

Investigations on the Reactions of Acetoxy Allenates and Propargylic Alcohols with Indole Substrates

A THESIS
SUBMITTED FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

By

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I dedicate this thesis to

*My Family,
Teachers, and
Friends.....*

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STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigation carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of Prof. K. C. Kumara Swamy.

In keeping with the general practice of reporting scientific observations, due acknowledgements have been made wherever the work described is based on the finding of other investigators.

Hyderabad

December 2022

S. Debnath
Shubham Debnath

DECLARATION

I, **Shubham Debnath**, hereby declare that this thesis entitled "**Investigations on the Reactions of Acetoxy Allenates and Propargylic Alcohols with Indole Substrates**" submitted by me under the guidance and supervision of **Professor K. C. Kumara Swamy** is a bonafide research work which is also free from plagiarism. I also declare that it has not been submitted previously in part or in full to this University or any other University or Institution for the award of any degree or diploma. I hereby agree that my thesis can be deposited in Shodganga/INFLIBNET.

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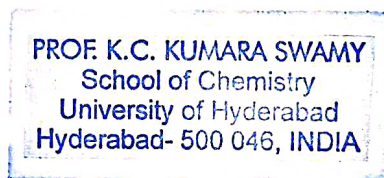
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Signature of the supervisor: Kumara Swamy





CERTIFICATE

This is to certify that the thesis entitled ***“Investigations on the Reactions of Acetoxy Allenoates and Propargylic Alcohols with Indole Substrates”*** submitted by **Mr. SHUBHAM DEBNATH** bearing registration number **16CHPH24** in partial fulfillment of the requirements for the award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by him under my supervision and guidance.

This thesis is free from plagiarism and has not been submitted previously in part or in full to this or any other University or Institution for the award of any degree or diploma. Further, the student has two publications before the submission of his thesis.

Part of this thesis has been published in the following publications:

1. Selvaraj, K.; **Debnath, S.**; Kumara Swamy, K. C. Reaction of indole carboxylic acid/amide with propargyl alcohols: (4 + 3) annulation, unexpected 3- to 2-carboxylate/amide migration and decarboxylative cyclization. *Org. Lett.* **2019**, *21*, 5451.
2. **Debnath, S[#]**; Kumar, A. S[#]; Chauhan, S.; Kumara Swamy, K. C. Divergent reactivity of δ and β' - acetoxy allenoates with 2-sulfonamidoindoles via phosphine catalysis: Entry to dihydro- α -carboiline, α -carboiline and spiro cyclopentene motifs. *J. Org. Chem.* **2021**, *86*, 11583.
3. **Debnath, S.**; Kumar, A. S.; Chauhan, S.; Kumara Swamy, K. C. Lewis base dependent (3 + 3) annulation of acetoxy allenoates with iminoindlines: α -Carboiline scaffolds with varied substituents. *Adv. Synth. Catal.* (doi.org/10.1002/adsc.202200997).

The following paper has to be communicated.

4. **Debnath, S.**; Kumara Swamy, K. C. (to be communicated).

The following is the list of presentations at conferences/symposia:

1. Poster presentation in the “Chemfest-2019” (Annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, February 2019.

3. Poster presentation in the "CRSI-NSC-26, 26th National Symposium in Chemistry", Department of Chemistry, School of Advanced Science, VIT Vellore, February 2020.
4. Oral presentation in the "Chemfest-2021" (Annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, March 2021.
5. Poster presentation in the "Chemfest-2022" (Annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, April 2022.

Further, the student has passed the following courses towards the fulfillment of the coursework requirement for Ph. D:

Sl. No	Course No	Title of the course	No of Credits	Grade
1.	CY801	Research proposal	3	Pass
2.	CY805	Instrumental methods-A	3	Pass
3.	CY806	Instrumental methods-B	3	Pass
4.	CY452	Organic Reactions and Mechanisms	3	Pass

Final Result: Passed.

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December 2022


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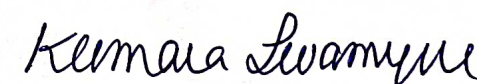
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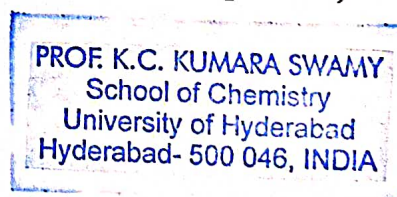
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Prof. K. C. Kumara Swamy

(Thesis supervisor)



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I thank the present and former Deans, School of Chemistry, for providing me with the instrumental facilities that are required for my research. I extend my sincere thanks to all the faculty members of the School of Chemistry for their cooperation and help in different aspects.

I am deeply indebted to all my teachers right from my school to my university for the support and training I received in my academic career.

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Talking about my drama team, I was fortunate enough to direct some dramas in several cultural programs observed at HCU. At least two of them became very famous. I was lucky

enough to have a bunch of talented actors on my team and it is the perfect platform to acknowledge them. I would like to express my gratitude towards Sugata da, Tirtha, Soumik, Izaz, Arkaprava, Shubhadeep, Ripan, Debjyoti, Niladri, Sneha, Dibyendu, Soumyajit, Sreejani, Dipanjali, Shilpi, Supriyo, Tanmay and Kamalika.

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Shubham...

LIST OF PUBLICATIONS

(A) *Published papers:*

1. Reaction of allenylphosphonates/allenylphosphine oxides with thiocyanates/isothiocyanates or oxalyl chloride/AgNO₃
K. C. Kumara Swamy*, Manab Chakaravarty, **Shubham Debnath**, and M. N. Reddy
Phosphorus Sulfur Silicon Rel. Elem. **2017**, 192, 763.
2. Reactivity of allenylphosphonates/allenyl phosphine oxides-some new addition/cycloaddition and cyclization pathways
K. C. Kumara Swamy*, Mandala Anitha, **Shubham Debnath**, and Mallepalli Shankar
Pure Appl. Chem. **2019**, 91, 773.
3. Reaction of indole carboxylic acid/amide with propargyl alcohols: (4 + 3) annulation, unexpected 3- to 2- carboxylate/amide migration and decarboxylative cyclization
Karuppu Selvaraj, **Shubham Debnath** and K. C. Kumara Swamy*
Org. Lett. **2019**, 21, 5451.
4. Divergent reactivity of δ and β' - acetoxy allenates with 2-sulfonamidoindoles via phosphine catalysis: Entry to dihydro- α -carboiline, α -carboiline and spiro cyclopentene motifs
Shubham Debnath[#], A Sanjeeva Kumar[#], Sachin Chauhan, and K. C. Kumara Swamy*
J. Org. Chem. **2021**, 86, 11583.
5. Lewis base dependent (3 + 3) annulation of acetoxy allenates with iminoindolines: α -Carboline scaffolds with varied substituents
Shubham Debnath, A. Sanjeeva Kumar, Sachin Chauhan, and K. C. Kumara Swamy*
Adv. Synth. Catal. (doi.org/10.1002/adsc.202200997).

(B) *The following paper is to be communicated.*

6. Lewis base catalyzed (3 + 3) annulation of acetoxy allenates with *N*-Boc-oxindole, benzofuranone and pyrazolone: Synthesis of pyran scaffolds
Shubham Debnath and K. C. Kumara Swamy*

Participation in Conferences/ Symposia

1. ϵ -lactones and ϵ -lactams via (4 + 3) Annulation and 3,4-dihydrocyclopenta[*b*]indoles via Decarboxylative Cyclization using Indole Carboxylic Acids/Amides and Propargyl Alcohol
Shubham Debnath, Karuppu Selvaraj, K. C. Kumara Swamy*
“*Chemfest-2019*” (Annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, February-2019.
2. Reaction of Indole Carboxylic Acid/Amide with Propargyl alcohols: Unexpected 3 to 2 Carboxylate/Amide Migration, Decarboxylative Cyclization and Reaction of Allenylphosphine Oxides with NH_4SCN and ICl
Shubham Debnath, K. C. Kumara Swamy*
“*INSPIRE Fellowship Review Meeting-2019*”, K L Deemed to be University, Vaddeswaram, Guntur district, June-2019.
3. ϵ -Lactones and ϵ -Lactams via (4 + 3) Annulation and 3,4-Dihydrocyclopenta[*b*]indoles via Decarboxylative Cyclization Using Indole Carboxylic Acids/Amides and Propargyl Alcohols
Shubham Debnath, Karuppu Selvaraj, K. C. Kumara Swamy*
“*CRSI-NSC-26, 26th National Symposium in Chemistry*”, Department of Chemistry, School of Advanced Science, VIT Vellore, February-2020.
4. Complex Reactivity of δ - and β' -Acetoxy Allenates with 2-Sulfonamidoindoles mediated by PPh_3 and DBU
Shubham Debnath, A. Sanjeeva Kumar, K. C. Kumara swamy*
“*Chemfest-2021*” (annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, March-2021.
5. Lewis Base Catalyzed Complex Reactivity of δ and β' -Acetoxy Allenates with 2-sulfonamidoindoles in (3 + 3) Annulation Reactions
Shubham Debnath, A. Sanjeeva Kumar, K. C. Kumara Swamy*
“*Chemfest-2022*” (Annual in-house symposium), School of Chemistry, University of Hyderabad, Hyderabad, April-2022.

Synopsis

This thesis is divided into two parts: **Part-A** and **Part-B**. **Part-A** deals with the following topics: (i) Divergent reactivity of δ - and β '-acetoxy allenates with 2-sulfonamido indoles *via* phosphine catalysis- Synthesis of dihydro- α -carboline, α -carboline and spiro cyclopentene motifs, and (ii) Lewis base dependent (3 + 3) annulations of acetoxy allenates with iminoindolines, Boc-protected oxindole, benzofuranone and pyrazolone. **Part-B** deals with the reaction of indole carboxylic acids/amides with propargylic alcohols that involve one or more of (4 + 3) annulation, indole 3- to 2-carboxylate/amide migration and decarboxylative cyclization.

The compounds synthesized in the present study are, in general, characterized by melting point, IR and NMR (^1H , $^{13}\text{C}\{^1\text{H}\}$ and $^{19}\text{F}\{^1\text{H}\}$) techniques in conjunction with LC-MS/ HRMS/ elemental (CHN) analyses. X-ray structure determination has been undertaken wherever required. A summary, as well as references, are given at the end of each part.

PART A

In Chapter 1, a review of the literature on aspects relevant to this part is presented. In Chapter 2, the results obtained are discussed while in Chapter 3, the experimental details are described. The precursors used in the present study are shown in Chart 1 [**Note:** The numbering of compounds given here is different from that in the main part of the thesis]. They are prepared by methodologies available (with modifications where necessary) in the literature.

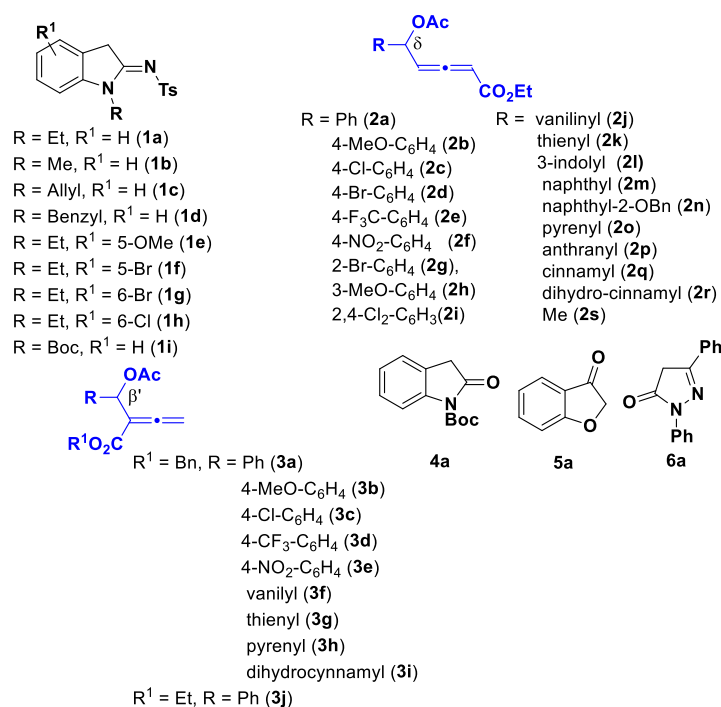
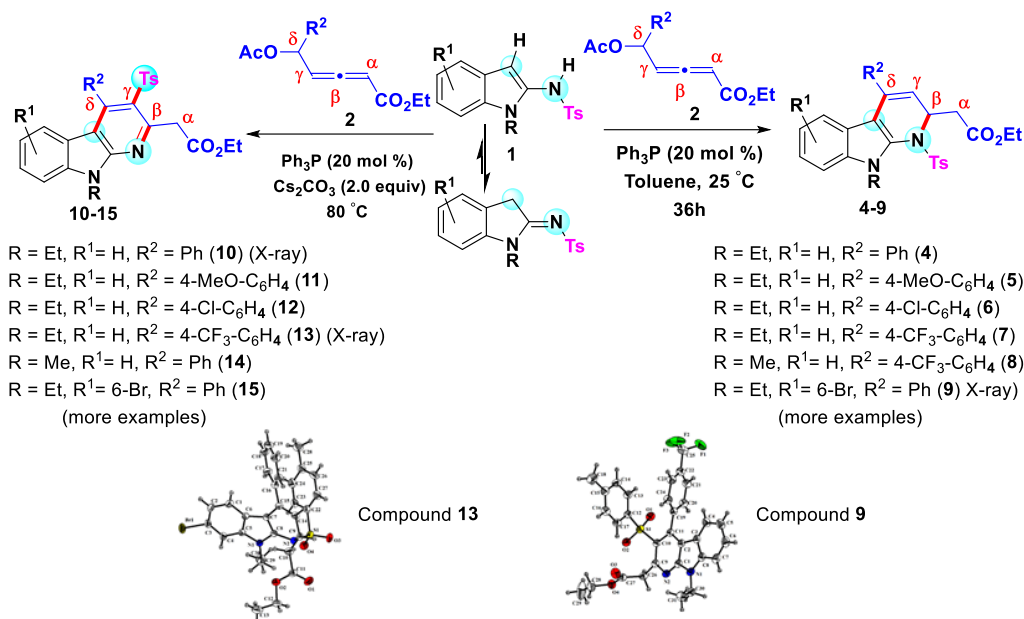


Chart 1. Precursors used in the present study (part A)

(i) Synthesis of dihydrocarbolines and tosyl-migrated carbolines from δ -acetoxy allenoates and 2-sulfonamidoindoles

As mentioned above, the primary objective of this part of the work was to explore the chemistry of acetoxy allenoates. In this context, we obtained α -carbolines as products in many cases. It is noted that carboline scaffold is present in many biologically active compounds and natural products. In the current study, we have developed a new synthetic methodology for the construction of carbolines and related compounds.

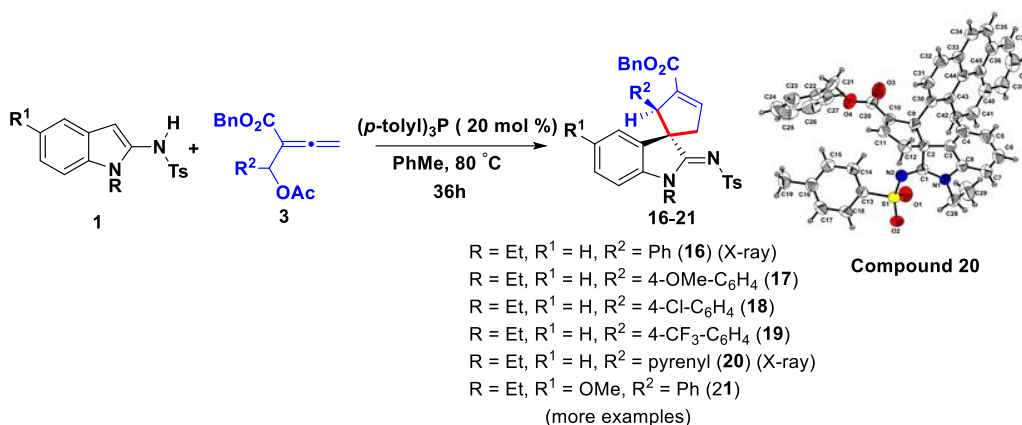
Under phosphine-catalysis, at ambient temperature, 2-sulfonamido indoles **1** react with δ -acetoxy allenoates **2** to produce dihydrocarbolines **4-9** via (3 + 3) annulation in good to excellent yields (Scheme 1). On the other hand, by the addition of Cs_2CO_3 as an additive at 80 °C, carbolines with the migration of tosyl group to the γ -position (cf. **10-15**) are obtained. Structures of compounds **9**, **10**, and **13** were confirmed by single crystal X-ray crystallography. Mechanistic details on these have been discussed.



Scheme 1: Synthesis of dihydrocarbolines and tosyl-migrated carbolines

(ii) Formation of spirocyclopentenones from β' -acetoxy allenates and 2-sulfonamido indoles

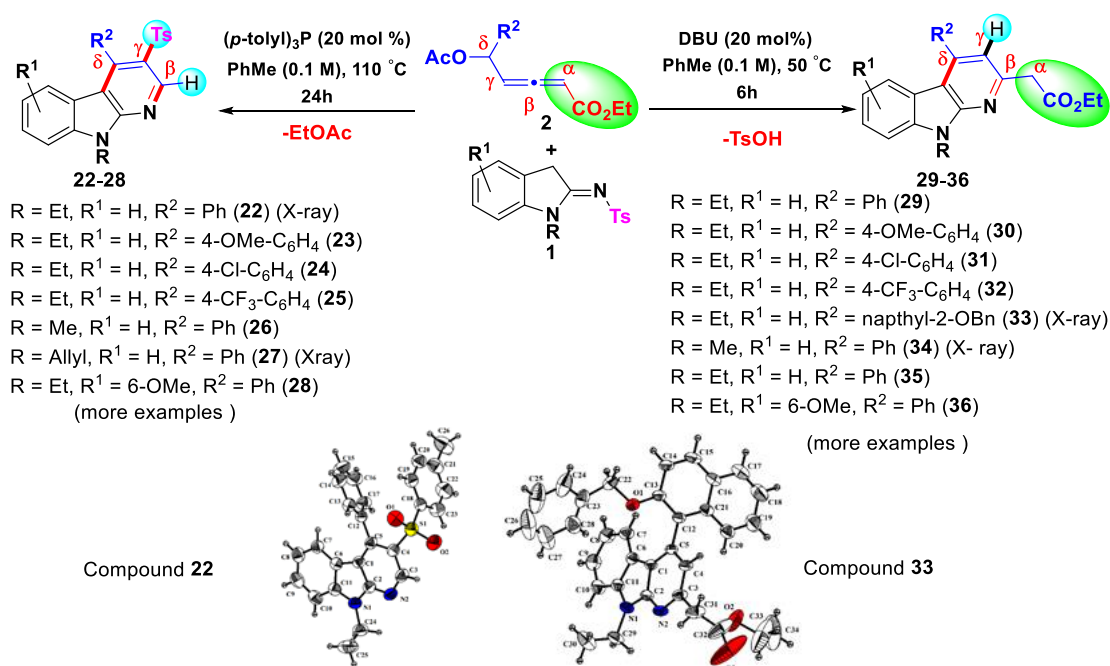
Taking a cue from the reactivity of δ -acetoxy allenates as described above, we expected the formation of a seven-membered fused heterocycle using β' -acetoxy allenates via (4 + 3) annulation. Surprisingly, under tri(*p*-tolyl)phosphine catalysis, β' -acetoxy allenates undergo (4 + 1) annulation to form spirocyclopentene motifs **16-21** (Scheme 2). Details on the mechanistic pathways leading to these spirocyclopentenones have been explored and discussed.



Scheme 2: Synthesis of indole fused cyclopentenones from β' -acetoxy allenates

(iii) DBU or PPh_3 mediated/ catalyzed reactions of δ -acetoxy allenates with 2-sulfonamidoindoles: Carbolines with tosyl migration and $-\text{CH}_2\text{CO}_2\text{Et}$ elimination

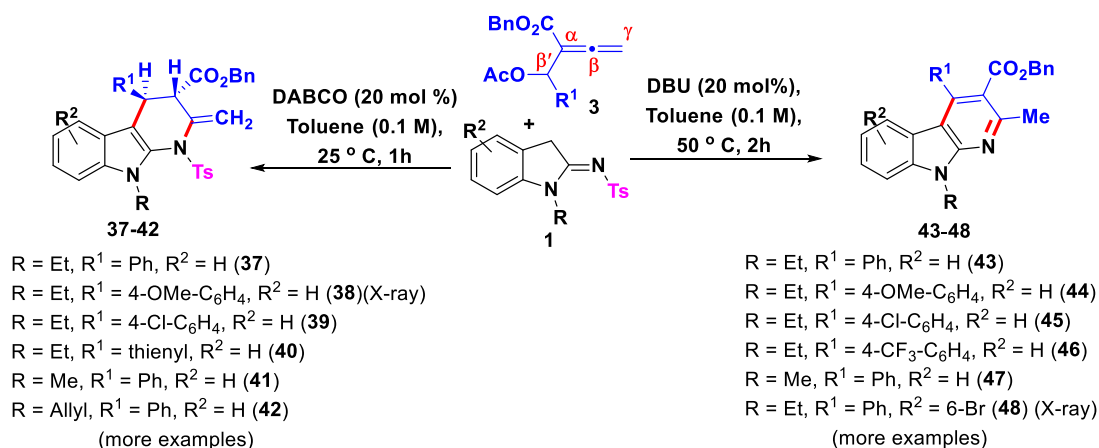
The phosphine-catalyzed reaction of δ -acetoxy allenolate with 2-sulfonamido indoles at room temperature (25 °C) as described above gave carbolines. Interestingly, at higher temperatures (e.g., 110 °C), the tosyl group migrated to the γ position of carboline moiety along with the elimination of $-\text{CH}_2\text{CO}_2\text{Et}$ moiety probably *via retro*-Mannich pathway leading to tosyl migrated carbolines **22-28**. Several control experiments and HRMS studies on reaction mixture revealed that the reaction takes place through dihydro-carboline intermediate **4**. Carbolines with varied substitutions could also be constructed using nitrogen-containing Lewis bases such as DBU/DABCO. Thus at 50 °C, 2-sulfonamidoindole **1** reacted with δ -acetoxy allenolates **2** to form carbolines **29-36** through (3 + 3) annulation. Thus the nature of the Lewis base plays a crucial role in these reactions (Scheme 3).



Scheme 3: Synthesis of tosyl migrated/eliminated carbolines from acetoxy allenolates

(iv) Reaction of β' -acetoxy allenolates with 2-sulfonamidoindole under DBU or DABCO mediation: Formation of carbolines/tetrahydrocarbolines

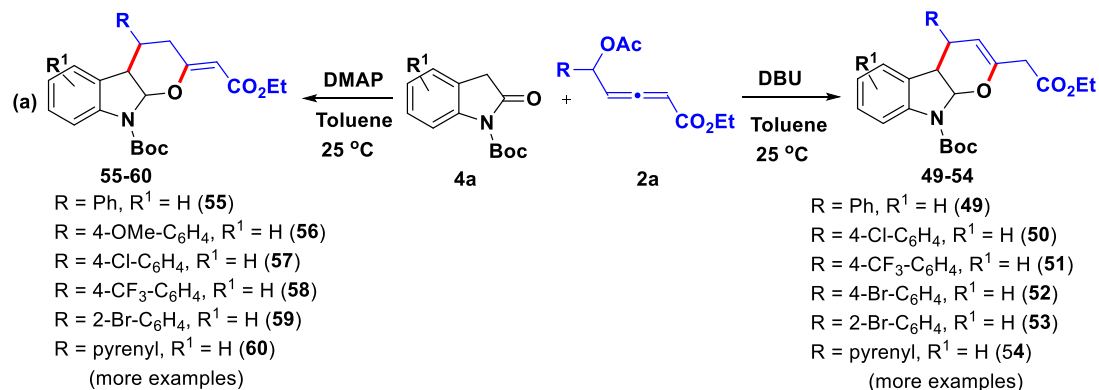
In continuation of the above studies, β' -acetoxy allenolates when reacted with 2-sulfonamidoindole in the presence of DBU produced the fully aromatized carbolines **43-48** whereas, in the presence of DABCO base, partial reduction occurred leading to the formation of tetrahydrocarbolines **37-42** containing two consecutive chiral centers (Scheme 4).



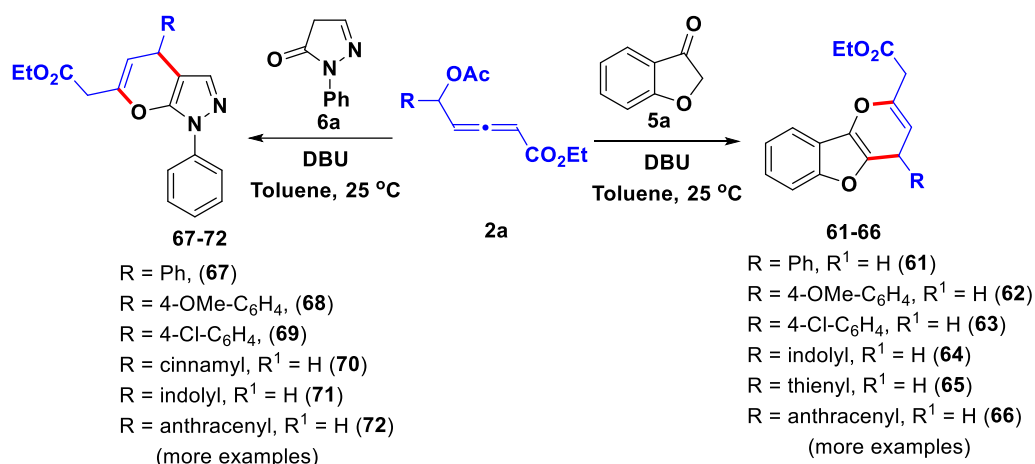
Scheme 4: Reaction of β' -acetoxy allenates with 2-sulfonamidoindoles

(v) DBU or DMAP mediated reaction of δ -acetoxy allenates with oxoindolines, pyrazolones and benzofuranones: Formation of pyrans

The reaction of keto-substrates possessing an adjacent $-\text{CH}_2$ group (e.g., *tert*-2-oxoindolinone carboxylate, benzofuranone, and pyrazolone) with δ -acetoxy allenates was the theme of investigations in this part. The products are indole fused pyrans/ dihydropyrans formed by (3 + 3) annulation. Both DBU and DMAP lead to pyrans, but with marginally different structures (Schemes 5-6). Details on the mechanistic pathways are discussed.



Scheme 5: Reaction of δ -acetoxy allenates with *tert*-2-oxoindolinone carboxylates



Scheme 6: Reaction of δ -acetoxy allenates with benzofuranone and pyrazolone

PART B

In Chapter 4, a review of the literature on aspects relevant to this part is presented. In Chapter 5, the results obtained on these aspects are discussed while in Chapter 6, the experimental details are described. The precursors used in this part are shown in Chart 2.

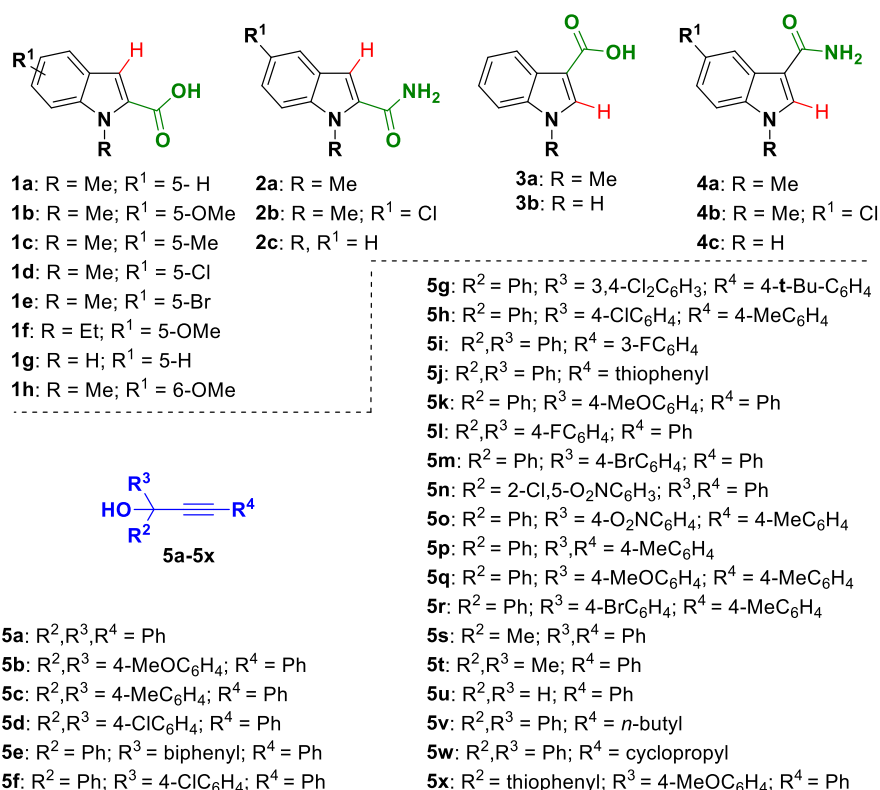
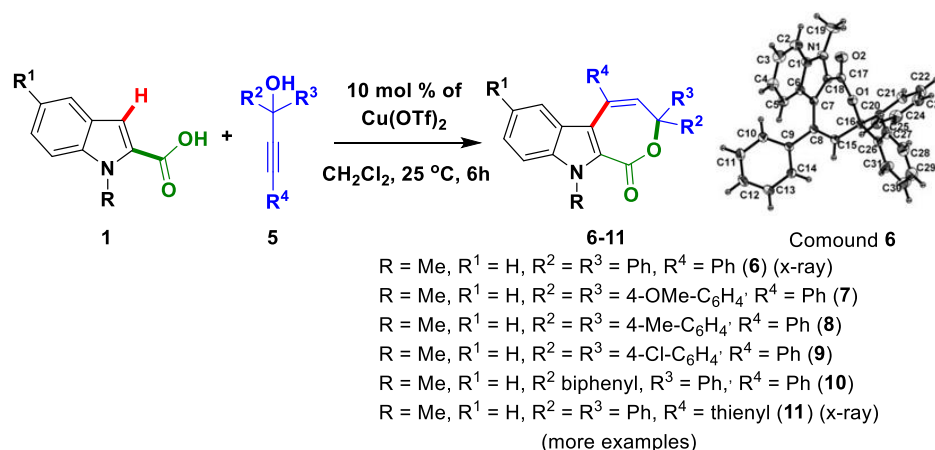


Chart 2: Precursors used in the present study (Part B)

(i) Synthesis of ε -lactones from indole-2-carboxylic acids and propargylic alcohols

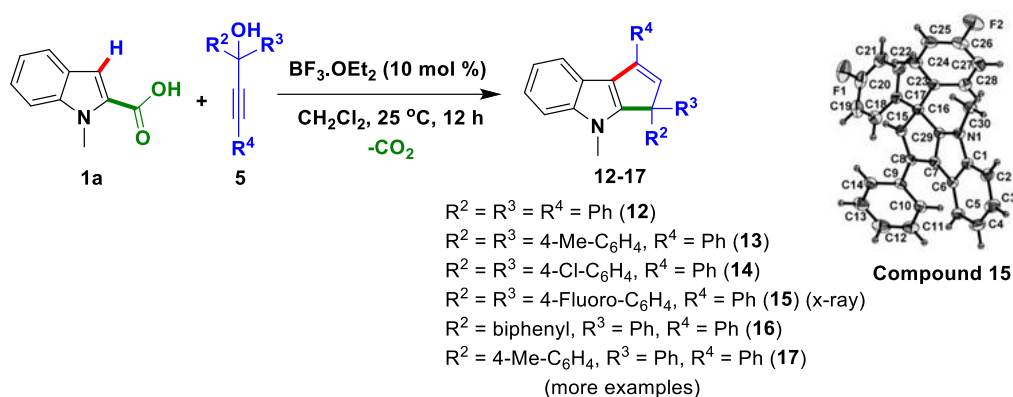
Propargylic alcohols have an interesting reactivity due to the presence of the triple bond as well as the $-CRR'OH$ group. In the presence of catalytic amounts of Lewis acid such as $Cu(OTf)_2$, *N*-alkylated indole-2-carboxylic acids **1** and propargylic alcohols **5** undergo (4 + 3) annulation leading to seven-membered ε -lactones **6-11** at room temperature (Scheme 7). Although the high reactivity at indole-3 carbon is expected isolation of the ε -lactones like what is obtained here is unprecedented.



Scheme 7: Synthesis of indole-fused ε -lactones from propargylic alcohols

(ii) $BF_3 \cdot OEt_2$ mediated decarboxylative cyclization of 1-methylindole-2-carboxylic acids with propargylic alcohols

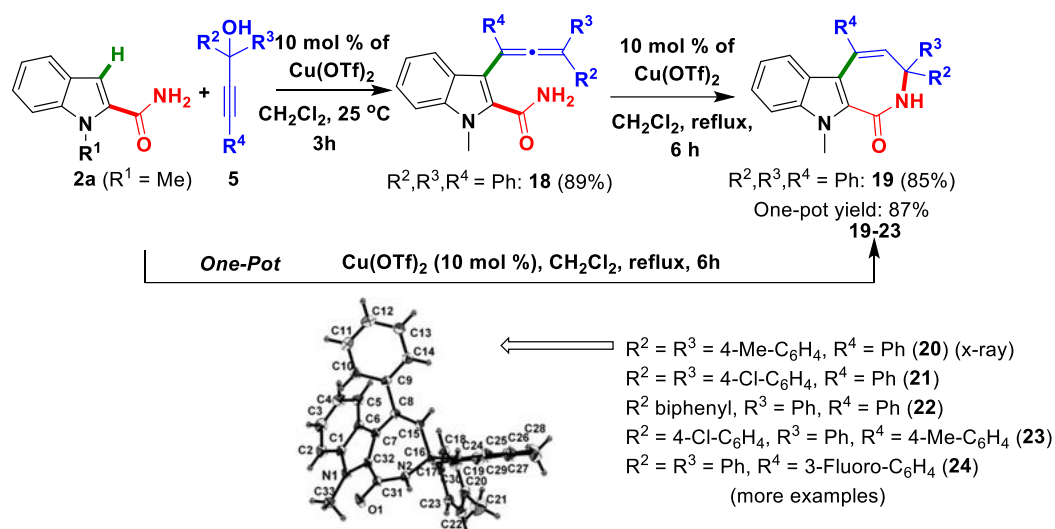
In the presence of a catalytic amount of strong Lewis acid such as $BF_3 \cdot OEt_2$, the reaction of 1-methylindole-2-carboxylic acids with propargylic alcohols goes through the same intermediate as above but ends up as 3,4-dihydrocyclopenta[*b*]indole **12-17** via decarboxylation followed by cyclization (Scheme 8).



Scheme 8: Synthesis of indole-fused cyclopentenenes using substituted propargylic alcohols

(iii) Reaction of indole-2-carboxamides with propargylic alcohols: Synthesis of ϵ -lactams and isolation of an intermediate allenamide

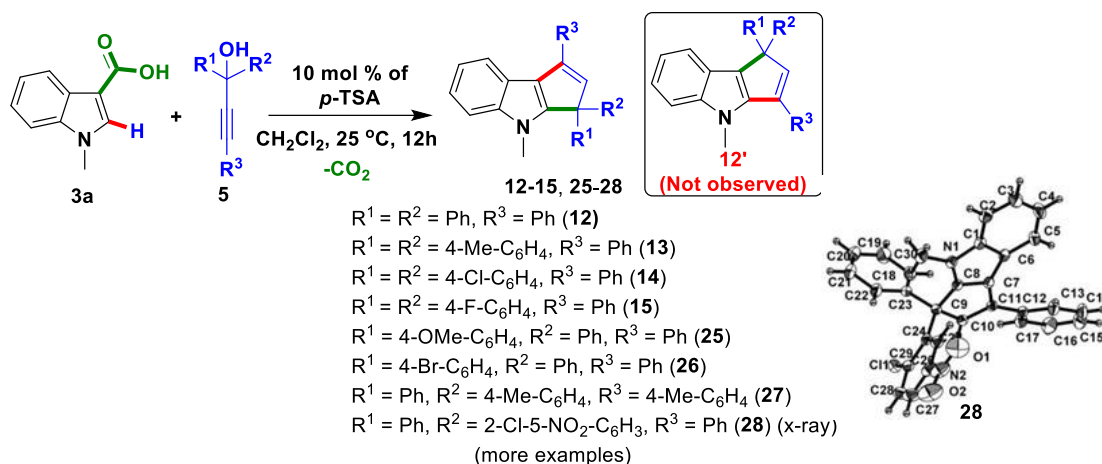
Interestingly, under $\text{Cu}(\text{OTf})_2$ catalyzed conditions, the use of 1-methylindole-2-carboxamide and propargylic alcohol ($\text{R}^1, \text{R}^2, \text{R}^3 = \text{Ph}$) afforded only the allene product **18** in 89% yield. This allene underwent nucleophilic attack of the NH_2 group in the presence of 10 mol % of $\text{Cu}(\text{OTf})_2$ in refluxing DCM for 6 h to afford the ϵ -lactam **19** in 85% yield. Hence we surmised that direct one-pot treatment of **2a** with **5** using $\text{Cu}(\text{OTf})_2$ catalyst should give **19-24**, which was proved to be correct (Scheme 9).



Scheme 9: Synthesis of ϵ -lactams using propargylic alcohols

(iv) *p*-TSA mediated reaction of 1-methylindole-3-carboxylic acids with propargylic alcohols

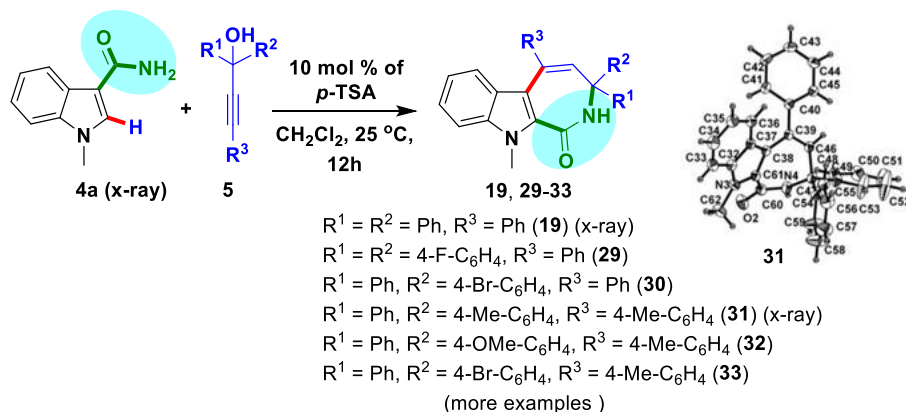
With the expectation that 3-substituted ϵ -lactone and 1,4-dihydrocyclopenta[*b*]indole will be formed when the carboxyl group is at the indole-3-position, we treated 1-methylindole-3-carboxylic acid **3a** with propargylic alcohol **5** in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ but the reaction did not occur. Surprisingly, in the presence of *p*-TSA, the unexpected 3,4-dihydrocyclopenta[*b*]indole **12-15**, and **25-28** formed, rather than the expected 1,4-dihydrocyclopenta[*b*]indoles are obtained (Scheme 10). This result indicates that the reaction must go through a seven-membered ϵ -lactone intermediate which means there is a possibility that the carboxylic acid group migrated from the indole 3- to 2-position.



Scheme 10: Synthesis of indole fused cyclopentenones from 1-methylindole-3-carboxylic acid

(v) *p*-TSA mediated reaction of 1-methylindole-3-carboxamides with propargylic alcohols: Indole 3- to 2-amide migration

The migration of the carboxylic acid group from the indole 3- to 2- position was proved unambiguously by choosing indole-3-carboxamide **4a** as the reaction partner to isolate ϵ -lactams **19**, and **29-33** in the presence of *p*-TSA (Scheme 11). The X-ray structures of *N*-methyl indole-3-carboxamide **4a** as well as the final compounds **19/31** were also determined. Thus it was concluded that the formation of **19** and **29-33** from **3a** and **5** occurs *via* carboxylate migration from 3- to 2- position on indole, followed by decarboxylative cyclization.



Scheme 11: Synthesis of ϵ -lactams from indole-3-carboxamide **4a**

PART A

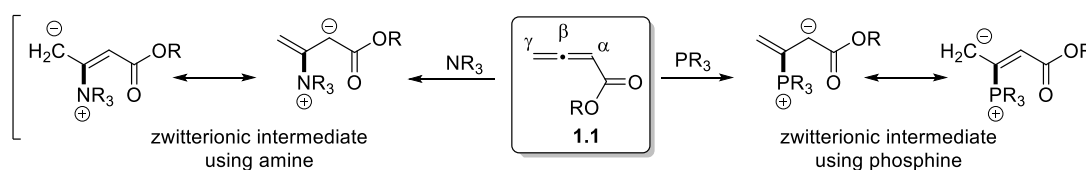
DIVERGENT REACTIVITY OF δ - AND β' -ACETOXY ALLENATES WITH 2-SULFONAMIDO INDOLES, *N*-BOC- OXINDOLE, BENZOFURANONE AND PYRAZOLONE

INTRODUCTION

This chapter serves with the literature relevant to the topics that will be thoroughly discussed in Chapter 2. General Introduction on allene as well as allenolate chemistry is presented in sections 1.1-1.2. Recent developments in the chemistry of allenolates are deliberated in section 1.3. Sections 1.4-1.5, delve into the reactivity of 2-sulfonamido-indoles and carbolines.

1.1 General Introduction: Allene Chemistry

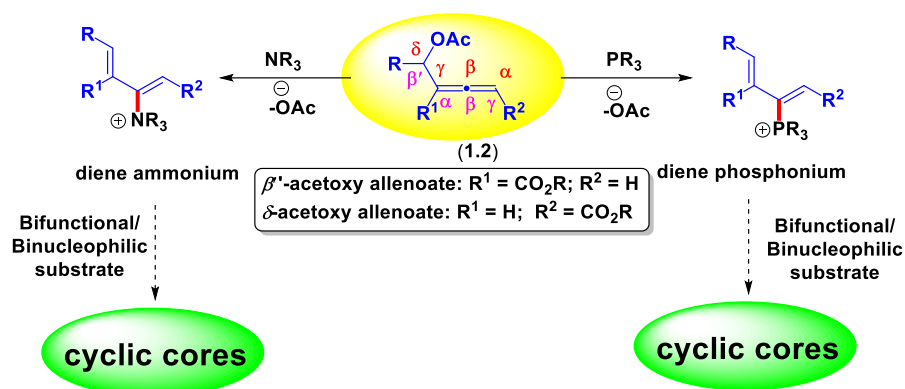
Over the past few decades, transformations involving allenes have evolved as powerful tools in organic synthesis.¹⁻³ The main reason behind the high reactivity of allene is its unique structure in which the two cumulative and mutually perpendicular π -bonds make it amenable for functionalization. Allenolates (**1.1**) belong to a unique class of compounds in which the allene moiety is directly attached to an ester group. Our main focus in this work is on allenolate chemistry. The negative charge generated after the attack of Lewis base at the sp hybridized carbon atom of allene can be easily stabilized by electron-withdrawing ester group leading to a zwitterionic intermediate which can attack an electrophilic partner (Scheme 1.1).



Scheme 1.1: Zwitterionic intermediates formed from allenolates

Since the discovery of Lu's (3 + 2) cycloaddition of allenolates using phosphine catalysis,⁴ numerous other Lewis base-catalyzed/mediated annulations of allenolates have been reported.^{5,6} To make allenolate chemistry more interesting and practically applicable, chemists have introduced easily removable groups like acetoxy in the allenolate moiety; among these, δ - and β' -acetoxy allenolates (cf. **1.2**) have been studied in greater detail. Here, the Lewis base (mainly nitrogen or phosphorus-based) tends to attack the sp hybridized carbon atom to make it a dipolarophile (zwitterionic species) leading to the formation of diene

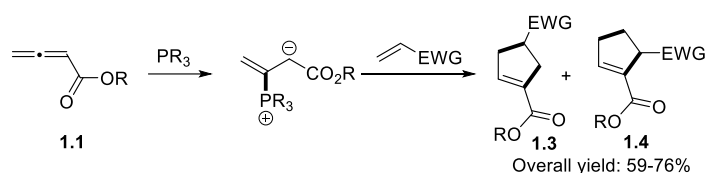
ammonium/phosphonium intermediate after the elimination of the acetoxy group. Subsequently, annulation occurs in the presence of a suitable bifunctional substrate to form carbocycles as well as heterocycles (Scheme 1.2).



Scheme 1.2: Formation of diene ammonium/phosphonium intermediates from acetoxy allenoates

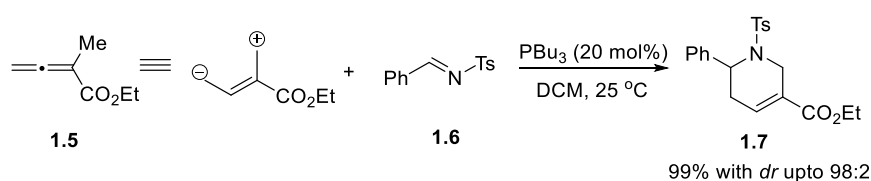
1.2 Reactions of allenoates

Lu and co-workers reported a unique (3 + 2) cycloaddition leading to cyclopentenones **1.3** or **1.4** from 2,3-butadienoates **1.1** and electron-deficient alkenes under phosphine catalysis (Scheme 1.3).^{4a} This discovery pivoted numerous other reactions using allenoates as outlined below.



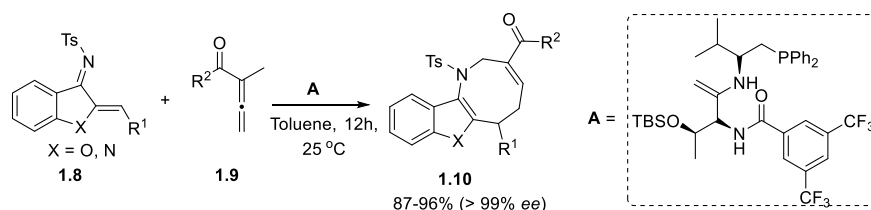
Scheme 1.3: Synthesis of cyclopentenones from allenoates by phosphine catalysis

Kwon's group reported the formation of tetrahydropyridines **1.7** from *N*-tosyl aldimine **1.6** and ethyl-2-methyl-2,3-butadienoate **1.5**.⁷ The (4 + 2) annulation occurs via 1,4-dipolar cycloaddition for the construction of six-membered ring which is rare. Here, they chose tributylphosphine as the catalyst (Scheme 1.4).



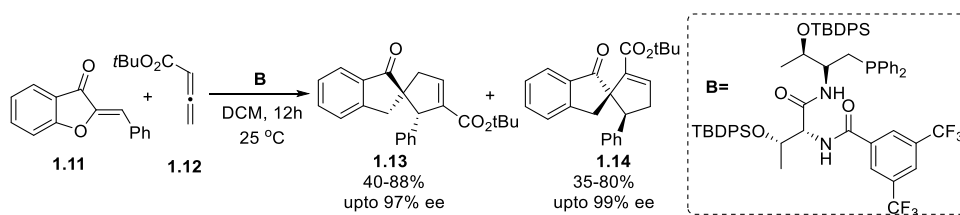
Scheme 1.4: Synthesis of tetrahydropyridine from allenoates by phosphine catalysis

In the year 2017, Lu *et al* developed the first highly enantioselective formal (4 + 4) annulation using allenates. The unusual (4 + 4) annulation between α,β -unsaturated imines **1.8** and allenic ketones **1.9** (that are close in structure to allenates) went smoothly in the presence of amino-acid-containing phosphines, producing azocines **1.10** in the presence of benzofuran or an indole moiety in good yields and with excellent enantioselectivities (>98% *ee* in most cases). This work represents the first effective asymmetric phosphine catalysis leading to optically enriched eight-membered rings (azocines, Scheme 1.5).⁸



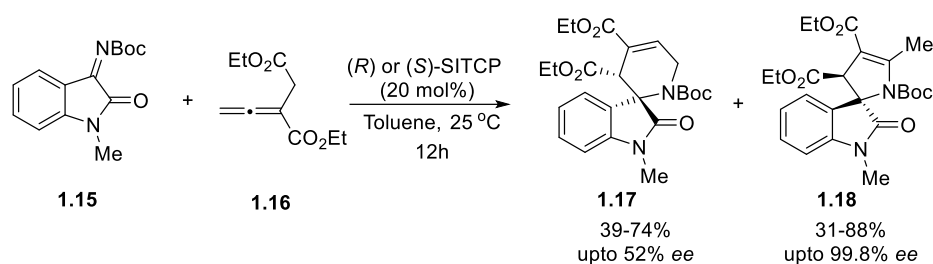
Scheme 1.5: Synthesis of azocines by chiral phosphine catalysis

Regiodivergent (3 + 2) annulations of aurone **1.11** with allenolate **1.12** using a chiral phosphine catalyst have also been developed by Lu *et al*.⁹ Thus α -selective cyclization products with good regio- and enantioselectivities could be obtained using a dipeptide phosphine catalyst. The γ -selective annulation products with outstanding enantioselectivities could be generated by using L-L dipeptide phosphines. A large variety of α -selective **1.13** or γ -selective **1.14** spirocyclic benzofuranones with either aryl or alkyl substitutions could be easily produced by simply adjusting the catalyst design (Scheme 1.6).



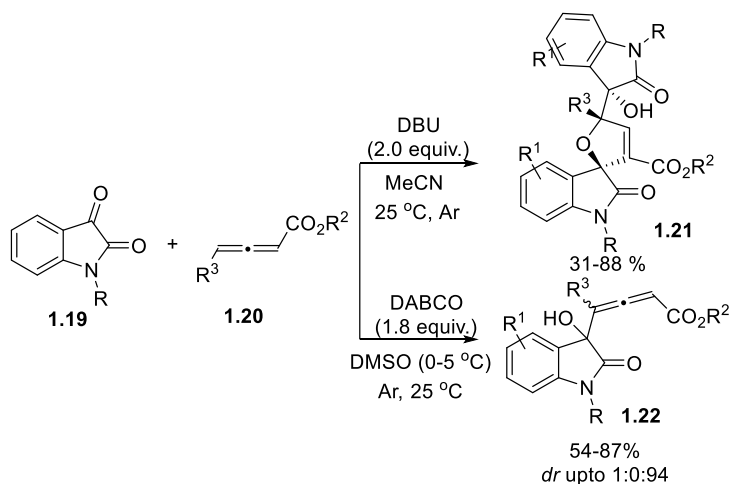
Scheme 1.6: Synthesis of benzofuranones from aurone and allenolate

Annulation reactions of allenyl esters **1.16** with a variety of electrophilic reagents by nucleophilic phosphine catalysis had been utilized by Kumar's group. A zwitterionic dipole was generated by the addition of chiral phosphine catalytically, specifically, (R)- or (S)-SITCP, to α -substituted ester allene **1.16**.¹⁰ This dipole could engage *N*-Boc-ketimines **1.15** produced from isatin in a (3 + 2) annulation reaction under optimal reaction conditions. As a result, pyrrolinyl spirooxindoles **1.17** and **1.18** were produced in good yields and with great enantioselectivity (Scheme 1.7).



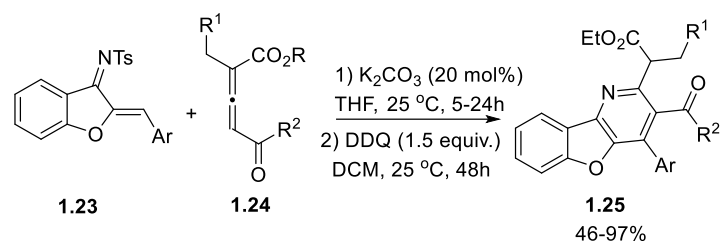
Scheme 1.7: Synthesis of spirooxindoles from *N*-Boc-ketimines and allenolate **1.16**

To produce spirofuran oxindoles **1.21** and γ -functionalized allenates **1.22**, base-assisted divergent reactivity of isatin **1.19** and allenolate **1.20** was studied by Somappa *et al.*¹¹ The spiro-framework was produced by the Morita-Baylis-Hillman (MBH) reaction mediated by DBU, subsequently the cascade annulation occurred through the stabilized β -ammonium enolate intermediate. By contrast, DABCO provided the γ -functionalized allenates. Under mild reaction conditions, the approach provides access to physiologically responsible functionalized oxindole scaffolds with good substrate scope (Scheme 1.8).



Scheme 1.8: Synthesis of spiro-furan oxindoles and γ -functionalized allenates from **1.20**

Using trisubstituted allenates **1.24** and aurone-derived 1-azadiene **1.23**, an effective 1,4-addition/intramolecular cyclization followed by aromatization procedure was established by Guo and coworkers that produced a variety of benzofuro[3,2-*b*]pyridines **1.25** in decent to good yields.¹² Without the aid of transition metal catalysts, the reaction was successfully carried out in an open atmosphere (Scheme 1.9).



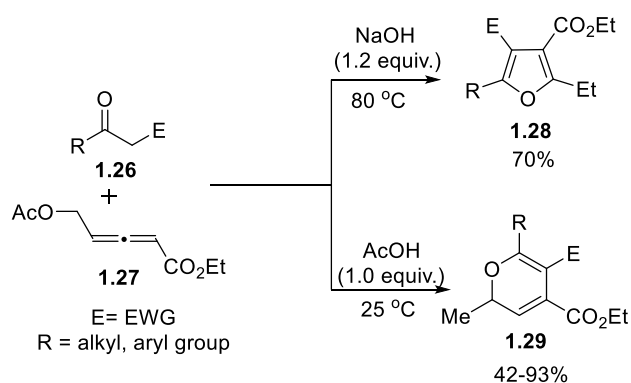
Scheme 1.9: Synthesis of benzofuro[3,2-*b*]pyridines from aurone-derived 1-azadiene and allenolate **1.24**

1.3 Reactions of acetoxy allenates

As depicted in Scheme 1.2 above, δ - and β' -acetoxy allenates have been utilized as synthons in a variety of annulations.^{13,14} These annulations are demonstrated as reliable approaches in organic synthesis leading to a wide array of carbo- and heterocycles. In this section, the chemistry of δ -acetoxy allenates and β' -acetoxy allenates is covered.

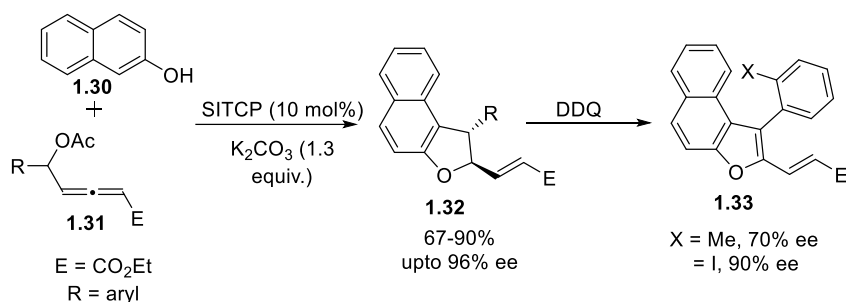
1.3.1 δ -Acetoxy allenolate chemistry

In 2012, Tong and co-workers reported the formation of tetrasubstituted furans **1.28** and dihydropyrans **1.29** from δ -acetoxy allenolate **1.27** and carbonyl compounds having active methylene group **1.26** which behave as a 1C-3O binucleophiles.¹⁵ This phosphine catalyzed (3 + 2) annulation requires basic conditions whereas, in (3 + 3) annulation, the reaction worked well under acidic conditions (Scheme 1.10).



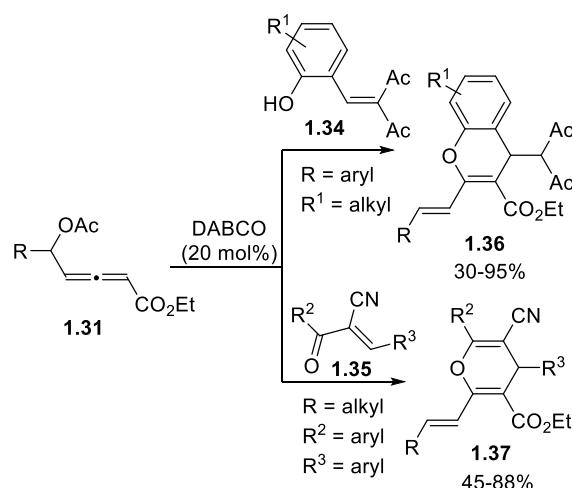
Scheme 1.10: Synthesis of furans and dihydropyrans from acetoxy allenolate **1.27**

Recently, Tong and coworkers reported phosphine catalyzed (3 + 2) annulation involving δ -acetoxy allenolate **1.31** and 2-naphthols **1.30** leading to the formation of 1,2-dihydronaphtho-[2,1-*b*]naphthols **1.32** which exhibit good anti-inflammatory activity.¹⁶ A chiral phosphine catalyst such as SITCP renders good enantioselectivity. The enantioenriched dihydrofuran on treatment with DDQ produced axially chiral furans **1.33** (Scheme 1.11).



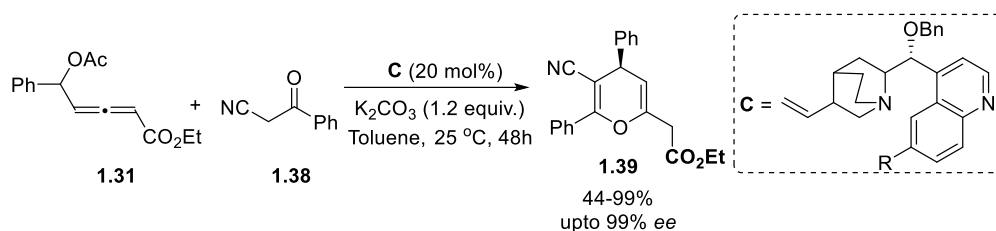
Scheme 1.11: Synthesis of chiral dihydrofurans from allenates

Annulation reactions using acetoxy allenates have also been conducted in the presence of nitrogen bases. Tong *et al.* reported a divergent (4 + 2) annulation using δ -acetoxy allenate **1.31** and substituted salicylaldehyde **1.34** or α -cyano carbonyl compound **1.35** in the presence of DABCO catalyst that led to 4*H*-chromenes **1.36** or 4*H*-pyrans **1.37**.¹⁷ The reaction is substrate dependent. When R = Ar, chromenes are formed, and when R = alkyl group, pyrans **1.37** are obtained (Scheme 1.12).



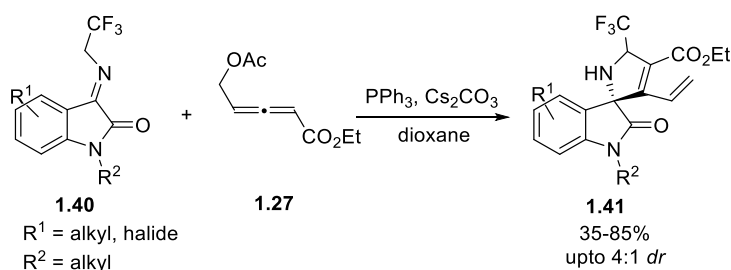
Scheme 1.12: Synthesis of 4*H*-chromenes and 4*H*-pyrans via acetoxy allenates

The formal (3 + 3) annulations of δ -acetoxy allenates **1.31** with 1C,3O-bisnucleophiles **1.38** have been reported by Tong *et al.*¹⁸ The catalyst used in this reaction is 6'-deoxy-6'-perfluorobenzamido-quinine, which enables quick formation of 4*H*-pyrans **1.39** with high enantioselectivity. Wide substrate scope and lenient reaction conditions are hallmarks of this reaction (Scheme 1.13).



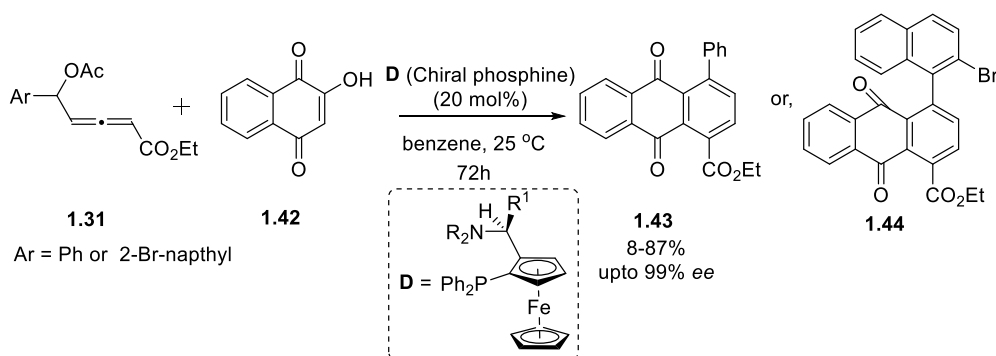
Scheme 1.13: Synthesis of 4*H*-pyran **1.39** from acetoxy allenolate **1.31**

In 2019, Min Shi disclosed the formation of spiro[indoline-3,2'-pyrrole] scaffolds **1.41** using *N*-2,2,2-trifluoroethyl isatin ketimines **1.40** and δ -acetoxy allenolate **1.27** via phosphine catalyzed (3 + 2) annulation (Scheme 1.14).¹⁹ Here, *N*-2,2,2-trifluoroethyl isatin ketimines play a vital role in the reaction as azomethine ylide precursors. The synthetic methodology has broad substrate scope and can be utilized to produce spiro-oxindoles containing a CF₃ moiety.



Scheme 1.14: Synthesis of spiro[indoline-3,2' pyrroles] via acetoxy allenolate **1.27**

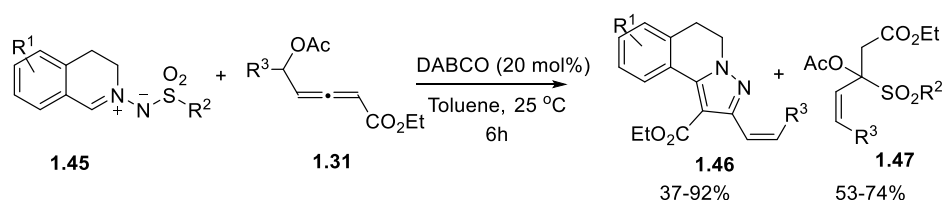
Tong *et al.* described chiral phosphine catalyzed atroposelective (4 + 2) annulation of 2-hydroxy quinone **1.42** with δ -acetoxy allenolate **1.31** with the introduction of a new benzene ring with simultaneous creation of axial chirality to produce aryl naphthaquinone atropisomers **1.43** and **1.44** in high enantioselectivities (Scheme 1.15).²⁰



Scheme 1.15: Synthesis of aryl naphtha-quinones via acetoxy allenolate

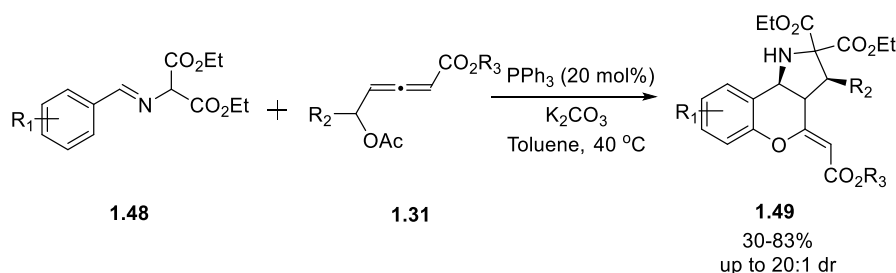
Min Shi and coworkers reported DABCO catalyzed (3 + 2) annulation of *C*, *N*-cyclic azomethine imine **1.45** with δ -acetoxy allenolate **1.31** to afford 5,6-dihydropyrazolo [5,1-

a]isoquinoline **1.46** and ethyl (*Z*)-3-acetoxy-3-tosylpent-4-enoate **1.47** (Scheme 1.16).²¹ This synthetic protocol provides an amenable route to synthesize dinitrogen-fused heterocycles **1.46** and ethyl (*Z*)-3-acetoxy-3-tosylpent-4-enoates **1.47** simultaneously.



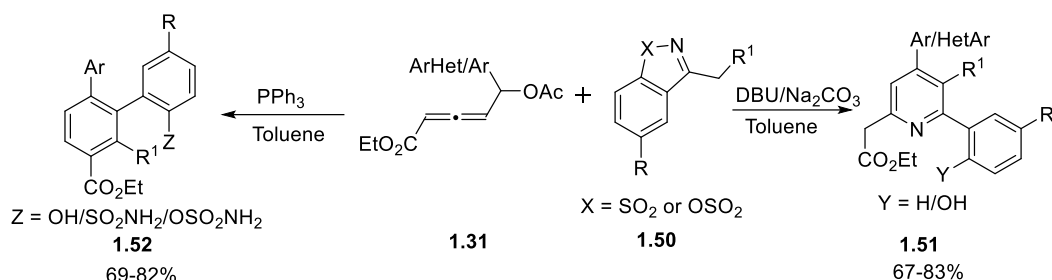
Scheme 1.16: Synthesis of dihydropyrazolo[5,1-*a*]isoquinolines and ethyl (*Z*)-3-acetoxy-3-tosylpent-4-enoates using acetoxy allenolate **1.31**

Zhou *et al.* reported phosphine-catalyzed tandem cyclization using aldimine ester **1.48** and δ -acetoxy allenolate **1.31** to produce chromeno[4.3-*b*]pyrrole **1.49** consisting of three consecutive stereocenters with good yield and high stereoselectivity (Scheme 1.17).²² The reaction takes place under lenient conditions with excellent efficiency and high chemo- and enantioselectivity.



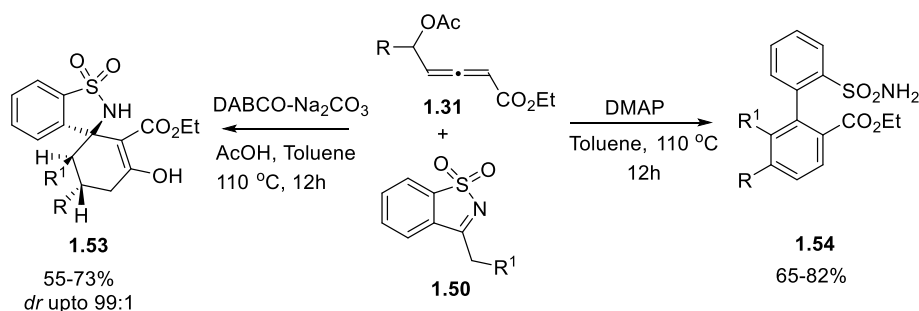
Scheme 1.17: Synthesis of chromeno [4.3-*b*]pyrroles from acetoxy allenolates **1.31**

During the last couple of years, our group has also made significant contributions towards allenolate chemistry. In 2020, our group described the formation of functionalized 2-pyridinyl acetate **1.51** and teraryl motifs **1.52** starting from *N*-sulfonyl ketimine **1.50** and δ -acetoxy allenolate **1.31** by simply changing the Lewis base. The (3 + 3) annulation employing DBU/ Na_2CO_3 combination involved sulfonyl elimination leading to 2-pyridinyl acetate **1.51** whereas PPh_3 catalyzed (4 + 2) annulation produced functionalized teraryls **1.52** with the retention of sulfamoyloxy group (Scheme 1.18).^{13c}



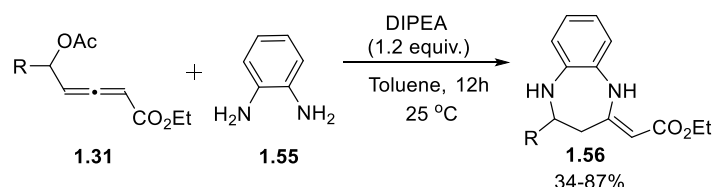
Scheme 1.18: Synthesis of 2-pyridinyl acetate and teraryl motifs from acetoxy allenates

In 2021, our research group reported a reaction involving δ -acetoxy allenates **1.31** and *N*-sulfonyl ketimines **1.50** by varying nitrogen-containing Lewis base such as DABCO or DMAP. In this scheme, for the first time, δ -acetoxy allenate acted as a 4-carbon synthon in the annulation. The DABCO-AcOH combination led to essentially single diastereomers of **1.53** via (4 + 2) spiro-annulation. On the other hand, in the case of DMAP-catalyzed benzannulation, unsymmetrical meta-teraryls **1.54** were formed (Scheme 1.19).^{13d}



Scheme 1.19: Synthesis of spiro-carbocyclic and *m*-teraryl scaffolds from acetoxy allenates

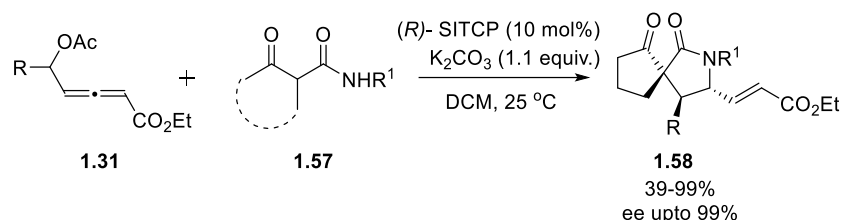
Tong's group reported diisopropylamine catalyzed (4 + 3) annulation using δ -acetoxy allenate **1.31** and *o*-diaminobenzene **1.55** leading to the formation of 1,5-benzodiazepines **1.56** (Scheme 1.20).²³ This method involves lenient reaction conditions, has wide variety of substrate scope, and utilizes easily available starting materials.



Scheme 1.20: Synthesis of 1,5-benzodiazepines from acetoxy allenates *o*-diaminobenzene

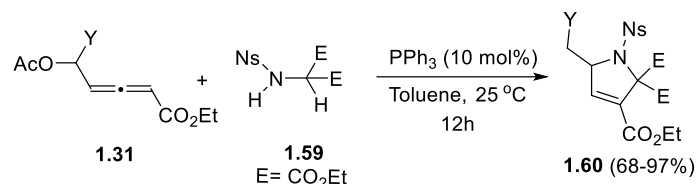
Zhou *et al.* disclosed the synthesis of chiral γ -lactams **1.58** through asymmetric (3 + 2) annulation of δ -acetoxy allenate **1.31** with β -carbonyl amides **1.57** (Scheme 1.21).²⁴ The chiral

phosphine-catalyzed annulation reactions of lactams are unusual. Here they chose R-SITCP as the chiral phosphine catalyst.



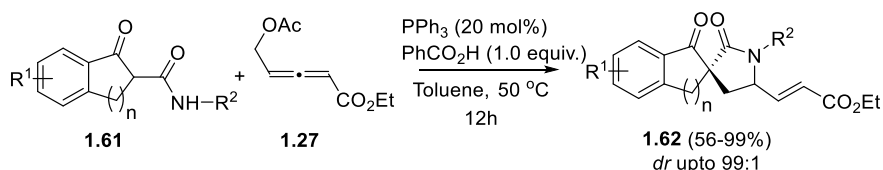
Scheme 1.21: Synthesis of chiral γ -lactams from acetoxy allenoates

In 2018, Tong and co-workers described the synthesis of 3-pyrrolines **1.60** from δ -acetoxy allenoates **1.31** and 2-sulfonamido malonates **1.59** via phosphine catalyzed (3 + 2) annulation. They also explored the asymmetric version by using I-SITCP as the catalyst and achieved up to 83% *ee* (Scheme 1.22).²⁵



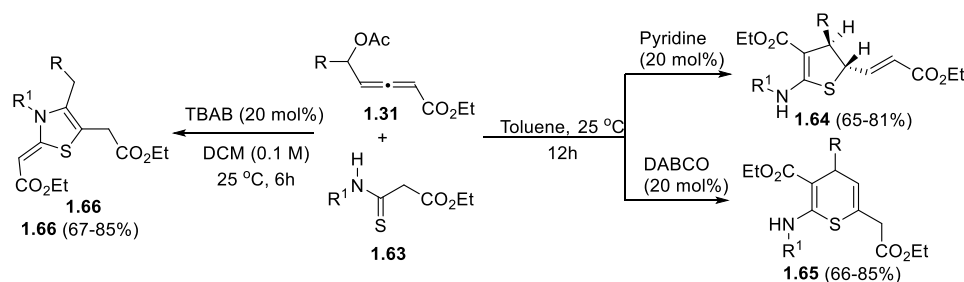
Scheme 1.22: Synthesis of 3-pyrrolines from acetoxy allenoates

Min Shi and coworkers reported the synthesis of five-membered heterocycles **1.61** that have a quaternary stereocenter *via* (3 + 2) annulation of δ -acetoxy allenoate **1.27** with α -substituted secondary β -ketoamides **1.60** under phosphine catalysis.²⁶ Here, β -ketoamides **1.60** acted as bis-nucleophiles (Scheme 1.23).



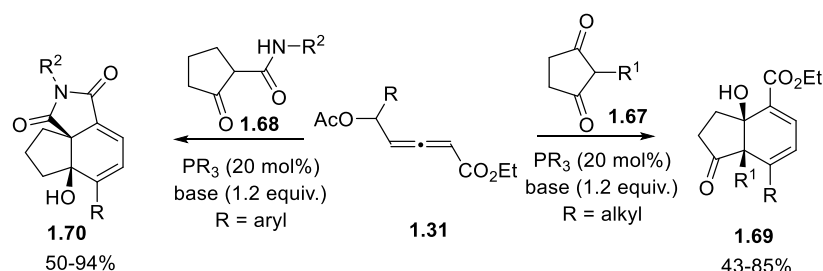
Scheme 1.23: Synthesis of spiro-heterocycles from acetoxy allenoate **1.27**

Very recently our group has developed an innovative protocol for the synthesis of dihydrothiophene (**1.63**), thiopyran (**1.64**), and thiazole (**1.65**) frameworks starting from δ -acetoxy allenoate **1.31** and thioamides **1.62** by the modulation of nitrogen-bases.²⁷ Use of pyridine as the base afforded dihydrothiophenes **1.63**, whereas by using DABCO, thiopyrans **1.64** were obtained. In contrast to these, tetrabutyl ammonium bromide led to the formation of thiazoles **1.65** (Scheme 1.24).



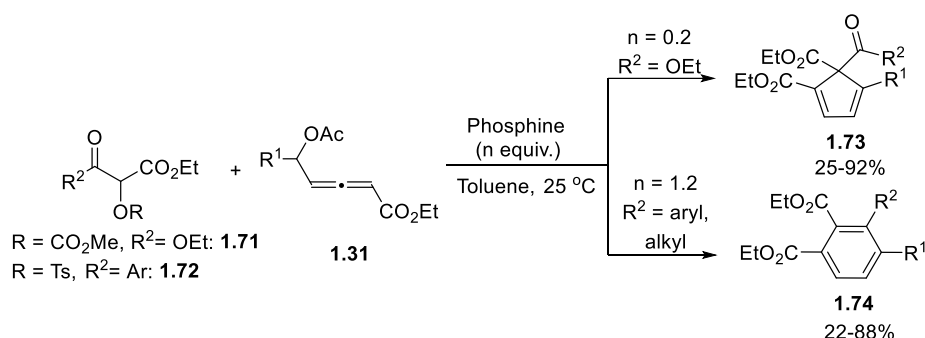
Scheme 1.24: Synthesis of dihydrothiophene, thiopyran, and thiazole frameworks by starting with acetoxy allenates **1.31**

By combining acetoxy allenates **1.31** with ketones in phosphine-catalyzed substrate-dependent (4 + 2) annulations, Tong and coworkers found an elegant way to access 1,3-cyclohexadienes **1.69** and **1.70**, which are structurally complicated but rich in functional groups (Scheme 1.25).²⁸ Allenates containing alkyl group at the δ -carbon show δ -C electrophilicity and α -C nucleophilicity during the reaction with cyclic 1,3-diketones **1.67** whereas aryl-containing allenates showed the opposite reactivity when encountered with cyclic β -carbonyl amides **1.68**. The catalytic cycle, a novelty in the realm of phosphine-catalyzed annulations, is based on 1,3-diene isomerization.



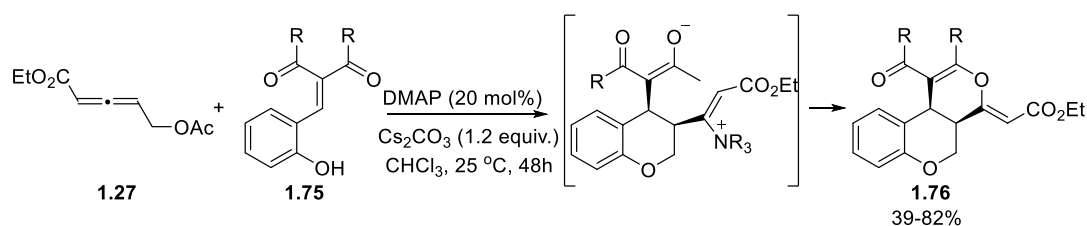
Scheme 1.25: Synthesis of fused 1,3-cyclohexadienes from acetoxy allenates

In the year 2019, Tong *et al.* reported that acetoxy allenate can function as a 1,4-disubstituted diene synthon. Thus in the presence of a catalytic quantity of phosphine, 2-[(methoxycarbonyl)oxy]malonate **1.71** can engage as a nucleophilic partner in (4 + 1) annulation with allenates to produce cyclopentadienes **1.73** in good yields. On the other hand, with the aid of stoichiometric phosphine and base, (4 + 2) annulation of allenates with 2-(tosyloxy)-3-ketoesters **1.72** resulting in tetrasubstituted benzene products **1.74** was observed (Scheme 1.26).^{13b}



Scheme 1.26: Synthesis of multi-substituted cyclopentadienes and aryls from acetoxy allenates

An easy way to create polycyclic frameworks **1.76** has been described by Tong's group *via* addition followed by (4 + 2) annulation and domino reaction of δ -acetoxy allenate **1.27** with either salicylaldehyde-derived or pyrrolealdehyde-derived oxadiene **1.75** *via* DMAP catalysis.²⁹ The addition-elimination process between an allenate and a catalyst is proposed to entail the cationic 3-ammonium-2,4-dienoate intermediate (Scheme 1.27).

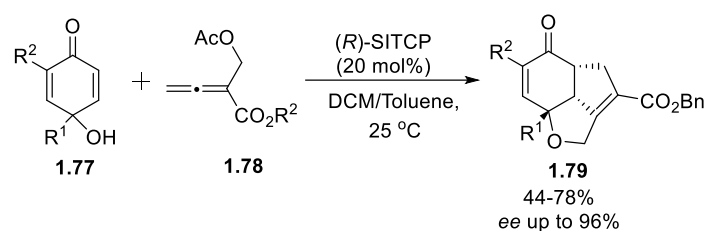


Scheme 1.27: Synthesis of heteropolycyclic frameworks from acetoxy allenates

To the best of our knowledge, (3 + 3) annulation involving β , γ , and δ -carbons of δ -acetoxy allenates as well as *functional group migration* and annulation involving C-C bond cleavage using phosphine has not been reported till now.

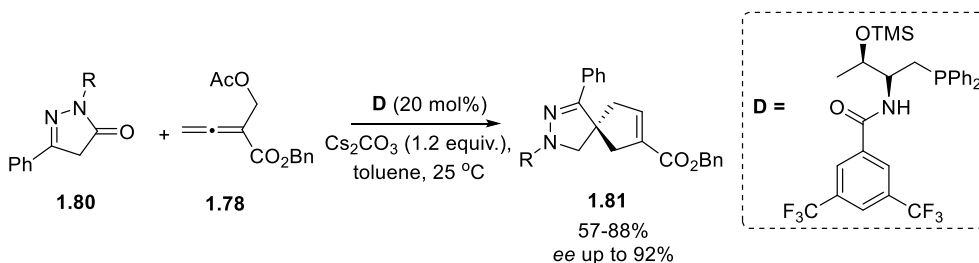
1.3.2 β' -Acetoxy allenate chemistry

Min Shi and co-workers reported the synthesis of highly functionalized multiple-ring fused hexahydroindeno derivatives **1.79** consisting of three consecutive stereogenic centers in a single step starting from *p*-quinols **1.77** and β' -acetoxy allenates **1.78** (Scheme 1.28).³⁰ This phosphine-catalyzed cyclization has some advantages such as the participation of *p*-quinol's three active centers in the reaction, wide substrate scope, mild reaction conditions, asymmetric version, and good yields.



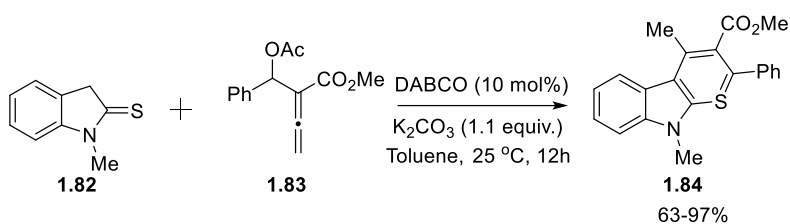
Scheme 1.28: Synthesis of hexahydroindeno derivatives

In the year 2014, Lu *et al.* described the asymmetric synthesis of spiropyrazolone derivatives **1.81** *via* chiral phosphine catalyzed (4 + 1) spiroannulation. They chose allenolate-derived MBH acetate **1.78** and pyrazolones **1.80** as the precursors where MBH acetate **1.78** played a key role as C₁ synthon (Scheme 1.29).³¹



Scheme 1.29: Synthesis of spiropyrazolones from acetoxy allenates

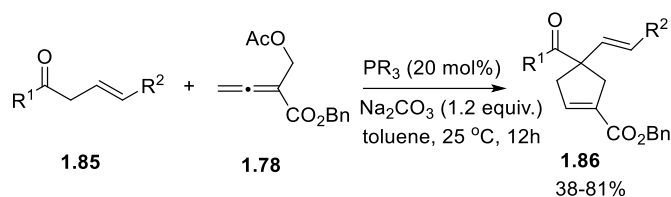
Easy access to thiopyrano[2,3-*b*]indole **1.84** under benign reaction conditions was achieved by Tong and coworkers *via* formal (3 + 3) annulation of β' -acetoxy allenolate **1.83** with indoline-2-thione **1.82** catalyzed by DABCO (Scheme 1.30).³² Here, indoline-2-thione **1.82** served as 1C-3S bis-nucleophile.



Scheme 1.30: Synthesis of thiopyrano[2,3-*b*]indole

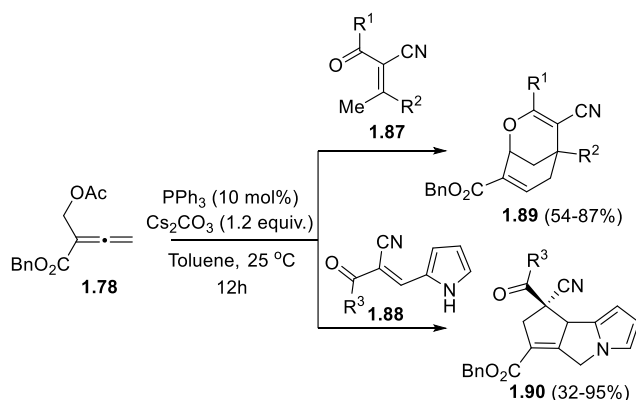
Although β,γ -unsaturated carbonyl compounds **1.85** have been extensively employed as γ -C or α -C nucleophiles, the field is still fertile with respect to their potential α -C, α -C-bisnucleophilic reactivity. In one such study, Tong and co-workers described phosphine-catalyzed (4 + 1) annulation of β' -acetoxy allenolate **1.78** with β,γ -unsaturated carbonyl compounds **1.85** leading to spirocyclopentenones **1.86**.³³ Here, β' -acetoxy allenolate **1.78** behaved

as the 1,4-biselectrophilic species and the β,γ -unsaturated carbonyl compounds **1.85** behaved as the α -C, α -C-bisnucleophiles leading to the formation of cyclopentenones **1.86** (Scheme 1.31).



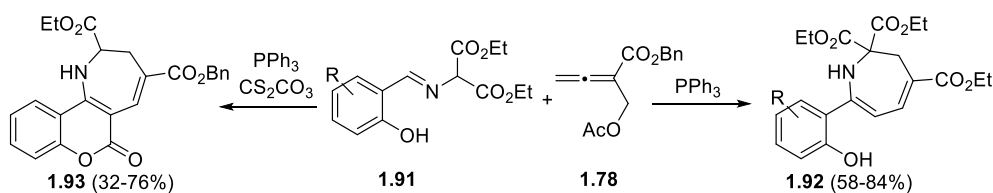
Scheme 1.31: Synthesis of spirocyclopentenones from β' -acetoxy allenolate **1.78**

Tong's group reported two types of addition/cycloaddition domino reactions of β' -acetoxy allenolate. When β' -acetoxy allenolate **1.78** and 2-acyl-3-methyl-acrylonitriles **1.87** are combined, the result is 2-oxabicyclo[3.3.1]nonanes **1.89**, which provides the domino reaction sequence of β' -addition/(4 + 4) cycloaddition.^{14a} β' -C functions as an electrophilic center in this sequence, and its β' -C and γ -C act as 1,4-dipole. When the other reaction partner is changed to 2-acyl-3-(2-pyrrole)-acrylonitriles **1.88**, allenolate displays dual electrophilic reactivity of γ -C and 1,3-dipolar chemical behavior of β -C and β' -C in a γ -addition/(3 + 2) cycloaddition domino reaction leading to cyclopenta[*a*]pyrrolizines **1.90**. Additionally, each of these two asymmetric forms was obtained in up to 93% *ee* (Scheme 1.32).



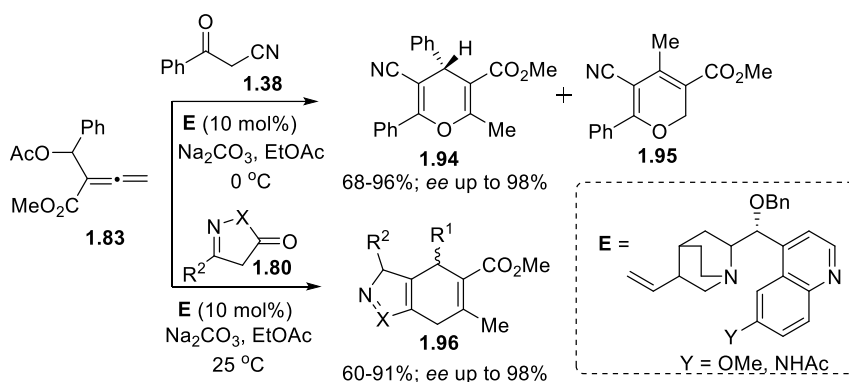
Scheme 1.32: Synthesis of 2-oxabicyclo[3.3.1]nonanes and cyclopenta[*a*]pyrrolizines from β' -acetoxy allenolate **1.78**

Zhou and co-workers described the synthesis of azepines from esters containing imine group **1.91** and β' -acetoxy allenolate **1.78**. Thus under phosphine catalysis, 1,3-dihydro-2*H*-azepine-2,2,4-tricarboxylates **1.92** were synthesized in decent yields whereas a variety of 2,3-dihydrchromeno[4,3-*b*]azepine-6(1*H*)-ones **1.93** were selectively produced when the reaction was carried out in presence of PPh_3 and Cs_2CO_3 (Scheme 1.33).^{14d}



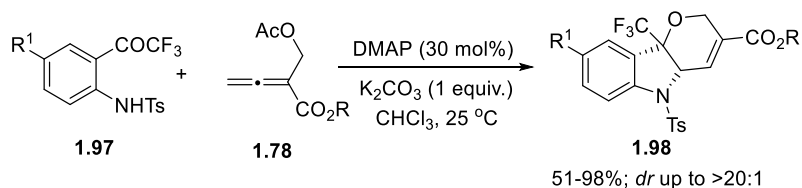
Scheme 1.33: Synthesis of azepines and chromenoazepine-6-ones from β' -acetoxy allenolate **1.78**

Using the catalyst 6'-deoxy-6'-[(L)-*N,N*-(2,2'-oxidiethyl)-valine amido]quinine, the asymmetric version of (3 + 3) annulations of β' -acetoxy allenolates **1.83** with 3-oxo-nitriles **1.38** and pyrazolones **1.80** have been carried out by Tong's group.³⁴ Lewis base (quinuclidine N), H-bond donor (amide NH), and Brønsted base (morpholine N) collectively play critical roles in the chemo- and enantioselectivity, enabling the synthesis of 4*H*-pyrans **1.94**/ **1.95** and 4*H*-pyrano[2,3-*c*]pyrazoles **1.96** in excellent yields and good enantioselectivity (Scheme 1.34).



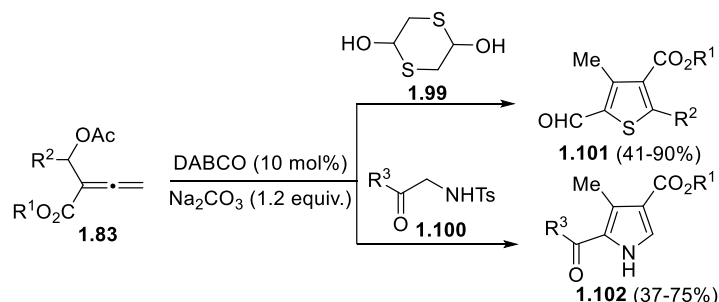
Scheme 1.34: Synthesis of 4*H*-pyrans and 4*H*-pyrano-pyrazoles from β' -acetoxy allenolate

Huang's group observed that DMAP facilitates a (4 + 1)/ (3 + 3) domino sequential annulation reaction between *o*-aminotrifluoroacetophenones **1.97** and β' -acetoxy allenolates **1.78**. Under benign conditions, a variety of tetrahydropyrano[3,2-*b*]indoles **1.98** containing the CF₃ moiety were produced in excellent yields (98%) as single diastereomers (Scheme 1.35).^{14e} As a result of the reaction, one C-N bond, one C-C bond, and one C-O bond were consecutively formed.



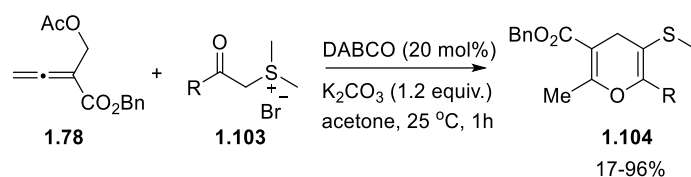
Scheme 1.35: Synthesis of 4*H*-pyran and tetrahydropyranoindoles from acetoxy allenolates

In the year 2016, Tong and coworkers described a cascade (3 + 2) annulation and aromatization sequence between 1,2-bisnucleophiles and β' -acetoxy allenoates **1.83**. The reaction produces fully substituted thiophene-2-carbaldehydes **1.101** when 1,4-dithane-2,5-diol **1.99** is utilized as the bisnucleophile partner. This reaction may went through the amine-catalyzed (3 + 2) annulation followed by oxidative aromatization.³⁵ The reaction is also amenable to 2-tosylamino-carbonyl bisnucleophiles **1.100** in which a tosyl group is 1,2-eliminated, followed by isomerization to produce a 1*H*-pyrroles **1.102** (Scheme 1.36).



