Reactivity of Acetoxy Allenoates with Bisnucleophiles

and

Annulation Reactions of Allenylphosphine Oxides

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

By

Sachin Chauhan

Reg. No. 18CHPH13

SCHOOL OF CHEMISTRY
UNIVERSITY OF HYDERABAD
HYDERABAD-500 046
INDIA
SEPTEMBER 2024

कायेन वाचा मनसेन्द्रियैर्वा
बुद्ध्यात्मना वा प्रकृतिस्वभावात् ।
करोमि यद्यत्सकलं परस्मै
नारायणयेति समर्पयामि ॥

(श्रीमद्भागवतं 11.2.36)

CONTENTS

Reactivity of Acetoxy Allenoates with Bisnucleophiles and Annulation Reactions of Allenylphosphine Oxides

STATEMENT

I hereby declare that the matter embodied in this thesis is the result of investigations 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 acknowledgments have been made wherever the work described is based on the findings of other investigators.

Hyderabad
September 2024

(05-09-2024)
Sachin Chauhan

DECLARATION

I, **Sachin Chauhan**, hereby declare that this thesis entitled ***"Reactivity of Acetoxy allenoates with Bisnucleophiles and Annulation Reactions of Allenylphosphine Oxides"*** 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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Date: 05-09-2024

Name: Sachin Chauhan
Reg. No. 18CHPH13

Kumara Swamy

Signature of the supervisor

Signature of the student

PROF. K.C. KUMARA SWAMY
School of Chemistry
University of Hyderabad
Hyderabad- 500 046, INDIA

CERTIFICATE

This is to certify that the thesis entitled ***"Reactivity of Acetoxy Allenoates with Bisnucleophiles and Annulation Reactions of Allenylphosphine Oxides"*** submitted by **Mr. Sachin Chauhan** bearing registration number **18CHPH13** 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 three publications before the submission of his thesis.

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

1. Kumar, A. S.; **Chauhan, S.**; Kumara Swamy, K. C. Contrasting Carboannulation Involving δ-Acetoxy Allenoate as a Four-Carbon Synthon Using DABCO and DMAP: Access to Spirocarbocyclic and *m*-Teraryl Scaffolds. *Org. Lett.* **2021**, *23*, 1123.
2. **Chauhan, S.;** Kumar, A. S.; Kumara Swamy, K. C. δ-Acetoxy Allenoate as a 5C-Synthon in Domino-Annulation with Sulfamidate Imines: Ready Access to Coumarins. *J. Org. Chem.*, **2023**, *88*, 12432.
3. **Chauhan, S.**; Kumara Swamy, K. C. Phosphine vs DBU Catalyzed Annulation Reactions of β'-Acetoxy Allenoates with Acyl-tethered Benzothiazole Bisnucleophiles: (4 + 3) or (4 + 1) vs (3 + 3) Annulation. *J. Org. Chem.*, **2024**, *89*, 10816.

It is planned to communicate the following paper:

4. **Chauhan, S.;** Kumara Swamy, K. C. [Pd] catalyzed domino (4 + 1)/(5 + 1) annulation reactions of allenylphosphine oxides with terminal alkynes and annulation reactions of sulfonamide-tethered vinylic propargyl alcohols with Ph_2PCl.

He has also made presentations in the following conferences:

1. Oral presentation in the XVIIth JNOST Conference for Research Scholars, University of Hyderabad, INDIA, January 2022.
2. Poster presentation in the Chemfest-2022 (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, April 2022.
3. Oral and Poster presentation in the Chemfest-2023 (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, March 2023.
4. Poster presentation in the FCSB-2024 (Indo-French Seminar), School of Chemistry, University of Hyderabad, INDIA, January 2024.

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

S.No.	Course No.	Title of the course	No. of credits	Grade
1	CY801	Research proposal	4	Pass
2	CY805	Instrumental methods-A	4	Pass
3	CY806	Instrumental methods-B	4	Pass

Final Result: Passed

Kumara Swamy

Prof. K. C. Kumara Swamy

(Thesis supervisor)

PROF. K.C. KUMARA SWAMY
School of Chemistry
University of Hyderabad
Hyderabad- 500 046, INDIA

Hyderabad

September 2024

Dean

School of Chemistry

University of Hyderabad

Hyderabad, 500046

INDIA

Dean
School of Chemistry
University of Hyderabad
Hyderabad-500 046.

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I want to express my heartfelt thanks to my parents, Mrs. Meena Devi and Mr. Rajender Singh Chauhan, and my nephew Anant for their immense love and support.

Sachin Chauhan..........

LIST OF PUBLICATIONS

(A) Published papers:

1. Advances in [4+3]-Annulation/ Cycloaddition Reactions Leading to Homo- and Heterocycles with Seven-Membered Rings
K. Selvaraj, **Sachin Chauhan,** K. Sandeep, .and K. C. Kumara Swamy*
Chem. Asian J. **2020**, *15*, 2380 (review).

2. Contrasting Carboannulation Involving δ-Acetoxy Allenoate as a Four-Carbon Synthon Using DABCO and DMAP: Access to Spirocarbocyclic and *m*-Teraryl Scaffolds
A. Sanjeeva Kumar, **Sachin Chauhan** and K. C. Kumara Swamy*
Org. Lett. **2021**, *23*, 1123.

3. Divergent Reactivity of δ- and β′-Acetoxy Allenoates with 2-Sulfonamidoindoles via Phosphine Catalysis: Entry to Dihydro-α-carboline, α-Carboline, and Spiro-cyclopentene Motifs
Subham Debnath, A. Sanjeeva Kumar, **Sachin Chauhan** and K. C. Kumara Swamy*
J. Org. Chem. **2021**, *17,* 11583.

4. Stereo-and Regioselective (3 + 2) Cycloaddition of Acetoxy Allenoates with Azides: Metal-Free Synthesis of Multisubstituted Triazoles
Asif Ali Qureshi, A. Sanjeeva Kumar, **Sachin Chauhan** and K. C. Kumara Swamy*
Synthesis **2022**, *54,* 965.

5. Palladium catalyzed nitrile insertion and cyanation of biindoles: Synthesis of indole fused α-carboline scaffolds *via* double C-H activation
A. Kalyani, R. N. P. Tulichala, **Sachin Chauhan** and K. C. Kumara Swamy*
Tetrahedron Lett. **2022**, *89,* 153600.

6. Annulations of Acetoxy Allenoates with Iminoindolines: α-Carboline Scaffolds with Varied Substituents
Subham Debnath, A. Sanjeeva Kumar**, Sachin Chauhan** and K. C. Kumara Swamy*
Adv. Synth. Catal. **2022**, *364,* 4316.

7. Annulation of acetoxy allenoates with enolisable carbonyl substrates leading to fused pyrans
Subham Debnath, **Sachin Chauhan** and K. C. Kumara Swamy*
Org. Biomol. Chem. **2023**, *21,* 5021.

8. δ-Acetoxy Allenoate as a 5C-Synthon in Domino-Annulation with Sulfamidate Imines: Ready Access to Coumarins

Sachin Chauhan, A. Sanjeeva Kumar and K. C. Kumara Swamy*

J. Org. Chem. **2023**, *88,* 12432.

9. Phosphine vs DBU Catalyzed Annulation Reactions of *β'*-Acetoxy Allenoates with Acyl-tethered Benzothiazole Bisnucleophiles: (4 + 3) or (4 + 1) vs (3 + 3) Annulation

Sachin Chauhan, and K. C. Kumara Swamy*

J. Org. Chem. **2024**, *89,* 10816.

10. DBU catalyzed (3 + 3) annulation of δ/β′-acetoxy allenoates with benzo-oxathiin-dioxide and phenylthiazolone: Synthesis of fused dihydropyrans.

Asif Ali Qureshi, **Sachin Chauhan** and K. C. Kumara Swamy*

J. Chem. Sci. **2024** (doi.org/10.1007/s12039-024-02302-5)

(B) To be published:

11. [Pd] catalyzed domino (4 + 1)/(5 + 1) annulation reactions of allenylphosphine oxides with terminal alkynes and annulation reactions of sulfonamide-tethered vinylic propargyl alcohols with Ph_2PCl

Sachin Chauhan and K. C. Kumara Swamy*

PARTICIPATION IN CONFERENCES/ SYMPOSIA

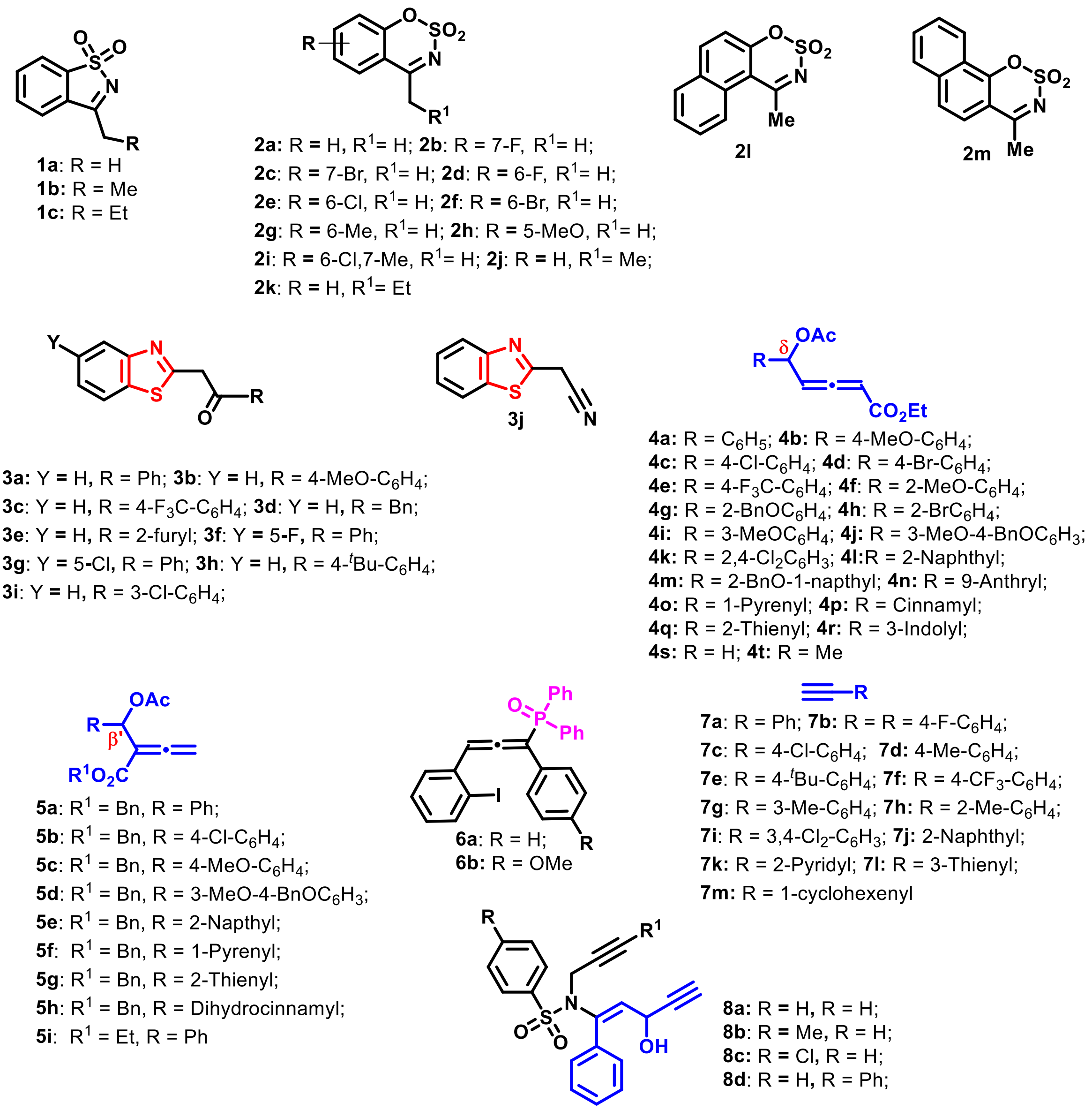
1. **Sachin Chauhan**, A. Sanjeeva Kumar, and K. C. Kumara Swamy
   δ-Acetoxy Allenoate as a Four-Carbon Synthon in Carboannulations Using DABCO and DMAP
   Oral presentation in the *XVII*th JNOST Conference for Research Scholars, University of Hyderabad, INDIA, January **2022**.
2. **Sachin Chauhan**, A. Sanjeeva Kumar, and K. C. Kumara Swamy
   δ-Acetoxy Allenoate as a Four or Five-Carbon Synthon in Carboannulations
   Poster presentation in the *Chemfest-2022* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, April **2022**.
3. **Sachin Chauhan**, A. Sanjeeva Kumar, and K. C. Kumara Swamy
   Exploration of δ-Acetoxy Allenoates as *3C* or *5C* Synthons in Annulation Reactions
   Oral and Poster presentation in the *Chemfest-2023* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, March **2023**.
4. **Sachin Chauhan** and K. C. Kumara Swamy
   (4 + 1), (3 + 3) and (4 + 3) Annulation reactions of β'-acetoxy allenoates under Lewis's base catalysis
   Poster presentation in the *FCSB-2024* (Indo-French Seminar), School of Chemistry, University of Hyderabad, INDIA, January **2024**.

Synopsis

This thesis is divided into three chapters. Chapter 1 deals with the literature relevant to the present study. In Chapter 2, the results obtained in the present work are discussed. The following topics are covered: (i) Contrasting carboannulation involving δ-acetoxy allenoate as a four-carbon synthon using DABCO or DMAP to access spirocarbocyclics or *m*-teraryls, respectively, (ii) δ-Acetoxy allenoate as a 5C-synthon in domino-annulation with sulfamidate imines to afford coumarins, (iii) Phosphine vs DBU catalyzed reactions of β'-acetoxy allenoates with acyl-tethered benzothiazole bisnucleophiles involving (4 + 3)/ (4 + 1) or (3 + 3) annulations, and (iv) [Pd]-catalyzed domino (4 + 1)/(5 + 1) annulation reactions of *o*-iodoaryl substituted allenylphosphine oxides with terminal alkynes as well as reaction of vinylic propargyl alcohols with Ph_2PCl resulting in 4-aminonaphthalenyl-diphenylphosphine oxides.

The compounds synthesized in the present study are, in general, characterized by melting point, IR, and NMR (^{1}H, ^{13}C, ^{19}F, and ^{31}P) techniques in conjunction with HRMS. X-ray structure determination has been undertaken wherever required. The references are compiled after Chapter 3.

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 using the available methodologies (with modifications where necessary) in the literature.



1a: R = H
1b: R = Me
1c: R = Et

2a: R = H, R^1= H; **2b**: R = 7-F, R^1= H;
2c: R = 7-Br, R^1= H; **2d**: R = 6-F, R^1= H;
2e: R = 6-Cl, R^1= H; **2f**: R = 6-Br, R^1= H;
2g: R = 6-Me, R^1= H; **2h**: R = 5-MeO, R^1= H;
2i: R = 6-Cl,7-Me, R^1= H; **2j**: R = H, R^1= Me;
2k: R = H, R^1= Et

2l

2m

3j

3a: Y = H, R = Ph; **3b**: Y = H, R = 4-MeO-C_6H_4;
3c: Y = H, R = 4-F_3C-C_6H_4; **3d**: Y = H, R = Bn;
3e: Y = H, R = 2-furyl; **3f**: Y = 5-F, R = Ph;
3g: Y = 5-Cl, R = Ph; **3h**: Y = H, R = 4-^{t}Bu-C_6H_4;
3i: Y = H, R = 3-Cl-C_6H_4;

4a: R = C_6H_5; **4b:** R = 4-MeO-C_6H_4;
4c: R = 4-Cl-C_6H_4; **4d**: R = 4-Br-C_6H_4;
4e: R = 4-F_3C-C_6H_4; **4f**: R = 2-MeO-C_6H_4;
4g: R = 2-BnOC_6H_4; **4h**: R = 2-BrC_6H_4;
4i: R = 3-MeOC_6H_4; **4j:** R = 3-MeO-4-BnOC_6H_3;
4k: R = 2,4-$Cl_2C_6H_3$; **4l:**R = 2-Naphthyl;
4m: R = 2-BnO-1-napthyl; **4n:** R = 9-Anthryl;
4o: R = 1-Pyrenyl; **4p:** R = Cinnamyl;
4q: R = 2-Thienyl; **4r:** R = 3-Indolyl;
4s: R = H; **4t:** R = Me

5a: R^1 = Bn, R = Ph;
5b: R^1 = Bn, R = 4-Cl-C_6H_4;
5c: R^1 = Bn, R = 4-MeO-C_6H_4;
5d: R^1 = Bn, R = 3-MeO-4-BnOC_6H_3;
5e: R^1 = Bn, R = 2-Napthyl;
5f: R^1 = Bn, R = 1-Pyrenyl;
5g: R^1 = Bn, R = 2-Thienyl;
5h: R^1 = Bn, R = Dihydrocinnamyl;
5i: R^1 = Et, R = Ph

6a: R = H;
6b: R = OMe

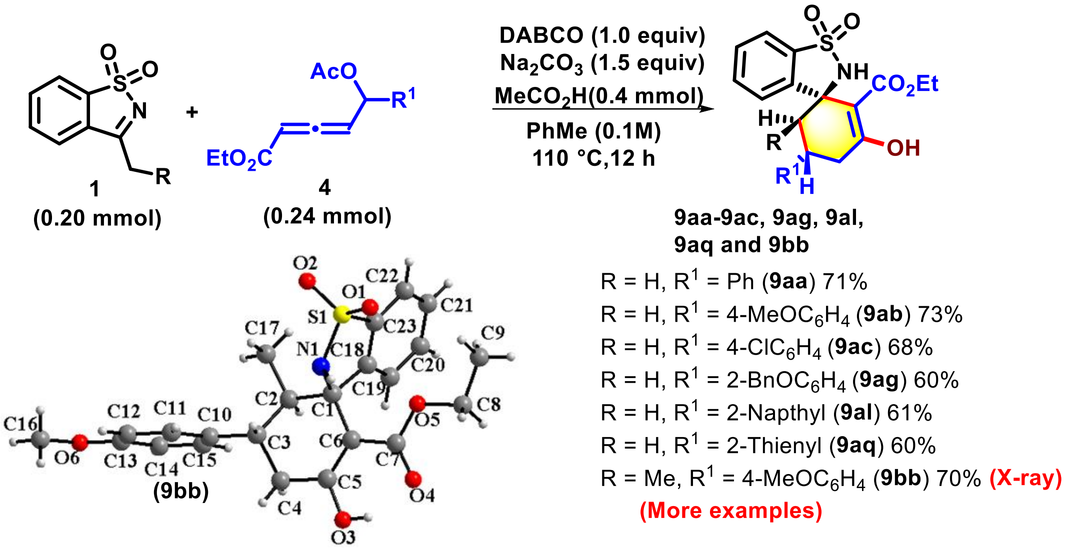
7a: R = Ph; **7b**: R = R = 4-F-C_6H_4;
7c: R = 4-Cl-C_6H_4; **7d**: 4-Me-C_6H_4;
7e: R = 4-^{t}Bu-C_6H_4; **7f:** R = 4-CF_3-C_6H_4;
7g: R = 3-Me-C_6H_4; **7h:** R = 2-Me-C_6H_4;
7i: R = 3,4-Cl_2-C_6H_3; **7j:** 2-Naphthyl;
7k: R = 2-Pyridyl; **7l:** R = 3-Thienyl;
7m: R = 1-cyclohexenyl

8a: R = H, R = H;
8b: R = Me, R = H;
8c: R = Cl, R = H;
8d: R = H, R = Ph;

Chart 1: Precursors used in the present study

(i) DABCO-mediated synthesis of spirocyclic sultams from *δ*-acetoxy allenoates and cyclic sulfonamide imines *via* (4 + 2) annulation

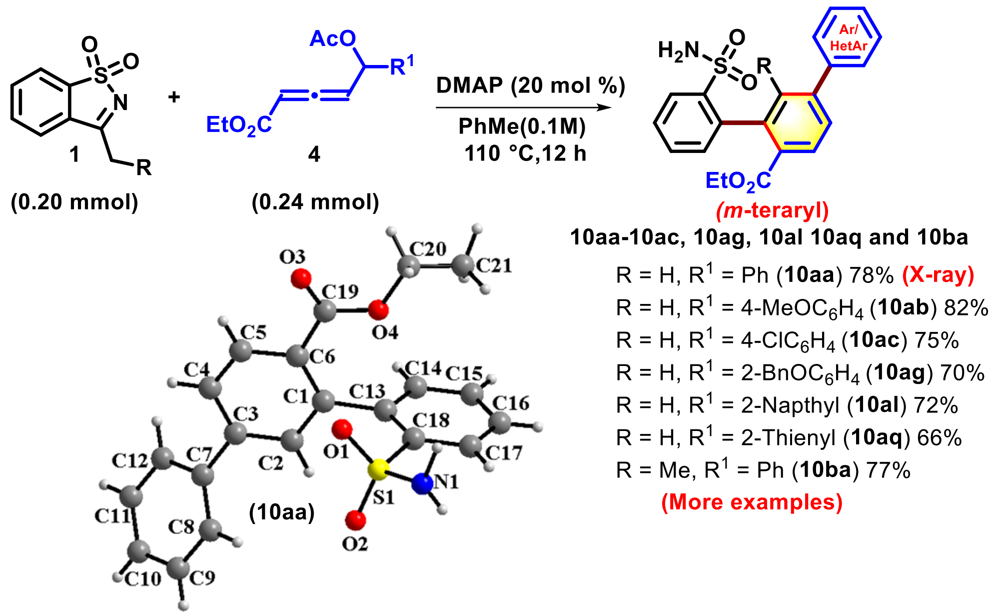
The spiro-annulation reaction between alkyl benzoisothiazole dioxides (*N*-sulfonyl ketimines) **1a**-**b** and *δ*-acetoxy allenoates (e.g., **4a-c**, **4g**, **4l**, and **4q**), facilitated by a combination of DABCO and acetic acid, results in the formation of a predominantly single diastereomeric product through chemo- and regio-selective (4 + 2)-carbo-annulation. This process affords spirocyclic sultams (e.g., **9aa-9ac**, **9ag**, **9al**, **9aq**, and **9bb**) in good yields (Scheme 1). In this reaction, the *δ*-acetoxy allenoate functions as a *4C*-synthon. Possible mechanistic pathways for the formation of these products are discussed.



Scheme 1: Synthesis of spirocyclic sultams from δ-acetoxy allenoates and cyclic sulfonamide imines (alkyl benzoisothiazole dioxides)

(ii) DMAP catalyzed synthesis of *m*-teraryls from δ-acetoxy allenoates and cyclic sulfonamide imines *via* (4 + 2) annulation

Based on the above successful annulation of sulfonamide imines **1** with δ-acetoxy allenoates **4**, we performed a reaction by changing the base from DABCO to DMAP. In this case, however, we obtained the benzannulated unsymmetrical *m*-teraryl scaffolds **10** in good yields. Optimization of the conditions revealed that the reaction took place in the presence of catalytic DMAP and there was no requirement of AcOH or Na_2CO_3. We were able to generalize the reaction using sulfonamide imines **1a-1c** and δ-acetoxy allenoates **4a-c**, **4g**, **4l**, and **4q** that furnished the *m*-teraryls **10aa-10ac**, **10ag**, **10al**, **10aq**, and **10ba** (Scheme 2). The reaction proceeds *via* Mannich coupling, proton transfers, and C-N bond cleavage. Remarkably, the products obtained by using DABCO and DMAP are mutually exclusive. Thus, in the reaction with allenoate using DABCO, teraryls were not found, and in the reaction using DMAP, spirocyclics were not at all observed.



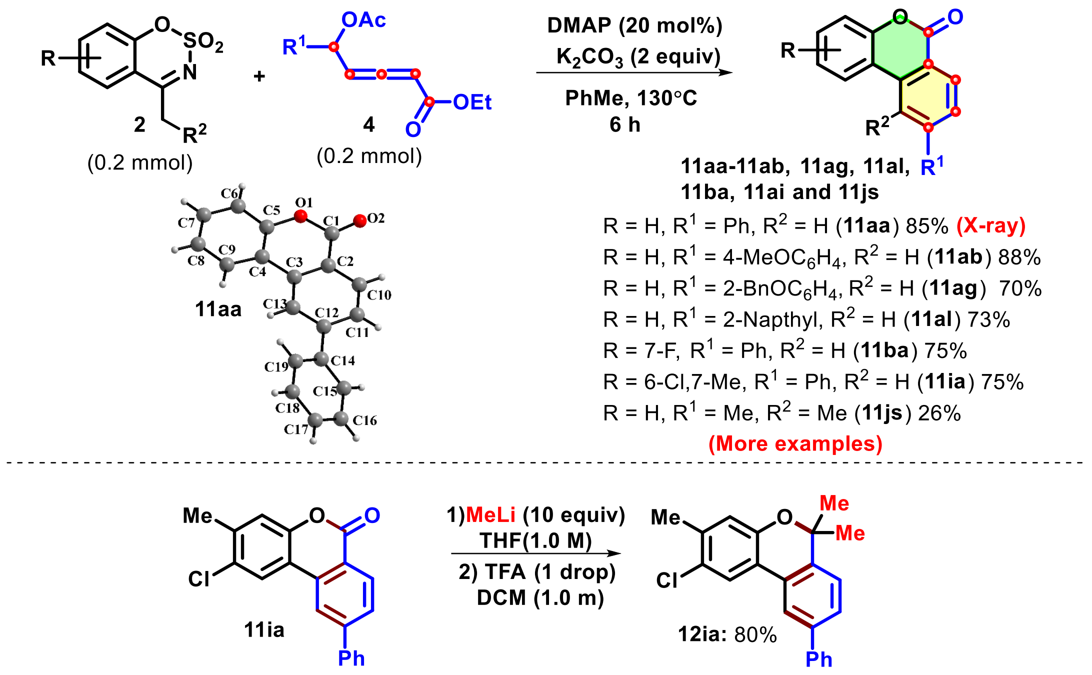
10aa-10ac, 10ag, 10al 10aq and 10ba

R = H, R^1 = Ph (**10aa**) 78% **(X-ray)**
R = H, R^1 = 4-$MeOC_6H_4$ (**10ab**) 82%
R = H, R^1 = 4-ClC_6H_4 (**10ac**) 75%
R = H, R^1 = 2-$BnOC_6H_4$ (**10ag**) 70%
R = H, R^1 = 2-Napthyl (**10al**) 72%
R = H, R^1 = 2-Thienyl (**10aq**) 66%
R = Me, R^1 = Ph (**10ba**) 77%
(More examples)

Scheme 2: Synthesis of *m*-teraaryl scaffolds from *δ*-acetoxy allenoates and cyclic sulfonamide imines

(iii) *δ*-Acetoxy allenoate as a 5C-synthon in domino-annulation with sulfamidate imines: Ready access to coumarins

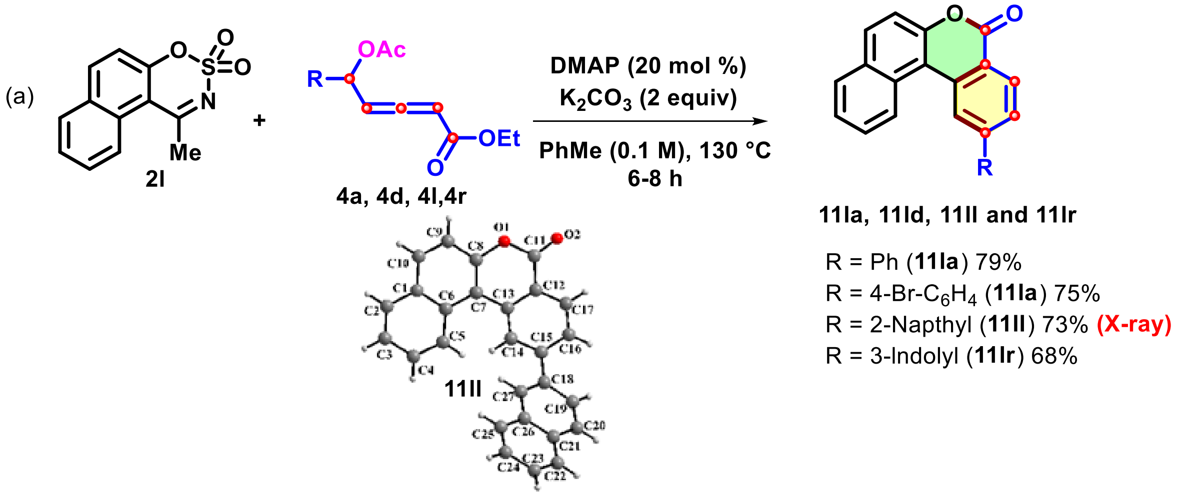
In the above reaction leading to teraryls, it is possible that the elimination of sulfonyl moiety by condensation with ester moiety may take place to lead to new cyclization products in an overall process wherein the *δ*-acetoxy allenoate **4** acts as *5C*-synthon. Indeed, by such an annulation reaction with sulfamidate imines **2** using DMAP catalysis, *via* diene-ammonium intermediate, we were able to obtain benzocoumarin scaffolds **11** by (4+2)/ (5+1) domino annulation. The reaction was generalized by using sulfamidate imine **2a-2b, 2i, 2j** and *δ*-acetoxy allenoates (e.g., **4a-b**, **4g**, **4l**, and **4s**) to give benzocoumarins (**11aa, 11ab, 11ag, 11al, 11ba, 11ia** and **11js**). As a demonstration of the synthetic utility of the developed strategy, the obtained products were utilized in nucleophilic addition-cyclization. Thus, the treatment of **11ia** with methyllithium followed by trifluoroacetic acid gave Cannabinol analogue **12ia** in high yield (85%; Scheme 3).

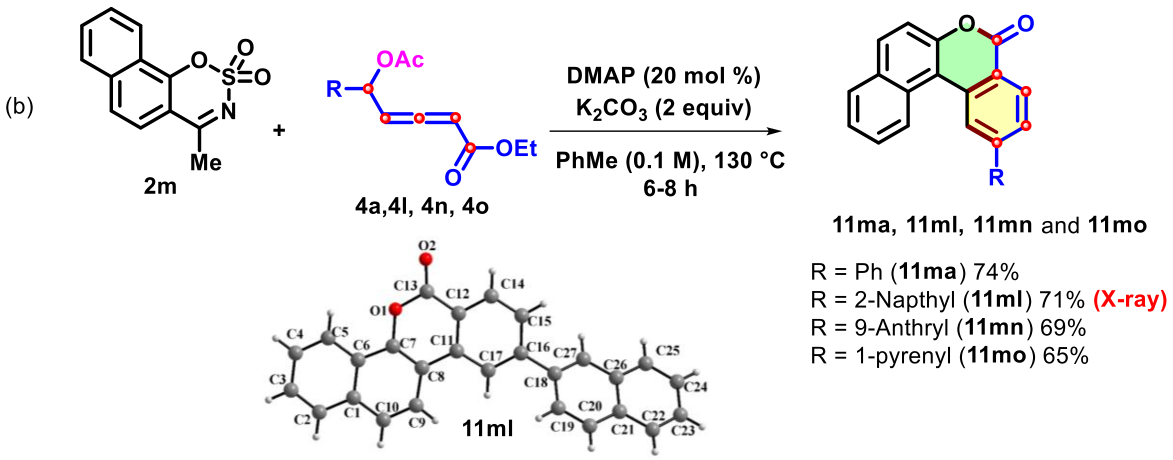


Scheme 3: Formation of chromenones (coumarins) from sulfamidate imines and δ-acetoxy allenoates

(iv) Extension of the scope of *sulfamidate imines* for the synthesis of dibenzochromenones

The above-developed strategy was extended for the synthesis of π-expanded coumarin entities. Here, we reacted cyclic sulfamidate imines **2l** and **2m**, possessing naphthalene as a part of the ring, with aryl/poly aryl substituted allenoates using the same conditions mentioned in Scheme 3. The expected dibenzo[*c*,*h*]/ [*c*,*f*]chromenones [**11la**, **11ld**, **11ll** and **11lr** (Scheme 4a) and **11ma**, **11ml**, **11mn** and **11mo** (Scheme 4b)] were obtained in acceptable yields. Plausible mechanistic pathways for these transformations are discussed.



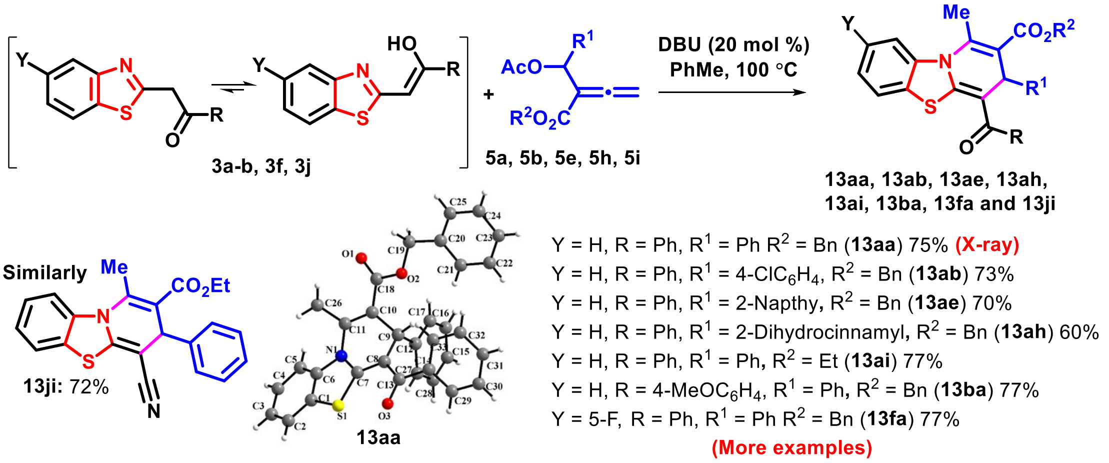


R = Ph (**11ma**) 74%
R = 2-Napthyl (**11ml**) 71% **(X-ray)**
R = 9-Anthryl (**11mn**) 69%
R = 1-pyrenyl (**11mo**) 65%

Scheme 4: Formation of dibenzochromenones from δ-acetoxy allenoates

(v) DBU-catalyzed (3 + 3) dearomative annulation of 2-acyl-tethered benzothiazoles with *β′*-acetoxy allenoates

β′-Acetoxy allenoates differ from the δ-acetoxy allenoates with respect to the position of the ester moiety. This could have implications for the final outcome of the products. In the current work, we have developed a DBU catalyzed dearomative (3 + 3) annulation of 2-acyl-tethered benzothiazole **3** with *β′*-acetoxy allenoates **5** affording fused 1,4-dihydropyridines possessing varying substituents (Scheme 5). The reaction is highly chemoselective, and the acyl group is not involved in the reaction. We did not observe the formation of the alternative pyran products. This reaction involves allylic elimination, followed by *aza*-Michael addition and dearomatization as key steps in delivering fused hydropyridines. The intermediates in this reaction have been identified by in-process HRMS studies.

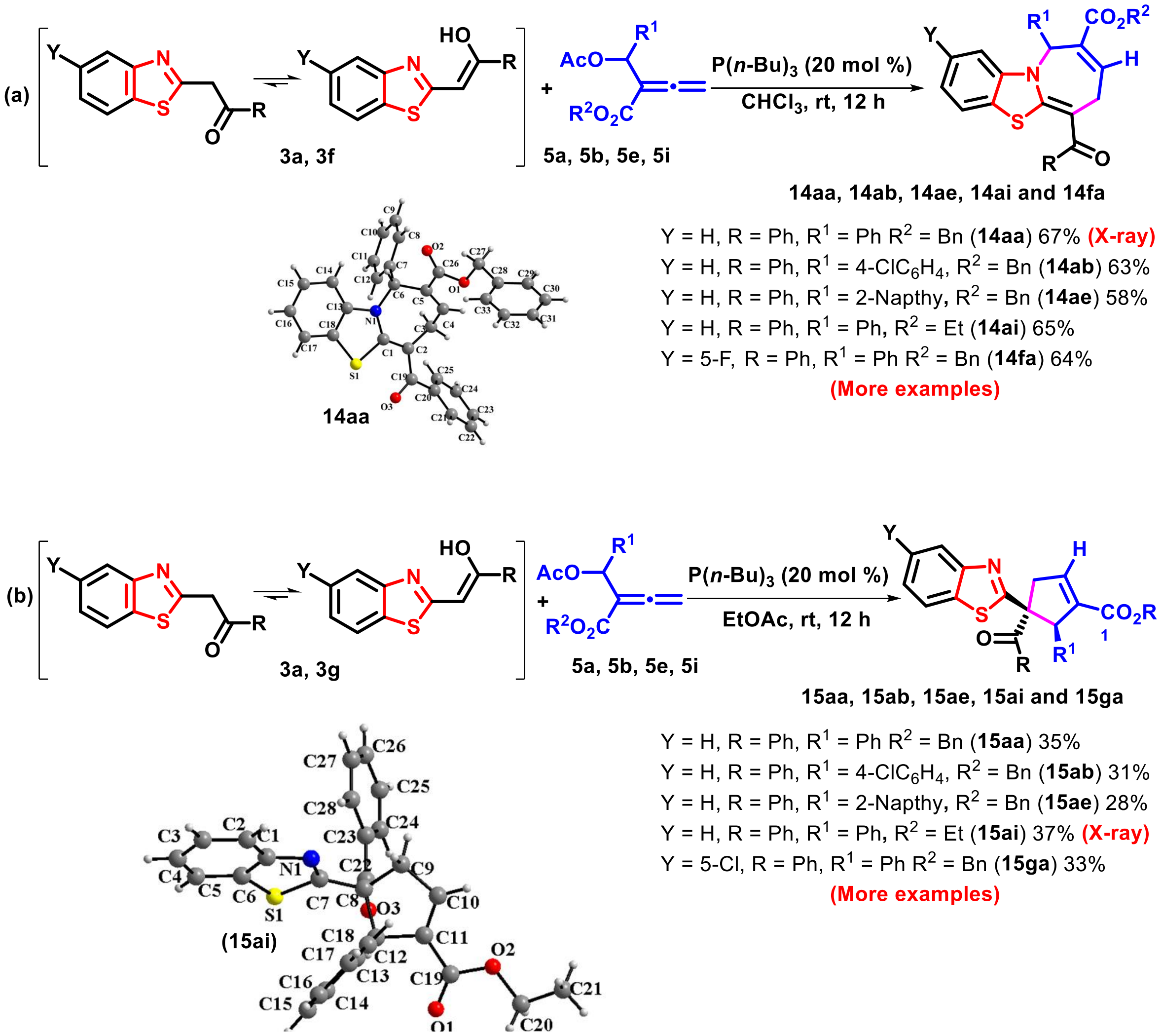


Y = H, R = Ph, R^1 = Ph R^2 = Bn (**13aa**) 75% **(X-ray)**
Y = H, R = Ph, R^1 = 4-ClC_6H_4, R^2 = Bn (**13ab**) 73%
Y = H, R = Ph, R^1 = 2-Napthy, R^2 = Bn (**13ae**) 70%
Y = H, R = Ph, R^1 = 2-Dihydrocinnamyl, R^2 = Bn (**13ah**) 60%
Y = H, R = Ph, R^1 = Ph, R^2 = Et (**13ai**) 77%
Y = H, R = 4-$MeOC_6H_4$, R^1 = Ph, R^2 = Bn (**13ba**) 77%
Y = 5-F, R = Ph, R^1 = Ph R^2 = Bn (**13fa**) 77%
(More examples)

Scheme 5: Synthesis of fused hydropyridines from acyl-tethered benzothiazoles and *β′*-acetoxy allenoates

(vi) P(*n*-Bu)$_3$-Catalyzed (4 + 3) and (4 + 1) annulation reactions of 2-acyl-tethered benzothiazoles with *β′*-acetoxy allenoates

We have been interested in investigating the divergent reactivity of allenoates under amine and phosphine catalysis. In this context, we envisioned that the above 2-acyl-tethered benzothiazoles **3** can react with *β′*-acetoxy allenoates **5** and undergo (4 + 3) annulation. This was indeed possible in the reaction using P(*n*-Bu)$_3$-catalyzed reaction which gave the (4 + 3) dearomative cyclization products **14** along with (4 + 1) cyclization derivatives **15** (Scheme 6). In this phosphine-catalyzed reaction, there is also a significant solvent effect on the ratio of (4 + 3) and (4 + 1) annulation processes. While chloroform favors the (4 + 3) product, ethyl acetate affords both products in nearly equal quantities.



