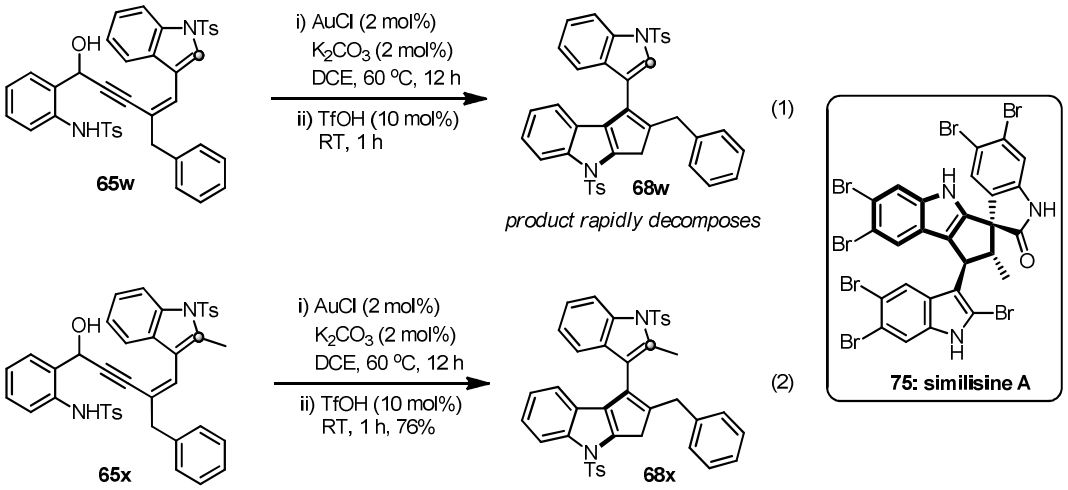
In order to further demonstrate the generality of this methodology, we considered an elaboration towards the synthesis of the bis-indole fragment present in the polybrominated spiro-trisindole natural product similisine A **75**.[87] Accordingly, the enynols **65w** and **65x** were prepared by following the literature procedure from **69f** and **69g**, Scheme 62.[88]



Scheme 62: Synthesis of enynols **65w** and **65x**.

Reaction of **65w** under the optimized conditions furnished the bis-indole derivative **68w** (Scheme 63, Eq. 1). However, it was found to be rapidly decomposing under ambient conditions. Though the reasons for its instability are unclear at this stage, assuming that the lack of substitution at the indole C-2 is the most likely reason, the enynol **65x** possessing a methyl group at C-2 was subjected to the optimized conditions, which successfully generated the expected bisindole **68x**. (Scheme 63, Eq. 2). The bis-indole **68x** represents the part structure of the brominated tris-indole natural product similisine A **75**. With the realization of several bioactive

bis-indole derivatives and the concept of 'pruning of biomolecules and natural products' gaining more relevance in various drug discovery programs,[89] bis-indole **68x** thus represents an important analogue of similisine A **75**, apart from being an advanced intermediate amenable for further synthetic manoeuvres.



Scheme 63: Elaboration to the part structure of similisine A.

4.4: Efforts towards the synthesis of 8-nor-polyveolinone

To demonstrate the synthetic utility of our method, we have undertaken the enantioselective synthesis of the core carbon skeleton of polyveoline family of natural products. The first member of this family, polyveoline **76** was isolated from the bark of *Greenwayodendron suaveolens* in 1978,[90] and the latest member 8α-polyveolinone **77** was isolated in 2014, Fig. 22.[2m] The structure and absolute configuration of indolosesquiterpene polyveoline **76** was elucidated by single crystal X-ray diffraction analysis. Natural products belonging to this family possess complex molecular architectures having driman[11,8-*b*]indole framework and found to exhibit a wide variety of biological activities, including significant antiparasitic properties.[91] Even though these terpenoids show impressive biological activity, surprisingly, no total synthesis of any member of polyveoline family has been reported thus far. However, in 1987, Mirand and co-workers reported synthesis of **78a**, an analogue of the natural product polyveoline **76**, by cyclization of a 3'-ω-epoxide-2-farnesyl indole **78b**, Scheme 64.[92]

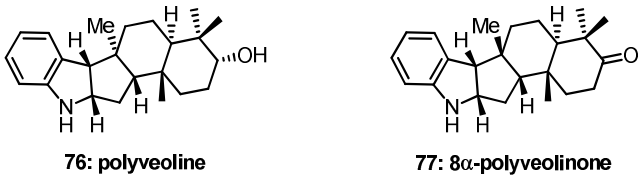
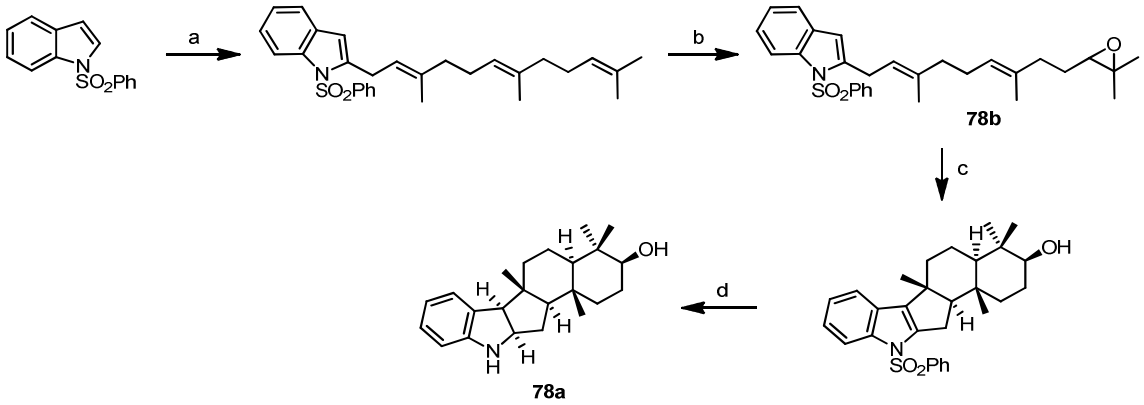
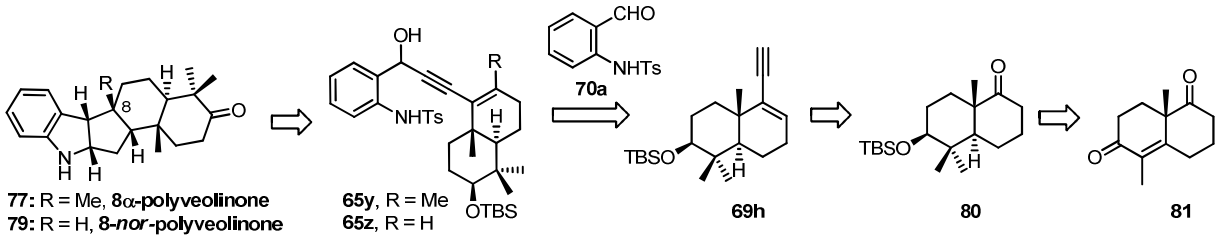


Figure 22: Natural products belonging to polyveoline family.



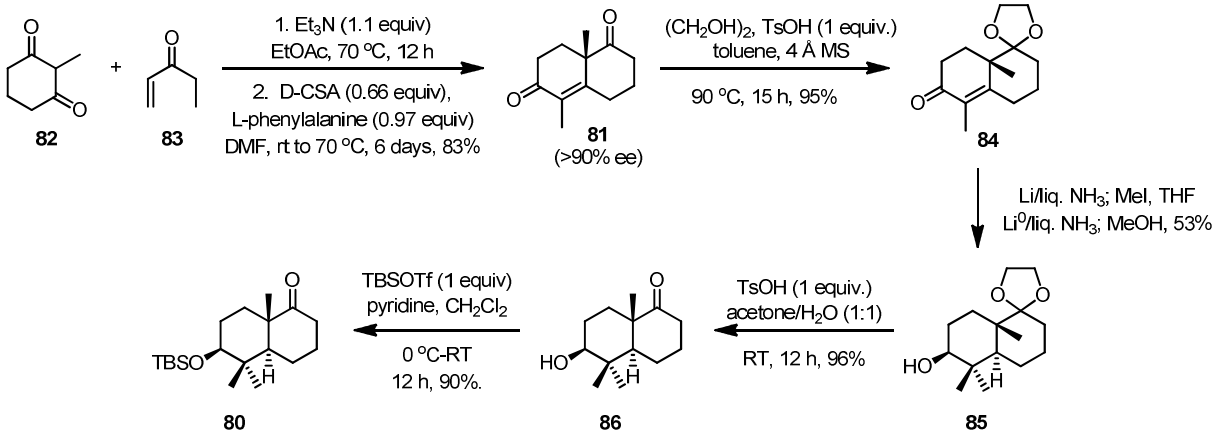
Scheme 64: Synthesis of polyveoline analogue **78a**. Reagents and conditions: (a) *n*-BuLi, *E*,*E*-farnesyl bromide, 70%. (b) NBS, K_2CO_3/MeOH, RT 1 h, 95%. (c) $BF_3.Et_2O$, 13%. (d) KOH/EtOH, $NaBH_3CN$/TFA, 65%.

Retrosynthetic analysis of 8α-polyveolinone **77** is depicted in Scheme 65. The enynol **65y** was identified as the suitable precursor for the synthesis of the complete carbon framework of **77**. However, as shown earlier (see Scheme 61), Au(I)-mediated reaction of enynols such as **65u** where the olefin is *tetrasubstituted*, generated only the respective quinolines. Thus we targeted the synthesis of the 8-*nor*-polyveolinone **79**. For this purpose, enynol **65z** serves as the suitable retrosynthetic precursor which can be readily obtained from the enyne **69h** and the amino benzaldehyde **70a**. The enyne **69h** can be obtained from the ketone **80** which in turn can be easily derived from the Wieland–Miescher ketone analogue **81**, Scheme 65.



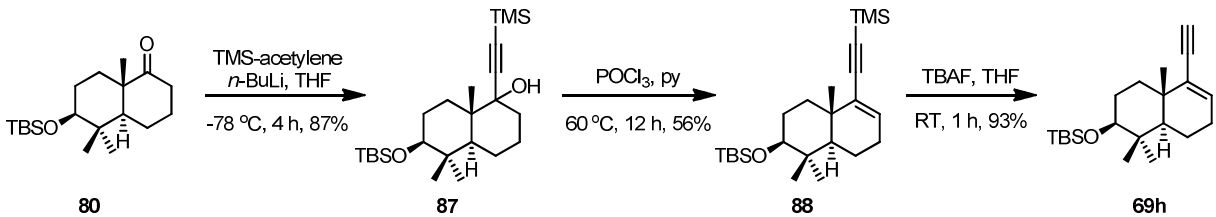
Scheme 65: Retrosynthesis of 8α-polyveolinone.

Accordingly, the synthetic efforts have been initiated from the commercially available 2-methyl cyclohexane-1,3-dione **82** and ethyl vinyl ketone **83**, Scheme 66. L-Phenylalanine-mediated asymmetric Robinson annulation of **82** provided the Weiland-Meischer-type ketone **81** in 83% yield, and in >90% ee.[93] Selective protection of the ketone over enone with ethylene glycol and *p*-toluenesulfonic acid (PTSA) in the presence of 4 A° molecular sieves provided the enone **84** in 95% yield. Lithium-liquid ammonia mediated reductive alkylation of **84** followed by *in situ* reduction of ketone with an additional amount of lithium metal produced the alcohol **85** as a single isomer in 53%. Structure of the secondary alcohol **85** was confirmed from its spectral data. The ketal group of **85** was then hydrolyzed with a catalytic amount of PTSA to the ketone **86** and the alcohol protected as the TBS ether **80** in 83% yield.[94]



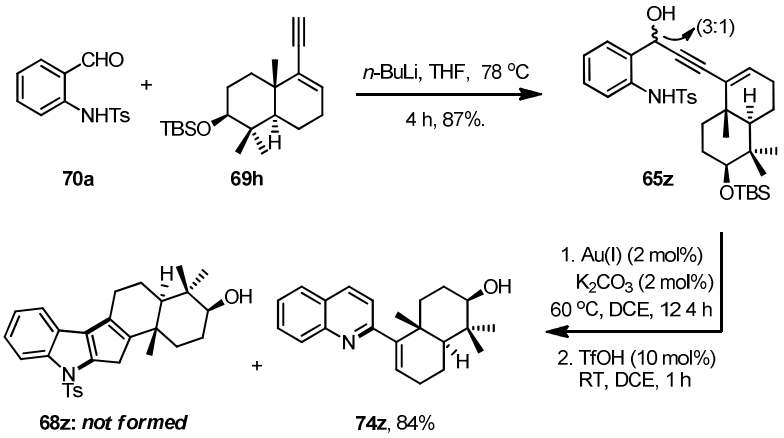
Scheme 66: Synthesis of the key intermediate **80**.

Treatment of **80** with TMS-acetylene furnished tertiary alcohol **87** and $POCl_3$-mediated dehydration of ynol **87** generated the enyne **88**, Scheme 67. Selective deprotection of TMS group in **88** was accomplished with TBAF in excellent yield. The structure of enyne **69h** was further confirmed from its spectral data.



Scheme 67: Efforts towards the synthesis of enyne **69h**.

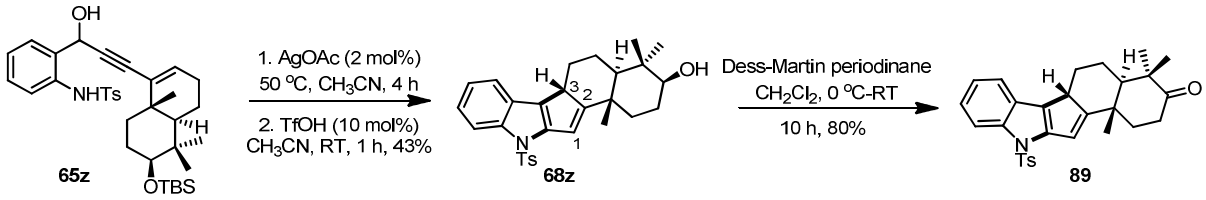
With the key intermediate **69h** in hand, we next attempted the synthesis of the desired enynol **65z**. Thus, addition of lithiated **69h** to the aldehyde **70a** generated the enynol **65z** in 87% yield as a 3:1 diastereomeric mixture, an inconsequential aspect in the succeeding steps, Scheme 68. With the formation of enynol **65z**, stage was set for employing the key step. Unfortunately, the Au(I)-catalyzed hydroamination followed by TfOH-catalyzed Nazarov-type cyclization of the enynol **65z**, exclusively generated quinoline **74z** in 84% yield.



Scheme 68: Efforts towards the synthesis of carbon framework of **77**.

After several attempts, we were gratified that the Ag(I)-catalyzed hydroamination[68] followed by TfOH-catalyzed Nazarov-type cyclization furnished the TBS-deprotected pentacyclic indole **68z** in 43% yield along with 55% of the respective quinoline **74z**, Scheme 69. The broad absorption band at 3324 cm^{-1} due to the secondary alcohol in the IR spectrum indicated the formation of **68z**. In the ^{1}H NMR spectrum, presence of a characteristic singlet at δ 6.62 due to the olefinic proton (C-1), a multiplet in δ 3.67-3.53 ppm due to allylic proton (C-3) and in the ^{13}C NMR spectrum presence of a quaternary carbon at δ 169.1 and a methine at 117.8 due to the olefinic carbon (C-2 and C-1) of the indole fused cyclopentene ring, a methine at the 35.0 due to the C-3 carbon confirmed the structure of the pentacyclic indole **68z**.The protonated molecular ion at 476.2259 (M+H) in the high resolution mass spectrum further established the structure of **68z**.

Dess-Martin oxidation of the alcohol **68z** resulted in the formation of ketone **89**. Indoles **68z** and **89** possess the complete carbon framework present in 8-*nor*-polyveolinone **80**, Scheme 69.



Scheme 69: Synthesis of carbon framework of **77**.

In conclusion, an expedient relay gold(I) and Brønsted acid catalyzed hydroamination/Nazarov cyclization of 1-(2aminophenyl)pent-4-en-2-ynols for the synthesis of various polyfunctionalized cyclopenta[*b*]indoles is developed. The synthetic utility of this method is demonstrated by the synthesis of a few unprecedented pentacyclic indoles and indole-steroidal hybrids. Further, the new methodology has been successfully applied to the enantioselective synthesis of core carbon structure of the polyveoline family of natural products.

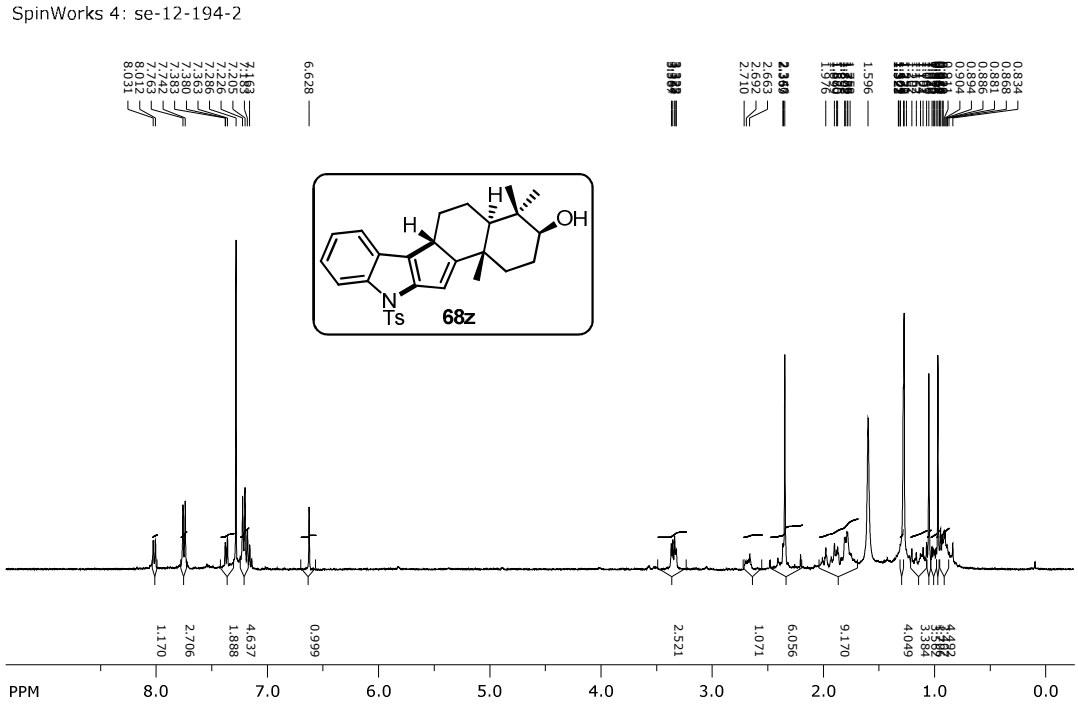


Figure 23: ^{1}H NMR spectrum of **68z**.

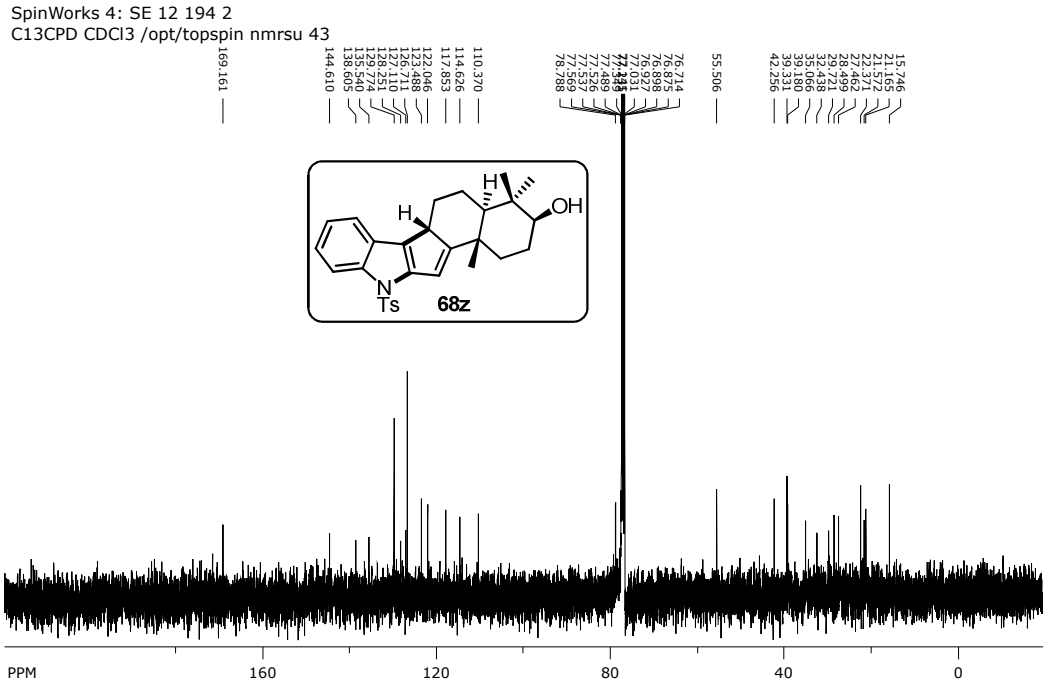


Figure 24: ^{13}C NMR spectrum of **68z**.

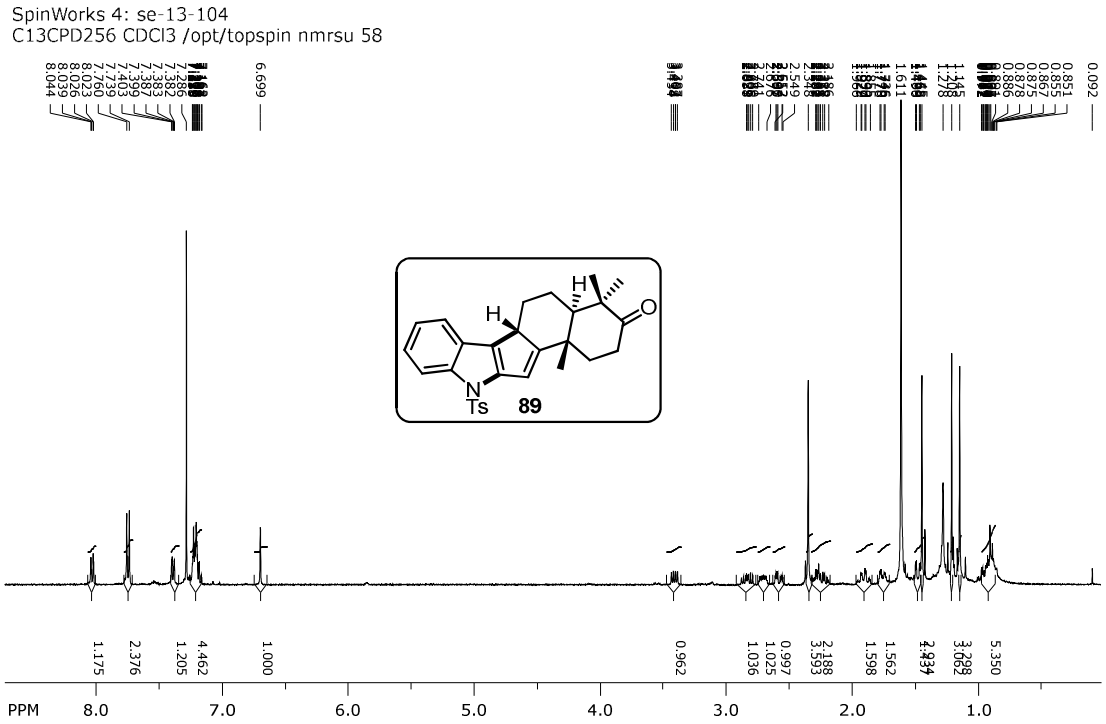


Figure 25: ^{1}H NMR spectrum of **89**.

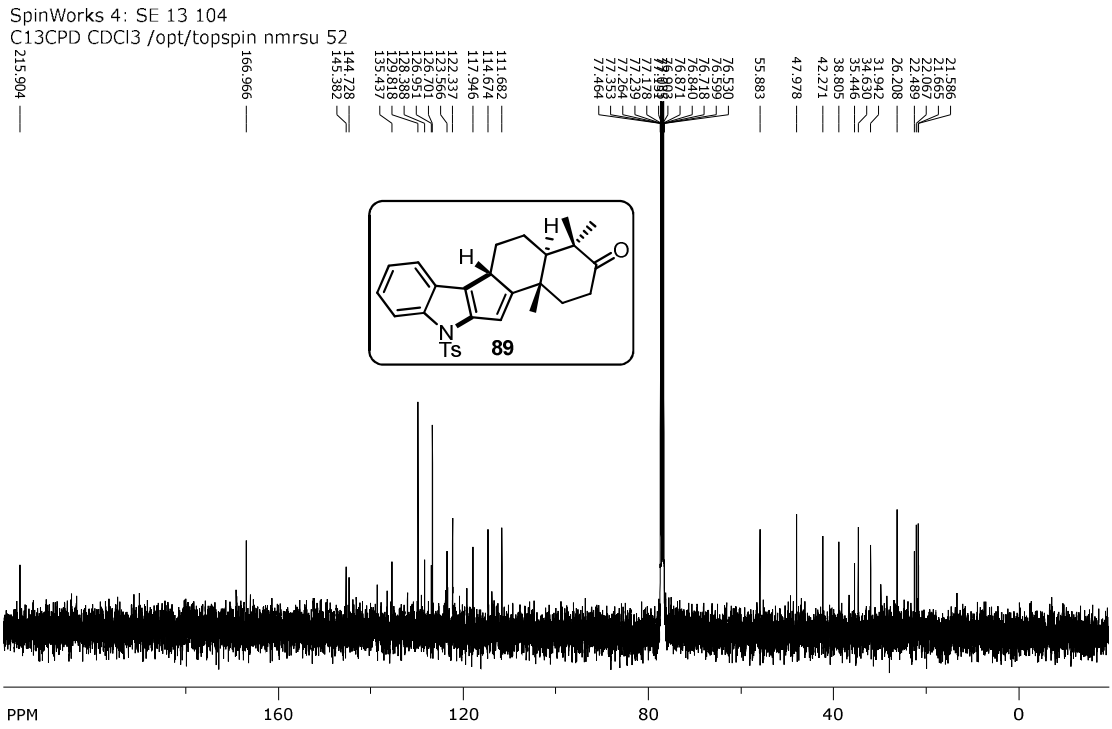


Figure 26: ^{13}C NMR spectrum of **89**.

Section 5

Synthesis of β-carbolines and other [c]-fused pyridines via one-pot triple orthogonal-relay catalysis

Having developed one-pot relay processes for the construction of complex indole derivatives, we planned to extend these strategies for the synthesis of other annulated indoles. Among them, tetrahydro-*β*-carbolines (THβCs) attracted our attention owing to their widespread occurrence in several natural products and medicinally interesting molecules, Fig. 27.[95] THβCs are well known for their neuroactive, antimicrobial, antioxidant, antiviral, anticarcinogenic and cytotoxic actions.[96] Not only the vast pharmacological properties but also the presence of THβCs under the physiological conditions in mammalian tissues and fluids especially fabricated them as indispensable biologically interesting molecules.

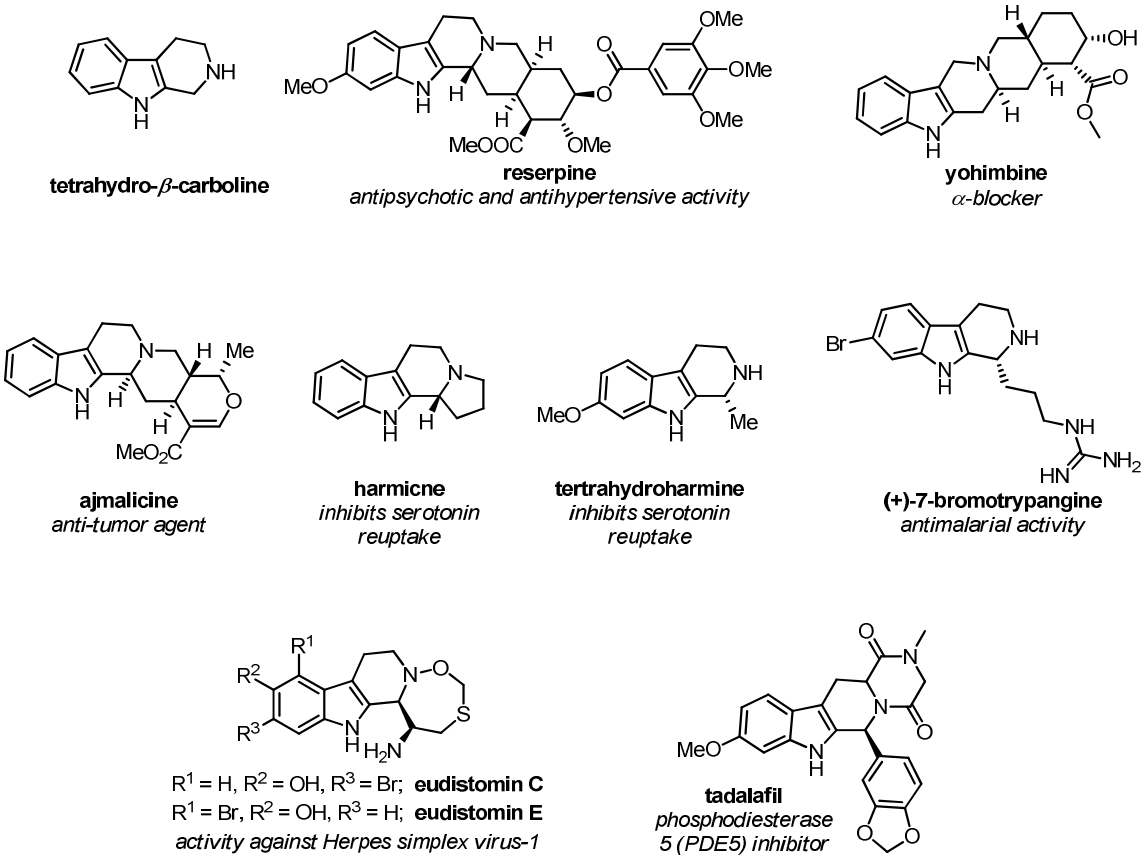
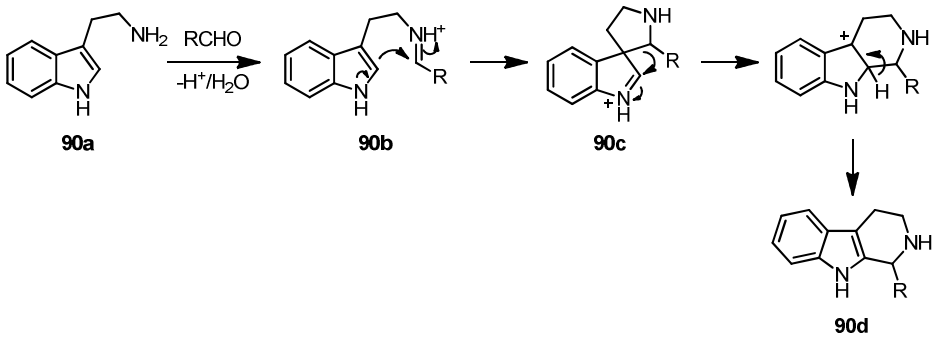


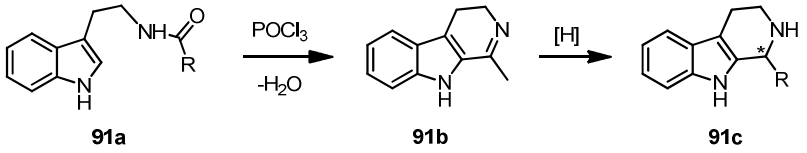
Figure 27: Representative examples of biologically active tetrahydro-*β*-carbolines.

Due to their substantial biological activity and natural occurrence, THβCs are important targets for chemical synthesis. The most common approach to this tricyclic core is by way of the Pictet-Spengler (P-S) reaction which is also considered as a biomimetic approach.[97] P-S reaction is basically a two component reaction, which involves the condensation of *β*-arylethylamine **90a** with an aldehyde to form an iminium ion **90b**. The attack on the iminium species **90b** from the 3-position of indole, forms a spiroindolenines **90c** which finally rearranges to yield the THβCs **90d**, Scheme 70. Over a century after its discovery, P-S reaction is evolved as one of the most powerful methods for the construction of THβCs. Numerous THβCs, with a wide range of important biological and pharmaceutical properties have been synthesized by this method. In addition, enantioselective variants of P-S reaction by the use of various chiral auxiliaries, transition metal catalysts, organocatalysts, and biocatalysts have been well reported.[98]



Scheme 70: Pictet-Spengler synthesis of THβCs.

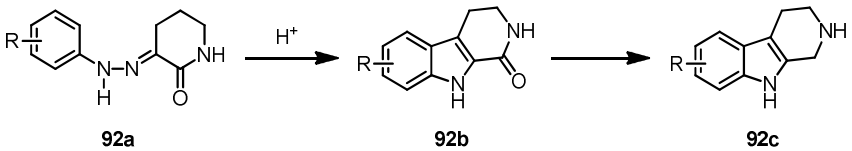
Bischler-Napieralski (B-N) cyclization is another commonly employed approach for the synthesis of THβCs.[99] B-N cyclization is an intramolecular electrophilic aromatic substitution reaction of β-arylethylamides or β-arylethylcarbamates **91a** and usually requires dehydrating reagents, such as PCl_5, $POCl_3$, $SOCl_2$ or $ZnCl_2$, to promote the loss of water, Scheme 71. The product of the B-N reaction is a DHβC **91b** which can then be further reduced to form the corresponding THβC **91c**, Scheme 71. Asymmetric transfer hydrogenation (ATH) of imines using chiral catalysts offers a powerful method to access a chiral THβC skeleton.



Scheme 71: Bischler-Napieralski cyclization for the synthesis of THβCs.

As described above, Pictet–Spengler (P-S) reaction and Bischler–Napieralski (B-N) reaction-based approaches are the most widely employed methods. Only a few, alternative synthetic methodologies independent of P-S or B-N reactions have emerged for procuring THβCs, some of which are outlined below.

In 1956, Abramovitch and Shapiro[100] reported orthophosphoric acid mediated Fischer indole cyclization of **92a** to provide the ketocarbolines **92b**, and which can be further reduced to form the corresponding THβCs **92c**, Scheme 72.

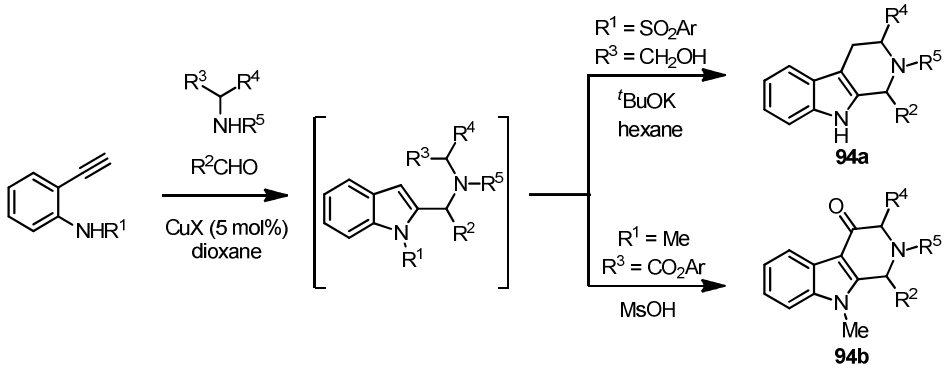


Scheme 72: Fischer indole based synthesis of THβCs.

In 2003, Soderberg *et al.*[101] developed a Pd(0)-catalyzed N-heteroannulation of 2-nitro styrenes **93a** for the generation of THβC derivatives **93b**. However, the substrate scope was limited as starting material synthesis required many tedious synthetic transformations, Scheme 73.

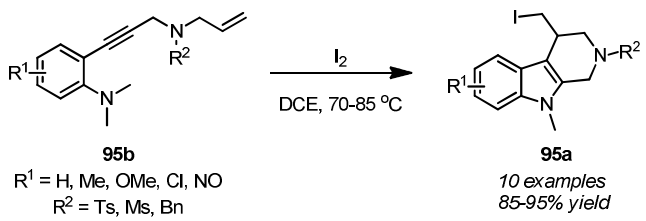
Scheme 73: Palladium catalyzed synthesis of THβCs.

In 2009, Ohno *et al.*[102] reported a direct synthetic route to THβC derivatives **94a** and **94b** by copper-catalyzed three-component indole formation followed by successive cyclization at the 3-position of indole, Scheme 74.



Scheme 74: Synthesis of THβC derivatives.

In 2013, Wang *et al.*[103] reported a one-pot synthesis of substituted THβCs **95a** by an iodine-promoted cascade electrophilic iodocyclization of 2-(3-(allylamino)prop-1-ynyl)anilines **95b**, Scheme 75. This strategy includes sequential electrophilic iodocyclization reactions on the alkyne and alkene, successively in one pot.



Scheme 75: Wang synthesis of THβCs.

β-Carbolines, represent yet another important class of annulated heteroarenes. *β*-Carbolines are significant scaffolds prevalent in several bioactive natural products and drug-like molecules. *β*-Carboline derivatives are known to exhibit diverse biological properties such as anti-HIV, antitumor, antimalarial, and antibacterial activities, to mention a few. The biological significance of these molecules inspired us to investigate this method further for the development of a new approach for the synthesis of *β*-carboline derivatives. *β*-Carbolines (pyrido [3,4-*b*] indoles) are important scaffolds prevalent in several bioactive natural products and drug-like molecules, Fig. 28. They exhibit a broad range of biological and pharmacological activities. These activities go notably from enzyme inhibition to suppression of the activity of the topoisomerase.[104] Some *β*-carbolines can bind to benzodiazepine (BZRs)[105] or 5-HT2 serotonin receptors.[106] Some of them are the main physiologically active components of plants used for a long time by african or asian tribes for their therapeutic effects. Many *β*-carbolines have effectively shown a wide range of pharmacological properties such as antidepressive, anxiolytic or anticonvulsant effects. Some of them were also shown to possess antitumor properties or, more recently, anti-HIV activity.[107] However, their use is limited due to inconvenient side effects such as hallucinogenic effects. Furthermore, some carbolines can interact with DNA, conferring them mutagenic or carcinogenic properties.[108]

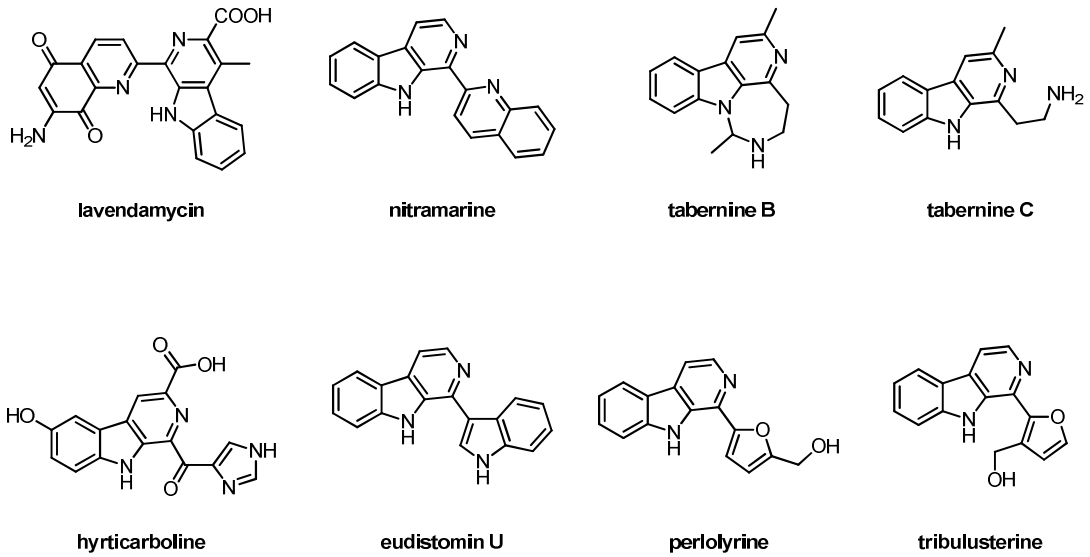
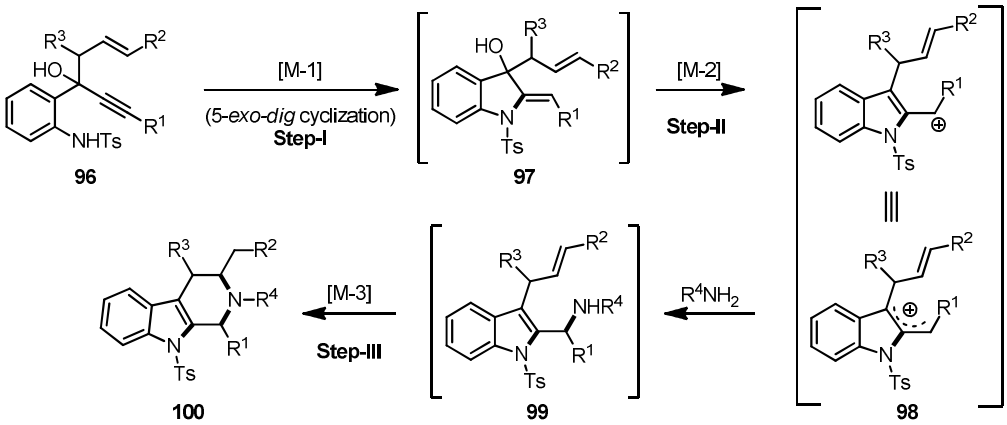


Figure 28: A few representative bioactive *β*-carboline natural products.

The Pictet-Spengler and the Bischler-Napieralski reactions are the two classical methods for the synthesis of *β*-carbolines. However, these two well-known methods do not lead directly to the fully aromatic carbolines, but respectively to their tetrahydro- or dihydro derivatives. Moreover, dehydrogenation of these compounds to *β*-carboline is oftentimes hard to perform. Furthermore, these methodologies start from tryptophan derivatives which are not always easy to prepare when a multi-substituted *β*-carboline is desired. Recently, alternative methods leading directly to fully aromatic *β*-carbolines have been developed.[109]

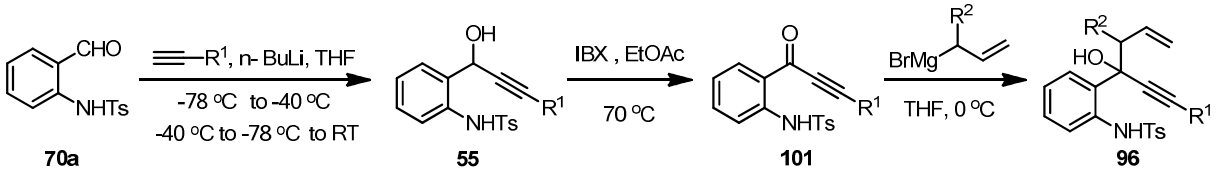
5.1: Results and discussion

Our experience in the development of relay catalytic processes and lack of general one-pot approaches independent of P-S and B-N based reactions for accessing THβCs derivatives, prompted us to develop an efficient one-pot approach for the synthesis of THβCs. In line with this, we envisioned that an intramolecular hydroamination of alkynols **96** promoted by an appropriate metal catalyst M-1 could provide the indolines **97**, Scheme 76. However, obtaining a 5-*exo-dig* cyclized product from among the other competing cyclization pathways could be a challenge.[110] On the other hand, a cascade acid-catalyzed 1,3-allylic alcohol isomerization (1,3-AAI) and dehydrative nucleophilic amination of **97** was considered for the synthesis of ε,ω-unsaturated amine **99**. Ideally, the acid catalyst M-2 should not drive the *tert*-alcohols **97** towards unintended dehydration. It was further hypothesized that M-3 mediated intramolecular hydroamination of appropriately positioned ε,ω-unsaturated olefin in **99** could afford the THβCs **100**.[111]



Scheme 76: Hypothesis for the one-pot synthesis of THβCs.

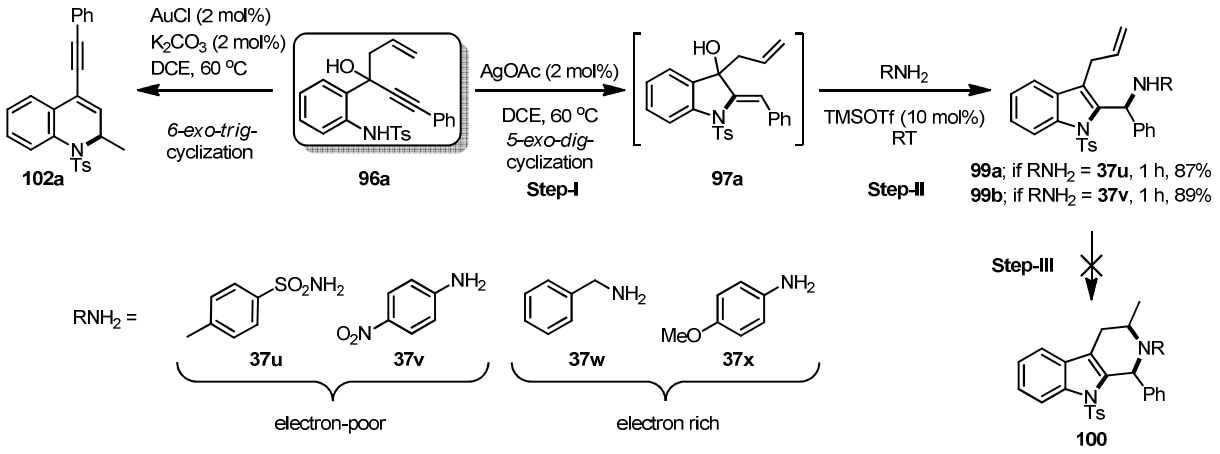
The 3-(2-aminophenyl)-5-hexenyn-3-ols **96** can be easily procured from the amino benzaldehydes **70a** by following three straightforward steps, Scheme 77.[112] *n*-Butyllithium mediated addition of alkynes to amino benzaldehydes **70a** affords ynols **55** which upon IBX oxidation generate the ynones **101**. Further, addition of allyl Grignard reagents to ynones **101** furnish 3-(2-aminophenyl)hex-5-en-1-yn-3-ols **96**. Since modular access to 3-(2-aminophenyl)-5-hexenyn-3-ols **96** can be readily achieved, this method thus can serve as a potential alternative to the existing approaches describing the synthesis of *β*-carboline derivatives.



70a **55** **101** **96**

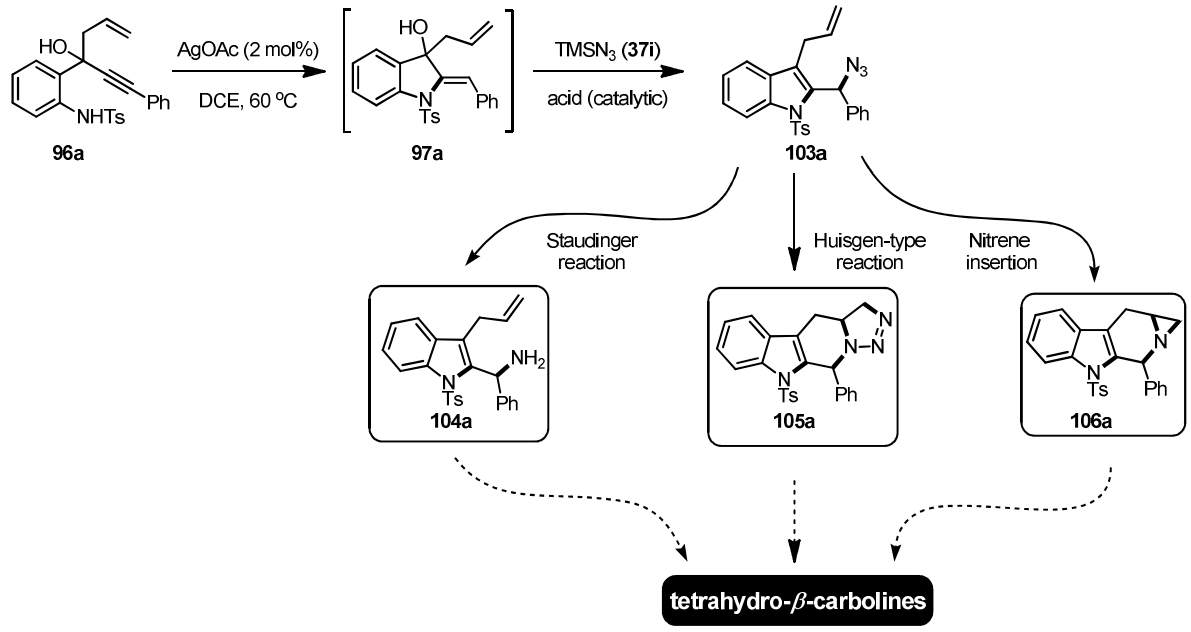
Scheme 77: Synthesis of 3-(2-aminophenyl)-5-hexenyn-3-ols **96**.

In order to validate the mechanistic hypothesis proposed in Scheme 76, enynol **96a** was chosen as the model substrate. We initiated our efforts towards identifying an efficient catalytic system. Initially, a step-wise protocol was followed with an intention to combine appropriately to a one-pot process for the synthesis of THβCs **100**, Scheme 78. At the outset, Au(I)-catalyzed intramolecular hydroamination condition reported earlier by our group was evaluated for step-I.[78] However, only the 6-*exo-trig* product **102a** was isolated, Scheme 78. Among few other variations attempted, AgOAc successfully produced the desired 5-*exo-dig* product **97a** in excellent chemo- and regioselectivity. During the screening of various acids evaluated for the cascade 1,3-AAI/nucleophilic amination (Step-II), TMSOTf was found to be optimal. An interesting dependence on the electronic nature of the amines was observed; electron-poor amines **37u** and **37v** were found to be very efficient and furnished the respective aminated products in good yields **99a** and **99b**.[113] On the other hand, electron-rich amines **37w** and **37x** led to the recovery of the starting material **97a**. In order to achieve the final intramolecular hydroamination (step-III), various lierature procedure were followed, but unfortunately all the attempts were unsuccessful, possibly due to the electron poor nature of amine. Interestingly, (most of the) olefin hydroaminations were achieved with electron-rich amines.



Scheme 78: Efforts towards the synthesis of THβCs.

In order to achieve the one-pot synthesis of THβCs; we intended to employ azide as an amine equivalent. Azides are particularly attractive due to their interesting reactivity patterns with alkenes. We hypothesized that a phosphine mediated reduction of azide **103a** to the free amino group **104a** followed by intramolecular hydroamination or a thermal or metal-catalyzed intramolecular azide-alkene [3+2]-cycloaddition **105a**, or a metal-catalyzed nitrene insertion **106a** into the appropriately positioned ε,ω-unsaturated olefin in **103a**, and subsequent bond reorganizations could afford THβCs,[114] Scheme 79.

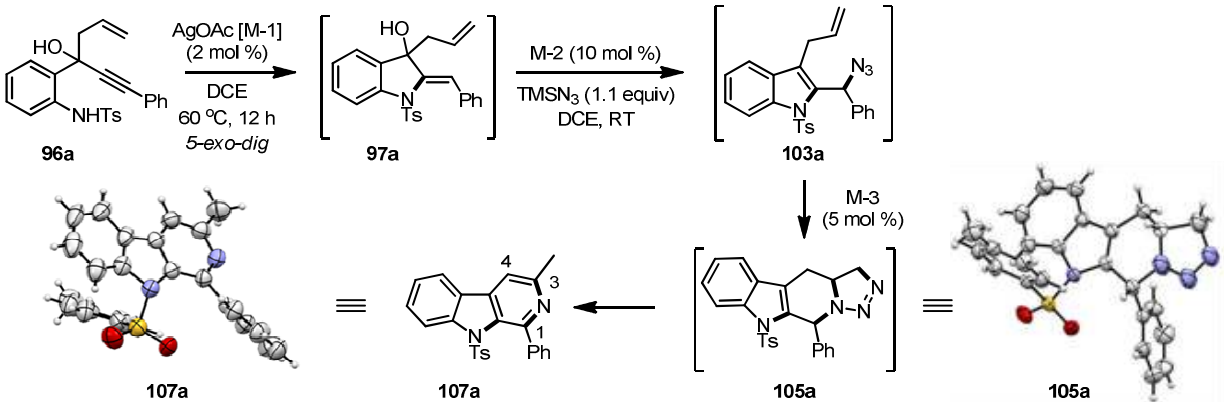


Scheme 79: Azide-mediated pathway for the synthesis of THβCs.

With the renewed approach, we initiated our efforts again towards identifying an efficient catalytic system for the synthesis of THβCs by using azide as an amine equivalent. During the screening of different Lewis acids for the cascade 1,3-AAI/nucleophilic azidation, to our surprise, Lewis acids such as $BiCl_3$ directly delivered the *β*-carboline **107a**, plausibly *via* the intermediacy of the azide **103a** and the triazole **105a**, (Table 19, entry 1). The structure of **105a** and **107a** were confirmed by single crystal X-ray diffraction analysis. In the ^{1}H NMR spectrum, presence of a characteristic singlet at δ 7.39 (1H) due to the C-4 proton, a singlet at δ 2.74 (3H) due to the pyridyl methyl and a singlet at 2.20 ppm due to tosyl methyl indicated the formation of **107a**. In ^{13}C NMR spectrum, presence of two methyl signals at δ 24.6 and 21.4 ppm due to C-2 methyl and tosyl methyl established the structure of *β*-carboline **107a**. The presence of the protonated molecular ion m/z 413.1311 in high resolution mass spectrum further confirmed the formation of **107a**.

After having an intial success with $BiCl_3$ (Table 19, entry 1), further attempts were made to improve the yield with different Lewis acids. However, our efforts in this direction were discouraging (Table 19, entries 2-6). To enhance the efficiency of the reaction, optimization studies were carried out with Cu and Pd-based catalysts.[115] Though the *β*-carboline **107a** was isolated in moderate yields in the presence of Cu catalysts (Table 19, entries 7 and 8), our intentions to improve the yield with Pd catalysts were met with success (Table 19, entries 9-18). Worth noting is the temperature dependant yield improvement, especially with $Pd(OAc)_2$ as the catalyst (Table 19, entries 9-11). Success with the palladium catalysis in step-III led us to develop an example of triple relay catalysis, which integrates silver, bismuth and palladium catalysts towards the synthesis of *β*-carbolines through a one-pot cascade involving an intramolecular hydroamination, Friedel-Crafts-type dehydrative azidation, and an unprecedented pyridine annulation of the ε,ω-unsaturated azides. Further, to the best of our knowledge, reactions promoted by *three* orthogonal relay metal catalytic systems are not reported thus far.

Table 19: Optimization of reaction parameters.



Entry	M-2, time	M-3	Conditions	Yield of 107a [%]
1	$BiCl_3$, 4 h	-	-	62
2	$Bi(OTf)_3$, 4 h	-	-	23
3	TMSOTf, 12 h	-	-	37
4	$TiCl_4$, 12 h	-	-	21
5	$Yb(OTf)_3$, 12 h	-	-	54
6	$Cu(OTf)_2$, 48 h	-	-	23
7	$BiCl_3$, 1 h	$CuCl_2$	24 h, 80 °C	23
8	$BiCl_3$, 1 h	$Cu(OTf)_2$	24 h, 80 °C	47
9	$BiCl_3$, 1 h	$Pd(OAc)_2$	RT, 48 h	68
10	$BiCl_3$, 1 h	$Pd(OAc)_2$	60 °C, 48 h	70
11	$BiCl_3$, 1 h	$Pd(OAc)_2$	80 °C, 4 h	78
12	$BiCl_3$, 1 h	$Pd(dppf)Cl_2$	80 °C, 4 h	56
13	$BiCl_3$, 1 h	$Pd(PPh_3)_4$	80 °C, 24 h	67
14	$BiCl_3$, 1 h	$Pd_2(dba)_3$	80 °C, 6 h	73
15	$FeCl_3$, 1 h	$Pd(OAc)_2$	80 °C, 4 h	74
16	$Sc(OTf)_3$, 1 h	$Pd(OAc)_2$	80 °C, 16 h	63
17[a]	$BiCl_3$, 1 h	$Pd(OAc)_2$	80 °C, 4 h	80
18[b]	**$BiCl_3$, 1 h**	**$Pd(OAc)_2$**	**80 °C, 4 h**	**82**

[a]5 mol % $BiCl_3$ was employed. [b]In the presence of 5 mol % $BiCl_3$ and at 60 °C.

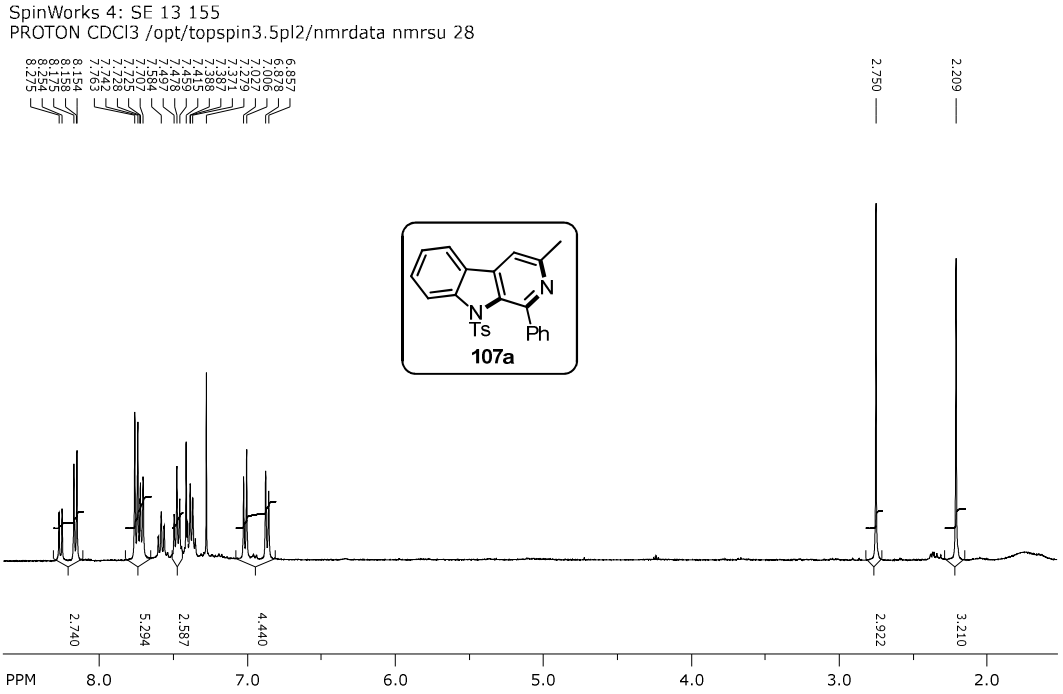


Figure 29: ^{1}H NMR spectrum of **107a**.