Scheme 1.36: Synthesis of thiophene-2-carbaldehydes and 1*H*-pyrroles from β' -acetoxy allenoates

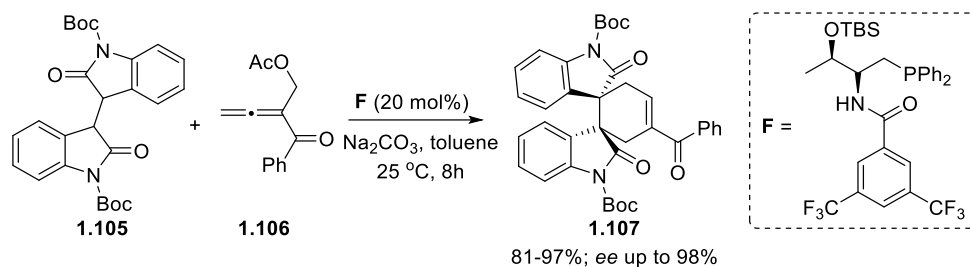
To produce 4*H*-pyrans **1.99** with a vinyl sulfide group, a DABCO-catalyzed (3 + 3) annulation between 2-(acetoxymethyl)buta-2,3-dienoate **1.78** and sulfur ylides **1.103** has been reported by Tong *et al.* Here, sulfur ylide serves two purposes: (i) strong nucleophilicity to initiate the addition to an electrophilic carbon center, and (ii) strong leaving power to guarantee the production of a three-membered product. Here, they obtained S-containing 4*H*-pyrans **1.104** from allenoate and sulfur ylide **1.103**, which is produced *in situ* by the reaction of a base and sulfonium salt (Scheme 1.37).³⁶



Scheme 1.37: Synthesis of 4*H*-pyrans from β' -acetoxy allenoate **1.78**

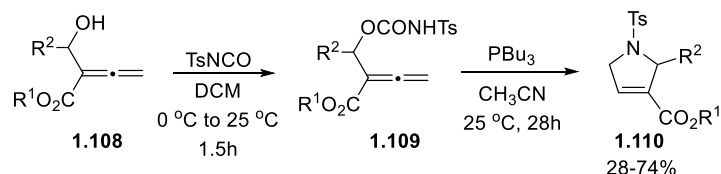
Very recently, Lu and co-workers developed a phosphine-mediated reaction by introducing a specific class of allenic ketone **1.106** as a dielectrophilic C4 synthon. Because of the high electrophilicity of the intermediates produced by phosphine activation, it was possible to easily produce spirocyclic bisindolines **1.107** with two adjacent quaternary stereogenic centers by using 3,3'-bisoxindoles **1.105** as two-carbon reaction partners in a highly

enantioselective (4 + 2) annulation (Scheme 1.38).³⁷ (-)-Folicanthine was concisely synthesized using modification of the (4 + 2) annulation product.



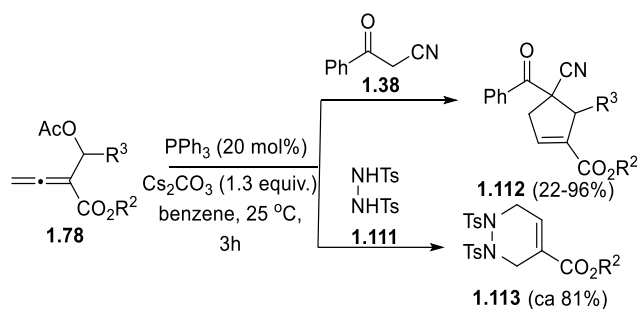
Scheme 1.38: Synthesis of spirocyclic bisindoline using acetoxy allenolate **1.106**

Kwon's group discovered a phosphine-catalyzed (4 + 1) annulative rearrangement that transformed allenylic carbamates **1.109** (obtained from allenylic hydroxide **1.108**) into 3-pyrrolines **1.110** via phosphonium diene intermediate. They used this technique to create a variety of substituted-3-pyrrolines **1.110** (Scheme 1.39).³⁸ A mechanistic analysis using mono-nucleophiles and allenylic acetates revealed that the (4 + 1) cyclization was catalyzed by phosphine.



Scheme 1.39: Synthesis of 3-pyrrolines *via* acetoxy allenolate **1.109**

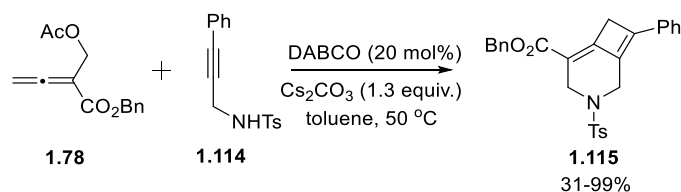
Tong and coworkers reported PPh₃-catalyzed (4 + 1) and (4 + 2) annulations of 2,3-butadienoates **1.78** that effectively gave easy access to cyclopentenones **1.112** and tetrahydropyridazines **1.113**, respectively.³⁹ The inversion of the 2,3-butadienoate's typical phosphine-catalyzed reaction modes depends critically on the presence of an acetate group at the β'-position (Scheme 1.40).



Scheme 1.40: Synthesis of cyclopentenones and tetrahydropyridazines *via* 2,3-butadienoates

1.78

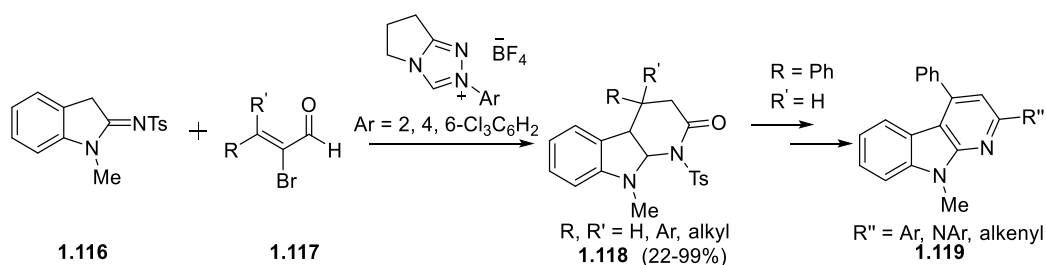
Tong and coworkers developed an effective S_N2 /cycloaddition cascade reaction of 2-(acetoxymethyl)buta-2,3-dienoate **1.78** with different functionalized tosylamides **1.114** in the presence of a catalytic amount of DABCO, which allowed a simple production of azaheterocycles **1.115** (Scheme 1.41).⁴⁰ The reaction required mild reaction conditions and readily accessible ingredients. More crucially, the formation of three new σ -bonds, up to three rings, and quaternary stereocenters during this cascade reaction enhances the molecular complexity.



Scheme 1.41: Synthesis of azaheterocycle **1.115** via acetoxy allenoate **1.78**

1.4 Sulfonamido indoles

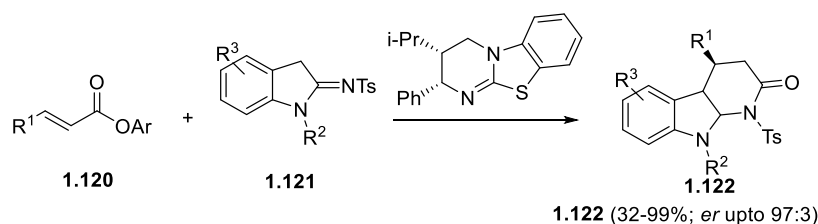
2-Sulfonamido indole, an important annulation partner, can act as a 1C-3N precursor and a versatile building block for the construction of six/ seven-membered aza-heterocyclic cores. Due to the presence of $=N\text{-Ts}$ group, the two hydrogen atoms on the adjacent carbon (C3) become highly acidic. In the presence of a base, after deprotonation, it can act as a good nucleophile to attack at the electrophilic center, thereby leading to a wide variety of carbo- and heterocycles.⁴¹ Ye and coworkers described the NHC-catalyzed (3 + 3) annulation of 2-sulfonamidoindole **1.116** with bromoenals **1.117** to produce dihydropyridinone-fused indoles **1.118**, which could then be converted to carbolines with various 2-substituents **1.119** through a process of dehydrogenation, tosylation, followed by C-C or C-N coupling reaction (Scheme 1.42).^{41b}



Scheme 1.42: Synthesis of carbolines through NHC catalysis

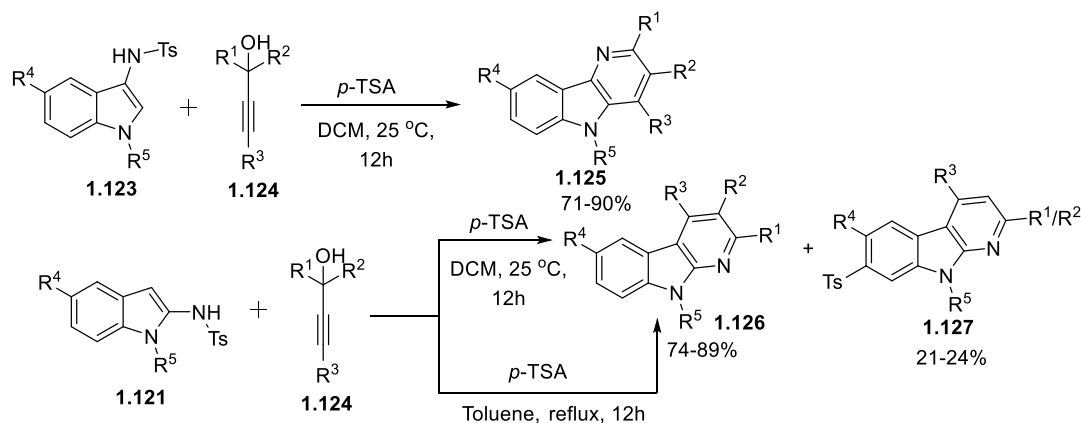
Recently, tetrahydro-carbolinones **1.122** were synthesized by Smith and coworkers using an isothiourea catalyzed enantioselective annulation process by combining indolin-2-imines **1.121** with several α,β -unsaturated *p*-nitrophenyl esters **1.120**.^{41f} This method enabled

the enantioselective formation of a variety of C(4)-substituted tetrahydro-carbolinones in decent to outstanding yield (32-99 %) with excellent enantioselectivity (up to 99:1 *er*) by employing 5 mol% of the isothioureia hyper-BTM as the Lewis base catalyst (Scheme 1.43).



Scheme 1.43: Synthesis of tetrahydrocarboline from indolin-2-imines **1.121**

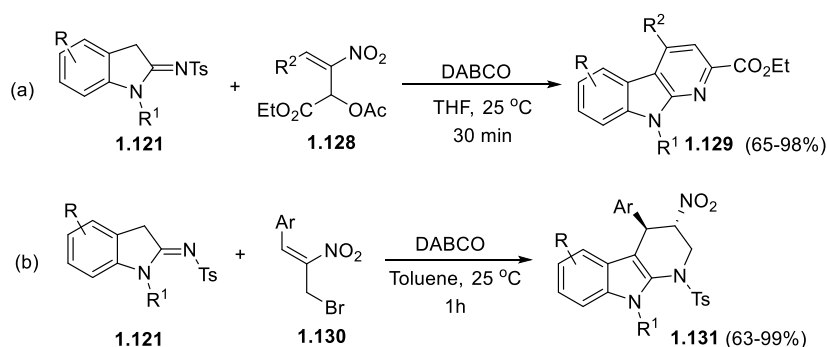
Recently, our group also worked on iminoindolines to furnish α - and δ -carbolines. Thus, propargylic alcohols **1.124** and sulfonamido-indoles/indolines **1.123** or **1.121** react in the presence of a Brønsted acid to produce highly substituted α - or δ -carbolines (**1.126** or **1.125**) in good yields.^{41c} Friedel-Crafts alkylation, [1,5]-hydrogen shift, electrocyclization, elimination, [1,2]-aryl migration, followed by aromatization are the steps involved in this cascade reaction sequence. There has also been evidence of an unanticipated regioselective tosyl group migration from the indole 2- to 6-position and arene elimination resulting in α -carbolines **1.127** (Scheme 1.44).



Scheme 1.44: Synthesis of α and δ -carbolines from iminoindolines and propargylic alcohols

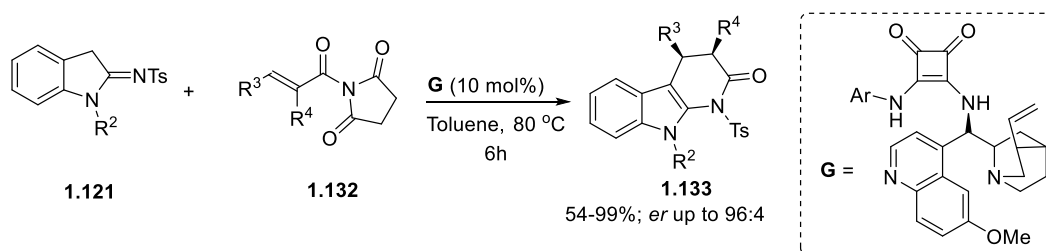
Very recently, Namboothiri and coworkers reported the formation of substituted carbolines **1.124** from secondary Morita-Baylis-Hillman (MBH) acetates of nitroalkenes **1.123** as a metal-free process. Thus, MBH acetates react in a cascade fashion with tosyliminoindolines **1.115** regioselectively to produce a variety of carbolines with a wide range of substrates.⁴² The reaction happens under benign conditions and forms products in high yields within a short time (Scheme 1.45a). The same group has also prepared tetrahydrocarbolines

1.131 by varying the electrophilic entity in the reaction medium. The one-pot synthesis of highly substituted tetrahydro- α -carbolines **1.131** from Morita-Baylis-Hillman (MBH) bromides of nitroalkenes **1.130** and 2-sulfonamidoindole **1.121** has been described using a metal-free technique.⁴³ A formal (3 + 3) cascade reaction occurred with high regio- and diastereoselectivity to produce a variety of tetrahydro- α -carbolines with a broad substrate scope (Scheme 1.45b).



Scheme 1.45: Synthesis of α -carbolines and tetrahydro- α -carbolines from MBH acetates

Li and co-workers made decent contribution to the asymmetric synthesis of α -carbolinones **1.133** by employing noncovalent bonding catalysis. Thus an asymmetric (3 + 3) cyclization of 2-sulfonamidoindole **1.115** and α,β -unsaturated *N*-acylated succinimides **1.132** was invented.^{41e} Tetrahydro- α -carbolinones **1.133** with various substituents were produced using this organocatalytic approach with up to 99% yield and up to 96:4 *er* (Scheme 1.46).



Scheme 1.46: Synthesis of tetrahydro- α -carbolinones from indolin-2-imines

1.5 Carbolines: Importance and synthetic approaches

The prevalence of indole and its fused heterocycle derivatives (e. g., carbolines) in natural products renders this class of compounds fascinating in synthetic chemistry.⁴⁴ The analogs of β - and γ -carbolines are frequently found in nature, and synthetic methods to produce them have received a great deal of attention.⁴⁵ Although α -carbolines are less common than β -carbolines, many compounds such as the neuronal cell-protective agent mescengricin and the anticancer agents grossularine-1 and grossularine-2 are based on the α -carboline moiety.

Additionally, there are reports on the potential use of α -carboline in organic semiconductors, organic thin-film transistors, and phosphorescent organic light emitting devices utilize α -carboline based thiophene derivatives.⁴⁶⁻⁴⁷ Hence several synthetic strategies have been developed for their synthesis. A summary of earlier synthetic methods for α -carboline (cf. Scheme 1.47) was published in 2015 by Wadsworth *et al.*⁴⁶

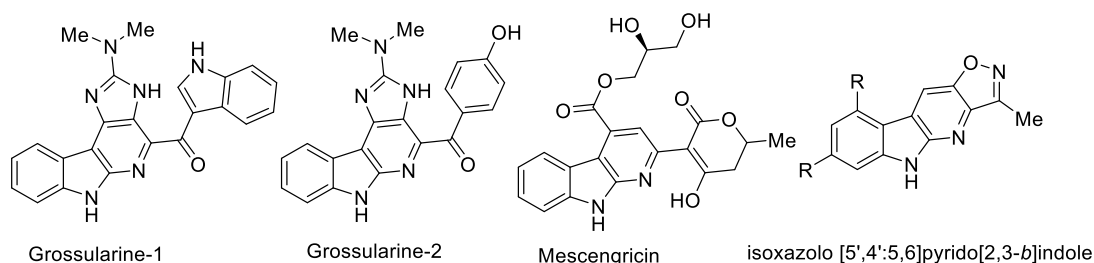
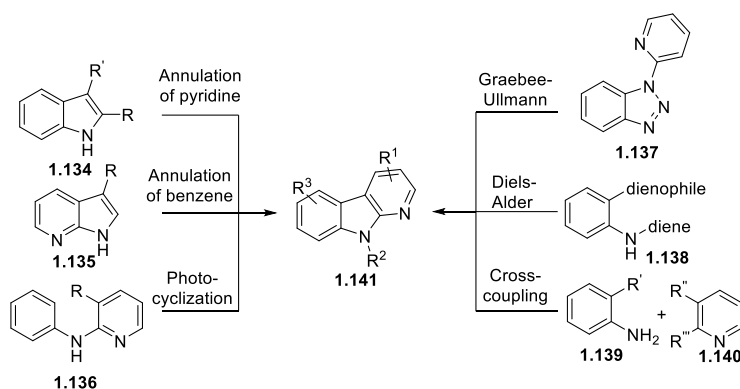
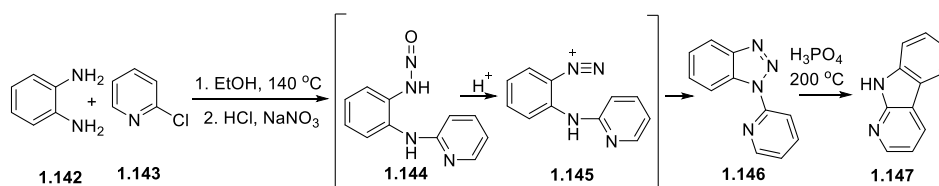


Figure 1: Examples of naturally occurring or biologically active compounds with α -carboline skeleton



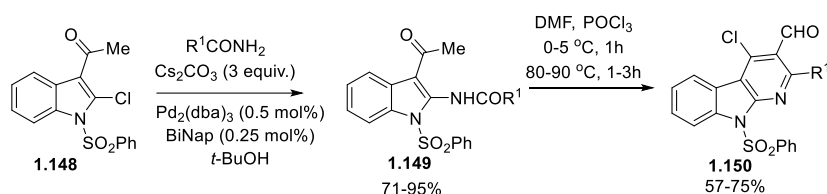
Scheme 1.47: Selected synthetic routes to α -carboline⁴⁶

The first known synthesis of α -carboline was documented in 1924 by Robinson *et al.*⁴⁸ The Graebbe-Ullmann carbazole synthesis was modified for the synthesis of α -carboline **1.147**. Thus 2-chloropyridine **1.143** and *o*-phenylenediamine **1.142** upon heating delivered the intermediate **1.144**. This underwent a further reaction with nitrous acid to produce the diazonium salt **1.145**, which spontaneously transformed into the intermediate 1,2,3-triazole **1.146**. The triazole **1.146** upon heating in the presence of phosphoric acid produced carboline **1.147** (Scheme 1.48).



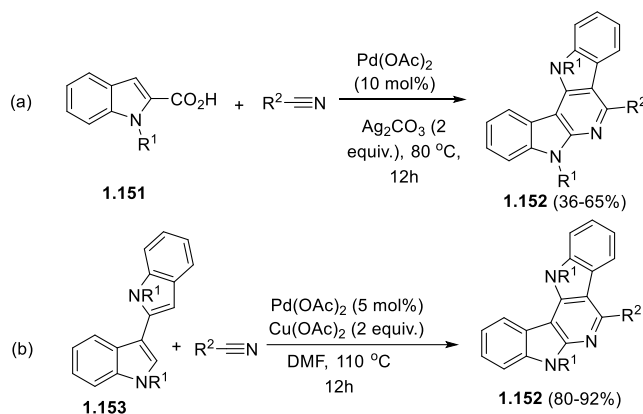
Scheme 1.48: Synthesis of α -carboline from 2-chloropyridine and *o*-phenylenediamine

Nagarajan and coworkers reported a different class of α -carbolines **1.150** via $\text{Pd}_2(\text{dba})_3/\text{BINAP}$ catalyzed amidation of 3-acetyl-2-chloroindole **1.148** leading to 1-(2-chloro-1-(phenylsulfonyl)-1*H*-indol-3-yl)ethenone **1.149**. Subsequently, **1.149** underwent Vilsmeier-Haack formylation to afford α -carboline **1.150** (Scheme 1.49).⁴⁹



Scheme 1.49: Synthesis of α -carboline from 3-acetyl-2-chloroindoles

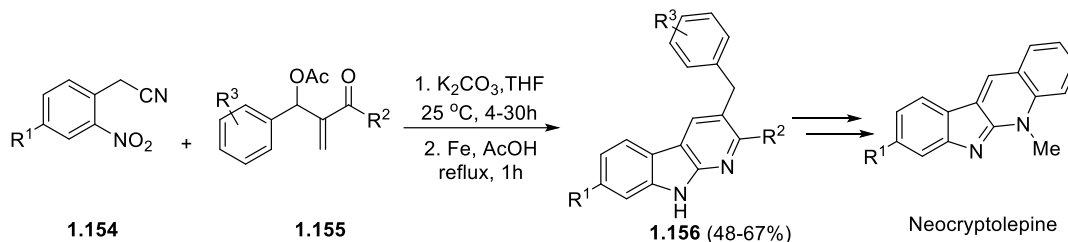
Our group reported the palladium catalyzed synthesis of triazaindenofluorenes (indolocarbolines) **1.152** as the nitrile insertion products from indole carboxylic acids **1.151** and nitriles in presence of Ag_2CO_3 (Scheme 1.50a).⁵⁰ Very recently, our group also discovered a new method for synthesizing indole fused α -carbolines **1.152** from 2,3'-biindoles **1.153** and aromatic nitriles. This method entails the formation of C-C and C-N bonds in a single step, as well as the double C-H bond activation and ring annulation of 2,3'-biindoles with nitriles (Scheme 1.50b).⁵¹



Scheme 1.50: Synthesis of indolocarbolines from indole carboxylic acid or bi-indoles

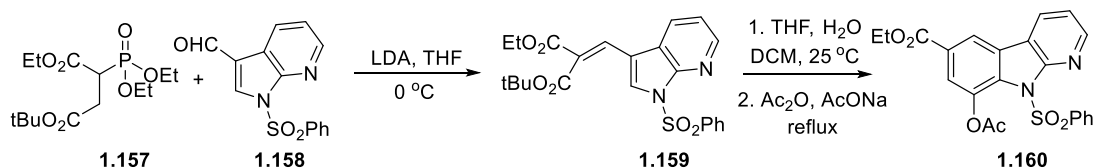
Basavaiah and Reddy described a one-pot synthesis of the α -carboline frameworks **1.156** during the synthesis of the naturally occurring alkaloid neocryptolepine, which is produced from α -carbolines. In this process, Baylis-Hillman acetates **1.155** were converted into pyrido[2,3-*b*]indole structures **1.156**. At the initial stage, under basic conditions, 2-nitroarylacetonitriles **1.154** were $\text{S}_{\text{N}}2'$ mono alkylated with Baylis-Hillman acetates **1.155**. The

desired α -carboline **1.156** were produced by reducing the nitro group with iron in acetic acid that was refluxing and initiating two further cyclization events (Scheme 1.51).⁵²



Scheme 1.51: Synthesis of α -carboline from Baylis-Hillman acetates

Synthesis of α -carboline **1.160** using the annulation of the benzene ring onto a derivative of 7-azaindole **1.158** to complete the tricyclic core has been documented by Joseph and coworkers.⁵³ Horner-Wadsworth-Emmons (HWE) reaction between diester phosphonate **1.157** and 1-(benzenesulfonyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carboxaldehyde **1.158** produced the ring closure precursor **1.159**. Hydrolysis of *tert*-butyl ester **1.159** produced the corresponding acid which underwent intramolecular cyclization to produce substituted α -carboline **1.160** (Scheme 1.52).



Scheme 1.52: Synthesis of α -carboline **1.160** from 7-azaindole **1.159**

OBJECTIVES OF THE WORK-PART A

The objective of the work was to investigate the annulation reactions of acetoxy allenoates with 2-sulfonamido indole/ benzofuran/pyrazoles in the presence of nitrogen-based as well as phosphorus-based Lewis bases. More specifically, it was intended to

- (i) Explore the complex reactivity of δ - and β' -acetoxy allenoates with 2-sulfonamido indoles *via* phosphine catalysis that could lead to the formation of dihydro- α -carbolines, α -carbolines, or spirocyclopentene motifs.
- (ii) Investigate Lewis-base (nitrogen as well as phosphorus) dependent (3 + 3) annulations of acetoxy allenoates with 2-sulfnamido indole for the possible generation of α -carboline scaffolds.
- (iii) Study the reactivity of δ -acetoxy allenoates with keto-substrates possessing an adjacent $-\text{CH}_2$ group (e.g., *tert*-2-oxoindolinone carboxylate, benzofuranone and pyrazolone) to synthesize fused pyrans/ dihydropyrans.

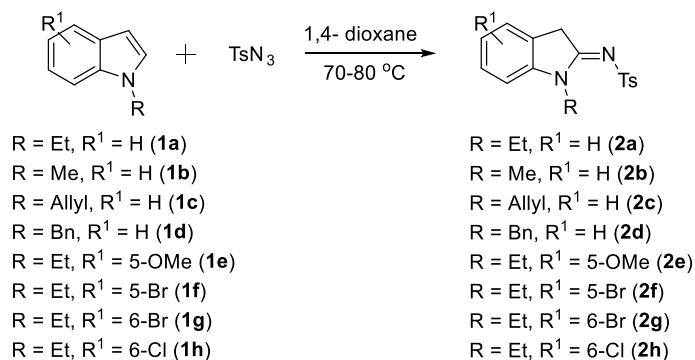
RESULTS AND DISCUSSION

This chapter describes the results on various transformations of acetoxy allenates with 2-sulfonamido indoles leading to carboline scaffolds as well as indole-fused cyclopentene motifs. It also deals with the reactivity of Boc-protected oxindole benzofuranone and pyrazolone with δ -acetoxy allenates. All the final products are well-characterized by using IR, NMR, LCMS/CHN, or HRMS and Mp (for solids); the regio- or stereo-chemistry of the compounds are generally based upon X-ray crystallographic studies

2.1 Synthesis of precursors

2.1.1 2-Sulfonamidoindoles 2a-h

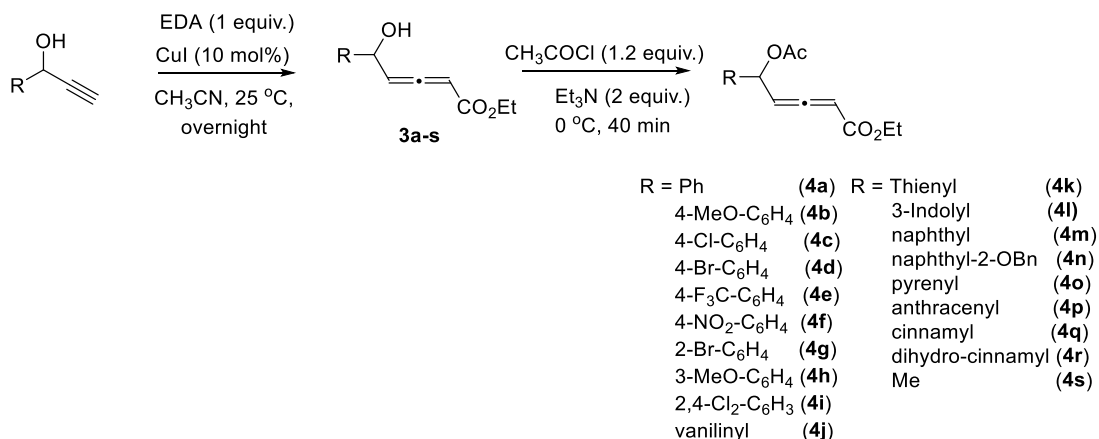
2-Sulfonamidoindoles **2a-h** were prepared from *N*-alkylated indole **1a-h** and tosyl azide following a literature procedure.^{41c} *N*-Boc protected sulfonamido indole **2i** was prepared using Chang's method.⁵⁴ In the presence of tosyl azide, indole substrates **1a-h** undergo (3 + 2) cycloaddition followed by elimination of N₂ leading to *N*-substituted 2-sulfonamido indoles **2a-h** (Scheme 1).



Scheme 1: Synthesis of 2-sulfonamido indoles **2a-h**

2.1.2 δ -Acetoxy allenoates **4a-s**

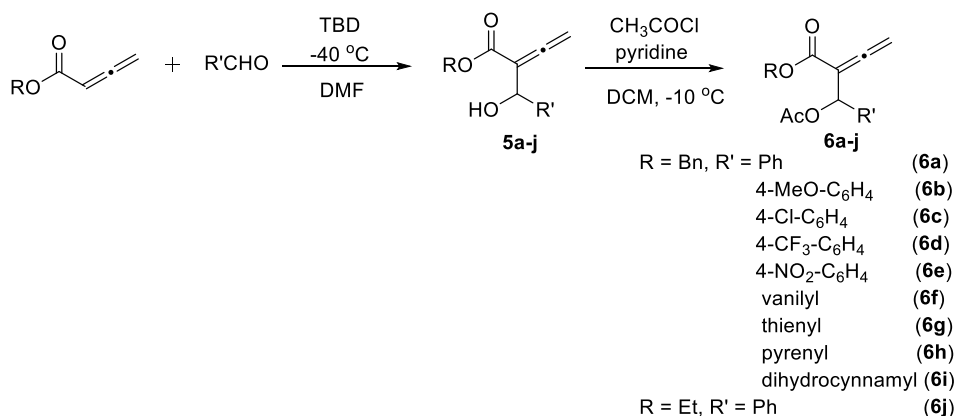
Propargylic alcohols react with ethyl diazoacetate in the presence of cuprous iodide and triethylamine in acetonitrile to deliver δ -hydroxy allenoates **3a-s**.^{13d, 55} The hydroxyl group of δ -hydroxy allenoates **3a-s** was converted to the easily removable acetoxy group in the presence of acetyl chloride and triethylamine (Scheme 2).^{13d, 55}



Scheme 2: Synthesis of δ -acetoxy allenoates **4a-s** from propargylic alcohols via δ -hydroxy allenoates **3a-s**

2.1.3 β' -Acetoxy allenoates **5a-j**

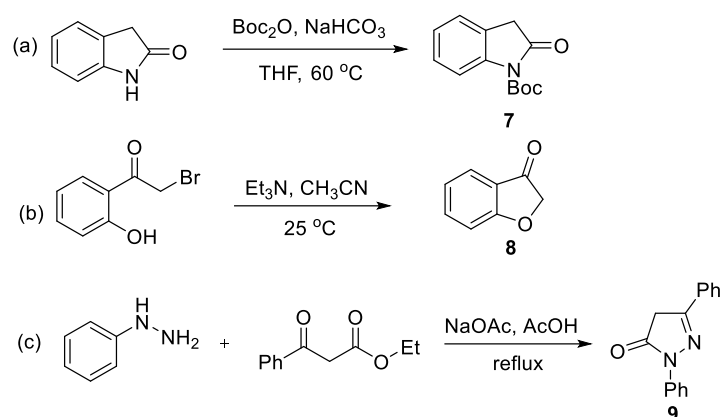
For the preparation of β' -acetoxy allenoates, as the first step, allenic esters were prepared using a literature procedure.⁵⁶ In the next step, allenic esters on treatment with aldehydes in the presence of triazabicyclodecene (TBD) in DMF solvent at -40 °C formed β' -hydroxy allenoates **5a-j**.⁵⁶ β' -Hydroxy allenoates **5a-j** were then acetylated using acetyl chloride/pyridine at -10 °C to produce β' -acetoxy allenoate **6a-j** (Scheme 3).⁵⁶



Scheme 3: Synthesis of β' -acetoxy allenoates **6a-j** from allenic esters via β' -hydroxy allenoates **5a-j**

2.1.4 *N*-Boc protected oxindole, benzofuranone and pyrazolone

The Boc protection of oxindole to obtain **7** has been done using Boc-anhydride under basic conditions (Scheme 4a).⁵⁷ Benzofuranone **8** has been prepared from 2-bromo-1-(2-hydroxyphenyl)ethan-1-one (Scheme 4b).⁵⁸ Pyrazolone **9** has been prepared using a standard literature procedure;⁵⁹ thus phenyl hydrazine and ethyl benzoylacetate, in the presence of sodium acetate under reflux conditions, delivered pyrazolone **9** (Scheme 4c).



Scheme 4: Synthesis of precursors **7-9**

2.2 Divergent reactivity of δ - and β' -acetoxy allenates with 2-sulfonamidoindoles via phosphine catalysis: Entry to dihydro- α -carboline, α -carboline, and spiro-cyclopentene motifs

In this present work, we have explored the reactivity of 2-sulfonamido indoles with δ - as well as β' -acetoxy allenates using phosphine catalysis. Using different conditions, we obtained dihydro-carbolines or tosyl-migrated carbolines *via* (3 + 3) annulation and spirocyclopentenones *via* (4 + 1) annulation. The best that we can tell, there had been no report for these types of reactions. Details are presented below.

2.2.1 Reaction of δ -acetoxy allenates with 2-sulfonamido indoles: Synthesis of dihydrocarbolines and tosyl-migrated carbolines

Initially, we tested the reaction between **2a** (0.20 mmol) and **4a** (0.24 mmol) in the presence of Ph_3P (20 mol %) in toluene at rt (25 °C) and obtained the product **10aa** in 45% yield after 24h (Table 1, entry 1). The yield (67%) of **10aa** could be enhanced by using degassed toluene (entry 2). Satisfyingly, we isolated the α -carboline **10aa** in 83% yield (entry 3) after 36h. Several other phosphines were screened but all of them were less effective (entries 4-7). Both electron-poor phosphines [$(p\text{-FC}_6\text{H}_4)_3\text{P}$ and $(p\text{-ClC}_6\text{H}_4)_3\text{P}$] and electron-rich phosphines [MePPh_2 and $(n\text{-Bu})_3\text{P}$] gave lower yields compared to Ph_3P . Hence, we believe

that optimum electron density and steric factors around phosphorus are crucial for this reaction. Further screening of reaction conditions using different solvents (DCE, DMF, MeOH, 1,4-dioxane, and H₂O; entries 8-12) revealed that toluene was the best solvent for this annulation, providing **10aa** in 83% yield (entry 3). To further increase the yield, we performed a reaction at a higher temperature (80 °C) but found the completely different product **11aa** (10%) along with **10aa** (61%); we identified product **11aa** as the tosyl migrated and aromatized carboline (entry 13) using analytical data (*vide infra*). Inspired by this unexpected result, we performed several reactions to get **11aa** as the sole product by minimizing the yield of **10aa**. First, we tested a reaction by using Cs₂CO₃ as an additive; fortunately, **11aa** was obtained in 75% yield (entry 14). Other additives (K₂CO₃ and ^tBuOK) were less effective (entries 15 and 16) compared to Cs₂CO₃. At room temperature, the Ph₃P-Cs₂CO₃ combination did not give a clear-cut reaction leading to either **10aa** or **11aa** (entry 17). Also, low catalytic loading (10 mol %) of phosphine did not lead to reactions efficiently (entries 18 and 19). Use of 50 mol % or 100 mol % of phosphine gave essentially the same yield as that from 20 mol % (entries 20-24).

Table 1. Optimization of reaction conditions for 10aa and 11aa^a

Reaction scheme: 2a + 4a $\xrightarrow{\text{Conditions}}$ 10aa + 11aa

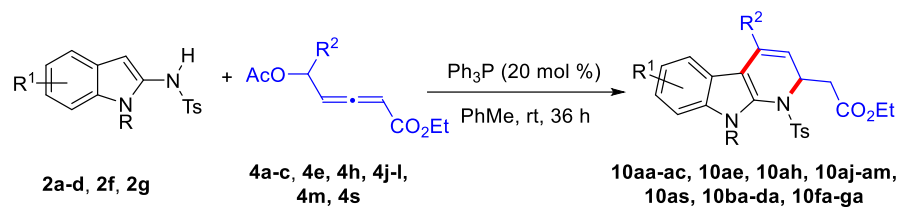
Entry	Base	Additive	Solvent	Temperature (°C)	Time (h)	Yield ^b 10aa:11aa
1	Ph ₃ P	-	PhMe	25	24	45:00
2	Ph ₃ P	-	PhMe	25	24	67:00
3	Ph₃P	-	PhMe	25	36	83:00
4	(<i>p</i> -ClC ₆ H ₄) ₃ P	-	PhMe	25	36	61:00
5	Bu ₃ P	-	PhMe	25	36	57:00
6	(<i>p</i> -FC ₆ H ₄) ₃ P	-	PhMe	25	36	58:00
7	Ph ₂ Pme	-	PhMe	25	36	65:00
8	Ph ₃ P	-	DCE	25	36	26:00
9	Ph ₃ P	-	DMF	25	36	29:00
10	Ph ₃ P	-	MeOH	25	36	-
11	Ph ₃ P	-	Dioxane	25	36	31:00

12	Ph ₃ P	-	H ₂ O	25	36	-
13	Ph ₃ P	-	PhMe	80	36	61:<10
14	Ph₃P	Cs₂CO₃	PhMe	80	36	≤5:75
15	Ph ₃ P	K ₂ CO ₃	PhMe	80	36	≤5:61
16	Ph ₃ P	^t BuOK	PhMe	80	36	≤5:64
17	Ph ₃ P	Cs ₂ CO ₃	PhMe	80	36	Complex
18	Ph ₃ P	Cs ₂ CO ₃	PhMe	80	36	≤5:53
19	Ph ₃ P	-	PhMe	25	36	61:00
20	Ph ₃ P	-	PhMe	25	36	83:00
21	Ph ₃ P	Cs ₂ CO ₃	PhMe	80	36	≤5:75
22	Ph ₃ P	-	PhMe	25	36	83:00
23	Ph ₃ P	Cs ₂ CO ₃	PhMe	80	36	≤5:75

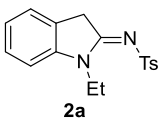
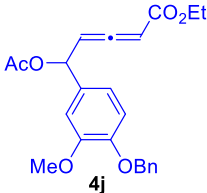
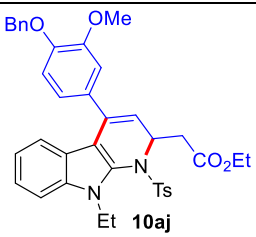
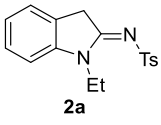
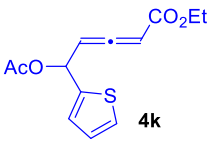
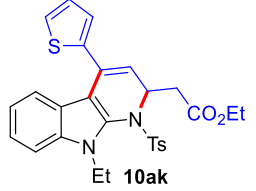
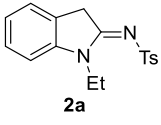
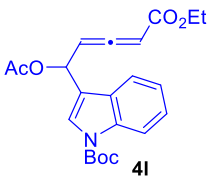
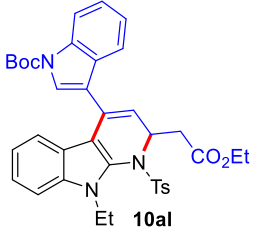
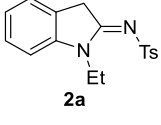
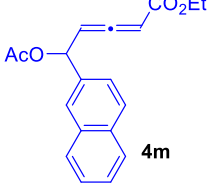
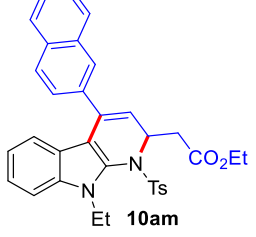
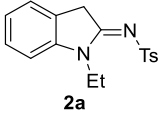
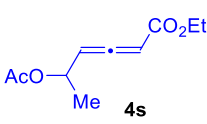
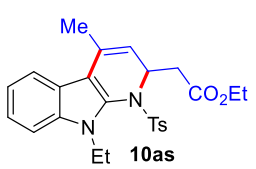
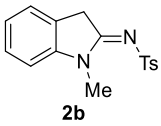
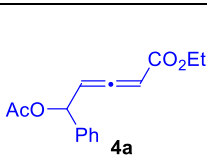
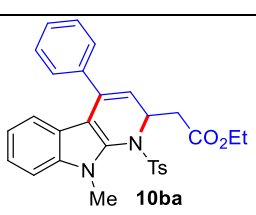
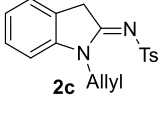
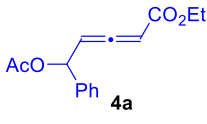
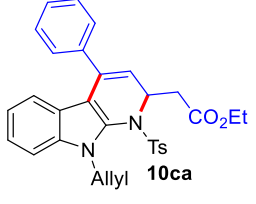
^aReaction conditions: **2a** (0.20 mmol), **4a** (0.24 mmol), phosphine (0.04 mmol for entries 1-18; 0.02 mmol for entries 18 and 19; 0.10 mmol for entries 20 and 21; 0.20 mmol for entries 22 and 23) and additive (entries 14-18, 0.40 mmol) in solvent (2.0 mL). ^bIsolated yield.

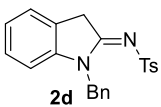
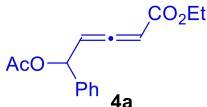
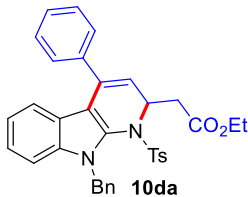
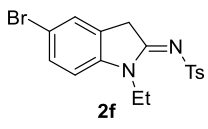
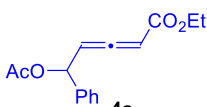
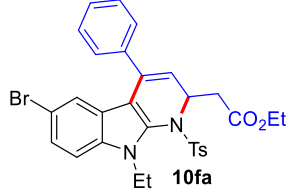
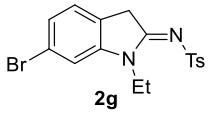
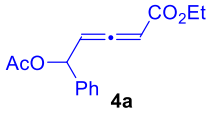
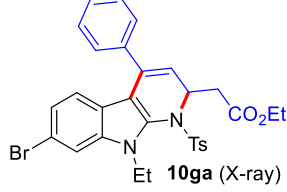
After establishing the best reaction conditions, we investigated the scope and limitations of the (3 + 3) annulation by using several 2-sulfonamidoindoles as *C/ N*-donors and a range of δ -acetoxy allenates as 3C-synthons (β , γ , δ -carbon donor). As shown in Table 2, regardless of the nature of substituents (OMe, Cl, or CF₃) at the 3rd/ 4th position on the phenyl ring, allenates (**4a-4c**, **4e**, **4h**) showed good reactivity with sulfonamidoindole **2a** and afforded dihydro- α -carboline **10aa-ac**, **10ae** and **10ah** in yields of 76-85%. Similarly, disubstituted allenate **4j** also reacted efficiently to afford **10aj** in 75% yield. The δ -polyaryl-substituted allenate **4m** was completely consumed to deliver **10am** in decent yield (72%). δ -Thienyl and indolyl substituted allenates **4k** and **4l** gave the desired products **10ak** and **10al** in yields of 73-75%. Moreover, this methodology was also effective with aliphatic allenate **4s** to deliver the (3 + 3) annulated product **10as** in 71% yield. Different substituents on the nitrogen atom in the nucleophile (**2b-d**) were well-tolerated affording high yields (73-84%) of **10ba-da**. Finally, this methodology was also amenable with 5- or 6-substituted sulfonamidoindoles (**2f** and **2g**), providing dihydrocarboline **10fa** and **10ga** in good yields (74% and 71%). The structure of compound **10ga** as revealed by single crystal X-ray diffraction is shown in Figure 1.

Table 2. Substrate scope for the synthesis of 1,2-dihydrocarboline from 2-sulfonamido indoles and δ -acetoxy allenates^a



Entry	2-Sulfonamido indole	δ -Acetoxy allenate	1,2-Dihydro carboline	Yield (%) ^b
1				83
2				85
3				78
4				77
5				76

6	 2a	 4j	 10aj	75
7	 2a	 4k	 10ak	73
8	 2a	 4l	 10al	75
9	 2a	 4m	 10am	72
10	 2a	 4s	 10as	71
11	 2b	 4a	 10ba	84
12	 2c	 4a	 10ca	78

13	 2d	 4a	 10da	73
14	 2f	 4a	 10fa	74
15	 2g	 4a	 10ga (X-ray)	71

^aReaction conditions: **2a-d**, **2f**, or **2g** (0.20 mmol), **4a-c**, **4e**, **4h**, **4j-l**, **4m**, or **4s** (0.24 mmol) and Ph₃P (0.04 mmol) in toluene (0.1 M) at rt (25 °C). ^bIsolated yield.

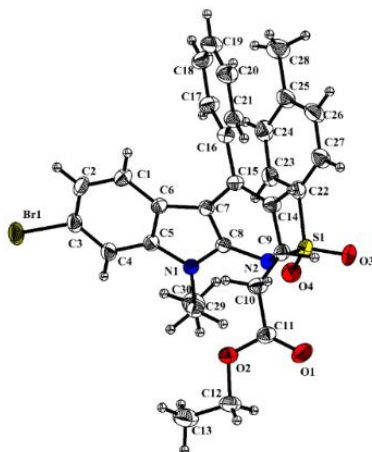
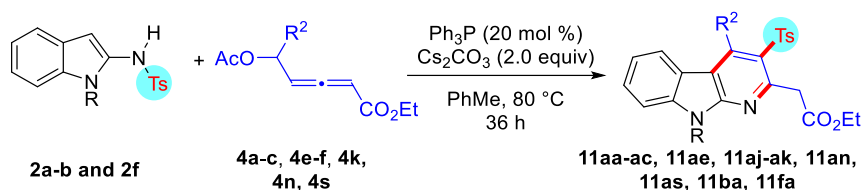


Figure 1. ORTEP view of **10ga** with a 30% probability of ellipsoids. Selected distances: N2 C9 1.502(4) Å, C7 C15 1.463(4) Å. CCDC No.: 2064415

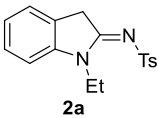
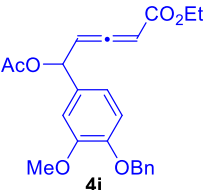
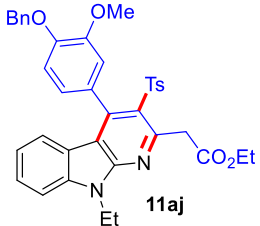
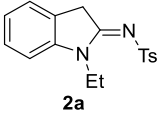
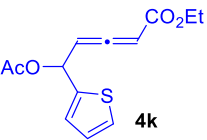
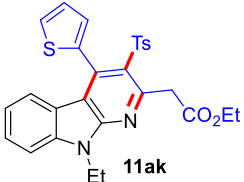
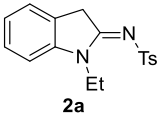
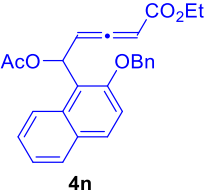
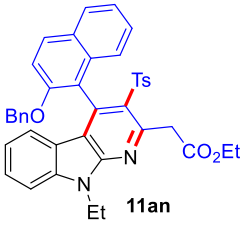
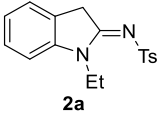
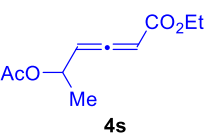
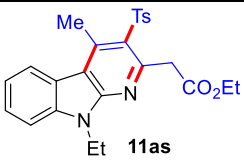
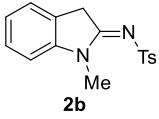
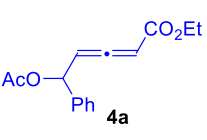
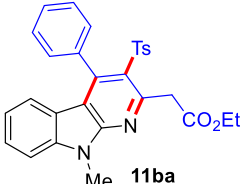
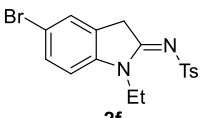
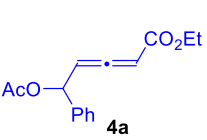
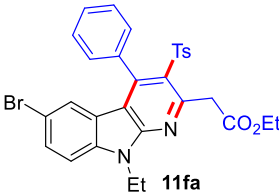
Next, we explored the substrate scope involving δ -acetoxy allenoates and sulfonamidoindoles in annulation and tosyl migration cascade processes leading to product **11aa**. As indicated in Table 3, allenoates **4a-c**, and **4e** afforded products **11aa-ac**, and **11ae** in 70-78% yields. To our delight, allenoate derived from vanillin **4j** and the heterocyclic allenoate **4k** also provided carbolines **11aj** and **11ak** in good yields (68% and 64%, respectively). Allenoate **4n** with naphthyl group at the fifth position also showed decent reactivity with **2a** to lead to the corresponding product **11an** in 72% yield. δ -Methyl substituted allenoate **4s** reacted

nicely in the cascade process and afforded **11as** in good yield (68%). Finally, *N*-substituted and 5-substituted sulfonamidoindoles (**2b** and **2f**) also afforded **11ba** and **11fa** in decent yields (76% and 65%) with **2a**. It is known that Cs₂CO₃ has fair solubility in many organic solvents, and quite low in toluene but the dramatic effect of tosyl group transfer as observed here is rather unexpected.⁶⁰ The structures of compounds **11aa** and **11ae** as revealed by single crystal X-ray diffraction are shown in Figure 2.

Table 3. Substrate scope for the synthesis of tosyl-migrated carbolines from 2-sulfonamido indole and δ -acetoxy allenates^a



Entry	2-Sulfonamido indole	δ -Acetoxy allenate	1,2-Dihydro carboline	Yield (%) ^b
1				75
2				78
3				73
4				70

5	 2a	 4j	 11aj	68
6	 2a	 4k	 11ak	64
7	 2a	 4n	 11an	72
8	 2a	 4s	 11as	68
9	 2b	 4a	 11ba	76
10	 2f	 4a	 11fa	65

^aReaction conditions: **2a-b** or **2f** (0.20 mmol), **4a-c**, **4e-f**, **4k**, **4n** or **4s** (0.24 mmol) and Ph₃P (0.04 mmol), Cs₂CO₃ (0.40 mmol) in toluene (0.1 M) at 80 °C. ^bIsolated yield.

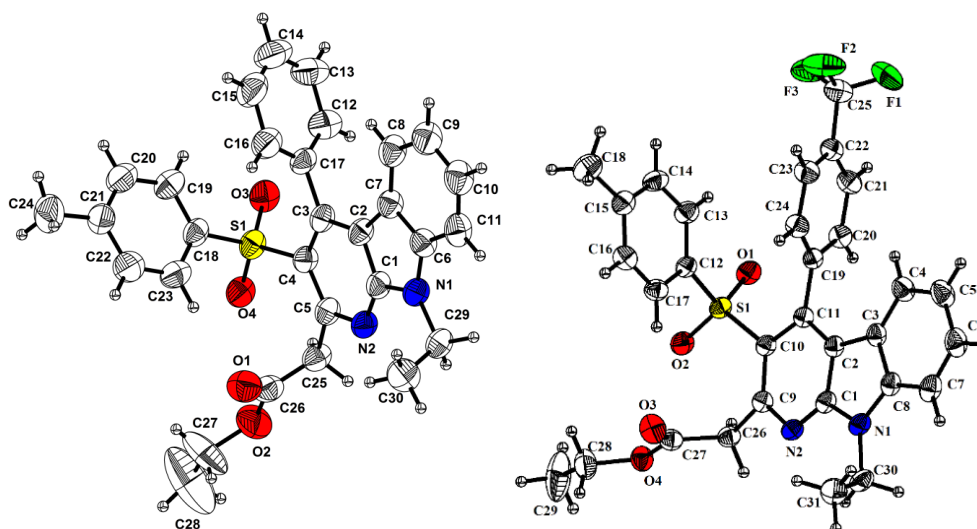
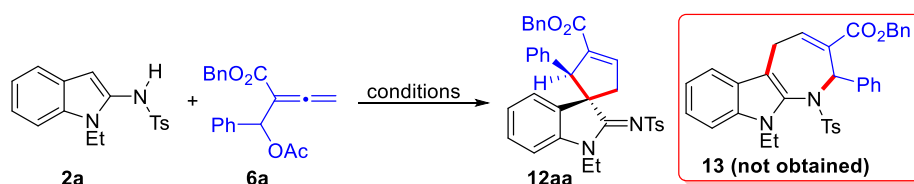


Figure 2: ORTEP views of **11aa** and **11ae** with 30% probability of ellipsoids. Selected distances: Compound **11aa** N2 C5 1.350(4) Å, C3 C4 1.410(4) Å, CCDC No.: 2064416. Compound **11ae** N2 C9 1.337(3) Å, C10 C11 1.407(3) Å. CCDC No.: 2064417.

2.2.2 Synthesis of spirocyclopentenenes from β' -acetoxy allenates and 2-sulfonamido indoles

Taking a cue from the reactivity of δ -acetoxy allenates as described above, we expected the formation of a seven-membered fused heterocycle **13** using β' -acetoxy allenates. Thus, as depicted in Table 4, we performed a reaction between 2-sulfonamidoindole **2a** (0.20 mmol) and β' -acetoxy allenate **6a** (0.24 mmol) using the conditions shown for entry 3, Table 1. Surprisingly, we isolated product **12aa** in 47% yield and identified it as the (4 + 1) product *via* spiro-annulation but not (4 + 3) annulated product **13** (Table 4, entry 1). This result motivated us to investigate the (4 + 1) annulation reaction in a systematic way for improving the yield of **12aa**. Increasing the reaction temperature from 25 °C to 80 °C afforded **12aa** in 69% yield (entry 2). Investigation of several phosphines (entries 3-7) indicated that (*p*-tolyl)₃P was the best choice as the catalyst (entry 7). A solvent study showed that toluene was the best (entry 7); protic polar and aprotic solvents (entries 8-11) gave inferior results. The addition of Cs₂CO₃ did not show any dramatic effect on the reactivity (entry 12). Thus, conditions under entry 7 were found to be the best for this (4 + 1)-spiro-annulation.

Table 4. Optimization of reaction conditions for the synthesis of 12aa^a

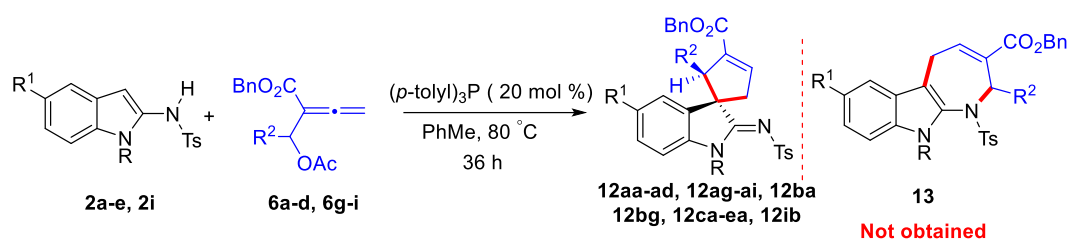
Entry	Base	Solvent	Temperature (°C)	Time (h)	Yield ^b		<i>dr</i> of ^c
					12aa	12aa ^c	
1	Ph ₃ P	PhMe	25	36	47		20:1
2	Ph ₃ P	PhMe	80	36	69		20:1
3	Ph ₂ PMe	PhMe	80	36	54		20:1
4	(<i>p</i> -ClC ₆ H ₄) ₃ P	PhMe	80	36	49		20:1
5	Bu ₃ P	PhMe	80	36	52		20:1
6	(<i>p</i> -FC ₆ H ₄) ₃ P	PhMe	80	36	45		20:1
7	(<i>p</i>-tolyl)₃P	PhMe	80	36	79		20:1
8	(<i>p</i> -tolyl) ₃ P	MeCN	80	36	26		20:1
9	(<i>p</i> -tolyl) ₃ P	DMF	80	36	29		20:1
10	(<i>p</i> -tolyl) ₃ P	MeOH	80	36	trace		-
11	(<i>p</i> -tolyl) ₃ P	H ₂ O	80	36	trace		-
12	(<i>p</i> -tolyl) ₃ P	PhMe	80	36	79		20:1

^aReaction conditions: **2a** (0.20 mmol), **6a** (0.24 mmol), phosphine (0.04 mmol), and additive (0.40 mmol for entry 12) in solvent (2.0 mL). ^bIsolated yield. ^cDiastereomeric ratio.

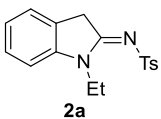
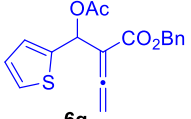
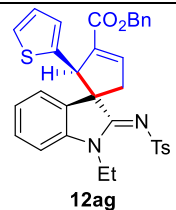
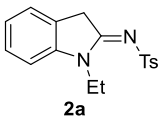
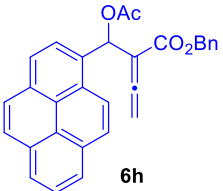
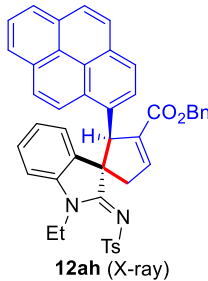
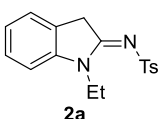
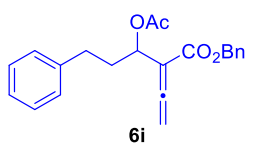
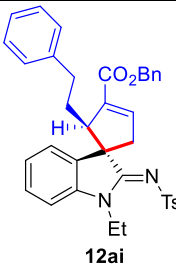
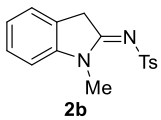
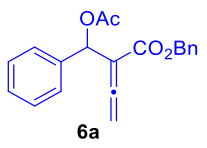
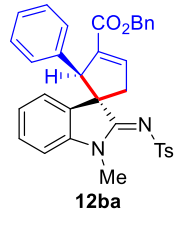
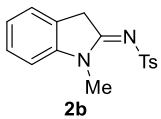
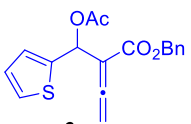
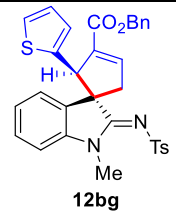
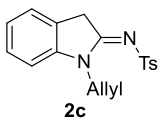
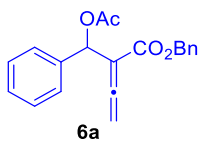
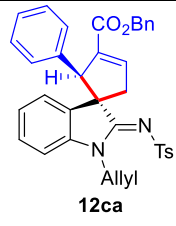
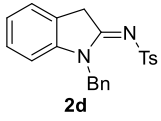
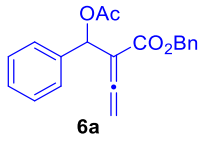
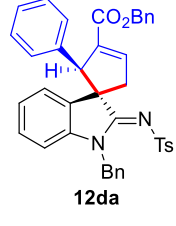
As depicted in Table 5, various β' -acetoxy allenolates reacted efficiently with **2a** under standard conditions to afford the corresponding spirocyclic cyclopentene carboxylate motifs with excellent diastereoselectivity (*dr* up to >20:1). The substituents on the phenyl ring (**6a-d**) had no significant effect in this methodology and spirocyclic products **12aa-ad** were isolated in yields of 71-83%. Even the pyrenyl allenolate **6h** and heterocyclic allenolate **6g** reacted well with **2a** and delivered **12ah** and **12ag** in yields of 65% and 70%, respectively. Aliphatic allenolate **6i** also reacted nicely in the spiro-annulation to lead **12ai** in 69% yield. Substituted indolines (**2b-e**, **2i**) were also suitable for this reaction and gave spirocyclic motifs **12ba**, **12bg**, **12ca-ea**, and **12ib** in good to high yields (71-84%). The relative configuration of substituents in these products was ascertained by X-ray crystal structures of **12aa** and **12ah** (Figure 3). The allenol precursors corresponding to the acetates **4a** and **6a** did not undergo any perceptible

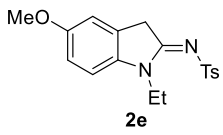
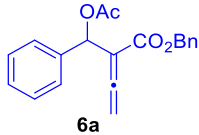
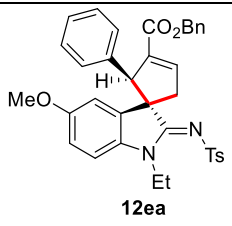
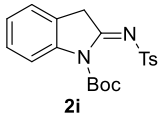
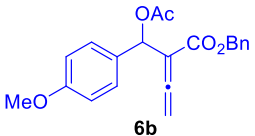
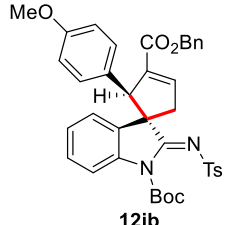
reaction even after 48h suggesting that the acetate leaving group is essential. Also, the use of (S)-BINAP as the phosphine did not give product **12aa**; although derivative **10aa** (*vide supra*) could be obtained, chiral induction did not occur.

Table 5. Substrate scope for the synthesis of indole fused spirocyclopentenes from 2-sulfonamido indoles and β' -acetoxy allenates^a



Entry	2-Sulfonamido indole	β' -Acetoxy allenate	Spiro-cyclopentene	Yield ^b (%)
1				79
2				83
3				76
4				71

5	 2a	 6g	 12ag	70
6	 2a	 6h	 12ah (X-ray)	65
7	 2a	 6i	 12ai	69
8	 2b	 6a	 12ba	82
9	 2b	 6g	 12bg	73
10	 2c	 6a	 12ca	79
11	 2d	 6a	 12da	75

12	 2e	 6a	 12ea	71
13	 2i	 6b	 12ib	84

^aReaction conditions: **2a-e**, **2i** (0.20 mmol), **6a-d**, **6g-i** (0.24 mmol) and (*p*-tolyl)₃P (0.04 mmol), in toluene (0.1 M) at 80 °C. ^bIsolated yield.

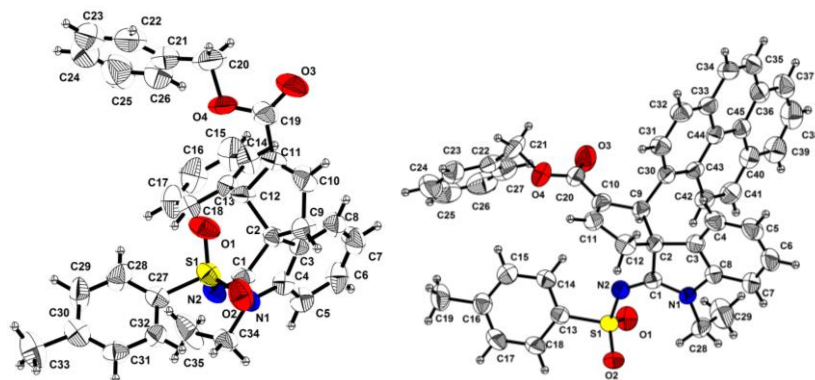
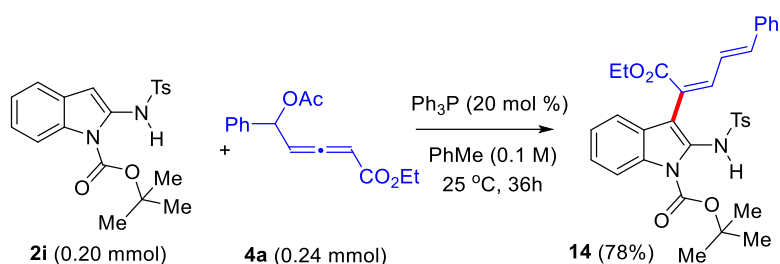


Figure 3: ORTEP views of **12aa** (left) and **12ah** (right) with 30% probability of ellipsoids. Selected distances: Compound **12aa** C2 C9 1.553(5) Å, C2 C12 1.596(5) Å. CCDC No.: 2064418. Compound **12ah** C2 C9 1.595(4) Å, C2 C12 1.552(4) Å. CCDC No.: 2064419.

2.2.3 Isolation of dienolate from the reaction of *N*-Boc-sulfonamidoindole with δ -acetoxy allenolate

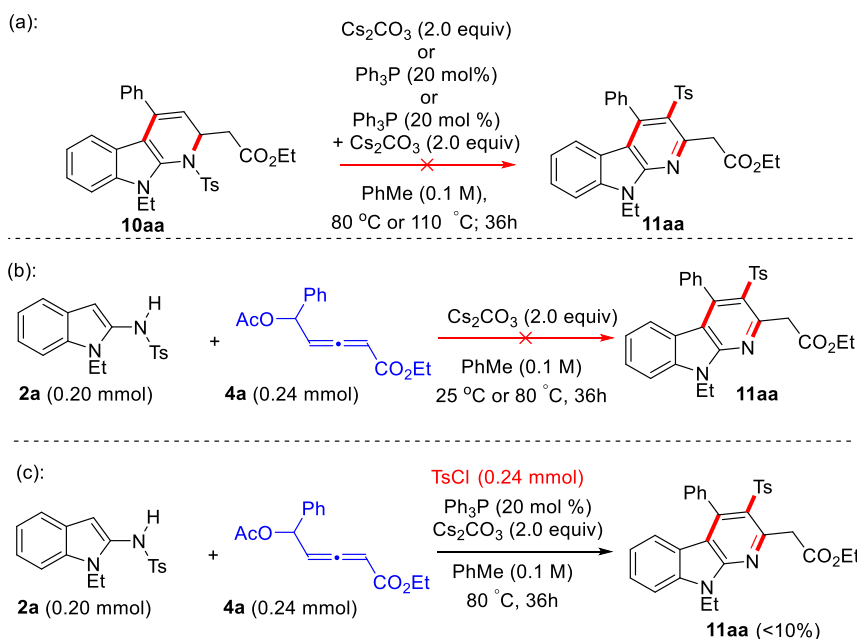
In the reaction of *N*-Boc protected 2-sulfonamidoindole **2i** with acetoxy allenolate **4a** under optimized conditions (Table 1, entry 3), surprisingly, we observed the non-cyclized dienolate **14** as the sole product *via* α -umpolung addition (Scheme 5). Since this was not the theme of the work, we did not check this aspect further.



Scheme 5: Synthesis of dienolate **14** from *N*-Boc-sulfonamido indole **2i** and **4a**

2.2.4 Control experiments

It can be noted that the aromatized tosyl migrated product **11aa** has two hydrogen atoms missing when compared to **10aa**. To investigate the mechanism of tosyl migration cum (3 + 3) annulation, we performed a few experiments. Heating compound **10aa** individually with (i) Cs_2CO_3 or (ii) Ph_3P or (iii) $\text{Ph}_3\text{P} + \text{Cs}_2\text{CO}_3$ at 80 °C or 110 °C even for 36h did not yield compound **11aa** (Scheme 6a). Thus, it is likely that (3 + 3) annulation *with and without* tosyl migration occurs by different pathways. Also, in the absence of Ph_3P , we did not observe any product at rt as well as at 80 °C (Scheme 6b). The yield of **11aa** dramatically dropped when we used tosyl chloride as tosyl cation source (Scheme 6c). Based on these experiments, we infer that (i) the presence of Ph_3P is essential, (ii) temperature and gradual addition of allenolate play a key role, and (iii) tosyl anion (not cation) is most likely involved in the migration leading to **11aa**.

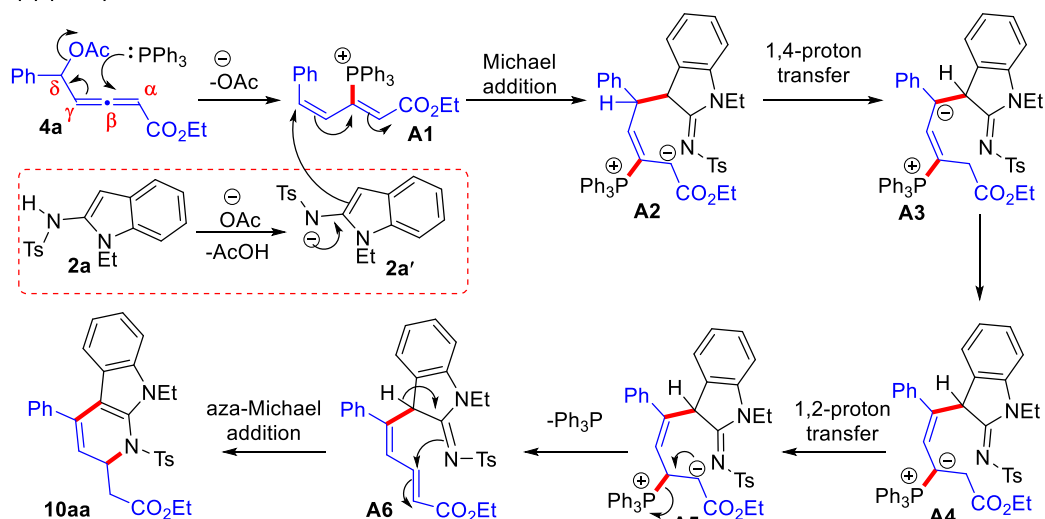


Scheme 6: Control experiments

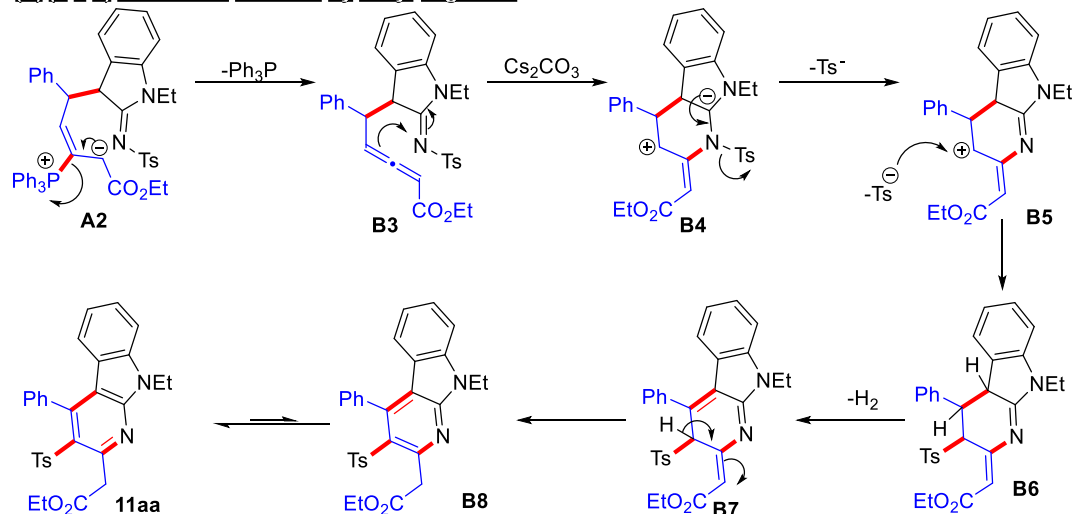
2.2.5 Proposed pathways for (3 + 3) and (4 + 1) annulations

Plausible pathways for the (3 + 3) and (4 + 1) annulations are shown in Scheme 7. These divergent annulations may be initiated through the phosphonium intermediate **A1** or **C1** via the addition-elimination process between phosphine and **4a** or **6a**. In the (3 + 3) annulation, the addition of **2a'** (generated from **2a**) to the phosphonium ion **A1** at the δ -carbon gives zwitterionic intermediate **A2** (Scheme 7a). Immediately, **A2** undergoes 1,4-proton transfer and affords **A3**. Subsequently, **A3** upon double bond isomerization, 1,2-proton transfer, and phosphine elimination leads to dienolate **A6** via **A4** and **A5**. Finally, **A6** after intramolecular aza-Michael addition^{13c} yields **10aa**. For the formation of tosyl migration product **11aa**, one possible pathway is shown in Scheme 7b. In this, **A1** undergoes a second addition-elimination process with **2a'** to give the allenic intermediate **B3**. Intermediate **B3** is involved in the aza-Claisen rearrangement⁶⁰ to give zwitterionic intermediate **B4**. Finally, tosyl group elimination/re-addition, and aromatization involving species **B4-B7** are expected to be involved in the formation of the unexpected α -carboline **11aa** with tosyl functionality at the γ -carbon. The nitrogen atom of intermediate **B3** may be electron deficient due to the double bond and sulfonyl functionality.⁶⁰ Hence one of the double bonds of the allene moiety attacks this nitrogen to deliver zwitterionic intermediate **B4**. Furthermore, at rt, proton shift is faster than addition-elimination but at 80 °C and addition-elimination is faster than proton shift. Therefore, the two (3 + 3) leading to **10aa** and **11aa** annulations occur in distinct ways. In the (*p*-tolyl)₃P mediated (4 + 1) stereoselective spiro-annulation (Scheme 7c), nucleophile **2a'** selectively attacks at the γ -carbon of **C1** to offer the ylide intermediate **C2**. Then; **C2** is involved in 1,3-proton transfer to produce **C3**. Finally, **C3** undergoes addition-elimination (S_N2' -attack) leading to **12aa**. It should be noted that in the (4 + 1) spiro-carbo-annulation the key step is ylide formation and the formation of the C-C bond is more favorable than the C-N bond in the final step. Although the possibility of the formation of a 7-membered ring exists (*cf.* structure **13**), we have not observed it in the present study.

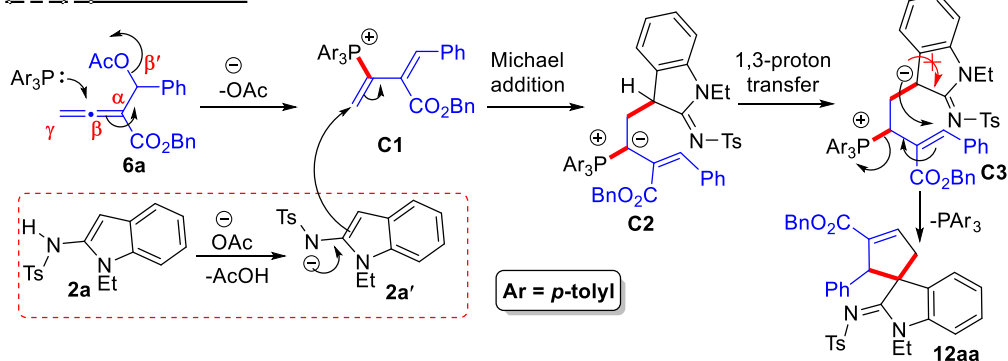
(a) (3 + 3) Annulation:



(b) (3 + 3) Annulation followed by Tosyl Migration:



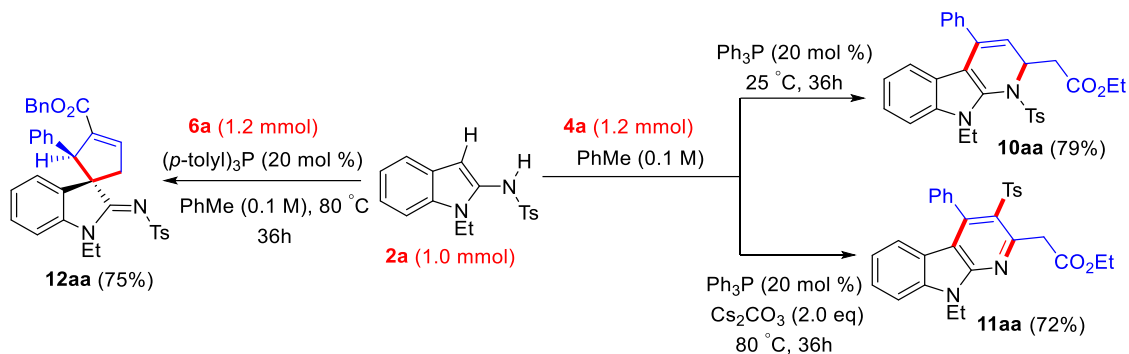
(c) (4 + 1) Spiro-Annulation:



Scheme 7: Plausible mechanism for the formation of 10aa, 11aa, and 12aa

2.2.6 Scale-up experiments for the synthesis of **10aa**, **11aa**, and **12aa**

The robustness of our divergent annulations is exemplified by 1.0 mmol scale reactions of **2a** with **4a** or **6a** under the optimal conditions to afford **10aa**, **11aa**, and **12aa** in high yields (Scheme 8).



Scheme 8: Scale up experiments

2.3 Lewis-base dependent (3 + 3) annulations of acetoxy allenates with iminoindolines: α -Carboline scaffolds with varied substituents

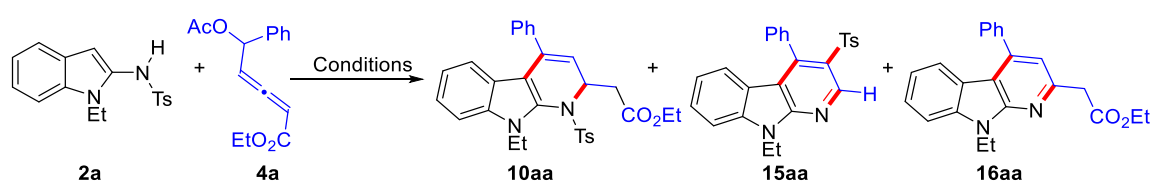
The concept of utilizing β' / δ -acetoxy allenates as electrophilic entities involving diene-ammonium/ phosphonium ion in several annulation reactions has been explored in recent years.¹³⁻¹⁴ However, none of them involved C-C bond cleavage. In this section, we describe the reactivity of β' / δ -acetoxy allenates with 2-sulfonamido indoles by phosphine as well as amine catalysis that involve C-C bond cleavage.

2.3.1 Synthesis of tosyl-migrated carbolines with the expulsion of $-\text{CH}_2\text{CO}_2\text{Et}$ moiety from the reaction of 2-sulfonamido indoles with δ -acetoxy allenates

We started with the reaction of 2-iminoindoline **2a** (0.20 mmol) with δ -acetoxy allenoate **4a** (0.24 mmol) in the presence of $(p\text{-tolyl})_3\text{P}$ (20 mol %; 0.04 mmol) at rt (25 °C). We obtained a mixture of dihydrocarboline **10aa** (75%) and C-C bond cleaved product **15aa** (<5%) after 24h (Table 6, entry 1). At 80 °C, the ratio changed to 23:61 (**10aa**:**15aa**, entry 2). The same reaction at a higher temperature (110 °C) afforded **15aa** (isolated yield: 81%) with the complete exclusion of **10aa** (entry 3). Then different phosphine catalysts were examined, but we found that $(p\text{-tolyl})_3\text{P}$ was still the best for **15aa** (entries 4-7). Among the solvents checked (entries 3, 8-11), toluene gave the optimum yield (entry 3). Increasing the quantity of phosphine to 50 and 100 mol% did not improve the yield of **15aa** (entries 12-13); decreasing the reaction time to 6h reduced the yield (entry 14). To our surprise, the use of DBU afforded a different product, identified as 2-(α)-carbolinyll acetate **16aa** (87%; entry 15). Even at a lower

temperature (50 °C; entry 16), the reaction delivered **16aa** with the same yield (entry 16). Among the tested tertiary amines, DBU delivered **16aa** in the highest yield (entries 15, 17-20). Among the solvents tested (entries 15 and 21-24) toluene was again the best for **16aa**; pleasingly, though, we obtained the same yield of **16aa** (87%) even after 6h (entry 25). A higher mole ratio (50 or 100 mol%) of DBU did not give better yields (entries 26-27); Hence, we proceeded with the substrate scope by taking entry 3 for **15aa** and entry 24 for **16aa** as optimal conditions.

Table 6. Optimization of reaction conditions for the synthesis of 15aa and 16aa^{a,b}



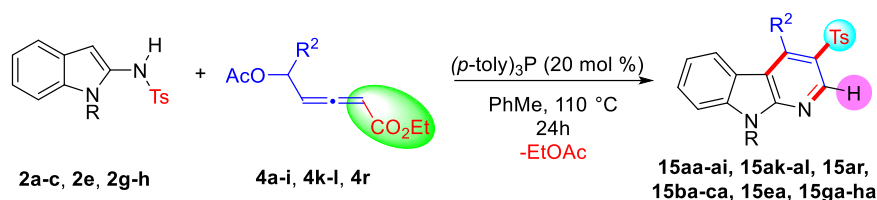
Entry	Lewis Base	Solvent	T/ °C	Time/h	Yield/ %		
					10aa	15aa	16aa
1	(<i>p</i> -tolyl) ₃ P	PhMe	25	24	75	<5	ND
2	(<i>p</i> -tolyl) ₃ P	PhMe	80	24	23	61	ND
3	(<i>p</i> -tolyl) ₃ P	PhMe	110	24	ND	81	ND
4	(<i>p</i> -ClC ₆ H ₄) ₃ P	PhMe	110	24	<5	49	ND
5	Bu ₃ P	PhMe	110	24	<5	56	ND
6	(<i>p</i> -FC ₆ H ₄) ₃ P	PhMe	110	24	<5	42	ND
7	Ph ₂ Pme	PhMe	110	24	<5	62	ND
8	(<i>p</i> -tolyl) ₃ P	THF	110	24	ND	35	ND
9	(<i>p</i> -tolyl) ₃ P	DMF	110	24	ND	43	ND
10	(<i>p</i> -tolyl) ₃ P	Dioxane	110	24	ND	26	ND
11	(<i>p</i> -tolyl) ₃ P	DCE	110	24	ND	45	ND
12	(<i>p</i> -tolyl) ₃ P	PhMe	110	24	ND	81	ND
13	(<i>p</i> -tolyl) ₃ P	PhMe	110	24	ND	81	ND
14	(<i>p</i> -tolyl) ₃ P	PhMe	110	6	ND	45	ND
15	DBU	PhMe	110	24	ND	ND	87
16	DBU	PhMe	50	24	ND	ND	87
17	TBD	PhMe	50	24	ND	ND	65
18	Et ₃ N	PhMe	50	24	ND	ND	62

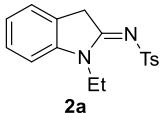
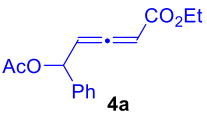
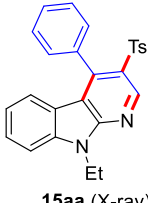
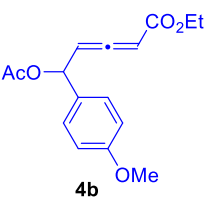
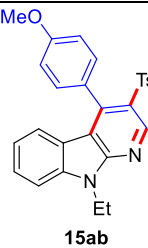
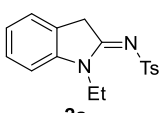
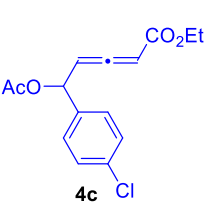
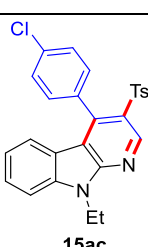
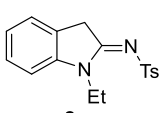
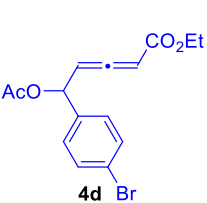
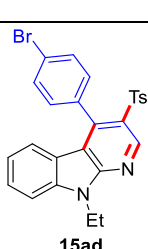
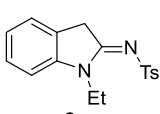
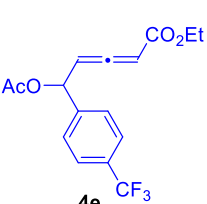
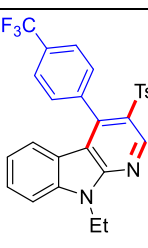
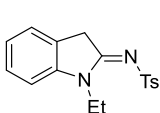
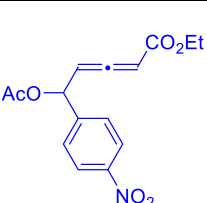
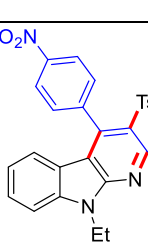
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20	DABCO	PhMe	50	24	ND	ND	52
21	DBU	DMF	50	24	ND	ND	45
22	DBU	dioxane	50	24	ND	ND	61
23	DBU	DCE	50	24	ND	ND	53
24	DBU	THF	50	24	ND	ND	65
25	DBU	PhMe	50	6 (or 24)	ND	ND	87
26	DBU	PhMe	50	6	ND	ND	87
27	DBU	PhMe	50	6	ND	ND	87

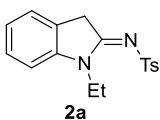
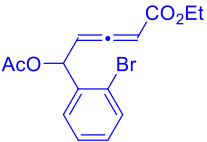
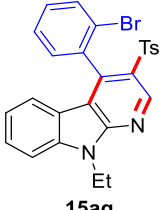
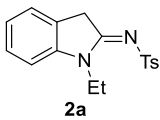
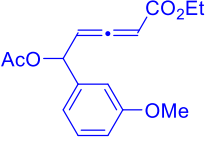
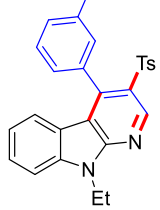
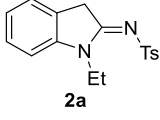
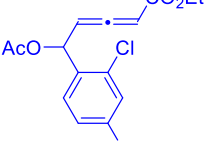
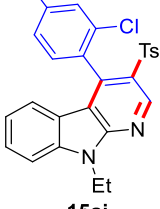
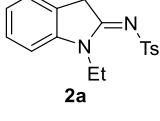
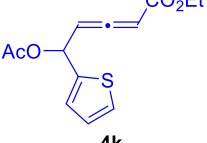
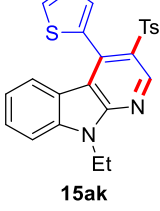
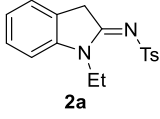
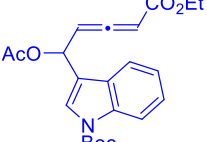
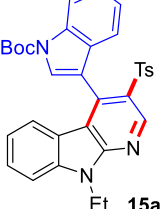
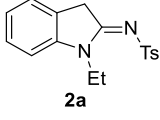
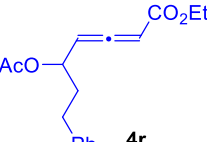
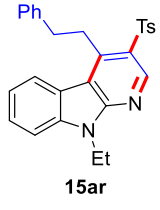
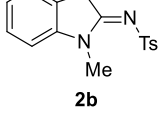
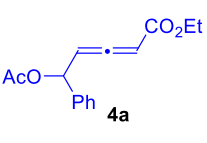
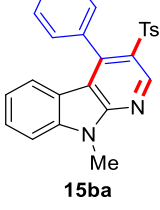
^aReaction conditions: **2a** (0.20 mmol; 1.0 equiv.), **4a** (0.24 mmol; 1.2 equiv.), Lewis base (0.04 mmol, 0.2 equiv. for entries 1-11, 14 and 15-25; 0.10 mmol, 0.5 equiv. for entries 12 and 26; 0.20 mmol, 1.0 equiv. for entries 13 and 27) in solvent (2.0 mL). ^bIsolated yield.

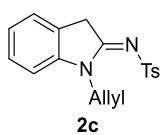
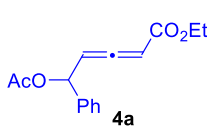
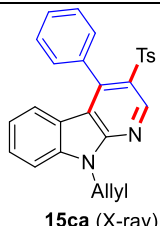
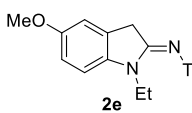
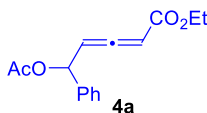
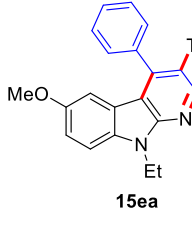
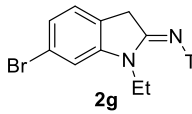
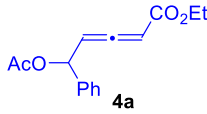
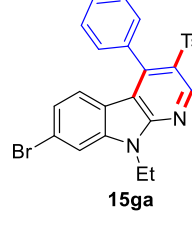
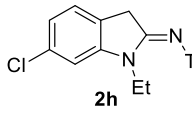
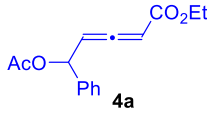
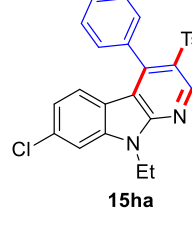
As shown in Table 7, the reaction efficiency is not affected by the electronic disparity at the *para*-position (MeO, Cl, Br, CF₃, NO₂) of the phenyl ring of allenolate moiety, and the corresponding products **15aa-af** are isolated in yields of 69-83%. The precursors with *ortho*-(2-Br) and *meta*-substitution (3-OMe) as well as the disubstituted one (2,4-Cl₂) are also viable in the present protocol and offered the products **15ag-ai** in 72-78% yield. Even the heteroaryl (thienyl, indolyl) and aliphatic allenolates afforded the respective products **15ak**, **15al** and **15ar** in decent yields of 65-73%. The different *N*-substituted and 5/6-substituted iminoindolines **2b-c**, **2e** and **2g-h** worked well and produced **15ba**, **15ea**, **15ga-ha** in good yields (69-78%). An interesting observation is that in the HRMS, we noticed another peak almost double in intensity to that of the base peak in most cases [2M + H]⁺. The molecular structures of **15aa** and **15ca** are shown in Figure 4.

Table 7. Substrate scope for the synthesis of tosyl migrated carbolines from 2-sulfonamido indole and δ -acetoxy allenolates^a



Entry	2-Sulfonamido indole	δ -Acetoxy allenolate	Carboline	Yield ^b (%)
1				81
2				83
3				79
4				77
5				75
6				69

7	 2a	 4g	 15ag	73
8	 2a	 4h	 15ah	78
9	 2a	 4i	 15ai	72
10	 2a	 4k	 15ak	73
11	 2a	 4l	 15al	69
12	 2a	 4r	 15ar	65
13	 2b	 4a	 15ba	78

14	 2c	 4a	 15ca (X-ray)	74
15	 2e	 4a	 15ea	69
16	 2g	 4a	 15ga	71
17	 2h	 4a	 15ha	73

^aReaction conditions: **2a-c**, **2e**, or **2g-h** (0.20 mmol; 1.0 equiv.), **4a-I**, **4k-I**, or **4r** (0.24 mmol; 1.2 equiv.), (*p*-tolyl)₃P (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 110 °C. ^bIsolated yield.