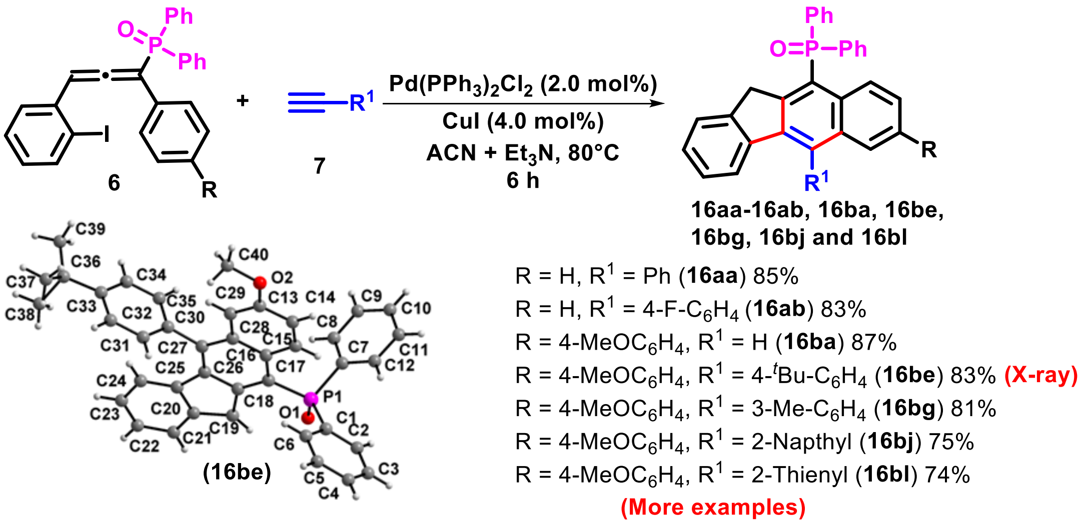
Y = H, R = Ph, R^1 = Ph R^2 = Bn (**14aa**) 67% **(X-ray)**
Y = H, R = Ph, R^1 = 4-ClC$_6$H$_4$, R^2 = Bn (**14ab**) 63%
Y = H, R = Ph, R^1 = 2-Napthy, R^2 = Bn (**14ae**) 58%
Y = H, R = Ph, R^1 = Ph, R^2 = Et (**14ai**) 65%
Y = 5-F, R = Ph, R^1 = Ph R^2 = Bn (**14fa**) 64%
(More examples)

Y = H, R = Ph, R^1 = Ph R^2 = Bn (**15aa**) 35%
Y = H, R = Ph, R^1 = 4-ClC$_6$H$_4$, R^2 = Bn (**15ab**) 31%
Y = H, R = Ph, R^1 = 2-Napthy, R^2 = Bn (**15ae**) 28%
Y = H, R = Ph, R^1 = Ph, R^2 = Et (**15ai**) 37% **(X-ray)**
Y = 5-Cl, R = Ph, R^1 = Ph R^2 = Bn (**15ga**) 33%
(More examples)

Scheme 6: Phosphine-catalyzed (4 + 3) or (4 + 1) annulation reactions of *β’*-acetoxy allenoates with acyl-tethered benzothiazoles

(vii) [Pd]-Catalyzed cascade annulation reaction of *o*-iodoaryl-substituted allenylphosphine oxides with terminal alkynes

Functionalized allenes can be versatile substrates in annulation reactions. For this purpose, we first synthesized the *o*-iodoaryl substituted allenylphosphine oxides **6**. The [Pd]-catalyzed domino annulation reaction of **6** with terminal alkynes **7** that involved (4 + 1)/(5 + 1) annulations furnished benzo[*b*]fluorenes **16**. In the first step, Sonogashira coupling in the presence of [Pd]/[Cu]-catalyst gives an allene-yne intermediate, which then undergoes (4 + 1) annulation and C-H functionalization leading to ring formation and subsequent aromatization to afford benzofluorenes **16**.

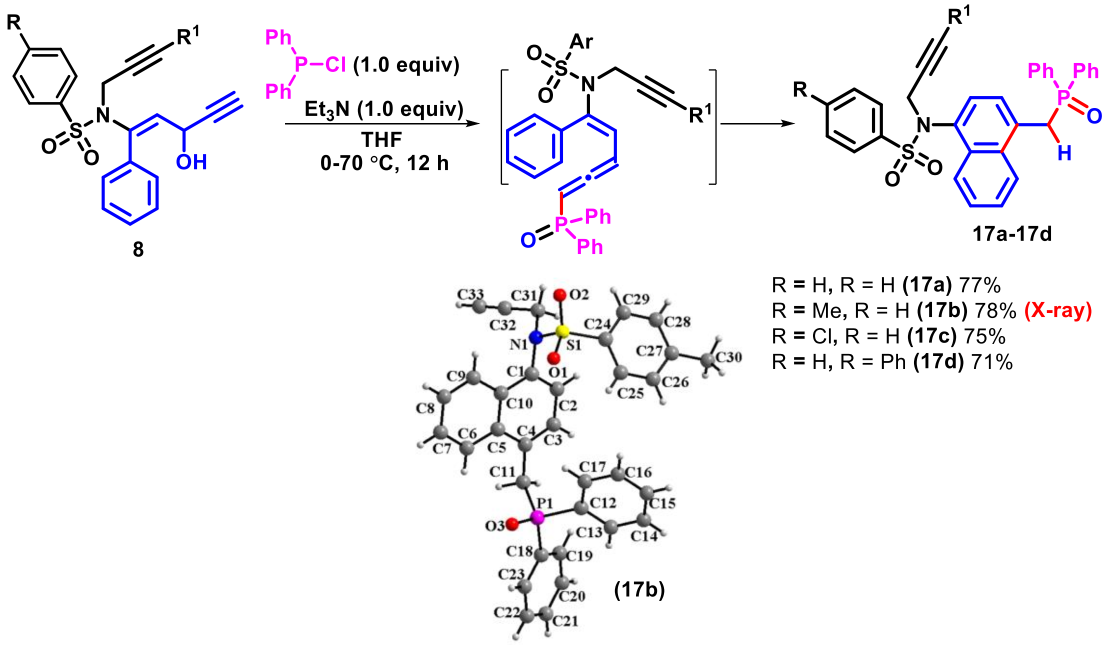


R = H, R^1 = Ph (**16aa**) 85%
R = H, R^1 = 4-F-C_6H_4 (**16ab**) 83%
R = 4-MeOC_6H_4, R^1 = H (**16ba**) 87%
R = 4-MeOC_6H_4, R^1 = 4-^{t}Bu-C_6H_4 (**16be**) 83% **(X-ray)**
R = 4-MeOC_6H_4, R^1 = 3-Me-C_6H_4 (**16bg**) 81%
R = 4-MeOC_6H_4, R^1 = 2-Napthyl (**16bj**) 75%
R = 4-MeOC_6H_4, R^1 = 2-Thienyl (**16bl**) 74%
(More examples)

Scheme 7: [Pd]-catalyzed formation of benzo[*b*]fluorenes from *o*-iodoaryl substituted allenylphosphine oxides

(viii) Reaction of vinylic propargyl alcohols with Ph_2PCl affording substituted 4-amino-naphthalenes

In continuation of the above part (vii), we intended to use functionalized propargyl alcohols to study their reactivity in anticipation of obtaining annulation products *via* the intermediate allenylphosphine oxides. Thus in this part of the work, synthesis of 4-amino-naphthalenyl diphenylphosphine oxides that involves 6π-electrocyclization, followed by Alder-Ene reaction of the allenic intermediate is accomplished. It may be noted here that the sulfonamide-alkyne part does not participate in the cyclization. Hence it may be possible to obtain similar products with other vinyl-tethered propargyl alcohols devoid of the sulfonamide-alkyne moiety.



R = H, R = H **(17a)** 77%

R = Me, R = H **(17b)** 78% **(X-ray)**

R = Cl, R = H **(17c)** 75%

R = H, R = Ph **(17d)** 71%

Scheme 8: Formation of 4-amino-naphthalenyl diphenylphosphine oxides from vinylic propargylic alcohols

Chapter 1

INTRODUCTION

In this thesis, the chemistry of acetoxy allenoates and phosphorus-based allenes is explored. The current chapter reviews the literature pertinent to the discussion in Chapter 2. Sections 1.1-1.2 provide an introduction to allene/ allenoate chemistry. Recent advances in acetoxy allenoate chemistry are examined in section 1.3. Additionally, since the current work involves *N*-sulfonyl-ketimines, dearomative cyclization, and phosphorus-based allenes, relevant literature on these topics is covered in sections 1.4-1.6.

1.1 Allenes: Useful Synthons in Organic Chemistry

Allenes are compounds consisting of three carbon atoms connected by consecutive double bonds. Their distinctive reactivity, which encompasses both the cumulative double bonds, makes them highly useful synthons in organic chemistry. This characteristic feature renders them valuable as intermediates in the synthesis of natural products, pharmaceuticals, dyes, and polymers.[1-2] The MAPP gas that is useful as a fuel is basically a mixture of **M**ethyl**A**cetylene, **P**ropadiene [allene **1.1** (R^1-R^4 = H, Figure 1.1], and **P**ropane. Allenes can be produced by a variety of synthetic protocols.[3] Although multisubstituted allenes possess chirality, this feature frequently disappears during the normal course of reactions and hence is not frequently employed. Introducing another functional group to the allene moiety can improve its versatility as a synthon. Allenoates (2,3-butadienoates; **1.2**), which have an ester group linked to the terminal carbon of the allene, react with a Lewis base to produce zwitterionic intermediates. These intermediates may serve as one-[2a], two-[2b], three-[2c], four-[2d], or five-carbon[2e] precursors, leading to the creation of cyclic structures with varying ring sizes. Substitution of a terminal hydrogen in the allene $H_2C=C=CH_2$ by an $R_2P(O)$-, $(RO)_2P(O)$- or $RS(O)_2$- moiety results in allenylphosphine oxide (**1.3a**), allenylphosphonate (**1.3b**) or allenylsulfonyl oxide (**1.4**). The chemistry of allenylphosphonates/allenylphosphine oxides has been extensively investigated in our laboratory.[4]

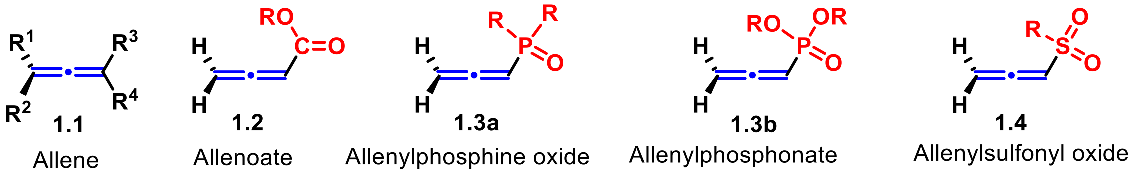
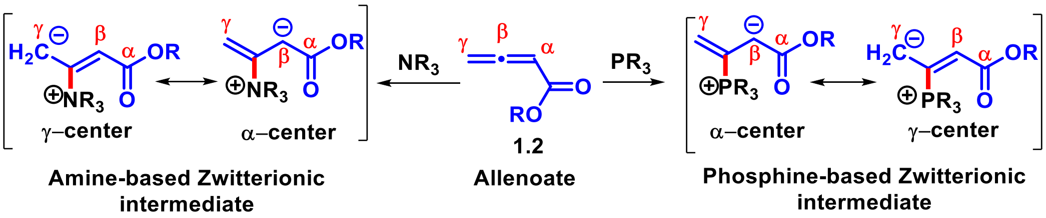


Figure 1.1: Structural varieties of allenes

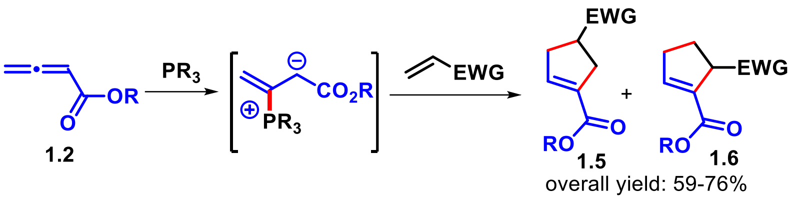
In this thesis, the primary focus is on exploring allenoate chemistry. Specifically, attention is directed towards understanding the reaction mechanism initiated when a Lewis base (NR_3 or PR_3) attacks the C(*sp*) atom of allenoate, generating a negative charge. This negative charge is stabilized by the presence of the electron-withdrawing ester group, resulting in the formation of a zwitterionic species capable of reacting with electrophilic substrates (Scheme 1.1). Due to their larger size and probable (but limited) involvement of available d-orbitals, zwitterionic intermediates exhibit enhanced stability in the presence of phosphines compared to amines. Consequently, this stabilizing effect by phosphine bases leads to distinct reactivity patterns compared to reactions mediated by amines.



Scheme 1.1: Resonance forms of zwitterions generated from allenoates Lewis base.

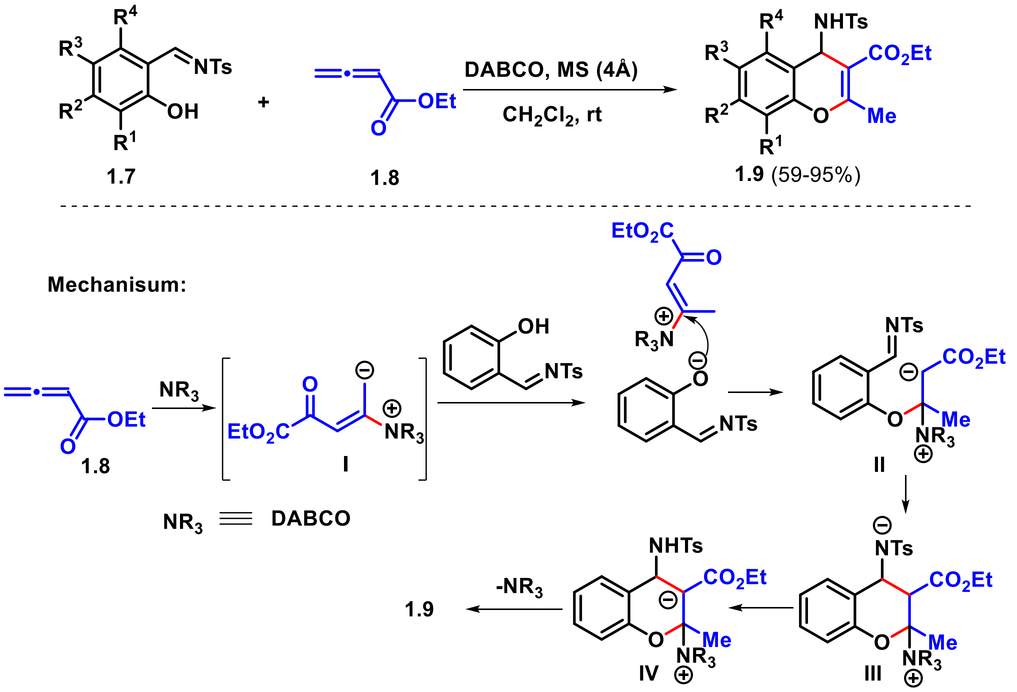
1.2. Reactivity of Allenoates Under Lewis Base Catalysis

In the year 1995, Lu's research team published the pioneering phosphine-catalyzed (3 + 2) annulation reaction involving allenoates **1.2** [*Note*: In the annulation reactions using allenes in the current work, we are concerned with the number of atoms of each substrate involved; for this reason, we have used normal parenthesis to depict annulation. The mechanistic intermediates, where given, are indicated by Roman numerals] and electron-deficient alkenes, resulting in cyclopentene products **1.5-1.6** (Scheme 1.2).[5] This breakthrough served as the cornerstone for a myriad of subsequent studies in allenoate chemistry. Consequently, allenoates have demonstrated their versatility by acting as 1,3-dipolarophiles in cycloaddition reactions with various electrophilic partners.[6,7] Moreover, asymmetric synthesis employing suitable catalysts has enabled highly stereoselective transformations. This section highlights some of these advancements, with particular emphasis on the recent literature.



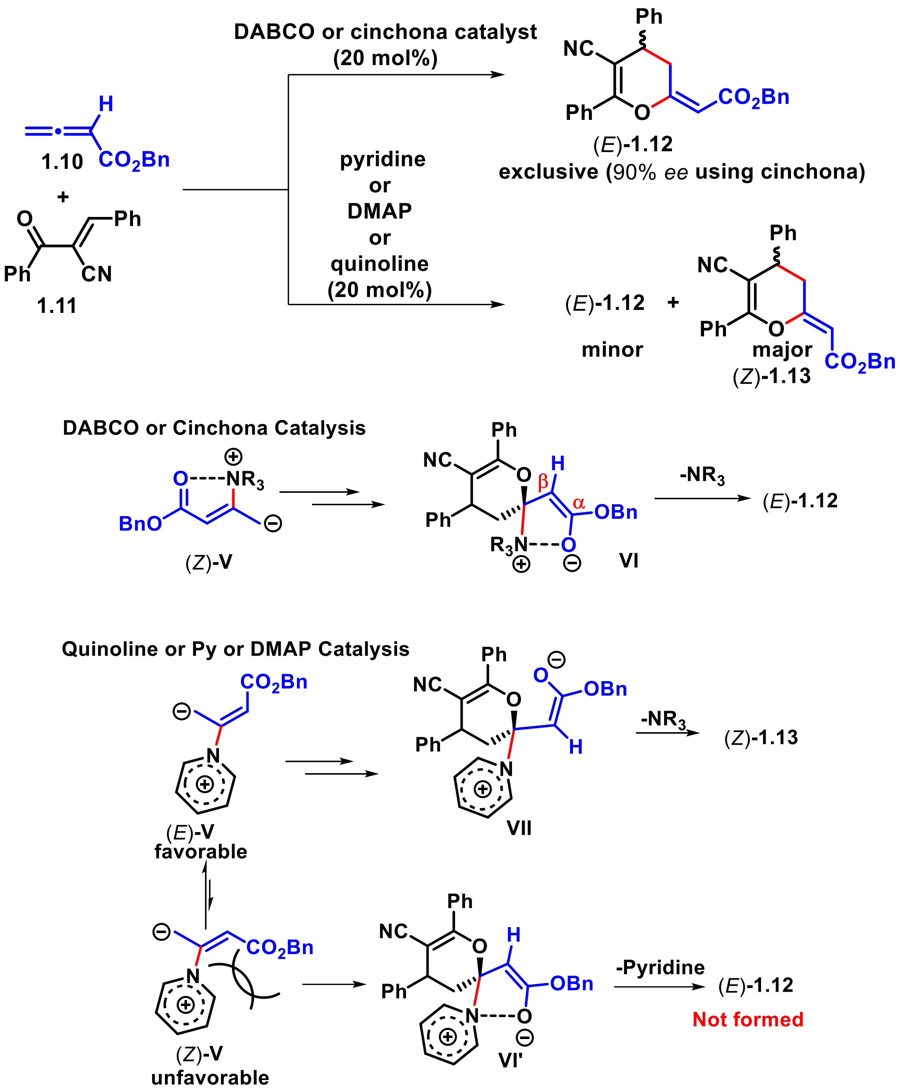
Scheme 1.2: Lu's synthesis of cyclopentenes from allenoates under phosphine catalysis

Shi *et al.* reported the DABCO catalyzed synthesis of functionalized chromenes in good yields from the reaction of allenoate **1.8** with salicyl-*N*-tosylimines **1.7** under mild reaction conditions. Here, the zwitterionic intermediate **I** deprotonates the phenolic -OH of the aryl-imine. Subsequent Michael addition/Mannich coupling affords intermediate **III** (via **II**) which undergoes proton shift followed by NR$_3$ elimination resulting in the formation of product **1.9** (Scheme 1.3).[8]



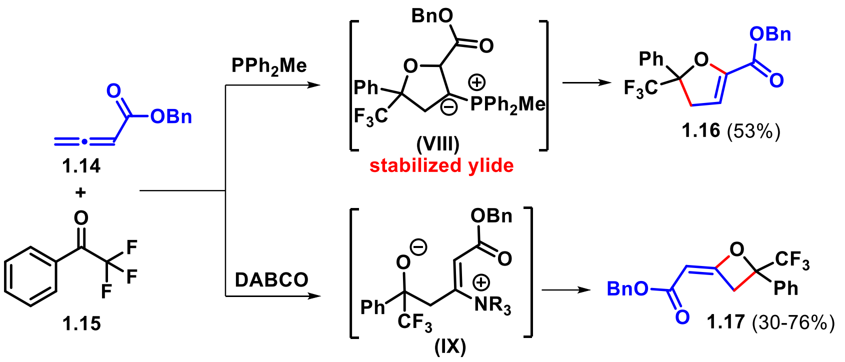
Scheme 1.3: Synthesis of chromenes **1.9** from allenoates **1.8** and salicyl-*N*-tosylimines **1.7**

In 2011, Tong and co-workers developed an amine-dependent (4 + 2) annulation of allenoate **1.10** with cyano-oxo-dienes **1.11**. The tertiary amine (DABCO or cinchona alkaloid) exclusively gives (*E*)-**1.12** selectivity because of the electrostatic interaction between the oxygen atom of the ester group and ammonium ion intermediate as in **V-VI**. In the case of pyridine, the positive charge on nitrogen in intermediate **V** is delocalized onto the aromatic ring. The relief of steric hindrance between the pyridyl ring and the ester group in intermediate (*E*)-**V** favors enolate **VII** to form (*Z*)-**1.13** as the major product (Scheme 1.4).[9]



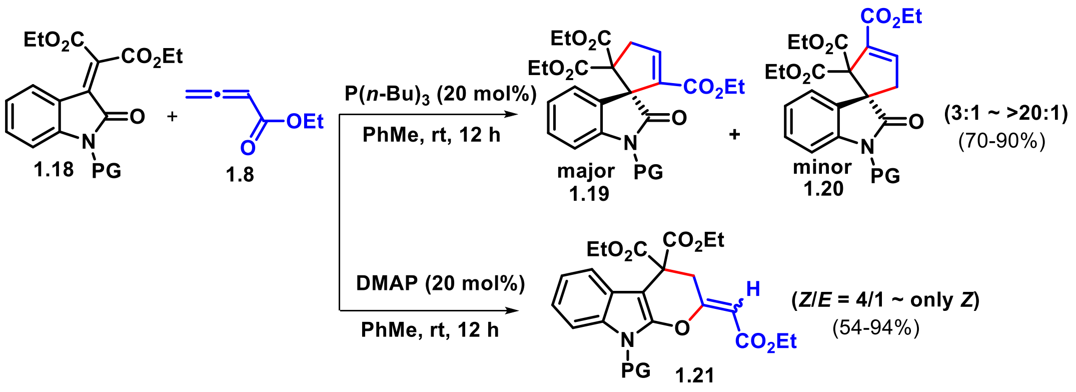
Scheme 1.4: Synthesis of substituted 2*H*-pyrans **1.12/1.13** from allenoate **1.10**

Miller's group reported the divergent reactivity of allenoate **1.14** with 2,2,2-trifluoroacetophenones **1.15** under Lewis base catalysis. In the Ph_2PMe catalyzed reaction, the (3 + 2) cycloaddition to form dihydrofurans **1.16** is favored because of the formation of stabilized ylide **VIII**, whereas in DABCO catalysis, γ-addition takes place to give the zwitterionic intermediate **IX** which is followed by (2 + 2) cycloaddition to form oxetanes **1.17** (Scheme 1.5).[10]



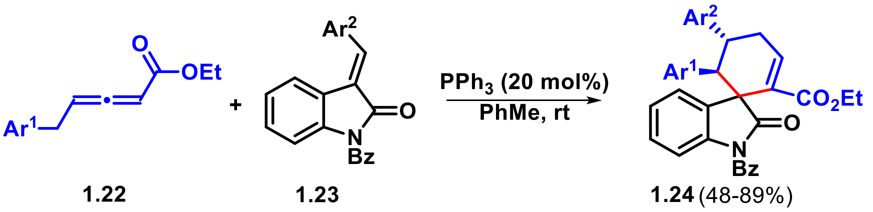
Scheme 1.5: Divergent reactivity of allenoate **1.14** with 2,2,2-trifluoromethyl-1-phenyl-ethan-1-one **1.15**

Shi *et al*. reported an interesting difference in the reactivity of α-allenic ester **1.8** with isatin derived *α,β*-unsaturated diesters **1.18**. Under P(*n*-Bu)$_3$ catalysis, the reaction takes place *via* regioselective (3 + 2) cycloaddition to afford functionalized spirocyclic products **1.19-1.20**. By contrast, the DMAP-catalyzed reaction proceeds by selective (4 + 2) cycloaddition to give the corresponding 4*H*-pyrans **1.21** in good yields (Scheme 1.6).[11]



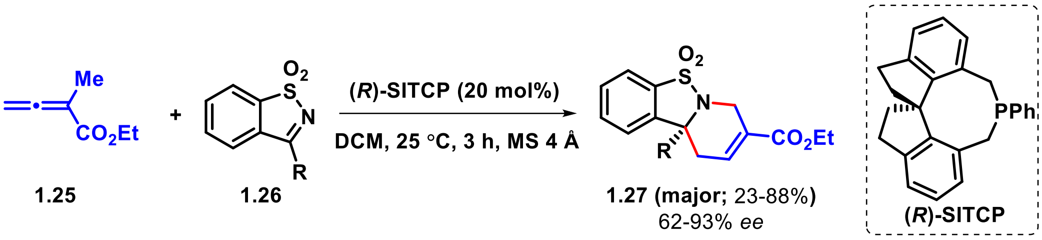
Scheme 1.6: Divergent reactivity of allenoate **1.8** with **1.17** under phosphine and amine catalysis

Marinetti and co-workers developed Ph$_3$P catalyzed (4 + 2) annulation reaction of δ-aryl penta-2,3-dienoates **1.22** and 3-arylideneoxindoles **1.23** for the synthesis of spirocyclic oxindoles **1.24**. Here, the allenoate serves as a 4-C source (Scheme 1.7).[12]



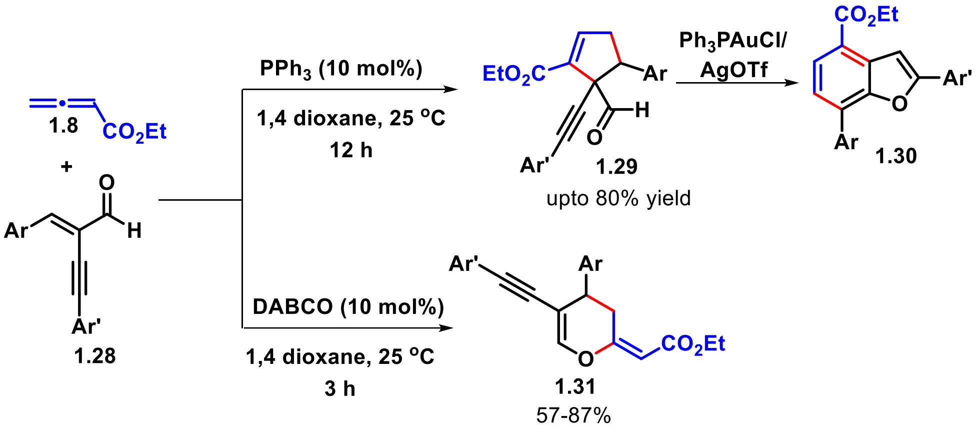
Scheme 1.7: Phosphine-catalyzed spirocyclization of allenoates **1.22**

Sasai's group reported the (4 + 2) cycloaddition of α-methylallenoate **1.25** with cyclic sulfonyl imines **1.26** using a chiral phosphine catalyst for the enantioselective synthesis of tetrahydropyridines **1.27** (Scheme 1.8).[13]



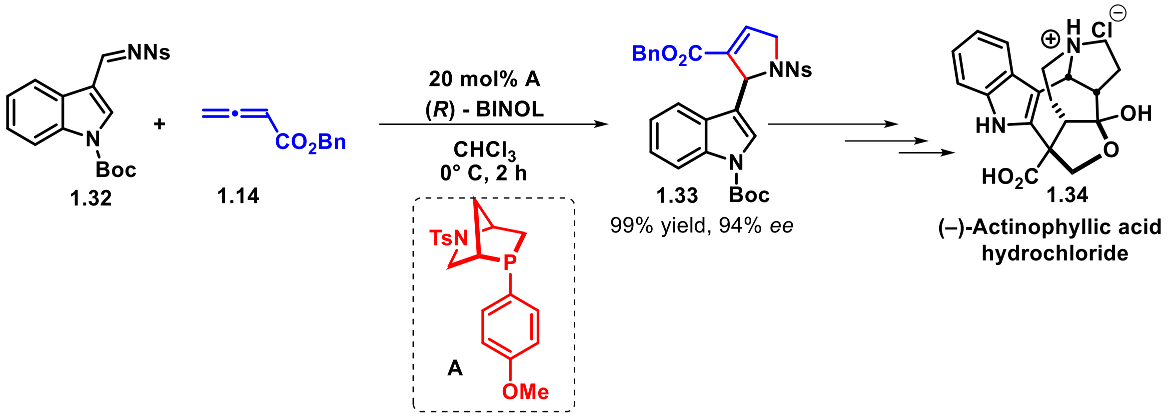
Scheme 1.8: Synthesis of tetrahydropyridines **1.27** from allenoate **1.25** and cyclic sulfonyl imines **1.26**

Our group reported the divergent reactivity of allenoate **1.8** with enynals **1.28** under PPh_3-catalyzed conditions. The reactants undergo (3 + 2) cycloaddition to give functionalized cyclopentene carboxylates **1.29** which are further converted into benzofurans **1.30** under the influence of a gold catalyst. However, under DABCO catalysis, the reaction takes place *via* (4 + 2) cycloaddition to afford 4*H*-dihydropyrans **1.31** (Scheme 1.9).[14]



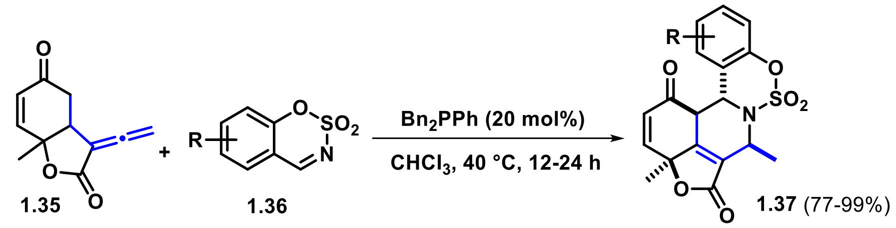
Scheme 1.9: Synthesis of cyclopentenes **1.29** and dihydropyrans **1.31** and from allenoate **1.8**

Kwon *et al* synthesized (–)-actinophyllic acid as its hydrochloride **1.34** by using chiral phosphine catalyzed (3 + 2) annulation between allenoate **1.14** and imine **1.32** *via* the pyrroline intermediate **1.33** which was obtained in 99% yield and 94% *ee*. The synthesis also features CuI-catalyzed coupling between a ketoester and 2-iodoindole to shape the tetrahydroazocine ring by intramolecular alkylative lactonizaton. SmI_2 mediated intramolecular pinacol coupling between ketone lactone subunits was used to assemble the complex skeleton of (-)-actinophyllic acid (Scheme 1.10).[15]



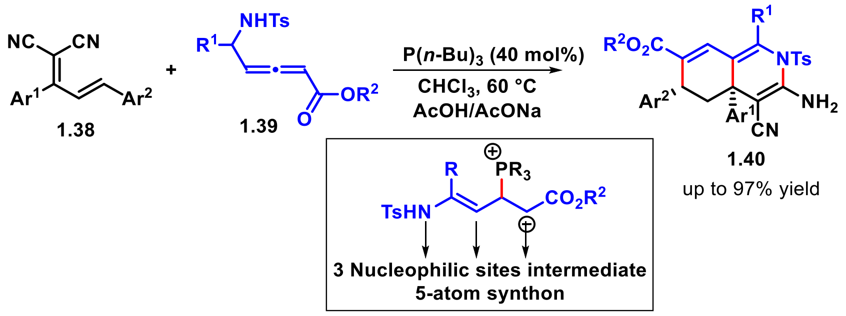
Scheme 1.10: Synthesis of (–)-actinophyllic acid hydrochloride **1.34** from allenoate **1.14**

Guo *et al* reported the first reaction where the γ′-carbon of α-substituted allenoate **1.35** is involved in (4 + 2) cycloaddition with cyclic sulfamate imines **1.36** by using $(PhCH_2)_2PPh$ as the nucleophilic catalyst. The reaction gives 3a,6,13b,13c-tetrahydro-1*H*,5*H*-benzo[5,6][1,2,3]oxathiazino-[4,3-*a*]furo[4,3,2-*de*]isoquinoline derivatives **1.37** with four chiral centers in good to excellent yields (Scheme-1.11).[16]



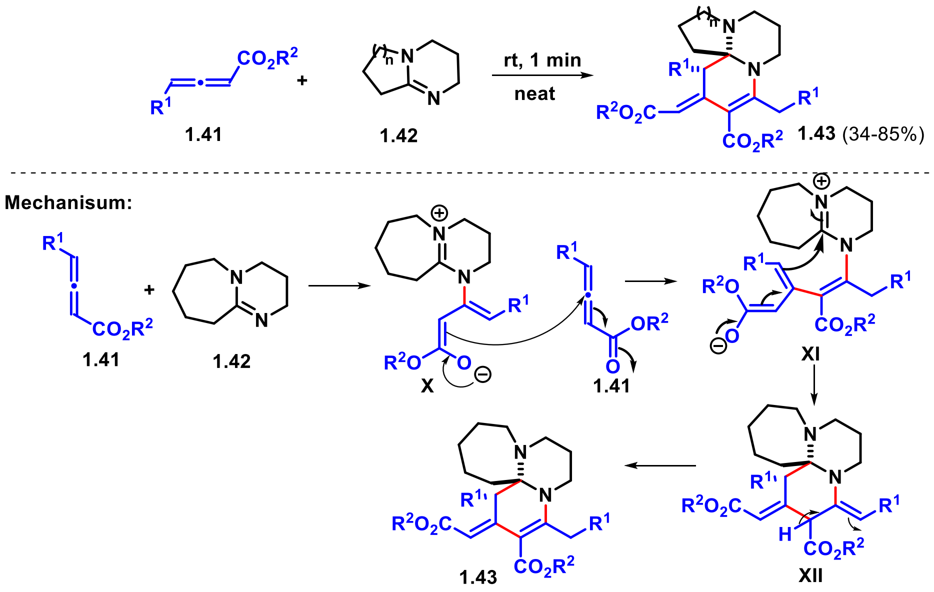
Scheme 1.11: Synthesis of multicyclic heterocycles **1.37** from allenoate **1.35**

Huang *et al* developed phosphine-catalyzed domino annulation of dienes **1.38** with δ-sulfonamido-allenoates **1.39** for the synthesis of highly functionalized hydroisoquinolines **1.40**. Here, δ-sulfonamido-allenoates **1.39** act as 5-atom synthons (Scheme 1.12).[17]



Scheme 1.12: Synthesis of functionalized hydroisoquinolines **1.40** from δ-sulfonamido-allenoates **1.39**

Very recently, Somappa's group developed atom economic annulation of allenoates **1.41** with cyclic amidines **1.42** for the synthesis of functionalized tricyclic pyridopyrimidine scaffolds **1.43**. The reaction proceeds *via* addition of DBU at the β position of allenoate **1.41**, forming stabilized diene-ammonium enolate **X** which then attacks on another molecule of allenoate, resulting in intermediate **XI**, which upon intramolecular cyclization (cf. **XII**) followed by isomerization furnishes the final conjugated ene system **1.43** (Scheme 1.13).[18]

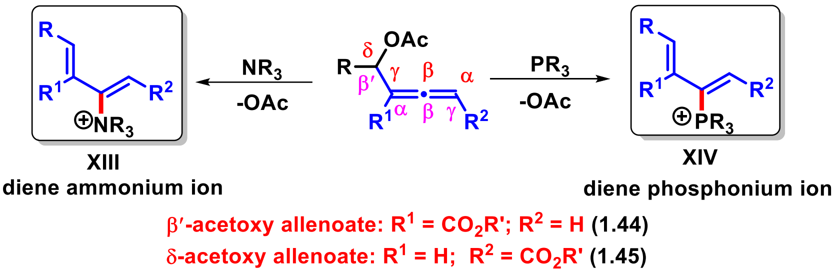


Scheme 1.13: Synthesis of fused tricyclic pyridopyrimidines **1.43** from allenoate **1.41**

In addition to the above, there are a few reactions where similar allenoates are used in (4 + 2) annulation with benzofuran-derived azadienes,[19a] Michael acceptors (using catalytic isochalcogenoureas),[19b-c] *N*-phosphoryl imine (using catalytic Cs_2CO_3),[19d] and methyleneindolinones.[19e] In addition, (5 + 1) annulation with pyrazolone using catalytic MeOK),[19f] and enantioselective Claisen rearrangement with (*E*)-cinnamyl pyrrolidine in the presence of chiral phosphate sodium salts[19g] have also been reported. There is also excellent work on allenyl acetates by Volla and co-workers; in these substrates, the ester group is absent on the allenic part, but the –OAc group is readily detachable as in the case of acetoxy allenoates that are discussed below.[19h-j]

1.3. Acetoxy Allenoate Chemistry

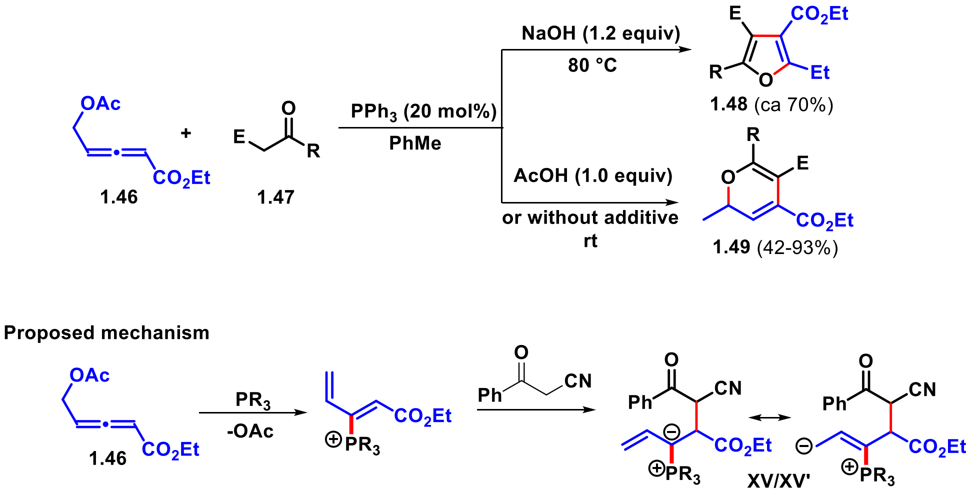
In the previous section, we discussed annulation reactions of normal allenoates under Lewis base catalysis *via* nucleophilic zwitterionic intermediates. The limitation of this process is the requirement of electrophile which is difficult to have each time, so by adding the readily detachable -OAc group in δ- or β'-allenoates (cf. **1.44/ 1.45**) the polarity of allenoates can be reversed. The addition of Lewis base at the *sp* carbon of acetoxy allenoate *via* S_N2' attack and elimination of -OAc group generates a reactive electrophilic diene-ammonium (**XIII**) /phosphonium (**XIV**) intermediate. This diene-ammonium/phosphonium intermediate can participate in annulation with a bifunctional substrate that can lead to the formation of cyclic frameworks (Scheme 1.14). Relevant work on this topic is delineated below.