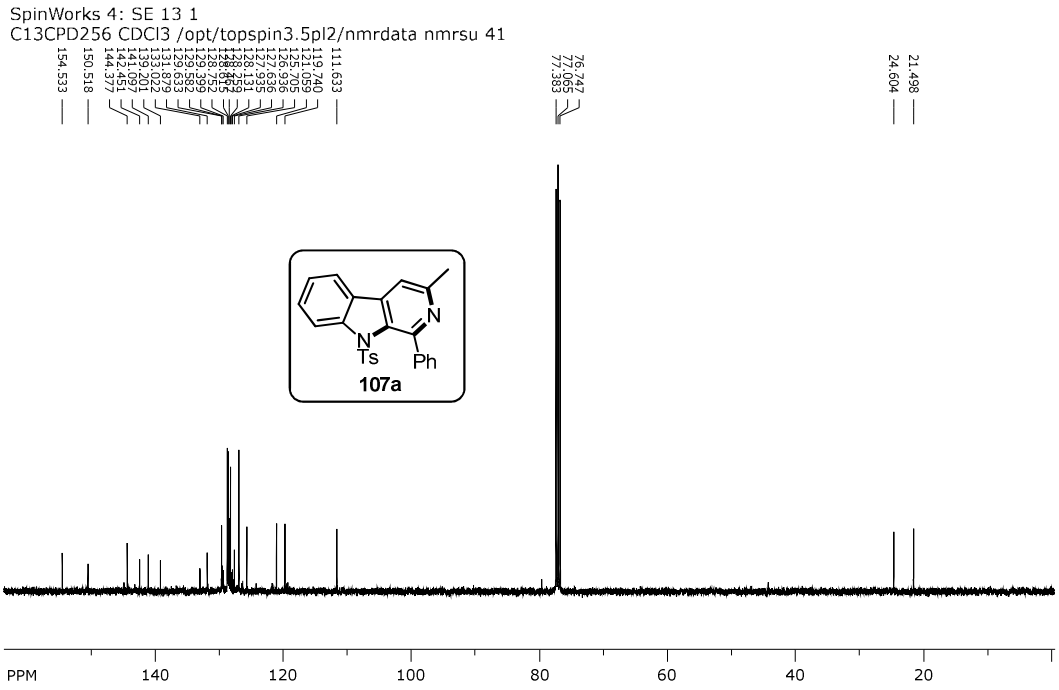
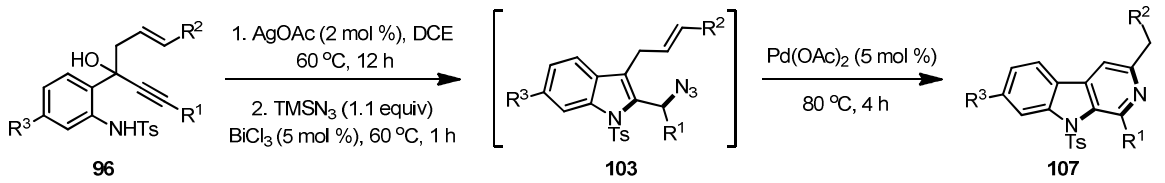
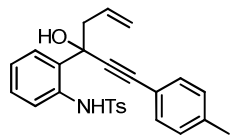
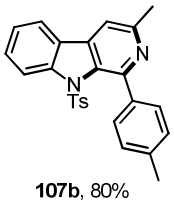
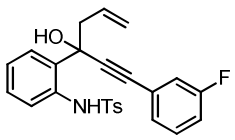
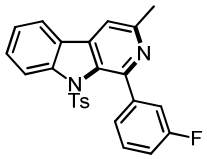
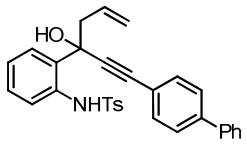
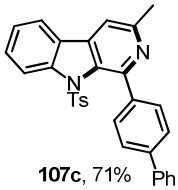
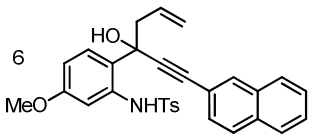
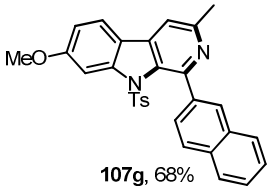
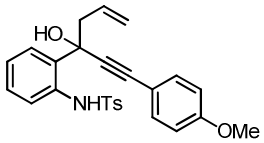
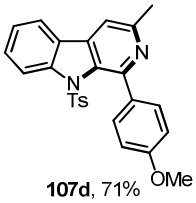
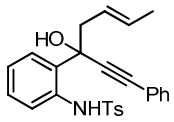
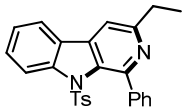
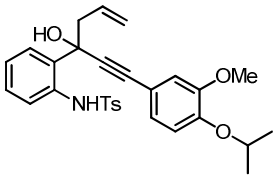
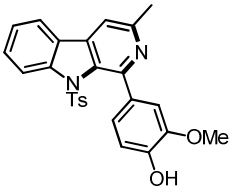
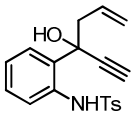
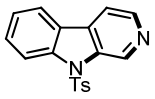


Figure 30: ^{13}C NMR spectrum of compound **107a**.

Table 20: Substrate scope.

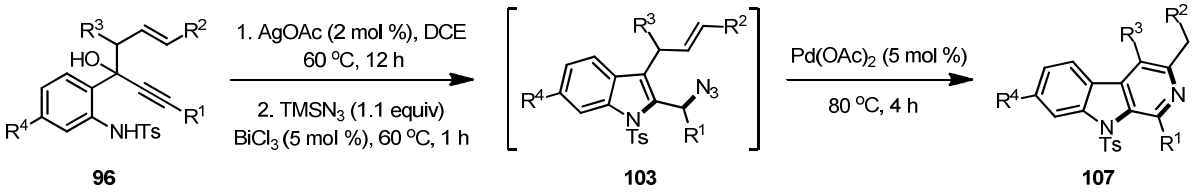


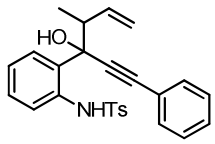
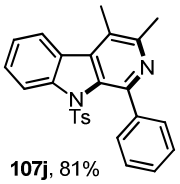
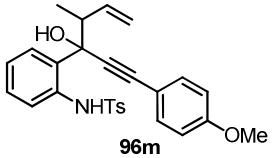
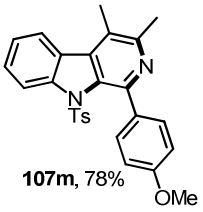
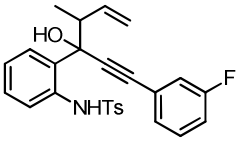
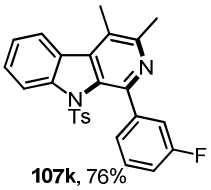
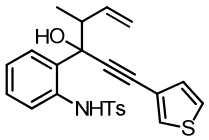
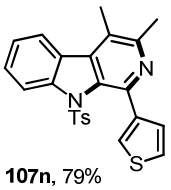
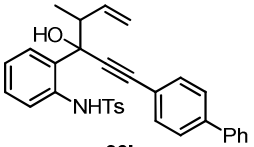
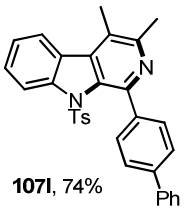
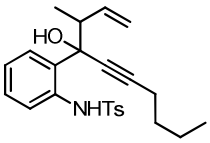
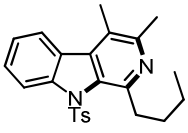
Entry	Substrate	Product	Entry	Substrate	Product
1	 **96b**	 **107b**, 80%	5	 **96f**	 **107f**, 78%
2	 **96c**	 **107c**, 71%	6	 **96g**	 **107g**, 68%
3	 **96d**	 **107d**, 71%	7	 **96h**	 **107h**, 0%
4	 **96e**	 **107e**, 65%	8	 **96i**	 **107i**, 0%

With the optimized conditions in hand, we next turned our attention towards evaluating the substrate scope, Table 20. Various electronically diverse 3-(2-aminophenyl)-5-hexenyn-3-ols **96b-96i** were subjected under the optimized conditions. Alkynols having a mild electron donating group such as tolyl and biphenyl on the acetylenic carbon centre, furnished the respective 1,3-disubstituted-*β*-carbolines **107b** and **107c** in good yields, (Table 20, entries 1 and 2). Triple relay catalytic system was found to be efficient even with the alkynols **96d** and **96e** bearing strong electron donating groups such as –OMe and –O*i*Pr, (Table 20, entries 3 and 4). Treatment of the alkynol **96e**, under the optimized conditions generated **107e**, with the deprotection of –*i*Pr group. The fluorinated 1,3-disubstituted-*β*-carboline **107f** can also be easily

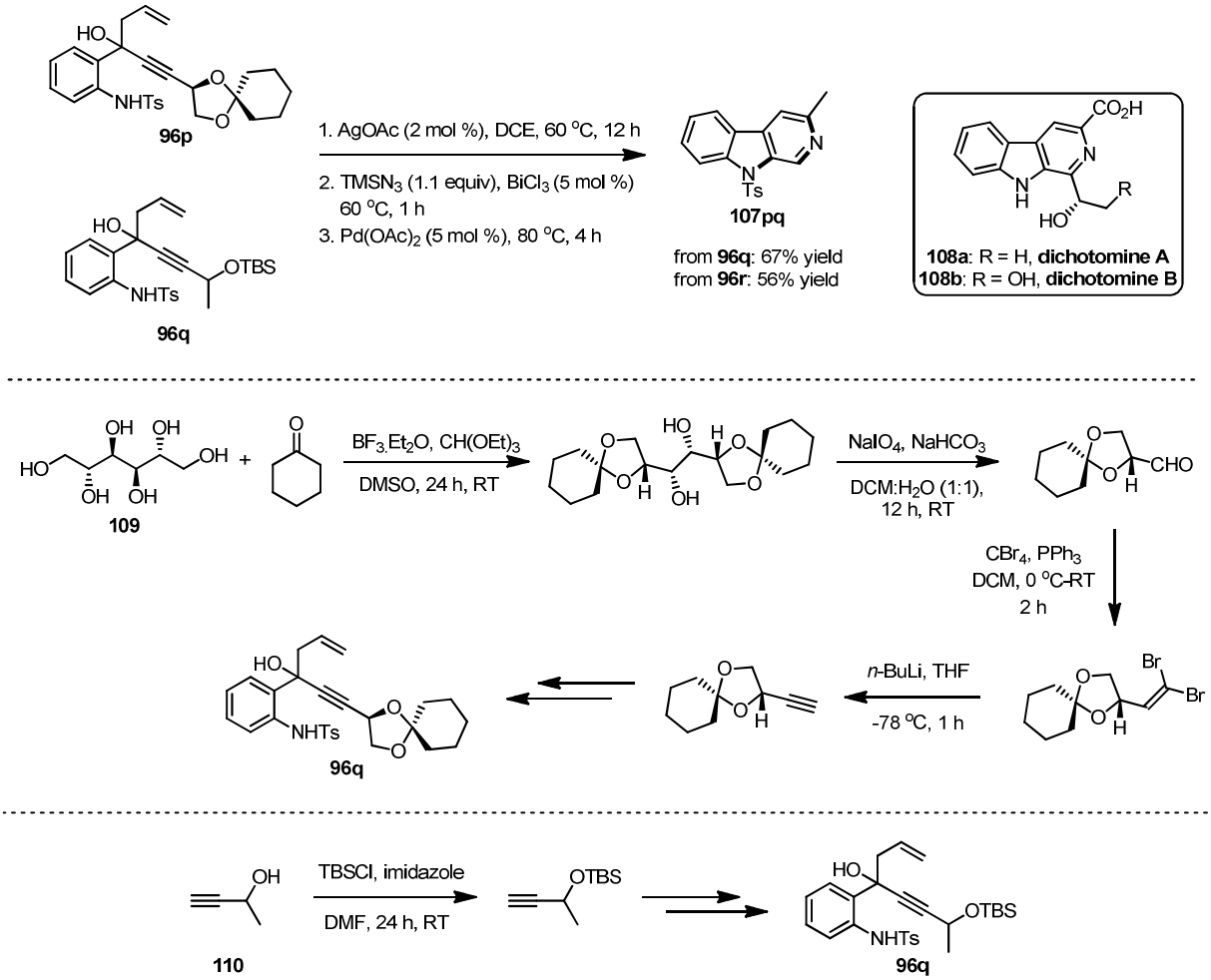
accessed by this method, (Table 20, entry 5). Fluorinated compounds are known to possess unique properties which make them valuable candidates for drug discovery. The alkynol **96g** under the optimized conditions furnished the highly conjugated 1,3-disubstituted-*β*-carboline **107g**, which can potentially exhibit interesting photophysical properties (Table 20, entry 6). A slim substitution-dependence was realized while studying the substrate scope. For example, the enynols **96h** and **96i** failed to proceed beyond the respective azides (**103h** and **103i**) and thus could not yield the respective carbolines **107h** and **107i**, despite our repeated attempts (Table 20, entries 7 and 8). Apparent decomposition of the azide under the reaction conditions could be possibly due to its inability to undergo the azide-alkene [3+2]-cycloaddition, while in the case of **107i**, most likely because of the instability or insufficient activation of the 1°-azide functionality.

Table 21: Substrate scope.



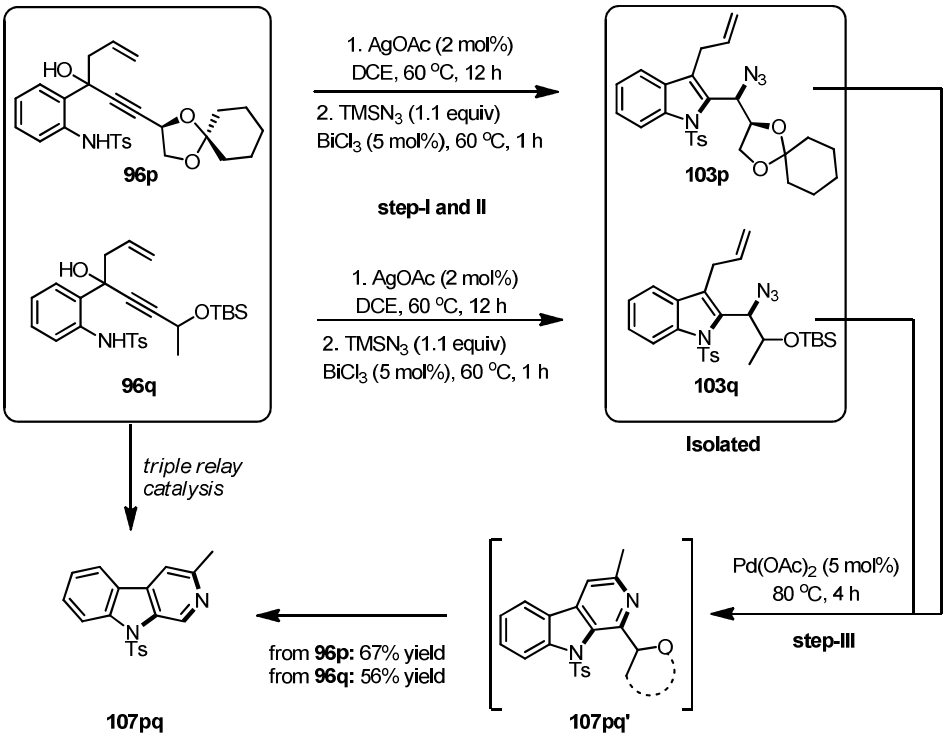
Entry	Substrate	Product	Entry	Substrate	Product
1	 **96j**	 **107j**, 81%	4	 **96m**	 **107m**, 78%
2	 **96k**	 **107k**, 76%	5	 **96n**	 **107n**, 79%
3	 **96l**	 **107l**, 74%	6	 **96o**	 **107o**, 67%

Various 1,3,4-trisubstituted-*β*-carbolines, were also assembled in a mere one-pot process in good to excellent yields. Table 21 outlines the scope of the electronically different aromatic substituents across the alkyne (R^1), such as phenyl, tolyl, *p*-biphenyl, *m*-flurobenzene and *p*-methoxybenzene for the synthesis of 1,3,4-trisubstituted-*β*-carbolines, (Table 21, entries 1-4). Alkynol **96n** having heteroaromatic group (such as thienyl) on the acetylenic carbon centre was well tolerated (Table 21, entry 5). Interestingly, reaction of **96o**, having a pendent alkyl group on the actylenic carbon centre, under the optimized conditions furnished the respective 1,3,4-trisubstituted-*β*-carboline **107o**, though in moderate yield, but enhanced the scope of this method (Table 21, entry 6).



Scheme 80: Unusual formation of 3-substituted-*β*-carboline and synthesis of enynes.

With the intention to attempt the total synthesis of *β*-carboline natural products dichotomine A **108a** and dichotomine B **108b**, the enynols **96p** and **96q** were designed, Scheme 80. Enynol **96p** was prepared by following a multistep synthetic sequences starting from commercially available and inexpensive sugar D-mannitol **109**.[116] Enynol **96q**, on the other hand, was prepared from the readily available ynol **110** as in Scheme 80. However, surprisingly, the reaction of **96p** or **96q** under the optimized conditions generated only the *β*-carboline **107pq**.

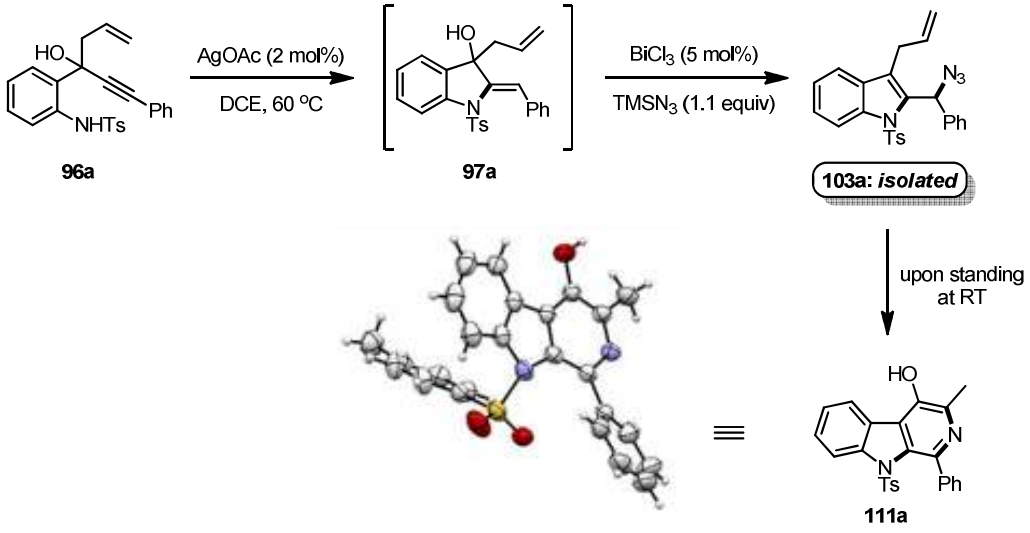


Scheme 81: Experiment undertaken to get insights about the conversion of **96p** and **96q** to **107pq**.

We were intrigued by the unusual formation of **107pq** from **96p** and **96q**. This observation leads to the hypothesize that the substrates possessing propargylic ethers follow a domino sequence involving benzylic ether deprotection/ benzylic alcohol oxidation/ retro-Claisen condensation of the intermediate **107pq'**(Scheme 81). TLC follow-up of the reaction provided sufficient indication that the domino sequence leading to the formation of **107pq** was occurring most likely during the third step [$Pd(OAc)_2$ (5 mol%), 80 °C]. To support this observation experimentally, azides **103p** and **103q** were isolated and subjected to the optimized conditions of step-III and obtained **107pq** as the only product. This proves that Pd(II)-mediated conditions alone are responsible for the domino sequence of the azides (**103p** and **103q**) to the *β*-

carboline **107pq**. In addition to the Pd(II) catalyst, temperature also must be playing a crucial role during this transformation. Complete mechanistic details of this process are not understood yet.

During our efforts to isolate the azide **103a** (Scheme 82), we made a remarkable observation. The isolated sample of the azide **103a** was found to be unstable under ambient conditions and slowly transformed to a crystalline material, which was characterized to be the 1,3-disubstituted-4-hydroxy-*β*-carboline **111a**.[117] In the ^{1}H NMR spectrum, presence of three doublet at δ 8.22 (1H), 8.08 (1H), 7.93 (2H), two triplets at 7.54 (1H), 7.14 (2H), two multiplets at 7.46-7.40 (1H), 7.39-7.31 (2H), and two doublet at 7.00 (2H), 6.86 (2H) due to the 16 aromatic protons, singlet at 2.59 due to methyl attached to the pyridine ring, another singlet at 2.27 ppm due to the tosyl methyl indicated the structure of 4-hydroxy-*β*-carboline **111a**. In addition, presence of 19 peaks between 145.1 and 118.9 due to aromatic carbons, and two characteristic methyl signals at 21.4 and 18.1 ppm in the ^{13}C NMR spectrum confirmed the structure **111a**. The presence of protonated molecular ion at *m/z* 429.1267 in high resolution mass spectrum, further established the structure of 4-hydroxy-*β*-carboline **111a**. The structure of **111a** was further confirmed by the single crystal x-ray diffraction analysis.



Scheme 82: Serendipitous formation of the 4-hydroxy-*β*-carboline.

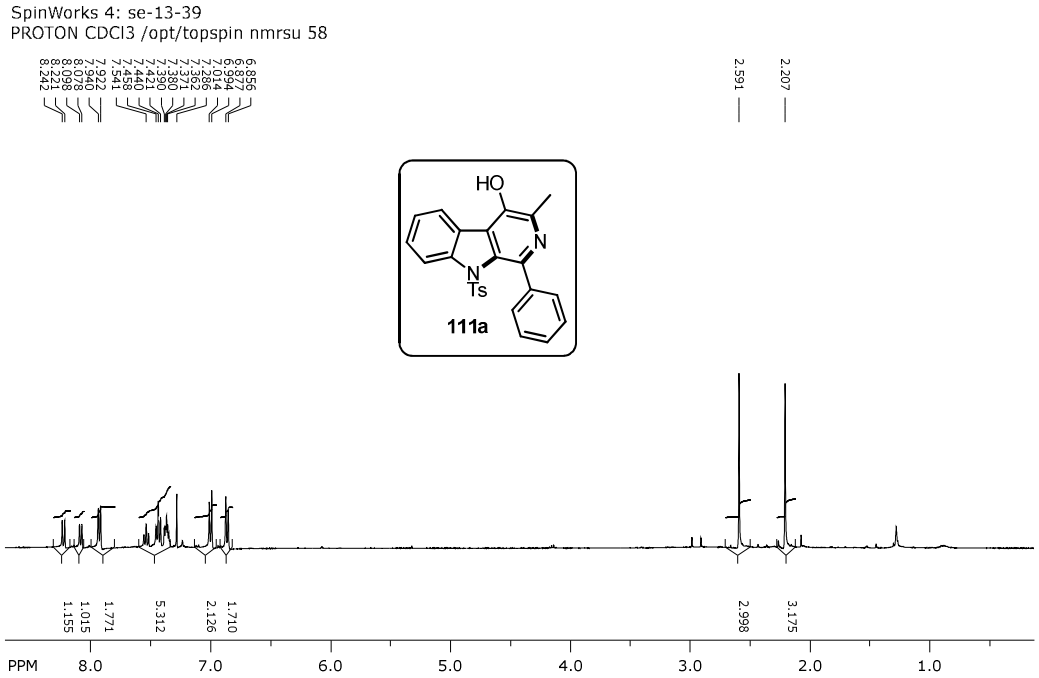


Figure 31: ^{1}H NMR spectrum of compound **111a.**

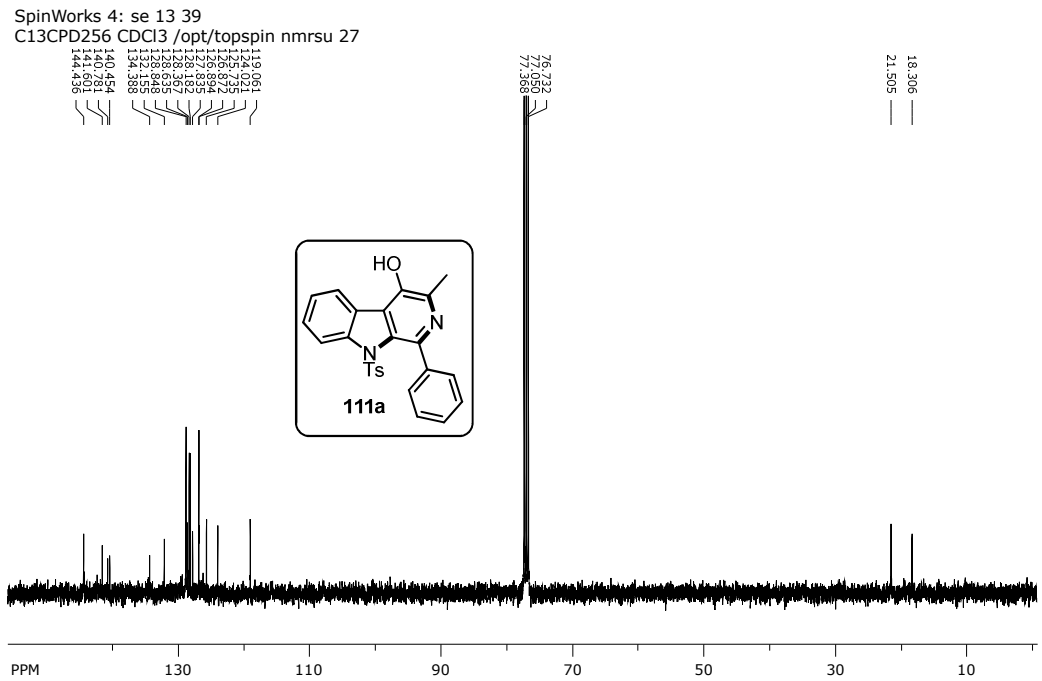
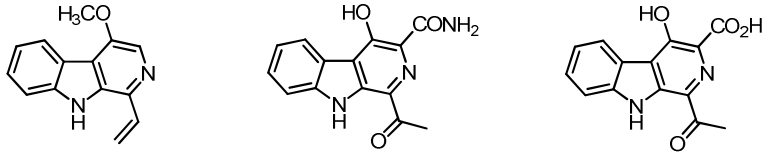


Figure 32:^{13}C NMR spectrum of compound **111a**.

Realizing that there exists no general methodology aimed at the synthesis of 4-hydroxy-*β*-carbolines and also prompted by the occurrence of several bioactive 4-hydroxy-*β*-carboline natural products (Fig. 33),[118] we commenced to explore the generality of the observation.

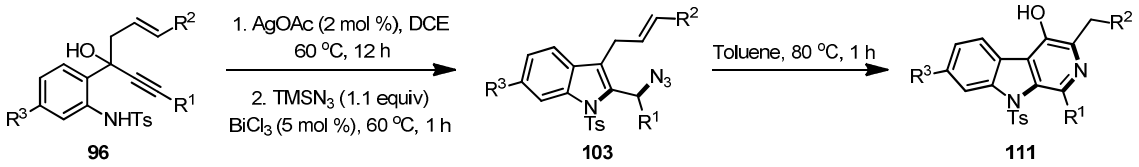


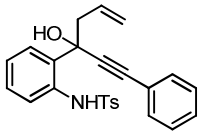
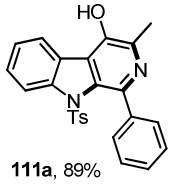
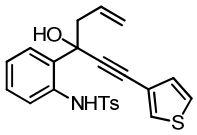
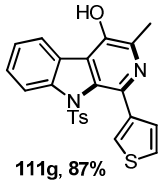
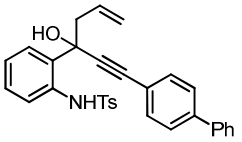
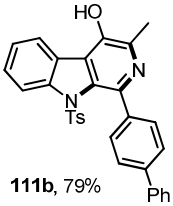
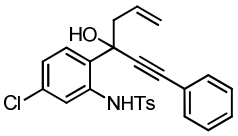
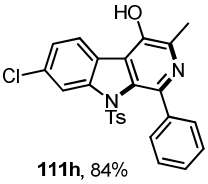
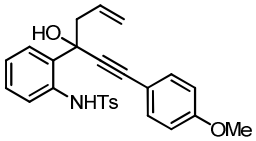
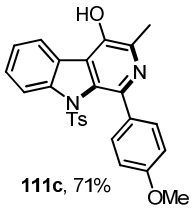
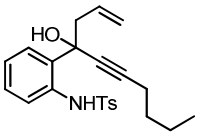
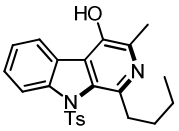
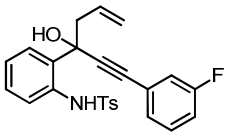
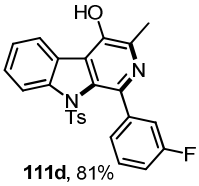
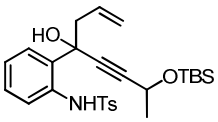
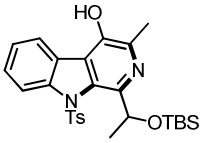
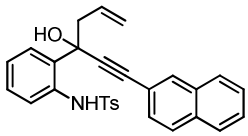
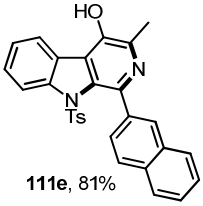
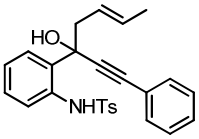
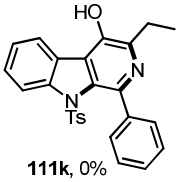
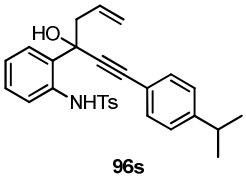
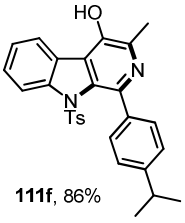
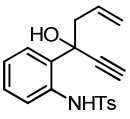
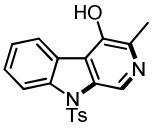
112a: dehydrocrenatine **112b: dichotomide IX** **112c: tunicoidine D**

Figure 33: Repersentative examples of 4-hydroxy-*β*-carboline natural products.

Before commencing towards the substrate scope, the reaction conditions were further refined though the transformation of **96a** to **111a** takes place even at room temperature. In order to expedite the formation of **111a**, the reaction conditions were optimized to heating the azide **103a** in toluene at 80 ^{o}C. Under these conditions, the generality of the reaction was examined. It can be inferred from Table 22 that the substrate scope of this protocol is significantly broad. All the 4-hydroxy-*β*-carbolines (**111a-111j**) were obtained in consistent turnaround times and in excellent yields. It is worth noting that the enynols bearing electronically diverse substituents (R^1), both aromatic and heteroaromatic, were well-tolerated under the reaction conditions (Table 22, entries 1-9). Enynol **96v** having aliphatic substituent at R^1 furnished the respective carbinol **111i** in good yield, extending the generality of this method (Table 22, entry 10). As a substantial advancement, the enynol **96p** possessing the propargylic TBS-ether moiety generated the expected product **111j** (unlike **96p** in Scheme 80). It is worth mentioning that compound **111j** is an advanced precursor possessing the complete carbon framework present in the *β*-carboline natural products, dichotomide IX **112b** and tunicoidine D **112c** (Fig. 33). Substitution across the olefin (R^2) was not tolerated, and no product formation could be observed (Table 22, entry 12). With the enynol **96i** having no substituent across the alkyne, our efforts were unsuccessful in obtaining the respective product **111l** (Table 22, entry 13).

Table 22: Substrate scope.

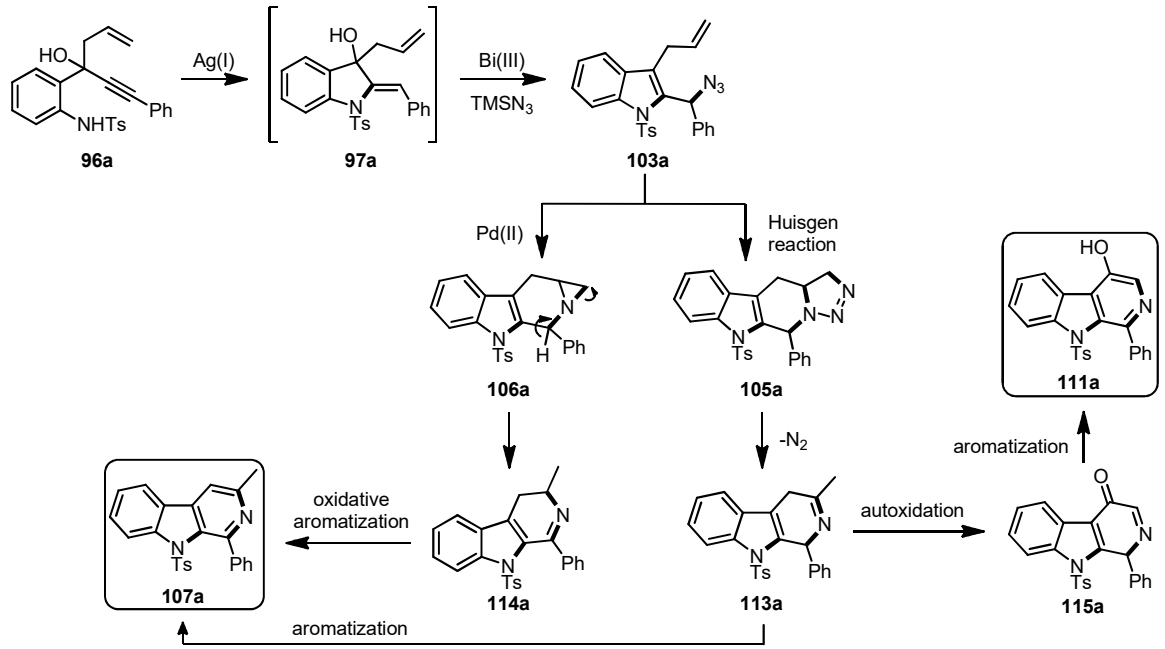


Entry	Substrate	Product	Entry	Substrate	Product
1	 **96a**	 **111a**, 89%	8	 **96t**	 **111g**, **87%**
2	 **96c**	 **111b**, 79%	9	 **96u**	 **111h**, 84%
3	 **96d**	 **111c**, 71%	10	 **96v**	 **111i**, 78%
4	 **96f**	 **111d**, 81%	11	 **96q**	 **111j**, 76%
5	 **96r**	 **111e**, 81%	12	 **96h**	 **111k**, 0%
6	 **96s**	 **111f**, 86%	13	 **96i**	 **111l**, 0%

5.2: Mechanistic insights

Based on the experimental observations and in conjunction with literature reports,[119] a plausible mechanism that explains the formation of **107a** and **111a** from **96a** is proposed in Scheme 83. The enynol **96a** undergoes a selective Ag(I)-catalyzed 5-*exo-dig* cyclization and protodemetallation to furnish the indoline **97a**. Bi(III)-promoted cascade 1,3-allylic alcohol isomerization (1,3-AAI) and nucleophilic azidation generates the azide **103a**, which undergoes a Huisgen-type intramolecular azide-alkene [3+2]-cycloaddition leading to the formation of **105a**. Transformation of the triazole **105a** to the **113a** and eventual aromatization provides **107a**.

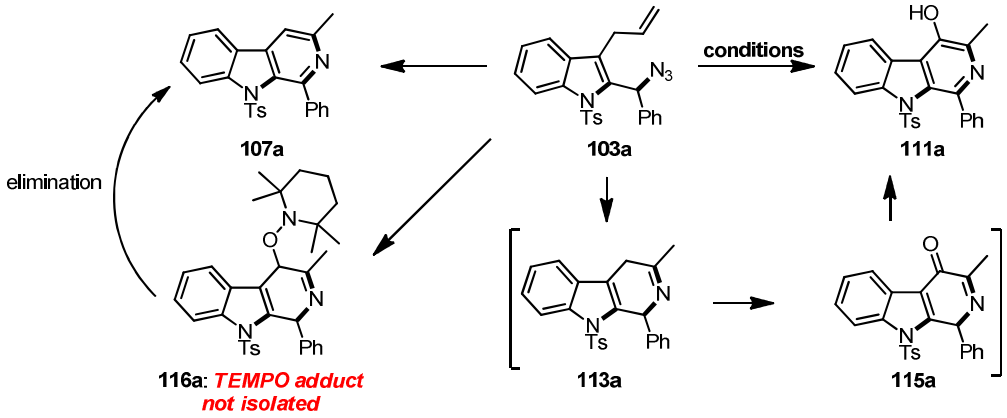
On the other hand, the azide **103a** converts to the aziridine intermediate **106a** in the presence of a Pd(II) complex. Aziridine **106a** undergoes deprotonation followed by ring opening to generate **114a**, which upon aromatization delivers **107a**. Thus, the Pd(II) complex plays a remarkable role in the exclusive formation of **107a**; this also explains the marked yield enhancement in the presence of Pd(II) complexes (see Table 19). In the absence of a Pd(II) complex, **103a** forms **113a**, and it takes an interesting detour. Presumably, **113a** undergoes an autoxidation and aromatization sequence, generating the 4-hydroxy-*β*-carboline **111a**, Scheme 83.



Scheme 83: Plausible mechanism for the formation *β*-carboline **107a** and 4-hydroxy-*β*-carboline **111a**.

Although the mechanism of the conversion of **96a** to **107a** is relatively straightforward, we intended to further understand the mechanism of the conversion of **96a** to **111a**. Towards this, we performed few experiments which are described below.

It is presumed that **111a** forms *via* an autoxidation and aromatization sequence involving **113a**. Since autoxidation is a free radical mediated process, quenching or trapping of the free radical species formed during the autoxidation process by a free radical scavenger such as TEMPO, should provide the TEMPO-adduct **116a**, Scheme 84. To validate this hypothesis, azide **103a** was heated to 80 °C in toluene (optimized conditions) in the presence of 3 equiv of TEMPO, which resulted in the formation of **111a** in 76% yield (Table 23, entry 1). Gradual decrease in the yield of **111a** was observed by increasing the amount of TEMPO (Table 23, entries 2 and 3). Increasing amount of unreacted starting compound (**103a**) was also recovered with increasing amounts of TEMPO which support the autoxidation and aromatization sequence for the formation of **111a**. However, no TEMPO adduct **116a** could be isolated. It can be reasoned that that the TEMPO adduct **116a** may not have formed due to the faster rate of the autoxidation process or due to the very short life-time of any radical intermediate involved or the TEMPO adduct **116a** can undergo elimination to give **107a**.



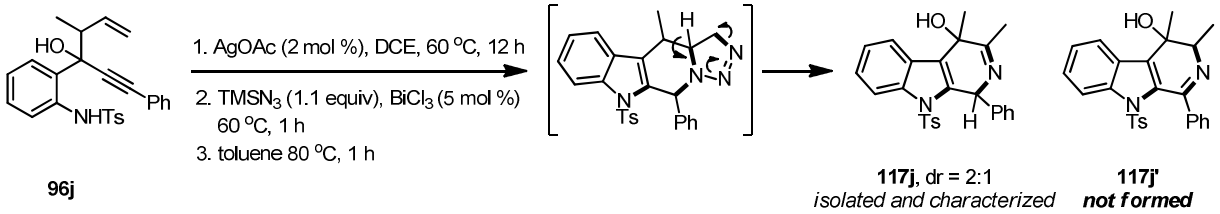
Scheme 84: Proposed mechanism of the formation of **103a** from **111a**.

Table 23: Experiments performed to get insights about the mechanism of the conversion of **103a** to **111a**.

Entry	Conditions	Time / Yield of 111a	Recovered 103a/107a
1	TEMPO (3 equiv), toulene, 80 °C	3 h, 76%	5% / -
2	TEMPO (5 equiv), toulene, 80 °C	3 h, 62%	12% / 7%
3	TEMPO (10 equiv), toulene, 80 °C	3 h, 56%	20% / 14%

After having an idea about the involvement of autoxidation process, we wanted to establish the role of atmospheric oxygen during the conversion of **113a** to **115a**, thus an isotopic labeling experiment was conducted using $^{18}O_2$. The reaction of **103a** under $^{18}O_2$ enriched atmosphere was carried out. Freshly prepared **103a** (30 mg) was taken in a 5 mL round bottom flask and anhydrous toluene (1 mL) under argon atmosphere. The flask was evacuated under vacuum and oxygen-18 balloon was introduced [100 mL oxygen-18 cylinder was purchased from Sigma-Aldrich and was transferred to a balloon]. The solution was initially heated to 50 ^{o}C and subsequently at 80 ^{o}C over a period of four hours. The reaction was continued at 80 ^{o}C for another four hours before commencing to purification. The ^{1}H NMR spectrum and high-resolution mass spectrum of the purified product was recorded. The ^{18}O abundance in **111a-^{18}O** was found to be ~25% more than the respective abundance of **111a-^{18}O** obtained under aerobic conditions (atmospheric oxygen) (Figs. 34 and 35), clearly indicating the incorporation of oxygen-18 supplied externally. The HRMS spectrum (Fig. 34) clearly showed the presence of **111a-^{18}O** (calcd for $C_{25}H_{21}N_2O_2{}^{18}OS$ $(M+H)^+$: 431.1315, Found: 431.1302) along with the expected **111a-^{16}O**.

In an attempt to interrupt and perceive the proposed autoxidation of **113a** to **115a**, we designed the enynol **96j** with a methyl group positioned at the allylic position, Scheme 85. It was expected that the methyl group should restrict the autoxidation process up to the *tert*-alcohol **117j**, since the formation ketone and subsequent isomerization to the respective 4-hydroxy-*β*-carboline is not feasible. Indeed, to our surprise and delight, dihydrocarboline **117j** formed, and was isolated. In addition to supporting an autoxidation process, this result also provides valuable information about the triazole decomposition pathway. Interestingly, the reaction did not form **117j'**, which can be energetically stable compared to **117j**.



Scheme 85: Isolation of the dihydrocarboline **117j**, proposed intermediate during the autoxidation process.

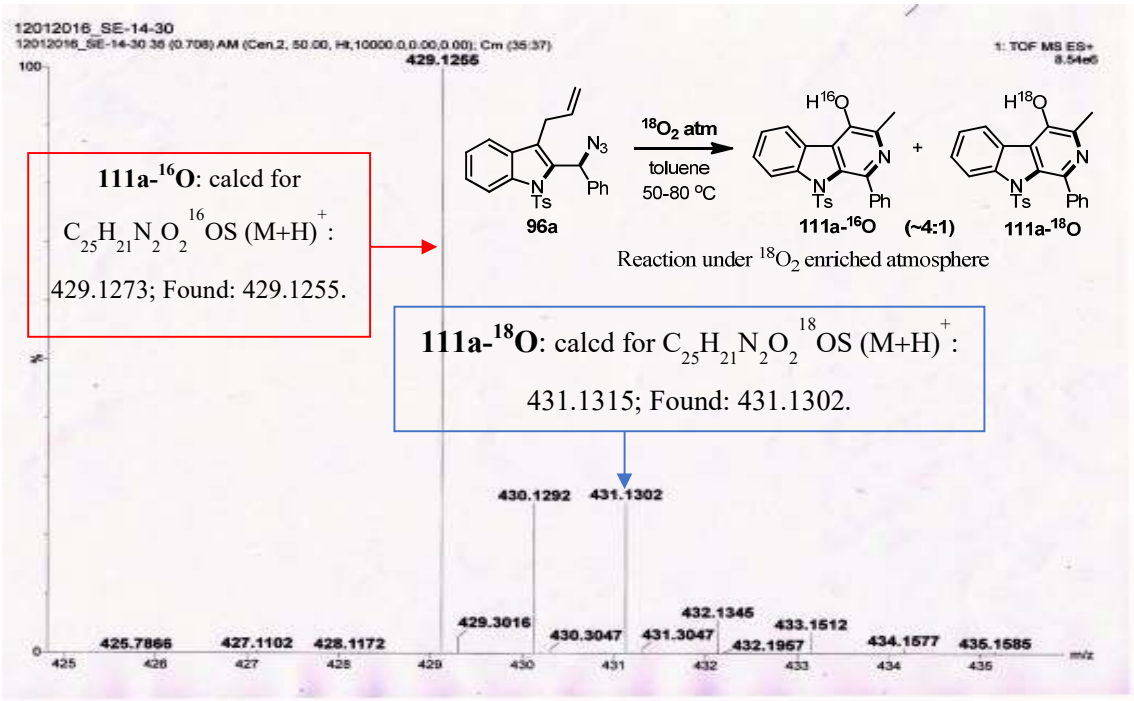


Figure 34: HRMS spectrum of the purified sample (mixture of **111a-^{16}O** and **111a-^{18}O**) from $^{18}O_2$ enriched experiment.

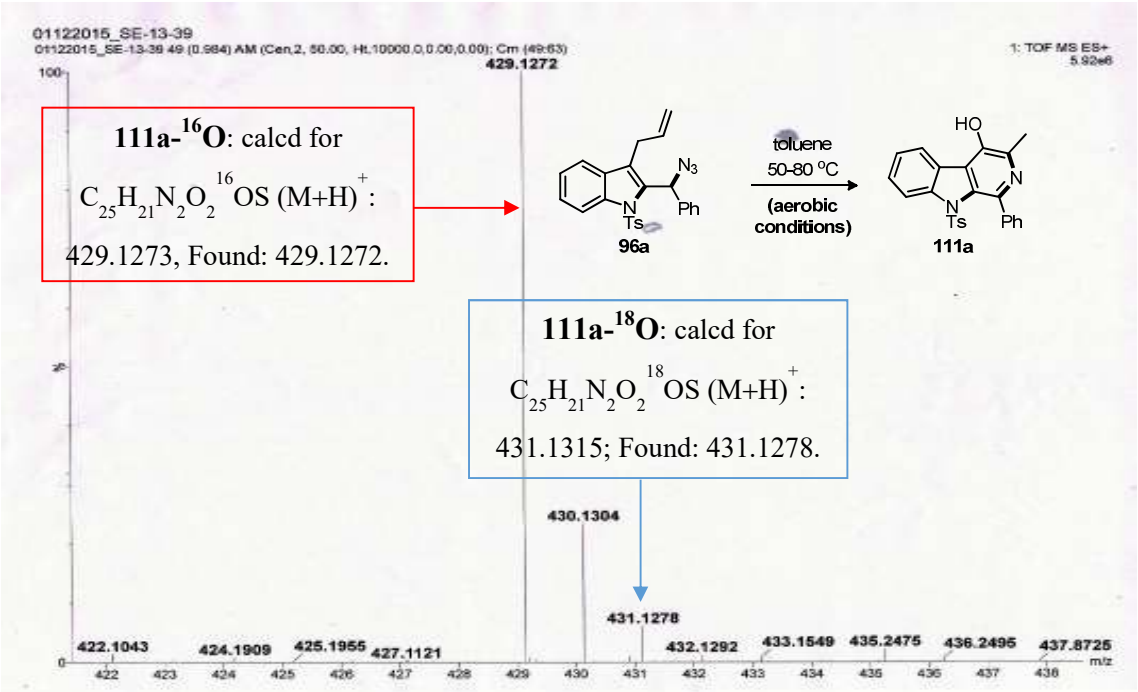


Figure 35: HRMS spectrum of the purified sample (mixture of **111a-^{16}O** and **111a-^{18}O**) obtained under aerobic conditions.

5.3: *Application towards the synthesis of other [c]-fused pyridines*

After successfully establishing one-pot relay processes for the facile synthesis of unusual *β*-carbolines by effectively accommodating orthogonal metal-catalytic cycles, we intended to extend this strategy for the synthesis of other important [*c*]-fused pyridines such as benzofuropyridines, benzothienopyridines and isoquinolines.

Benzofuropyridines and their derivatives are the primary molecular architectures present in many heterocyclic compounds that exhibit a wide range of biological and pharmaceutical activities, including antitumor, antibacterial and antimalarial activities.[120] For example, ethyl benzofuro[2,3-*c*]pyridine-3-carboxylate **118a** (Fig. 36) and its derivatives are known to act as non-benzodiazepine structural ligands, binding to benzodiazepine receptors in anxiolytics, tranquilizers, and anticonvulsants. Benzofuro-[2,3-*c*]pyridin-3-yl(quinuclidin-3-yl)methanone **118b** (Fig. 36) has been reported for central nervous system activity, whereas, benzofuro-[2,3-*c*]pyridine derivative **118c** is realized to be useful as phosphodiesterase-10 inhibitor.

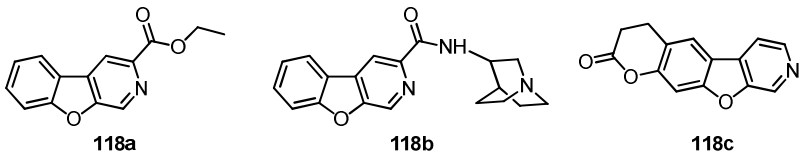
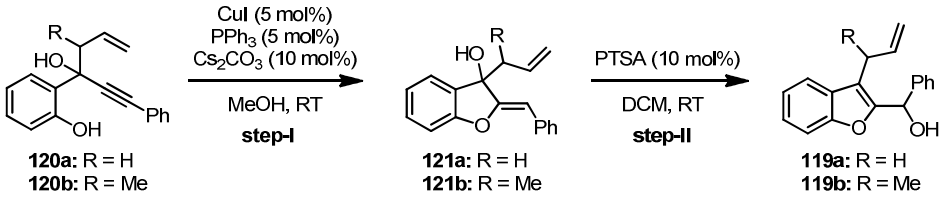


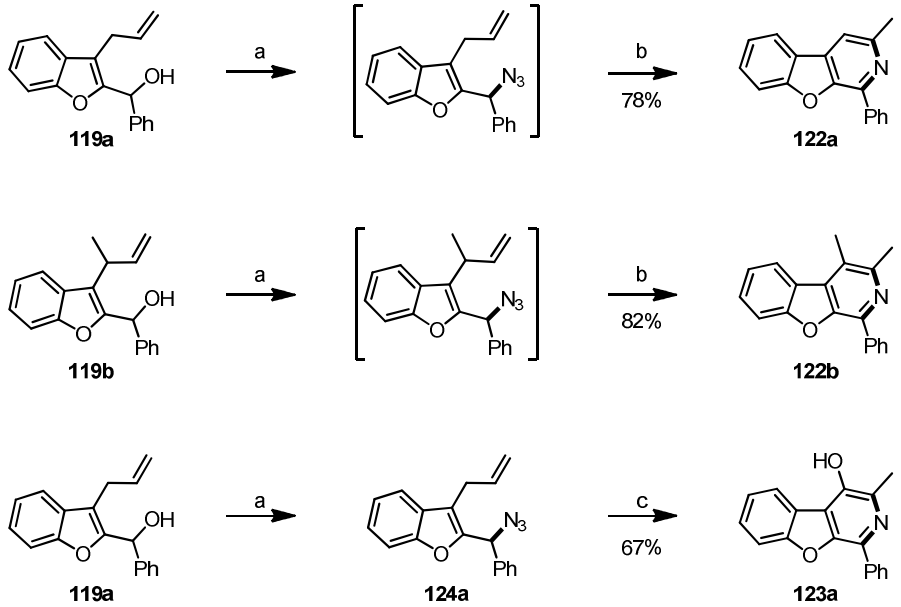
Figure 36: Some biologically active benzofuro-[2,3-*c*]pyridines.

Owing to their interesting biological activity, we elaborated the triple relay catalytic approach for the synthesis of benzofuro[2,3-*c*]pyridines from easily accessible 3-allylbenzo[*b*]furan-2-carbinols, Scheme 86.[121] 3-Allylbenzo[*b*]furan-2-carbinols **119a** and **119b** were prepared in two-steps from 2-(3-hydroxy-1-phenylhex-5-en-1-yn-3-yl)phenols **120a** and **120b** by following the literature procedures.[121] Copper(I)-catalyzed cycloetherification of the ynols **120a** and **120b** followed by PTSA-catalyzed allylic isomerization of **121a** and **121b** generated the respective, 3-allylbenzo[*b*]furan-2-carbinols **119a** and **119b**.



Scheme 86: Synthesis of 3-allylbenzo[*b*]furan-2-carbinols (**119a** and **119b**).

Gratifyingly, reaction of 3-allylbenzo[*b*]furan-2-carbinols **119a** and **119b** under the optimized conditions generated 1,3-disubstituted benzofuro[2,3-*c*]pyridine **122a** and 1,3,4-trisubstituted benzofuro[2,3-*c*]pyridine **122b**, respectively, Scheme 87. In addition, an unprecedented 1,3-disubstituted-4-hydroxybenzofuro[2,3-*c*]pyridine **123a** was easily constructed in good yield, merely by the thermal treatment of isolated ε,ω-unsaturated azide **124a** in toluene.



Scheme 87: Reaction of 3-allylbenzo[*b*]furan-2-carbinols **119a** and **119b**. Reagents and conditions: (a) $TMSN_3$ (1.1 equiv.), $BiCl_3$ (5 mol%), DCE, 60 °C, 1 h. (b) $Pd(OAc)_2$ (5 mol%), 80 °C, 10 h. (c) Toluene, 80 °C, 12 h.

Benzothienopyridines are another important class of [*c*]-fused pyridines and have found significant applications in supramolecular chemistry and materials science. Benzothienopyridines are well-known for their optico-electronic properties and therefore, synthesis of benzothiophene fused pyridines can offer potential opportunities to validate their physicochemical properties.[122] Towards this, 3-allylbenzo[*b*]thiophene-2-carbinols (**125a** and **125b**) were prepared by following a three-step protocol starting from benzothiophene **126** (Scheme 88).[123] NBS mediated bromination, magnesium mediated allylation, and further, *n*-BuLi mediated alkylation of 3-allylbenzo[*b*]thiophene **127** with respective aldehydes furnished 3-allylbenzothiphene-2-carbinols **125a** and **125b**.

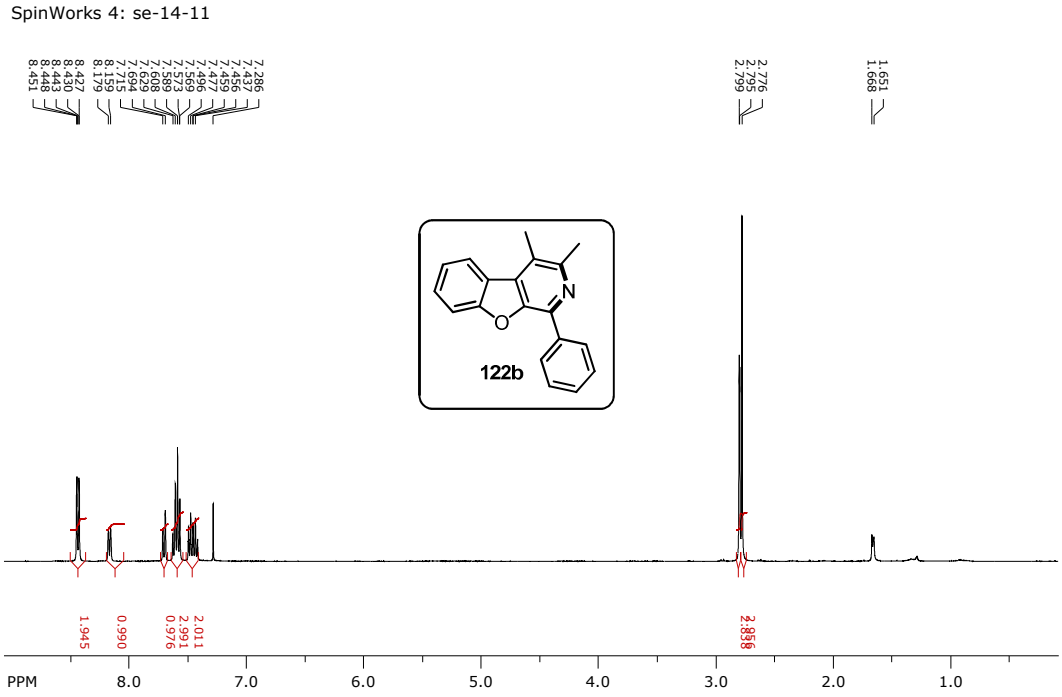


Figure 37: ^{1}H NMR spectrum of **122b**.

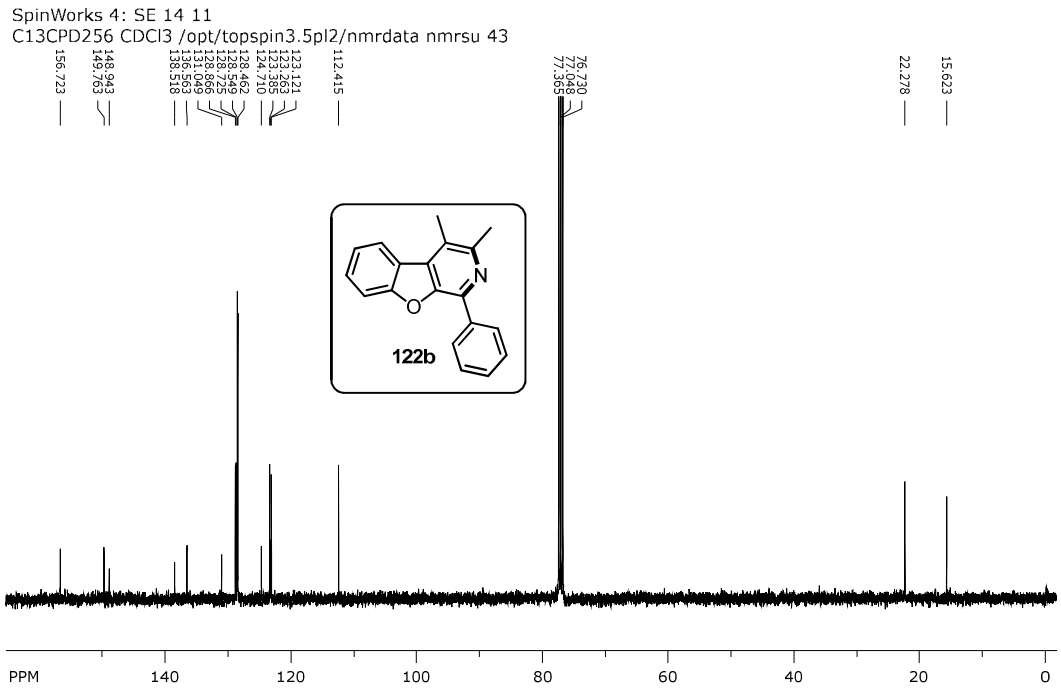
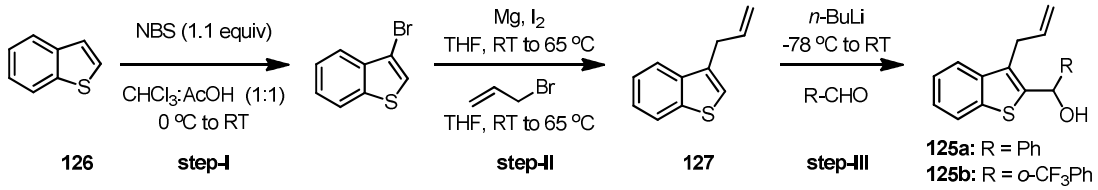
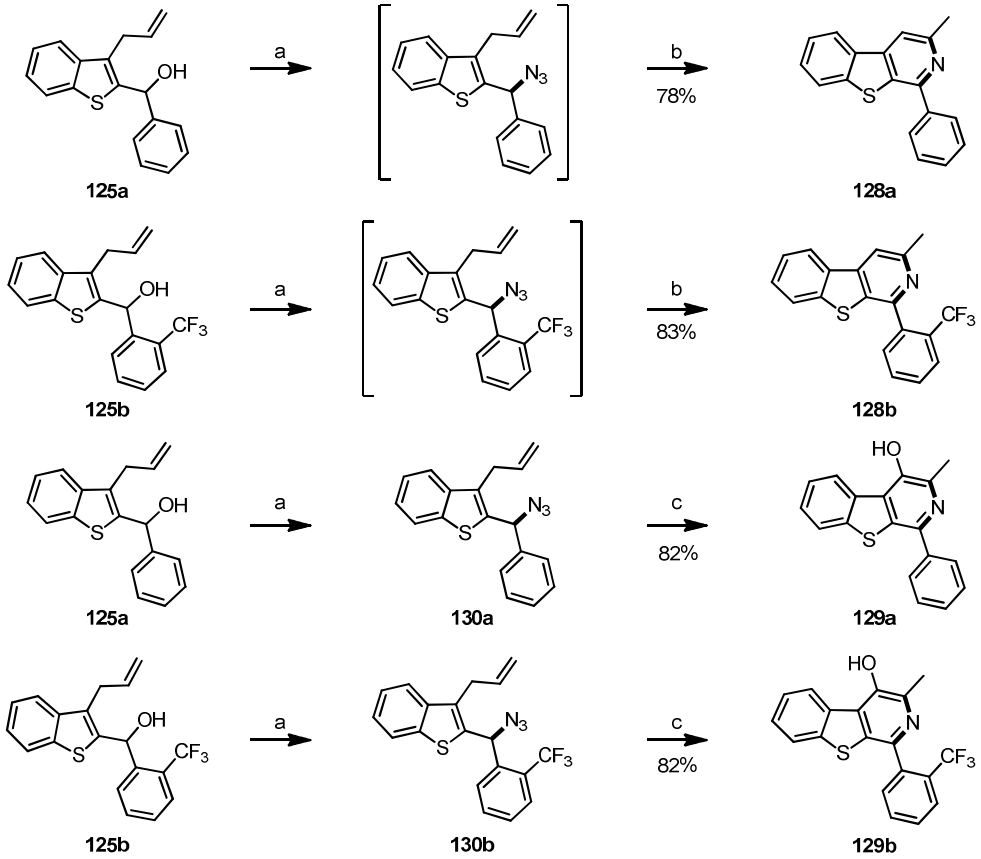


Figure 38: ^{13}C NMR spectrum of **122b**.