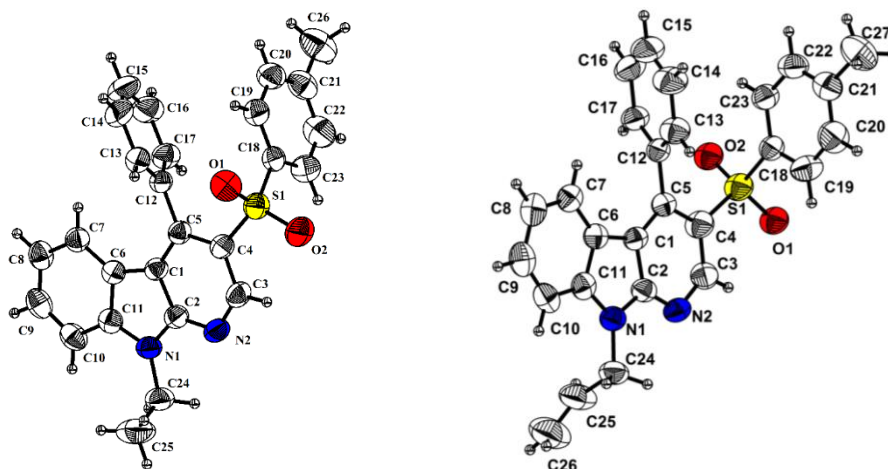
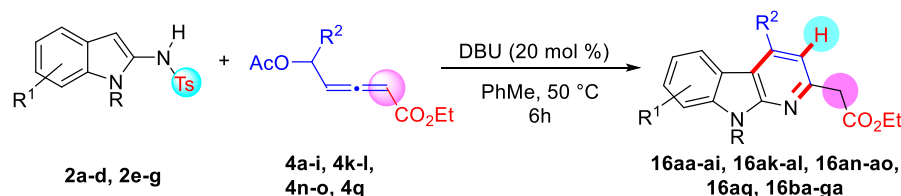


Figure 4: Molecular structures of compounds **15aa** (left) and **15ca** (right). Selected bond parameters: Compound **15aa** C(1)-C(5) 1.391(3), C(5)-C(4) 1.407(3), C(4)-C(3) 1.398(3), N(2)- C(3) 1.334(3), N(2)- C(2) 1.336 (3) [Å]. CCDC No. 2206241, Compound **15ca** C(1)-

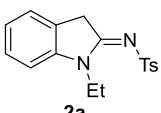
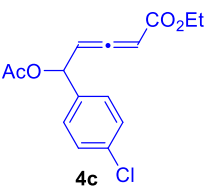
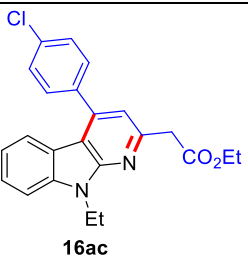
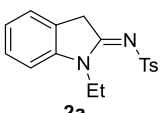
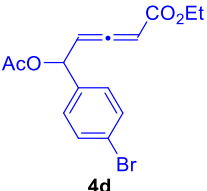
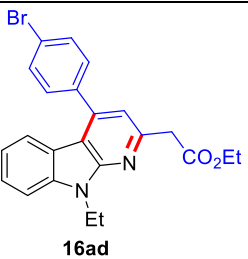
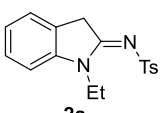
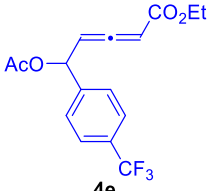
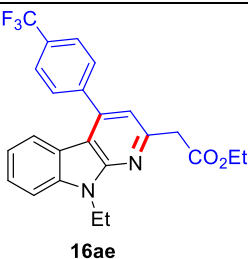
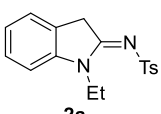
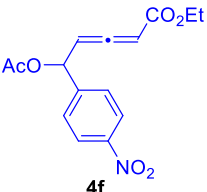
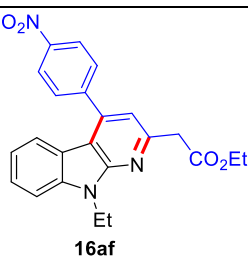
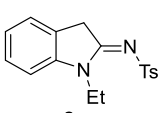
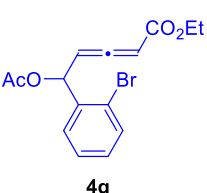
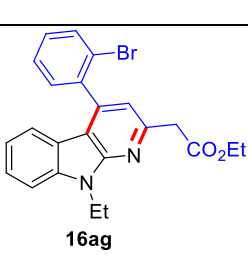
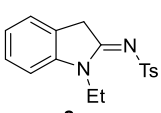
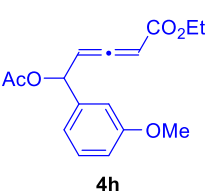
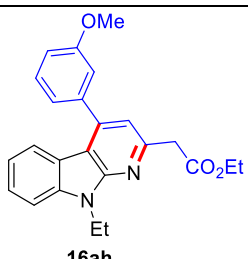
C(5) 1.374(5), C(5)-C(4) 1.406(5), N(2)-C(3) 1.340(5), N(2)-C(2) 1.335(5). CCDC No. 2206242.

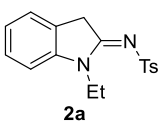
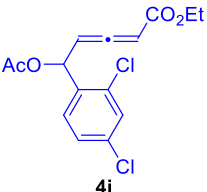
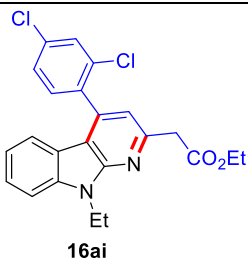
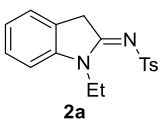
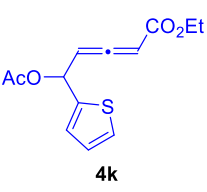
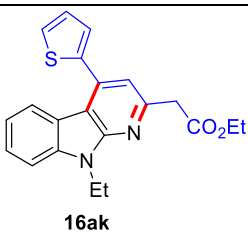
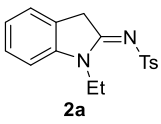
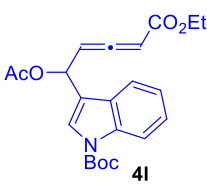
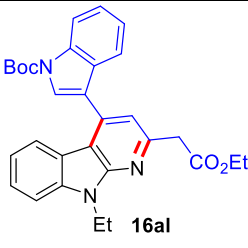
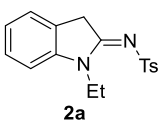
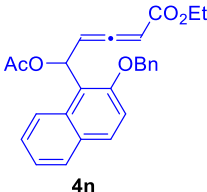
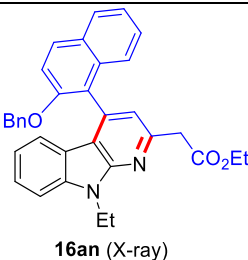
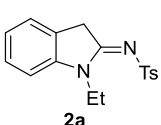
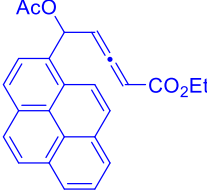
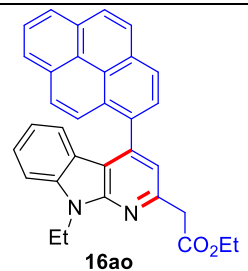
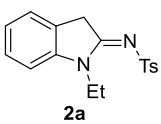
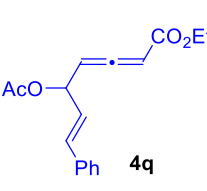
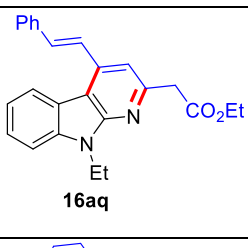
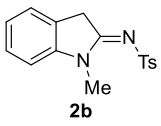
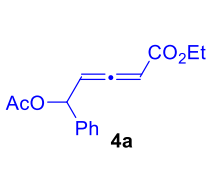
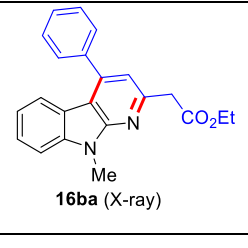
Coming to the DBU-catalyzed (3 + 3) annulation (Table 8), the position of the substituents on the phenyl ring of allenates (*cf.* **4b-h**) appears to have no noticeable effect on the reactivity and produced annulated products **16aa-ah** in good to high yields (72%-87%). The 2,4-dichloro substituted (**4i**), 2-thienyl (**4k**), and *N*-Boc-3-indolyl (**4l**) substrates also afforded the expected products **16ai**, and **16ak-al** in 71-76% yields. Moreover, polyaryl allenates with 2-BnO-1-naphthyl and 1-pyrenyl substituents (**4n-o**) delivered the annulated products **16an-ao** in good yields (65-69%). The aliphatic allenate **4q** nicely fitted in this procedure and produced **16aq** in decent yield (68%). This annulation reaction also worked efficiently with other *N*-substituted precursors (*N*-Me, *N*-allyl and *N*-Bn) and aryl ring substituted (5-MeO/Br, 6-Br) indole precursors in delivering the corresponding products **16ba-da** (72%-82%) and **16ea-ga** (67%-70%).

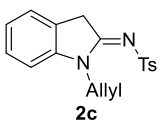
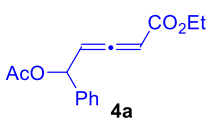
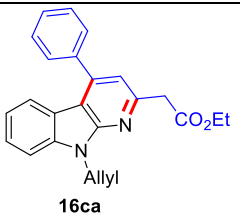
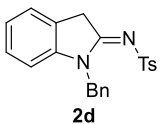
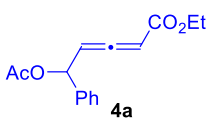
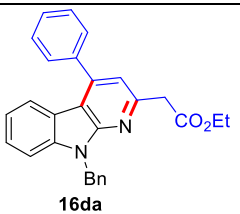
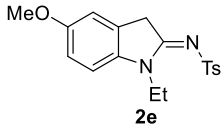
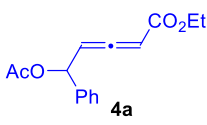
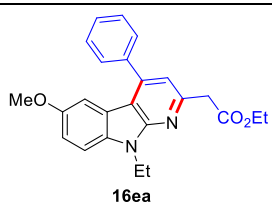
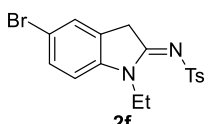
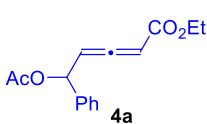
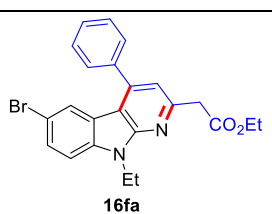
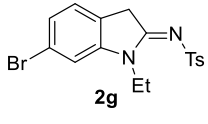
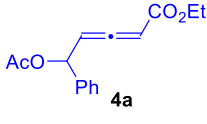
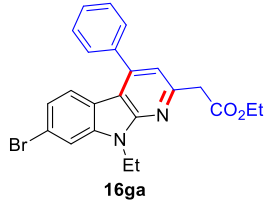
Table 8. Substrate scope for the synthesis of carbolines from 2-sulfonamido indoles and δ -acetoxy allenates^a



Entry	2-Sulfonamido indole	δ -Acetoxy allenate	Carboline	Yield ^b (%)
1	 2a	 4a	 16aa	87
2	 2a	 4b	 16ab	92

3	 2a	 4c	 16ac	80
4	 2a	 4d	 16ad	83
5	 2a	 4e	 16ae	78
6	 2a	 4f	 16af	72
7	 2a	 4g	 16ag	74
8	 2a	 4h	 16ah	81

9	 2a	 4i	 16ai	76
10	 2a	 4k	 16ak	75
11	 2a	 4l	 16al	71
12	 2a	 4n	 16an (X-ray)	69
13	 2a	 4o	 16ao	65
14	 2a	 4q	 16aq	68
15	 2b	 4a	 16ba (X-ray)	82

16	 2c	 4a	 16ca	76
17	 2d	 4a	 16da	72
18	 2e	 4a	 16ea	70
19	 2f	 4a	 16fa	67
20	 2g	 4a	 16ga	69

^aReaction conditions: **2a-d**, **2e-g** (0.20 mmol; 1.0 equiv.), **4a-l**, **4k-l**, **4n-o**, **4q** (0.24 mmol; 1.2 equiv.), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 50 °C. ^bIsolated yield.

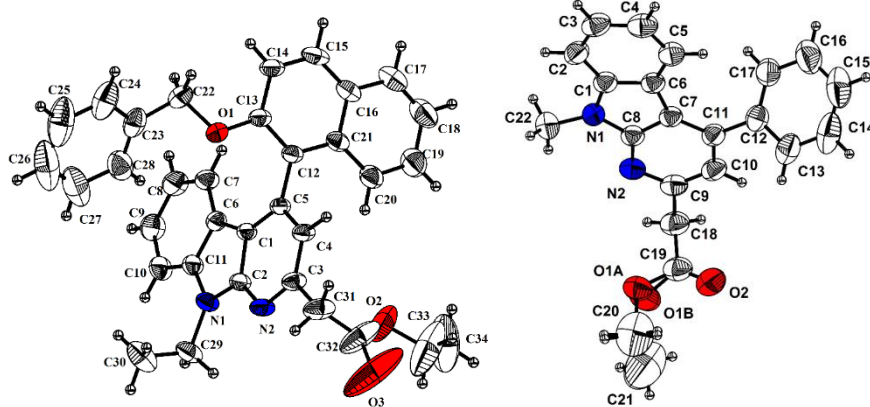
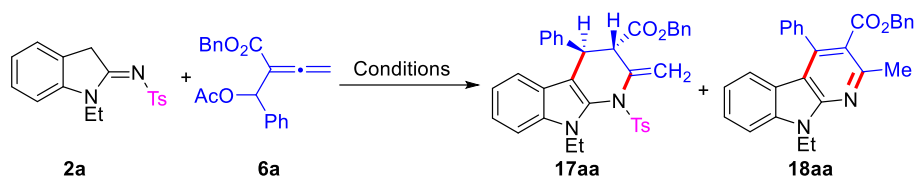


Figure 5: Molecular structures of compounds **16an** and **16ba**. Selected bond parameters: Compound **16an** C(1)-C(5) 1.387(4), C(5)-C(4) 1.394(4), N(2)-C(3) 1.345(4), N(2)-C(2) 1.327(4). CCDC No. 2206243, Compound **16ba** C(7)-C(11) 1.400(3), C(11)-C(10) 1.389(4), N(2)-C(9) 1.340(3), N(2)-C(8) 1.329(3). CCDC No. 2206244.

2.3.2 Synthesis of tetrahydro-carbolines and carbolines from 2-sulfonamido indoles and β' -acetoxy allenates

For the reaction of β' -acetoxy allenates with 2-sulfonamido indoles, we began our investigation utilizing **2a** (0.20 mmol) and **6a** (0.24 mmol) in the presence of DABCO (20 mol %) at rt and obtained the tetrahydrocarboline **17aa** in just 30% yield (Table 9, entry 1). However, a better yield was observed at 50 °C (73%, entry 2). By switching the base to DBU, the reaction provided the completely aromatized α -carboline **18aa** (entry 3). Attempts using other tertiary amines like TBD and DMAP resulted in lower yields of **18aa** (entries 4 and 5). Overall, among the screened solvents, toluene provided the highest yield for both **17aa** (entries 2 and 6-8) and **18aa** (entries 3 and 11-14). At higher temperatures, the yield of **17aa** or **18aa** remained essentially unaltered (entries 9 and 15). The desired carboline **18aa** was isolated only in 45% yield at rt (entry 10) using DBU as the base.

Table 9. Optimization of reaction conditions for the synthesis of 17aa and 18aa^{a-c}



Entry	Base	Solvent	Temperature (°C)	Time (h)	Yield ^b 17aa:18aa	dr for 17aa
1	DABCO	PhMe	25	6	30:00	-19:1
2	DABCO	PhMe	50	6	73:00	-19:1
3	DBU	PhMe	50	6	00:85	-
4	TBD	PhMe	50	6	00:70	-
5	DMAP	PhMe	50	6	00:27	
6	DABCO	DCE	50	6	41:00	-19:1
7	DABCO	Dioxane	50	6	37:00	-19:1
8	DABCO	THF	50	6	35:00	-19:1

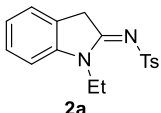
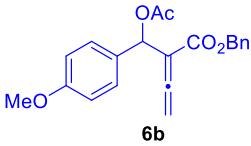
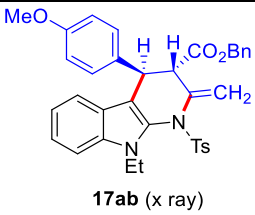
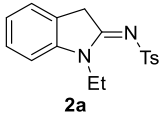
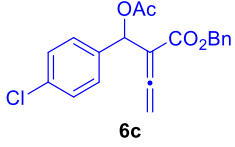
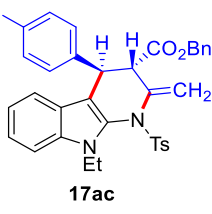
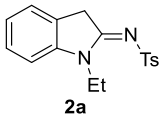
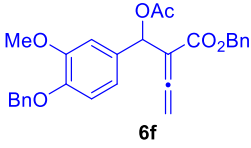
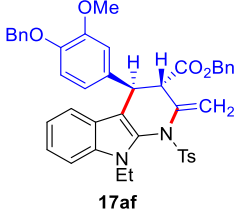
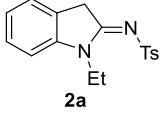
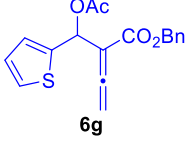
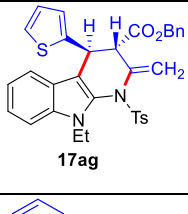
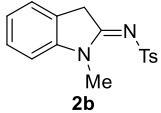
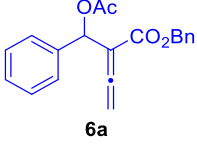
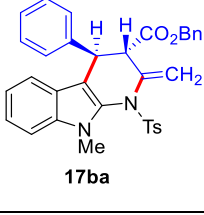
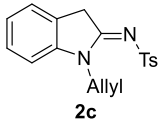
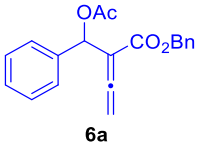
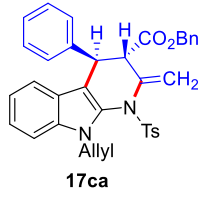
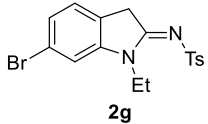
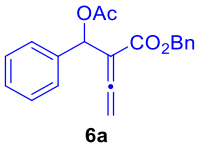
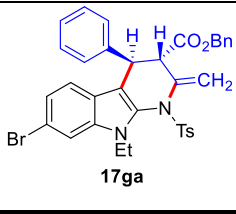
9	DABCO	Toluene	110	6	73:00	-19:1
10	DBU	PhMe	25	6	00:45	-
11	DBU	DMF	50	6	00:58	
12	DBU	Dioxane	50	6	00:48	
13	DBU	DCE	50	6	00:26	
14	DBU	THF	50	6	00:51	
15	DBU	PhMe	110	6	00:85	

^aReaction conditions: **2a** (0.20 mmol; 1.0 equiv.), **6a** (0.24 mmol; 1.2 equiv.), amine (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M). ^bIsolated yield. ^cDiastereomeric ratio of **17aa**.

Using the optimal conditions (Table 9, entry 2), different aryl groups such as Ph, 4-MeOC₆H₄, 4-ClC₆H₄, 3-MeO-4BnO-C₆H₃, and 2-thienyl at the β' -position of the allenolate **6a-c** and **6f-g** displayed good compatibility in reaction with **2a**, offering the products **17aa-ac**, **17af-ag** in 63-77% yields with excellent stereoselectivity (19:1 ratio) (Table 10). *N*-Alkyl substituted (**2b**, **2c**) and 6-Br (**2g**) substituted 2-imino-indolines were also viable with this DABCO catalyzed stereoselective annulation to produce **17ba-ca**, **17ga** in moderate to good yields (56-71%).

Table 10. Substrate Scope for the synthesis of tetrahydro-carbolines from 2-sulfonamido indoles and β' -acetoxy allenolates^a

Entry	2-Sulfonamido indole	β' -Acetoxy allenolate	Tetrahydro carboline	Yield ^b (%)
1	 2a	 6a	 17aa	73

2	 2a	 6b	 17ab (x ray)	77
3	 2a	 6c	 17ac	70
4	 2a	 6f	 17af	68
5	 2a	 6g	 17ag	63
6	 2b	 6a	 17ba	71
7	 2c	 6a	 17ca	67
8	 2g	 6a	 17ga	56

^aReaction conditions: **2a-c** or **2g** (0.20 mmol; 1.0 equiv.), **6a-c**, **6f**, or **6g** (0.24 mmol; 1.2 equiv.), DABCO (0.04 mmol; 0.2 equiv.), toluene (2.0 mL; 0.1 M) at 50 °C. ^bIsolated yield.

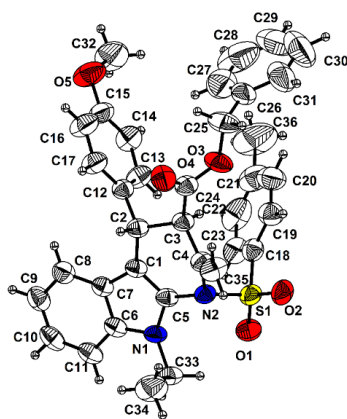
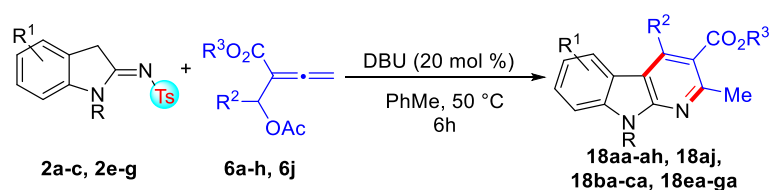


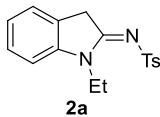
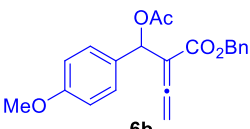
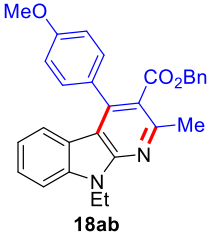
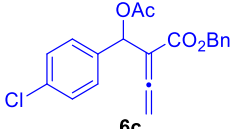
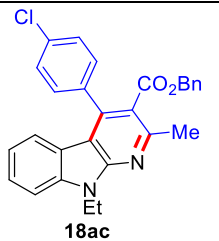
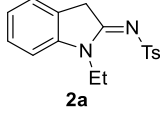
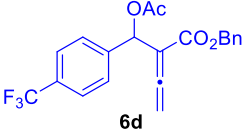
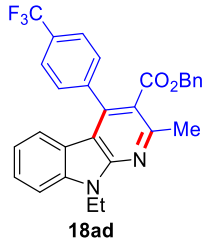
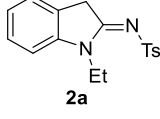
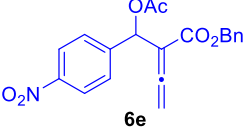
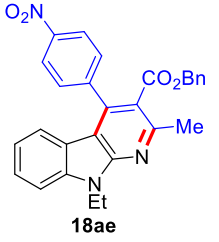
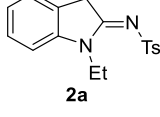
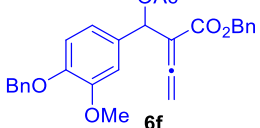
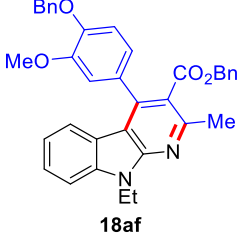
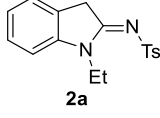
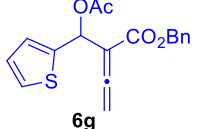
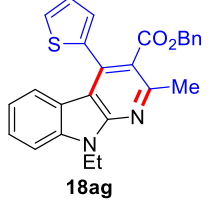
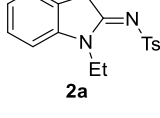
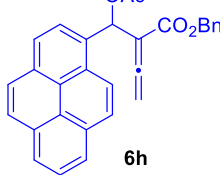
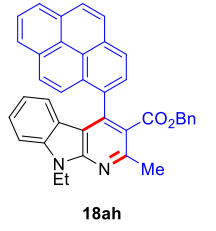
Figure 6: Molecular structure of compound **17ab**. Selected bond parameters: C(1)-C(2) 1.498(3), C(3)-C(2) 1.542(3), N(2)-C(4) 1.458(3), N(2)-C(5) 1.424(3). CCDC No. 2206245.

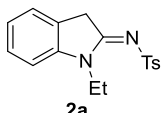
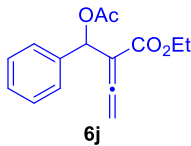
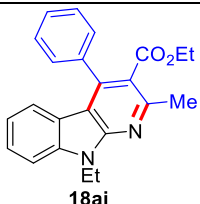
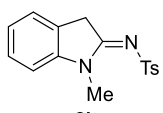
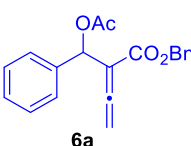
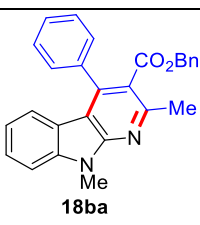
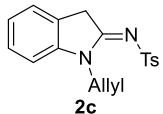
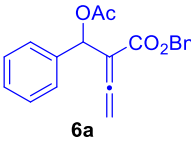
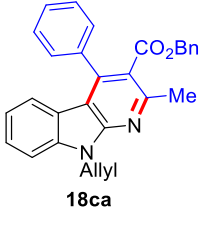
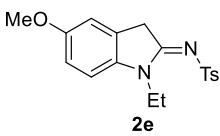
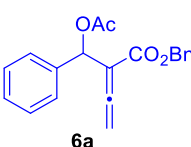
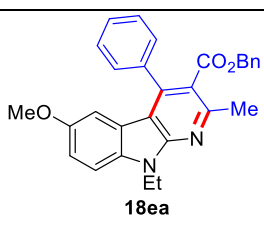
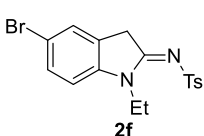
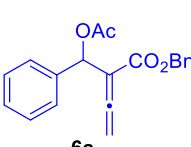
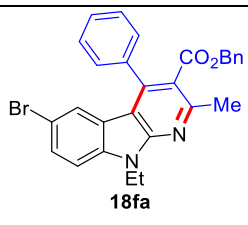
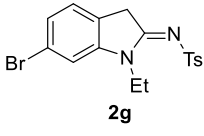
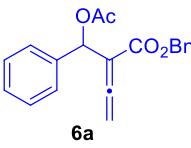
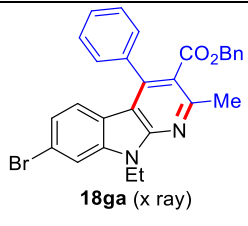
For the synthesis of carboline frameworks under DBU catalysis (*cf.* Table 9, entry 3), the vast array of functionalized β' -acetoxy allenates possessing different functionalities on the phenyl ring performed well to deliver the corresponding annulated products (Table 11). Thus, allenates **6a-e** worked efficiently with **2a** and offered carboline cores **18aa-ae** in good to high yields (69%-87%). The disubstituted (**6f**), hetero-aryl (**6g**) and polyaryl (**6h**) substrates were nicely involved in the annulation reaction and gave **18af-ah** in 75%, 71%, and 63% yields, respectively. The allenate **6j** also worked well and the product **18aj** was obtained in 76% yield. Other iminoindolines **2b-c** and **2e-g** worked smoothly in delivering the products **18ba-ca** and **18ea-ga** (59%-80%).

Table 11. Substrate scope for the synthesis of carbolines from 2-sulfonamido indoles and β' -acetoxy allenates^a



Entry	2-Sulfonamido indole	β' -Acetoxy allenate	Carboline	Yield ^b (%)
1	 2a	 6a	 18aa	85

2	 2a	 6b	 18ab	87
3	 2a	 6c	 18ac	80
4	 2a	 6d	 18ad	77
5	 2a	 6e	 18ae	69
6	 2a	 6f	 18af	75
7	 2a	 6g	 18ag	71
8	 2a	 6h	 18ah	63

9	 2a	 6j	 18aj	76
10	 2b	 6a	 18ba	80
11	 2c	 6a	 18ca	73
12	 2e	 6a	 18ea	67
13	 2f	 6a	 18fa	63
14	 2g	 6a	 18ga (x ray)	59

^aReaction conditions: **2a-c** and **2e-g** (0.20 mmol; 1.0 equiv.), **6a-h** and **6j** (0.24 mmol; 1.2 equiv.), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 50 °C. ^bIsolated yield.

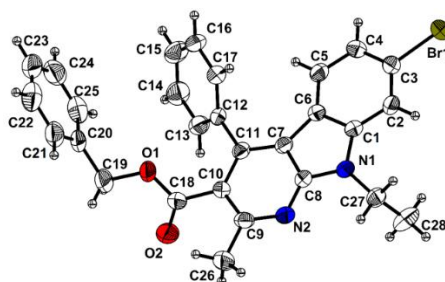
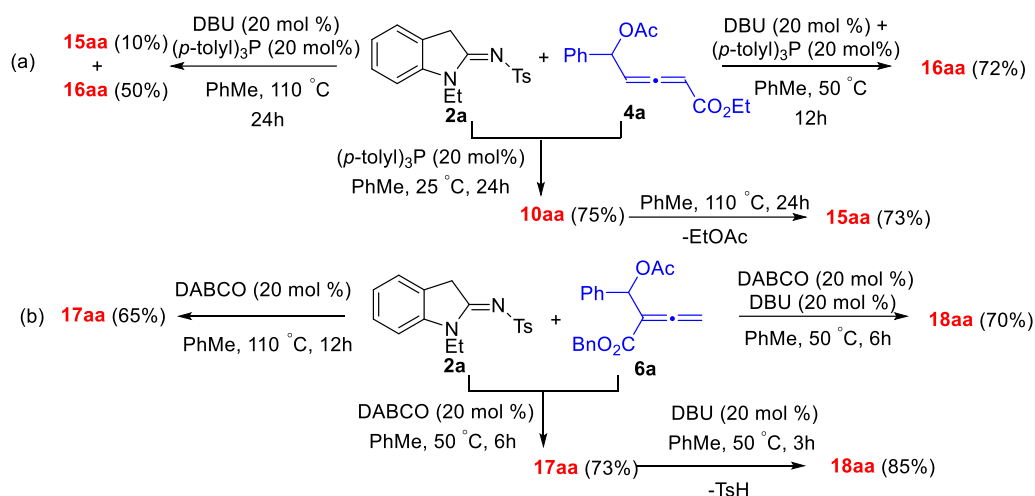


Figure 7: Molecular structure of compound **18ga**. Selected bond parameters: C(7)-C(11) 1.396(3), C(10)-C(11) 1.409(3), N(2)-C(9) 1.337(3), N(2)-C(8) 1.329(3). CCDC No. 2206246.

2.3.3 Control experiments

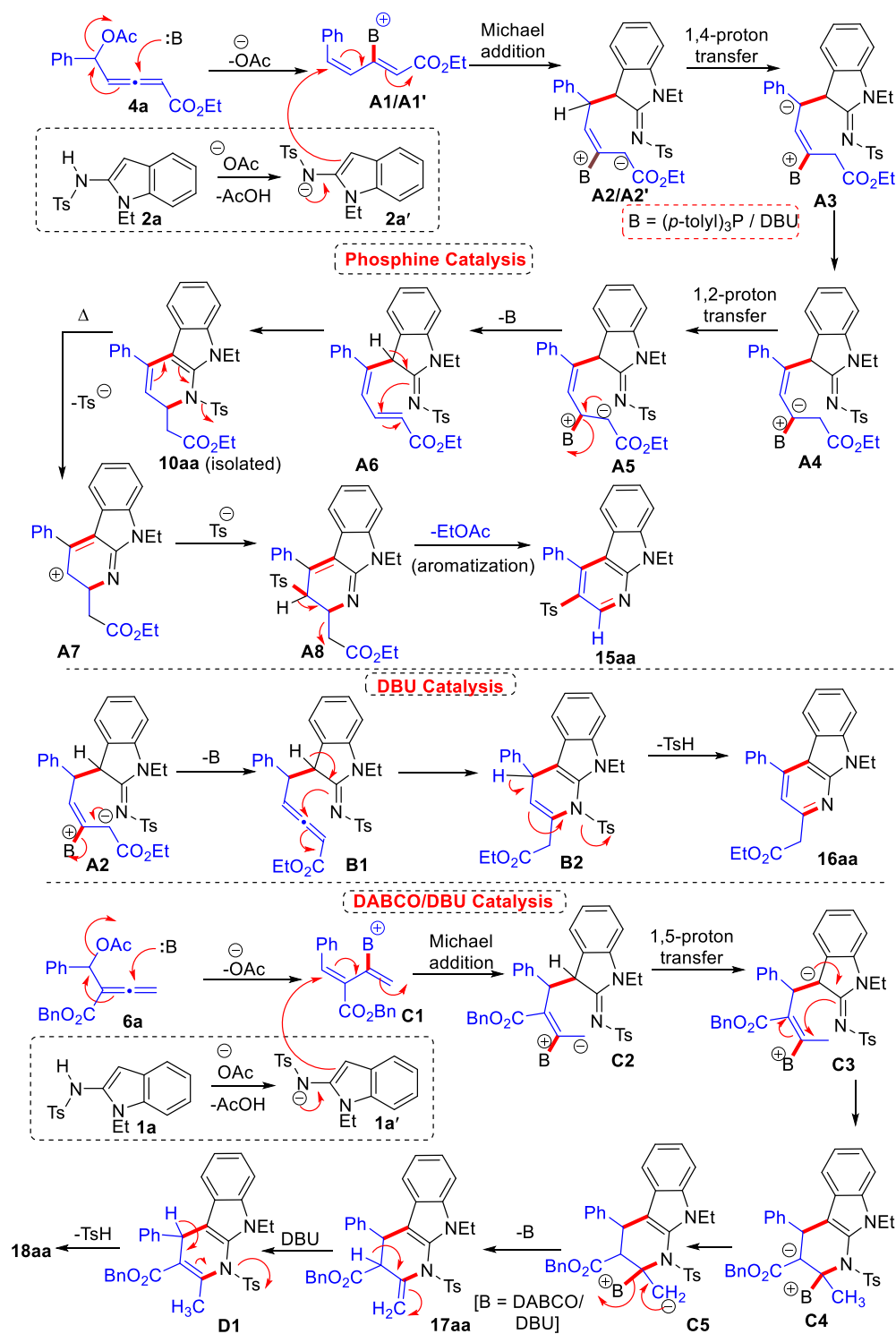
To elucidate the details of the reaction mechanism, we performed control experiments using **2a** and **4a** or **6a**. First, we tested the reaction using a combination of DBU and (*p*-tolyl)₃P (each 20 mol %) at two different temperatures (50 °C and 110 °C) (Scheme 9a). Only **16aa** was obtained in 72% yield at 50 °C; product **16aa** (50%) was obtained along with **15aa** (10%) at 110 °C (Scheme 9a). This study indicated that DBU overrides (*p*-tolyl)₃P in this reaction. Next, intermediate **10aa** was isolated in 75% yield at rt^{13g} and was converted to the corresponding carboline **15aa** by simply heating at 110 °C in toluene. Next, we examined a reaction between **2a** and **6a** using DABCO+DBU (each 20 mol%) and obtained the corresponding aromatized carboline derivative **18aa** in 70% yield (Scheme 9b); the use of only DABCO gave **17aa** (65%). The isolated **17aa** was also transformed into **18aa** using DBU at 50 °C after 3h. These experiments suggest that **15aa** is formed *via* **10aa** and **18aa** is formed *via* **17aa**. In a competitive sense, DBU overrides phosphine or DABCO.



Scheme 9: Control experiments

2.3.4 Proposed mechanistic pathways for phosphine and DBU catalysis

Based on the control experiments and previous literature,^{13g} plausible pathways for the formation of **15aa**, **16aa**, **17aa**, and **18aa** are shown in Scheme 10. These hetero-annulations may be initiated through the formation of diene-phosphonium/ ammonium intermediate **A1**, **A1'/ C1** via the addition-elimination process between Lewis base (tertiary amine or phosphine) and **4a** {**A1**: B = tri(*p*-tolyl)phosphine, found [M + H]⁺ 506.2366, **A1'**: B = DBU, found [M + H]⁺ 354.2294, **C1** (positive ion): B = DBU, [M]⁺ 445.2484}. Next, the addition of **2a'** (*in situ* generated from **2a**) to **A1**, **A1'/C1** at the δ -carbon gives zwitterionic intermediate **A2**, **A2'/ C2** {**A2**: B = tri(*p*-tolyl)phosphine, found [M + H]⁺ 819.3384, **A2'**: B = DBU, found [M + H]⁺ 668.3400, **C2**: B = DBU, found [M + H]⁺ 759.3580}. In the phosphine-catalyzed (3 + 3) annulation, **A2** undergoes 1,4-proton transfer rather than 1,2-elimination and affords **A3**. Subsequently, double bond isomerization followed by proton transfer, phosphine elimination, and 6-*exo-trig* cyclization leads to **10aa** {**10aa**: B = tri(*p*-tolyl)phosphine, found [M + H]⁺ 515.1990}. Next, the elimination of tosyl-anion from intermediate **10aa** gives **A7**. Instantly, the cationic intermediate **A7** attracts the *in situ* generated tosyl-anion at the γ -carbon atom to afford **A8**.⁶¹ Finally, C-C bond cleavage in intermediate **A8** delivers **15aa** via a *retro*-Mannich pathway under metal-free conditions.⁶² In sharp contrast to this, 1,2-elimination is dominates in DBU-catalysis and offers allenolate intermediate **B1** {**B1**: B = DBU, found [M + H]⁺ 515.2011}. In the end, 6-*exo-dig* cyclization and aromatization occurred to deliver **16aa**. In the case of β' -acetoxy allenolate, **C2** is involved in 1,5-proton transfer, 6-*endo-trig* cyclization, 1,3-proton transfer, and base elimination to provide **17aa**. DBU is stronger base than DABCO.¹¹ Hence **17aa** underwent rearrangement and TsH⁶³ elimination via **D1** and produced **18aa** exclusively. In the case of DBU catalysis, there is also a chance of **C4** going directly to **D1** leading to the formation of **18aa** via aromatization.



Scheme 10: Plausible pathways for the formation of 15aa, 16aa, 17aa, and 18aa

2.3.5 Photophysical properties of carbolines

To highlight the utility of the synthesized compounds, UV-visible and fluorescence spectra were recorded for the compounds **16aa**, **16ab**, **16ac**, **16ak**, **16an**, and **16ao**. The emission spectra of the compounds were recorded upon excitation at 300 nm and showed excellent fluorescence emission intensity. The molar extinction coefficient, (ϵ) absorption peak wavelength at which ϵ is calculated (λ_{abs}), and emission maxima of the compound (λ_{em}), excitation wavelength (λ_{ex}) in solution have been summarized in Table 12 and Figure 6.

Table 12. UV-visible absorption and fluorescence emission data for selected carbolines

Entry	Compound	λ_{abs} (nm)	$\epsilon(10^4 \text{ M}^{-1}\text{cm}^{-1})$	λ_{ex} (nm)	λ_{em} (nm)
1	16aa	300	1.17	300	406
2	16ab	300	1.09	300	399
3	16ac	300	1.19	300	412
4	16ak	300	1.06	300	424
5	16an	300	1.10	300	397
6	16ao	300	1.14	300	422

The absorption wavelength at which ϵ is calculated, molar extinction coefficient, excitation wavelength, emission maxima of the compound at room temperature in chloroform at concentration 10^{-5} M.

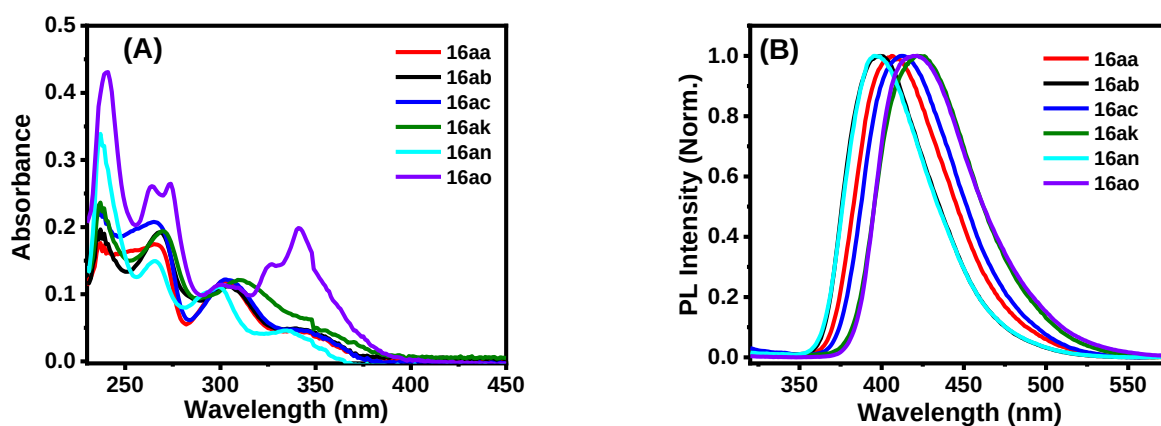
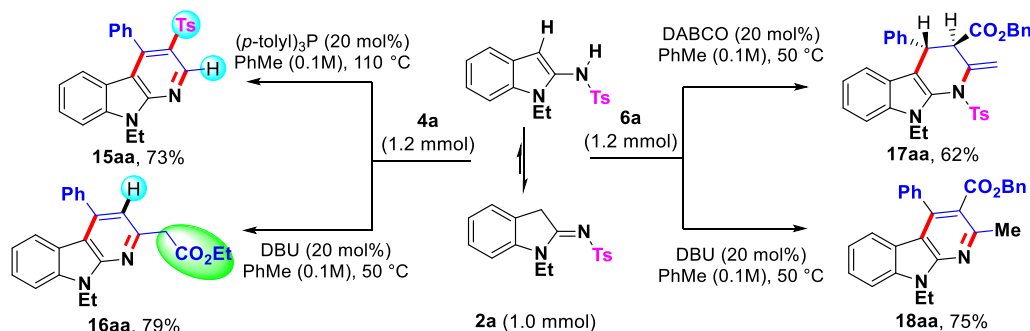


Figure 8: (A) Absorbance and (B) fluorescence emission spectra of compounds **16aa**, **16ab**, **16ac**, **16ak**, **16an**, and **16ao**

2.3.6 Scale-up experiments

The robustness of the (3 + 3) annulations is exemplified by 1.0 mmol scale reaction of **2a** with **4a** or **6a** under the optimized reaction conditions to obtain **15aa**, **16aa**, **17aa**, and **18aa** in high yields (Scheme 11).



Scheme 11: Scale-up experiments for the synthesis **15aa**, **16aa**, **17aa**, and **18aa**

2.4 Lewis-base dependent (3 + 3) annulations of acetoxy allenoates with Boc-protected oxindole, benzofuranone, and pyrazolone: Synthesis of pyran scaffolds

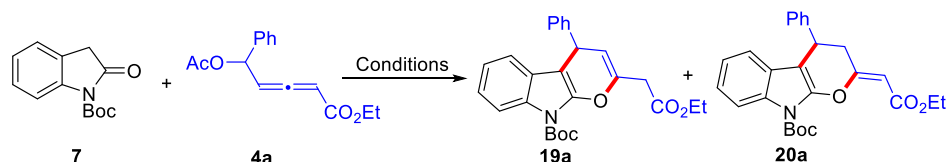
The introduction of the acetoxy group in the allenoate moiety was a breakthrough concept in allenoate chemistry. Nitrogen or phosphorus-based Lewis bases form diene-ammonium or phosphonium intermediates with allenoates making them electrophilic entities. A suitable nucleophile present in the vicinity can undergo an annulation reaction to afford carbo- or heterocycles.¹³⁻¹⁴ The presence of an active methylene group (e. g., oxindole, benzofuranone, pyrazolone) in the nucleophile plays a crucial role in the annulation. In the presence of Lewis bases such as DBU or DMAP, they can undergo (3 + 3) annulation reaction leading to the formation of pyran scaffolds. The results of these reactions are discussed below.

2.4.1 Synthesis of indole-fused pyrans and dihydropyrans from δ -acetoxy allenoates and *N*-Boc-oxindole

We started with the reaction of δ -acetoxy allenoate **4a** (0.24 mmol) with Boc-protected oxindole **7** (0.20 mmol) in the presence of DBU (20 mol %; 0.04 mmol) at rt (25 °C) for 1h (Table 12, entry 1). The product, indole-fused pyran **19a** was obtained in an excellent yield (87%). This result encouraged us to check other nitrogen containing bases such as DABCO, TBD, and Et₃N (entries 2-4). DABCO did not give any clear-cut product, but with TBD and Et₃N, we obtained the same product **19a** in low yields of 38 and 25%, respectively. Surprisingly

when we used DMAP base, we obtained dihydropyran **20a** in 85% yield with the complete exclusion of **19a** (entry 5). Several other solvents such as DMF, 1,4-dioxane, THF, and DCE have been examined for (entries 6-13), but toluene proved to be the best in both the cases. The increase in temperature (50 °C) (entries 14-15) or time (entries 16-17) did not alter the yield of the final product appreciably.

Table 13. Optimization of reaction conditions for 19a and 20a^a

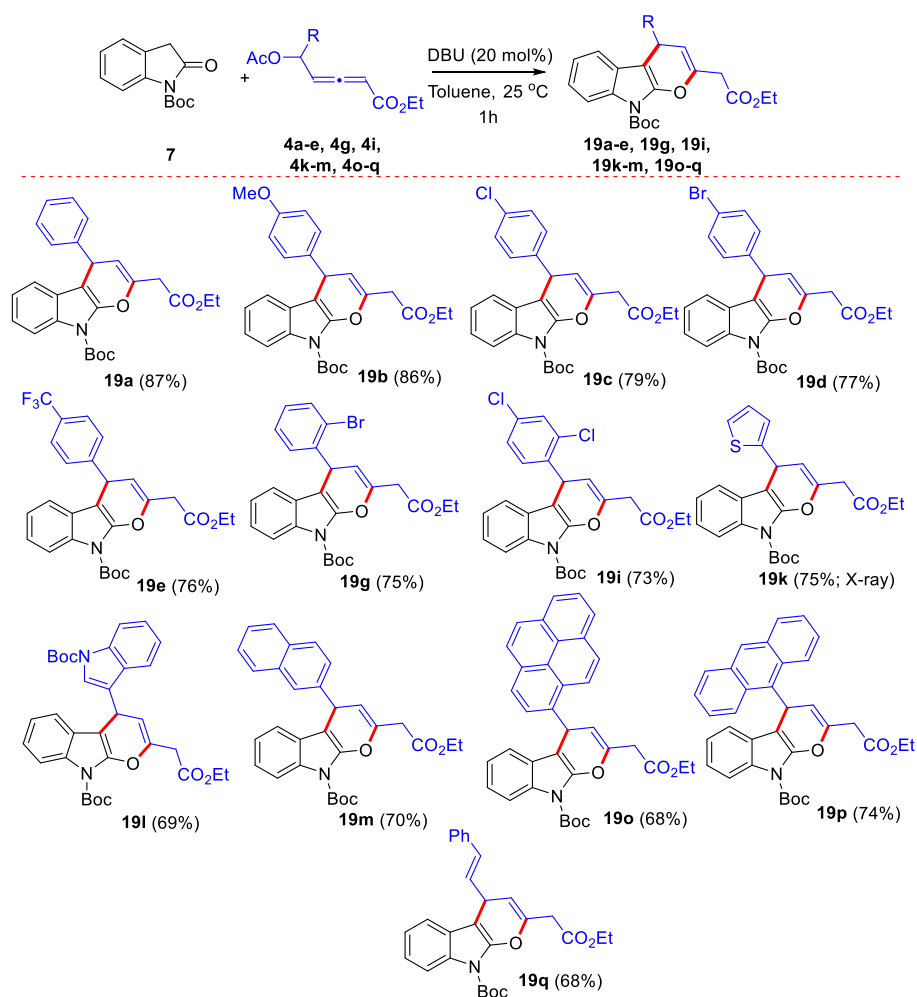


Entry	Base	Solvent	Temperature (°C)	Time (h)	Yield ^b 19a:20a
1	DBU	PhMe	25	1	87:00
2	DABCO	PhMe	25	1	NA
3	TBD	PhMe	25	1	38:00
4	Et ₃ N	PhMe	25	1	25:00
5	DMAP	PhMe	25	1	00:85
6	DBU	DMF	25	1	61:00
7	DBU	dioxane	25	1	45:00
8	DBU	THF	25	1	38:00
9	DBU	DCE	25	1	41:00
10	DMAP	DMF	25	1	00:65
11	DMAP	Dioxane	25	1	00:56
12	DMAP	THF	25	1	00:42
13	DMAP	DCE	25	1	00:28
14	DBU	PhMe	50	1	81:00
15	DMAP	PhMe	50	1	00:79
16	DBU	PhMe	25	6	80:00
17	DMAP	PhMe	25	6	00:82

^aReaction conditions: **2a** (0.20 mmol), **4a** (0.24 mmol), DBU or DMAP (0.04 mmol in solvent (2.0 mL)). ^bIsolated yield.

Using the optimized reaction conditions (*cf.* Table 13, entry 1), the scope and limitations

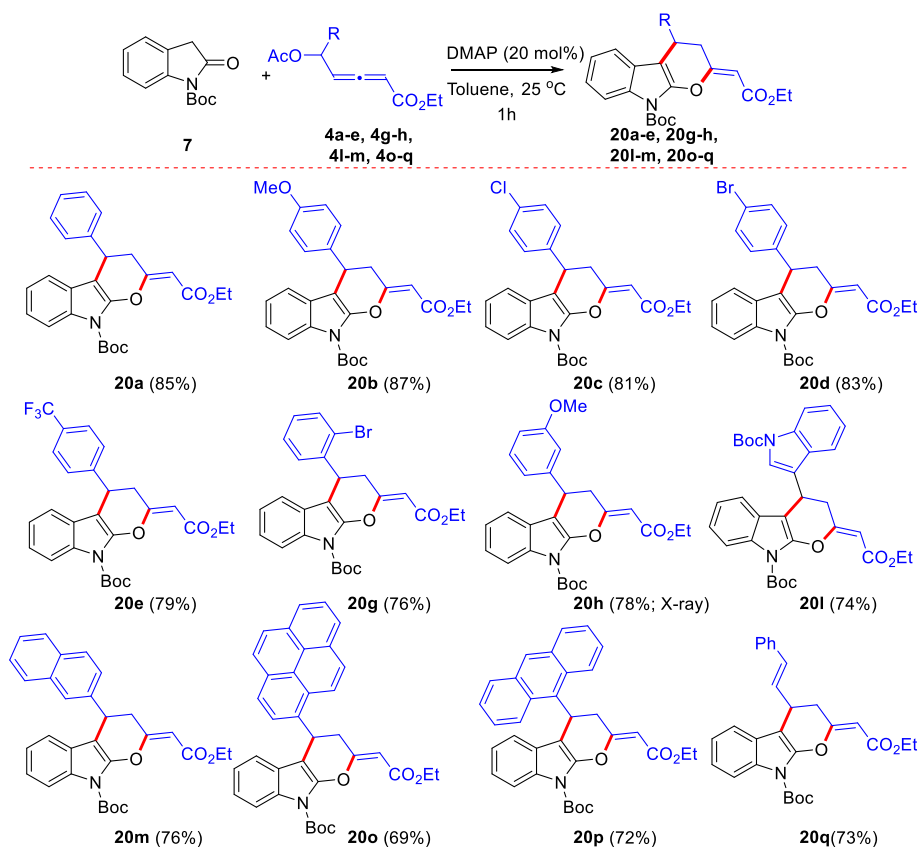
of (3 + 3) annulation leading to indole fused *pyrans* was investigated (Scheme 12). The reaction efficiency is not affected by the electronic factors at the *para*-position (H, MeO, Cl, Br, CF₃) of the aryl ring of the allenolate moiety, and the corresponding products **19a-e** are isolated in yields of 76-87%. The precursors with *ortho*-substitution (2-Br, 2,4-Cl₂) are also viable under the present protocol and offer the products **19g** and **19i** in 73-75% yield. The heteroaryl (thienyl, indolyl) and polyaryl substituted allenolates worked well to offer **19k** (X-ray), **19l-m**, and **19o-p** in good yields (68-75%). The cinnamyl substituted allenolate was also compatible with this protocol leading to **19q** in 68% yield.



Scheme 12: Substrate scope for the synthesis of indole -fused *pyrans* from *N*-Boc-oxindole and δ -acetoxy allenolates. Reaction conditions: **7** (0.20 mmol, 1.0 equiv.), **4a-e**, **4g**, **4i**, **4k-m**, or **4o-q** (0.24 mmol, 1.2 equiv.) and DBU (0.04 mmol, 0.02 equiv.) in toluene (0.1 M) at rt. Yields given are after isolation.

Next, we focussed on the synthesis of indole-fused *dihydropyrans* under DMAP catalysis (cf. Table 13, entry 5). Functionalized δ -acetoxy allenolates possessing different functionalities on the phenyl ring performed well to deliver the corresponding annulated

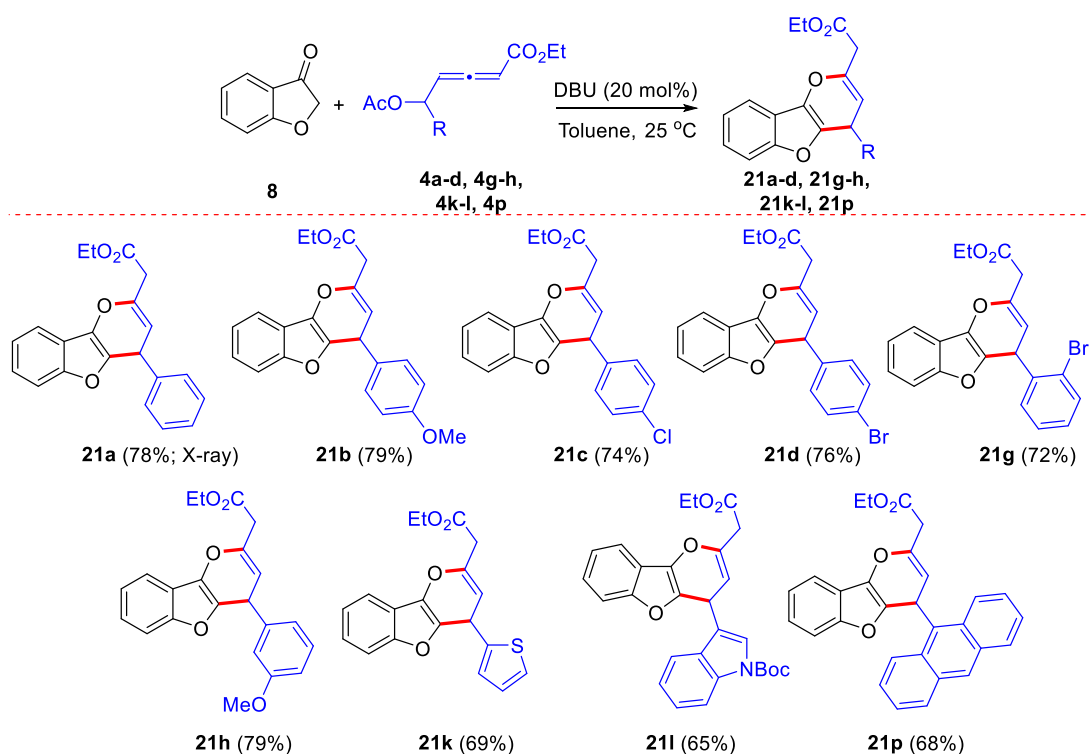
products (Scheme 13). The position of the substituents on the aryl ring of allenates (cf. **4a-e**) had no noticeable effect on the reactivity/yield and annulated products **20a-e** were obtained in high yields (79%-87%). Allenates with 2-/3-substituted aryl or indolyl (**4g-h**, **4l**) group also reacted smoothly with *N*-Boc-oxindole to afford **20g**, **20h** (X-ray), and **20l** in good yields (74-78%). The polyaryl (naphthyl, pyrenyl, anthracenyl) and cinnamyl allenates were also viable for the reaction leading to **20m**, and **20o-q** in good yields (69-76%).



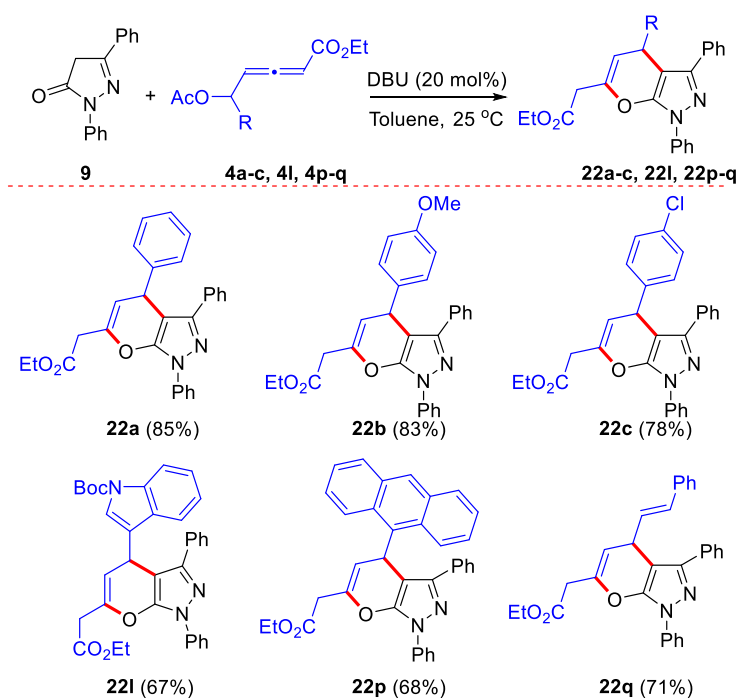
Scheme 13: Substrate scope for the synthesis of indole fused *dihydropyrans* from *N*-Boc-oxindole and δ -acetoxy allenates. Reaction conditions: **7** (0.20 mmol, 1.0 equiv.), **4a-e**, **4g-h**, **4l-m** or **4o-q** (0.24 mmol, 1.2 equiv.) and DMAP (0.04 mmol, 0.20 equiv.) in toluene (0.1 M) at rt (25 °C). Yields are after isolation.

2.4.2 Synthesis of benzofuran-fused pyrans and pyrazole-fused pyrans using δ -acetoxy allenates

We extended the above reaction of δ -acetoxy allenates with benzofuranone **8** and pyrazolone **9** by using the standard reaction conditions (Schemes 14-15). Here again, the yields of the products **21a** (X-ray), **21b-d**, **21g-h**, **21k-l**, **21p** and **22a-c**, **22l**, **22p-q** were good in all the cases, showing the reaction is fairly general. X-ray structures for the products (**19k**, **20h**, and **21a**,) have been determined (Figure 9).



Scheme 14: Substrate scope for the synthesis of benzofuran-fused pyrans. Reaction conditions: **8a** (0.20 mmol; 1.0 equiv.), **4a-d, 4g-h, 4k-l** or **4p** (0.24 mmol; 1.2 equiv.), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 25 °C. Yields given are after isolation.



Scheme 15: Synthesis of pyrazole fused pyran from pyrazolone and δ -acetoxy allenoate
 Reaction conditions: **9** (0.20 mmol; 1.0 equiv.), **4a-c**, **4l**, **4p-q** (0.24 mmol; 1.2 equiv.), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 25 °C. Yields given are after isolation.

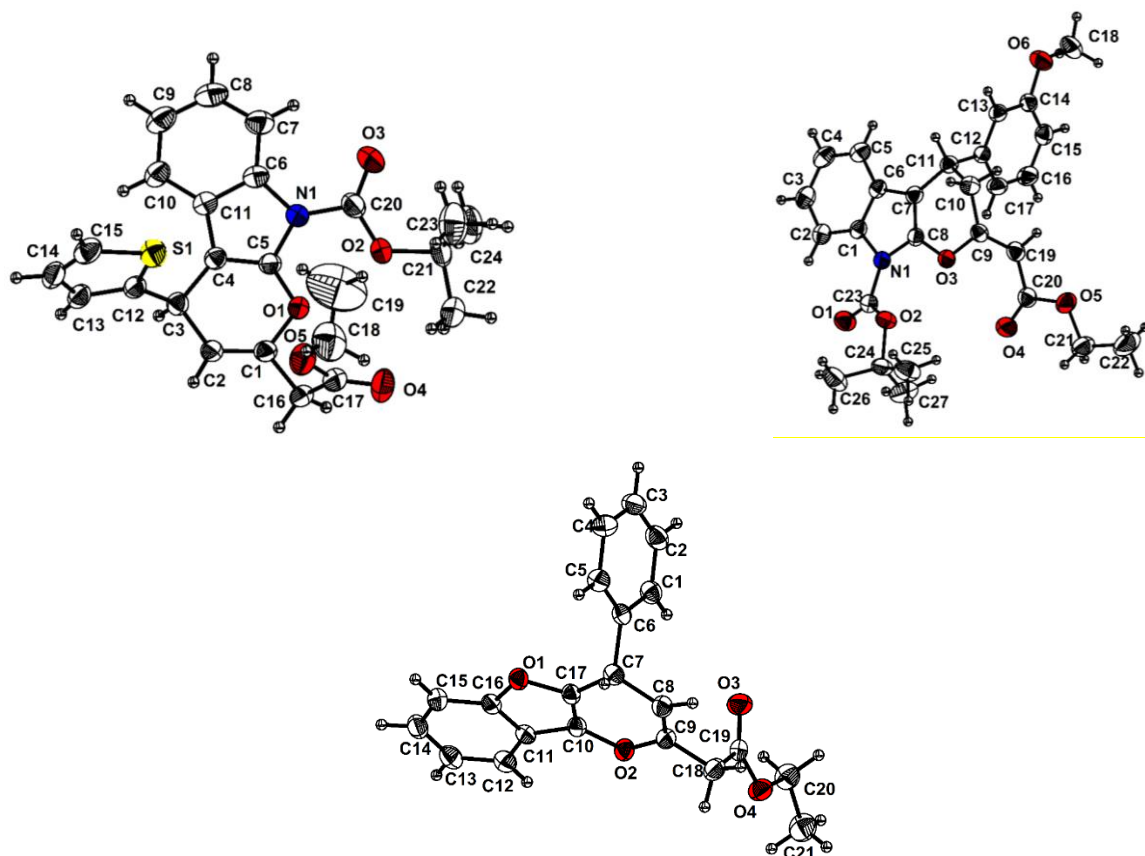
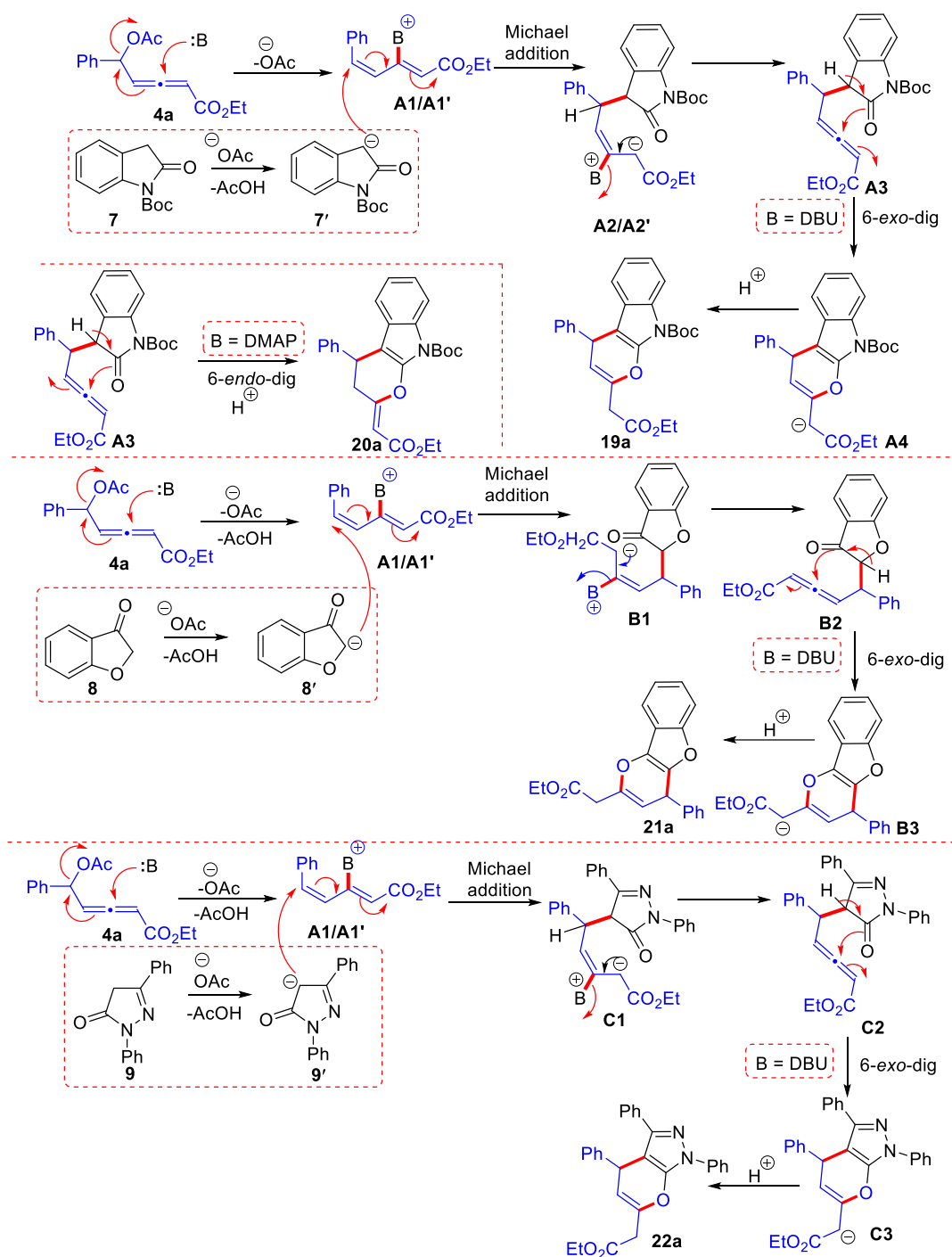


Figure 9: Molecular structures of compounds **19k** (top left), **20h** (top right), and **21a** (bottom).

2.4.3 Proposed mechanistic pathways for DBU and DMAP catalysis

Plausible pathways for the (3 + 3) annulations are shown in Scheme 16. These hetero-annulations may be initiated through the formation of diene-ammonium intermediate **A1**, **A1'** via the addition-elimination process between Lewis base (tertiary amine) and **4a** {**A1**: B = DBU, **A1'**: B = DMAP}. Next, the addition of **7'** (*in situ* generated from **7**) to **A1** or **A1'** at the δ -carbon gives zwitterionic intermediate **A2** or **A2'** {**A2**: B = DBU, **A2'**: B = DMAP}. Next, base will be eliminated leading to the formation of allenic intermediate **A3**. In case of DBU catalysis, 6-*exo*-dig cyclization will occur for the ring closure to form the final compound **19a** whereas the DMAP catalysis will lead to product **20a** via 6-*endo*-dig cyclization. In the case of **8/9**, in the presence of DBU base, at first diene-ammonium intermediate **A1** will form. Next, the addition of **8'/9'** (*in situ* generated from **8/9**) to **A1** at the δ -carbon gives zwitterionic intermediate **B1/C1**. Subsequently, the base is eliminated from **B1/C1** leading to allenic

intermediate **B2/C2**. Finally, ring closing 6-*exo*-dig cyclization will occur for both cases to deliver products **21a** and **22a**.



Scheme 16: Plausible pathways for the formation of **19a**, **20a**, **21a**, and **22a**

Summary (PART-A)

- (1) We have developed phosphine-catalyzed divergent annulations utilizing β' / δ -acetoxy allenates (as carbo-electrophiles) and 2-sulfonamidoindoles to obtain either carboline or spirocyclopentene motifs depending on the reaction conditions. In the temperature-dependent phosphine catalyzed (3 + 3) annulation, δ -acetoxy allenates act as β -, γ - and δ -carbon donors with 2-sulfonamidoindoles. At room temperature, 1,2-dihydro-carbolines are obtained in good yields; in sharp contrast, at a higher temperature (80 °C), tosyl migration and aromatization/ cascade process occurred to deliver α -carboline motifs with tosyl functionality at the γ -carbon.
- (2) In the phosphine catalyzed reaction of β' -acetoxy allenates with 2-sulfonamidoindoles, the latter substrates act as 1C synthons in a stereoselective (4 + 1) spiro-carbo-annulation to provide a novel class of spirocyclopentene carboxylates with excellent diastereomeric ratio (dr up to 20:1).
- (3) We have developed a Lewis base-dependent and mutually exclusive (3 + 3) annulation strategy for the construction of α -carbolines from acetoxy allenates and 2-imino-indoles. Thus in the phosphine catalyzed (3 + 3) annulation, C $_{\alpha}$ -C $_{\beta}$ bond of the δ -acetoxy allenate is cleaved, and tosyl cation migration, and elimination of -CH₂CO₂Et functionality occur in the formation of the products. In a similar reaction using DBU in place of the phosphine, 1,2-elimination is faster than proton shift and α -carbolines are obtained by the cleavage of C-H and N-S bonds.
- (4) Annulation involving β' -acetoxy allenates and 2-iminoindolines is tertiary amine dependent and mutually exclusive. The use of DABCO leads to tetrahydrocarbolines with excellent stereoselectivity while DBU catalyzed reaction involves rearrangement and TsH elimination to produce aromatized β -methyl- α -carboline frameworks.
- (5) We have also developed tertiary amine catalyzed (3 + 3) annulation for the construction of pyran scaffolds from δ -acetoxy allenates and *N*-Boc-oxindole, benzofuranone or pyrazolone in the absence of metal. In the reaction of δ -acetoxy allenates with *N*-Boc-oxindole, the use of a catalytic amount of DBU led to the formation of indole-fused pyrans whereas the use of DMAP resulted in indole-fused dihydropyrans. In a similar manner, use of δ -acetoxy allenates and benzofuranone or pyrazolone led to benzofuran-fused pyrans or pyrazole-fused pyrans, respectively.

EXPERIMENTAL SECTION

General information: Chemicals and solvents were procured from Aldrich or local manufacturers. Further purification of solvents was done according to standard procedures wherever required.⁶⁴ All operations, unless otherwise specified, were carried out under dry nitrogen atmosphere using standard vacuum line techniques.⁶⁵

Melting point: Melting points were determined using a SUPERFIT hot stage apparatus and are uncorrected.

Elemental analyses: Elemental analyses were carried out on a Perkin-Elmer 240C CHN or Thermo Finnigan EA1112 CHNS analyzer.

Infrared spectroscopy: IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer.

NMR spectroscopy: NMR spectra were recorded using 5 mm tubes on a Bruker 400 MHz [¹H and ¹³C{¹H}] operating at 400 and 100 MHz, respectively] or 500 MHz [¹H, ¹³C{¹H} and ¹⁹F operating at field strengths: 500, 125 and 470 MHz, respectively] NMR spectrometer in CDCl₃ solution (unless specified otherwise) with shifts referenced to SiMe₄ (¹H, ¹³C) and CFCl₃ (¹⁹F) ($\delta = 0$), respectively. All *J* values are in Hz.

LC-MS and HRMS: LC-MS equipment was used to record mass spectra for isolated compounds where appropriate. LC-MS data were obtained using electrospray ionization (positive mode) on a C-18 column. Mass spectra were recorded using HRMS (ESI-TOF and ESI-EXACTIVE ORBITRAP analyzer) equipment.

2-Sulfonamidoindoles **2a-h** were prepared using *N*-alkylated indoles **1a-h** and tosyl azide following a literature procedure.^{41c} *N*-Boc protected sulfonamido indole **2i** was prepared using Chang's method.⁵⁴ δ -Acetoxy allenates^{13d, 55} and β' -acetoxy allenates⁵⁶ were prepared using literature procedure. Among sulfonamido indoles, **2g** and **2i** are new and among β' -acetoxy allenates **6a-d**, **6g-I** are new. The solvent/s of crystallization for all the products was ethyl acetate-hexane (ca 4:1 v/v).

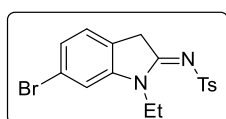
Steady-state optical measurements: UV-Vis absorption and photoluminescence (PL) spectra were recorded using Cary 100 (Varian) spectrophotometer and FluoroLog-3 (Horiba Jobin Yvon) spectrofluorimeter, respectively. For these measurements, a dilute colloidal solution of the samples (optical density of < 0.10 at the excitation wavelengths in 1 cm path length cuvette) was used.

3.1 Synthesis of starting materials

3.1.1. Synthesis of *N*-(6-bromo-1-ethylindolin-2-ylidene)-4-methylbenzenesulfonamide **2g**^{13g}

An oven-dried 25 mL round-bottomed flask was charged with 6-bromo-1-ethyl-1*H*-indole (1.11 g, 5.0 mmol) and *p*-toluenesulfonyl azide (1.38 g, 7.0 mmol) in 10.0 mL of dry 1,4-dioxane under nitrogen atmosphere. The mixture was stirred with heating (oil bath temperature at 75-80 °C) for 18-24h and cooled. Addition of ethanol (40 mL) resulted in most of 2-sulfonamidoindole **2g** to crystallize/precipitate from the solution. The solvent was removed from the mother liquor and the residue purified by column chromatography on silica gel using ethyl acetate/hexane (1:4) as eluent to obtain 2-sulfonamidoindole **2g**.

Compound **2g**



Yield: 1.17 g (60%, brown solid, R_f = 0.53 (4:1 hexane/ethyl acetate)).

Mp: 137-139 °C.

IR (neat): 3056, 2985, 2945, 2907, 2306, 1735, 1566, 1445, 1374, 1266, 1246, 1156, 1102, 1046, 943, 897, 848, 743, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.89-7.88 (m, 2H), 7.31 (d, J = 7.5 Hz, 2H), 7.25 (dd, J = 8.0, 2.0 Hz, 1H), 7.20-7.19 (m, 1H), 7.11-7.10 (m, 1H), 4.17 (s, 2H), 3.89 (q, J = 7.5 Hz, 2H), 2.43 (s, 3H), 1.27 (t, J = 7.5 Hz, 3H) ppm.

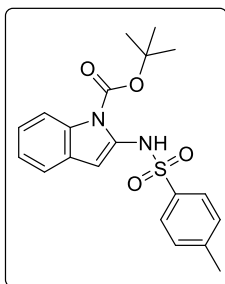
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 144.5, 142.9, 139.2, 129.4, 126.7, 126.3, 125.7, 125.5, 121.6, 112.6, 37.1, 35.9, 21.5, 11.9 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{17}\text{H}_{18}\text{BrN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 393.0267. Found: 393.0261.

3.1.2 Synthesis of *tert*-butyl 2-((4-methylphenyl)sulfonamido)-1*H*-indole-1-carboxylate **2i**.

An oven-dried 25 mL round-bottomed flask was charged with *tert*-butyl 1*H*-indole-1-carboxylate (500 mg, 2.30 mmol), 4-methylbenzenesulfonyl azide (500 mg, 2.54 mmol), AgNTf_2 (89.2 mg, 0.23 mmol) and AgOAc (76.7 mg, 0.26 mmol) in 5.0 mL of DCE. The mixture was stirred with heating (oil bath temperature at 40 °C) for 12h and cooled. The reaction mixture was cooled to room temperature and filtered through a plug of celite and then washed with EtOAc . The solvent was removed from the filtrate and the residue purified by column chromatography on silica gel using ethyl acetate/hexane (1:4) as the eluent to obtain 2-sulfonamidoindole **2e** as a white solid.

Compound 2i



Yield: 100.0 mg (13%, white solid, R_f = 0.53 (4:1 hexane/ethyl acetate)).

Mp: 145-147 °C.

IR (neat): 3244, 2979, 2931, 1705, 1598, 1453, 1371, 1330, 1210, 1157, 1089, 886, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.65 (s, 1H), 7.77-7.76 (m, 3H), 7.44 (d, J = 7.0 Hz, 1H), 7.24-7.16 (m, 4H), 6.56 (s, 1H), 2.38 (s, 3H), 1.65 (s, 9H) ppm.

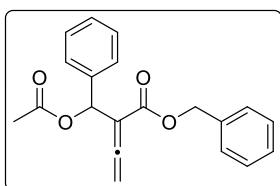
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 151.8, 144.2, 136.0, 133.7, 132.4, 129.7, 128.5, 127.4, 123.6, 123.2, 120.2, 115.2, 96.8, 86.2, 28.1, 21.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 387.1373. Found 387.1376.

3.1.3 General procedure for the synthesis of allenates 6a-d, and 6g-i

A literature procedure was followed.⁵⁶ To a solution of benzyl 2-(hydroxy-4-aryl/heteroaryl)buta-2,3-dienoate (10.0 mmol, 1.0 equiv) in dry dichloromethane (20 mL) at -5 °C was added pyridine (15.0 mmol, 1.5 equiv), and then the mixture stirred for 5.0 min at the same temperature. After that, acetyl chloride (15.0 mmol, 1.5 equiv) was slowly added into the mixture over 5 min, and the contents were stirred for 45 min. After completion of the reaction (TLC), the aqueous layer was extracted with dichloromethane (3 $\times$ 25 mL). Then the combined organic layer was washed with brine (2 $\times$ 20 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as the eluent.

Compound 6a



Yield: 1.84 g (57%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

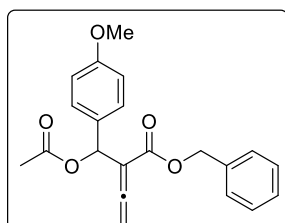
IR (neat): $\nu_{\max}$ 3019, 2400, 1968, 1738, 1713, 1601, 1523, 1499, 1461, 1424, 1372, 1215, 1090, 1025, 979, 929, 853, 759, 698, 669 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.31-7.28 (m, 2H), 7.23-7.21 (m, 5H), 7.19-7.16 (m, 3H), 6.53-6.52 (m, 1H), 5.19 (d, J = 2.5 Hz, 1H), 5.17 (d, J = 2.5 Hz, 1H), 5.06 (d, J = 3.5 Hz, 2H), 1.95 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 213.8, 169.6, 164.7, 138.1, 135.7, 128.5, 128.4₁, 128.3₈, 128.2, 128.0, 127.4, 102.6, 82.3, 71.7, 66.8, 21.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{20}\text{H}_{18}\text{NaO}_4$ [$\text{M}^+ + \text{Na}$]: m/z 345.1097. Found 345.1091.

Compound 6b



Yield: 1.86 g (53%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

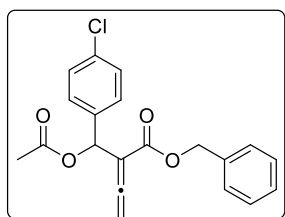
IR (neat): $\nu_{\max}$ 3019, 2961, 2839, 2400, 2254, 1969, 1713, 1612, 1514, 1462, 1424, 1373, 1216, 1176, 1091, 1029, 910, 854, 770, 669, 650 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.37-7.32 (m, 5H), 7.31-7.28 (m, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.59-6.58 (m, 1H), 5.35-5.33 (m, 2H), 5.19-5.17 (m, 2H), 3.82 (s, 3H), 2.07 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 213.5, 169.7, 164.8, 159.7, 135.7, 130.1, 128.9, 128.5, 128.2, 128.0, 113.8, 102.7, 82.3, 71.3, 66.8, 55.3, 21.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{20}\text{NaO}_5$ [$\text{M}^+ + \text{Na}$]: m/z 375.1203. Found 375.1204.

Compound 6c



Yield: 1.99 g (56%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

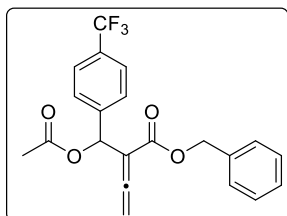
IR (neat): $\nu_{\max}$ 3054, 2986, 2308, 1742, 1712, 1498, 1425, 1265, 1090, 1026, 896, 743 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.36-7.30 (m, 9H), 6.60-6.59 (m, 1H), 5.35 (d, J = 2.5 Hz, 1H), 5.32 (d, J = 2.5 Hz, 1H), 5.19 (d, J = 4.5 Hz, 2H), 2.09 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 213.6, 169.4, 164.6, 136.7, 135.6, 134.2, 128.7, 128.6, 128.5, 128.2, 128.0, 102.3, 82.4, 71.0, 66.9, 21.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{20}\text{H}_{18}\text{ClO}_4$ [$\text{M}^+ + \text{H}$]: m/z 357.0888. Found 357.0875.

Compound 6d



Yield: Yield 2.30 g (60%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 3019, 2400, 2254, 1969, 1742, 1712, 1422, 1374, 1326, 1216, 1170, 1131, 1067, 1019, 909, 856, 760, 668, 650 cm^{-1} .

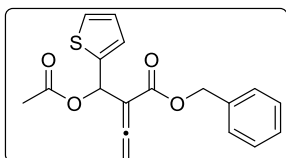
^1H NMR (500 MHz, CDCl_3): δ 7.62-7.60 (m, 2H), 7.53-7.52 (m, 2H), 7.37-7.34 (m, 3H), 7.31-7.30 (m, 2H), 6.68 (s, 1H), 5.36-5.35 (m, 1H), 5.33 (d, J = 1.5 Hz, 1H), 5.21-5.20 (m, 2H), 2.11 (s, 3H) ppm.

^{19}F NMR (470 MHz, CDCl_3): δ -62.6 ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 213.8, 169.4, 164.5, 142.1, 135.5, 130.4 (q, $^2J_{\text{C-F}}$ = 32.4 Hz), 128.5, 128.3, 128.0, 127.5, 125.4 (q, $^3J_{\text{C-F}}$ = 3.6 Hz), 124.0 (q, $^1J_{\text{C-F}}$ = 270.3 Hz), 102.1, 82.6, 71.0, 67.0, 20.9 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{17}\text{F}_3\text{NaO}_4$ [$\text{M}^+ + \text{Na}$]: m/z 413.0971. Found 413.0970.

Compound 6g



Yield: 1.87 g (57%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

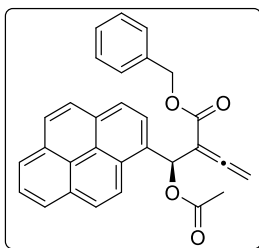
IR (neat): ν_{max} 3019, 2400, 2254, 1969, 1739, 1713, 1601, 1531, 1424, 1373, 1216, 1092, 1022, 909, 855, 769, 669, 650 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.38-7.28 (m, 6H), 7.13 (d, J = 3.0 Hz, 1H), 6.99-6.97 (m, 1H), 6.91 (s, 1H), 5.41 (s, 2H), 5.22-5.21 (m, 2H), 2.09 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 213.3, 169.4, 164.5, 141.0, 135.6, 128.5, 128.2, 128.0, 126.9, 126.6, 126.0, 102.6, 82.9, 67.3, 66.9, 21.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{18}\text{H}_{17}\text{NaO}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 351.0662. Found: 351.0666.

Compound 6h



Yield: 2.0 g (45%) (45%, brown coloured solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 114-116 °C.

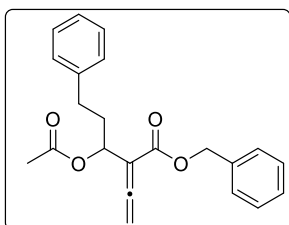
IR (neat): $\nu_{\max}$ 3019, 2400, 2253, 1970, 1714, 1611, 1528, 1477, 1423, 1374, 1216, 1091, 1022, 909, 850, 760, 669, 650 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.46-8.43 (m, 1H), 8.23-8.19 (m, 2H), 8.19-8.03 (m, 7H), 7.76-7.74 (m, 1H), 7.28-7.27 (m, 4H), 5.28-5.5.24 (m, 1H), 5.22-5.21 (m 2H), 5.14-5.11 (m, 1H), 2.15 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 214.3, 169.8, 164.9, 135.6, 131.4, 131.3, 131.1, 130.6, 128.4, 128.2, 128.1, 128.0, 127.8, 127.4, 126.1, 125.5, 125.4, 125.1, 124.9, 124.74, 124.67, 123.0, 102.8, 82.4, 69.5, 66.9, 21.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{26}\text{NO}_4$ [$\text{M}^+ + \text{NH}_4$]: m/z 464.1856. Found 464.1861

Compound 6i



Yield: 1.72 g (49%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

IR (neat): 3027, 2927, 2856, 2237, 1963, 1739, 1713, 1496, 1372, 1229, 1102, 1029, 752, 698 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.41-7.33 (m, 5H), 7.31-7.28 (m, 2H), 7.23-7.18 (m, 3H), 5.70-5.67 (m, 1H), 5.37-5.36 (m, 2H), 5.27-5.21 (m, 2H), 2.76-2.65 (m, 2H), 2.18-2.10 (m, 2H), 2.05 (s, 3H) ppm.

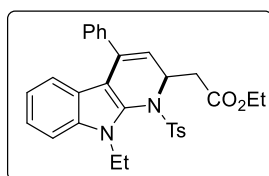
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 213.5, 170.0, 165.0, 141.2, 135.8, 128.5, 128.4, 128.3, 128.2, 128.0, 126.0, 101.6, 81.8, 69.9, 66.8, 35.1, 31.8, 21.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{22}\text{H}_{26}\text{NO}_4$ [$\text{M}^+ + \text{NH}_4$]: m/z 368.1856. Found: 368.1853.

3.2 General procedure for the synthesis of compounds 10aa-ac, 10ae, 10ah, 10aj-am, 10as, 10ba-da and 10fa-ga

A Schlenk tube was charged with 2-sulfonamido indole **2** (0.20 mmol), δ -acetoxy allenoate **4** (0.24 mmol), and toluene (2.0 mL). Subsequently, Ph_3P (0.04 mmol) was added to the contents at rt (25 °C), the mixture was stirred at the same temperature for 36h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). Then, the combined organic layer was washed with brine solution (20.0 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:9) as the eluent.

Compound 10aa



Yield: 85.4 mg (83%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 148-150 °C.

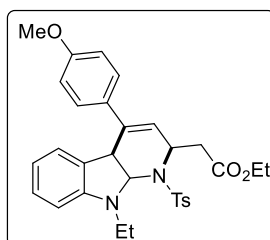
IR (neat): ν_{max} 3054, 2987, 1712, 1422, 1362, 1223, 1167, 896, 737, 706, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.46 (d, J = 8.5 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.30-7.27 (m, 1H), 7.27-7.21 (m, 3H), 6.96-6.92 (m, 5H), 6.82 (d, J = 8.0 Hz, 1H), 5.41-5.37 (m, 1H), 5.14 (d, J = 6.0 Hz, 1H), 4.72-4.65 (m, 1H), 4.45-4.38 (m, 1H), 4.26-4.18 (m, 2H), 2.48-2.38 (m, 2H), 2.13 (s, 3H), 1.49 (t, J = 7.0 Hz, 3H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.9, 144.3, 137.7, 136.1, 135.2, 134.0, 131.7, 129.0, 128.2, 127.9, 127.7, 122.9, 122.1, 120.7, 120.1, 116.1, 110.7, 105.6, 60.9, 55.4, 39.1, 37.9, 21.3, 14.7, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{31}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 515.1999. Found 515.2006.

Compound 10ab



Yield: 92.5 mg (85%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 155-157 °C.

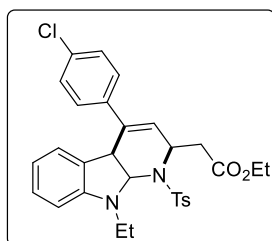
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1422, 1360, 1265, 1163, 896, 737, 706, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.48 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.26-7.23 (m, 1H), 6.98-6.96 (m, 3H), 6.91-6.88 (m, 3H), 6.80 (d, J = 8.5 Hz, 2H), 5.39 (q, J = 7.5 Hz, 1H), 5.08 (d, J = 5.5 Hz, 1H), 4.73-4.66 (m, 1H), 4.46-4.39 (m, 1H), 4.27-4.17 (m, 2H), 3.85 (s, 3H), 2.48-2.38 (m, 2H), 2.17 (s, 3H), 1.51 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.9, 159.3, 144.2, 135.6, 135.2, 134.1, 131.7, 129.1, 129.0, 128.8, 128.2, 126.1, 123.0, 122.0, 120.7, 120.0, 115.0, 113.1, 110.7, 105.8, 60.8, 55.3, 39.1, 38.0, 21.3, 14.7, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{33}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 545.2105. Found 545.2104.

Compound 10ac



Yield: 85.5 mg (78%, yellow solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 142-144 °C.

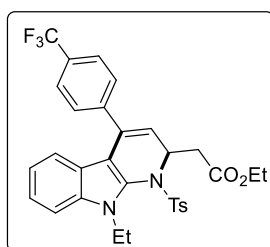
IR (neat): $\nu_{\max}$ 3054, 2986, 1731, 1598, 1535, 1492, 1440, 1422, 1360, 1265, 1168, 1090, 1016, 896, 738, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.49 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.26-7.23 (m, 3H), 7.01-6.97 (m, 3H), 6.92 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 8.0 Hz, 1H), 5.43-5.39 (m, 1H), 5.16 (d, J = 5.5 Hz, 1H), 4.73-4.66 (m, 1H), 4.45-4.41 (m, 1H), 4.25-4.18 (m, 2H), 2.49-2.38 (m, 2H), 2.18 (s, 3H), 1.51 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 144.3, 136.1, 135.2, 135.0, 134.0, 133.6, 131.9, 129.2, 129.0, 128.2, 127.9, 122.7, 122.2, 120.4, 120.3, 116.6, 110.8, 105.1, 60.9, 55.2, 39.2, 37.8, 21.4, 14.7, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{30}\text{H}_{30}\text{ClN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 549.1609. Found 549.1634.

Compound 10ad



Yield: 90.0 mg (77%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 156-158 °C.

IR (neat): $\nu_{\max}$ 3054, 2986, 1732, 1714, 1611, 1535, 1441, 1422, 1361, 1325, 1265, 1168, 1126, 1089, 1068, 1018, 896, 851, 744, 706, 666 cm^{-1} .

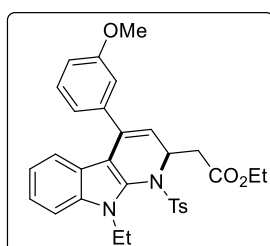
^1H NMR (500 MHz, CDCl_3): δ 7.53-7.50 (m, 3H), 7.41 (d, J = 8.5 Hz, 2H), 7.30-7.26 (m, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.02-6.99 (m, 1H), 6.97 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 1H), 5.45-5.41 (m, 1H), 5.23 (d, J = 5.5 Hz, 1H), 4.75-4.67 (m, 1H), 4.48-4.41 (m, 1H), 4.28-4.18 (m, 2H), 2.51-2.41 (m, 2H), 2.14 (s, 3H), 1.52 (t, J = 7.0 Hz, 3H), 1.33 (t, J = 7.0 Hz, 3H) ppm.

^{19}F NMR (470 MHz, CDCl_3): δ -62.5 ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.9, 144.5, 141.3, 135.3, 135.0, 134.1, 132.1, 130.0 (q, $^2J_{\text{C-F}}$ = 32.0 Hz), 129.2, 128.3, 128.2, 124.8 (q, $^3J_{\text{C-F}}$ = 3.5 Hz), 124.3 (q, $^1J_{\text{C-F}}$ = 270.5 Hz), 122.7, 122.5, 120.5, 120.4, 118.0, 111.0, 104.9, 61.1, 55.3, 39.4, 37.9, 21.4, 14.8, 14.4 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{31}\text{H}_{30}\text{F}_3\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 583.1873.
Found 583.1894.

Compound 10ah



Yield: 82.7 mg (76%, yellow solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 153-155 °C.

IR (neat): $\nu_{\max}$ 3054, 2986, 1738, 1712, 1422, 1360, 1265, 1167, 896, 739, 706, 666 cm^{-1} .