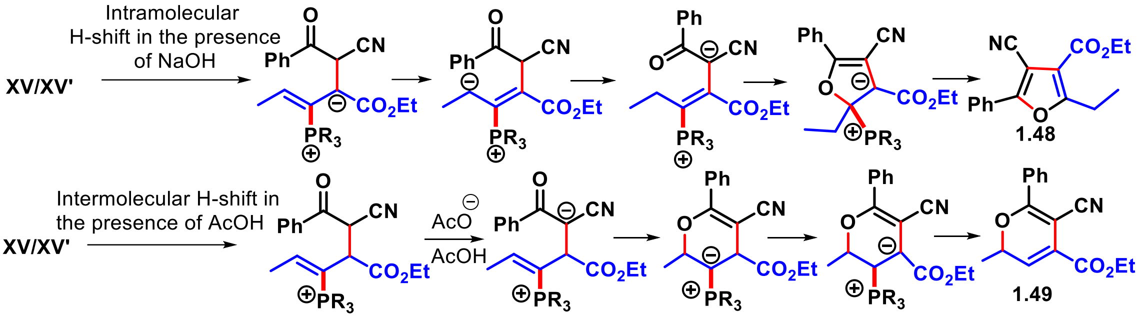


Scheme 1.14: Generation of diene-ammonium/phosphonium intermediates from acetoxy allenoates

1.3.1 *δ-Acetoxy allenoate chemistry*

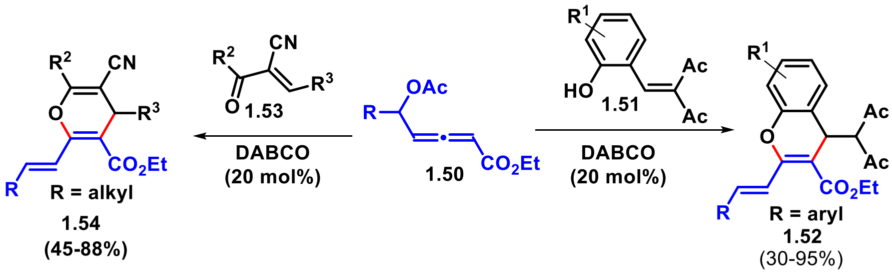
In the year 2012, Tong *et al.* developed the additive dependent phosphine-catalyzed (3 + 2) and (3 + 3) annulation *δ*-acetoxy allenoate **1.46** with carbonyl compounds **1.47**. In the presence of NaOH, intramolecular H-shift takes place to form the zwitterion **XV/XV'** which undergoes *oxo*-Michael addition in a 5-*endo* fashion followed by elimination of PPh_3 to give the furan products **1.48**. Under acidic conditions, intermolecular H-abstraction from HOAc generates **XV/XV'**. Selective deprotonation followed by 6-*endo* oxo-Michael addition and PPh_3 elimination gives the 2*H*-pyrans **1.49** (Scheme 1.15).[20]





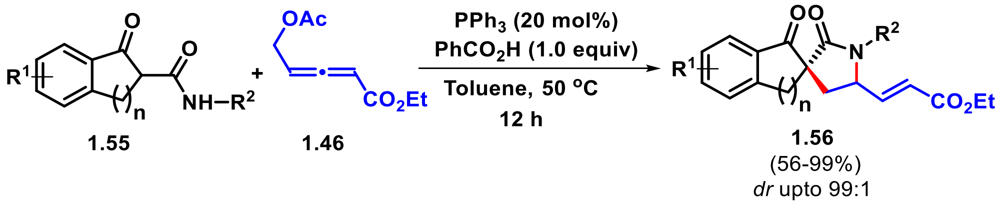
Scheme 1.15: Synthesis of furans **1.48** and dihydropyrans **1.49** from acetoxy allenoate **1.46**

Tong's group reported a DABCO-catalyzed divergent (4 + 2) annulation reaction of *δ*-acetoxy allenoates **1.50** in which the reactivity was substrate-dependent. Allenoates with an aromatic group at *δ*-C reacted with substituted salicylaldehydes **1.51** and favored the formation of 4*H*-chromenes **1.52** but the alkyl group tethered allenoates at *δ*-C reacted with oxo-diene substrates **1.53** to afford 4*H*-pyrans **1.54** (Scheme 1.16).[21]



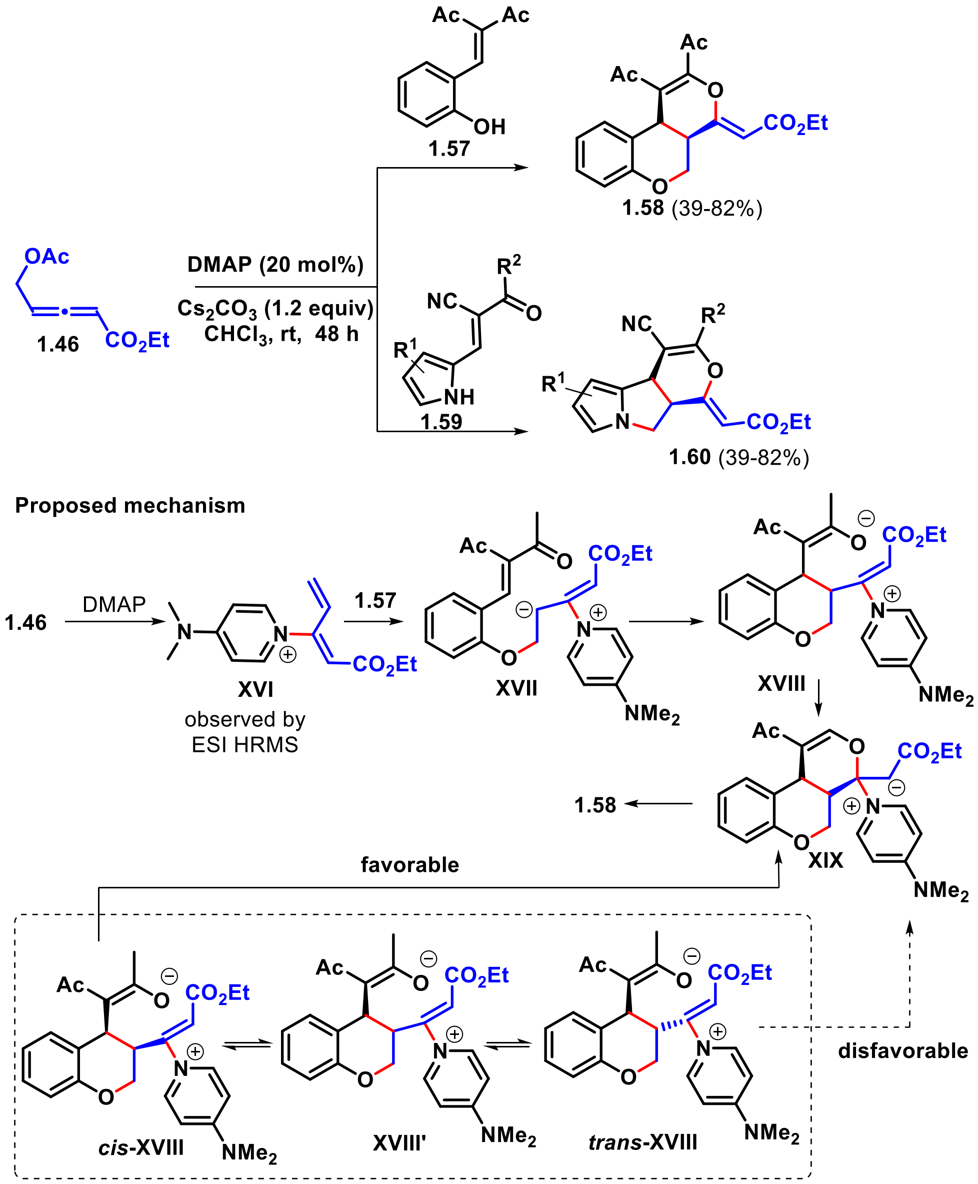
Scheme 1.16: Synthesis of 4*H*-chromenes and 4*H*-pyrans from acetoxy allenoates

Xing *et al.* reported Ph_3P-catalyzed (3 + 2) annulation of *δ*-acetoxy allenoates **1.46** with α-substituted *β*-ketoamides **1.55** giving five-membered spirolactam derivatives **1.56** under mild conditions with high diastereoselectivity. Here, *δ*-acetoxy allenoate **1.46** acts as a 2*C* synthon and *β*-ketoamides **1.52** serve as 1*C*,3*N* donors with $PhCO_2H$ acting as the proton source (Scheme 1.17).[22]



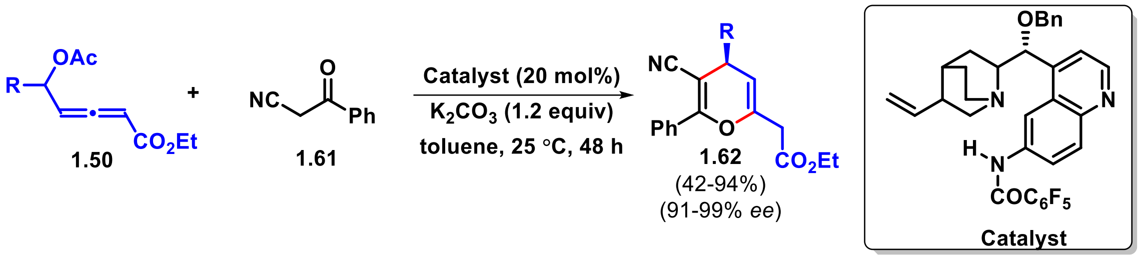
Scheme 1.17: Synthesis of spiro-heterocycles **1.56** from acetoxy allenoate **1.46**

Ni *et al.* reported DMAP-catalyzed domino annulation reaction of δ-acetoxy allenoate **1.46** with **1.57** or pyrrole aldehyde-derived oxadiene **1.58** for the construction of polycyclic frameworks. The reaction proceeds by addition of DMAP to the allenoate *via* addition and elimination to generate diene-ammonium intermediate **XVI** which was observed by ESI HRMS. With the help of Cs_2CO_3, addition of **1.57** to **XVI** generates **XVII** which upon intramolecular Michael addition gives enolate **XVIII** which exists in isomeric *cis* and *trans* forms that are interconvertible *via* zwitterionic intermediate **XVIII'**. *Cis*-**XVII** is more favorable for the oxa-Michael addition giving *cis*-**1.58** as a single product *via* species **XIX** (Scheme 1.18).[23]



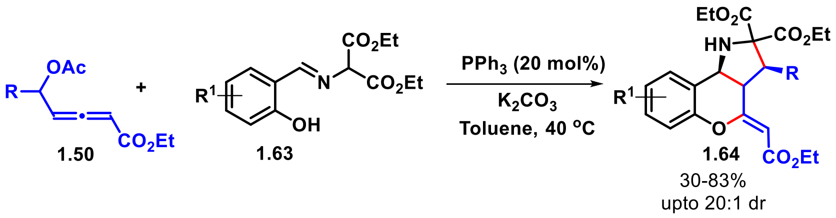
Scheme 1.18: Synthesis of hetero-polycyclic frameworks **1.58** and **1.60** from *δ*-acetoxy allenoate **1.46**

In 2017, Tong and colleagues reported a highly efficient method for the synthesis of 4*H*-pyran **1.62**. This process, catalyzed by a bifunctional amine, proceeded *via* asymmetric (3 + 3) annulation of δ-acetoxy allenoates **1.50** with 1C,3O-bisnucleophiles **1.61**, leading to the formation of 4*H*-pyran scaffolds **1.62** with high enantioselectivity. Notably, this methodology demonstrated versatility with allenoates bearing either electron-donating (EDG) or electron-withdrawing (EWG) groups, yielding the desired products in good yields under mild reaction conditions (Scheme 1.19).[24]



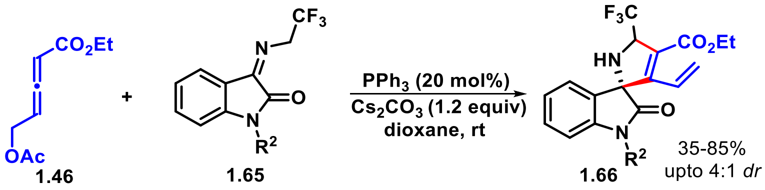
Scheme 1.19: Synthesis of 4*H*-pyran **1.62** from δ- acetoxy allenoates **1.50**

Zhou's group developed PPh$_3$-catalyzed domino cycloaddition of *δ*-acetoxy allenoates **1.50** with aldimine esters **1.63** for the synthesis of chromeno-pyrrole derivatives **1.64** having three continuous chiral centers with high diastereoselectivity in good yields. In addition, asymmetric version of this cycloaddition was performed with a chiral phosphine giving outstanding selectivity (Scheme 1.20).[25]



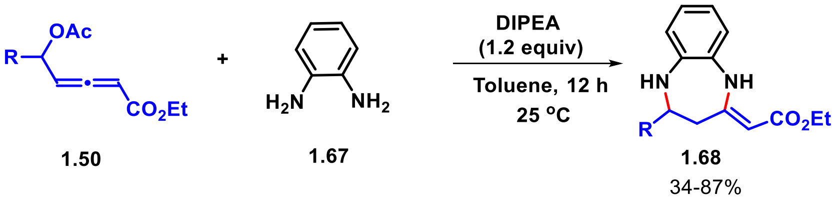
Scheme 1.20: Synthesis of compounds **1.64** from *δ*-acetoxy allenoates **1.50**

Shi's group developed PPh$_3$-catalyzed (3 + 2) cycloaddition pathway for synthesis of CF$_3$-containing spiro[indoline-3,2′-pyrrole] scaffolds **1.66** from δ-acetoxy allenoates **1.46** and *N*-2,2,2-trifluoroethylisatin ketimines **1.65**. This process employs mild conditions, yielding spirooxindoles with decent efficiency. The reactive *N*-2,2,2-trifluoroethylisatin ketimines **1.65** serve a crucial role as azomethine ylide precursors in this reaction (Scheme 1.21).[26]



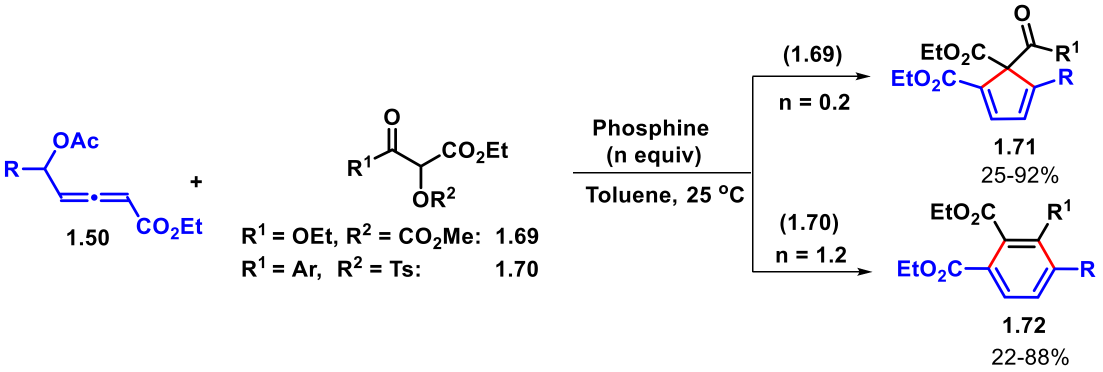
Scheme 1.21: Synthesis of spirooxindoles **1.66** from acetoxy allenoate **1.46**

Tong and co-workers have developed a novel method for synthesizing 1,5-benzodiazepines **1.68** through the (3 + 4) annulation of δ-acetoxy allenoates **1.50** with o-diaminobenzenes **1.67**. This annulation likely proceeds through the *aza*-Michael addition of diaminobenzene to the allenoate, followed by the removal of the acetate group, and subsequent 1,6-addition. This approach exhibits a broad substrate scope, utilizes readily available starting materials, operates under moderate reaction conditions, and demonstrates high reaction efficiency (Scheme 1.22).[27]



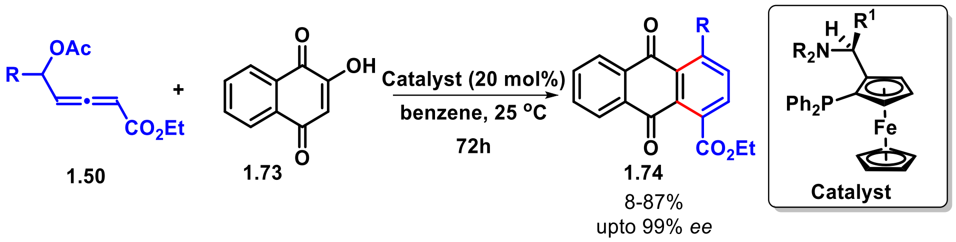
Scheme 1.22: Synthesis of 1,5-benzodiazepines **1.68** from δ-acetoxy allenoates **1.50**

Tong *et al*. showcased the synthesis of substituted cyclopentadienes **1.71** through a PPh_3-catalyzed (4 + 1) annulation reaction of unsymmetrical malonate **1.69** with δ-acetoxy allenoates **1.50**. Interestingly, by employing 1.2 equivalents of phosphine along with Na_2CO_3, similar starting materials **1.70** underwent (4 + 2) annulation, leading to the formation of tetrasubstituted benzenes **1.72** (Scheme 1.23).[28]



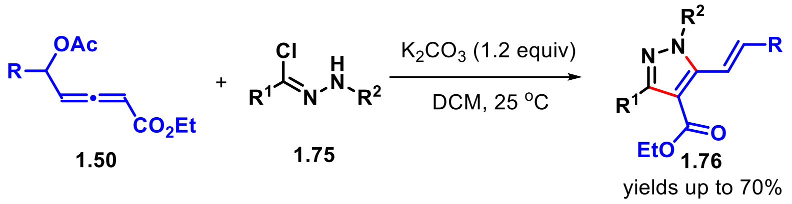
Scheme 1.23: Synthesis of cyclopentadienes **1.71** and tetrasubstituted aryls and **1.72** from acetoxy allenoates **1.50**

Tong and colleagues pioneered the chiral phosphine-catalyzed atroposelective (4 + 2) annulation of δ-acetoxy allenoates **1.50** with 2-hydroxy-quinone **1.73**, resulting in the *de novo* synthesis of an aryl ring and axial chirality. This approach yields aryl-naphthoquinone atropisomers **1.74** with excellent enantioselectivity. The essential (4 + 2) cycloaddition, which occurs in a *pseudo*-intramolecular way, is well-known for its high efficiency and adaptability with a variety of substrates (Scheme 1.24).[29]



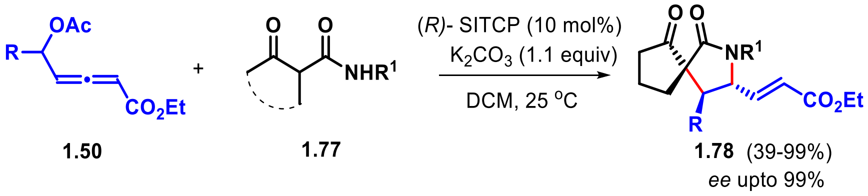
Scheme 1.24: Synthesis of aryl naphtha-quinones **1.74** from acetoxy allenoate **1.50**

Zhou *et al*. developed K_2CO_3 mediated (3 + 2) cycloaddition of δ-acetoxy allenoates **1.50** with nitrilimines **1.75** for synthesizing 1,3,5-trisubstituted pyrazoles **1.76**. The reaction proceeds *via* a 1,3-dipolar cycloaddition. The R group of allenoate **1.50** has a significant electronic effect on the yield of the reaction; an electron-withdrawing nitro group on the benzene ring of the nitrilimines decreased the product yield, whereas a methoxy group enhanced the yield (Scheme 1.25).[30]



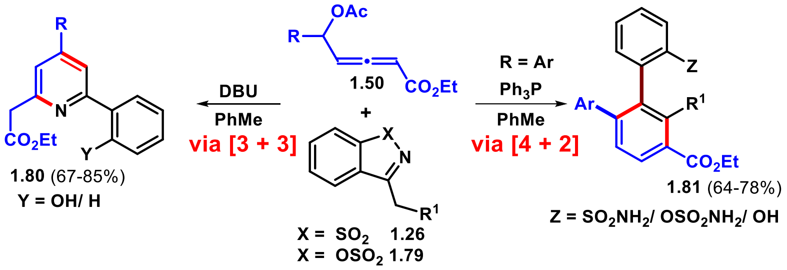
Scheme 1.25: Synthesis of trisubstituted pyrazoles **1.76** from δ-acetoxy allenoates **1.50**

Zhou and co-workers described an unusual asymmetric (3 + 2) annulation of δ-acetoxy allenoates **1.50** with β-carbonyl amides **1.77** using the chiral phosphine (*R*)-SITCP as a catalyst. In this reaction, the δ-C and γ-C positions of the allenoate serve as electrophilic sites that engage with the α-C and N of the amide, respectively. This technique accommodates a wide range of allenoates and β-carbonyl amides, providing a robust method for synthesizing various γ-lactams **1.78** with high stereoselectivity (up to 97% *ee*) and >20:1 *dr* (Scheme 1.26).[31]



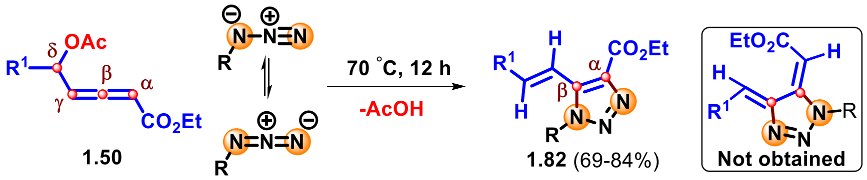
Scheme 1.26: Synthesis of γ-lactams **1.78** from δ-acetoxy allenoates **1.50**

Our group synthesized α-pyridyl acetates or *o*-teraryl scaffolds by treating *δ*-acetoxy allenoates **1.50** with cyclic *N*-sulfonyl imines (sulfamidate imines/sulfonyl imines **1.26**/**1.79**) *via* Lewis base-switching. In the DBU-mediated process, **1.26**/**1.79** acts as a C/N donor, leading to α-pyridyl acetates **1.80** through *aza*-Michael addition and SO_2 elimination/aromatization. In PPh_3-catalyzed (4 + 2) annulation, **1.26**/**1.79** serves as a C/C donor, yielding *o*-terphenyl carboxylates **1.81** *via* Michael addition, vinylogous Mannich coupling, and C-N bond cleavage/aromatization (Scheme 1.27).[32]



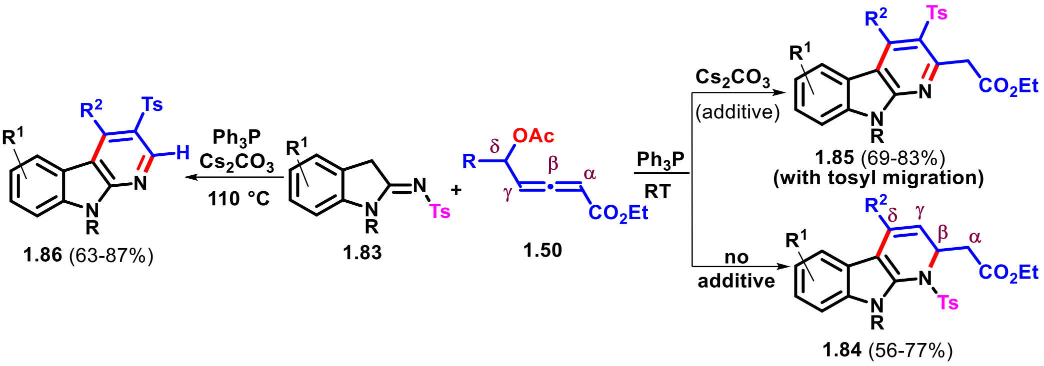
Scheme 1.27: Synthesis of functionalized *α*-pyridyl acetates **1.80** and *o*-teraryl scaffolds **1.81** from *δ*-acetoxy allenoates **1.50**

Our group has also reported regio-and stereo-selective (3 + 2) thermal cycloaddition of *δ*-acetoxy allenoates **1.50** with organic azides for the synthesis of 1,4,5-trisubstituted-1,2,3-triazoles **1.82** under metal-free conditions. This cycloaddition is initiated by the addition of an aryl-attached nitrogen atom at the β-carbon of allenoate chemoselectively to deliver the (*E*)-isomer exclusively (Scheme 1.28).[33]



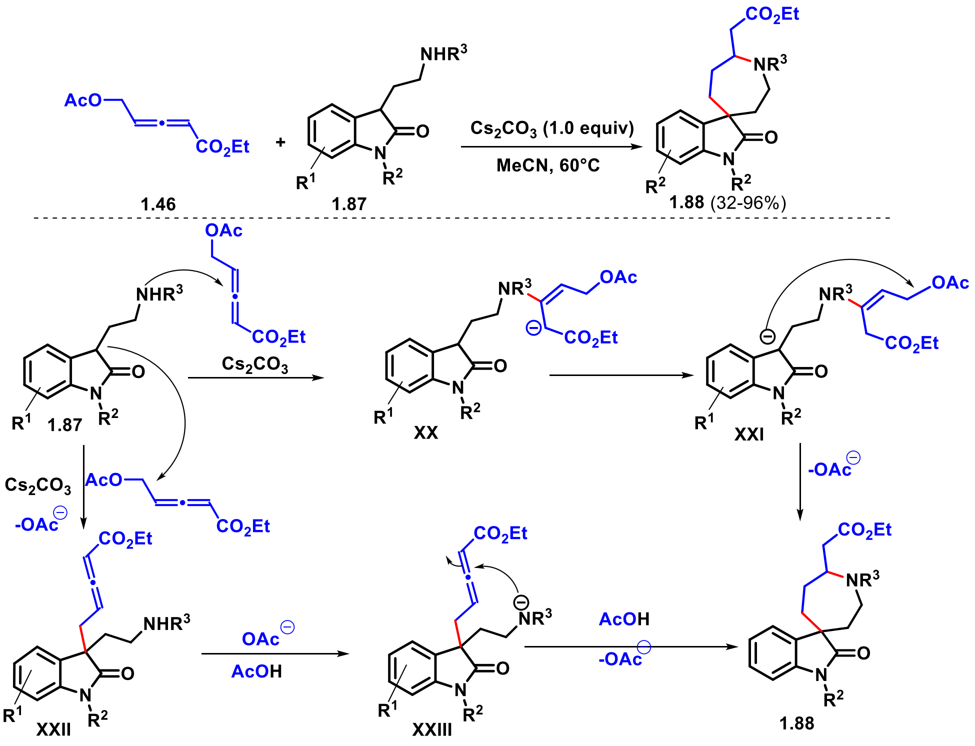
Scheme 1.28: Synthesis of multiubstituted triazoles from allenoate **1.50**

The PR_3 catalyzed (3 + 3) annulation of *δ'*-acetoxy allenoates **1.50** with iminoindolines **1.83** has been reported from our group. The type of product is controlled by the temperature and the additive used. When the reaction was performed at room temperature under PR_3 catalysis, dihydro-α-carboline core **1.84** was obtained whereas PR_3/Cs_2CO_3 combination yielded tosyl migrated α-carboline **1.85**. When the reaction was performed at 110 °C, $-CH_2CO_2Et$ moiety elimination (by C_α-C_β bond cleavage) was observed to give **1.86** (Scheme 1.29).[34]



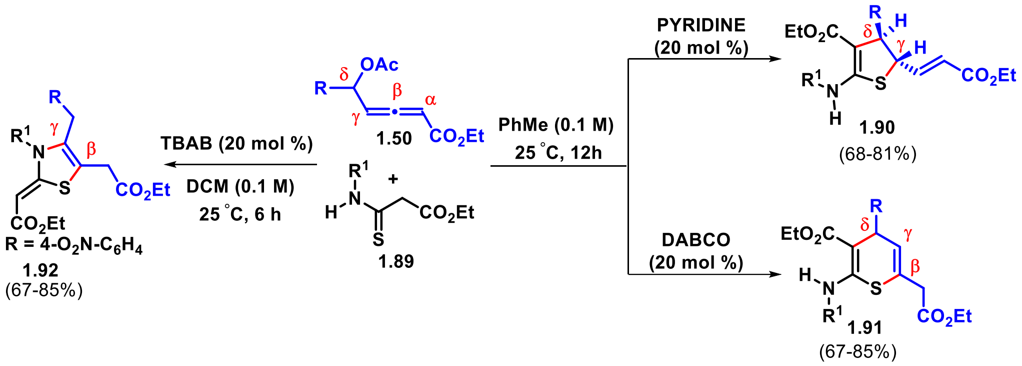
Scheme 1.29: Synthesis of α-carboline derivatives from acetoxy allenoate **1.50**

Yang *et al.* reported Cs_2CO_3 mediated (4 + 3) cyclization of oxotryptamines with δ-acetoxy allenoates **1.46** and oxotryptamines **1.87** for the construction of spiro-[azepane 4,3′-indol]-2′(1′H)-ones **1.88** in excellent yields. The pK_a value of the amide group in oxotryptamines plays an important role in this reaction. The authors proposed two pathways for the formation of **1.88**. The amide group in **1.87** is first deprotonated to give an anionic intermediate that attacks the β-carbon of the **1.46** to furnish intermediate **XX**. This intermediate undergoes H-shift to give intermediate **XXI**, which is followed by cyclization through an intramolecular nucleophilic addition to afford product **1.88** (Scheme 1.30).[35] An alternative pathway involving **XXII**/**XXIII** is also possible.



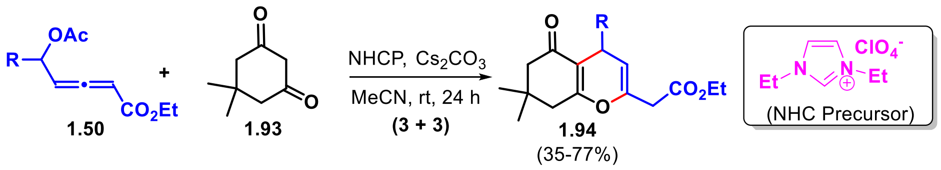
Scheme 1.30: Synthesis of spiro-heterocycles **1.88** from δ-acetoxy allenoates **1.46**

Amine-catalyzed chemoselective annulations of δ-acetoxy allenoates **1.50** with thioamides **1.89** result in the formation of dihydrothiophene **1.90** or thiopyran **1.91** scaffolds through distinct mechanisms. Pyridine-catalyzed (3 + 2) annulation yields dihydrothiophenes **1.90** as nearly single diastereomers. Conversely, DABCO-catalyzed (3 + 3) annulation produces thiopyrans **1.91** through addition-elimination and 6-*exo*-dig cyclization steps. In a markedly different pathway, TBAB-catalyzed (3 + 2) annulation generates a novel class of thiazole motifs **1.92** featuring a (*Z*)-isomeric exocyclic double bond involving the β- and γ-carbons of the allenoate in the cyclization process. These three distinct pathways significantly expand the scope of acetoxy allenoate chemistry (Scheme 1.31).[36]



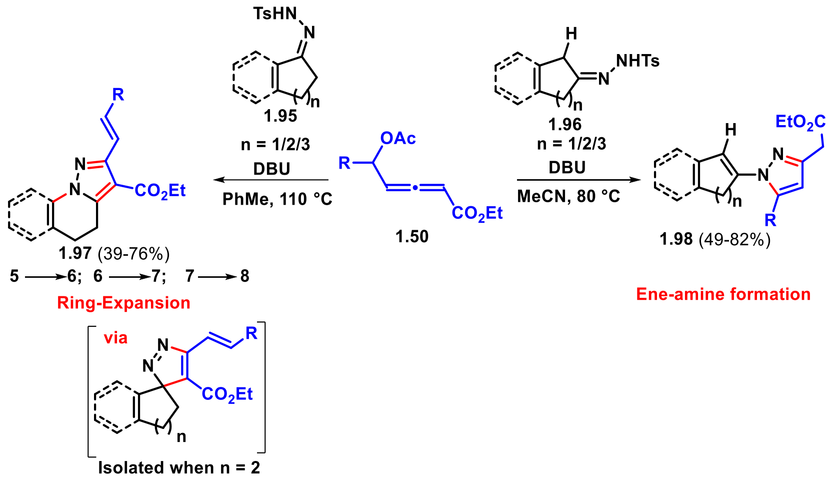
Scheme 1.31: Synthesis of dihydrothiophenes, thiopyrans, and thiazoles from δ-acetoxy allenoates **1.50**

Yao *et al.* reported NHC-catalyzed (3 + 3) annulation of δ-acetoxy allenoates **1.50** with 5,5-dimethyl-1,3-cyclohexanedione **1.93** that acts as 1C, 3O bisnucleophile for the synthesis of fused-4*H*-pyrans 1.94 with good yield and broad substrate scope. Here, the NHC catalyst forms a cationic intermediate species with **1.50** which reacts with **1.93** in the presence of Cs_2CO_3 to form zwitterionic intermediate. Elimination of NHC and oxa-Michael addition gives **1.94** (Scheme 1.32).[37]



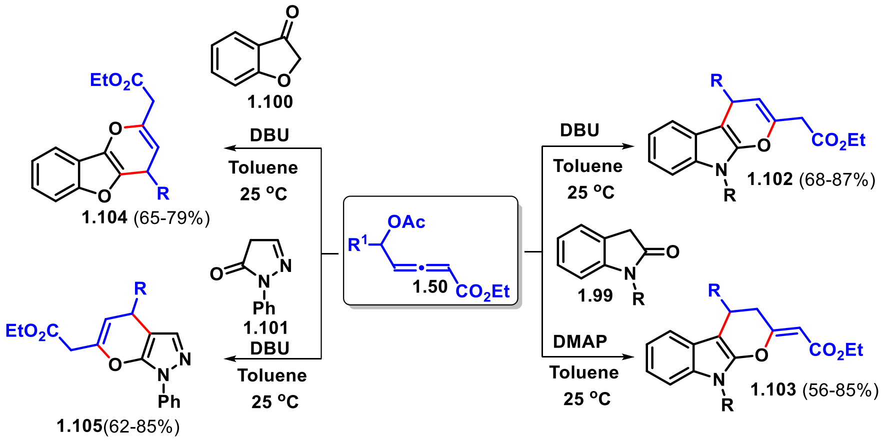
Scheme 1.32: Synthesis of fused 4*H*-pyrans **1.94** from δ-acetoxy allenoates **1.50**

Our group reported DBU-catalyzed hetero-annulation of δ-acetoxy allenoates **1.50** with *N*-sulfonylhydrazone (**1.95**/**1.96**). Here, cycl-2-ene-*N*-sulfonyl hydrazides **1.95** react with **1.50** and deliver the ring expansion products **1.97** (5 → 6, 6 → 7, and 7 → 8) *via* vinyl amine -imine coupling. This strategy was extended to carvone derived substrates also. By contrast, cycl-3-ene-*N*-sulfonyl hydrazides **1.96** react with **1.50** in a different manner and afford *N*-alkenyl-1,2-pyrazoles **1.98** *via* sequential allylic elimination. Here, allenoates **1.50** act as 3C synthons. The products **1.97-1.98** are mutually exclusive (Scheme 1.33).[38]



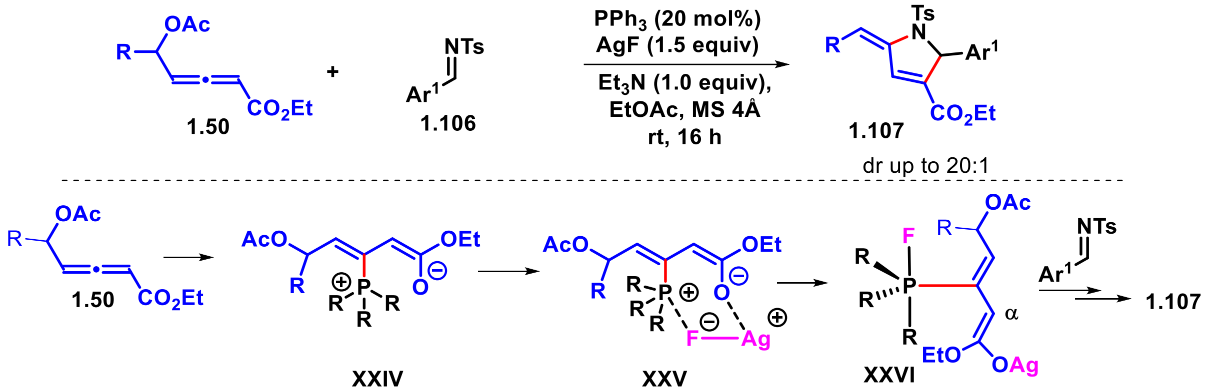
Scheme 1.33: Ring expansion and normal pyrazole products **1.97**/ **1.98** from δ-acetoxy allenoates **1.50**

Our group has also developed Lewis base dependent (3 + 3) annulation of δ-acetoxy allenoates **1.50** with Boc-protected oxindole (**1.99**), benzofuranone (**1.100**), and pyrazolone (**1.101**) *via* 6-*exo*-dig cyclization. The reaction occurs at rt (25 °C) and the products are fused pyrans **1.102-1.105**. The DBU-catalyzed reaction gives products with an endocyclic double bond while the DMAP-catalyzed reaction affords products with an exocyclic double bond (Scheme 1.34).[39a]



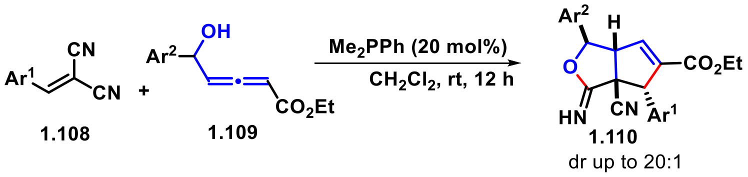
Scheme 1.34: Synthesis of 4*H*-pyrans from δ-acetoxy allenoates **1.50**

Qian *et al.* developed phosphine catalyzed (3 + 2) annulation of δ-acetoxy allenoates **1.50** with aldimine **1.106** facilitated by AgF. The effectiveness of this reaction depends on the metathesis between the enolate-phosphonium zwitterion **XXIV** and AgF, resulting in a critical intermediate consisting of a silver enolate and fluorophosphorane **XXV**. The silver enolate can participate in a Mannich reaction with aldimine, while the fluorophosphorane initiates a cascade reaction *via* **XXVI** that includes acetate elimination followed by *aza*-addition, allowing for P(III)/P(V) catalysis and affording dihydropyrroles **1.107** (Scheme 1.35).[40]



Scheme 1.35: Synthesis of dihydropyrroles **1.107** from δ-acetoxy allenoates **1.50**

Guo's group reported the phosphine-catalyzed domino annulation reaction of 1,1-dicyanoalkenes **1.108** with allenylic alcohols **1.109** as an innovative reaction that enabled the synthesis of bicyclic fused furans **1.110**. The bicyclic product **1.110** is formed through sequential (3 + 2) annulation and nucleophilic addition reactions, with significant diastereoselectivity and in yields of 40-89% (Scheme 1.36).[41]

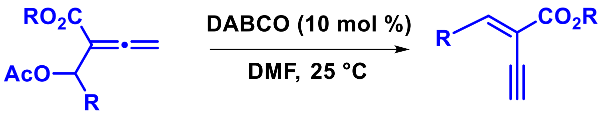


Scheme 1.36: Synthesis of tetrahydrocyclopentafurans**110** from δ-acetoxy allenoates **1.50**

1.3.2 *β'-Acetoxy allenoate chemistry*

These substrates do not differ much from the *δ*-acetoxy allenoates, but since the removable acetoxy group is positioned closer to the electron-withdrawing CO$_2$R group connected to the α-carbon, some differences in the reactivity may be observed. Relevant details are highlighted here.