Scheme 88: Synthesis of 3-allylbenzo[*b*]furan-2-carbinols (**125a** and **125b**).

By subjecting the 3-allylbenzo[*b*]thiophene-2-carbinols (**125a** and **125b**) to the optimized conditions, an interesting range of 1,3-disubstituted benzothieno[2,3-*c*]pyridines (**128a** and **128b**) were efficiently assembled in one-pot in good yields, Scheme 89. In addition, an unprecedented 3-substituted-4-hydroxy-*β*-carbolines **129a** and **129b** were also easily synthesized by the thermal treatment of the isolated ε,ω-unsaturated azides **130a** and **130b** in toluene.



Scheme 89: Reaction of 3-allylbenzo[*b*]thieno-2-carbinols. Reagents and conditions: (a) $TMSN_3$ (1.1 equiv.), $BiCl_3$ (5 mol%), DCE, 60 °C, 1 h. (b) $Pd(OAc)_2$ (5 mol%), 80 °C, 10 h. (c) Toluene, 80 °C, 12 h.

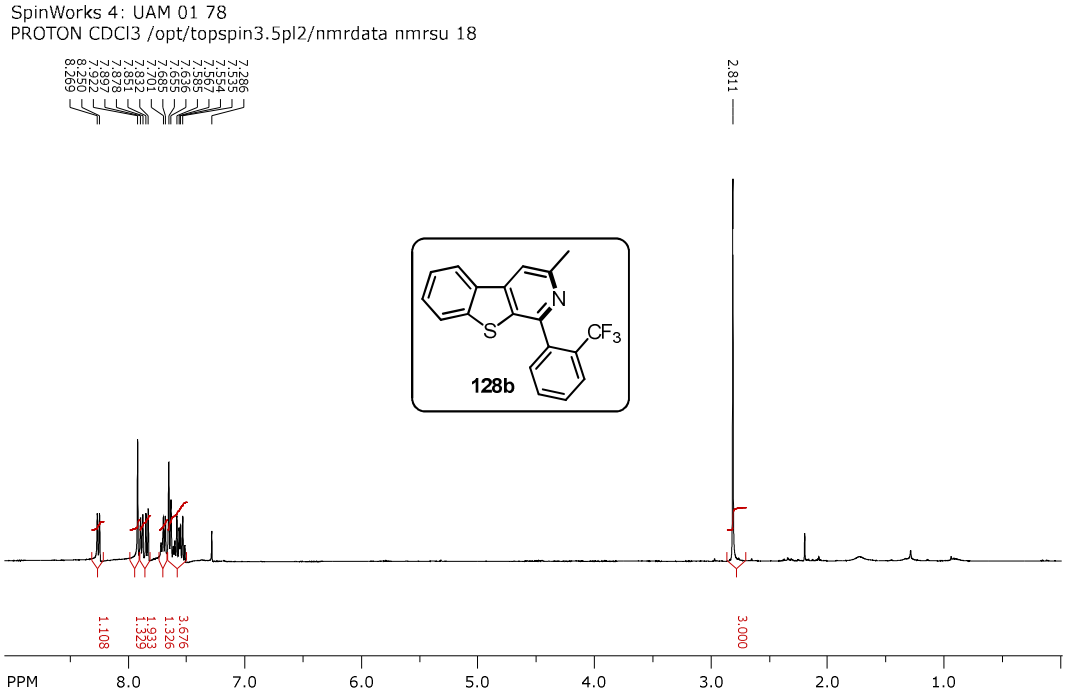


Figure 39: ^{1}H NMR spectrum of **128b**.

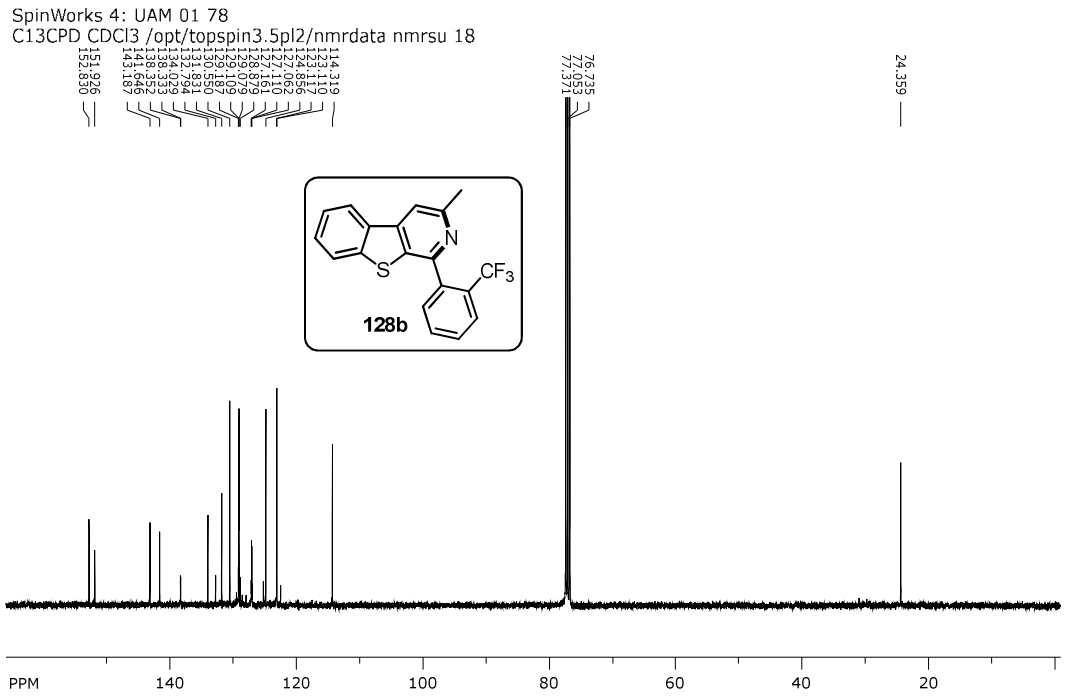


Figure 40: ^{13}C NMR spectrum of **128b**.

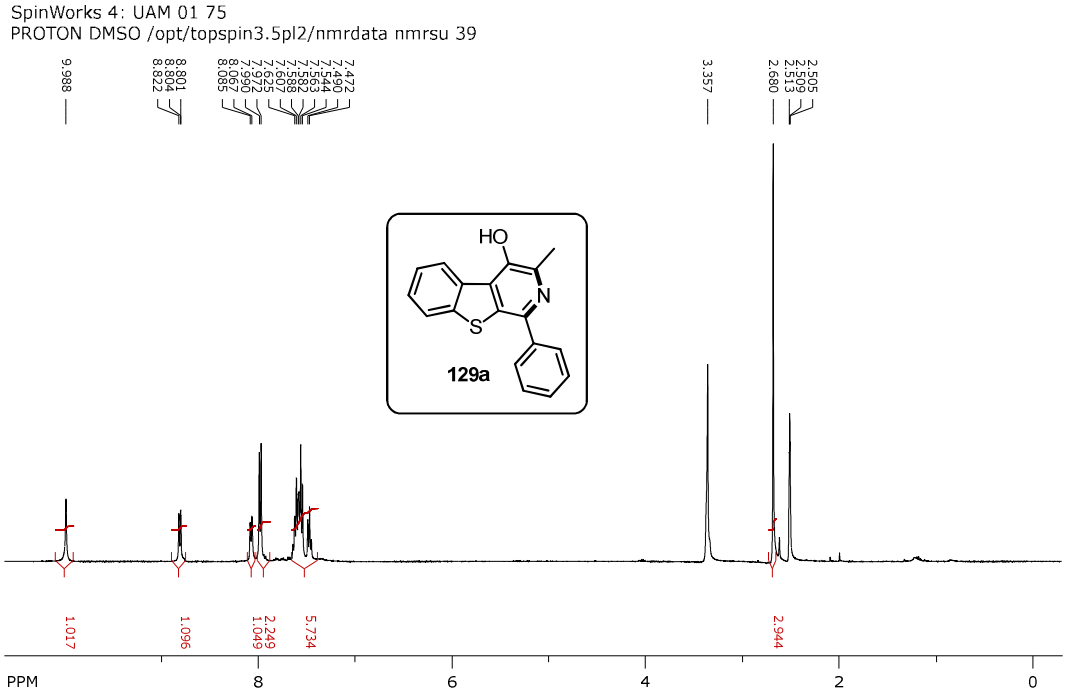


Figure 41: ^{1}H NMR spectrum of **129a**.

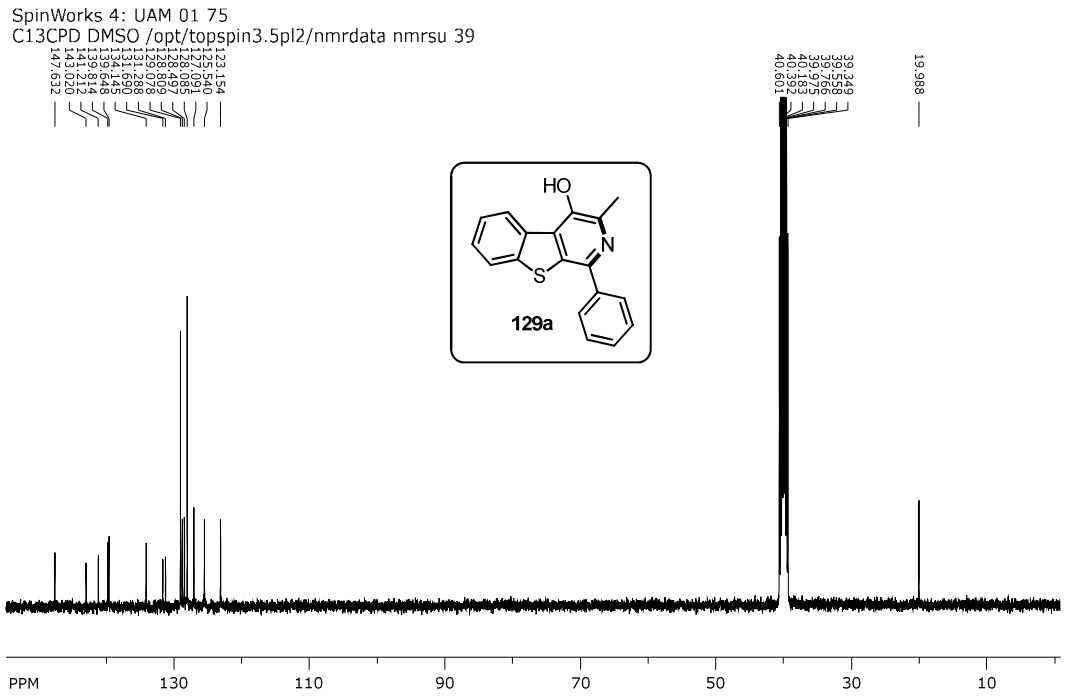


Figure 42: ^{13}C NMR spectrum of **129a**.

Synthetic utility of this method was further flourished by attempting the one-pot synthesis of substituted isoquinolines. Isoquinolines are privileged class of compounds commonly found in natural products and medicinally interesting molecules, Fig. 43.[124] Their biological activities have resulted in them often being used as building blocks in pharmaceutical compounds, as chiral ligands for transition metal catalysts, and their iridium complexes as organic light emitting diodes (OLEDs). Owing to their significance, we have shown a new approach for the synthesis of isoquinolines from easily accessible 1-(2-allylphenyl) carbinols.

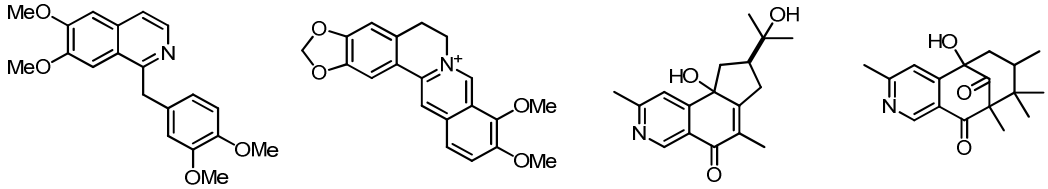
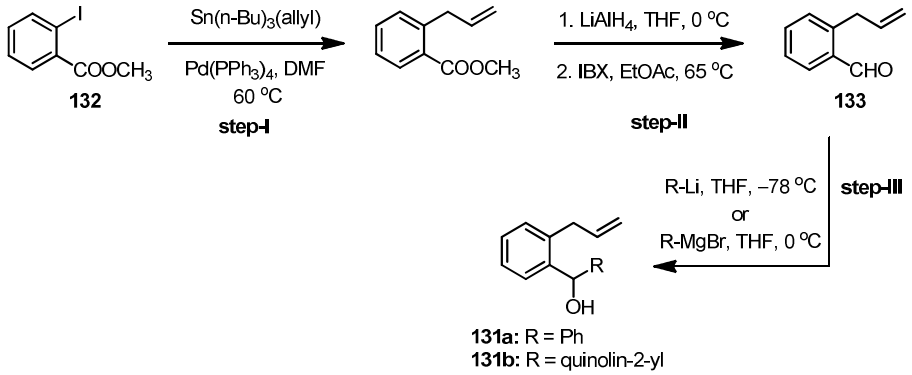


Figure 43: Representative examples of isoquinoline alkaloids.

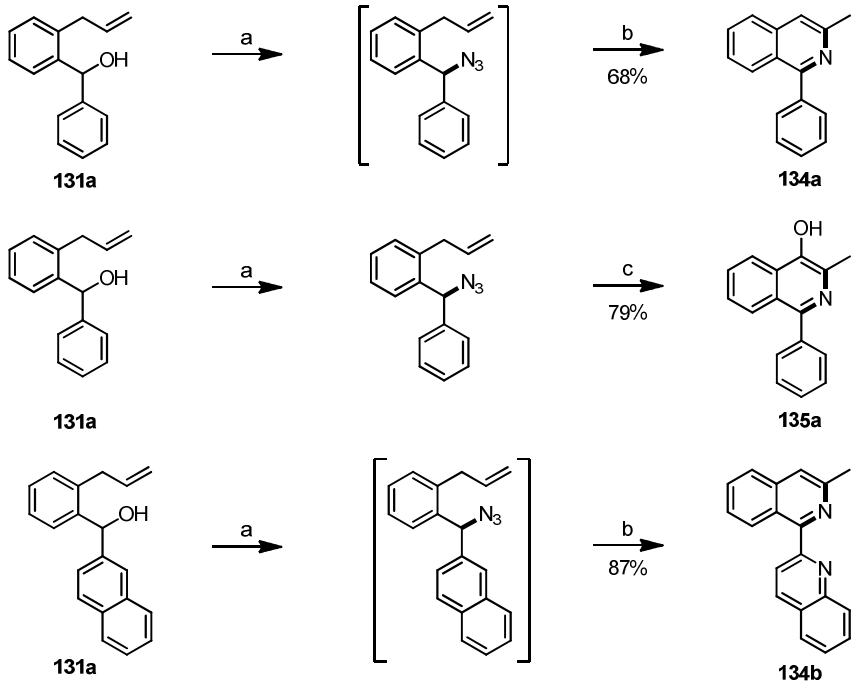
The required starting compounds, 1-(2-allylphenyl) carbinols **131a** and **131b** were easily prepared by following a three-step protocol starting from methyl 2-iodobenzoate **132**, Scheme 90.[125] Allylation of aryl iodide under Stille protocol followed by reduction and oxidation sequence afforded 2-allylbenzaldehyde **133**. Further addition of the respective organolithium reagents at –78 °C (or organomagnesium reagents at 0 °C) to 2-allylbenzaldehyde **132** provided 1-(2-allylphenyl) carbinols **131a** and **131b** in good yields.



Scheme 90: Synthesis of 1-(2-allylphenyl) carbinols (**131a** and **131b**).

Reaction of 1-(2-allylphenyl) carbinols under the optimized conditions provided access to 1,3-disubstituted isoquinolines **134a** and 1,3-disubstituted-4-hydroxyisoquinolines **135a**, which

otherwise require a multistep synthesis, Scheme 91. Especially, synthesis of a novel isoquinoline derivatives such as 2-(isoquinolin-1-yl)quinolones **134b** has also been accomplished.



Scheme 91: Reaction of 1-(2-allylphenyl) carbinols (**131a** and **131b**). Reagents and conditions: (a) $TMSN_3$ (1.1 equiv.), $BiCl_3$ (5 mol%), DCE, 60 ^oC, 1 h. (b) $Pd(OAc)_2$ (5 mol%), 80 ^oC, 12 h. (c) Toluene, 80 ^oC, 8 h.

In conclusion an unprecedented examples of relay catalysis through the sequential employment of silver, bismuth and palladium catalysts to access an array of distinct *β*-carbolines and subsequently extended towards the synthesis of the intriguing [*c*]-fused pyridines such as benzofuro- and benzothieno[2,3-*c*]pyridines, and isoquinolines has been developed. Intriguing mechanistic details governing these processes were also elucidated.

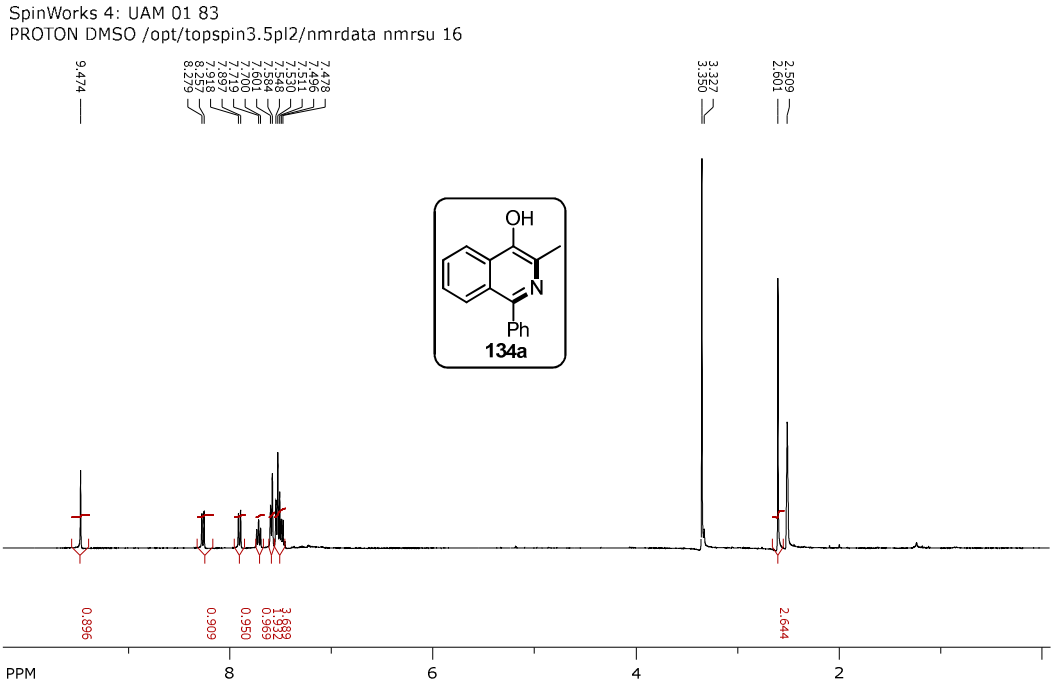


Figure 44: ^{1}H NMR spectrum of **134a**.

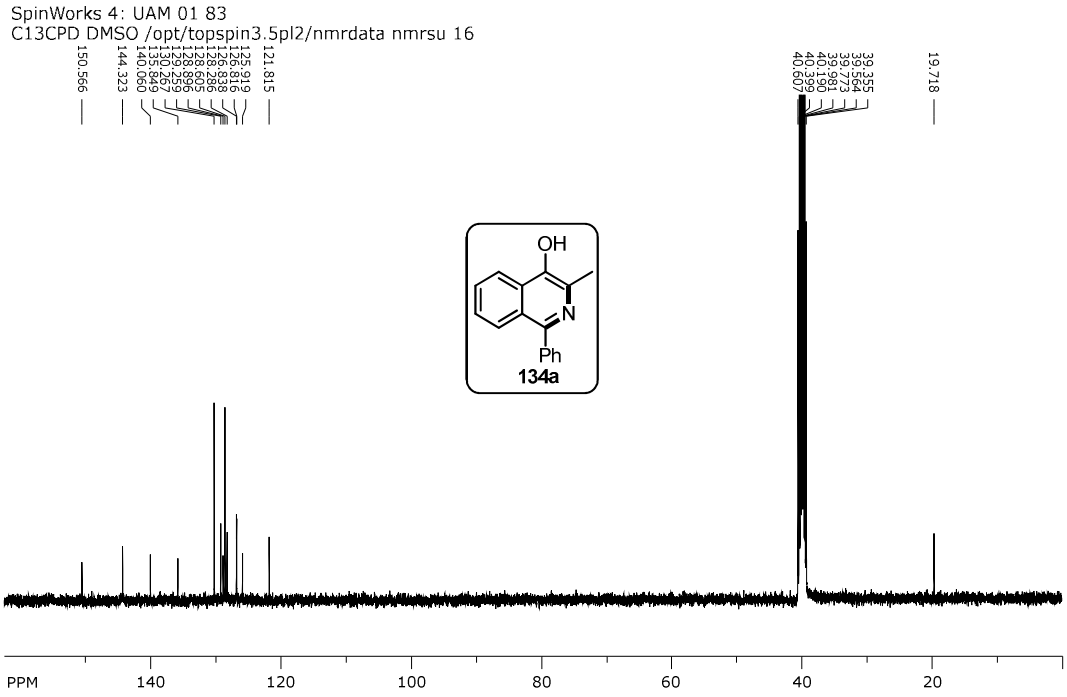


Figure 45: ^{13}C NMR spectrum of **134a**.

CONCLUSIONS

In conclusion, we have described the systematic generation of furfuryl cations from furyl/benzofuryl carbinols under $BiCl_3$ catalysis, their reactions with various nucleophiles and elaboration to some architecturally novel scaffolds. Whereas the treatment of furyl/benzofuryl carbinols with 1,3-dicarbonyls under the TfOH catalysis generated functionalized, and polysubstituted furans in good to excellent yields, synthesis of 1,2,3-trisubstituted cyclopenta[*b*]thiophenes was achieved through a PPA mediated domino process under solvent-free conditions. After successfully deliberating a method for the cyclopentannulation of benzothiophenes, we next focused on the construction of cyclopentannulated indoles. In this context, we developed a one-pot relay catalytic process involving gold(I) and Brønsted acid to access various polysubstituted cyclopentannulated indoles. A practical and efficient relay catalytic system for indole cyclopentannulation *via* Nazarov-type cyclization also has been demonstrated. This approach is successfully elaborated to the synthesis of a natural product-like complex pentacyclic structures, indole steroidal conjugates and core carbon scaffold of 8-*nor*-polyveolinone.

Having developed one-pot relay processes for the construction of complex indole derivatives, we extended these strategies for the synthesis of *β*-carbolines. In line with this, one-pot triple relay catalytic approach, which constitutes sequential employment of silver, bismuth and palladium catalysts towards the synthesis of *β*-carbolines has been established. In addition, a one-pot bimetallic relay catalytic approach has been developed to access novel 3-substituted-4-hydroxy-*β*-carbolines in good to excellent yields. Further, we elaborated this strategy for the synthesis of other significant [*c*]-fused pyridines such as 1,3-disubstituted and 1,3,4-trisubstituted benzofuro[2,3-*c*]pyridines, benzothieno[2,3-*c*]pyridines and isoquinolines.

EXPERIMENTAL SECTION

General experimental methods: All the starting compounds and catalysts employed in this study were procured from Sigma-Aldrich and were used without further purification. For thin layer chromatography (TLC), silica aluminium foils with fluorescent indicator 254 nm (from Aldrich) were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of *p*-anisaldehyde (23 mL), conc. H_2SO_4 (35 mL), and acetic acid (10 mL) in ethanol (900 mL) followed by heating. Column chromatography was performed using SD Fine silica gel 100-200 mesh (approximately 15–20 g per 1 g of the crude product). Dry THF was obtained by distillation over sodium and stored over sodium wire. IR spectra were recorded on a Perkin–Elmer FT IR spectrometer as thin films or KBr pellet, as indicated, with ν_{max} in inverse centimetres. Melting points were recorded on a digital melting point apparatus Stuart SMP30. ^{1}H NMR and ^{13}C NMR spectra were recorded on a 400 MHz Bruker Biospin Avance III FT-NMR spectrometer. NMR shifts are reported as delta (δ) units in parts per million (ppm) and coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are utilized to describe peak patterns when appropriate: br=broad, s=singlet, d=doublet, t=triplet, q=quartet and m=multiplet. Proton chemical shifts are given in δ relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$ or in $(CD_3)_2SO$ (δ 2.50 ppm) or in $(CD_3)_2CO$ (δ 2.05 ppm). Carbon chemical shifts are internally referenced to the deuterated solvent signals in $CDCl_3$ (δ 77.1 ppm) or in $(CD_3)_2SO$ (δ 39.5 ppm) or in $(CD_3)_2CO$ at δ 29.9 and 206.7. Single crystal X-ray analysis was carried on a Bruker AXS KAPPA APEX II system or Rigaku XtaLAB mini X-ray diffractometer. High-resolution mass spectra were recorded on a Waters QTOF mass spectrometer. Optical rotations were recorded on Rudolph APIII/2W.

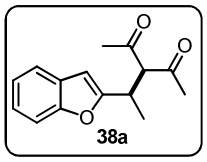
Procedure A: General procedure for synthesis of furyl and thienyl carbinols.

Furyl and thienyl carbinols were prepared based on literature procedures,[43] either by the addition of organolithium reagents or organomagnesium reagents to aldehydes or by the generation of furyllithium/ thienyllithium/ benzofuranyllithium and addition to aldehydes/lactones.

Procedure B: General procedure for $BiCl_3$ catalyzed reactions of various heteroatyl alcohols.

To a solution of furfuryl alcohol (0.1 mmol, 1 equiv) in nitromethane (1 mL) were added an appropriate nucleophile (0.11 mmol, 1.1 equiv) followed by $BiCl_3$ (0.02 mmol, 0.2 equiv) at room temperature. The reaction mixture was stirred at room temperature until the alcohol was consumed as monitored by TLC. Quenched the reaction mixture with aqueous saturated sodium bicarbonate solution (1-2 mL). Diluted the reaction mixture with ethyl acetate (1-2 mL) and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1-2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexanes/ethyl acetate) to afford product.

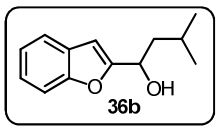
3-(1-(Benzofuran-2-yl)ethyl)pentane-2,4-dione (38a).



Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 2936, 2880, 1724, 1700, 1598, 1455, 1422, 1358, 1253, 1167, 1011, 942. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.19-7.10 (m, 2H), 6.34 (s, 1H), 4.10 (d, *J* = 10.2 Hz, 1H), 3.77 (dq, *J* = 10.2 and 6.7 Hz, 1H), 2.15 (s, 3H), 1.96 (s, 3H), 1.23 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 202.8, 202.6, 159.0, 154.5, 128.2, 123.8, 122.8, 120.7, 110.9, 102.7, 73.1, 33.7, 30.0, 29.3, 17.4. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}O_3Na$ (M+Na): 267.0997. Found: 267.0994.

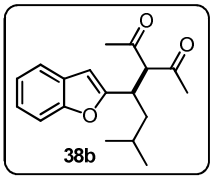
1-(Benzofuran-2-yl)-3-methylbutan-1-ol (36b).

Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3367, 2956, 2871, 1457, 1253, 1172, 807, 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46 (d, *J* =7.2 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.20-7.11 (m, 2H), 6.53 (s, 1H), 4.87 (t, *J* = 7.7 Hz, 1H), 1.95 (d, *J* =5.9 Hz, 1H), 1.80-1.68 (m, 3H), 0.90 (d, *J* = 5.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): 159.7, 154.7, 128.1, 124.1, 122.7, 121.0, 111.1, 102.4, 66.0, 44.5, 24.6, 23.0, 22.1. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}O_2Na$ (M+Na): 204.1150. Found: 204.1148.



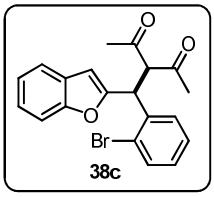
3-(1-(Benzofuran-2-yl)-3-methylbutyl)pentane-2,4-dione (38b).

Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2969, 2894, 1732, 1683, 1450, 1366, 1265, 1074, 745. **^{1}H**



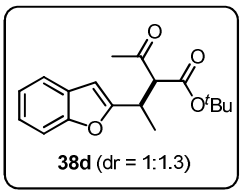
NMR (400 MHz, $CDCl_3$): δ 7.42 (d, *J* = 7.1 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.18-7.07 (m, 2H), 6.40 (s, 1H), 4.16 (d, *J* = 10.0 Hz, 1H), 3.79 (dt, *J* = 11.5 and 3.3 Hz, 1H), 3.01 (s, 3H), 1.80 (s, 3H), 1.73-1.65 (m, 1H), 1.33-1.28 (m, 1H), 1.13-1.04 (m, 1H), 0.85 (d, *J* = 6.4 Hz, 3H), 0.72 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 202.7, 202.4, 156.9, 154.3, 128.2, 123.8, 122.8, 120.4, 111.0, 102.2, 73.2, 41.3, 37.9, 29.5, 25.4, 24.3, 23.7, 20.8. HRMS (ESI): *m/z* calcd for $C_{18}H_{22}O_3Na$ (M+Na): 309.1467. Found: 309.1463.

3-((Benzofuran-2-yl)(2-bromophenyl)methyl)pentane-2,4-dione (38c).



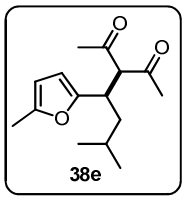
Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2932, 1723, 1703, 1471, 1358, 1252, 1172, 1022, 765. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.51-7.56 (m, 8H), 5.59 (s, 1H), 5.57 (d, *J* = 10.1 Hz, 1H), 4.83 (d, *J* = 10.1 Hz, 1H), 2.14 (s, 3H), 1.98 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 201.6, 201.4, 155.2, 154.7, 136.9, 133.6, 129.2, 129.1, 128.1, 128.0, 124.9, 124.0, 122.9, 120.9, 111.0, 104.4, 72.1, 43.2, 30.0, 28.4. HRMS (ESI): *m/z* calcd for $C_{20}H_{17}BrO_3Na$ (M+Na): 384.0361. Found: 384.0363.

***tert*-Butyl 2-acetyl-3-(benzofuran-2-yl)butanoate (38d, Major).**



Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2982, 1714, 1732, 1258, 1145, 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45-7.31 (m, 2H), 7.17-7.08 (m, 2H), 6.38 (s, 1H), 3.77 (d, *J* = 11.2 Hz, 1H), 3.72-3.66 (m, 1H), 2.20 (s, 3H), 1.38 (s, 9H), 1.33 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 202.1, 201.9, 167.2, 159.5, 128.4, 123.6, 122.6, 120.6, 110.8, 102.6, 82.4, 65.2, 33.3, 29.9, 27.8, 17.4. HRMS (ESI): *m/z* calcd for $C_{18}H_{22}O_4Na$ (M+Na): 325.1416. Found: 325.1414.

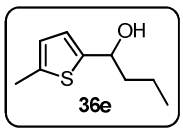
3-(3-Methyl-1-(5-methylfuran-2-yl)butyl)pentane-2,4-dione (38e).



Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2954, 2871, 1726, 1701, 1374, 1226, 1073, 1018, 785. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.83 (d, *J* = 3.0 Hz, 1H), 5.75-5.73 (m, 1H), 3.97 (d, *J* = 10.8 Hz, 1H), 3.49 (dt, *J* = 11.4 and 3.3

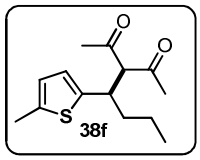
Hz, 1H), 2.14 (s, 3H), 1.86 (s, 3H), 1.49 (s, 3H), 1.30-0.95 (m, 3H), 0.80 (d, *J* = 4.8 Hz, 3H), 0.72 (d, *J* = 4.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 203.4, 203.1, 151.9, 151.8, 108.0, 105.9, 73.8, 41.2, 37.7, 29.9, 29.5, 25.4, 23.7, 20.9, 13.5. HRMS (ESI): *m/z* calcd for $C_{15}H_{22}O_3Na$ (M+Na): 273.1467. Found: 273.1461.

1-(5-Methylthiophen-2-yl)butan-1-ol (36e).



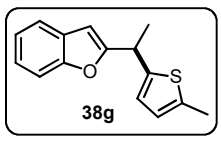
Prepared by following the procedure **A** and isolated as colorless oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3374, 2958, 2928, 2870, 1455, 1097, 1020, 800. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.73 (d, *J* = 3.3 Hz, 1H), 6.61 (d, *J* = 3.3 Hz, 1H), 4.48 (t, *J* = 6.9 Hz, 1H), 2.48 (s, 3H), 1.90-1.69 (m, 2H), 1.53-1.28 (m, 2H), 0.96 (t, *J* = 6.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 146.5, 139.0, 124.5, 123.6, 70.1, 41.1, 19.2, 15.4, 13.8. HRMS (ESI): *m/z* calcd for $C_9H_{14}OSNa$ (M+Na): 193.0663. Found: 193.0662.

3-(1-(5-Methylthiophen-2-yl)butyl)pentane-2,4-dione (38f).



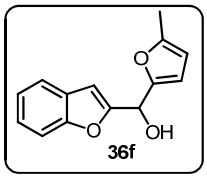
Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.4 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2979, 1724, 1723, 1455, 1362, 1254, 1178, 781. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.56 (d, *J* = 3.1 Hz, 1H), 6.50 (d, *J* = 3.1 Hz, 1H), 4.11 (d, *J* = 11.2 Hz, 1H), 3.70 (m, 1H), 2.41 (s, 3H), 2.23 (s, 3H), 1.94 (s, 3H), 1.47-1.36 (m, 2H), 1.27-1.17 (m, 2H), 0.83 (t, *J* = 11.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 203.1, 203.1, 147.4, 141.9, 138.3, 125.6, 124.7, 41.4, 37.6, 29.7, 24.8, 20.0, 14.2, 13.6. HRMS (ESI): *m/z* calcd for $C_{14}H_{20}O_2NaS$ (M+Na): 275.1082. Found: 275.1078.

2-(1-(5-Methylthiophen-2-yl)ethyl)benzofuran (38g).



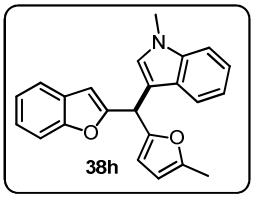
Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.6 (hexane/EtOAc = 9.5/0.5). IR (thin film, neat): ν_{max}/cm^{-1} 2974, 2925, 1585, 1453, 1374, 1253, 1166, 1046, 929, 881, 800, 744. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.41-7.38 (m, 2H), 7.16-7.06 (m, 2H), 6.66 (s, 1H), 6.56 (s, 1H), 6.62 (d, *J* = 3.2 Hz, 1H), 4.37 (q, *J* = 7.1 Hz, 1H), 2.34 (s, 3H), 1.67 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.4, 154.7, 144.1, 138.3, 128.5, 124.6, 124.0, 123.5, 122.5, 120.6, 111.0, 101.7, 35.1, 21.0, 15.3. HRMS (ESI): *m/z* calcd for $C_{15}H_{14}OSNa$ (M+Na): 265.0663. Found: 265.0658.

Benzofuran-2-yl(5-methylfuran-2-yl)methanol (36f).



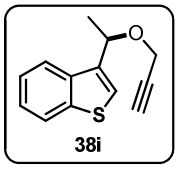
Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3390, 1614, 1557, 1451, 1220, 1020, 779, 674. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.2 Hz, 1H), 7.38 (d, *J* = 7.4 Hz, 1H), 7.20-7.12 (s, 2H), 7.14 (s, 1H), 6.17 (s, 1H), 5.88 (s, 1H), 5.87 (s, 1H), 2.53 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 156.6, 154.9, 152.8, 150.8, 128.0, 124.4, 122.9, 111.2, 111.4, 109.2, 106.4, 104.1, 64.6, 13.6. HRMS (ESI): *m/z* calcd for $C_{14}H_{12}O_2Na$ (M+Na): 251.0684. Found: 251.0682.

2-((Benzofuran-2-yl)(5-methylfuran-2-yl)methyl)-1-methyl-1*H*-indole (38h).



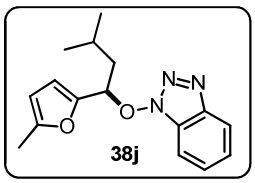
Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 9.5/0.5). IR (thin film, neat): ν_{max} /cm^{-1} 2920, 1583, 1562, 1453, 1372, 1242, 1245, 1132, 1021, 784, 741. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45-7.37 (m, 3H), 7.24-6.97 (m, 5H), 6.99 (s, 1H), 6.38 (s, 1H), 5.94 (s, 1H), 5.84 (s, 1H), 5.72 (s, 1H), 3.71 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.2, 154.9, 152.0, 151.4, 137.1, 128.6, 127.7, 126.8, 123.5, 122.2, 121.7, 120.6, 119.5, 119.3, 112.5, 111.2, 109.3, 107.9, 106.2, 103.9, 37.0, 32.8, 13.2. HRMS (ESI): *m/z* calcd for $C_{23}H_{19}O_2NNa$ (M+Na): 364.1314. Found: 364.1318.

3-(1-(Prop-2-yn-1-yloxy)ethyl)benzo[*b*]thiophene (38i).



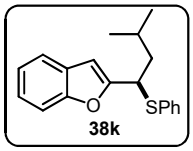
Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.7 (hexane/EtOAc = 9.5/0.5). IR (thin film, neat): ν_{max}/cm^{-1} 3292, 2979, 2932, 2855, 1457, 1427, 1442, 1372, 1354, 1254, 1007, 763. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03-8.00 (m,1H), 7.93-7.88 (m,1H), 7.43-7.56 (m, 3H), 5.14 (q, *J* = 6.5 Hz, 1H), 4.22 (dd, *J* = 15.7 and 2.4 Hz, 1H), 4.03 (dd, *J* = 15.6 and 2.4 Hz, 1H), 2.46 (t, *J* = 2.4 Hz, 1H), 1.68 (d, *J* = 6.5 Hz,3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 141.1, 37.4, 124.4, 124.1, 123.3, 122.9, 122.6, 80.0, 137.2, 74.2, 72.3, 55.6, 21.8. HRMS (ESI): *m/z* calcd for $C_{13}H_{12}OSNa$ (M+Na): 239.0507. Found: 239.0502.

1-(3-Methyl-1-(5-methylfuran-2-yl)butoxy)-1*H*-benzo[*d*][1,2,3]triazole (38j).



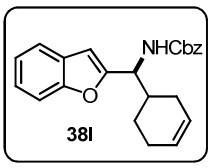
Prepared by following the procedure **B** and isolated as colorless solid. M.P. = 138-140 ˚C. R_f = 0.50 (hexane/EtOAc = 3/7). IR (KBr): ν_{max}/cm^{-1} 2973, 1737, 1461, 1422, 1373, 1244, 1046. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.5 Hz, 1H), 7.48-7.40 (m, 2H), 7.29-7.25 (m, 1H), 6.23 (d, *J* = 3.1 Hz, 1H), 5.83 (t, *J* = 6.0 Hz, 1H), 5.65 (q, *J* = 3.4 Hz, 1H), 2.40-2.32 (m, 1H), 2.20 (s, 3H), 2.10-2.02 (m, 1H), 1.39-1.34 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 3H); 0.83 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.8, 148.6, 133.4, 130.5, 130.1, 124.2, 115.6, 111.0, 109.5, 106.5, 56.1, 40.4, 24.6, 22.6, 21.7, 13.3. HRMS (ESI): *m/z* calcd for $C_{16}H_{19}O_2N_3Na$ (M+Na): 308.1375. Found: 308.1374.

2-(3-Methyl-1-(phenylthio)butyl)benzofuran (38k).



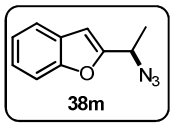
Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3015, 2958, 1583, 1454, 1253, 1216, 738. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45-7.40 (m, 2H), 7.29-7.13 (m, 7H), 6.28 (s, 1H), 4.30 (t, *J* = 7.1 Hz, 1H), 2.03-1.92 (m, 1H), 1.85 -1.70 (m, 2H), 0.90 (d, *J* = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.5, 154.7, 133.7, 133.4, 129.1, 128.7 (2C), 128.2, 127.5, 123.8, 122.6, 120.6, 111.1, 103.9, 45.4, 42.2, 26.0, 22.5, 22.1. HRMS (ESI): *m/z* calcd for $C_{19}H_{20}OSNa$ (M+Na): 319.1133; Found; 319.1130.

Benzyl (benzofuran-2-yl)(cyclohex-3-enyl)methylcarbamate (38l).



Prepared by following the procedure **B** and isolated as colorless waxy solid. R_f = 0.6 (hexane/EtOAc = 1/4). IR (thin film): ν_{max}/cm^{-1} 3104, 2954, 2867, 1698, 1530, 1045, 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 6.9 Hz, 1H), 7.20 (m, 7H), 6.62 (s, 1H), 5.73-5.64 (m, 2H), 5.21 (brs, 1H), 5.12 (ABq, *J* = 5.2 Hz, 2H), 4.85 (d, *J* = 6.6 Hz, 1H), 2.26 (m, 1H), 2.16-2.00 (m, 2H), 2.00-1.77 (m, 2H), 1.50-1.24 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.2, 156.1, 136.2, 128.5 (2CH), 128.2 (2C), 128.0, 128.3, 127.0, 126.9, 125.5, 124.0, 122.8, 120.9, 111.1, 103.9, 67.0, 54.3, 37.5, 28.5, 27.8, 24.9. HRMS (ESI): *m/z* calcd for $C_{23}H_{23}O_3NNa$ (M+Na): 384.1576. Found: 384.1572.

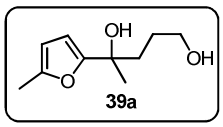
2-(1-Azidoethyl)benzofuran (38m).



38m

Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.7 (hexane/EtOAc = 9.5/0.5). IR (thin film, neat): ν_{max} /cm^{-1} 2929, 2106, 1454, 1153, 1043, 820, 746. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49-7.39 (m, 2H), 7.24-7.13 (m, 2H), 6.59 (s, 1H), 4.6 (q, *J* = 6.8 Hz, 1H), 1.59 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.9, 154.9, 127.7, 124.6, 123.0, 121.2, 111.3, 103.6, 54.4, 18.0. HRMS (ESI): *m/z* calcd for $C_{10}H_9N_3ONa$ (M+Na): 210.0644. Found: 210.0644.

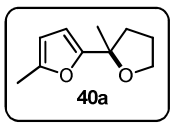
4-(5-Methylfuran-2-yl)pentane-1,4-diol (39a).



39a

Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.60 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3351, 2929, 2919, 1454, 1254, 1171, 958, 754. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.07 (s, 1H), 5.90 (s, 1H), 3.94 (t, *J* = 6.12 Hz, 2H), 2.28 (s, 3H), 1.91 (m, 2H), 1.73 (m, 2H), 1.58 (m, 2H) 1.46 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 157.9, 156.9, 119.4, 108.9, 79.8, 62.3, 29.7, 27.0, 20.0, 13.4. HRMS (ESI): *m/z* calcd for $C_{10}H_{16}O_3Na$ (M+Na): 193.0841. Found: 193.0839.

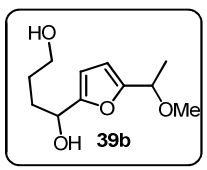
2-(Tetrahydro-2-methylfuran-2-yl)-5-methylfuran (40a).



40a

Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.80 (hexane/EtOAc = 9.5/0.5); IR (thin film, neat): ν_{max}/cm^{-1} 2956, 2925, 2624, 1686, 1536, 1467, 1220, 969, 771, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.97 (s, 1H), 5.78 (s, 1H), 3.91-3.72 (m, 1H), 2.29-2.20 (m, 1H), 2.18 (s, 6H), 1.97-1.86 (m, 2H), 1.79-1.71 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$+CCl_4): δ 156.8, 151.3, 105.7, 105.3, 79.3, 67.8, 37.0, 26.0 (2C), 13.6. HRMS (ESI): *m/z* calcd for $C_{10}H_{14}O_2Na$ (M+Na): 189.0891. Found: 189.0891.

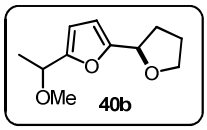
1-(5-(1-Methoxyethyl)furan-2-yl)butane-1,4-diol (39b).



39b

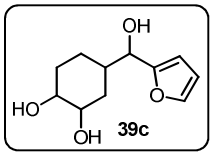
Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.6 (EtOAc/MeOH = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3354, 2954, 2874, 1253, 1108, 1098, 854, 763. **^{1}H NMR** (400 MHz, CD_3OD): δ 6.28 (d, *J* = 2.7 Hz, 1H), 6.23 (d, *J* = 2.7 Hz, 1H), 4.62 (t, *J* = 6.5 Hz, 1H), 4.38 (q, *J* = 6.5 Hz, 1H), 3.57 (t, *J* = 6.5 Hz, 2H), 3.26 (s, 3H), 1.92-1.79 (m, 2H), 1.72-1.51 (m, 2H), 1.47 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, CD_3OD): δ 156.0, 153.0, 107.0, 105.8, 71.0, 66.8, 61.3, 54.8, 31.7, 28.3, 18.0. HRMS (ESI): *m/z* calcd for $C_{11}H_{18}O_4Na$ (M+Na): 237.1103. Found: 237.1117.

2-(Tetrahydrofuran-2-yl)-5-(1-methoxyethyl)furan (40b).



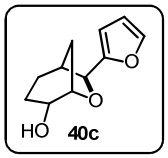
Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2855, 1564, 1340, 240, 1174, 1110, 784, 543. **^{1}H NMR** (400 MHz, C_3D_6O): δ 6.25 (s, 2H), 4.83 (t, *J* = 6.4 Hz, 1H), 4.32 (q, *J* = 6.6 Hz, 1H), 3.87 (t, *J* = 6.8 Hz, 1H), 3.78 (t, *J* = 6.8 Hz, 1H), 3.20 (s, 3H), 2.23 (m, 1H), 2.08 (m, 3H), 1.42 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (100 MHz, C_3D_6O): δ 155.2, 155.0, 107.4, 106.6, 73.5, 71.6, 67.5, 55.1, 30.1, 25.6, 18.8. HRMS (ESI): *m/z* calcd for $C_{11}H_{16}O_3Na$ (M+Na): 219.0997. Found: 219.0995.

4-(Furan-2-yl(hydroxy)methyl)cyclohexane-1,2-diol (39c).



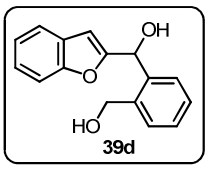
Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.6 (EtOAc). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 2924, 1563, 1260, 1021, 765, 561. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.42 (s, 1H), 6.31 (s, 1H), 6.2 (s, 1H), 4.34 (dt, *J* = 9.5 and 2.8 Hz, 1H), 3.98 (s, 1H), 3.63-3.47 (m, 2H), 1.96-1.81 (m, 2H), 1.51-1.32 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.3, 141.4, 109.5, 106.1, 71.5, 71.3, 68.6, 41.3, 29.3, 27.8, 21.3. HRMS (ESI): *m/z* calcd for $C_{11}H_{16}O_4K$ (M+K): 251.0686. Found: 251.0654.

7-(Furan-2-yl)-6-oxabicyclo[3.2.1]octan-4-ol (40c).



Prepared by following the procedure **B** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 3/2). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2855, 1563, 1434, 1260, 1218, 1021, 959, 784, 765, 561. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.30 (s, 1H), 6.39 (s, 1H), 6.20 (s, 1H), 4.88 (s, 1H), 4.40 (d, *J* = 6.7 Hz, 1H), 4.15 (q, *J* = 7.0 Hz, 2H), 3.54 (t, *J* = 7.8 Hz, 1H), 2.53 (s, 1H), 2.35-1.90 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.7, 141.9, 106.1 (2C), 81.5, 77.9, 71.9, 38.3, 34.2, 29.2, 28.1. HRMS (ESI): *m/z* calcd for $C_{11}H_{14}O_3Na$ (M +Na): 217.0841. Found: 217.0860.

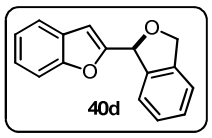
Benzofuran-2-yl(2-(hydroxymethyl)phenyl)methanol (39d).



Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 3/7). IR (thin film, neat): ν_{max}/cm^{-1} 3332, 2927, 1453, 1253 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.0 Hz, 1H), 7.37 (d, *J*

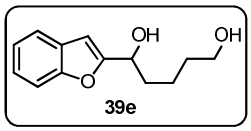
= 7.3 Hz, 1H), 7.35-7.12 (m, 6H), 6.57 (s, 1H), 6.09 (s, 1H), 4.63 (AB q, *J* = 12.0 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): 157.9, 155.0, 139.1, 138.3, 130.1, 128.5 (2CH), 128.0, 124.2, 122.9 (2CH), 121.1, 111.3, 104.0, 69.3, 63.8. HRMS (ESI): *m/z* calcd for $C_{16}H_{14}O_3Na$ (M+Na): 277.0841. Found: 277.0836.

2,3-Dihydro-2,2'-bibenzofuran (40d).



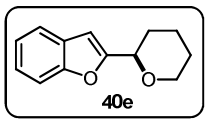
Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.6 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3050, 2858, 1602, 1456, 1353, 1254, 1172, 1030, 854. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46 (d, *J* = 7.4 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.31-7.11 (m, 5H), 6.85 (s, 1H), 6.30 (s, 1H), 5.28 (dd, *J* = 12.1 and 2.5 Hz, 1H), 5.16 (d, *J* = 12.0 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.8, 155.4, 139.5, 138.4, 128.3, 128.0, 127.6, 124.4, 122.8, 122.4, 121.2 (2CH), 111.5, 104.5, 79.5, 73.3. HRMS (ESI): *m/z* calcd for $C_{16}H_{12}O_2Na$ (M+Na): 259.0735. Found: 259.0732.

1-(Benzofuran-2-yl)pentane-1,5-diol (39e).



Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.60 (hexane/EtOAc = 2/3). IR (thin film, neat): ν_{max}/cm^{-1} 3338, 2938, 1453, 1253, 1173, 1069. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 7.1 Hz, 1H), 7.29 (d, *J* = 7.4 Hz, 1H), 7.13-7.02 (m, 2H), 6.42 (s, 1H), 4.65 (t, *J* = 6.8 Hz, 1H), 3.43 (t, *J* = 5.8 Hz, 2H), 2.79 (br s, 2H), 1.77-1.72 (m, 2H), 1.48-1.20 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): 159.6, 154.7, 126.1, 124.0, 122.7, 121.0, 111.1, 102.3, 67.9, 62.2, 35.0, 31.9, 21.6. HRMS (ESI): *m/z* calcd for $C_{13}H_{16}O_3Na$ (M+Na): 243.0997. Found: 243.0993.

2-(Tetrahydro-2*H*-pyran-2-yl)benzofuran (40e).



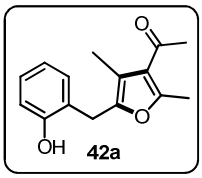
Prepared by following the procedure **B** and isolated as pale yellow oil. R_f = 0.70 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2941, 2851, 1371, 1453, 1173, 1086, 1046, 1010, 784. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 7.4 Hz, 1H), 7.37 (d, *J* = 7.04, Hz, 1H), 7.18-7.07 (m, 2H), 6.52 (s, 1H), 4.45 (dd, *J* = 10.6 and 2.0 Hz, 1H), 4.06-4.00 (m, 1H), 3.55 (dt, *J* = 11.3 and 1.36 Hz, 1H), 1.94-1.79 (m, 3H), 1.65-1.48 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.8, 154.7, 128.1, 124.1, 122.6, 121.0, 111.3,

102.7, 73.4, 68.8, 29.8, 25.7, 23.1. HRMS (ESI): *m/z* calcd for $C_{13}H_{14}O_2Na$ (M +Na): 225.0891. Found: 225.0895.

Procedure C: General procedure for triflic acid catalyzed reactions of furyl and benzofuranyl carbinols with different 1,3-dicarbonyl.

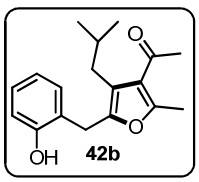
To a solution of an alcohol (0.25 mmol, 1 equiv) in nitromethane (2 mL) were added an appropriate 1,3-dicarbonyl (0.27 mmol, 1.1 equiv) followed by triflic acid (0.05 mmol, 0.2 equiv) at room temperature (30-35 ^oC). The reaction mixture was stirred at room temperature until the alcohol was consumed as monitored by TLC. Reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1-2 mL). Diluted the reaction mixture with ethyl acetate (1-2 mL) and the layers were separated. The aqueous layer was further extracted with ethyl acetate (1-2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (hexanes/ethyl acetate) to afford product **42**.

1-(5-(2-Hydroxybenzyl)-2,4-dimethylfuran-3-yl)ethanone (42a).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3354, 2925, 2851, 1650, 1455, 1253, 751. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.13 (dt, *J* = 7.7 and 1.4 Hz, 1H), 7.07 (dd, *J* = 7.4 and 1.3 Hz, 1H), 6.86 (m, 2H), 6.19 (brs, 1H, O*H*), 3.92 (s, 2H), 2.59 (s, 3H), 2.45 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.8, 157.4, 153.8, 147.7, 130.0, 127.8, 124.5, 123.1, 120.6, 115.6, 115.4, 30.8, 26.0, 15.4, 10.6. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}O_3Na$ (M+Na): 281.1154. Found: 281.1153.

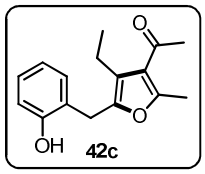
1-(5-(2-Hydroxybenzyl)-4-isobutyl-2-methylfuran-3-yl)ethanone (42b).



Prepared by following the procedure **C** and isolated as colorless solid. M.P = 98-112 ^oC. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3372, 2966, 1643, 1595, 1455, 1070, 752. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.02 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 7.1 Hz, 1H), 6.80-6.73 (m, 2H), 6.08 (brs, 1H, O*H*), 3.83 (s, 2H), 2.44 (s, 3H), 2.42 (d, *J* = 7.1 Hz, 2H), 2.35 (s, 3H), 1.75-1.62 (m, 1H), 0.81 (d, *J* = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.5, 157.2, 153.8, 148.3, 130.1, 127.8, 124.5,

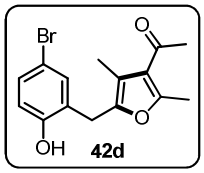
122.8, 120.6, 119.8, 115.6, 33.2, 30.7, 29.3, 26.2, 24.4, 15.6. HRMS (ESI): *m/z* calcd for $C_{18}H_{22}O_3Na$ (M+Na): 309. 1467. Found: 309.1459.

1-(5-(2-Hydroxybenzyl)-4-ethyl-2-methylfuran-3-yl)ethanone (42c).



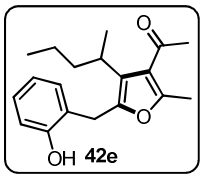
Prepared by following the procedure **C** and isolated as colorless solid. M.P = 165-170 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3354, 2925, 2851, 1667, 1455, 1234, 751. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.12 (dt, *J* = 7.7 and 1.6 Hz, 1H), 7.06 (dd, *J* = 7.4 and 1.4 Hz, 1H), 6.90-6.83 (m, 2H), 6.29 (brs, 1H, OH), 3.93 (s, 2H), 2.67 (q, *J* = 7.4 Hz, 2H), 2.54 (s, 3H), 2.47 (s, 3H), 1.10 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.5, 157.3, 153.8, 147.4, 130.0, 127.8, 124.6, 122.5, 122.3, 120.6, 115.6, 30.6, 25.9, 17.7, 15.6, 15.3. HRMS (ESI): *m/z* calcd for $C_{16}H_{18}O_3Na$ (M+Na): 281.1154. Found: 281.1157.

1-(5-(5-Bromo-2-hydroxybenzyl)-2,4-dimethylfuran-3-yl)ethanone (42d).



Prepared by following the procedure **C** and isolated as colorless solid. M.P = 132-122 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3216, 1651, 1556, 1453, 1092, 739. **^{1}H NMR** (400 MHz, 1:4 $CDCl_3$ + $(CD_3)_2CO$): δ 7.19 (d, *J* = 8.5 Hz, 1H), 7.10 (s, 1H), 6.83 (d, *J* = 8.5, 1H), 3.86 (s, 2H), 2.51 (s, 3H), 2.40 (s, 3H), 2.18 (s, 3H). **^{13}C NMR** (100 MHz, 1:4 $CDCl_3$ + $(CD_3)_2CO$): δ 193.9, 156.6, 154.2, 147.1, 132.0, 130.1, 127.5, 122.9, 116.6, 115.6, 110.8, 30.1, 24.9, 14.4, 9.0. HRMS (ESI): *m/z* calcd for $C_{15}H_{14}BrO_3$ (M+H): 321.0127. Found: 321.0121.

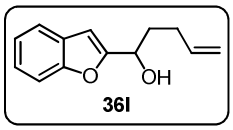
1-(5-(2-Hydroxybenzyl)-2-methyl-4-(pentan-2-yl)furan-3-yl)ethanone (42e).



Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3342, 2958, 2871, 1644, 1455, 1235, 964, 739. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.13 (dt, *J* = 7.5 and 1.5 Hz, 1H), 7.02 (dd, *J* = 7.5 and 1.5 Hz, 1H), 6.88 (dt, *J* = 7.4 and, 1.1 Hz, 1H), 6.83 (dd, *J* = 7.8 and 1.1 Hz, 1H), 3.96 (s, 2H), 3.12 (m, 1H), 2.52 (s, 3H), 2.45 (s, 3H), 1.71-1.49 (m, 4H), 1.23 (d, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.5, 156.1, 153.6, 147.0, 130.0, 127.8, 125.6, 124.6, 123.6, 120.8, 115.7, 38.3, 31.5, 29.6, 27.3,

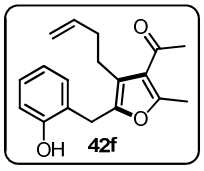
21.3, 20.3, 15.7, 14.1. HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O_3Na$ (M+Na): 323.1623. Found: 323.1628.

1-(Benzofuran-2-yl)pent-4-en-1-ol (36l).



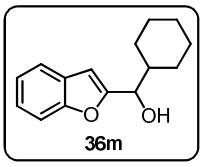
Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 3423, 1651, 1556, 1455, 1265, 1233, 754. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.2 Hz, 1H), 7.49 (d, *J* = 7.32 Hz, 1H), 7.32-7.22 (m, 2H), 6.63 (s, 1H), 5.94-5.82 (m, 1H), 5.07 (m, 2H), 4.86 (t, *J* = 6.4 Hz, 1H), 2.44 (brs, 1H, O*H*), 2.32-2.16 (m, 2H), 2.14-1.98 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.2, 154.7, 137.7, 128.1, 124.1, 122.8, 121.0, 115.4, 111.2, 102.6, 67.7, 34.5, 29.6. HRMS (ESI): *m/z* calcd for $C_{13}H_{13}O$ (M-OH): 185.0966. Found: 185.0964.

1-(4-(But-3-en-1-yl)-5-(2-hydroxybenzyl)-2-methylfuran-3-yl)ethanone (42f).



Prepared by following the procedure **C** and isolated as colorless solid. M.P = 159-162 °C. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3423, 1651, 1556, 1455, 1265, 1233, 754. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.14 (dt, *J* = 7.8 and 1.3 Hz, 1H), 7.08 (dd, *J* = 7.4 and 1.3 Hz, 1H), 6.89 (dt, *J* = 7.4 and 1.1 Hz, 1H), 6.82 (dd, *J* = 7.8 and 1.1 Hz, 1H), 5.90-5.81(m, 1H), 5.53 (brs, 1H, O*H*), 5.06-4.89 (m, 2H), 3.90 (s, 2H), 2.73 (t, *J* = 7.2 Hz, 2H), 2.55 (s, 3H), 2.45 (s, 3H), 2.21 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.9, 157.1, 153.6, 147.8, 138.3, 130.2, 128.0, 124.4, 122.7, 120.8, 120.1, 115.7, 114.9, 34.7, 30.7, 26.2, 24.0, 15.6. HRMS (ESI): *m/z* calcd for $C_{18}H_{20}O_3Na$ (M+Na): 307.1310. Found: 307.1316.