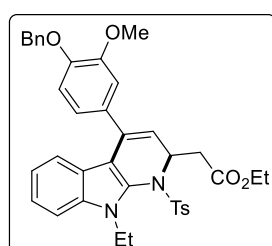
^1H NMR (500 MHz, CDCl_3): δ 7.48 (d, J = 8.5 Hz, 1H), 7.42 (d, J = 7.5 Hz, 2H), 7.26-7.23 (m, 1H), 7.20-7.17 (m, 1H), 7.00-6.96 (m, 3H), 6.90 (d, J = 8.0 Hz, 1H), 6.86-

6.84 (m, 1H), 6.56 (d, $J = 7.5$ Hz, 1H), 6.50 (s, 1H), 5.44-5.40 (m, 1H), 5.19-5.18 (m, 1H), 4.74-4.66 (m, 1H), 4.47-4.40 (m, 1H), 4.28-4.18 (m, 2H), 3.78 (s, 3H), 2.50-2.40 (m, 2H), 2.18 (s, 3H), 1.51 (t, $J = 7.0$ Hz, 3H), 1.34-1.32 (m, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.0, 159.2, 144.5, 139.3, 136.1, 135.3, 134.1, 131.7, 129.2, 128.9, 128.8, 128.3, 123.0, 122.2, 120.8, 120.6, 120.2, 116.3, 113.9, 113.1, 110.8, 61.0, 55.5, 55.3, 39.3, 38.0, 21.4, 14.8, 14.4 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{31}\text{H}_{33}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 545.2105.
Found 545.2126.

Compound 10aj



Yield: 97.5 mg (75%, yellow solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 132-134 °C.

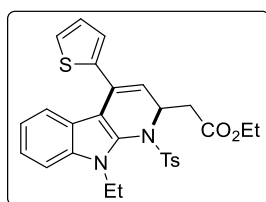
IR (neat): ν_{max} 3054, 2986, 1731, 1712, 1600, 1511, 1439, 1422, 1360, 1265, 1167, 1089, 1023, 896, 730 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.49-7.48 (m, 3H), 7.43-7.41 (m, 4H), 7.36-7.33 (m, 1H), 7.27-7.24 (m, 1H), 7.00-6.92 (m, 4H), 6.79-6.77 (m, 1H), 6.55 (s, 1H), 6.48 (d, $J = 8.0$ Hz, 1H), 5.41-5.38 (m, 1H), 5.23-5.17 (m, 2H), 5.13-5.12 (m, 1H), 4.71-4.65 (m, 1H), 4.45-4.40 (m, 1H), 4.27-4.18 (m, 2H), 3.81 (s, 3H), 2.48-2.38 (m, 2H), 2.10 (s, 3H), 1.51 (t, $J = 6.5$ Hz, 3H), 1.32 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.0, 148.8, 147.8, 144.2, 137.1, 135.7, 135.2, 134.1, 131.7, 131.0, 129.0, 128.6, 128.2, 128.0, 127.4, 122.9, 122.1, 120.8, 120.4, 120.1, 115.1, 113.2, 111.7, 110.7, 105.6, 71.0, 60.9, 56.0, 55.4, 39.1, 38.0, 21.4, 14.7, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{38}\text{H}_{39}\text{N}_2\text{O}_6\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 651.2523.
Found 651.2550.

Compound 10ak



Yield: 76.0 mg (73%, brown solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 135-137 °C.

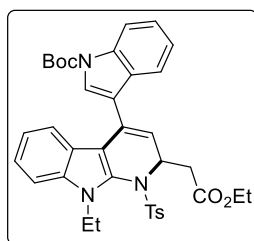
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1597, 1422, 1361, 1265, 1168, 1085, 896, 739, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.49 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.5 Hz, 2H), 7.30-7.26 (m, 1H), 7.20-7.18 (m, 2H), 7.05-7.03 (m, 1H), 6.99-6.97 (m, 3H), 6.75-6.74 (m, 1H), 5.36-5.32 (m, 1H), 5.19 (d, J = 6.0 Hz, 1H), 4.71-4.64 (m, 1H), 4.46-4.38 (m, 1H), 4.27-4.18 (m, 2H), 2.47-2.36 (m, 2H), 2.17 (s, 3H), 1.51 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 144.4, 140.0, 135.1, 133.8, 131.7, 129.3, 129.1, 128.0, 126.7, 126.6, 124.6, 122.7, 122.2, 120.7, 120.2, 116.8, 110.7, 105.2, 60.9, 55.1, 39.1, 37.6, 21.4, 14.7, 14.2 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{28}\text{H}_{29}\text{N}_2\text{O}_4\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 521.1563. Found 521.1581.

Compound 10al



Yield: 98.0 mg (75%, brown solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 114-116 °C.

IR (neat): $\nu_{\max}$ 3054, 2986, 2931, 1732, 1709, 1600, 1451, 1422, 1368, 1265, 1165, 1097, 1052, 896, 746, 706 cm^{-1} .

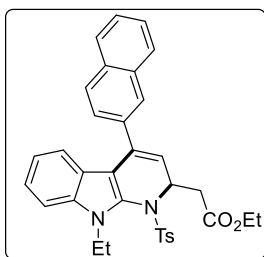
^1H NMR (500 MHz, CDCl_3): δ 8.14 (d, J = 7.0 Hz, 1H), 7.48-7.45 (m, 3H), 7.32-7.29 (m, 1H), 7.26 (s, 1H), 7.24-7.20 (m, 1H), 7.10-7.07 (m, 1H), 7.01 (d, J = 8.0 Hz, 1H), 6.97 (d, J = 8.0 Hz, 2H), 6.90-6.87 (m, 2H), 5.47-5.42 (m, 1H), 5.38 (d, J = 5.5 Hz, 1H), 4.74-4.67 (m, 1H), 4.48-4.41 (m, 1H), 4.30-4.21 (m, 2H), 2.57-

2.47 (m, 2H), 2.06 (s, 3H), 1.70 (s, 9H), 1.53 (t, $J = 7.0$ Hz, 3H), 1.34 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.9, 149.6, 144.3, 135.2, 135.1, 134.2, 131.4, 129.1, 128.9, 128.2, 127.3, 124.4, 124.3, 122.9, 122.5, 122.1, 120.9, 120.7, 120.2, 118.5, 116.5, 115.0, 110.6, 105.6, 84.0, 60.9, 55.3, 39.2, 38.2, 28.2, 21.3, 14.7, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{37}\text{H}_{40}\text{N}_3\text{O}_6\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 654.2632. Found 654.2635.

Compound 10am



Yield: 81.2 mg (72%, yellow solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 141-143 °C.

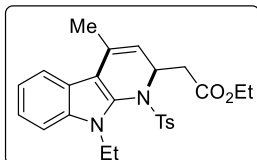
IR (neat): ν_{max} 3054, 2986, 1712, 1606, 1422, 1362, 1265, 1167, 896, 706, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.87-7.85 (m, 1H), 7.77-7.72 (m, 2H), 7.52-7.50 (m, 4H), 7.44 (d, $J = 8.0$ Hz, 2H), 7.27-7.24 (m, 1H), 7.07 (d, $J = 8.5$ Hz, 1H), 6.97-6.90 (m, 3H), 6.84 (d, $J = 8.0$ Hz, 1H), 5.49-5.45 (m, 1H), 5.29 (d, $J = 5.5$ Hz, 1H), 4.76-4.69 (m, 1H), 4.50-4.43 (m, 1H), 4.31-4.24 (m, 2H), 2.55-2.46 (m, 2H), 2.00 (s, 3H), 1.54 (t, $J = 7.0$ Hz, 3H), 1.35 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.0, 144.5, 136.2, 135.3₃, 135.3₁, 134.2, 133.1₄, 133.0₉, 132.0, 129.1, 128.4, 128.1, 127.8, 127.3, 126.9, 126.3, 126.1, 123.1, 122.3, 120.9, 120.3, 116.9, 110.9, 105.8, 61.1, 55.6, 39.3, 38.1, 21.4, 14.9, 14.4 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{34}\text{H}_{33}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 565.2156. Found 565.2179.

Compound 10as



Yield: 64.2 mg (71%, gummy liquid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

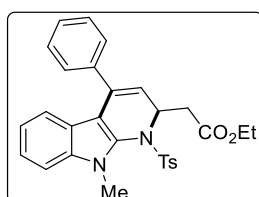
IR (neat): ν_{max} 2981, 1732, 1537, 1440, 1372, 1266, 1241, 1168, 1089, 1045, 733, 703 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.64 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 7.31-7.27 (m, 3H), 7.17-7.14 (m, 1H), 7.08 (d, J = 8.0 Hz, 2H), 5.13-5.09 (m, 1H), 4.72-4.65 (m, 2H), 4.38-4.31 (m, 1H), 4.25-4.14 (m, 2H), 2.44-2.39 (m, 1H), 2.37 (s, 3H), 2.35-2.30 (m, 1H), 1.75 (s, 3H), 1.45 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.1, 144.0, 135.0, 134.2, 130.7, 128.7, 128.2, 123.3, 121.9, 120.3, 120.0, 114.3, 110.9, 107.1, 60.8, 55.3, 39.1, 38.0, 21.5, 18.8, 14.6, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{25}\text{H}_{29}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 453.1843. Found 453.1846.

Compound 10ba



Yield: 84.0 mg (84%, yellow solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 125-127 $^\circ\text{C}$.

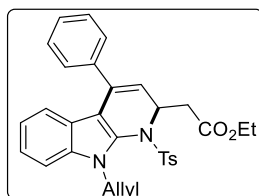
IR (neat): ν_{max} 3054, 2986, 1732, 1598, 1536, 1421, 1361, 1265, 1168, 1090, 1026, 896, 738, 705 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.46-7.40 (m, 3H), 7.33-7.26 (m, 4H), 7.01-6.98 (m, 5H), 6.86 (d, J = 8.0 Hz, 1H), 5.39-5.35 (m, 1H), 5.11 (d, J = 5.5 Hz, 1H), 4.29-4.17 (m, 2H), 3.95 (s, 3H), 2.48-2.40 (m, 2H), 2.16 (s, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.9, 144.3, 137.7, 136.2, 136.1, 134.1, 132.3, 129.1, 128.1, 127.9, 127.7, 122.4, 122.2, 120.5, 120.2, 115.7, 110.1, 105.2, 60.9, 55.5, 38.1, 31.1, 21.3, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{29}\text{H}_{29}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 501.1843. Found 501.1861.

Compound 10ca



Yield: 82.0 mg (78%, yellow solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 124-126 $^\circ\text{C}$.

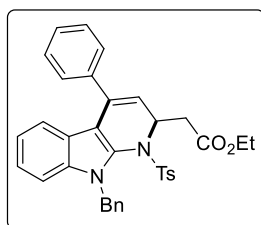
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1600, 1422, 1363, 1265, 1167, 896, 740, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.47 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 7.5 Hz, 2H), 7.30-7.25 (m, 3H), 7.24-7.21 (m, 1H), 6.99-6.95 (m, 5H), 6.83 (d, J = 8.0 Hz, 1H), 6.12-6.04 (m, 1H), 5.42-5.38 (m, 1H), 5.29-5.17 (m, 4H), 5.06-5.02 (m, 1H), 4.27-4.16 (m, 2H), 2.49-2.40 (m, 2H), 2.16 (s, 3H), 1.33 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.9, 144.3, 137.6, 136.0, 135.9, 134.1, 133.9, 131.9, 129.1, 128.2, 127.9, 127.8, 127.7, 122.8, 122.2, 120.6, 120.3, 117.4, 116.2, 111.4, 105.7, 60.9, 55.3, 47.3, 38.0, 21.3, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{31}\text{H}_{31}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 527.1999. Found 527.2019.

Compound 10da



Yield: 84.1 mg (73%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 124-126 $^{\circ}\text{C}$.

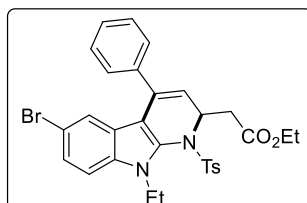
IR (neat): $\nu_{\max}$ 3053, 3020, 2986, 1722, 1607, 1422, 1265, 1216, 1169, 909, 738, 668, 650 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.43 (d, J = 7.5 Hz, 2H), 7.27-7.23 (m, 8H), 7.13-7.09 (m, 4H), 6.99-6.91 (m, 5H), 6.83 (d, J = 7.5 Hz, 1H), 5.93-5.90 (m, 1H), 5.59-5.55 (m, 1H), 5.30 (d, J = 6.0 Hz, 1H), 5.14 (d, J = 5.0 Hz, 1H), 4.11-4.06 (m, 2H), 2.15 (s, 3H), 1.20 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.0, 144.4, 137.6, 137.5, 135.9, 135.8, 134.0, 132.3, 129.1, 128.5, 128.2, 128.0, 127.7₃, 127.7₁, 127.3, 127.0, 122.8, 122.4, 120.6, 120.3, 116.7, 111.4, 106.1, 60.7, 55.1, 48.0, 37.8, 21.3, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{33}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 577.2156. Found 577.2157.

Compound 10fa



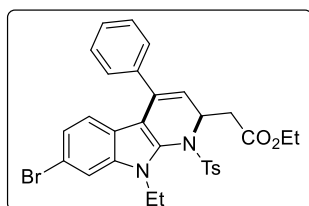
Yield: 87.6 mg (74%, brown solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).
Mp: 160-162 °C.
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1603, 1422, 1361, 1265, 1169, 896, 743, 705, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.40-7.39 (m, 2H), 7.36-7.27 (m, 5H), 6.99 (d, $J = 7.5$ Hz, 2H), 6.95-6.92 (m, 3H), 5.43-5.39 (m, 1H), 5.18 (d, $J = 5.5$ Hz, 1H), 4.74-4.67 (m, 1H), 4.43-4.36 (m, 1H), 4.29-4.18 (m, 2H), 2.48-2.40 (m, 2H), 2.17 (s, 3H), 1.49 (t, $J = 7.0$ Hz, 3H), 1.33 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.7, 144.5, 137.1, 135.6, 133.9, 133.8, 132.6, 129.1, 128.0₉, 128.0₅, 127.9, 127.7, 125.0, 124.4, 123.1, 116.6, 113.5, 112.1, 105.2, 60.9, 55.4, 39.4, 38.0, 21.3, 14.6, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{30}\text{H}_{30}\text{BrN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 593.1104
Found 593.1126.

Compound 10ga



Yield: 84.0 mg (71%, brown solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).
IR (neat): $\nu_{\max}$ 3054, 2986, 1732, 1711, 1603, 1422, 1371, 1265, 1168, 1090, 1025, 896, 739, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.63 (s, 1H), 7.40 (d, $J = 8.5$ Hz, 2H), 7.32-7.25 (m, 3H), 7.06-7.04 (m, 1H), 6.98 (d, $J = 8.0$ Hz, 2H), 6.93-6.92 (m, 2H), 6.68 (d, $J = 8.5$ Hz, 1H), 5.48-5.41 (m, 1H), 5.19 (d, $J = 6.0$ Hz, 1H), 4.73-4.65 (m, 1H), 4.41-4.34 (m, 1H), 4.28-4.20 (m, 2H), 2.49-2.40 (m, 2H), 2.16 (s, 3H), 1.50 (t, $J = 7.0$ Hz, 3H), 1.33 (t, $J = 7.5$ Hz, 3H) ppm.

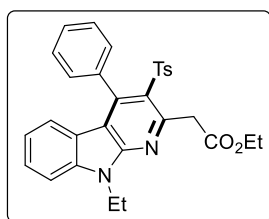
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 144.5, 137.3, 135.9, 135.6, 133.8, 132.2, 129.1, 128.1, 127.9, 127.8₁, 127.8₀, 123.4, 121.9, 121.6, 116.6, 115.8, 113.6, 105.8, 61.0, 55.4, 39.3, 38.0, 21.3, 14.7, 14.3 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{30}\text{H}_{30}\text{BrN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 593.1104.
Found 593.1128.

3.3 General procedure for the synthesis of compounds 11aa-ac, 11ae, 11aj-ak, 11an, 11as, 11ba, and 11fa

A Schlenk tube was charged with 2-sulfonamidoindole **2** (0.20 mmol), Ph_3P (0.04 mmol), cesium carbonate (0.40 mmol) and toluene (1.0 mL). Subsequently, δ -acetoxy allenoate **4** (0.24 mmol) in toluene (1.0 mL) was added gradually over 30 min at 80 °C and mixture was stirred at the same temperature for 36h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 $\times$ 15 mL). Then, the combined organic layer was washed with brine solution (20 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:9) as the eluent.

Compound 11aa



Yield: 77.0 mg (75%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 162-164 °C.

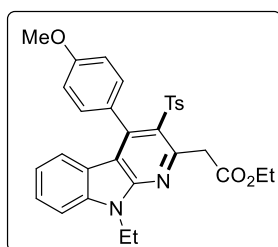
IR (neat): ν_{max} 3054, 2985, 1712, 1563, 1495, 1470, 1420, 1366, 1311, 1265, 1223, 1190, 1150, 1092, 1032, 896, 739, 705, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.43-7.39 (m, 3H), 7.30-7.25 (m, 4H), 7.01 (d, J = 8.0 Hz, 2H), 6.96-6.94 (m, 2H), 6.91-6.87 (m, 1H), 6.23 (d, J = 8.0 Hz, 1H), 4.72 (s, 2H), 4.56 (q, J = 7.0 Hz, 2H), 4.28 (q, J = 7.0 Hz, 2H), 2.34 (s, 3H), 1.49 (t, J = 7.0 Hz, 3H), 1.34 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.9, 151.6, 150.7, 146.4, 142.9, 141.0, 140.1, 135.4, 129.3, 129.0, 128.0, 127.9, 127.3, 126.9, 126.5, 122.9, 120.7, 120.6, 115.3, 109.3, 60.9, 45.6, 36.4, 21.5, 14.3, 13.9 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 513.1843
Found 513.1852.

Compound 11ab



Yield: 85.0 mg (78%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 164-166 °C.

IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1422, 1365, 1265, 1152, 896, 743, 706, 666 cm^{-1} .

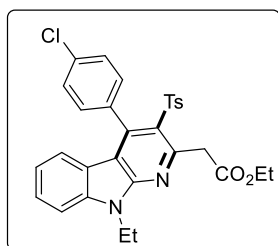
^1H NMR (500 MHz, CDCl_3): δ 7.43-7.42 (m, 2H), 7.30-7.28 (m, 2H), 7.03 (d, J = 8.0 Hz, 2H), 6.95-6.92 (m, 1H), 6.86 (d, J = 8.5 Hz, 2H), 6.80 (d, J = 8.5 Hz, 2H), 6.41 (d, J = 8.0 Hz, 1H), 4.72 (s, 2H), 4.56 (q, J = 7.0 Hz, 2H), 4.29 (q, J = 7.0 Hz, 2H), 3.93 (s, 3H), 2.35 (s, 3H), 1.50 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.9, 159.4, 151.6, 150.7, 146.4, 142.7, 141.2, 140.1, 130.6, 128.9, 127.5, 127.2, 127.1, 126.8, 123.0, 120.7, 120.6, 115.7, 113.3, 109.3, 60.9, 55.4, 45.6, 36.4, 22.3, 14.3, 13.9 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{31}\text{H}_{31}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 543.1948.

Found 543.1963.

Compound 11ac



Yield: 80.0 mg (73%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 189-191 °C.

IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1612, 1561, 1422, 1265, 1164, 1092, 896, 742, 706, 666 cm^{-1} .

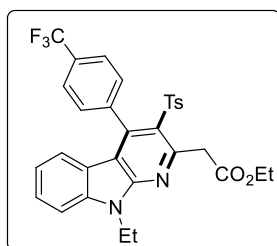
^1H NMR (500 MHz, CDCl_3): δ 7.46-7.45 (m, 2H), 7.33 (d, J = 8.5 Hz, 2H), 7.28-7.25 (m, 2H), 7.07 (d, J = 8.5 Hz, 2H), 6.98-6.95 (m, 1H), 6.91 (d, J = 8.5 Hz, 2H), 6.38 (d, J = 8.0 Hz, 1H), 4.72 (s, 2H), 4.58 (q, J = 7.0 Hz, 2H), 4.29 (q, J = 7.0 Hz, 2H), 2.38 (s, 3H), 1.50 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.9, 151.7, 150.7, 145.0, 143.2, 140.9, 140.2, 134.3, 133.8, 130.8, 129.0, 128.1, 127.5, 126.8, 126.6, 122.8, 120.8, 120.3, 115.1, 109.5, 60.9, 45.6, 36.4, 21.6, 14.3, 13.9 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{30}\text{H}_{28}\text{ClN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 547.14539.

Found 547.1457.

Compound 11ae



Yield: 81.0 mg (70%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 138-140 °C.

IR (neat): ν_{max} 3054, 2986, 1712, 1562, 1422, 1365, 1324, 1265, 1151, 1092, 1021, 896, 744, 706, 666 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.54 (d, J = 8.0 Hz, 2H), 7.48-7.46 (m, 2H), 7.31-7.28 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.04 (d, J = 8.0 Hz, 2H), 6.97-6.93 (m, 1H), 6.25 (d, J = 8.0 Hz, 1H), 4.73 (s, 2H), 4.60 (q, J = 7.2 Hz, 2H), 4.30 (q, J = 7.2 Hz, 2H), 2.38 (s, 3H), 1.52 (t, J = 7.2 Hz, 3H), 1.36 (t, J = 7.2 Hz, 3H) ppm.

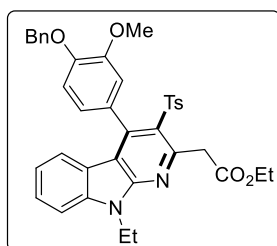
^{19}F NMR (470 MHz, CDCl_3): δ -62.6 ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.8, 151.7, 150.7, 144.5, 143.3, 140.8, 140.3, 139.3, 130.2 (q, $^2J_{\text{C-F}}$ = 32.3 Hz), 129.9, 129.1, 127.6, 126.8, 126.5, 124.7 (q, $^3J_{\text{C-F}}$ = 3.1 Hz), 124.1 (q, $^1J_{\text{C-F}}$ = 270.6 Hz), 122.5, 120.9, 120.2, 114.7, 109.6, 61.0, 45.5, 36.5, 21.5, 14.3, 13.9 ppm.

HRMS (ESI-EXACTIVE ORBITRAP): Calcd. For $\text{C}_{31}\text{H}_{28}\text{F}_3\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 581.1716.

Found 581.1716.

Compound 11aj



Yield: 88.0 mg (68%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 176-178 °C.

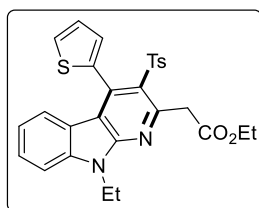
IR (neat): $\nu_{\max}$ 3054, 2986, 2928, 2856, 1731, 1611, 1511, 1422, 1265, 1164, 896, 746, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57 (d, J = 7.5 Hz, 2H), 7.50-7.47 (m, 2H), 7.44-7.39 (m, 3H), 7.25 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 3H), 6.85 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 6.5 Hz, 1H), 6.42 (d, J = 7.5 Hz, 1H), 6.29 (s, 1H), 5.36-5.28 (m, 2H), 4.85-4.81 (m, 1H), 4.65-4.62 (m, 1H), 4.59-4.55 (m, 2H), 4.33-4.28 (m, 2H), 3.57 (s, 3H), 2.30 (s, 3H), 1.50 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.2, 151.4, 150.7, 149.1, 147.6, 146.1, 142.7, 141.1, 140.1, 137.0, 128.8, 128.7, 128.1, 127.8, 127.3, 127.2, 127.1, 123.1, 122.2, 120.7, 120.6, 115.6, 113.3, 112.6, 109.4, 70.9, 60.9, 55.4, 45.8, 36.4, 21.5, 14.3, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{38}\text{H}_{37}\text{N}_2\text{O}_6\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 649.2367. Found 649.2367.

Compound 11ak



Yield: 66.3 mg (64%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 148-150 $^{\circ}\text{C}$.

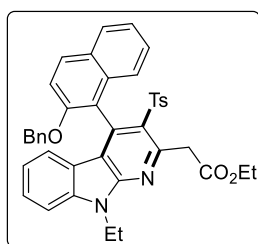
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1605, 1422, 1265, 1147, 896, 745, 706, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.48-7.42 (m, 5H), 7.10-7.07 (m, 3H), 7.03-6.99 (m, 1H), 6.83-6.82 (m, 1H), 6.42 (d, J = 8.0 Hz, 1H), 4.79-4.76 (m, 1H), 4.69-4.65 (m, 1H), 4.57 (q, J = 7.0 Hz, 2H), 4.31-4.27 (m, 2H), 2.37 (s, 3H), 1.50 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.8, 151.7, 150.6, 142.9, 140.9, 140.3, 139.2, 134.9, 129.4, 129.1, 128.0, 127.9, 127.6, 126.8, 126.7, 123.2, 120.9, 120.3, 117.0, 109.4, 60.9, 45.6, 36.4, 21.6, 14.3, 13.9 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{27}\text{N}_2\text{O}_4\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 519.1407. Found 519.1408.

Compound 11an



Yield: 96.2 mg (72%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 115-117 °C.

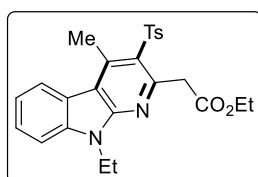
IR (neat): $\nu_{\max}$ 3054, 2986, 1738, 1601, 1557, 1422, 1265, 1153, 896, 748, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.99 (d, J = 9.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.40 (d, J = 8.5 Hz, 1H), 7.35-7.30 (m, 2H), 7.23-7.20 (m, 3H), 7.15-7.08 (m, 3H), 6.96-6.93 (m, 3H), 6.77 (d, J = 8.5 Hz, 1H), 6.73-6.69 (m, 3H), 5.97 (d, J = 8.0 Hz, 1H), 5.02-4.99 (m, 1H), 4.94-4.91 (m, 1H), 4.86-4.82 (m, 1H), 4.61-4.56 (m, 3H), 4.29 (q, J = 7.0 Hz, 2H), 2.20 (s, 3H), 1.53 (t, J = 7.0 Hz, 3H), 1.34 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.6, 153.2, 152.2, 151.0, 142.7, 142.3, 140.2, 140.0, 137.3, 132.4, 130.7, 128.6, 128.5, 128.2, 127.7, 127.6, 127.3, 127.0, 126.7, 126.5, 124.5, 123.4, 122.5, 120.7, 120.6, 118.9, 115.4, 114.4, 109.2, 70.5, 60.8, 45.5, 36.5, 21.3, 14.3, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{41}\text{H}_{37}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 669.2418. Found 669.2396.

Compound 11as



Yield: 61.2 mg (68%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 133-135 °C.

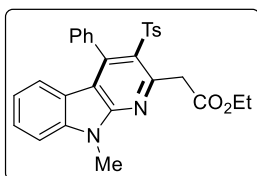
IR (neat): $\nu_{\max}$ 2926, 1711, 1568, 1495, 1409, 1362, 1304, 1220, 1162, 1146, 1107, 1088, 1027, 816, 740, 706, 679 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.11 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.59-7.52 (m, 2H), 7.34-7.28 (m, 3H), 4.64 (s, 2H), 4.56 (q, J = 7.0 Hz, 2H), 4.25 (q, J = 7.0 Hz, 2H), 2.96 (s, 3H), 2.41 (s, 3H), 1.48 (t, J = 7.0 Hz, 3H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.7, 152.3, 150.7, 145.0, 143.4, 141.4, 140.0, 129.5, 127.0, 126.6, 126.0, 123.6, 121.1, 120.9, 115.0, 109.7, 60.8, 45.5, 36.3, 21.6, 18.5, 14.3, 13.9.

HRMS (ESI-TOF): Calcd. For $\text{C}_{25}\text{H}_{27}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 451.1686. Found 451.1687.

Compound 11ba



Yield: 76.0 mg (76%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 130-132 °C

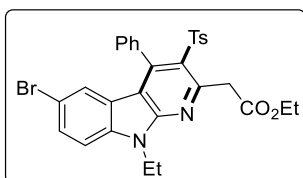
IR (neat): ν_{max} 3004, 2966, 2925, 1716, 1421, 1362, 1222, 1092, 902, 787, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.46-7.41 (m, 3H), 7.30-7.26 (m, 4H), 7.01 (d, J = 8.5 Hz, 2H), 6.96-6.91 (m, 3H), 6.24 (d, J = 8.0 Hz, 1H), 4.73 (s, 2H), 4.30 (q, J = 7.0 Hz, 2H), 4.00 (s, 3H), 2.36 (s, 3H), 1.36 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.9, 151.6, 151.3, 146.5, 142.9, 141.2, 141.0, 135.4, 129.3, 129.0, 128.0, 127.9, 127.4, 126.9, 126.6, 122.8, 120.9, 120.4, 115.4, 109.2, 60.9, 45.6, 27.8, 21.5, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 499.1686. Found 499.1687.

Compound 11fa



Yield: 77.0 mg (65%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 202-204 °C.

IR (neat): ν_{max} 3054, 2985, 2927, 1711, 1604, 1574, 1422, 1365, 1265, 1167, 1091, 1027, 976, 896, 858, 737, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.51 (d, J = 8.5 Hz, 1H), 7.47-7.44 (m, 1H), 7.31-7.28 (m, 5H), 7.02 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 7.5 Hz, 2H), 6.27 (s, 1H), 4.72 (s, 2H), 4.55 (q, J = 6.5 Hz, 2H), 4.30 (q, J = 7.0 Hz, 2H), 2.36 (s, 3H), 1.49 (t, J = 7.0 Hz, 3H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

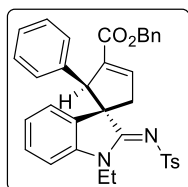
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.9, 152.3, 150.7, 147.0, 143.1, 140.8, 138.8, 134.9, 130.0, 129.0, 128.3, 128.1, 127.2, 127.0, 125.7, 122.2, 114.6, 113.5, 110.8, 61.0, 45.6, 36.6, 21.6, 14.3, 13.9 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{28}\text{BrN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 591.0948. Found 591.0948.

3.4 General procedure for the synthesis of compounds 12aa-ad, 12ag-ai, 12ba, 12bg, 12ca-ea, and 12ib

A Schlenk tube was charged with 2-sulfonamido indole **2** (0.20 mmol), tri(*p*-tolyl)phosphine (0.04 mmol), and toluene (1.0 mL). Subsequently, β' -acetoxy allenolate **6** (0.24 mmol) in toluene (1.0 mL) was added gradually over 30 min at 80 °C and the mixture was stirred at the same temperature for the stipulated time (36h). After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×15 mL). Then the combined organic layer was washed with brine solution (20 mL), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/hexane (1:4) as the eluent.

Compound 12aa



Yield: 91.0 mg (79%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 148-150 °C.

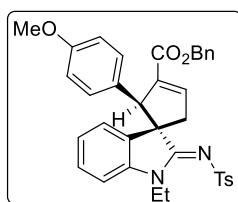
IR (neat): ν_{max} 3054, 2986, 1712, 1603, 1565, 1473, 1422, 1265, 1165, 1086, 896, 705, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.99-7.96 (m, 2H), 7.28-7.20 (m, 6H), 7.16-7.14 (m, 1H), 7.05-7.02 (m, 1H), 6.97-6.87 (m, 6H), 6.72-6.71 (m, 2H), 6.57 (d, J = 8.0 Hz, 1H), 5.65-5.63 (m, 1H), 5.20-5.17 (m, 1H), 5.01-4.98 (m, 1H), 4.19-4.15 (m, 1H), 4.08-4.01 (m, 1H), 3.75-3.68 (m, 1H), 2.97-2.92 (m, 1H), 2.43 (s, 3H), 1.20 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.2, 164.2, 144.3, 142.3, 141.0, 140.4, 136.8, 136.7, 135.7, 134.3, 129.3, 128.3, 128.1, 127.8, 127.7, 127.3, 126.6, 126.4, 124.1, 123.2, 108.6, 66.1, 62.3, 60.1, 42.8, 37.6, 21.5, 12.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{33}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 577.2156. Found 577.2162.

Compound 12ab



Yield: 100.6 mg (83%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 175-177 °C.

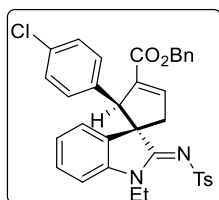
IR (neat): $\nu_{\max}$ 3054, 2986, 2925, 1712, 1556, 1422, 1363, 1265, 1149, 1087, 896, 745, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.96 (d, J = 7.5 Hz, 2H), 7.28-7.24 (m, 6H), 7.15 (d, J = 7.0 Hz, 1H), 7.06-6.99 (m, 3H), 6.91-6.88 (m, 1H), 6.64-6.58 (m, 3H), 6.44 (d, J = 8.0 Hz, 2H), 5.58 (s, 1H), 5.21-5.19 (m, 1H), 4.99-4.97 (m, 1H), 4.15-4.12 (m, 1H), 4.05-4.01 (m, 1H), 3.74-3.70 (m, 1H), 3.64 (s, 3H), 2.94-2.90 (m, 1H), 2.43 (s, 3H), 1.20 (t, J = 6.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.2, 164.2, 158.2, 143.9, 142.2, 141.1, 140.5, 137.1, 135.8, 134.4, 129.2₃, 129.1₇, 128.9, 128.2, 128.1, 127.8, 126.3, 124.0, 123.2, 112.8, 108.7, 66.0, 62.5, 59.5, 55.0, 42.6, 37.6, 21.5, 12.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 607.2261. Found 607.2263.

Compound 12ac



Yield: 92.7 mg (76%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 °C.

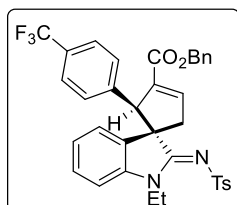
IR (neat): $\nu_{\max}$ 3054, 2986, 2928, 1712, 1624, 1560, 1490, 1422, 1376, 1265, 1148, 1087, 1046, 1015, 958, 896, 818, 739 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.98-7.95 (m, 2H), 7.31-7.24 (m, 6H), 7.17 (d, J = 7.5 Hz, 1H), 7.10-7.06 (m, 1H), 7.01-6.99 (m, 2H), 6.93-6.90 (m, 1H), 6.86 (d, J = 8.0 Hz, 2H), 6.65 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 8.0 Hz, 1H), 5.65 (d, J = 2.5 Hz, 1H), 5.24-5.21 (m, 1H), 4.97-4.95 (m, 1H), 4.24-4.19 (m, 1H), 4.04-3.97 (m, 1H), 3.74-3.67 (m, 1H), 2.95-2.91 (m, 1H), 2.44 (s, 3H), 1.19 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 163.9, 144.7, 142.4, 140.9, 140.3, 136.4, 135.6, 135.3, 134.0, 132.3, 129.5, 129.3, 128.5, 128.3, 128.0, 127.9, 127.5, 126.3, 123.9, 123.3, 108.8, 62.2, 59.4, 42.7, 37.6, 21.5, 12.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{32}\text{ClN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 611.1766. Found 611.1766.

Compound 12ad



Yield: 91.5 mg (71%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 123-125 °C.

IR (neat): ν_{max} 3054, 2986, 1712, 1561, 1422, 1363, 1326, 1265, 1223, 1087, 896, 740, 705, 665 cm^{-1} .

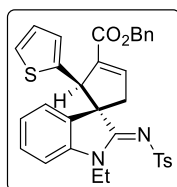
^1H NMR (500 MHz, CDCl_3): δ 7.98 (d, J = 8.5 Hz, 2H), 7.35-7.31 (m, 3H), 7.27-7.21 (m, 3H), 7.18 (d, J = 7.5 Hz, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.07-7.05 (m, 1H), 6.98 (d, J = 7.0 Hz, 2H), 6.92-6.89 (m, 1H), 6.83 (d, J = 8.0 Hz, 2H), 6.58 (d, J = 8.0 Hz, 1H), 5.75 (d, J = 2.0 Hz, 1H), 5.25-5.23 (m, 1H), 4.96-4.94 (m, 1H), 4.29-4.24 (m, 1H), 4.03-3.96 (m, 1H), 3.74-3.67 (m, 1H), 2.98-2.93 (m, 1H), 2.45 (s, 3H), 1.18 (t, J = 7.0 Hz, 3H) ppm.

^{19}F NMR (376 MHz, CDCl_3): δ -62.5 ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 163.8, 145.2, 142.5, 141.0, 140.8, 140.2, 136.0, 135.4, 133.7, 129.3, 128.3 (q, $^2J_{\text{C-F}}$ = 32.4 Hz), 128.5, 128.4, 128.3, 128.1, 128.0, 126.3, 124.1 (q, $^3J_{\text{C-F}}$ = 3.5 Hz), 124.0 (q, $^1J_{\text{C-F}}$ = 270.3 Hz), 123.8, 123.3, 108.8, 66.3, 62.2, 59.6, 42.8, 37.5, 21.5, 12.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{32}\text{F}_3\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 645.2029. Found 645.2029.

Compound 12ag



Yield: 81.5 mg (70%, brown solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 77-79 °C.

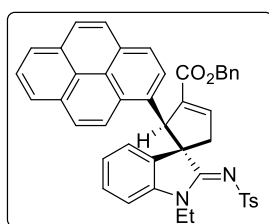
IR (neat): ν_{max} 3054, 2986, 1713, 1632, 1561, 1488, 1422, 1379, 1265, 1148, 1087, 1014, 896, 819, 738, 705, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.93 (d, J = 8.5 Hz, 2H), 7.28-7.25 (m, 5H), 7.23-7.22 (m, 1H), 7.16-7.13 (m, 2H), 7.09-7.07 (m, 2H), 6.95-6.92 (m, 1H), 6.88 (d, J = 5.0 Hz, 1H), 6.72-6.70 (m, 1H), 6.63-6.61 (m, 1H), 6.46-6.45 (m, 1H), 5.83 (d, J = 2.5 Hz, 1H), 5.22-5.20 (m, 1H), 5.05-5.03 (m, 1H), 4.10-4.03 (m, 2H), 3.85-3.78 (m, 1H), 2.98-2.94 (m, 1H), 2.42 (s, 3H), 1.25 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 163.8, 143.9, 142.3, 140.9₂, 140.8₆, 140.0, 137.0, 135.8, 133.9, 129.2, 128.4, 128.3, 127.9, 127.8, 126.3, 126.1, 125.9, 124.2, 124.0, 123.4, 108.8, 66.2, 62.1, 55.0, 43.1, 37.8, 21.5, 12.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{31}\text{N}_2\text{O}_4\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 583.1720. Found 583.1722.

Compound 12ah



Yield: 91.0 mg (65%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 194-196 °C.

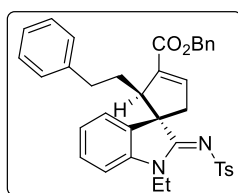
IR (neat): ν_{max} 3054, 2986, 1713, 1560, 1488, 1421, 1375, 1265, 1148, 1087, 1016, 959, 896, 841, 818, 739 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.15-8.07 (m, 5H), 7.98-7.95 (m, 2H), 7.87 (d, J = 8.5 Hz, 1H), 7.77-7.52 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.43-7.42 (m, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.10-7.09 (m, 1H), 6.97-6.94 (m, 1H), 6.77-6.68 (m, 5H), 6.59 (d, J = 7.5 Hz, 2H), 6.24 (d, J = 7.5 Hz, 1H), 5.11-5.08 (m, 1H), 4.88-4.85 (m, 1H), 4.25-4.21 (m, 1H), 3.78-3.63 (m, 2H), 3.15-3.11 (m, 1H), 2.48 (s, 3H), 0.99 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.8, 164.2, 143.9, 142.4, 141.1, 140.4, 137.9, 135.5, 134.2, 131.8, 131.2, 130.6, 130.0, 129.4, 129.3, 127.9₄, 127.8₉, 127.5₁, 127.4₅, 127.3₆, 127.1, 126.9, 126.8, 126.5, 125.7, 124.9, 124.6, 124.5₃, 124.4₇, 123.9, 123.1, 123.0, 108.7, 66.0, 62.2, 55.8, 44.1, 38.0, 21.6, 11.4. ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{45}\text{H}_{37}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 701.2469. Found 701.2469.

Compound 12ai



Yield: 83.4 mg (69%, gummy liquid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

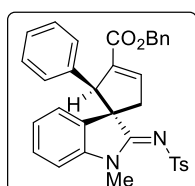
IR (neat): $\nu_{\max}$ 2923, 2853, 1710, 1556, 1487, 1468, 1373, 1336, 1282, 1236, 1172, 1146, 1084, 955, 900, 815, 772, 753, 698, 679 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, J = 7.5 Hz, 2H), 7.41-7.36 (m, 7H), 7.29 (d, J = 6.5 Hz, 2H), 7.16-7.02 (m, 6H), 6.55 (d, J = 6.5 Hz, 2H), 5.29-5.26 (m, 1H), 5.19-5.16 (m, 1H), 4.54 (d, J = 11.0 Hz, 1H), 4.14-4.10 (m, 1H), 4.01-3.97 (m, 1H), 3.88-3.83 (m, 1H), 2.71-2.67 (m, 1H), 2.44-2.41 (m, 4H), 2.13-2.08 (m, 1H), 1.65-1.59 (m, 1H), 1.44-1.37 (m, 1H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 164.1, 142.3, 141.9, 141.8, 141.1, 140.9, 137.9, 135.9, 134.7, 129.2, 128.5₈, 128.5₅, 128.3, 128.2, 128.1, 128.0, 126.4, 125.6, 123.9, 123.8, 109.4, 66.3, 59.9, 52.8, 45.1, 37.6, 33.6, 31.7, 21.5, 11.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{37}\text{H}_{37}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 605.2469. Found 605.2463.

Compound 12ba



Yield: 92.2 mg (82%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 105-107 $^\circ\text{C}$.

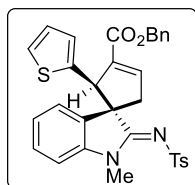
IR (neat): $\nu_{\max}$ 3054, 2986, 2928, 1713, 1626, 1564, 1492, 1469, 1422, 1378, 1265, 1147, 1086, 1014, 933, 896, 746 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.97 (d, J = 8.0 Hz, 2H), 7.29-7.22 (m, 6H), 7.08-6.95 (m, 7H), 6.89-6.86 (m, 1H), 6.76 (d, J = 7.0 Hz, 2H), 6.61 (d, J = 8.0 Hz, 1H), 5.49 (s, 1H), 5.20-5.18 (m, 1H), 5.01-4.98 (m, 1H), 4.02-3.98 (m, 1H), 3.41 (s, 3H), 2.97-2.94 (m, 1H), 2.44 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.0, 164.1, 144.1, 142.3, 141.8, 140.9, 136.9, 136.8, 135.8, 133.6, 129.3, 128.3, 128.2, 128.0, 127.8, 127.7, 127.5, 126.7, 126.4, 124.0, 123.4, 66.1, 62.5, 60.3, 42.9, 30.1, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{31}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 563.1999. Found 563.2001.

Compound 12bg



Yield: 83.0 mg (73%, brown solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 66-68 °C.

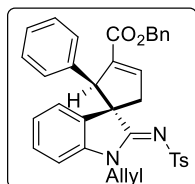
IR (neat): $\nu_{\max}$ 3054, 2986, 1724, 1564, 1422, 1265, 1150, 1084, 896, 740, 705, 665 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, $J = 8.0$ Hz, 2H), 7.28-7.24 (m, 5H), 7.19-7.16 (m, 2H), 7.10-7.09 (m, 2H), 6.98 (d, $J = 7.5$ Hz, 1H), 6.94-6.90 (m, 2H), 6.75 (d, $J = 7.5$ Hz, 1H), 6.68-6.67 (m, 1H), 6.49 (d, $J = 3.0$ Hz, 1H), 5.60 (s, 1H), 5.21-5.19 (m, 1H), 5.05-5.02 (m, 1H), 3.84-3.80 (m, 1H), 3.50 (s, 3H), 3.00-2.96 (m, 1H), 2.42 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.6, 163.7, 143.6, 142.4, 142.3, 140.9, 140.4, 137.2, 135.8, 133.0, 129.2, 128.5, 128.3, 127.9, 127.7, 127.3, 126.2, 126.0, 124.1, 124.0, 123.6, 108.9, 66.2, 62.2, 55.1, 43.2, 30.6, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{29}\text{N}_2\text{O}_4\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 569.1563. Found 569.1563.

Compound 12ca



Yield: 93.0 mg (79%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 96-98 °C.

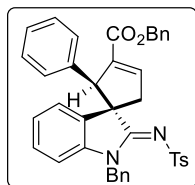
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1561, 1422, 1265, 1148, 1087, 896, 738, 706, 666 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.95 (d, $J = 7.0$ Hz, 2H), 7.28-7.16 (m, 7H), 7.01-6.88 (m, 7H), 6.74 (d, $J = 6.0$ Hz, 2H), 6.57 (d, $J = 7.5$ Hz, 1H), 5.74-5.69 (m, 2H), 5.20-5.17 (m, 2H), 5.10-5.07 (m, 1H), 5.00-4.98 (m, 1H), 4.62-4.60 (m, 1H), 4.29-4.18 (m, 2H), 2.97-2.93 (m, 1H), 2.43 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.5, 164.2, 144.2, 142.4, 140.8, 140.6, 136.9, 136.7, 135.7, 134.0, 130.2, 129.3, 128.3, 128.2, 128.1, 127.8, 127.7, 127.4, 126.7, 126.4, 124.0, 123.2, 118.6, 109.3, 66.1, 62.4, 59.9, 45.2, 43.1, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{36}H_{33}N_2O_4S$ [$M^+ + H$]: m/z 589.2156. Found 589.2151.

Compound 12da



Yield: 96.0 mg (75%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 75-77 °C.

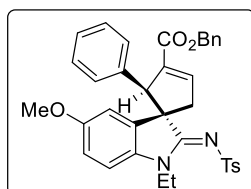
IR (neat): $\nu_{\max}$ 3054, 2986, 1715, 1637, 1422, 1265, 1147, 1083, 896, 740, 705, 665 cm^{-1} .

1H NMR (400 MHz, $CDCl_3$): δ 7.92-7.90 (m, 2H), 7.32-7.19 (m, 10H), 7.13-7.11 (m, 2H), 7.01-6.81 (m, 7H), 6.65-6.63 (m, 2H), 6.58 (d, J = 8.0 Hz, 1H), 5.79-5.77 (m, 1H), 5.21-5.12 (m, 2H), 5.01-4.98 (m, 1H), 4.79-4.76 (m, 1H), 4.34-4.29 (m, 1H), 3.02-2.96 (m, 1H), 2.44 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 171.0, 164.2, 144.1, 142.4, 140.7, 140.6, 137.1, 136.7, 135.8, 134.8, 134.3, 129.2, 128.6, 128.3₂, 128.2₆, 128.1, 127.8₃, 127.8₁, 127.7, 127.4, 127.0, 126.6, 126.5, 124.2, 123.2, 109.2, 66.1, 62.2, 59.6, 46.2, 43.4, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{40}H_{35}N_2O_4S$ [$M^+ + H$]: m/z 639.2312. Found 639.2309.

Compound 12ea



Yield: 86.1 mg (71%, brown solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 96-98 °C.

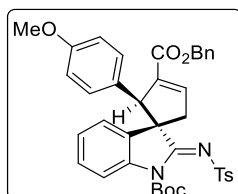
IR (neat): $\nu_{\max}$ 3054, 2986, 1712, 1559, 1493, 1422, 1265, 1148, 1087, 1028, 896, 736, 706 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ 7.95 (d, J = 8.5 Hz, 2H), 7.32-7.20 (m, 6H), 6.99-6.94 (m, 5H), 6.75 (d, J = 7.0 Hz, 2H), 6.67 (d, J = 2.0 Hz, 1H), 6.58-6.56 (m, 1H), 6.50 (d, J = 8.5 Hz, 1H), 5.58 (d, J = 1.5 Hz, 1H), 5.20-5.18 (m, 1H), 5.00-4.98 (m, 1H), 4.10-4.04 (m, 2H), 3.75-3.71 (m, 1H), 3.68 (s, 3H), 2.94-2.91 (m, 1H), 2.42 (s, 3H), 1.22 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.7, 164.1, 156.4, 144.2, 142.1, 141.2, 136.9, 136.8, 135.7, 135.5, 134.2, 129.2, 128.1, 127.9, 127.7, 127.5, 126.7, 126.3, 113.0, 111.3, 109.1, 66.1, 62.4, 60.0, 56.0, 43.1, 37.9, 21.5, 12.1.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 607.2261. Found 607.2262.

Compound 12ib



Yield: 114.0 mg (84%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 63-65 °C.

IR (neat): ν_{max} 3034, 2933, 2834, 1715, 1631, 1596 1511, 1461, 1318, 1282, 1176, 1084, 1031, 810, 697 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.88 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.26-7.24 (m, 5H), 7.10-7.07 (m, 2H), 6.99 (d, J = 6.0 Hz, 2H), 6.87-6.84 (m, 1H), 6.77-6.73 (m, 3H), 6.56 (d, J = 8.5 Hz, 2H), 5.17 (d, J = 12.5 Hz, 1H), 4.95-4.90 (m, 2H), 3.70 (s, 3H), 3.29-3.26 (m, 1H), 2.88-2.84 (m, 1H), 2.40 (s, 3H), 1.66 (s, 9H) ppm.

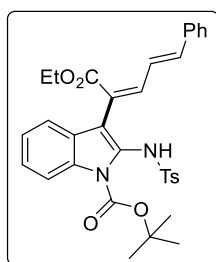
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 163.8, 158.6, 148.9, 143.1, 142.8, 140.0, 139.9, 136.5, 135.8, 130.8, 129.3, 129.2, 129.1, 128.5, 128.3, 127.8, 127.6, 126.7, 124.1₇, 124.1₅, 113.2₀, 113.1₆, 86.7, 66.0, 62.3, 61.3, 55.1, 43.4, 27.7, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{39}\text{H}_{39}\text{N}_2\text{O}_7\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 679.2472. Found 679.2473.

3.5 Synthesis of *tert*-butyl 3-((2*Z*,4*E*)-1-ethoxy-1-oxo-5-phenylpenta-2,4-dien-2-yl)-((4-methylphenyl)sulfonamido)-1*H*-indole-1-carboxylate **14**

A Schlenk tube was charged with 2-sulfonamido indole **2i** (77.2 mg, 0.20 mmol), δ -acetoxy allenolate **4a** (62.4 mg, 0.24 mmol), and toluene (2.0 mL). Subsequently, Ph_3P (10.5 mg, 0.04 mmol) was added at rt (25 °C) and mixture was stirred at the same temperature for 36h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). Then, the combined organic layer was washed with brine solution (20.0 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (2:8) as the eluent to obtain **14** as a white solid.

Compound 14



Yield: 91.4 mg (78%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 103-105 °C.

IR (neat): $\nu_{\max}$ 3235, 2971, 1701, 1619, 1452, 1362, 1274, 1186, 1037, 700 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.19 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 2H), 7.32-7.24 (m, 8H), 7.11-7.06 (m, 3H), 6.95 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 11.5 Hz, 1H), 5.99 (d, J = 15.0 Hz, 1H), 4.18 (q, J = 7.0 Hz, 2H), 2.32 (s, 3H), 1.64 (s, 9H), 1.27 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 167.2, 150.5, 143.7, 142.3, 140.1, 139.3, 136.6, 133.4, 129.5, 129.2, 128.7, 128.2, 127.8₄, 127.7₆, 127.6, 127.3, 125.2, 123.5, 122.4, 120.8, 115.3, 115.2, 86.0, 60.2, 28.1, 21.5, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{35}\text{N}_2\text{O}_6\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 587.2210. Found: 587.2220.

3.6 Scale-up Experiments for 10aa, 11aa and 12aa

Synthesis of compound 10aa: A 25 mL RB flask was charged with **2a** (314.0 mg, 1.0 mmol), **4a** (312.0 mg, 1.20 mmol), and toluene (10.0 mL). Subsequently, Ph_3P (52.5 mg, 0.20 mmol) was added to the reaction mixture at rt (25 °C), and the mixture was stirred at the same temperature for 36h. Then it was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with brine (20 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as the eluent to obtain **10aa** (406.2 mg; 79%).

Synthesis of compound 11aa: A 25 mL RB flask was charged with **2a** (314.0 mg, 1.0 mmol), Ph_3P (52.5 mg, 0.20 mmol), cesium carbonate (651.6 mg, 2.0 mmol), and toluene (5.0 mL). Subsequently, **4a** (312.0 mg, 1.20 mmol) in toluene (5.0 mL) was added gradually over a period of 45 min at 80 °C (oil bath), and the mixture was stirred at the same temperature for 36h. Then it was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). Then the combined organic layer was washed with brine (20 mL), dried over

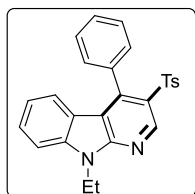
anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as the eluent to obtain **11aa** (369.0 mg; 72%).

Synthesis of compound 12aa: A 25 mL RB flask was charged with **2a** (314.0 mg, 1.0 mmol), tri(*p*-tolyl)phosphine (61.0 mg, 0.20 mmol), and toluene (5.0 mL). Subsequently, **6a** (386.5 mg, 1.20 mmol) in toluene (5.0 mL) was added gradually over a period of 45 min at 80 °C (oil bath), and the mixture was stirred at the same temperature for 36h. Then it was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 10 mL). Then the combined organic layer was washed with brine (20 mL), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:4) as the eluent to obtain **12aa** (432.0 mg; 75%).

3.7 General procedure for the synthesis of compounds 15aa-ai, 15ak-al, 15ar, 15ba-ca, 15ea, and 15ga-ha

A Schlenk tube was charged with 2-sulfonamido indole **2** (0.20 mmol), δ -acetoxy allenolate **4** (0.24 mmol) in toluene (2.0 mL) and PPh₃ (0.04 mmol). The mixture was kept stirring at 110 °C for 24h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 5 mL). Then, the combined organic layer was washed with brine (2 x 30 mL), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (10:90) as the eluent.

Compound 15aa



Yield: 69.0 mg (81%, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 170-172 °C.

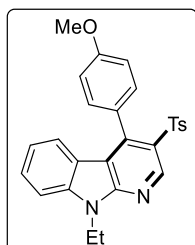
IR (neat): ν_{max} 3060, 2977, 2927, 1596, 1568, 1549, 1492, 1469, 1446, 1415, 1312, 1226, 1208, 1175, 1145, 1117, 1089, 1017 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 9.46 (s, 1H), 7.51-7.48 (m, 1H), 7.46-7.42 (m, 2H), 7.39-7.36 (m, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.05-7.04 (m, 4H), 6.96-6.92 (m, 1H), 6.53 (d, *J* = 8.0 Hz, 1H), 4.61 (q, *J* = 7.5 Hz, 2H), 2.35 (s, 3H), 1.51 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 147.0, 144.6, 143.4, 140.3, 139.4, 134.4, 129.2, 128.7, 128.3, 127.9, 127.6, 127.5, 123.2, 120.9, 120.6, 115.7, 109.5, 36.7, 21.6, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 427.1469. Found 427.1477.

Compound 15ab



Yield: 75.8 mg (83%, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: above 200 °C

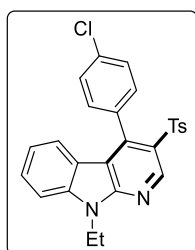
IR (neat): ν_{max} 3058, 2934, 2840, 1606, 1574, 1416, 1330, 1146, 1032, 847, 787, 689 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.36 (s, 1H), 7.37-7.36 (m, 2H), 7.18 (d, J = 8.0 Hz, 2H), 6.98 (d, J = 8.0 Hz, 2H), 6.90-6.88 (m, 3H), 6.83 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 8.0 Hz, 1H), 4.51 (q, J = 7.0 Hz, 2H), 3.86 (s, 3H), 2.26 (s, 3H), 1.42 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 160.0, 153.0, 147.0, 144.6, 143.4, 140.2, 139.5, 130.6, 129.1, 127.9₃, 127.8₇, 127.6, 126.5, 123.3, 120.9, 120.7, 116.1, 113.7, 109.5, 55.5, 36.7, 21.6, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 457.1580. Found 457.1583.

Compound 15ac



Yield: 72.8 mg (79%, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: above 200 °C

IR (neat): ν_{max} 3054, 2979, 2925, 2853, 1708, 1554, 1491, 1265, 1147, 1088, 1014, 737 cm^{-1} .

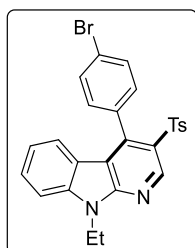
^1H NMR (500 MHz, CDCl_3): δ 9.44 (s, 1H), 7.47-7.46 (m, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.01-6.98 (m, 3H), 6.63 (d, J =

8.0 Hz, 1H), 4.61 (q, $J = 7.0$ Hz, 2H), 2.37 (s, 3H), 1.51 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 147.0, 143.8, 143.1, 140.3, 139.3, 135.0, 132.8, 130.7, 129.3, 128.6, 127.9, 127.8, 127.5, 123.1, 121.1, 120.3, 115.5, 109.7, 36.8, 21.7, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{ClN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 461.1080. Found 461.1087.

Compound 15ad



Yield: 77.7 mg (77%, white solid, $R_f = 0.53$ (85:15 hexane/ethyl acetate)).

Mp: above 200 °C

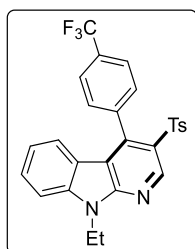
IR (neat): ν_{max} 2980, 2924, 2853, 1732, 1566, 1490, 1467, 1414, 1373, 1302, 1234, 1147, 1117, 1086, 1011, 812, 745, 706 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.43 (s, 1H), 7.51 (d, $J = 8.0$ Hz, 2H), 7.46 (m, 2H), 7.28-7.26 (m, 2H), 7.09 (d, $J = 8.0$ Hz, 2H), 7.00-6.99 (m, 1H), 6.93 (d, $J = 8.0$ Hz, 2H), 6.63 (d, $J = 8.0$ Hz, 1H), 4.60 (q, $J = 7.0$ Hz, 2H), 2.36 (s, 3H), 1.50 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 152.9, 147.0, 143.8, 143.0, 140.3, 139.3, 133.3, 131.5, 131.0, 129.3, 127.9, 127.8, 127.4, 123.1₃, 123.0₆, 121.1, 120.3, 115.3, 109.7, 36.8, 21.7, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{BrN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 505.0580. Found: 505.0583.

Compound 15ae



Yield: 74.1 mg (75%, white solid, $R_f = 0.53$ (85:15 hexane/ethyl acetate)).

Mp: 200-202 °C.

IR (neat): ν_{max} 3056, 2986, 1617, 1547, 1567, 1493, 1415, 1322, 1168, 1067, 1016, 862, 801, 645 cm^{-1} .

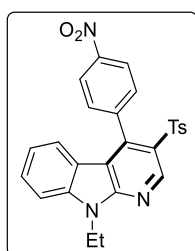
^1H NMR (500 MHz, CDCl_3): 9.47 (s, 1H), 7.63 (d, $J = 8.0$ Hz, 2H), 7.48-7.47 (m, 2H), 7.23-7.18 (m, 4H), 7.05 (d, $J = 8.0$ Hz, 2H), 6.99-6.96 (m, 1H), 6.51 (d, $J = 8.0$ Hz, 1H), 4.62 (q, $J = 7.0$ Hz, 2H), 2.36 (s, 3H), 1.52 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 147.0, 143.9, 142.5, 140.4, 139.1, 138.2, 131.0 ($^2J_{\text{C-F}} = 32.3$ Hz), 129.9, 129.4, 128.0, 127.8, 127.4, 125.2 ($^3J_{\text{C-F}} = 3.6$ Hz), 124.2 ($^1J_{\text{C-F}} = 270.8$ Hz), 122.9, 121.2, 120.2, 115.1, 109.8, 36.9, 21.6, 14.1 ppm.

^{19}F NMR (470 MHz, CDCl_3): -62.5 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 495.1349. Found: 495.1351.

Compound 15af



Yield: 65.0 mg (69 %, white solid, $R_f = 0.53$ (85:15 hexane/ethyl acetate)).

Mp: 85-87 $^{\circ}\text{C}$.

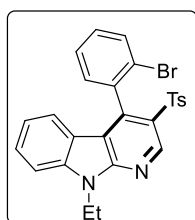
IR (neat): ν_{max} 2980, 2927, 2856, 1735, 1597, 1533, 1521, 1493, 1416, 1347, 1312, 1238, 1175, 1146, 1118, 1086, 855 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.44 (s, 1H), 8.28-8.26 (m, 2H), 7.50-7.49 (m, 2H), 7.30-7.28 (m, 3H), 7.27-7.26 (m, 1H), 7.11 (d, $J = 8.0$ Hz, 2H), 7.01-6.96 (m, 1H), 6.48 (d, $J = 7.5$ Hz, 1H), 4.63 (q, $J = 7.0$ Hz, 2H), 2.38 (s, 3H), 1.52 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 152.9, 148.2, 147.2, 144.2, 141.6, 141.5, 140.5, 139.3, 130.6, 129.5, 128.3, 127.7, 127.1, 123.4, 122.7, 121.3, 119.9, 114.8, 110.0, 36.9, 21.7, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{N}_3\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 472.1326, found: 472.1327.

Compound 15ag



Yield: 73.8 mg (73 %, white solid, $R_f = 0.53$ (85:15 hexane/ethyl acetate)).

Mp: above 200 °C

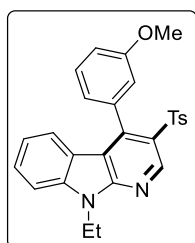
IR (neat): $\nu_{\max}$ 3054, 2979, 2924, 2853, 1552, 1493, 1415, 1313, 1176, 1146, 1117, 1087, 737, 705, 683 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.47 (s, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.47-7.42 (m, 4H), 7.32-7.31 (m, 3H), 7.10 (d, J = 7.0 Hz, 2H), 7.00 (s, 1H), 6.54 (d, J = 7.0 Hz, 1H), 4.66-4.57 (m, 2H), 2.37 (s, 3H), 1.52 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 147.3, 143.9, 142.4, 140.4, 138.8, 135.2, 132.6, 131.9, 130.6, 129.4, 128.4, 127.9, 127.4, 127.0, 123.8, 122.7, 121.2, 120.4, 115.3, 109.7, 36.9, 21.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{BrN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 505.0580. Found: 505.0584.

Compound 15ah



Yield: 71.2 mg (78 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 160-162 °C.

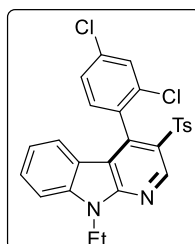
IR (neat): $\nu_{\max}$ 2983, 2925, 2859, 1594, 1565, 1549, 1410, 1312, 1246, 1218, 1085, 1037, 838, 756 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.47 (s, 1H), 7.46-7.43 (m, 2H), 7.33-7.26 (m, 3H), 7.07-7.02 (m, 3H), 7.00-6.95 (m, 1H), 6.71 (d, J = 7.0 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.43 (s, 1H), 4.61 (q, J = 7.0 Hz, 2H), 3.65 (s, 3H), 2.35 (s, 3H), 1.51 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 159.4, 152.9, 146.8, 144.2, 143.4, 140.2, 139.3, 135.3, 129.4, 129.1, 128.0, 127.7, 127.4, 123.3, 121.6, 120.9, 120.4, 115.4, 115.2, 113.6, 109.5, 55.1, 36.7, 21.6, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 457.1580. Found: 457.1582.

Compound 15ai



Yield: 71.3 mg (72 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 186-188 °C.

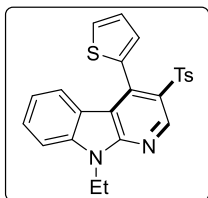
IR (neat): $\nu_{\max}$ 3057, 2925, 2859, 1551, 1492, 1311, 1175, 1086, 842, 736, 675 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.46 (s, 1H), 7.49 (s, 2H), 7.43-7.40 (m, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.26-7.24 (m, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.07-7.04 (m, 1H), 6.64 (d, J = 7.5 Hz, 1H), 4.66-4.56 (m, 2H), 2.39 (s, 3H), 1.52 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 152.9, 147.3, 144.1, 140.4, 139.6, 138.7, 135.9, 134.8, 132.7, 131.9, 129.5, 129.4, 128.1₂, 128.0₈, 127.3, 127.2, 122.5, 121.4, 120.1, 115.2, 109.8, 36.9, 21.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{21}\text{Cl}_2\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 495.0695. Found: 495.0699.

Compound 15ak



Yield: 63.0 mg (73 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 90-92 °C.

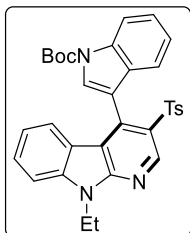
IR (neat): $\nu_{\max}$ 3064, 2978, 2923, 2852, 1708, 1612, 1552, 1431, 1407, 1301, 1147, 1088, 704, 685 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.46 (s, 1H), 7.53-7.52 (m, 1H), 7.50-7.45 (m, 2H), 7.37 (d, J = 8.5 Hz, 2H), 7.17-7.16 (m, 1H), 7.11 (d, J = 8.0 Hz, 2H), 7.07-7.02 (m, 1H), 6.94-6.93 (m, 1H), 6.72 (d, J = 7.5 Hz, 1H), 4.63-4.58 (m, 2H), 2.36 (s, 3H), 1.51 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 152.9, 147.0, 143.6, 140.5, 139.2, 137.4, 133.4, 129.5, 129.3, 128.8, 128.1, 128.0, 127.8, 127.2, 123.5, 121.1, 120.2, 117.4, 109.6, 36.8, 21.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_2\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 433.1033. Found: 433.1040.

Compound 15al



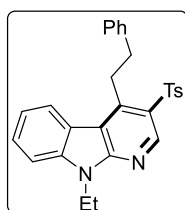
Yield: 78.0 mg (69 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).
Mp: 165-167 °C.
IR (neat): $\nu_{\max}$ 3059, 2979, 2929, 1732, 1551, 1451, 1369, 1246, 1144, 1097, 1056, 734, 679 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.54 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.67 (s, 1H), 7.47-7.41 (m, 2H), 7.24-7.22 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 6.89-6.86 (m, 1H), 6.82-6.79 (m, 1H), 6.74-6.70 (m, 3H), 6.38 (d, J = 8.0 Hz, 1H), 4.64 (q, J = 7.0 Hz, 2H), 2.07 (s, 3H), 1.74 (s, 9H), 1.54 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 149.7, 146.9, 143.2, 140.3, 138.2, 135.8, 134.7, 129.3, 128.9, 128.6, 127.7, 127.4, 126.6, 124.7, 123.8, 122.8, 121.0, 120.1, 119.8, 116.4, 115.3, 113.5, 109.5, 84.5, 36.8, 28.4, 21.3, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{31}\text{N}_3\text{NaO}_4\text{S}$ [$\text{M}^+ + \text{Na}$]: m/z 588.1927. Found: 588.1925.

Compound 15ar



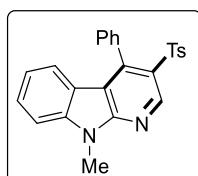
Yield: 59.0 mg (65 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).
Mp: 128-130 °C.
IR (neat): $\nu_{\max}$ 3024, 2973, 2923, 1737, 1569, 1553, 1492, 1414, 1307, 1181, 1086, 832, 700, 679 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.31 (s, 1H), 8.15 (d, J = 7.5 Hz, 1H), 7.83 (d, J = 7.5 Hz, 2H), 7.60-7.55 (m, 2H), 7.42-7.38 (m, 5H), 7.29-7.25 (m, 3H), 4.61-4.59 (m, 2H), 3.69 (s, 2H), 2.96 (t, J = 8.0 Hz, 2H), 2.36 (s, 3H), 1.50 (t, J = 6.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.2, 148.3, 146.4, 143.9, 141.4, 140.1, 130.0, 128.9, 128.4, 127.5, 127.4, 126.9, 126.6, 123.5, 121.4, 120.3, 115.1, 110.0, 36.7, 34.9, 32.8, 21.6, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 455.1788. Found: 455.1786.

Compound 15ba



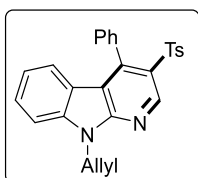
Yield: 64.3 mg (78 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).
Mp: 95-97 °C.
IR (neat): $\nu_{\max}$ 3056, 2923, 2853, 1711, 1574, 1494, 1471, 1400, 1302, 1148, 1087, 1019, 739, 702, 685 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.47 (s, 1H), 7.52-7.47 (m, 1H), 7.46-7.43 (m, 2H), 7.39-7.34 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.05-7.03 (m, 4H), 6.97-6.94 (m, 1H), 6.53 (d, J = 8.0 Hz, 1H), 4.03 (s, 3H), 2.34 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.6, 147.1, 144.8, 143.5, 141.3, 139.3, 134.3, 129.2, 128.7, 128.3, 127.9, 127.7, 127.5, 123.0, 121.1, 120.4, 115.7, 109.5, 28.1, 21.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 413.1318. Found 413.1319.

Compound 15ca



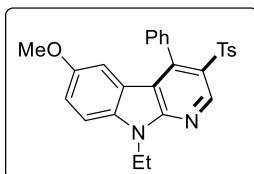
Yield: 65.0 mg (74 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).
Mp: 175-177 °C.
IR (neat): $\nu_{\max}$ 3063, 2920, 2853, 1571, 1550, 1493, 1469, 1412, 1306, 1164, 1143, 1119, 994, 808, 749 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.46 (s, 1H), 7.52-7.49 (m, 1H), 7.42-7.37 (m, 4H), 7.26-7.23 (m, 2H), 7.05 (d, J = 7.0 Hz, 4H), 6.95-6.94 (m, 1H), 6.53 (d, J = 8.0 Hz, 1H), 6.10-6.03 (m, 1H), 5.24 (d, J = 10.0 Hz, 1H), 5.13 (m, 3H), 2.35 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.2, 147.1, 144.7, 143.5, 140.6, 139.3, 134.3, 132.0, 129.2, 128.7, 128.3, 128.0, 127.9, 127.7, 123.1, 121.1, 120.6, 117.6, 115.7, 110.2, 44.1, 21.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 439.1475. Found: 439.1477.

Compound 15ea



Yield: 63.0 mg (69 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).
Mp: 173-175 °C.

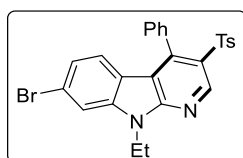
IR (neat): $\nu_{\max}$ 3027, 2969, 2942, 1739, 1572, 1554, 1482, 1375, 1199, 1139, 1085, 1038, 905, 808, 680 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.42 (s, 1H), 7.51-7.48 (m, 1H), 7.41-7.38 (m, 2H), 7.35-7.33 (m, 1H), 7.27 (s, 1H), 7.260-7.256 (m, 1H), 7.07-7.05 (m, 5H), 5.95 (d, J = 2.5 Hz, 1H), 4.57 (q, J = 7.5 Hz, 2H), 3.44 (s, 3H), 2.35 (s, 3H), 1.49 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 154.5, 153.0, 146.9, 144.5, 143.4, 139.6, 134.9, 134.5, 129.3, 129.2, 128.6, 128.2, 128.0, 126.9, 121.0, 116.8, 115.5, 110.3, 105.8, 55.4, 36.8, 21.6, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_3\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 457.1580. Found: 457.1580.

Compound 15ga



Yield: 71.7 mg (71 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 110-112 $^{\circ}\text{C}$.

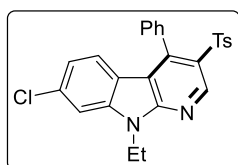
IR (neat): $\nu_{\max}$ 3059, 2966, 2921, 1737, 1611, 1568, 1409, 1307, 1228, 1122, 932, 844, 736 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.47 (s, 1H), 7.59 (s, 1H), 7.52-7.49 (m, 1H), 7.39-7.36 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.05-7.01 (m, 5H), 6.35 (d, J = 8.5 Hz, 1H), 4.56 (q, J = 7.0 Hz, 2H), 2.34 (s, 3H), 1.50 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.0, 147.4, 144.7, 143.6, 141.1, 139.1, 134.0, 129.2, 129.0, 128.9, 128.4, 128.2, 127.9, 124.3, 124.2, 121.5, 119.5, 115.3, 112.7, 36.9, 21.7, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{BrN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 505.0580. Found: 505.0579.

Compound 15ha



Yield: 67.3 mg (73 %, white solid, R_f = 0.53 (85:15 hexane/ethyl acetate)).

Mp: 90-92 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3062, 3024, 2976, 1737, 1570, 1549, 1487, 1379, 1308, 1210, 1175, 1125, 1086, 939, 754, 663 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.46 (s, 1H), 7.52-7.49 (m, 1H), 7.43₂-7.42₉ (m, 1H), 7.39-7.36 (m, 2H), 7.23 (d, J = 8.0 Hz, 2H), 7.05-7.02 (m, 4H), 6.91-6.89 (m, 1H), 6.41 (d, J = 8.5 Hz, 1H), 4.56 (q, J = 7.5 Hz, 2H), 2.35 (s, 3H), 1.51 (t, J = 7.0 Hz, 3H) ppm.

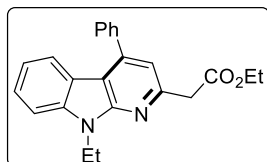
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.2, 147.2, 144.6, 143.6, 140.9, 139.1, 134.0, 133.6, 129.2, 129.0, 128.9, 128.4, 128.1, 127.9, 124.0, 121.4, 119.0, 115.3, 109.7, 36.9, 21.7, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{22}\text{ClN}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 461.1085. Found: 461.1083.

3.8 General procedure for the synthesis of compounds 16aa-ai, 16ak-al, 16an-ao, 16aq, and 16ba-ga

A Schlenk tube was charged with 2-sulfonamido indole **2** (0.20 mmol), δ -acetoxy allenoate **4** (0.24 mmol) in toluene (2.0 mL) and kept for stirring at 50 °C. Subsequently, DBU (0.04 mmol) was added and the stirring continued for 2h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×5 mL). Then, the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (10:90) as the eluent.

Compound 16aa



Yield: 62.3 mg (87 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 88-90 °C.

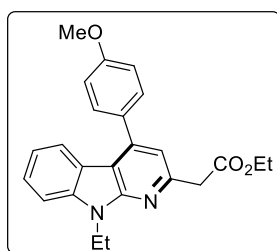
IR (neat): ν_{max} 3032, 2971, 2931, 1723, 1616, 1582, 1559, 1405, 1214, 995, 708 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.69- 7.65 (m, 3H), 7.58-7.49 (m, 3H), 7.47-7.43 (m, 2H), 7.05-7.01 (m, 2H), 4.58 (q, J = 7.0 Hz, 2H), 4.23 (q, J = 7.0 Hz, 2H), 4.01 (s, 2H), 1.48 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 151.6, 150.9, 145.5, 139.5, 139.2, 128.8, 128.7, 128.6, 126.3, 122.7, 120.3, 119.3, 116.4, 111.9, 109.1, 61.0, 44.5, 36.3, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 359.1754. Found 359.1750.

Compound 16ab



Yield: 71.5 mg (92 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 123-125 °C.

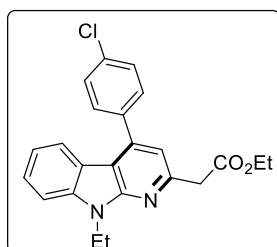
IR (neat): $\nu_{\max}$ 2986, 2963, 2938, 1729, 1608, 1578, 1473, 1296, 1086, 1026, 841, 774 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.74 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.5 Hz, 2H), 7.46-7.42 (m, 2H), 7.09-7.04 (m, 3H), 7.03 (s, 1H), 4.57 (q, J = 7.0 Hz, 2H), 4.22 (q, J = 7.0 Hz, 2H), 3.99 (s, 2H), 3.93 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.3, 160.1, 151.7, 150.9, 145.4, 139.6, 131.6, 130.2, 126.2, 122.8, 120.5, 119.3, 116.4, 114.2, 112.0, 109.1, 61.0, 55.5, 44.5, 36.3, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 389.1860. Found 389.1861.

Compound 16ac



Yield: 63.0 mg (80 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 106-108 °C.

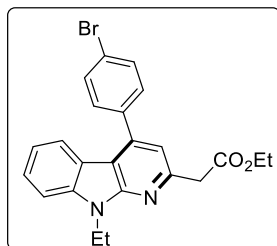
IR (neat): $\nu_{\max}$ 2962, 2927, 2853, 1726, 1608, 1577, 1490, 1362, 1293, 1029, 867, 740 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.65-7.60 (m, 3H), 7.54-7.52 (m, 2H), 7.48-7.46 (m, 2H), 7.08-7.05 (m, 1H), 7.01 (s, 1H), 4.57 (q, J = 7.0 Hz, 2H), 4.22 (q, J = 7.0 Hz, 2H), 4.00 (s, 2H), 1.47 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H). ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 151.7, 151.1, 144.1, 139.6, 137.7, 134.7, 130.3, 129.1, 126.5, 122.6, 120.2, 119.5, 116.2, 111.8, 109.3, 61.1, 44.5, 36.4, 14.4, 14.1 ppm.

HRMS (ESI-TOF): m/z Calcd. For $C_{23}H_{22}ClN_2O_2$ [$M^+ + H$]: 393.1364. Found 393.1365.

Compound 16ad



Yield: 87.5 mg (83 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 120-122 °C.

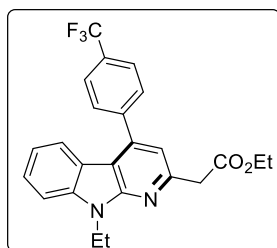
IR (neat): $\nu_{\max}$ 2971, 2930, 1724, 1615, 1552, 1488, 1473, 1354, 1236, 1178, 1071, 1011, 892, 739 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.69 (d, J = 8.5 Hz, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 4.0 Hz, 2H), 7.08-7.04 (m, 1H), 7.01 (s, 1H), 4.57 (q, J = 7.0 Hz, 2H), 4.22 (q, J = 7.0 Hz, 2H), 4.00 (s, 2H), 1.47 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 151.6, 151.1, 144.1, 139.6, 138.1, 132.0, 130.6, 126.5, 122.9, 122.6, 120.1, 119.5, 116.1, 111.7, 109.2, 61.1, 44.4, 36.4, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{22}\text{BrN}_2\text{O}_2$ [$M^+ + H$]: m/z 437.0859. Found 437.0860.

Compound 16ae



Yield: 66.2 mg (78 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 100-102 °C.

IR (neat): $\nu_{\max}$ 2980, 2934, 1729, 1618, 1581, 1560, 1489, 1322, 1125, 1018, 890, 649 cm^{-1} .

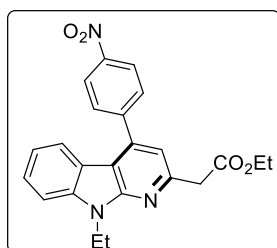
^1H NMR (500 MHz, CDCl_3): δ 7.83-7.79 (m, 4H), 7.57 (d, J = 8.0 Hz, 1H), 7.48-7.47 (m, 2H), 7.09-7.05 (m, 1H), 7.04 (s, 1H), 4.59 (q, J = 7.0 Hz, 2H), 4.23 (q, J = 7.0 Hz, 2H), 4.02 (s, 2H), 1.48 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.0, 151.5, 151.0, 143.6, 142.8, 139.6, 130.7 ($^2J_{\text{C-F}} = 32.5$ Hz), 129.2, 126.6, 125.7 ($^3J_{\text{C-F}} = 3.75$ Hz), 124.2 ($^1J_{\text{C-F}} = 271.3$ Hz), 122.4, 119.8, 119.5, 116.0, 111.6, 109.2, 61.0, 44.3, 36.3, 14.3, 14.0 ppm.

^{19}F NMR (470 MHz, CDCl_3): -62.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{22}\text{F}_3\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 427.1628 Found 427.1627.

Compound 16af



Yield: 58.0 mg (72 %, white solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 73-75 °C.

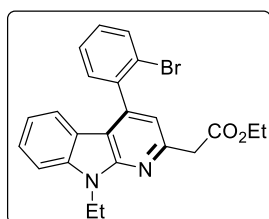
IR (neat): ν_{max} 3111, 2940, 2847, 1738, 1561, 1354, 1248, 1145, 1034, 870, 742 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.44-8.41 (m, 2H), 7.87-7.85 (m, 2H), 7.53 (d, $J = 8.0$ Hz, 1H), 7.50-7.47 (m, 2H), 7.09-7.06 (m, 1H), 7.05 (s, 1H), 4.59 (q, $J = 7.0$ Hz, 2H), 4.23 (q, $J = 7.0$ Hz, 2H), 4.03 (s, 2H), 1.48 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 151.6, 151.3, 148.2, 146.0, 142.7, 139.8, 130.0, 126.9, 124.1, 122.4, 119.8, 119.7, 115.8, 111.5, 109.5, 61.1, 44.4, 36.5, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{22}\text{N}_3\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 404.1605. Found 404.1606.

Compound 16ag



Yield: 62.1 mg (71 %, brown solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 84-86 °C.

IR (neat): ν_{max} 3050, 2926, 2853, 1736, 1650, 1595, 1468, 1429, 1362, 1236, 1172, 1087, 1025, 968, 811, 746 cm^{-1} .

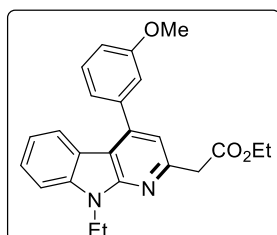
^1H NMR (500 MHz, CDCl_3): δ 7.70 (d, $J = 8.0$ Hz, 1H), 7.39-7.32 (m, 4H), 7.30-7.27 (m, 1H), 7.04 (d, $J = 8.0$ Hz, 1H), 6.94-6.92 (m, 2H), 4.55-4.42 (m, 2H), 4.14 (q, $J =$

7.0 Hz, 2H), 3.97-3.91 (m, 2H), 1.40 (t, $J = 7.0$ Hz, 3H), 1.19 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.2, 151.3, 150.8, 143.6, 139.8, 139.6, 133.2, 130.8, 130.0, 127.7, 126.4, 122.7, 122.5, 120.2, 119.7, 116.2, 112.5, 109.1, 61.0, 44.5, 36.4, 14.4, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{22}\text{BrN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 437.0859. Found 437.0858.

Compound 16ah



Yield: 77.7 mg (81 %, gummy liquid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

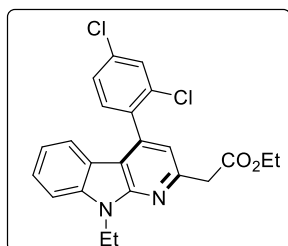
IR (neat): ν_{max} 2971, 2934, 1734, 1582, 1562, 1487, 1470, 1263, 1121, 1034, 782, 733 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.77 (d, $J = 8.0$ Hz, 1H), 7.51-7.48 (m, 3H), 7.31-7.26 (m, 2H), 7.11-7.09 (m, 3H), 4.62 (q, $J = 7.0$ Hz, 2H), 4.27 (q, $J = 7.0$ Hz, 2H), 4.06 (s, 2H), 3.89 (s, 3H), 1.52 (t, $J = 7.0$ Hz, 3H), 1.34 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 159.8, 151.6, 150.9, 145.3, 140.5, 139.5, 129.8, 126.3, 122.8, 121.2, 120.3, 119.4, 116.2, 114.5, 114.0, 111.8, 109.1, 61.0, 55.5, 44.4, 36.3, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 389.1860. Found 389.1861.

Compound 16ai



Yield: 65.0 mg (76 %, white solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 78-80 $^{\circ}\text{C}$.

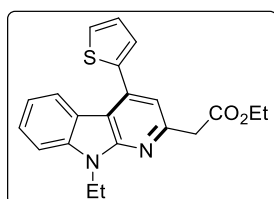
IR (neat): ν_{max} 2976, 2923, 2858, 1735, 1595, 1567, 1483, 1409, 1347, 1255, 1122, 1031, 995, 867, 823, 783 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.53 (s, 1H), 7.35-7.34 (m, 2H), 7.31 (s, 2H), 7.14-7.10 (m, 1H), 6.97-6.93 (m, 1H), 6.91 (s, 1H), 4.53-4.41 (m, 2H), 4.12 (q, $J = 7.0$ Hz, 2H), 3.96-3.89 (m, 2H), 1.38 (t, $J = 7.0$ Hz, 3H), 1.18 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 151.3, 150.9, 140.7, 139.5, 136.3, 135.1, 133.9, 131.7, 129.9, 127.5, 126.6, 122.3, 120.0, 119.7, 116.2, 112.5, 61.0, 44.4, 36.4, 14.3, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{21}\text{Cl}_2\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 427.0975. Found 427.0975.

Compound 16ak



Yield: 54.7 mg (75 %, brown solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 123-125 $^{\circ}\text{C}$.

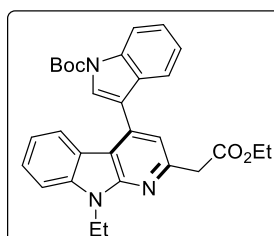
IR (neat): ν_{max} 3063, 2973, 2925, 1724, 1561, 1468, 1333, 1196, 1025, 750, 655 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.05-8.03 (m, 1H), 7.54₄-7.53₅ (m, 1H), 7.52-7.50 (m, 1H), 7.48-7.46 (m, 2H), 7.25-7.24 (m, 1H), 7.14-7.10 (m, 2H), 4.57 (q, $J = 7.0$ Hz, 2H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.99 (s, 2H), 1.47 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 151.8, 150.8, 140.3, 139.6, 138.0, 127.6₉, 127.6₇, 126.9, 126.6, 122.8, 120.3, 119.5, 117.0, 112.0, 109.2, 61.0, 44.4, 36.4, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{21}\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 365.1318. Found 365.1318.

Compound 16al



Yield: 71.0 mg (71 %, white solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 65-67 $^{\circ}\text{C}$.

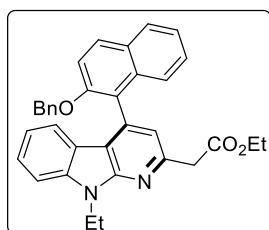
IR (neat): ν_{max} 2977, 2932, 1731, 1566, 1471, 1451, 1368, 1245, 1149, 1096, 848, 747 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.30 (d, $J = 7.5$ Hz, 1H), 7.91 (s, 1H), 7.50-7.44 (m, 2H), 7.43-7.38 (m, 3H), 7.21-7.18 (m, 2H), 7.00-6.97 (m, 1H), 4.60 (q, $J = 7.0$ Hz, 2H), 4.23 (q, $J = 7.0$ Hz, 2H), 4.02 (s, 2H), 1.72 (s, 9H), 1.50 (t, $J = 7.0$ Hz, 3H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.3, 151.8, 150.9, 149.8, 139.6, 136.7, 135.6, 129.2, 126.2, 125.1, 124.6, 123.5, 123.2, 121.0, 120.4, 119.7, 119.4, 117.0, 115.6, 112.9, 109.0, 84.3, 61.1, 44.5, 36.4, 28.4, 14.4, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{32}\text{N}_3\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 498.2387. Found 498.2388.

Compound 16an



Yield: 71.0 mg (69 %, yellow solid, $R_f = 0.50$ (90:10 hexane/ethyl acetate)).

Mp: 122-124 $^{\circ}\text{C}$.

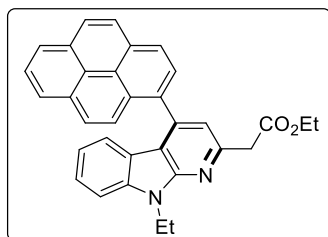
IR (neat): ν_{max} 3059, 2970, 1721, 1621, 1592, 1567, 1450, 1264, 1081, 1035, 939, 785, 741 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.98 (d, $J = 9.0$ Hz, 1H), 7.89 (d, $J = 8.0$ Hz, 1H), 7.46 (d, $J = 9.0$ Hz, 1H), 7.43 (d, $J = 8.0$ Hz, 1H), 7.39-7.33 (m, 3H), 7.26-7.23 (m, 1H), 7.15-7.09 (m, 4H), 6.93 (d, $J = 6.5$ Hz, 2H), 6.83-6.80 (m, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 5.12-5.09 (m, 1H), 5.03-5.00 (m, 1H), 4.68-4.57 (m, 2H), 4.24-4.20 (m, 2H), 4.06 (s, 2H), 1.54 (t, $J = 7.0$ Hz, 3H), 1.27 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 153.1, 151.6, 150.8, 139.8, 139.6, 137.1, 132.8, 130.2, 129.4, 128.3, 128.1, 127.6, 127.1, 127.0, 126.1, 125.2, 124.3, 122.9, 122.5, 120.8, 119.5, 118.0, 116.0, 114.2, 108.8, 71.7, 60.9, 44.7, 36.4, 14.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{31}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 515.2329. Found 515.2327.

Compound 16ao



Yield: 62.7 mg (65 %, yellow solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 70-72 °C.

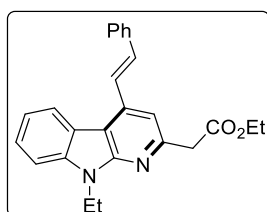
IR (neat): $\nu_{\max}$ 3046, 2974, 2934, 1731, 1564, 1485, 1469, 1214, 1029, 846, 739, 664 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.34 (d, J = 8.0 Hz, 1H), 8.26 (dd, J = 7.5, 1.0 Hz, 1H), 8.22-8.18 (m, 2H), 8.17-8.16 (m, 1H), 8.12 (d, J = 8.0 Hz, 1H), 8.06-8.03 (m, 1H), 7.92 (d, J = 9.0 Hz, 1H), 7.87 (d, J = 9.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.35-7.32 (m, 1H), 7.26 (s, 1H), 6.71-6.68 (m, 1H), 6.65-6.64 (m, 1H), 4.69-4.60 (m, 2H), 4.26 (q, J = 7.0 Hz, 2H), 4.10 (s, 2H), 1.56 (t, J = 7.0 Hz, 3H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.3, 151.5, 150.9, 144.0, 139.7, 134.1, 131.5₉, 131.5₇, 131.2, 128.7, 128.2, 128.1, 127.6, 127.1, 126.3₂, 126.3₀, 125.5, 125.4, 125.3, 125.0, 124.9, 122.9, 120.4, 119.5, 117.8, 113.8, 109.0, 61.1, 44.7, 36.5, 14.4, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{27}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 483.2062. Found 483.2068.

Compound 16aq



Yield: 52.2 mg (68 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 100-102 °C.

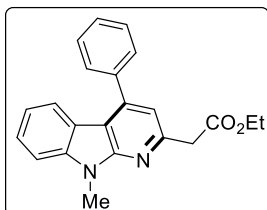
IR (neat): $\nu_{\max}$ 3051, 2980, 2929, 1734, 1635, 1470, 1450, 1302, 1150, 959, 744 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.22 (d, J = 7.5 Hz, 1H), 7.99-7.95 (m, 1H), 7.67 (d, J = 7.5 Hz, 2H), 7.53-7.43 (m, 5H), 7.38-7.36 (m, 2H), 7.30-7.27 (m, 1H), 4.55 (q, J = 7.0 Hz, 2H), 4.24 (q, J = 7.0 Hz, 2H), 4.00 (s, 2H), 1.45 (t, J = 7.0 Hz, 3H), 1.30 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.4, 152.0, 150.9, 141.0, 139.7, 136.9, 134.3, 129.0, 128.8, 127.3, 126.1, 124.7, 123.4, 121.0, 119.9, 112.0, 111.4, 109.3, 61.0, 44.6, 36.3, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{25}\text{H}_{25}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 385.1911. Found 385.1912.

Compound 16ba



Yield: 56.4 mg (82 %, brown solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 120-122 °C.