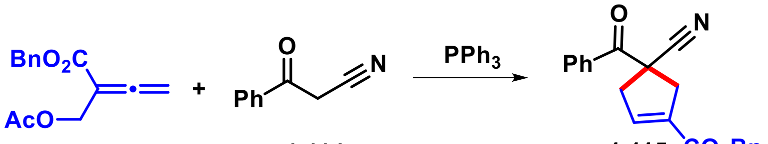
Lee's group developed a highly stereoselective synthesis of (*E*)-α-ethynyl-α,β-unsaturated ester **1.112** from allenyl acetate esters **1.111** under DABCO catalysis at room temperature in DMF (Scheme 1.37).[42]



1.111 **1.112** (70-88%)

Scheme 1.37: (*E*)-α-ethynyl-α,β-unsaturated ester **1.112** from *β′*-acetoxy allenoate **1.111**

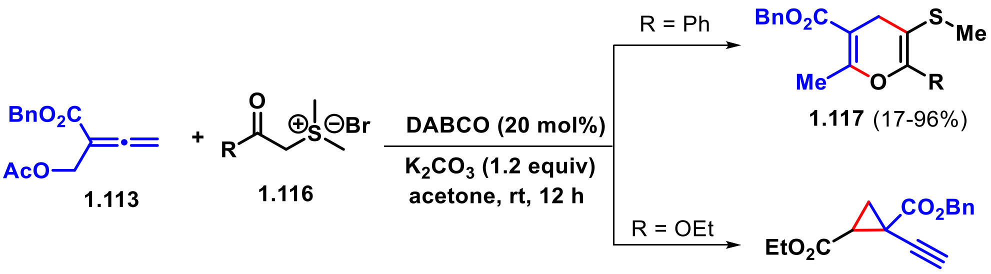
Tong *et al.* reported the first PPh_3 catalyzed (4 + 1) annulation of *β′*-acetoxy allenoate **1.113** with 1C,1C-bisnucleophiles **1.114** for the synthesis of cyclopentene carboxylate **1.115**.[43a] Here, allenoate **1.113** acts as a 1,4-biselectrophile. Later, Fu's group developed enantioselective variant of this (4 + 1) annulation using biphenyl derived phosphine (Scheme 1.38).[43b]



1.113 **1.114** **1.115** (22-95%)

Scheme 1.38: Synthesis of cyclopentene **1.115** from *β′*-acetoxy allenoate **1.113**

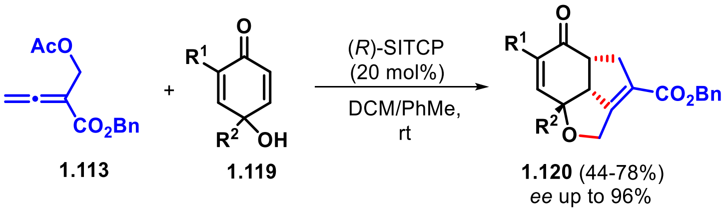
Tong's group developed amine catalyzed distinct annulation of *β′*-acetoxy allenoate **1.113** with sulfur ylides **1.116. Here,** the ketone stabilized sulfur ylide delivered 4*H* pyrans **1.117** and ester stabilized ylide gave cyclopropane carboxylate **1.118**. The deprotonation in ketone stabilized sulfur ylide is faster than that in the corresponding ester-stabilized ylide. Therefore, diene-ammonium intermediate in reaction with ester-stabilized ylide gives cyclopropane carboxylate **1.118** (Scheme 1.39).[44]



1.113 **1.116** **1.117** (17-96%) **1.118** (53%)

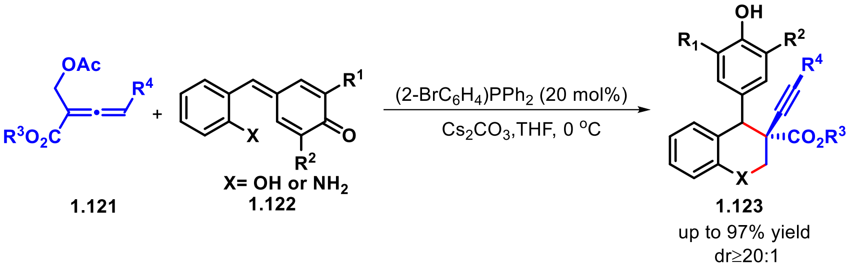
Scheme 1.39: Synthesis of 4H-pyrans and cyclopropane carboxylates from *β′*-acetoxy allenoate **1.113**

Min Shi and co-workers discovered a one-step phosphine catalyzed highly diastereoselective cascade annulation reaction between *p*-quinols **1.119** and *β′*-acetoxy allenoates **1.113** to obtain multiple ring-fused hexahydroindeno furans **1.120** containing three consecutive stereogenic carbon centers. The important points in this phosphine-catalyzed process are (i) excellent tolerance for the functional group, (ii) vast substrate scope, (iii) asymmetric version, (iv) mild conditions, (v) ease of scale-up to gram scale, (vi) good yields, and (vii) subsequent reactions (Scheme 1.40).[45]



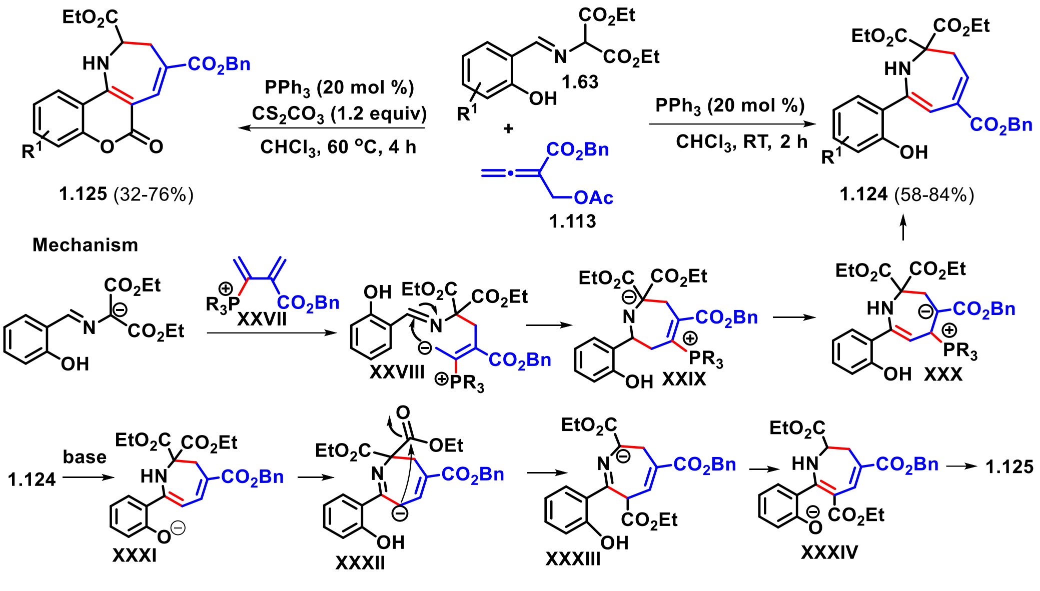
Scheme 1.40: Synthesis of hexahydroindeno furans **1.120** from *β′*-acetoxy allenoate **1.113**

Huang and co-workers developed a new domino (4 + 2) cycloaddition of *β′*-acetoxy allenoates **1.121** with *p*-quinone methides (*p*-QMs) **1.122** under phosphine-catalysis affording a new class of chromane and tetrahydroquinolines (**1.123**) that have an alkynyl-substituted quaternary carbon. This is the first time that the *α*- and *β′*-carbon atoms of *α*-substituted allenoates participated in the (4 + 2) cycloaddition. Products with either terminal or internal alkynes at the quaternary carbon center could be synthesized readily (Scheme 1.41).[46]



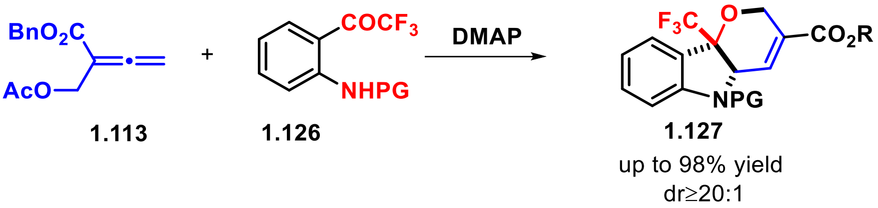
Scheme 1.41: Synthesis of chromane and tetrahydroquinolines **1.123** from *β′*-acetoxy allenoate **1.121**

Zhou's group obtained azepines from *β′*-acetoxy allenoates **1.113** and aldimine esters **1.63** by employing phosphine catalysis using a reaction tunable for the formation of azepine-2,2,4-tricarboxylates **1.124** in the presence of catalytic PPh_3 or (4 + 3)/1,5-ethoxycarbonyl migration/lactonization cascade reaction for the formation of chromeno[4,3-*b*]azepin-6(1*H*)-ones **1.125** when the reaction was performed in the presence of PPh_3 and Cs_2CO_3.[48] For the formation of the latter compounds **1.125**, the authors proposed the initial formation of **1.124** (Scheme 1.42).[47]



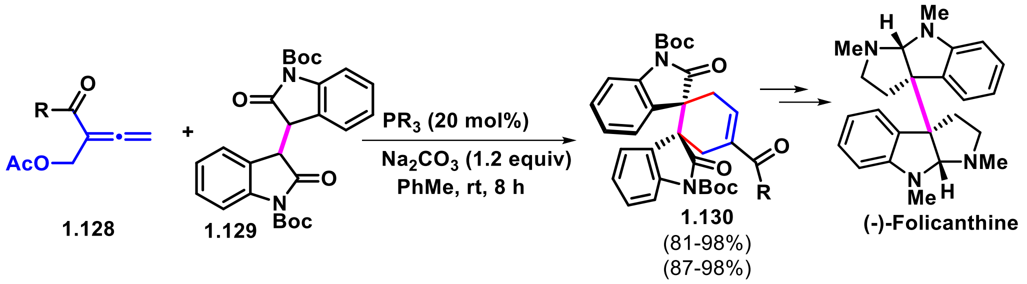
Scheme 1.42: Synthesis of azepine-carboxylates **1.124/1.125** from *β′*-acetoxy allenoate **1.113**

Huang *et al.* developed DMAP catalyzed (4 + 1)/(3 + 3) domino sequential annulation of *β′*-acetoxy allenoates **1.113** with *o*-aminotrifluoroacetophenones **1.126** for the synthesis of CF_3 moiety containing tetrahydropyrano[3,2-*b*]indoles **1.127** as single diastereomers in good yields. The reaction may follow two paths from the ammonium ylide. It can either go through intramolecular Diels-Alder reaction or *oxa*-Michael addition but because of excellent diastereoselctivity, the former process is more probable. In the formation of the product, one each of C-N, C-C, and C-O bonds are generated in a single step (Scheme 1.43).[48]



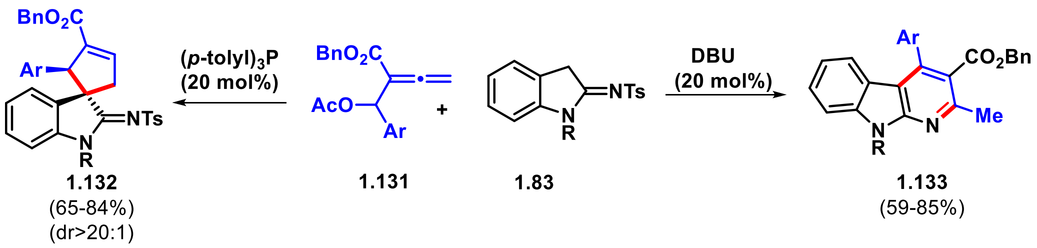
Scheme 1.43: Synthesis of tetrahydropyrano[3,2-*b*]indoles **1.127** from the *β′*-acetoxy allenoate **1.113**

Lu’s group reported asymmetric (4 + 2) annulation of allenic ketone **1.128** as a dielectrophilic C4 synthon. The introduction of ketone group provided high reactivity to the dielectrophile which can efficiently react with weak dinucleophile bisoxindoles **1.129**. The reaction produced spirocyclic bisoxindole scaffolds **1.130** having two vicinal stereogenic centers with high enantioselectivities. This methodology was used in the total synthesis of (−)-folicanthine (Scheme 1.44).[49]



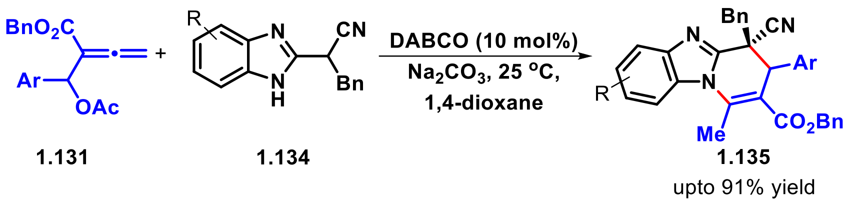
Scheme 1.44: Synthesis of (−)-folicanthine from allenoate **1.128**

Our group reported Lewis base catalyzed annulation of *β′*-acetoxy allenoates **1.131** with iminoindolines **1.83**. Under PR$_3$ catalysis,[50a] the reaction follows (4 + 1) pathway to give spirocyclic cyclopentene carboxylates **1.132** in good yields and high diastereoselectivity. The DBU catalyzed reaction,[50b] by contrast, affords α-carbolines **1.133** *via* (3 + 3) annulation (Scheme 1.45).[50]



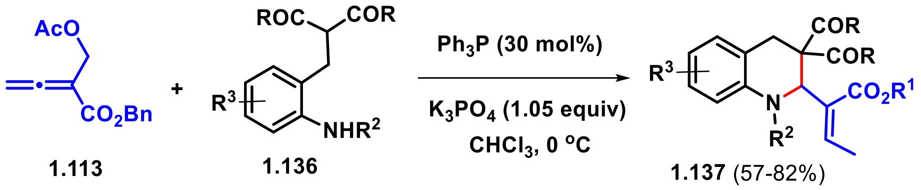
Scheme 1.45: Synthesis of spirocyclic cyclopentene carboxylates **1.132** and substituted α-carbolines **1.133**

Qin and co-workers established an amine-catalyzed (3 + 3) annulation of *β′*-acetoxy allenoates **1.131** with 1*C*,3*N*-bisnucleophiles **1.134** in the presence of DABCO assisted by sodium carbonate in 1,4-dioxane at room temperature. Under the optimized conditions, this synthetic process worked well with a large number of substrates furnishing 1,2-fused benzimidazoles **1.135** in good yields. Additionally, the asymmetric version of this reaction has been checked by using cinchona alkaloid-based tertiary amines. They obtained 80% *ee* in one case albeit in 38% yield (Scheme 1.46).[51]



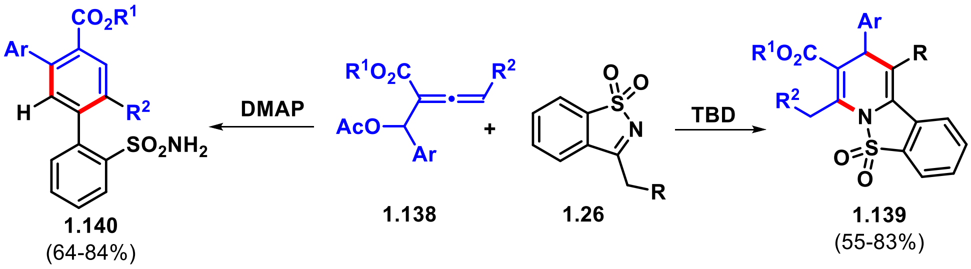
Scheme 1.46: Synthesis of 1,2-fused benzimidazoles from *β′*-acetoxy allenoates **1.131**

Wan and co-workers reported PPh_3 catalyzed (5 + 1) annulation of 1,5-dinucleophiles **1.136** with *β′*-acetoxy allenoate **1.113** for the synthesis of novel tetrahydroquinolines **1.137** The use of K_3PO_4 as a base has a significant role in enhancing the yield because it helps the easy removal of proton from nucleophilic carbon in **1.136**. This is the first reaction where *β′* carbon of *β′*-acetoxy allenoates is involved in the annulation reaction with allenoate acting as a 1*C* synthon (Scheme 1.47).[52]



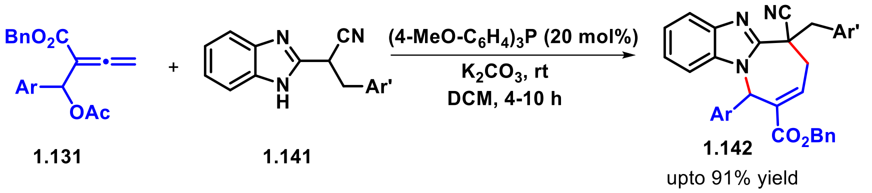
Scheme 1.47: Synthesis of tetrahydroquinolines from *β′*-acetoxy allenoates **1.113**

Our group reported an amine-controlled annulation of *β′*-acetoxy allenoates **1.138** with *N*-sulfonyl ketimines **1.26**. Here, the TBD catalyzed reaction offers dihydropyridines **1.139** *via* (3 + 3) annulation which involves an allenic intermediate *via* 1,2-elimination. However, DMAP catalyzed reaction occurs by (4 + 2) annulation offering *m*-teraryls **1.140** *via* Mannich coupling and aromatization (Scheme 1.48).[53] The key intermediates of the reaction were identified by HRMS studies



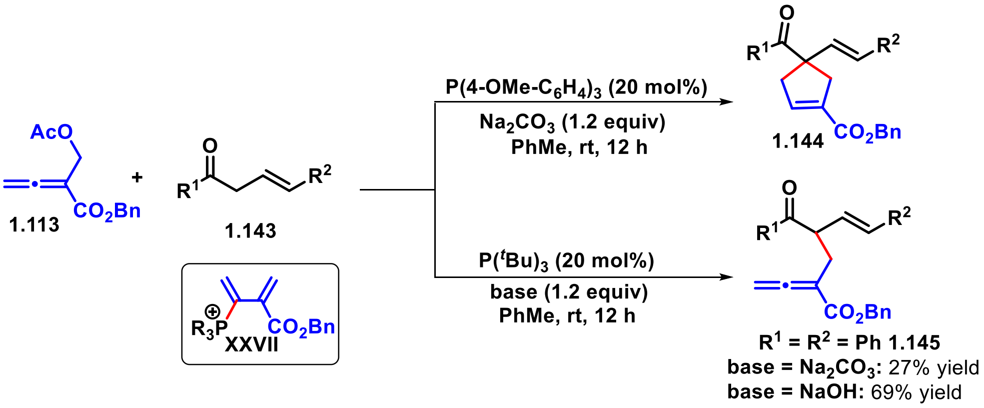
Scheme 1.48: Synthesis of substituted dihydropyridine **1.139** and *m*-teraryl **1.140** from *β′*-acetoxy allenoates **1.138**

Ni and co-workers reported the synthesis of azepine derivatives **1.142** *via* PR_3-catalyzed (4 + 3) annulation of benzimidazole **1.141** with *β′*-acetoxy allenoates **1.131** under mild conditions. Here, benzimidazole tethered substrates act as 1*C*,3*N*-bisnucleophiles. The asymmetric variant of this reaction has been conducted utilizing phosphine (*R*)-SITCP as the catalyst (Scheme 1.49).[54]



Scheme 1.49: Synthesis of 1,2-fused benzimidazoles **1.141** from *β′*-acetoxy allenoates **1.131**

Tong's group reported PR_3-catalyzed annulation of *β′*-acetoxy allenoate **1.113** with *β,γ*-unsaturated carbonyl substrates **1.143.** Under $P(4\text{-MeO-}C_6H_4)_3$ catalysis, the reaction follows (4 + 1) pathway to furnish cyclopentenes. Here, precursors **1.143** act as αC, αC-bisnucleophiles. On the other hand, under $P(^tBu)_3$ catalysis, the reaction follows a different mechanistic pathway because the *γ*-position of diene-phosphonium species **XXVII** is more hindered and hence the attack of **1.143** at the *β′*-position gives allenic compound **1.145** (Scheme 1.50).[55]



Scheme 1.50: Synthesis of cyclopentene from *β′*-acetoxy allenoates **1.113**

Thus acetoxy allenoates are wonderful substrates if one can judiciously use the bis-nuleophilic partner; this is what we intend to do in the present work.

1.4. Reaction Chemistry of Cyclic *N*-Sulfonyl-Ketimines

Cyclic sulfamidate imines as components of 5- or 6-membered rings are emerging as valuable precursors for organic chemists because of their versatile reactivity.[56] Bearing a reactive prochiral C=N bond moiety, these are widely used as substrates to synthesize important natural products, biologically active heterocyclic compounds, and macromolecules.[57] These scaffolds comprehensively participate in reactions like hydrogenation,[58] nucleophilic addition,[59] ring expansion,[60] and annulation reaction.[61] Some of them are also key units in anticancer, antipsychotic, and antituberculosis drugs.[62]

The electrophilic imine moiety character of the C=N bonds allows sulfamidate imines to undergo the Mannich type reaction. The acidity of α-C_{sp3}-H protons is increased because of the C=N double bond character (Figure 1.2). Under basic conditions, aza-enolates are formed, and under photocatalysis they undergo single electron transfer to form α-iminyl C-centered radical. These generally tautomerize to form enamines under neutral conditions. The sulfonyl moiety in α-alkyl cyclic *N*-sulfonyl ketimines containing heteroatoms increases the acidity of their α-Csp^3–H protons. The proton can be removed by a base, subsequently rendering the resulting intermediates as excellent carbonucleophiles. The *N*-sulfonyl moiety of ketimines can also act as a leaving group opening more synthetic avenues in organic synthesis.

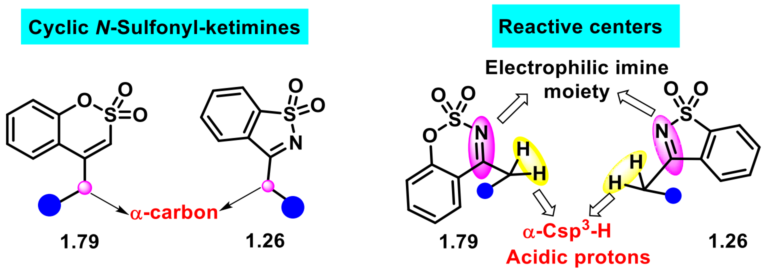
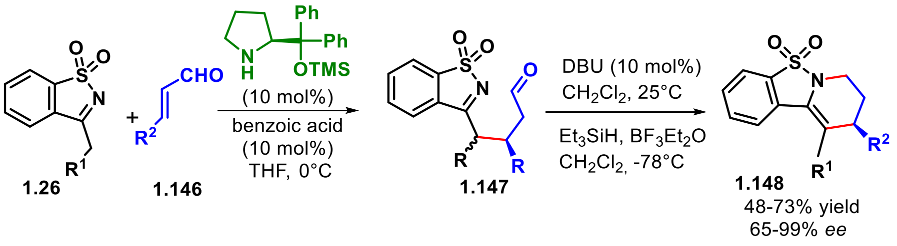


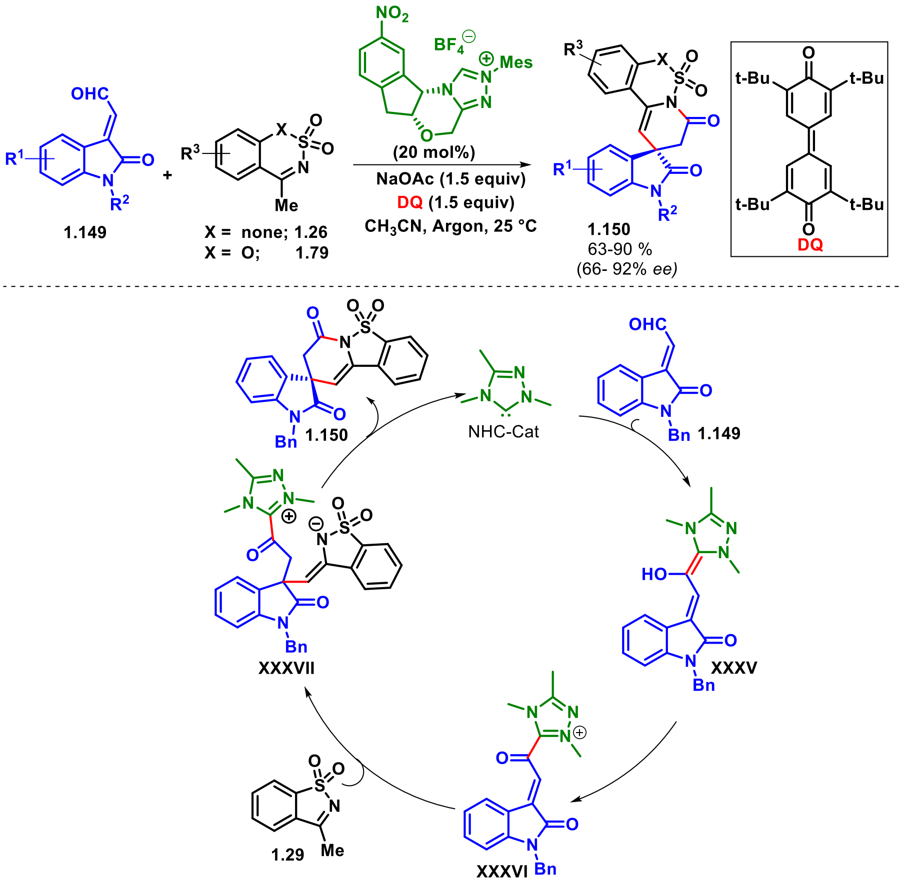
Figure 1.2: General structure and reactive centers of cyclic *N*-sulfonyl ketimines

Chen's group has reported the reversal of electrophilic reactivity of cyclic *N*-sulfonylimines **1.26** *via* asymmetric Michael addition reaction with α,β-unsaturated aldehydes **1.146** by using α,α-diphenylprolinol-*O*-TMS ether as a catalyst to give diastereomeric mixture of **1.147** which can be converted into tricyclic piperidine **1.148** with excellent enantioselectivity by a tandem cyclization that involves tautomerization, hemiaminal formation, and dehydroxylation catalyzed by DBU (Scheme 1.51).[63]



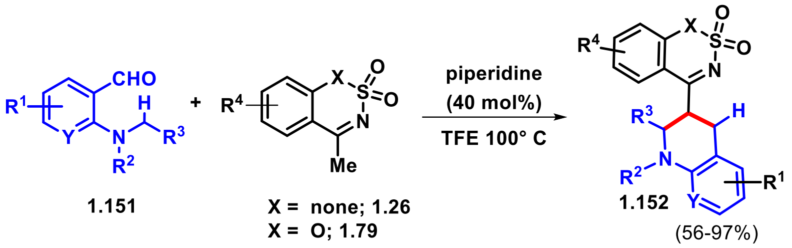
Scheme 1.51: Synthesis of tricyclic piperidine from cyclic *N*-sulfonylimines

Enders' group reported (3 + 3) annulation of *N*-sulfonyl ketimines (**1.26** or **1.79**) with isatin-derived enals **1.149** using a NHC-catalyst for the synthesis of pentacyclic spirooxindoles in good yields and good to high enantiomeric ratios. The reaction proceeds by the addition of NHC-catalyst to **1.149** to form Breslow intermediate **XXXV** which upon oxidation with bisquinone affords the α,β-unsaturated acyl azolium intermediate **XXXVI**. This intermediate undergoes Michael addition with **1.29** in the presence of a base to give intermediate **XXXVII** from which intramolecular lactamization and regeneration of the NHC catalyst gives **1.150** (Scheme 1.52).[64]



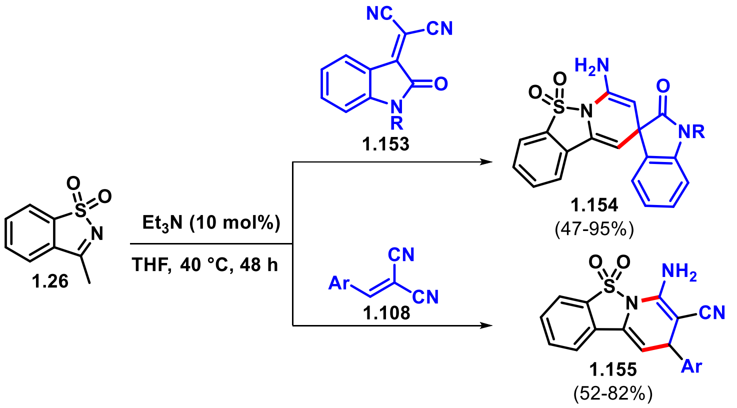
Scheme 1.52: NHC-catalyzed (3 + 3) annulation of *N*-sulfonyl ketimines with isatin-derived enals

Yuan *et al.* developed dual alkylation of the C(sp^3)-H bond of cyclic *N*-sulfonyl-ketimines (**1.26** or **1.79**) with *o*-aminobenzaldehyde **1.151** catalyzed by piperidine for the construction of tetrahydroquinolines **1.152** in good yields. The reaction involves sequential condensation followed by [1,5]-hydride transfer and trifluoroethanol (TFE) assisted cyclization (Scheme 1.53).[65]



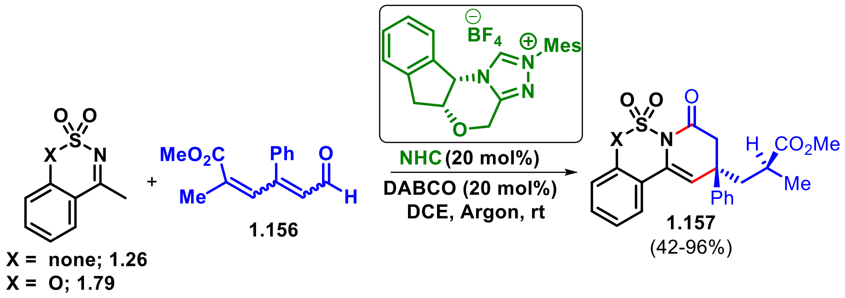
Scheme 1.53: Synthesis of tetrahydroquinolines from cyclic *N*-sulfonyl-ketimines

Mei's group reported the synthesis of saccharin-fused 1,4-dihydropyridines **1.154** (1,4-DHPs) *via* Et_3N-catalyzed (3 + 3) tandem Michael/aza-Pinner reaction, by employing cyclic *N*-sulfonyl ketimines **1.26** as nucleophiles and α,α-dicyanoolefins **1.108/1.153** as electrophiles. This methodology has broad functional group compatibility, works under mild conditions and gives the desired products in good to excellent yields (Scheme 1.54).[66]



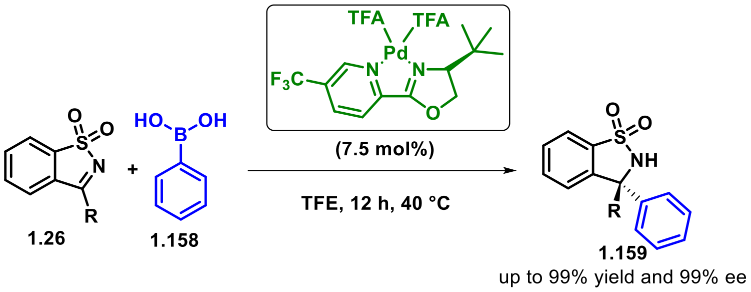
Scheme 1.54: Synthesis of saccharin-fused 1,4-dihydropyridines from cyclic *N*-sulfonyl ketimines

Dong *et al.* reported NHC-catalyzed enantioselective δ-protonation/(3 + 3) annulation reaction of α,β-γ,δ-diunsaturated enals **1.156** with cyclic-*N*-sulfonyl ketimines (**1.26** or **1.79**) for the synthesis of dihydropyridinone scaffolds **1.157** in moderate to high yields. The reaction provides two chiral centers, including a quaternary stereocenter, in a single step. In this process, a chiral NHC catalyst reacts with **1.156** to form the extended Breslow intermediate which generates two nucleophilic carbon centers (β and γ). The acyl azolium ion thus formed adds to **1.26** or **1.79** *via* nucleophilic addition; followed by tautomerization and *N*-acylation giving **1.157** (Scheme 1.55).[67]



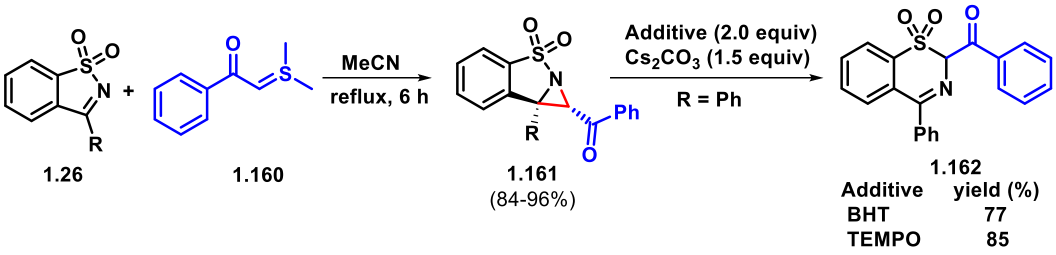
Scheme 1.55: Synthesis of dihydropyridinone **1.157** from cyclic-*N*-sulfonyl ketimines

Sedlák's group developed an improved version of the enantioselective addition of aryl boronic acid **1.158** to the cyclic *N*-sulfonyl ketimines **1.26** using (*S*)-4-(*tert*-butyl)-2-(5-(trifluoromethyl) pyridin-2-yl)-4,5-dihydrooxazole ligand with excellent yield as well as *ee*. This reaction was successfully tested on a continuous flow system and gave a high turnover (Scheme 1.56).[68]



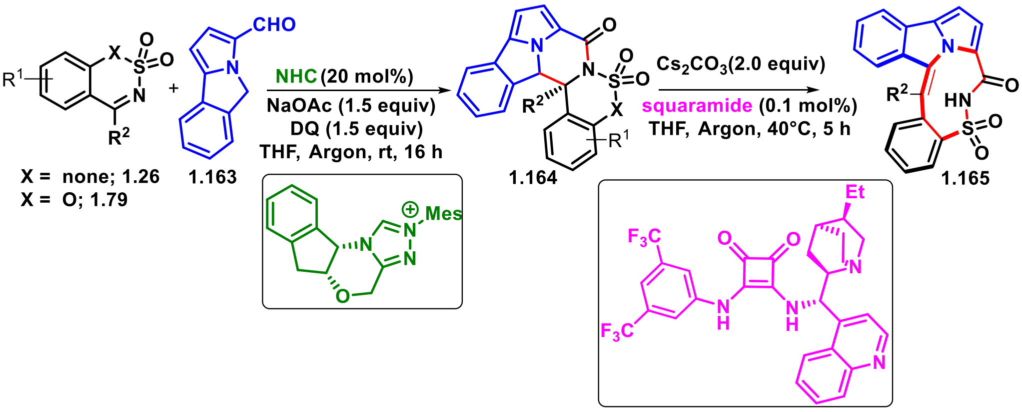
Scheme 1.56: [Pd]-catalyzed asymmetric arylation of cyclic *N*-sulfonyl ketimines with boronic acids

A concise and efficient method for synthesizing aziridines has been developed by Liu's group utilizing intermolecular (2 + 1) cycloaddition reaction of cyclic *N*-ketimines **1.26** and sulfur ylides **1.160**. This reaction has high atom economy, broad substrate scope, excellent yields, and high diastereoselectivity (>20:1 dr). Furthermore, **1.161** can be converted into benzothiazines **1.162** in the presence of Cs_2CO_3 *via* an intramolecular S_N2-type nucleophilic substitution (Scheme 1.57).[69]