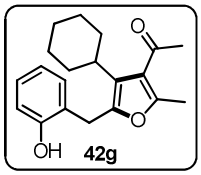
1-(Benzofuran-2-yl)-2-methylpentan-1-ol (36m).



Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3408, 2960, 2872, 14543, 1380, 1253, 1171, 1151, 963, 803, 744. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.0 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.19-7.10 (m, 2H), 6.52 (s, 1H), 4.59 (d, *J* = 5.5 Hz, 1H), 2.08 (br s, 1H), 1.37- 1.05 (m, 5H), 0.89 (d, *J* = 6.8 Hz, 3H), 0.86–0.78 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.2, 154.6, 128.2, 123.9, 122.7, 120.9, 111.2, 103.4,

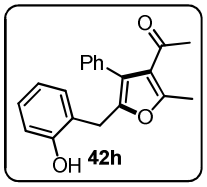
73.0, 38.3, 35.2, 20.2, 15.5, 11.4. HRMS (ESI): *m/z* calcd for $C_{14}H_{18}O_2Na$ (M+Na): 241.1204. Found: 241.1206.

1-(5-(2-Hydroxybenzyl)-4-cyclohexyl-2-methylfuran-3-yl)ethanone (42g).



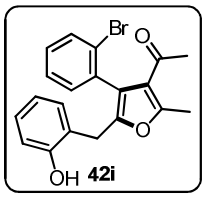
Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3354, 2925, 1644, 1455, 1217, 751. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.13 (dt, *J* = 7.6 and 1.4 Hz, 1H), 7.00 (dd, *J* = 7.6 and 1.4 Hz, 1H), 6.87 (dt, *J* = 7.1 and 1.1 Hz, 1H), 6.85 (dd, *J* = 7.8 and 1.1 Hz, 1H), 5.82 (br s, 1H, O*H*), 4.02 (s, 2H), 2.96 (tt, *J* = 11.8 and 3.6 Hz, 1H), 2.51 (s, 3H), 2.47 (s, 3H), 1.87-1.58 (m, 6H), 1.42-1.12 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.0, 156.2, 153.6, 146.9, 129.9, 127.7, 125.9, 124.8, 123.3, 120.7, 115.6, 35.0, 32.3 ($2CH_2$), 31.4, 27.6, 27.1 ($2CH_2$), 26.0, 15.6. HRMS (ESI): *m/z* calcd for $C_{20}H_{24}O_3Na$ (M+Na): 335.1623. Found: 335.1623.

1-(5-(2-Hydroxybenzyl)-2-methyl-4-phenylfuran-3-yl)ethanone (42h).



Prepared by following the procedure **C** and isolated as colorless solid. M.P = 175-179 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3216, 1651, 1556, 1453, 1092, 739, 696. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46-7.34 (m, 3H), 7.34-7.26 (m, 2H), 7.12 (dt, *J* = 7.5 and 1.6 Hz, 1H), 6.99 (dd, *J* = 7.5 and 1.5 Hz, 1H), 6.87 (dt, *J* = 7.4 and 1.1 Hz, 1H), 6.81 (dd, *J* = 8.0 and 1.0 Hz, 1H), 5.72 (brs, 1H, O*H*), 3.85 (s, 2H), 2.56 (s, 3H), 1.96 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.5, 157.4, 153.7, 148.3, 133.1, 130.0 (3CH), 128.6 (2CH), 128.0, 127.7, 124.3, 123.0, 122.0, 120.7, 115.7, 30.7, 26.4, 14.5. HRMS (ESI): *m/z* calcd for $C_{20}H_{18}O_3Na$ (M+Na): 329.1154. Found: 329.1151.

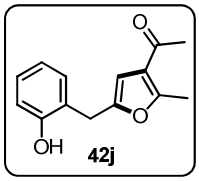
1-(5-(2-Hydroxybenzyl)-4-(2-bromophenyl)-2-methylfuran-3-yl)ethanone (42i).



Prepared by following the procedure **C** and isolated as colorless solid. M.P = 159-164 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3224, 1651, 1556, 1453, 1092, 739, 696. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.68 (dd, *J* = 8.0 and 1.0 Hz, 1H), 7.37 (dt, *J* = 7.4 and 1.2 Hz, 1H), 7.33-7.23 (m, 2H), 7.11 (dt, *J* = 7.6 and 1.6 Hz, 1H), 6.98 (dd, *J* = 7.6 and 1.6 Hz, 1H), 6.84 (dt, *J* = 7.6 and 1.0

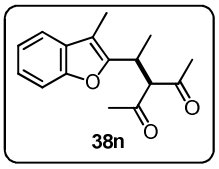
Hz, 1H), 6.77 (dd, *J* = 8.0 and 1.0 Hz, 1H), 5.31 (brs, 1H, O*H*), 3.76 (AB q, *J* = 16.2 Hz, 2H), 2.59 (s, 3H), 1.95 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.3, 157.7, 153.5, 148.6, 134.5, 132.8, 132.1, 130.3, 129.7, 128.0, 127.5, 125.5, 123.7, 122.5, 121.0, 120.8, 115.7, 29.9, 26.7, 14.8. HRMS (ESI): *m/z* calcd for $C_{20}H_{17}BrO_3Na$ (M+Na): 407.0259. Found: 407.0257.

1-(5-(2-Hydroxybenzyl)-2-methylfuran-3-yl)ethanone (42j).



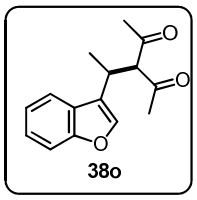
Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 3359, 2925, 2881, 1643, 1455, 1253, 741. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.17 (d, *J* = 7.5 Hz, 2H), 6.93 (dt, *J* = 6.5 and 0.9 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.23 (s, 1H), 5.23 (brs, 1H, OH), 3.95 (s, 2H), 2.57 (s, 3H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.4, 157.6, 153.6, 151.7, 130.7, 128.3, 123.6, 122.1, 121.0, 115.8, 106.7, 29.1, 28.6, 14.4. HRMS (ESI): *m/z* calcd for $C_{14}H_{14}O_3Na$ (M+Na): 253.0841. Found: 253.0891.

3-(1-(3-Methylbenzofuran-2-yl)ethyl)pentane-2,4-dione (38n).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2969, 1736, 1732, 1561, 1377, 1248, 1099, 1045, 743. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 7.4 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.17-7.09 (m, 2H), 4.30 (d, *J* = 12.7 Hz, 1H), 3.84, (dq, *J* = 12.7 and 7.0 Hz, 1H), 2.20 (s, 3H), 2.09 (s, 3H), 1.84 (s, 3H), 1.19 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 202.6, 202.4, 153.8, 153.2, 129.8, 123.7, 122.3, 119.2, 110.7, 110.5, 72.8, 31.8, 29.9, 29.7, 17.8, 7.7. HRMS (ESI): *m/z* calcd for $C_{16}H_{19}O_3Na$ (M+Na+1): 259.1256. Found: 259.1253.

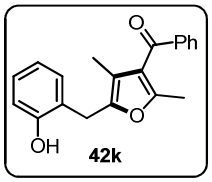
3-(-1-(Benzofuran-3-yl)ethyl)pentane-2,4-dione (38o).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2936, 2880, 1724, 1700, 1598, 1455, 1422, 1358, 1253, 1167, 1011, 942, 809, 752. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.61-7.06 (m, 5H), 4.12 (d, *J* = 11.2 Hz, 1H), 3.77 (m, 1H), 2.27 (s,

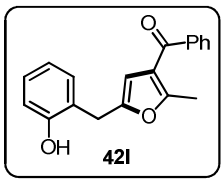
3H), 1.84 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 203.2, 203.2, 154.4, 142.2, 126.3, 124.6, 122.8, 122.0, 119.8, 111.0, 75.0, 30.4, 30.1, 29.0, 19.5. HRMS (ESI): *m/z* calcd for $C_{15}H_{16}O_3Na$ (M+Na): 267.0997. Found: 267.0994.

(5-(2-Hydroxybenzyl)-2,4-dimethylfuran-3-yl)(phenyl)methanone (42k).



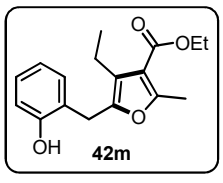
Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3342, 2958, 2871, 1644, 1455, 1235, 964, 739. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.78 (dd, *J* = 8.1 and 1.2 Hz, 2H), 7.52 (tt, *J* = 7.8 and 1.2 Hz, 1H), 7.47 (dt, *J* = 8.1 and 1.2 Hz, 2H), 7.13 (d, *J* = 7.4 Hz, 2H), 6.90 (dt, *J* = 7.4 and 1.0 Hz, 1H), 6.85 (dd, *J* = 8.3 and 1.0 Hz, 1H), 5.90 (brs, 1H, OH), 3.95 (s, 2H), 2.14 (s, 3H), 2.02 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.6, 155.5, 153.8, 147.9, 139.4, 132.5, 130.2, 129.2 (2CH), 128.4 (2CH), 127.9, 124.5, 122.6, 120.7, 115.9, 115.7, 26.3, 14.3, 9.4. HRMS (ESI): *m/z* calcd for $C_{20}H_{18}O_3K$ (M+K): 354.0893. Found: 354.0843.

5-(2-Hydroxybenzyl)-2-methylfuran-3-yl(phenyl)methanone (42l).



Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 3359, 2935, 2881, 1643, 1423, 1253, 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80-7.76 (m, 2H), 7.59-7.52 (m, 1H), 7.49-7.43 (m, 2H), 7.21-7.13 (m, 2H), 6.92 (dt, *J* = 7.4 and 1.1 Hz, 1H), 6.83 (d, *J* = 7.9 Hz, 1H), 6.25 (s, 1H), 3.98 (s, 2H), 2.49 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.5, 158.6, 153.6, 151.6, 139.2, 132.0, 130.6, 128.9 (2CH), 128.3 (2CH), 123.7, 121.2, 121.0, 115.8, 110.7, 108.1, 28.6, 14.6. HRMS (ESI): *m/z* calcd for $C_{19}H_{16}O_3Na$ (M+Na): 315.0997. Found: 315.0995.

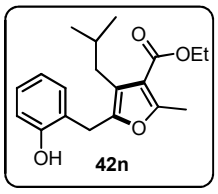
Ethyl 5-(2-hydroxybenzyl)-4-ethyl-2-methylfuran-3-carboxylate (42m).



Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3227, 2957, 2931, 1713, 1455, 1292, 724. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.13 (dt, *J* = 7.7 and 1.6 Hz, 1H), 7.07 (dd, *J* = 7.4 and 1.4 Hz, 1H), 6.89 (dt, *J* = 7.4 and 1.0 Hz, 1H), 6.83 (dd, *J* = 7.9 and 1.0 Hz, 1H), 5.47 (brs, 1H, OH), 4.3 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 2H),

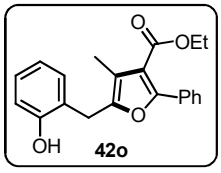
2.64 (q, *J* = 7.4 Hz, 2H), 2.52 (s, 3H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.7, 158.4, 153.6, 146.8, 130.1, 127.9, 124.7, 122.5, 120.9, 115.8, 113.1, 59.8, 26.3, 17.6, 15.3, 14.4, 14.2. HRMS (ESI): *m/z* calcd for $C_{17}H_{20}O_4$ (M^+): 288.1362. Found: 288.1312.

Ethyl 5-(2-hydroxybenzyl)-4-isobutyl-2-methylfuran-3-carboxylate (42n).



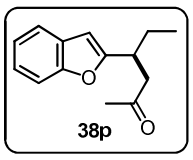
Prepared by following the procedure **C** and isolated as colorless solid. M.P = 98-102 °C. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3224, 2957, 2931, 1713, 1454, 1292, 724. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.14 (dt, *J* = 7.5 and 1.6 Hz, 1H), 7.07 (dd, *J* = 7.5 and 1.6 Hz, 1H), 6.88 (dt, *J* = 7.4 and 1.1 Hz, 1H), 6.83 (dd, *J* = 7.6 and 1.0 Hz, 1H), 5.45 (brs, 1H, OH), 4.29 (q, *J* = 7.1 Hz, 2H), 3.91 (s, 2H), 2.53 (s, 3H), 2.49 (d, *J* = 7.0 Hz, 2H), 1.91-1.79 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.9, 158.5, 153.6, 147.7, 130.2, 127.9, 124.5, 120.8, 119.9, 115.8, 113.5, 59.8, 33.2, 29.2, 26.5, 22.4 ($2CH_3$), 14.4, 14.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O_4Na$ (M+Na): 339.1572. Found: 339.1573.

Ethyl 5-(2-hydroxybenzyl)-4-methyl-2-phenylfuran-3-carboxylate (42o).



Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.4 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max} /cm^{-1} 3227, 2967, 2931, 1717, 1459, 1292, 724. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.77-7.73 (m, 2H), 7.43-7.34 (m, 3H), 7.15-7.10 (m, 2H), 6.89 (dt, *J* = 7.6 and 1.0 Hz, 1H), 6.81 (dd, *J* = 8.3 and 1.0 Hz, 1H), 5.70 (br s, 1H, OH), 4.31 (q, *J* =7.1 Hz, 2H), 4.01 (s, 2H), 2.25 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.8, 155.7, 153.5, 149.0, 130.3, 130.1, 128.8, 128.3 (2CH), 127.9 (3CH), 124.4, 120.9, 117.5, 115.6, 114.6, 60.4, 26.4, 14.1, 10.0. HRMS (ESI): *m/z* calcd for $C_{21}H_{20}O_4Na$ (M+Na): 359.1259. Found: 359.1261.

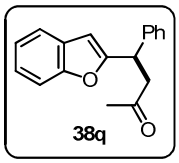
4-(Benzofuran-2-yl)hexan-2-one (38p).



Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 2963, 1716, 1455, 1359, 1253, 751. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.26-7.15 (m, 2H), 6.44 (s, 1H), 3.36 (quin, *J* = 7.0 Hz, 1H), 2.95 (dd, *J* = 16.8 and

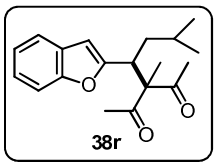
7.3 Hz, 1H), 2.77 (dd, *J* = 16.8 and 7.3 Hz, 1H), 2.14 (s, 3H), 1.75 (dq, *J* = 13.2 and 5.7 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.1, 160.3, 154.5, 128.6, 123.3, 122.5, 120.4, 110.8, 102.5, 47.2, 36.2, 30.5, 26.6, 11.6. HRMS (ESI): *m/z* calcd for $C_{14}H_{17}O_2$ (M+H): 217.1229. Found: 217.1227.

4-(Benzofuran-2-yl)-4-phenylbutan-2-one (38q).



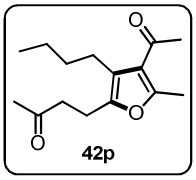
Prepared by following the procedure **C** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 2963, 1716, 1455, 1359, 1253, 751. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.37-71.7 (m, 7H), 6.43 (s, 1H), 4.78 (t, *J* = 7.3 Hz, 1H), 3.40 (dd, *J* = 17.0 and 7.3 Hz, 1H), 3.15 (dd, *J* = 17.0 and 7.3 Hz, 1H), 2.17 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.9, 159.6, 154.7, 140.9, 128.7, 128.5 (2CH), 127.9 (2CH), 127.1, 123.6, 122.6, 120.6, 111.0, 102.9, 48.0, 40.5, 30.5. HRMS (ESI): *m/z* calcd for $C_{18}H_{16}O_2Na$ (M+Na): 287.1048. Found: 287.1046.

3-(1-(Benzofuran-2-yl)-3-methylbutyl)-3-methylpentane-2,4-dione (38r).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.7 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 1732, 1698, 1454, 1373, 1094, 1046, 911, 736. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 1H),7.32 (d, *J* = 7.5 Hz, 1H), 7.18-7.08 (m, 2H), 6.41 (s, 1H), 4.03 (dd, *J* = 12.1 and 2.3 Hz, 1H), 2.08 (s, 3H), 1.92 (s, 3H), 1.76 (m, 1H), 1.43 (s, 3H), 1.26 (m, 1H), 0.98 (m, 1H), 0.88 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 206.0, 206.1, 157.1, 154.5, 128.1, 123.7, 122.7, 120.6, 111.0, 105.6, 71.1, 40.8, 37.9, 27.1, 26.9, 26.0, 23.9, 21.0, 14.9. HRMS (ESI): *m/z* calcd for $C_{19}H_{24}O_3Na$ (M+Na): 323.1623. Found: 323.1623.

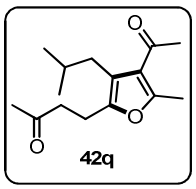
4-(4-Acetyl-3-butyl-5-methylfuran-2-yl)butan-2-one (42p).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 3055, 2959, 1715, 1665, 1359, 1265, 738. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.82-2.71 (m, 4H), 2.51 (s, 3H), 2.42 (s, 3H), 2.18 (s, 3H), 1.45-1.21 (m, 6H), 0.98 (t, *J* = 7.1 Hz, 3H, CH_2CH_3). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.3, 194.8, 156.5, 148.2, 122.6, 119.9, 41.9, 33.1,

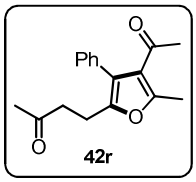
30.7, 29.9, 23.9, 22.6, 19.6, 15.4, 13.9. HRMS (ESI): *m/z* calcd for $C_{15}H_{22}O_3Na$ (M+Na): 273.1467. Found: 273.1454.

Ethyl 4-butyl-2-methyl-5-(3-oxobutyl)furan-3-carboxylate (42q).



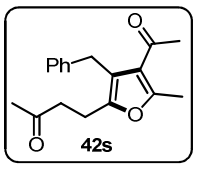
Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 2957, 2931, 1719, 1713, 1367, 1292, 1165, 754. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.28 (q, *J* = 7.1 Hz, 2H), 2.84-2.67 (m, 4H), 2.51(t, *J* = 7.3 Hz, 2H), 2.50 (s, 3H), 2.18 (s, 3H), 1.47-1.22 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.5, 164.8, 158.0, 148.2, 119.7, 112.9, 59.7, 42.0, 32.1, 30.0, 23.9, 22.7 ($2CH_2$), 19.7, 14.3, 14.0. HRMS (ESI): *m/z* calcd for $C_{16}H_{23}O_4$ (M+H): 279.1591. Found: 279.1596.

4-(4-Acetyl-3-isobutyl-5-methylfuran-2-yl)butan-2-one (42r).



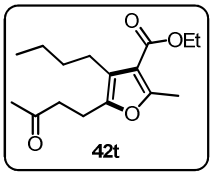
Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 3055, 2959, 1715, 1665, 1359, 1265, 738. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.69 (m, 4H), 2.43 (s, 3H), 2.33 (s, 3H), 2.31 (d, *J* = 8.1 Hz, 2H), 2.15 (s, 3H, CH_3), 1.63 (m, 1H), 0.79 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.3, 194.9, 156.4, 148.8, 122.8, 118.8, 41.7, 33.2, 30.7, 29.7, 29.2, 22.3 ($2CH_3$), 19.7, 15.4. HRMS (ESI): *m/z* calcd for $C_{15}H_{22}O_3K$ (M+K): 289.1206. Found: 289.1405.

4-(4-Acetyl-5-methyl-3-phenylfuran-2-yl)butan-2-one (42s).



Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 1716, 1673, 1561, 1418, 1315, 952, 761. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.44-7.33 (m, 3H), 7.28-7.23 (m, 2H), 2.80-2.69 (m, 4H), 2.54 (s, 3H), 2.12 (s, 3H), 1.91 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.0, 196.0, 156.5, 148.9, 133.2, 129.9 (2CH), 128.5 (2CH), 127.6, 123.0, 121.1, 41.6, 30.7, 29.8, 20.1, 14.3. HRMS (ESI): *m/z* calcd for $C_{17}H_{18}O_3Na$ (M+Na): 293.1154. Found: 293.1163.

4-(4-Acetyl-3-benzyl-5-methylfuran-2-yl)butan-2-one (42t).

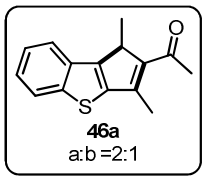


Prepared by following the procedure **C** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 2957, 2931, 1719, 1713, 1367, 1292, 1165, 754. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 4.28 (q, *J* = 7.1 Hz, 2H), 2.84-2.67 (m, 4H), 2.51(t, *J* = 7.3 Hz, 2H), 2.50 (s, 3H), 2.18 (s, 3H), 1.47-1.22 (m, 4H), 1.35 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 207.5, 164.8, 158.0, 148.2, 119.7, 112.9, 59.7, 42.0, 32.1, 30.0, 23.9, 22.7 ($2CH_2$), 19.7, 14.3, 14.0. HRMS (ESI): *m/z* calcd for $C_{16}H_{23}O_4$ $(M+1)^+$: 279.1591. Found: 279.1596.

Procedure D: General procedure for the cyclization of benzothienyl alcohols.

A mixture of the alcohol (0.1 mmol), 1,3-dicarbonyl (0.11 mmol, 1.1 equiv), and PPA (0.1 mmol, 1 equiv) in a 5 mL vial was stirred at 70 °C for an appropriate time. The reaction was monitored by using TLC periodically. Upon complete disappearance of starting material, the reaction mixture was quenched carefully with saturated aqueous solution of sodium bicarbonate, extracted 2-3 times with ethyl acetate. All the volatile organics were removed under reduced pressure. The crude product was purified by flash chromatography using silica gel to afford cyclopentannulated benzothiophenes **46**.

1-(1,3-Dimethyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)ethanone (46a, Major).

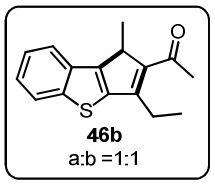


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.4 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2965, 2918, 1638, 1421, 1363, 758. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.84 (dd, *J* = 8.0 and 0.5 Hz, 1H), 7.45-7.41 (m, 1H), 7.38-7.34 (m, 1H), 3.96 (q, *J* = 7.3 Hz, 1H), 2.85 (d, *J* = 2.0 Hz, 3H), 2.51 (s, 3H), 1.54 (d, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.6, 149.8, 147.0, 146.7, 146.4, 145.0, 134.1, 124.9, 124.5, 124.1, 121.9, 43.2, 30.5, 16.2, 15.8. HRMS (ESI): *m/z* calcd for $C_{15}H_{15}OS$ $(M+H)^+$: 243.0844; Found: 243.0842.

1-(1,3-Dimethyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)ethanone (46a, Minor).

R_f = 0.4 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 1H), 7.38-7.34 (m, 1H), 3.96 (q, *J* = 7.3 Hz, 1H), 2.58 (d, *J* = 2.0 Hz, 3H), 2.49 (s, 3H), 1.49 (d, *J* = 7.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.5, 156.9, 148.2, 146.8, 146.3, 144.8, 142.0, 133.2, 124.8, 124.0, 123.9, 44.9, 30.6, 18.2, 15.6.

1-(3-Ethyl-1-methyl-1H-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)ethanone (46b, Major)

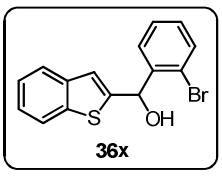


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.4 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2968, 2907, 1638, 1432, 1335, 758. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.82 (dd, *J* = 8.0 and 0.5 Hz, 1H), 7.42-7.40 (m, 1H), 7.39-7.37 (m, 1H), 3.96 (q, *J* = 7.3 Hz, 1H), 2.83 (d, *J* = 2.0 Hz, 3H), 2.51 (s, 3H), 2.12-1.98 (m, 1H), 1.54 (t, *J* = 6.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.6, 147.8, 146.3, 146.0, 145.5, 145.0, 134.1, 124.9, 124.5, 124.1, 121.9, 43.2, 30.5, 16.2, 14.2, 15.8. HRMS (ESI): *m/z* calcd for $C_{16}H_{16}OSNa$ $(M+Na)^+$: 278.0820; Found: 278.0838.

1-(3-Ethyl-1-methyl-3H-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)ethanone (46b, Minor).

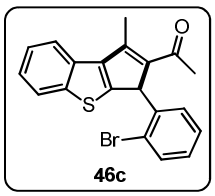
R_f = 0.4 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.41-7.39 (m, 1H), 7.38-7.34 (m, 1H), 3.96 (q, *J* = 7.3 Hz, 1H), 2.58 (d, *J* = 2.0 Hz, 3H), 2.49 (s, 3H), 2.12-1.96 (m, 2H), 1.49 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.5, 156.9, 148.2, 146.8, 146.3, 144.8, 142.0, 133.2, 124.8, 124.0, 123.9, 44.9, 30.6, 18.2, 14.2, 15.6.

Benzo[*b*]thiophen-2-yl(2-bromophenyl)methanol (36x).



Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.3 (EtOAc/Hexane = 1/9). IR (thin film, neat): ν_{max} /cm^{-1} 3350, 3058, 145.8, 1016, 746, 726. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82-7.79 (m, 1H), 7.75 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.73-7.70 (m, 1H), 7.59 (dd, J = 8.0 Hz, 1H), 7.43-7.39 (m, 1H), 7.37-7.30 (m, 2H), 7.25-7.21 (m, 1H), 7.17 (t, *J* = 0.9 Hz, 1H), 6.49 (s, 1H), 2.87 (d, *J* = 3.0 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.8, 141.5, 139.8, 139.3, 132.9, 129.6, 128.1, 127.9, 124.4, 124.3, 123.7, 122.5, 122.4, 121.9, 71.7. HRMS (ESI): *m/z* calcd for $C_{15}H_{10}BrS$ $(M+OH)^+$: 300.9687; Found: 300.9680.

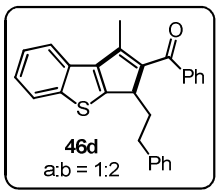
1-(3-(2-Bromophenyl)-1-methyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)ethanone (46c).



Prepared by following the procedure **D** and isolated as pale yellow solid. M.P = 165-167 °C. R_f = 0.4 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3061, 2921, 1651, 1463, 1358, 757, 740. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.12-8.10 (m, 1H), 7.82 (dt, *J* = 8.0 and 1.0 Hz, 1H), 7.72-7.70 (m, 1H), 7.46

(ddd, *J* = 8.2, 7.2 and 1.3 Hz, 1H), 7.36 (ddd, *J* = 8.2, 7.2 and 1.3 Hz, 1H), 7.16-7.10 (m, 2H), 6.82-6.79 (m, 1H), 5.63 (q, *J* = 2.3 Hz, 1H), 2.99 (d, *J* = 2.3 Hz, 3H), 2.15 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.9, 154.7, 151.9, 145.0, 143.2, 142.4, 137.7, 133.3, 132.7, 129.2, 128.3, 127.4, 125.0, 124.6, 124.4, 123.9, 121.8, 54.1, 30.1, 15.4. HRMS (ESI): *m/z* calcd for $C_{20}H_{16}BrOS$ $(M+H)^+$: 383.0105; Found: 383.0122. $[(M+2)+H]^+$: 385.0084; Found 385.0104.

(1-methyl-3-phenethyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-yl)(phenyl)methanone (46d, Major).

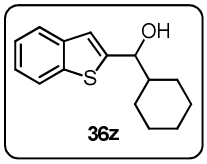


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.6 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3059, 2926, 1623, 1493, 1340, 732. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04-8.01 (m, 1H), 7.96-7.94 (m,1H), 7.81-7.78 (m, 1H), 7.60-7.52 (m, 1H), 7.50-7.46 (m, 3H), 7.44-7.40 (m, 1H), 7.26-7.14 (m, 6H), 4.35 (ddq, *J* = 8.6, 4.2 and 2.1 Hz, 1H), 3.04-2.91 (m, 3H), 2.67-2.59 (m, 1H), 2.39 (d, *J* = 2.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.1, 153.7, 148.3, 147.8, 147.2, 145.2, 144.8, 141.3 (2CH), 132.1 (2CH), 128.8 (2CH), 128.5 (2CH), 128.4 (2CH), 125.9, 124.9 (2CH), 124.1, 123.8, 121.4, 50.1, 32.3, 32.0, 16.1. HRMS (ESI): *m/z* calcd for $C_{27}H_{23}OS$ $(M+H)^+$: 395.1470; Found: 395.1519.

Ethyl 3-phenethyl-1-phenyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46d, Minor).

R_f = 0.6 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95-7.93 (m, 1H), 7.89-7.87 (m, 1H), 7.87-7.78 (m, 1H), 7.6-7.5 (m, 1H), 7.48-7.46 (m, 3H), 7.44-7.40 (m, 1H), 7.26-7.14 (m, 5H), 7.00-6.98 (m, 1H), 4.25 (q, *J* = 7.5 Hz, 1H), 2.41-2.32 (m, 2H), 1.99 (dddd, *J* = 13.5, 10.7, 8.7 and 4.8 Hz, 2H), 1.47 (d, *J* = 7.5 Hz, 3H) . **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.5, 149.7, 145.2, 145.0, 144.5, 143.2, 140.7 (2CH), 140.6 (2CH), 134.0, 132.0, 128.6, 128.5 (2CH), 128.4 (2CH), 128.3 (2CH), 126.2, 124.4, 124.1, 121.8, 44.4, 34.8, 31.1, 14.8.

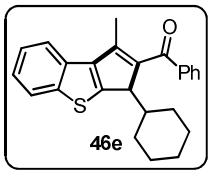
Benzo[*b*]thiophen-2-yl(cyclohexyl)methanol (36z).



Prepared by following the procedure **A** and isolated as pale yellow oil. R_f = 0.50 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max} /cm^{-1} 3397, 2952, 2851, 1449.6, 1440, 1016, 744. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.84-7.82 (m, 1H), 7.75-7.72 (m, 1H), 7.38-7.30 (m, 2H), 7.16 (s, 1H), 4.73 (dd, *J* = 7.3 and 3.3

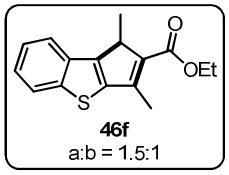
Hz, 1H), 2.16 (d, *J* = 3.5 Hz, 1H), 2.09-2.05 (m, 1H), 1.84-1.66 (m, 4H), 1.59-1.55 (m, 1H), 1.34-1.00 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.3, 139.4, 130.3, 124.3, 124.0, 123.3, 122.4, 120.8, 75.7, 45.2, 29.3, 28.6, 26.3, 25.9, 25.8. HRMS (ESI): *m/z* calcd for $C_{15}H_{17}S$ $(M+OH)^+$: 229.1051; Found: 229.1075.

3-Cyclohexyl-1-methyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophen-2-yl(phenyl)methanone (46e).



Prepared by following the procedure **D** and isolated as colorless solid. M.P = 171-173 ˚C. R_f = 0.50 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 2917, 2848, 1607, 1574, 1463, 1339, 909, 745. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (dt, *J* = 8.1 and 0.8 Hz, 3H), 7.89 (dt, *J* = 8.3 and 0.8 Hz, 2H), 7.62-7.58 (m, 1H), 7.53-7.49 (m, 1H), 7.44-7.34 (m, 2H), 4.25 (dq, *J* = 4.0 and 2.2 Hz, 1H), 2.32 (d, *J* = 2.3 Hz, 3H), 2.21-2.14 (m, 1H), 1.84-0.73 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.1, 152.2, 146.8, 144.8, 144.9, 143.5, 140.5, 132.8, 132.1, 129.1 (2CH), 128.5 (2CH), 124.7, 123.9, 121.2, 57.0, 38.4, 31.9, 27.2, 26.6 ($2CH_2$), 26.0, 16.2. HRMS (ESI): *m/z* calcd for $C_{25}H_{25}OS$ $(M+H)^+$: 373.1626; Found: 373.1625.

Ethyl 1,3-dimethyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46f, Major).

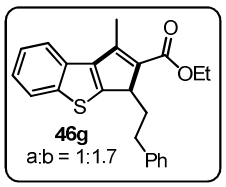


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.7 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2978, 2927, 1693, 1423, 1096, 757. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.91-7.87 (m, 1H), 7.84 (dd, *J* = 7.9 and 0.8 Hz, 1H), 7.46-7.41 (m, 1H), 7.37-7.33 (m, 1H), 4.42-4.28 (m, 2H), 3.91 (q, *J* = 7.5 Hz, 1H), 2.86 (d, *J* = 2.1 Hz, 3H), 1.59 (d, *J* = 7.5 Hz, 3H), 1.44 (t, *J* = 8.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.8, 149.4, 148.4, 145.7, 144.8, 137.2, 134.2, 124.8, 124.2, 124.1, 121.8, 59.9, 44.1, 16.0, 14.8, 14.5. HRMS (ESI): *m/z* calcd for $C_{16}H_{17}O_2S$ $(M+H)^+$: 273.0949; Found: 273.0960.

Ethyl 1,3-dimethyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46f, Minor).

R_f = 0.7 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ. 8.05 (d, *J* = 8.0 Hz, 1H), 7.91-7.87 (m,1H), 7.46-7.41 (m, 1H), 7.37-7.33 (m, 1H), 4.42-4.28 (m, 2H), 3.90 (q, *J* = 7.5 Hz, 1H), 2.59 (d, *J* = 2.1 Hz, 3H), 1.52 (d, *J* = 7.5 Hz, 3H), 1.41 (t, *J* = 8.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.8, 155.9, 149.9, 144.7, 141.8, 136.4, 133.2, 124.7, 124.2, 123.9, 121.5, 59.8, 44.1, 17.9, 14.8, 14.5.

Ethyl 1-methyl-3-phenethyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46g, Major).

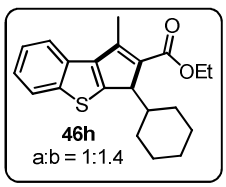


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.8 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3026, 2927, 1693, 1464, 1209, 1069, 757. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10-8.08 (m, 1H), 7.94-7.91 (m, 1H), 7.47 (td, *J* = 7.6 and 1.1 Hz, 1H), 7.41-7.36 (m, 1H), 7.32-7.28 (m, 2H), 7.23-7.18 (m, 3H), 4.41-4.23 (m, 2H), 3.98-3.91 (m, 1H), 2.87 (d, *J* = 2.3 Hz, 3H), 2.73-2.69 (m, 1H), 2.59-2.53 (m, 2H), 2.15-2.07 (m, 1H), 1.40 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.7, 153.3, 150.6, 144.6, 142.9, 141.6, 134.4, 133.0, 128.5 (2CH), 128.3 (2CH), 125.9, 124.8, 123.9, 123.7, 121.5, 59.7, 49.0, 32.7, 31.7, 14.9, 14.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{23}O_2S$ $(M+H)^+$: 363.1419; Found: 363.1412.

Ethyl 1-methyl-3-phenethyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46g, Minor).

R_f = 0.8 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92-7.90 (m, 1H), 7.86-7.84 (m, 1H), 7.44 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.38-7.34 (m, 1H), 7.32-7.28 (m, 2H), 7.23-7.18 (m, 3H), 4.41-4.23 (m, 2H), 3.88-3.94 (m, 1H), 3.38-3.33 (m, 2H), 3.06 (td, *J* = 8.2 and 3.0 Hz, 2H), 1.58 (d, *J* = 7.5 Hz, 3H), 1.41 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.7, 151.7, 149.7, 144.9, 142.9, 141.2, 137.5, 134.1, 128.5 (2CH), 128.4 (2CH), 126.1, 124.7, 124.3, 124.0, 121.7, 59.9, 43.3, 35.0, 30.9, 16.1, 14.5.

Ethyl 3-cyclohexyl-1-methyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46h, Major).

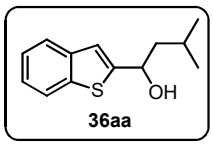


Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max} /cm^{-1} 2926, 2693, 1694, 1328, 1158, 1214, 1067, 758. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07-8.04 (m, 1H), 7.89-7.87 (m, 1H), 7.37-7.32 (m, 1H), 4.44-4.36 (m, 1H), 4.33-4.25 (m, 1H), 3.86-3.84 (m, 1H), 2.84 (d, *J* = 2.3 Hz, 3H), 2.56-2.47 (m, 1H), 1.98-1.67 (m, 9H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.21-1.06 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.9, 151.6, 144.6, 143.3, 133.8, 132.9, 124.6, 123.8, 123.4, 121.3, 59.8, 55.9, 38.4, 31.9, 26.9, 26.4, 26.3, 26.1, 26.2, 26.0, 14.9. HRMS (ESI): *m/z* calcd for $C_{21}H_{25}O_2S$ $(M+H)^+$: 341.1575; Found: 341.1578.

Ethyl 3-cyclohexyl-1-methyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46h, Minor).

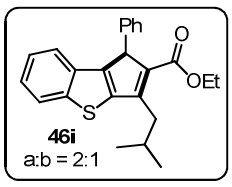
R_f = 0.5 (hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07-8.04 (m, 1H), 7.84-7.82 (m, 1H), 7.48-7.39 (m, 1H), 7.35-7.31 (m, 1H), 4.44-4.36 (m, 1H), 4.33-4.25 (m, 1H), 3.89 (q, *J* = 7.5 Hz, 1H), 2.54-2.47 (m, 1H), 1.98-1.67 (m, 8H), 1.56 (d, *J* = 7.5 Hz, 3H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.21-1.06 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.8, 158.0, 150.4, 145.3, 145.3, 141.9, 135.9, 133.5, 124.6, 124.3, 123.5, 121.6, 59.8, 42.8, 37.6, 31.8, 31.9, 26.4, 26.1, 16.2, 14.5.

1-(Benzo[*b*]thiophen-2-yl)-3-methylbutan-1-ol (36aa).



Prepared by following the procedure **A** and isolated as white solid. M.P = 76-78 ˚C. R_f = 0.4 (EtOAc/Hexane = 1/9). IR (thin film, neat): ν_{max} /cm^{-1} 3253, 2918, 2867, 1465, 1030, 747, 728. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.85-7.83 (m, 1H), 7.75-7.73 (m, 1H), 7.39-7.31 (m, 2H), 7.22 (s, 1H), 5.12-5.08 (m, 1H), 2.09 (s, 1H), 1.92-1.70 (m, 3H), 1.01 (d, *J* = 6.3 Hz, 3H), 1.00 (d, *J* = 6.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 149.8, 139.4, 139.3, 124.2, 124.1, 123.4, 122.5, 120.1, 69.1, 48.0, 24.8, 22.9, 22.8. HRMS (ESI): *m/z* calcd for $C_{13}H_{15}S$ $(M+OH)^+$: 203.0894; Found: 203.0890.

Ethyl 3-isobutyl-1-methyl-1*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46i, Major).



Prepared by following the procedure **D** and isolated as pale yellow oil. R_f = 0.7 (Hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2958, 2869, 1693, 1465, 1293, 758, 731. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.43 (td, *J* = 7.5 and 1.1 Hz, 1H), 7.37-7.32 (m, 1H), 4.41-4.26 (m, 2H), 3.94 (q, *J* = 7.5 Hz, 2H), 2.95 (d, *J* = 7.3 Hz, 2H), 2.20 (m, 1H), 1.58 (d, *J* = 7.4 Hz, 3H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 3H), 1.02 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.7, 152.3, 149.6, 145.2, 144.9, 137.8, 134.0, 124.7, 124.2, 123.9, 121.7, 59.8, 43.3, 37.6, 28.8, 22.9, 22.8, 16.3, 14.5. HRMS (ESI): *m/z* calcd for $C_{19}H_{23}O_2S$ $(M+H)^+$: 315.1419; Found: 315.1413.

Ethyl 3-isobutyl-1-methyl-3*H*-benzo[*b*]cyclopenta[*d*]thiophene-2-carboxylate (46i, Minor).

R_f = 0.7 (Hexane/EtOAc = 9/1). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.44 (td, *J* = 7.5 and 1.3 Hz, 1H), 7.35 (td, *J* = 7.5 and 1.3 Hz, 1H), 4.40-4.26

(m, 2H), 3.94 (q, *J* = 7.7 Hz, 1H), 2.94 (d, *J* = 7.5 Hz, 2H), 2.85 (d, *J* = 2.3 Hz, 3H), 2.20 (d quin, *J* = 13.6 and 6.9 Hz, 1H), 1.41 (d, *J* = 7.2, 3H), 1.10 (d, *J* = 6.5 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.7, 153.9, 149.6, 145.2, 144.9, 137.8, 134.0, 124.7, 124.2, 123.8, 121.4, 59.7, 43.3, 39.7, 28.8, 26.1, 24.1, 21.7, 14.8.

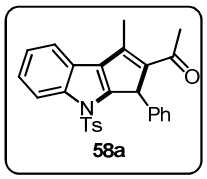
Procedure E: General procedure for the preparation of 1-(2-aminophenyl)prop-2-ynols.

To a stirred solution of the alkyne (2.2 equiv) in anhydrous THF at -78 °C was added n-butyllithium (2.0 M in cyclohexane solution, 2.2 equiv) drop wise, and the resulting solution was allowed to stir at the same temperature for 10 min. The reaction was warmed to -40 °C. The resulting mixture was stirred at the same temperature for 1 h. After 1 h reaction mixture was cooled to -78 °C. The aminoaldehyde **70** (1 mmol) was dissolved in THF (2 mL) and added to the reaction mixture drop wise at -78 °C and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **55** in 80-90% yields.

Procedure F: General procedure for the synthesis of polysubstitued cyclopenta[*b*]indoles *via* realy Au(I)/Brønsted acid catalyzed one-pot process.

A 5 mL glass vial was charged with alcohol (0.1 mmol), AuCl (2 mol%) and K_2CO_3 (2 mol%) in 1 mL of dichloroethane (DCE) and stirred at 60 ^{o}C until the alcohol was consumed as monitored by TLC. Upon disappearance of alcohol **55**, 1,3-dicarbonyls (1.1 equiv) and triflic acid (10 mol%) were added and continued stirring at 60 ^{o}C until indoline **56** and 1,3 dicarbonyl adducts **57** disappeared. Reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1-2 mL). Diluted the reaction mixture with dichloromethane (1-2 mL) and the layers were separated. The aqueous layer was further extracted with solvent (1-2 mL). The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford polysubstituted cyclopenta[*b*]indoles **58**.

1-(1-Methyl-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)ethanone (58a).

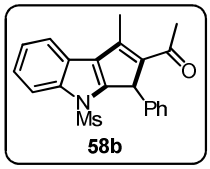


58a

Prepared by following the procedure **F** and isolated as colorless amorphous solid. M.P = 195-197 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2919, 1630, 1511, 1481, 1447, 1371, 1275, 1171, 1091, 749. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97-7.95 (m, 1H), 7.81-7.79 (m, 1H), 7.37-7.19 (m, 7H), 7.03-6.97 (m, 4H), 5.27 (q, *J* = 2.0 Hz, 1H), 2.84 (d, *J* = 2.0 Hz, 3H), 2.29 (s, 3H), 2.18 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.7 (C=O), 152.2, 148.6, 144.9, 142.1, 139.6, 135.4, 134.8, 129.6 (2CH), 129.5, 129.4, 128.6 (2CH, C), 127.2, 127.1 (2CH), 124.4, 124.1, 123.8, 119.5, 114.6, 52.8, 30.4, 21.5, 15.6. HRMS (ESI): *m/z* calcd for $C_{27}H_{24}NO_3S$ $(M+H)^+$: 442.1477, Found: 442.1484.

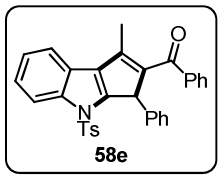
1-(2-Methyl-4-(methylsulfonyl)-3-phenyl-3,4-dihydrocyclopenta[*b*]indol-1-yl)ethanone (58b).

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 130-132 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2919, 1630, 1511, 1481, 1447, 1371, 1275, 1171, 1091, 749. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96-7.94 (m, 1H), 7.88-7.86 (m, 1H), 7.42-7.29 (m, 3H), 7.27-7.17 (m, 4H), 5.17 (q, *J* = 2.0 Hz, 1H), 2.89 (d, *J* = 2.0 Hz, 3H), 2.37 (s, 3H), 2.17 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.7, 152.3, 149.4, 141.3, 140.0, 134.6, 129.2 (2CH, 1C), 128.7 (2CH), 127.6 (2CH), 124.6, 124.0, 119.7, 114.2, 52.4, 41.5, 30.2, 15.7. HRMS (ESI): *m/z* calcd for $C_{21}H_{20}NO_3S$ $(M+H)^+$: 366.1164, Found: 366.1149.



58b

(1-Methyl-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl(phenyl)methanone (58e).

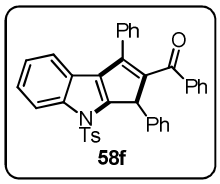


58e

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 195-197 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3503, 2915, 2852, 1608, 1474, 1445, 1375, 1174, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07-8.05 (m, 1H), 7.77-7.05 (m, 1H), 7.59-7.53 (m, 2H), 7.53-7.46 (m, 1H), 7.44-7.31 (m, 4H), 7.22-7.11 (m, 5H), 7.11-6.98 (m, 4H), 5.55 (q, *J* = 2.0 Hz, 1H), 2.34 (d, *J* = 2.0 Hz, 3H), 2.31 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.9, 152.0, 145.9, 145.7, 144.9, 143.2, 140.7, 139.8, 135.3, 134.9, 131.6, 130.0, 129.6 (2CH), 128.6, 128.5 (2CH),

128.4 (2CH), 128.2 (2CH), 127.1 (2CH), 126.9, 124.4, 124.1, 123.8, 119.3, 114.7, 63.4, 21.5, 16.6. HRMS (ESI): *m/z* calcd for $C_{32}H_{26}NO_3S$ $(M+H)^+$: 504.1633, Found: 504.1637.

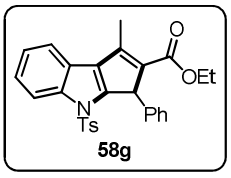
(1,3-Diphenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)(phenyl)methanone (58f).



58f

Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3057, 2918, 1658, 1608, 1467, 1375, 1174, 839, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.50-7.52 (m, 1H), 7.42-7.29 (m, 7H), 7.27-7.20 (m, 6H), 7.20-7.12 (m, 4H), 7.09-6.98 (m, 4H), 5.75 (s, 1H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.4, 151.9, 147.1, 145.0, 143.3, 139.8, 138.3, 135.2, 135.0, 133.9, 131.3, 129.7 (2CH), 129.3 (2CH), 129.2 (2CH, C), 128.7 (2CH, C), 128.6, 128.3, 127.9 (2CH), 127.4 (2CH), 127.2 (2CH, C), 124.4, 124.0, 123.6, 120.0, 114.6, 53.7, 21.5. HRMS (ESI): *m/z* calcd for $C_{37}H_{28}NO_3S$ $(M+H)^+$: 566.1790, Found: 566.1793.

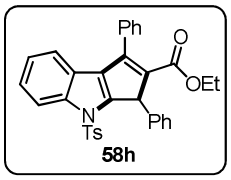
Ethyl 1-methyl-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxylate (58g).



58g

Prepared by following the procedure **F** and isolated as pale yellow solid. M.P = 166-168 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2981, 2931, 1693, 1597, 1373, 1275, 1174, 982, 703, 682. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03-8.01 (m, 1H), 7.79-7.76 (m, 1H), 7.36-7.37 (m, 2H), 7.11-7.09 (m, 2H), 7.09-6.97 (m, 6H), 5.19 (q, *J* = 2.0 Hz, 1H), 4.11 (m, 2H), 2.80 (d, *J* = 2.0 Hz, 3H), 2.31 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.5 (C=O), 151.7, 148.8, 144.7, 139.6, 136.3, 135.1, 133.1, 132.8, 129.5 (2CH), 129.3, 129.0 (2CH), 128.8 (2CH), 127.1 (2CH), 124.2, 124.1, 123.7, 119.3, 114.6, 59.6, 52.3, 21.5, 21.2, 14.8, 14.1. HRMS (ESI): *m/z* calcd for $C_{29}H_{28}NO_4S$ $(M+H)^+$: 472.1583, Found: 472.1581.

Ethyl 1,3-diphenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxylate (58h).

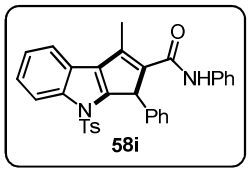


58h

Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3057, 2918, 1658, 1608, 1467, 1375, 1174, 839, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.50-7.52 (m, 1H), 7.42-7.29 (m, 7H), 7.27-7.20 (m, 6H), 7.20-7.12 (m, 4H), 7.09-6.98 (m, 4H), 5.75 (s, 1H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ

165.6, 151.9, 147.1, 145.0, 143.3, 139.8, 138.3, 135.2, 135.0, 133.9, 131.3, 129.7 (2CH), 129.3 (2CH), 129.2 (2CH, C), 128.7 (2CH, C), 128.6, 128.3, 127.9 (2CH), 127.4 (2CH), 127.2 (2CH, C), 124.4, 124.0, 123.6, 120.0, 114.6, 58.7, 53.7, 21.5 (CH_3), 21.3, 14.1. HRMS (ESI): *m/z* calcd for $C_{33}H_{28}NO_4S$ $(M+H)^+$: 534.1739, Found: 534.1728.

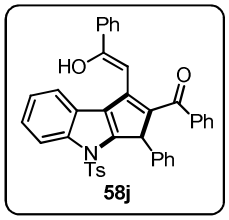
1-Methyl-N,3-diphenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxamide (58i).



58i

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 185-187 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3094, 2924, 2856, 1658, 1597, 1529, 1495, 1372, 1174, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.02-7.98 (m, 1H), 7.82-7.78 (m, 1H), 7.44-7.30 (m, 6H), 7.26-7.24 (m, 4H), 7.21-7.01 (m, 7H), 5.17 (q, *J* = 1.8 Hz, 1H), 2.90 (d, *J* = 1.8 Hz, 3H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.1, 150.0, 148.0, 144.9, 139.6, 138.0, 135.4, 134.9, 130.0, 129.6 (3CH), 129.5 (2CH), 129.3 (2CH), 128.8 (2CH), 128.3, 126.9 (2CH), 124.5, 124.1, 123.9, 123.8, 119.6 (2CH), 119.5, 114.7, 52.3, 21.5, 15.0. HRMS (ESI): *m/z* calcd for $C_{32}H_{27}N_2O_3S$ $(M+H)^+$: 519.1742, Found: 519.1757.

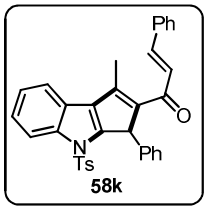
1-((2-Hydroxy-2-phenylvinyl)-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)(phenyl)methanone (58j).



58j

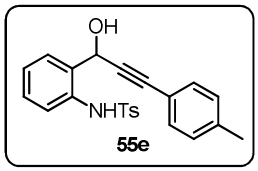
Prepared by following the procedure **F** and isolated as pale yellow solid. M.P = 225-227 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3004, 2945, 2910, 1639, 1563, 1446, 1371, 1275, 1187, 767, 664. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 16.15 (s, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.72-7.68 (m, 2H), 7.64-7.55 (m, 3H), 7.46-7.40 (m, 3H), 7.36-7.29 (m, 7H), 7.28-7.25 (m, 2H), 7.21-7.16 (m, 2H), 7.13-7.09 (m, 2H), 7.06-7.00 (m, 2H), 6.00 (s, 1H), 5.61 (s, 1H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.2, 181.8, 152.3, 147.8, 145.0, 140.9, 139.6, 135.7, 135.4, 135.1, 134.8, 131.6, 129.7 (2CH), 129.2, 129.1, 128.9 (2CH), 128.8 (4CH), 128.6 (2CH), 128.3 (2CH), 127.2 (2CH), 127.1, 126.6 (2CH), 124.5, 123.6, 119.7, 115.0, 104.5, 97.1, 52.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{39}H_{30}NO_4S$ $(M+H)^+$: 608.1896, Found: 608.1904.

1-(1-Methyl-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)-3-phenylprop-2-en-1-one (58k).



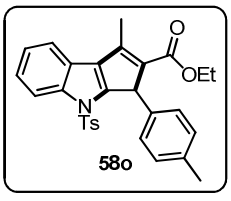
Prepared by following the procedure **F** and isolated as pale yellow solid. M.P = 114-116 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2919, 1610, 1511, 1481, 1447, 1371, 1275, 1171, 1091, 749. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.00-7.98 (m, 1H), 7.89-7.81 (m, 1H), 7.61-7.47 (m, 3H), 7.45-7.34 (m, 8H), 7.21-7.11 (m, 2H), 7.07-6.96 (m, 5H), 5.47 (q, *J* = 2.0 Hz, 1H), 2.91 (d, *J* = 2.0 Hz, 3H), 2.30 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 186.2, 152.3, 149.5, 144.9, 142.7, 141.8, 139.7, 135.3, 135.2, 134.8, 130.3, 130.0, 129.7 (2CH), 129.3, 129.0, 128.8 (2CH), 128.7 (2CH), 128.6, 128.2, 127.3, 127.2, 127.1 (2CH), 125.5, 124.5, 123.9, 119.6, 114.7, 52.7, 21.5, 15.9. HRMS (ESI): *m/z* calcd for $C_{34}H_{28}NO_3S$ $(M+H)^+$: 530.1790, Found: 530.1798.

N-(2-(1-Hydroxy-3-(*p*-tolyl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (55e).



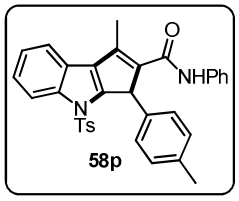
Prepared by following the procedure **E** and isolated as colorless solid. M.P = 153-155 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3446, 3276, 2897, 2356, 2229, 1597, 1494, 1330, 1158, 1021, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (br s, 1H), 7.72-7.70 (m, 3H), 7.58 (dd, *J* = 7.7 and 1.6 Hz, 1H), 7.48 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.32-7.28 (m, 2H), 7.19-7.13 (m, 5H), 5.50 (d, *J* = 5.5 Hz, 1H), 2.70 (d, *J* = 5.5 Hz, 1H), 2.38 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 139.2, 136.7, 135.5, 131.7 (2CH), 130.7, 129.7 (2CH, C), 129.1 (2CH, C), 128.3, 127.2 (2CH), 125.1, 122.7, 118.7, 88.7, 85.5, 63.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{20}NO_2S$ $(M–OH)^+$: 374.1215, Found: 374.1201.

Ethyl-1-methyl-3-(*p*-tolyl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxylate (58o).



Prepared by following the procedure **F** and isolated as colorless solid. M.P = 166-168 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2981, 2931, 1693, 1597, 1373, 1275, 1174, 982, 703, 682. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03-8.01 (m, 1H), 7.79-7.76 (m, 1H), 7.36-7.37 (m, 2H), 7.11-7.09 (m, 2H), 7.09-6.97 (m, 6H), 5.19 (q, *J* = 2.0 Hz, 1H), 4.11 (m, 2H), 2.80 (d, *J* = 2.0 Hz, 3H), 2.37 (s, 3H), 2.31 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.5, 151.7, 148.8, 144.7, 139.6, 136.3, 135.1, 133.1, 132.8, 129.5 (2CH), 129.3, 129.0 (2CH), 128.8 (2CH), 127.1 (2CH), 124.2, 124.1, 123.7, 119.3, 114.6, 59.6, 52.3, 21.5, 21.2, 14.8, 14.1. HRMS (ESI): *m/z* calcd for $C_{29}H_{28}NO_4S$ $(M+H)^+$: 486.1739, Found: 486.1733.

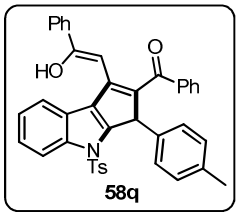
1-Methyl-N-phenyl-3-(*p*-tolyl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxamide (58p).



58p

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 193-195 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3056, 2915, 1632, 1596, 1374, 1221, 1176, 1087, 818. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03-8.00 (m, 1H), 7.81-7.79 (m, 1H), 7.38-7.34 (m, 2H), 7.29-7.24 (m, 5H), 7.20 (m, 3H), 7.13-7.14 (m, 2H), 7.05-6.92 (m, 3H), 5.13 (q, *J* = 2.0 Hz, 1H), 2.89 (d, *J* = 2.0 Hz 3H), 2.43 (s, 3H), 2.01 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.1, 150.1, 148.0, 144.8, 139.7, 138.2 (2CH), 135.0, 134.5, 132.1, 132.0, 130.1 (2CH), 130.0, 129.5 (2CH), 129.1, 128.8 (2CH), 127.0 (2CH), 124.4, 124.1, 123.9, 123.7, 119.5 (2CH), 119.4, 114.7, 51.9, 21.5, 21.2, 15.0. HRMS (ESI): *m/z* calcd for $C_{33}H_{29}N_2O_3S$ $(M+H)^+$: 533.1899, Found: 533.1877.

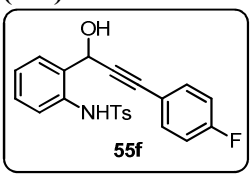
(1-(2-Hydroxy-2-phenylvinyl)-3-(*p*-tolyl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)(phenyl)methanone (58q).



58q

Prepared by following the procedure **F** and isolated as yellow coloured solid. M.P = 240-242 °C. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3178, 2965, 2930, 1629, 1563, 1436, 1376, 1275, 1197, 767, 664. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 16.15 (s, 1H), 8.02 (d, *J* = 7.2 Hz, 1H), 7.72-7.76 (m, 2H), 7.64-7.56 (m, 3H), 7.47-7.29 (m, 3H), 7.35-7.29 (m, 3H), 7.28-7.06 (m, 8H), 7.05-6.99 (m, 2H), 6.00 (s, 1H), 5.57 (s, 1H), 2.38 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 182.3, 181.8, 152.4, 147.7, 144.8, 140.9, 139.7, 136.7, 135.5, 135.2, 135.0, 132.4, 131.6, 129.6 (2CH), 129.2 (2CH), 129.0 (2CH), 128.9, 128.9, 128.8 (4CH), 128.3 (2CH), 127.2 (2CH), 126.6 (2CH), 124.6, 123.6, 123.5, 119.7, 114.5, 91.1, 52.2, 21.6, 22.3. HRMS (ESI): *m/z* calcd for $C_{40}H_{32}NO_4S$ $(M+H)^+$: 622.2052, Found: 622.2070.

N-(2-(3-(4-Fluorophenyl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzene sulfonamide (55f).

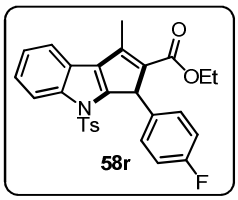


55f

Prepared by following the procedure **E** and isolated as colorless amorphous solid. M.P = 152-154 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 (br s, 1H), 7.73-7.70 (m, 2H), 7.57-7.55 (m, 1H),

7.47-7.44 (m, 2H), 7.40 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.28 (td, *J* = 7.7 and 1.6 Hz, 1H), 7.20-7.16 (m, 3H), 7.06-7.01 (m, 2H), 6.56 (s, 1H), 3.06 (br s, 1H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.8 (d, *J* = 248.2 Hz, 1C), 143.9, 136.6, 135.4, 133.4, 133.7 (2CH), 131.0, 129.7 (2CH), 128.4, 127.2 (2CH), 125.3, 122.8, 118 (d, *J* = 3.7 Hz), 115.8, 115.6 (d, *J* = 3.5 Hz), 87.2, 86.2, 63.3, 21.5. HRMS (ESI): *m/z* calcd for $C_{22}H_{17}FNO_3S$ $(M–H)^+$: 394.0913, Found: 394.0909.

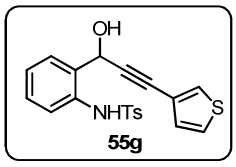
Ethyl 3-(4-fluorophenyl)-1-methyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxylate (58r).



58r

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 143-145 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3056, 2981, 2930, 1693, 1598, 1507, 1373, 1174, 1219, 737, 575. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.05-8.02 (m, 1H), 7.78-7.77 (m, 1H), 7.36-7.28 (m, 2H), 7.16-7.14 (m, 2H), 7.06-7.05 (m, 4H), 6.89 (t, *J* = 8.8 Hz, 2H), 5.19 (q, *J* = 2.0 Hz, 1H), 4.17-4.05 (m, 2H), 2.80 (d, *J* = 2.0 Hz, 3H), 2.32 (s, 3H), 1.81 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 164.4, 162.0 (d, *J* = 243.1 Hz), 151.2, 149.2, 145.0, 139.7, 135.1, 132.9, 131.7 (d, *J* = 3.5 Hz), 130.6 (d, *J* = 31.4 Hz), 129.6 (2CH, 1C), 129.5, 126.8 (2CH, 1C), 124.4, 124.0, 123.8, 119.3 (d, *J* = 11.2) 115.0, 114.3 (d, *J* = 11.6 Hz), 59.7, 51.8, 21.5, 14.8, 14.1. HRMS (ESI): *m/z* calcd for $C_{28}H_{25}FNO_4S$ $(M+H)^+$: 490.1488, Found: 490.1488.