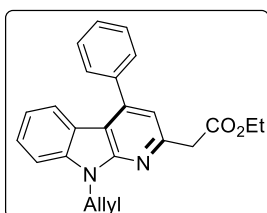
IR (neat): ν_{max} 3059, 2922, 1725, 1618, 1580, 1496, 1478, 1317, 1245, 1028, 886, 706 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.69-7.68 (m, 1H), 7.67-7.65 (m, 2H), 7.57-7.50 (m, 3H), 7.48-7.43 (m, 2H), 7.07-7.04 (m, 2H), 4.23 (q, J = 7.0 Hz, 2H), 4.02 (s, 2H), 3.99 (s, 3H), 1.30 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 152.3, 150.9, 145.5, 140.6, 139.1, 128.9, 128.7, 128.6, 126.4, 122.6, 120.2, 119.5, 116.4, 111.9, 109.0, 61.0, 44.4, 27.9, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{22}\text{H}_{21}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 345.1598. Found 345.1599.

Compound 16ca



Yield: 56.3 mg (76 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 57-59 °C.

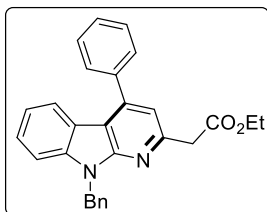
IR (neat): ν_{max} 3059, 2980, 2931, 1732, 1644, 1484, 1405, 1301, 1126, 1029, 995, 923, 861 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.72-7.68 (m, 3H), 7.59-7.52 (m, 3H), 7.44₂-7.43₅ (m, 2H), 7.10-7.05 (m, 2H), 6.11-6.04 (m, 1H), 5.22-5.17 (m, 4H), 4.25 (q, J = 7.0 Hz, 2H), 4.03 (s, 2H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 151.8, 151.0, 145.6, 139.9, 139.1, 133.1, 128.9, 128.8, 128.6, 126.4, 122.6, 120.4, 119.6, 116.9, 116.7, 111.9, 109.8, 61.0, 44.4, 43.9, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{23}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 371.1754. Found 371.1753.

Compound 16da



Yield: 57.1 mg (68 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 80-82 °C.

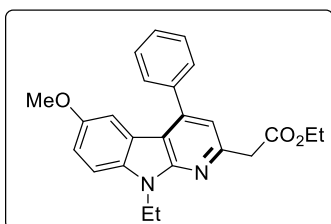
IR (neat): ν_{max} 2970, 2921, 2850, 1718, 1578, 1556, 1488, 1412, 1296, 1246, 1028, 992, 770 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.62-7.57 (m, 3H), 7.49-7.43 (m, 3H), 7.27-7.12 (m, 7H), 7.02 (s, 1H), 6.96-6.93 (m, 1H), 5.65 (s, 2H), 4.12 (q, J = 7.0 Hz, 2H), 3.93 (s, 2H), 1.17 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 152.2, 151.2, 145.7, 139.9, 139.2, 137.7, 128.9, 128.8, 128.7₁, 128.6₉, 127.5, 126.5, 122.7, 120.5, 119.8, 116.8, 111.9, 109.9, 61.0, 45.2, 44.5, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{25}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 421.911. Found 421.913.

Compound 16ea



Yield: 54.4 mg (70 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 80-82 °C.

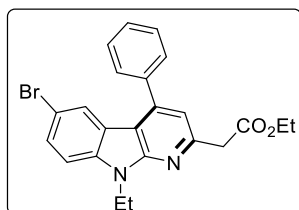
IR (neat): ν_{max} 2978, 2932, 1732, 1623, 1581, 1561, 1472, 1365, 1277, 1030, 941, 876, 704 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57 (d, J = 7.0 Hz, 2H), 7.46-7.38 (m, 3H), 7.24 (d, J = 9.0 Hz, 1H), 7.05₂-7.04₈ (m, 1H), 6.99-6.97 (m, 1H), 6.93 (s, 1H), 4.43 (q, J = 7.0 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H), 3.90 (s, 2H), 3.57 (s, 3H), 1.35 (t, J = 7.0 Hz, 3H), 1.19 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.2, 153.5, 151.8, 150.9, 145.4, 139.0, 134.4, 128.9, 128.6, 120.6, 115.8, 115.1, 111.7, 109.7, 106.2, 61.0, 55.8, 44.5, 36.3, 14.3, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{25}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 389.1860. Found 389.1861.

Compound 16fa



Yield: 58.6 mg (67 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 113-115 $^{\circ}\text{C}$.

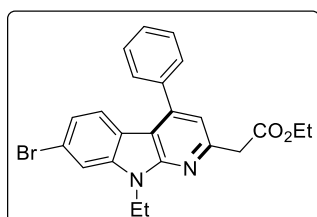
IR (neat): ν_{max} 2972, 2938, 1729, 1582, 1561, 1471, 1397, 1299, 1173, 1030, 867, 76 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.77₀-7.76₇ (m, 1H), 7.66-7.63 (m, 2H), 7.59-7.52 (m, 4H), 7.33 (d, J = 8.5 Hz, 1H), 7.07 (s, 1H), 4.55 (q, J = 7.0 Hz, 2H), 4.23 (q, J = 7.0 Hz, 2H), 4.00 (s, 2H), 1.45 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 151.8, 151.7, 146.0, 138.6, 138.2, 129.0₄, 129.0₁, 128.9, 128.7, 125.3, 122.0, 116.8, 112.1, 111.0, 110.6, 61.1, 44.5, 36.5, 14.4, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{22}\text{BrN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 437.0859. Found 437.0858.

Compound 16ga



Yield: 60.4 mg (69 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 125-127 $^{\circ}\text{C}$.

IR (neat): ν_{max} 2963, 2923, 1729, 1613, 1563, 1476, 1368, 1263, 1129, 993, 811, 770 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.65-7.64 (m, 1H), 7.64-7.62 (m, 1H), 7.60-7.59 (m, 1H), 7.57-7.51 (m, 3H), 7.51-7.49 (m, 1H), 7.14 (dd, J = 8.0, 1.5 Hz, 1H), 7.07 (s, 1H), 4.53 (q, J = 7.0 Hz, 2H), 4.22 (q, J = 7.0 Hz, 2H), 3.99 (s, 2H), 1.47 (t, J = 7.0 Hz, 3H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

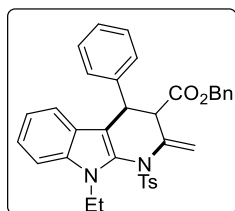
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 171.1, 151.7, 151.5, 145.6, 140.4, 138.9, 128.9, 128.8_i, 128.7_s, 123.9, 122.6, 120.0, 119.3, 116.9, 112.2, 111.5, 61.1, 44.5, 36.5, 14.4, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{22}\text{BrN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 437.0859. Found 437.0859.

3.9 General procedure for the synthesis of compounds 17aa-ac, 17af-ag, 17ba-ca, and 17ga

A solution of 2-sulfonamido indole **2** (0.20 mmol) and β' -acetoxy allenolate **6** (0.24 mmol) in toluene (2.0 mL) was stirred in a Schlenk tube at room temperature for 1h. Subsequently, DABCO (0.04 mmol) was added to the reaction mixture and the stirring continued for 1h more. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×5 mL). Then, the combined organic layer was washed with brine (2 x 30 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:19) as the eluent.

Compound 17aa



Yield: 76.0 mg (66 %, yellow solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 134-136 °C.

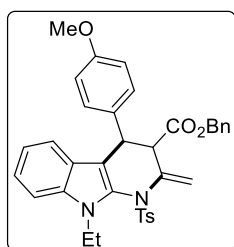
IR (neat): ν_{max} 3062, 3030, 2925, 2877, 1735, 1653, 1596, 1493, 1454, 1364, 1341, 1236, 1168, 1086, 930, 813.

^1H NMR (500 MHz, CDCl_3): δ 7.63 (d, J = 7.5 Hz, 2H), 7.40 (d, J = 8.5 Hz, 1H), 7.34-7.32 (m, 3H), 7.18-7.15 (m, 3H), 7.12-7.11 (m, 5H), 6.86-6.82 (m, 3H), 6.62 (d, J = 7.5 Hz, 1H), 5.58 (s, 1H), 5.07-5.04 (m, 3H), 4.67-4.63 (m, 1H), 4.44-4.39 (m, 2H), 2.75-2.74 (m, 1H), 2.25 (s, 3H), 1.39 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.7, 145.3, 141.5, 141.1, 136.6, 135.4, 133.1, 130.1, 129.2, 128.6, 128.4, 128.2, 128.1, 127.2, 125.9, 122.2, 119.9, 119.6, 116.1, 110.7, 105.0, 66.8, 51.8, 43.5, 40.4, 21.7, 14.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{33}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 577.2156. Found 577.2154.

Compound 17ab



Yield: 87.3 mg (72 %, brown solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 130-132 °C.

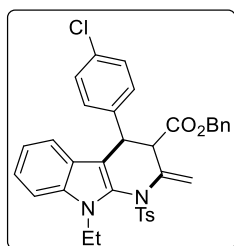
IR (neat): $\nu_{\max}$ 3059, 2929, 2848, 1720, 1610, 1564, 1512, 1488, 1469, 1407, 1335, 1301, 1246, 1232, 1189, 1081, 1056, 1031, 836, 782.

^1H NMR (500 MHz, CDCl_3): δ 7.63 (d, J = 7.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 1H), 7.33 (s, 3H), 7.18-7.12 (m, 5H), 6.87-6.84 (m, 1H), 6.74 (d, J = 8.0 Hz, 2H), 6.65 (s, 3H), 5.57 (s, 1H), 5.05 (s, 3H), 4.65-4.64 (m, 1H), 4.43-4.40 (m, 1H), 4.35-4.33 (m, 1H), 3.77 (s, 3H), 2.72-2.70 (m, 1H), 2.27 (s, 3H), 1.38 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.7, 158.7, 145.2, 141.3, 136.6, 135.5, 133.5, 133.1, 130.1, 129.2, 129.1, 128.6, 128.4, 128.2, 126.0, 122.2, 119.8, 119.7, 115.9, 113.7, 110.7, 105.3, 66.7, 55.3, 52.0, 42.8, 40.4, 21.7, 14.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{35}\text{N}_2\text{O}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 607.2261. Found 607.2266.

Compound 17ac



Yield: 75.7 mg (62 %, white solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 130-132 °C.

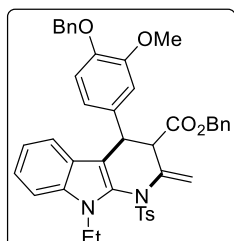
IR (neat): $\nu_{\max}$ 3043, 2977, 2880, 1733, 1655, 1595, 1489, 1455, 1421, 1365, 1341, 1237, 1153, 1087, 1044, 1014, 923, 815, 739.

^1H NMR (500 MHz, CDCl_3): δ 7.63 (d, J = 7.0 Hz, 2H), 7.41 (d, J = 8.5 Hz, 1H), 7.36-7.35 (m, 3H), 7.20-7.18 (m, 1H), 7.14-7.12 (m, 4H), 7.07 (d, J = 7.5 Hz, 2H), 6.89-6.86 (m, 1H), 6.77 (d, J = 8.0 Hz, 2H), 6.62 (d, J = 7.0 Hz, 1H), 5.57 (s, 1H), 5.06 (s, 3H), 4.65-4.62 (m, 1H), 4.44-4.37 (m, 2H), 2.71-2.69 (m, 1H), 2.28 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.7, 158.7, 145.2, 141.3, 136.6, 135.5, 133.5, 133.1, 130.1, 129.2, 129.1, 128.6, 128.4, 128.2, 126.0, 122.2, 119.8, 119.7, 115.9, 113.7, 110.7, 105.3, 66.7, 55.3, 52.0, 42.8, 40.4, 21.7, 14.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{32}\text{ClN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 611.1766. Found 611.1768.

Compound 17af



Yield: 79.8 mg (56 %, white solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 135-137 °C.

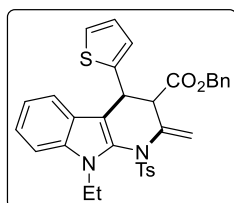
IR (neat): ν_{max} 3031, 2934, 2877, 1735, 1653, 1594, 1511, 1454, 1421, 1362, 1341, 1256, 1231, 1155, 1086, 1021, 919, 813, 742, 698 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.63 (d, J = 7.0 Hz, 2H), 7.44 (d, J = 7.5 Hz, 2H), 7.40-7.36 (m, 3H), 7.33-7.31 (m, 4H), 7.19-7.16 (m, 1H), 7.12 (s, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.89-6.86 (m, 1H), 6.68 (d, J = 7.5 Hz, 1H), 6.64-6.62 (m, 2H), 6.27 (d, J = 7.5 Hz, 1H), 5.52 (s, 1H), 5.14-5.10 (m, 2H), 5.07-5.04 (m, 3H), 4.65-4.60 (m, 1H), 4.42-4.34 (m, 2H), 3.71 (s, 3H), 2.77-2.75 (m, 1H), 2.19 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.9, 149.5, 147.5, 147.4₁, 147.3₅, 145.2, 141.3, 137.4, 135.5, 134.7, 133.1, 132.9, 130.0, 129.2, 128.6₉, 128.6₆, 128.5, 128.1, 128.0, 127.5, 122.2, 120.2, 119.8, 115.9, 114.0, 112.4, 110.6, 105.1, 71.3, 66.8, 56.3, 52.0, 43.2, 40.3, 21.7, 14.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{43}\text{H}_{41}\text{N}_2\text{O}_6\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 713.2680. Found 713.2675.

Compound 17ag



Yield: 74.5 mg (64 %, yellow solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 135-137 °C.

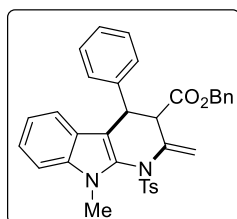
IR (neat): ν_{max} 3062, 2977, 2934, 2870, 1733, 1454, 1422, 1368, 1340, 1240, 1155, 1086, 1044, 922, 852, 738 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.59 (s, 2H), 7.42-7.36 (m, 4H), 7.20 (s, 3H), 7.10 (s, 3H), 6.93-6.82 (m, 3H), 6.66 (s, 1H), 5.60 (s, 1H), 5.09 (s, 2H), 5.03 (s, 1H), 4.75-4.74 (m, 1H), 4.63 (s, 1H), 4.41 (s, 1H), 2.66-2.64 (s, 1H), 2.24 (s, 3H), 1.39 (t, J = 6.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.5, 145.2, 140.6, 136.4, 135.4, 132.8, 130.3, 129.5, 129.1, 128.7, 128.5, 128.3, 126.4, 125.9, 124.5, 122.3, 120.0, 119.6, 116.3, 110.7, 104.4, 67.0, 52.2, 40.4, 38.5, 21.7, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{31}\text{N}_2\text{O}_4\text{S}_2$ [$\text{M}^+ + \text{H}$]: m/z 583.1720. Found 583.1719.

Compound 17ba



Yield: 70.0 mg (62 %, brown solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 140-142 $^{\circ}\text{C}$.

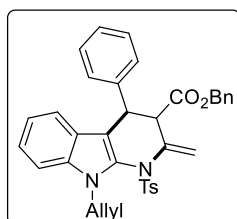
IR (neat): ν_{max} 3062, 3029, 2924, 1735, 1653, 1595, 1492, 1466, 1362, 1239, 1167, 1087, 1043, 925, 814, 742, 701 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.62 (s, 2H), 7.35-7.33 (m, 4H), 7.26-7.16 (m, 2H), 7.14-7.08 (m, 6H), 6.88-6.84 (m, 3H), 6.62 (s, 1H), 5.62 (s, 1H), 5.09 (s, 1H), 5.01 (s, 2H), 4.37-4.36 (m, 1H), 3.91 (s, 3H), 2.63 (s, 1H), 2.24 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.6, 145.3, 141.5, 140.9, 137.3, 135.4, 133.3, 133.0, 130.1, 129.2, 128.6, 128.4, 128.2, 127.3, 125.1, 122.2, 119.9, 119.5, 116.3, 110.0, 104.0, 66.8, 51.8, 43.4, 32.7, 21.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{31}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 563.1999. Found 563.1993.

Compound 17ca



Yield: 70.6 mg (60 %, yellowish white solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 142-144 $^{\circ}\text{C}$.

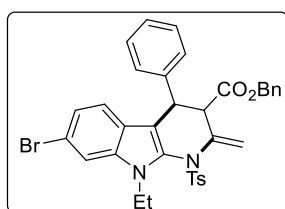
IR (neat): ν_{max} 2923, 2853, 1737, 1567, 1488, 1464, 1405, 1371, 1336, 1300, 1267, 1226, 1169, 1092, 1057, 920, 743 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.64 (d, J = 7.0 Hz, 2H), 7.40 (d, J = 8.5 Hz, 1H), 7.33-7.32 (m, 3H), 7.19-7.18 (m, 1H), 7.15-7.12 (m, 7H), 6.84 (d, J = 7.5 Hz, 3H), 6.62 (d, J = 7.5 Hz, 1H), 6.08-6.00 (m, 1H), 5.56 (s, 1H), 5.20-5.18 (m, 1H), 5.16-5.12 (m, 1H), 5.07-5.04 (m, 5H), 4.41-4.39 (m, 1H), 2.75-2.73 (m, 1H), 2.26 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.6, 145.3, 141.4, 141.0, 137.3, 135.4, 134.7, 133.3, 133.0, 130.1, 129.2, 128.7, 128.4, 128.2, 128.1, 127.2, 125.8, 122.3, 120.1, 119.6, 116.9, 116.3, 111.3, 105.1, 66.8, 51.8, 48.4, 43.5, 29.8, 21.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{33}\text{N}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 589.2156. Found 589.2159.

Compound 17ga



Yield: 84.0 mg (64 %, brown solid, R_f = 0.50 (95:5 hexane/ethyl acetate)).

Mp: 136-138 $^{\circ}\text{C}$.

IR (neat): ν_{max} 3069, 3034, 2976, 1734, 1654, 1596, 1493, 1465, 1365, 1338, 1236, 1153, 1086, 1044, 933, 907, 812, 735 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.63 (d, J = 6.5 Hz, 2H), 7.54 (s, 1H), 7.34-7.33 (m, 3H), 7.20-7.19 (m, 1H), 7.13-7.12 (m, 6H), 6.94 (d, J = 7.5 Hz, 1H), 6.81 (d, J = 7.0 Hz, 2H), 6.45 (d, J = 8.0 Hz, 1H), 5.58 (s, 1H), 5.07-5.04 (m, 3H), 4.64-4.63 (m, 1H), 4.38-4.36 (m, 2H), 2.73-2.71 (m, 1H), 2.26 (s, 3H), 1.38 (t, J = 7.0 Hz, 3H) ppm.

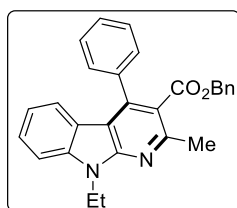
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.5, 145.4, 141.2, 140.9, 137.3, 135.4, 133.6, 132.9, 130.2, 129.2, 128.7, 128.5₁, 128.4₇, 128.2, 128.0, 127.4, 124.7, 123.2, 120.8, 116.3, 115.9, 113.7, 105.2, 66.9, 51.7, 43.3, 40.6, 21.7, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{32}\text{BrN}_2\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 655.1261. Found 655.1258.

3.10 General Procedure for the Synthesis of Compounds 18aa-ah, 18aj, 18ba-ca, and 18ea-ga

A Schlenk tube was charged with 2-sulfonamido indole **2** (0.20 mmol), β' -acetoxy allenoate **6** (0.24 mmol) in toluene (2.0 mL) and the mixture stirred at 50 °C. Subsequently, DBU base (0.04 mmol) was added and the stirring continued for 2h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 $\times$ 5 mL). Then, the combined organic layer was washed with brine, dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (10:90) as the eluent.

Compound 18aa



Yield: 71.5 mg (85 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 120-122 °C.

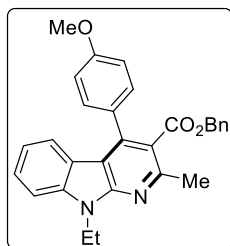
IR (neat): $\nu_{\max}$ 3049, 2966, 2876, 1696, 1561, 1233, 1077, 1057, 955, 913 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 7.49-7.44 (m, 5H), 7.43-7.40 (m, 2H), 7.28-7.27 (m, 3H), 7.10 (d, J = 8.0 Hz, 1H), 7.07-7.05 (m, 2H), 6.99-6.96 (m, 1H), 5.00 (s, 2H), 4.57 (q, J = 7.0 Hz, 2H), 2.76 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H) ppm.

¹³C{¹H} NMR (125 MHz, CDCl₃): δ 169.6, 153.1, 150.9, 143.4, 139.7, 137.4, 135.4, 128.7₁, 128.6₈, 128.6, 128.5, 128.3, 126.4, 122.6, 121.1, 120.8, 119.8, 111.5, 109.3, 67.3, 36.3, 23.9, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For C₂₈H₂₅N₂O₂ [M^+ + H]: m/z 421.1911. Found 421.1917.

Compound 18ab



Yield: 78.3 mg (87 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 125-127 °C.

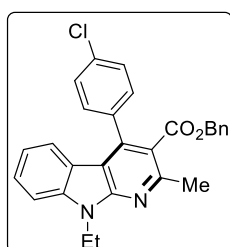
IR (neat): $\nu_{\max}$ 2975, 2928, 2842, 1695, 1609, 1580, 1561, 1512, 1406, 1375, 1234, 1178, 1055, 1029, 916, 845 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.44-7.42 (m, 2H), 7.39-7.36 (m, 2H), 7.30-7.28 (m, 3H), 7.23 (d, J = 8.0 Hz, 1H), 7.13-7.10 (m, 2H), 7.02-6.96 (m, 3H), 5.06 (s, 2H), 4.57 (q, J = 7.0 Hz, 2H), 3.91 (s, 3H), 2.76 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.7, 159.9, 152.8, 150.8, 143.3, 139.7, 135.5, 129.9, 129.4, 128.7, 128.5, 128.3, 126.4, 122.6, 121.6, 120.9, 119.8, 114.1, 111.8, 109.2, 67.2, 55.4, 36.3, 23.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 451.2016. Found 451.2014.

Compound 18ac



Yield: 76.0 mg (83 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 145-147 $^{\circ}\text{C}$.

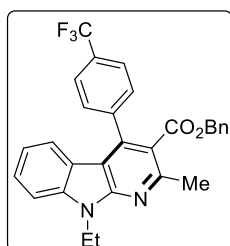
IR (neat): $\nu_{\max}$ 2967, 2928, 1617, 1599, 1577, 1557, 1370, 1334, 1301, 1209, 1132, 1077, 844 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.45-7.43 (m, 2H), 7.39-7.36 (m, 2H), 7.34-7.29 (m, 5H), 7.10-7.07 (m, 3H), 7.03-7.00 (m, 1H), 5.05 (s, 2H), 4.56 (q, J = 7.0 Hz, 2H), 2.77 (s, 3H), 1.46 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 153.3, 150.8, 142.0, 139.7, 135.7, 135.2, 134.6, 129.9, 128.94, 128.89, 128.53, 128.45, 126.6, 122.4, 120.9, 120.5, 120.0, 111.3, 109.4, 67.3, 36.3, 23.9, 14. Ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{24}\text{ClN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 455.1521. Found 455.1522.

Compound 18ad



Yield: 79.0 mg (81 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 105-107 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3066, 2980, 2918, 2845, 1711, 1616, 1581, 1561, 1489, 1471, 1449, 1316, 1182, 1130, 1003, 951, 838, 814 cm^{-1} .

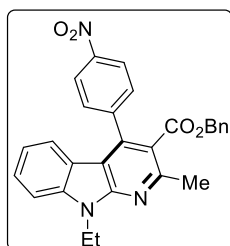
^1H NMR (500 MHz, CDCl_3): δ 7.58 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.36 (s, 2H), 7.22-7.17 (m, 3H), 6.97 (d, J = 6.5 Hz, 2H), 6.92-6.86 (m, 2H), 4.93 (s, 2H), 4.49 (q, J = 7.0 Hz, 2H), 2.71 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 153.6, 150.8, 141.8, 141.2, 139.8, 135.1, 130.6 ($^2J_{\text{C-F}}$ = 32.5 Hz), 129.1, 128.9, 128.6, 126.8, 125.6 ($^3J_{\text{C-F}}$ = 2.5 Hz), 124.3 ($^1J_{\text{C-F}}$ = 271.3 Hz), 122.2, 120.6, 120.3, 120.1, 111.2, 109.5, 67.5, 36.4, 24.0, 14.1 ppm.

^{19}F NMR (470 MHz, CDCl_3): -62.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{24}\text{F}_3\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 489.1784 Found 489.1782.

Compound 18ae



Yield: 77.0 mg (83 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 142-144 $^{\circ}\text{C}$.

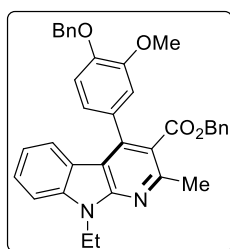
IR (neat): $\nu_{\max}$ 3050, 2959, 2922, 2848, 1712, 1602, 1570, 1515, 1491, 1469, 1452, 1346, 1334, 1299, 1228, 1191, 1105, 1053, 933, 913, 854 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.13 (d, J = 8.5 Hz, 2H), 7.50-7.48 (m, 2H), 7.44-7.43 (m, 2H), 7.30-7.28 (m, 1H), 7.25-7.22 (m, 2H), 7.08 (d, J = 7.5 Hz, 2H), 7.00-6.96 (m, 1H), 6.88 (d, J = 7.5 Hz, 1H), 5.04 (s, 2H), 4.44 (q, J = 7.5 Hz, 2H), 2.82 (s, 3H), 1.48 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 168.7, 154.1, 150.8, 147.8, 144.3, 141.1, 139.8, 134.9, 129.5, 129.2, 128.7, 128.5, 127.0, 123.8, 122.1, 120.2, 120.1, 119.9, 110.9, 109.6, 67.3, 36.4, 24.2, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{24}\text{N}_3\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 466.1761. Found 466.1763.

Compound 18af



Yield: 83.4 mg (75 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 148-150 °C.

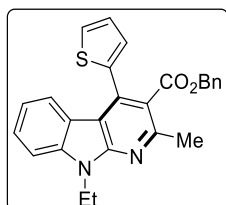
IR (neat): $\nu_{\max}$ 3069, 3030, 2931, 2874, 1718, 1607, 1564, 1510, 1467, 1412, 1373, 1249, 1226, 1133, 1055, 1027, 855 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.51 (d, J = 7.0 Hz, 2H), 7.41-7.37 (m, 4H), 7.34-7.31 (m, 1H), 7.26-7.20 (m, 4H), 7.06-7.03 (m, 2H), 6.99-6.91 (m, 4H), 5.25-5.23 (m, 2H), 5.00 (q, J = 12.0 Hz, 2H), 4.54-4.53 (m, 2H), 3.73 (s, 3H), 2.74 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H). ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.8, 153.0, 150.9, 149.8, 148.3, 143.1, 139.7, 137.1, 135.4, 130.3, 128.7, 128.6, 128.5, 128.3, 128.1, 127.6, 126.4, 122.7, 121.3, 120.8, 119.8, 114.0, 112.3, 111.6, 109.2, 71.2, 67.3, 56.0, 36.3, 23.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{33}\text{N}_2\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 557.2435. Found 557.2431.

Compound 18ag



Yield: 64.0 mg (75 %, brown solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 117-119 °C.

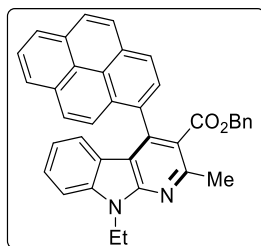
IR (neat): $\nu_{\max}$ 2973, 2924, 2848, 1724, 1577, 1562, 1490, 1471, 1371, 1355, 1332, 1275, 1173, 1052, 949, 914, 842 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.51-7.49 (m, 1H), 7.47-7.44 (m, 2H), 7.33-7.30 (m, 4H), 7.22-7.18 (m, 3H), 7.17-7.16 (m, 1H), 7.07-7.04 (m, 1H), 5.12 (s, 2H), 4.56 (q, J = 7.0 Hz, 2H), 2.73 (s, 3H), 1.46 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.4, 152.7, 150.7, 139.8, 136.8, 135.9, 135.4, 128.8, 128.6, 128.4, 127.9, 127.5, 127.1, 126.7, 122.7, 122.4, 120.5, 120.0, 112.7, 109.3, 67.5, 36.3, 23.7, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 427.1475. Found 427.1477.

Compound 18ah



Yield: 80.6 mg (74 %, yellowish white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: above 200 °C.

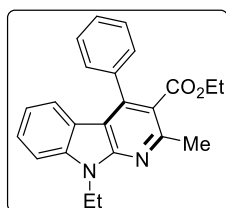
IR (neat): $\nu_{\max}$ 3038, 2925, 2852, 1718, 1566, 1510, 1488, 1469, 1455, 1372, 1336, 1297, 1285, 1229, 1206, 1183, 1105, 1080, 913, 847, 744 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.28-8.27 (m, 1H), 8.20-8.18 (m, 2H), 8.16-8.14 (m, 1H), 8.13-8.11 (m, 1H), 8.06-8.03 (m, 1H), 7.92 (d, J = 7.5 Hz, 1H), 7.80 (d, J = 9.0 Hz, 1H), 7.66 (d, J = 9.5 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.30-7.27 (m, 1H), 6.71-6.68 (m, 1H), 6.60-6.57 (m, 1H), 6.51-6.48 (m, 2H), 6.35-6.33 (m, 2H), 6.13 (d, J = 7.5 Hz, 1H), 4.67-4.64 (m, 1H), 4.64-4.58 (m, 3H), 2.90 (s, 3H), 1.54 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 154.0, 150.8, 142.5, 139.8, 134.4, 132.4, 131.6, 131.5, 131.3, 128.8, 128.1, 127.9, 127.7, 127.6₂, 127.5₅, 126.4₀, 126.3₇, 126.2, 125.4₂, 125.3₈, 125.1, 125.0, 124.8₄, 124.7₅, 122.5, 122.0, 120.7, 120.0, 112.9, 109.2, 67.1, 36.4, 24.2, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{38}\text{H}_{29}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 545.2224. Found 545.2226.

Compound 18aj



Yield: 53.7 mg (75 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 112-114 °C.

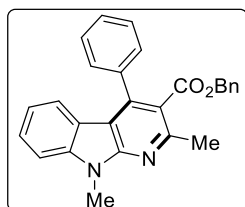
IR (neat): $\nu_{\max}$ 3059, 2976, 2931, 1715, 1617, 1566, 1488, 1469, 1445, 1369, 1334, 1301, 1230, 1133, 1058, 1027, 895, 749 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.51-7.46 (m, 5H), 7.44-7.41 (m, 2H), 7.11 (d, J = 8.0 Hz, 1H), 7.00-6.97 (m, 1H), 4.58 (q, J = 7.0 Hz, 2H), 4.03 (q, J = 7.0 Hz, 2H), 2.79 (s, 3H), 1.47 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.7, 153.1, 150.8, 143.5, 139.7, 137.6, 128.6₀, 128.5₅, 128.4, 126.4, 122.6, 121.4, 120.8, 119.8, 111.5, 109.3, 61.1, 36.3, 23.8, 14.1, 13.8 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{23}\text{H}_{23}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 359.1754. Found 359.1755.

Compound 18ba



Yield: 66.5 mg (82 %, brown solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 100-102 °C.

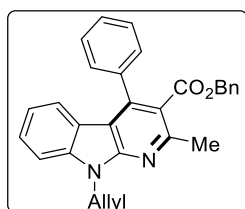
IR (neat): ν_{max} 3037, 2920, 2848, 1707, 1578, 1561, 1498, 1401, 1372, 1333, 1301, 1245, 1201, 1132, 1088, 1075, 1056, 959, 797 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.48-7.40 (m, 7H), 7.28-7.26 (m, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.06-7.05 (m, 2H), 7.01-6.98 (m, 1H), 5.00 (s, 2H), 3.98 (s, 3H), 2.77 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 153.3, 151.5, 143.5, 140.8, 137.3, 135.4, 128.7₂, 128.6₉, 128.5₈, 128.5₂, 128.3, 126.6, 122.4, 121.2, 120.6, 120.1, 111.6, 109.1, 67.3, 27.9, 23.8 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 407.1754. Found 407.1758.

Compound 18ca



Yield: 72.6 mg (84 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 130-132 °C.

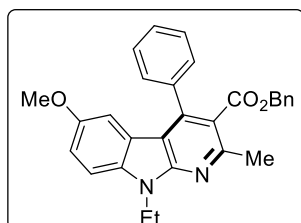
IR (neat): ν_{max} 2920, 2848, 1713, 1581, 1485, 1402, 1368, 1311, 1270, 1226, 1148, 1070, 802, 778, 752 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.49-7.47 (m, 5H), 7.40-7.39 (m, 2H), 7.28-7.27 (m, 3H), 7.11 (d, J = 8.0 Hz, 1H), 7.06-7.05 (m, 2H), 7.00-6.97 (m, 1H), 6.07-6.00 (m, 1H), 5.20-5.18 (m, 1H), 5.15-5.14 (m, 2H), 5.10-5.07 (m, 1H), 5.00 (m, 2H), 2.75 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 153.3, 151.1, 143.5, 140.1, 137.3, 135.4, 132.8, 128.7₄, 128.6₉, 128.6₀, 128.5, 128.3, 126.5, 122.5, 121.5, 120.8, 120.1, 117.0, 111.5, 110.0, 67.3, 43.8, 23.8 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{25}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 433.1911. Found 433.1912.

Compound 18ea



Yield: 72.0 mg (80 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 124-126 °C.

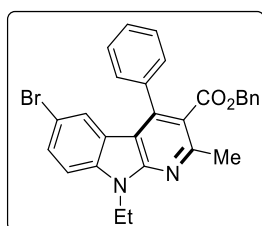
IR (neat): ν_{max} 2995, 2916, 2851, 1708, 1629, 1572, 1479, 1343, 1280, 1242, 1167, 1063, 921, 871 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.48-7.44 (m, 5H), 7.33 (d, J = 8.5 Hz, 1H), 7.29-7.26 (m, 3H), 7.06-7.04 (m, 3H), 6.55-6.54 (m, 1H), 5.00 (s, 2H), 4.53 (q, J = 7.0 Hz, 2H), 3.57 (s, 3H), 2.76 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 153.8, 153.3, 151.0, 143.5, 137.3, 135.4, 134.4, 128.6₄, 128.6₁, 128.5₁, 128.4₈, 128.2, 121.1, 120.5, 115.2, 111.4, 109.9, 105.7, 67.2, 55.6, 36.3, 23.9, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 451.2016. Found 451.2017.

Compound 18fa



Yield: 76.0 mg (76 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 140-142 °C.

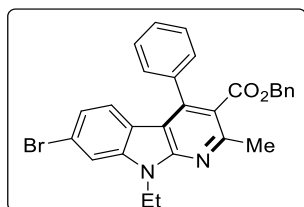
IR (neat): ν_{max} 2976, 2934, 1701, 1580, 1560, 1499, 1476, 1442, 1338, 1275, 1231, 1196, 1079, 1053, 950, 914 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.53-7.47 (m, 4H), 7.44-7.42 (m, 2H), 7.31 (d, J = 8.5 Hz, 1H), 7.28-7.27 (m, 3H), 7.19₂-7.18₈ (m, 1H), 7.06-7.04 (m, 2H), 5.00 (s, 2H), 4.54 (q, J = 7.0 Hz, 2H), 2.75 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 154.0, 150.9, 143.8, 138.3, 136.8, 135.3, 129.2, 128.9₃, 128.8₇, 128.7, 128.5, 128.4, 128.3, 125.2, 122.4, 121.6, 112.7, 110.6₈, 110.6₅, 67.4, 36.5, 23.9, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{24}\text{BrN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 499.1016. Found 499.1019.

Compound 18ga



Yield: 78.0 mg (78 %, white solid, R_f = 0.50 (90:10 hexane/ethyl acetate)).

Mp: 150-152 °C.

IR (neat): ν_{max} 2976, 2925, 1702, 1559, 1405, 1331, 1301, 1230, 1049, 941, 917, 841 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57₄-7.57₁ (m, 1H), 7.49-7.45 (m, 3H), 7.43-7.41 (m, 2H), 7.29-7.27 (m, 3H), 7.09-7.07 (m, 1H), 7.06-7.04 (m, 2H), 6.93 (d, J = 8.5 Hz, 1H), 5.00 (s, 2H), 4.52 (q, J = 7.0 Hz, 2H), 2.74 (s, 3H), 1.46 (t, J = 7.0 Hz, 3H) ppm.

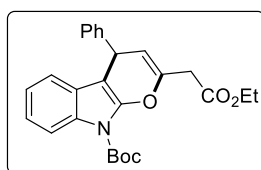
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 153.7, 150.9, 143.5, 140.6, 137.0, 135.3, 128.8, 128.7₂, 128.6₇, 128.5₂, 128.4₆, 128.3, 123.7, 123.1, 121.7, 120.2, 119.7, 112.4, 111.1, 67.3, 36.5, 23.8, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{24}\text{BrN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 499.1016. Found 499.1019.

3.11 General procedure for the synthesis of compounds 19a-e, 19g, 19i, 19k-m, and 19o-q

A Schlenk tube was charged with δ -acetoxy allenolate **4** (0.24 mmol), *tert*-butyl 2-oxoindoline-1-carboxylate **7** (0.20 mmol), and toluene (2.0 mL). Subsequently, DBU (0.04 mmol) was added at rt (25 °C) and mixture stirred for 1h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 $\times$ 10 mL). The combined organic layer was washed with brine solution (20.0 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:19) as the eluent.

Compound 19a



Yield: 75.4 mg (87%, white solid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

Mp: 125-127 °C.

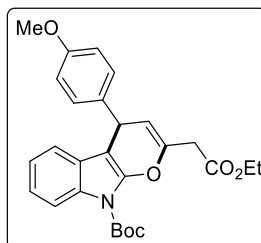
IR (neat): $\nu_{\max}$ 2978, 1736, 1693, 1633, 1599, 1454, 1416, 1362, 1336, 1150, 1133, 1025, 837, 761 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, J = 8.0 Hz, 1H), 7.35-7.34 (m, 2H), 7.32-7.29 (m, 2H), 7.23-7.20 (m, 1H), 7.16-7.12 (m, 1H), 7.04-7.01 (m, 1H), 6.94 (d, J = 7.5 Hz, 1H), 5.09 (d, J = 3.5 Hz, 1H), 4.85 (d, J = 3.0 Hz, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.34-3.27 (m, 2H), 1.66 (s, 9H), 1.29 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.4, 149.1, 144.3, 144.2, 143.8, 131.8, 128.7, 128.2, 127.0, 126.6, 123.1, 122.8, 118.2, 114.9, 106.5, 94.1, 83.9, 61.3, 39.4, 38.1, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{28}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 434.1962. Found 434.1963.

Compound 19b



Yield: 79.7 mg (86%, gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

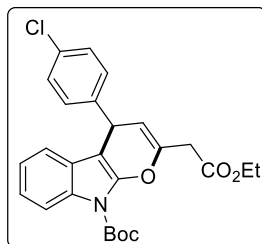
IR (neat): $\nu_{\max}$ 2979, 2936, 1731, 1691, 1630, 1599, 1457, 1358, 1318, 1258, 1220, 1137, 1043, 991, 763, 744, 699 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.13 (d, J = 8.0 Hz, 1H), 7.29-7.24 (m, 1H), 7.20-7.17 (m, 1H), 7.09-7.06 (m, 1H), 7.02 (d, J = 7.0 Hz, 1H), 6.99 (d, J = 7.5 Hz, 1H), 6.94-6.93 (m, 1H), 6.80-6.78 (m, 1H), 5.12 (d, J = 3.5 Hz, 1H), 4.86 (d, J = 3.5 Hz, 1H), 4.24 (q, J = 7.0 Hz, 2H), 3.80 (s, 3H), 3.38-3.31 (m, 2H), 1.70 (s, 9H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 160.1, 149.1, 146.0, 144.2, 143.9, 131.9, 129.7, 126.6, 123.1, 122.8, 120.6, 118.3, 114.9, 114.3, 112.1, 106.3, 94.1, 83.9, 61.3, 55.3, 39.4, 38.2, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{30}NO_6$ [$M^+ + H$]: m/z 464.2068. Found 464.2069.

Compound 19c



Yield: 74.0 mg (79%, yellow solid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

Mp: 110-112 °C.

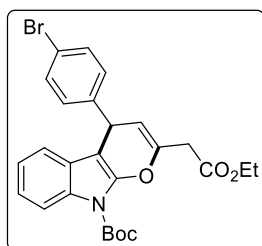
IR (neat): ν_{max} 2979, 2926, 2854, 1732, 1689, 1630, 1487, 1458, 1358, 1320, 1220, 1141, 1014, 991, 834, 745 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 8.5 Hz, 1H), 7.27-7.26 (m, 4H), 7.17-7.14 (m, 1H), 7.06-7.03 (m, 1H), 6.90 (d, J = 7.5 Hz, 1H), 5.05-5.04 (m, 1H), 4.84-4.83 (m, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.30 (s, 2H), 1.66 (s, 9H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.3, 149.0, 144.2, 144.1, 142.8, 132.8, 131.8, 129.5, 128.9, 126.3, 123.1, 123.0, 118.1, 115.0, 106.0, 93.7, 84.0, 61.4, 39.3, 37.6, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{27}ClNO_5$ [$M^+ + H$]: m/z 468.1572. Found 468.1570.

Compound 19d



Yield: 79.0 mg (77%, yellow gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

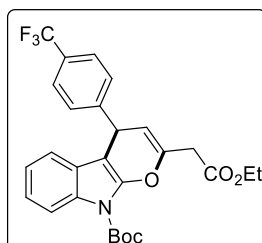
IR (neat): ν_{max} 2979, 2925, 2854, 1732, 1689, 1630, 1482, 1458, 1358, 1140, 1071, 1011, 991, 850, 743 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 8.5 Hz, 1H), 7.42 (d, J = 7.5 Hz, 2H), 7.22 (d, J = 7.5 Hz, 2H), 7.18-7.14 (m, 1H), 7.06-7.03 (m, 1H), 6.90 (d, J = 7.5 Hz, 1H), 5.047-5.040 (m, 1H), 4.827-4.820 (m, 1H), 4.20 (q, J = 7.0 Hz, 2H), 3.30 (s, 2H), 1.66 (s, 9H), 1.28 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.2, 149.0, 144.2, 144.1, 143.3, 131.8, 129.9, 126.2, 123.1, 123.0, 120.9, 118.1, 115.0, 105.9, 93.6, 84.0, 61.3, 39.3, 37.6, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{27}\text{BrNO}_5$ [$\text{M}^+ + \text{H}$]: m/z 512.1067. Found 512.1063.

Compound 19e



Yield: 76.0 mg (76%, white gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 2981, 2930, 2856, 1733, 1458, 1321, 1142, 1067, 992, 843, 750 cm^{-1} .

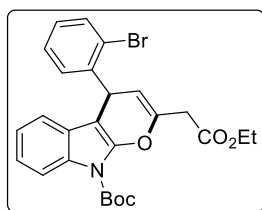
^1H NMR (500 MHz, CDCl_3): δ 8.10 (d, J = 8.0 Hz, 1H), 7.56-7.55 (m, 2H), 7.47-7.46 (m, 2H), 7.18-7.15 (m, 1H), 7.06-7.03 (m, 1H), 6.89 (d, J = 7.5 Hz, 1H), 5.06 (s, 1H), 4.93 (s, 1H), 4.21 (q, J = 7.0 Hz, 2H), 3.31 (s, 2H), 1.66 (s, 9H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 148.9, 148.0, 144.3, 144.2, 131.7, 129.2 (J_2 = 32.3 Hz), 128.4, 126.0, 125.7 (J_3 = 3.8 Hz), 124.2 (J_1 = 270.2 Hz), 123.1, 123.0, 117.8, 114.9, 105.5, 93.2, 84.0, 61.3, 39.2, 37.9, 28.2, 14.2 ppm.

^{19}F NMR (470 MHz, CDCl_3): -62.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{27}\text{F}_3\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 502.1836. Found 502.1831.

Compound 19g



Yield: 77.0 mg (75%, white solid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

Mp: 98-100 $^{\circ}\text{C}$.

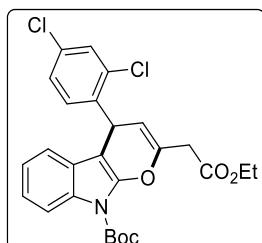
IR (neat): ν_{max} 2979, 2934, 1732, 1690, 1631, 1458, 1359, 1255, 1219, 1140, 1024, 991, 840, 746 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.11 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.20-7.15 (m, 3H), 7.06-7.04 (m, 2H), 6.94 (d, J = 7.5 Hz, 1H), 5.39 (d, J = 3.0 Hz, 1H), 5.16 (d, J = 3.0 Hz, 1H), 4.19 (q, J = 7.5 Hz, 2H), 3.29 (s, 2H), 1.66 (s, 9H), 1.27 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.2, 149.0, 144.9, 144.2, 142.4, 132.8, 131.8, 131.2, 128.5, 128.1, 126.2, 123.2, 123.0, 122.9, 118.3, 114.9, 104.9, 93.5, 84.0, 61.3, 39.4, 37.0, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{27}\text{BrNO}_5$ [$\text{M}^+ + \text{H}$]: m/z 512.1067. Found 512.1064.

Compound 19i



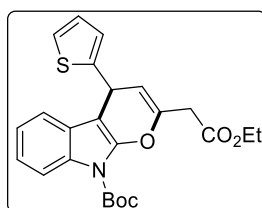
Yield: 73.0 mg (73%, yellow gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 2979, 2932, 1771, 1732, 1585, 1519, 1459, 1368, 1240, 1144, 1045, 930, 740, 635 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.13 (d, J = 8.0 Hz, 1H), 7.42₆-7.42₂ (m, 1H), 7.21-7.16 (m, 1H), 7.14-7.06 (m, 3H), 6.93 (d, J = 7.5 Hz, 1H), 5.37₆-5.36₉ (m, 1H), 5.13₂-5.12₅ (m, 1H), 4.21 (q, J = 7.0 Hz, 2H), 3.30 (s, 2H), 1.68 (s, 9H), 1.29 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 148.9, 144.9, 144.7, 139.5, 133.2, 133.0, 131.9, 131.8, 129.2, 127.8, 125.9, 123.3, 123.2, 118.0, 115.0, 104.3, 92.8, 84.0, 61.3, 39.3, 33.8, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{26}\text{Cl}_2\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 502.1183. Found 502.1182.



Yield: 66.0 mg (75%, white solid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

Mp: 110-112 $^{\circ}\text{C}$

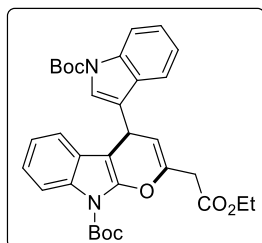
IR (neat): ν_{max} 2979, 2932, 1734, 1691, 1629, 1458, 1421, 1356, 1320, 1255, 1222, 1142, 1030, 992, 854, 748 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.10 (d, J = 8.5 Hz, 1H), 7.18-7.08 (m, 4H), 7.00 (s, 1H), 6.94-6.93 (m, 1H), 5.19 (s, 2H), 4.21 (q, J = 7.0 Hz, 2H), 3.35-3.28 (m, 2H), 1.66 (s, 9H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.2, 149.2, 149.1, 144.1, 143.8, 131.8, 126.8, 126.4, 124.7, 124.5, 123.1, 123.0, 118.1, 115.0, 106.0, 94.1, 84.0, 61.4, 39.4, 33.0, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{24}\text{H}_{26}\text{NO}_5\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 440.1526. Found 440.1528.

Compound 19l



Yield: 79.0 mg (69%, yellow gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

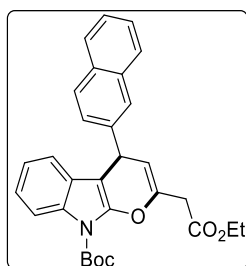
IR (neat): ν_{max} 2979, 2928, 2848, 1730, 1454, 1368, 1150, 990, 855, 748 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.10 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.31-7.28 (m, 1H), 7.22-7.19 (m, 1H), 7.16-7.13 (m, 1H), 7.09 (d, J = 7.5 Hz, 1H), 7.05-7.02 (m, 1H), 5.17-5.15 (m, 2H), 4.21 (q, J = 7.0 Hz, 2H), 3.36-3.28 (m, 2H), 1.69 (s, 9H), 1.66 (s, 9H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.3, 149.9, 149.1, 144.4, 144.1, 136.0, 131.8, 129.4, 126.6, 124.5, 123.7, 123.0, 122.9, 122.6, 119.5, 118.2, 115.5, 114.9, 105.3, 93.1, 84.0, 83.8, 61.3, 39.4, 29.0, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{37}\text{N}_2\text{O}_7$ [$\text{M}^+ + \text{H}$]: m/z 573.2595. Found 573.2599.

Compound 19m



Yield: 67.6 mg (70%, red gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

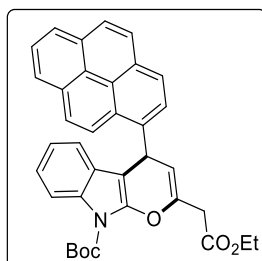
IR (neat): ν_{max} 3056, 2980, 2936, 1731, 1630, 1510, 1458, 1357, 1319, 1240, 1142, 1044, 991, 819, 734 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.17 (d, J = 8.5 Hz, 1H), 7.86-7.81 (m, 4H), 7.54-7.45 (m, 3H), 7.19-7.16 (m, 1H), 7.04-6.98 (m, 2H), 5.17 (d, J = 3.5 Hz, 1H), 5.07 (d, J = 3.5 Hz, 1H), 4.26 (q, J = 7.0 Hz, 2H), 3.41-3.33 (m, 2H), 1.73 (s, 9H), 1.34 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.3, 149.1, 144.2, 144.0, 141.5, 133.6, 132.7, 131.8, 128.6, 127.9, 127.8, 126.5, 126.4, 126.2, 125.7, 123.1, 122.8, 118.2, 114.9, 106.3, 93.9, 83.9, 61.3, 39.4, 38.3, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{30}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 484.2118. Found 484.2119.

Compound 19o



Yield: 75.8 mg (68%, brown gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

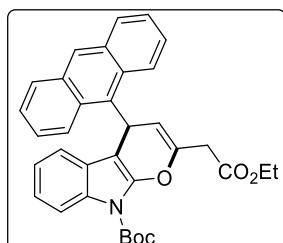
IR (neat): ν_{max} 3045, 2979, 2932, 1731, 1689, 1601, 1457, 1421, 1357, 1320, 1220, 1138, 1028, 990, 844, 733, 682 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.62 (d, J = 9.0 Hz, 1H), 8.24-8.20 (m, 3H), 8.12 (d, J = 7.5 Hz, 1H), 8.08-8.00 (m, 4H), 7.93 (d, J = 8.0 Hz, 1H), 7.12-7.09 (m, 1H), 6.86-6.83 (m, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.04 (s, 1H), 5.30₁-5.29₅ (m, 1H), 4.21 (q, J = 7.0 Hz, 2H), 3.36-3.28 (m, 2H), 1.71 (s, 9H), 1.29 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.4, 149.2, 144.9, 143.9₆, 143.9₄, 137.2, 131.9, 131.6, 130.9, 130.3, 130.2, 128.3, 127.9, 127.7, 127.3, 126.5, 126.1, 125.6, 125.4, 125.2, 125.0, 123.1, 122.9, 122.3, 118.4, 114.9, 106.2, 94.0, 84.0, 61.3, 39.4, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{32}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 558.2275. Found 558.2278.

Compound 19p



Yield: 79.0 mg (74%, red gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

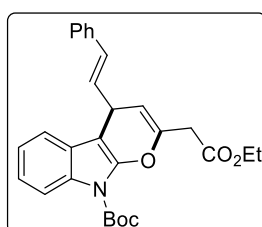
IR (neat): ν_{max} 3056, 2979, 2928, 1729, 1628, 1517, 1455, 1367, 1247, 1144, 1025, 888, 840, 732, 701 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.72 (d, J = 8.5 Hz, 1H), 8.62 (d, J = 9.0 Hz, 1H), 8.46 (s, 1H), 8.10 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.63-7.60 (m, 1H), 7.56-7.53 (m, 1H), 7.36-7.30 (m, 2H), 7.01-6.98 (m, 1H), 6.69-6.66 (m, 1H), 6.58 (s, 1H), 6.27 (d, J = 7.5 Hz, 1H), 5.21 (s, 1H), 4.25 (q, J = 7.0 Hz, 2H), 3.38 (s, 2H), 1.73 (s, 9H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.4, 149.2, 144.2, 143.5, 132.8, 132.3, 131.7, 131.4, 131.3, 130.3, 129.9, 129.3, 128.3, 126.7, 126.6, 125.3, 125.2, 124.9, 124.9, 123.2, 123.0, 122.7, 118.1, 114.8, 107.1, 95.6, 84.0, 61.3, 39.4, 32.0, 28.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{32}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 534.2275. Found 534.2279.

Compound 19q



Yield: 62.4 mg (68%, brown gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 2978, 2929, 2853, 1731, 1690, 1629, 1458, 1421, 1364, 1319, 1249, 1220, 1142, 1029, 990, 748 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.09 (d, J = 8.5 Hz, 1H), 7.34-7.31 (m, 3H), 7.28-7.23 (m, 2H), 7.20-7.15 (m, 2H), 7.13-7.10 (m, 1H), 6.59-6.56 (m, 1H), 6.27-6.22 (m, 1H), 5.01 (d, J = 3.5 Hz, 1H), 4.46-4.44 (m, 1H), 4.18 (q, J = 7.0 Hz, 2H), 3.28 (s, 2H), 1.62 (s, 9H), 1.27 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.3, 149.1, 144.7, 143.8, 137.1, 132.0, 131.8, 130.1, 128.7, 127.6, 126.9, 126.5, 123.2, 122.9, 118.2, 115.0, 104.8, 93.3, 83.9, 61.3, 39.4, 35.6, 28.3, 14.3 ppm.

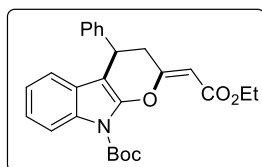
HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{30}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 460.2118. Found 460.2122.

3.12 General procedure for the synthesis of compounds 20a-e, 20g-h, 20l-m, and 20o-q

A Schlenk tube was charged with *tert*-butyl-2-oxoindoline-1-carboxylate **7** (0.20 mmol), δ -acetoxy allenolate **4** (0.24 mmol), and toluene (2.0 mL). Subsequently, DMAP (0.04 mmol) was added at rt (25 °C) and mixture stirred for 1h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 $\times$ 10 mL). Then the combined organic layer was washed with brine

solution (20.0 mL), dried over anhydrous Na₂SO₄, and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/hexane (1:19) as the eluent.

Compound 20a



Yield: 73.6 mg (85%, yellow gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

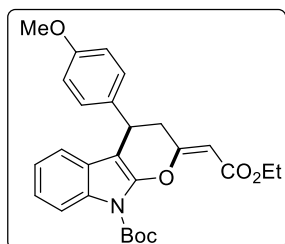
IR (neat): $\nu_{\max}$ 2979, 2934, 1731, 1651, 1610, 1456, 1369, 1346, 1288, 1247, 1146, 1111, 1044, 837, 751, 699 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 8.03 (d, J = 8.0 Hz, 1H), 7.30-7.24 (m, 3H), 7.21 (d, J = 7.0 Hz, 2H), 7.17-7.14 (m, 1H), 7.05-7.02 (m, 1H), 6.82 (d, J = 7.5 Hz, 1H), 5.14 (s, 1H), 4.24-4.19 (m, 3H), 3.08 (dd, J_1 = 14.5 Hz, J_2 = 6.5 Hz, 1H), 2.75 (dd, J_1 = 14.5 Hz, J_2 = 6.0 Hz, 1H), 1.73 (s, 9H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 163.9, 159.5, 148.7, 145.4, 141.7, 131.6, 128.8, 127.8, 127.3, 126.1, 123.1, 122.8, 118.1, 115.2, 101.7, 96.2, 84.8, 60.1, 37.7, 35.5, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For C₂₆H₂₇NNaO₅ [M^+ + H]: m/z 456.1781. Found 456.1780.

Compound 20b



Yield: 80.6 mg (87%, brown gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

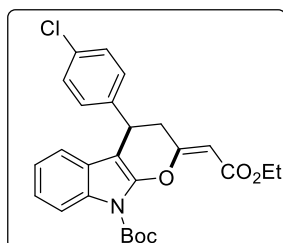
IR (neat): $\nu_{\max}$ 2978, 2931, 2835, 1723, 1665, 1608, 1511, 1413, 1249, 1142, 1115, 1036, 994, 910, 832, 747 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 8.04 (d, J = 8.0 Hz, 1H), 7.18-7.12 (m, 3H), 7.06-7.03 (m, 1H), 6.86-6.82 (m, 3H), 5.15 (s, 1H), 4.24-4.18 (m, 3H), 3.78 (s, 3H), 3.06 (dd, J_1 = 14.5 Hz, J_2 = 6.0 Hz, 1H), 2.73 (dd, J_1 = 14.5 Hz, J_2 = 5.5 Hz, 1H), 1.74 (s, 9H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.8, 159.7, 158.8, 148.7, 145.3, 133.7, 131.7, 128.8, 126.2, 123.1, 122.8, 118.1, 115.2, 114.2, 101.6, 96.5, 84.7, 60.1, 55.3, 38.0, 34.7, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{30}\text{NO}_6$ [$\text{M}^+ + \text{H}$]: m/z 464.2068. Found 464.2063.

Compound 20c



Yield: 75.8 mg (81%, red gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

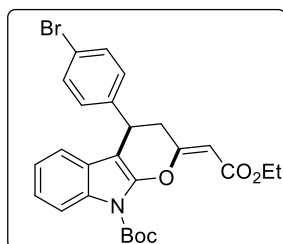
IR (neat): ν_{max} 2979, 2925, 2851, 1725, 1456, 1144, 1043, 831, 749 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.04 (d, J = 8.5 Hz, 1H), 7.28-7.26 (m, 2H), 7.20-7.14 (m, 3H), 7.08-7.05 (m, 1H), 6.85 (d, J = 7.5 Hz, 1H), 5.15 (s, 1H), 4.24-4.19 (m, 3H), 3.09 (dd, J_1 = 14.5 Hz, J_2 = 6.0 Hz, 1H), 2.70 (dd, J_1 = 14.5 Hz, J_2 = 5.5 Hz, 1H), 1.74 (s, 9H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 163.7, 159.0, 148.6, 145.5, 140.3, 133.1, 131.7, 129.1, 129.0, 125.9, 123.2, 123.0, 117.8, 115.3, 102.1, 95.6, 84.9, 60.2, 37.6, 34.9, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{27}\text{ClNO}_5$ [$\text{M}^+ + \text{H}$]: m/z 468.1572. Found 468.1574.

Compound 20d



Yield: 85.0 mg (83%, red gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

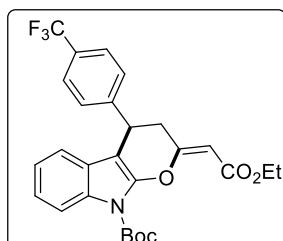
IR (neat): ν_{max} 3024, 2978, 2929, 1725, 1668, 1456, 1209, 1144, 1043, 1010, 830, 751 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.03 (d, J = 8.5 Hz, 1H), 7.41 (d, J = 8.5 Hz, 2H), 7.19-7.16 (m, 1H), 7.09-7.05 (m, 3H), 6.84 (d, J = 7.5 Hz, 1H), 5.14 (s, 1H), 4.23-4.19 (m, 3H), 3.09 (dd, J_1 = 14.0 Hz, J_2 = 6.0 Hz, 1H), 2.69 (dd, J_1 = 14.5 Hz, J_2 = 6.5 Hz, 1H), 1.73 (s, 9H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.7, 158.9, 148.6, 145.6, 140.8, 132.0, 131.7, 129.5, 125.9, 123.2, 123.0, 121.2, 117.8, 115.3, 102.1, 95.5, 84.9, 60.2, 37.5, 34.9, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{27}\text{BrNO}_5$ [$\text{M}^+ + \text{H}$]: m/z 512.1067. Found 512.1069.

Compound 20e



Yield: 79.0 mg (79%, brown gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 2979, 2931, 1725, 1669, 1456, 1321, 1119, 1066, 1018, 840, 748 cm^{-1} .

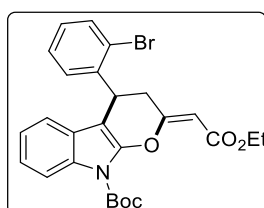
^1H NMR (500 MHz, CDCl_3): δ 8.05 (d, J = 8.5 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 7.20-7.17 (m, 1H), 7.09-7.06 (m, 1H), 6.84 (d, J = 7.5 Hz, 1H), 5.15 (s, 1H), 4.31 (t, J = 5.5 Hz, 1H), 4.21 (q, J = 7.0 Hz, 2H), 3.14 (dd, J_1 = 14.5 Hz, J_2 = 6.5 Hz, 1H), 2.72 (dd, J_1 = 14.5 Hz, J_2 = 5.0 Hz, 1H), 1.74 (s, 9H), 1.31 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.6, 158.6, 148.6, 145.9, 145.6, 131.7, 129.7 (J_2 = 32.6 Hz), 128.2, 125.9 (J_3 = 3.4 Hz), 125.8, 124.2 (J_1 = 271.5 Hz), 123.3, 123.1, 117.7, 115.4, 102.3, 95.1, 85.0, 60.2, 37.3, 35.2, 28.3, 14.4 ppm.

^{19}F NMR (470 MHz, CDCl_3): -62.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{27}\text{F}_3\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 502.1836. Found 502.1835.

Compound 20g



Yield: 77.8 mg (76%, red gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

Mp: 148-150 $^{\circ}\text{C}$.

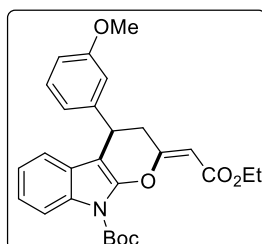
IR (neat): ν_{max} 2978, 2929, 1725, 1668, 1629, 1456, 1419, 1358, 1318, 1209, 1144, 1117, 1043, 996, 830 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.05 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.20-7.17 (m, 1H), 7.14-7.07 (m, 3H), 6.96-6.93 (m, 2H), 5.11 (s, 1H), 4.76-4.74 (m,

1H), 4.20 (q, $J = 7.0$ Hz, 2H), 3.16 (dd, $J_1 = 14.5$ Hz, $J_2 = 6.5$ Hz, 1H), 2.73 (dd, $J_1 = 14.5$ Hz, $J_2 = 4.0$ Hz, 1H), 1.75 (s, 9H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.
 $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.7, 158.9, 148.6, 146.1, 140.1, 133.1, 131.7, 129.8, 128.9, 127.9, 125.8, 123.7, 123.2, 123.0, 117.9, 115.3, 102.3, 95.2, 84.9, 60.1, 35.6, 34.3, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{26}\text{H}_{27}\text{BrNO}_5$ [$\text{M}^+ + \text{H}$]: m/z 512.1067. Found 512.1069.

Compound 20h



Yield: 72.3 mg (78%, white solid, $R_f = 0.53$ (19:1 hexane/ethyl acetate)).

Mp: 110-112 °C.

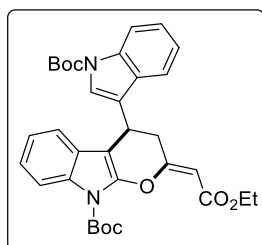
IR (neat): ν_{max} 2978, 2934, 1724, 1667, 1629, 1601, 1455, 1415, 1359, 1318, 1262, 1204, 1177, 1141, 1042, 995, 851, 746 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): 8.02 (d, $J = 8.0$ Hz, 1H), 7.22-7.19 (m, 1H), 7.17-7.14 (m, 1H), 7.06-7.03 (m, 1H), 6.87 (d, $J = 8.0$ Hz, 1H), 6.80-6.78 (m, 2H), 6.76 (s, 1H), 5.15 (s, 1H), 4.23-4.19 (m, 3H), 3.75 (s, 3H), 3.09-3.05 (m, 1H), 2.79-2.74 (m, 1H), 1.73 (s, 9H), 1.31 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.9, 160.0, 159.5, 148.7, 145.4, 143.5, 131.7, 129.9, 126.2, 123.1, 122.8, 120.2, 118.1, 115.2, 113.7, 112.5, 101.7, 96.1, 84.8, 60.2, 55.4, 37.7, 35.6, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{27}\text{H}_{29}\text{NNaO}_6$ [$\text{M}^+ + \text{Na}$]: m/z 486.1887. Found 486.1886.

Compound 20l



Yield: 84.7 mg (74%, yellow gummy liquid, $R_f = 0.53$ (19:1 hexane/ethyl acetate)).

IR (neat): ν_{max} 2977, 2927, 2854, 1727, 1454, 1368, 1146, 1084, 997, 854, 747 cm^{-1} .

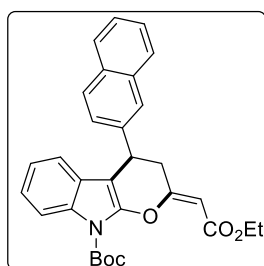
^1H NMR (500 MHz, CDCl_3): δ 8.18 (s, 1H), 8.06 (d, $J = 8.5$ Hz, 1H), 7.57 (d, $J = 7.5$ Hz, 1H), 7.38-7.35 (m, 1H), 7.28-7.26 (m, 1H), 7.21-7.19 (m, 2H), 7.11-7.07 (m, 2H),

5.11 (s, 1H), 4.55 (t, $J = 5.0$ Hz, 1H), 4.22 (q, $J = 7.5$ Hz, 2H), 3.14 (dd, $J_1 = 14.5$ Hz, $J_2 = 6.5$ Hz, 1H), 2.99 (dd, $J_1 = 14.5$ Hz, $J_2 = 4.0$ Hz, 1H), 1.78 (s, 9H), 1.64 (s, 9H), 1.32 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.8, 159.3, 149.7, 148.7, 145.4, 136.1, 131.6, 129.0, 126.1, 124.7, 124.3, 123.2, 122.9, 122.7, 120.6, 118.8, 117.8, 115.8, 115.3, 102.3, 95.2, 84.9, 84.0, 60.1, 35.4, 28.4, 28.3, 26.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{36}\text{N}_2\text{NaO}_7$ [$\text{M}^+ + \text{Na}$]: m/z 595.2415. Found 595.2413.

Compound 20m



Yield: 73.4 mg (76%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 67-69 °C.

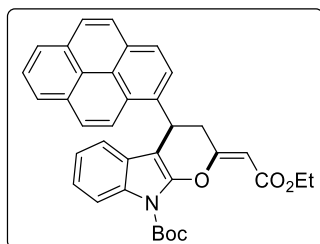
IR (neat): ν_{max} 2978, 2931, 1725, 1665, 1629, 1602, 1456, 1415, 1353, 1201, 1141, 1042, 994, 820, 746 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): 8.05 (d, $J = 8.5$ Hz, 1H), 7.83-7.75 (m, 3H), 7.66 (s, 1H), 7.47-7.45 (m, 2H), 7.35-7.34 (m, 1H), 7.18-7.15 (m, 1H), 7.01-6.98 (m, 1H), 6.83 (d, $J = 7.5$ Hz, 1H), 5.14 (s, 1H), 4.42 (t, $J = 6.0$ Hz, 1H), 4.21 (q, $J = 7.0$ Hz, 2H), 3.15 (dd, $J_1 = 14.5$ Hz, $J_2 = 6.5$ Hz, 1H), 2.86 (dd, $J_1 = 14.5$ Hz, $J_2 = 5.5$ Hz, 1H), 1.76 (s, 9H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.8, 159.5, 148.7, 145.6, 139.2, 133.5, 132.8, 131.7, 128.8, 128.0, 127.8, 126.6, 126.3, 126.2, 126.0, 125.8, 123.2, 122.9, 118.1, 115.3, 101.8, 96.0, 84.9, 60.1, 37.7, 35.7, 28.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{29}\text{NnaO}_5$ [$\text{M}^+ + \text{Na}$]: m/z 506.1938. Found 506.1937.

Compound 20o



Yield: 77.0 mg (69%, brown gummy liquid, $R_f = 0.53$ (19:1 hexane/ethyl acetate)).

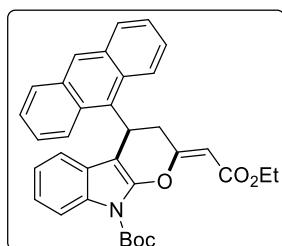
IR (neat): $\nu_{\max}$ 3024, 2979, 2931, 1721, 1666, 1455, 1213, 1143, 995, 909, 847 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.46 (d, $J = 9.5$ Hz, 1H), 8.25-8.21 (m, 3H), 8.11 (d, $J = 8.0$ Hz, 1H), 8.07-8.00 (m, 4H), 7.69 (d, $J = 7.5$ Hz, 1H), 7.19-7.16 (m, 1H), 6.96-6.93 (m, 1H), 6.72 (d, $J = 7.5$ Hz, 1H), 5.41 (t, $J = 5.5$ Hz, 1H), 5.02 (s, 1H), 4.20 (q, $J = 7.0$ Hz, 2H), 3.38 (dd, $J_1 = 14.5$ Hz, $J_2 = 6.5$ Hz, 1H), 3.00 (dd, $J_1 = 14.5$ Hz, $J_2 = 5.5$ Hz, 1H), 1.80 (s, 9H), 1.28 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.7, 159.3, 148.8, 146.2, 134.7, 131.8, 131.5, 130.8, 130.6, 128.3, 128.1, 127.7, 127.4, 126.2, 126.0, 125.6, 125.3, 125.2₃, 125.1₆, 123.2, 122.9, 122.0, 118.1, 115.3, 102.1, 96.0, 84.9, 60.1, 37.4, 31.4, 28.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{36}\text{H}_{31}\text{NnaO}_5$ [$\text{M}^+ + \text{Na}$]: m/z 580.2094. Found 580.2097.

Compound 20p



Yield: 76.8 mg (72%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 167-169 $^{\circ}\text{C}$.

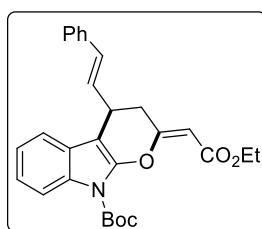
IR (neat): $\nu_{\max}$ 2970, 2924, 2854, 1735, 1720, 1666, 1621, 1455, 1410, 1369, 1341, 1316, 1196, 1145, 1040, 994, 886, 752, 733 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): 8.50 (s, 1H), 8.41 (d, $J = 9.0$ Hz, 1H), 8.17 (d, $J = 9.0$ Hz, 1H), 8.11 (d, $J = 8.5$ Hz, 1H), 8.00-7.96 (m, 2H), 7.60-7.52 (m, 2H), 7.33-7.30 (m, 1H), 7.14-7.10 (m, 1H), 7.01-6.98 (m, 1H), 6.60-6.57 (m, 1H), 5.91 (d, $J = 7.5$ Hz, 1H), 5.81-5.77 (m, 1H), 5.32 (s, 1H), 4.31-4.27 (m, 2H), 3.78-3.73 (m, 1H), 2.91-2.87 (m, 1H), 1.79 (s, 9H), 1.37 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.1, 160.5, 148.8, 143.8, 131.9, 131.8, 131.4, 130.6, 130.2, 129.9, 129.6, 128.4, 126.8, 126.0, 125.6, 125.0₂, 124.9₆, 124.9, 123.1, 122.9, 122.7, 118.4, 115.0, 101.3, 98.5, 84.9, 60.3, 35.1, 30.8, 28.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{31}\text{NnaO}_5$ [$\text{M}^+ + \text{Na}$]: m/z 556.2094. Found 556.2096.

Compound 20q



Yield: 67.0 mg (73%, yellow gummy liquid, R_f = 0.53 (19:1 hexane/ethyl acetate)).

IR (neat): $\nu_{\max}$ 3024, 2978, 2924, 2854, 1725, 1668, 1456, 1210, 1146, 1041, 909, 839 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.03 (d, J = 8.0 Hz, 1H), 7.37-7.32 (m, 3H), 7.30-7.27 (m, 2H), 7.23-7.14 (m, 3H), 6.55-6.52 (m, 1H), 6.24-6.20 (m, 1H), 5.27 (s, 1H), 4.22 (q, J = 7.5 Hz, 2H), 3.87-3.83 (m, 1H), 2.95 (dd, J_1 = 15.0 Hz, J_2 = 6.0 Hz, 1H), 2.68 (dd, J_1 = 14.0 Hz, J_2 = 5.0 Hz, 1H), 1.72 (s, 9H), 1.32 (t, J = 7.0 Hz, 3H) ppm.

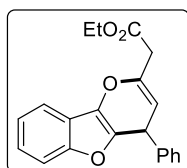
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.9, 159.6, 148.7, 144.7, 136.8, 131.9, 131.6, 129.8, 128.7, 127.8, 126.5, 126.4, 123.3, 122.8, 117.7, 115.4, 101.9, 95.7, 84.8, 60.2, 35.2, 33.0, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{30}\text{NO}_5$ [$\text{M}^+ + \text{H}$]: m/z 460.2118. Found 460.2113.

3.13 General procedure for the synthesis of compounds 21a-d, 21g-h, 21k-l, and 21p

A Schlenk tube was charged with benzofuran-3(2H)-one **8** (0.20 mmol), δ -acetoxy allenoate **4** (0.24 mmol), and toluene (2.0 mL). Subsequently, DBU (0.04 mmol) was added at rt (25 °C) and mixture stirred for 1h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 $\times$ 10 mL). Then the combined organic layer was washed with brine solution (20.0 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:9) as the eluent.

Compound 21a



Yield: 78.0 mg (78%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 120-122 °C.

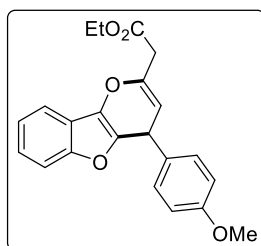
IR (neat): $\nu_{\max}$ 2870, 1724, 1447, 1406, 1368, 1339, 1307, 1243, 1217, 1164, 1024, 1000, 847, 832, 784, 745 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.58-7.54 (m, 1H), 7.35-7.31 (m, 5H), 7.28-7.27 (m, 1H), 7.25-7.23 (m, 1H), 7.23-7.22 (m, 1H), 5.07 (d, $J = 3.5$ Hz, 1H), 4.97 (d, $J = 4.0$ Hz, 1H), 4.23 (q, $J = 7.5$ Hz, 2H), 3.38-3.32 (m, 2H), 1.31 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.6, 152.7, 145.3, 142.5, 137.6, 134.4, 128.8, 128.2, 127.4, 124.5, 122.8, 120.1, 117.9, 111.9, 104.0, 61.4, 39.6, 39.5, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{19}\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 335.1278. Found 335.1279.

Compound 21b



Yield: 86.3 mg (79%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 95-97 $^{\circ}\text{C}$.

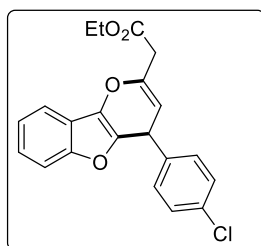
IR (neat): $\nu_{\max}$ 2955, 2901, 2834, 1722, 1696, 1649, 1609, 1509, 1447, 1406, 1369, 1342, 1303, 1253, 1210, 1160, 1097, 1027, 999, 852, 824, 745 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57-7.54 (m, 1H), 7.34-7.30 (m, 1H), 7.27₃-7.26₉ (m, 1H), 7.26-7.25 (m, 1H), 7.24-7.21 (m, 2H), 6.89-6.88 (m, 2H), 5.05 (d, $J = 3.5$ Hz, 1H), 4.93 (d, $J = 3.0$ Hz, 1H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.79 (s, 3H), 3.25 (s, 2H), 1.31 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 159.0, 152.7, 145.2, 137.9, 134.8, 134.3, 129.2, 124.4, 122.8, 120.1, 117.9, 114.2, 111.9, 104.2, 61.4, 55.4, 39.5, 38.8, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{22}\text{H}_{21}\text{O}_5$ [$\text{M}^+ + \text{H}$]: m/z 365.1384. Found 365.1391.

Compound 21c



Yield: 81.8 mg (74%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 104-106 $^{\circ}\text{C}$.

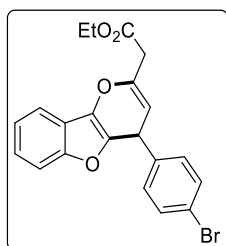
IR (neat): $\nu_{\max}$ 2969, 2929, 2843, 1720, 1649, 1486, 1450, 1406, 1366, 1345, 1276, 1240, 1163, 1088, 1027, 897, 820, 745 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57-7.55 (m, 1H), 7.32-7.31 (m, 3H), 7.29-7.27 (m, 2H), 7.25-7.22 (m, 2H), 5.03 (d, $J = 3.5$ Hz, 1H), 4.95 (d, $J = 3.5$ Hz, 1H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.35 (s, 2H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.5, 152.7, 145.7, 141.0, 137.0, 134.5, 133.3, 129.5, 129.0, 124.7, 122.9, 120.0, 118.0, 111.9, 103.5, 61.4, 39.5, 39.0, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{18}\text{ClO}_4$ [$\text{M}^+ + \text{H}$]: m/z 369.0888. Found 369.0887.

Compound 21d



Yield: 94.0 mg (76%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 105-107 $^{\circ}\text{C}$.

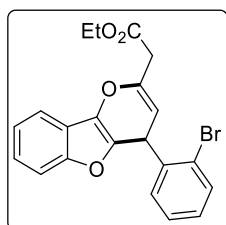
IR (neat): $\nu_{\max}$ 2986, 2840, 1729, 1696, 1649, 1484, 1447, 1401, 1368, 1342, 1272, 1231, 1160, 1072, 895, 821, 797, 747 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57-7.55 (m, 1H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.33-7.32 (m, 1H), 7.25-7.21 (m, 4H), 5.03 (d, $J = 3.5$ Hz, 1H), 4.94 (d, $J = 3.5$ Hz, 1H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.35 (s, 2H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.5, 152.8, 145.7, 141.5, 137.0, 134.6, 132.0, 129.9, 124.7, 122.9, 121.4, 120.0, 118.0, 111.9, 103.4, 61.4, 39.5, 39.1, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{18}\text{BrO}_4$ [$\text{M}^+ + \text{H}$]: m/z 413.0383. Found 413.0384.

Compound 21g



Yield: 89.0 mg (72%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 120-122 $^{\circ}\text{C}$.

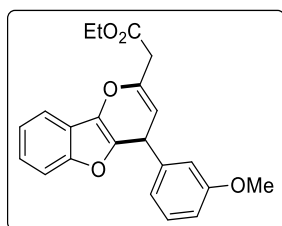
IR (neat): $\nu_{\max}$ 2969, 2939, 1723, 1695, 1648, 1466, 1448, 1410, 1370, 1350, 1214, 1169, 1135, 1027, 999, 899 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.60-7.58 (m, 2H), 7.37-7.36 (m, 1H), 7.29-7.27 (m, 1H), 7.25-7.23 (m, 2H), 7.16-7.14 (m, 1H), 7.12-7.09 (m, 1H), 5.53 (d, $J = 3.5$ Hz, 1H), 5.11 (d, $J = 3.5$ Hz, 1H), 4.22 (q, $J = 7.0$ Hz, 2H), 3.33 (s, 2H), 1.29 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.5, 152.8, 145.5, 141.3, 136.4, 135.7, 133.0, 130.7, 128.9, 128.1, 124.7, 123.2, 122.9, 119.9, 117.9, 112.0, 103.0, 61.4, 39.5, 38.8, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{21}\text{H}_{18}\text{BrO}_4$ [$\text{M}^+ + \text{H}$]: m/z 413.0383. Found 413.0390.

Compound 21h



Yield: 86.3 mg (79%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 100-102 $^{\circ}\text{C}$.

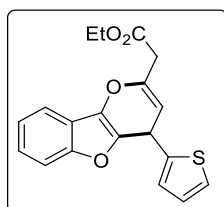
IR (neat): ν_{max} 2975, 2842, 1728, 1695, 1649, 1607, 1582, 1448, 1368, 1299, 1262, 1228, 1207, 1041, 1000, 900, 870, 787, 746 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.57-7.55 (m, 1H), 7.34-7.32 (m, 1H), 7.28-7.26 (m, 1H), 7.25-7.21 (m, 2H), 6.94 (d, $J = 7.5$ Hz, 1H), 6.89 (s, 1H), 6.82-6.80 (m, 1H), 5.06 (d, $J = 3.5$ Hz, 1H), 4.94 (d, $J = 3.5$ Hz, 1H), 4.23 (q, $J = 7.5$ Hz, 2H), 3.79 (s, 3H), 3.38-3.31 (m, 2H), 1.30 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 160.1, 152.7, 145.4, 144.2, 137.5, 134.5, 129.8, 124.5, 122.8, 120.5, 120.1, 117.9, 114.1, 112.8, 111.9, 103.9, 61.4, 55.4, 39.6, 39.5, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{22}\text{H}_{21}\text{O}_5$ [$\text{M}^+ + \text{H}$]: m/z 365.1384. Found 365.1388.

Compound 21k



Yield: 70.4 mg (69%, brown solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 108-110 $^{\circ}\text{C}$.

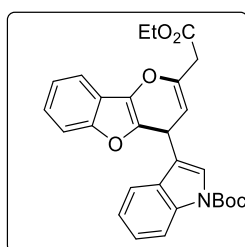
IR (neat): $\nu_{\max}$ 2986, 2853, 1726, 1695, 1650, 1447, 1407, 1366, 1306, 1272, 1236, 1166, 1030, 998, 895, 826, 744, 711 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.56 (d, $J = 7.0$ Hz, 1H), 7.37 (d, $J = 7.5$ Hz, 1H), 7.27-7.24 (m, 3H), 7.04-7.03 (m, 1H), 6.99-6.97 (m, 1H), 5.28 (d, $J = 3.0$ Hz, 1H), 5.18 (d, $J = 3.5$ Hz, 1H), 4.24 (q, $J = 7.0$ Hz, 2H), 3.39-3.32 (m, 2H), 1.31 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.4, 152.7, 146.9, 145.6, 136.9, 134.1, 127.0, 125.1, 124.9, 124.7, 122.9, 120.0, 118.1, 112.0, 103.5, 61.4, 39.5, 34.6, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{19}\text{H}_{17}\text{O}_4\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 341.0842. Found 341.0846.

Compound 21l



Yield: 92.3 mg (65%, red gummy liquid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

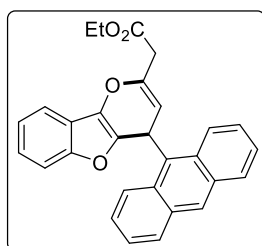
IR (neat): $\nu_{\max}$ 2980, 2932, 1734, 1451, 1367, 1308, 1249, 1156, 1083, 1029, 820, 747, 670 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.13 (s, 1H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.59-7.57 (m, 1H), 7.55 (s, 1H), 7.32-7.29 (m, 2H), 7.25-7.22 (m, 2H), 7.20-7.17 (m, 1H), 5.23 (d, $J = 3.0$ Hz, 1H), 5.14 (d, $J = 3.5$ Hz, 1H), 4.23 (q, $J = 7.5$ Hz, 2H), 3.37 (s, 2H), 1.66 (s, 9H), 1.30 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.5, 152.7, 149.9, 145.9, 136.8, 136.1, 134.5, 129.4, 124.6, 124.5, 123.8, 122.9, 122.7, 121.4, 120.0, 119.8, 117.9, 115.5, 111.9, 102.9, 83.9, 61.4, 39.5, 31.2, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{28}\text{NO}_6$ [$\text{M}^+ + \text{H}$]: m/z 474.1911. Found 474.1914.

Compound 21p



Yield: 88.6 mg (68%, brown gummy liquid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

IR (neat): $\nu_{\max}$ 2982, 2932, 1733, 1677, 1607, 1449, 1370, 1173, 1028, 890, 815, 732, 701 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.60 (d, J = 9.0 Hz, 1H), 8.50-8.48 (m, 2H), 8.07 (d, J = 8.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.62-7.59 (m, 1H), 7.53-7.50 (m, 1H), 7.38-7.35 (m, 1H), 7.30-7.29 (m, 1H), 7.25-7.22 (m, 1H), 7.18 (d, J = 3.5 Hz, 2H), 6.67 (s, 1H), 5.20 (d, J = 2.5 Hz, 1H), 4.25 (q, J = 6.0 Hz, 2H), 3.39 (s, 2H), 1.29 (t, J = 7.5 Hz, 3H) ppm.

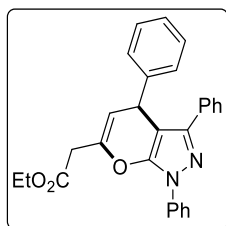
$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.6, 152.7, 145.2, 138.6, 134.3, 132.3, 131.6, 131.0, 130.7₇, 130.7₅, 129.7, 129.4, 128.7, 126.9, 125.6, 125.0, 124.9, 124.7, 124.3, 123.1, 122.9, 120.0, 117.9, 111.9, 105.1, 61.4, 39.5, 33.9, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{23}\text{O}_4$ [$\text{M}^+ + \text{H}$]: m/z 435.1591. Found 435.1596.

3.14 General procedure for the synthesis of compounds 22a-c, 22l, and 22p-q

A Schlenk tube was charged with 2,5-diphenyl-2,4-dihydro-3H-pyrazol-3-one **9** (0.20 mmol), δ -acetoxy allenolate **4** (0.24 mmol), and toluene (2.0 mL). Subsequently, DBU (0.04 mmol) was added at rt (25 °C) and mixture stirred for 1h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3×10 mL). Then the combined organic layer was washed with brine solution (20.0 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as the eluent.

Compound 22a



Yield: 55.5 mg (71%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 118-120 °C.

IR (neat): $\nu_{\max}$ 3066, 3027, 2982, 1737, 1688, 1598, 1513, 1486, 1456, 1384, 1161, 1028, 848, 759, 694 cm^{-1} .

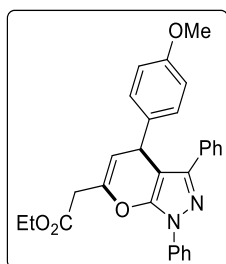
^1H NMR (500 MHz, CDCl_3): δ 7.92 (d, J = 7.5 Hz, 2H), 7.56-7.54 (m, 2H), 7.51-7.48 (m, 2H), 7.35-7.30 (m, 1H), 7.29-7.28 (m, 2H), 7.26-7.25 (m, 2H), 7.25-7.22 (m, 3H),

7.20-7.17 (m, 1H), 5.15 (d, $J = 4.0$ Hz, 1H), 4.97 (d, $J = 4.0$ Hz, 1H), 4.23 (q, $J = 7.0$ Hz, 2H), 3.37-3.29 (m, 2H), 1.29 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.2, 148.1, 148.0, 144.7, 142.6, 138.5, 133.2, 129.2, 128.8, 128.2, 127.9, 127.1, 126.9, 126.3, 121.0, 107.3, 97.2, 61.4, 39.1, 38.7, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $[\text{M}^+ + \text{H}]$: m/z $\text{C}_{28}\text{H}_{25}\text{N}_2\text{O}_3$ 437.1860. Found 437.1862.

Compound 22b



Yield: 65.4 mg (83%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 90-92 °C.

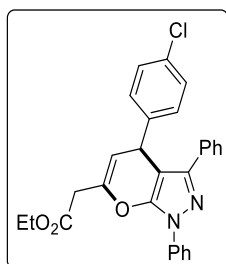
IR (neat): ν_{max} 3062, 2980, 2938, 1734, 1689, 1597, 1511, 1485, 1455, 1382, 1257, 1141, 1040, 994, 754, 691 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.90-7.88 (m, 2H), 7.56-7.54 (m, 2H), 7.49-7.45 (m, 2H), 7.31-7.27 (m, 1H), 7.26-7.21 (m, 3H), 7.20-7.16 (m, 1H), 6.84-6.82 (m, 1H), 6.76-6.75 (m, 1H), 6.71-6.69 (m, 1H), 5.13 (d, $J = 4.5$ Hz, 1H), 4.92 (d, $J = 4.5$ Hz, 1H), 4.21 (q, $J = 7.0$ Hz, 2H), 3.71 (s, 3H), 3.35-3.27 (m, 2H), 1.27 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.1, 160.0, 148.1, 147.9, 146.4, 142.7, 138.5, 133.3, 129.8, 129.2, 128.2, 127.9, 127.2, 126.3, 121.0, 120.3, 113.7, 112.3, 107.1, 97.1, 61.4, 55.3, 39.1, 38.6, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $[\text{M}^+ + \text{H}]$: m/z $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_4$ 467.1965. Found 467.1960.

Compound 22c



Yield: 62.0 mg (78%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 140-142 °C.

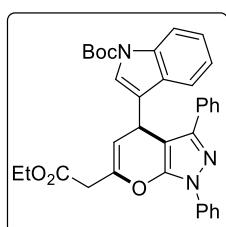
IR (neat): $\nu_{\max}$ 3066, 2983, 1736, 1689, 1598, 1574, 1513, 1487, 1456, 1383, 1264, 1160, 1089, 851, 735, 697 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.89-7.87 (m, 2H), 7.53-7.51 (m, 2H), 7.49-7.45 (m, 2H), 7.32-7.28 (m, 2H), 7.25-7.19 (m, 4H), 7.16-7.13 (m, 2H), 5.08 (d, $J = 4.0$ Hz, 1H), 4.95 (d, $J = 4.0$ Hz, 1H), 4.21 (q, $J = 7.5$ Hz, 2H), 3.35-3.27 (m, 2H), 1.27 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.1, 148.0, 147.9, 143.2, 143.0, 138.5, 133.1, 132.7, 129.24, 129.22, 129.0, 128.4, 128.1, 127.1, 126.5, 121.0, 106.8, 96.8, 61.5, 39.1, 38.1, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{28}\text{H}_{24}\text{ClN}_2\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 471.1470. Found 471.1471.

Compound 22l



Yield: 65.0 mg (67%, brown gummy liquid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

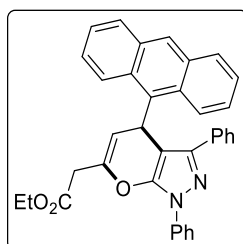
IR (neat): $\nu_{\max}$ 2979, 2931, 1732, 1696, 1599, 1514, 1484, 1453, 1369, 1307, 1249, 1154, 1081, 1027, 853, 759 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.09 (s, 1H), 7.92 (d, $J = 8.0$ Hz, 2H), 7.63-7.62 (m, 2H), 7.55 (d, $J = 7.5$ Hz, 1H), 7.50-7.47 (m, 2H), 7.32-7.28 (m, 3H), 7.22-7.21 (m, 4H), 5.27-5.24 (m, 2H), 4.20 (q, $J = 7.0$ Hz, 2H), 3.35-3.27 (m, 2H), 1.60 (s, 9H), 1.26 (t, $J = 7.0$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 169.1, 149.8, 148.1, 147.8, 143.4, 138.5, 136.1, 133.3, 129.2, 128.9, 128.3, 127.9, 127.1, 126.4, 124.5, 124.0, 123.2, 122.6, 121.1, 119.2, 115.6, 105.7, 96.0, 83.7, 61.5, 39.1, 29.9, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{34}\text{N}_3\text{O}_5$ [$\text{M}^+ + \text{H}$]: m/z 576.2493. Found 576.2498.

Compound 22p



Yield: 61.6 mg (68%, brown solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 145-147 °C.