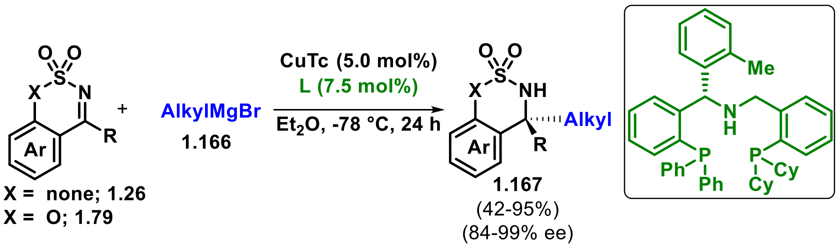
Scheme 1.57: Synthesis of benzothiazines from cyclic *N*-ketimines

Ren *et al.* have introduced a significant advancement in catalytic asymmetric synthesis through their work on NHC-catalyzed diastereoselective and enantioselective higher-order cycloadditions. They have demonstrated the transformation of 5*H*-benzo[*a*]-pyrrolizine-3-carbaldehydes **1.163** with cyclic-*N*-sulfonyl ketimines (**1.26** or **1.79**) into optically pure polycyclic piperazin-2-ones **1.164** under mild reaction conditions with excellent diastereoselectivities and enantioselectivities. Additionally, they have illustrated the potential for further diversification by converting these chiral polycyclic piperazin-2-ones into chiral nine-membered cyclic amides **1.165** *via* squaramide-catalyzed asymmetric ring-expansion reactions (Scheme 1.58).[70]



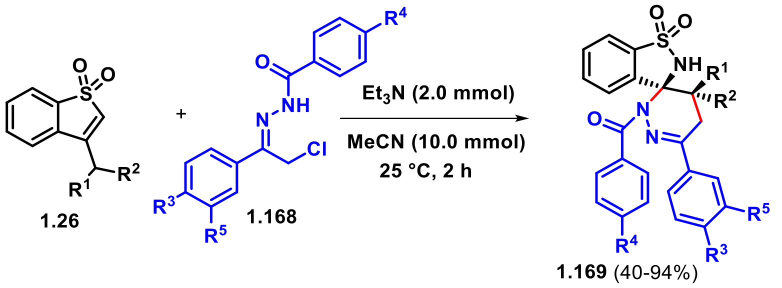
Scheme 1.58 Synthesis of polycyclic piperazin-2-ones from cyclic *N*-sulfonyl ketimines

Zhang's group recently reported a catalytic asymmetric alkylation using their newly developed PNP-type ligand W-Phos and a copper catalyst. This innovation enables the efficient alkylation of both cyclic *N*-sulfonyl ketimines (**1.26** or **1.79**) with alkyl Grignard reagents **1.166**. The success of this method lies in the utilization of a newly identified ancillary, which facilitates the formation of chiral aza-quaternary stereocenters (α-tertiary amines) with high enantioselectivities and good yields. Importantly, this strategy is applicable to a wide range of substrates, demonstrating its versatility. Furthermore, the scalability of the reaction and its potential for further derivatization underscore the practical utility of this protocol in organic synthesis (Scheme 1.59).[71]



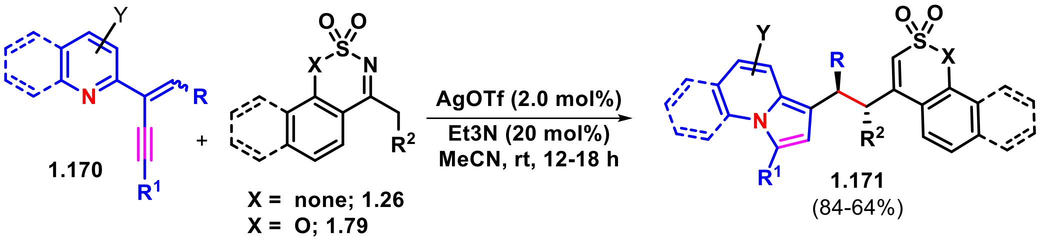
Scheme 1.59: Asymmetric alkylation of cyclic *N*-sulfonyl ketimines with Grignard reagents

Cao's group developed (4 + 2) annulation of cyclic *N*-sulfonyl ketimines **1.26** with 1,2-diaza-1,3-dienes **1.168** mediated by Et_3N for the synthesis of spiropyridazine benzosultams **1.169** under mild reaction conditions (Scheme 1.60).[72]



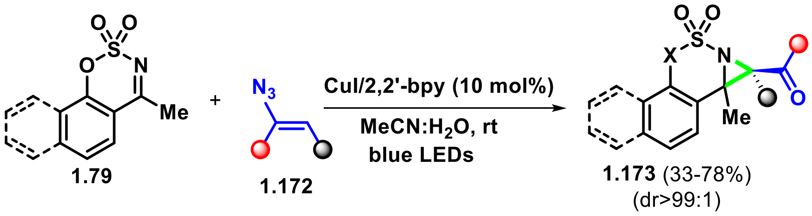
Scheme 1.60 Synthesis of spiropyridazine benzosultams from cyclic *N*-sulfonyl ketimines

Samanta's group reported AgOTf catalyzed domino cyclization of cyclic N-sulfonyl ketimines (**1.26** or **1.79**) with alkyne **1.170** to give 4-(indolizinylethyl)-substituted ketimine **1.171** having broad substrate scope in good yields with 100% atom economy. This reaction creates C-N and C-C bonds. The synthesized products were further derivatized to give coumarinyl/benzofuranyl-substituted indolizines (Scheme 1.61).[73]



Scheme 1.61 Synthesis of indolizinylethyl-substituted ketimine **1.171** from cyclic *N*-sulfonyl ketimines (**1.26** or **1.79**)

Recently Samanta's group also reported the CuI and blue LEDs assisted (2 + 1) aza-cyclization reaction of cyclic N-sulfamidate imine **1.79** with vinyl azides **1.172** for the synthesis of benzo[*f*][1,2,3]oxathiazepine dioxides in good yields and high diastereoselectivity. This reaction generates C-C/C-N/C=O bonds (Scheme 1.61).[74a] In addition to this, they have also done more substantial work on similar systems earlier.[74b-g]

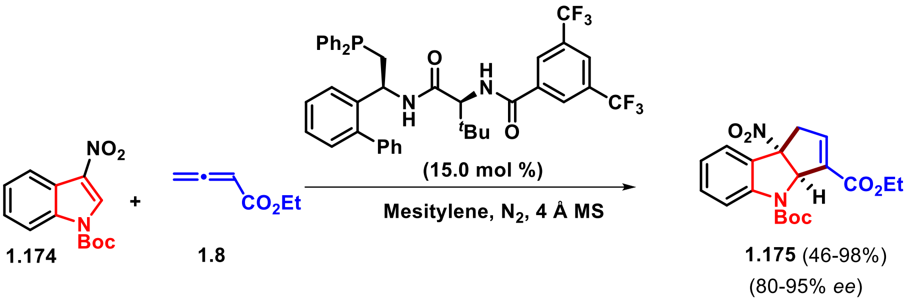


Scheme 1.62 Synthesis of spiropyridazine benzosultams from cyclic *N*-sulfonyl ketimines

1.5 Dearomative Cycloaddition/ Cyclization

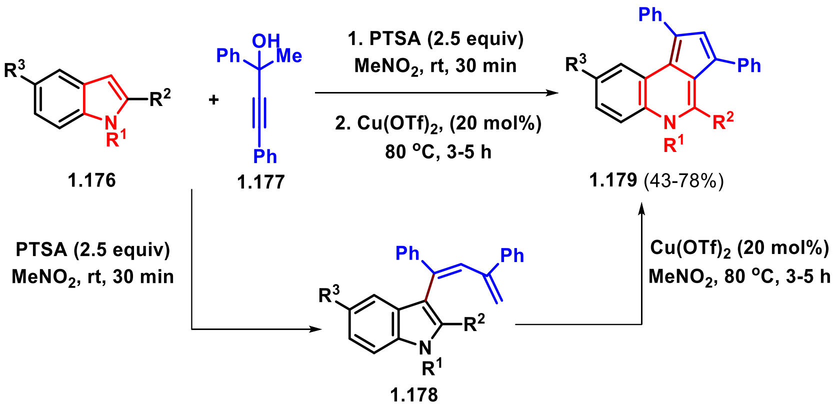
Dearomative cycloaddition and cyclization are general topics but in the following lines a brief survey of recent literature that is close to the present work is highlighted.

Zhang's group reported the asymmetric dearomative (3 + 2) cycloaddition of 3-nitroindoles **1.174** and allenoate **1.8** using a chiral phosphine for the synthesis of chiral 2,3-fused cyclopentannulated indolines **1.175** in moderate to excellent yields and high enantioselectivities. The allenoate **1.8** generates α-centered zwitterionic intermediate with PR_3 (*cf* Scheme 1.1) which upon conjugate addition to **1.174,** subsequent cyclization and regeneration of PR_3 gives **1.175** (Scheme 1.63).[76]



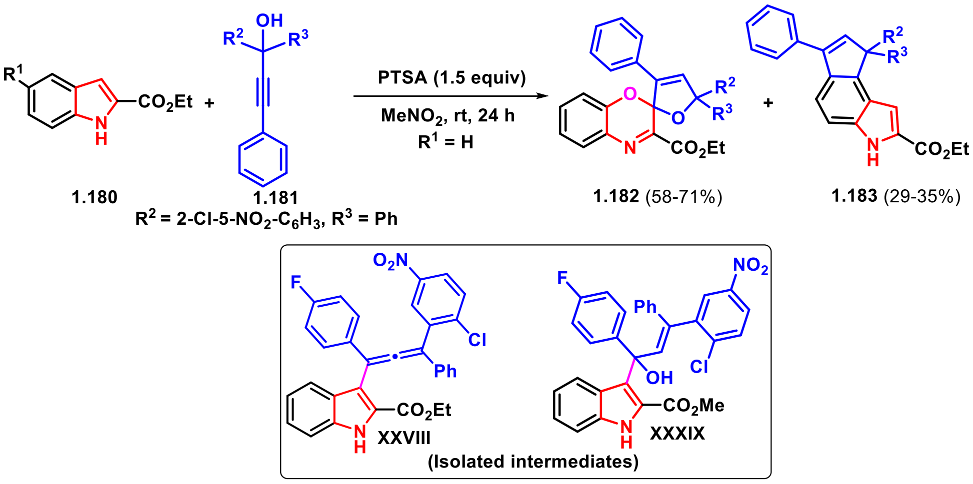
Scheme 1.63: Synthesis of cyclopentannulated indolines from allenoate **1.8**

Our group successfully demonstrated a novel sequential one-pot methodology for constructing highly conjugated cyclopenta[*c*]quinolines **1.179**. This was achieved using propargyl alcohol **1.173** and 2-substituted indoles **1.176**, catalyzed by $Cu(OTf)_2$ and PTSA, through the dearomatized oxidative ring expansion of intermediate **1.178** with air as the sole oxidant The reaction involves Brønsted acid-mediated allenylation and isomerization to form intermediate **1.178**, which then undergoes copper-catalyzed dearomatization and oxidative ring expansion to yield the final product **1.179** (Scheme 1.64).[77]



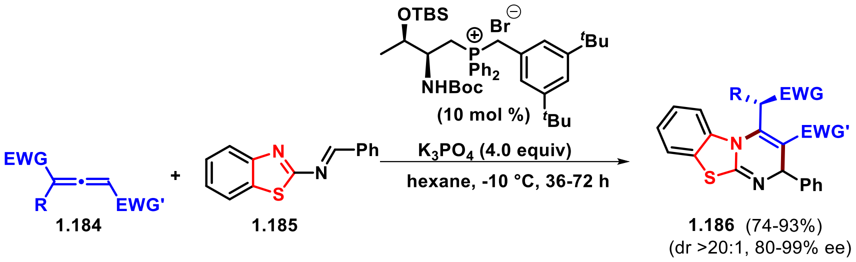
Scheme 1.64: Synthesis of cyclopenta[*c*]quinoline from propargyl alcohol **1.179**

Our group also reported PTSA mediated dearomative ring expansion followed by spirocyclization (*via* oxygen insertion) of indole-2-carboxylates **1.180** with propargylic alcohols **1.181** The disadvantage of this reaction, however, is the requirement of 2-Cl,5-NO_2-C_6H_3 group on the propargylic alcohol. The lone pairs of chlorine and electron withdrawing effect of NO_2 work synergistically to generate intermediate **XXXIX** from **XXVIII.** The intermediate **XXXIX** undergoes cyclopropanation, oxygen insertion, and ring expansion to afford **1.182** (Scheme 1.65).[78]



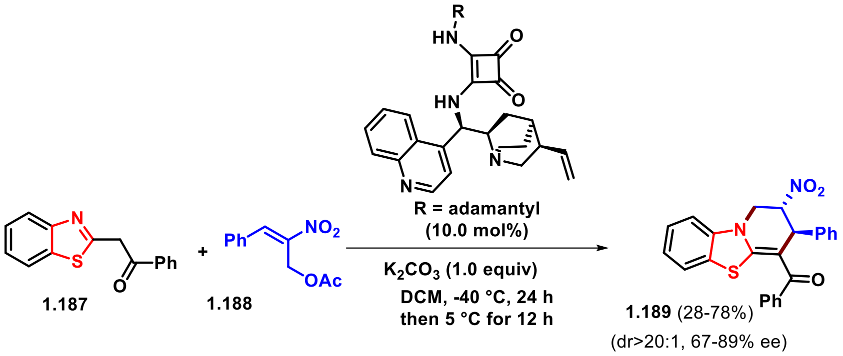
Scheme 1.65: Dearomative ring expansion of indole-2-carboxylates **1.180** with propargylic alcohols **1.181**

Lu *et al.* developed an efficient annulation between allenoate **1.184** and 2-benzothiazolimines **1.185** catalyzed by amino acid-derived bifunctional phosphonium salt catalyst. This (4 + 2) annulation gives thiourea-based benzothiazolopyrimidines **1.186** with excellent diastereo- and enantio-selectivities under mild reaction conditions (Scheme 1.66).[79]



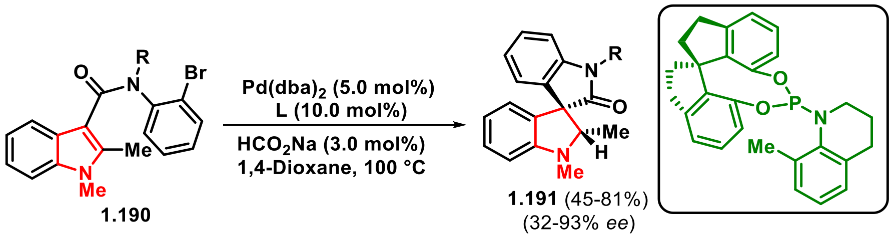
Scheme 1.66: Synthesis of benzothiazolopyrimidine from allenoates **1.184**

Song *et al*. developed a squaramide-catalyzed dearomative (3 + 3) cycloaddition of 2-acyl benzothiazoles **1.187** with 2-nitroallylic acetates **1.188**, leading to the synthesis of benzothiazolopyridines **1.189**. This reaction produces products with two adjacent stereogenic centers, achieving moderate to good yields with good to excellent stereocontrol. The protocol regiospecifically involves the desired *aza*-Michael cyclization, rather than the *oxa*-Michael cyclization (Scheme 1.67).[80]



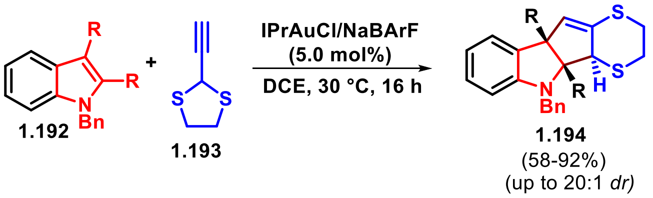
Scheme 1.67: (3 + 3) Cycloaddition between 2- acylbenzothiazole **1.187** and nitroacetates **1.188**

Wang *et al.* developed an enantioselective [Pd]-catalyzed intramolecular dearomative reductive Heck reaction of indole **1.190** by employing Pd(dba)$_2$/SPINOL-based phosphoramidite as the chiral catalyst. The protocol provides an efficient method to afford spirooxindoles **1.191** bearing vicinal stereocenters in moderate to good yields and excellent enantioselectivities for most cases. It represents asymmetric reductive Heck reaction of a formal sterically congested tetrasubstituted endocyclic alkene (Scheme 1.68).[81]



Scheme 1.68: [Pd]- catalyzed synthesis of spirooxindoles **1.191**

Winne's group developed gold(I) catalyzed (3 + 2) dearomative annulation of indoles **1.192** with 2-ethynyl-1,3-dithiolane **1.193** to generate functionalized cyclopentenes **1.194** having three continuous stereocenters with excellent control of relative stereochemistry and high functional group tolerance (Scheme 1.69).[82]

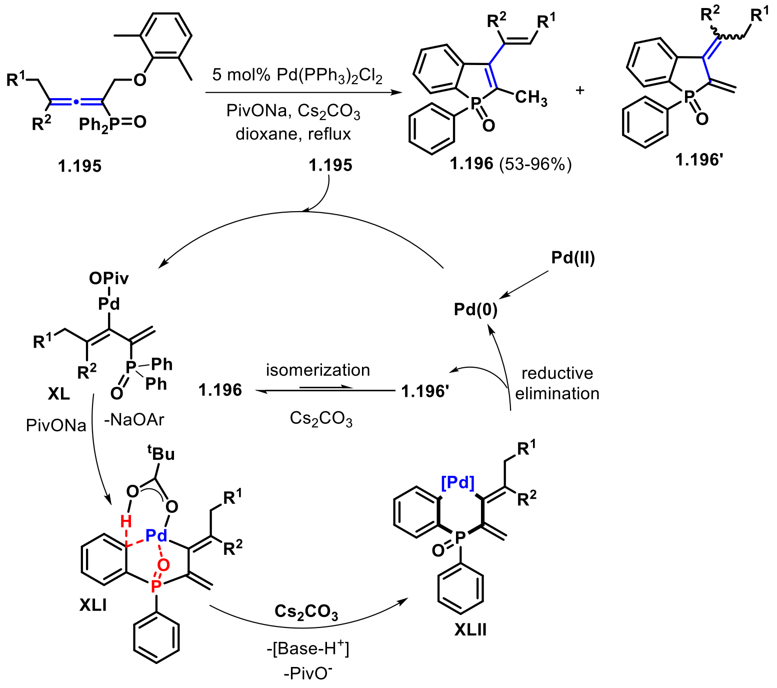


Scheme 1.69: Dearomative (3 + 2) annulation of indoles **1.192**

1.6 Annulation Reactions of Phosphorus-Based Allenes

Phosphorus-based allenes are readily prepared and are useful substrates in cyclization/cycloaddition reactions.[83] Recent literature that is more relevant to the work done in this thesis is presented in this section.

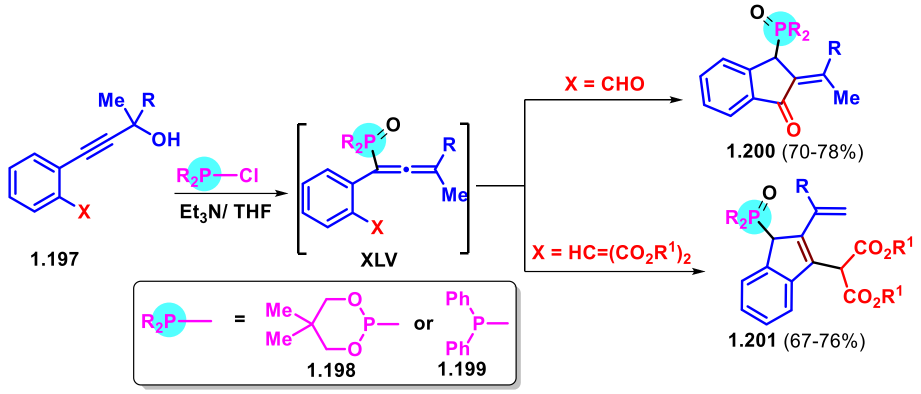
Wu and co-workers reported the [Pd]-catalyzed intramolecular cyclization of allenylphosphine oxides **1.195** to obtain 3-alkenyl benzo[*b*]phosphole oxides **1.196**. This transformation encompasses oxidative addition followed by the immediate cleavage of the C-O bond to form intermediate **XL**. Subsequently, C-H activation occurs in the presence of pivalate, generating intermediate **XLI**. The elimination of pivalic acid then leads to the formation of the six-membered palladium complex **XLII**. Through reductive elimination, this complex yields the isomer **1.196′**, which in the presence of a Cs_2CO_3 converts to the final product **1.196**, while regenerating the Pd(0) catalyst (Scheme 1.70).[84]



Scheme 1.70: Intramolecular [Pd]-catalyzed cyclization of allenylphosphine oxides **1.195**

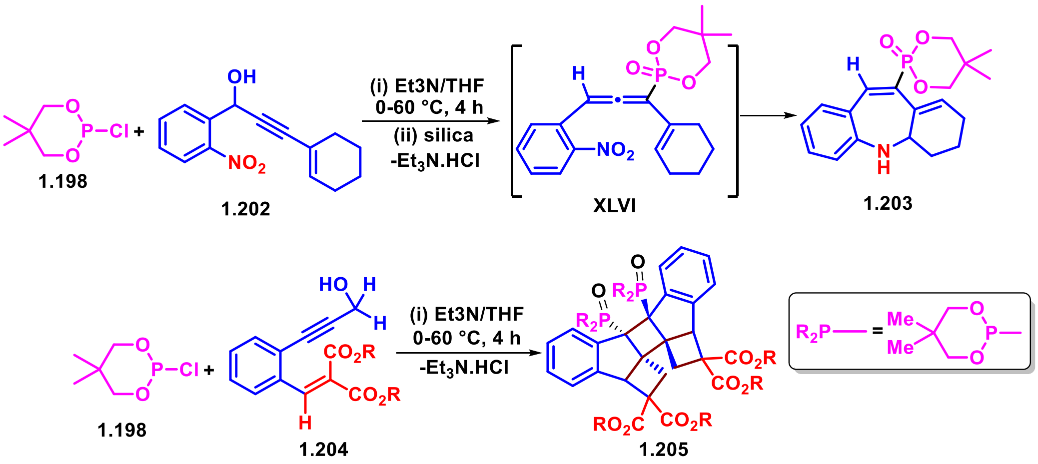
Our group reported new cyclization pathways involving reaction of *o*-substituted propargylic alcohols **1.197** with P^{III}–Cl substrates (**1.198** or **1.199**). The reaction proceeds *via* intramolecular *ene*-type or cycloaddition reaction. Here the *o*-CHO containing propargylic alcohol gives phosphono-indenone derivatives *via* allene intermediate **XLV**. It should be noted that in the normal reaction without the *o*-CHO functionality, this type of allene is the final product. (2 + 2)-Cycloaddition involving allenic β and γ carbons and CHO group affords a polycyclic intermediate; then H-migration and ring opening gives **1.200**. When X is *o*-

alkylidene moiety, the products are phosphono-indenes **1.201** formed *via* intramolecular ene reaction and H-migration (Scheme 1.71).[85]



Scheme 1.71: Cyclization of *o*-functionalized propargylic alcohols *via* an allene

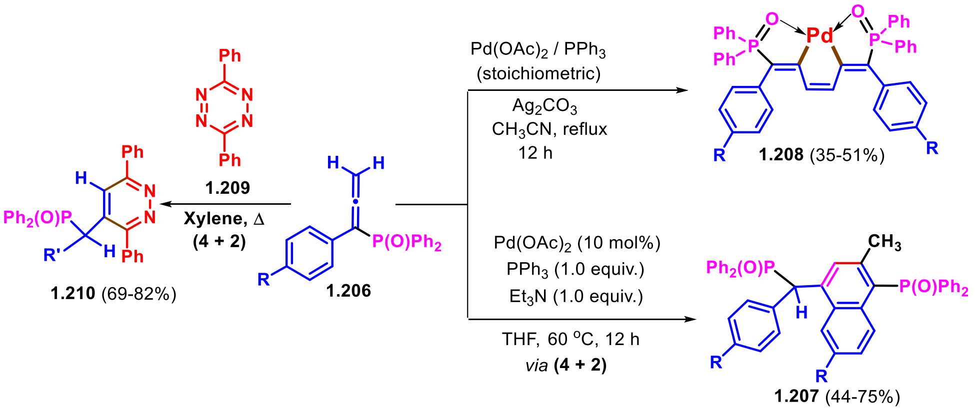
Our group also reported the rather unusual reaction of substituted propargyl alcohols possessing *o*-nitro and *o*-alkylidene moieties with the P(III)-Cl precursor **1.198** to afford novel phosphono(tetrahydro)dibenzazepines **1.203** or polycyclic molecules **1.205** with three fused four-membered rings. In both reactions, the intermediate is an allene **XLVI** (Scheme 1.72).[86]



Scheme 1.72: Cyclization of *o*- functionalized propargylic alcohols in reactions with P(III)-Cl substrates

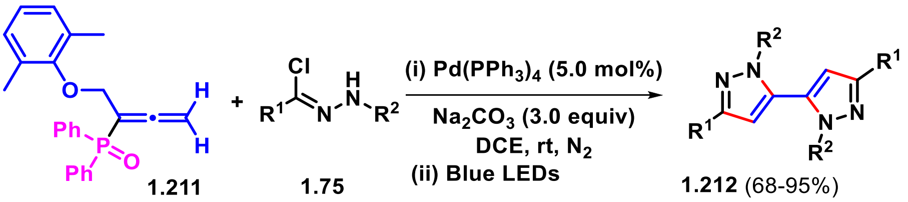
Very recently our group reported the divergent reactivity of allenyl phosphine oxides **1.206** which, under $Pd(OAc)_2$ catalyzed reaction, undergo self-dimerization-cum-cyclization to give phosphorus-based naphthalenes **1.207** while the use of stoichiometric amount of $Pd(OAc)_2$/ PPh_3 and replacing Et_3N by Ag_2CO_3 gives palladium incorporated metal complexes **1.208** which can be used as catalysts in the reactions involving allenes and 2-iodophenol. When allene **1.206** was treated with 3,6-diphenyltetrazine **1.209** at high temperature, it underwent

Inverse Electron Demand Diels−Alder (IEDDA) reaction furnishing 3,6-diphenylpyridazines **1.210** (Scheme 1.73).[87]



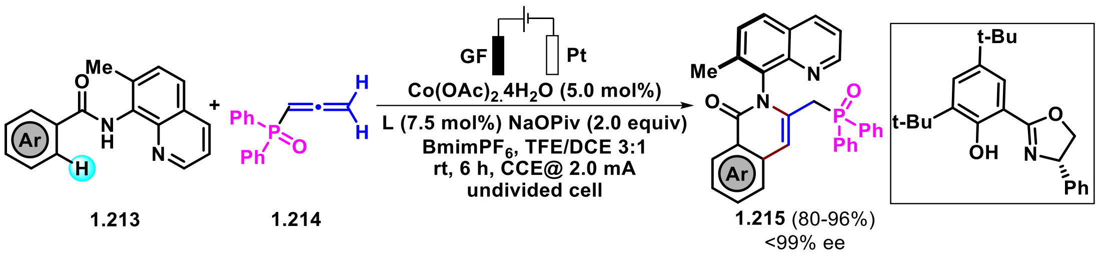
Scheme 1.73: Reactivity of allenylphosphine oxides **1.206**

Zhang *et al.* developed a one-pot method for the synthesis of polyarylbipyrazole **1.212** in good yields and excellent atom-economy *via* palladium-catalyzed, visible-light-driven domino reaction of allenylphosphine oxide **1.211** with *in situ* generated nitrile. This reaction involves double 1,3-dipolar and photocatalyst-free C(sp^3) −P(V) bond cleavage. The reaction has a broad substrate scope encompassing drug molecular fragments (Scheme 1.75).[88]



Scheme 1.74: Intermolecular [Pd]-catalyzed reaction of allenylphosphine oxide **1.211** with **1.75**

Ackermann's group developed cobalta-electro-catalyzed C−H annulation of phosphorus allenes **1.214** with benzamides **1.212** for the synthesis of C-N axially chiral compounds in good yields with high enantioselectivities. The reaction has broad functional group tolerance which was evidenced by late-stage annulation of complex bioactive compounds and drug molecules as well as decagram scale enantioselective electrocatalysis in continuous flow (Scheme 1.79).[89]



Scheme 1.75: Cobalta-electro-catalyzed atroposelective C-H annulation of **1.232**

In the above reactions it is apparent that the presence of additional functionalities on the propargylic alcohols in their reactions with P^{III}-Cl substrates can lead to unique cyclization processes. It is also clear that phosphorus-based allenes are versatile substrates in cycloaddition/cyclization reactions which is what we intend to explore in the current work.

OBJECTIVES OF THE PRESENT WORK

The major objective of the work was to explore the reactivity of acetoxy allenoates with *N*-sulfonyl ketimines, acyl-tethered benzothiazole binucleophiles and cyclization reaction of P-based allenes. More specifically, it was intended

(i) To explore the reactivity of *δ*-acetoxy allenoates with cyclic *N*-sulfonyl imines using DABCO or DMAP in an effort to assess the role of bases while accessing spirocarbocyclic and *m*-teraryl scaffolds,

(ii) To check the feasibility of using *δ*-acetoxy allenoate as a 5C-synthon in domino-annulation with sulfamidate imines,

(iii) To investigate the divergent effect of catalytic phosphine and DBU on the reactivity of *β'*-acetoxy allenoates with bisnucleophiles, and

(iv) To explore [Pd]-catalyzed domino (4 + 1)/(5 + 1) annulation reaction of phosphorus-based allenes with terminal alkynes, and to study the cyclization reactions of propargylic alcohol-tethered benzenesulfonamides with Ph_2PCl with the possible intermediacy of allenic species.

Chapter 2

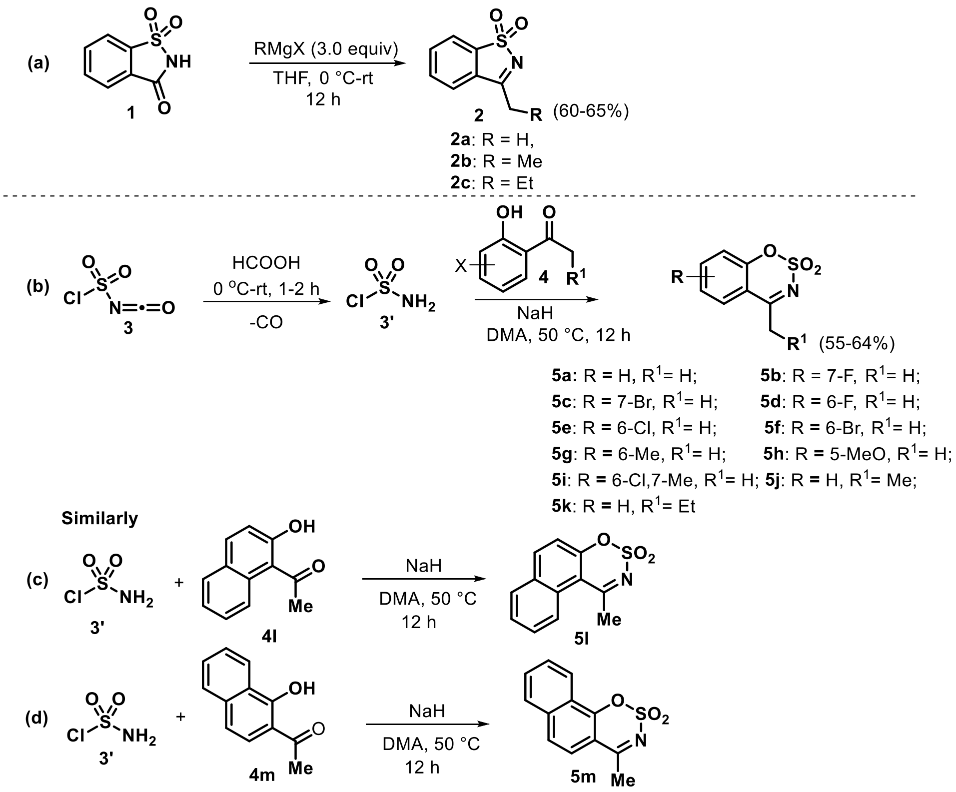
RESULTS AND DISCUSSION

This chapter deals with the results of various transformations involving *δ*-acetoxy allenoates and cyclic *N*-sulfonyl ketimines, catalyzed or mediated by a tertiary amine, leading to spirocyclic sultam, *m*-teraaryl or coumarin motifs. It also deals with the reactivity of *β'*-acetoxy allenoates and acyl-tethered benzothiazoles under phosphine and amine catalysis. The last part of this chapter is related to [Pd]-catalyzed annulation reaction of allenyl phosphine oxide with alkynes to give benzo[*b*]fluorenes and reactivity of sulfonamide substituted vinylic propargyl alcohols with Ph_2PCl leading to 4-amino-naphthalenyl phosphine oxides. The products obtained in this work are characterized by Mp (for solids), IR, NMR, and HRMS. The assigned regio- and stereo-chemistry of the products are generally based on X-ray crystallographic studies of representative compounds.

2.1 Synthesis of Precursors

2.1.1 *Cyclic N-sulfonyl ketimines 2a-c and 5a-m*

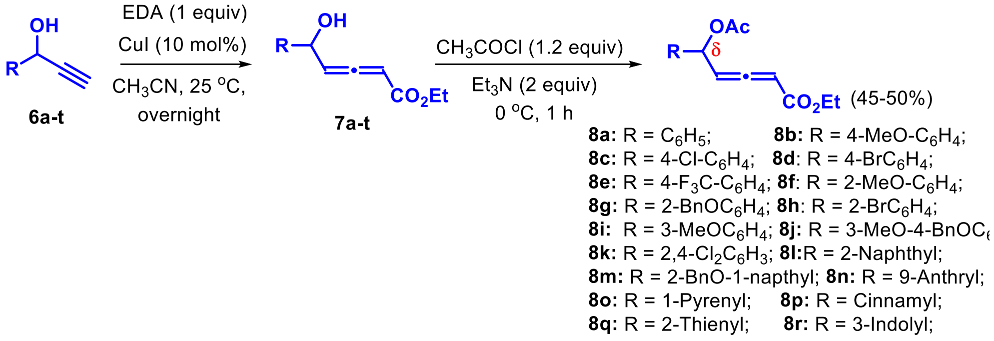
Cyclic *N*-sulfonyl ketimines were prepared by using one of the two methodologies available in the literature.[90-91] 3-Alkyl-substituted *N*-sulfonylketimines **2** were prepared by the addition of Grignard or organolithium reagents to saccharin **1** (Scheme 1a).[90] Treatment of sulfamoyl chloride (NH_2SO_2Cl, generated *in situ* from a mixture of $ClSO_2NCO$ and HCO_2H) with α-hydroxyl ketone or *ortho*-hydroxy arylketone **4** in the presence of a base at 50 °C furnished *N*-sulfonylketimine **5a-k** (Scheme 1b).[91] In an analogous manner, precursors **5l-m** have been prepared (Scheme 1c-d). These compounds are fairly air-stable. The signal for –N=*C* for these compounds appears around δ 175 ppm in the ^{13}C NMR spectra.



Scheme 1: Synthesis of cyclic *N*-sulfonyl ketimines **2a-c** and **5a-m**.

2.1.2 ***δ-Acetoxy allenoates 8a-r***

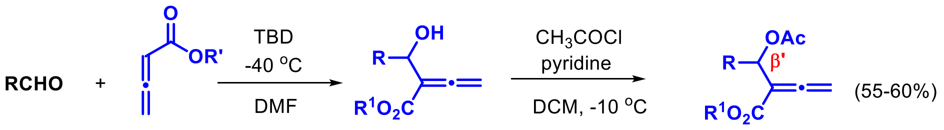
Treatment of propargylic alcohols **6a-t** with ethyl diazoacetate in acetonitrile solvent with a catalytic amount of CuI gave the corresponding *δ*-hydroxy allenoates **7a-t** as per literature.[32, 92] The hydroxyl group was transformed into the acetoxy group in the presence of acetyl chloride and Et_3N to afford the required *δ*-acetoxy allenoates **8a-s** (Scheme 2). The characteristic peaks for the *sp*-hybridized central carbon and the sp^2-hybridized adjacent carbons appear around δ 212 and 91-97 ppm, respectively, in the ^{13}C NMR spectra. These compounds exist as diastereomers, but this part is not investigated in the current study.



Scheme 2: Synthesis of *δ*-acetoxy allenoates **8a-r**

2.1.3 *β′-Acetoxy allenoates 12a-i*

We prepared *β′*-hydroxy allenoates **11a-i** by treating allenic esters **10** with appropriate aldehydes **9** using a catalytic amount of triazabicyclodecene (TBD) in DMF solvent at -45 °C.[4] We then acetylated the *β′*-hydroxy allenoates **11a-i** with acetyl chloride and pyridine in DCM solvent at -10 °C, which furnished the *β*'-acetoxy allenoates **12a-i** (Scheme 3).[50] The characteristic peaks for the *sp*-hybridized central carbon and the two sp^2-hybridized adjacent carbons appear around δ 213, 102 and 82 ppm in the ^{13}C NMR spectra. However, the $=CH_2$ signals [δ: 5.35-5.30 ppm] in the ^{1}H NMR spectra are more distinguishable, since in *δ*-acetoxy allenoates, this moiety is not present.



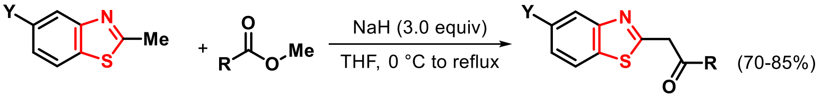
9 **10** **11a-i**

12a: R^1 = Bn, R = Ph;
12b: R^1 = Bn, R = 4-Cl-C_6H_4;
12c: R^1 = Bn, R = 4-MeO-C_6H_4;
12d: R^1 = Bn, R = 3-MeO-4-BnOC_6H_3;
12e: R^1 = Bn, R = Napthyl;
12f: R^1 = Bn, R = pyrenyl;
12g: R^1 = Bn, R = thienyl;
12h: R^1 = Bn, R = CH_2Bn
12i: R^1 = Et, R = Ph

Scheme 3: Synthesis of *β*'-acetoxy allenoates **12a-i**

2.1.4 *2-Acyl-tethered benzothiazoles 15a-j*

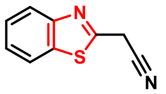
Following a literature procedure,[93] the reaction of 2-methylbenzothiazoles **13** with methyl aroylates/methyl-phenylacetate **14a-i** afforded the acyl thiazoles **15a-i** (Scheme 4). Precursor **15j** is commercially available. The -CH_2 hydrogen atoms connected to the benzothiazole part are fairly acidic; this feature coupled with the involvement of ring nitrogen makes the system bisnucleophilic that can be exploited in several reactions.