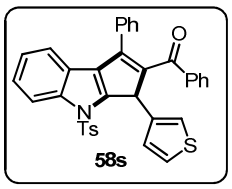
N-(2-(1-Hydroxy-3-(thiophen-3-yl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (55g).



55g

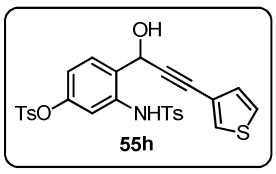
Prepared by following the procedure **E** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3430, 3263, 3107, 2925, 2232, 1597, 1492, 1400, 1330, 1157, 1090, 926, 813, 759. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (br s, 1H), 7.73-7.70 (m, 2H), 7.57-7.52 (m, 2H), 7.45 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.32-7.28 (m, 2H), 7.22-7.21 (m, 2H), 7.16-7.13 (m, 2H), 5.52 (s, 1H), 2.77 (br s, 1H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 136.7, 135.5, 130.7, 129.8 (2CH), 129.7, 129.6 (2CH), 128.4, 127.2 (2CH), 125.6, 125.2, 122.8, 120.8, 86.0, 83.7, 63.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{20}H_{16}NO_3S_2$ $(M–H)^+$: 382.0572, Found: 382.0575.

Phenyl(1-phenyl-3-(thiophen-2-yl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)methanone (58s).



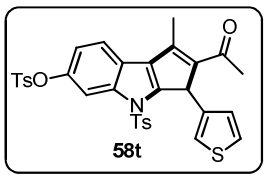
Prepared by following the procedure **F** and isolated as colorless solid. M.P = 208-210 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3068, 2915, 2852, 1612, 1578, 1174, 1092, 836, 747. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.4 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.39-7.34 (m, 8H), 7.24-7.12 (m, 8H), 7.02 (t, *J* = 7.9 Hz, 2H), 6.86 (dd, *J* = 5.0 and 1.3 Hz, 1H), 5.97 (s, 1H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.5, 150.9, 146.8, 145.0, 142.1, 139.9, 138.3, 135.1, 134.6, 133.8, 131.4 (2CH), 129.8 (2CH), 129.2 (2CH), 129.1 (2CH), 128.6 (2CH), 127.9 (2CH), 127.5 (2CH), 127.1 (2CH), 126.8, 125.1, 124.0, 123.7, 123.6, 120.0, 114.7, 49.0, 21.6. HRMS (ESI): *m/z* calcd for $C_{35}H_{26}NO_3S_2$ $(M+H)^+$: 572.1354, Found: 572.1359.

4-(1-Hydroxy-3-(thiophen-3-yl)prop-2-yn-1-yl)-3-(4-methylphenylsulfonamido)phenyl 4-methylbenzenesulfonate (55h).



Prepared by following the procedure **E** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3481, 3269, 2926, 2235, 1596, 1493, 1374, 1266, 1194, 1031, 790. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.97 c(br s, 1H), 7.69-7.66 (m, 4H), 7.53 (dd, *J* = 8.8 Hz, 1H), 7.34 (dd, *J* = 5.0 and 3.0 Hz, 1H), 7.28-7.21 (m, 6H), 7.14 (dd, *J* = 4.9 and 1.0 Hz, 1H), 6.84 (dd, *J* = 8.9 and 2.9 Hz, 1H), 5.36 (br s, 1H), 2.43 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.1, 145.6, 144.2, 136.4, 134.7, 132.0, 130.1, 129.8 (2CH, C), 129.7 (2CH), 128.4 (3CH), 127.1 (2CH), 123.5, 123.3, 124.4, 120.5, 84.9, 84.3, 62.9, 21.7, 21.6. HRMS (ESI): *m/z* calcd for $C_{27}H_{22}NO_6S_3$ $(M-H)^+$: 552.0609, Found: 552.0604.

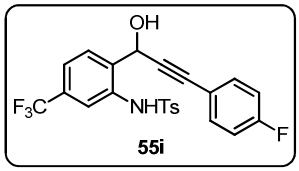
2-Acetyl-1-methyl-3-(thiophen-3-yl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-6-yl 4-methylbenzenesulfonate (58t).



Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 3/2). IR (thin film, neat): ν_{max}/cm^{-1} 2926, 2924, 1654, 1592, 1521, 1450, 1367, 1157, 1245, 1024, 690. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 9.0 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 3H), 7.41-7.31 (m, 6H), 7.19 (dd, *J* = 5.6 Hz and 3.0 Hz, 1H), 6.92 (dd, *J* = 9.0 Hz and 2.4 Hz, 1H), 6.68

(dd, *J* = 5.0 Hz and 1.2 Hz, 1H), 5.44 (q, *J* = 1.9 Hz, 1H), 2.67 (d, *J* = 1.9 Hz, 3H), 2.49 (s, 3H), 2.33 (s, 3H), 2.18 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.8, 152.3, 147.5, 145.9, 145.6, 145.4, 140.9, 137.7, 134.6 (2CH), 132.3, 129.9 (2CH), 129.8 (2CH), 128.7, 128.6 (2CH), 127.5, 127.0 (2CH), 125.5, 124.6, 124.5, 118.7, 115.2, 113.3, 48.1, 30.1, 21.7, 21.5, 15.3. HRMS (ESI): *m/z* calcd for $C_{32}H_{27}NO_6S_3$ $(M)^+$: 617.1000. Found: 617.1046.

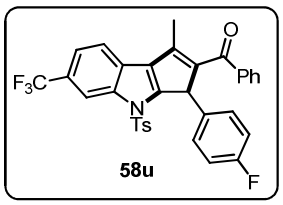
N-(2-(3-(4-Fluorophenyl)-1-hydroxyprop-2-yn-1-yl)-5-(trifluoromethyl)phenyl)-4-methylbenzenesulfonamide (55i).



55i

Prepared by following the procedure **E** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3469, 3252, 2199, 1599, 1507, 1420, 130, 1232, 1131, 1091, 968, 665, 565. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.15 (br s, 1H), 7.75-7.73 (m, 2H), 7.71 (d, *J* = 1.3 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.48-7.44 (m, 2H), 7.39-7.37 (m, 1H), 7.28-7.21 (m, 2H), 7.09-7.03 (m, 2H), 5.62 (s, 1H), 3.01 (br s, 1H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.9 (d, *J* = 249.7 Hz, 1C), 144.4, 136.3, 136.1, 133.9, 133.8, 133.4, 132.0, 129.8 (2CH, 1C), 128.9 (q, *J* = 246.0 Hz), 127.3 (2CH), 121.5 (q, *J* = 3.8 Hz), 118.9 (q, *J* = 3.8), 117.5 (d, *J* = 4.0 Hz), 115.9, 115.7, 88.0, 85.2, 63.2, 21.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{16}F_4NO_2S$ $(M–OH)^+$: 446.0838, Found: 446.0839.

(3-(4-Fluorophenyl)-1-methyl-4-tosyl-6-(trifluoromethyl)-3,4-dihydrocyclopenta[*b*]indol-2-yl)(phenyl)methanone (58u).

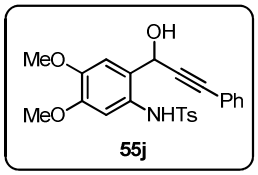


58u

Prepared by following the procedure **F** and isolated as colorless amorphous solid. M.P = 128-131 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3503, 2960, 2925, 1638, 1449, 1363, 1218, 1173, 1091, 917, 733, 665, 542. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.62-7.50 (m, 4H), 7.45-7.39 (m, 2H), 7.24-7.17 (m, 2H), 7.11-7.09 (m, 2H), 7.04-6.96 (m, 2H), 6.88-6.79 (m, 2H), 5.56 (d, *J* = 2.0 Hz, 1H), 2.35 (s, 3H), 2.33 (d, *J* = 2.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.3, 161.2 (d, *J* = 244.1 Hz), 153.7, 145.6, 144.5, 143.6, 140.2, 139.1, 134.5, 132.0, 130.5 (d, *J* = 2.9 Hz), 130.0 (2CH, C), 129.9 (2CH), 129.5 (q, *J* = 265.0 Hz), 128.5 (2CH, C), 128.4 (2CH), 126.8 (2CH), 126.4, 120.8 (q, *J* =

3.0 Hz), 119.6, 115.5, 115.3, 112.2 (q, *J* = 3.0 Hz), 52.7, 21.5, 15.7. HRMS (ESI): *m/z* calcd for $C_{33}H_{24}F_4NO_3S$ $(M+H)^+$: 590.1413, Found: 590.1416.

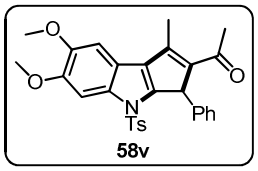
N-(2-(1-Hydroxy-3-phenylprop-2-yn-1-yl)-4,5-dimethoxyphenyl)-4-methyl benzenesulfonamide (55j).



55j

Prepared by following the procedure **E** and isolated as colorless amorphous solid. M.P = 58-60 °C. Rf = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): νmax/cm-1 3446, 3276, 2897, 2356, 2229, 1597, 1494, 1330, 1158, 1130, 1021, 815. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.09 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.38-7.34 (m, 4H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.1 (s, 1H), 6.72 (s, 1H), 5.51 (s, 1H), 3.88 (s, 3H), 3.74 (s, 3H), 3.08 (brs, 1H), 2.38 (s, 3H). 13C NMR (100 MHz, $CDCl_3$): δ 149.1, 147.2, 144.0, 136.1, 131.7 (2CH), 129.7 (2CH), 128.8, 128.4 (2CH), 127.4 (2CH), 127.1, 126.8, 122.0, 110.9, 109.2, 87.7, 81.1, 62.0, 56.0, 55.9, 21.5. HRMS (ESI): *m/z* calcd for $C_{24}H_{22}NO_4S$ $(M–OH)^+$: 420.1270, Found: 420.1265.

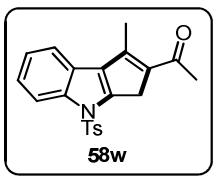
1-(6,7-Dimethoxy-1-methyl-3-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2- yl)ethanone (58v).



58v

Prepared by following the procedure **F** and isolated as colorless amorphous solid. M.P = 174-176 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): νmax/cm^{-1} 3060, 2917, 1649, 1579, 1492, 1366, 1301, 1169, 1086, 907. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (s, 1H), 7.28-7.23 (m, 3H), 7.71 (s, 3H), 7.06-6.99 (m, 4H), 6.17 (s, 1H), 3.97 (s, 6H), 2.81 (s, 3H), 2.30 (s, 3H), 2.15 (s, 3H). 13C NMR (100 MHz, $CDCl_3$): δ 194.9, 150.7, 148.8, 147.8, 147.4, 145.0, 142.1, 135.7, 134.9, 134.0, 130.0, 129.7 (2CH), 129.4, 128.6 (2CH), 127.2, 126.9 (2CH, 1C), 117.0, 101.2, 98.7, 56.4 ($2CH_3$), 52.9, 30.5, 21.6, 15.8. HRMS (ESI): *m/z* calcd for $C_{29}H_{28}NO_5S$ $(M+H)^+$: 502.1688, Found: 502.1676.

1-(1-Methyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-2-yl)ethanone (58w).

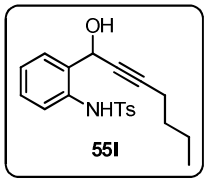


58w

Prepared by following the procedure **F** and isolated as colorless solid. M.P = 185-187 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3082, 2922, 2856, 1646, 1598, 1493, 1369, 1275, 1174, 1090, 915, 748. **^{1}H**

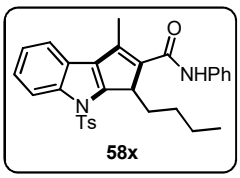
NMR (400 MHz, $CDCl_3$): δ 8.13-8.06 (m, 1H), 7.85-7.79 (m, 3H), 7.74-7.69 (m, 4H), 4.04 (q, *J* = 2.4 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 3H), 2.45 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 194.7, 149.2, 146.8, 145.6, 139.8, 134.9, 134.4, 131.2, 130.1 (2CH), 126.6 (2CH), 124.6, 124.4, 123.9, 119.3, 114.5, 36.2, 29.6, 21.6, 15.6. HRMS (ESI): *m/z* calcd for $C_{21}H_{20}NO_3S$ $(M+H)^+$: 366.1164, Found: 366.1169.

N-(2-(1-Hydroxyhept-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (55l).



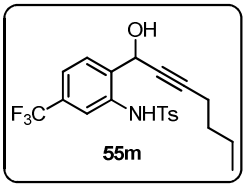
Prepared by following the procedure **E** and isolated as colorless amorphous solid. M.P = 93-95 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3487, 3262, 2956, 2165, 1598, 1493, 1331, 1159, 1091, 924, 759. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71-7.68 (m, 2H), 7.51-7.49 (m, 2H), 7.29-7.23 (m, 3H), 7.13 (td, *J* = 7.5, 7.5 and 1.3 Hz, 1H), 5.23 (s, 1H), 2.40 (s, 3H), 2.29 (td, *J* = 7.2 and 2.0 Hz, 2H), 1.56-1.51 (m, 2H), 1.46-1.40 (m, 4H), 0.94 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 136.8, 135.5, 131.2, 129.6 (2CH), 129.4, 128.1, 127.1 (2CH), 125.0, 122.7, 89.6, 77.6, 63.0, 30.4, 22.0, 21.5, 18.5, 13.5. HRMS (ESI): *m/z* calcd for $C_{20}H_{23}NNaO_3S$ $(M+Na)^+$: 380.1296, Found: 380.1299.

3-Butyl-1-methyl-N-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole-2-carboxamide (58x).



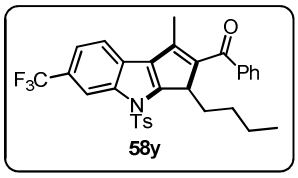
Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2958, 2957, 1598, 1530, 1498, 1442, 1371, 1174, 1023, 750, 665. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.15-8.07 (m, 1H), 7.76-7.61 (m, 4H), 7.45-7.29 (m, 6H), 7.23-7.13 (m, 3H), 4.31 (m, 1H), 2.74 (d, *J* = 1.9 Hz, 3H), 2.58 (m, 1H), 2.33 (s, 3H), 1.47-1.14 (m, 3H), 0.97-0.85 (m, 2H), 0.74 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.4, 140.9, 145.2, 143.6, 140.8, 138.0, 135.5, 134.6, 131.5, 129.8 (2CH), 129.1 (2CH), 126.6 (2CH), 124.9, 124.3 (2CH), 124.2, 120.0 (2CH), 119.1, 115.4, 47.8, 30.0, 25.6, 22.7, 21.5, 14.7, 13.8. HRMS (ESI): *m/z* calcd for $C_{30}H_{31}N_2O_3S$ $(M+H)^+$: 499.2055, Found: 499.2062.

N-(2-(1-Hydroxyhept-2-yn-1-yl)-5-(trifluoromethyl)phenyl)-4- methylbenzene sulfonamide (55m).



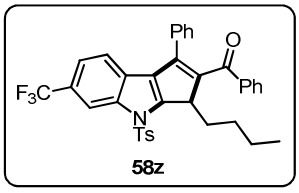
Prepared by following the procedure **E** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3469, 3252, 2198, 1579, 1507, 1470, 130, 1232, 1131, 1091, 968, 665, 565. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.16 (br s, 1H), 7.73-7.71(m, 3H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.36-7.34 (m, 1H), 7.27-7.25 (m, 2H), 5.29 (s, 1H), 2.41 (s, 3H), 2.29 (dt, *J* = 7.3 Hz and 5.2 Hz, 2H), 1.56-1.51 (m, 2H), 1.47-1.40 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): 144.3, 136.3, 136.2, 138.8, 131.7, 131.4, 129.8 (2CH), 128.7, 127.1, 127.1 (q, *J* = 245.0 Hz), 121.3 (q, *J* = 6.0 Hz), 110.3 (q, *J* = 4.0 Hz), 90.8 (2C), 62.8, 30.3, 22.0, 21.5, 18.4, 13.5. HRMS (ESI): *m/z* calcd for $C_{21}H_{21}F_3NO_2S$ $(M–OH)^+$: 408.1245, Found: 408.1246.

(3-Butyl-1-phenyl-4-tosyl-6-(trifluoromethyl)-3,4-dihydrocyclopenta[*b*]indol-2-yl) (phenyl)methanone (58y).



Prepared by following the procedure **F** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 2957, 2923, 2883, 1629, 1577, 1515, 1148, 1325, 1173, 1124, 981, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.82-7.66 (m, 4H), 7.63-7.48 (m, 5H), 7.23 (d, *J* = 8.0 Hz, 2H), 4.61 (m, 1H), 2.52-2.39 (m, 2H), 2.36 (s, 3H), 2.18 (d, *J* = 2.0 Hz, 3H), 1.17 (m, 2H), 1.03-0.78 (m, 2H), 0.75 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 193.3, 153.9, 144.5, 144.6, 142.6, 140.4, 140.1, 134.3, 132.2, 130.9 (q, *J* = 256.0 Hz), 130.1 (3CH), 128.8 (3CH), 128.6 (3CH), 127.4, 126.7, 121.0 (q, *J* = 3.0 Hz), 119.3, 112.8 (q, *J* = 3.0 Hz), 49.1, 29.5, 26.5, 22.6, 21.6, 15.8, 13.8. HRMS (ESI): *m/z* calcd for $C_{31}H_{29}F_3NO_3S$ $(M+H)^+$: 552.1820, Found: 552.1824.

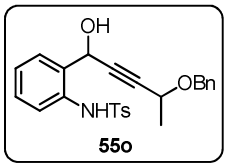
(3-Butyl-1-phenyl-4-tosyl-6-(trifluoromethyl)-3,4-dihydrocyclopenta[*b*]indol-2-yl) (phenyl)methanone (58z).



Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 2959, 2929, 2873, 1619, 1577, 1515, 1148, 1325, 1173, 1124, 981, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.48 (s, 1H), 7.78 (d, *J* = 8.4 Hz, 2H), 7.56-7.52 (m, 2H), 7.48-7.42 (m, 2H), 7.29-7.23 (m, 5H), 7.19-1.08 (m, 5H), 4.79 (t, *J* = 4.0 Hz, 1H), 2.69-2.56 (m, 1H), 2.36 (s, 3H), 2.34-2.27 (m, 1H), 1.29-1.17 (m, 2H), 1.12-0.87 (m, 2H),

0.76 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.3, 153.7, 145.6, 144.5, 142.7, 140.1, 138.1, 134.2, 133.8, 131.7, 130.1 (2CH), 129.3 (2CH), 129.1 (3CH), 128.5 (q, *J* = 267.0 Hz), 128.0 (3CH), 127.7 (2CH), 127.2, 126.7, 126.4, 120.8, 120.3 (q, *J* = 2.0 Hz), 120.0, 112.6 (q, *J* = 2.0 Hz), 49.5, 29.5, 26.5, 22.6, 21.6, 13.8. HRMS (ESI): *m/z* calcd for $C_{36}H_{29}F_3NO_3S$ $(M–H)^+$: 612.1820, Found: 612.1829.

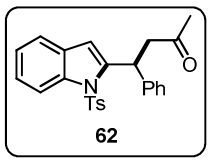
N-(2-(4-(Benzyloxy)-1-hydroxypent-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (55o).



55o

Prepared by following the procedure **E** and isolated as colorless amorphous solid. M.P = 102-105 °C. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3413, 3171, 2983, 2862, 2213, 1597, 1456, 1380, 1276, 1119, 986, 738. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71-6.68 (m, 2H), 7.53 (dd, *J* = 7.5 and 1.5 Hz, 1H), 7.38-7.34 (m, 6H), 7.25-7.22 (m, 3H), 7.15 (td, *J* = 7.5 and 1.5 Hz, 1H), 5.38 (s, 1H), 4.77 (d, *J* = 11.5 and 2.8 Hz, 1H), 4.54 (dd, *J* = 11.8 and 5.3 Hz, 1H), 4.35-4.30 (m, 1H), 2.38 (s, 3H), 1.52 (t, *J* = 7.3 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 137.6, 136.7, 135.4, 131.1, 129.7 (2CH), 129.6, 128.4 (2CH), 128.3, 128.0 (2CH), 127.8, 127.1 (2CH), 125.3, 122.9, 88.4, 82.7, 70.8, 64.5, 62.6, 21.5, 21.4. HRMS (ESI): *m/z* calcd for $C_{25}H_{25}NNaO_4S$ $(M+Na)^+$: 458.1402, Found: 458.1406.

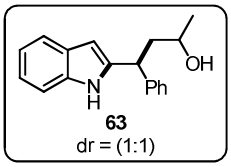
4-Phenyl-4-(1-tosyl-1*H*-indol-2-yl)butan-2-one (62).



62

Prepared by following the procedure **F** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2958, 973, 2872, 1713, 1513, 1475, 1372, 1308, 1211, 1188, 1175, 1090, 748. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (d, *J* = 8.2 Hz, 1H), 7.58-7.53 (m, 3H), 7.33-7.18 (m, 7H), 7.15-7.11 (m, 2H), 6.44 (s, 1H), 5.40 (t, *J* = 7.4 Hz, 1H), 3.34 (dd, *J* = 17.2 and 7.6 Hz, 1H), 3.08 (dd, *J* = 17.1 and 7.6 Hz, 1H), 2.32 (s, 3H), 2.17 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.8, 144.6, 143.5, 141.8, 135.6, 129.6 (2CH), 129.2, 128.6 (2CH), 128.1 (2CH, C), 126.8, 126.7 (2CH), 124.0, 123.6, 120.4, 115.1, 109.8, 51.0, 39.5, 30.1, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{23}NO_3SNa$ $(M+Na)^+$: 440.1296, Found: 440.1287.

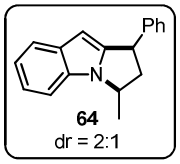
4-(1*H*-Indol-2-yl)-4-phenylbutan-2-ol (63).



63
dr = (1:1)

Prepared by following the literature procedure[77] and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 3/2). IR (thin film, neat): ν_{max}/cm^{-1} 3537, 3063, 2925, 1597, 1493, 1451, 1368, 1172, 1053, 916, 701. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.40 (br s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.37-7.22 (m, 6H), 7.15-7.07 (m, 2H), 6.40 (s, 1H), 4.40-4.35 (m, 1H), 3.92-3.66 (m, 1H), 2.32 (ddd, *J* = 12.1, 8.6 and 6.7 Hz, 1H), 2.14 (ddd, *J* = 12.1, 8.6 and 6.7 Hz, 1H), 1.29 (d, *J* = 6.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.1, 142.4, 136.1, 128.8 (2CH, 1C), 128.3 (2CH), 126.9, 121.3, 120.0, 119.6, 110.5, 98.4, 66.0, 44.5, 41.7, 24.0. HRMS (ESI): *m/z* calcd for $C_{18}H_{18}NO$ $(M–H)^+$: 264.1389, Found: 264.1380.

3-Methyl-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (64, Major).



64
dr = 2:1

Prepared by following the literature procedure[2] and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2915, 1567, 1451, 1430, 1192, 1153, 926, 701. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.60-7.58 (m, 2H), 7.40-7.36 (m, 5H), 7.19-7.16 (m, 2H), 6.12 (s, 1H), 4.54 (t, *J* = 8.5 Hz, 1H), 4.77 (qt, *J* = 8.5 and 6.7 Hz, 1H), 3.23 (ddd, *J* = 12.7, 8.5 and 6.7 Hz, 1H), 2.22 (ddd, *J* = 12.8, 8.5 and 7.8 Hz, 1H), 1.74 (t, *J* = 6.7 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.8, 142.9, 133.4, 132.2, 128.6 (2CH, C), 127.6 (2CH), 120.8, 120.3, 119.1, 109.7, 93.5, 53.2, 47.7, 43.2, 20.9. HRMS (ESI): *m/z* calcd for $C_{18}H_{18}N$ $(M+H)^+$: 248.1439, Found: 248.1475.

3-Methyl-1-phenyl-2,3-dihydro-1*H*-pyrrolo[1,2-*a*]indole (64, Minor).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.45 (m, 2H), 7.40-7.36 (m, 5H), 7.18-7.16 (m, 2H), 6.10 (s, 1H), 4.78-4.74 (m, 2H), 2.76-2.70 (m, 2H), 1.57 (d, *J* = 6.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.3, 142.8, 133.3, 132.2, 131.9, 127.7 (2CH, C), 126.8 (2CH), 120.7, 120.2, 109.5, 93.3, 51.7, 47.0, 42.2, 20.0.

Procedure G: General procedure for the preparation of 1-(2-aminophenyl)prop-2-ynols .

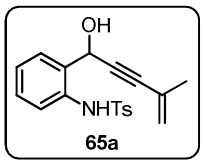
To a stirred solution of the enyne (2.2 equiv) in anhydrous THF at -78 °C was added *n*-butyllithium (2.0 M in cyclohexane solution, 2.2 equiv) drop wise, and the resulting solution was allowed to stir at the same temperature for 10 min. The reaction was warmed to -40 °C. The resulting mixture was stirred at the same temperature for 1 h. After 1 h reaction mixture was cooled to -78 °C. The aminoaldehyde **70** (1 mmol) was dissolved in THF (2 mL) and added to the reaction mixture drop wise at -78 °C and allowed to stir for 1 h at the same temperature. The

reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **65** in 80-90% yields.

Procedure H: General procedure for the synthesis of disubstitued cyclopenta[*b*]indoles *via* realy Au(I)/Brønsted acid catalyzed Nazarov-type cyclization.

To a 0.01 M solution of the alcohol **65** in DCE, AuCl (2 mol%) and K_2CO_3 (2 mol%) were added and stirred at 60 ^oC until the alcohol was consumed as monitored by TLC. Upon the disappearance of alcohol **65** an acid (10 mol%) were added and continued stirring at RT until indoline **66** disappeared. The reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1-2 mL). Diluted the reaction mixture with DCM (1-2 mL) and the layers were separated. The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by neutral alumina column chromatography (2% EtOAc/hexane) to afford product **68** and quinoline **74**.

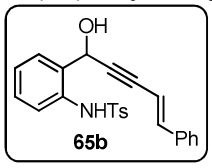
N-(2-(1-Hydroxy-4-methylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65a).



65a

Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3453, 3243, 2924, 2286, 1616, 1476, 1220, 1164, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (br s, 1H), 7.17-7.69 (m, 2H), 7.51 (dd, *J* = 7.8 and 1.5 Hz, 1H), 7.39 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.28-7.23 (m, 3H), 7.14 (td, *J* = 7.5 and 1.3 Hz, 1H), 5.41 (d, *J* = 13.8 Hz, 2H), 5.33 (d, *J* = 1.6 Hz, 1H), 2.98 (br s, 1H), 2.39 (s, 3H), 1.93 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 136.6, 135.3, 131.0, 129.7 (2CH), 129.6, 128.3, 127.2 (2CH), 125.8, 125.2, 123.3, 122.8, 89.3, 85.4, 63.1, 23.2, 21.5. HRMS (ESI): *m/z* calcd for $C_{19}H_{18}NO_2S$ $(M–OH)^+$: 324.1058, Found: 324.1060.

N-(2-(1-Hydroxy-5-phenylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65b).

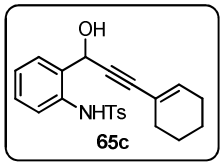


65b

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3398, 2970, 2922,

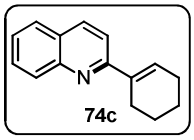
2175, 1598, 1492, 1217, 1091, 947. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (br s, 1H), 7.73-7.71 (m, 2H), 7.54 (dd, *J* = 7.7 and 1.6 Hz, 1H), 7.46 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.40-7.30 (m, 6H), 7.29-7.25 (m, 2H), 7.16 (td, *J* = 7.6 and 1.1 Hz, 1H), 7.02 (d, *J* = 16.3 Hz, 1H), 6.20 (d, *J* = 16.3 Hz, 1H), 5.49 (s, 1H), 2.82 (br s, 1H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 142.7, 136.7, 135.7, 135.4, 130.9, 129.7 (2CH, 1C), 129.0, 128.8 (2CH), 128.3, 127.2 (2CH), 126.4 (2CH), 125.2, 122.8, 106.7, 88.3, 87.6, 63.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{24}H_{20}NO_2S$ $(M–OH)^+$: 386.1215, Found: 386.1219.

N-(2-(3-(Cyclohex-1-en-1-yl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65c).



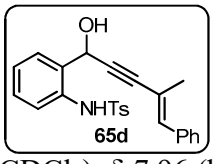
Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3343, 2914, 2286, 1624, 1396, 1220, 1154, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (br s, 1H), 7.71-7.69 (m, 2H), 7.50 (dd, *J* = 7.8 and 1.5 Hz, 1H), 7.44 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.29-7.22 (m, 3H), 7.13 (td, *J* = 7.6 and 1.1 Hz, 1H), 6.20 (t, *J* = 1.9 Hz, 1H), 5.30 (s, 1H), 2.73 (br s, 1H), 2.39 (s, 3H), 2.16-2.12 (m, 4H), 1.66-1.61 (m, 4H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 136.7, 136.6, 135.5, 130.9, 129.7 (2CH), 129.5, 128.2, 127.1 (2CH), 125.0, 122.7, 119.6, 96.5, 83.5, 63.3, 28.9, 25.6, 22.1, 21.6, 21.3. HRMS (ESI): *m/z* calcd for $C_{22}H_{22}NO_2S$ $(M–OH)^+$: 364.1371, Found: 364.1379.

2-(Cyclohex-1-en-1-yl)quinoline (74c).



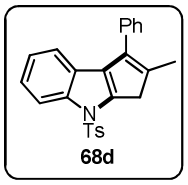
Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2925, 2916, 1491, 1371, 1174, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10-8.06 (m, 2H), 7.78 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.69 (ddd, *J* = 8.4, 6.9 and 1.5 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.49 (ddd, *J* = 8.1, 6.8 and 1.1 Hz, 1H), 6.80 (t, *J* = 3.8 Hz, 1H), 2.72 (dt, *J* = 3.8 and 1.8 Hz, 2H), 2.53-2.34 (m, 2H), 1.88-1.85 (m, 2H), 1.76-1.73 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.2, 137.7, 135.8, 130.0, 129.4 (2CH), 129.2, 127.3, 127.0, 125.6, 118.0, 26.1, 26.0, 22.8, 22.1. HRMS (ESI): *m/z* calcd for $C_{15}H_{15}N$ $(M)^+$: 209.1204, Found: 209.1208.

N-(2-(1-Hydroxy-4-methyl-5-phenylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65d).



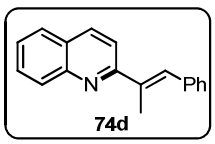
Prepared by following the procedure **G** and isolated as colorless solid. M.P = 134-136 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3072, 2921, 2853, 2212, 1494, 1323, 1173, 1092, 1018. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.96 (br s, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.56 (dd, *J* = 7.7 and 1.4 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.45-7.40 (d, *J* = 8.0 Hz, 1H), 7.40-7.36 (m, 2H), 7.31-7.24 (m, 5H), 7.19-7.14 (m, 1H), 6.91 (s, 1H), 5.47 (d, *J* = 4.3 Hz, 1H), 2.78 (brs, 1H), 2.39 (s, 3H), 2.11 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 137.3, 136.7, 136.2, 135.5, 130.9, 129.7 (2CH), 129.6, 129.0 (2CH, 1C), 128.3 (2CH), 127.5, 127.2 (2CH), 125.2, 122.8, 118.5, 92.2, 85.0, 63.3, 21.5, 19.0. HRMS (ESI): *m/z* calcd for $C_{25}H_{22}NO_2S$ $(M–OH)^+$: 400.1371, Found: 400.1362.

2-Methyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68d).



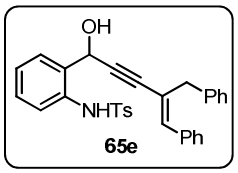
Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2929, 1598, 1450, 1375, 1163, 1091, 814. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.52-7.46 (m, 2H), 7.39-7.36 (m, 3H), 7.28-7.23 (m, 4H), 7.17-7.14 (m, 1H), 3.75 (s, 2H), 2.36 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 142.0, 139.5, 135.6, 135.4, 135.3, 134.5, 130.4, 129.9 (2CH), 128.8 (2CH), 128.3 (2CH), 127.1, 126.5 (2CH), 124.8, 123.1, 123.2, 119.6, 114.4, 40.1, 21.6, 14.8. HRMS (ESI): *m/z* calcd for $C_{25}H_{21}NO_2SNa$ $(M+Na)^+$: 422.1191, Found: 422.1192.

2-(1-Phenylprop-1-en-2-yl)quinoline (74d).



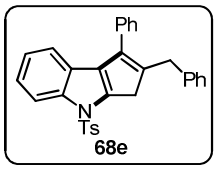
Prepared by following the procedure **H** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2935, 2925, 1498, 1396, 1186, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.8 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 8.5 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.53 (m, 4H), 7.44 (t, *J* = 7.7 Hz, 2H), 7.33 (s, 1H), 2.54 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.1, 147.7, 137.68, 137.64, 136.1, 131.7, 129.58, 129.50, 129.4 (2CH), 128.2 (2CH), 127.3, 127.1, 127.0, 126.1, 118.7, 16.1. HRMS (ESI): *m/z* calcd for $C_{18}H_{15}NNa$ $(M+Na)^+$: 268.1102, Found: 268.1113.

N-(2-(4-Benzyl-1-hydroxy-5-phenylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65e).



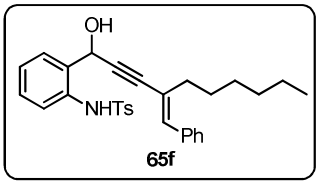
Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3471, 3272, 3063, 2186, 1598, 1494, 1375, 1164, 1091, 911. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.67 (br s, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.36-7.34 (m, 3H), 7.34-7.31 (m, 5H), 7.28-7.22 (m, 6H), 7.17-7.12 (m, 2H), 7.01 (s, 1H), 5.29 (d, *J* = 5.5 Hz, 1H), 3.81 (s, 2H), 2.53 (d, *J* = 5.5 Hz, 1H), 2.39 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 138.6, 139.4, 136.8, 135.8, 135.4, 130.8, 129.7 (2CH, 1C), 128.7 (2CH), 128.6 (2CH), 128.5 (2CH), 128.4 (2CH), 128.2, 127.9, 127.1 (2CH), 126.5, 125.2, 122.9, 122.0, 91.0, 86.5, 63.1, 37.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{31}H_{28}NO_3S$ $(M+H)^+$: 494.1790, Found: 494.1794.

2-Benzyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68e).



Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3056, 2926, 1597, 1448, 1368, 1173, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.3 Hz, 2H), 7.43-7.33 (m, 6H), 7.28-7.21 (m, 6H), 7.17 (t, *J* = 7.7 Hz, 1H), 3.93 (s, 2H), 3.70 (s, 2H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, DMSO-d_6): δ 146.2, 143.2, 141.0, 139.1, 139.0, 135.3, 129.2 (2CH, 1C), 129.1 (2CH, 1C), 128.85 (2CH, 1C), 128.81 (4CH), 126.9 (2CH, 1C), 126.6, 124.4, 124.09, 124.07, 119.5, 114.6, 37.9, 34.7, 21.4. HRMS (ESI): *m/z* calcd for $C_{31}H_{25}NNaO_2S$ $(M+Na)^+$: 498.1504, Found: 498.1512.

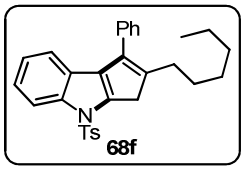
N-(2-(4-Benzylidene-1-hydroxydec-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65f).



Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3474, 3271, 3208, 2211, 1599, 1494, 1160, 1020, 924. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (br s, 1H), 7.75-7.72 (m, 2H), 7.60 (dd, *J* = 7.7 and 1.6 Hz, 1H), 7.44 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.33- 7.36 (m, 2H), 7.29-7.28 (m, 6H), 7.17 (td, *J* =7.5 and 1.3 Hz, 1H), 6.93 (s, 1H), 5.51 (s, 1H), 3.03 (br s, 1H), 2.44-2.40 (m, 2H), 2.38 (s,

3H), 1.64 (m, 2H), 1.38-1.24 (m, 6H), 0.89 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 137.1, 136.7, 136.3, 135.4, 131.3, 129.7 (2CH), 129.6, 128.8 (2CH), 128.3 (2CH, 1C), 127.4, 127.2 (2CH), 125.2, 124.5, 122.9, 90.0, 86.0, 63.2, 31.6, 31.3, 28.9, 28.5, 22.6, 21.5, 14.1. HRMS (ESI): *m/z* calcd for $C_{30}H_{33}KNO_3S$ $(M+K)^+$: 526.1818, Found: 526.1791.

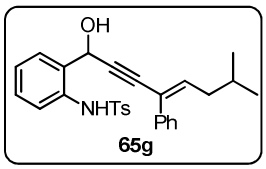
2-Hexyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68f).



68f

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2939, 1578, 1450, 1363, 1173, 1091, 814. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 (dt, *J* = 8.2 and 0.9 Hz, 1H), 7.83-7.80 (m, 2H), 7.40 (s, 1H), 7.48-7.47 (m, 2H), 7.40-7.36 (m, 1H), 7.34-7.32 (m, 3H), 7.27-7.23 (m, 2H), 7.16-7.14 (m, 1H), 3.76 (s, 2H), 2.57-2.53 (m, 2H), 2.36 (s, 3H), 1.66-1.59 (m, 2H), 1.37-1.38 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 142.3, 140.9, 139.5, 135.6, 135.4, 134.3, 130.4, 129.9 (2CH), 128.3 (3CH), 127.1 (2CH), 126.5 (2CH), 124.8, 123.1 (2CH), 119.6, 114.3, 37.6, 31.6, 30.7, 29.3, 28.9, 22.6, 21.6, 14.1. HRMS (ESI): *m/z* calcd for $C_{30}H_{32}NO_2S$ $(M+H)^+$: 470.2154, Found: 470.2154.

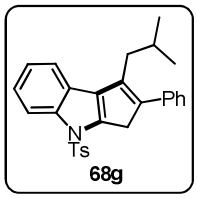
N-(2-(1-hydroxy-7-methyl-4-phenyloct-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65g).



65g

Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (br s, 1H), 7.70-7.67 (m, 2H), 7.51 (dd, *J* = 7.8 and 1.5 Hz, 1H), 7.41-7.39 (m, 1H), 7.37 (d, *J* = 2.3 Hz, 3H), 7.35-7.29 (m, 2H), 7.26-7.24 (m, 1H), 7.22-7.20 (m, 2H), 7.12 (td, *J* = 7.5 Hz, 1H), 6.33 (t, *J* = 7.7 Hz, 1H), 5.40 (s, 1H), 2.91 (br s, 1H), 2.37 (s, 3H), 2.15 (t, *J* = 7.7 Hz, 2H), 1.76-1.71 (m, 1H), 0.91 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 141.1, 137.0, 136.7, 135.4, 130.9, 129.7 (2CH), 129.5, 128.7 (2CH), 128.3, 128.2 (2CH), 127.5, 127.1 (2CH), 125.1, 122.83, 122.80, 90.6, 84.0, 63.2, 38.4, 28.5, 22.4 ($2CH_3$), 21.5. HRMS (ESI): *m/z* calcd for $C_{28}H_{29}NNaO_3S$ $(M+Na)^+$: 482.1766, Found: 482.1758.

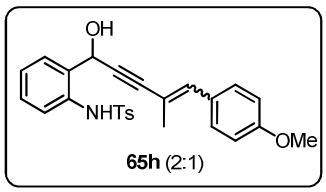
1-Isobutyl-2-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68g).



68g

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2957, 2945, 1534, 1468, 1317, 1123, 1109, 976. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.13-8.11 (m, 1H), 7.82-7.80 (m, 2H), 7.60-7.58 (m, 1H), 7.48-7.46 (m, 2H), 7.44-7.40 (m, 2H), 7.32-7.29 (m, 3H), 7.27-7.22 (m, 2H), 4.03 (s, 2H), 2.74 (d, *J* = 7.0 Hz, 2H), 2.35 (s, 3H), 2.15-2.10 (m, 1H), 0.79 (d, *J* = 6.5 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.0, 143.3, 139.5, 137.4, 137.2, 135.8, 135.3, 131.6, 129.9 (2CH), 128.4 (2CH), 128.2 (2CH), 126.6, 126.5 (2CH), 126.3, 125.1, 123.4, 119.4, 114.5, 38.2, 36.5, 28.8, 22.9 ($2CH_3$), 21.6. HRMS (ESI): *m/z* calcd for $C_{28}H_{28}NO_2S$ $(M+H)^+$: 442.1841, Found: 442.1850.

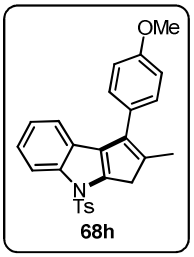
N-(2-(1-Hydroxy-5-(4-methoxyphenyl)-4-methylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65h, Major isomer).



65h (2:1)

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.82 (br s, 1H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.55 (d, *J* = 7.0 Hz, 1H), 7.43-7.40 (m, 2H), 7.28-7.15 (m, 5H), 6.99-6.84 (m, 3H), 5.47 (s, 1H), 3.83 (s, 3H), 3.04 (br s, 1H), 2.37 (s, 3H), 2.09 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.9, 143.9, 136.9, 136.7, 135.5, 133.3, 131.1, 130.4 (2CH), 129.7 (2CH), 129.5, 128.4, 128.3, 127.2, 125.1, 122.7, 116.5, 114.0, 113.8, 92.5, 84.6, 63.4, 55.3, 21.5, 19.0. HRMS (ESI): *m/z* calcd for $C_{26}H_{24}NO_4S$ $(M–H)^+$: 446.1426, Found: 446.1415.

1-(4-Methoxyphenyl)-2-methyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68h).

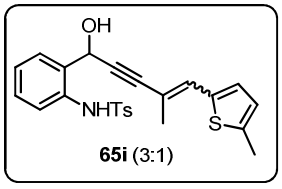


68h

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2970, 2936, 1596, 1453, 1366, 1216, 1178, 1090, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.45-7.43 (m, 3H), 7.25-7.23 (m, 3H), 7.22-7.16 (m, 1H), 7.03-7.01 (m, 2H), 3.89 (s, 3H), 3.73 (s, 2H), 2.35(s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.6, 144.9, 142.0, 139.5, 135.4, 134.6, 130.6, 129.9 (2CH), 129.8 (2CH, 1C), 127.8, 126.5 (2CH), 124.9, 123.1 (2CH), 119.6, 114.4, 113.7 (2CH),

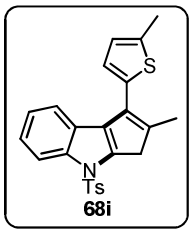
55.3, 40.0, 21.6, 14.8. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}NO_3S$ $(M)^+$: 429.1399, Found: 429.1389.

N-(2-(1-Hydroxy-4-methyl-5-(5-methylthiophen-2-yl)pent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65i, Major isomer).



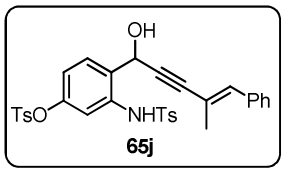
Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3398, 2970, 2922, 2175, 1598, 1492, 1217, 1091, 947. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17 (br s, 1H), 7.77-7.73 (m, 2H), 7.54-7.52 (m, 1H), 7.43-7.39 (d, *J* = 8.0 Hz, 1H), 7.28-7.22 (m, 3H), 7.10-7.07 (m, 1H), 6.93 (s, 1H), 6.88 (d, *J* = 3.2 Hz, 1H), 6.74-6.73 (m, 1H), 5.40 (d, *J* = 4.0 Hz, 1H), 2.73 (d, *J* = 4.0 Hz, 1H), 2.52 (s, 3H), 2.39 (s, 3H), 2.13 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.2, 142.4, 137.6, 136.8, 136.4, 135.2, 133.4, 131.0, 129.8 (2CH), 129.4, 129.3, 128.4, 127.2 (2CH), 125.4, 124.6, 122.1, 113.5, 93.2, 84.6, 63.3, 21.5, 15.4. HRMS (ESI): *m/z* calcd for $C_{24}H_{23}NNaO_3S_2$ $(M+Na)^+$: 460.1017, Found: 460.1021.

2-Methyl-1-(5-methylthiophen-2-yl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68i).



Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2925, 2916, 2149, 1371, 1174, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.11 (s, 1H), 7.80 (d, *J* = 7.2 Hz, 2H), 7.26-7.24 (m, 4H), 7.19 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 3.5 Hz, 1H), 3.70 (s, 2H), 2.59 (s, 3H), 2.38 (s, 3H), 2.27 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.3, 142.9, 139.6, 136.9, 135.0, 134.3, 130.1 (2CH), 129.8, 129.1 (2CH), 127.7, 126.6, 126.5, 126.5 (2CH), 125.3, 123.7, 120.6, 114.5, 40.0, 21.6, 15.6, 15.5. HRMS (ESI): *m/z* calcd for $C_{24}H_{21}NNaO_2S_2$ $(M+Na)^+$: 442.0911, Found: 442.0923.

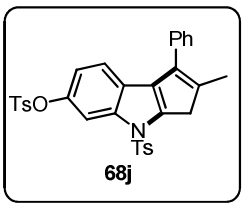
4-(1-Hydroxy-4-methyl-5-phenylpent-4-en-2-yn-1-yl)-3-(4-methylphenylsulfonamido)phenyl 4-methylbenzenesulfonate (65j).



Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3279,

2923, 2201, 1598, 1494, 1159, 1091, 922, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (br s, 1H), 7.69 (dd, *J* = 8.3 and 2.0 Hz, 4H), 7.41-7.36 (m, 4H), 7.31-7.28 (m, 6H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.87 (s, 1H), 6.84 (dd, *J* = 8.3 and 2.1 Hz, 1H), 5.33 (s, 1H), 2.42 (s, 3H), 2.39 (s, 3H), 2.08 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.1, 145.6, 144.2, 137.6, 136.4, 136.2, 134.4, 132.3, 132.0, 129.8 (2CH, 1C), 129.0 (2CH, 1C), 128.4 (2CH), 128.3 (2CH), 127.6, 127.1 (2CH), 123.5, 123.1, 122.4, 118.2, 92.6, 84.1, 62.8, 21.7, 21.6, 18.9. HRMS (ESI): *m/z* calcd for $C_{32}H_{29}NNaO_6S_2$ $(M+Na)^+$: 610.1334, Found: 610.1318.

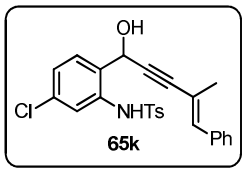
2-Methyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-6-yl, 4-methylbenzenesulfonate (68j).



68j

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3056, 2926, 1597, 1484, 1368, 1173, 919, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 9.0 and 0.5 Hz, 1H), 7.81-7.75 (m, 2H), 7.03-7.61 (m, 3H), 7.48-7.38 (m, 3H), 7.31-7.25 (m, 5H), 6.95 (dd, *J* = 9.0 and 2.5 Hz, 1H), 6.85 (d, *J* = 2.0 Hz, 1H), 3.71 (s, 2H), 2.43 (s, 3H), 2.39 (s, 3H), 2.19 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.6, 145.4, 145.1, 143.7, 137.5, 135.8, 135.0, 134.8, 133.9, 132.1, 130.0 (2CH), 129.8, 129.7, 129.5 (2CH), 129.4, 128.5 (2CH), 128.3 (2CH), 128.2, 127.2, 126.5, 124.9, 117.6, 114.8, 113.2, 40.0, 21.7, 21.6, 14.8. HRMS (ESI): *m/z* calcd for $C_{32}H_{28}NO_5S_2$ $(M+H)^+$: 570.1409, Found: 570.1403.

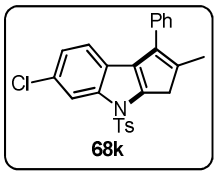
N-(5-Chloro-2-(1-hydroxy-4-methyl-5-phenylpent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65k).



65k

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3373, 3042, 2215, 1598, 1442, 1335, 1160, 937, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (br s, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.59-7.19 (m, 9H), 7.10 (d, *J* = 8.3 Hz, 1H), 6.90 (br s, 1H), 5.45 (s, 1H), 3.13 (br s, 1H), 2.38 (s, 3H), 2.09 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.3, 137.5, 136.7, 136.3, 136.2, 135.2, 129.9 (2CH), 129.4, 129.0 (2CH), 128.7, 128.4 (2CH), 127.6, 127.2 (2CH), 124.8, 121.9, 118.4, 92.4, 84.6, 63.1, 21.6, 19.0. HRMS (ESI): *m/z* calcd for $C_{25}H_{21}ClNO_3S$ $(M-H)^+$: 450.0931, Found: 450.0943.

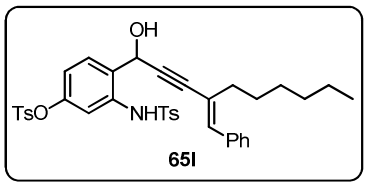
6-Chloro-2-methyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68k).



68k

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 3065, 2928, 1598, 1341, 1164, 1090, 947. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.12 (d, *J* = 1.8 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.50-7.42 (m, 4H), 7.40-7.35 (m, 1H), 7.28 (dd, *J* = 6.4 and 2.1 Hz, 3H), 7.13 (dd, *J* = 8.5 and 1.8 Hz, 1H), 3.73 (s, 2H), 2.31 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.3, 142.5, 139.7, 135.9, 135.2, 135.1, 134.2, 130.1 (2CH), 130.0, 129.0, 128.7 (2CH), 128.4 (2CH), 127.2, 126.5 (2CH), 123.7, 123.2, 120.2, 114.5, 40.0, 21.6, 14.8. HRMS (ESI): *m/z* calcd for $C_{25}H_{20}ClNNaO_2S$ $(M+Na)^+$: 456.0801, Found: 456.0804.

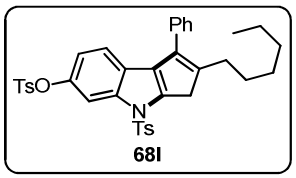
4-(4-Benzylidene-1-hydroxydec-2-yn-1-yl)-3-(4-methylphenylsulfonamido)phenyl4-methylbenzenesulfonate (65l).



65l

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.00 (br s, 1H), 7.69 (d, *J* = 8.3 Hz, 4H), 7.41-7.37 (m, 3H), 7.32-7.25 (m, 8H), 6.89 (s, 1H), 6.82 (dd, *J* = 8.9 and 2.9 Hz, 1H), 5.32 (s, 1H), 2.27 (br s, 1H), 2.43 (s, 3H), 2.41 (s, 3H), 1.66-1.57 (m, 3H), 1.35-1.26 (m, 7H), 0.88 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 146.1, 145.6, 144.2, 137.6, 136.5, 136.1, 134.4, 132.2, 129.8 (2CH, 1C), 129.7 (2CH), 128.8 (2CH), 128.4 (2CH), 128.3 (2CH), 127.6, 127.1 (2CH), 124.1, 123.4, 123.1, 122.5, 91.8, 84.6, 62.9, 31.5, 31.2, 28.9, 28.5, 22.6, 21.7, 21.6, 14.0. HRMS (ESI): *m/z* calcd for $C_{37}H_{38}NO_5S_2$ $(M–OH)^+$: 640.2191, Found: 640.2187.

2-Hexyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indol-6-yl 4-methylbenzenesulfonate (68l).

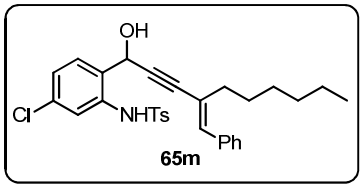


68l

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2929, 2859, 1598, 1376, 1177, 1091, 894. **^{1}H NMR** (400 MHz, $CDCl_3$): δ

7.98 (d, *J* = 9.0 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 3H), 7.41-7.36 (m, 3H), 7.29-7.23 (m, 7H), 6.94 (dd, *J* = 9.0 and 2.0 Hz, 1H), 6.80 (d, *J* = 2.3 Hz, 1H), 3.72 (s, 2H), 2.53 (m, 2H), 2.44 (s, 3H), 2.39 (s, 3H), 1.61 (m, 4H), 1.32-1.28 (m, 4H), 0.87 (t, *J* = 7.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.6, 145.3, 145.1, 144.0, 141.0, 137.6, 135.1, 135.0, 133.8, 132.1, 130.0 (2CH), 129.8, 129.5 (2CH), 128.6 (3CH), 128.4 (2CH), 128.3 (2CH), 127.2, 126.5, 125.0, 117.6, 114.8, 113.2, 37.6, 31.6, 30.6, 29.2, 28.9, 22.6, 21.7, 21.6, 14.0. HRMS (ESI): *m/z* calcd for $C_{37}H_{38}NO_5S_2$ $(M+H)^+$: 640.2191, Found: 640.2178.

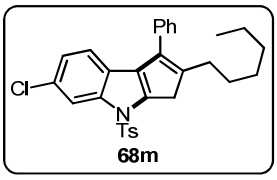
N-(2-(4-Benzylidene-1-hydroxydec-2-yn-1-yl)-5-chlorophenyl)-4-methylbenzenesulfonamide (65m).



65m

Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3424, 3269, 3062, 2956, 2928, 2176, 1598, 1493, 1373, 1091, 941. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.21 (br s, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 1.8 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.50-7.36 (m, 2H), 7.31-7.26 (m, 5H), 7.11 (dd, *J* = 8.3 and 2.0 Hz, 1H), 6.91 (s, 1H), 5.45 (s, 1H), 2.99 (br s, 1H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.39 (s, 3H), 1.63-1.57 (m, 2H), 1.35-1.24 (m, 6H), 0.88 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.2, 137.4, 136.8, 136.3, 136.2, 135.2, 129.8 (2CH), 129.3, 128.8 (2CH), 128.7, 128.4 (2CH), 127.5, 127.2 (2CH), 124.7, 124.2, 122.0, 91.4, 85.3, 63.0, 31.6, 31.2, 28.9, 28.5, 22.6, 21.6, 14.1. HRMS (ESI): *m/z* calcd for $C_{30}H_{31}NClO_2S$ $(M–OH)^+$: 504.1764, Found: 504.1768.

6-Chloro-2-hexyl-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68m).

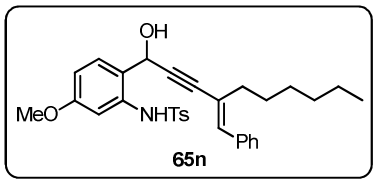


68m

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2929, 1598, 1461, 1368, 1198, 981. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 1.8 Hz, 1H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.50-7.44 (m, 4H), 7.40-7.38 (m, 1H), 7.29-7.27 (m, 2H), 7.23 (d, *J* = 8.5 Hz, 1H), 7.12 (dd, *J* = 8.4 and 1.4 Hz, 1H), 3.74 (s, 2H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.13 (s, 3H), 1.64-1.61 (m, 2H), 1.36-1.30 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.3, 142.7, 141.2, 139.7, 135.3, 135.1, 134.0, 130.0 (2CH), 130.0, 129.0, 128.7 (2CH), 128.4 (2CH), 127.2, 126.5 (2CH), 123.7, 123.2, 120.1, 114.5,

37.6, 31.6, 30.6, 29.3, 28.9, 22.6, 21.6, 14.1. HRMS (ESI): *m/z* calcd for $C_{30}H_{29}ClNO_2S$ $(M–H)^+$: 502.1608, Found: 502.1601.

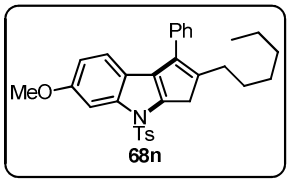
N-(2-(4-Benzylidene-1-hydroxydec-2-yn-1-yl)-5-methoxyphenyl)-4-methylbenzenesulfonamide (65n).



65n

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3243, 2924, 2186, 1614, 1496, 1220, 1164, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.37-7.28 (m, 2H), 7.27-7.25 (m, 6H), 7.16 (d, *J* = 8.8 Hz, 2H), 6.91 (s, 1H), 5.41 (s, 1H), 3.82 (s, 3H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.49 (s, 3H), 1.64-1.61 (m, 3H), 1.33-1.27 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.0, 143.9, 137.1, 136.5, 136.3, 136.1, 129.7 (2CH), 129.6, 128.8 (2CH), 128.3, 127.4, 127.2 (2CH), 127.0, 124.4, 114.4, 113.8, 90.5, 86.1, 62.3, 55.4, 31.6, 31.3, 29.7, 29.0, 28.5, 22.6, 21.6, 14.0. HRMS (ESI): *m/z* calcd for $C_{31}H_{34}NO_4S$ $(M–H)^+$: 516.2209, Found: 516.2205.

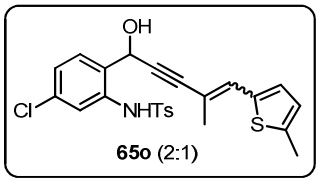
2-Hexyl-6-methoxy-1-phenyl-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68n).



68n

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2920, 2858, 1598, 1489, 1377, 1214, 1163, 1035, 814. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.48-7.45 (m, 4H), 7.41-7.36 (m, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.85 (dd, *J* = 9.0 and 2.5 Hz, 1H), 6.80 (d, *J* = 2.5 Hz, 1H), 3.73 (s, 2H), 3.72 (s, 3H), 2.54 (t, *J* = 7.2 Hz, 2H), 2.13 (s, 3H), 1.64-1.61 (m, 2H), 1.36-1.30 (m, 6H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.1, 144.8, 143.2, 140.7, 135.3, 135.2, 134.4, 134.3, 130.4, 129.8 (2CH), 128.7 (2CH), 128.6 (2CH), 127.1, 126.4 (2CH), 125.8, 115.0, 111.0, 103.2, 55.1, 37.7, 31.6, 30.6, 29.3, 28.9, 22.6, 21.5, 14.1. HRMS (ESI): *m/z* calcd for $C_{31}H_{33}NO_3S$ $(M)^+$: 499.2181, Found: 499.2193.

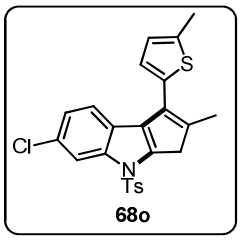
N-(5-Chloro-2-(1-hydroxy-4-methyl-5-(5-methylthiophen-2-yl)pent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65o, Major isomer).



65o (2:1)

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): 7.95-7.51 (m, 1H), 7.72-7.70 (m, 2H), 7.55-7.44 (m, 3H), 7.31-7.21 (m, 3H), 7.17-7.15 (m, 1H), 6.88 (d, *J* = 3.5 Hz, 1H), 6.73-6.66 (m, 1H), 5.43 (s, 1H), 2.73 (s, 3H), 2.39 (s, 3H), 2.14 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 142.9, 142.2, 137.7, 135.4, 133.3, 130.8, 128.7 (2CH), 129.6, 129.2, 128.3, 127.2 (2CH), 125.4, 125.2, 113.8, 92.8, 85.2, 82.3, 63.5, 21.5, 19.4, 15.4. HRMS (ESI): *m/z* calcd for $C_{24}H_{21}ClNO_2S_2$ $(M–OH)^+$: 454.0702, Found: 454.0710.

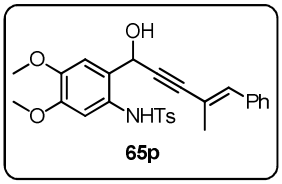
6-Chloro-2-methyl-1-(5-methylthiophen-2-yl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68o).



68o

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2934, 2917, 1449, 1361, 1227, 1191, 1086, 865. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.2 Hz, 1H), 7.78 (dd, *J* = 7.56 and 0.4 Hz, 2H), 7.18-7.16 (m, 1H), 7.27-7.11 (m, 3H), 7.01 (d, *J* = 3.4 Hz, 1H), 6.81-6.80 (m, 1H), 3.73 (s, 2H), 2.57 (s, 3H), 2.56 (s, 3H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.0, 141.9, 139.4, 134.3, 134.6, 130.0, 129.9 (3CH), 128.0 (2CH), 126.6, 126.5 (2CH), 125.2, 124.7, 123.2, 122.3, 119.9, 114.3, 40.0, 21.6, 15.3, 15.2. HRMS (ESI): *m/z* calcd for $C_{24}H_{20}ClNNaO_2S_2$ $(M+Na)^+$: 476.0522, Found: 476.0529.