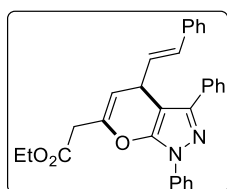
IR (neat): $\nu_{\max}$ 3053, 2976, 2927, 1736, 1690, 1597, 1512, 1485, 1455, 1378, 1244, 1157, 1028, 992, 758, 730, 692 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.42-8.37 (m, 2H), 8.32 (s, 1H), 8.00-7.96 (m, 3H), 7.88 (d, J = 8.0 Hz, 1H), 7.56-7.46 (m, 4H), 7.34-7.30 (m, 2H), 7.28-7.26 (m, 1H), 6.92 (d, J = 7.5 Hz, 2H), 6.82-6.79 (m, 1H), 6.63-6.60 (m, 2H), 6.56 (s, 1H), 5.28 (d, J = 3.0 Hz, 1H), 4.25-4.22 (m, 2H), 3.43-3.35 (m, 2H), 1.28 (t, J = 7.0 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 170.0, 148.8, 147.0, 143.4, 138.6, 133.3, 132.4, 132.3, 131.3, 130.6, 130.3, 129.7, 129.4, 129.3, 128.3, 127.4, 127.1, 126.8, 126.4, 125.3, 124.9, 124.7, 122.9, 121.1, 106.8, 99.2, 61.5, 39.2, 32.6, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $[\text{M}^+ + \text{H}]$: m/z $\text{C}_{36}\text{H}_{29}\text{N}_2\text{O}_3$ 537.2173. Found 537.2171.

Compound 22q



Yield: 55.5 mg (71%, brown solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 78-80 °C.

IR (neat): $\nu_{\max}$ 3062, 2980, 2928, 1736, 1688, 1597, 1573, 1486, 1456, 1383, 1157, 1028, 966, 757, 692 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.85 (d, J = 7.5 Hz, 2H), 7.82 (d, J = 7.5 Hz, 2H), 7.47-7.44 (m, 2H), 7.37-7.34 (m, 2H), 7.30-7.28 (m, 2H), 7.24-7.23 (m, 4H), 7.20-7.15 (m, 1H), 6.43-6.40 (m, 1H), 6.20-6.15 (m, 1H), 5.08 (d, J = 4.0 Hz, 1H), 4.60-4.58 (m, 1H), 4.22 (q, J = 7.5 Hz, 2H), 3.38-3.31 (m, 2H), 1.28 (t, J = 7.5 Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.2, 148.3, 147.3, 144.0, 138.5, 137.2, 133.5, 131.9, 130.4, 129.2, 128.6, 128.5, 128.1, 127.5, 127.3, 126.5, 126.4, 121.1, 105.1, 96.7, 61.5, 39.2, 35.8, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{27}\text{N}_2\text{O}_3$ $[\text{M}^+ + \text{H}]$: m/z 463.2016. Found 463.2018.

3.15 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **10ga**, **11aa**, **11ae**, **12aa**, **12ah**, **15aa**, **15ca**, **16an**, **16ba**, **17ab**, **18ga**, **19k**, **20h**, and **21a**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer [Mo-K α (λ = 0.71073 Å) or Cu-K α (λ = 1.54184 Å)]. Structures were solved and refined using standard methods.⁶⁶ Crystal data are summarized in Tables 14-17.

Table 14: Crystal data for compounds **10ga**, **11aa**, **11ae**, **12aa** and **12ah**^a

Compound	10ga	11aa	11ae	12aa	12ah
Emp. Formula	C ₃₀ H ₂₉ BrN ₂ O ₄ S	C ₃₀ H ₂₈ N ₂ O ₄ S	C ₃₁ H ₂₇ F ₃ N ₂ O ₄ S	C ₃₅ H ₃₀ N ₂ O ₄ S	C ₄₅ H ₃₆ N ₂ O ₄ S
Formula weight	593.51	512.60	580.61	574.67	700.82
Crystal system	Triclinic	Monoclinic	Triclinic	Monoclinic	orthorhombic
Space group	$P\bar{1}$	$P 1 21/n 1$	$P\bar{1}$	$P 1 21/c 1$	$P n a 21$
a /Å	11.0248(4)	10.8561(5)	11.1131(10)	23.2361(13)	14.1493(3)
b /Å	11.4222(3)	19.8837(11)	11.1508(9)	8.7085(5)	13.3321(3)
c /Å	11.8064(3)	12.5756 (6)	13.6423(9)	15.3446(7)	20.5726 (5)
α /deg	90.858(2)	90	69.594(7)	90	90
β /deg	111.889(3)	103.077(5)	81.166(6)	102.289 (5)	90
γ /deg	96.888(3)	90	60.882(9)	90	90
V /Å ³	1366.73(7)	2644.2(2)	1383.95(19)	3033.9(3)	3880.51(15)
Z	2	4	2	4	4
D_{calc} /g cm ⁻³	1.442	1.288	1.393	1.258	1.199
μ /mm ⁻¹	1.619	0.161	0.178	0.148	0.128
$F(000)$	612.0	1080.0	604.0	1208.0	1472.0
Data/ restraints/ parameters	4803/0/346	4634/0/338	4416/0/373	5302/0/381	7793/1/471
S	0.983	0.988	1.081	0.933	1.037
R_1 [$I > 2\sigma(I)$]	0.0442	0.0667	0.0468	0.0688	0.0363
wR_2 [all data]	0.1422	0.1994	0.1269	0.2042	0.0886
Max./min. residual electron dens. [eÅ ⁻³]	0.50/-0.77	0.44/-0.39	0.22 /-0.30	0.41/-0.31	0.12/-0.22

$$^a R_1 = \sum ||F_o| - |F_c|| / \sum |F_o| \text{ and } wR_2 = [\sum w(F_o^2 - F_c^2)^2 / \sum wF_o^4]^{0.5}$$

Table 15: Crystal data for compounds **15aa**, **15ca** and **16an**

Compound	15aa	15ca	16an
Emp. Formula	C ₂₆ H ₂₂ N ₂ O ₂ S	C ₂₇ H ₂₂ N ₂ O ₂ S	C ₃₄ H ₃₀ N ₂ O ₃
Formula weight	426.52	438.53	514.60
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	<i>I</i> 2/ <i>a</i>	<i>I</i> 2/ <i>a</i>	<i>C</i> 2/ <i>c</i>
<i>a</i> /Å	18.7390(9)	18.6706(8)	24.0756(7)
<i>b</i> /Å	7.1964(3)	7.1074(3)	10.5637(3)
<i>c</i> /Å	32.6495(17)	33.8377(18)	22.5994(10)
α /deg	90	90	90
β /deg	98.519(5)	100.438(4)	101.340(4)
γ /deg	90	90	90
<i>V</i> /Å ³	4354.3(4) Å ³	4415.9(4)	5635.4(3)
<i>Z</i>	8	8	8
<i>D</i> _{calc} /g cm ⁻³	1.301	1.319	1.213
μ /mm ⁻¹	0.174	0.174	0.078
<i>F</i> (000)	1792.0	1840.0	2176.0
Data/ restraints/ parameters	4606/0/282	3890/1/279	6019/0/354
<i>S</i>	1.040	0.929	1.087
R1 [<i>I</i> >2σ(<i>I</i>)]	0.0542	0.0660	0.0912
wR2 [all data]	0.1644	0.2056	0.3146
Max./min. residual electron dens. [eÅ ⁻³]	0.21/-0.40	0.457/-0.636	0.60 /-0.59

$$^a\text{R1} = \sum ||\text{Fo}| - |\text{Fc}|| / \sum |\text{Fo}| \text{ and } \text{wR2} = [\sum w(\text{Fo}^2 - \text{Fc}^2)^2 / \sum w\text{Fo}^4]^{0.5}$$

Table 16: Crystal data for compounds **16ba**, **17ab** and **18ga**

Compound	16ba	17ab	18ga
Emp. Formula	C ₂₂ H ₂₀ N ₂ O ₂	C ₃₆ H ₃₄ N ₂ O ₅ S	C ₂₈ H ₂₃ BrN ₂ O ₂
Formula weight	344.40	606.71	499.38
Crystal system	Monoclinic	Triclinic	Monoclinic
Space group	P2(1)/c	<i>P</i> -1	<i>P</i> 21/ <i>c</i>
<i>a</i> /Å	9.8447(3)	10.3724(4)	9.4032(2)
<i>b</i> /Å	8.2108(3)	11.6754(2)	9.2208(2)
<i>c</i> /Å	22.3429(6)	13.7808(3)	26.5915(6)
α /deg	90	79.557(2)	90
β /deg	101.755(2)	72.793(3)	99.022(2)
γ /deg	90	87.940(2)	90
<i>V</i> /Å ³	1768.16(10)	1567.50(8)	2277.09(9)
<i>Z</i>	4	2	4
<i>D</i> _{calc} /g cm ⁻³	1.294	1.286	1.457
μ /mm ⁻¹	0.084	0.149	1.834
<i>F</i> (000)	728.0	640.0	1024.0
Data/ restraints/ parameters	3707/1/240	6529/0/408	4780/0/300
<i>S</i>	1.087	1.051	1.052
R1 [<i>I</i> >2 σ (<i>I</i>)]	0.0776	0.0576	0.0451
wR2 [all data]	0.2390	0.1599	0.0992
Max./min. residual electron dens. [eÅ ⁻³]	0.48/-0.45	0.27/-0.26	0.25/-0.53

$$^a R1 = \sum ||F_o| - |F_c|| / \sum |F_o| \text{ and } wR2 = [\sum w(F_o^2 - F_c^2)^2 / \sum wF_o^4]^{0.5}$$

Table 17: Crystal data for compounds **19k**, **20h** and **21a**

Compound	19k	20h	21a
Emp. Formula	C ₂₄ H ₂₅ NO ₅ S	C ₂₇ H ₂₉ NO ₆	C ₂₁ H ₁₈ O ₄
Formula weight	439.51	463.51	334.35
Crystal system	Triclinic	Monoclinic	Triclinic
Space group	<i>P</i> -1	<i>P</i> 21/ <i>c</i>	<i>P</i> -1
<i>a</i> /Å	10.3479(3)	11.7617(4)	8.2390(2)
<i>b</i> /Å	10.5057(3)	21.8252(8)	8.5305(2)
<i>c</i> /Å	11.7663(3)	9.9033(3)	12.8575(3)
α /deg	93.409(2)	90	72.914(2)
β /deg	114.609(3)	107.445(4)	83.275(2)
γ /deg	95.175(2)	90	75.314(2)
<i>V</i> /Å ³	1151.55(6)	2425.26(15)	834.67(4)
<i>Z</i>	2	4	2
<i>D</i> _{calc} /g cm ⁻³	1.268	1.270	1.330
μ /mm ⁻¹	0.175	0.090	0.092
<i>F</i> (000)	464.0	984.0	352.0
Data/ restraints/ parameters	4815/0/284	5137/0/312	3575/0/227
<i>S</i>	1.041	1.053	1.053
R1 [<i>I</i> >2σ(<i>I</i>)]	0.0656	0.0546	0.0416
wR2 [all data]	0.2083	0.1573	0.1170
Max./min. residual electron dens. [eÅ ⁻³]	0.435/-0.422	0.185/-0.223	0.132 /-0.211

$$^a\text{R1} = \Sigma||\text{Fo}| - |\text{Fc}||/\Sigma|\text{Fo}| \text{ and } \text{wR2} = [\Sigma\text{w}(\text{Fo}^2 - \text{Fc}^2)^2/\Sigma\text{wFo}^4]^{0.5}$$

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PART B

**REACTION OF INDOLE CARBOXYLIC ACIDS/AMIDES
WITH PROPARGYLIC ALCOHOLS: (4 + 3)-ANNULATION,
UNEXPECTED 3- TO 2-CARBOXYL/AMIDE MIGRATION,
AND DECARBOXYLATIVE CYCLIZATION**

INTRODUCTION

This chapter composed of literature relevant to the topics that will be further discussed in Chapter 4. General Introduction to the chemistry of indoles and propargylic alcohols is presented in sections 4.1 and 4.2. Recent literature on intermolecular annulation reactions of indole substrates with propargylic alcohols is discussed in section 4.3 while that on indole fused cyclopentenones is delved into in section 4.4.

4.1 General Introduction

Lewis/Brønsted acid-mediated annulation reaction using indole substrates has been an active area of research.¹ In general, indole 3-position is more nucleophilic as compared to that of 2-position. Because of its electronic distribution, it tends to attack an electrophile through 3-position. Substituted propargylic alcohols can act effectively as such electrophilic partners. In the presence of Lewis/ Brønsted acid, the carbocation intermediate formed can be attacked by indole acid/amide leading to annulated products.² Some of these products like indole-fused ϵ -lactams are often found as core structural motifs in natural products and biologically active compounds (Figure 4.1), but reported methods for their synthesis are very limited.³ The corresponding indole-fused ϵ -lactones are not common⁴ but their decarboxylated products, cyclopenta-indoles, are frequently found in natural products (Figure 4.1).⁵ The latter class of compounds with an indole-fused cyclopentane ring can be synthesized by many methods.⁶ Even for 3,3-disubstituted cyclopenta[*b*]indole, several elegant methods have been reported.⁷ From another perspective, decarboxylative cyclization has emerged as a powerful tool for the synthesis of acyclic/polycyclic compounds.⁸ Most of these decarboxylation reactions are assisted by expensive metal catalysts and reagents, while the reports on metal-free decarboxylation reactions are rather limited.⁹ To develop the metal-free Lewis acid-mediated decarboxylative cyclization, a variety of carboxylic acid substrates are used.¹⁰ However, this strategy has limitations in terms of substrate scope and affords products in poor yields in many cases. Relative to the well-established [1,2]-migration of alkyl, aryl, or other electron-donating groups (EDG),¹¹ migration of strongly electron-withdrawing groups (EWG) is less frequent.¹²

Carboxylate or amide group migration is interesting, but only a handful of examples are available in the literature because the relative order of the migrating aptitude is reverse (EDG < EWG).¹³ Some of these aspects as relevant to the present study are described in the following sections.

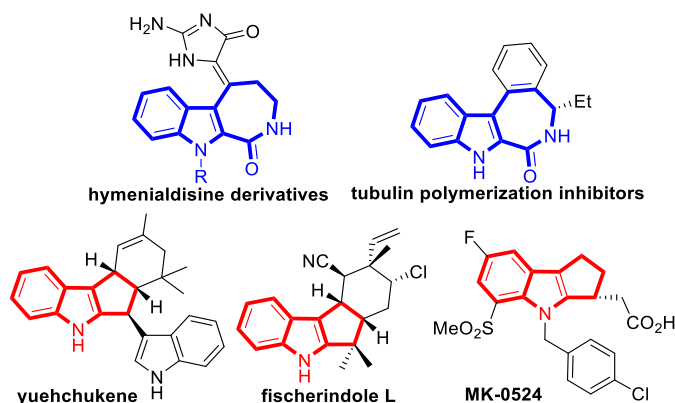


Figure 4.1: Selected examples of lactams, and 3,4-dihydrocyclopentaindoles relevant to the present study

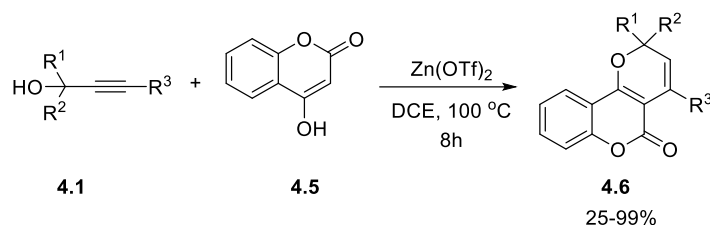
4.2 Propargylic alcohol chemistry

Meyer and Schuster published the classic Meyer–Schuster rearrangement of propargylic alcohols in 1922.¹⁴ This reaction produces the corresponding unsaturated aldehydes or ketones *via* a 1,3-shift of the hydroxyl group from **A** to allenol **B** in the presence of Brønsted or Lewis acid (Scheme 4.1, eq 1).¹⁵ Due to its great atom economy and effectiveness at producing a variety of useful enone derivatives from easily available sources, this reaction has been widely used in organic synthesis. The Rupe rearrangement is a closely comparable process that converts propargylic alcohols into α,β -unsaturated ketones by formally 1,2-shift of the hydroxy group through enyne **D** (Scheme 4.1, eq 2).

Propargylic alcohols have been the subject of thorough research.¹⁶ The strategies for the synthesis of various allene derivatives **4.4** by trapping the allenic carbocationic intermediates **H** is one indication of substantial advancement in this subject (Scheme 4.1, eq 3). In these instances, the use of the more potent nucleophiles effectively blocked the 1,3-hydroxyl shift in the traditional Meyer–Schuster rearrangement.

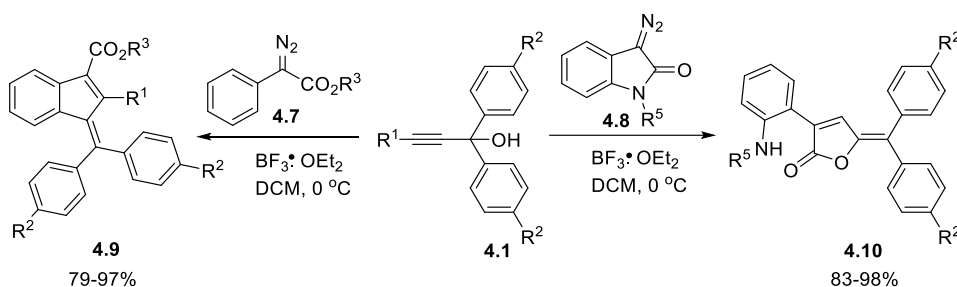
$$\begin{array}{c}
 \text{R}^1 \text{---} \text{C}(\text{OH}) \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\
 | \\
 \text{R}^2
 \end{array}
 \xrightarrow{\text{H}^+}
 \begin{array}{c}
 \text{R}^1 \text{---} \text{C}(\text{OH}_2^+) \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\
 | \\
 \text{R}^2
 \end{array}
 \xrightarrow{-\text{H}^+}
 \begin{array}{c}
 \text{R}^1 \text{---} \text{C} = \text{C}(\text{OH}) \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\
 | \qquad \qquad \qquad | \\
 \text{R}^2 \qquad \qquad \qquad \cdot
 \end{array}
 \rightleftharpoons
 \begin{array}{c}
 \text{R}^1 \text{---} \text{C} = \text{C} \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\
 | \qquad \qquad \qquad | \\
 \text{R}^2 \qquad \qquad \qquad \text{O}
 \end{array}
 \quad (\text{eq 1})$$
$$\begin{array}{c} \text{R}^1 \text{---} \text{C}(\text{OH}) \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\ | \\ \text{R}^2 \end{array} \xrightarrow{\text{LA}} \begin{array}{c} \text{AL}^+ \text{---} \text{OH}^- \\ | \\ \text{R}^1 \text{---} \text{C} \equiv \text{C} \text{---} \text{R}^3 \\ | \\ \text{R}^2 \end{array} \rightarrow \left[\begin{array}{c} \text{R}^1 \\ | \\ \text{C}^+ \equiv \text{C} \text{---} \text{R}^3 \\ | \\ \text{R}^2 \end{array} \right] \rightarrow \begin{array}{c} \text{R}^1 \\ \text{C} = \text{C}^+ \text{---} \text{R}^3 \\ | \\ \text{R}^2 \end{array} \xrightarrow{\text{Nu}^-} \begin{array}{c} \text{R}^1 \\ \text{C} = \text{C} \text{---} \text{Nu} \\ | \quad \quad | \\ \text{R}^2 \quad \quad \text{R}^3 \end{array} \quad (\text{eq 3})$$

Liang *et al.* reported a formal (3 + 3) cascade annulation method using a Lewis acid to create a variety of tricyclic compounds with functionalized pyrano[3,2-*c*]chromen-5(2*H*)-one fragments **4.6**.¹⁷ Propargylic alcohols **4.1** and 4-hydroxy-2*H*-chromen-2-ones **4.5** were used as the substrates. The approach offers a simple, one-step process with low environmental impact for obtaining a wide variety of pyrano[3,2-*c*]chromen-5(2*H*)-ones **4.6** in outstanding yields and with strong functional group tolerance (Scheme 4.2).



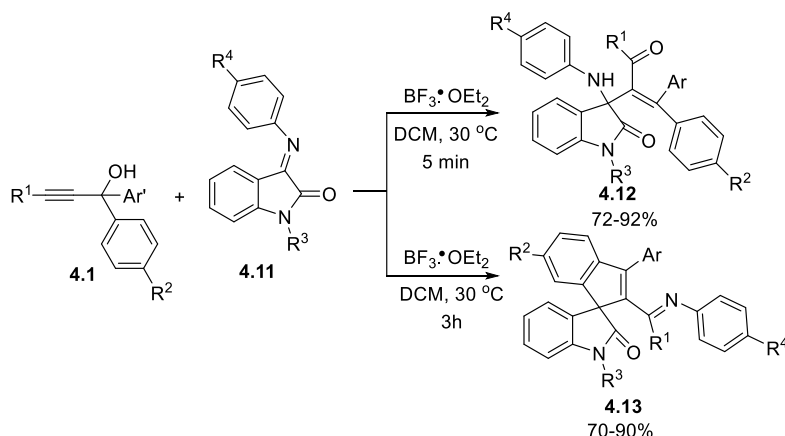
Scheme 4.2: Synthesis of pyrano[3,2-*c*]chromen-5(2*H*)-ones

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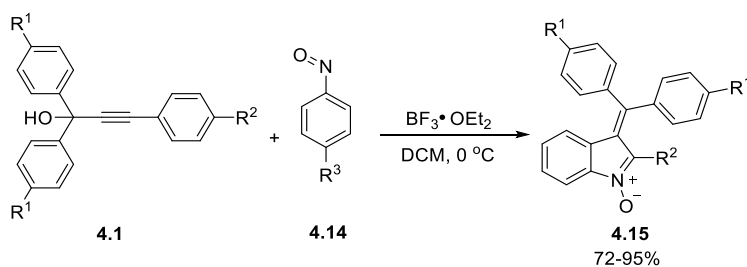
Scheme 4.3: Synthesis of indenenes **4.9** and furanones **4.10** from propargylic alcohols

3-Alkenyl-3-amino-2-oxindoles **4.12** could be made from inexpensive propargylic alcohols **4.1** and isatin imines **4.11** in the presence of catalytic $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in open-air as shown by Muthusamy and coworkers.¹⁹ The reaction was subsequently extended to produce highly substituted spiroindeneindolones **4.13** in one pot using Friedel-Crafts cyclization and 1,3-amino group migration (Scheme 4.4).



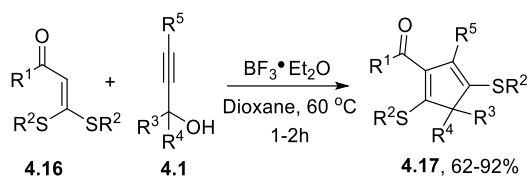
Scheme 4.4: Synthesis of 3-alkenyl-3-amino-2-oxindoles and spiroindeneindolones

By using boron trifluoride etherate ($\text{BF}_3 \cdot \text{Et}_2\text{O}$) as a catalyst in tandem with propargylic alcohols **4.1** and nitrosobenzene **4.14**, Muthusamy's group produced 3-alkylidene-3*H*-indole-*N*-oxides **4.15** (Scheme 4.5).²⁰



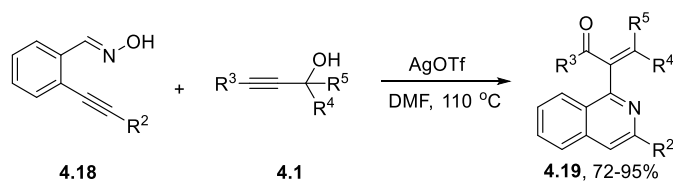
Scheme 4.5: Synthesis of 3*H*-indole-*N*-oxides from propargylic alcohols

In the year 2014, Bi *et al.* developed a novel method for the regiospecific (3 + 2) cycloaddition of propargylic alcohols **4.1** with α -oxo ketene dithioacetals **4.16** to produce cyclopentadienes **4.17**.²¹ A new family of completely substituted 2,5-dialkylthiocyclopentadienes **4.17** was produced in good to exceptional yields (Scheme 4.6). During the ring-closure process, a mechanistically unique 1,4-alkylthio group was observed.



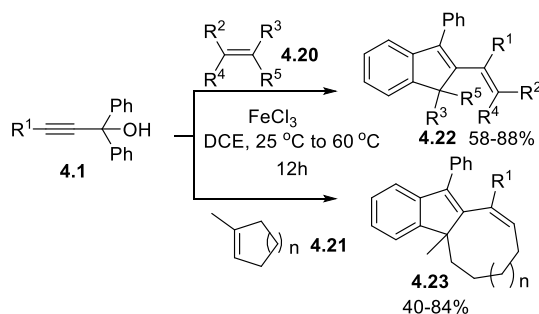
Scheme 4.6: Synthesis of 2,5-dialkylthiocyclopentadienes from propargylic alcohols

A novel method for one-pot formation of 2-(isoquinolin-1-yl) prop-2-en-1-ones **4.19** has been developed by Breit and coworkers through tandem 6-endo-cyclization followed by 1,3-dipolar cycloaddition and intramolecular dehydrative opening of the 2,3-dihydroisoxazole ring.²² in presence of silver(I)-catalyst. The reaction of *ortho*-alkynylbenzaloximes **4.18** with propargylic alcohols **4.1** produced the desired products in high yields (Scheme 4.7).



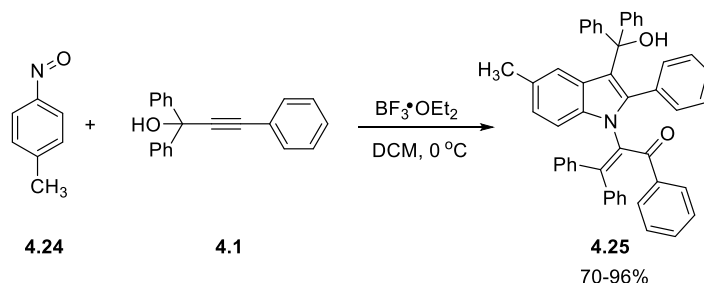
Scheme 4.7: Synthesis of 2-(isoquinolin-1-yl) propenones from propargylic alcohols

Chen's group invented a quick and regioselective cascade cyclization of simple alkenes **4.20** or **4.21** with propargylic alcohols **4.1**. This reaction went through a unique C-C bond cleavage, offering an easy route to polycyclic indenenes **4.22** or **4.23**.²³ Additionally, two new successive carbon rings could be produced in one step using catalytic FeCl_3 (Scheme 4.8).



Scheme 4.8: Synthesis of polycyclic indenenes from propargylic alcohols

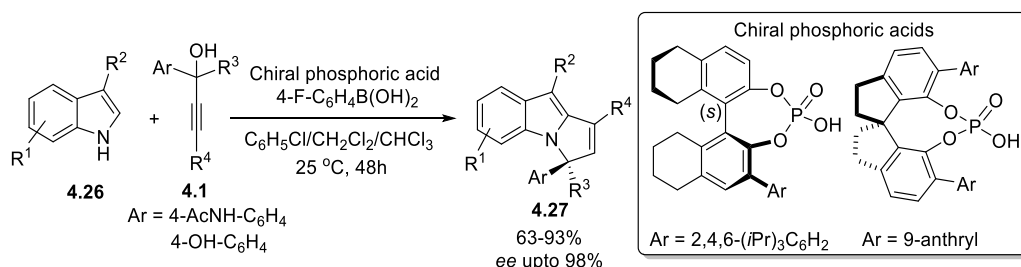
Muthusamy *et al.* developed a method to produce highly substituted indole-3-carbinols **4.25**, where nitrosobenzenes **4.24** and propargylic alcohols **4.1** were combined in $\text{BF}_3 \cdot \text{Et}_2\text{O}$ catalyzed process.²⁴ This approach operates in an open environment, is atom-efficient, and requires a low-cost Lewis acid catalyst (Scheme 4.9).



Scheme 4.9: Synthesis of indole-3-carbinols from propargylic alcohols

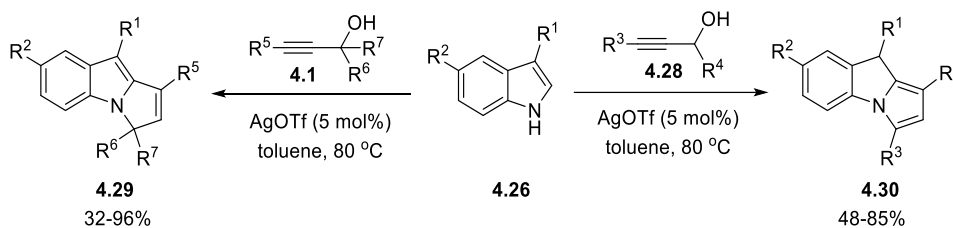
4.3 Intermolecular annulation reactions of indoles with propargylic alcohols

Li's group described the formal (3 + 2) cycloaddition of 3-substituted 1*H*-indoles **4.26** with propargylic alcohols **4.1** containing a directing group (*p*-NHAc or *p*-OH) using chiral phosphoric acid as the catalyst leading to chiral pyrrolo[1,2-*a*]indoles **4.27** with tetrasubstituted carbon stereocenters.^{1c} The reaction tolerates a variety of substrates producing chiral pyrrolo-indoles **4.27** with up to 93% yield and 98% *ee* (Scheme 4.10).



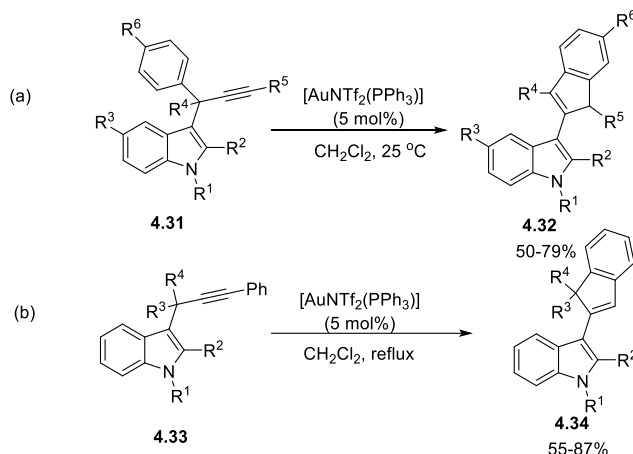
Scheme 4.10: Synthesis of pyrrolo[1,2-*a*]indoles from propargylic alcohols

An effective cascade process to synthesize 9*H*-pyrrolo[1,2-*a*]indole **4.29** or 3*H*-pyrrolo[1,2-*a*]indole **4.30** has been established by Zhan *et al.*^{1d} Here, propargylic alcohols **4.1** or **4.28** and 3-substituted-1*H*-indoles **4.26** undergo consecutive Friedel-Crafts reaction and N-C bond formation, catalyzed by silver(I) triflate. Base- and ligand-free conditions can be used to perform this Lewis acid-catalyzed N-C bond-forming reaction with excellent chemoselectivity (Scheme 4.11).



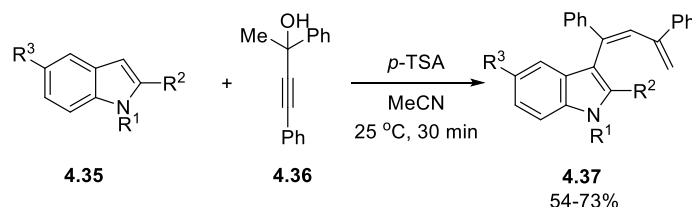
Scheme 4.11: Ag(I)-catalyzed chemoselective cascade synthesis of pyrroloindoles

Sanz *et al.* showed that under gold-catalysis, C3-propargylated indoles **4.31** react via unprecedented 1,2-indole migrations. The 1,2-indole migration and C-H insertion reactions and 1,2-indole migration and Nazarov cyclization reactions are two new tandem processes that have been described.²⁵ When indole **4.31** was treated with gold(I)-catalyst, 3-indenyl indole **4.32** was obtained (Scheme 4.12a).²⁵ On the other hand, **4.34** can also be synthesized directly from C3-propargylated indole **4.33** (Scheme 4.12b).



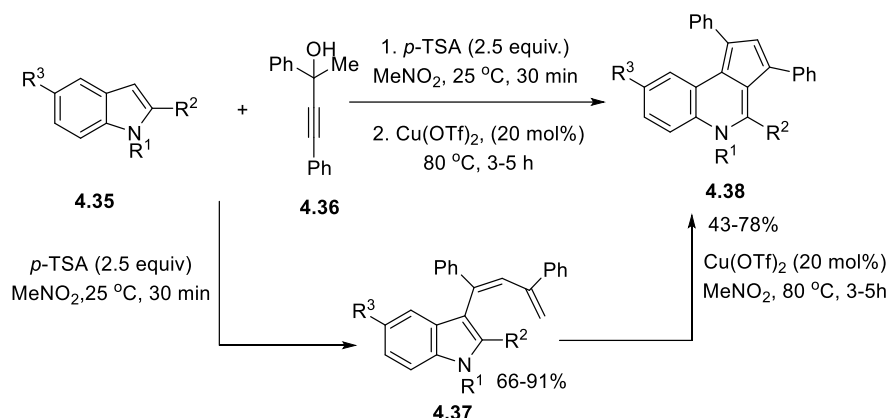
Scheme 4.12: Gold(I)-catalyzed annulations of the indoles with propargylic alcohols

Sanz's group obtained synthetically useful 3-(1,3-butadienyl)indoles **4.37** by the reaction of **4.35** with propargylic alcohol **4.36** under *p*-TSA catalysis at room temperature (Scheme 4.13).²⁶



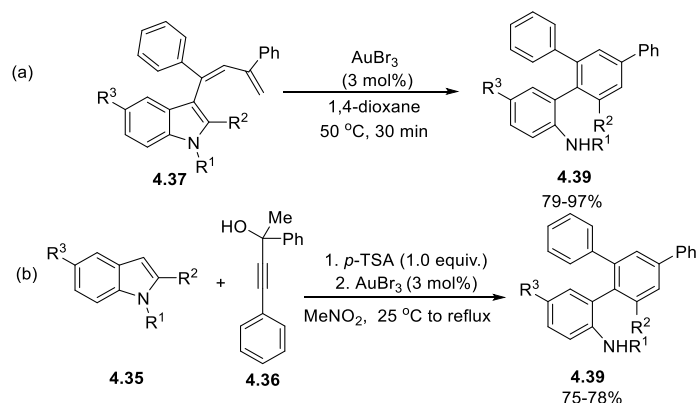
Scheme 4.13: *p*-TSA-catalyzed butadienylation of indoles with propargylic alcohols

In 2014, our group observed that under aerobic conditions, 3-dienylindoles **4.35** undergo copper-catalyzed oxidative ring-expansion and intramolecular electrophilic substitution that resulted in cyclopenta[*c*]quinolines **4.38**. The reaction went through Brønsted acid-catalyzed allenylation and isomerization to produce intermediate **4.37**, which upon copper-catalyzed dearomatizative oxidative ring expansion gave the desired product **4.38** (Scheme 4.14).^{1e}



Scheme 4.14: Sequential or one-pot synthesis of fused cyclopenta[*c*]quinolines using *p*-TSA and Cu(OTf)₂

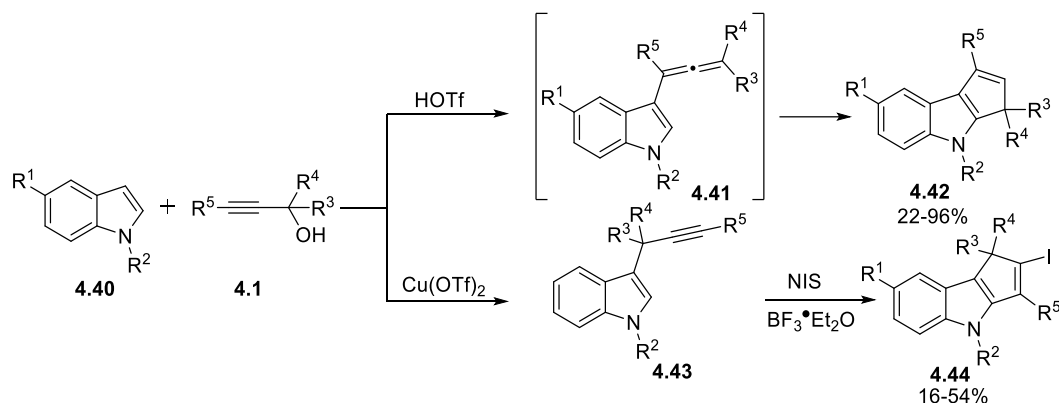
Recently our group also reported that 3-dienyl indoles **4.37** undergo a gold-catalyzed intramolecular reaction that resulted in the synthesis of functionalized terphenylamines **4.39** with high efficiency.²⁷ This reaction could also be carried out in a single pot starting with 2-arylidolines **4.35** and propargylic alcohol **4.36**. This reaction is expected to occur by cascade cyclization, aromatization, and fragmentation of the indole moiety (Scheme 4.15).



Scheme 4.15: Gold(III)-catalyzed sequential/one-pot synthesis of terphenylamines

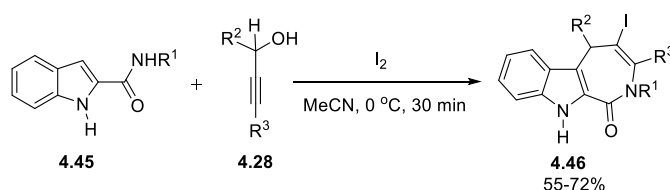
In the year 2012, Wang's group observed that an appropriate catalyst may effectively regulate 3-alkenylation or 3-alkylation of indole with propargylic alcohols. Thus in the

presence of triflic acid, indole **4.40** underwent 3-alkenylation to give intermediate **4.41**, and a cascade reaction successfully generated 3,4-dihydrocyclopenta[*b*]indole **4.42** in good yields.^{1a} In the presence of Cu(OTf)₂, 3-propargylic indoles **4.43** were produced. These indoles could then be transformed into 2-iodo-1,4-dihydrocyclopenta[*b*]indoles **4.44** in the presence of *N*-iodosuccinimide and BF₃·OEt₂ (Scheme 4.16).



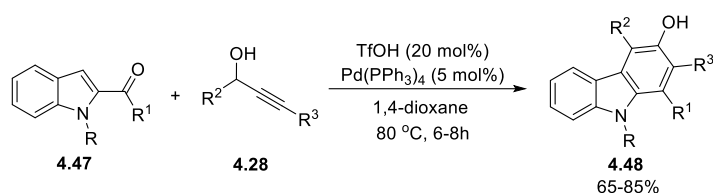
Scheme 4.16: Catalyst-driven divergent annulations of indoles and propargylic alcohols

Kundu and coworkers have reported the formation of naturally occurring indoloazepinone scaffolds **4.46** quickly and effectively using indole-2-carboxamides **4.45**, 1,3-disubstituted propargylic alcohols **4.28**, and I₂ (Scheme 4.17).²⁸ A domino sequence of C-H functionalization followed by alkyne activation, intramolecular hydroamidation, and deprotonation is operative in this method.



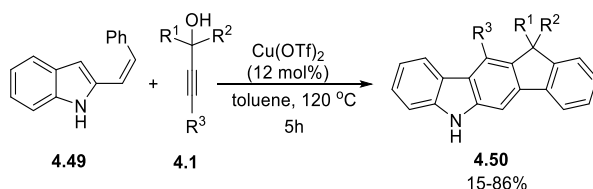
Scheme 4.17: Iodo-cyclization of indole-2-carboxamides and propargylic alcohols

A novel sequential propargylation of indole-2-carbonyls **4.47** with propargylic alcohols **4.28** followed by palladium-catalyzed hydroxylative benzannulation for the synthesis of 3-hydroxycarbazoles **4.48** was developed by Raji Reddy's group.²⁹ This one-pot method afforded substituted 3-hydroxycarbazoles **4.48** in high yield (Scheme 4.18). Tandem annulations were used to enhance the method's ability to access furano-carbazoles from dialkynols.



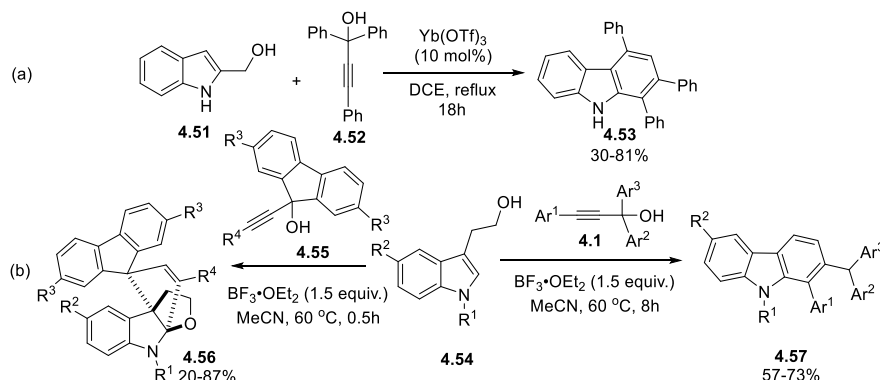
Scheme 4.18: Synthesis of 3-hydroxy carbazoles from indoles and propargylic alcohols

Propargylic alcohols **4.1** and (*Z*)-2-styryl-1-indoles **4.49** were used as the initial substrates in a unique copper(II) trifluoromethanesulfonate catalyzed intermolecular cascade annulation approach by Liang *et al.* allowing the synthesis of pentacyclic compounds **4.50** with desirable carbazole fragments.³⁰ This atom-efficient method involves a sequential Meyer-Schuster rearrangement, followed by isomerization, and cyclization cascade (Scheme 4.19).



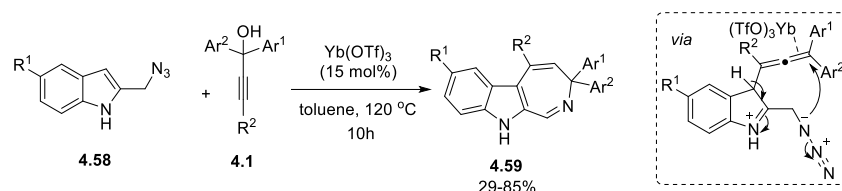
Scheme 4.19: Cu(II)-catalyzed annulation of propargylic alcohols with (*Z*)-2-styrylindoles

An innovative Lewis acid catalyzed dehydrative (3 + 3) annulation of indole alcohols **4.51** and propargylic alcohol **4.52** was devised to produce polysubstituted carbazoles **4.53** in good yields by Wang *et al.* (Scheme 4.20a).³¹ The cascade process involved Friedel-Crafts type allenylation, followed by 1,5-hydride shift, 6-electrocyclization, and Wagner-Meerwein rearrangement. Using a similar substrate, Wang and Lu reacted *tert*-propargylic alcohols **4.1** or tryptophols **4.55** with indolyl alcohol **4.54** in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ to obtain cyclopenta[*b*]furo[2,3-*b*]indoles **4.56** or carbazoles **4.57** (Scheme 4.20b).^{1f}



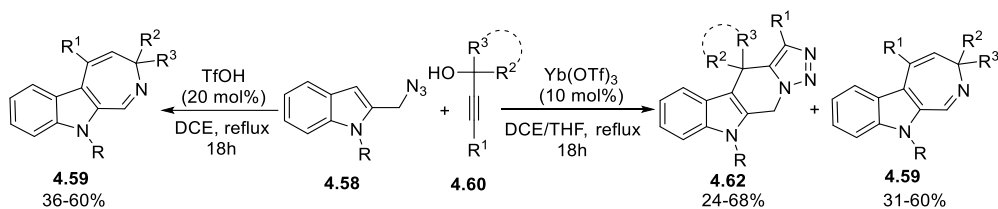
Scheme 4.20: Yb(III)-catalyzed dehydrative (3 + 3) cycloaddition reactions of indole alcohols with propargylic alcohols

Starting with easily accessible internal tertiary alkynols and azides, a novel Lewis acid catalyzed (4 + 3) cycloaddition reaction was reported by Liang *et al.*³² This reaction went through alkenylation/allenylation of indole azide **4.58** and propargylic alcohol **4.1** in the presence of Yb(OTf)₃ with subsequent intramolecular cyclization of azide and elimination of N₂ producing the indolo-azepines **4.59** (Scheme 4.21).



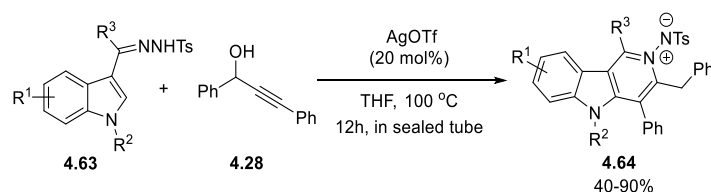
Scheme 4.21: Yb(III)-catalyzed (4 + 3) cycloaddition of indole azides with propargylic alcohols

Easy and quick access to tetrahydro- β -carbolines **4.62** and indole azepines **4.59** was achieved by Wang's group from 2-indolylmethyl azides **4.58** and propargylic alcohols **4.60** by using acid-catalyzed dehydrative annulation process.³³ Thus treatment of **4.58** with the propargylic alcohols **4.60** in the presence of Yb(OTf)₃ produced tetrahydro- β -carbolines **4.62** with the formation of substituted indole azepines **4.59**. On the contrary, same two starting materials when reacted with the Brønsted acidic catalyst TfOH, gave access to indole azepines **4.59** as the sole products (Scheme 4.22).



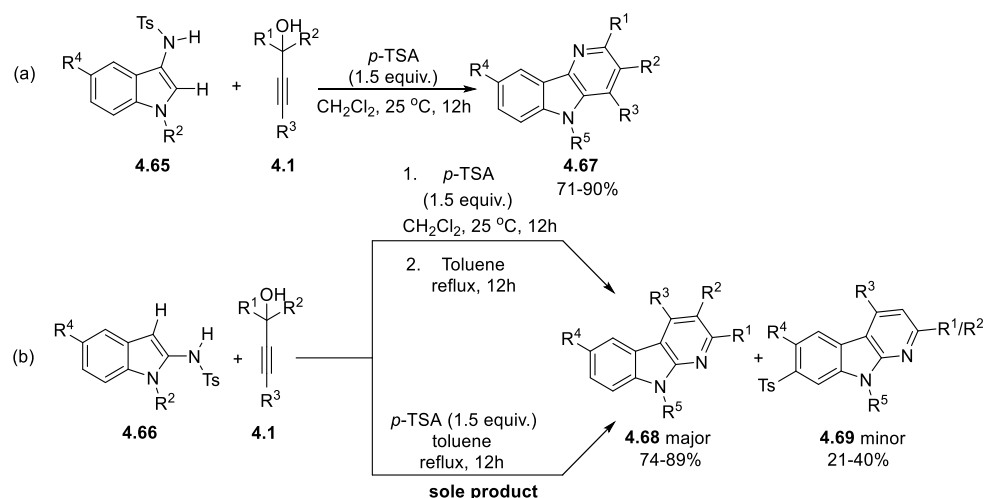
Scheme 4.22: Divergent annulations of the 2-indolylmethyl azides with propargylic alcohols

Zhan's group presented a straightforward and effective method for the regioselective synthesis of *N*-imino- γ -carbolinium ylides **4.64** starting from easily accessible hydrazones of indole-3-carbonyl derivatives **4.63** and propargylic alcohols **4.28** using a silver(I)-catalyst.³⁴ In this reaction, consecutive Friedel Crafts alkylation and intramolecular N-C bond formation takes place sequentially (Scheme 4.23).



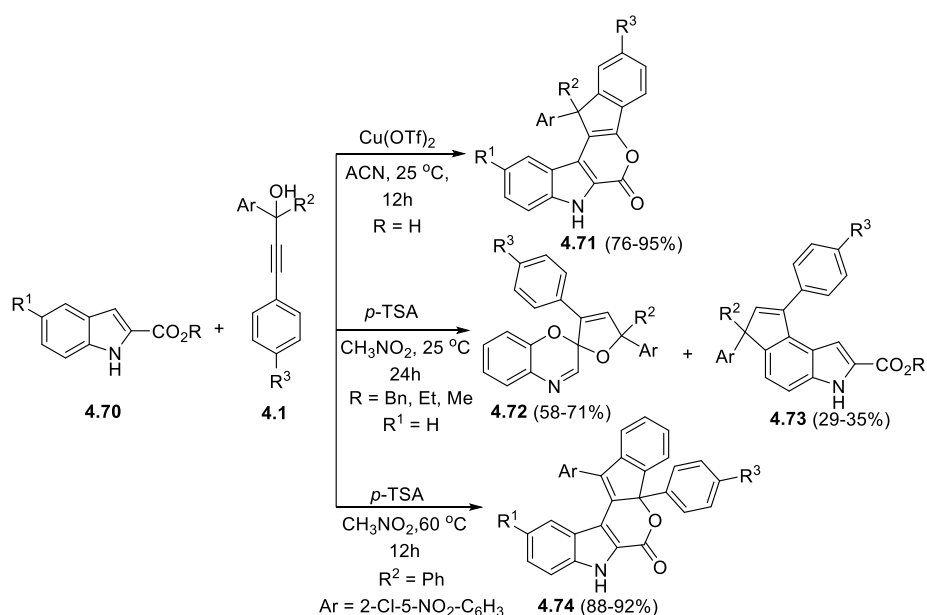
Scheme 4.23: Ag(I)-catalyzed annulation of indole-3-hydrazones with propargylic alcohols

Recently our group found that propargylic alcohols **4.1** react with sulfonamido-indoles/-indolines **4.65** and **4.66** in the presence of a Brønsted acid to produce highly substituted δ - or α -carboline **4.67** and **4.68** in good to outstanding yields. For this approach, Friedel-Crafts alkylation, [1,5]-hydrogen shift, electrocyclization, and elimination, [1,2]-aryl migration, and aromatization are cascade reaction sequences. There has also been evidence of an unanticipated regioselective tosyl group migration from the indole 2- to 6-position and arene elimination resulting in tosyl migrated α -carboline **4.69** (Scheme 4.24).^{1b}



Scheme 4.24: *p*-TSA-mediated annulation reactions of the sulfonamido-indoles/indolines

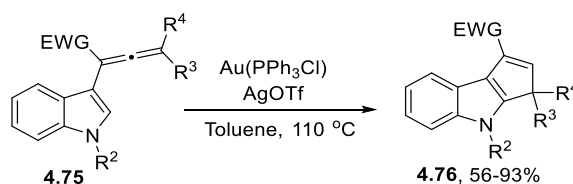
Our group recently discovered that in the presence of *p*-TSA, dearomative ring expansion/spirocyclization of indole-2-carboxylates **4.70** with propargylic alcohols **4.1** containing electron-withdrawing aromatic groups produced dihydrocyclopenta[*b*]indole-2-carboxylates **4.73** and spiro[benzo[*b*]oxazine-furans **4.72** via oxygen insertion.³⁵ The same reactants, when heated to a moderately high temperature, produced fused pyrano-indoles **4.74**. On the other hand, a distinct type of pentacyclic indene fused pyrano-indolones **4.71** could be quickly obtained through the annulation of indole-2-carboxylic acids **4.70** with propargylic alcohols **4.1** in the presence of Cu(OTf)₂ at room temperature (Scheme 4.25).



Scheme 4.25: Synthesis of indole fused scaffolds from indole carboxylates and propargylic alcohols

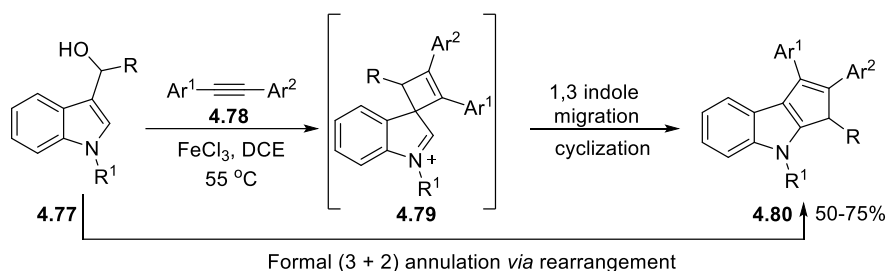
4.4 Indole fused cyclopentene scaffolds

Through the C2-H bond functionalization of the indole moiety, Ma's group created a method for the construction of dihydrocyclopenta[*b*]indoles **4.76** in good yields *via* gold-catalyzed cyclization of indole substrates with an electron-deficient allene moiety at the 3-position **4.75**.³⁶ This reaction depends strongly on the presence of the electron-withdrawing alkoxy carbonyl, dialkoxyphosphono or phenyl group on the allenic carbon (Scheme 4.26).



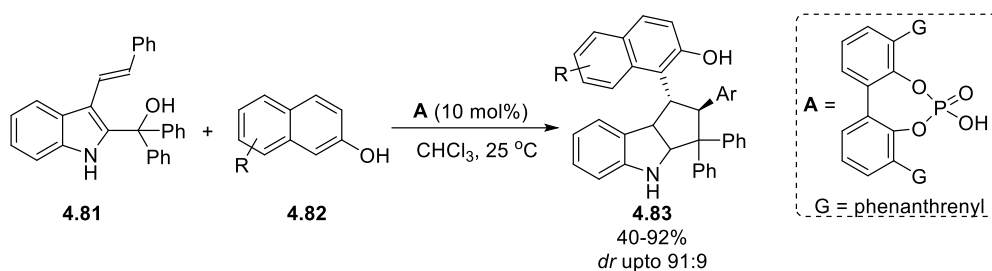
Scheme 4.26: Synthesis of dihydrocyclopenta[*b*]indole using gold catalysis

Baire *et al.* reported the synthesis of cyclopenta[*b*]indole framework **4.80** from 3-indolylmethanols **4.77** and alkynes **4.78** *via* formal (3 + 2) annulation. This method produced cyclopenta[*b*]indoles **4.80** and exhibited universality for both alkynes and carbinol substrates.⁷¹ Based on an isolated vinyl chloride intermediate, involvement of the vinylic carbocation intermediate **4.79** was proposed. A 1,3-indole migration process *via* a ring-opening/ ring-closing cascade has been postulated for the mechanism (Scheme 4.27).



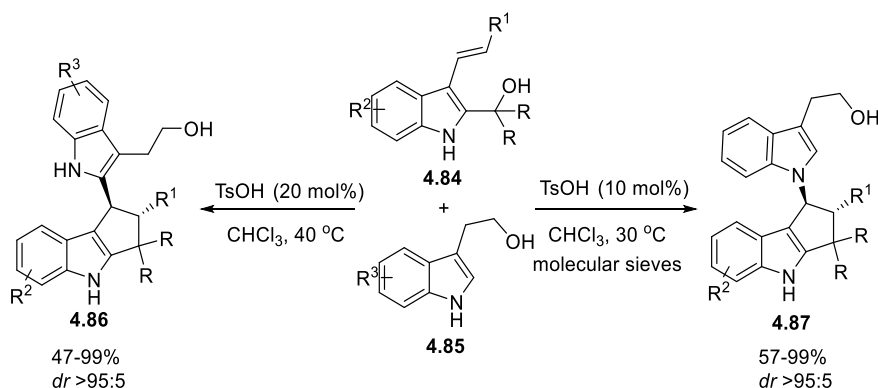
Scheme 4.27: Synthesis of dihydrocyclopenta[*b*]indole from indolylmethanols and alkynes

Shi and co-workers achieved the synthesis of chiral cyclopenta[*b*]indole frameworks **4.83** through the catalytic asymmetric tandem cyclization of 2-indolylmethanols **4.81** with 2-naphthols **4.82** in presence of chiral phosphoric acids, with good yields (up to 90%), high diastereoselectivities (up to >95:5 *dr*), and excellent enantioselectivities (up to 96% *ee*) (Scheme 4.28).^{7d}



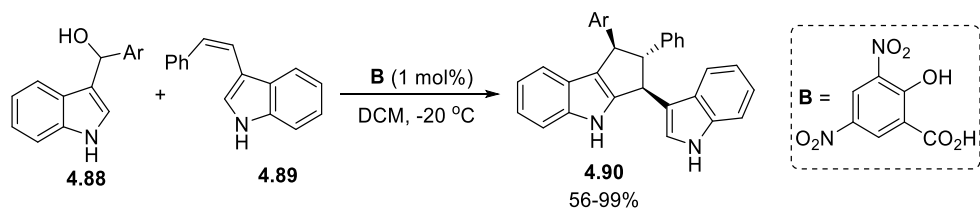
Scheme 4.28: Synthesis of asymmetric cyclopenta[*b*]indole using a chiral phosphoric acid

Through an interrupted Nazarov-type cyclization in the presence of Brønsted acid, a chemodivergent reaction of 2-indolylmethanols **4.85** with tryptophols **4.84** resulting in an effective synthesis of two kind of cyclopenta[*b*]indole derivatives **4.86** and **4.87** in good yields and excellent diastereoselectivities has been established by Shi *et al* (Scheme 4.29).^{7c} The chemoselectivity of the reaction was significantly influenced by the presence or absence of molecular sieves.



Scheme 4.29: Synthesis of cyclopenta[*b*]indole from 2-indolylmethanols and tryptophols

In 2014, Guo and coworkers described an effective (3 + 2) annulation reaction involving 3-vinyliindoles **4.89** and 3-indolylmethanols **4.88**. With the aid of 1 mol% 2-hydroxy-3,5-dinitrobenzoic acid, novel 2,3-bisindolylmethanes **4.90** were produced in high yields as single diastereoisomers (Scheme 4.30).^{7g}



Scheme 4.30: Synthesis of asymmetric 2,3-bisindolylmethanes from 3-vinyliindoles and 3-indolylmethanols

OBJECTIVES OF THE WORK-PART B

The vital objective of the current work was to investigate the reactivity of indole carboxylic acids/amides with substituted propargylic alcohols in the presence of different Lewis/Brønsted acids. More specifically, it was planned to

- (i) Explore the reactivity of indole-2-carboxylic acid/amide with propargylic alcohol in presence of a suitable catalyst [e.g., $\text{Cu}(\text{OTf})_2$, $\text{BF}_3 \cdot \text{OEt}_2$] to see if products like ϵ -lactones, or indole fused cyclopentenones may be obtained or not, and
- (ii) Investigate the reactions of indole-3-carboxylic acid/amide with substituted propargylic alcohols and compare the reactivity with that of indole-2-carboxylic acid/amide.

RESULTS AND DISCUSSION

This chapter deals with the reaction of indole carboxylic acid/amide with propargylic alcohol in the presence of different Lewis and Brønsted acids resulting in seven-membered indole fused lactone/lactam unit, five-membered indole fused cyclopentenones through decarboxylative cyclization. Unexpected 3- to 2- carboxylate/amide migration is the breakthrough for this reaction. General characterization techniques are similar to what has been presented in Chapter 2.

5.1 Precursors used in the present study

Substituted indole-2-carboxylic acids **1a-1g**,^{37a} and **1h**,^{37b} indole-2-carboxamides **2a-2c**,^{37c} indole-3-carboxamides **4a-4c**,^{37d} and propargylic alcohols **5a-5x**^{37e} (Chart 1) were prepared by using literature methods.

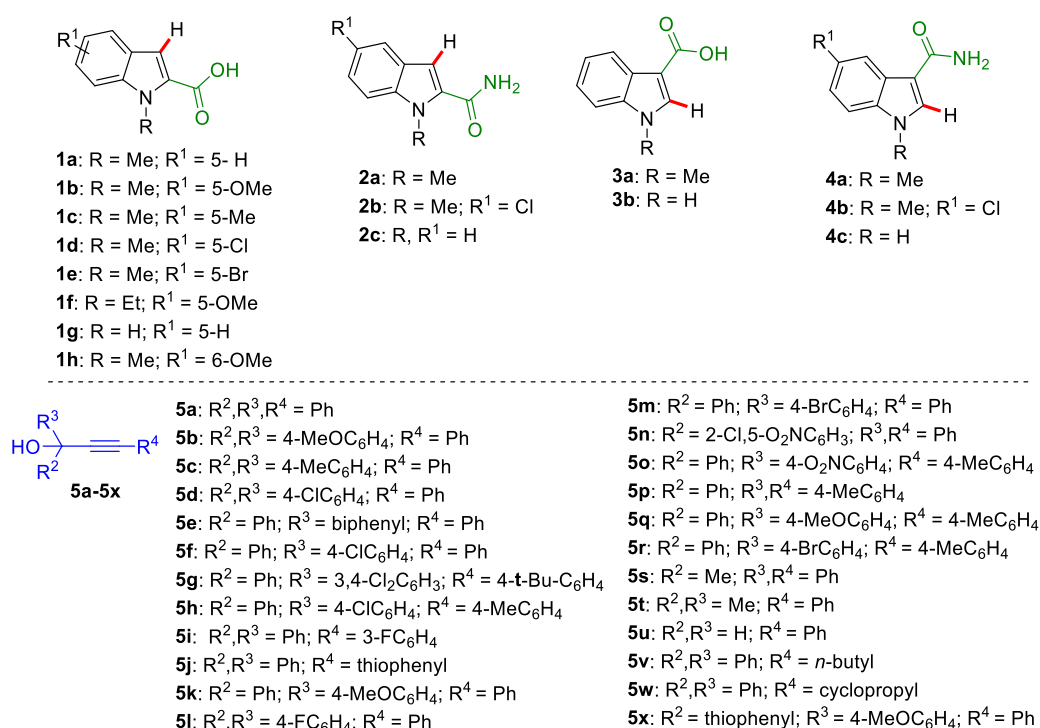


Chart 1: Indole-2/3-carboxylic acids, indole-2/3-carboxamides, and propargylic alcohols used in the present study

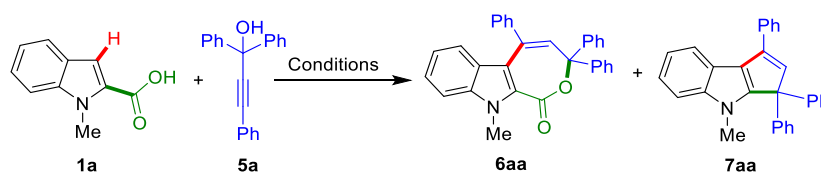
5.2 Reaction of indole carboxylic acids/amides with propargylic alcohols: (4+3)-Annulation, unexpected 3- to 2- carboxylate/amide migration and decarboxylative cyclization

In this section, results obtained in the reactions of indole carboxylic acids/ amides with propargylic alcohols in the presence of different Lewis/ Brønsted acid are discussed. The unobvious carboxylate or amide migration from indole 3- to 2-position is an interesting finding of this scheme. The resulting products such as indole fused seven-membered ε -lactone/lactams, and indole fused cyclopentenones may have pharmacological significance.⁴⁻⁶

5.2.1 Synthesis of ε -lactones and indole-fused cyclopentenones from *N*-alkylated indole-2-carboxylic acids and propargylic alcohols

The initial reaction was performed between 1-methylindole-2-carboxylic acid **1a** and propargylic alcohol **5a** in the presence of $\text{Sc}(\text{OTf})_3$ at rt (25 °C). The oxepino-indolone (ε -lactone) **6aa** via direct (4 + 3)-annulation and the unexpected dihydrocyclopenta-indole **7aa** via decarboxylative cyclization of the ε -lactone were obtained after 12h in 74% and 10% yields, respectively, (Table 1, entry 1). Based on this result, we screened the catalysts, solvents, reaction temperature, reaction time, and quantity of the catalyst. First, the effectiveness of other catalysts $\text{Zn}(\text{OTf})_2$, $\text{In}(\text{OTf})_3$, $\text{Bi}(\text{OTf})_3$, AgOTf , NaOTf , and FeCl_3 was checked; in these cases, products **6aa** and **7aa** were obtained in moderate yields. The sole product **6aa** in slightly increased yield was obtained using $\text{Yb}(\text{OTf})_3$ or $\text{Fe}(\text{OTf})_3$. The highest yield of **6aa** (93%) was observed by conducting the reaction for 6h using $\text{Cu}(\text{OTf})_2$ as the catalyst in DCM solvent (Table 1, entry 10); increasing the reaction time to 12h also afforded the same yield. The reaction when conducted at 0 or 40 °C gave a lower yield. Other solvents like dichloroethane, chloroform, 1,4-dioxane, acetonitrile, tetrahydrofuran, toluene, and dimethyl sulfoxide afforded lower yields. No reaction occurred in the absence of the catalyst. Increasing the catalyst loading from 10 mol% to 15 and 20 mol%, did not improve yield. Thus $\text{Cu}(\text{OTf})_2$ in DCM at rt (25 °C) was found to be optimal for obtaining **6aa**.

Table 1. Optimization of reaction conditions for obtaining 6aa and 7aa^a



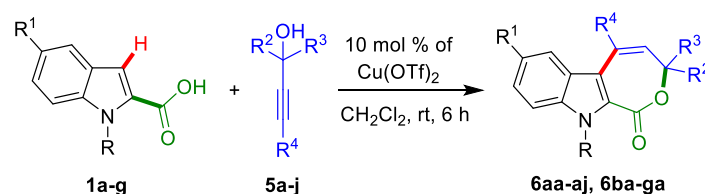
Entry	Catalyst (10 mol %)	Solvent	T (°C)	Time (h)	Yield (%) ^b	
					6aa	7aa
1	Sc(OTf) ₃	DCM	25	12	74	10
2	Zn(OTf) ₂	DCM	25	12	70	5
3	In(OTf) ₃	DCM	25	12	60	16
4	Bi(OTf) ₃	DCM	25	12	65	15
5	AgOTf	DCM	25	12	72	10
6	NaOTf	DCM	25	12	63	7
7	FeCl ₃	DCM	25	12	83	9
8	Yb(OTf) ₃	DCM	25	12	85	--
9	Fe(OTf) ₃	DCM	25	12	88	--
10	Cu(OTf)₂	DCM	25	6	93	--
11	Cu(OTf) ₂	DCM	25	12	93	--
12	Cu(OTf) ₂	DCM	25	6	70	--
13	Cu(OTf) ₂	DCM	40	6	75	--
14	Cu(OTf) ₂	DCE	25	6	87	--
15	Cu(OTf) ₂	CHCl ₃	25	6	78	--
16	Cu(OTf) ₂	Dioxane	25	6	76	--
17	Cu(OTf) ₂	CH ₃ CN	25	6	46	--
18	Cu(OTf) ₂	THF	25	6	40	--
19	Cu(OTf) ₂	Toluene	25	6	43	--
20	Cu(OTf) ₂	DMSO	25	6	44	--
21	no catalyst	DCM	25	6	nr ^c	--
22	Cu(OTf) ₂	DCM	25	6	93	--
23	Cu(OTf) ₂	DCM	25	6	93	--

^aReaction conditions: **1a** (0.100 g, 0.57 mmol), **5a** (0.178 g, 0.62 mmol), solvent (5 mL).

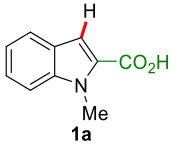
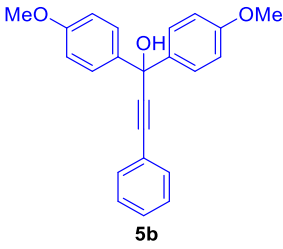
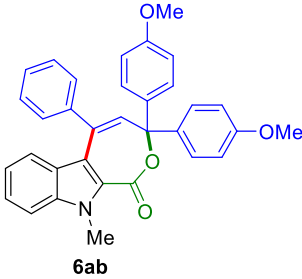
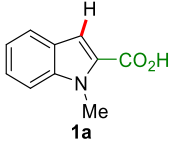
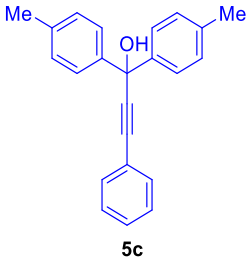
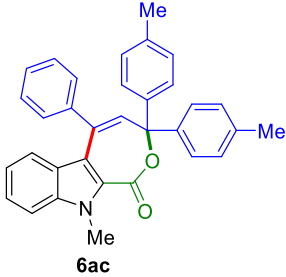
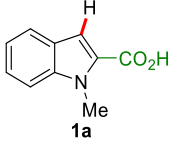
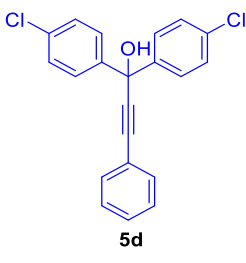
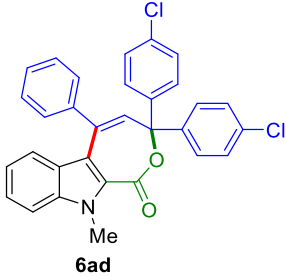
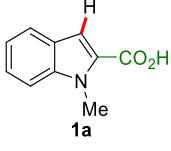
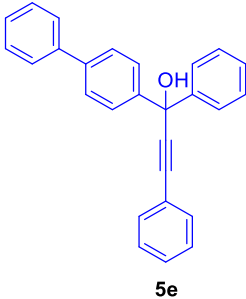
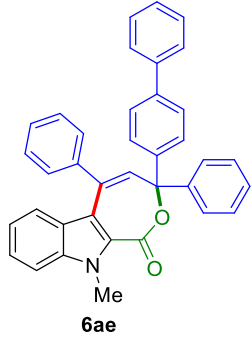
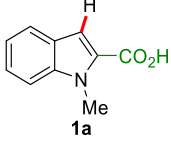
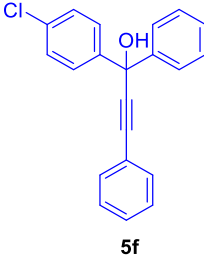
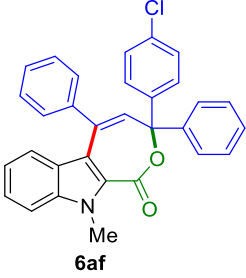
^bYield after isolation is based on **1a**. ^cnr = no reaction.

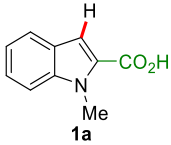
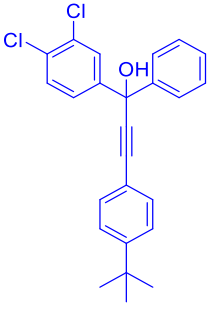
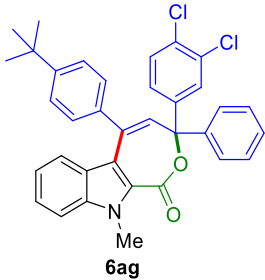
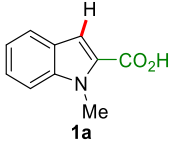
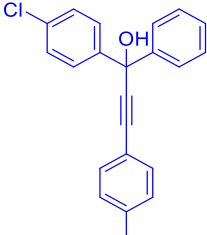
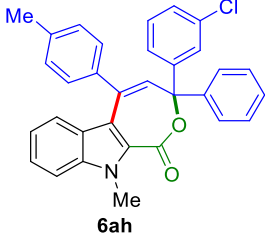
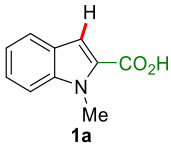
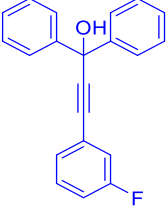
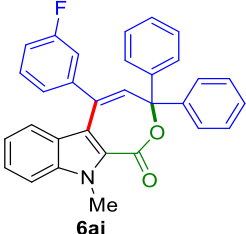
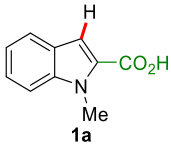
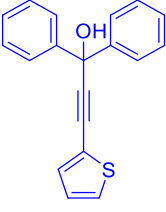
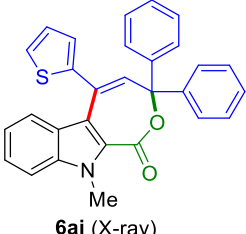
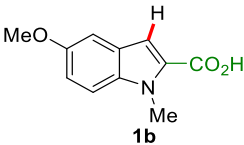
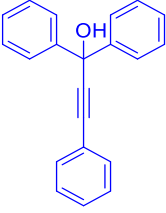
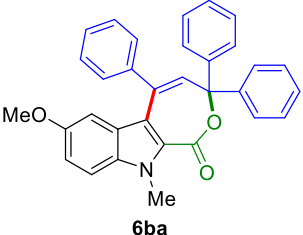
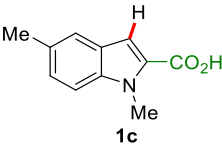
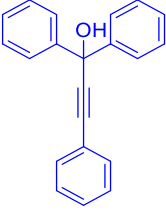
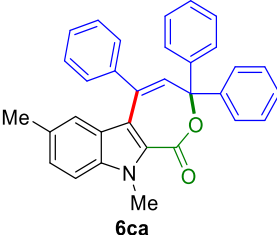
For the substrate scope, we checked a wide variety of indole-2-carboxylic acids **1** and propargylic alcohols **5** to obtain substituted indole fused ϵ -lactones **6** (Table 2; Figure 1 for X-ray structures). First, a series of substituted propargylic alcohols **5b-5e** were reacted with **1a** to examine the substituent effect (e. g., **6ab-6ae**). Propargylic alcohols **5** bearing an electron-donating substituent (OMe, Me; **6ab-6ac**) at the *para*-position of the aromatic ring provided slightly higher yields than those bearing the electron-withdrawing substituent (Cl; **6ad**). With $R^2 = \text{Ph}$ and $R^3 = \text{biphenyl}$, ϵ -lactone **6ae** could be obtained as a single product in 67% yield. Other unsymmetrical propargylic alcohols **5f-5h** also gave products **6af-6ah** in good to excellent yields. Propargylic alcohols with an electron-donating *para*-substituent on the phenyl ring (*tert*-Bu, Me; **6ag-6ah**) gave a higher yield than that with electron-withdrawing group at *meta*-position (F; **6ai**). The reaction also worked well when R^4 was thiophenyl (**5j**) giving the product **6aj** (X-ray; Figure 1). The 5-substituted indole-2-carboxylic acids ($R^1 = \text{OMe, Me, Cl, Br, 1b-1e}$) with electron-donating or electron-withdrawing groups led to products **6ba-6ea** in good yields. Lastly, 1-ethyl-indole-2-carboxylic acid **1f** ($R = \text{Et}$) provided the ϵ -lactone **6fa** in 76% yield. The parent 1*H*-indole-2-carboxylic acid **1g** ($R = \text{H}$) also reacted with the propargylic alcohol **5a** at 0 °C affording the product **6ga** in good yield.

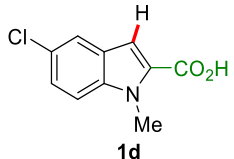
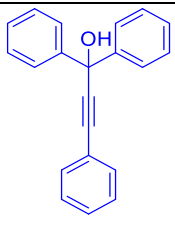
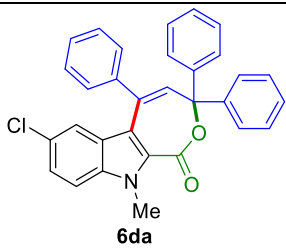
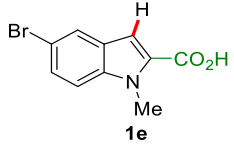
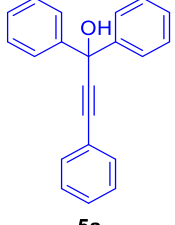
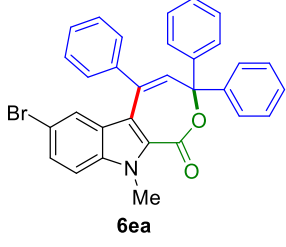
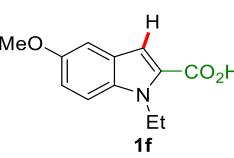
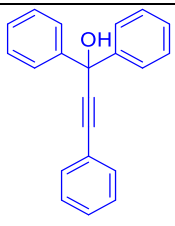
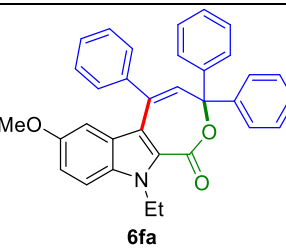
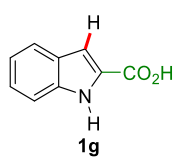
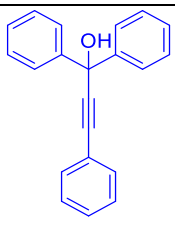
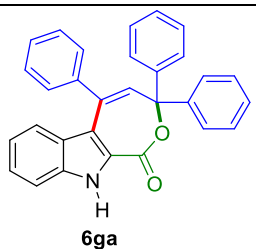
Table 2. Substrate Scope for the synthesis of ϵ -lactones from *N*-alkylated indole-2-carboxylic acids and propargylic alcohols^a



Entry	Indole-carboxylic acid	Propargylic alcohol	ϵ -lactone	Yield ^b (%)
1	 1a	 5a	 6aa (X-ray)	93

2	 1a	 5b	 6ab	91
3	 1a	 5c	 6ac	94
4	 1a	 5d	 6ad	81
5	 1a	 5e	 6ae	67
6	 1a	 5f	 6af	87

7	 1a	 5g	 6ag	78
8	 1a	 5h	 6ah	84
9	 1a	 5i	 6ai	77
10	 1a	 5j	 6aj (X-ray)	75
11	 1b	 5a	 6ba	90
12	 1c	 5a	 6ca	88

13	 1d	 5a	 6da	88
14	 1e	 5a	 6ea	84
15	 1f	 5a	 6fa	76
16	 1g	 5a	 6ga	71

^aReaction conditions: indole-2-carboxylic acid **1** (0.57 mmol), propargylic alcohol **5** (0.62 mmol), solvent (DCM, 10 mL), 6h, 25 °C. ^bYield of the isolated product.

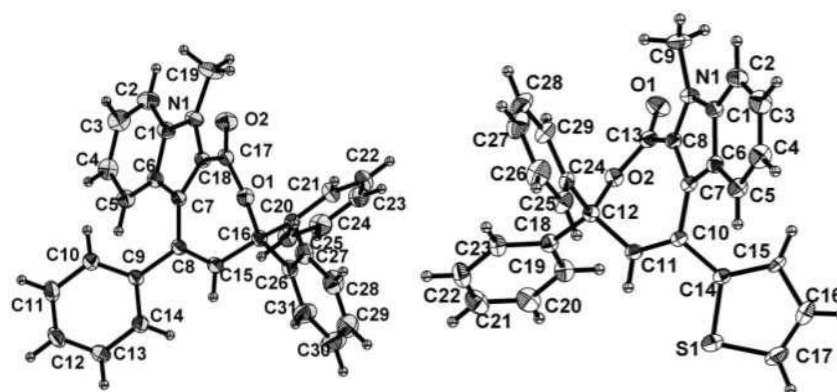
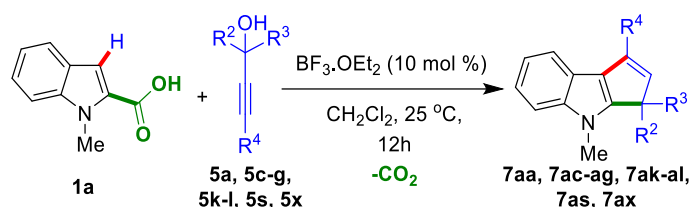


Figure 1: ORTEP views of **6aa** (CCDC 1915530) and **6aj** (CCDC No: 1915531) with a 30% probability of ellipsoids

In the above reaction, the CO₂ moiety is intact in the ϵ -lactones **6aa** and the decarboxylated product **7aa** is either minor or present in trace quantities during optimization. However, if we use the Lewis acid BF₃·OEt₂ in DCM at rt for 12h, **7aa** was obtained in 81% yield from 1-methylindole-2-carboxylic acid **1a** via decarboxylation followed by cyclization. Although TfOH, MsOH, and *p*-TSA also worked (yields: 71%, 64%, and 76%, respectively), BF₃·OEt₂ was the best and 3,4-dihydrocyclopenta[*b*]indoles **7aa**, **7ac-7ag** and **7ak-7al** [cf. Figure 2 for **7al**, X-ray] were readily obtained in good to excellent yields (Table 3). Propargylic alcohol **5s** bearing an alkyl substituent (R² = Me, R³ = Ph) gave **7as** in 75% yield. The reaction worked well when R² was thiophenyl (**5x**) giving the product **7ax** in 79% yield.

Table 3. Substrate Scope for the synthesis of indole-fused cyclopentenenes from *N*-alkyl-indole-2-carboxylic acids and propargylic alcohols^a



Entry	Indole-carboxylic acid	Propargylic alcohol	Cyclopentene	Yield ^b (%)
1				81
2				78
3				87

10				79
11				trace

^aReaction conditions: 1-methylindole-2-carboxylic acid **1** (0.100 g, 0.57 mmol), propargylic alcohols **5** (0.62 mmol), solvent (DCM, 10 mL), 12h, 25 °C. ^bYield of the isolated product. ^c0.39 mmol was used; key peaks in the ¹H NMR: 3.54 (*OCH*₃), 3.91 (*NCH*₃), 6.46 (*PhC = CH*), 6.80-7.86 (*Ar-H*), LCMS 428 [*M* + 1].

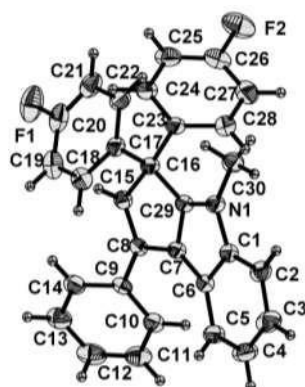
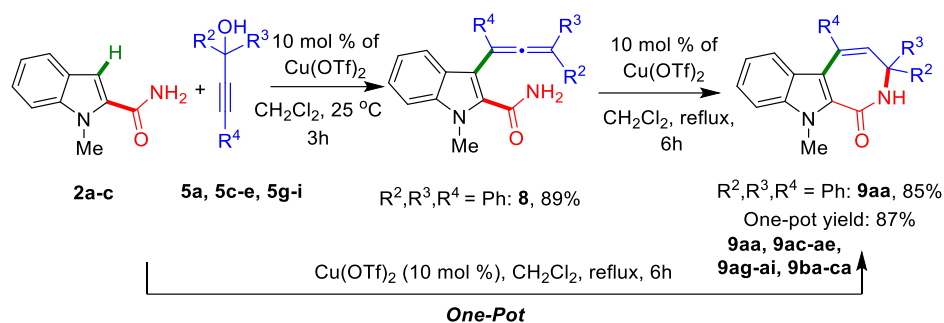


Figure 2: ORTEP view of **7al** with 30% probability of ellipsoids. CCDC No: 1915532.

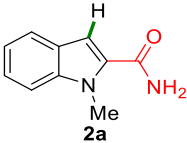
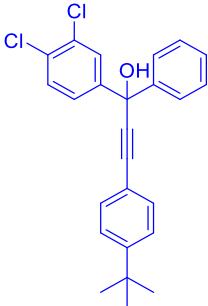
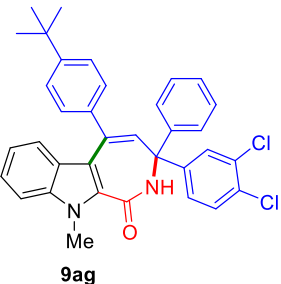
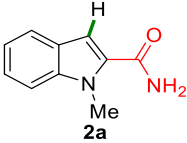
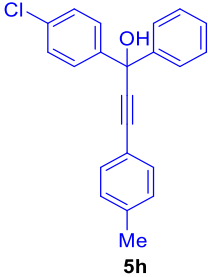
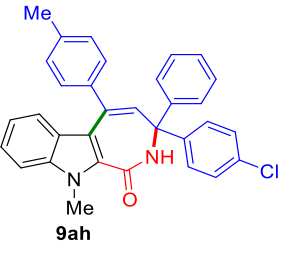
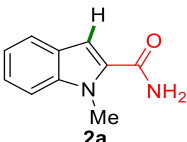
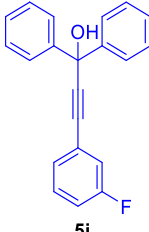
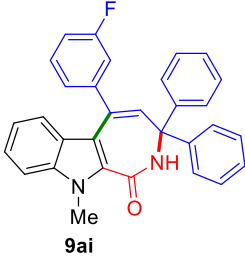
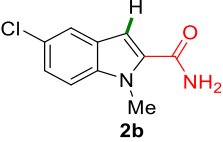
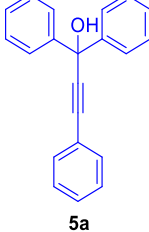
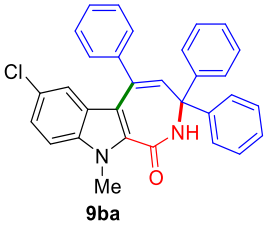
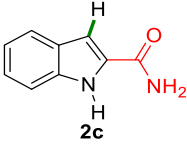
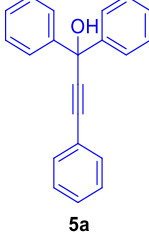
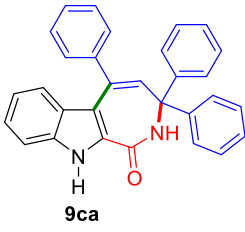
5.2.2 Synthesis of allenamide **8**, ϵ -lactams **9aa**, **9ac-ae**, **9ag-ai** and **9ba-ca** from *N*-alkylated indole-2-carboxamides and substituted propargylic alcohols

Interestingly, under the above Cu(OTf)₂ catalyzed conditions, use of 1-methylindole-2-carboxamide **2a** and propargylic alcohol **5a** afforded only the allene product **8** in 89% yield. This allene underwent nucleophilic attack of NH₂ group in the presence of 10 mol% of Cu(OTf)₂ in refluxing DCM for 6h to afford the ϵ -lactam **9aa** in 85% yield. Hence we surmised that direct one-pot treatment of **2a** with **5a** using Cu(OTf)₂ catalyst should give **9aa**, which was proved to be correct. Pleasingly, the other ϵ -lactams **9ac-ae**, **9ag-ai** and **9ba-ca** were obtained in good yields (Table 4). The structure of product **9ac** has been determined by single crystal X-ray crystallography (Figure 3).

Table 4. Substrate scope for the synthesis of allenamide **8 and ϵ -lactams **9aa**, **9ac-ae**, **9ag-ai**, and **9ba-ca** from *N*-alkyl-indole-2-carboxamides and propargylic alcohols^a**



Entry	Indole-carboxamide	Propargylic alcohol	ϵ -lactam	Yield ^b (%)
1.				85
2.				85
3.				82
4.				88

5.	 2a	 5g	 9ag	83
6.	 2a	 5h	 9ah	83
7.	 2a	 5i	 9ai	79
8.	 2b	 5a	 9ba	80
9.	 2c	 5a	 9ca	78

^aReaction conditions: Indole-2-carboxamide **2** (0.100 g, 0.57 mmol), propargylic alcohol **5** (0.62 mmol), solvent (DCM, 10 mL), 6h, 60 °C. ^bYield of the isolated product.

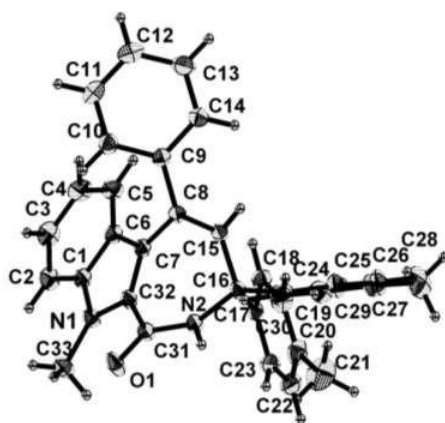
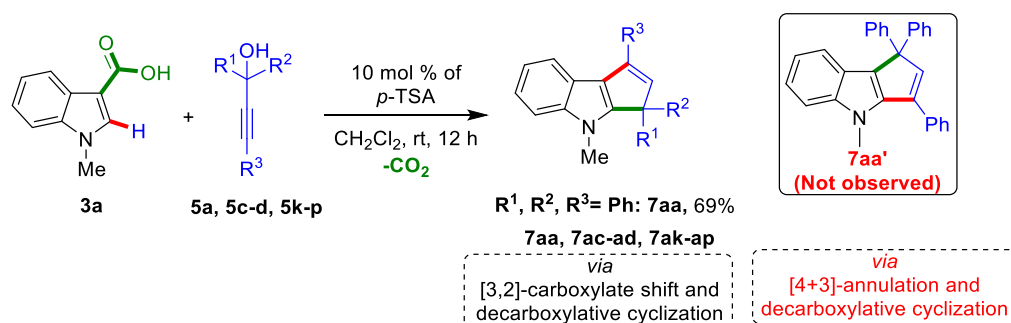


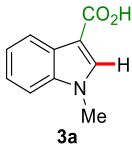
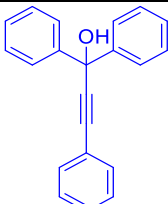
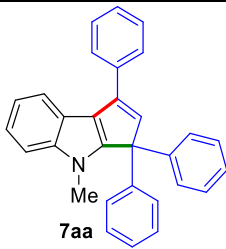
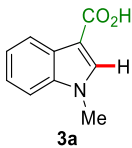
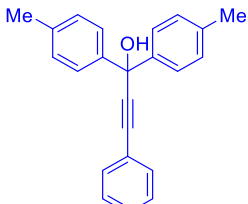
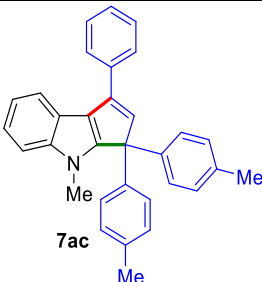
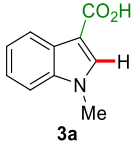
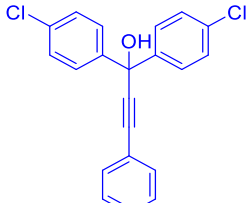
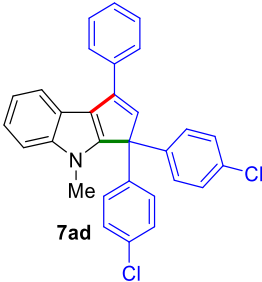
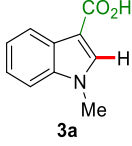
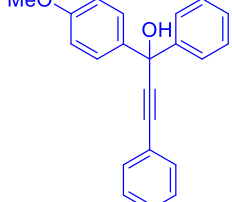
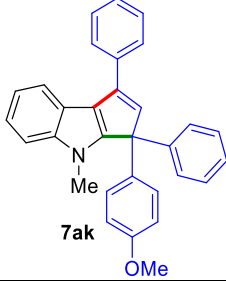
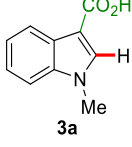
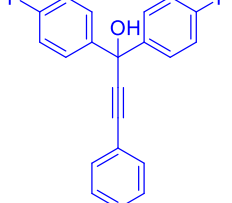
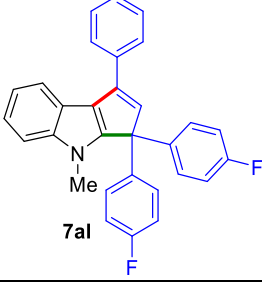
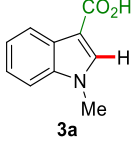
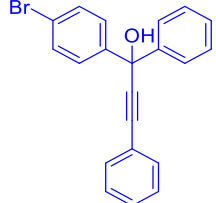
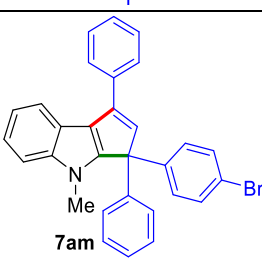
Figure 3: ORTEP view of **9ac** with 30% probability of ellipsoids. CCDC No: 1915533

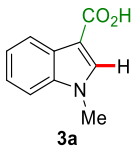
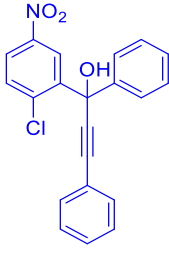
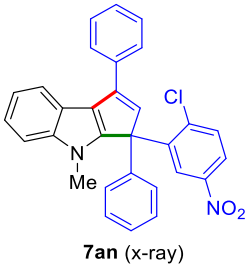
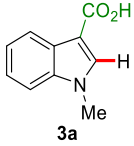
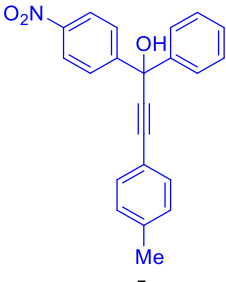
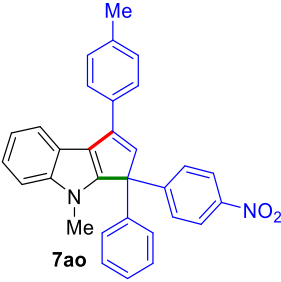
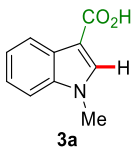
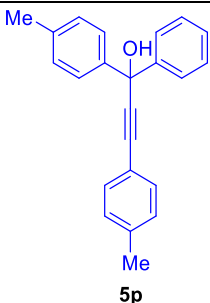
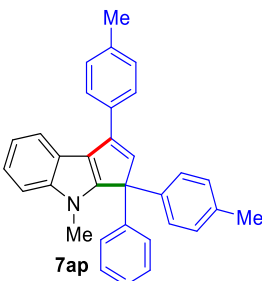
5.2.3 *p*-TSA mediated reaction of 1-methylindole-3-carboxylic acid with propargylic alcohols: Unexpected [3,2]-carboxylate/carboxamide migration and (4 + 3)-annulation of 1-methylindole-3-carboxylic acids/amides

With the expectation that 3-substituted ϵ -lactone and 1,4-dihydrocyclopenta[*b*]indole will be formed when the carboxyl group is at the indole-3-position, we treated 1-methylindole-3-carboxylic acid **3a** with propargylic alcohol **5a** under above conditions (cf. Tables 2 and 3), but the reaction did not occur. Surprisingly, in the presence of *p*-TSA, the unexpected 3,4-dihydrocyclopenta[*b*]indole **7aa**, rather than the expected 1,4-dihydrocyclopenta[*b*]indole **7aa'**, was obtained in 69% yield. Analogous [3,2]-carboxylate migration cum decarboxylative cyclization products **7ac-7ad**, **7ak-ap** were similarly prepared in good yields (Table 5; Figure 4 for the structure of **7an**). In this reaction, we could not isolate the ϵ -lactone intermediate. The 1*H*-indole-3-carboxylic acid **3b** with propargylic alcohol **5a** did not afford an isolable product under these conditions.