13
(Y = H, F, or Cl)

14a-i

15a: Y = H, R = Ph; **15b**: Y = H, R = 4-MeO-C_6H_4;
15c: Y = H, R = 4-F_3C-C_6H_4; **15d**: Y = H, R = Bn;
15e: Y = H, R = 2-furyl; **15f**: Y = 5-F, R = Ph;
15g: Y = 5-Cl, R = Ph; **15h**: Y = H, R = 4-^{t}Bu-C_6H_4;
15i: Y = H, R = 3-Cl-C_6H_4



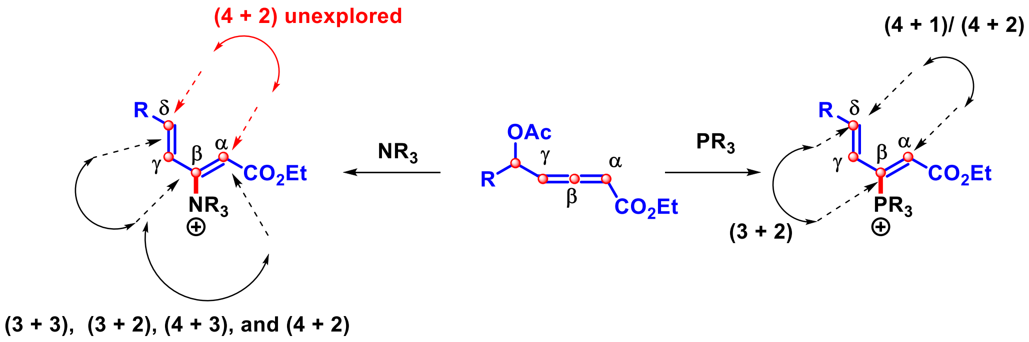
15j (commercially avialable)

Scheme 4: Synthesis of acyl-tethered benzothiazoles **15a-j**

2.2 Contrasting Carbo-Annulation Involving δ-Acetoxy Allenoate as a 4-Carbon Synthon Using DABCO and DMAP: Access to Spiro-Carbocyclic and *m*-Teraryl Scaffolds

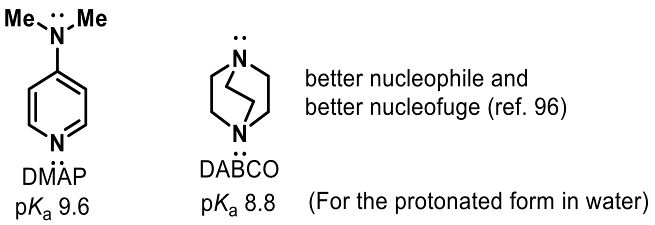
In the present work, we wanted to explore the reactivity of *δ*-acetoxy allenoates as 4C-synthons with alkyl benzoisothiazole dioxides (*N*-sulfonyl ketimines) under tertiary amine (DABCO and DMAP) mediation/catalysis. Interestingly, the DABCO-mediated reaction, δ-acetoxy allenoates afforded a new class of six-membered spirocyclic sultams containing multiple chiral centers with excellent stereoselectivity (*dr* up to 99:1) *via* enol acetate-imine coupling. On the other hand, DMAP-catalyzed benzannulation led to unsymmetrical *m*-teraryl scaffolds *via* Mannich coupling, proton transfers, and C-N bond cleavage. Remarkably, the products obtained by using DABCO and DMAP are mutually exclusive. Thus, in the reaction with allenoate using DABCO, teraryls were not found, and in the reaction using DMAP, spirocyclics were not at all observed.

In phosphine (PR_3) catalyzed/mediated reactions reported prior to the current work, δ-substituted or β′-substituted allenoates acted as 4C-synthons in (4 + 2) or (4 + 1) annulation/cycloaddition (Scheme 5).[12,94] In the presence of an amine, however, these allenoates acted primarily as 2C or 3C partners but not as 4C-synthons except in one case.[48] The reactions of δ-acetoxy allenoates that act as 4C or 2C-partners, was elegantly developed by Tong[28,29,31] and Shi[22] along with one of our own.[32]

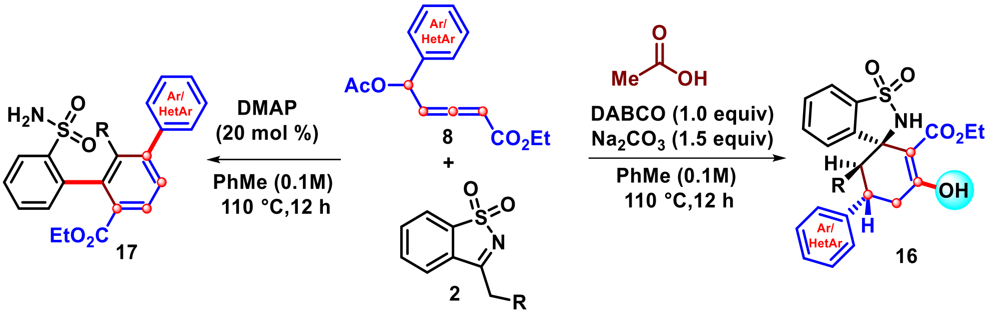


Scheme 5: Previous reports of δ-acetoxy allenoates

The distinction between DABCO and DMAP becomes important when we realize that even in the well-known Baylis-Hillman reaction,[95] significant differences in reactivity exist while using these bases, as analyzed by Mayr et al.[96] Although the standard catalyst/base DABCO is preferred in most cases, for reactions of cyclohexenone with acrylates, DMAP is supposed to work better. Since both DABCO[97a] and DMAP[97b] are explored as nucleophilic organocatalysts[98] in numerous reactions,[99,100] we believe that the distinction observed in the current work is significant.

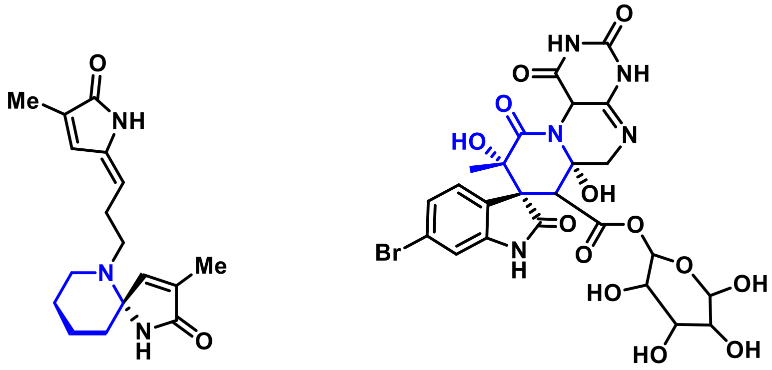


Two distinct pathways involving tertiary amine-controlled chemo-, regio-, and stereo-selective carbo-annulation between **2** and bifunctional isothiazole dioxides **8** with the allenoate still acting as a *4C*-synthon are described herein. The results include (a) DABCO-triggered diastereoselective spiro-annulation affording multiple chiral-centered spirocyclic hybrid cores with the introduction of a new –OH moiety, and (b) DMAP-catalyzed benzannulation leading to *m*-teraryls substitutionally different from those using phosphine catalysis (Scheme 6).[32]



Scheme 6: Contrasting carbo-annulation of *δ*-acetoxy allenoate with cyclic sulfonamide imines (present work)

Spirocycles have a good balance of conformational rigidity and flexibility compared to linear molecules or flat aromatic heterocycles. They may be able to adapt to many proteins as biological targets; thus, increasing the chances of discovering bioactive hits.[101] Two natural products featuring (6,5)-spiro system are depicted in Figure 1. The other type of products, teraryls, observed herein (cf. Scheme 6 above), are atropisomers with moderate stereoselectivity.



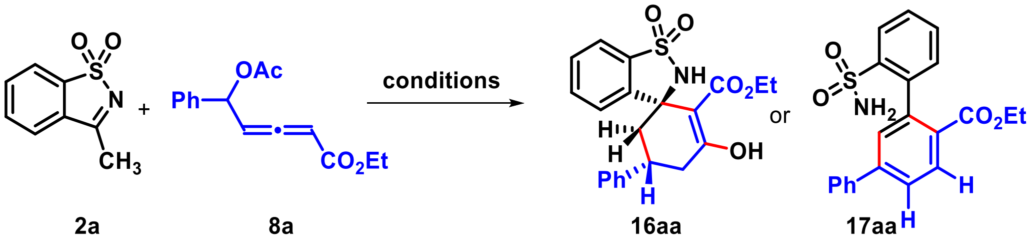
(a) (b)

Figure 1: (a) Alkaloid (±)-pandamarine isolated from *Pandanus amaryllif olius*, and (b) Surugatoxin isolated from the toxic Japanese ivory shell (*Babylonica japonica*)

2.2.1 *Reaction of δ-acetoxy allenoates with cyclic N-sulfonyl ketimines: Optimization study*

We commenced our investigations by exploring the reaction between 3-methyl isothiazole dioxide **2a** (0.20 mmol) and δ-acetoxy allenoate **8a** (0.24 mmol) in the presence of DABCO (0.20 mmol) in toluene solvent at 80 °C. After 12 h, we observed the unexpected product **16aa** in 15% yield *via* (4 + 2) annulation (Table 1, entry 1). The enolic O-H and the ring NH are clearly discernible in the ^{1}H NMR spectrum [δ 13.01, 4.85]. In the ^{13}C{^{1}H} NMR, six peaks in the aliphatic region are consistent with the structure; two peaks in the most downfield region [δ 179.2, 170.7] support the presence of the enolic as well as the carbonyl carbon. However final structural confirmation is given by single crystal X-ray diffraction (Figure 3, *vide infra*) since the reaction did not have a literature precedence. Based on this result, we assumed that an *in situ* generated acetate ion/ acetic acid might have played a key role in this carbo-annulation. Thus, we tested the sodium acetate as the acetate ion source; unfortunately, a better result was not obtained (entry 2). However, an increased yield of **16aa** (45%; entry 3) was found using acetic acid (0.20 mmol). Then, we shifted our focus on the amount of acetic acid and found that 2.0 equivalents of acetic acid delivered **16aa** in 58% yield (entry 4). Inspired by this promising result, several inorganic bases such as Na_2CO_3 (entry 5), $NaHCO_3$ (entry 6), and ^{t}BuOK (entry 7) were screened as additives to facilitate Mannich coupling; Na_2CO_3 delivered **16aa** in slightly better yield (66%). Increasing the temperature from 80 °C to 110 °C improved the yield of **16aa** from 66% to 71% (entry 8). The solvent variation (entries 9-12) showed that toluene was the best choice for optimum conversion (entry 8). Inferior results were obtained with a decreased amount of DABCO (entries 19 and 20). We then examined other bases such as DBN, TBD, and DIPEA, but found that they failed to give the **16aa** (entries 12-14). By adding DMAP instead of DABCO, the reaction proceeded well but furnished an entirely different product **17aa** (72%; entry 15). In the ^{1}H NMR spectrum, the aliphatic region for this compound exhibited only –NH_2 signal apart from those due to the ester ethyl group; the ^{13}C{^{1}H} NMR spectrum showed only aromatic, ethyl and carbonyl peaks. Thus, this compound has a structure completely different from **16aa**. A single crystal X-ray diffraction study confirmed the teraryl structure for this compound (cf. Figure 2 below). This unusual finding disclosed that AcOH and base additive might be unnecessary for the reaction of **2a** with **8a** (entry 16). No decrease in the yield was observed by reducing the amount (20 mol% and 50 mol%) of DMAP (entries 17-18). Thus, the optimized condition has been established for this benzannulation leading to **17aa** (entry 18). It should be noted that no product was detected at room temperature (entries 21 and 22).

Table 1. Optimization of Reaction Conditions for 16aa and 17aa[a]



Entry	Base[b]	Acid	Additive	Solvent	Yield[c] **16aa**:**17aa**	dr of **16aa**[d]
1	DABCO	-	-	PhMe	15:0	97:3
2	DABCO	-	NaOAc	PhMe	15:0	97:3
3	DABCO	AcOH	-	PhMe	45:0	97:3
4	DABCO	AcOH	-	PhMe	58:0	97:3
5	DABCO	AcOH	Na_2CO_3	PhMe	66:0	97:3
6	DABCO	AcOH	$NaHCO_3$	PhMe	60:0	97:3
7	DABCO	AcOH	^{t}BuOK	PhMe	55:0	97:3
8	**DABCO**	**AcOH**	**Na_2CO_3**	**PhMe**	**71:0**	**97:3**
9	DABCO	AcOH	Na_2CO_3	DMF	25:0	97:3
10	DABCO	AcOH	Na_2CO_3	DMSO	27:0	97:3
11	DABCO	AcOH	Na_2CO_3	H_2O	-	-
12	DIPEA	AcOH	Na_2CO_3	PhMe	-	-

13	DBN	AcOH	Na_2CO_3	PhMe	-	-
14	TBD	AcOH	Na_2CO_3	PhMe	-	-
15	DMAP	AcOH	Na_2CO_3	PhMe	0:72	-
16	DMAP	-	-	PhMe	0:78	-
17	DMAP	-	-	PhMe	0:78	-
18	**DMAP**	**-**	**-**	**PhMe**	**0:78**	**-**
19	DABCO	AcOH	Na_2CO_3	PhMe	55:0	97:3
20	DABCO	AcOH	Na_2CO_3	PhMe	33:0	97:3
21	DABCO	AcOH	Na_2CO_3	PhMe	-	-
22	DMAP	-	-	PhMe	-	-

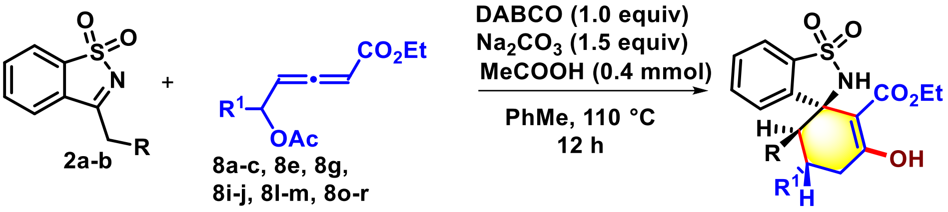
[a]Reaction conditions: **2a** (0.20 mmol), **8a** (0.24 mmol), base (100 mol% for entries 1-16 and 21; 50 mol% for entries 17 and 19; and 20 mol% for entries 18, 20 and 22), AcOH (0.20 mmol for entry 3; 0.40 mmol for entries 4-15 and 19-21) and additive (0.30 mmol) in toluene (2.0 mL); temperature is that of oil bath (80 °C for entries 1-7; 110 °C for entries 8-20 and 25 °C for entries 21 and 22). [b]DABCO = 1,4-Diazabicyclo[2.2.2]octane, DMAP = 4-(Dimethylamino)pyridine, DIPEA = N,N-Diisopropylethylamine, DBN = 1,5-Diazabicyclo[4.3.0]non-5-ene, TBD = 1,5,7-Triazabicyclo[4.4.0]dec-5-ene. [c]Isolated yield after 12h. [d]Diastereomeric ratio.

2.2.2 *Substrate scope for (4 + 2) spiro-annulation*

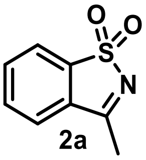
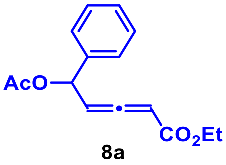
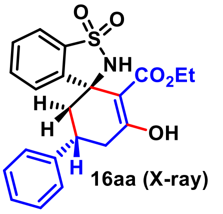
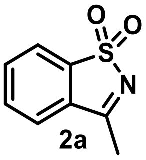
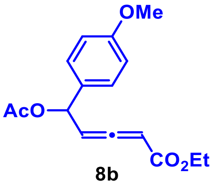
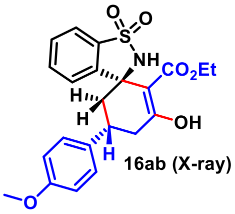
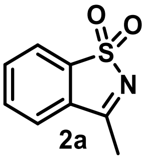
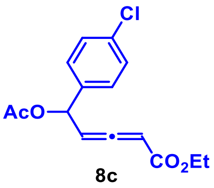
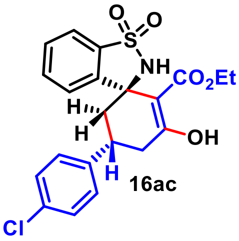
As depicted in Table 2, a variety of acetoxy allenoates were screened as four carbon synthons to evaluate the generality and limitations of (4 + 2) spiro carbo-annulation, different types of δ-acetoxy allenoates were well tolerated with **2a**, and the corresponding products were obtained with excellent diastereoselectivity (dr up to 99:1). Allenoates having different substituents (OMe, Cl, and CF_3) at the *meta*/*para* position of the phenyl ring **8a-c**, **8e**, and **8i** reacted well and afforded spirocyclic sultams **16aa-16ac, 16ae**, and **16ai** in 65-71% yields. In the case of **8g**, we obtained **16ag** in lower yield (60%) with 99:1 diastereomeric ratio; this may be attributed to steric hindrance. Additionally, disubstituted allenoate **8j** derived from vanillin also delivered **16aj** in 66% yield. Polycyclic aromatic allenoates such as 2-naphthyl and 2-benzyloxy-1-naphthyl allenoates (**8l** and **8m**) participated well, leading to **16al-16am** in good yields (60-61%). 5-Cinnamyl substituted allenoate **8p** also furnished **16ap** in 57% yield. Even heterocyclic allenoates **8q** and **8r** readily underwent annulation to afford the desired products **16aq** and **16ar** in moderate yields (60-63%).

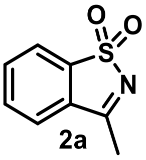
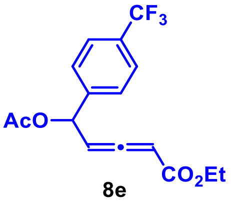
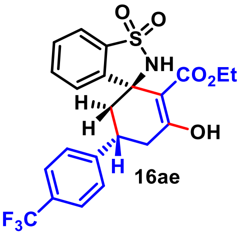
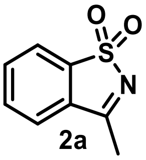
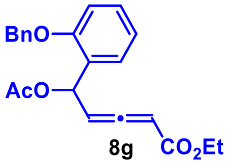
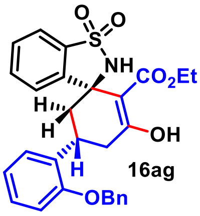
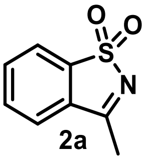
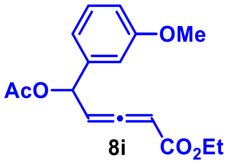
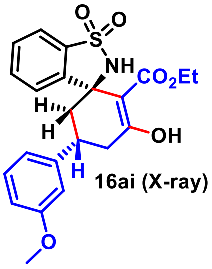
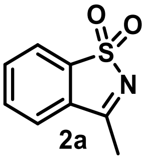
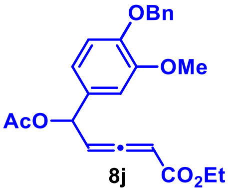
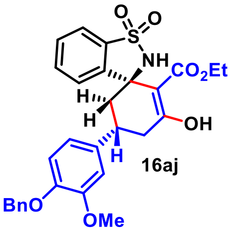
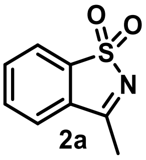
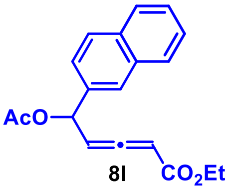
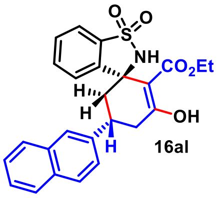
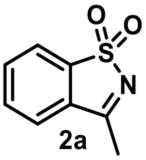
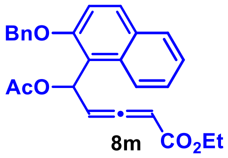
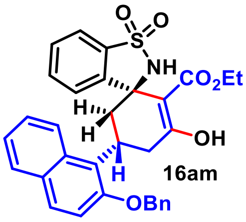
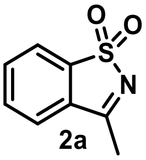
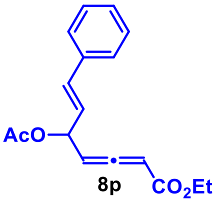
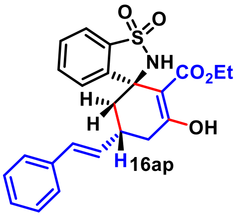
The above products involving three contiguous chiral centered spirocyclic motifs motivated us to probe using 3-ethyl isothiazole dioxide (**2b**) with **8a-c**,**8e, 8l, 8o 8q** under optimized conditions. Satisfyingly, all reactions proceeded nicely and gave **16ba-bc** (62-70%), **16bl**, **16bo,** and **6bq** (55-58%). Use of cinchona alkaloids in place of DABCO in this reaction did not give any clear-cut and isolable product. Since there are two or three chiral centers in these compounds, we wanted make sure that there was no other diastereomer by using X-ray crystallography [**16aa** (Figure 2, left), **16ab**, **16ai** (Figure 2, right), **16ba**, **16bb**, and **16bo**)] but found that in each case, only one diastereomer was formed preferentially.

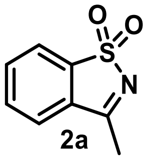
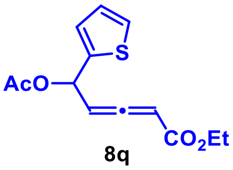
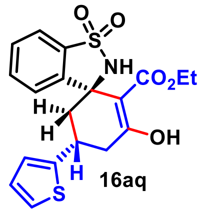
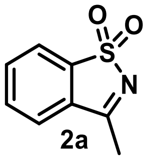
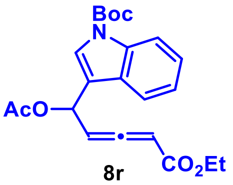
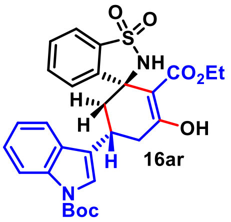
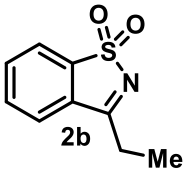
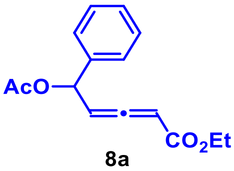
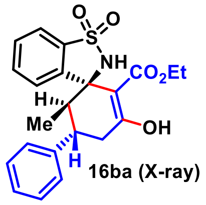
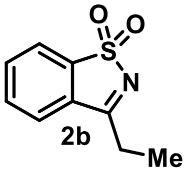
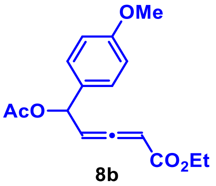
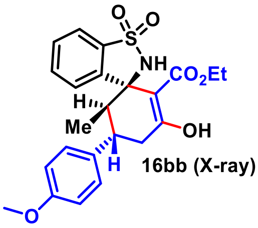
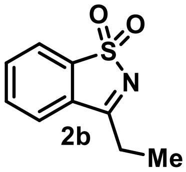
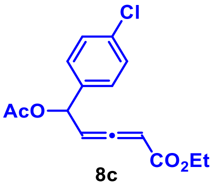
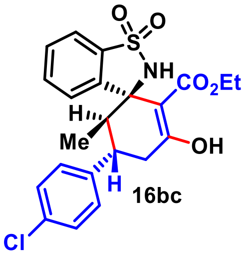
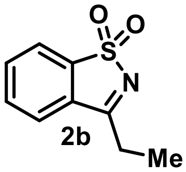
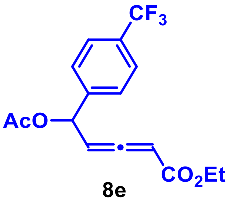
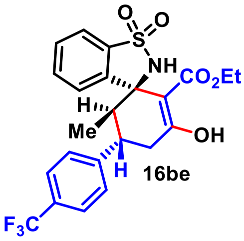
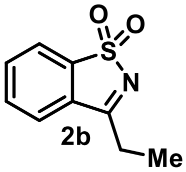
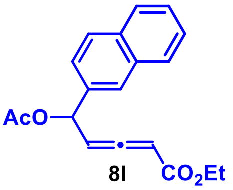
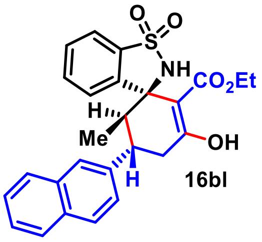
Table 2. Substrate Scope for (4 + 2) Spiro-Annulation[a,b,c]

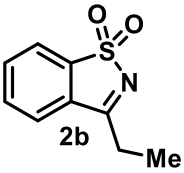
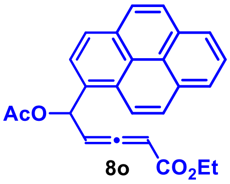
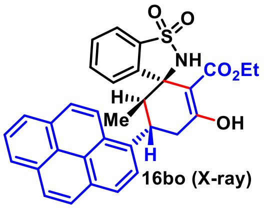
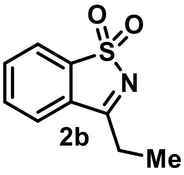
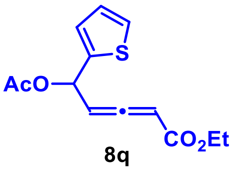
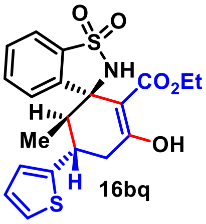


16aa-ac, 16ae, 16ag, 16ai, 16aj, 16al-am,16ap-ar, 16ba-16bc, 16be, 16bl, 16bo, and **16bq**

Entry	*N*-Sulfonyl imine	δ-Acetoxy allenoate	Spirocyclic sultams	Yield (%)[b]	dr
1	 **2a**	 **8a**	 **16aa (X-ray)**	71	97:3
2	 **2a**	 **8b**	 **16ab (X-ray)**	73	97:3
3	 **2a**	 **8c**	 **16ac**	68	98:2

4	 2a	 8e	 16ae	65	99:1
5	 2a	 8g	 16ag	60	96:4
6	 2a	 8i	 16ai (X-ray)	66	98:2
7	 2a	 8j	 16aj	66	97:3
8	 2a	 8l	 16al	61	97:3
9	 2a	 8m	 16am	60	99:1
10	 2a	 8p	 16ap	55	95:5

11	 **2a**	 **8q**	 **16aq**	60	96:4
12	 **2a**	 **8r**	 **16ar**	63	98:2
13	 **2b**	 **8a**	 **16ba (X-ray)**	69	99:1
14	 **2b**	 **8b**	 **16bb (X-ray)**	70	98:2
15	 **2b**	 **8c**	 **16bc**	65	98:2
16	 **2b**	 **8e**	 **16be**	62	99:1
17	 **2b**	 **8l**	 **16bl**	57	99:1

18	 2b	 8o	 16bo (X-ray)	55	99:1
19	 2b	 8q	 16bq	58	99:1

[a]Reaction conditions: **2a-b** (0.20 mmol), **8a-c, 8e, 8g, 8i, 8j, 8l-m, 8o-r** (0.24 mmol), DABCO (0.20 mmol), AcOH (0.40 mmol) and Na_2CO_3 (0.30 mmol) in toluene (2.0 mL) at 110 °C. [b]Isolated yield. [c]Diastereomeric ratio.

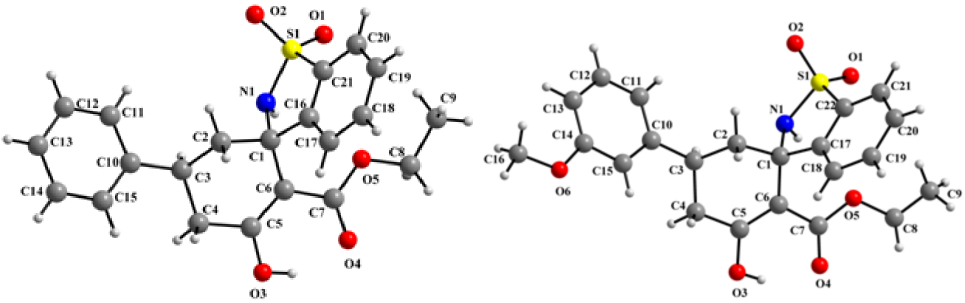
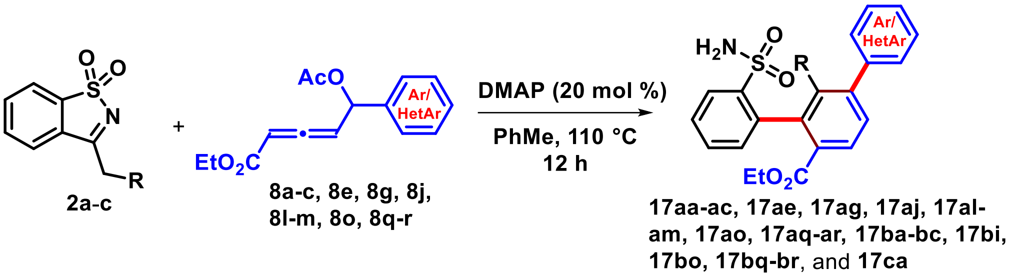


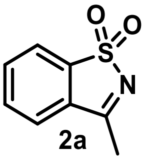
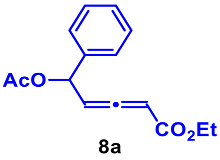
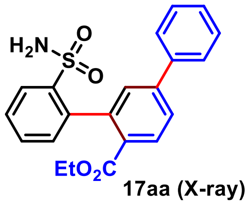
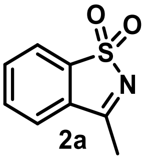
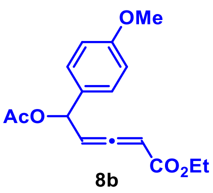
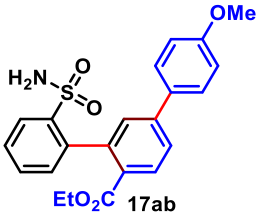
Figure 2. Molecular structures of compounds **16aa** (left, CCDC No. 2047794) and **16ai** (right, CCDC No. 2047796). only one of the two molecules in the asymmetric unit is shown, Selected bond distances: **16aa** C1-C2 1.533(4), C2-C3 1.522(4), C3-C4 1.512(4), C4-C5 1.490(4), C5-C6 1.356(4), C6-C1 1.514(4), N1-C1 1.496(4) Å. **16ai** C1-C2 1.537(4), C2-C3 1.535(4), C3-C4 1.518(4), C4-C5 1.482(5), C5-C6 1.359(5), C6-C1 1.521(4), N1-C1 1.507(4) Å.

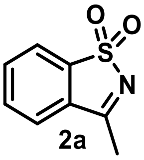
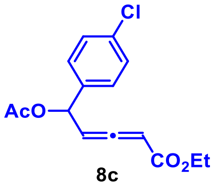
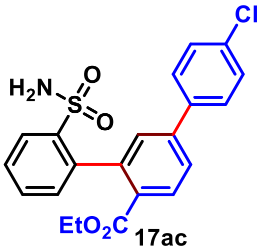
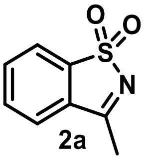
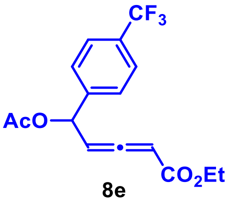
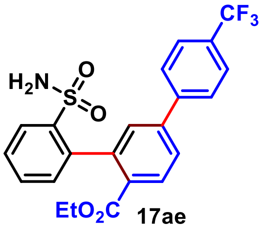
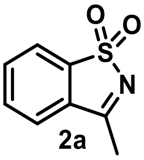
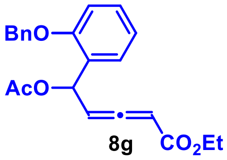
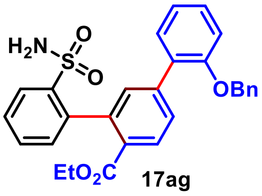
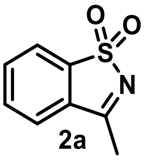
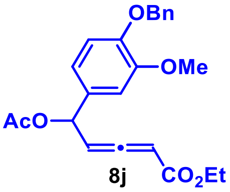
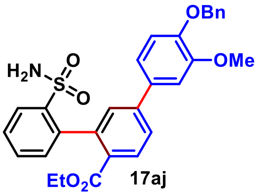
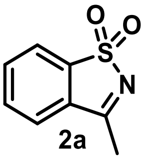
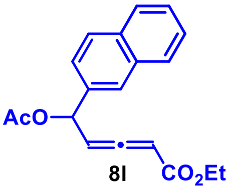
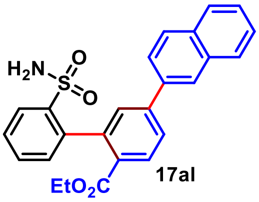
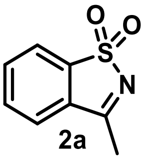
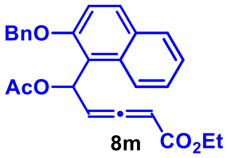
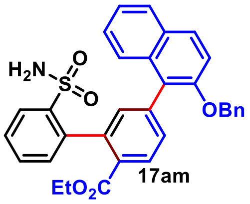
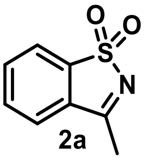
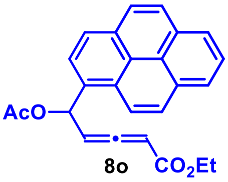
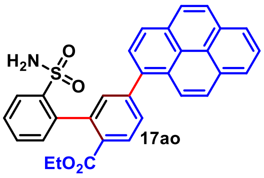
2.2.3 *Substrate scope for (4 + 2) benzannulation*

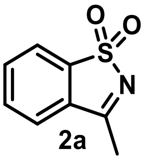
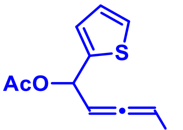
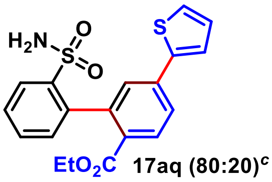
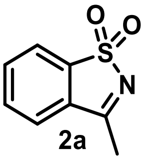
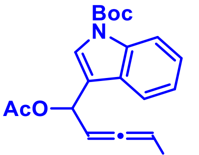
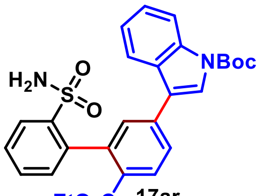
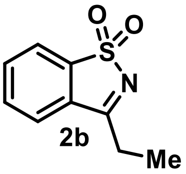
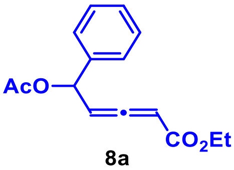
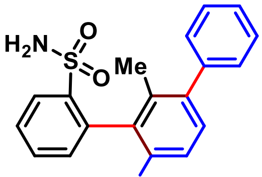
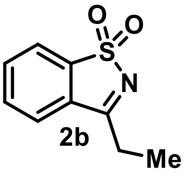
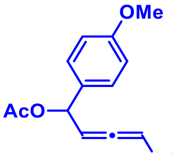
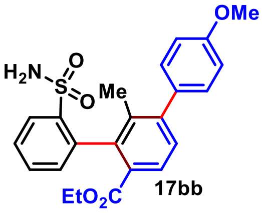
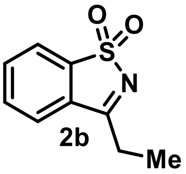
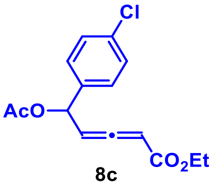
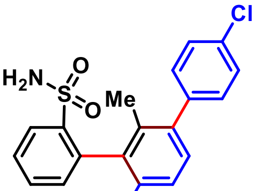
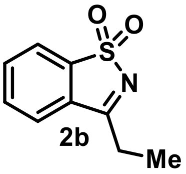
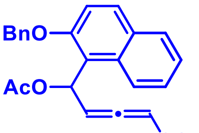
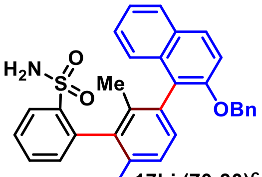
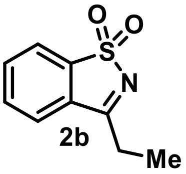
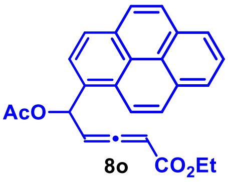
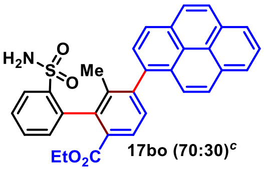
The results on the reactivity of allenoates (**8a-8c**, **8e**, **8g**, **8j**, **8l-m**, **8o**, and **8q-r**) in the DMAP-catalyzed benzannulation affording unsymmetrical *m*-teraryls are summarized in Table 3. The reaction in the presence of MeCOOH/Na_2CO_3 also gave only teraryls with the exclusion of spirocyclics. It is important to note that the regiochemistry here is different from that observed by using Ph_3P.[32] Regardless of the nature and position of the functionalities on the phenyl ring of allenoate (**8a-c**, **8e**, **8g**, **8j**), the reaction worked well with **2a** and furnished annulated products **17aa-17ac**, **17ae, 17ag**, and **17aj** in 70-82% yields. As expected, polyaromatic allenoates **8l, 8m** and **8o** also afforded **17al**, **17am** and **17ao** in good yields. Heterocyclic allenoates **8q-r** also allowed access to the desired products **17aq** and **17ar** in 69-71% yield. In the case of **17aq**, we observed a second isomer [atropisomer(?); dr 80:20], probably due to different orientations for sulfur in the thiophene residue. Inspired by the atropselectivity, we explored the reaction of allenoates with **2b-c** and isolated **17ba-17bc**, **17bm, 17bo**, **17bq-17br**, and **17ca** in good to high yields. Low diastereomeric ratio was observed for **17bm** and **17bo** possessing bulky aryl groups such as naphthyl and pyryl. However, we observed only one isomer in the NMR spectra of compounds **17ba-17bc**, **17bq-17br**, and **17ca**. The molecular structures of **17aa** and **17bq** are depicted in Figures 3; the fully aromatic middle ring confirms the structures as drawn.