N-(2-(1-Hydroxy-4-methyl-5-phenylpent-4-en-2-yn-1-yl)-4,5-dimethoxyphenyl)-4-methylbenzenesulfonamide (65p).

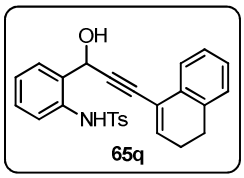


65p

Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3457, 3269, 2937, 2214, 1598, 1515, 1346, 1265, 1162, 1009, 737. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.82 (d, *J* = 8.5 Hz, 1H), 7.66-7.64 (m, 2H), 7.38-7.31 (m, 2H), 7.28-7.24 (m, 6H), 7.16 (s, 1H), 6.86 (s, 1H), 6.68 (s, 1H), 5.47 (s, 1H), 3.82 (s, 3H), 3.71 (s, 3H), 2.39 (s, 3H), 2.03 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 149.0, 147.2, 144.0, 137.0, 136.3, 136.2, 129.7 (2CH, 1C), 128.9 (2CH), 128.3 (2CH), 127.49, 127.43, 127.1,

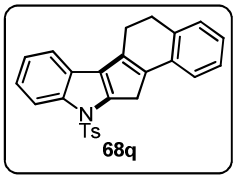
126.4, 118.7, 110.9, 109.2, 91.2, 86.1, 61.9, 55.9, 30.9, 21.5, 19.0. HRMS (ESI): *m/z* calcd for $C_{27}H_{26}NO_5S$ $(M–H)^+$: 476.1526, Found: 476.1526.

N-(2-(3-(3,4-Dihydronaphthalen-1-yl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65q).



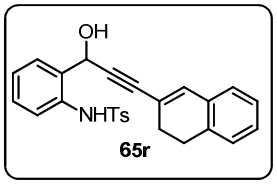
Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250, 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73-7.70 (m, 2H), 7.61 (dd, *J* = 7.7 and 1.6 Hz, 1H), 7.49-7.47 (m, 2H), 7.45 (dd, *J* = 8.0 and 1.3 Hz, 1H), 7.31-7.23 (m, 2H), 7.23-7.20 (m, 4H), 7.19-7.14 (m, 2H), 6.55 (t, *J* = 4.9 Hz, 1H), 5.53 (s, 1H), 2.83 (t, *J* = 8.0 Hz, 2H), 2.43 (m, 2H), 2.31 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 137.0, 136.6, 135.5, 134.9, 132.1, 131.0, 129.7 (2CH), 129.6, 128.3, 127.9, 127.5, 127.2 (2CH), 126.7, 125.2, 124.9, 122.9, 120.8, 87.2, 86.4, 63.3, 27.0, 23.6, 21.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}NNaO_3S$ $(M+Na)^+$: 452.1296, Found: 452.1295.

11-Tosyl-5,6,11,12-tetrahydrobenzo[4,5]indeno[2,1-*b*]indole (68q).



Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2969, 2945, 1574, 1498, 1367, 1123, 1119, 976, 854. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17-8.15 (m, 2H), 7.96-7.94 (m, 2H), 7.80-7.78 (m, 3H), 7.38-7.32 (m, 1H), 7.24-7.21 (m, 4H), 3.81 (s, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.68 (t, *J* = 7.9 Hz, 2H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.2, 144.0, 139.6, 135.3, 135.2, 133.9, 133.6, 129.6 (2CH, 1C), 127.8, 126.8, 126.4 (2CH, 1C), 125.8, 124.8, 123.64, 123.62, 121.4, 119.2, 114.6, 33.6, 28.4, 22.4, 21.6. HRMS (ESI): *m/z* calcd for $C_{26}H_{21}NO_2S$ $(M)^+$: 411.1293, Found: 411.1303.

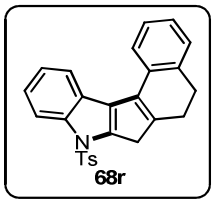
N-(2-(3-(3,4-Dihydronaphthalen-2-yl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65r).



Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3250,

2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.70 (dd, *J* = 7.7 Hz and 1.4 HZ, 2H), 7.45 (dd, *J* = 8.0 and 1.0 Hz, 2H), 7.32-7.24 (m, 3H), 7.19-7.14 (m, 4H), 7.07 (dd, *J* = 5.0 and 3.8 Hz, 1H), 6.85 (s, 1H), 5.49 (s, 1H), 2.88 (t, *J* = 8.3 Hz, 2H), 2.49 (t, *J* = 8.3 Hz, 2H), 2.40 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.9, 136.7, 135.5, 134.8, 134.6, 133.2, 130.9, 129.74 (2CH, 1C), 129.70, 128.3, 128.1, 127.5, 127.2 (2CH), 126.7, 126.6, 125.2, 122.8, 119.7, 89.9, 88.0, 63.5, 27.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}NNaO_3S$ $(M+Na)^+$: 452.1296, Found: 452.1295.

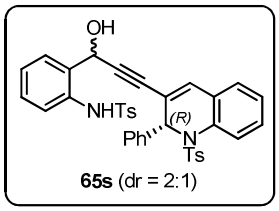
8-Tosyl-5,6,7,8-tetrahydrobenzo[6,7]indeno[2,1-*b*]indole (68r).



68r

Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2969, 2945, 1574, 1498, 1367, 1123, 1119, 976, 854. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.17-8.15 (m, 2H), 7.96-7.94 (m, 1H), 7.80-7.78 (m, 3H), 7.38-7.32 (m, 2H), 7.24-7.21 (m, 4H), 3.81 (s, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.68 (t, *J* = 7.9 Hz, 2H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.2, 144.0, 139.6, 135.3, 135.2, 133.9, 133.6, 129.6 (2CH, 1C), 127.8, 126.8, 126.4 (2CH, 1C), 125.8, 124.8, 123.64, 123.62, 121.4, 119.2, 114.6, 33.6, 28.4, 22.4, 21.6. HRMS (ESI): *m/z* calcd for $C_{26}H_{22}NO_2S$ $(M+H)^+$: 412.1371, Found: 412.1379

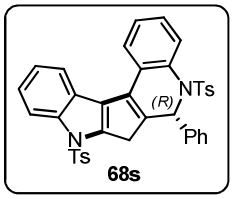
N-(2-(1-Hydroxy-3-((*R*)-2-phenyl-1-tosyl-1,2-dihydroquinolin-3-yl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65s).



65s (dr = 2:1)

Prepared by following the procedure **G** and isolated as pale yellow semi-solid. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3072, 2921, 2853, 2212, 1494, 1323, 1173, 1092, 1018, 809. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (br s, 1H), 7.71-7.65 (m, 3H), 7.41-7.38 (m, 4H), 7.37-7.33 (m, 3H), 7.32-7.24 (m, 7H), 7.18-7.09 (m, 3H), 7.05-6.97 (m, 2H), 6.57 (s, 1H), 6.07 (s, 1H), 5.52 (s, 1H), 2.23 (s, 3H), 2.34 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.0, 143.9, 136.87, 136.83, 136.5, 135.3, 135.1, 132.3, 131.5, 131.3, 129.7 (2CH), 129.28, 129.27, 128.5 (2CH), 128.3, 128.2, 128.1, 127.9, 127.4 (2CH), 127.2 (2CH), 127.1 (2CH), 126.9, 126.7, 125.4, 123.2, 118.6, 96.1, 90.6, 86.3, 63.0, 59.7, 21.6 ($2CH_3$). HRMS (ESI): *m/z* calcd for $C_{38}H_{31}N_2O_4S_2$ $(M–OH)^+$: 643.1725, Found: 643.1735.

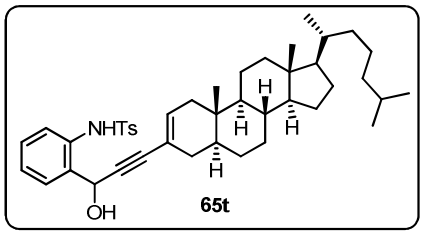
(*R*)-6-Phenyl-5,8-ditosyl-5,6,7,8-tetrahydroindolo[3',2':3,4]cyclopenta[1,2-*c*]quinoline (68s).



68s

Prepared by following the procedure **H** and isolated as colorless solid. M.P = 126-128 °C. $[\alpha]_D^{22}$ = –130.00 (*c* 0.18, $CHCl_3$). R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2934, 2221, 1599, 1506, 1330, 1228, 1158, 1090, 923. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.9 Hz, 1H), 7.90 (d, *J* = 8.3 Hz, 2H), 7.66 (dt, *J* = 7.7 and 3.8 Hz, 3H), 7.41-7.28 (m, 7H), 7.25 (s, 5H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.34 (d, *J* = 8.3 Hz, 1H), 6.29 (s, 1H), 3.83 (d, *J* = 23.8 Hz, 1H), 3.37 (d, *J* = 23.8 Hz, 1H), 2.41 (s, 3H), 1.27 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.6, 143.9, 143.4, 139.2, 137.4, 135.7, 135.3, 133.8, 132.9, 132.8, 130.1 (2CH), 128.5 (2CH), 128.3, 128.2, 128.1, 127.9 (3CH), 127.8 (2CH), 127.6, 126.7 (2CH), 126.3 (2CH), 125.5, 124.1, 123.7, 123.6, 123.5, 119.9, 114.4, 58.7, 36.6, 21.6, 20.1. HRMS (ESI): *m/z* calcd for $C_{38}H_{31}N_2O_4S_2$ $(M+H)^+$: 643.1725, Found: 643.1717.

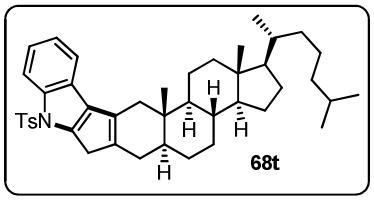
N-(2-(3-((5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65t).



65t

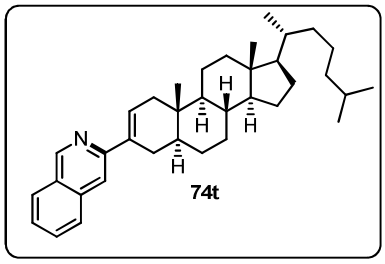
Prepared by following the procedure **G** and isolated as colorless solid. M.P = 143-145 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3243, 2924, 2186, 1614, 1496, 1220, 1164, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.72-7.68 (m, 2H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.30-7.33 (m, 3H), 7.15-7.11 (m, 1H), 6.13 (m, 1H), 5.35 (d, *J* = 5.3 Hz, 1H), 2.52 (br s, 1H), 2.41 (s, 3H), 2.11-0.99 (m, 29H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H), 0.83 (s, 3H), 0.81 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 136.8, 135.7, 135.5, 130.7, 129.74, 129.70 (2CH), 129.5, 128.2, 127.2 (2CH), 125.0, 122.69, 122.68, 118.4, 90.2, 83.5, 63.4, 56.3, 56.2, 53.6, 42.4, 41.2, 40.3, 39.9, 39.5, 36.1, 35.8, 34.0, 33.7, 31.6, 28.3, 28.2, 28.0, 24.2, 23.8, 22.5, 21.5, 21.0, 18.7, 11.99, 11.96. HRMS (ESI): *m/z* calcd for $C_{43}H_{58}NO_2S$ $(M–OH)^+$: 652.4188, Found: 652.4179.

(1*R*,3a*S*,3b*R*,5a*S*,13a*S*,13b*S*,15a*R*)-13a,15a-Dimethyl-1-((*R*)-6-methylheptan-2-yl)-8-tosyl-2,3,3a,3b,4,5,5a,6,7,8,13,13a,13b,14,15,15a-hexadecahydro-1*H*-cyclopenta[5',6']naphtho[2',1':5,6]indeno[2,1-*b*]indole (68t).



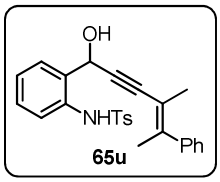
Prepared by following the procedure **H** and isolated as colorless solid. M.P = 96-98 °C. $[\alpha]_D^{22}$ = –33.00 (*c* 0.06, $CHCl_3$). R_f = 0.5 (hexane/EtOAc = 5/1). IR (thin film, neat): ν_{max}/cm^{-1} 2932, 2868, 1600, 1494, 1338, 1160, 1091, 923, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98-7.96 (m, 1H), 7.70-7.64 (m, 2H), 7.44-7.43 (m, 1H), 7.15-7.10 (m, 4H), 3.41-3.38 (m, 2H), 2.56-2.52 (m, 1H), 2.25 (s, 3H), 2.11-0.99 (m, 28H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H), 0.83 (s, 3H), 0.81 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.4, 140.4, 137.4, 136.9, 135.6, 129.3 (2CH), 129.0, 126.6 (2CH), 124.5, 123.8, 120.3, 115.9, 115.4, 112.2, 56.5, 56.2, 50.8, 44.1, 42.7, 40.0, 39.5, 38.6, 38.0, 36.1, 35.8, 35.7, 31.8, 31.3, 28.2, 28.1, 28.0 ($2CH_2$), 24.2, 23.8, 22.8, 22.5, 21.5, 21.1, 18.6, 14.1, 12.2. HRMS (ESI): *m/z* calcd for $C_{43}H_{58}NO_2S$ $(M+H)^+$: 652.4188, Found: 652.4194.

2-((5*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-4,5,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl)quinoline (74t).



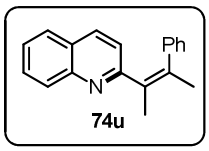
Prepared by following the procedure **H** and isolated as colorless solid. M.P = 130-132 °C. $[\alpha]_D^{22}$ = –133.00 (*c* 0.01, $CHCl_3$). R_f = 0.5 (hexane/EtOAc = 5/1). IR (thin film, neat): ν_{max}/cm^{-1} 2932, 2868, 1600, 1494, 1338, 1160, 1091, 923, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.5 Hz, 2H), 7.77 (d, *J* = 7.0 Hz, 1H), 7.67-7.63 (m, 2H), 7.49-7.45 (m, 1H), 6.77-6.75 (m, 1H), 2.76 (d, *J* = 17.1 Hz, 1H), 2.57-2.51 (m, 1H), 2.22-0.97 (m, 27H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H), 0.84 (s, 3H), 0.83 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 158.9, 135.8, 135.7, 129.2, 127.3 (2CH), 126.9, 125.6, 120.3, 117.9 (2CH), 56.4, 56.2, 53.9, 42.5, 41.7, 40.9, 36.1, 35.8, 35.6, 34.5, 31.9, 30.7, 29.6, 28.8, 28.7, 28.0, 24.2, 23.8, 22.8, 22.7, 22.5, 21.1, 14.2, 12.1, 12.0. HRMS (ESI): *m/z* calcd for $C_{36}H_{51}NNa$ $(M+Na)^+$: 520.3919, Found: 520.3910.

N-(2-(1-Hydroxy-4-methyl-5-phenylhex-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65u).



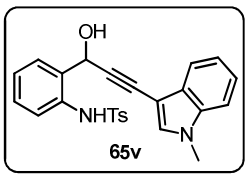
Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3343, 2914, 2286, 1624, 1396, 1220, 1154, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.01 (s, 1H, NH), 7.73 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 7.1 Hz, 1H), 7.45 (dd, *J* = 8.2 and 1.1 Hz, 2H), 7.36-7.30 (m, 3H), 7.22-7.17 (m, 3H), 6.50 (s, 1H), 2.40 (s, 3H), 2.27 (d, *J* = 1.5 Hz, 3H), 1.82 (d, *J* = 1.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.2, 143.9, 141.7, 136.7, 135.2, 131.2, 129.7 (2CH), 129.6, 128.2 (2CH), 127.9, 127.7 (2CH), 127.5, 127.2, 127.1, 125.2, 122.9, 113.1, 90.1, 89.7, 63.4, 24.0, 21.5, 20.6. HRMS (ESI): *m/z* calcd for $C_{26}H_{24}NO_2S$ $(M\text{-}OH)^+$: 414.1528, Found: 444.1532.

2-(3-Phenylbut-2-en-2-yl)quinoline (74u).



Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 9/1). IR (thin film, neat): ν_{max}/cm^{-1} 2925, 2916, 1491, 1371, 1174, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (t, *J* = 7.2 Hz, 2H), 7.86 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.75 (ddd, *J* = 8.5, 7.0 and 1.5 Hz, 1H), 7.70-7.69 (m, 1H), 7.57 (ddd, *J* = 8.2, 6.9 and 1.0 Hz, 1H), 7.49-7.41 (m, 3H), 7.10-7.07 (m, 2H), 2.10 (s, 3H), 2.02 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.1, 147.9, 143.8, 136.1, 134.8, 131.0, 129.6, 129.4, 129.0, 128.2 (2CH), 127.8, 127.5, 126.5, 126.1, 123.8, 122.1, 22.3, 20.9.

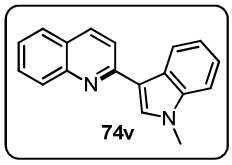
N-(2-(1-Hydroxy-3-(1-methyl-1*H*-indol-3-yl)prop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65v).



Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3243, 2924, 2186, 1614, 1496, 1220, 1164, 1090, 815. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (br s, 1H), 7.73-7.69 (m, 2H), 7.69-7.64 (m, 3H), 7.49 (dd, *J* = 8.2 and 1.1 Hz, 1H), 7.31-7.28 (m, 4H), 7.21 (s, 1H), 7.17-7.15 (m, 3H), 5.56 (s, 1H), 3.77 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 136.8, 136.1, 135.6, 133.1, 131.1, 129.7 (2CH), 129.4, 129.0, 128.4, 127.1 (2CH), 125.0, 122.8, 122.6, 120.6, 119.9, 109.7, 95.4, 88.0, 82.8,

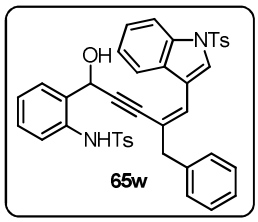
63.7, 33.1, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{21}N_2O_2S$ $(M–OH)^+$: 413.1324, Found: 413.1344.

2-(1-Methyl-1H-indol-3-yl)quinoline (74v).



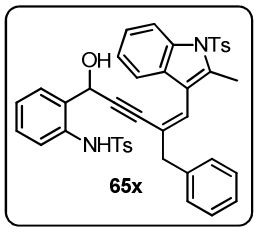
Prepared by following the procedure **H** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 2935, 2925, 1498, 1396, 1186, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.02-9.00 (m, 1H), 8.22-8.18 (m, 1H), 8.11 (s, 1H), 8.10-8.08 (m, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.86 (dd, *J* = 8.8 and 1.5 Hz, 1H), 7.72 (ddd, *J* = 8.4, 6.9 and 1.5 Hz, 1H), 7.50-7.48 (m, 2H), 7.30 (s, 1H), 3.97 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.5, 148.5, 138.1, 135.5, 130.9, 129.1, 128.8 (2CH), 127.5, 126.6, 126.2, 124.8, 123.2, 122.2, 120.5, 118.9, 109.6, 32.4. HRMS (ESI): *m/z* calcd for $C_{18}H_{14}N_2$ $(M)^+$: 258.1157, Found: 258.1168.

N-(2-(4-Benzyl-1-hydroxy-5-(1-tosyl-1*H*-indol-3-yl)pent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65w).



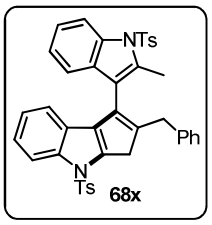
Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3457, 3269, 2937, 2214, 1598, 1515, 1346, 1265, 1162, 1009, 737. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.02 (d, *J* = 8.3 Hz, 1H), 7.82 (s, 1H), 7.71-7.68 (m, 3H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.57 (s, 1H), 7.38-7.28 (m, 7H), 7.27-7.21 (m, 7H), 7.10 (s, 1H), 7.06-7.04 (m, 1H), 7.10 (s, 1H), 7.06-7.04 (m, 1H), 5.37 (s, 1H), 3.85 (s, 2H), 2.363 (s, 3H), 2.361 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.2, 143.9, 137.9, 135.4, 134.8, 134.5, 130.8, 130.2, 130.0, 129.9 (2CH), 129.7 (2CH), 128.5, 128.7 (2CH, 1C), 128.3, 127.1 (2CH), 127.0, 126.8, 126.6, 125.3, 125.2, 124.5, 123.6, 122.8, 122.7, 119.4, 117.8, 113.6, 90.9, 87.6, 63.2, 38.8, 29.6, 21.56, 21.55, 14.1. HRMS (ESI): *m/z* calcd for $C_{40}H_{34}N_2NaO_5S_2$ $(M+Na)^+$: 709.1807, Found: 709.1815.

N-(2-(4-Benzyl-1-hydroxy-5-(2-methyl-1-tosyl-1*H*-indol-3-yl)pent-4-en-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65x).



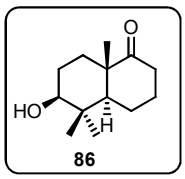
Prepared by following the procedure **G** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3457, 3269, 2937, 2214, 1598, 1515, 1346, 1265, 1162, 1009, 737. **^{1}H NMR** (400 MHz, $CDCl_3$): 8.25 (d, *J* = 8.3 Hz, 1H), 7.69-7.66 (m, 5H), 7.46-7.34 (m, 1H), 7.32-7.16 (m, 4H), 7.23-7.16 (m, 8H), 7.11-7.01 (m, 2H), 6.83 (s, 1H), 5.33 (s, 1H), 4.40 (s, 1H), 3.76 (s, 1H), 3.33 (s, 2H), 2.53 (s, 3H), 2.40 (s, 3H), 2.28 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.9, 143.9, 138.2, 136.8, 136.5, 135.3, 134.3, 130.9, 129.9 (2CH, 1C), 129.0, 128.8 (2CH, 1C), 128.3, 128.32 (2CH), 128.2, 127.1 (2CH), 127.0, 126.8, 126.4, 126.2 (2CH), 125.3, 124.5, 123.8, 123.4, 123.0, 119.2, 117.4, 114.8, 89.6, 87.1, 63.0, 38.5, 21.52, 21.51, 14.3. HRMS (ESI): *m/z* calcd for $C_{41}H_{36}N_2NaO_5S_2$ $(M+Na)^+$: 723.1963, Found: 723.1950.

2-Benzyl-1-(2-methyl-1-tosyl-1*H*-indol-3-yl)-4-tosyl-3,4-dihydrocyclopenta[*b*]indole (68x).



Prepared by following the procedure **H** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3063, 2938, 1598, 1494, 1453, 1366, 1174, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.5 Hz, 1H), 8.00 (d, *J* = 8.3 Hz, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.68 (d, *J* = 8.3 Hz, 3H), 7.36-7.35 (m, 2H), 7.27-7.18 (m, 8H), 6.99 (d, *J* = 7.5 Hz, 2H), 6.91-6.89 (m, 1H), 6.53 (d, *J* = 7.8 Hz, 1H), 3.69 (s, 2H), 3.57 (s, 2H), 2.53 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.1, 144.8, 142.8, 142.2, 140.2, 139.1, 136.9, 136.0, 135.3, 134.4, 130.2, 130.1, 129.9 (2CH, 1C), 129.8 (2CH), 128.5 (2CH, 1C), 128.4 (2CH), 126.6 (2CH, 1C), 126.2 (2CH), 126.2, 126.1, 124.5, 124.4, 123.8, 123.2, 119.8, 116.8, 114.9, 114.1, 37.5, 35.8, 21.5, 14.3. HRMS (ESI): *m/z* calcd for $C_{41}H_{34}N_2O_4S_2$ $(M)^+$: 682.1960, Found: 682.1971.

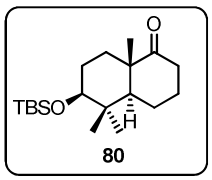
(4a*S*,6*S*,8a*S*)-6-Hydroxy-5,5,8a-trimethyloctahydronaphthalen-1(2*H*)-one (86).



Prepared by following the literature procedure[126]and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). $[\alpha]_D^{22}$ = -30.00 (*c* 0.20, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 3447, 2946, 2923, 2869, 1705, 1496, 1438, 1234, 1113, 1042, 964. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.28-3.20 (m, 1H), 2.63-2.54 (m, 1H), 2.24-2.18 (m, 1H), 2.14-2.07 (m, 1H), 1.84-1.52 (m, 9H), 1.64 (s, 3H), 1.04 (s, 3H), 0.91 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 215.4, 78.1, 52.5, 48.6, 39.7, 37.4, 31.1, 27.9, 26.8, 26.2, 20.7, 18.6, 15.8. HRMS (ESI): *m/z* calcd for $C_{13}H_{22}O_2Na$ $(M+Na)^+$: 233.1517, Found: 233.1516.

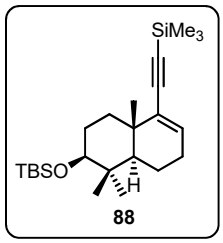
(4a*S*,6*S*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8a-trimethyloctahydronaphthalen-1(2*H*)-one (80).



80

Prepared by following the literature procedure[126] and isolated as white oily solid. R_f = 0.5 (hexane/EtOAc = 9/1). $[\alpha]_D^{22}$ = -13.00 (*c* 1.00, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 2937, 2921, 2843, 1705, 1549, 1445, 1250, 1100, 1076, 833. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.18-3.15 (m, 1H), 2.61-2.54 (m, 1H), 2.23-2.18 (m, 1H), 2.12-2.06 (m, 2H), 1.78-1.52 (m, 7H), 1.64 (s, 3H), 0.94 (s, 3H), 0.91 (s, 9H), 0.90 (s, 3H), 0.05 (d, *J* = 8.6 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 215.6, 78.6, 52.7, 48.6, 40.3, 37.5, 31.1, 28.4, 27.2, 26.3, 25.9 ($3CH_3$), 20.9, 18.6, 18.0, 16.2, -3.7, -4.9. HRMS (ESI): *m/z* calcd for $C_{19}H_{36}O_2Si$ $(M)^+$: 324.2485, Found: 324.2489.

***tert*-Butyldimethyl(((2*S*,4a*S*,8a*R*)-1,1,4a-trimethyl-5-((trimethylsilyl)ethynyl)-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl)oxy)silane (88).**

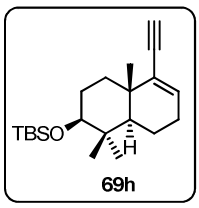


88

Prepared by following the literature procedure[127] and isolated as colorless oil. R_f = 0.5 (hexane). $[\alpha]_D^{22}$ = -13.00 (*c* 1.00, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 2950, 2856, 2087, 1472, 1361, 1255, 1105, 1070, 883, 836, 773. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.04 (t, *J* = 4.8 Hz, 1H), 3.52-3.21 (m, 1H), 2.26-2.18 (m, 1H), 2.14-2.03 (m, 1H), 1.98-1.92 (m, 3H), 1.75-1.60 (m, 3H), 1.51-1.39 (m, 1H), 1.01 (s, 3H), 0.94 (s, 3H), 0.91 (s, 9H), 0.79 (s, 3H), 0.76 (s, 9H), 0.06 (d, *J* = 8.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 134.0, 133.0, 104.6, 92.5, 79.3, 49.9, 39.4, 36.9, 35.6, 29.7, 27.2, 28.3, 28.1, 27.5, 25.9 ($3CH_3$), 20.6, 18.15, 18.14, 15.8, 0.17, -3.7, -4.9. HRMS (ESI): *m/z* calcd for $C_{24}H_{44}OSi_2$ $(M)^+$: 404.2931, Found: 404.2942.

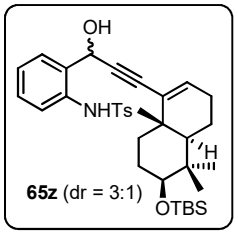
***tert*-Butyl(((2*S*,4a*S*,8a*R*)-5-ethynyl-1,1,4a-trimethyl-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-yl)oxy)dimethylsilane (69h).**

Prepared by following the literature procedure[127] and isolated as colorless oil. R_f = 0.5 (hexane). $[\alpha]_D^{22}$ = +58.65 (*c* 0.96, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 3331, 2947, 2832, 2017, 1472, 1361, 1255, 1105, 1070, 883, 836, 773. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 6.03 (t, *J* = 4.6 Hz, 1H),



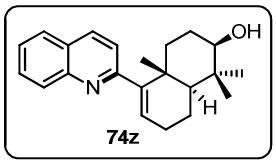
3.26-3.22 (m, 1H), 2.79 (s, 1H), 2.29-2.15 (m, 1H), 2.15-1.97 (m, 1H), 1.96-1.94 (m, 3H), 1.78-1.61 (m, 3H), 1.51-1.45 (m, 1H), 1.12 (s, 3H), 0.97 (s, 3H), 0.91 (s, 9H), 0.80 (s, 3H), 0.07 (d, J = 8.1 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 134.9, 132.1, 82.9, 79.3, 75.8, 49.9, 39.4, 36.8, 29.3, 28.3, 27.5, 25.9 ($3CH_3$), 20.5, 18.16, 18.12, 15.8, 14.1, -3.7, -4.9. HRMS (ESI): *m/z* calcd for $C_{21}H_{36}OSi$ $(M)^+$: 332.2535, Found: 332.2535.

N-(2-(3-((4a*R*,6*S*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8a-trimethyl-3,4,4a,5,6,7,8,8a-octahydronaphthalen-1-yl)-1-hydroxyprop-2-yn-1-yl)phenyl)-4-methylbenzenesulfonamide (65z, Major isomer).



Prepared by following the procedure **G** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). $[\alpha]_D^{22}$ = +76.24 (*c* 0.24, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 2967, 2945, 2832, 2122, 1601, 1578, 1420, 1361, 1255, 1105, 1070, 883, 836, 776. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.92 (brs, 1H), 7.92 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.45 (m, 3H), 7.16-7.12 (m, 1H), 6.02 (t, J = 3.2 Hz, 1H), 5.34 (s, 1H), 3.26 (m, 1H), 2.50 (brs, 1H), 2.40 (s, 3H), 2.30-2.22 (m, 1H), 1.92-1.86 (m, 1H), 1.78-1.73 (m, 1H), 1.67-1.61 (m, 3H), 1.54-1.50 (m, 1H), 1.36-1.27 (m, 2H), 1.16 (s, 3H), 0.95 (s, 3H), 0.91 (s, 9H), 0.79 (s, 3H), 0.06 (d, J = 8.1 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 136.8, 135.5, 131.9, 131.0, 129.7 (2CH), 129.5, 128.17, 127.1 (2CH), 125.1, 122.86, 122.83, 88.2, 85.0, 79.2, 63.3, 49.9, 39.4, 37.1, 35.8, 35.2, 28.3, 18.0, 27.6, 25.9 ($3CH_3$), 21.5, 20.9, 18.1, 15.8, -3.7 -4.9. HRMS (ESI): *m/z* calcd for $C_{35}H_{48}NO_3SSi$ $(M\text{-}OH)^+$: 590.3124, Found: 590.3129.

(2*R*,4a*R*,8a*S*)-1,1,4a-Trimethyl-5-(quinolin-2-yl)-1,2,3,4,4a,7,8,8a-octahydronaphthalen-2-ol (74z).

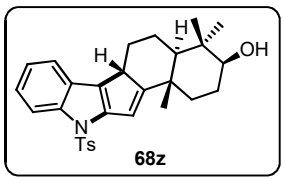


Prepared by following the procedure **H** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). $[\alpha]_D^{22}$ = +33.69 (*c* 0.24, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 2925, 2916, 1491, 1371, 1174, 1089, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.79 (dd, J = 8.0 and 0.8 Hz, 1H), 7.71-7.76 (m, 1H), 7.52-7.48 (m, 1H), 7.32 (d, J = 8.4 Hz, 1H), 5.75 (t, J = 4.3 Hz, 1H), 3.35-3.26 (m, 1H), 2.45-2.33 (m, 2H), 1.89-1.76 (m, 1H), 1.66-1.60 (m, 4H), 1.58 (s,

3H), 1.44-1.30 (m, 3H), 1.09 (s, 3H), 0.92 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 161.3, 149.8, 147.1, 135.4, 129.6, 128.1, 127.3, 126.5 (2CH), 125.8, 122.4, 78.9, 50.8, 39.0, 38.4, 29.7, 28.2, 27.5, 27.1, 20.9, 18.3, 15.5. HRMS (ESI): *m/z* calcd for $C_{22}H_{27}NO$ $(M)^+$: 321.2093, Found: 321.2096.

Procedure I: General procedure of Ag(I)-catalyzed hydroamination reaction of enynol 65z.
To a stirred solution of enynol **65z** (200 mg, 0.32 mmol) in CH_3CN (3 mL), AgOAc (2.73 mg, 0.01 mmol) was added and stirred at 50 °C for 5 h. Upon the disappearance of enynol **65z**, TfOH (3.08 μL, 0.032 mmol) was added and continued stirring at RT for next 2 h. The reaction mixture was quenched with aqueous saturated sodium bicarbonate solution (1-2 mL). Diluted the reaction mixture with DCM (2 mL) and the layers were separated. The organic layers were combined, dried over Na_2SO_4, concentrated, and purified by neutral alumina column chromatography to afford product **68z** (43% yield) and **74z** (51% yield) as colorless oil.

(3*S*,12b*S*)-4,4,12b-Trimethyl-11-tosyl-1,2,3,4,4a,5,6,6a,11,12b-decahydrobenzo[4,5]indeno[2,1-*b*]indol-3-ol (68z).



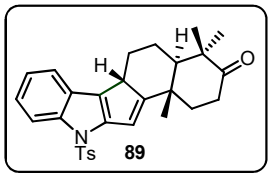
68z

Prepared by following the procedure **I** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). $[\alpha]_D^{22}$ = -198.15 (*c* 0.20, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 3324, 2932, 2868, 1600, 1494, 1338, 1160, 1091, 923, 813. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 7.6 HZ, 1H), 7.76 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.22-7.16 (m, 3H), 6.62 (s, 1H), 3.67-3.53 (m, 1H), 3.37-3.22 (m, 1H), 2.70-2.65 (m, 1H), 2.36 (s, 3H), 1.97-1.75 (m, 5H), 1.72 (s, 3H), 1.62-1.06 (m, 1H), 1.04 (s, 3H), 0.96 (s, 3H), 0.94-0.86 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.1, 144.6, 138.4, 135.5, 129.7 (2CH), 128.2, 127.1, 126.7 (2CH), 123.4, 122.0, 117.8, 114.6, 110.3, 78.7, 55.5, 42.2, 39.3, 39.1, 35.0, 32.4, 29.7, 28.4, 27.4, 22.3, 21.5, 21.1, 15.7. HRMS (ESI): *m/z* calcd for $C_{29}H_{34}NOS$ $(M+H)^+$: 476.2259, Found: 476.2259.

Procedure J: General procedure of oxidation of 89.
To a stirring solution of the alcohol **68z** (10 mg, 0.02 mmol) in anhydrous DCM (1 mL) at 0 °C, Dess–Martin periodinane (10 mg, 0.02 mmol) was added. The solution was allowed to warm to room temperature and stirred for 10 h. Upon completion, the reaction mixture was quenched by

adding saturated $NaHCO_3$ (1 mL) and extracted with DCM three time. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by neutral alumina gel column chromatography to afford the ketone **89.**

(4a*R*,12b*S*)-4,4,12b-Trimethyl-11-tosyl-1,4,4a,5,6,6a,11,12b-octahydrobenzo[4,5]indeno[2,1-*b*]indol-3(2*H*)-one (89).



Prepared by following the procedure **J** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 9/1). $[\alpha]_D^{22}$ = -57.00 (*c* 0.10, $CHCl_3$). IR (thin film, neat): ν_{max}/cm^{-1} 2924, 2853, 1704, 1445, 1371, 1275, 1173, 1086, 965. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04-8.02 (m, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.41-7.38 (m, 1H), 6.69 (s, 1H), 3.40 (dd, *J* = 12.4 and 6.0 Hz, 1H), 2.88-2.77 (m, 1H), 2.74-2.67 (m, 1H), 2.34 (s, 3H), 2.22-2.18 (m, 2H), 1.96-1.85 (m, 2H), 1.77-1.73 (m, 1H), 1.49-1.45 (m, 1H), 1.44 (s, 3H), 1.20 (s, 3H), 1.14 (s, 3H), 0.97-0.85 (m, 5H).**^{13}C NMR** (100 MHz, $CDCl_3$): δ 215.19, 166.9, 145.3, 144.7, 135.4, 129.8 (2CH, 1C), 128.3, 126.9, 126.7 (2CH), 123.5, 122.3, 117.9, 114.6, 111.6, 55.8, 47.9, 42.2, 38.8, 35.4, 34.6, 31.9, 26.2, 22.4, 22.0, 21.6, 21.5. HRMS (ESI): *m/z* calcd for $C_{29}H_{30}NO_3S$ $(M-H)^+$: 472.1947, Found: 472.1930.

Procedure K: General procedure for the preparation of 3-(2-aminophenyl)hex-5-en-1-yn-3-ols.

Step-I: To a stirred solution of the alkyne (2.2 equiv.) in anhydrous THF at -78 °C, was added *n*-butyllithium (2.0 M in cyclohexane solution, 2.2 equiv.) drop wise, and the resulting solution was allowed to stir at the same temperature for 10 min. The reaction was warmed to -40 °C. The resulting mixture was stirred at the same temperature for 1 h. After 1 h, reaction mixture was cooled to -78 °C. The N-(2-formylphenyl)-4-methylbenzenesulfonamide **70** (1 mmol) was dissolved in THF (2 mL) and added to the reaction mixture drop wise at -78 °C and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for a further 1 h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **55** (80-90% yields).

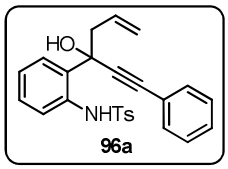
Step-II: Ynol **55** (1 mmol) was dissolved in EtOAc (5 mL), and IBX (1.5 mmol) was added. The resulting suspension was stirred at 75 °C until alcohol **55** disappeared as monitored by TLC. Cooled the reaction mixture to room temperature and filtered through celite. The residue was washed with ethyl acetate (3×2 mL). Organic extracts were combined and washed with saturated aq. $NaHCO_3$ solution to remove excess iodobenzoic acid. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford **101** (in 75-85% yields).

Step-III: An oven dried round bottom flask was charged with ynone **101** (1.0 mmol), 5 mL dry THF and placed at 0^{o}C. Allylmagnesium chloride (2.2 mmol) were added drop wise at the same temperature and stirred for 1h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **96** (in 90-95% yields).

Procedure L: General procedure for the synthesis of 1,3-disubstituted-*β*-carbolines.

A 5 mL glass vial was charged with 3-(2-aminophenyl)hex-5-en-1-yn-3-ol **96** (0.1 mmol), AgOAc (2 mol%) in DCE (1 mL) and stirred at 60 ^{o}C. Upon disappearance of the starting compound **96** (by TLC), $TMSN_3$ (0.11 mmol) and $BiCl_3$ (5 mol%) were introduced and continued stirring at 60 ^{o}C until the respective intermediate disappeared (TLC). Upon complete formation of **103**, $Pd(OAc)_2$ (5 mol%) was introduced and continued stirring at 80 ^{o}C until intermediate **103** disappeared (TLC). The reaction mixture was quenched by adding saturated aq. $NaHCO_3$ (1 mL) and extracted with EtOAc (2x1 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **107** (in 56-81% yields).

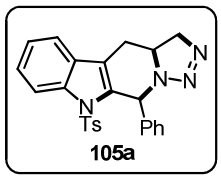
N-(2-(3-Hydroxy-1-phenylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96a).



96a

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3437, 3239, 2231, 1599, 1511, 1338, 927. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.22 (s, 1H, NH), 7.80 (d, *J* = 8.4 Hz, 2H), 7.63 (dt, *J* = 7.6 and 1.2 Hz, 2H), 7.49 (dd, *J* = 7.2 and 1.6 Hz, 2H), 7.41-7.32 (m, 3H), 7.24 (d, *J* = 8.4 Hz, 3H), 7.05 (s, 1H), 5.92-5.80 (m, 1H), 5.23 (dd, *J* = 9.6 and 0.8 Hz, 1H), 5.10 (d, *J* = 17.2 Hz, 1H), 3.23 (brs, 1H), 2.63-2.55 (m, 2H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 137.2, 135.6, 132.0, 131.8 (2CH), 129.9, 129.7 (2CH, 1C), 129.1, 128.6, 128.4 (2CH, 1C), 127.2 (2CH), 121.8, 121.0, 120.1, 89.2, 88.1, 74.7, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{23}NNaO_3S$ $(M+Na)^+$: 440.1296, Found: 440.1278.

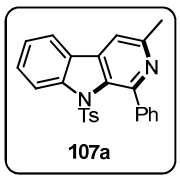
10-Phenyl-9-tosyl-3a,4,9,10-tetrahydro-3*H*-[1,2,3]triazolo[1',5':1,6]pyrido[3,4-*b*]indole (105a).



105a

Prepared by following the procedure **L** and isolated as colorless solid. M.P = 155-157 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3061, 2922, 1601, 1450, 1371, 1172, 747. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.04 (d, *J* = 8.0 Hz, 1H), 7.49-7.29 (m, 4H), 7.27-7.12 (m, 6H), 7.03 (d, *J* = 8.4 Hz, 2H), 5.69 (s, 1H), 3.57 (d, *J* = 5.6 Hz, 2H), 3.25-3.14 (m, 1H), 2.88-2.76 (m, 1H), 2.66-2.56 (m, 1H), 2.31 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.1, 143.1, 137.2, 135.3, 129.7, 129.6, 129.4 (2CH), 128.6 (2CH), 128.3 (2CH), 127.6, 126.4 (2CH), 124.8, 123.6, 120.7, 118.4, 115.2, 58.9, 55.7, 52.6, 27.1, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{23}N_4O_2S$ $(M+H)^+$: 443.1542, Found: 443.1573.

3-Methyl-1-phenyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107a).

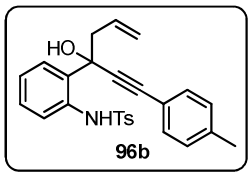


107a

Prepared by following the procedure **L** and isolated as colorless solid. M.P = 230-231 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2925, 1610, 1372, 1175, 752. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.4 Hz, 1H), 8.10-8.06 (m, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.61-7.49 (m, 3H), 7.48-7.33 (m, 3H), 7.01-6.96 (m, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 2.74 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.5, 150.5, 144.3, 142.4, 141.0, 139.2, 133.0, 131.8, 129.6, 128.7 (2CH),

128.6 (2CH, 1C), 128.4, 128.2 (2CH), 127.6, 126.9, 125.7, 121.0, 119.7, 111.6, 24.6, 21.4. HRMS (ESI): *m/z* calcd for $C_{25}H_{21}N_2O_2S$ $(M+H)^+$: 413.1324, Found: 413.1311.

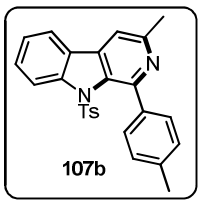
N-(2-(3-Hydroxy-1-(*p*-tolyl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96b).



96b

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.24 (s, 1H, NH), 7.79 (d, *J* = 8.4 Hz, 2H), 7.62 (dt, *J* = 9.2 and 1.2 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.15 (dt, *J* = 7.6 and 1.2 Hz, 1H), 5.91-5.79 (m, 1H), 5.21 (dd, *J* = 16.8 and 1.2 Hz, 1H), 5.08 (dd, *J* = 16.8 and 1.2 Hz, 1H), 3.28 (brs, 1H, OH), 2.64-2.57 (m, 2H), 2.38 (s, 3H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 139.2, 137.1, 135.6, 132.1, 131.6 (2CH), 130.0, 129.7 (2CH), 129.1 (2CH), 129.0, 128.4, 127.2 (2CH), 123.4, 120.1, 120.0, 118.6, 88.5, 88.3, 74.7, 47.4, 21.56, 21.53. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}NNaO_3S$ $(M+Na)^+$: 454.1453, Found: 454.1435.

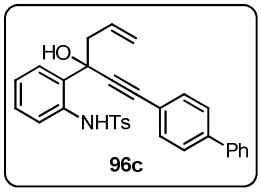
3-Methyl-1-(*p*-tolyl)-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107b).



107b

Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 178-180 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3051, 2921, 1596, 1373, 1174, 1089. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 2H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.56 (dt, *J* = 7.2 and 1.2 Hz, 1H), 7.39 (s, 1H), 7.37-7.34 (m, 3H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 2.72 (s, 3H), 2.45 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.4, 150.6, 144.3, 142.4, 139.1, 138.2, 138.1, 132.9, 131.8, 129.5, 128.9 (2CH), 128.7 (2CH, 1C), 128.4 (2CH), 127.7, 126.9 (2CH), 125.6, 121.0, 111.3, 24.5, 21.5, 21.4. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}N_2O_2S$ $(M+H)^+$:427.1480, Found: 427.1464.

N-(2-(1-([1,1'-Biphenyl]-4-yl)-3-hydroxyhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96c).

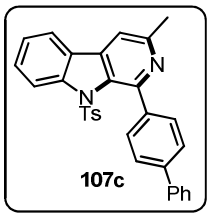


96c

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3412, 3257,

3025, 2856, 2230, 1582, 1449, 1266, 1171, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.28 (s, 1H, NH), 7.81 (d, *J* = 8.4 Hz, 2H), 7.69-7.50 (m, 8H), 7.48 (t, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.30-7.21 (m, 3H), 7.07 (dt, *J* = 8.0 and 0.8 Hz, 1H), 5.94-5.82 (m, 1H), 5.24 (dd, *J* = 10.4 and 1.2 Hz, 1H), 5.11 (dd, *J* = 17.2 and 0.8 Hz, 1H), 3.42 (brs, 1H), 2.68-2.57 (m, 2H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 141.7, 140.1, 137.2, 135.7, 132.2 (2CH), 132.0, 129.9, 129.7 (2CH), 129.1, 128.9 (2CH), 128.4, 127.8, 127.2 (2CH), 127.1 (2CH), 127.0 (2CH), 123.4, 120.9, 120.6, 120.1, 89.9, 88.0, 74.8, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{31}H_{27}NNaO_3S$ $(M+Na)^+$: 516.1609, Found: 516.1591.

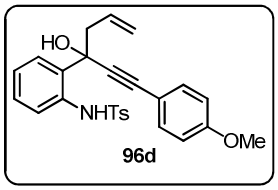
1-([1,1'-Biphenyl]-4-yl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107c).



107c

Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 215-217 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 7.81-7.69 (m, 5H), 7.59 (dt, *J* = 7.6 and 1.2 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.42 (s, 1H), 7.39 (t, *J* = 6.8 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 2.75 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.5, 150.1, 144.3, 142.4, 141.1, 141.0, 140.0, 139.1, 133.0, 132.0, 129.6, 128.9 (2CH), 128.7 (2CH), 128.6 (2CH), 127.6, 127.2 (2CH, 1C), 126.9 (2CH), 126.9 (2CH), 125.7, 121.0, 119.7, 111.6, 24.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{31}H_{25}N_2O_2S$ $(M+H)^+$: 489.1637, Found: 489.1620.

N-(2-(3-hydroxy-1-(4-methoxyphenyl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96d).

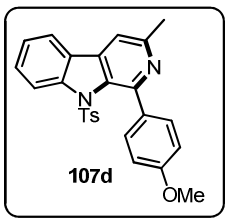


96d

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3443, 3267, 3017, 2920, 2221, 1573, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.30 (s, 1H, NH), 7.79 (d, *J* = 8.4 Hz, 2H), 7.62 (dt, *J* = 8.0 and 1.2 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 3H), 7.03 (dt, *J* = 7.6 and 0.8 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.89-5.79 (m, 2H), 5.19 (dd, *J* = 10.0 and 1.6 Hz, 1H), 5.06 (dd, *J* = 17.2 and 1.6 Hz, 1H), 3.82 (s, 3H), 2.62-2.51 (m, 2H), 2.36 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.0, 143.7, 137.1, 135.7, 133.3 (2CH), 132.2, 130.1, 129.7 (2CH), 129.0, 128.5,

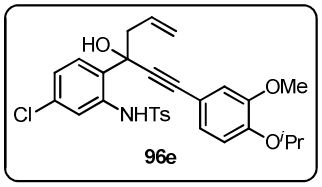
127.2 (2CH), 123.3, 120.6, 119.9, 114.0 (2CH), 113.8, 88.1, 88.0, 74.7, 55.3, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}NNaO_4S$ $(M+Na)^+$: 470.1402, Found: 470.1386.

1-(4-Methoxyphenyl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107d).



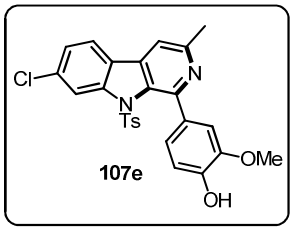
Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 167-169 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2925, 1513, 1372, 1248, 1175, 752. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.24 (d, *J* = 8.4 Hz, 1H), 8.10-8.06 (m, 2H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.56 (dt, *J* = 7.3 and 1.2 Hz, 1H), 7.40-7.33 (m, 2H), 7.09-7.04 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 3.90 (s, 3H), 2.27 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.9, 154.4, 150.2, 144.3, 142.5, 139.3, 133.6, 132.7, 131.7, 129.9 (2CH), 129.5, 128.6 (2CH), 127.8, 126.9 (2CH), 125.7, 121.0, 119.8, 113.6 (2CH), 111.0, 55.2, 24.5, 21.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}N_2O_3S$ $(M+H)^+$: 443.1429, Found: 443.1413.

N-(5-Chloro-2-(3-hydroxy-1-(4-isopropoxy-3-methoxyphenyl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96e).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3442, 3216, 2939, 2235, 1597, 1470, 1263, 1163, 1091. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.38 (brs, 1H, NH), 7.78 (d, *J* = 8.4 Hz, 2H), 7.65-7.64 (m, 2H), 7.62 (s, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.03-6.95 (m, 3H), 6.93-6.88 (m, 1H), 5.86-5.75 (m, 1H), 5.11 (dd, *J* = 10.4 Hz, 1H), 4.93 (dd, *J* = 17.2 and 1.2 Hz, 1H), 4.62-4.54 (m, 1H), 3.83 (s, 3H), 2.61-2.44 (m, 2H), 2.37 (s, 3H), 1.27 (d, *J* = 6.4 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.0, 148.1, 144.0, 136.79, 136.76, 134.6, 132.0, 130.0, 129.8 (2CH), 128.4, 127.1 (2CH), 124.9, 123.7, 123.1, 120.5, 119.6, 117.5, 113.3, 92.3, 85.4, 75.9, 74.8, 55.8, 47.3, 22.5, 21.5 ($2CH_3$). HRMS (ESI): *m/z* calcd for $C_{29}H_{30}NaO_2S$ $(M+Na)^+$: 562.1431, Found: 562.1410.

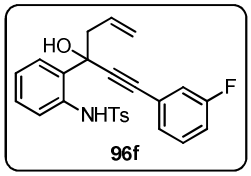
4-(7-Chloro-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-1-yl)-2-methoxyphenol (107e).



107e

Prepared by following the procedure **L** and isolated as pale yellow oil. M.P = 201-203°C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3069, 2978, 1471, 1377, 1261, 1177, 1045. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 1.6 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.46 (s, 1H), 7.39-7.35 (m, 3H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.4 Hz, 2H), 7.00 (dd, *J* = 8.0 and 1.6 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 2.71 (s, 3H), 2.24 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.3, 153.0, 147.9, 145.1, 144.2, 142.5, 136.7, 136.4, 135.2, 134.2, 133.3, 128.9 (2CH), 126.7 (2CH), 125.5, 124.9, 123.7, 122.1, 119.1, 112.3, 111.5, 75.0, 55.8, 24.3, 21.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{22}ClN_2O_4S$ $(M+H)^+$: 493.0989, Found: 493.1025.

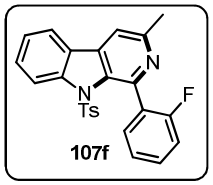
N-(2-(1-(3-Fluorophenyl)-3-hydroxyhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96f).



96f

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3444, 3267, 3067, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.23 (s, 1H, NH), 7.79 (d, *J* = 8.4 Hz, 2H), 7.66 (dd, *J* = 4.0 and 2.6 Hz, 1H), 7.63 (dd, *J* = 8.0 and 2.0 Hz, 1H), 7.36-7.29 (m, 4H), 7.26-7.14 (m, 3H), 7.07 (dt, *J* = 7.6 and 0.8 Hz, 1H), 5.99-5.87 (m, 1H), 5.37 (d, *J* = 2.0 Hz, 1H), 4.83 (dd, *J* = 10.4 and 0.8 Hz, 1H), 3.46 (brs, 1H, OH), 2.59-2.52 (m, 2H), 2.39 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.3 (d, *J* = 245.6 Hz), 143.8, 138.5, 137.2, 135.6, 130.1 (d, *J* = 8.5 Hz), 129.7 (2CH, 1C), 129.5, 129.0, 127.7 (d, *J* = 29 Hz), 127.2 (2CH, 1C), 123.6 (d, *J* = 37.6 Hz), 123.5, 120.7, 118.7 (d, *J* = 22.9 Hz), 116.9, 88.0, 87.9, 78.4, 48.1, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{22}FNaNO_3S$ $(M+Na)^+$: 434.1304, Found: 435.1343.

1-(2-Fluorophenyl)-3-methyl-9-tosyl-9H-pyrido[3,4-b]indole (107f).

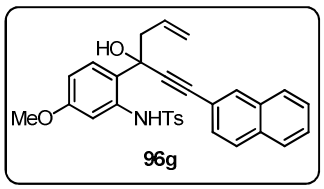


107f

Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 175-178 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3069, 2925, 1448, 1373, 1175, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 8.4 Hz, 1H), 7.98 (t, *J* = 1.8 Hz, 1H), 8.03 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.50-7.47 (m, 2H), 7.45-7.35 (m, 3H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 2.74 (s,

3H), 2.62 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.0 (d, *J* = 243.6 Hz), 153.1, 146.0, 144.4, 143.4 (d, *J* = 8.1 Hz), 142.3, 137.1, 135.6, 133.0, 131.8, 129.5 (d, *J* = 7.9 Hz), 128.8, 128.7 (2CH), 126.9 (2CH), 126.3 (d, *J* = 11.7 Hz), 125.7, 124.3 (d, *J* = 8.0 Hz), 123.5 (d, *J* = 5.6 Hz), 119.6, 115.4 (d, *J* = 22.3 Hz), 114.9 (d, *J* = 23.5 Hz), 26.6, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{19}FN_2O_2S$ $(M+H)^+$: 453.1949, Found: 453.1958.

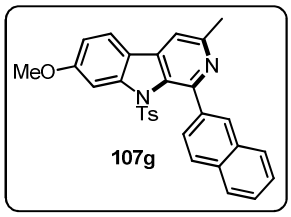
N-(2-(3-Hydroxy-1-(naphthalen-2-yl)hex-5-en-1-yn-3-yl)-5-methoxyphenyl)-4-methylbenzenesulfonamide (96g).



96g

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3444, 3267, 3067, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.83 (brs, 1H, NH), 7.99 (s, 1H), 7.86-7.79 (m, 3H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.55-7.47 (m, 4H), 7.26-7.22 (m, 3H), 6.82 (dd, *J* = 8.8 and 2.8 Hz, 1H), 5.92-5.80 (m, 1H), 5.23 (dd, *J* = 10.4 and 1.6 Hz, 1H), 5.10 (dd, *J* = 17.2 and 1.2 Hz, 1H), 3.78 (s, 3H), 2.54-2.46 (m, 2H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.7, 143.6, 137.2, 133.0, 132.8, 132.5, 132.0, 131.9, 129.6 (2CH), 128.5, 128.1 (2CH), 127.8 (2CH), 127.1 (2CH), 127.0, 126.7, 122.8, 120.9, 118.9, 114.7, 113.4, 89.4, 88.4, 74.6, 55.4, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{30}H_{27}NNaO_4S$ $(M+Na)^+$: 520.1558, Found: 520.1540.

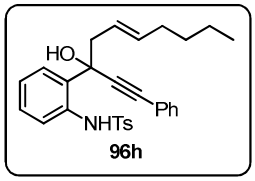
7-Methoxy-3-methyl-1-(naphthalen-2-yl)-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107g).



107g

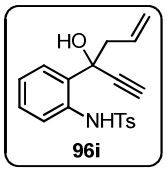
Prepared by following the procedure **L** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2925, 1563, 1419, 1371, 1172, 682. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.24 (dd, *J* = 8.4 and 1.6 Hz, 1H), 8.17 (dd, *J* = 9.2 and 0.4 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.96-7.88 (m, 2H), 7.51-7.49 (m, 2H), 7.40 (s, 1H), 7.22-7.15 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 3.91 (s, 3H), 2.76 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 157.9, 154.4, 150.4, 144.2, 139.4, 138.4, 136.3, 133.9, 133.46, 133.41, 131.9, 128.8, 128.7 (2CH), 128.6, 127.8, 127.7, 127.6, 126.9 (2CH), 126.7, 126.1, 125.7, 120.7, 117.5, 111.6, 104.0, 55.7, 24.6, 21.5. HRMS (ESI): *m/z* calcd for $C_{30}H_{25}N_2O_3S$ $(M+H)^+$: 493.1586, Found: 493.1579.

N-(2-(3-Hydroxy-1-phenyldec-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96h).



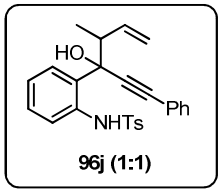
Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.22 (s, 1H, NH), 7.80 (dd, *J* = 8.0 and 1.2 Hz, 2H), 7.64-7.53 (m, 2H), 7.52-7.41 (m, 2H), 7.40-7.33 (m, 3H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.04 (dt, *J* = 8.0 and 1.2 Hz, 1H), 5.51-5.46 (m, 2H), 3.81 (s, 1H, OH), 2.55 (d, *J* = 5.6 Hz, 2H), 2.37 (s, 3H), 2.11-2.07 (m, 2H), 1.31-1.15 (m, 5H), 0.90 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.6, 138.2, 137.2, 135.7 (2CH), 129.9, 129.6 (2CH), 129.5, 129.0, 128.9, 128.4 (2CH, 1C), 127.2 (2CH), 123.3, 122.9, 121.9, 119.9, 89.5, 87.7, 74.7, 46.3, 32.3, 31.4, 22.1, 21.5, 13.9. HRMS (ESI): *m/z* calcd for $C_{29}H_{31}NNaO_3S$ $(M+Na)^+$: 496.1922, Found: 496.1909.

N-(2-(3-Hydroxyhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96i).



Prepared by following the procedure **L** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3467, 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.07 (s, 1H, NH), 7.78 (d, *J* = 8.4 Hz, 2H), 7.60 (dd, *J* = 8.4 and 1.2 Hz, 1H), 7.56 (dd, *J* = 8.0 and 1.2 Hz, 1H), 7.29-7.21 (m, 3H), 7.04 (dt, *J* = 8.0 and 1,6 Hz, 1H), 5.86-5.78 (m, 1H), 5.22 (d, *J* = 10.0 Hz, 1H), 5.07 (d, *J* = 16.8 Hz, 1H), 3.51 (brs, 1H, OH), 2.79 (s, 1H), 2.56-2.47 (m, 2H), 2.48 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 137.2, 135.6, 131.6, 129.7 (2CH), 129.3, 129.2, 128.3, 127.1 (2CH), 123.4, 121.3, 120.2, 84.0, 76.3, 74.1, 47.0, 21.5. HRMS (ESI): *m/z* calcd for $C_{19}H_{19}NNaO_3S$ $(M+Na)^+$: 364.0983, Found: 364.0970.

N-(2-(3-Hydroxy-4-methyl-1-phenylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96j).