Table 5. Substrate scope for the synthesis of 3,4-dihydrocyclopenta[*b*]indoles from *N*-alkylated indole-2-carboxylic acids and propargylic alcohols^a



Entry	Indole-3-carboxylic acid	Propargylic alcohol	Cyclopentene	Yield ^b (%)
1.	 3a	 5a	 7aa	69
2.	 3a	 5c	 7ac	80
3.	 3a	 5d	 7ad	86
4.	 3a	 5k	 7ak	83
5.	 3a	 5l	 7al	89
6.	 3a	 5m	 7am	83

7.				88
8.				86
9.				79

^aReaction conditions: 1-methylindole-3-carboxylic acid **3a** (0.100 g, 0.57 mmol), propargylic alcohol **5** (0.62 mmol), solvent (DCM, 10 mL), 12h, 25 °C. ^bYield of the isolated product.

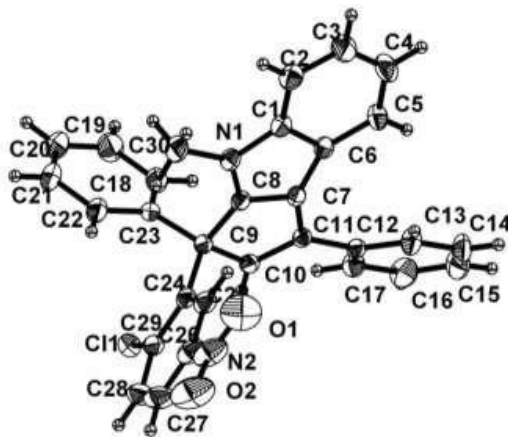


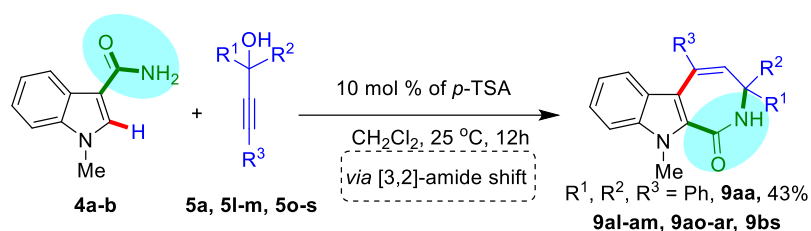
Figure 4: ORTEP view of **7an** with 30% probability of ellipsoids. CCDC No: 1915534.

5.2.4 *p*-TSA mediated reaction of 1-methylindole-3-carboxamides and propargylic alcohols: Indole 3- to 2-amide migration

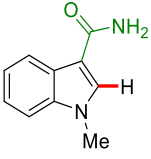
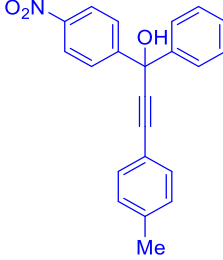
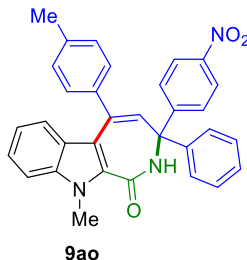
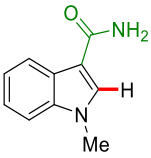
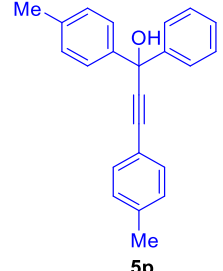
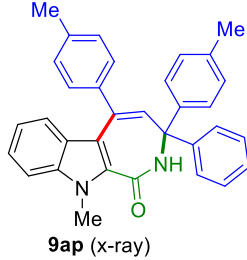
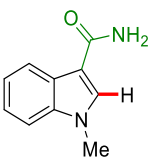
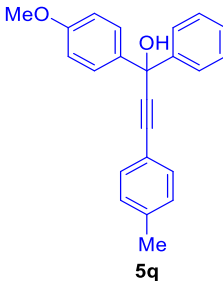
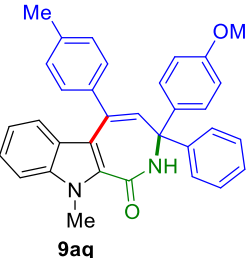
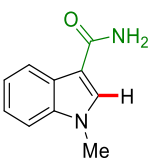
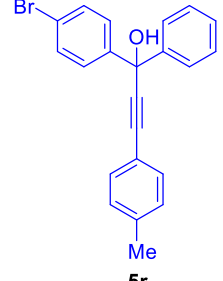
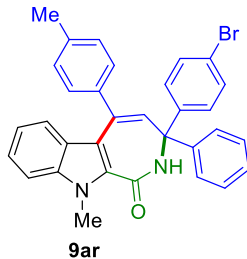
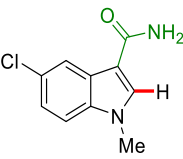
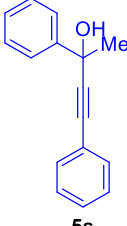
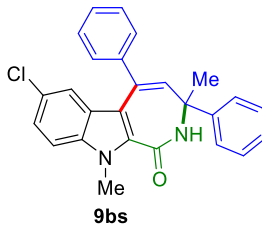
In continuation of the above studies, 1-methylindole-3-carboxamide **4a** upon treatment with propargylic alcohol **5a** in the presence of *p*-TSA afforded the ϵ -lactam **9aa** in 43% yield

via [3,2]-carboxamide migration (Table 6). Compounds **9al-am**, **9ao-ar** and **9bs** could be similarly isolated. For unambiguous proof of [3,2]-carboxylate/carboxamide migration, we have determined the X-ray structures of **4a**, **9aa**, and **9ap** (Figure 5). Thus, we conclude that the formation of **7aa** from **3a** and **5a** also occurs *via* carboxylate migration from 3- to 2-position on indole, followed by decarboxylative cyclization as shown in Table 6. We also performed the reaction to obtain **9aa** using catalytic $\text{BF}_3 \cdot \text{OEt}_2$ or $\text{Cu}(\text{OTf})_2$; in the former case, the reaction did not occur and in the latter case, the yield of **9aa** was lower (30%).

Table 6. Substrate scope for the synthesis of ϵ -lactams from *N*-alkylated indole-3-carboxamides and propargylic alcohols^a



Entry	Indole-3-carboxamide	Propargylic alcohol	ϵ -Lactam	Yield ^b (%)
1	 4a (x-ray)	 5a	 9aa (x-ray)	43
2	 4a (x-ray)	 5l	 9al	38
3	 4a (x-ray)	 5m	 9am	39

4	 4a (x-ray)	 5o	 9ao	40
5	 4a (x-ray)	 5p	 9ap (x-ray)	36
6	 4a (x-ray)	 5q	 9aq	37
7	 4a (x-ray)	 5r	 9ar	39
8	 4b	 5s	 9bs	34

^aReaction conditions: 1-methylindole-3-carboxamide **4** (0.100 g, 0.57 mmol), propargylic alcohol **5** (0.62 mmol), solvent (DCM, 10 mL), 12h, 25 °C. ^bYield of the isolated product.

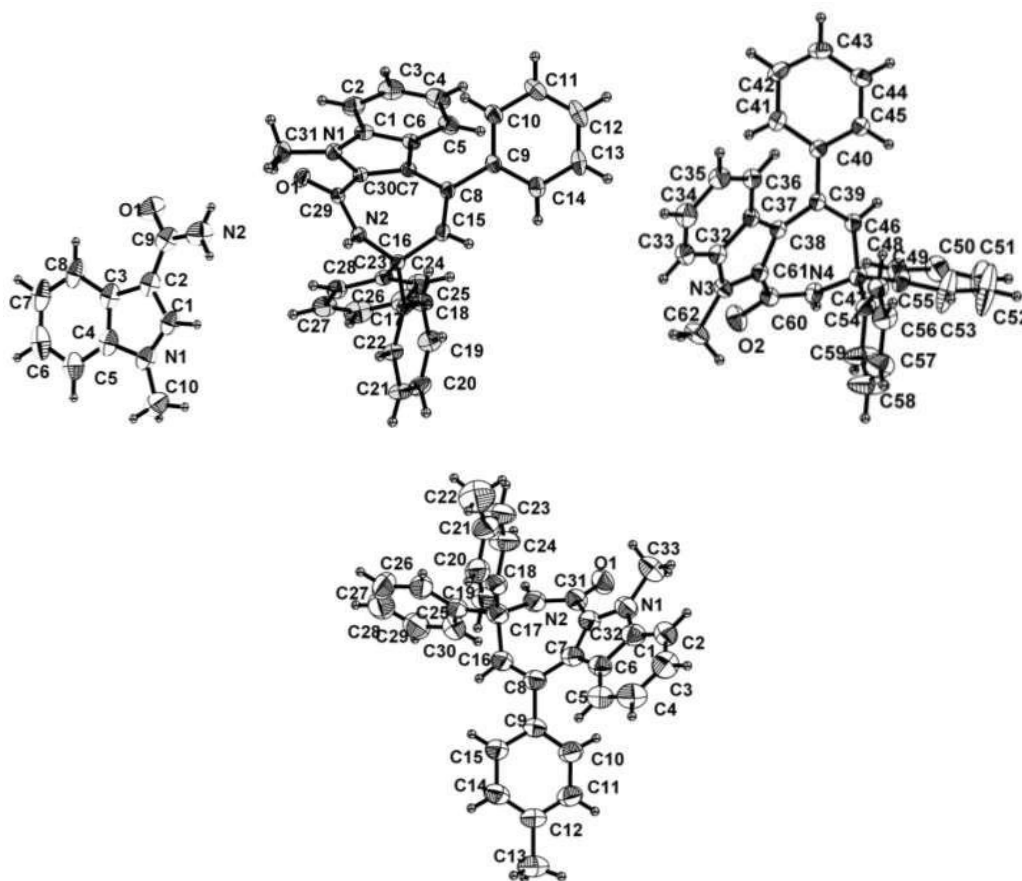
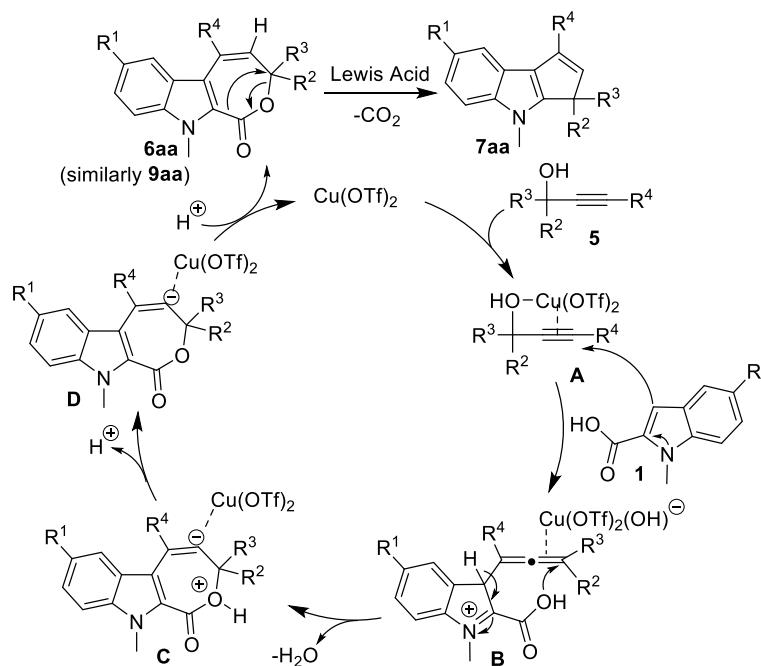


Figure 5: ORTEP views of **4a** (top left; CCDC 1915537), **9aa** (two molecules in the asymmetric unit, top middle and right; CCDC 1915535) and **9ap** (bottom, CCDC 1915536) with 30% probability of ellipsoids.

5.2.5 Possible mechanistic pathways for the (4 + 3) annulation, decarboxylative cyclization and [3,2]-carboxylate/carboxamide migration on indole

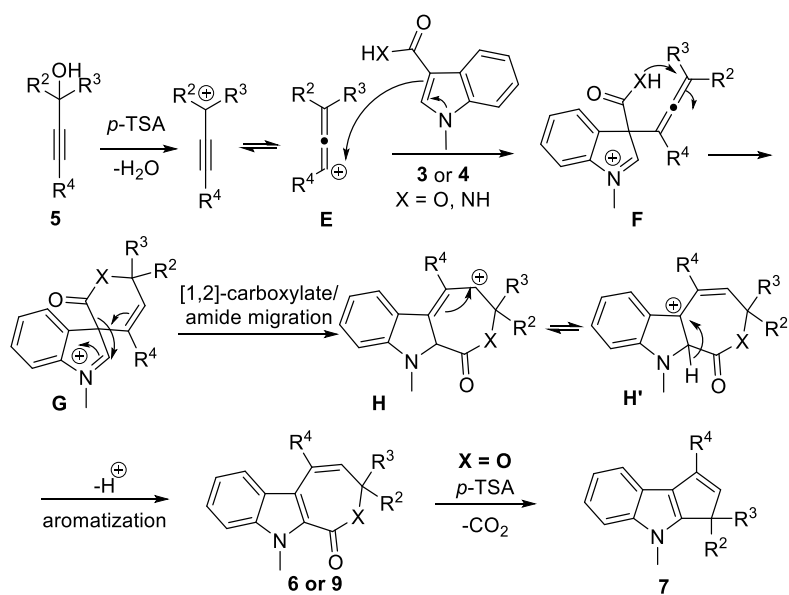
A possible pathway for the formation of ϵ -lactone **6aa**, dihydrocyclopenta[*b*]indole **7aa**, and ϵ -lactam **9aa** based on literature³⁸ is shown in Scheme 1. First, the propargylic alcohol **5** is converted to the intermediate **A** in the presence of Cu(OTf)₂. Species **A** undergoes Friedel-Crafts-type reaction with indole-2-carboxylic acid **1** to form the allene intermediate **B**. Subsequently, **B** is transformed to intermediate **C** and then to **D** via intramolecular nucleophilic attack of -OH group of carboxylic acid. The product **6aa** and the regenerated catalyst Cu(OTf)₂ are formed by subsequent protonation. This step is supported by the isolation of **6aa** (cf. Table 1). This ϵ -lactone **6aa** undergoes decarboxylative cyclization in the presence of Lewis acid to give compound **7aa**. The ϵ -lactam **9aa** is formed in a manner similar to that of **6aa**.



Scheme 1: Plausible pathway for the formation of **6aa** or **9aa** and **7aa**

5.2.6 Proposed pathway for the *p*-TSA mediated [1,2]-carboxylate or amide migration and formation of **7aa/9aa**

The reaction using indole-3-carboxylate/carboxamide must take place by the migration of the carboxylate/carboxamide group from indole-3- to indole-2-position (1,2-migration; Scheme 2). Some literature is available on somewhat different reactions.^{7k, 12-13} First, in the presence of *p*-TSA, the propargylic alcohol **5** is converted to the allene intermediate **E**, which would then undergo Friedel-Crafts-type reaction with 1-methylindole-3-carboxylic acid **3** or amide **4** to form the allene intermediate **F**. This intermediate **F** is transformed into the six-membered spirocycle **G** via intramolecular nucleophilic attack of OH/NH₂ group. The resulting *N*-heterocycles contain an indolinium ion, which can undergo a carboxylate or amide migration to produce **H/H'**. Finally, aromatization of intermediate **H'** affords ϵ -lactone **6** or ϵ -lactam **9**. The indole fused ϵ -lactone **6** undergoes decarboxylative cyclization in the presence of *p*-TSA to give dihydrocyclopenta-indoles **7** as described above.



Scheme 2: *p*-TSA mediated [1,2]-carboxylate/ amide migration and formation of **6/9** and **7**

Summary of PART-B

- (1) Indole-2-carboxylic acids/amides undergo (4 + 3) annulation with propargylic alcohols under mild Lewis acidic conditions to form indole-fused ε -lactones/ ε -lactams. Indole-2-carboxylic acids and propargylic alcohols, in the presence of strong Lewis acid $\text{BF}_3 \cdot \text{OEt}_2$, undergo decarboxylative cyclization leading to indole-fused cyclopentenones.
- (2) In contrast to the above reactions, in the presence of Brønsted acid *p*-TSA, indole-3-carboxylic acids produced the same indole-fused cyclopentenones as those from indole-2-carboxylic acids.
- (3) Indole-3-carboxamide in the presence of *p*-TSA delivered indole-fused seven-membered ε -lactams which indicates that an unexpected carboxylic acid/amide group migration takes place from indole 3- to 2- position during the course of the reaction.

EXPERIMENTAL SECTION

General information about the chemicals, solvents, equipment used etc. is already given in Chapter 3.

6.1 Synthesis of starting materials

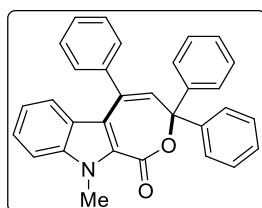
6.1.1 Synthesis of *N*-protected indole-2-carboxylic acids, substituted indole-3-carboxylic acids, indole-2-carboxamides, indole-3-carboxamides, and propargylic alcohols

Substituted indole-2-carboxylic acids **1a-1g**,^{37a} and **1h**,^{37b} indole-2-carboxamides **2a-2c**,^{37c} indole-3-carboxamides **4a-4c**,^{37d} and propargylic alcohols **5a-5x**^{37e} were prepared using literature methods.

6.2 General procedure for the synthesis of ϵ -lactones **6aa-aj**, and **6ba-ga**

An oven dried 25 mL round-bottomed flask was charged with 1-methylindole-2-carboxylic acid **1a** (0.100g, 0.57 mmol), propargylic alcohol **5a** (0.178 g, 0.62 mmol) and Cu(OTf)₂ (0.020 g, 0.057 mmol (10 mol %)) in dichloromethane (10 mL). The mixture was stirred at rt (25 °C) in open air for 6h and monitored by TLC for the disappearance of starting materials. After completion of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na₂SO₄ and the solvent removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:9) afforded the desired product **6aa** as a white solid. Compounds **6ab-aj**, **6ba-ga** were prepared from appropriate indole-2-carboxylic acids and propargylic alcohols by using the same procedure and same molar quantities.

Compound **6aa**



Yield: 0.235 g (93%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 168-170 °C.

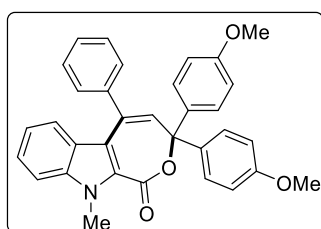
IR (neat): 3027, 1691, 1513, 1470, 1448, 1274, 1235, 1161, 1032, 986, 967, 799, 747, 696 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 7.54-7.39 (m, 9H), 7.26-7.10 (m, 8H), 6.89-6.85 (m, 1H), 6.65 (d, *J* = 8.4 Hz, 1H), 6.47 (s, 1H), 3.76 (s, 3H) ppm.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 162.5, 142.0, 140.0, 138.7, 131.8, 131.2, 128.7, 128.5, 128.2, 127.5, 126.1, 125.2, 123.9, 122.9, 120.7, 118.3, 110.0, 85.9, 31.7 ppm.

HRMS (ESI-TOF): Calcd. For C₃₁H₂₄NO₂ [M⁺ + H]: *m/z* 442.1807. Found: 442.1808.

Compound 6ab



Yield: 0.259 g (91%, white solid, *R*_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 160-162 °C.

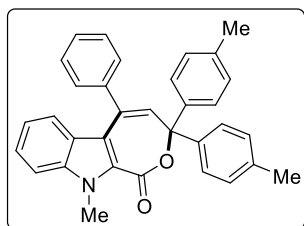
IR (neat): 2934, 2835, 1689, 1605, 1506, 1464, 1405, 1382, 1233, 1175, 1122, 1030, 829, 738, 698 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 7.50-7.49 (m, 2H), 7.46-7.40 (m, 3H), 7.32 (d, *J* = 9.0 Hz, 4H), 7.26-7.22 (m, 2H), 6.88- 6.85 (m, 1H), 6.72 (d, *J* = 8.0 Hz, 4H), 6.60 (d, *J* = 7.0 Hz, 1H), 6.40 (s, 1H), 3.80 (s, 3H), 3.72 (s, 6H) ppm.

¹³C{¹H} NMR (125 MHz, CDCl₃): δ 162.6, 158.8, 141.7, 140.2, 138.7, 132.3, 131.1, 128.5₄, 128.4₆, 127.5, 125.1, 124.0, 122.9, 120.5, 118.1, 113.5, 110.1, 85.9, 55.1, 31.7 ppm.

HRMS (ESI-TOF): Calcd. For C₃₃H₂₈NO₄ [M⁺ + H]: *m/z* 502.2018. Found: 502.2019.

Compound 6ac



Yield: 0.252 g (94%, white solid, *R*_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 °C.

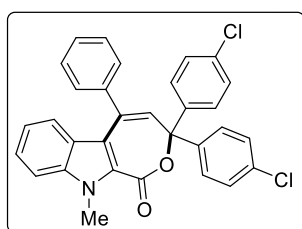
IR (neat): $\nu_{\max}$ 3055, 2946, 1692, 1522, 1509, 1407, 1274, 1233, 1122, 1090, 822, 785, 770, 737, 672 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.51-7.50(m, 2H), 7.44-7.39 (m, 3H), 7.31 (d, J = 8.0 Hz, 4H), 7.26-7.21 (m, 2H), 6.99 (d, J = 7.5 Hz, 4H), 6.89-6.86 (m, 1H), 6.62 (d, J = 8.0 Hz, 1H), 6.42 (s, 1H), 3.78 (s, 3H), 2.29 (s, 6H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.6, 141.7, 140.2, 138.7, 137.1, 132.3, 131.2, 128.9, 128.6, 128.5, 126.0, 125.1, 124.0, 123.0, 120.5, 118.2, 110.0, 85.9, 31.8, 21.0 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{33}\text{H}_{28}\text{NO}_2$ [$\text{M}^+ + \text{H}$]: m/z 470.2120. Found: 470.2121.

Compound 6ad



Yield: 0.234 g (80%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 172-174 $^{\circ}\text{C}$.

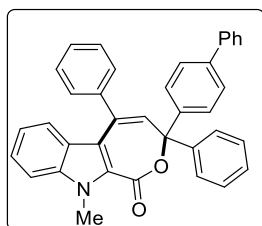
IR (neat): $\nu_{\max}$ 3057, 2948, 1697, 1534, 1486, 1384, 1232, 1121, 1087, 1015, 989, 836, 818, 787, 755, 743, 697 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.50-7.40(m, 5H), 7.36 (d, J = 8.5 Hz, 4H), 7.30-7.25 (m, 2H), 7.18 (d, J = 7.5 Hz, 4H), 6.91-6.88 (m, 1H), 6.62 (d, J = 8.5 Hz, 1H), 6.32 (s, 1H), 3.81 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 161.9, 142.7, 139.7, 138.8, 133.6, 130.5, 130.3, 128.9, 128.6₂, 128.5₆, 128.5, 127.4, 125.7, 123.8, 122.9, 121.0, 118.3, 110.3, 84.8, 31.9 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{22}\text{Cl}_2\text{NO}_2$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H}+2$], [$\text{M}^+ + \text{H}+4$]: m/z 510.1028, 512.0998, 514.0968. Found: 510.1023, 512.0998, 514.0986.

Compound 6ae



Yield: 0.198 g (67%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 140-143 $^{\circ}\text{C}$.

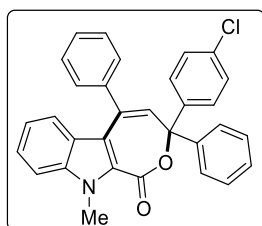
IR (neat): $\nu_{\max}$ 3021, 2919, 1605, 1507, 1460, 1334, 1237, 1185, 1115, 1071, 1019, 911, 817, 740, 722, 696 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.55-7.39(m, 15H), 7.35-7.31 (m, 1H), 7.26-7.13 (m, 5H), 6.90-6.86 (m, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.49 (s, 1H), 3.78 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.5, 142.1, 140.3, 140.2, 140.0, 138.7, 131.6, 131.1, 128.8, 128.7, 128.6, 128.5, 128.2, 127.6, 127.4, 127.0, 126.9, 126.6, 126.1, 125.2, 123.9, 122.9, 120.7, 118.3, 110.1, 85.8, 31.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{37}\text{H}_{28}\text{NO}_2$ [$\text{M}^+ + \text{H}$]: m/z 518.2120. Found: 518.2120.

Compound 6af



Yield: 0.235 g (87%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 155-157 $^{\circ}\text{C}$.

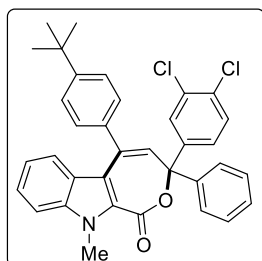
IR (neat): $\nu_{\max}$ 3053, 1695, 1518, 1445, 1402, 1273, 1229, 1086, 1034, 982, 896, 765, 742, 718, 696 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.52-7.39 (m, 9H), 7.26-7.12 (m, 7H), 6.91-6.87 (m, 1H), 6.63 (dd, J = 8.4, 0.8 Hz, 1H), 6.39 (s, 1H), 3.79 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.2, 142.4, 139.8, 138.7, 133.4, 131.0, 130.9, 128.8, 128.6, 128.5, 128.4, 128.3, 127.7, 127.5, 126.0, 125.4, 123.9, 122.9, 120.8, 118.3, 110.1, 85.3, 31.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{23}\text{ClNO}_2$ [$\text{M}^+ + \text{H}$], ($\text{M}^+ + \text{H} + 2$): m/z 476.1417, 478.1387. Found: 476.1419, 478.1393.

Compound 6ag



Yield: 0.253 g (78%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 171-173 $^{\circ}\text{C}$.

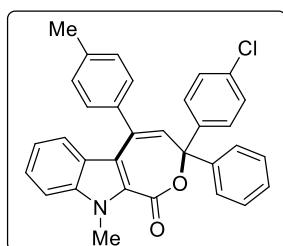
IR (neat): ν_{max} 2966, 1705, 1599, 1561, 1525, 1468, 1449, 1273, 1224, 1123, 1084, 1026, 997, 849, 783, 768, 744, 671 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.59 (s, 1H), 7.43-7.40 (m, 6H), 7.29- 7.13 (m, 7H), 6.90 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 8.4 Hz, 1H), 6.34 (d, J = 0.8 Hz, 1H), 3.79 (s, 3H), 1.39 (s, 9H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.0, 152.2, 142.5, 138.7, 136.6, 132.6, 131.6, 130.7, 130.2, 129.8, 128.4, 128.2, 127.9, 126.0, 125.5, 123.9, 123.0, 120.8, 118.5, 110.1, 84.9, 34.8, 31.7, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{35}\text{H}_{30}\text{Cl}_2\text{NO}_2$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H}+2$], [$\text{M}^+ + \text{H}+4$]: m/z 566.1654, 568.1624, 570.1594. Found: 566.1654, 568.1610, 570.1594.

Compound 6ah



Yield: 0.236 g (84%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 164-166 $^{\circ}\text{C}$.

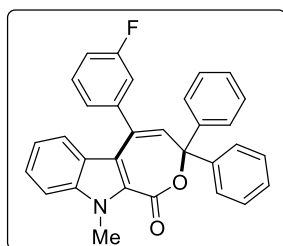
IR (neat): ν_{max} 3024, 1704, 1688, 1488, 1446, 1401, 1275, 1228, 1086, 807, 781, 743, 710, 698 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.43-7.39 (m, 6H), 7.26-7.13 (m, 9H), 6.92-6.89 (m, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.37 (s, 1H), 3.78 (s, 3H), 2.45 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.3, 142.3, 138.8, 138.7, 136.9, 133.3, 130.9, 130.4, 129.3, 128.4, 128.3, 127.7, 127.6, 126.0, 125.4, 123.9, 123.1, 120.7, 118.5, 110.1, 85.4, 31.8, 21.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{25}\text{ClNO}_2$ [$\text{M}^+ + \text{H}$], ($\text{M}^+ + \text{H}+2$): m/z 490.1574, 492.1544. Found: 490.1572, 492.1540.

Compound 6ai



Yield: 0.203 g (77%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 162-164 °C.

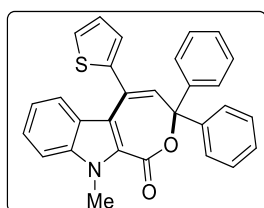
IR (neat): $\nu_{\max}$ 3059, 1692, 1608, 1470, 1448, 1266, 1238, 1094, 1033, 976, 886, 781, 737, 698 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.44-7.36 (m, 5H), 7.30-7.13 (m, 11H), 6.92-6.89 (m, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.47 (s, 1H), 3.76 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 163.8 (d, J = 245.1 Hz), 162.3, 142.2 (d, J = 7.5 Hz), 141.0, 138.6, 132.5, 131.2, 130.1 (d, J = 8.1 Hz), 128.3, 127.6, 126.0, 125.3, 124.4 (d, J = 2.4 Hz), 123.7, 122.6, 120.9, 117.6, 115.7 (d, J = 20.9 Hz), 115.5 (d, J = 21.8 Hz), 110.1, 85.8, 31.7 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{23}\text{FNO}_2$ [$\text{M}^+ + \text{H}$]: m/z 460.1713. Found: 460.1714.

Compound 6aj



Yield: 0.193 g (75%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 185-187 °C.

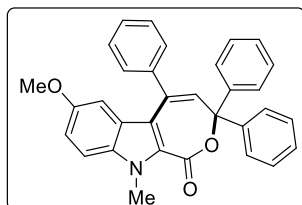
IR (neat): $\nu_{\max}$ 3052, 1690, 1600, 1528, 1487, 1468, 1342, 1227, 1081, 955, 697, 660, 632 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.42 (d, J = 7.5 Hz, 4H), 7.38 (dd, J = 5.0, 1.0 Hz, 1H), 7.29-7.07 (m, 10H), 7.02-6.96 (m, 2H), 6.59 (s, 1H), 3.74 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.4, 141.9, 138.4, 135.0, 131.2, 131.0, 128.2, 127.9, 127.5₂, 127.4₆, 126.0, 125.3, 123.8, 122.8, 120.7, 117.7, 110.0, 86.0, 31.6 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{29}\text{H}_{22}\text{NO}_2\text{S}$ [$\text{M}^+ + \text{H}$]: m/z 448.1371. Found: 448.1370.

Compound 6ba



Yield: 0.206 g (90%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 158-160 °C.

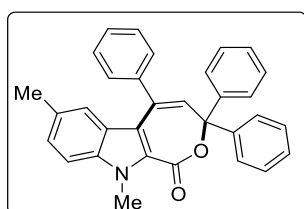
IR (neat): $\nu_{\max}$ 3032, 2940, 1699, 1515, 1485, 1290, 1201, 1121, 1094, 1069, 967, 794, 782, 697 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.54-7.52 (m, 2H), 7.47-7.42 (m, 7H), 7.22-7.12 (m, 6H), 7.09 (d, J = 9.0 Hz, 1H), 6.89 (dd, J = 9.0, 2.5 Hz, 1H), 6.42 (s, 1H), 5.94 (d, J = 2.5 Hz, 1H), 3.74 (s, 3H), 3.43 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.4, 154.2, 142.1, 140.0, 134.2, 131.1, 131.0, 128.7, 128.5, 128.5, 128.2, 127.4, 126.1, 124.2, 117.8, 116.6, 110.9, 103.2, 85.8, 55.1, 31.8 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{26}\text{NO}_3$ [$\text{M}^+ + \text{H}$]: m/z 472.1912. Found: 472.1914.

Compound 6ca



Yield: 0.213 g (88%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 169-171 $^{\circ}\text{C}$.

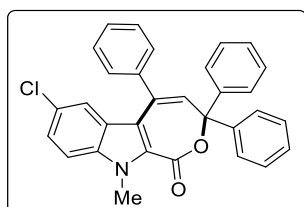
IR (neat): $\nu_{\max}$ 3029, 2934, 1703, 1485, 1446, 1424, 1293, 1228, 1072, 981, 874, 744, 696 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.53-7.50 (m, 2H), 7.47-7.40 (m, 7H), 7.23-7.04 (m, 8H), 6.43 (s, 1H), 6.36 (d, J = 0.4 Hz, 1H), 3.73 (s, 3H), 2.18 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.6, 142.2, 140.0, 137.3, 131.4, 131.1, 129.9, 128.6, 128.5, 128.5, 128.2, 127.4, 127.2, 126.1, 124.1, 122.3, 117.8, 109.7, 85.8, 31.7, 21.5 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{26}\text{NO}_2$ [$\text{M}^+ + \text{H}$]: m/z 456.1963. Found: 456.1964.

Compound 6da



Yield: 0.189 g (86%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 166-168 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3030, 1703, 1601, 1523, 1470, 1545, 1470, 1233, 1096, 1063, 977, 959, 791, 770, 694 cm^{-1} .

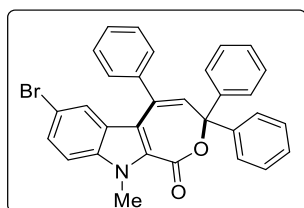
^1H NMR (400 MHz, CDCl_3): δ 7.51-7.41(m, 9H), 7.23-7.11 (m, 8H), 6.57 (d, J = 1.6 Hz, 1H), 6.47 (s, 1H), 3.73 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.2, 141.6, 139.3, 136.9, 132.2₀, 132.1₆, 129.1, 128.7, 128.4, 128.3, 127.6, 126.3, 126.1, 125.8, 124.7, 122.1, 117.6, 111.3, 86.0, 31.9 ppm.

LCMS: m/z 476 [$\text{M}^+ + 1$].

Anal. Calcd. For $\text{C}_{31}\text{H}_{22}\text{ClNO}_2$: C, 78.23; H, 4.66; N, 2.94. Found: C, 78.15; H, 4.62; N, 2.98.

Compound 6ea



Yield: 0.170 g (84%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 169-171 $^\circ\text{C}$.

IR (neat): ν_{max} 3030, 1701, 1601, 1523, 1468, 1444, 1407, 1233, 1095, 1052, 975, 958, 896, 789, 757, 744, 694 cm^{-1} .

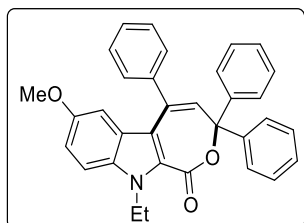
^1H NMR (400 MHz, CDCl_3): δ 7.51-7.42 (m, 9H), 7.31 (dd, J = 8.8 Hz, 1.6 Hz, 1H), 7.23-7.12 (m, 6H), 6.08 (d, J = 8.8 Hz, 1H), 6.72 (d, J = 2.0 Hz, 1H), 6.48 (s, 1H), 3.73 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 162.2, 141.5, 139.3, 137.1, 132.2, 132.0, 129.0, 128.7, 128.4, 128.3, 127.6, 126.1, 125.3, 125.2, 117.5, 113.9, 111.6, 86.0, 31.8 ppm.

LCMS: m/z 519 [$\text{M}^+ - 1$].

Anal. Calcd. For $\text{C}_{31}\text{H}_{22}\text{BrNO}_2$: C, 71.55; H, 4.26; N, 2.69. Found: C, 71.45; H, 4.29; N, 2.63.

Compound 6fa



Yield: 0.199 g (76%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 159-161 $^\circ\text{C}$.

IR (neat): $\nu_{\max}$ 2929, 1701, 1513, 1483, 1446, 1290, 1200, 1167, 1097, 1074, 795, 747, 695 cm^{-1} .

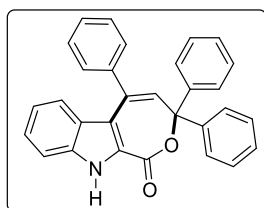
^1H NMR (500 MHz, CDCl_3): δ 7.53-7.51 (m, 2H), 7.47-7.42 (m, 7H), 7.22-7.19 (m, 4H), 7.15-7.11 (m, 3H), 6.89 (dd, $J = 9.0, 2.5$ Hz, 1H), 6.37 (s, 1H), 5.93 (d, $J = 2.0$ Hz, 1H), 4.37 (d, $J = 6.0$ Hz, 2H), 3.42 (s, 3H), 1.04 (t, $J = 7.5$ Hz, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.1, 154.1, 142.0, 140.2, 133.2, 130.9, 129.8, 128.7, 128.4, 128.2, 127.4, 126.2, 124.5, 118.3, 116.7, 111.0, 103.4, 85.6, 55.0, 39.7, 15.0 ppm.

LCMS: m/z 486 [$\text{M}^+ + 1$].

Anal. Calcd. For $\text{C}_{33}\text{H}_{27}\text{NO}_3$: C, 81.63; H, 5.60; N, 2.88. Found: C, 81.52; H, 5.65; N, 2.84.

Compound 6ga



Yield: 0.260 g (71%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: 179-181 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3308, 3053, 1660, 1613, 1528, 1457, 1381, 1331, 1243, 1180, 1099, 958, 745, 696 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 8.99 (s, 1H), 7.52-7.41 (m, 9H), 7.29-7.28 (m, 1H), 7.25-7.22 (m, 5H), 7.19-7.16 (m, 2H), 6.89-6.86 (m, 1H), 6.62 (dd, $J = 8.0, 0.5$ Hz, 1H), 6.36 (s, 1H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 163.4, 143.9, 141.7, 140.1, 136.3, 131.3, 128.8, 128.7₂, 128.6₇, 128.5, 128.4, 127.7, 126.3, 125.8, 124.9, 123.2, 120.8, 118.8, 112.1, 86.6 ppm.

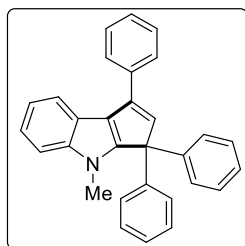
LCMS: m/z 428 [$\text{M}^+ + 1$].

Anal. Calcd. For $\text{C}_{30}\text{H}_{21}\text{NO}_2$: C, 84.29; H, 4.95; N, 3.28. Found: C, 84.19; H, 4.91; N, 3.25.

6.3 General procedure for the synthesis of 3,4-dihydrocyclopenta[*b*]indoles **7aa**, **7ac-ag**, **7ak-al**, **7as**, and **7ax** by using 1-methylindole-2-carboxylic acids and propargylic alcohols

An oven dried 25 mL round- bottomed flask was charged with 1-methylindole-2-carboxylic acid **1** (0.100 g, 0.57 mmol), propargylic alcohol **5** (0.178 g, 0.62 mmol) and BF₃.OEt₂ [0.008 g (0.1 mL), 0.057 mmol] (10 mol %) in dichloromethane (10 mL). The mixture was stirred at rt (25 °C) in open air for 12h and monitored by TLC. After completion of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:9) afforded the desired product **7aa** as a white solid. Compounds **7ac-ag**, **7ak-al**, **7as**, and **7ax** were prepared from 1-methylindole-2-carboxylic acid and appropriate propargylic alcohols by using the same procedure and same molar quantities.

Compound **7aa**



Yield: 0.184 g (81%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 180-182 °C.

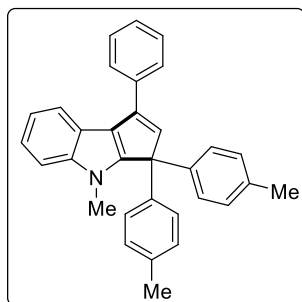
IR (neat): ν_{max} 3019, 2922, 2851, 1747, 1596, 1511, 1490, 1475, 1459, 1441, 753, 739, 694 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 7.91-7.89(m, 2H), 7.87-7.85 (m, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.43-7.40 (m, 1H), 7.39-7.36 (m, 5H), 7.36-7.29 (m, 6H), 7.28-7.19 (m, 2H), 6.50 (s, 1H), 3.61 (s, 3H) ppm.

¹³C{¹H} NMR (125 MHz, CDCl₃): δ 154.9, 141.3, 141.0, 139.9, 136.3, 136.0, 128.6₄, 128.6₀, 128.4, 127.9, 127.5, 127.2, 121.8, 120.7, 120.2, 120.1, 118.9, 110.1, 62.1, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For C₃₀H₂₄N [M⁺ + H]: *m/z* 398.1909. Found: 398.1906.

Compound 7ac



Yield: 0.196 g (81%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 °C.

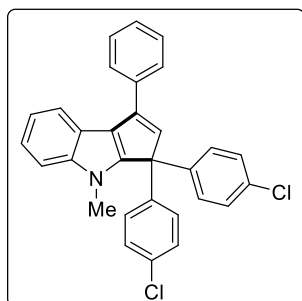
IR (neat): $\nu_{\max}$ 3022, 2920, 1905, 1737, 1604, 1507, 1460, 1020, 816, 782, 722 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.90-7.88 (m, 2H), 7.87-7.85 (m, 1H), 7.52-7.49 (m, 2H), 7.42-7.37 (m, 2H), 7.28-7.25 (m, 5H), 7.23-7.19 (m, 1H), 7.14 (d, J = 8.0 Hz, 4H), 6.46 (s, 1H), 3.62 (s, 3H), 2.38 (s, 6H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 155.2, 141.3, 140.7, 136.9, 136.7, 136.5, 136.2, 129.2, 128.6, 128.3, 127.8, 127.5, 121.8, 120.6, 120.1, 120.0, 118.7, 110.0, 61.4, 31.4, 21.2 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{28}\text{N}$ [$\text{M}^+ + \text{H}$]: m/z 426.2222. Found: 426.2222.

Compound 7ad



Yield: 0.228 g (86%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 185-187 °C.

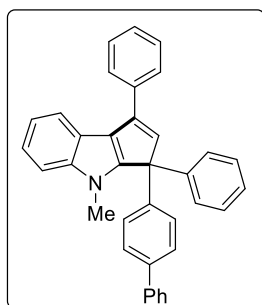
IR (neat): $\nu_{\max}$ 3058, 2947, 1507, 1478, 1396, 1335, 1234, 1089, 1012, 909, 828, 809, 738, 707, 692 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.85-7.82 (m, 3H), 7.51-7.48 (m, 2H), 7.42-7.39 (m, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.29-7.24 (m, 9H), 7.20 (td, J = 8.0, 1.0 Hz, 1H), 6.36 (s, 1H), 3.57 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.8, 141.6, 141.3, 138.0, 135.8, 135.0, 133.1, 129.5, 128.8, 128.6, 128.1, 127.4, 121.5, 121.1, 120.3, 120.2, 119.0, 110.1, 60.8, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{30}H_{22}Cl_2N$ $[M^+ + H]$, $[M^+ + H+2]$, $[M^+ + H+4]$: m/z 466.1129, 468.1099, 470.1069. Found: 466.1126, 468.1100, 470.1089.

Compound 7ae



Yield: 0.216 g (80%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 117-119 °C.

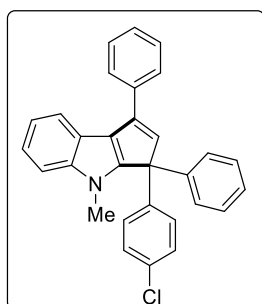
IR (neat): ν_{max} 3026, 1598, 1508, 1483, 1461, 1333, 1235, 1157, 1115, 1006, 914, 839, 739, 694 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ 7.90-7.88(m, 2H), 7.85 (d, J = 7.5 Hz, 1H), 7.61-7.59 (m, 2H), 7.54-7.30 (m, 16H), 7.26-7.23 (m, 1H), 7.21-7.18 (m, 1H), 6.50 (s, 1H), 3.62 (s, 3H). ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 154.8, 141.2, 141.0, 140.7, 139.9, 139.7, 138.9, 136.2, 135.7, 128.8, 128.7, 128.5, 128.3, 127.8, 127.4, 127.3, 127.2, 127.1, 127.0, 121.6, 120.6, 120.1, 120.0, 118.8, 110.0, 61.7, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{36}H_{28}N$ $[M^+ + H]$: m/z 474.2222. Found: 474.2222.

Compound 7af



Yield: 0.207 g (84%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 145-147 °C

IR (neat): ν_{max} 3051, 2924, 1596, 1506, 1477, 1455, 1335, 1089, 1013, 972, 829, 796, 739 cm^{-1} .

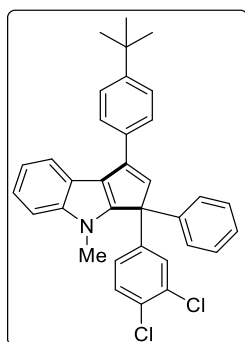
1H NMR (400 MHz, $CDCl_3$): δ 7.91-7.86 (m, 3H), 7.54-7.51 (m, 2H), 7.45-7.21 (m, 13H), 6.46 (s, 1H), 3.61 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 154.3, 141.3₁, 141.2₈, 139.3, 138.6, 136.0, 135.5, 132.9, 129.7, 128.6₅, 128.6₀, 128.2, 127.9, 127.4, 127.3, 121.6, 120.9, 120.2, 120.1, 119.0, 110.0, 61.4, 31.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{23}\text{ClN}$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H} + 2$]: m/z 432.1519, 434.1489.

Found: 432.1518, 434.1497.

Compound 7ag



Yield: 0.246 g (83%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 182-184 °C.

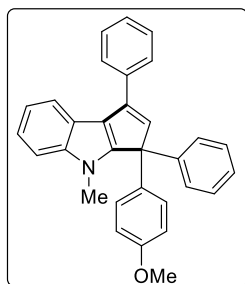
IR (neat): ν_{max} 2964, 1737, 1592, 1512, 1463, 1375, 1268, 1204, 1115, 1026, 925, 882, 831, 792, 764, 742, 699 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.91-7.89 (m, 1H), 7.84-7.82 (m, 2H), 7.56-7.54 (m, 2H), 7.46-7.45 (m, 1H), 7.40-7.17 (m, 10H), 6.38 (s, 1H), 3.61 (s, 3H), 1.42 (s, 9H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 153.8, 151.3, 141.5, 141.4, 140.9, 138.9, 134.5, 132.9, 132.7, 131.2, 130.4, 130.1, 128.8, 128.2, 127.9, 127.5, 127.2, 125.6, 121.7, 121.1, 120.4, 120.3, 119.3, 110.1, 61.1, 34.8, 31.5₀, 31.4₇ ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{34}\text{H}_{30}\text{Cl}_2\text{N}$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H} + 2$], [$\text{M}^+ + \text{H} + 4$]: m/z 522.1755, 524.1725, 526.1695. Found: 522.1754, 524.1726, 526.1694.

Compound 7ak



Yield: 0.195 g (80%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 184-186 °C.

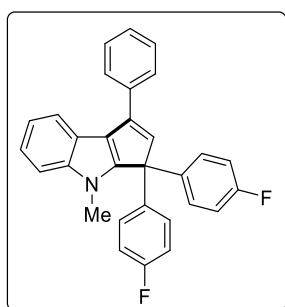
IR (neat): $\nu_{\max}$ 3058, 2837, 1743, 1606, 1505, 1458, 1246, 1176, 1025, 830, 742, 698 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.89-7.87(m, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.51-7.47 (m, 2H), 7.41-7.17 (m, 11H), 6.87-6.83 (m, 2H), 6.46 (s, 1H), 3.82 (s, 3H), 3.60 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 158.6, 155.0, 141.2, 140.6, 140.1, 136.3, 136.1, 131.6, 129.4, 128.5₀, 128.4₆, 128.2, 127.7, 127.4, 127.0, 121.7, 120.5, 120.0, 119.9, 118.6, 113.8, 109.9, 61.3, 55.3, 31.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{26}\text{NO}$ [$\text{M}^+ + \text{H}$]: m/z 428.2014. Found: 428.2016.

Compound 7al



Yield: 0.213 g (86%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 162-164 $^{\circ}\text{C}$.

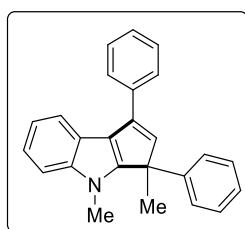
IR (neat): $\nu_{\max}$ 3069, 2924, 1898, 1598, 1500, 1475, 1459, 1411, 1338, 1219, 1155, 1014, 911, 835, 739, 722, 692, 591 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.88-7.83(m, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.43-7.37 (m, 2H), 7.33-7.19 (m, 6H), 7.04-6.99 (m, 4H), 6.41 (s, 1H), 3.59 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 162.0 (d, J = 244.8 Hz), 154.4, 141.3, 141.1, 136.0, 135.6, 135.4 (d, J = 3.3 Hz), 129.8 (d, J = 7.9 Hz), 128.6, 128.0, 127.4, 121.6, 121.0, 120.2 (d, J = 11.6 Hz), 118.9, 115.4 (d, J = 21.1 Hz), 110.0, 60.7, 31.3 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{22}\text{F}_2\text{N}$ [$\text{M}^+ + \text{H}$]: m/z 434.1720. Found: 434.1723.

Compound 7as



Yield: 0.143 g (75%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 155-157 °C.

IR (neat): $\nu_{\max}$ 3049, 2931, 1598, 1509, 1489, 1476, 1460, 1335, 1236, 1176, 1016, 918, 737, 717, 696 cm^{-1} .

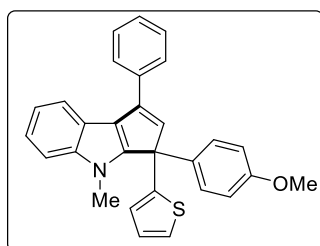
^1H NMR (500 MHz, CDCl_3): δ 7.86-7.82 (m, 3H), 7.51-7.48 (m, 2H), 7.41-7.35 (m, 2H), 7.32-7.27 (m, 4H), 7.26-7.17 (m, 3H), 6.16 (s, 1H), 3.63 (s, 3H), 1.98 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 156.4, 141.1, 140.5, 140.1, 136.6, 128.7, 128.5, 127.6, 127.3, 126.8, 126.2, 121.7, 120.4, 119.9, 118.7, 109.8, 51.7, 30.8, 19.8 ppm.

LC-MS: m/z 336 [$\text{M}^+ + 1$].

Anal. Calcd. For $\text{C}_{25}\text{H}_{21}\text{N}$: C, 89.51; H, 6.31; N, 4.18. Found: C, 89.42; H, 6.34; N, 4.21.

Compound 7ax



Yield: 0.196 g (79%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 °C.

IR (neat): $\nu_{\max}$ 3064, 3000, 2929, 1606, 1506, 1458, 1299, 1247, 1176, 1114, 1025, 919, 838, 826, 742, 695 cm^{-1} .

^1H NMR(500 MHz, CDCl_3): δ 7.87 (dd, J = 8.5, 1.5 Hz, 2H), 7.82 (d, J = 8.0 Hz, 1H), 7.51-7.48 (m, 2H), 7.42-7.40 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.32-7.29 (m, 2H), 7.24 (dd, J = 7.5, 1.5 Hz, 1H), 7.21-7.17 (m, 2H), 7.04 (dd, J = 3.5, 1.0 Hz, 1H), 6.99 (dd, J = 5.0, 3.5 Hz, 1H), 6.85-6.82 (m, 2H), 6.42 (s, 1H), 3.81 (s, 3H), 3.70 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 158.9, 154.2, 144.2, 141.3, 140.4, 136.1, 135.8, 131.7, 128.6, 128.5, 127.8, 127.4, 126.5₄, 126.4₇, 124.2, 121.6, 120.6, 120.1, 120.0, 118.6, 113.9, 110.0, 57.7, 55.3, 31.4 ppm.

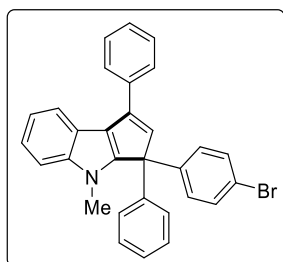
LC-MS: m/z 434 [$\text{M}^+ + 1$].

Anal. Calcd. For $\text{C}_{29}\text{H}_{23}\text{NOS}$: C, 80.34; H, 5.35; N, 3.23. Found: C, 80.41; H, 5.31; N, 3.26.

6.4 General procedure for the synthesis of 3,4-dihydrocyclopenta[*b*]indoles **7aa-ad**, **7ak-ap** by using 1-methylindole-3-carboxylic acids and propargylic alcohols

An oven-dried 25 mL round-bottomed flask was charged with 1-methylindole-3-carboxylic acid **3a** (0.100 g, 0.57 mmol), propargylic alcohol **5** (0.178 g, 0.62 mmol) and *p*-TSA (0.010 g, 0.057 mmol (10mol %)) in dichloromethane (10 mL). The mixture was stirred at rt (25 °C) in open air for 12h and monitored by TLC. After completion of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:9) afforded the desired product **7aa** as a white solid. Compounds **7ab-ad**, and **7ak-ap** were prepared from 1-methylindole-3-carboxylic acid and appropriate propargylic alcohols by using the same procedure and same molar quantities.

Compound **7am**



Yield: 0.224 g (83%, white solid, *R*_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 173-175 °C.

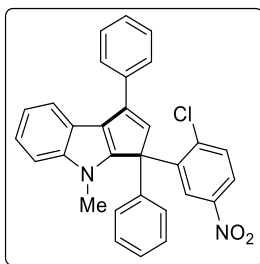
IR (neat): ν_{max} 3055, 1883, 1737, 1594, 1508, 1482, 1465, 1444, 1048, 1007, 910, 827, 743, 696 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ 7.87-7.82 (m, 3H), 7.51-7.47 (m, 2H), 7.43-7.40 (m, 3H), 7.38-7.29 (m, 6H), 7.27-7.18 (m, 4H), 6.41 (s, 1H), 3.58 (s, 3H) ppm.

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 154.3, 141.3, 141.2₆, 139.2₀, 139.1₆, 136.0, 135.4, 131.6, 130.0, 128.6₃, 128.6₀, 128.2, 127.9, 127.4, 127.3, 121.6, 121.0, 120.8, 120.1, 118.9, 110.0, 61.5, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For C₃₀H₂₃BrN [M⁺ + H], [M⁺ + H+2]: *m/z* 476.1014, 478.0994. Found: 476.1015, 478.1004.

Compound 7an



Yield: 0.239 g (88%, red solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 220-222 °C.

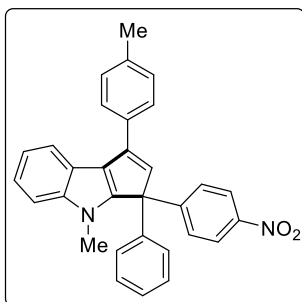
IR (neat): $\nu_{\max}$ 3060, 1570, 1517, 1462, 1344, 1289, 1259, 1156, 1112, 1049, 924, 904, 856, 743, 699, 630 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 8.25 (d, J = 2.8 Hz, 1H), 8.19 (dd, J = 8.4, 2.4 Hz, 1H), 7.92-7.90 (m, 2H), 7.83 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.55-7.51 (m, 2H), 7.46-7.39 (m, 2H), 7.31-7.19 (m, 7H), 6.98 (s, 1H), 3.61 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 152.6, 146.8, 144.3, 134.0, 141.7, 139.2, 137.0, 135.7, 132.4, 129.5, 128.8, 128.7, 128.3, 127.4, 127.3, 136.7, 123.6, 123.5, 121.5, 121.4, 120.5, 120.3, 119.1, 110.3, 62.2, 31.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{30}\text{H}_{22}\text{ClN}_2\text{O}_2$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H} + 2$]: m/z 477.1370, 479.1340.
Found: 477.1370, 479.1348.

Compound 7ao



Yield: 0.224 g (86%, red solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 146-148 °C.

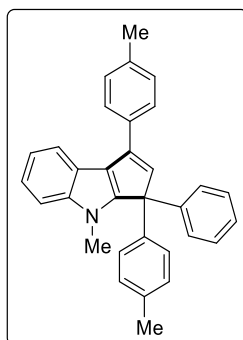
IR (neat): $\nu_{\max}$ 2922, 1593, 1510, 1463, 1343, 1243, 1180, 1110, 1044, 911, 852, 825, 722, 700 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 8.16-8.14 (m, 2H), 7.86-7.84 (m, 1H), 7.76 (d, J = 8.4 Hz, 2H), 7.52-7.48 (m, 2H), 7.38-7.20 (m, 10H), 6.38 (s, 1H), 3.58 (s, 3H), 2.45 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 153.5, 148.5, 146.9, 142.0, 141.3, 138.4, 138.1, 134.0, 132.7, 129.3, 129.0, 128.8, 128.1, 127.6, 127.3, 123.7, 121.5, 121.2, 120.3₁, 120.2₅, 119.5, 110.1, 61.7, 31.4, 21.4 ppm.

HRMS (ESI-TOF): Calcd. For $\text{C}_{31}\text{H}_{25}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 457.1925. Found: 457.1917.

Compound 7ap



Yield: 0.193 g (79%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 182-184 °C.

IR (neat): ν_{max} 2939, 1738, 1594, 1509, 1463, 1335, 1234, 1179, 1158, 1112, 1034, 1017, 817, 765, 724 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.86-7.84 (m, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.37-7.17 (m, 12H), 7.13-7.11 (m, 2H), 6.42 (s, 1H), 3.60 (s, 3H), 2.45 (s, 3H), 2.36 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 155.0, 141.2, 140.6, 140.2, 137.5, 136.8, 136.7, 135.4, 133.5, 129.2, 128.5, 128.3₂, 128.2₆, 127.3, 127.0, 121.7, 120.5, 120.1, 119.9, 118.9, 109.9, 61.6, 31.4, 21.4, 21.1 ppm.

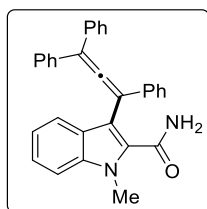
HRMS (ESI-TOF): Calcd. For $\text{C}_{32}\text{H}_{28}\text{N}$ [$\text{M}^+ + \text{H}$]: m/z 426.2222. Found: 426.2219.

6.5 Synthesis of 1-methyl-3-(1,3,3-triphenylpropa-1,2-dien-1-yl)-1H-indole-2-carboxamide 8

An oven dried 25 mL round-bottomed flask was charged with 1- methylindole-2-carboxamide **2a** (0.100 g, 0.57 mmol), propargylic alcohol **5a** (0.178 g, 0.62 mmol) and $\text{Cu}(\text{OTf})_2$ (0.020 g, 0.057 mmol (10 mol %)) in dichloromethane (10 mL). The mixture was stirred at rt (25 °C) in open air for 6h and monitored by TLC. After the completeness of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na_2SO_4 and the

solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:4) afforded the desired product **8**.

Compound 8



Yield: 0.224 g (89%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 192-194 °C.

IR (neat): $\nu_{\max}$ 3446, 3027, 1883, 1665, 1611, 1520, 1487, 1468, 1440, 1321, 1072, 1026, 758, 738, 693 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.48-7.46 (m, 2H), 7.45-7.25 (m, 17H), 7.11 (td, J = 7.6, 0.8 Hz, 1H), 6.27 (s, 1H), 5.10 (s, 1H), 4.14 (s, 3H) ppm.

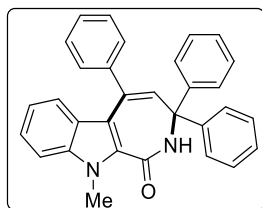
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 208.3, 163.8, 138.4, 135.9, 135.3, 129.0, 128.8, 128.7, 128.6, 128.1, 128.0, 126.8, 126.7, 124.9, 121.4, 120.8, 113.1, 112.7, 110.3, 104.1, 32.3 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{31}\text{H}_{24}\text{N}_2\text{NaO}$ [$\text{M}^+ + \text{Na}$]: m/z 463.1786. Found: 463.1787.

6.6 Synthesis of 10-methyl-3,3,5-triphenyl-2,3-dihydroazepino[3,4-*b*]indol-1(10*H*)-one **9aa**

An oven dried 25 mL round-bottomed flask was charged with compound **8** (0.100 g, 0.16 mmol) in DCM (10 mL). The mixture was stirred at reflux temperature with ice-cold water circulation using a condenser for 6h and monitored by TLC. After completeness of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:4) afforded the desired product **9aa**.

Compound 9aa

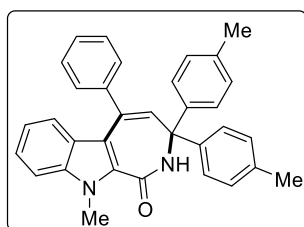


Yield: 0.085 g (85%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).
Mp: above 220 °C.
IR (neat): $\nu_{\max}$ 3166, 3029, 1629, 1521, 1473, 1444, 1315, 1236, 1137, 894, 790, 741, 697, 663 cm^{-1} .
 ^1H NMR (400 MHz, CDCl_3): δ 7.48-7.44 (m, 2H), 7.42-7.39 (m, 3H), 7.37-7.34 (m, 4H), 7.24-7.16 (m, 8H), 6.88 (s, 1H), 6.81-6.77 (m, 1H), 6.60 (s, 1H), 6.49 (d, J = 8.4 Hz, 1H), 3.93 (s, 3H) ppm.
 $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 163.4, 145.3, 141.2, 139.5, 138.3, 135.3, 132.3, 128.7, 128.4, 128.2, 127.7, 127.1, 124.4, 124.2, 122.7, 119.9, 117.2, 109.7, 64.5, 31.7 ppm.
HRMS (ESI-TOF): Calcd. for $\text{C}_{31}\text{H}_{25}\text{N}_2\text{O}$ [$\text{M}^+ + \text{H}$]: m/z 441.1967. Found: 441.1966.

6.7 General procedure for the synthesis of ϵ -lactams **9aa**, **9ac-ae**, **9ag-ai**, and **9ba-ca** by using indole-2-carboxamides and propargylic alcohols

An oven dried 25 mL round-bottomed flask was charged with indole-2-carboxamides **3** (0.100 g, 0.57 mmol), one of the propargylic alcohols **5** (0.62 mmol) and $\text{Cu}(\text{OTf})_2$ (0.020 g, 0.057 mmol (10 mol %)) in dichloromethane (10 mL). The mixture was stirred at reflux temperature with ice-cold water circulation using a condenser for 6h and monitored by TLC. After completeness of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:4) afforded the desired products **9aa**, **9ac-ae**, **9ag-ai** and **9ba-ca**.

Compound **9ac**



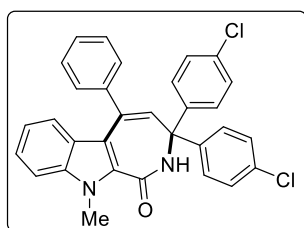
Yield: 0.226 g (85%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).
Mp: above 220 °C.
IR (neat): $\nu_{\max}$ 3376, 3025, 2916, 1915, 1640, 1509, 1468, 1438, 1311, 1187, 1019, 819, 736, 702 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.46-7.36 (m, 5H), 7.25-7.16 (m, 6H), 7.00 (d, J = 8.0 Hz, 4H), 6.81-6.77 (m, 2H), 6.57 (s, 1H), 6.49 (d, J = 8.0 Hz, 1H), 3.95 (s, 3H), 2.26 (s, 6H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): δ 163.3, 142.5, 141.4, 139.2, 138.3, 137.3, 135.6, 132.2, 128.8, 128.7, 128.3, 128.0, 127.0, 124.5, 124.1, 122.9, 119.8, 117.2, 109.8, 64.0, 31.8, 21.0 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{33}\text{H}_{29}\text{N}_2\text{O}$ [$\text{M}^+ + \text{H}$]: m/z 469.2280. Found: 469.2281.

Compound 9ad



Yield: 0.238 g (82%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 $^\circ\text{C}$.

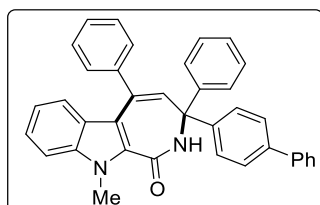
IR (neat): ν_{max} 3374, 3050, 1644, 1513, 1486, 1469, 1314, 1093, 1012, 819, 737, 695 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.45-7.38 (m, 5H), 7.28-7.26 (m, 5H), 7.23-7.20 (m, 5H), 7.03 (s, 1H), 6.83-6.80 (m, 1H), 6.48 (d, J = 8.0 Hz, 1H), 6.47 (s, 1H), 3.94 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.1, 143.5, 140.9, 140.2, 138.4, 133.8₃, 133.8₀, 131.8, 128.6, 128.5, 128.4₆, 128.4₀, 128.3₇, 124.6, 124.3, 122.7, 120.2, 117.2, 110.0, 63.7, 31.8 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{31}\text{H}_{23}\text{Cl}_2\text{N}_2\text{O}$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H}+2$], [$\text{M}^+ + \text{H}+4$]: m/z 509.1187, 511.1157, 513.1127. Found: 509.1187, 511.1162, 513.1146.

Compound 9ae



Yield: 0.259 g (88%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 $^\circ\text{C}$.

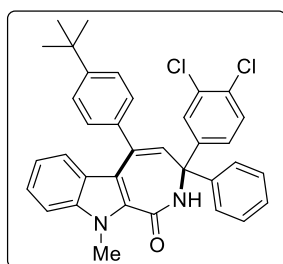
IR (neat): ν_{max} 3160, 3026, 2161, 2001, 1627, 1517, 1474, 1442, 1313, 832, 767, 695 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.53-7.43 (m, 6H), 7.41-7.35 (m, 9H), 7.36-7.28 (m, 1H), 7.26-7.15 (m, 5H), 6.93 (s, 1H), 6.81-6.77 (m, 1H), 6.63 (s, 1H), 6.51 (d, J = 8.4 Hz, 1H), 3.94 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 160.5, 145.3, 144.5, 141.3, 140.4, 140.2, 139.6, 138.3, 135.2, 132.3, 128.8₄, 128.7₅, 128.5, 128.2₃, 128.2₀, 127.7₃, 127.6₉, 127.5, 127.2, 127.0, 126.8, 124.4, 124.3, 122.8, 120.0, 117.3, 109.8, 64.4, 31.8 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{37}\text{H}_{29}\text{N}_2\text{O}$ [$\text{M}^+ + \text{H}$]: m/z 517.2280. Found: 517.2283.

Compound 9ag



Yield: 0.253 g (79%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 177-179 °C.

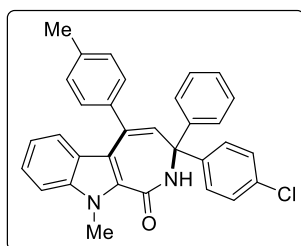
IR (neat): ν_{max} 3179, 3031, 2958, 1636, 1519, 1469, 1444, 1378, 1316, 1028, 820, 737, 701 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.53 (s, 1H), 7.42-7.36 (m, 4H), 7.29-7.20 (m, 9H), 6.99 (s, 1H), 6.84-6.81 (m, 1H), 6.55-6.53 (m, 2H), 3.94 (s, 3H), 1.39 (s, 9H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.4, 151.6, 145.3, 139.9, 138.3, 137.8, 133.6, 132.3, 132.1, 131.6, 129.9, 129.3, 128.6, 128.3, 128.1, 127.1, 126.5, 125.3, 124.5, 124.4, 122.9, 120.1, 117.4, 109.9, 64.0, 34.7, 31.7, 31.4 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{35}\text{H}_{30}\text{Cl}_2\text{N}_2\text{NaO}$ [$\text{M}^+ + \text{Na}$], [$\text{M}^+ + \text{Na}+2$], [$\text{M}^+ + \text{Na}+4$]: m/z 587.1633, 589.1603, 591.1573. Found: 587.1632, 589.1607, 591.1592.

Compound 9ah



Yield: 0.231 g (83%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 190-192 °C.

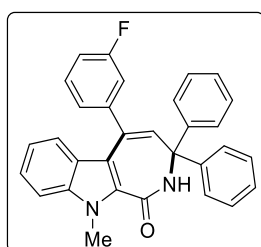
IR (neat): $\nu_{\max}$ 3171, 3031, 2001, 1877, 1801, 1630, 1520, 1486, 1469, 1443, 1383, 1319, 1093, 1014, 739, 697 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.34-7.15 (m, 15H), 6.86-6.80 (m, 2H), 6.55 (d, $J = 8.4$ Hz, 1H), 6.51 (s, 1H), 3.93 (s, 3H), 2.44 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 163.3, 145.5, 143.5, 139.7, 138.3, 138.2, 138.1, 134.1, 133.4, 132.0, 129.1, 128.5, 128.4, 128.2, 127.9, 127.1, 124.4, 122.9, 120.0, 117.4, 109.9, 64.1, 31.7, 21.3 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{32}\text{H}_{26}\text{ClN}_2\text{O}$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H} + 2$]: m/z 489.1734, 491.1704.
Found: 489.1734, 491.1698.

Compound 9ai



Yield: 0.216 g (83%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: above 220 $^{\circ}\text{C}$.

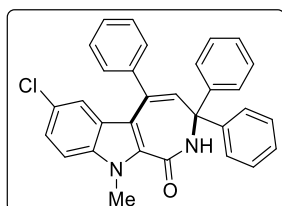
IR (neat): $\nu_{\max}$ 3163, 3027, 2886, 2236, 1629, 1612, 1579, 1523, 1470, 1444, 1325, 1182, 914, 878, 726, 700 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.38-7.33(m, 5H), 7.24-7.17 (m, 10H), 7.14-7.09 (m, 1H), 7.06 (s, 1H), 6.85-6.81 (m, 1H), 6.63 (s, 1H), 6.54 (d, $J = 8.4$ Hz, 1H), 3.91 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.8 (d, $J = 244.6$ Hz), 163.3, 145.1, 143.4 (d, $J = 7.5$ Hz), 138.5, 138.2, 136.0, 132.4, 129.9 (d, $J = 8.3$ Hz), 128.2, 127.8, 127.1, 124.5 (d, $J = 2.4$ Hz), 124.3, 124.2, 122.5, 120.1, 116.5, 115.5 (d, $J = 21.6$ Hz), 115.0 (d, $J = 20.9$ Hz), 109.9, 64.5, 31.7 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{31}\text{H}_{24}\text{FN}_2\text{O}$ [$\text{M}^+ + \text{H}$]: m/z 459.1873. Found: 459.1874.

Compound 9ba



Yield: 0.178 g (80%, white solid, $R_f = 0.53$ (9:1 hexane/ethyl acetate)).

Mp: above 220 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3182, 3025, 2986, 1737, 1625, 1523, 1470, 1443, 1323, 1235, 1069, 836, 743, 696 cm^{-1} .

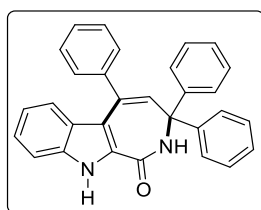
^1H NMR (500 MHz, CDCl_3): δ 7.46-7.39 (m, 5H), 7.34-7.32 (m, 4H), 7.24-7.17 (m, 6H), 7.14-7.10 (m, 2H), 6.94 (s, 1H), 6.63 (s, 1H), 6.43-6.42 (m, 1H), 3.89 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.0, 140.5, 139.1, 136.5, 135.7, 133.3, 128.5₄, 128.4₅, 128.2, 127.7, 127.0, 125.5, 125.2, 124.7, 121.9, 116.6, 110.9, 64.5, 31.8 ppm.

LC-MS: m/z 475 [$\text{M}^+ + 1$].

Anal. Calcd. for $\text{C}_{31}\text{H}_{23}\text{ClN}_2\text{O}$: C, 78.39; H, 4.88; N, 5.90. Found: C, 78.31; H, 4.92; N, 5.85.

Compound 9ca



Yield: 0.207 g (78%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 $^{\circ}\text{C}$.

IR (neat): $\nu_{\max}$ 3382, 3254, 1623, 1524, 1490, 1467, 1445, 1400, 1334, 1286, 1013, 776, 744, 698 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 9.48 (s, 1H), 7.45-7.38 (m, 5H), 7.36-7.34 (m, 4H), 7.32 (d, J = 8.0 Hz, 1H), 7.26-7.19 (m, 6H), 7.17-7.14 (m, 1H), 6.85 (s, 1H), 6.81-6.78 (m, 1H), 6.49 (d, J = 8.5 Hz, 1H), 6.44 (s, 1H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.8, 145.6, 141.3, 139.2, 135.8, 133.9, 130.4, 128.9, 128.3, 128.1, 127.8, 127.3, 125.6, 124.8, 123.1, 120.1, 117.1, 111.8, 64.8 ppm.

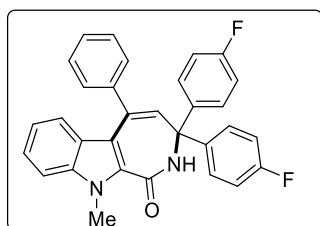
LC-MS: m/z 427 [$\text{M}^+ + 1$].

Anal. Calcd. for $\text{C}_{30}\text{H}_{22}\text{N}_2\text{O}$: C, 84.48; H, 5.20; N, 6.57. Found: C, 84.39; H, 5.16; N, 6.63.

6.8 General procedure for the synthesis of ϵ -lactams **9aa**, **9al-am**, **9ao-ar**, and **9bs** by using 1-methylindole-3-carboxamide and propargylic alcohols

An oven dried 25 mL round-bottomed flask was charged with 1-methylindole-3-carboxamide **4a** (0.100 g, 0.57 mmol), propargylic alcohol **5a** (0.178 g, 0.62 mmol) and *p*-TSA (0.010 g, 0.057 mmol (10 mol %)) in dichloromethane (10 mL). The mixture was stirred at rt (25 °C) in open air for 12h and monitored by TLC. After completeness of the reaction, the mixture was treated with dichloromethane (10 mL) and water (15 mL). The organic phase was separated and the aqueous layer washed with dichloromethane (10 mL) and brine solution (10 mL). The combined organic part was dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography (ethyl acetate: hexane 1:4) afforded the desired product **9aa** as a white solid. Compounds **9al-am**, **9ao-ar**, and **9bs** were prepared from appropriate indole-3-carboxamide and propargylic alcohol by using the same procedure and same molar quantities.

Compound **9al**



Yield: 0.105 g (38%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 °C.

IR (neat): $\nu_{\max}$ 3161, 3033, 1632, 1600, 1503, 1470, 1443, 1323, 1220, 1163, 833, 739, 700 cm⁻¹.

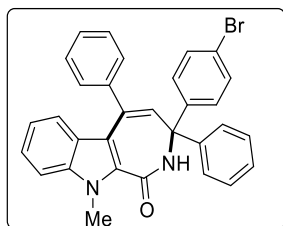
¹H NMR (400 MHz, CDCl₃): δ 7.46-7.37 (m, 5H), 7.34-7.30 (m, 4H), 7.27-7.19 (m, 2H), 7.05 (s, 1H), 6.94-6.91 (m, 4H), 6.83-6.79 (m, 1H), 6.52 (s, 1H), 6.49 (d, J = 8.0 Hz, 1H), 3.92 (s, 3H) ppm.

¹³C{¹H} NMR (125 MHz, CDCl₃) δ 163.5, 162.0 (d, J = 245.8 Hz), 141.0, 139.9, 138.3, 134.7, 132.1, 128.9 (d, J = 8.0 Hz), 128.7, 128.5, 128.3, 124.5, 124.3, 122.7, 120.2, 117.2, 115.2 (d, J = 21.3 Hz), 109.9, 63.7, 31.7 ppm.

LC-MS: m/z 475 [M^+ - 1].

Anal. Calcd. for C₃₁H₂₂F₂N₂O: C, 78.14; H, 4.65; N, 5.88. Found: C, 78.07; H, 4.63; N, 5.82.

Compound 9am



Yield: 0.116 g (39%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 °C.

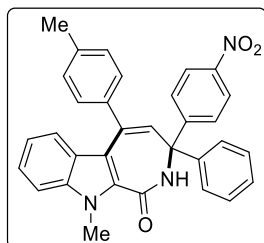
IR (neat): 3162, 3027, 1634, 1520, 1470, 1441, 1317, 1261, 1072, 1007, 818, 738, 698 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.46-7.37 (m, 5H), 7.34-7.18 (m, 11H), 6.95 (s, 1H), 6.50-6.48 (m, 1H), 6.54 (s, 1H), 6.50-6.48 (m, 1H), 3.93 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.5, 141.1, 139.8, 138.3, 134.6, 132.1, 131.2, 128.9, 128.7, 128.4₃, 128.3₉, 128.3, 127.9, 127.1, 124.4₃, 124.3₅, 122.8, 121.7, 120.1, 117.2, 109.9, 64.2, 31.7 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{31}\text{H}_{24}\text{BrN}_2\text{O}$ [$\text{M}^+ + \text{H}$], [$\text{M}^+ + \text{H} + 2$]: m/z 519.1072, 521.1052.
Found: 519.1073, 521.1056.

Compound 9ao



Yield: 0.115 g (40%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 139-141 °C.

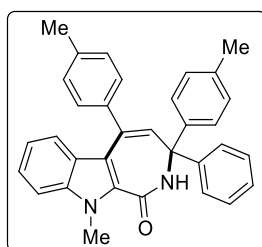
IR (neat): ν_{max} 3173, 3028, 1634, 1516, 1470, 1443, 1343, 1315, 1237, 1110, 905, 876, 849, 814, 735, 700 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 8.00 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.8 Hz, 2H), 7.35-7.20 (m, 11H), 6.95 (s, 1H), 6.85-6.81 (m, 1H), 6.57 (s, 1H), 6.58 (d, J = 10.4 Hz, 1H), 3.94 (s, 3H), 2.44 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 163.2, 152.1, 147.1, 145.3, 140.3, 138.4, 138.3, 137.7, 133.0, 131.8, 129.2, 128.9, 128.5, 128.4, 127.8, 126.9, 124.8, 124.3, 123.1, 122.8, 120.3, 117.5, 109.9, 64.3, 31.8, 21.3 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{32}\text{H}_{26}\text{N}_3\text{O}_3$ [$\text{M}^+ + \text{H}$]: m/z 500.1974. Found: 500.1974.

Compound 9ap



Yield: 0.097 g (36%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 °C.

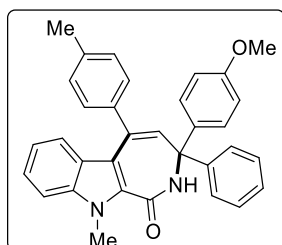
IR (neat): $\nu_{\max}$ 3173, 3029, 1633, 1518, 1476, 1468, 1448, 1381, 1320, 1095, 1014, 730, 699 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.34 (d, J = 8.0 Hz, 4H), 7.28-7.14 (m, 9H), 7.03 (d, J = 8.0 Hz, 2H), 6.90 (s, 1H), 6.82-6.79 (m, 1H), 6.56 (d, J = 8.0 Hz, 1H), 6.56 (s, 1H), 3.92 (s, 3H), 2.43 (s, 3H), 2.27 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.3, 139.2, 138.4, 138.3, 137.9, 137.3, 134.9, 132.2, 129.0, 128.9, 128.5, 128.0, 127.5, 127.1, 127.0, 124.5, 124.1, 122.9, 119.8, 117.4, 109.7, 64.3, 31.7, 21.3, 20.9 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{33}\text{H}_{29}\text{N}_2\text{O}$ [$\text{M}^+ + \text{H}$]: m/z 469.2280. Found: 469.2280.

Compound 9aq



Yield: 0.103 g (37%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 °C.

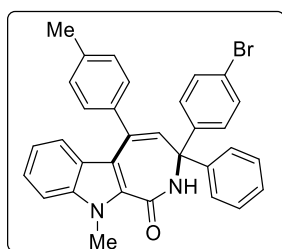
IR (neat): $\nu_{\max}$ 3159, 3018, 1626, 1604, 1508, 1473, 1442, 1315, 1254, 1182, 1032, 815, 757, 701, 671 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ 7.34 (d, J = 7.5 Hz, 4H), 7.24-7.14 (m, 9H), 6.88 (s, 1H), 6.80 (t, J = 7.5 Hz, 1H), 6.75 (d, J = 8.5 Hz, 2H), 6.56-6.55 (m, 2H), 3.92 (s, 3H), 3.74 (s, 3H), 2.43 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.3, 158.8, 139.3, 138.4, 138.3, 137.9, 134.9, 132.2, 129.0, 128.5, 128.3, 128.0, 127.5, 127.0, 124.5, 124.1, 122.9, 119.8, 117.4, 113.5, 109.7, 64.1, 55.2, 31.7, 21.3 ppm.

HRMS (ESI-TOF): Calcd. for $\text{C}_{33}\text{H}_{29}\text{N}_2\text{O}_2$ [$\text{M}^+ + \text{H}$]: m/z 485.2229. Found: 485.2232.

Compound 9ar



Yield: 0.119 g (39%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 170-172 °C.

IR (neat): $\nu_{\max}$ 3161, 3024, 1632, 1509, 1472, 1443, 1315, 1237, 1074, 1008, 874, 814, 782, 702 cm^{-1} .

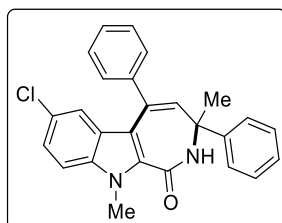
^1H NMR (400 MHz, CDCl_3): δ 7.34-7.19 (m, 15H), 6.98 (s, 1H), 6.84-6.80 (m, 1H), 6.56 (d, J = 8.4 Hz, 1H), 6.50 (s, 1H), 3.92 (s, 3H), 2.44 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) δ 163.3, 139.7, 138.3, 138.1₄, 138.1₁, 134.0, 132.0, 131.2, 129.1, 128.9, 128.5, 128.4, 127.9, 127.0, 124.4, 122.9, 121.6, 112.0, 117.4, 109.9, 64.2, 31.8, 21.3 ppm.

LC-MS: m/z 533 [$\text{M}^+ - 1$].

Anal. Calcd. For $\text{C}_{32}\text{H}_{25}\text{BrN}_2\text{O}$: C, 72.05; H, 4.72; N, 5.25. Found: C, 72.15; H, 4.68; N, 5.28.

Compound 9bs



Yield: 0.065 g (34%, white solid, R_f = 0.53 (9:1 hexane/ethyl acetate)).

Mp: above 220 °C.

IR (neat): $\nu_{\max}$ 3175, 3040, 2971, 1640, 1521, 1468, 1441, 1321, 1067, 1025, 819, 794, 743, 723, 696 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.44-7.42 (m, 5H), 7.39-7.37 (m, 2H), 7.11-7.10 (m, 2H), 7.07-7.03 (m, 2H), 6.99-6.95 (m, 1H), 6.86 (s, 1H), 6.45-6.44 (m, 1H), 6.31 (s, 1H), 3.88 (s, 3H), 1.78 (s, 3H) ppm.

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 163.5, 145.8, 140.3, 139.0, 136.5, 134.2, 133.4, 128.5, 128.4₄, 128.4₁, 127.8, 126.8, 125.1, 124.7, 121.8, 116.9, 110.8, 57.1, 34.3, 31.7 ppm.

LC-MS: m/z 413 [$M^+ + 1$].

Anal. Calcd. for $C_{26}H_{21}ClN_2O$: C, 75.63; H, 5.13; N, 6.78. Found: C, 75.52; H, 5.16; N, 6.73.

6.9 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **6aa**, **6aj**, **7al**, **9ac**, **7an**, **4a**, **9aa**, and **9ap**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer using Mo-K α ($\lambda = 0.71073$ Å) or Cu-K α ($\lambda = 1.54184$ Å) radiation]. Structures were solved and refined using standard methods.⁴¹ Crystal data are summarized in Tables 7-8.