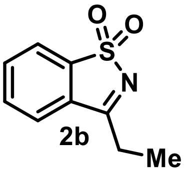
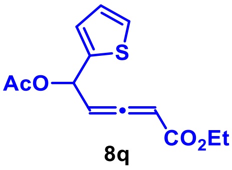
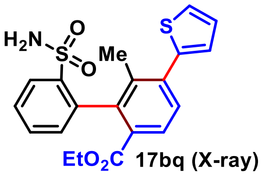
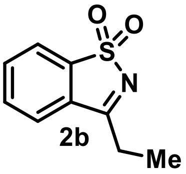
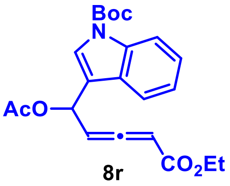
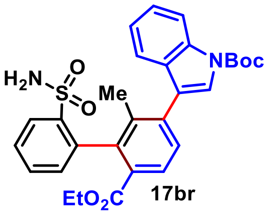
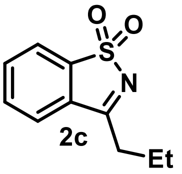
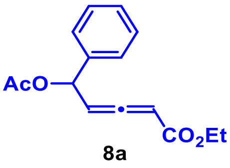
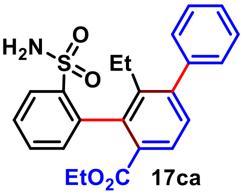
Table 3. Substrate Scope for (4 + 2) Benzannulation[a,b,c]



Entry	*N*-Sulfonyl imine	*δ*-Acetoxy allenoate	*m*-Teraryl	Yield (%)[b]
1	 **2a**	 **8a**	 **17aa (X-ray)**	78
2	 **2a**	 **8b**	 **17ab**	82

3	 **2a**	 **8c**	 **17ac**	75
4	 **2a**	 **8e**	 **17ae**	71
5	 **2a**	 **8g**	 **17ag**	70
6	 **2a**	 **8j**	 **17aj**	73
7	 **2a**	 **8l**	 **17al**	72
8	 **2a**	 **8m**	 **17am**	71
9	 **2a**	 **8o**	 **17ao**	69

10	 **2a**	 **8q**	 **17aq (80:20)^c**	71
11	 **2a**	 **8r**	 **17ar**	69
12	 **2b**	 **8a**	 **17ba**	74
13	 **2b**	 **8b**	 **17bb**	77
14	 **2b**	 **8c**	 **17bc**	72
15	 **2b**	 **8m**	 **17bi (70:30)^c**	68
16	 **2b**	 **8o**	 **17bo (70:30)^c**	65

17	 2b	 8q	 17bq (X-ray)	68
18	 2b	 8r	 17br	66
19	 2c	 8a	 17ca	71

[a]Reaction conditions: **2a-c** (0.20 mmol), **8a-c, 8e, 8g, 8j, 8l, 8m, 8o,** and **8q-r** (0.24 mmol) and DMAP (0.04 mmol) in toluene (2.0 mL) at 110 °C. [b]Isolated yield. [c]Diastereomeric ratio.

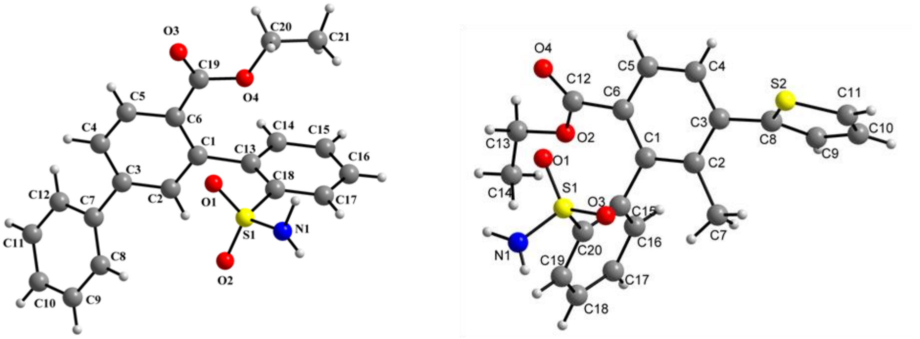
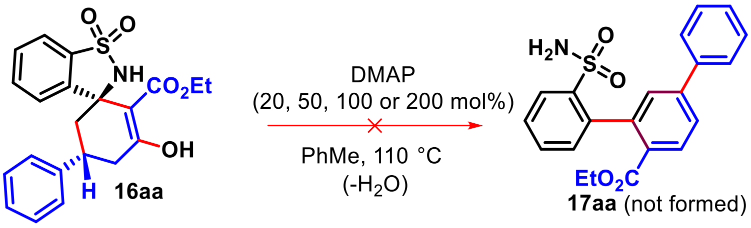


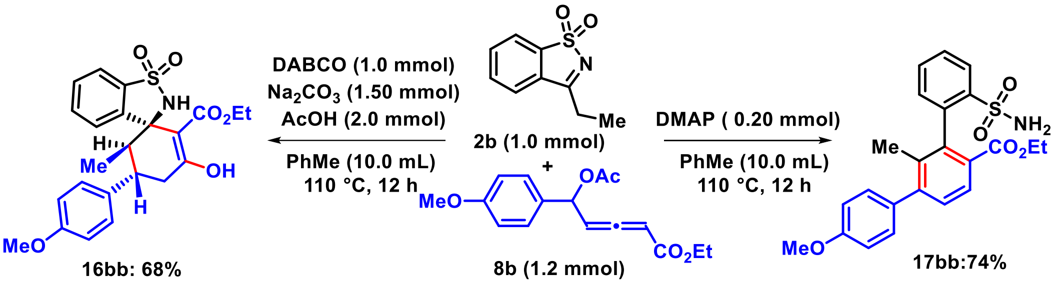
Figure 3. Molecular structures of compounds **17aa** (left, CCDC No. 2047800) and **17bq** (right, CCDC No. 2047801). Selected bond distances: **17aa** C1-C2 1.394(6), C2-C3 1.395(7), C3-C4 1.382(7), C4-C5 1.368(7), C5-C6 1.384(7), C6-C1 1.384(6) Å. **17bq** C1-C2 1.402(4), C2-C3 1.405(4), C3-C4 1.386(4), C4-C5 1.379(4), C5-C6 1.387(4), C6-C1 1.403(4) Å.

We also conducted experiments using different stoichiometries of DMAP (Scheme 7). However, even at elevated temperatures, we did not observe C-N bond cleavage or dehydration from **16aa** using various mole ratios of DMAP. Therefore, it is possible that the spirocyclic (**16**) and *m*-teraryl (**17**) motifs are formed through entirely different pathways at later stages.



Scheme 7: Control Experiment

To establish the utility of the present (4 + 2) carbo-annulations, we performed 1.0 mmol scale reaction of **2b** with **8b** (1.2 mmol) using standard reaction conditions as shown in Scheme 8. The reactions proceeded nicely and we obtained the corresponding products **16bb** and **17bb** in yields of 68% and 74%, respectively.

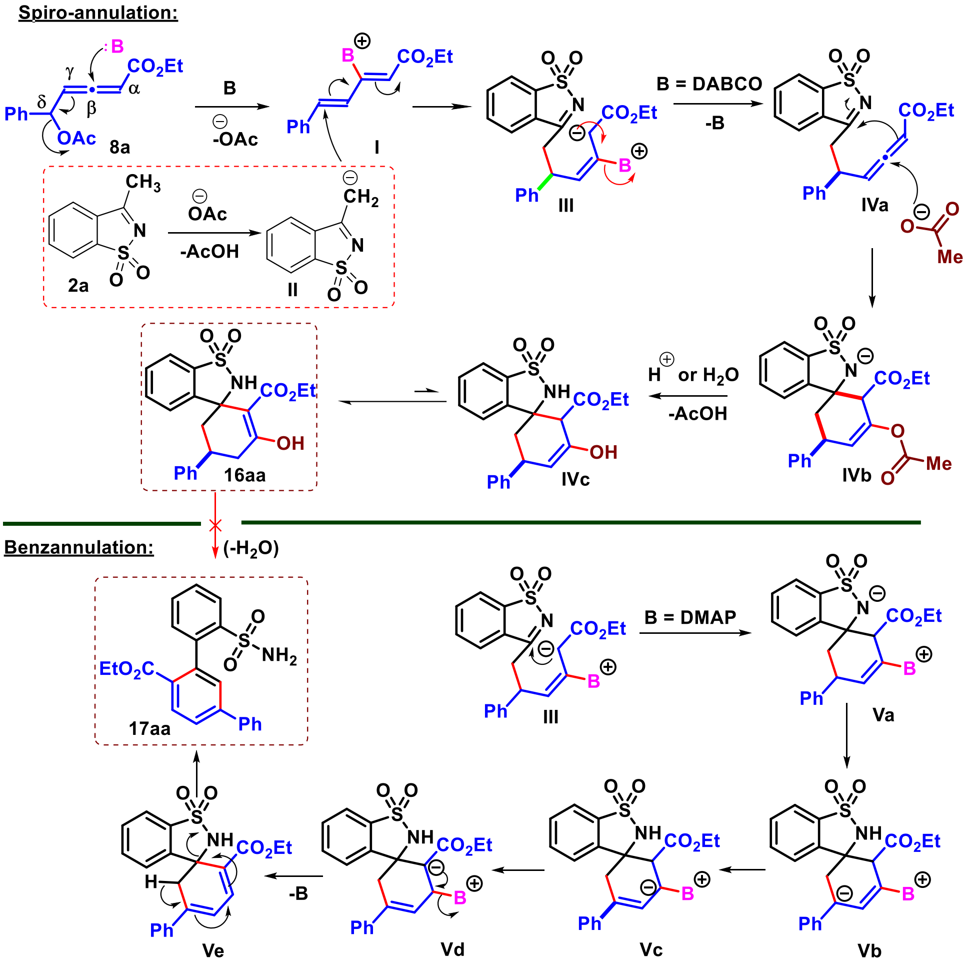


Scheme 8: Scale-up Experiments

2.2.4 Proposed pathways for (4 + 2) carbo-annulations

A plausible pathway for the (4 + 2) carbo-annulation is proposed in Scheme 9. This annulation reaction is facilitated by the addition of a tertiary amine to β-carbon of the δ-acetoxy allenoate **8a** *via* an addition-elimination fashion to deliver the reactive electrophilic intermediate **I**. This species upon 1,6-addition with the anion **II** provides zwitterionic intermediate **III**. In the DABCO-mediated spiro-annulation, **III** rapidly undergoes 1,2-elimination and delivers the allenic intermediate **IVa**. Subsequently, **IVa** undergoes nucleophilic addition with the acetate ion to give anionic intermediate **IVb**. Finally, Mannich coupling[102] followed by proton abstraction and hydrolysis affords **IVc** that transforms into the unexpected six-membered spirocyclic sultam **16aa**. By contrast, in the DMAP catalyzed benzannulation, the negative charge is stabilized at the δ-carbon of allenoate. Thus, the intermediate **III** immediately participates in intramolecular Mannich coupling[102] rather than 1,2-elimination to give spirocyclic zwitterionic species **Va**. Then intermediate **Va** undergoes 1,4-proton transfer (cf. **Vb**) followed by isomerization (cf. **Vc**), 1,2-proton transfer (cf. **Vd**), and DMAP elimination affording the spirocyclic diene **Ve** which upon C-N bond cleavage/ aromatization leads to the unsymmetrical *m*-teraryl **17aa**.

In this DMAP catalyzed benzannulation, it is likely that the intermediate ylide **Vc** is stabilized because of the delocalization effect of the attached aromatic ring and the –NMe_2 group (which is not so in the spiro-annulation using DABCO).[103]

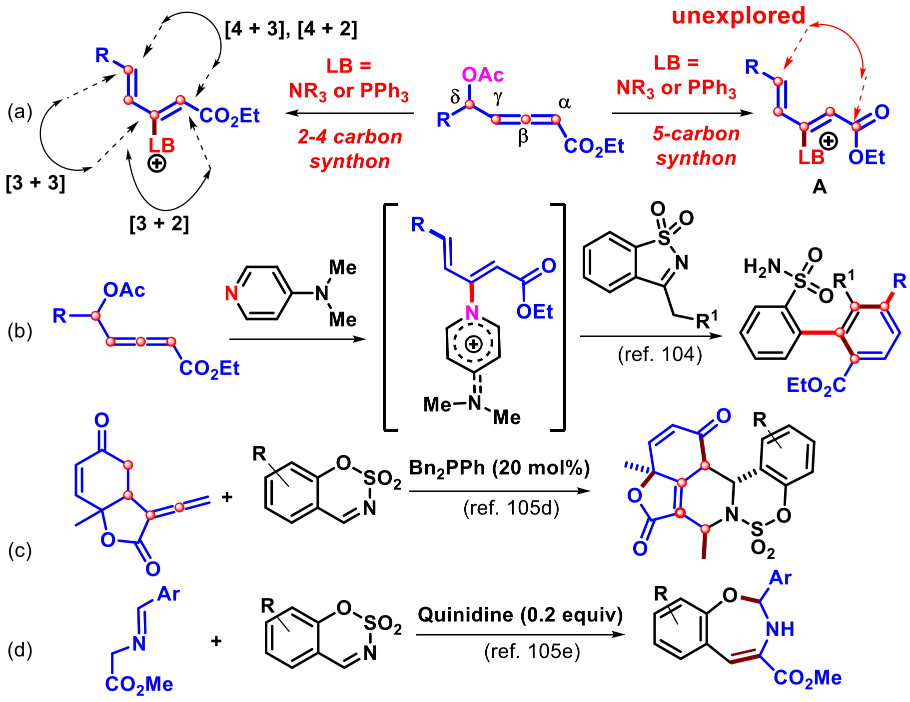


Scheme 9: Proposed Pathways for (4 + 2) Spiro-and Benzannulations

2.3 *δ*-Acetoxy Allenoate as a 5C-Synthon in Domino-Annulation with Sulfamidate Imines: Ready Access to Coumarins

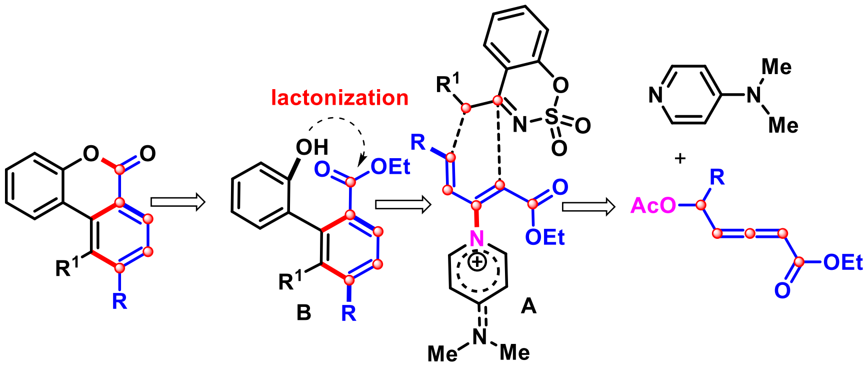
In Lewis base mediated/catalyzed annulations, *δ*-acetoxy allenoates can offer 5-8 membered ring scaffolds by the attack of the nucleophile at the *δ*- or *α*-carbon of electrophilic intermediate, wherein the allenoate part offers *1C-4C* for the framework, but till this (current) work none of them utilized acetoxy allenoates as *5C*-synthons (Scheme 10a-b).[21,25,29,32,36,38,50b]

Our interest in allene chemistry[4] prompted us to explore annulations *via* diene-ammonium intermediate, and in this context, we envisioned that annulation involving *δ*-acetoxy allenoate as *5C-synthon via* diene-ammonium intermediate is feasible with a suitable reaction partner such as sulfamidate derived cyclic imines.[32,104] The latter imines have been explored in cyclization/annulation reactions in recent years, with sulfamidate as a disposable entity in a couple of cases (Scheme 10c-d).[105]



Scheme 10: Selected Annulation Reactions of δ-Acetoxy allenoates and/ or Sulfamidate Imines

In the current work, we have designed the chromone synthesis in a single operation as depicted in Scheme 11. The key diene-ammonium intermediate **A** is formed by the addition of a base to acetoxy allenoate **8** *via* allylic elimination of the acetate group. Electrophilic intermediate **A** may interact with the cyclic-sulfamidate imine **5** to form intermediate **B** which can undergo the lactonization process to form the coumarin framework. Coumarin (2*H*-chromen-2-one) scaffold is ubiquitous in natural products and has significant medicinal relevance.[106] A large number of benzocoumarins and related scaffolds are also found in nature (cf. Figure 4).[107,108] However, methods to access π-expanded coumarin entities are less encountered.[107b] Herein, we highlight (i) use -$SO_2(NH_2)$ of sulfamidate imine as a disposable moiety and δ-acetoxy allenoates as a *5C-synthon*, an operationally simple route to benzocoumarins, and (ii) the utility of as-synthesized coumarins to obtain a cannabinol analogue.



Scheme 11: Retrosynthesis approach for the synthesis of benzocoumarin

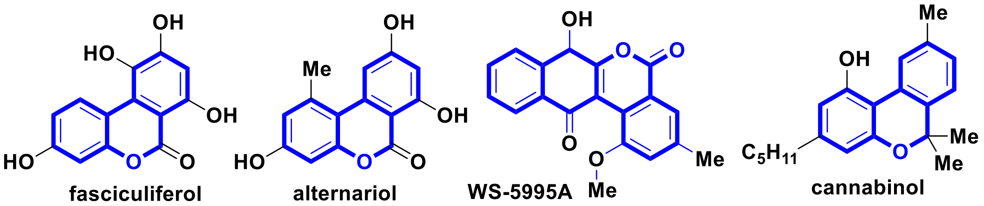


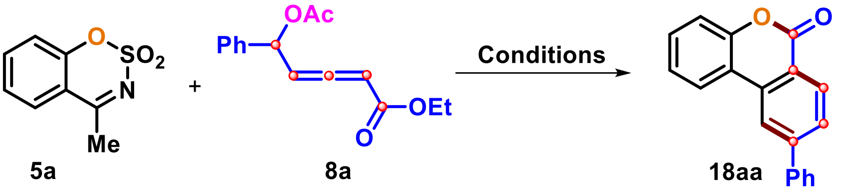
Figure 4: Selected 3,4-benzocoumarin/chromene and related natural products.

2.3.1 Domino-annulation reactions of δ-acetoxy allenoates with N-sulfamidate imines: Optimization study

Initially, we examined a reaction between **5a** (0.20 mmol) and **8a** (0.20 mmol) in the presence of DMAP (20 mol%) in toluene at rt but did not observe the formation of **18aa** even after two days (Table 4, entry 1). By increasing the reaction temperature to 50 °C we observed the benzocoumarin product **18aa** in 15% isolated yield after 12 h *via* (4 + 2)/(5 + 1) annulation (entry 2). The absence of the peaks due to ethyl-ester protons and the appearance of only aromatic protons in the ^{1}H NMR, in conjunction with the presence of the carbonyl peak in the $^{13}C\{^1H\}$ NMR, suggested the structure as depicted. A single crystal X-ray diffraction study confirmed the structure of **18aa** (Figure 5, *vide infra*) as given here. Based on this result, we surmised that a higher temperature was required for this domino sequential annulation. Thus, it was realized that the reflux temperature of toluene (oil bath maintained a 130 °C) was the best and product **18aa** obtained in 66% yield (entries 2-5). Then we examined the effect of additives. Thus, by adding $NaHCO_3$ (2 equiv), **18aa** was obtained in 75% yield (entry 6); the same yield was obtained within 6 h. Among the other additives Na_2CO_3, K_2CO_3, and Cs_2CO_3 (entries 7-9), K_2CO_3 was the best (85% yield). We screened the reaction in high boiling solvents like *p*-xylene, DMSO, and, DMF but they were not better than toluene (entries 10-12). We then examined DMAP analogues 4-PPY, and 4-APY (entries 13-14); while 4-PPY and

DABCO gave a lower yield, 4-APY was ineffective. Use of DBU afforded the previously reported pyridine derivative (entry 16).[32] Lowering the amount of DMAP from 20 mol% to 10 mol% decreased the yield (entry 17). No reaction occurred without DMAP catalyst (entry 18). Thus, the optimal reaction condition to get **18aa** was by using DMAP (20 mol%) as the catalyst, K_2CO_3 (2.0 equiv) as the additive, and by performing the reaction at 130 °C in toluene (2.0 mL) for 6 h.

Table 4. Optimization of Reaction Conditions for 18aa[a]



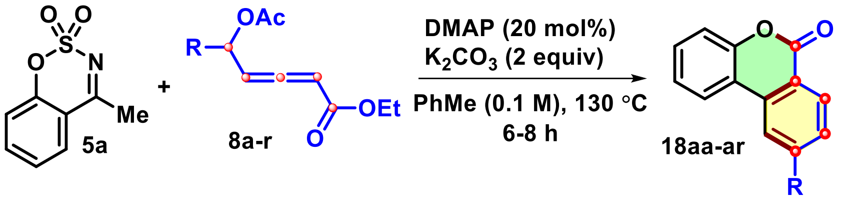
Entry	Catalyst	Base	Solvent	Temp (oil bath, °C)/ time	Yield (%)[c]
1	DMAP	-	PhMe	rt/48h	NR
2	DMAP	-	PhMe	50/12h	15
3	DMAP	-	PhMe	80/12h	45
4	DMAP	-	PhMe	110/12h	58
5	DMAP	-	PhMe	130/12h	66
6	DMAP	$NaHCO_3$	PhMe	130/12h (or 6h)	75
7	DMAP	Na_2CO_3	PhMe	130/6h	79
8	**DMAP**	**K_2CO_3**	**PhMe**	**130**	**85**
9	DMAP	Cs_2CO_3	PhMe	130	84
10	DMAP	K_2CO_3	*p*-Xylene	130	85
11	DMAP	K_2CO_3	DMSO	130	25
12	DMAP	K_2CO_3	DMF	130	20
13	4-PPY	K_2CO_3	PhMe	130	74
14	4-APY	K_2CO_3	PhMe	130	-
15	DABCO	K_2CO_3	PhMe	130	40
16	DBU	K_2CO_3	PhMe	130	-[d]
17	DMAP	K_2CO_3	PhMe	130	68[e]
18	-	K_2CO_3	PhMe	130	NR

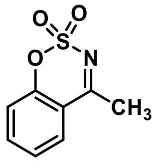
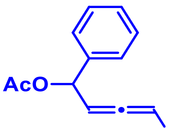
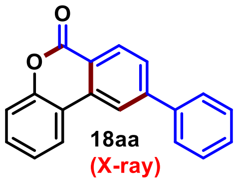
[a] Reaction conditions: **5a** (0.20 mmol), **8a** (0.20 mmol), Catalyst (20 mol% for entries 1-15), and base (0.40 mmol) in toluene (2.0 mL), 130 °C (oil bath) in a stoppered Schlenk tube. [b] DABCO = 1,4-Diazabicyclo[2.2.2]octane, DMAP = 4-(Dimethylamino)pyridine, 4-PPY = 4-Pyrrolidinopyridine, 4-APY = 4-Aminopyridine. [c] Isolated yield after 8h. [d] A different product (substituted pyridine) was obtained (cf. ref. 32). [e] 10 mol% of DMAP was used.

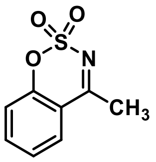
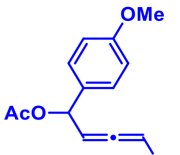
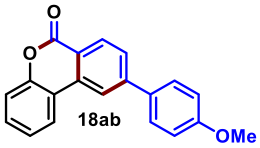
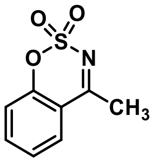
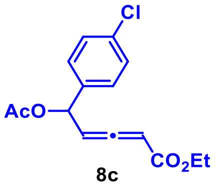
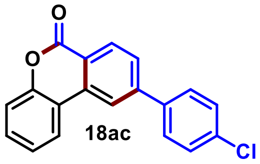
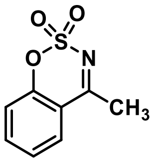
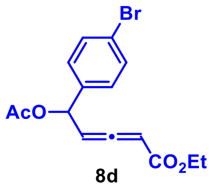
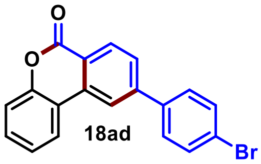
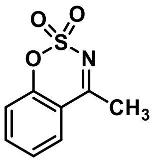
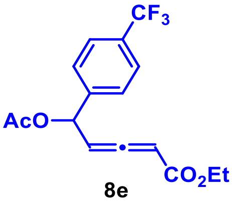
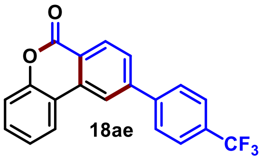
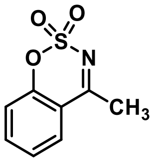
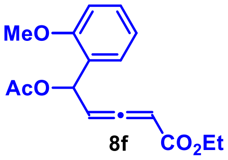
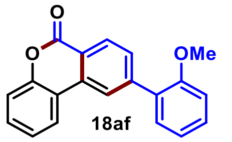
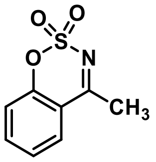
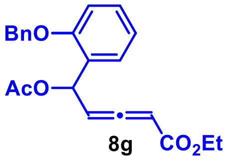
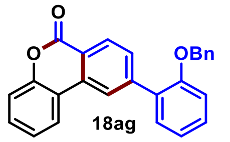
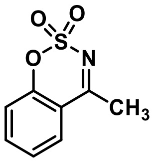
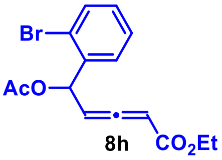
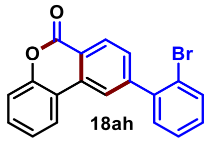
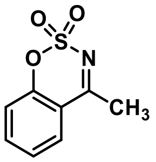
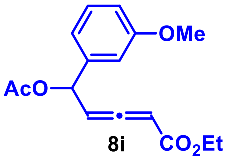
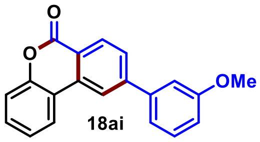
2.3.2 *Formation of benzocoumarins: Substrate scope for δ-acetoxy allenoates*

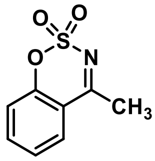
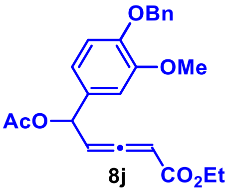
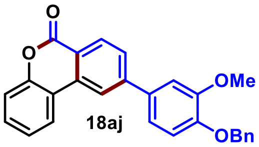
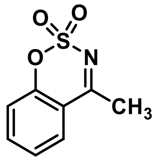
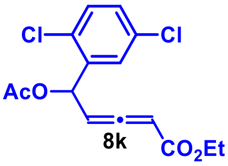
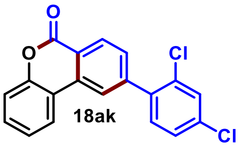
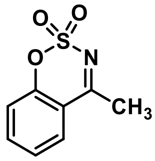
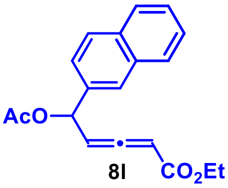
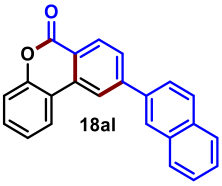
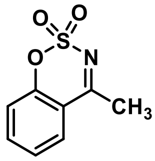
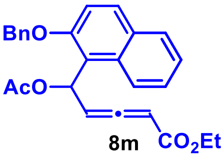
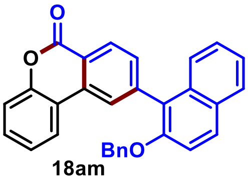
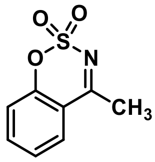
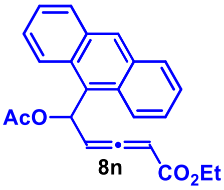
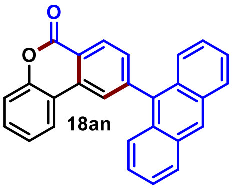
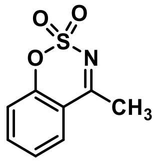
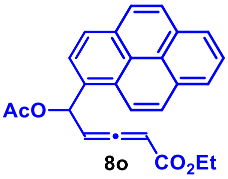
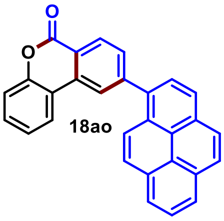
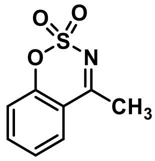
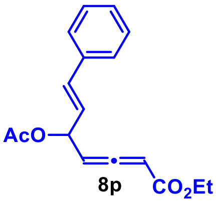
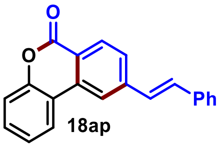
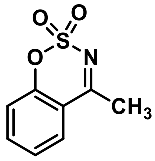
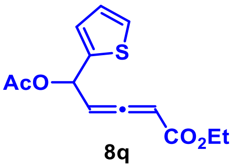
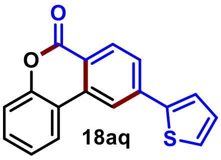
Next, we examined the substrate scope of allenoates **8a-r** in their reaction with **5a** using optimal reaction conditions, and the results are depicted in Table 5. Different electronic disparity functional groups at the *p*-position of the allenoate did not show any significant deviation and afforded the corresponding domino-annulation lactone cores **18aa-ae** in high yields (71%-85%). Apart from this, *meta*/ *ortho*-substituted allenoates **8f-i** were involved nicely to offer **18af-ai** in good yields (70%-80%). To our delight, disubstituted (**8k**), poly-aryl (**8l-o**), alkenyl, and heteroaryl substituents at the *δ*-position of allenoate did not hamper the reactivity and gave the corresponding scaffolds (**18ak-ao**) in acceptable yields (69-82%). The yields of **18ao** and **18ar** in the case of the pyrene or indole substituted allenoate were marginally lower but still decent. Thus, although some steric effects are observed, no significant electronic effects are discernible.

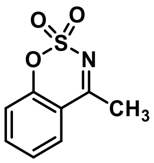
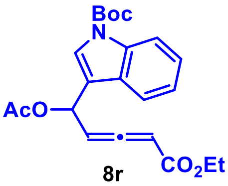
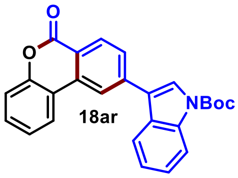
Table 5. Substrate Scope for *δ*-Acetoxy Allenoates[a]



Entry	*N*-Sulfonyl imine	*δ*-Acetoxy allenoate	Benzocoumarin	Yield (%)[b]
1	 **5a**	 **8a**	 **18aa** (X-ray)	85

2	 5a	 8b	 18ab	88
3	 5a	 8c	 18ac	81
4	 5a	 8d	 18ad	78
5	 5a	 8e	 18ae	71
6	 5a	 8f	 18af	75
7	 5a	 8g	 18ag	70
8	 5a	 8h	 18ah	73
9	 5a	 8i	 18ai	80

10	 5a	 8j	 18aj	77
11	 5a	 8k	 18ak	82
12	 5a	 8l	 18al	73
13	 5a	 8m	 18am	70
14	 5a	 8n	 18an	71
15	 5a	 8o	 18ao	69
16	 5a	 8p	 18ap	65
17	 5a	 8q	 18aq	74

18	 5a	 8r	 18ar	69

[a]Reaction conditions: **5a** (0.20 mmol), **8a-r** (0.20 mmol), DMAP (0.04 mmol) and K_2CO_3 (0.40 mmol) in toluene (2.0 mL) at 130 °C (oil bath). [b]Isolated yield.

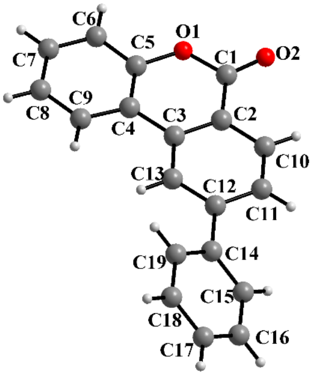
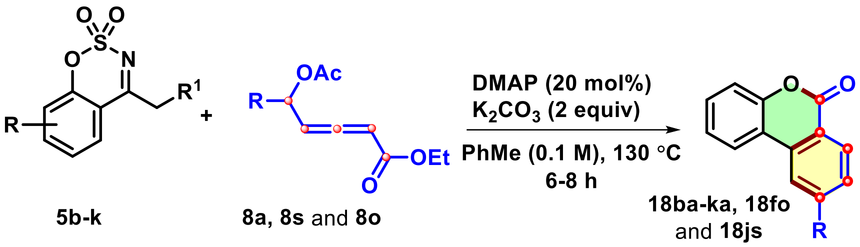


Figure 5. Molecular structure of compound **18aa** (CCDC No. 2258035). Selected bond lengths: C3-C2 1.402(2), C3-C13 1.395(2), C13-C12 1.390(2), C12-C11 1.394(2), C2-C10 1.391(2), C10-C11 1.373(2) Å

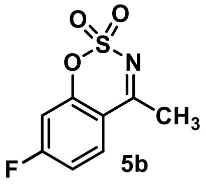
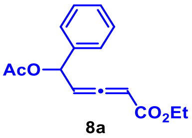
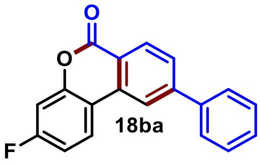
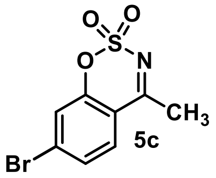
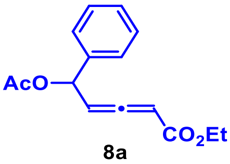
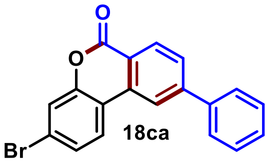
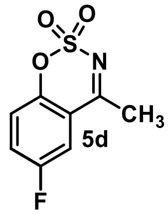
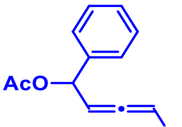
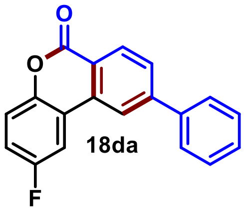
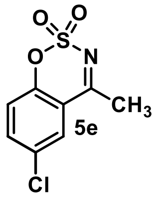
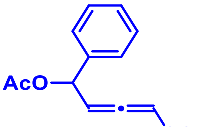
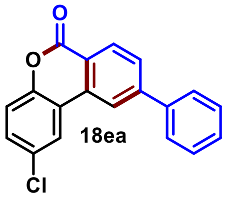
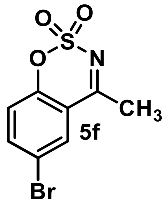
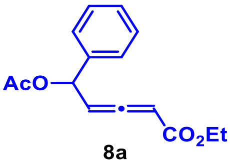
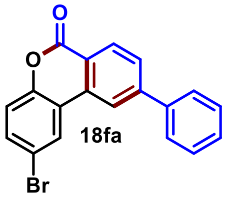
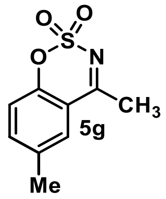
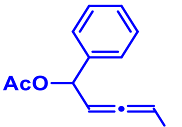
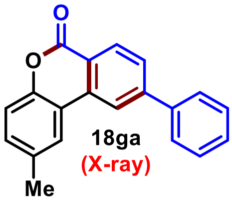
2.3.3 Formation of benzocoumarins: Substrate scope for sulfamidate imines

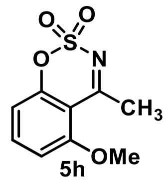
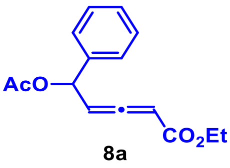
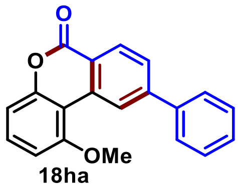
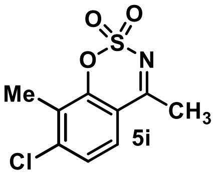
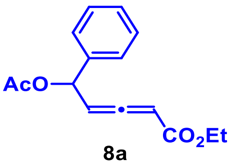
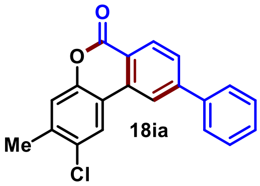
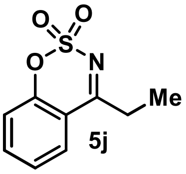
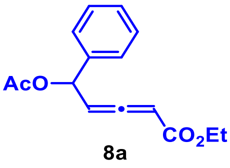
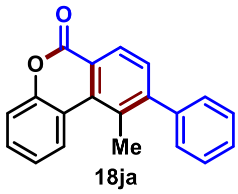
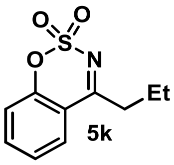
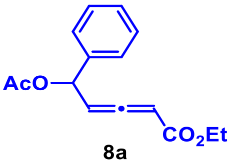
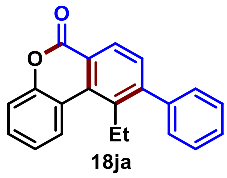
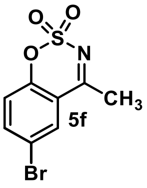
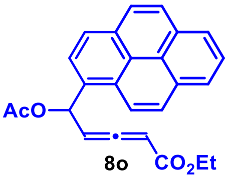
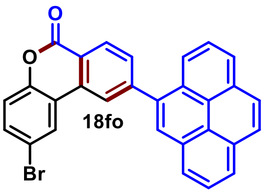
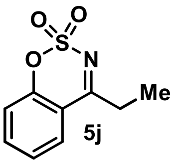
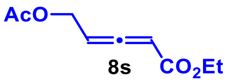
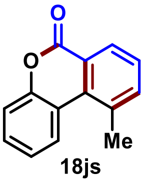
After examining the substrate scope of *δ*-acetoxy allenoates **8** in their reaction with **5a**, we moved to check the same with respect to cyclic sulfamidate imine (**5b-k**) and *δ*-acetoxy allenoate (**8a**, **8s**, and **8o**). As shown in Table 6, the products are obtained in very good yields suggesting the generality of our synthetic route to benzocoumarins. The structure of **18ga** has been confirmed by X-ray crystallography (Figure 6). The reaction using CH(Me)(OAc)-CH=C=CH(CO_2Et) (**8t**) with **5a** under these conditions gave only traces of the product. Satisfyingly, though, treatment of *δ*-acetoxy allenoate CH_2(OAc)-CH=C=CH(CO_2Et) (**2s**; R = H) with **5j** afforded **18js**, but the yield was rather low (26%).

Table 6. Substrate Scope for Cyclic Sulfamidate Imines[a]



5b-k + **8a, 8s and 8o** → **18ba-ka, 18fo and 18js**

Entry	*N*-Sulfonyl imine	*δ*-Acetoxy allenoate	Benzocoumarins (chromenone)	Yield (%)[b]
1	 **5b**	 **8a**	 **18ba**	75
2	 **5c**	 **8a**	 **18ca**	70
3	 **5d**	 **8a**	 **18da**	73
4	 **5e**	 **8a**	 **18ea**	75
5	 **5f**	 **8a**	 **18fa**	71
6	 **5g**	 **8a**	 **18ga** (X-ray)	78

7	 5h	 8a	 18ha	81
8	 5i	 8a	 18ia	75
9	 5j	 8a	 18ja	79
10	 5k	 8a	 18ja	75
11	 5f	 8o	 18fo	63
12	 5j	 8s	 18js	72

[a]Reaction conditions: **5b-k** (0.20 mmol), **8a, 8o** and **8s** (0.20 mmol), DMAP (0.04 mmol) and K_2CO_3 (0.40 mmol) in toluene (2.0 mL) at 130 °C (oil bath). [b]Isolated yield.