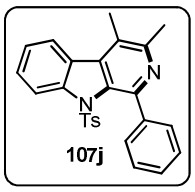


Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3443, 3267, 3017, 2920, 2221, 1573, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.25 (s, 1H, NH), 7.82 (d, *J* = 8.4 Hz, 2H), 7.71 (dd, *J* = 7.6 and 1.6 Hz, 1H), 7.64 (dd, *J* = 4.0 and 1.2 Hz, 1H), 7.52-7.47 (m, 2H), 7.41-7.33 (m, 6H), 7.07 (dt, *J* = 7.6 and 1.2

Hz, 1H), 6.02-5.91 (m, 1H), 5.36 (s, 1H), 4.81 (dd, *J* = 10.4 and 0.8 Hz, 1H), 3.43 (brs, 1H, OH), 2.59-2.52 (m, 1H), 2.39 (s, 3H), 1.22 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 138.7, 137.3, 135.6, 131.8 (2CH), 130.0, 129.73 (2CH), 129.7 (2CH), 129.2 (2CH), 128.5, 127.2 (2CH), 123.2, 121.8, 120.6, 119.9, 89.2, 88.0, 78.8, 48.1, 21.52, 16.4.

2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.18 (s, 1H, NH), 7.76 (d, *J* = 8.4 Hz, 2H), 7.66 (dd, *J* = 4.0 and 1.2 Hz, 1H), 7.55 (dd, *J* = 8.0 and 1.6 Hz, 1H), 7.52-7.47 (m, 3H), 7.27-7.21 (m, 6H), 7.00 (dt, *J* = 8.0 and 1.2 Hz, 1H), 5.60-5.50 (m, 1H), 5.33 (dd, *J* = 8.0 and 1.6 Hz, 1H), 4.43 (dt, *J* = 17.2 Hz and 1.2 Hz, 1H), 3.36 (brs, 1H, OH), 2.52-2.49 (m, 1H), 2.37 (s, 3H), 0.69 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 138.2, 137.1, 135.6, 131.8 (2CH), 129.8, 129.0, 128.9, 128.48 (2CH, 1C), 128.47 (2CH), 128.5, 127.0 (2CH), 123.8, 121.8, 120.0, 116.8, 88.9, 78.7, 47.6, 21.5, 14.5. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}NNaO_3S$ $(M+Na)^+$: 454.1453, Found: 454.1427.

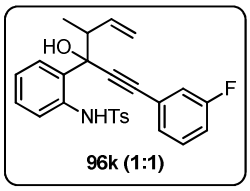
3,4-Dimethyl-1-phenyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107j).



107j

Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 130-132 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 8.4 Hz, 1H), 8.08 (t, *J* = 1.6 Hz, 1H), 8.06 (s, 1H), 7.93 (d, *J* = 7.6 Hz, 1H), 7.60-7.47 (m, 3H), 7.45-7.35 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 2.74 (s, 3H), 2.62 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.0, 147.5, 144.2, 142.3, 137.0, 133.1, 132.0, 128.7, 128.6 (2CH, 1C), 128.4 (2CH), 128.2 (2CH, 1C), 128.1, 126.9 (2CH), 125.5, 123.4, 122.9, 119.6, 22.6, 21.4, 15.3. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}N_2O_2S$ $(M+H)^+$: 427.1480, Found: 427.1467.

N-(2-(1-(3-Fluorophenyl)-3-hydroxy-4-methylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96k).



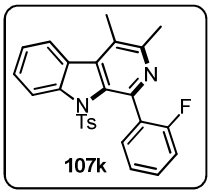
96k (1:1)

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3444, 3267, 3067, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.23 (s, 1H, NH), 7.79 (d, *J* = 8.4 Hz, 2H), 7.66 (dd, *J* = 4.0 and 2.6 Hz, 1H), 7.63 (dd, *J* = 8.0 and 2.0 Hz, 1H), 7.36-7.29 (m, 4H), 7.26-7.14 (m, 3H), 7.07 (dt, *J* = 7.6

and 0.8 Hz, 1H), 5.99-5.87 (m, 1H), 5.37 (d, *J* = 2.0 Hz, 1H), 4.83 (dd, *J* = 10.4 and 0.8 Hz, 1H), 3.46 (brs, 1H, OH), 2.59-2.52 (m, 1H), 2.39 (s, 3H), 1.21 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.3 (d, *J* = 245.6 Hz), 143.8, 138.5, 137.2, 135.6, 130.1 (d, *J* = 8.5 Hz), 129.7 (2CH, 1C), 129.5, 129.0, 127.7 (d, *J* = 29 Hz), 127.2 (2CH, 1C), 123.6 (d, *J* = 37.6 Hz), 123.5, 120.7, 118.7 (d, *J* = 22.9 Hz), 116.9, 88.0, 87.9, 78.4, 48.1, 21.5, 16.4.

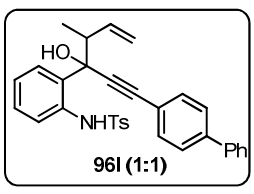
2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H, NH), 7.76 (d, *J* = 8.0 Hz, 2H), 7.65 (dd, *J* = 4.1 and 1.2 Hz, 1H), 7.51 (dd, *J* = 8.0 and 11.6 Hz, 1H), 7.27-7.24 (m, 5H), 7.26-7.06 (m, 2H), 7.00 (dt, *J* = 7.6 and 0.8 Hz, 1H), 5.59-5.47 (m, 1H), 5.33 (dd, *J* = 10.4 and 1.6 HZ, 1H), 4.46 (dt, *J* = 16.8 and 1.2 Hz, 1H), 3.44 (brs, 1H, OH), 2.52-2.45 (m, 1H), 2.37 (s, 3H), 0.68 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 162.2 (d, *J* = 245.6 Hz), 143.8, 138.0, 137.1, 130.3, 130.1 (d, *J* = 8.5 Hz), 129.7 (2CH, 1C), 129.3, 128.2, 127.7 (d, *J* = 2.9 Hz), 127.0 (2CH, 1C), 123.5 (d, *J* = 37.6 Hz), 122.9, 120.5, 126.0, 116.3 (d, *J* = 22.4 Hz), 88.4, 87.8, 78.6, 47.5, 21.5, 14.4. HRMS (ESI): *m/z* calcd for $C_{26}H_{24}FNaNO_3S$ $(M+Na)^+$: 472.1359, Found: 472.1343.

1-(2-Fluorophenyl)-3,4-dimethyl-9-tosyl-9H-pyrido[3,4-*b*]indole (107k).



Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 175-178 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3069, 2925, 1448, 1373, 1175, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 8.4 Hz, 1H), 7.98 (t, *J* = 1.8 Hz, 1H), 8.03 (s, 1H), 7.90 (d, *J* = 7.6 Hz, 1H), 7.50-7.47 (m, 2H), 7.45-7.35 (m, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 2.74 (s, 3H), 2.62 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 163.0 (d, *J* = 243.6 Hz), 153.1, 146.0, 144.4, 143.4 (d, *J* = 8.1 Hz), 142.3, 137.1, 135.6, 133.0, 131.8, 129.5 (d, *J* = 7.9 Hz), 128.8, 128.7 (2CH), 126.9 (2CH), 126.3 (d, *J* = 11.7 Hz), 125.7, 124.3 (d, *J* = 8.0 Hz), 123.5 (d, *J* = 5.6 Hz), 119.6, 115.4 (d, *J* = 22.3 Hz), 114.9 (d, *J* = 23.5 Hz), 26.6, 21.5, 15.4. HRMS (ESI): *m/z* calcd for $C_{26}H_{22}FN_2O_2S$ $(M+H)^+$: 445.1386, Found: 445.1371.

N-(2-(1-([1,1'-Biphenyl]-4-yl)-3-hydroxy-4-methylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96l).

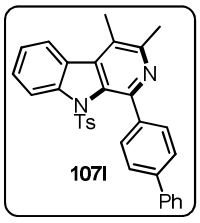


Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3451, 3229, 2973, 2231, 1510, 1493, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$):

δ 9.20 (s, 1H, NH), 7.81 (dd, *J* = 8.0 and 1.6 Hz, 1H), 7.66 (tt, *J* = 8.0 and 1.2 Hz, 1H), 7.63-7.54 (m, 7H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 2H), 7.31-7.22 (m, 3H), 7.08 (dt, *J* = 7.6 and 1.2 Hz, 1H), 6.04-5.92 (m, 1H), 5.38 (s, 1H), 4.83 (dd, *J* = 10.4 and 0.8 Hz, 1H), 3.35 (brs, 1H, OH), 2.63-2.55 (m, 1H), 2.40 (s, 3H), 1.28 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 141.8, 141.0, 138.1, 137.2, 135.6, 132.2 (2CH, 1C), 130.4, 129.7 (2CH, 1C), 129.2, 128.9 (2CH, 1C), 128.4, 127.2, 127.0 (2CH), 127.0, 123.3, 120.6, 120.1, 116.9, 89.1, 88.6, 78.9, 48.2, 21.5, 16.4.

2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H, NH), 7.78 (d, *J* = 10.4 Hz, 1H), 7.66 (dt, *J* = 8.0 and 1.2 Hz, 1H), 7.63-7.54 (m, 7H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.43-7.37 (m, 2H), 7.31-7.22 (m, 3H), 7.02 (dt, *J* = 8.0 and 1.2 Hz, 1H), 5.64-5.52 (m, 1H), 5.35 (d, *J* = 4.4 and 1.6 Hz, 1H), 4.48 (dt, *J* = 17.2 and 1.6 Hz, 1H), 3.11 (brs, 1H, OH), 2.55-2.48 (m, 1H), 2.58 (s, 3H), 0.71 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 141.8, 138.7, 137.3, 135.6, 132.2 (2CH, 1C), 130.4, 129.8, 129.7 (2CH), 128.98, 128.94 (2CH, 1C), 127.8, 127.1 (2CH, 1C), 127.04, 122.9, 120.63, 120.61, 120.0, 116.9, 88.9, 88.0, 78.7, 47.5, 21.5, 14.4. HRMS (ESI): *m/z* calcd for $C_{32}H_{30}NO_3S$ $(M+H)^+$: 508.1946, Found: 508.1918.

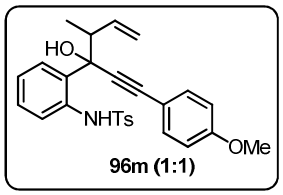
1-([1,1'-Biphenyl]-4-yl)-3,4-dimethyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107l).



107l

Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 219-220 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3025, 2924, 1449, 1372, 1173, 749. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 8.4 Hz, 1H), 8.18-8.14 (m, 2H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.76-7.69 (m, 3H), 7.61-7.55 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.44-7.34 (m, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 2.75 (s, 3H), 2.64 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.1, 147.0, 144.2, 143.2, 142.3, 141.1, 140.6, 137.0, 133.1, 132.1, 128.4 (2CH), 128.7 (2CH, 1C), 128.6 (2CH, 1C), 127.2 (2CH), 127.1, 127.0, 126.9 (2CH, 1C), 125.6, 123.5, 123.0, 119.6, 122.6, 21.4, 15.4. HRMS (ESI): *m/z* calcd for $C_{32}H_{27}N_2O_2S$ $(M+H)^+$: 503.1793, Found: 503.1775.

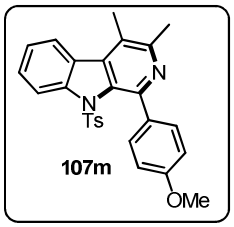
N-(2-(3-Hydroxy-1-(4-methoxyphenyl)-4-methylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (97m).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3443, 3267, 3017, 2920, 2221, 1573, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.23 (s, 1H, NH), 7.79 (d, *J* = 8.0 Hz, 2H), 7.70 (dd, *J* = 8.0 and 1.6 Hz, 1H), 7.63 (dd, *J* = 4.0 and 1.2 Hz, 1H), 7.46-7.40 (m, 4H), 7.29-7.26 (m, 1H), 7.05 (dt, *J* = 7.6 and 0.8 Hz, 1H), 6.89 (d, *J* = 2.8 Hz, 2H), 6.01-5.90 (m, 1H), 5.35 (s, 1H), 4.74 (dd, *J* = 11.6 and 1.2 Hz, 1H), 3.84 (s, 3H), 3.35 (s, 1H), 2.58-2.51 (m, 1H), 2.39 (s, 3H), 1.20 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 138.8, 137.3, 135.6, 133.2 (2CH), 130.4, 129.8, 129.6 (2CH, 1C), 128.8, 127.2 (2CH), 123.1, 120.5, 119.8, 114.0 (2CH), 113.9, 89.2, 86.7, 78.8, 55.3, 48.1, 21.5, 16.8.

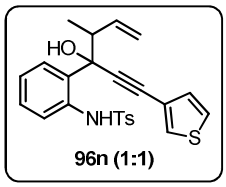
2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.19 (s, 1H, NH), 7.77 (d, *J* = 8.4 Hz, 2H), 7.65 (dd, *J* = 4.0 and 0.8 Hz, 1H), 7.55 (dd, *J* = 8.0 and 1.6 Hz, 1H), 7.29-7.20 (m, 4H), 6.99 (dt, *J* = 8.0 and 1.2 Hz, 1H), 6.87 (d, *J* = 3.2 Hz, 2H), 5.62-5.50 (m, 1H), 5.31 (dd, *J* = 8.4 and 1.6 Hz, 1H), 4.43 (dt, *J* = 17.2 Hz, 1H), 3.83 (s, 3H), 3.20 (s, 1H, OH), 2.51-2.45 (m, 2H), 2.37 (s, 3H), 0.68 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 138.3, 137.2, 135.6, 133.2 (2CH), 129.9, 129.7 (2CH, 1C), 129.1, 128.6, 127.0 (2CH), 122.8, 119.9, 116.6, 114.0 (2CH), 113.8, 89.0, 86.1, 78.7, 55.3, 47.5, 21.5, 14.3. HRMS (ESI): *m/z* calcd for $C_{27}H_{27}NNaO_4S$ $(M+Na)^+$: 484.1558, Found: 4484.1590.

1-(4-Methoxyphenyl)-3,4-dimethyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107m).



Prepared by following the procedure **L** and isolated as pale yellow solid. M.P = 203-205 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.0 Hz, 1H), 8.09-8.04 (m, 2H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.55 (dt, *J* = 7.4 and 1.2 Hz, 1H), 7.38 (dt, *J* = 8.0 and 0.8 Hz, 1H), 7.07-7.01 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 3.89 (s, 3H), 2.72 (s, 3H), 2.59 (s, 3H), 2.20 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.6, 153.0, 147.2, 144.2, 142.4, 137.1, 133.9, 132.8, 131.9, 129.7 (2CH), 128.9, 128.6 (2CH), 128.5, 127.0 (2CH), 125.5, 123.4, 122.3 119.7, 113.6 (2CH), 55.2, 22.6, 21.4, 15.3. HRMS (ESI): *m/z* calcd for $C_{27}H_{25}N_2O_3S$ $(M+H)^+$: 457.1586, Found: 457.1578.

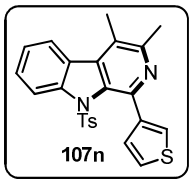
N-(2-(3-Hydroxy-4-methyl-1-(thiophen-3-yl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96n).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.18 (s, 1H, NH), 7.79 (d, *J* = 8.4 Hz, 1H), 7.68 (dd, *J* = 8.0 and 1.2 Hz, 1H), 7.69 (d, *J* = 6.0 and 1.0 Hz, 1H), 7.52-7.51 (m, 2H), 7.28-7.20 (m, 3H), 7.16 (dt, *J* = 5.2 and 1.2 Hz, 2H), 7.06 (dt, *J* = 7.6 and 0.8 Hz, 1H), 6.02-5.88 (m, 1H), 5.36 (s, 1H), 4.82 (d, *J* = 10.8 Hz, 1H), 3.31 (s, 1H, OH), 2.61-2.53 (m, 1H), 2.39 (s, 3H), 1.20 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 138.6, 137.3, 135.6, 130.0, 129.7 (2CH, 1C), 129.6, 129.2, 128.4, 127.2 (2CH), 125.7, 123.2, 120.8, 120.6, 119.9, 87.7, 84.4, 78.9, 48.1, 21.5, 16.4.

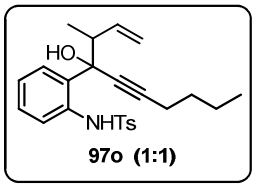
2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.15 (s, 1H, NH), 7.77 (d, *J* = 8.4 Hz, 1H), 7.64 (dd, *J* = 6.4 and 1.2 Hz, 1H), 7.54 (dd, *J* = 6.0 and 1.0 HZ, 1H), 7.34-7.31 (m, 2H), 7.28-7.20 (m, 3H), 7.16 (dt, *J* = 5.2 and 1.2 Hz, 1H), 7.00 (dt, *J* = 7.2 and 0.8 Hz, 2H), 5.61-5.50 (m, 1H), 5.33 (dd, *J* = 8.0 and 1.2 Hz, 1H), 4.47 (d, *J* = 17.2 Hz, 1H), 3.07 (s, 1H, OH), 2.53-2.45 (m, 1H), 2.38 (s, 3H), 0.68 (d, *J* = 6.4 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 138.1, 137.2, 135.6, 129.8, 129.6 (2CH, 1C), 129.65, 128.9, 127.0 (2CH, 1C), 125.7, 122.8, 120.7, 120.1, 116.8, 87.0, 84.2, 78.7, 47.5, 21.5, 14.4. HRMS (ESI): *m/z* calcd for $C_{24}H_{23}NNaO_3S_2$ $(M+Na)^+$: 460.1017, Found: 460.1009.

3,4-Dimethyl-1-(thiophen-3-yl)-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107n).



Prepared by following the procedure **L** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3062, 2928, 1420, 1373, 1188, 1175. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (s, 1H, NH), 8.07 (s, 1H), 7.92-7.86 (m, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.42 (dd, *J* = 4.8 and 2.8 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 2.72 (s, 3H), 2.59 (s, 3H), 2.21 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.9, 147.6, 144.1, 142.3, 137.6, 132.1, 129.0 (2CH), 128.7, 128.6 (2CH, 1C), 128.5, 128.3 (2CH), 126.9 (2CH), 125.5, 123.4, 122.6, 119.6, 26.6, 21.5, 15.3. HRMS (ESI): *m/z* calcd for $C_{24}H_{21}N_2O_2S_2$ $(M+H)^+$: 433.1044, Found: 433.1026.

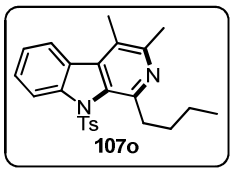
N-(2-(4-Hydroxy-3-methyldec-1-en-5-yn-4-yl)phenyl)-4-methylbenzenesulfonamide (97o).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3441, 3253, 3068, 2921, 2231, 1582, 1491, 1266, 1165, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.20 (s, 1H, NH), 7.77 (d, *J* = 8.0 Hz, 2H), 7.64-7.58 (m, 1H), 7.46 (dd, *J* = 8.0 and 1.2 Hz, 1H), 7.27-7.20 (m, 3H), 7.03 (dt, *J* = 8.0 and 0.8 Hz, 1H), 5.92-5.80 (m, 1H), 5.30 (s, 1H), 5.26 (dd, *J* = 12.8 and 1.6 Hz, 1H), 3.16 (brs, 1H, OH), 2.44-2.35 (m, 3H), 2.38 (s, 3H), 1.63-1.51 (m, 4H), 1.16 (d, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 4.0 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 139.0, 137.3, 135.6, 130.4, 129.8, 129.6 (2CH), 128.9, 127.1 (2CH), 123.0, 120.3, 119.5, 90.2, 79.3, 78.4, 48.0, 30.6, 22.0, 21.4, 18.4, 16.4, 13.5.

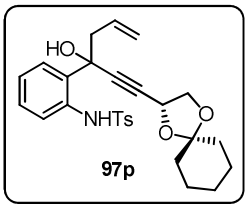
2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.17 (s, 1H, NH), 7.74 (d, *J* = 8.4 Hz, 2H), 7.64-7.58 (m, 1H), 7.27-7.20 (m, 3H), 7.19 (dd, *J* = 8.1 and 1.2 Hz, 1H), 6.97 (dt, *J* = 7.6 and 0.4 Hz, 1H), 5.52-5.41 (m, 1H), 4.74 (dd, *J* = 10.4 and 0.4 Hz, 1H), 4.36 (d, *J* = 17.2 Hz, 1H), 2.97 (brs, 1H, OH), 2.37 (s, 3H), 2.35-2.30 (m, 3H), 1.50-1.40 (m, 4H), 0.94 (t, *J* = 4.0 Hz, 3H), 0.59 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.6, 138.5, 137.2, 135.5, 130.1, 129.6 (2CH), 129.0, 128.7, 127.0 (2CH), 122.7, 119.8, 116.3, 90.1, 78.7, 78.3, 47.4, 30.5, 22.0, 21.4, 18.3, 14.9, 13.5. HRMS (ESI): *m/z* calcd for $C_{24}H_{29}NNaO_3S$ $(M+Na)^+$: 434.1766, Found: 434.1750.

1-Butyl-3,4-dimethyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107o).



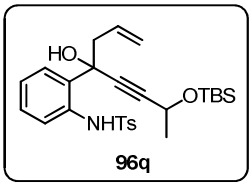
Prepared by following the procedure **L** and isolated as colorless solid. M.P = 152-155 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3064, 2934, 1597, 1447, 1187, 1172, 747. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 7.7 Hz, 2H), 3.44 (t, *J* = 7.6 Hz, 2H), 2.66 (s, 3H), 2.53 (s, 3H), 2.53 (s, 3H), 1.86-1.78 (m, 2H), 1.43-1.32 (m, 2H), 0.97 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.6, 151.1, 144.3, 142.5, 136.4, 134.1, 131.8, 129.1, 128.6 (2CH, 1C), 127.1 (2CH), 125.6, 123.4, 121.7, 119.9, 36.1, 31.3, 22.9, 22.3, 21.4, 15.2, 14.1. HRMS (ESI): *m/z* calcd for $C_{24}H_{27}N_2O_2S$ $(M+H)^+$: 407.1793, Found: 407.1777.

N-(2-(3-Hydroxy-1-(1,4-dioxaspiro[4.5]decan-2-yl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (97p).



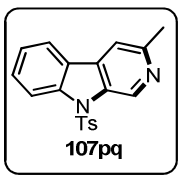
Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3427, 3231, 2938, 1599, 1337, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.18 (s, 1H, NH), 7.75 (dd, *J* = 8.4 and 1.6 Hz, 2H), 7.56 (dt, *J* = 8.0 and 1.2 Hz, 1H), 7.51-7.46 (m, 1H), 7.27-7.18 (m, 3H), 7.00 (t, *J* = 7.6 Hz, 1H), 5.77-5.63 (m, 1H), 5.14 (dd, *J* = 10.0 Hz, 1H), 4.99 (d, *J* = 17.2 Hz, 1H), 4.82 (dt, *J* = 6.0 and 2.8 Hz, 1H), 4.17 (t, *J* = 8.0 Hz, 1H), 3.99-3.94 (m, 1H), 3.63 (brs, 1H, OH), 2.55-2.40 (m, 2H), 2.37 (s, 3H), 1.76-1.70 (m, 2H), 1.64-1.57 (m, 6H), 1.45-1.39 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.8, 137.1, 135.6, 131.8, 129.7 (2CH, 1C), 129.5, 128.4, 127.1, 123.3, 120.7, 120.1, 111.3, 86.2, 85.7, 74.4, 69.5, 69.4, 60.0, 47.1, 35.6, 35.3, 24.9, 23.8, 23.7, 21.5. HRMS (ESI): *m/z* calcd for $C_{27}H_{31}NNaO_5S$ $(M+Na)^+$: 504.1821, Found: 504.1809.

N-(2-(7-((*tert*-Butyldimethylsilyl)oxy)-4-hydroxyoct-1-en-5-yn-4-yl)phenyl)-4-methylbenzenesulfonamide (96q).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3481, 2943, 2873, 2134, 1454, 1344, 702. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.18 (s, 1H, NH), 7.77 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 6.0 Hz, 1H), 7.56-7.51 (m, 1H), 7.30-7.19 (m, 2H), 7.01 (dt, *J* = 8.0 and 1.2 Hz, 1H), 5.79-5.69 (m, 1H), 5.79-5.69 (m, 1H), 5.15 (d, *J* = 10.4 Hz, 1H), 4.99 (d, *J* = 17.2 Hz, 1H), 4.63 (dq, *J* = 6.8 and 2.4 Hz, 1H), 3.19 (s, 1H), 2.54-2.39 (m, 2H), 2.38 (s, 3H), 1.46 (d, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), 0.12 (s, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 137.2, 135.6, 130.2, 129.8, 129.7 (2CH), 129.0, 128.6, 127.1 (2CH), 123.3, 120.7, 120.0, 90.9, 83.3, 74.7, 58.9, 472, 25.7 ($3CH_3$), 25.2, 21.5, 18.2, -4.6, 4.9. HRMS (ESI): *m/z* calcd for $C_{27}H_{37}NNaO_4SSi$ $(M+Na)^+$: 522.2110, Found: 522.2103.

3-Methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indole (107pq).



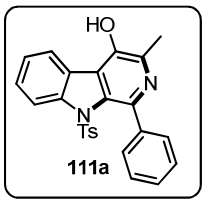
Prepared by following the procedure **L** and isolated as colorless solid. M.P = 87-90 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 2929, 2856, 1597, 1371, 1173, 934. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.51 (s, 1H, NH), 8.36 (d, *J* = 8.8 Hz, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.66 (s, 1H), 7.64-7.60 (m, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 2H), 2.71 (s, 3H), 2.28 (s,

3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.5, 145.3, 139.3, 136.3, 134.4, 135.5, 133.1, 129.9, 129.8 (2CH), 126.6 (2CH), 124.4, 124.2, 121.4, 115.3, 113.4, 24.2, 21.5. HRMS (ESI): *m/z* calcd for $C_{19}H_{17}N_2O_2S$ $(M+H)^+$: 337.1011, Found: 337.0996.

Procedure M: General procedure for the synthesis of 1,3-disubstituted-4-hydroxy-*β*-carbolines.

A 5 mL glass vial was charged with 3-(2-aminophenyl)hex-5-en-1-yn-3-ol **96** (0.1 mmol), AgOAc (2 mol%) in DCE (1 mL) and stirred at 60 °C. Upon disappearance of starting compound **96** (by TLC), $TMSN_3$ (0.11 mmol) and $BiCl_3$ (5 mol%) were introduced and continued stirring at 60 °C until intermediate **97** disappeared (TLC). On complete formation of **103**, the reaction mixture was quenched by adding saturated aq. $NaHCO_3$ (1 mL) and extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (10-20% EtOAc/hexane) to afford **103**. Isolated azide **103** was taken in a 5 mL glass vial and toluene (1 mL) was added, stirred at 80 °C for 1 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (50-70% EtOAc/hexane) to afford **111** in 76-89% yields.

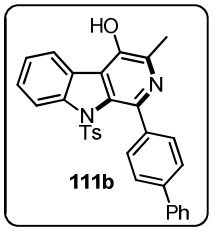
3-Methyl-1-phenyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111a).



111a

Prepared by following the procedure **M** and isolated as colorless solid. M.P = 178-180 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3446, 3064, 2921, 1447, 1372, 1173. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 8.4 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 2H), 7.46-7.40 (m, 1H), 7.39-7.31 (m, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 2.59 (s, 3H), 2.27 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.1, 144.4, 141.6, 141.5, 140.8, 140.4, 134.3, 132.2, 128.8 (2CH), 128.6, 128.4 (2CH), 128.1 (2CH), 127.8, 126.9, 126.8 (2CH), 126.7, 125.7, 124.1, 118.9, 21.4, 18.1. HRMS (ESI): *m/z* calcd for $C_{25}H_{21}N_2O_3S$ $(M+H)^+$: 429.1273, Found: 429.1267.

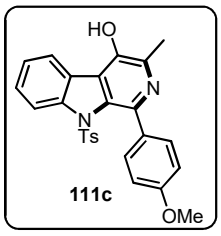
1-([1,1'-Biphenyl]-4-yl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111b).



111b

Prepared by following the procedure **M** and isolated as pale yellow oli. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 2930, 2834, 1513, 1371, 1247, 1175. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 9.88 (s, 1H, NH), 8.16-8.06 (m, 2H), 8.00 (d, *J* = 8.4 Hz, 2H), 7.82-7.35 (m, 4H), 7.66-7.33 (m, 6H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.94 (d, *J* = 8.4 Hz, 2H), 2.59 (s, 3H), 2.17 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 145.2, 145.1, 142.9, 141.1, 140.9, 139.2, 134.0, 133.3, 132.8, 133.9, 131.9, 129.6 (2CH, 1C), 129.1, 129.2, 128.7, 127.9, 127.39, 127.35, 127.0, 126.9 (2CH, 1C), 126.5, 126.3 (2CH), 124.2, 119.1, 21.3, 19.9. HRMS (ESI): *m/z* calcd for $C_{31}H_{25}N_2O_3S$ $(M+H)^+$: 505.1586, Found: 505.1569.

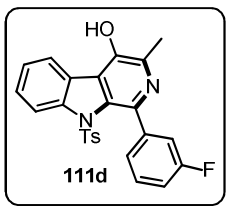
1-(4-Methoxyphenyl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111c).



111c

Prepared by following the procedure **M** and isolated a pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3342, 2931, 1428, 1532, 1176, 1152. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.86-6.82 (m, 4H), 3.78 (s, 3H), 2.45 (s, 3H), 2.18 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.2, 145.4, 144.4, 141.6, 140.9, 134.1, 132.2, 129.6 (2CH, 1C), 128.9 (2CH, 1C), 128.5, 127.2, 127.1, 126.8 (2CH, 1C), 125.7, 124.1, 118.9, 113.5, 55.1, 21.4, 17.9. HRMS (ESI): *m/z* calcd for $C_{26}H_{23}N_2O_4S$ $(M+H)^+$: 459.1379, Found: 459.1363.

1-(3-Fluorophenyl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (11d).

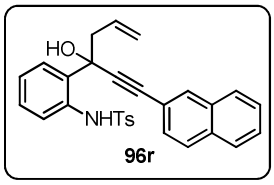


111d

Prepared by following the procedure **M** and isolated as pale yellow solid. M.P = 215-218 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): δ 8.20 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.80-7.55 (m, 1H), 7.61 (dt, *J* = 8.8 and 1.2 Hz, 1H), 7.50-7.39 (m, 2H), 7.11 (dt, *J* = 2.4 Hz, 1H), 7.05-6.98 (m, 4H), 2.97 (brs, 1H, OH), 2.66 (s, 3H), 2.19 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2CO$): δ 162.2 (d, *J* = 240.1 Hz), 145.0, 144.9, 144.0 (d, *J* = 7.9 Hz), 141.5 (d, *J* = 24.8 Hz), 140.1, 134.1, 132.0, 129.7 (d, *J* = 8.2 Hz), 128.9 (2CH, 1C), 128.5, 127.3, 126.9 (2CH), 126.1, 125.9, 124.4 (d, *J* = 2.0 Hz), 123.9, 118.9,

114.9 (d, *J* = 22.5 Hz), 113.7 (d, *J* = 22.5 Hz), 24.6, 18.6. HRMS (ESI): *m/z* calcd for $C_{25}H_{20}FN_2O_3S$ $(M+H)^+$: 447.1179, Found: 447.1165.

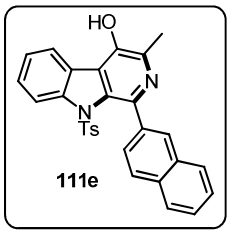
N-(2-(3-Hydroxy-1-(naphthalen-2-yl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96r).



96r

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3434, 3134, 2978, 2132, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.26 (s, 1H, NH), 8.01 (s, 1H), 7.90-7.78 (m, 5H), 7.68 (dd, *J* = 7.6 and 0.8 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.57-7.49 (m, 3H), 7.31-7.19 (m, 3H), 7.07 (t, *J* = 7.6 Hz, 1H), 5.97-5.84 (m, 1H), 5.25 (d, *J* = 10.0 Hz, 1H), 5.13 (d, *J* = 17.2 Hz, 1H), 3.33 (brs, 1H, OH), 2.61-2.60 (m, 2H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 137.2, 135.7, 133.0, 132.8, 132.0, 131.9, 129.9, 129.7 (2CH), 129.1, 128.4, 128.2, 128.1, 127.8 (2CH), 127.2 (2CH), 127.0, 126.7, 123.4, 121.0, 120.1, 90.0, 89.5, 88.4, 74.8, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{29}H_{25}NNaO_3S$ $(M+Na)^+$: 490.1453, Found: 490.1435.

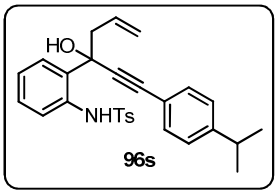
3-Methyl-1-(naphthalen-2-yl)-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111e).



111e

Prepared by following the procedure **M** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 9.25 (s, 1H, NH), 8.37 (s, 1H), 8.19-8.04 (m, 3H), 8.02-7.89 (m, 3H), 7.67-7.39 (m, 4H), 7.07-6.88 (m, 4H), 2.62 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 145.2, 145.1, 142.9, 141.1, 140.9, 139.2, 134.0, 133.3, 132.8, 131.9, 129.6 (2CH, 1C), 129.1, 128.7, 127.9, 127.39, 127.35, 127.0, 126.9 (2CH, 1C), 126.5, 126.3 (2CH), 124.2, 119.1, 21.3, 19.9. HRMS (ESI): *m/z* calcd for $C_{29}H_{23}N_2O_3S$ $(M+H)^+$: 479.1429, Found: 479.1411.

N-(2-(3-Hydroxy-1-(4-isopropylphenyl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96s).

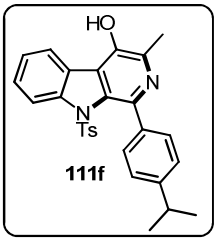


96s

Prepared by following the procedure **K** and isolated as pale yellow solid. M.P = 84-87 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat):

ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.25 (s, 1H, NH), 7.79 (d, *J* = 1.6 Hz, 2H), 7.61 (dt, *J* = 8.0 and 1.6 Hz, 2H), 7.42 (d, *J* = 6.4 Hz, 2H), 7.29-7.20 (m, 6H), 7.04 (dt, *J* = 8.0 and 1.6 Hz, 1H), 5.90-5.89 (m, 1H), 5.21 (dd, *J* = 10.0 and 1.6 Hz, 1H), 5.06 (dd, *J* = 17.2 and 1.6 Hz, 1H), 2.96 (sept, *J* = 6.8 Hz, 1H), 2.64-2.52 (m, 2H), 2.37 (s, 3H),1.26 (t, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 150.1, 143.7, 137.1, 135.6, 132.1, 131.8 (2CH), 130.0, 129.7 (2CH), 129.0, 128.5, 127.2 (2CH), 126.5 (2CH), 123.4, 120.8, 120.0, 119.0, 88.5, 88.3, 74.7, 47.4, 34.1, 23.8 ($2CH_3$), 21.5. HRMS (ESI): *m/z* calcd for $C_{28}H_{29}NNaO_3S$ $(M+Na)^+$: 482.1766, Found: 482.1754.

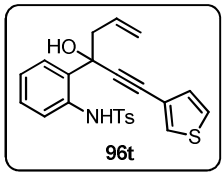
1-(4-Isopropylphenyl)-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111f).



111f

Prepared by following the procedure **M** and isolated as colourless solid. M.P = 194-196 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3477, 2961, 2878, 1426, 1372, 1172. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.21 (d, *J* = 8.4 Hz, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.32 (t, *J* = 7.2 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.00 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 2.96-2.84 (m, 1H), 2.45 (s, 3H), 2.19 (s, 3H), 1.24 (d, *J* = 6.8 Hz, 6H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 148.4, 144.4, 141.6, 140.9, 137.6, 134.2, 132.3, 128.8 (2CH), 128.5, 128.2 (2CH), 127.0, 127.1, 126.8 (2CH), 126.2 (2CH, 1C), 125.6, 124.1, 118.8, 33.8, 23.9 ($2CH_3$), 21.4, 17.9. HRMS (ESI): *m/z* calcd for $C_{28}H_{27}N_2O_3S$ $(M+H)^+$: 471.1742, Found: 471.1721.

N-(2-(3-Hydroxy-1-(thiophen-3-yl)hex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96t).

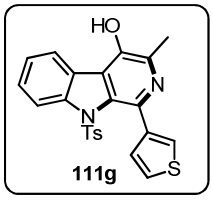


96t

Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3445, 3257, 3077, 2930, 2231, 1582, 1491, 1266, 1161, 1092. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.22 (s, 1H, NH), 7.80 (d, *J* = 8.4 Hz, 2H), 7.63 (dt, *J* = 7.6 and 1.2 Hz, 2H), 7.49 (dd, *J* = 7.2 and 1.6 Hz, 2H), 7.41-7.32 (m, 2H), 7.24 (d, *J* = 8.4 Hz, 3H), 7.05 (s, 1H), 5.92-5.80 (m, 1H), 5.23 (dd, *J* = 9.6 and 0.8 Hz, 1H), 5.10 (d, *J* = 17.2 Hz, 1H), 3.23 (brs, 1H), 2.63-2.55 (m, 1H), 2.37 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 137.2, 135.6, 132.0, 131.8 (2CH, 1C), 129.9, 129.7 (2CH), 129.1, 128.4 (2CH), 127.2 (2CH), 121.8, 121.0, 120.1, 89.2,

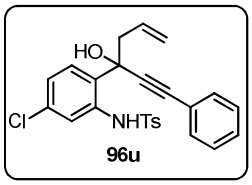
88.1, 74.7, 47.4, 21.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{21}NNaO_3S_2$ $(M+Na)^+$: 446.0861, Found: 446.0845.

3-Methyl-1-(thiophen-3-yl)-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111g).



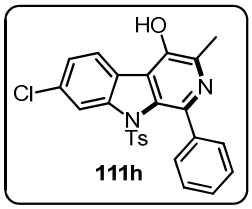
Prepared by following the procedure **M** and isolated as colorless solid. M.P = 149-151 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3416, 3051, 2920, 1451, 1369, 1174. **^{1}H NMR** (400 MHz, $(CD_3)_2CO$+ $CDCl_3$): δ 8.11 (dd, *J* = 8.0 and 2.4 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 8.00 (dd, *J* = 6.8 and 0.8 Hz, 1H), 7.88-7.84 (m, 1H), 7.79-7.71 (m, 1H), 7.46 (dt, *J* = 8.0 and 0.2 Hz, 1H), 7.35-7.23 (m, 2H), 6.93-6.81 (m, 4H), 2.62 (s, 3H), 2.15 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2CO$ + $CDCl_3$): δ 144.3, 141.7, 141.6, 133.9, 131.8, 129.5, 128.6 (2CH, 1C), 128.2, 128.1, 127.5, 126.9 (2CH, 1C), 126.3, 125.7, 124.0, 123.9, 123.1, 119.0, 21.0, 18.9. HRMS (ESI): *m/z* calcd for $C_{23}H_{19}N_2O_3S_2$ $(M+H)^+$: 435.0837, Found: 435.0822.

N-(5-Chloro-2-(3-hydroxy-1-phenylhex-5-en-1-yn-3-yl)phenyl)-4-methylbenzenesulfonamide (96u).



Prepared by following the procedure **K** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3444, 3216, 2970, 2231, 1492, 1228, 1091. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.28 (s, 1H, NH), 7.80 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 2.0 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.50-7.45 (m, 2H), 7.42-7.33 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.04 (dd, *J* = 8.4 and 2.0 Hz, 1H), 5.89-5.75 (m, 1H), 5.22 (d, *J* = 10.4 Hz, 1H), 5.06 (d, *J* = 17.2 Hz, 1H), 3.33 (brs, 1H, OH), 2.62-2.50 (m, 2H), 2.38 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 144.1, 136.8, 136.6, 134.8, 131.8 (2CH), 131.7, 129.8 (2CH), 129.5, 129.1, 128.4 (2CH), 128.2, 127.2 (2CH), 123.3, 121.5, 121.2, 19.7, 88.7, 88.4, 74.4, 47.3, 21.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{22}ClNNaO_3S$ $(M+Na)^+$: 474.0907, Found: 474.0892.

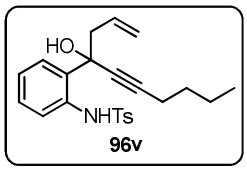
7-Chloro-3-methyl-1-phenyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111h).



Prepared by following the procedure **M** and isolated as colorless solid. M.P = 220-222 °C. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat):

ν_{max}/cm^{-1} 3341, 2917, 1597, 1360, 1171, 949. **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): δ 8.83 (s, 1H, NH), 8.18 (d, *J* = 2.0 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 8.01-7.97 (m, 2H), 7.48-7.4 (m, 3H), 7.38-7.32 (m, 1H), 7.07 (s, 4H), 2.64 (s, 3H), 2.23 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2CO$): δ 145.2, 144.4, 142.3, 141.7, 141.6, 141.3, 134.1, 133.5, 132.1, 129.1 (2CH, 1C), 128.4 (2CH), 127.6 (2CH), 127.3, 126.8 (2CH), 126.2, 126.0, 125.1, 118.9, 20.4, 18.5. HRMS (ESI): *m/z* calcd for $C_{25}H_{20}ClN_2O_3S$ $(M+H)^+$: 463.0883, Found: 463.0869.

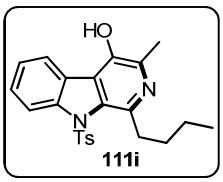
N-(2-(4-Hydroxydec-1-en-5-yn-4-yl)phenyl)-4-methylbenzenesulfonamide (96v).



96v

Prepared by following the procedure **K** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 1612, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.19 (s, 1H, NH), 7.78 (d, *J* =8.4 Hz, 2H), 7.60-7.54 (m, 2H), 7.27-7.18 (m, 3H), 7.02 (dt, *J* = 7.6 and 1.2 Hz, 1H), 5.84-5.69 (m, 1H), 5.17 (d, *J* = 10.0 Hz, 1H), 5.02 (d, *J* = 17.2 Hz, 1H), 2.95 (brs, 1H, OH), 2.52-2.39 (m, 2H), 2.38 (s, 3H), 2.31 (t, *J* = 6.8 Hz, 2H), 1.60-1.38 (m, 4H), 0.94 (t, *J* = 6.2 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.7, 137.2, 135.5, 132.3, 130.4, 129.6 (2CH), 128.9, 128.4, 127.1 (2CH), 123.2, 120.5, 119.9, 89.4, 80.7, 74.3, 47.4, 30.5, 22.0, 21.5, 18.4, 13.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{27}NNaO_3S$ $(M+Na)^+$: 420.1609, Found: 420.1596.

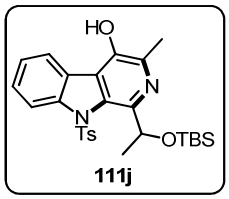
1-Butyl-3-methyl-9-tosyl-9*H*-pyrido[3,4-*b*]indol-4-ol (111i).



111i

Prepared by following the procedure **M** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3490, 2925, 1449, 1370, 1174, 1089. **^{1}H NMR** (400 MHz, $(CD_3)_2CO$): δ 8.42 (s, 1H, NH), 8.02 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 7.6 Hz, 1H), 7.56 (dt, *J* = 7.6 and 1.2 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.4 Hz, 2H), 3.33 (t, *J* = 7.6 Hz, 2H), 2.57 (s, 3H), 2.22 (s, 3H), 1.93-1.81 (m, 2H), 1.44-1.29 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2CO$): δ 144.8, 141.4, 141.2, 134.8, 132.4, 129.0 (2CH, 1C), 128.1, 127.6 (2CH), 126.9 (2CH), 125.7, 125.3, 123.8, 119.0, 35.5, 30.9, 22.5, 20.4, 18.4, 13.5. HRMS (ESI): *m/z* calcd for $C_{23}H_{25}N_2O_3S$ $(M+H)^+$: 409.1586, Found: 409.1564.

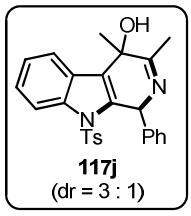
1-(1-((*tert*-Butyldimethylsilyl)oxy)ethyl)-3-methyl-9-tosyl-9H-pyrido[3,4-*b*]indol-4-ol (111j).



111j

Prepared by following the procedure **M** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3416, 3051, 2920, 1451, 1369, 1174, 798. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 8.23 (brs, 1H, OH), 8.16 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 2H), 7.28-7.19 (m, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.14 (q, *J* = 6.0 Hz, 1H), 2.57 (s, 3H), 2.15 (s, 3H), 1.74 (d, *J* = 6.0 Hz, 3H), 0.98 (s, 9H), 0.06 (s, 6H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 145.0, 141.2, 133.6, 131.6, 129.0 (2CH, 1C), 128.8, 128.3, 128.1, 127.0, 126.8 (2CH, 1C), 125.9, 124.5, 118.3, 67.2, 29.6, 25.9 ($3CH_3$), 23.0, 21.4, 18.2, -4.6, -4.9. HRMS (ESI): *m/z* calcd for $C_{27}H_{35}N_2O_4SSi$ $(M+H)^+$: 511.2087, Found: 511.2087.

3,4-Dimethyl-1-phenyl-9-tosyl-4,9-dihydro-1*H*-pyrido[3,4-*b*]indol-4-ol (117j, Major isomer).



117j
(dr = 3 : 1)

Prepared by following the procedure **M** and isolated as colourless oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3463, 3060, 2926, 1597, 1452, 1371, 1172, 740. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 11.6 (s, 1H, NH), 7.88 (dd, *J* = 7.0 and 1.6 Hz, 1H), 7.77-7.72 (m, 2H), 7.36-7.29 (m, 4H), 7.18-7.08 (m, 5H), 6.99 (d, *J* = 8.1 Hz, 1H), 6.27 (s, 1H), 2.25 (s, 3H), 2.13 (s, 3H), 1.54 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 163.9, 147.5, 145.3, 139.9, 138.1, 136.7, 134.3, 130.2, 130.1 (2CH), 129.3, 128.4, 127.7, 126.9 (2CH), 126.3 (2CH), 125.2, 124.4, 121.3, 115.1, 78.4, 62.0, 23.3, 21.4, 20.1. HRMS (ESI): *m/z* calcd for $C_{26}H_{25}N_2O_3S$ $(M+H)^+$: 445.1586, Found: 445.1599.

Procedure N: General procedure for the preparation of 3-allylbenzo[*b*]furan-2-carbinols.

Step-I: CuI (0.05 mmol), PPh_3 (0.05 mol) and Cs_2CO_3 (0.01 mmol, 3.3 mg) were added to a solution of diol **120** (1.0 mmol) in MeOH (1.0 mL). The mixture was stirred at room temperature until the reactant disappeared. The reaction mixture was quenched by adding saturated aq. $NaHCO_3$ (1 mL) and extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was used as such without any further purification.

Step-II: An oven dried round bottom flask was charged with 3-allyl-2-benzylidene-2,3-dihydrobenzofuran-3-ol **121** (1.0 mmol) in DCM (1 mL), placed at room temperature. PTSA (0.2 mmol) was added and stirred at room temperature until the reaction was complete (TLC). The

reaction mixture was quenched by adding saturated aq. $NaHCO_3$ (1 mL) and extracted with DCM. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **119** in 91% yield and used up immediately.

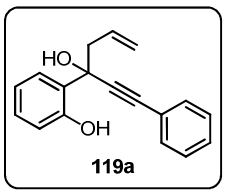
Procedure O: General procedure for the synthesis of benzofuro[2,3-*c*]pyridines, benzothieno[2,3-*c*]pyridines and isoquinolines.

A 5 mL glass vial was charged with the alcohol in DCE (1 mL), $TMSN_3$ (0.11 mmol) and $BiCl_3$ (5 mol%) were introduced and stirred at 60 ^oC until the complete disappearance of the alcohol (by TLC). Upon complete formation of the azide intermediate, $Pd(OAc)_2$ (5 mol%) was introduced and continued stirring at 80 ^oC until azide intermediate disappeared (by TLC). The reaction mixture was then quenched by adding saturated aq. $NaHCO_3$ (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford product in 68-87% yields.

Procedure P: General procedure for the synthesis of 4-hydroxy benzofuro[2,3-*c*]pyridine, benzothieno[2,3-*c*]pyridines and isoquinoline.

A 5 mL glass vial was charged with the azide in 1 mL of toluene and stirred at 80 ^oC till starting material disappeared (by TLC). The solvent was removed and the residue was purified by flash silica gel chromatography (50-70% EtOAc/hexane) to afford product in 67-83% yields.

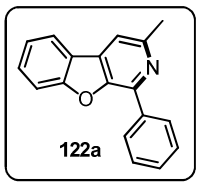
2-(3-Hydroxy-1-phenylhex-5-en-1-yn-3-yl)phenol (119a).



119a

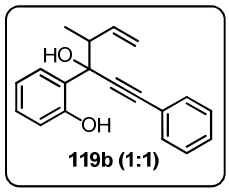
Prepared by following the procedure **N** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 2213, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.53 (s, 1H, OH), 7.59-7.47 (m, 3H), 7.44-7.35 (m, 3H), 7.29-7.20 (m, 1H), 7.02-6.86 (m, 2H), 6.11-5.96 (m, 1H), 5.34-5.22 (m, 2H), 3.61 (s, 1H), 2.97-2.82 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 154.9, 132.4, 131.8 (2CH, 1C), 129.7, 128.9 128.4 (2CH), 127.8, 126.3, 121.9, 120.8, 119.7, 89.1, 87.9, 75.4, 47.9. HRMS (ESI): *m/z* calcd for $C_{18}H_{15}O_2$ $(M–H)^+$: 263.1072, Found: 263.1060.

3-Methyl-1-phenylbenzofuro[2,3-*c*]pyridine (122a).



Prepared by following the procedure **O** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3068, 2924, 1581, 1419, 1192, 735. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.47 (m, 2H), 8.02 (dd, *J* = 7.6 and 0.4 Hz, 1H), 7.71-7.66 (m, 2H), 7.65-7.56 (m, 3H), 7.53-7.47 (m, 1H), 7.44 (dt, *J* = 8.0 and 0.8 Hz, 1H), 2.80 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.9, 151.4, 148.9, 141.3, 136.3 132.7, 129.6, 129.1, 128.6 (2CH), 128.5 (2CH), 123.2, 122.4, 121.8, 113.2, 112.4, 24.5. HRMS (ESI): *m/z* calcd for $C_{18}H_{14}NO$ $(M+H)^+$: 260.1075, Found: 260.1066.

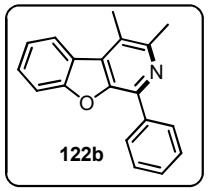
2-(3-Hydroxy-4-methyl-1-phenylhex-5-en-1-yn-3-yl)phenol (119b).



Prepared by following the procedure **N** and isolated as colourless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3134, 2978, 2232, 1488, 1230, 1159, 768. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.50 (brs, 1H, OH), 7.60-7.49 (m, 6H), 7.46-7.44 (m, 1H), 6.97-6.83 (m, 2H), 6.14-6.02 (m, 1H), 5.39 (d, *J* = 3.2 Hz, 1H), 5.08 (d, *J* = 10.4 Hz, 1H), 3.52 (brs, 1H, OH), 3.03-2.86 (m, 1H), 1.28 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.2, 139.0, 131.8 (2CH), 129.8, 129.5, 128.4 (2CH, 1C), 125.4, 122.0, 119.6, 119.3, 119.2, 88.9, 88.7, 79.2, 48.8, 16.5.

2nd isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (brs, 1H, OH), 7.41-7.34 (m, 6H), 7.26-7.18 (m, 1H), 6.97-6.83 (m, 2H), 5.97-5.83 (m, 1H), 5.36 (s, 1H), 5.09 (d, *J* = 17.2 Hz, 1H), 3.27 (brs, 1H, OH), 3.03-2.86 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 155.0, 138.3, 131.8 (2CH), 129.5, 129.9, 128.4 (2CH, 1C), 124.5, 121.9, 117.9, 117.6, 117.2, 88.3, 87.3, 78.6, 48.5, 14.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{18}NaO_2$ $(M+Na)^+$: 301.1204, Found: 301.1194.

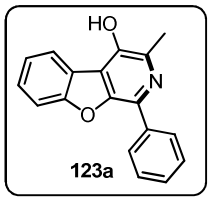
3,4-Dimethyl-1-phenylbenzofuro[2,3-*c*]pyridine (122b).



Prepared by following the procedure **O** and isolated as colorless solid. M.P = 121-123 °C. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3063, 2855, 1631, 1420, 1196, 767. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.43 (dd, *J* = 8.4 and 1.2 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.68-7.53 (m, 3H), 7.51-7.40 (m, 2H), 2.79 (s, 3H), 2.77 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ

156.7, 149.7, 148.9, 138.5, 136.5, 131.0, 128.8, 128.7, 128.5 (2CH), 128.4 (2CH), 124.7, 123.3, 123.2, 123.1, 112.4, 22.2, 15.6. HRMS (ESI): *m/z* calcd for $C_{19}H_{16}NO$ $(M+H)^+$: 274.1232, Found: 274.1219.

3-Methyl-1-phenylbenzofuro[2,3-*c*]pyridin-4-ol (123a).



123a

Prepared by following the procedure **P** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3432, 2956, 1445, 1375, 1258, 1096, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.4 Hz, 2H), 8.23 (d, *J* = 7.6 Hz, 1H), 7.72-7.66 (m, 1H), 7.64-7.54 (m, 4H), 7.48-7.41 (m, 2H), 2.74 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 156.2, 150.2, 141.6, 136.5, 134.2, 128.8, 128.6, 128.5 (2CH), 128.4, 128.0 (2CH, 1C), 123.6, 123.4, 121.6, 112.0, 18.1. HRMS (ESI): *m/z* calcd for $C_{18}H_{12}NO_2$ $(M–H)^+$: 274.0868, Found: 274.0857.

Procedure Q: General procedure for the preparation of 3-allylbenzo[*b*]thiophene-2-carbinols 125.

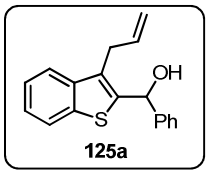
Step-I: To a stirred solution of the benzo[*b*]thiophene **126** (1.0 mmol) in 5 mL of $CHCl_3$/AcOH (1:1), NBS (1.5 mmol) was added in small portions. The reaction mixture was stirred at room temperature overnight before being poured into water. After extraction with CH_2Cl_2, the organic phase was separated and dried over anhydrous $MgSO_4$. The residue was purified by column chromatography to obtain 3-bromobenzothiophene.

Step-II: An oven dried round bottom flask was charged with magnesium turnings (1.0 mmol), catalytic amount of iodine and dry THF (0.5 mL). A solution of 3-bromobenzothiophene (1.1 mmol) in dry THF (1 mL) was slowly added to the suspension, which was heated under reflux for 2 h. The reaction mixture was cooled to room temperature and then it was treated with a solution of allyl bromide (1 mmol) in dry THF (0.5 mL). After heating under reflux for 2 h and cooling to room temperature, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane) to afford 3-allylbenzo[*b*]thiophene **127** in 76% yield.

Step-II: To a stirred solution of the 3-allylbenzo[*b*]thiophene **127** (1.0 equiv.) in anhydrous THF at -78 °C, was added *n*-butyllithium (2.0 *M* cyclohexane solution, 1.1 equiv.) drop wise, and the

resulting solution was allowed to stir at the same temperature for 1 h. Then, aldehyde (1 mmol) was dissolved in dry THF (1 mL) and added to the reaction mixture drop wise at -78 °C and allowed to stir for 1 h at the same temperature. The reaction mixture was slowly warmed up to room temperature and stirred for another 1 h. Upon completion (TLC), the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **125** in 80% yield.

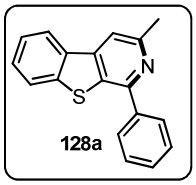
(3-Allylbenzo[*b*]thiophen-2-yl)(phenyl)methanol (125a).



125a

Prepared by following the procedure **Q** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3346, 3075, 2958, 1435, 1312, 1123, 1061. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.46-7.24 (m, 5H), 7.13-7.09 (m, 3H), 5.93 (s, 1H), 5.76-5.62 (m, 1H), 5.09 (s, 1H), 5.08 (dd, *J* = 7.2 and 1.6 Hz, 1H), 2.91-2.84 (m, 1H), 2.75-2.68 (m, 1H), 2.56 (brs, 1H, OH). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 159.5, 156.6, 134.5, 131.6, 130.2, 129.4, 128.7 (2CH), 128.4 (2CH), 126.7, 124.3, 122.7, 119.7, 110.5, 103.6, 79.5, 46.3. HRMS (ESI): *m/z* calcd for $C_{18}H_{15}S$ $(M–OH)^+$: 263.0894, Found: 263.0877.

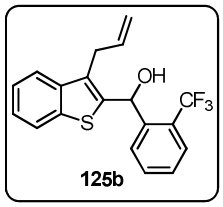
3-Methyl-1-phenylbenzo[4,5]thieno[2,3-*c*]pyridine (128a).



128a

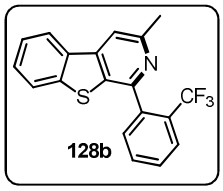
Prepared by following the procedure **O** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3060, 2956, 1599, 1542, 1399, 1026, 739. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.86 (s, 1H), 7.64-7.47 (m, 5H), 2.83 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 153.4, 152.8, 143.7, 141.5, 139.9, 134.0, 131.0, 129.1, 128.9, 128.7 (2CH), 128.3 (2CH), 124.7, 122.9, 122.8, 113.7, 24.5. HRMS (ESI): *m/z* calcd for $C_{18}H_{14}NS$ $(M+H)^+$: 276.0847, Found: 276.0838.

(3-Allylbenzo[*b*]thiophen-2-yl)(2-(trifluoromethyl)phenyl)methanol (125b).



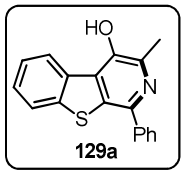
Prepared by following the procedure **Q** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3368, 2956, 2930, 1494, 1454, 1378, 1124, 762. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.0 Hz, 1H), 7.88-7.75 (m, 1H), 7.74-7.68 (m, 2H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.42-7.31 (m, 2H), 6.70 (s, 1H), 6.02-5.77 (m, 1H), 5.13 (brs, 1H, OH), 5.03 (s, 1H), 5.01-4.98 (m, 2H), 3.69-3.54 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 142.3, 140.9 (q, *J* = 7.1 Hz), 140.1, 138.9, 135.3, 132.4, 130.2, 128.9, 128.4, 127.3 (q, *J* = 271.0 Hz), 125.9 (q, *J* = 76.0 Hz), 124.4, 124.1, 122.4 (2CH), 122.1, 116.0, 66.3, 30.7. HRMS (ESI): *m/z* calcd for $C_{19}H_{14}F_2S$ $(M–OH)^+$: 331.0768, Found: 331.0754.

3-Methyl-1-(2-(trifluoromethyl)phenyl)benzo[4,5]thieno[2,3-*c*]pyridine (128b).



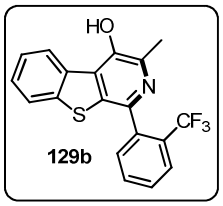
Prepared by following the procedure **O** and isolated as colourless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3067, 2956, 1575, 1399, 1023, 793. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.26 (d, *J* = 7.6 Hz, 1H), 7.92 (s, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.74-7.49 (m, 5H), 2.81 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 152.8, 151.9, 143.1, 141.6, 138.3 (q, *J* = 1.9 Hz), 134.0, 131.8, 130.5 (2CH), 129.0 (2CH), 129.0 (q, *J* = 30.9 Hz), 127.1 (q, *J* = 5.1 Hz), 125.2 (q, *J* = 272.5 Hz), 124.8, 123.1(2CH), 114.3, 24.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{13}F_3NS$ $(M+H)^+$: 344.0721, Found: 344.0709.

3-Methyl-1-phenylbenzo[4,5]thieno[2,3-*c*]pyridin-4-ol (129a).



Prepared by following the procedure **P** and isolated as colourless oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3341, 2923, 1360, 1260, 748. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 9.98 (s, 1H, OH), 8.81 (dd, *J* = 7.2 Hz and 1.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* =7.2 Hz, 2H), 7.66-7.43 (m, 5H), 2.68 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 147.6, 143.0, 141.2, 139.8, 139.6, 134.1, 131.6, 131.2, 129.0 (2CH), 128.8, 128.4, 128.0 (2CH), 127.0, 125.5, 123.1, 19.9. HRMS (ESI): m/z calcd for $C_{18}H_{14}NOS$ $(M+H)^+$: 292.0796, Found: 292.0789.

3-Methyl-1-(2-(trifluoromethyl)phenyl)benzo[4,5]thieno[2,3-*c*]pyridin-4-ol (129b).