Table 7: Crystal data for compounds **6aa**, **6aj**, **7al**, and **9ac**

Compound	6aa	6aj	7al	9ac
Emp. formula	C ₃₁ H ₂₃ NO ₂	C ₂₉ H ₂₁ NO ₂ S	C ₃₀ H ₂₁ F ₂ N	C ₃₃ H ₂₈ N ₂ O
Formula weight	441.50	447.53	433.48	468.57
Crystal system	Monoclinic	Monoclinic	Orthorhombic	Triclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2(1)/ <i>n</i>	<i>Pna</i> 21	<i>P</i> -1
<i>a</i> /Å	9.5504(9)	11.9339(13)	9.0702(4)	10.7428(4)
<i>b</i> /Å	17.3600(19)	10.8446(12)	20.8446(8)	11.5805(4)
<i>c</i> /Å	14.7835(16)	17.9980(17)	12.0332(4)	11.8540(5)
α /deg	90	90	90	102.3017(15)
β /deg	105.148(3)	103.711(3) ^o	90	103.6326(16)
γ /deg	90	90	90	108.3261(14) ^o
<i>V</i> /Å ³	2365.9(4)	2262.9(4)	2275.05(15)	1292.89(9)
<i>Z</i>	4	4	4	2
<i>D</i> _{calc} /g cm ⁻³	1.240	1.314	1.266	1.204
μ /mm ⁻¹	0.077	0.170	0.085	0.072
<i>F</i> (000)	928	936	904	496
Data/ restraints/ parameters	5396/0/307	3983/0/299	4474/1/298	4553/0/332
<i>S</i>	0.983	1.072	1.082	1.099
R1 [<i>I</i> >2 σ (<i>I</i>)]	0.0466	0.0519	0.0394	0.0429
wR2 [all data]	0.1377	0.1642	0.1031	0.1202
Max./min. residual electron dens. [eÅ ⁻³]	0.499/-0.767	0.397/-0.633	0.148/-0.159	0.216/-0.165

^aR1 = $\sum ||F_o| - |F_c|| / \sum |F_o|$ and wR2 = $[\sum w(F_o^2 - F_c^2)^2 / \sum wF_o^4]^{0.5}$

Table 8: Crystal data for compounds **7an**, **4a**, **9aa** and **9ap**

Compound	7an	4a	9aa	9ap
Emp. formula	C ₃₀ H ₂₁ ClN ₂ O ₂	C ₁₀ H ₁₀ N ₂ O	C ₃₁ H ₂₄ N ₂ O	C ₂₃ H ₂₈ N ₂ O
Formula weight	476.94	174.20	440.52	468.57
Crystal system	Orthorhombic	Monoclinic	Triclinic	Monoclinic
Space group	<i>Pbca</i>	<i>C2/c</i>	<i>P-1</i>	<i>C12/c1</i>
<i>a</i> /Å	13.8267(8)	20.717(2)	10.1870(4)	23.3055(12)
<i>b</i> /Å	17.2618(13)	11.7670(11)	12.0867(4)	12.5430(4)
<i>c</i> /Å	20.2956(15)	9.8845(8)	20.2712(7)	19.5823(12)
α /deg	90	90	76.231(2)	90
β /deg	90	101.146(3)	78.228(2)	114.108(7)
γ /deg	90	90	86.594(2)	90
<i>V</i> /Å ³	4844.0(6)	2364.2(4)	2373.07(15)	5225.0(5)
<i>Z</i>	8	8	4	8
<i>D</i> _{calc} /g cm ⁻³	1.308	0.979	1.233	1.191
μ /mm ⁻¹	0.188	0.065	0.075	0.072
<i>F</i> (000)	1984	736	928	1984
Data/ restraints/ parameters	4245/0/317	2074/0/120	9771/0/621	4598/1/332
<i>S</i>	1.042	1.076	1.053	1.031
R1 [<i>I</i> > 2σ(<i>I</i>)]	0.0425	0.0850	0.0625	0.0938
wR2 [all data]	0.1167	0.2753	0.1462	0.3380
Max./min. residual electron dens. [eÅ ⁻³]	0.244/-0.489	0.323/- 0.268	0.252/-0.226	0.759/-0.408

$$^a\text{R1} = \Sigma||\text{Fo}| - |\text{Fc}||/\Sigma|\text{Fo}| \text{ and } \text{wR2} = [\Sigma \text{w}(\text{Fo}^2 - \text{Fc}^2)^2/\Sigma \text{wFo}^4]^{0.5}$$

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APPENDIX

Copies of $^1\text{H}/^{13}\text{C}\{^1\text{H}\}$ NMR spectra for representative compounds

Part A: 10ab, 11aa, 12ah, 15aa, 16aa, 17aa, 18ac, 19a, 20b, 21a, 22a

Part B: 6aa, 7aa, and 9aa

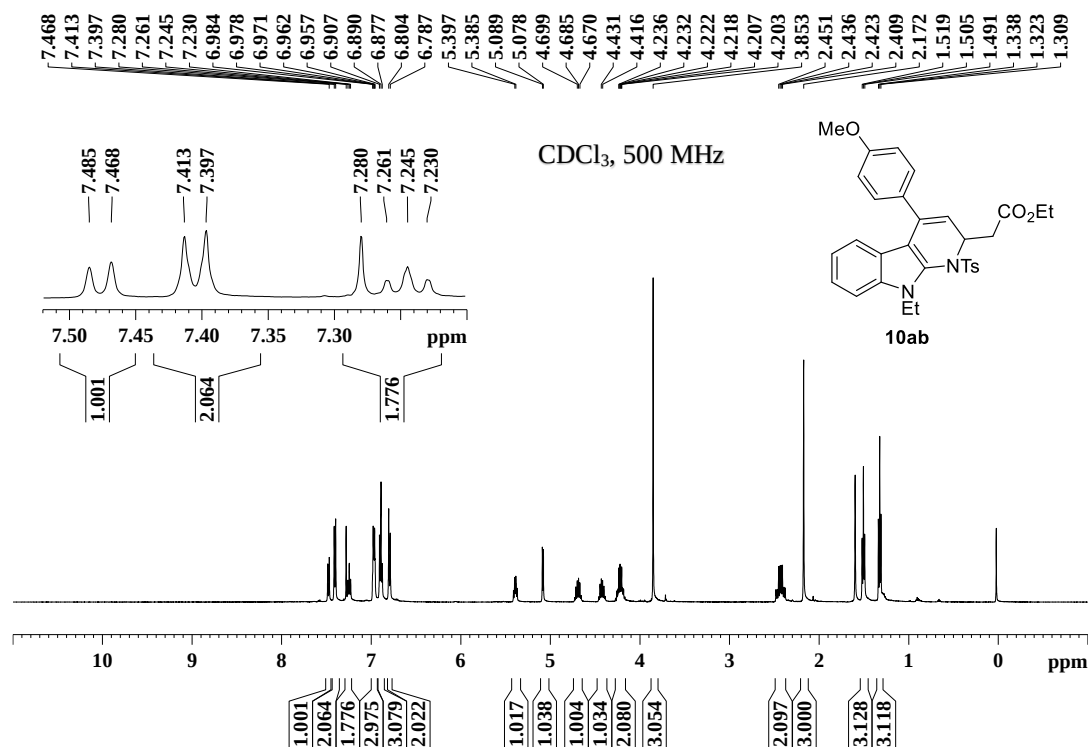


Figure A1: ^1H NMR spectrum of compound 10ab

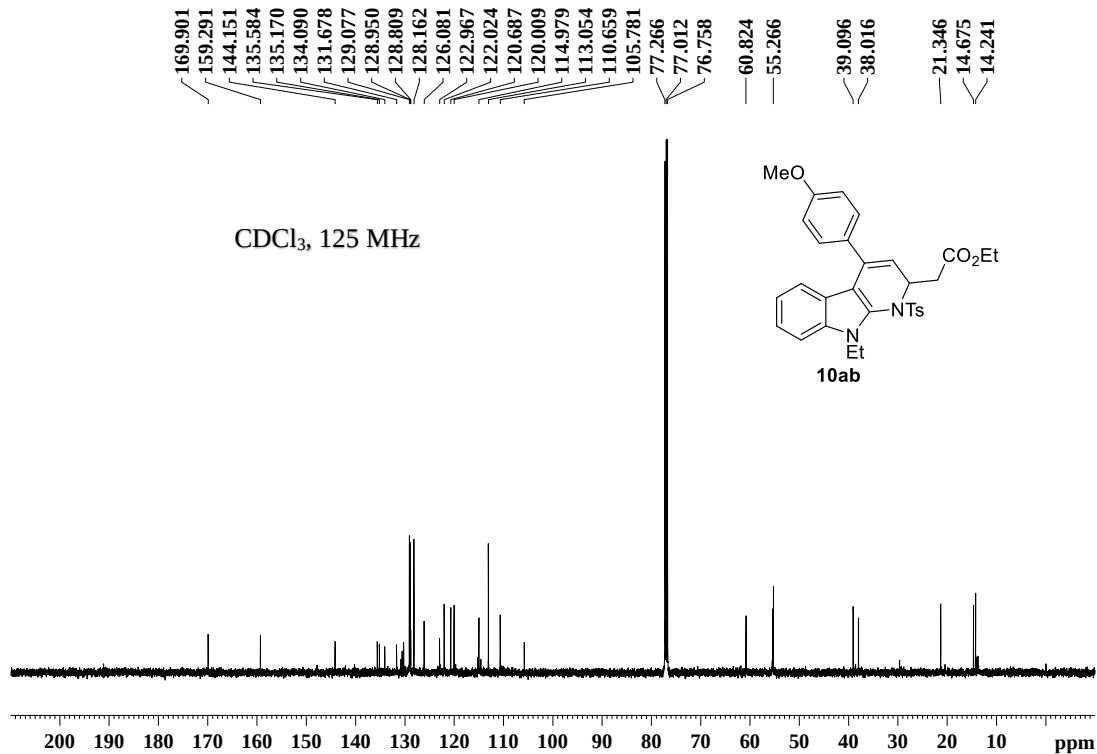


Figure A2: $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 10ab

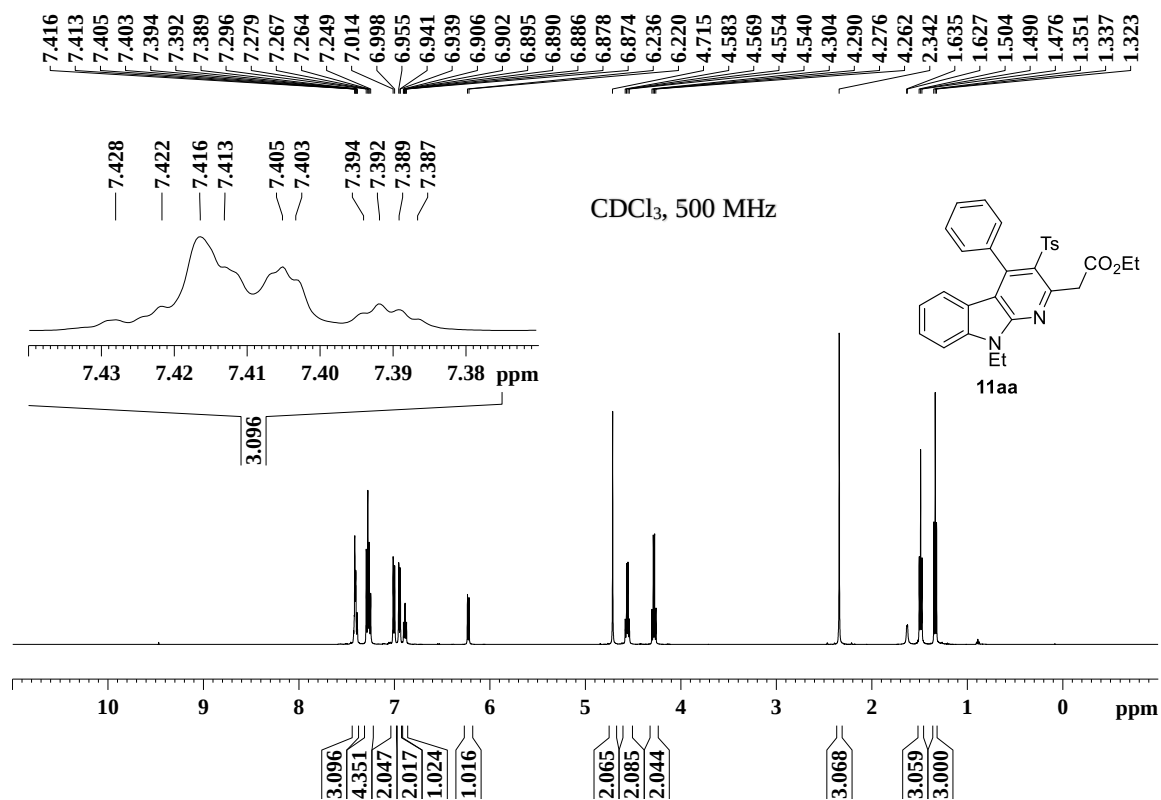


Figure A3: ¹H NMR spectrum of compound 11aa

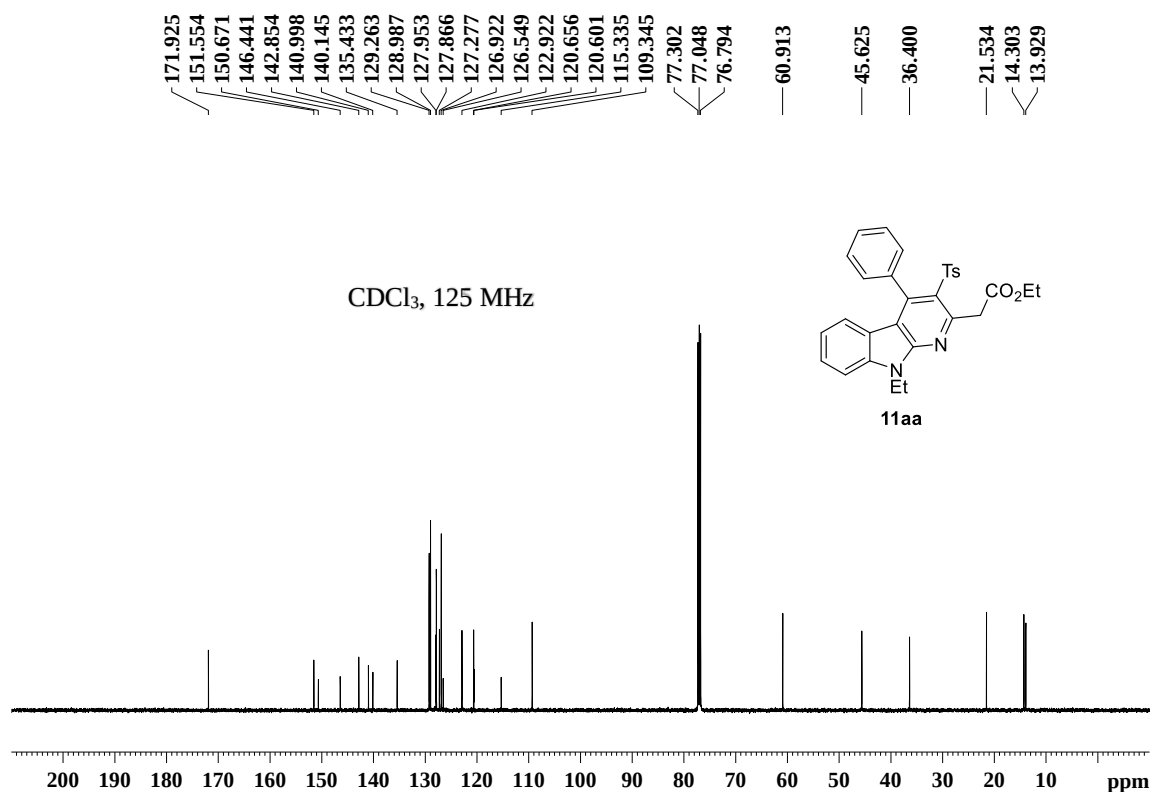


Figure A4. ¹³C{¹H} NMR spectrum of compound 11aa

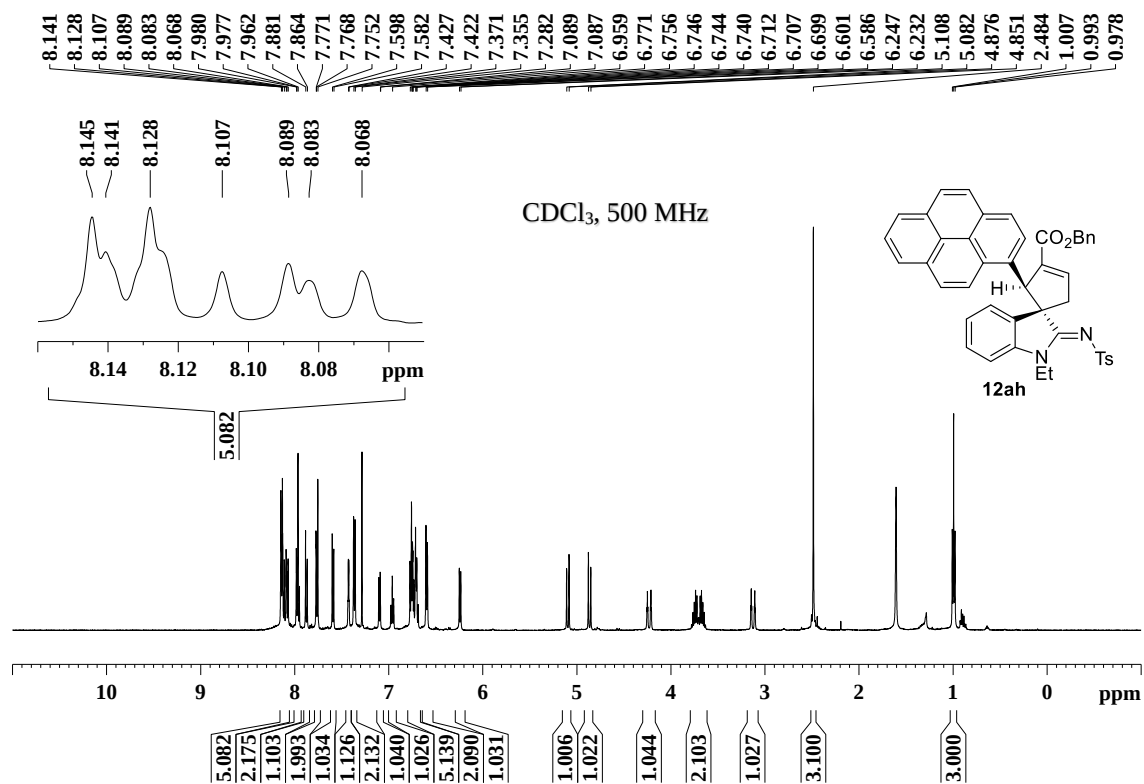


Figure A5: ¹H NMR spectrum of compound 12ah

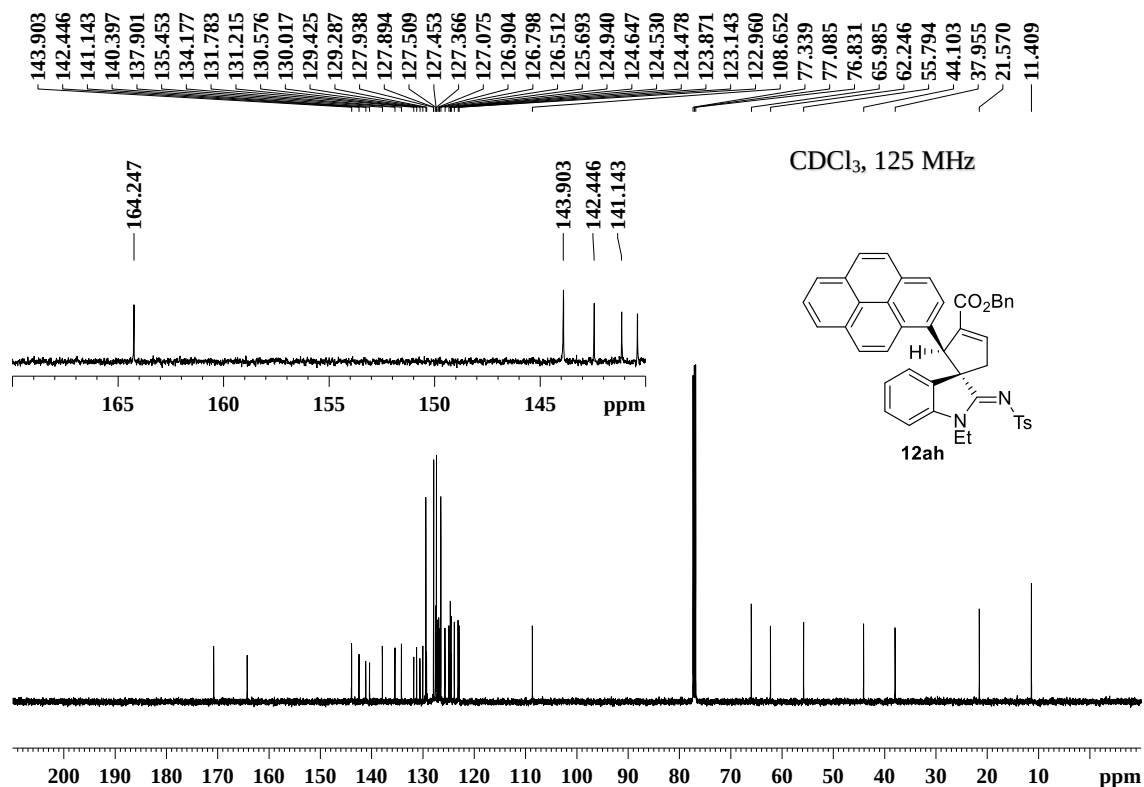


Figure A6: ¹³C{¹H} NMR spectrum of compound 12ah

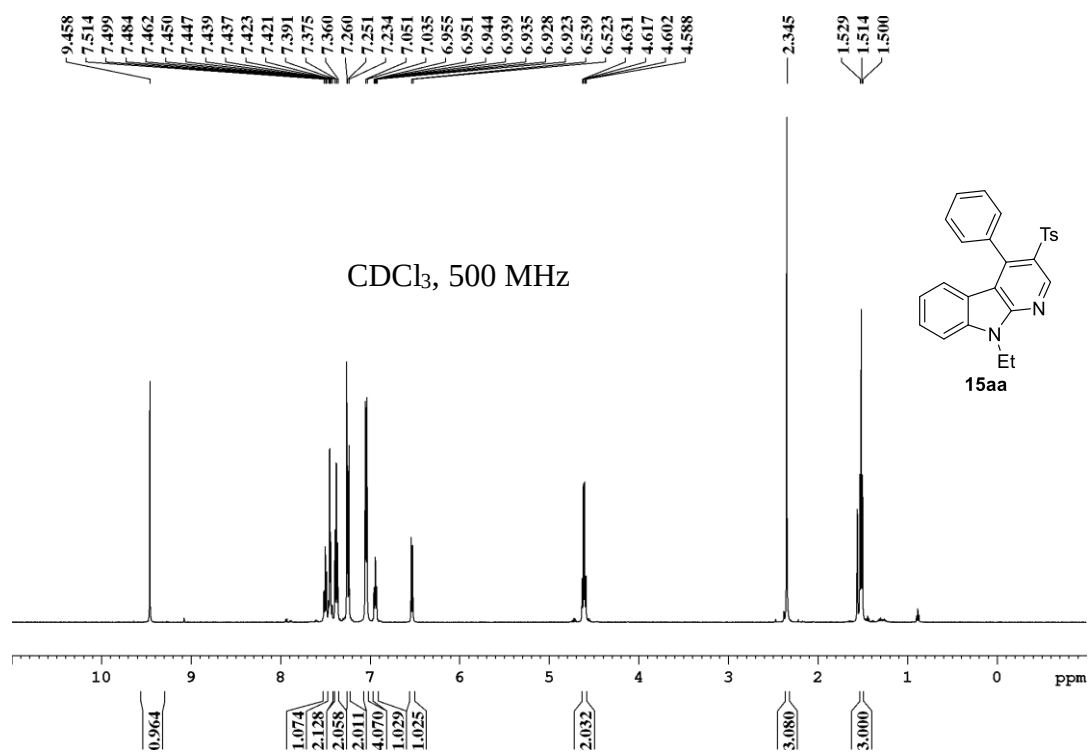


Figure A7: ^1H NMR spectrum of compound **15aa**

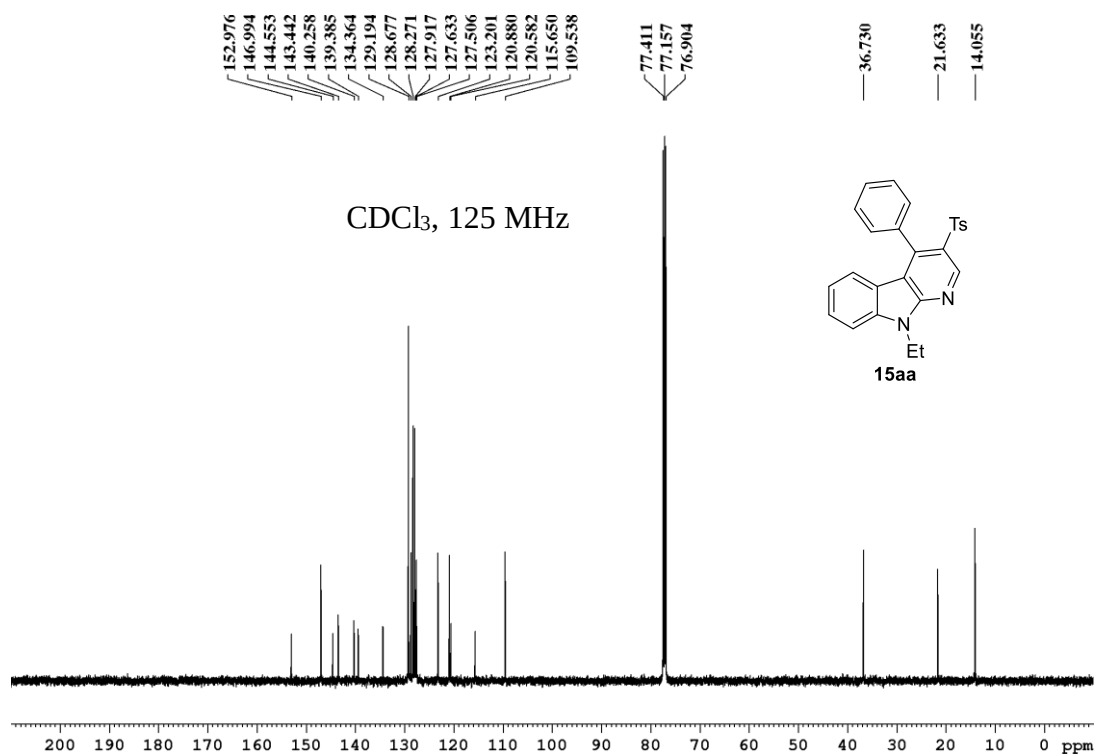


Figure A8: $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **15aa**

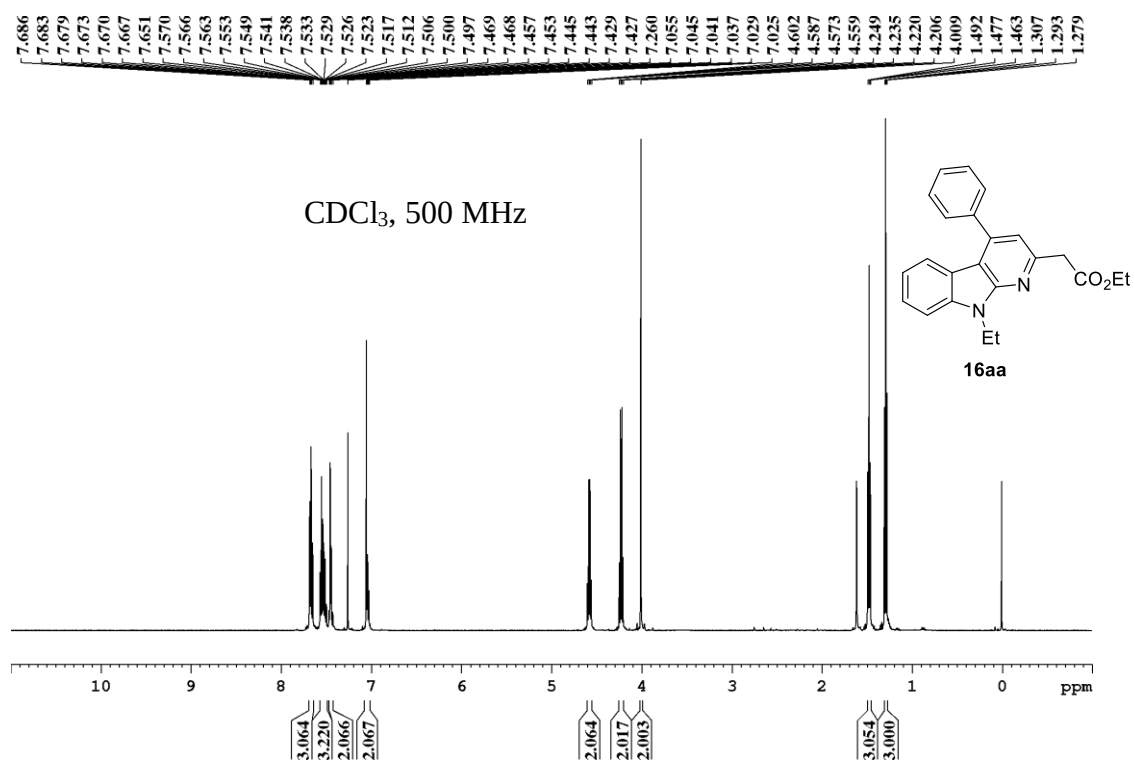


Figure A9: ¹H NMR spectrum of compound **16aa**

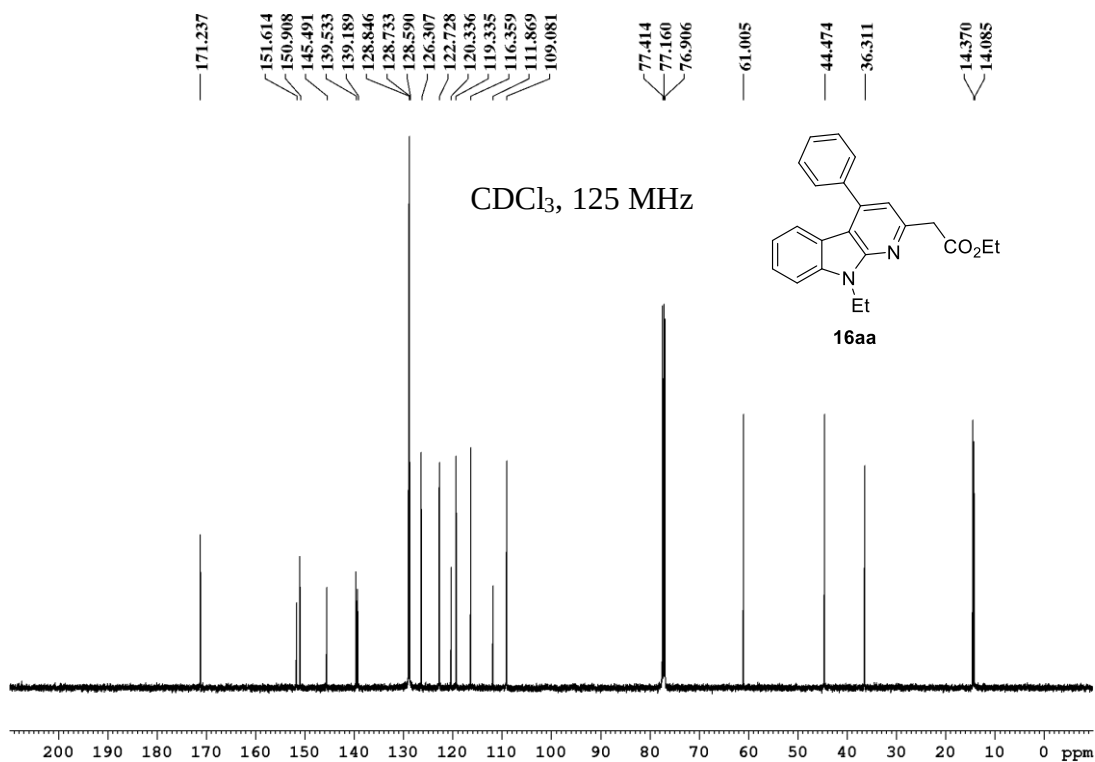


Figure A10: ¹³C{¹H} NMR spectrum of compound **16aa**

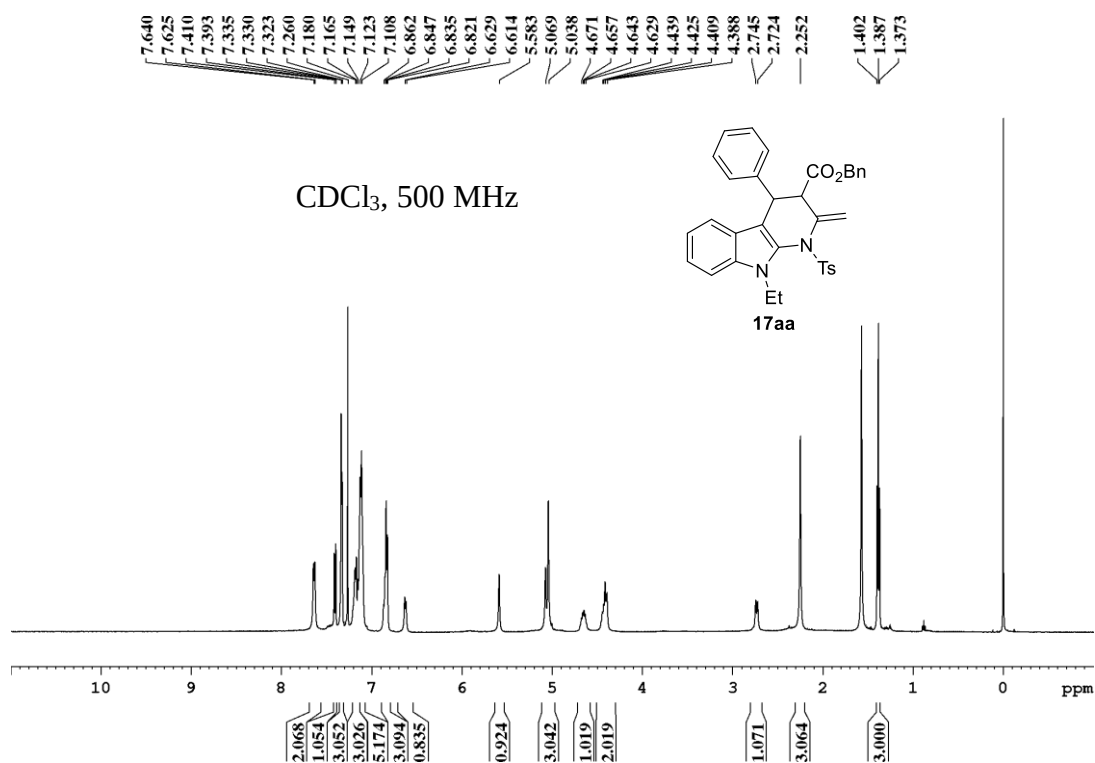


Figure A11: ¹H NMR spectrum of compound **17aa**

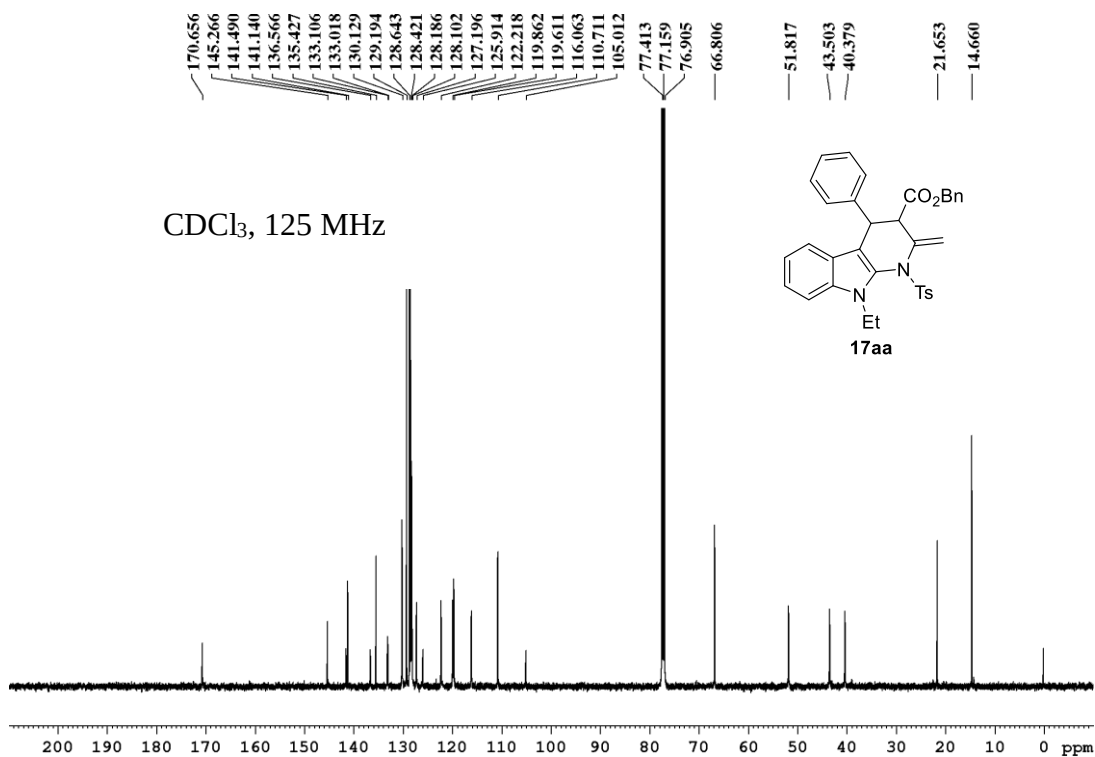


Figure A12: ¹³C{¹H} NMR spectrum of compound **17aa**

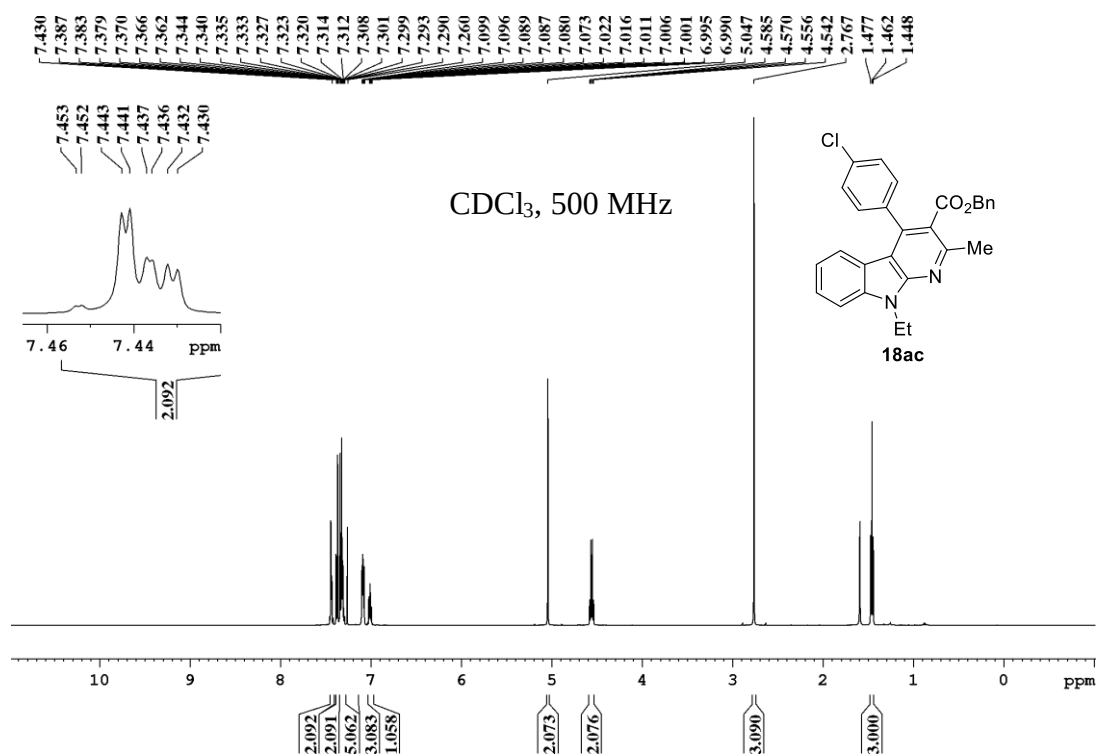


Figure A13: ¹H NMR spectrum of compound **18ac**

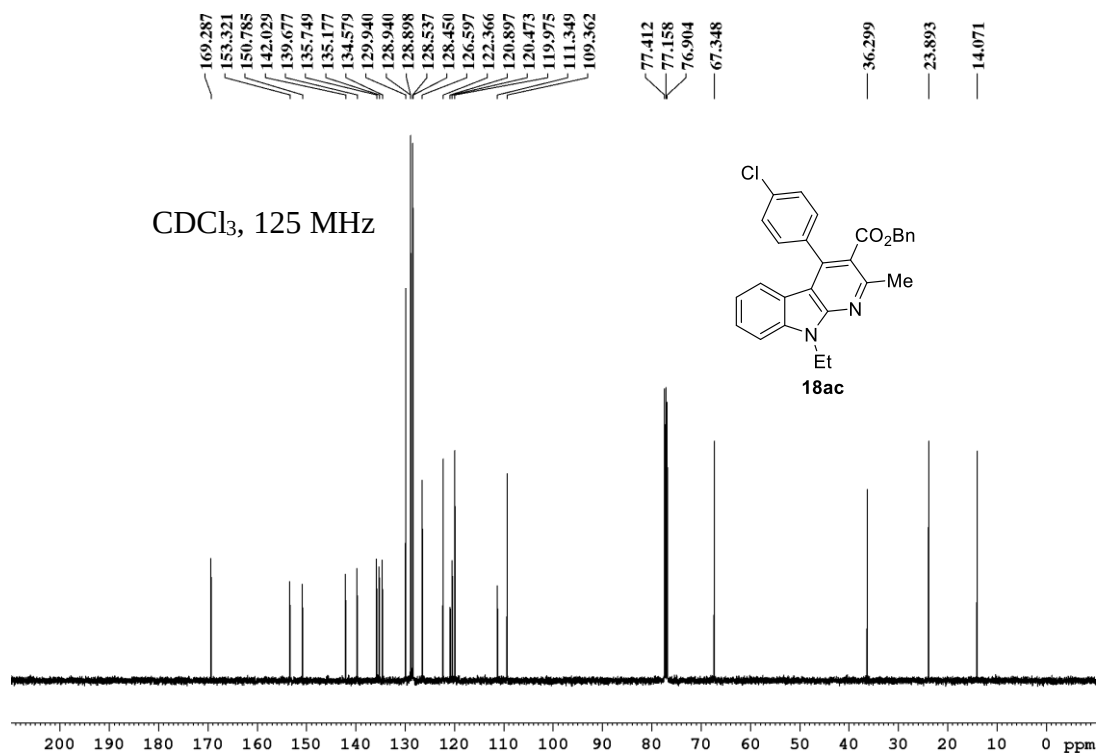


Figure A14: ¹³C{¹H} NMR spectrum of compound **18ac**

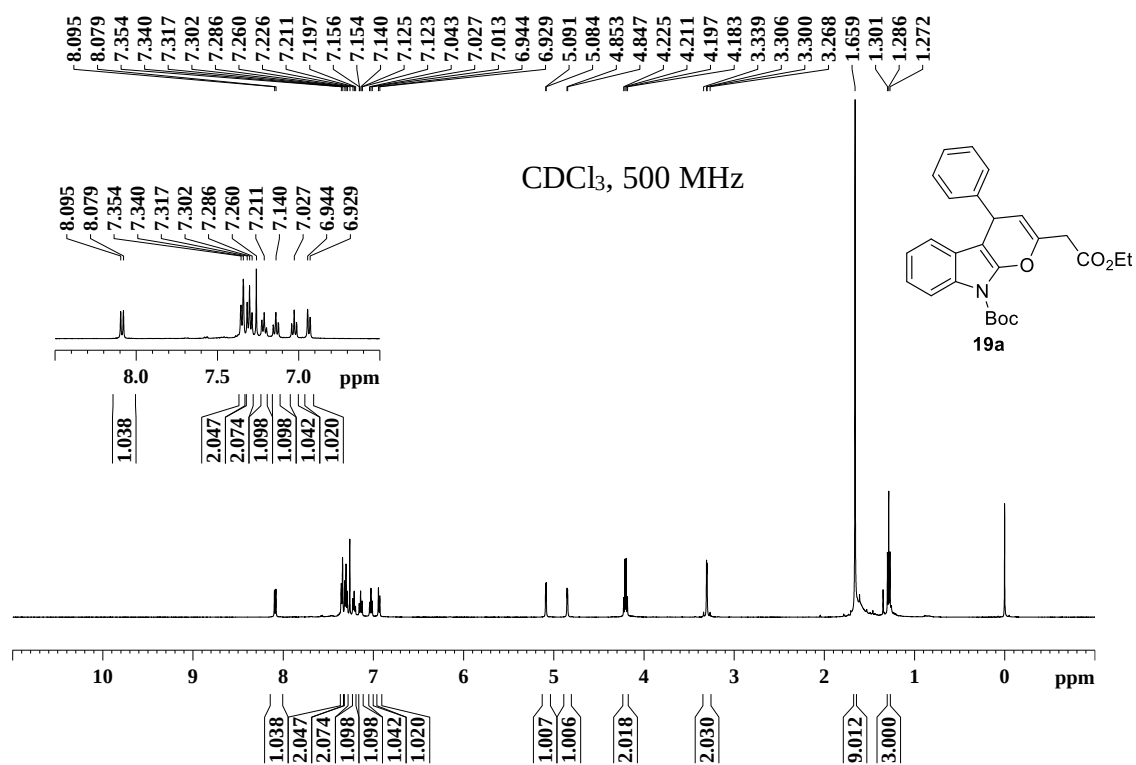


Figure A15: ¹H NMR spectrum of compound 19a

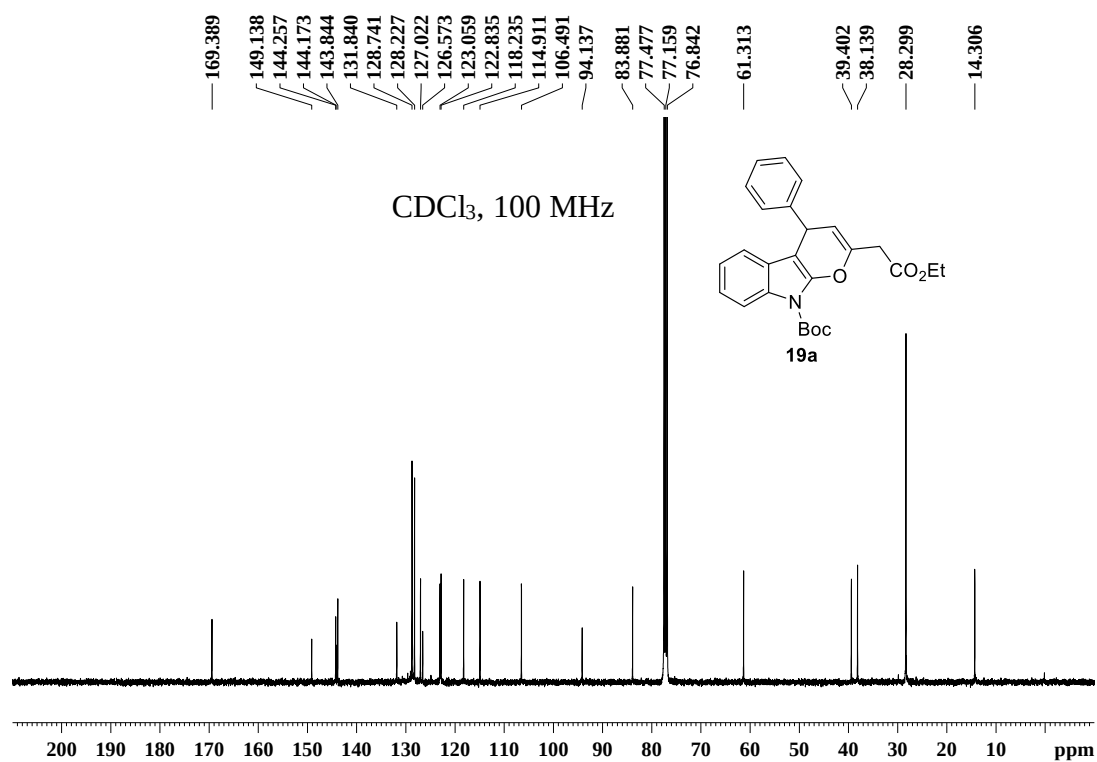


Figure A16: ¹³C{¹H} NMR spectrum of compound 19a

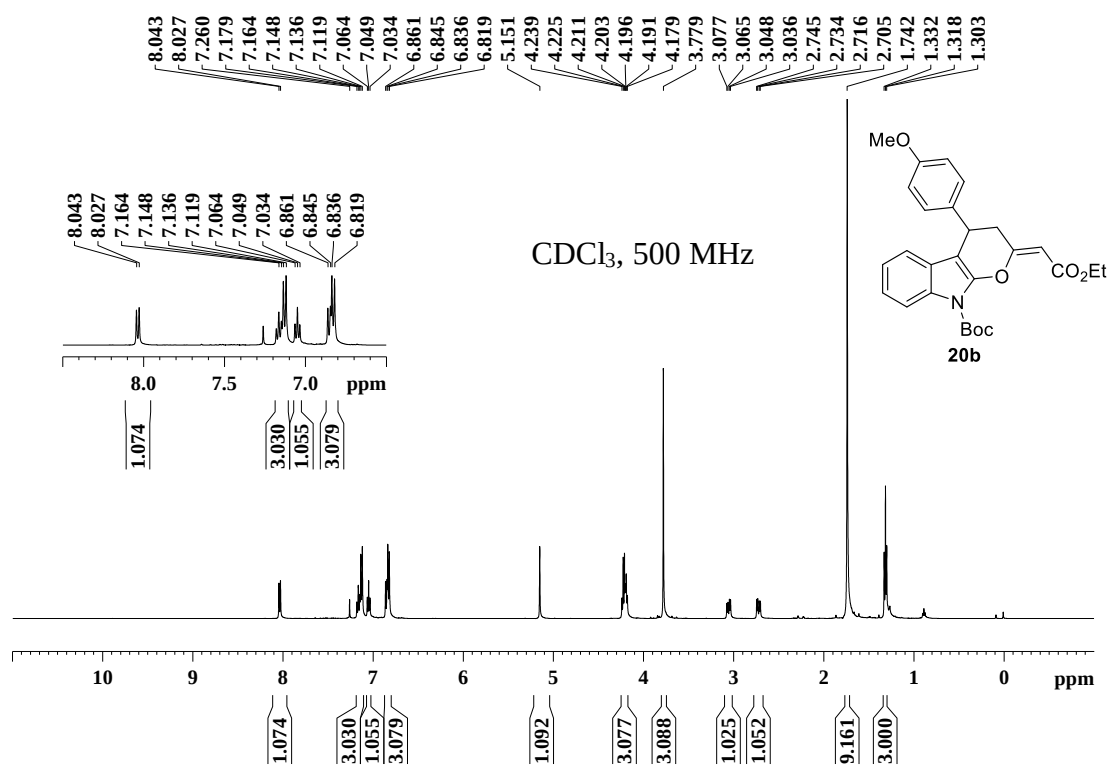


Figure A17: ¹H NMR spectrum of compound **20b**

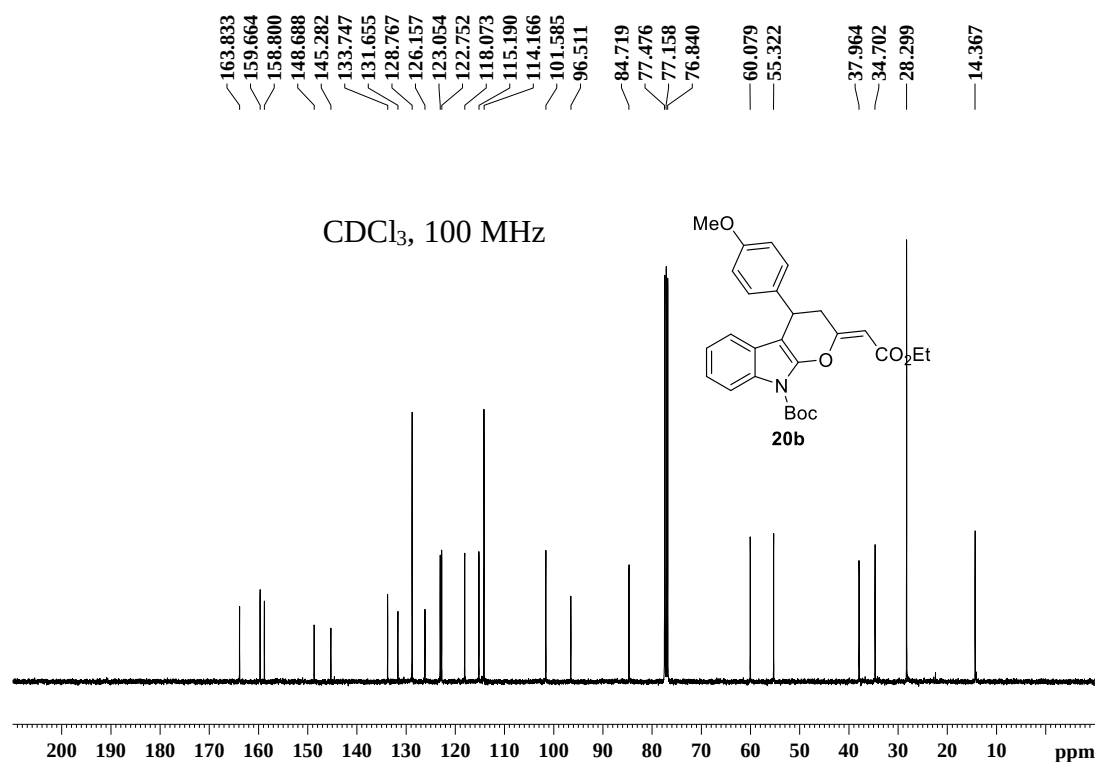


Figure A18: ¹³C{¹H} NMR spectrum of compound **20b**

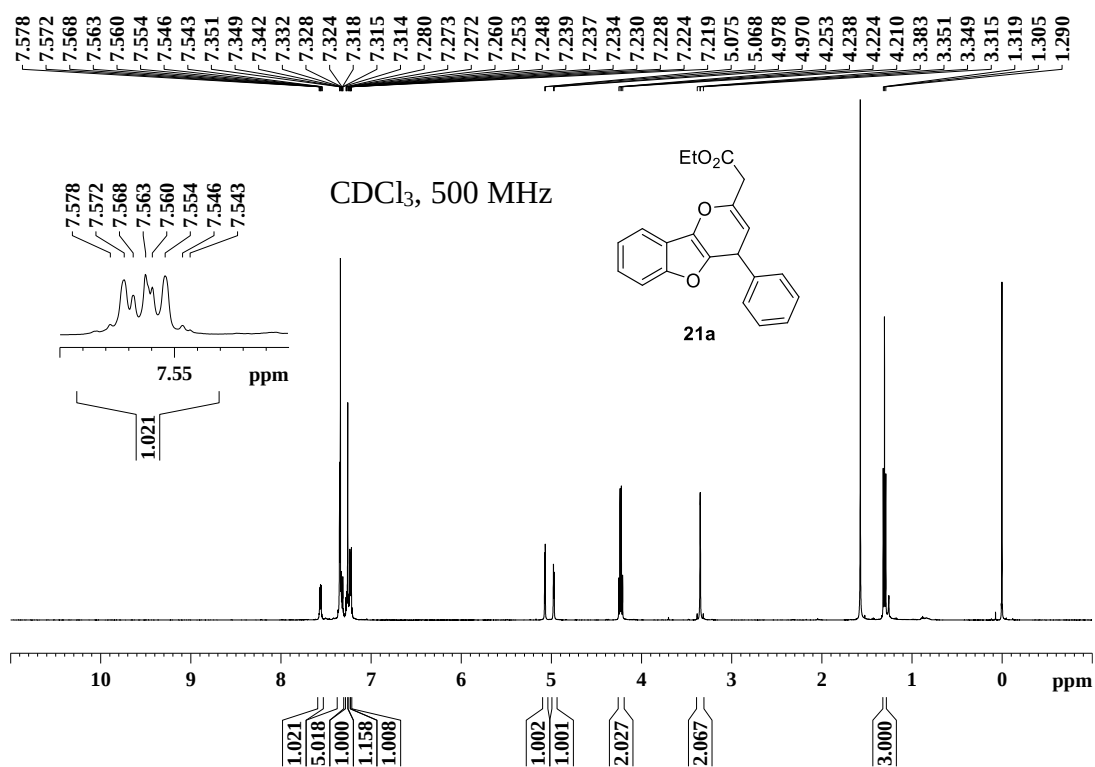


Figure A19: ^1H NMR spectrum of compound 21a

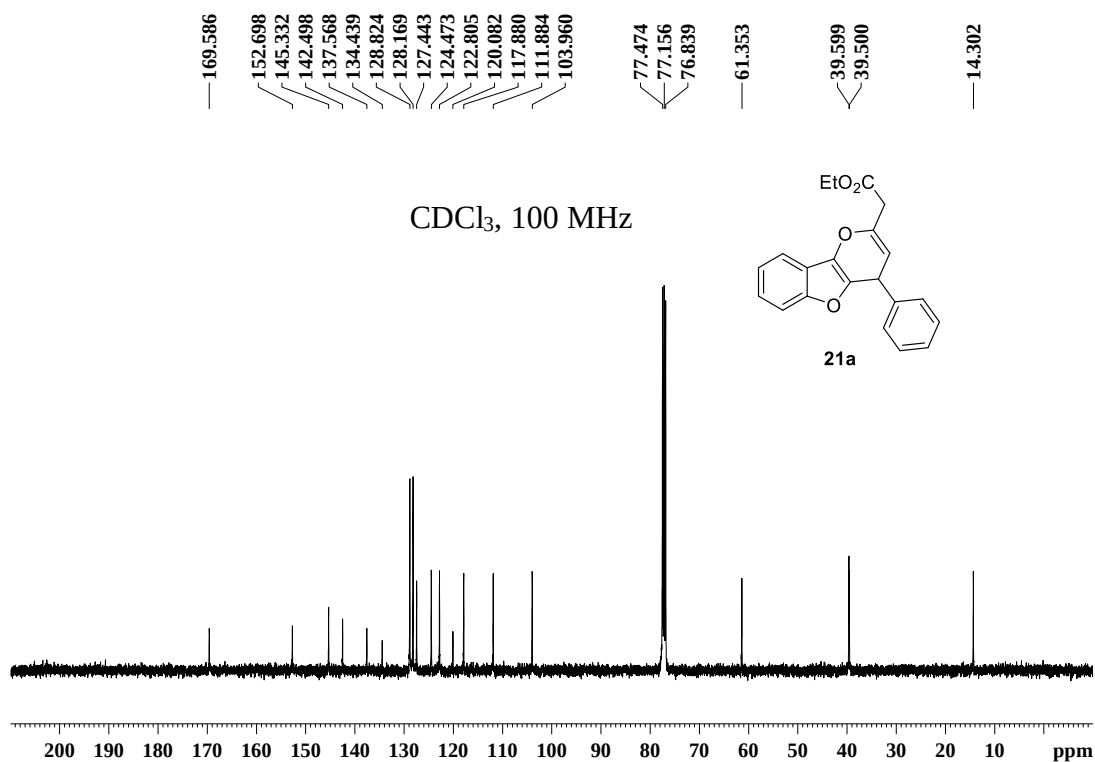


Figure A20: $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound 21a

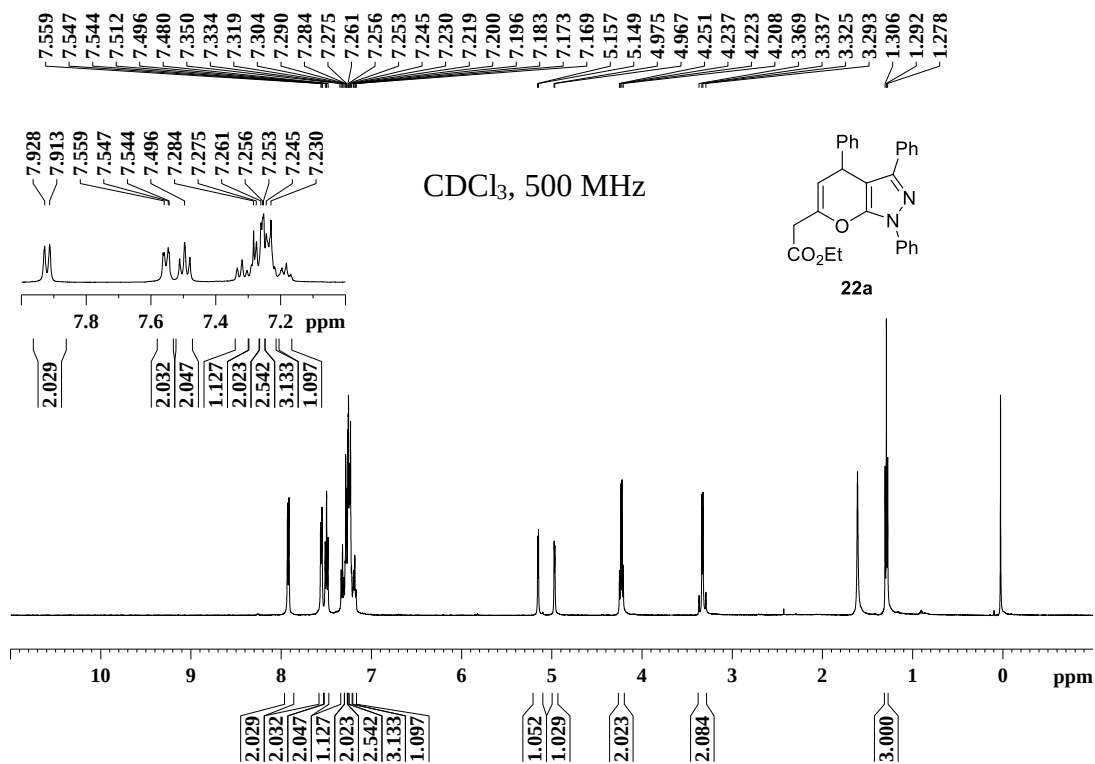


Figure A21: ¹H NMR spectrum of compound **22a**

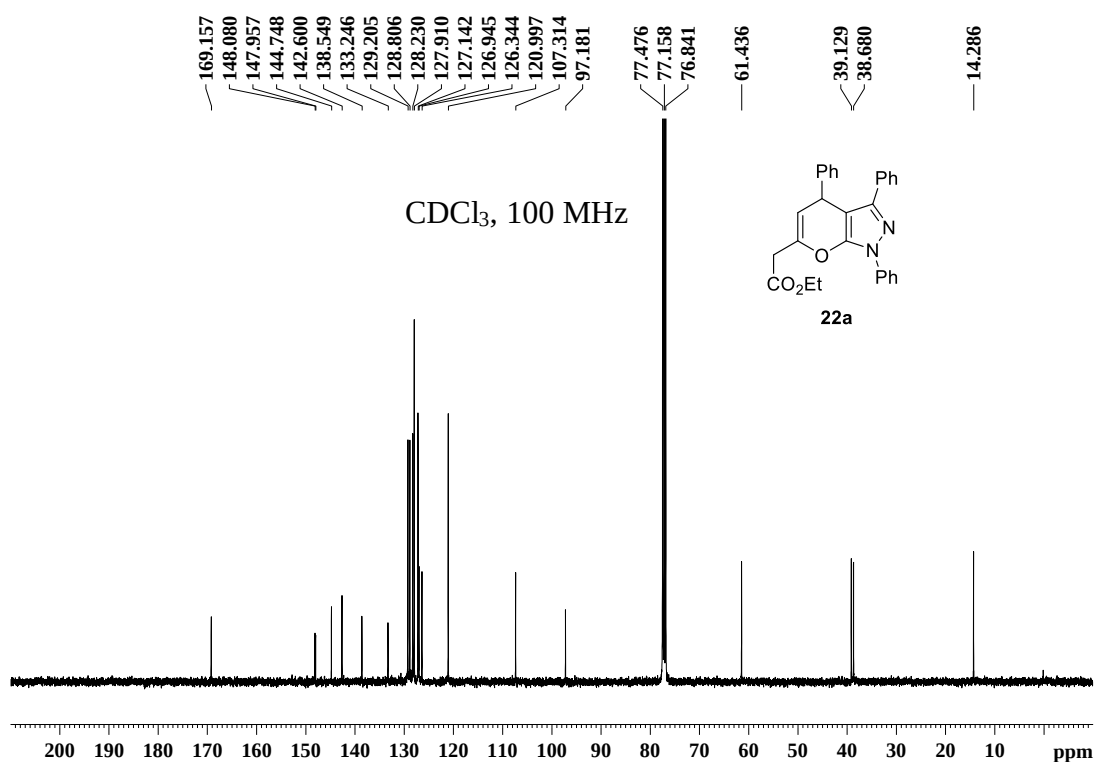


Figure A22: ¹³C{¹H} NMR spectrum of compound **22a**

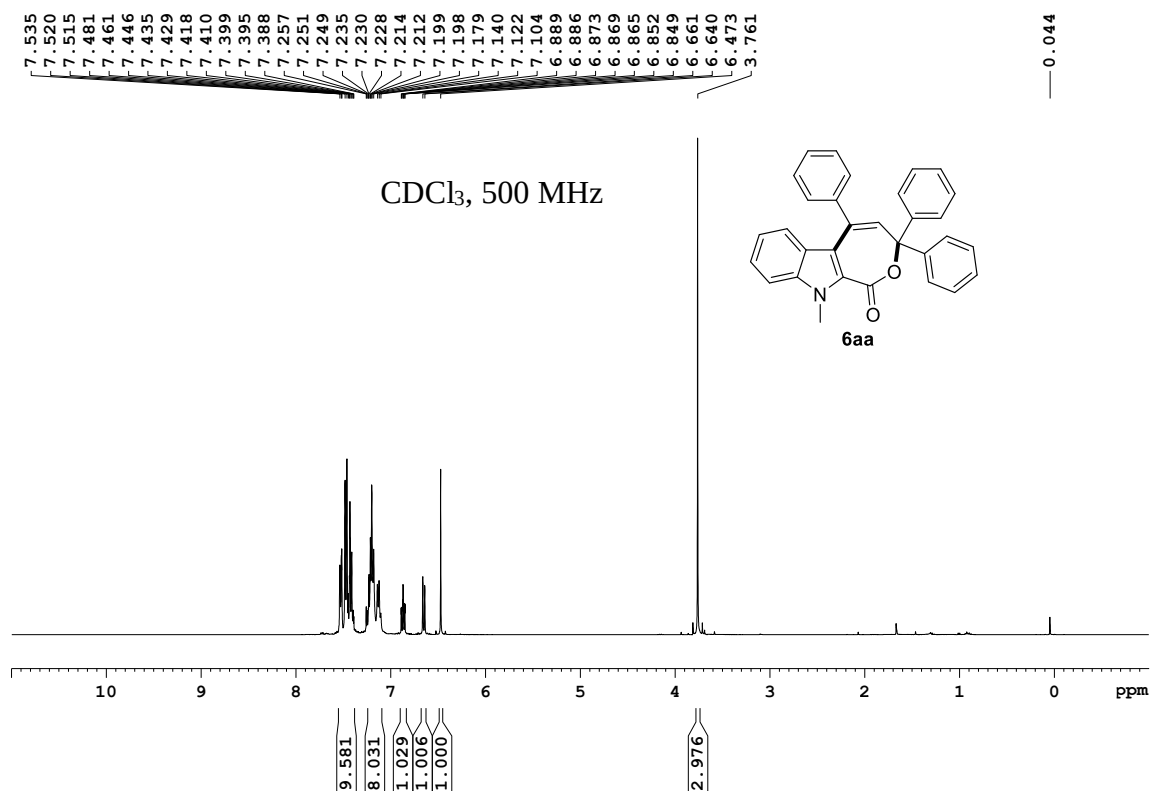


Figure A23: ¹H NMR spectrum of compound **6aa**

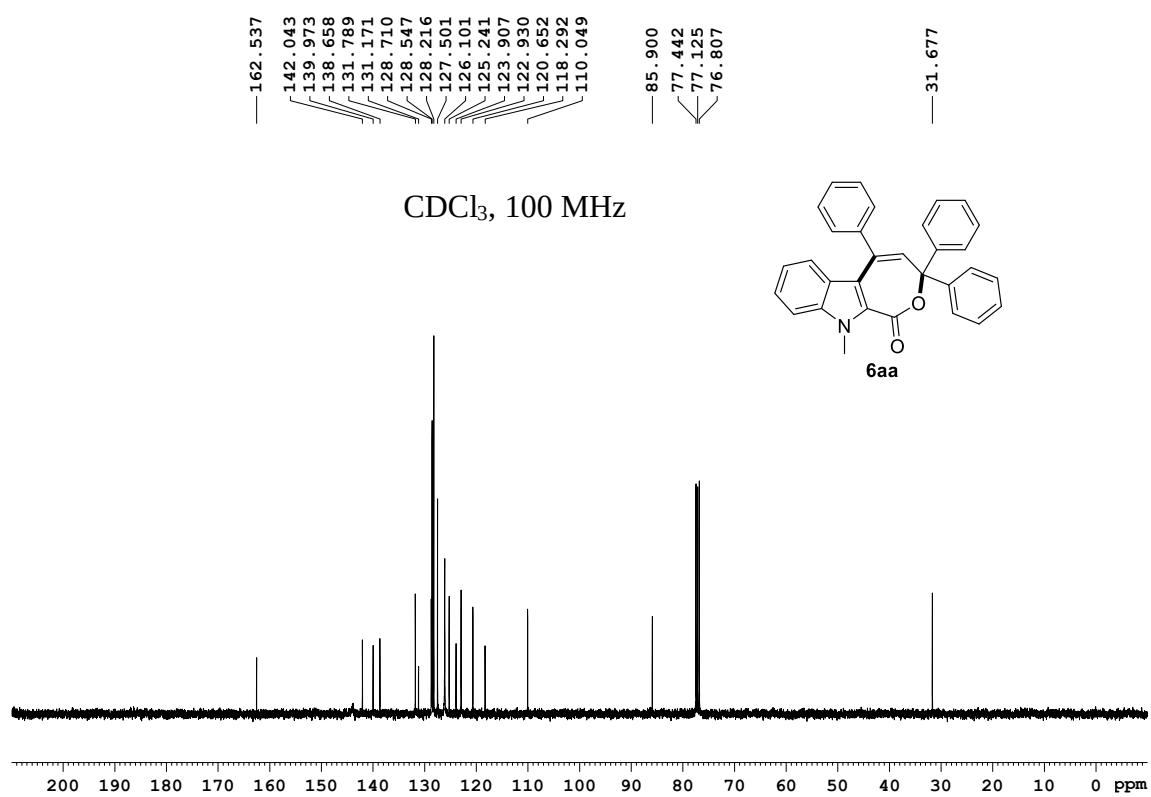


Figure A24: ¹³C{¹H} NMR spectrum of compound **6aa**

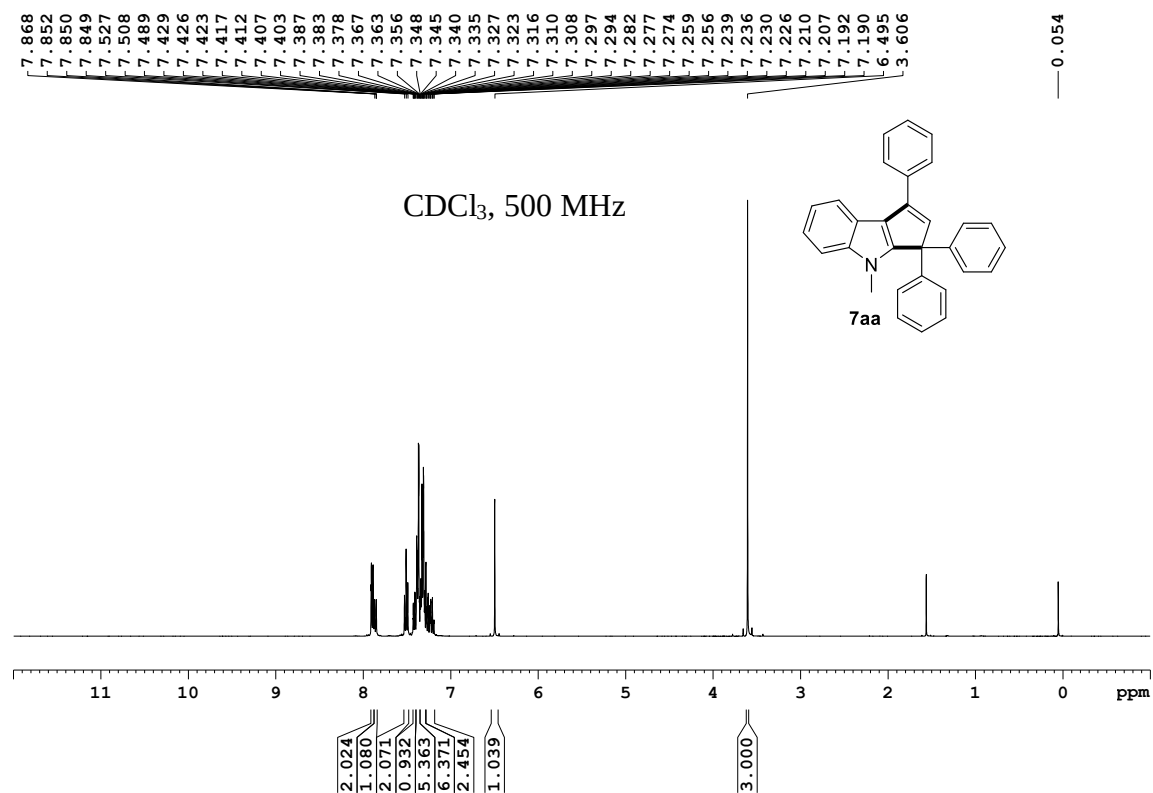


Figure A25: ¹H NMR spectrum of compound **7aa**

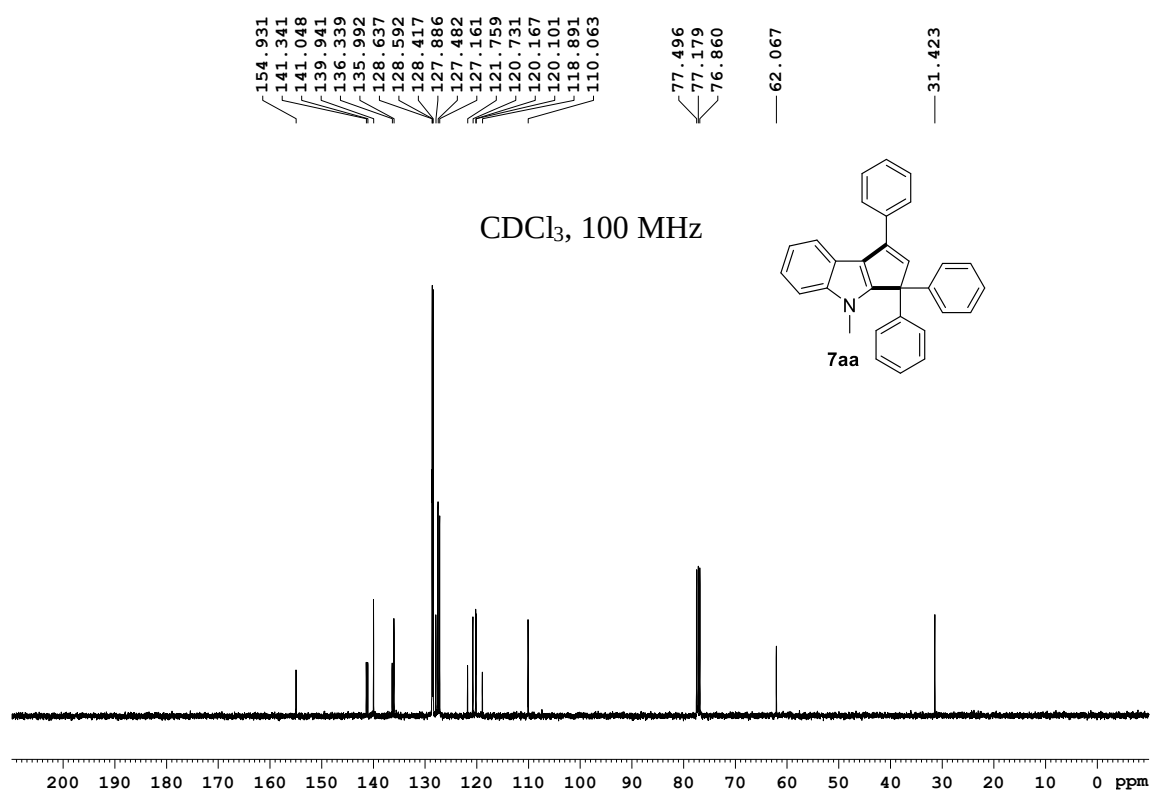


Figure A26: ¹³C{¹H} NMR spectrum of compound **7aa**

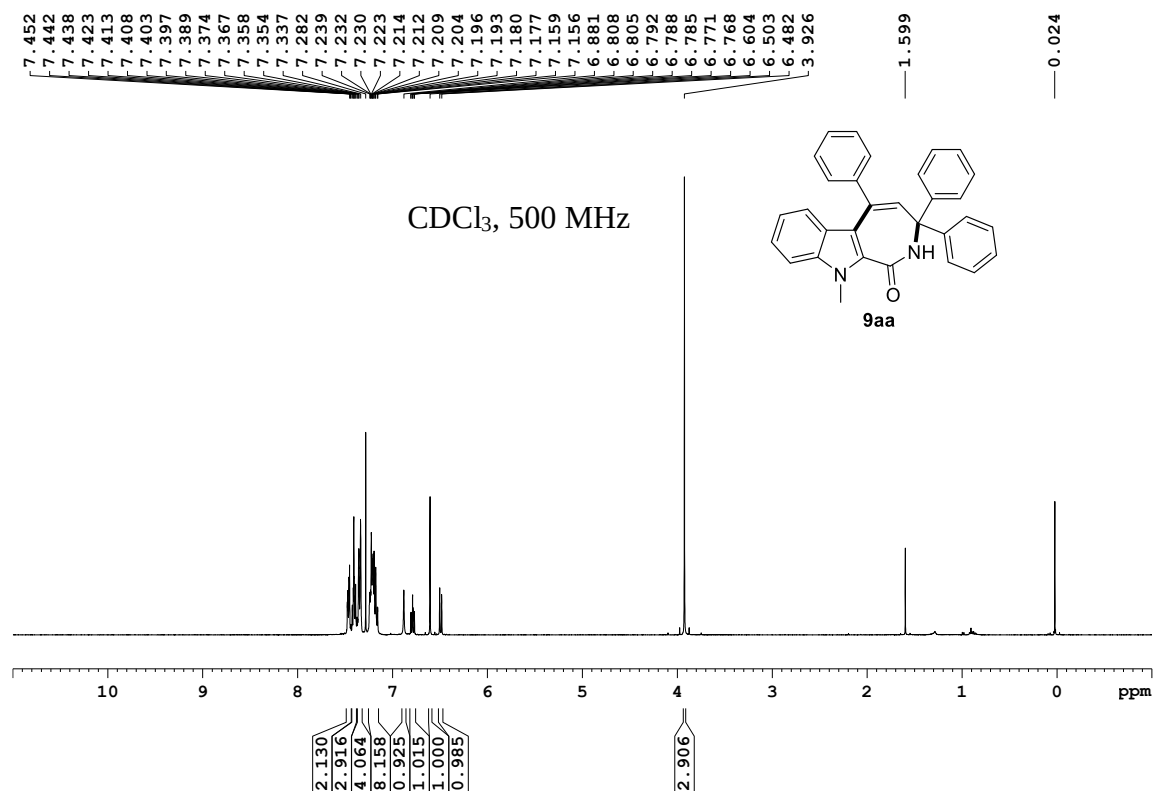


Figure A27: ^1H NMR spectrum of compound **9aa**

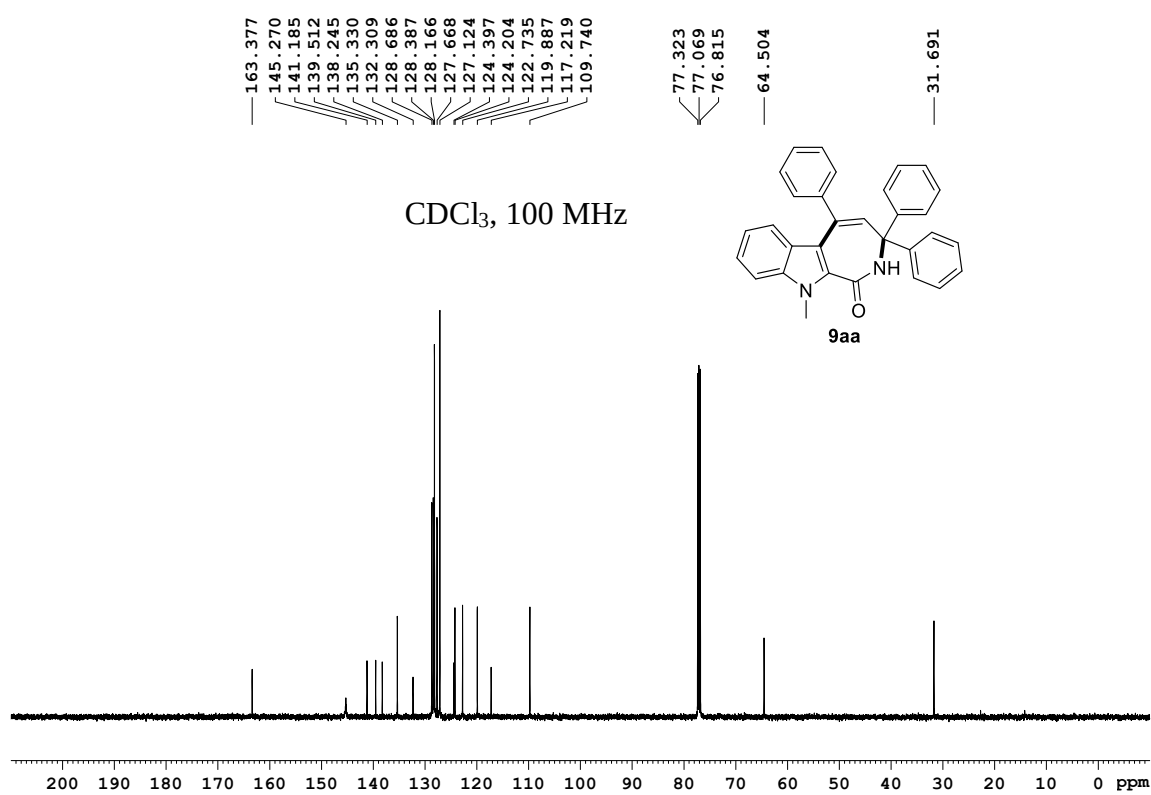


Figure A28: $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of compound **9aa**

B) CCDC numbers and atomic coordinates for X-ray structures reported in this thesis

CCDC numbers for the published compounds: 10ga, 11aa, 11ae, 12aa, 12ah, 15aa, 15ca, 16an, 16ba, 17ab, 18ga, 6aa, 6aj, 7al, 9ac, 7an, 4a, 9aa and 9ap are 2064415, 2064416, 2064417, 2064418, 2064419, 2206241, 2206242, 2206243, 2206244, 2206245, 2206246, 1915530, 1915531, 1915532, 1915533, 1915534, 1915537, 1915535, and 1915536, respectively.

Unpublished compounds: 19k, 20h, and 21a (part A)

Compound 19k

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck228

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck228

Bond precision:	C-C = 0.0051 Å	Wavelength=0.71073
Cell:	a=10.3479(3)	b=10.5057(3) c=11.7663(3)
	alpha=93.409(2)	beta=114.609(3) gamma=95.175(2)
Temperature:	299 K	

	Calculated	Reported
Volume	1151.55(6)	1151.54(6)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C24 H25 N O5 S	C24 H25 N O5 S
Sum formula	C24 H25 N O5 S	C24 H25 N O5 S
Mr	439.51	439.51
Dx, g cm ⁻³	1.268	1.268
Z	2	2
Mu (mm ⁻¹)	0.175	0.175
F000	464.0	464.0
F000'	464.47	
h,k,lmax	13,13,14	13,13,14
Nref	4994	4815
Tmin, Tmax	0.966, 0.976	0.587, 1.000
Tmin'	0.966	

Correction method= # Reported T Limits: Tmin=0.587 Tmax=1.000
AbsCorr = MULTI-SCAN

Data completeness= 0.964 Theta(max)= 26.923

R(reflections)= 0.0656(2815)	wR2(reflections)=
S = 1.041	0.2083(4815)
Npar= 284	

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

● **Alert level C**

PLAT220_ALERT_2_C	NonSolvent	Resd 1	C	Ueq(max)/Ueq(min)	Range	5.2	Ratio
PLAT222_ALERT_3_C	NonSolvent	Resd 1	H	Uiso(max)/Uiso(min)	Range	6.2	Ratio
PLAT230_ALERT_2_C	Hirshfeld	Test Diff	for	C18	--C19	.	6.6 s.u.
PLAT242_ALERT_2_C	Low	'MainMol'	Ueq	as Compared to	Neighbors of	C17	Check
PLAT242_ALERT_2_C	Low	'MainMol'	Ueq	as Compared to	Neighbors of	C18	Check
PLAT242_ALERT_2_C	Low	'MainMol'	Ueq	as Compared to	Neighbors of	C21	Check
PLAT340_ALERT_3_C	Low	Bond Precision	on	C-C Bonds		0.0051	Ang.
PLAT360_ALERT_2_C	Short	C(sp3)-C(sp3)	Bond	C18	- C19	.	1.34 Ang.

● **Alert level G**

PLAT793_ALERT_4_G	Model has Chirality at C3	(Centro SPGR)	R	Verify
PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L=	0.600	179	Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.		0	Info

- 0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
8 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
3 **ALERT level G** = General information/check it is not something unexpected
- 0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
7 ALERT type 2 Indicator that the structure model may be wrong or deficient
2 ALERT type 3 Indicator that the structure quality may be low
2 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check
-
-

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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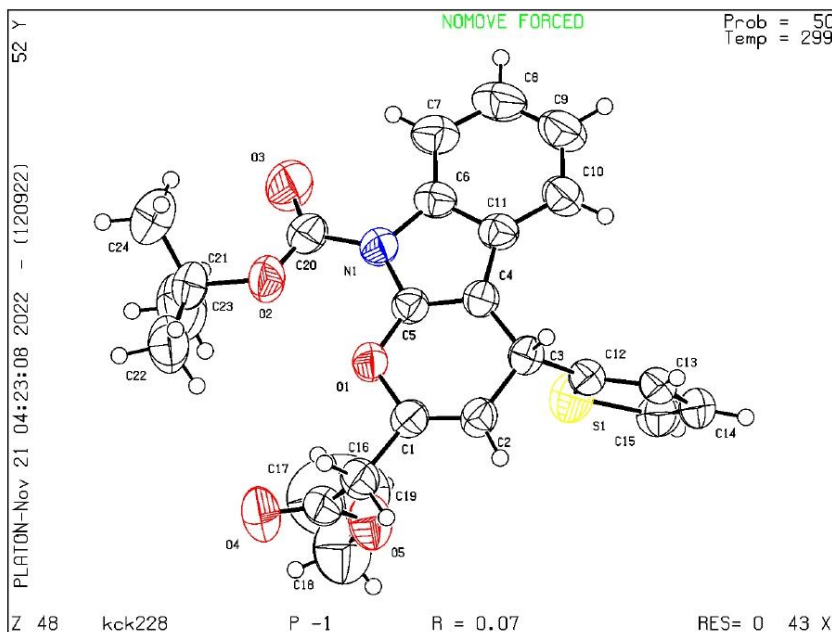
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Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

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Datablock kck228 - ellipsoid plot



Compound 20h

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck193

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck193

Bond precision: C-C = 0.0032 Å Wavelength=0.71073

Cell: a=11.7617 (4) b=21.8252 (8) c=9.9033 (3)
alpha=90 beta=107.445 (4) gamma=90

Temperature: 301 K

	Calculated	Reported
Volume	2425.26 (15)	2425.26 (15)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C27 H29 N O6	C27 H29 N O6
Sum formula	C27 H29 N O6	C27 H29 N O6
Mr	463.51	463.51
Dx, g cm ⁻³	1.270	1.269
Z	4	4
Mu (mm ⁻¹)	0.090	0.090
F000	984.0	984.0
F000'	984.51	
h, k, lmax	15, 28, 12	14, 27, 12
Nref	5445	5137
Tmin, Tmax	0.984, 0.991	0.651, 1.000
Tmin'	0.982	

```
Correction method= # Reported T Limits: Tmin=0.651 Tmax=1.000
AbsCorr = MULTI-SCAN
```

Data completeness= 0.943 Theta(max)= 27.267

```
R(reflections)= 0.0546( 2963)      wR2(reflections)=
S = 1.053                          0.1573( 5137)
Npar= 312
```

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

● **Alert level C**

PLAT220_ALERT_2_C	NonSolvent	Resd 1	C	Ueq(max)/Ueq(min) Range	3.1	Ratio
PLAT242_ALERT_2_C	Low	'MainMol'	Ueq as Compared to Neighbors of	C21	Check	
PLAT242_ALERT_2_C	Low	'MainMol'	Ueq as Compared to Neighbors of	C24	Check	
PLAT906_ALERT_3_C	Large K Value in the Analysis of Variance			2.965	Check	

● **Alert level G**

PLAT793_ALERT_4_G	Model has Chirality at C11	(Centro SPGR)	S	Verify
PLAT910_ALERT_3_G	Missing # of FCF Reflection(s) Below Theta(Min).		2	Note
PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L=	0.600	290	Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.		0	Info

0 **ALERT level A** = Most likely a serious problem - resolve or explain
0 **ALERT level B** = A potentially serious problem, consider carefully
4 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
4 **ALERT level G** = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
4 ALERT type 2 Indicator that the structure model may be wrong or deficient
2 ALERT type 3 Indicator that the structure quality may be low
2 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

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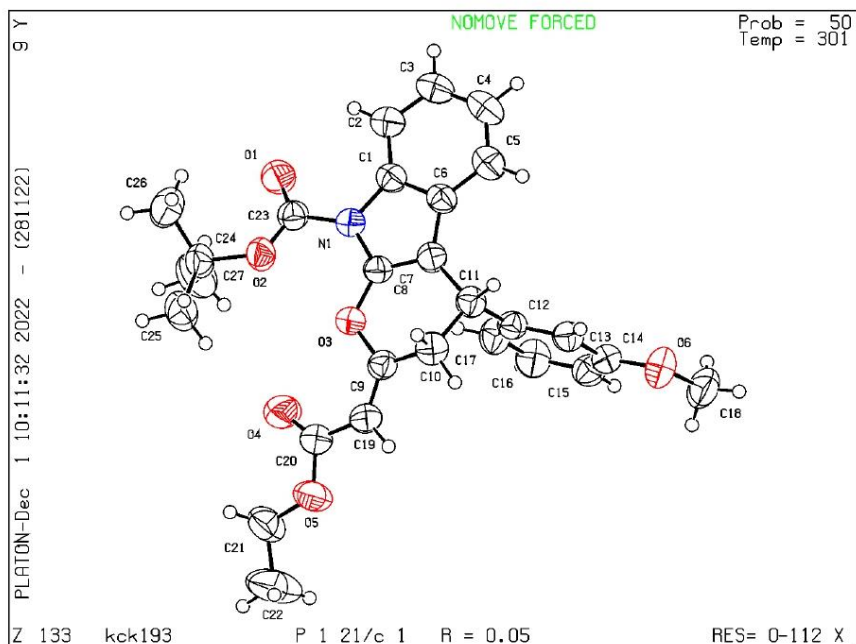
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Publication of your CIF in other journals

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Datablock kck193 - ellipsoid plot



Compound 21a

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck223

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck223

Bond precision: C-C = 0.0020 Å Wavelength=0.71073

Cell: a=8.2390 (2) b=8.5305 (2) c=12.8575 (3)
alpha=72.914 (2) beta=83.275 (2) gamma=75.314 (2)

Temperature: 297 K

	Calculated	Reported
Volume	834.67 (4)	834.67 (4)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C21 H18 O4	C21 H18 O4
Sum formula	C21 H18 O4	C21 H18 O4
Mr	334.35	334.35
Dx, g cm-3	1.330	1.330
Z	2	2
Mu (mm-1)	0.092	0.092
F000	352.0	352.0
F000'	352.18	
h,k,lmax	10,10,16	10,10,16
Nref	3724	3575
Tmin,Tmax	0.982,0.990	0.610,1.000
Tmin'	0.982	

```
Correction method= # Reported T Limits: Tmin=0.610 Tmax=1.000
AbsCorr = MULTI-SCAN
```

Data completeness= 0.960 Theta(max)= 27.218

```
R(reflections)= 0.0416( 2781)      wR2(reflections)=
S = 1.053                        0.1170( 3575)
Npar= 227
```

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

● **Alert level G**

PLAT154_ALERT_1_G	The s.u.'s on the Cell Angles are Equal ..(Note)	0.002 Degree
PLAT398_ALERT_2_G	Deviating C-O-C Angle From 120 for O1 .	105.3 Degree
PLAT793_ALERT_4_G	Model has Chirality at C7 (Centro SPGR)	S Verify
PLAT910_ALERT_3_G	Missing # of FCF Reflection(s) Below Theta(Min).	1 Note
PLAT912_ALERT_4_G	Missing # of FCF Reflections Above STh/L= 0.600	148 Note
PLAT978_ALERT_2_G	Number C-C Bonds with Positive Residual Density.	1 Info

0 **ALERT level A** = Most likely a serious problem - resolve or explain
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0 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
6 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
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1 ALERT type 3 Indicator that the structure quality may be low
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Publication of your CIF in IUCr journals

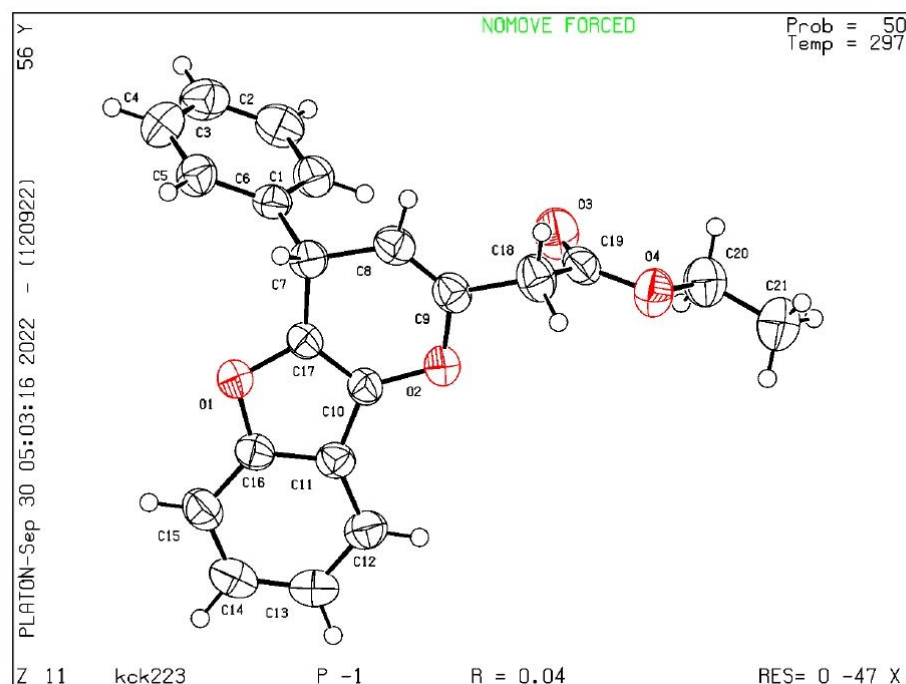
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Publication of your CIF in other journals

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Datablock kck223 - ellipsoid plot



Investigations on the Reactions of Acetoxy Allenates and Propargylic Alcohols with Indole Substrates

by Shubham Debnath

Submission date: 26-Dec-2022 03:58PM (UTC+0530)

Submission ID: 1986682568

File name: y_Allenates_and_Propargylic_Alcohols_with_Indole_Substrates.pdf (8.04M)

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