Prepared by following the procedure **P** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 1/1). IR (thin film, neat): ν_{max}/cm^{-1} 3432, 2924, 1412, 1313, 1229, 1160, 750. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.89 (brs, 1H, OH), 8.85 (d, *J* = 7.2 Hz, 1H), 7.95 (t, *J* = 8.8 Hz, 2H), 7.82 (t, *J* = 7.2 Hz, 1H), 7.78-7.68 (m, 2H), 7.67-7.53 (m, 2H), 2.72 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 147.2, 142.9, 140.0, 139.9, 138.7 (q, *J* = 1.7 Hz), 134.1, 132.1, 131.5 (q, *J* = 144.0 Hz), 131.8, 129.0, 127.9, 126.9, 126.8 (q, *J* = 10.0 Hz), 126.0 (q, *J* = 257.0 Hz), 124.9 (2CH), 122.5 (2CH), 18.3. HRMS (ESI): *m/z* calcd for $C_{19}H_{13}F_3NOS$ $(M+H)^+$: 360.0670, Found: 360.0655.

Procedure R: General procedure for the preparation of 1-(2-allylphenyl) carbinols.

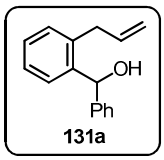
Step-I: An oven dried round bottom flask was charged with the methyl-2-iodobenzoate (1.1 mmol), and 2 mL dry THF under nitrogen atmosphere. $Pd(PPh_3)_4$ (0.05 mmol) and allyltributyltin (1.1 mmol) were added at room temperature. The resulting suspension was stirred at 60 °C until the aryl iodide disappeared as monitored by TLC. The black suspension was filtered through celite and the cake washed with EtOAc (5 mL). The filtrate washed with 1M HCl (2 x 5 mL), H_2O (5 mL), dried, filtered and concentrated. The residue was purified by silica gel column chromatography (5% EtOAc/hexane) to afford methyl-2-allylbenzoate in 90% yield.

Step-II: An oven dried round bottom flask was charged with methyl-2-allylbenzoate (1.0 mmol), 5 mL dry THF under nitrogen atmosphere and placed at 0^{o}C. $LiAlH_4$ (2.0 mmol) was added slowly at the same temperature and stirred for 1 h. Upon completion (TLC), the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure.

Crude 2-allyl benzyl alcohol (1 mmol) was dissolved in EtOAc (5 mL), and IBX (1.5 mmol) was added. The resulting suspension was stirred at 75 °C until alcohol disappeared as monitored by TLC. The reaction was cooled to room temperature and filtered through celite. The residue was washed with ethyl acetate (3× 2 mL). Organic extracts were combined and washed with saturated aq. $NaHCO_3$solution to remove excess iodobenzoic acid. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (20-30% EtOAc/hexane) to afford 2-allylbenzaldehyde **133** in 80% yield over two steps.

Step-III: An oven dried round bottom flask was charged with ynone **133** (1.0 mmol), 5 mL dry THF and placed at 0°C. Respective Grignard reagents (2.2 mmol) were added drop wise at the same temperature and stirred for 1h. Upon completion, the reaction mixture was quenched by adding saturated aq. NH_4Cl (1 mL) and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (10-20% EtOAc/hexane) to afford **131** (in 90-95% yields).

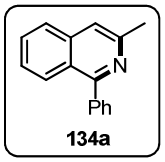
(2-Allylphenyl)(phenyl)methanol (131a).



131a

Prepared by following the procedure **R** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3351, 3063, 1493, 1451, 1015, 760. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.51-7.44 (m, 1H), 7.39-7.34 (m, 4H), 7.34-7.26 (m, 3H), 7.23-7.20 (m, 2H), 6.10 (s, 1H), 6.02-5.89 (m, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 5.02 (dd, *J* = 17.2 and 0.8 Hz, 1H), 3.55-3.35 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 143.1, 141.4, 137.3, 137.2, 130.0, 128.4 (2CH), 127.8, 127.5, 127.2, 126.9 (2CH), 126.7, 116.0, 72.7, 36.8. HRMS (ESI): *m/z* calcd for $C_{16}H_{15}O$ $(M–H)^+$: 223.1123, Found: 223.1113.

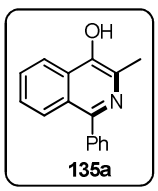
3-Methyl-1-phenylisoquinoline (134a).



134a

Prepared by following the procedure **O** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 4/1). IR (thin film, neat): ν_{max}/cm^{-1} 3054, 2923, 1588, 1622, 1357, 802, 753. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 9.47 (s, 1H, NH), 8.26 (d, *J* = 8.8 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.61-7.56 (m, 2H), 7.55-7.43 (m, 4H), 2.60 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.3, 150.8, 139.7, 137.5, 129.9, 129.8 (2CH), 128.4, 128.3 (2CH), 127.5, 126.3, 126.1, 124.9, 118.0, 24.4. HRMS (ESI): *m/z* calcd for $C_{16}H_{14}N$ $(M+H)^+$: 220.1126, Found: 220.1119.

3-Methyl-1-phenylisoquinolin-4-ol (135a).

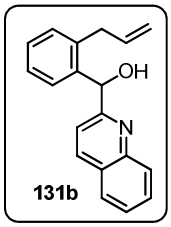


135a

Prepared by following the procedure **P** and isolated as colorless oil. R_f = 0.5 (hexane/EtOAc = 7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3432, 2967, 1553, 1367, 1021, 802, 753. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$): δ 9.47 (s, 1H, NH), 8.26 (d, *J* =

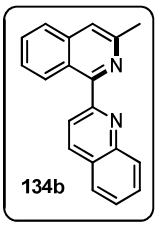
8.8 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.61-7.67 (m, 2H), 7.55-7.43 (m, 4H), 2.60 (s, 3H). **^{13}C NMR** (100 MHz, $(CD_3)_2SO$): δ 150.5, 144.3, 140.0, 135.8, 130.2 (2CH), 129.2, 128.8, 128.6 (2CH), 128.2, 126.8, 126.7, 125.9, 121.8, 19.7. HRMS (ESI): *m/z* calcd for $C_{16}H_{14}NO$ $(M+H)^+$: 236.1075, Found: 236.1056.

(2-Allylphenyl)(quinolin-2-yl)methanol (131b).



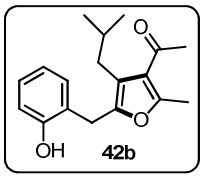
Prepared by following the procedure **R** and isolated as pale yellow oil. R_f = 0.5 (hexane/EtOAc =7/3). IR (thin film, neat): ν_{max}/cm^{-1} 3341, 3062, 1598, 1313, 1116, 965, 924, 757. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.8 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.79 (dt, *J* = 7.2 and 1.6 Hz, 1H), 7.59 (dt, *J* = 8.0 and 1.2 Hz, 1H), 7.31-7.25 (m, 3H), 7.22-7.13 (m, 2H), 7.13 (d, *J* = 8.4 Hz, 1H), 6.16 (s, 1H), 6.06-5.96 (m, 1H), 5.14-5.00 (m, 2H), 3.79-3.59 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.7, 146.0, 143.0, 138.4, 137.5, 136.9, 130.3, 129.9, 129.0, 128.8, 128.2, 127.6, 127.4, 126.8, 126.4, 119.3, 115.9, 72.0, 36.9. HRMS (ESI): *m/z* calcd for $C_{19}H_{18}NO$ $(M+H)^+$: 276.1388, Found: 276.1380.

2-(3-Methylisoquinolin-1-yl)quinolone (134b).



Prepared by following the procedure **O** and isolated as colourless oil. R_f = 0.5 (hexane/EtOAc =7/3). IR (thin film, neat): ν_{max}/cm^{-1} 2956, 2924, 2854, 1664, 1314, 952, 742. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.36 (d, *J* = 8.8 Hz, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 6.0 Hz, 1H), 7.81-7.75 (m, 2H), 7.68 (t, *J* = 8.0 Hz, 1H), 7.57 (dt, *J* = 7.2 and 0.8 Hz, 1H), 7.57 (dt, *J* = 7.2 and 0.8 Hz, 1H), 7.42-7.34 (m, 2H), 2.26 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.2, 169.7, 154.7, 147.0, 137.0, 136.0, 135.8, 133.2 132.7, 132.3, 131.8, 130.7, 130.1, 128.9, 128.5, 127.6, 126.4, 120.7, 22.5. HRMS (ESI): *m/z* calcd for $C_{19}H_{15}N_2$ $(M+H)^+$: 271.1235, Found: 271.1223.

Table 24: General data and structure refinement parameters for the compound 42b.



Chemical formula	$C_{18}H_{22}O_3$	
Formula weight	286.36	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 10.9516(7) Å	α = 90°
	b = 7.0293(4) Å	β = 99.065(4)°
	c = 21.4714(13) Å	γ = 90°
Volume	1632.27(17) $Å^3$	
Z	4	
Density (calculated)	1.165 Mg/cm^3	
Absorption coefficient	0.078 mm^{-1}	
F(000)	616	
Theta range for data collection	1.92 to 23.35°	
Reflections collected	7874	
Independent reflections	2359 [R(int) = 0.0584]	
Absorption correction	multi-scan	
Data / restraints / parameters	2359 / 0 / 195	
Index ranges	-12<=h<=12, -7<=k<=7, -23<=l<=23	
Goodness-of-fit on F^2	1.031	
Δ/σ_{max}	0.002	
Final R indices	1423 data; I>2σ(I)	R1 = 0.0799, wR2 = 0.2048
	all data	R1 = 0.1336, wR2 = 0.2358
CCDC number	947120	

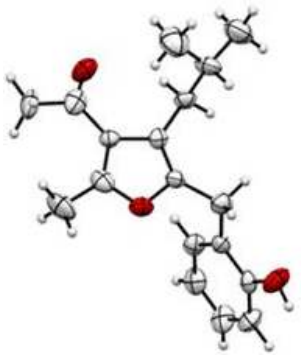
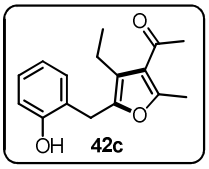


Table 25: General data and structure refinement parameters for the compound 42c.



Chemical formula	$C_{16}H_{18}O_3$	
Formula weight	258.30	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 7.3627(10) Å	α = 90°
	b = 16.577(2) Å	β = 93.907(7)°
	c = 11.7672(16) Å	γ = 90°
Volume	1432.9(3) $Å^3$	
Z	4	
Density (calculated)	1.197 Mg/cm^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	552	
Theta range for data collection	2.13 to 25.06°	
Reflections collected	12361	
Independent reflections	2513 [R(int) = 0.0346]	
Absorption correction	multi-scan	
Data / restraints / parameters	2513 / 0 / 176	
Index ranges	-8<=h<=8, -19<=k<=19, -7<=l<=13	
Goodness-of-fit on F^2	1.045	
Δ/σ_{max}	0.122	
Final R indices	1849 data; I>2σ(I)	R1 = 0.0670, wR2 = 0.2004
	all data	R1 = 0.0870, wR2 = 0.2224
CCDC number	947119	

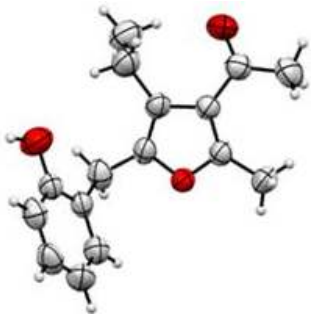
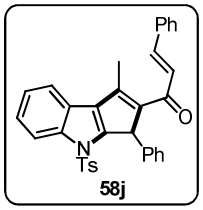


Table 26: General data and structure refinement parameters for the compound 58j.



58j

Chemical formula	$C_{34}H_{27}NO_3S$	
Formula weight	529.62	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 6.1013(8) Å	α = 90°
	b = 15.039(2) Å	β = 90.877(8)°
	c = 23.894(3) Å	γ = 90°
Volume	2192.2(5) $Å^3$	
Z	4	
Density (calculated)	1.605 g/cm^3	
Absorption coefficient	0.193 mm^{-1}	
F(000)	1112	
Theta range for data collection	1.60 to 25.24°	
Index ranges	-7<=h<=7, -16<=k<=17, -28<=l<=28	
Reflections collected	22157	
Independent reflections	3925 [R(int) = 0.0691]	
Data / restraints / parameters	3925 / 0 / 355	
Goodness-of-fit on F^2	1.080	
Δ/σ_{max}	0.005	
Final R indices	2599 data; I>2σ(I)	R1 = 0.0640, wR2 = 0.1539
	all data	R1 = 0.1080, wR2 = 0.1810
Extinction coefficient	0.0190(20)	
CCDC number	1029309	

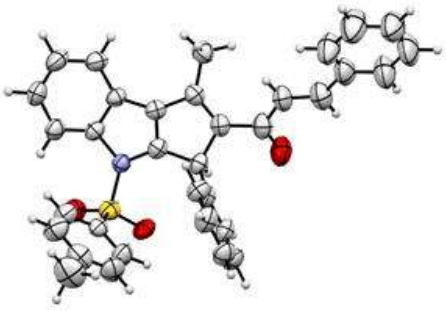
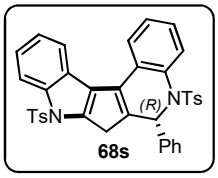


Table 27: General data and structure refinement parameters for the compound 68s.



Empirical formula	$C_{38}H_{30}N_2O_4S_2$	
Formula weight	642.16	
Temperature/K	296.15	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.370(3) Å	α = 90.830(3)°
	b = 12.582(4) Å	β = 105.888(3)°
	c = 14.702(4) Å	γ = 110.831(3)°
Volume/Å^3	1546.0(8)	
Z	2	
ρ_{calc}g/cm^3	1.376	
μ/mm^{-1}	0.217	
F(000)	670.0	
Reflections collected	33393	
Radiation	MoKα (λ = 0.71073)	
2Θ range for data collection/°	2.902 to 50.364	
Index ranges	-11 ≤ h ≤ 11, -15 ≤ k ≤ 15, -17 ≤ l ≤ 17	
Independent reflections	5526 [R_{int} = 0.0309, R_{sigma} = 0.0206]	
Data/restraints/parameters	5526/0/417	
Goodness-of-fit on F^2	1.029	
Final R indexes [I>=2σ (I)]	[I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.0972
	[all data]	R_1 = 0.0524, wR_2 = 0.1067
CCDC number	1062844	

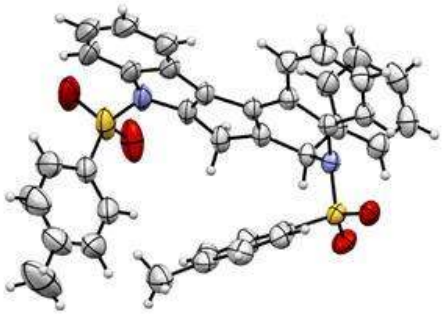
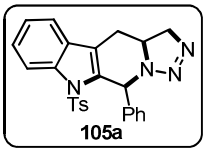


Table 28: General data and structure refinement parameters for the compound 105a.



105a

Empirical formula	$C_{25}H_{22}N_4O_2S$	
Formula weight	442.14	
Temperature/K	273.15	
Crystal system	triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.2947(7) Å	α = 90.522(4)°
	b = 10.8968(8) Å	β = 109.882(4)°
	c = 12.1332(8) Å	γ = 111.713(4)°
Volume/Å^3	1060.76(14)	
Z	2	
ρ_{calc}g/cm^3	1.3587	
μ/mm^{-1}	0.183	
F(000)	453.4	
Crystal size/mm^3	0.2 × 0.2 × 0.2	
2Θ range for data collection/°	3.62 to 50.7	
Radiation	Mo Kα (λ = 0.71073)	
Index ranges	-11 ≤ h ≤ 11, -13 ≤ k ≤ 13, -14 ≤ l ≤ 14	
Reflections collected	10216	
Independent reflections	3869 [R_{int} = 0.0136, R_{sigma} = 0.0159]	
Data/restraints/parameters	3869/0/265	
Goodness-of-fit on F^2	1.040	
Final R indexes	[I>=2σ (I)]	R_1 = 0.0810, wR_2 = 0.2307
	[all data]	R_1 = 0.0888, wR_2 = 0.2407
CCDC number	1449095	

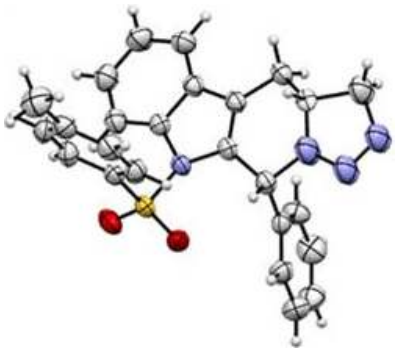
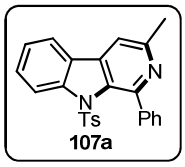


Table 29: General data and structure refinement parameters for the compound 107a.



Empirical formula	$C_{25}H_{20}N_2O_2S$	
Formula weight	412.52	
Temperature/K	293	
Crystal system	monoclinic	
Space group	$P2_1/n$	
Unit cell dimensions	a = 10.1775(19) Å	α = 90°
	b = 18.125(3) Å	β = 107.984(7)°
	c = 11.690(2) Å	γ = 90°
Volume/Å^3	2051.0(6)	
Z	4	
ρ_{calc}g/cm^3	1.3358	
μ/mm^{-1}	0.183	
F(000)	864.9	
2Θ range for data collection/°	6.16 to 54.96	
Radiation	Mo Kα (λ = 0.71075)	
Index ranges	$-13 \leq h \leq 13$, $-23 \leq k \leq 23$, $-15 \leq l \leq 15$	
Reflections collected	20892	
Independent reflections	4683 [R_{int} = 0.0921, R_{sigma} = 0.0712]	
Data/restraints/parameters	4683/0/266	
Goodness-of-fit on F^2	1.087	
Final R indexes	[I>=2σ (I)]	R_1 = 0.1038, wR_2 = 0.1553
	[all data]	R_1 = 0.1772, wR_2 = 0.1871
CCDC number	1447120	

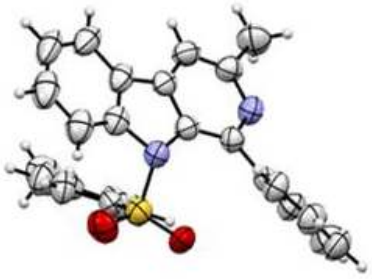
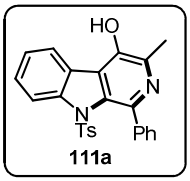
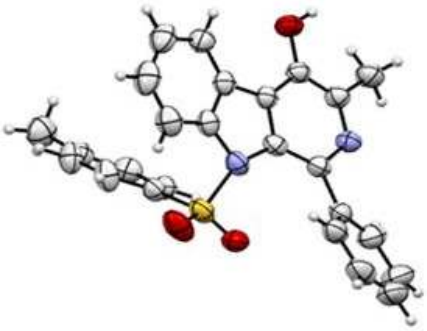


Table 30: General data and structure refinement parameters for the compound 111a.



111a

Empirical formula	$C_{25}H_{20}N_2O_3S$	
Formula weight	428.1195	
Temperature/K	296.15	
Crystal system	orthorhombic	
Space group	Pbca	
Unit cell dimension	a = 9.4216(7) Å	α = 90°
	b = 15.1001(10) Å	β = 90°
	c = 29.2713(19) Å	γ = 90°
Volume/Å^3	4164.3(5)	
Z	8	
ρ_{calc}g/cm^3	1.3701	
μ/mm^{-1}	0.186	
F(000)	1801.8	
2Θ range for data collection/°	5.14 to 50.28	
Radiation	Mo Kα (λ = 0.71073)	
Index ranges	-11 ≤ h ≤ 6, -17 ≤ k ≤ 17, -35 ≤ l ≤ 33	
Reflections collected	21116	
Independent reflections	3705 [R_{int} = 0.0464, R_{sigma} = 0.0338]	
Data/restraints/parameters	3705/0/282	
Goodness-of-fit on F^2	1.023	
Final R indexes	[I>=2σ (I)]	R_1 = 0.0481, wR_2 = 0.1256
	[all data]	R_1 = 0.0722, wR_2 = 0.1428
CCDC number	1447093	



REFERENCES

(1) Fan, H.; Peng, J.; Hamann M. T.; Hu, J. -F. *Chem. Rev.* **2008**, *108*, 264.

(2) For merrilactone A, see (a) Huang, J. -M.; Yokoyama, R.; Yang, C. -S.; Fukuyama, Y. *Tetrahedron Lett.* **2000**, *41*, 6111. For roseophilin, see (b) Hayakawa, Y.; Kawakami, K.; Seto, H.; Furihata, K. *Tetrahedron Lett*. **1992**, *33*, 2701. For (-)-nakadomarin, see (c) Kobayashi, J.; Watanabe, D.; Kawasaki, N.; Tsuda, M. *J. Org. Chem*. **1997**, *62*, 9236. For (-)-aplysin, see (d) Yamaur, S.; Liirata, Y. *Tetrahedron* **1963**, *19*, 1485. For beraprost, see (e) Melian, E. B.; Goa, K. L. *Drugs* **2002**, *62*, 107. For aglafolin, see (f) Wu, T. -S.; Liou, M.-J.; Kuoh, C. -S.; Teng, C. -M.; Nagao, T.; Lee, K. -H. *J. Nat. Prod*. **1997**, *60*, 606. For raloxifene analogue, see (g) Kalinin, A. V.; Reed, M. A.; Norman, B. H.; Snieckus, V. *J. Org. Chem.* **2003**, *68*, 5992. For bruceolline E, see (h) Guo, Z.; Vangapandu, S.; Sindelar, R. W.; Walker, L. A.; Sindelar, R. D. *Curr. Med. Chem*. **2005**, *12*, 173. For lacenindole D, see (i) Roll, D. M.; Barbieri, L. R.; Bigelis, R.; McDonald, L. A.; Arias, D. A.; Chang, L.-P.; Singh, M. P.; Luckman, S. W.; Berrodin, T. J.; Yudt, M. R. *J. Nat. Prod*. **2009**, *72*, 1944. For emindole SB, see (j) Nozawa, K.; Yuyama, M.; Nakajima S.; Kawai, K. *J. Chem. Soc. Perkin Trans. 1*, **1988**, 2155. For sespendole, sees (k) Yamaguchi, Y.; Masuma, R.; Kim, Y.-P.; Uchida, R.; Tomoda, H.; Omura, S. *Mycoscience* **2004**, *45*, 9. For terependole E, see (l) Nakazawa, J.; Yajima, J.; Usui, T.; Ueki, M.; Takatsuki, A.; Imoto, M.; Toyoshima, Y. Y.; Osada, H. *Chem. Biol.* **2005**, *10*, 131. For polyveoline see (m) Kouam, S. F.; Ngouonpe, A. W.; Lamshoft, M.; Talontsi, F. M.; Bauer, J. O.; Strohmann, C.; Ngadjui, B. T.; Laatsch, H.; Spiteller, M. *Phytochemistry* **2014**, *105*, 52. For fischerindole L, see (n) Richter, J. M.; Ishihara, Y.; Masuda, T.; Whitefield, B. W.; Llamas, T.; Pohjakallio, A.; Baran, P. S. *J. Am. Chem. Soc.* **2008**, *130*, 17938. For spiroindimicins B, see (o) Zhang, W.; Liu, Z.; Li, S.; Yang, T.; Zhang, Q.; Ma, L.; Tian, X.; Zhang, H.; Huang, C.; Zhang, S.; Ju, J.; Shen Y.; Zhang, C. *Org. Lett.* **2012**, *14*, 3364. For yeuhchukene, see (p) Kong, Y. –C.; Cheng, K. –F.; Cambie R. C.; Waterman, P. G. *J. Chem. Soc. Chem. Commun.* **1986**, 47. For sessilistemonamine F, see (q) Ramli, R. A.; Lie, W.; Pyne, S. G. *J. Nat. Prod.* **2014**, *77*, 894.

(3) Pouchain, L.; Alévêque, O.; Nicolas, Y.; Oger, A.; Régent, C. -H. L.; Allain, M.; Blanchard, P.; Roncali, J. *J. Org. Chem.* **2009**, *74*, 1054.

(4) Bergman, J.; Venemahn, L. *Tetrahedron* **1990**, *46*, 6067.

(5) Kang, K. -T.; S. K. Soung; Lee, J. C.; Sun, U. J. *Tetrahedron Lett*. **1992**, *33*, 3495.

(6) Malona, J. A.; Colbourne, J. M.; Frontier, A. J. *Org. Lett*. **2006**, *8*, 5661.

(7) Song, C.; Knight, D. W.; Whatton, M. A. *Org. Lett*. **2006**, *8*, 163.

(8) Wang, Z.; Xu, X.; Gu, Z.; Feng, W.; Qian, H.; Li, Z.; S, X.; Kwon, O. *Chem. Commun*. **2016**, *52*, 2811.

(9) Bergman, J.; Venemalm, L. *Tetrahedron Lett*. **1988**, *29*, 2993.

(10) Churruca, F.; Fousteris, Manolis.; Ishikawa, Y.; Rekowski, M. V. W.; Hounsou, C.; Surrey, T.; Giannis, A. *Org. Lett.* **2010**, *12*, 2096.

(11) Jordan, J. A.; Gribble, G. W.; Badenock, J. C. *Tetrahedron Lett*. **2011**, *52*, 6772.

(12) Magnus, P.; Freund, W. A.; Moorhead, E. J.; Rainey, T. *J. Am. Chem. Soc.* **2012**, *134*, 6140.

(13) Yadav, A. K.; Peruncheralathan, S.; Ila, H.; Junjappa, H. *J. Org. Chem.* **2007**, *72*, 1388.

(14) Xiong, H.; Xu, H.; Liao, S.; Xie, Z.; Tang, Y. *J. Am. Chem. Soc*. **2013**, *135*, 7851.

(15) Tan, W.; Li, X.; Gong, Y.-X.; Ge, M. -D.; Shi, F. *Chem. Commun.* **2014**, *50*, 15901.

(16) Lebée, C.; Kataja, A. O.; Blanchard, F.; Masson, G. *Chem. Eur. J*. **2015**, *21*, 8399.

(17) Galván, A.; Calleja, J.; González-Pérez, A. B.; Álvarez, R.; de Lera, A. R.; Fañanás, F. J.; Rodríguez. F. *Chem. Eur. J*. **2015**, *21*, 16769.

(18) Xu, B.; Guo, Z. -L.; Jin, W. -Y.; Wang, Z. -P.; Peng, Y. -G.; Guo, Q. -X. *Angew. Chem. Int. Ed*. **2012**, *51*, 1059.

(19) Iwama, T.; Birman, V. B.; Kozmin, S. A.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 673.

(20) Krafft, M. E.; Vidhani, D. V.; Cran, J. W.; Manoharan, M. *Chem. Commun*. **2011**, *47*, 6707.

(21) Chen, B.; Fan, W.; Chai, G.; Ma, S. *Org. Lett.* **2012**, *14*, 3616.

(22) Iqbal, N.; Sperger, C. A.; Fiksdahl, A. *Eur. J. Org. Chem*. **2013**, 907.

(23) Ishikura, M.; Matsuzaki, Y.; Agata, I. *Chem. Commun*. **1996**, 2409.

(24) Ma, Y.; You, J.; Song, F. *Chem. Eur. J.* **2013**, *19*, 1189.

(25) Saito, K.; Sogou, H.; Suga, T.; Kusama, H.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 689.

(26) Yoshida, M.; Maeyama, Y.; Al-Amin, M.; Shishido, K. *J. Org. Chem*. **2011**, *76*, 5813.

(27) Tseng, N. -W.; Lautens, M. *J. Org. Chem.* **2009**, *74*, 1809.

(28) Sun, K.; Liu, S.; Bec, P. M.; Driver, T. G. *Angew. Chem. Int. Ed.* **2011**, *50*, 1702.

(29) Meotti, F. C.; Silva, D. O.; dos Santos, A. R. S.; Zeni, G.; Rocha, J. B. T.; Nogueira, C. W. *Environ. Toxicol. Pharmacol*. **2003**, *15*, 37.

(30) (a) Iwanaga, K.; Yoneda, S.; Hamahata, Y.; Miyazaki, M.; Shibano, M.; Taniguchi, M.; Baba, K.; Kakemi, M. *Biol. Pharm. Bull.* **2011**, *34*, 1246. (b) Hikino, H; Konno, C. Heterocycles **1976**, *4*, 817. (c) Bissember, A. C.; Phillis, A. T.; Banwell, M. G.; Willis, A. C. *Org. Lett*. **2007**, *9*, 5421.

(31) (a) Chambers, J. M.; Huang, D. C. S.; Lindqvist, L. M.; Savage, G. P.; White, J. M.; Rizzacasa, M. A. *J. Nat. Prod.* **2012**, *75*, 1500. (b) Watanabe, M.; Su, W. -T.; Chang, Y. J.; Chao, T. -H.; Wen, Y. -S.; Chow, T. J. *Chem. Asian J.* **2012**, *8*, 60.

(32) Ghosh, A. K.; Leshchenko, S.; Noetzel, M. *J. Org. Chem.* **2004**, *69*, 7822.

(33) (a) Chen, Y.; Li, G.; Liu, Y. *Adv. Synth. Catal.* **2011**, *353*, 392. (b) Wang, C.; Chen, Y.; Xie, X.; Liu, J.; Liu, Y. *J. Org. Chem.* **2012**, *77*, 1915. (c) Pilipenko, A. S.; Melchin, V. V.; Trushkov, I. V.; Cheshkov, D. A.; Butin, A. V. *Tetrahedron* **2012**, *68*, 619. (d) Uchuskin, M. G.; Molodtsova, N. V.; Abaev, V. T.; Trushkov, I. V.; Butin, A. V. *Tetrahedron* **2012**, *68*, 4252. (e) Uchuskin, M. G.; Pilipenko, A. S.; Serdyuk, O. V.; Trushkov, I. V.; Butin, A. V. *Org. Biomol. Chem.* **2012**, *10*, 7262.

(34) Burke, M. D.; Berger E. M; Schreiber, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 14095.

(35) Achmatowicz, O.; Bukowski, Jr., P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, *27*, 1973.

(36) Piancatelli, G.; Scettri, A.; Barbadoro, S.; *Tetrahedron Lett.* **1976**, *17*, 3555.

(37) Deska, J.; T, D.; Gianolio, E. *Synthesis* **2015**, *47*, 3435.

(38) Nicolaou, K. C.; Kang, Q.; Ng, S. Y.; Chen, D. Y. -K. *J. Am. Chem. Soc.* **2010**, *132*, 8219.

(39) Ma, Y.; O'Doherty, G. A. *Org. Lett*. **2015**, *17*, 5280.

(40) Piutti, C.; Quartieri, F. *Molecules* **2013**, *18*, 12290.

(41) Dygos, J. H.; Adamek, J. P.; Babiak, K. A.; Behling, J. R.; Medich, J. R.; Ng, J. S.; Wieczorek, J. J. *J. Org. Chem.* **1991**, *56*, 2549.

(42) Katsuta, R.; Aoki, K.; Yajima, A.; Nukada, T. *Tetrahedron Lett*. **2013**, *54*, 347.

(43) Winne, J. M.; Catak, S.; Waroquier, M.; Speybroeck, V. V. *Angew. Chem. Int. Ed*. **2011**, *50*, 11990.

(44) Zhang, J.; Li, L.; Wang, Y.; Wang, W.; Xue, J.; Li, Y. *Org. Lett*. **2012**, *14*, 4528.

(45) Laplace, D. R.; Verbraeken, B.; Hecke, K. V.; Winne, J. M. *Chem. Eur. J*. **2014**, *20*, 253.

(46) Palframan, M. J.; Pattenden, G. *Chem. Commun.* **2014**, *50*, 7223.

(47) (a) Ikeda, M.; Miyake, Y.; Nishibayashi, Y. *Angew. Chem. Int. Ed.* **2010**, *49*, 7289. (b) Chatterjee, P. N.; Roy, S. *Tetrahedron* **2011**, *67*, 4569. (c) Das, B. G.; Nallagonda, R.; Ghorai, P. *J. Org. Chem.* **2012**, *77*, 5577.

(48) (*a*) Gaspard-Iloughmane, H.; Le Roux, C. *Eur. J. Org. Chem.* **2004**, *69*, 2517. (*b*) Bothwell, J. M.; Krabbez, S. W.; Mohan, R. S. *Chem. Soc. Rev.* **2011**, *40*, 4649. From www.sigmaaldrich.com, the price per 25 g in US dollars is \$75 and \$238 for $BiCl_3$ and $Bi(OTf)_3$, respectively. The LD_{50} of $BiCl_3$ is listed as 3.3 g/kg (oral, rat) in the MSDS provided by Sigma-Aldrich, which is lower than that of NaCl (3.8 g/Kg). The low toxicity of bismuth is attributed to the poor solubility of the metal in aqueous solutions at moderate pH levels similar to biological systems.

(49) (*a*) Nair, V.; Thomas, S.; Mathew, S. C.; Abhilash, K. G. *Tetrahedron* **2006**, *62*, 6731. (*b*) Thirupathi, P.; Kim, S. S. *J. Org. Chem.* **2010**, *75*, 5240.

(50) Dhiman, S.; Ramasastry, S. S. V. *Org. Biomol. Chem.* **2013**, *11*, 8030.

(51) Pettersson, T.; Eklund, A. -M.; Wahlberg, I. *J. Agric. Food Chem.* **1993**, *41*, 2097.

(52) Roberts, R. M. *Serendipity: Accidental Discoveries in Science*, Wiley-VCH: New York, 1989.

(53) (a) Tietze, L. F.; Brasche, G.; Gericke, K. In *Domino Reactions in Organic Synthesis*, Wiley VCH: Weinheim, 2006. (b) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442.

(54) (a) Huang, X.; Peng, B.; Luparia, M.; Gomes, L. F. R.; Veiros, L. F.; Maulide, N. *Angew. Chem. Int. Ed.* **2012**, *55*, 8886. (b) Watanabe, M.; Su, W. -T.; Chang, Y. J.; Chao, T. -H.; Wen, Y. -S.; Chow, T. J. *Chem. Asian J.* **2012**, *8*, 60.

(55) Friedrichsen, W. In *Furans and their Benzo Derivatives: Synthesis,* Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V. Ed., *Comprehensive heterocyclic chemistry II*, Pergamon, Elsevier Science Ltd, Oxford, 1996, *2*, 351.

(56) (a) Benary, E. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 489. (b) Calter, M. A.; Phillips, R. M.; Flaschenriem, C. *J. Am. Chem. Soc.* **2005***, 127,* 14566.

(57) Seki, M.; Sakamoto, T.; Suemune, H.; Kanematsu, K. *J. Chem. Soc., Perkin Trans. 1,* **1997**, 1707.

(58) (a) Gutnov, A. V.; Butin, A. V.; Abaev, V. T.; Krapivin, G. D.; Zavodnik, V. E. *Molecules*, **1999**, *4*, 204. (b) Butin, A. V.; Gutnov, A. V.; Abaev, V. T.; Krapivin, G. D. *Molecules*, **1999**, *4*, 52.

(59) (a) Feng, X.; Tan, Z.; Chen, D.; Shen, Y.; Guo, C. –C.; Xiang, J.; Zhu, C. *Tetrahedron Lett.* **2008**, *49*, 4110. (b) Pan, Y. –M.; Zhao, S. –Y.; Ji, W. –H.; Zhan, Z. –P. *J. Comb. Chem.* **2009**, *11,* 103.

(60) Yu, H.; Zhong, W.; He, T.; Gu, W.; Yin, B. *Tetrahedron Lett.* **2013**, *54*, 1256.

(61) Ie, Y.; Nishida, K.; Karakawa, M.; Tada, H.; Aso, Y. *J. Org. Chem*. **2011**, *76*, 6604.

(62) Arends, I.; Sheldon, R.; Hanefeld, U. *Green Chemistry and Catalysis*, Wiley-VCH: Weinheim, 2007.

(63) Hayashi, Y. *Chem. Sci.* **2016**, *7*, 866.

(64) Shao Z.; Zhang, H. *Chem. Soc. Rev*. **2009**, *38*, 2745.

(65) (a) Fürstner, A. *Chem. Soc. Rev.* **2009**, *38*, 3208. (b) Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. *Aldrich. Chim. Acta* **2010**, *43*, 37. (c) Bandini, M. *Chem. Soc. Rev*. **2011**, *40*, 1358. (d) Rudolph, M.; Hashmi, A. S. K. *Chem. Soc. Rev*. **2012**, *41*, 2448. (e) Fürstner, A. *Acc. Chem. Res*. **2014**, *47*, 925. (f) Dorel, R.; Echavarren, A. M. *Chem. Rev*. **2015**, *115*, 9028.

(66) (a) Han, Z. -Y.; Chen, D. -F.; Wang, Y. -Y.; Guo, R.; Wang, P. -S.; Wang, C.; Gong, L. -Z. *J. Am. Chem. Soc*. **2012**, *134*, 6532. (b) He, Y. -P.; Wu, H.; Chen, D. -F.; Yu, J.; Gong, L. -Z. *Chem. Eur. J*. **2013**, *19*, 5232. (c) Wang, P. -S.; Li, K. -N.; Zhou, X. -L.; Wu, X.; Han, Z. -Y.; Guo, R.; Gong, L. -Z. *Chem. Eur. J*. **2013**, *19*, 6234.

(67) Kothandaraman, P.; Rao, W.; Foo, S. J.; Chan, P. W. H. *Angew. Chem., Int. Ed*. **2010**, *49*, 4619.

(68) Susanti, D.; Koh, F.; Kusuma, J. A.; Kothandaraman, P.; Chan, P. W. H. *J. Org. Chem*. **2012**, *77*, 7166.

(69) Zhang, J.; Shao, J. -D.; Xue, J. -J.; Wang, Y. -X.; Li, Y. *RSC Adv.* **2014**, *4*, 63850.

(70) Li, H.; Li, X.; Wang, H. -Y.; Winston-McPherson, G. N.; Geng, H. -M. J.; Guzei, I. A.; Tang, W. *Chem. Commun*. **2014**, *50*, 12293.

(71) Thirupathi, N.; Babu, M. H.; Dwivedi, V.; Kant, R.; Reddy, M. S. *Org. Lett*., **2014**, *16*, 2908.

(72) (a) Dhiman, S.; Ramasastry, S. S. V. *J. Org. Chem.* **2013**, *78*, 10472. (b) Dhiman, S.; Ramasastry, S. S. V. *Indian J. Chem.* **2013**, *52A*, 1103.

(73) Satpathi, B.; Dhiman S.; Ramasastry, S. S. V. *Eur. J. Org. Chem*. **2014**, 2022.

(74) Fernandez, L. S.; Buchanan, M, S.; Carroll, A. R.; Feng, Y. J.; Quinn, R. J.; Avery, V. M. *Org. Lett.* **2009***, 11*, 329.

(75) Tillequin, F.; Koch, M.; Bert, M.; Sevenet, T. *J. Nat. Prod.* **1979**, *42*, 92.

(76) Ramos, L. A.; Lipman, R.; Tomasz, Maria; Basu, A. K. *Chem. Res. Toxicol*. **1998**, *11*, 64.

(77) Kuznetsov, A.; Makarov, A.; Rubtsov, A. E.; Butin, A. V.; Gevorgyan, V. *J. Org. Chem*. **2013**, *78*, 12144.

(78) Dhiman, S.; Ramasastry, S. S. V. *Chem. Commun*. **2015**, *51*, 557.

(79) Dhiman, S.; Ramasastry, S. S. V. *Org. Lett.* **2015**, *17*, 5116

(80) Torrado, A.; López, S.; Alvarez, R.; Lera, A. R. De. *Synthesis* **1995**, *3*, 285.

(81) Severin, R.; Reimer, J.; Doye, S. *J. Org. Chem.* **2010**, *75*, 3518.

(82) Cho, E. J.; Buchwald, S. L. *Org. Lett.* **2011**, *13*, 6552.

(83) Ali, S.; Zhu, H. -T.; Xia, X. -F.; Ji, K. -G.; Yang, Y. -F.; Song X. -R.; Liang, Y. -M. *Org. Lett.* **2011**, *13*, 2598.

(84) (a) Marcus, A. P.; Lee, A. S.; Davis, R. L.; Tantillo D. J.; Sarpong, R. *Angew. Chem. Int. Ed.* **2008**, *47*, 6379. (b) He, W.; Herrick, I. R.; Atesin, T. A.; Caruana, P. A.; Kellenberger, C. A.; Frontier, A. J. *J. Am. Chem. Soc*. **2008**, *130*, 1003. (d) Smith, C. D.; Rosocha, G.; Mui L.; Batey, R. A. *J. Org. Chem.* **2010**, *75*, 4716.

(85) (a) Antinarelli, L. M. R.; Carmo, A. M. L.; Pavan, F. R.; Leite, C. Q. F.; Silva, A. D. Da; Coimbra, E. S.; Salunke, D. B. *Org. Med. Chem. Lett.* **2012**, *2*, 16. (b) Singh, P. Shaveta, Sharma, S.; Bhatti, R. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 77.

(86) Alford, J. S.; Spangler J. E.; Davies, H. M. L. *J. Am. Chem. Soc.* **2013**, *135*, 11712.

(87) Sun, W. -S.; Su, S.; Zhu, R. -X.; Tu, G. -Z.; Cheng, W.; Liang, H.; Guo, X. -Y.; Zhao, Y. - Y.; Zhang, Q. -Y. *Tetrahedron Lett*. **2013**, *54*, 3617.

(88) Smithers, R. H. *J. Org. Chem.* **1980**, *45*, 173.

(89) Bathula, S. R.; Akondi, S. M.; Mainkar, P. S.; Chandrasekhar, S. *Org. Biomol. Chem.* **2015**, *13*, 6432.

(90) Cave, A.; Guinaudeau, H.; Leboeuf, M.; Ramahatra, A.; Razafindrazaka, *J. Planta Med*. **1978**, *33*, 243.

(91) Ngantchou, I.; Nyasse, B.; Denier, C.; Blonski, C.; Hannaert, V.; Schneider, B. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 3495.

(92) Mirand, C.; de Maindreville, M. D.; Cartier, D.; Levy, J. *Tetrahedron Lett*. **1987**, *28*, 3565.

(93) Hagiwara, H.; Uda, H. *J. Org. Chem*. **1988**, *53*, 2308.

(94) Yasui, K.; Kawada, K.; Kagawa, K.; Tokura, K.; Kitadokoro, K.; Ikenishi, Y. *Chem. Pharm. Bull*. **1993**, *41*, 1698.

(95) Hesse, M. *Alkaloids: Nature's Curse or Blessing*; *Wiley-VCH*: Zürich, Switzerland, **2002**, 14.

(96) (a) Rottmann, M.; McNamara, C.; Yeung, B. K. S.; Lee, M. C. S.; Zou, B.; Russell, B.; Seitz, P.; Plouffe, D. M.; Dharia, N. V.; Tan, J.; Cohen, S. B.; Spencer, K. R.; Gonzalez-Paez, G. E.; Lakshminarayana, S. B.; Goh, A.; Suwanarusk, R.; Jegla, T.; Schmitt, E. K.; Beck, H. -P.; Brun, R.; Nosten, F.; Renia, L.; Dartois, V.; Keller, T. H.; Fidock, D. A.; Winzeler, E. A.; Diagana, T. T. *Science* **2010**, *329*, 1175. (b) Chan, S. T. S.; Pearce, A. N.; Page, M. J.; Kaiser, M.; Copp, B. R. *J. Nat. Prod.* **2011**, *74*, 1972.

(97) Stöckigt, J.; Antonchick, A. P.; Wu, F.; Waldmann, H. *Angew. Chem. Int. Ed*. **2011**, *50*, 8538.

(98) Larghi, E. L.; Amongero, M.; Bracca, A. B. J.; Kaufman, T. S. *ARKIVOC* **2005**, 98.

(99) Bischler, A.; Napieralski, B. *Ber. Deutsch. Chem. Gesell.* **1893**, *26*, 1903.

(100) Abramovitch, R. A.; Shapiro, D. *J. Chem. Soc.* **1956**, 4589.

(101) Dantale, S. W.; Söderberg, B. C. G. *Tetrahedron* **2003**, *59*, 5507.

(102) Ohta, Y.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett.* **2009**, 11, 1979.

(103) Song, H.; Liu, Y.; Wang, Q. *Org*. *Lett*. **2013**, *15*, 3274.

(104) Funayama, Y.; Nishio, K.; Wakabayashi, K.; Nagao, M.; Shimoi, K.; Ohira, T.; Hasegawa, S.; Saijo, N. *Mutat. Res.* **1996**, *349*, 183.

(105) (a) Tenen, S.S.; Hirsch, J. D. *Nature,* **1980**, *218*, 609. (b) Guzman, F.; Cain, M.; Larscheid, P.; Hagen, T.; Cook, J. M. *J. Med. Chem.* **1984**, *27*, 564.

(106) Grella, B.; Teitler, M.; Smith, C.; Herrick-Davis, K.; Glennon, R. A. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 4421.

(107) Wang, Y. -H.; Tang, J. -G.; Wang, R. -R.; Yang, L. -M.; Dong, Z. -J.; Du, L.; Shen, X.; Liu, J. -K.; Zheng, Y. -T. *Bioch. Biophys. Res. Commun.* **2007**, *355*, 1091.

(108) de Meester, C. *Muta Res.* **1995**, *339*, 139.

(109) (a) Zhang, H.; Larock, R. C. *J. Org. Chem.* **2002**, *67*, 7048. (b) Kusurkar, R. S.; Goswami S.K. *Tetrahedron*, **2004**, *60*, 5315. (c) Ding, S.; Shi, Z.; Jiao, N. *Org. Lett.* **2010**, *12*, 1540. (d) Nissen, F.; Richard, V.; Alayrac, C.; Witulski, B. *Chem. Commun.* **2011**, *47*, 6656. (e) Mulcahy, S. P.; Varelas, J. G. *Tetrahedron Lett.* **2013**, *54*, 6599. (f) Panarese, J. D.; Waters, S. P. *Org. Biomol. Chem.* **2013**, *11*, 3428. (g) Tiruveedhula, V. V. N. P. B.; Methuku, K. R.; Deschamps, J. R.; Cook, J. M. *Org. Biomol. Chem.* **2015**, *13*, 10705. (h) Kamal, A.; Tangella, Y.; Manasa, K. L.; Sathish, M.; Srinivasulu, V.; Chetna, J.; Alarifi, A. *Org. Biomol. Chem.* **2015**, *13*, 8652.

(110) Thirupathi, N.; Puri, S.; Reddy, T. J.; Sridhar, B.; Reddy, M. S. *Adv. Synth. Catal.* **2015**, *358*, 303.

(111) Severin, R.; Doye, S. *Chem. Soc. Rev.* **2007**, *36*, 1407.

(112) Dhiman, S.; Mishra, U. K.; Ramasastry, S. S. V. *Angew. Chem. Intl. Ed.* **2016**, DOI: 10.1002/anie.201600840R1.

(113) (a) Watanabe, Y.; Morisaki, Y.; Kondo, T.; Mitsudo, T. *J. Org. Chem*. **1996**, *61*, 4214. (b) Zotto, A. D.; Baratta, W.; Sandri, M.; Verardo, G.; Rigo, P. *Eur. J. Inorg. Chem.* **2004**, 524. (c) Hollmann, D.; Tillack, A.; Michalik, D.; Jackstell R.; Beller, M. *Chem.–Asian J.* **2007**, *2*, 403.

(114) (a) Suman, K.; Srinu, L.; Thennarasu, S. *Org. Lett.* **2014**, *16*, 3732. (b) Moynihan, L.; Chadda, R.; McArdle, P.; Murphy, P. V. *Org. Lett.* **2015**, *17*, 6226.

(115) (a) Zhou, Y.; Murphy, P. V. *Org. Lett*. **2008**, *10*, 3777. (b) Hui, B. W. -Q.; Chiba, S. *Org. Lett*. **2009**, *11*, 729. (c) Janreddy, D.; Kavala, V.; Kuo, C. -W.; Chen, W. -C.; Ramesh, C.; Kotipalli, T.; Kuo, T. -S.; Chen, M. -L.; He, C. -H.; Yao, C. F. *Adv. Synth. Catal*. **2013**, *355*, 2918.

(116) Ganin, H.; Tang, X.; Meijler, M. M. *Bioorg. Med. Chem. Lett*. **2009**, *19*, 3941.

(117) (a) Suzuki, H.; Iwata, C.; Sakurai, K.; Tokumoto, K.; Takahashi, H.; Hanada, M.; Yokoyama, Y.; Murakami, Y. *Tetrahedron* **1997**, *53*, 1593. (b) Busacca, C. A.; Eriksson, M. C.; Dong, Y.; Prokopowicz, A. S.; Salvagno, A. M.; Tschantz, M. A. *J. Org. Chem.* **1999,** *64,* 4564.

(118) For dehydrocrenatine, see: (a) Joshi, B. S.; Kamat, V. N.; Gawad, D. H. *Heterocycles* **1977**, *7*, 193. For dichotomides, see: (b) Chen, Y. -F.; Kuo, P. -C.; Chan, H. -H.; Kuo, I. -J.; Lin, F. -W.; Su, C. -R.; Yang, M. -L.; Li, D. -T.; Wu, T. -S. *J. Nat. Prod.* **2010**, *73*, 1993. For tunicoidines, see: (c) Tian, J.; Shen, Y.; Li, H.; Liu, R.; Shan, L.; Gao, J.; Zhang, W. *Planta Med.* **2012**, *78*, 625.

(119) (a) Chiba, S.; Xu, Y. -J.; Wang, Y. -F. *J. Am. Chem. Soc.* **2009**, *131*, 12886. (b) Zhang, L.; Lee, J. -Y.; Yamazaki, N.; Chiba, S. *Synlett* **2011**, 2167. (c) Wang, Y.; Li, J.; He, Y.; Xie, Y.; Wang, H.; Pana, Y. *Adv. Synth. Catal.* **2015**, *357*, 3229. (d). Li, J. -L.; Wang, Y. -C.; Li, W. -Z.; Wang, H. -S.; Mo, D. -L.; Pan, Y. M. *Chem. Commun.* **2015**, *51*, 17772.

(120) (a) Yue, W. S.; Li, J. J. *Org. Lett*. **2002**, *4*, 2201. (b) Hu, J.; Deng, Z.; Zhang, X.; Zhang, F.; Zheng, H. *Org. Biomol. Chem.* **2014**, *12*, 4885.

(121) Li, X.; Xue, J.; Chen, R.; Li, Y. *Synlett* **2012**, *23*, 1043.

(122) Seo, J. -A.; Gong, M. -S.; Lee, J. Y. *Org. Electron.* **2014**, *15*, 2068.

(123) González, B. C.; Sánchez, S. C.; Sedes, D. A.; Blanco, R. B. *PCT Int. Appl*. 2010146125.

(124) Carver, C. T.; Williams, B. N.; Ogilby, K. R.; Diaconescu, P. L. *Organometallics* **2010**, *29*, 835.

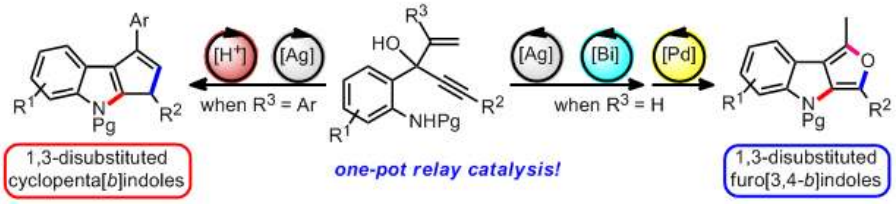
(125) Kotha, S.; Behera, M.; Shah, V. R. *Synlett* **2005**, *12*, 1877.

(126) Jung, M. E.; Duclos, B. A. *Tetrahedron* **2006,** *62,* 9321.

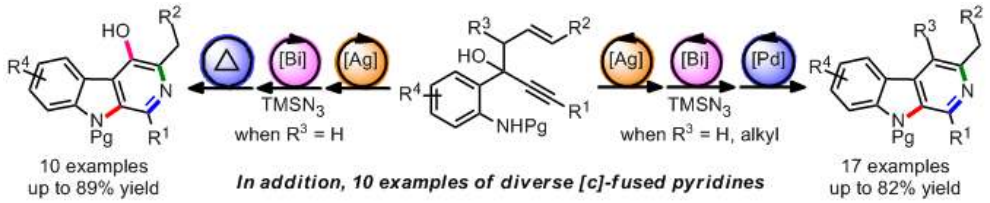
(127) Miller, B.; Lonescu, D. *Tetrahedron Lett.* **1994***, 35,* 6615.

LIST OF PUBLICATIONS

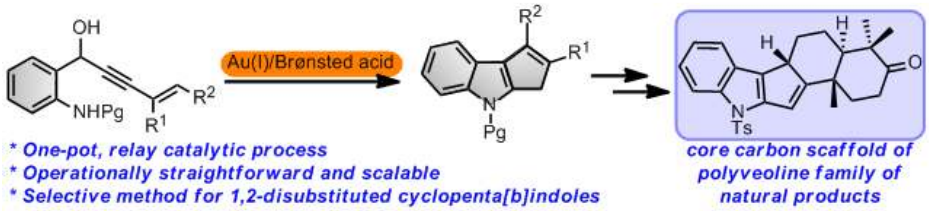
1. *"One-pot relay catalysis: Divergent synthesis of furo[3,4-b]indoles and cyclopenta[b]indoles from 3-(2-aminophenyl)-1,4-enynols"*
   Manisha.; Dhiman, S.; Mathew, J.; Ramasastry, S. S. V. *Org. Biomol. Chem.* **2016**, DOI: 10.1039/C6OB00319B. [*Invited article towards the thematic issue 'New Talent'*]



2. "*One-Pot Trimetallic Relay Catalysis: A Unified Approach for the Synthesis of β-Carbolines and Other [c]-Fused Pyridines*"
   Dhiman, S.; Mishra, U. K.; Ramasastry, S. S. V. *Angew. Chem. Intl. Ed.* **2016**, DOI: 10.1002/anie.201600840R1.

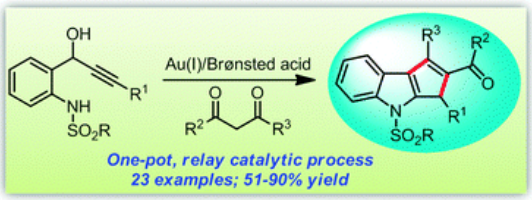


3. "*One-Pot Relay Gold(I) and Brønsted Acid Catalysis: Cyclopenta[b]annulation of Indoles via Hydroamination/Nazarov-Type Cyclization Cascade of Enynols*"
   Dhiman, S.; Ramasastry, S. S. V. *Org. Lett.* **2015**, *17*, 5116.



4. "*Synthesis of Polysubstituted Cyclopenta[b]indoles via Relay Gold(I)/Brønsted Acid Catalysis*"

   Dhiman, S.; Ramasastry, S. S. V. *Chem. Commun*. **2015**, *51*, 557.

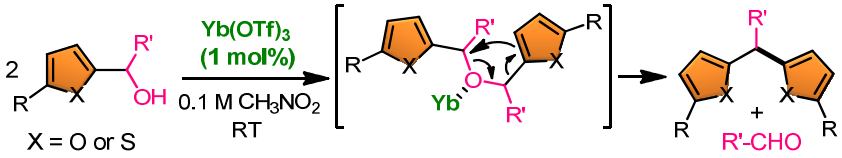


5. "*Synthesis of 1,2,3-Trisubstituted Cyclopentannulated Benzothiophenes through an Acid-Mediated, Solvent-Free, One-Pot Domino Process*"

   Satpathi, B.; Dhiman, S.; Ramasastry, S. S. V. *Eur. J. Org. Chem.* **2014**, 2022.

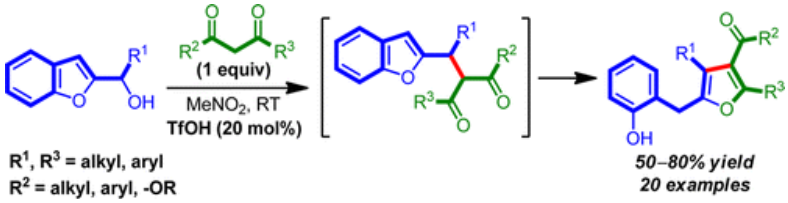
6. "*Di- and Triheteroarylalkanes via Self-Condensation and Intramolecular Friedel-Crafts Type Reaction of Heteroaryl alcohols*"

   Dhiman, S.; Ramasastry, S. S. V. *Org. Biomol. Chem.* **2013**, *11*, 4299.



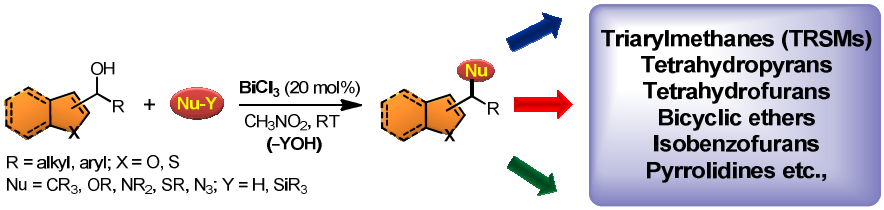
7. "*Acid Catalyzed Ring Transformation of Benzofurans to Tri- and Tetrasubstituted Furans*"

   Dhiman, S.; Ramasastry, S. S. V. *J. Org. Chem.* **2013**, *78*, 10472.



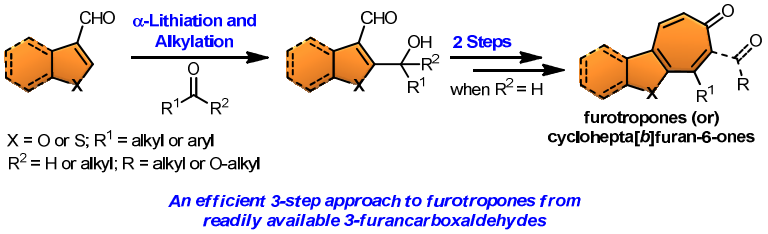
8. "*Taming Furfuryl Cations for the Synthesis of Privileged Structures and Novel Scaffolds*"

   Dhiman, S.; Ramasastry, S. S. V. *Org. Biomol. Chem.* **2013**, *11*, 8030.



9. "*One-Step Synthesis of 3-Formyl-2-furylcarbinols and Elaboration to Unprecedented Furotropones*"

   Dhiman, S.; Ramasastry, S. S. V. *Indian J. Chem.* **2013**, *52A*, 1103. [*Invited article towards the thematic issue 'Complex Chemical System'*]



An efficient 3-step approach to furotropones from readily available 3-furancarboxaldehydes

ABOUT THE AUTHOR

The author, Ms. Seema Rani was born in 1988 at Panipat, Haryana. After her intial schooling at Panipat; she obtained B. Sc. Degree in 2009 form S. D. College, Panipat, Kurukshetra University; and M. Sc. Degree from the Department of Chemistry, Kurukshetra University. She joined the Department of Chemical Sciences, Indian Institute of Science Education and Research (IISER) Mohali, in the Ph. D. programme in January 2012. She passed the comprehensive examination in January 2013. Presently she is continuing as a Senior Research Fellow of IISER Mohali, in the Department of Chemical Sciences.

CONFERENCES ATTENDED

- Delivered an invited talk at the **10th CRSI-RSC Symposium** held at Chandigarh, India during February 2016. Title of the presentation: *One-pot cascade processes for the synthesis of annulated heteroaryls*
- Presented a poster at the **Nascent Developments in Chemical Sciences (NDCS)** held at BITS-Pilani, India during October 2015. Title of the poster: *One-pot relay gold(I)/acid catalysis for the synthesis of annulated Indoles*
- Presented a poster at the **International Symposium on Recent Advances in Medicinal Chemistry (ISRAM)** held at NIPER-Mohali, India during September 2014. Title of the poster: *Previously unexplored chemistry of heteroaryl carbinols*
- Delivered an invited talk at the **XVI NOST-Organic Chemistry Conference (NOST-OCC)** held at Agra, India during April 2014. Title of the presentation: *Previously unexplored chemistry of heteroaryl carbinols*
- Delivered a talk at the **IX JNOST-Organic Chemistry Conference (JNOST-OCC)** held at IISER-Bhopal, India during December 2013. Title of the presentation: *An exciting chemistry of heteroaryl carbinols leading to the synthesis of privileged structures and novel scaffolds*