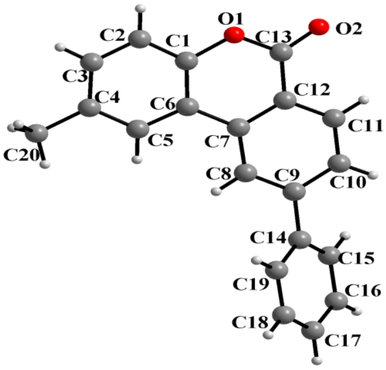
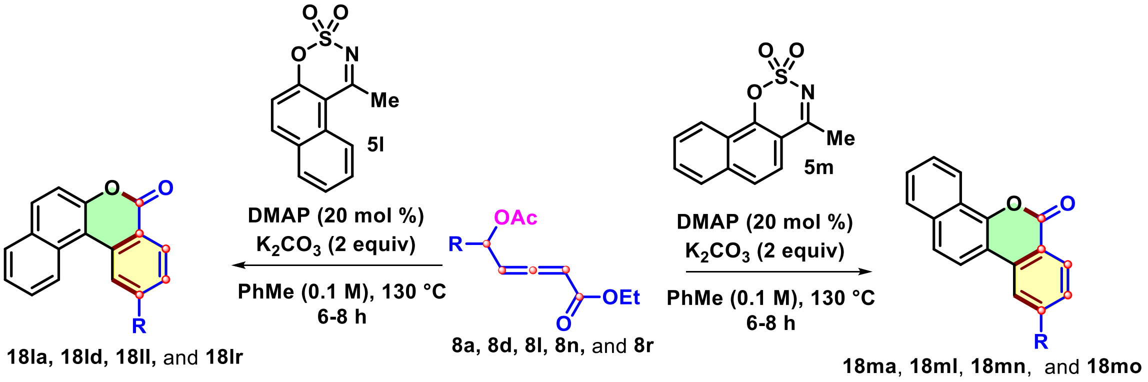


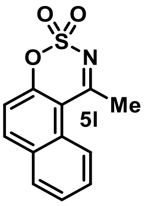
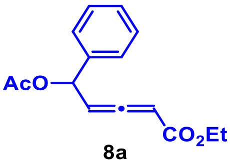
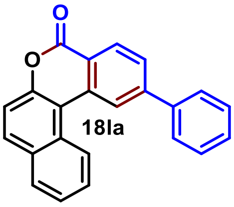
Figure 6: Molecular structure of compound **18ga** (CCDC No. 2258037). Relevant bond lengths: C7-C8 1.393(7), C8-C9 1.377(7), C9-C10 1.402(7), C10-C11 1.379(8), C11-C12 1.374(8), C12-C7 1.413(7) Å

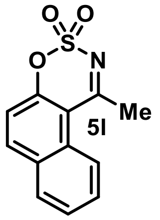
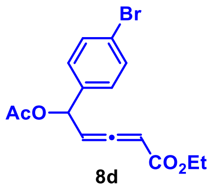
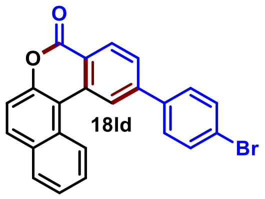
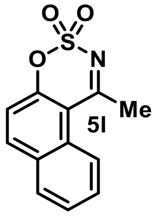
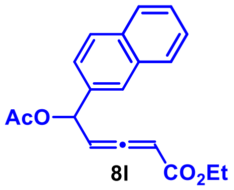
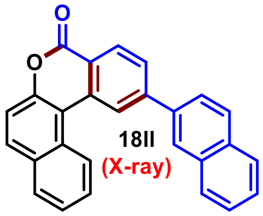
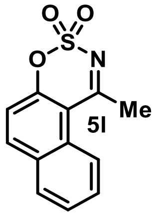
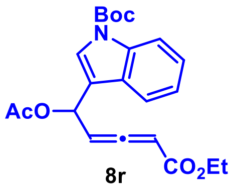
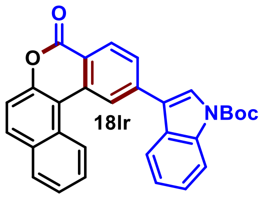
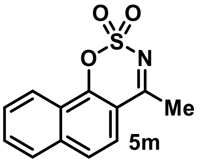
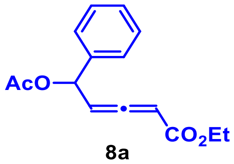
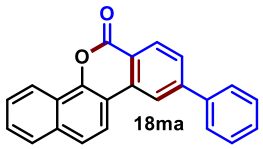
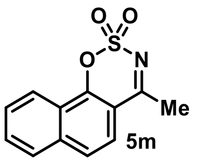
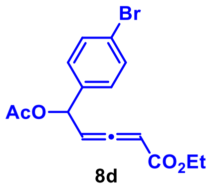
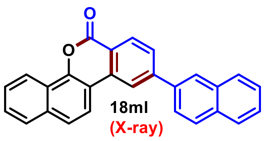
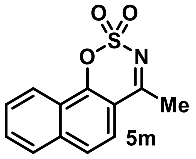
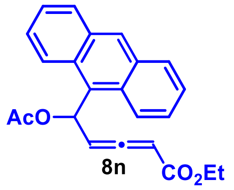
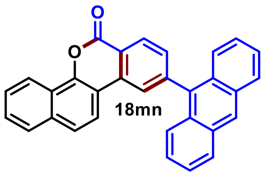
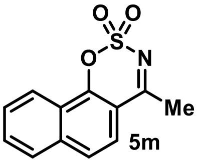
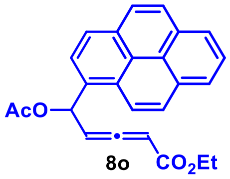
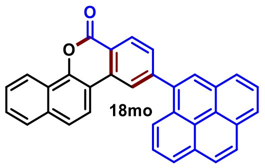
2.3.4 Extension to π-expanded coumarins (dibenzo[c,f]/ [c,h]-chromenones)

We extended the above protocol for cyclic sulfamidate imines **5l** and **5m**, possessing naphthalene as a part of the ring, with aryl/poly aryl substituted allenoates (Table 7). Here also, the expected dibenzo[*c*,*h*]/ [*c*,*f*]chromenones [**18la**, **18ld**, **18ll** (Figure 7, left), **18lr**, **18ma**, **18ml** (Figure 7, right), **18mn** and **18mo**] could be obtained in acceptable yields.

Table 7. Substrate Scope for Dibenzo[*c*,*f*]/ [*c*,*h*]-chromenones [a]



Entry	*N*-Sulfonyl imine	*δ*-Acetoxy allenoate	Chromenone	Yield (%)[b]
1	 5l	 8a	 18la	79

2	 **5l**	 **8d**	 **18ld**	75
3	 **5l**	 **8l**	 **18ll** **(X-ray)**	73
4	 **5l**	 **8r**	 **18lr**	68
5	 **5m**	 **8a**	 **18ma**	74
6	 **5m**	 **8d**	 **18ml** **(X-ray)**	71
7	 **5m**	 **8n**	 **18mn**	69
8	 **5m**	 **8o**	 **18mo**	65

[a]Reaction conditions: **5l**/ **5m** (0.20 mol), **8a, 8d, 8l, 8n,** and **8o** (0.20 mmol), DMAP (0.04 mmol) and K_2CO_3 (0.40 mmol) in toluene (2.0 mL) at 130 °C (oil bath). [b]Isolated yield.

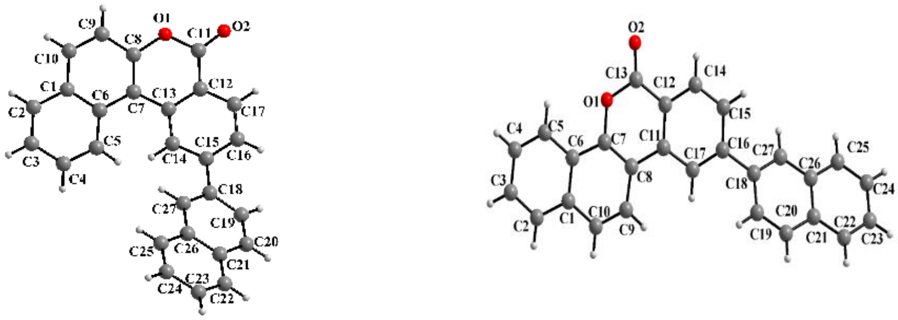
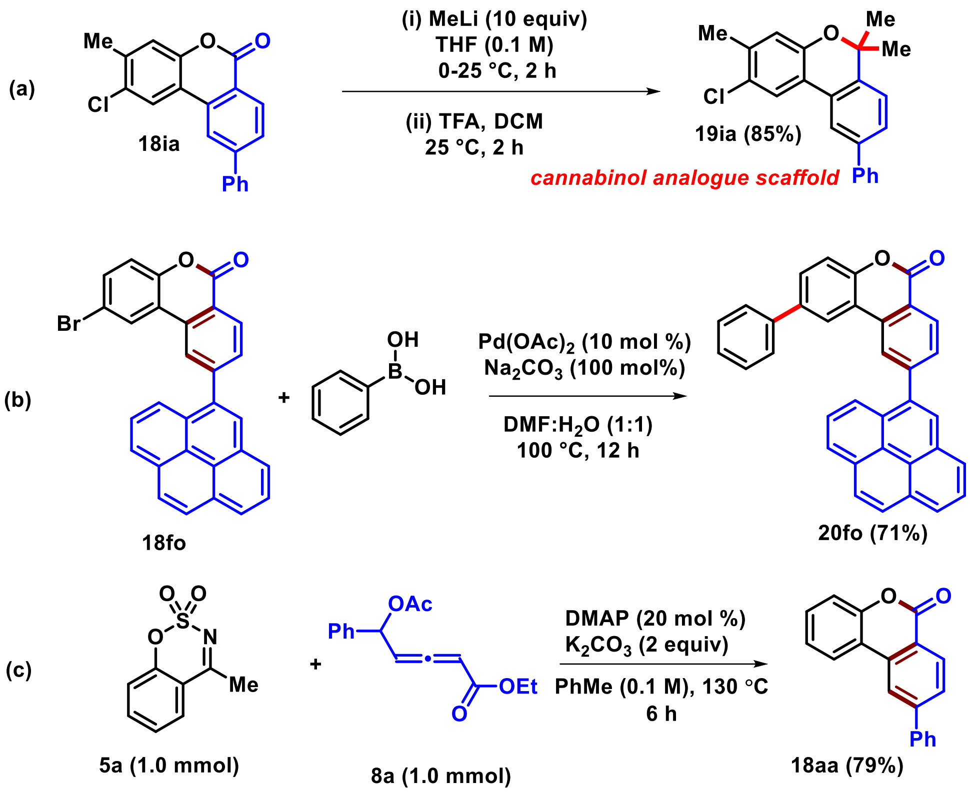


Figure 7: Molecular structures of compounds **18ll** (left, CCDC No. 2264275) and **18ml** (right, CCDC No. 2258038). Relevant bond distances: **18ll** C12-C13 1.406(3), C13-C14 1.402(3), C14-C15 1.392(3), C15-C16 1.403(3), C16-C17 1.374(3) C17-C12 1.391(3) Å. **18ml** C11-C12 1.403(2), C12-C14 1.394(2), C14-C15 1.369(2), C15-C16 1.396(2), C16-C17 1.391(2), C17-C11 1.399(2) Å.

2.3.5 Synthetic utility

To highlight the synthetic utility of the developed strategy, the obtained products were utilized in nucleophilic addition-cyclization and Suzuki coupling. Thus, the treatment of **18ia** with methyllithium followed by trifluoroacetic acid[108] gave Cannabinol analogue **19ia** in high yield (85%). The absence of the carbonyl peak in the $^{13}C\{^{1}H\}$ NMR and the appearance of the two methyl protons at δ 1.66 along with HRMS data confirmed the structure as proposed. Next, the product **18fo** was utilized in Suzuki coupling with phenylboronic acid to obtain the corresponding cross-coupled product **20fo** in 71% yield. We have also performed a 1.0 mmol scale reaction to obtain **18aa** in 79% yield (Scheme 12).

Benzocoumarins could be luminescent sensors.[109] Hence we checked the fluorescence properties of compounds **18aa**, **18an**, and **18ao** in dil. $CHCl_3$ solution (10^{-5} M). All these compounds displayed satisfactory fluorescence emission bands (Figure 8, Table 8). Compound **18ao** shows a remarkable bathochromic shift, probably because of the pyrene ring at the C9 position. The fluorescence quantum yield (59.64%) of **18ao** was calculated using 9,10 diphenyl anthracene as a standard.



Scheme 12. Synthetic Utility and mmol Scale Reaction[a]

[a]Reagents and conditions: (a) i) **18ia** (0.0625 mmol), MeLi (0.625 mmol), THF (0.1 M), rt; ii) TFA (1 µL, 0.012 mmol), DCM, rt. (b) **18fo** (0.042 mmol)**,** Pd(OAc)$_2$ (0.0042 mmol), Na$_2$CO$_3$ (0.042 mmol), DMF/H$_2$O (2.0 mL, 1:1), 12 h, at 100 °C (oil bath). (c) **5a** (1.0 mmol), **8a** (1.0 mmol), K$_2$CO$_3$ (2.0 mmol), DMAP (0.2 mmol), toluene (10 mL), 130 °C (oil bath), 6 h.

2.3.6 UV−Visible absorption and fluorescence emission spectra of benzocoumarins 18aa, 18an, and 18ao

Table 8. UV−Visible absorption and fluorescence emission properties of benzocoumarins 18aa, 18an, and 18ao

Entry	Compound	λ_{abs} (nm)[a]	ε (10^5 M^{-1} cm^{-1})	λ_{em} (nm)[b]
1	**18aa**	263	1.77	374
2	**18an**	256	1.83	361
3	**18ao**	244	0.60	442

[a]UV-visible absorption wavelengths. [b]Emission wavelengths at rt in CHCl$_3$ at a concentration of 1 × 10^{-5} M.

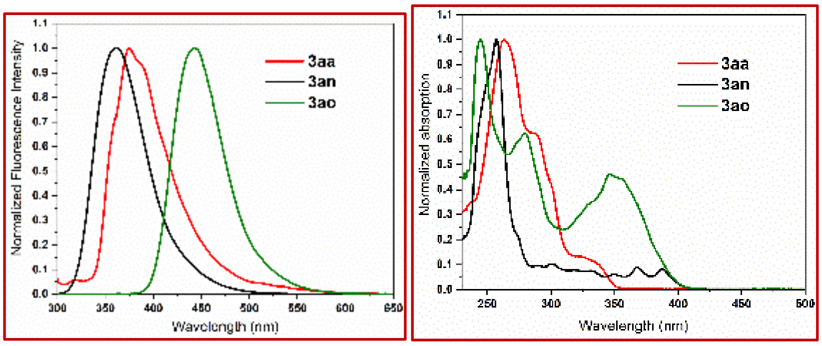
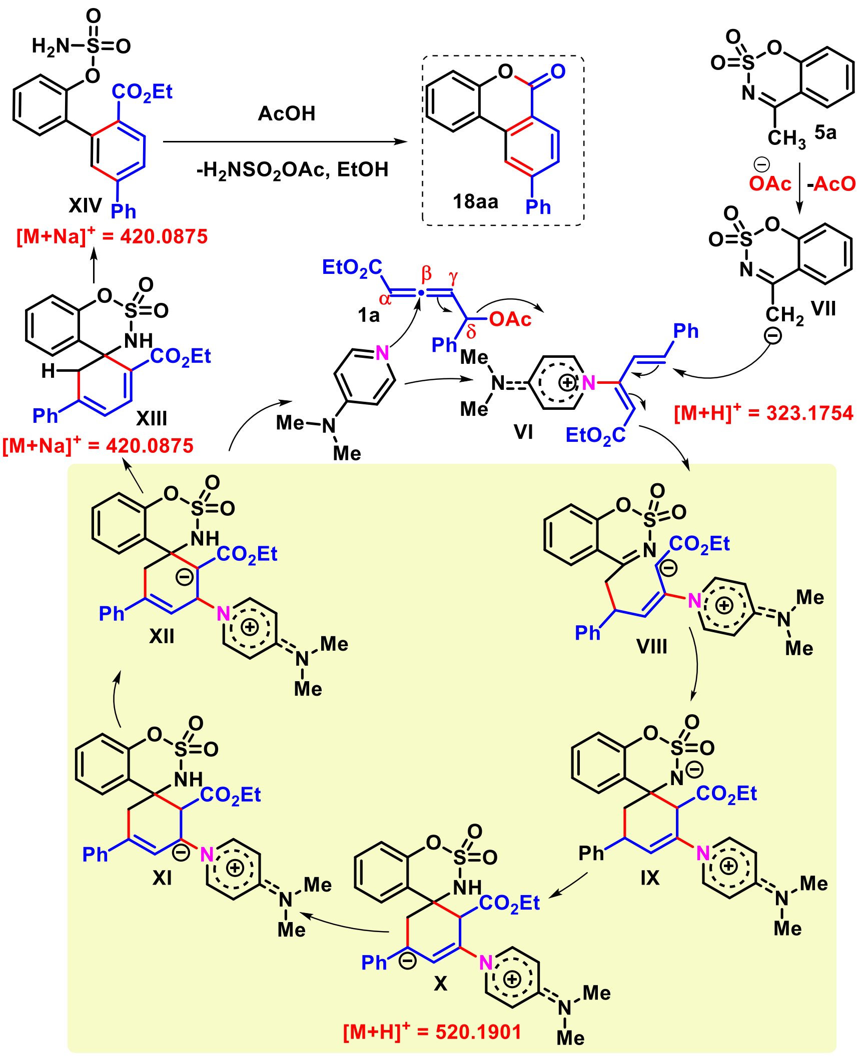


Figure 8. Absorbance and fluorescence emission spectra of compounds **18aa**, **18an**, and **18ao**.

2.3.7 Proposed pathway for the formation of benzocoumarins

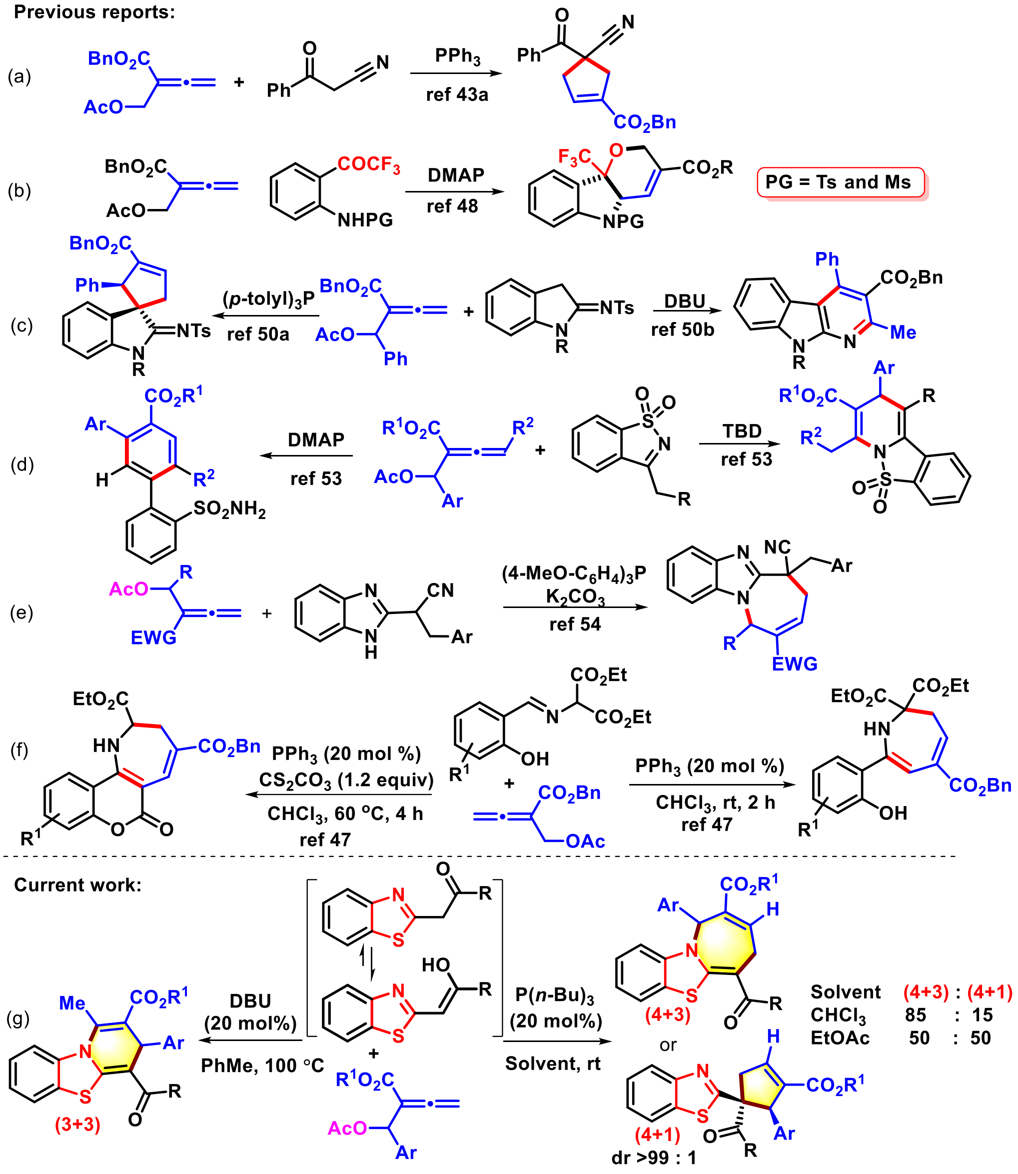
The above sequential (4 + 2) and (5 + 1) domino-annulation is initiated by the addition of nucleophilic base DMAP to the *β*-carbon of the *δ*-acetoxy allenoate **8a** via allylic elimination (S_N2') to give the diene-ammonium intermediate **VI** (Scheme 13). Next, the addition of the nucleophilic carbon of **VII** at the *δ*-carbon of **VI** leads to zwitterionic intermediate **VIII**. The positive charge on the nitrogen atom of **VIII** is weakened by the attached ring as well as nitrogen. Hence, **VIII** is involved in Mannich coupling rather than 1,2-elimination to afford intermediate **IX**. Subsequently, proton shift, double-bond isomerization, proton shift, and DMAP elimination give spirocyclic diene **XIII** *via* **X**-**XII**. Then aromatization of **XIII** provides sulfamyloxy carboxylate **XIV** *via* C-N bond cleavage. Finally, cleavage O-S bond and subsequent lactonization aided by acetic acid leads to chromenone **18aa** through phenolic intermediate due to proximal effect. These aforementioned intermediates were identified by an in-process HRMS study.



Scheme 13: Plausible mechanistic pathway for the formation of **18aa**

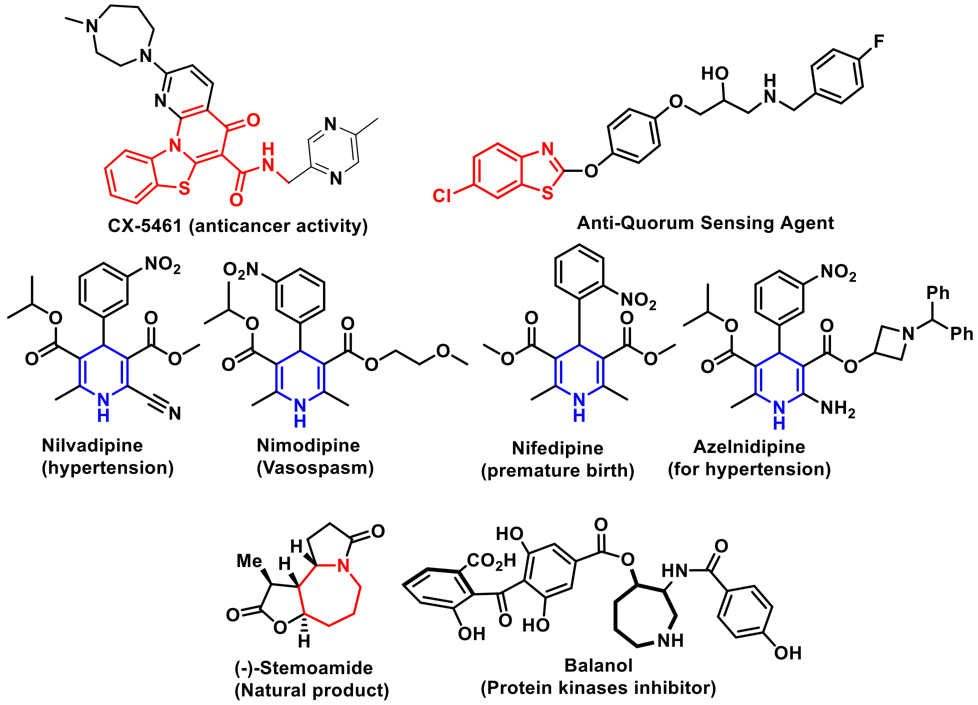
2.4 Phosphine vs DBU Catalyzed Annulation Reactions of *β*'-Acetoxy Allenoates with Acyl-tethered Benzothiazole Bisnucleophiles: (4 + 3) or (4 + 1) vs (3 + 3) Annulation

Lewis base catalyzed annulation of *β*'-acetoxy allenoates has been investigated by several research groups including ours (Scheme 14a-d).[43a,48, 50a, 50b, 53] As can be seen readily, the second substrate in all these cases acts as a bisnucleophile and the annulation products possess newly generated 5/6-membered rings. Compared to these, the (4 + 3) annulation is perhaps more fascinating and two cases involving *β*'-acetoxy allenoates are illustrated in Scheme 14e-f;[47, 54] in both these systems, the (4 + 3)-annulation products using phosphine catalysis are reported. There are also a few other reports on (4 + 3)-annulations involving allenoates.[110] We have been interested in the divergent reactivity of allenoates under amine vs phosphine catalysis and herein, we address the reactivity of *β*'-acetoxy allenoates with 2-acyl-tethered benzothiazole wherein a methylene group is flanked between the thiazole moiety and the carbonyl group. Although this 2-acyl-tethered benzothiazole acts as a bisnucleophile under both DBU and P(n-Bu)$_3$ catalyzed dearomative annulations, the DBU-catalyzed (3 + 3) dearomative and chemoselective cyclization gives benzothiazole-fused 1,4-dihydropyridines whereas P(n-Bu)$_3$-catalyzed reaction gives the (4 + 3) dearomative cyclization product[9] along with (4 + 1) cyclization derivative. In the phosphine-catalyzed reaction, there is also a significant solvent effect on the ratio of (4 + 3)/(4 + 1) annulation: While CHCl$_3$ favors (4 + 3) product, ethyl acetate affords both the products in a nearly equal ratio.



Scheme 14: Previous literature reports and the current work

Benzothiazole scaffolds are integral parts of many pharmaceutical agents.[111] Several important drugs based on 1,4-dihydropyridine scaffolds (e.g., nilvadipine, nimodipine, nifedipine, azeinidipine) are available (Figure 9).[112] Although 2,5-dihydroazepines *per se* are not that common, a good number of azepine derivatives are present as natural products or pharmaceutically active.[113]



CX-5461 (anticancer activity)

Anti-Quorum Sensing Agent

Nilvadipine
(hypertension)

Nimodipine
(Vasospasm)

Nifedipine
(premature birth)

Azelnidipine
(for hypertension)

(-)-Stemoamide
(Natural product)

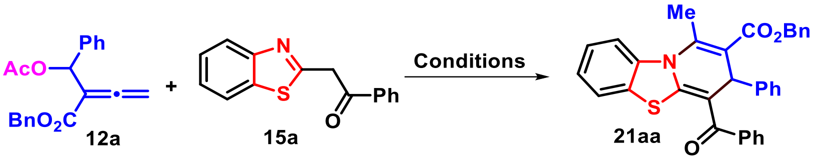
Balanol
(Protein kinases inhibitor)

Figure 9: Selected examples of bioactive benzothiazoles, dihydropyridines, and azepines

2.4.1 Dearomative (3 + 3) annulation reactions of β'-acetoxy allenoates with acyl-tethered benzothiazole: Optimization study

Initially, we examined a reaction between **12a** (0.20 mmol) and **15a** (0.20 mmol) in the presence of DABCO (20 mol%) in toluene at rt (25 °C) but did not observe the formation of **21aa** (Table 9, entry 1). By increasing the reaction temperature to 50 °C, we obtained the dearomative annulation product, 1,4-dihydropyridine **21aa**, in 10% isolated yield after 12 h (entry 2). Peaks at δ 5.65 for the unique C*H* proton and at 2.69 for the newly generated CH_3 protons in the ^{1}H NMR spectrum corroborate the structure as given here; the corresponding carbons exhibit peaks at δ 40.9 and 19.3, respectively, in the $^{13}C\{^1H\}$ NMR spectrum. Single crystal X-ray structure determination (Figure 10, *vide infra*) confirmed the structure as proposed. Shifting from DABCO to DBU increased the product yield to 35% (entry 3) and a higher temperature of 100 °C increased the yield to 75% (entry 4). As an additive, Na_2CO_3 (1.5 equiv) did not influence the yield of **21aa** (entry 5). We then examined other tertiary amine bases such as TMG, TBD, and DBN, which gave a lower yield of **21aa** (entries 6-8). The solvents DCE, DMF, and dioxane were not better than toluene (entries 9-11). Lowering the amount of DBU from 20 mol% to 10 mol% decreased the yield (entry 12). No reaction occurred without the DBU catalyst (entry 13). Thus, the optimal reaction conditions to get **21aa** were by using DBU (20 mol%) as the catalyst and by performing the reaction at 100 °C in toluene (2.0 mL) for 12 h.

Table 9. Optimization of Reaction Conditions for 21aa[a]



Entry	Base[b]	Solvent	Temp (oil bath, °C)	Yield (%)
1	DABCO	PhMe	25	NR
2	DABCO	PhMe	50	10
3	DBU	PhMe	50	35
4	DBU	PhMe	100	75
5	DBU (+Na_2CO_3)	PhMe	100	75
6	TMG	PhMe	100	60
7	TBD	PhMe	100	71
8	DBN	PhMe	100	65
9	DBU	DCE	100	25
10	DBU	DMF	100	NR
11	DBU	Dioxane	100	25
12	DBU	PhMe	100	50
13	-	PhMe	100	NR

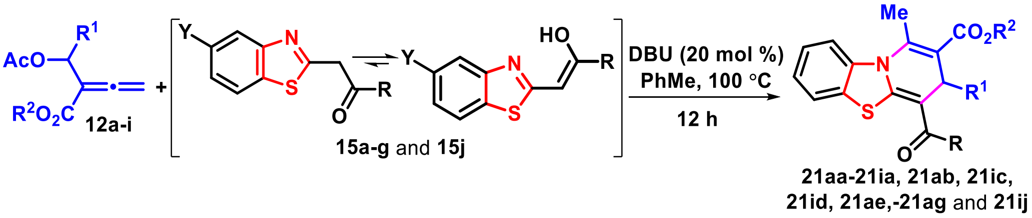
[a]Reaction conditions: **12a** (0.20 mmol), **15a** (0.20 mmol), base (20 mol% for entries 1-10 and 10 mol% for entry 11) in solvent (2.0 mL) in a stoppered Schlenk tube.[b]Na_2CO_3 (0.30 mmol) was used. [c]Isolated yield after 12h.

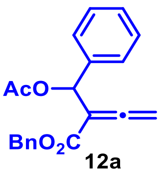
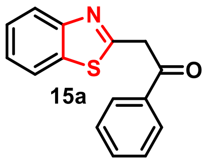
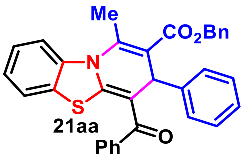
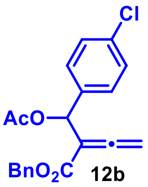
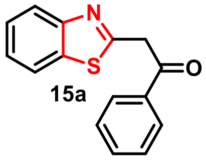
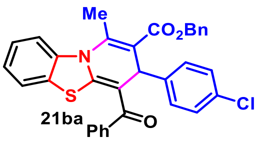
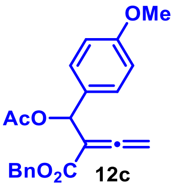
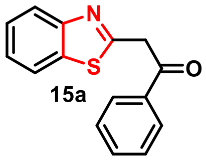
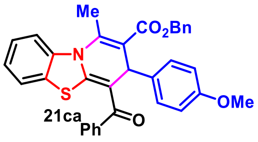
2.4.2 Substrate scope for dearomative (3 + 3) annulation reactions

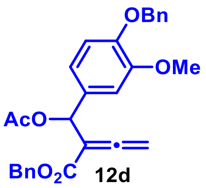
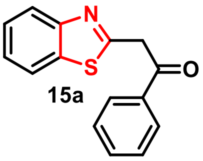
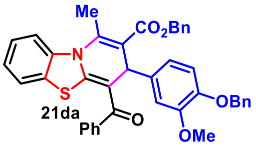
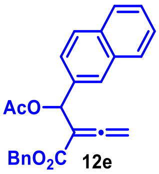
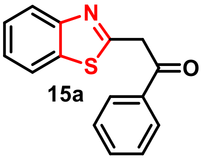
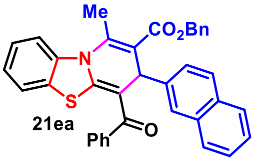
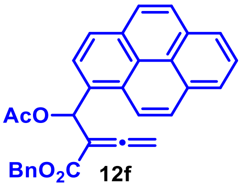
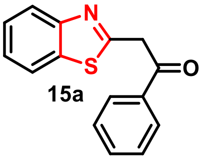
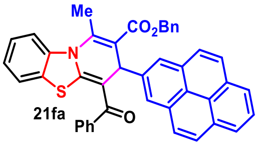
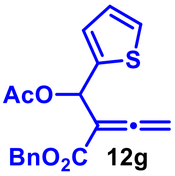
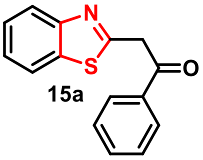
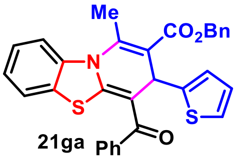
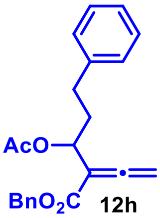
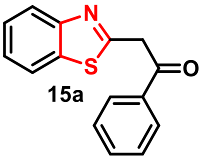
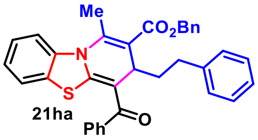
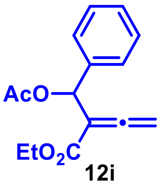
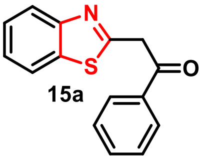
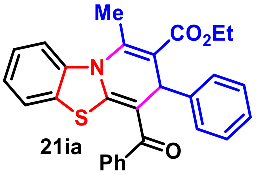
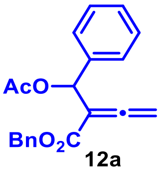
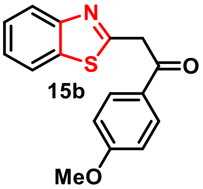
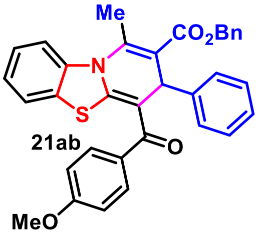
The substrate scope for the DBU-catalyzed (3 + 3) annulation between 2-acyl benzothiazoles **15** and *β*'-acetoxy allenoates **12**, is presented in Table 10. Different types of *β*'-acetoxy allenoates having functionalities (H, Cl, and OMe) at the *p*-position of the phenyl ring **12a-c** reacted well and afforded benzothiazole-fused 1,4-dihydropyridines **21aa-ca** in 75-81% yields. Disubstituted allenoate **12d** also delivered **21da** in 68% yield. The polycyclic aromatic and heterocyclic substituted allenoates (**12e-g**) gave products **21ea**, **21fa**, and **21ga** in yields of

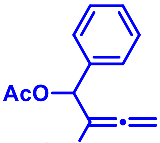
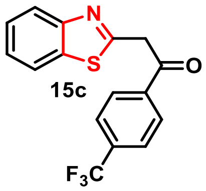
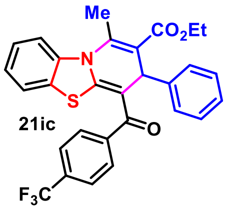
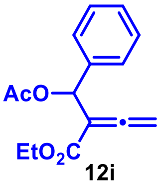
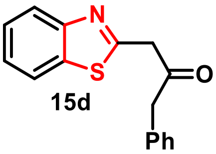
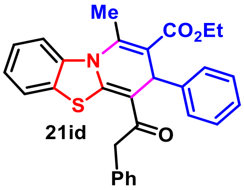
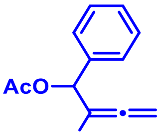
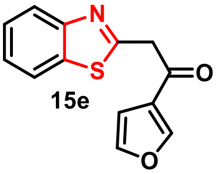
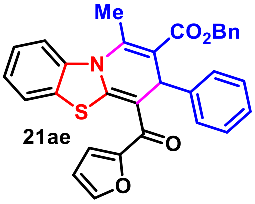
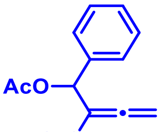
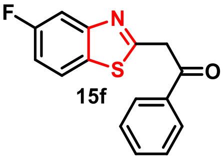
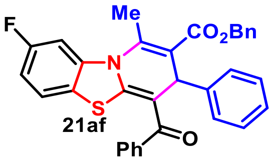
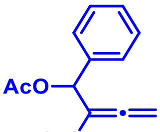
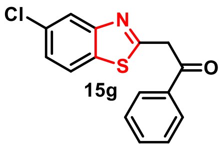
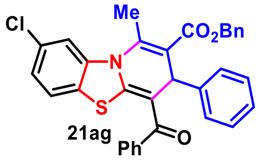
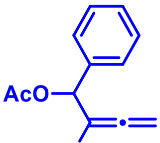
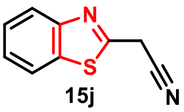
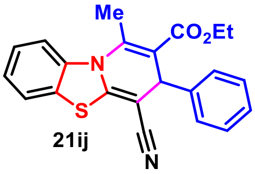
70%, 65%, and 69%, respectively. We could also obtain product **21ha** in 60% yield using the alkyl-substituted allenoate **12h**. The *β*'-acetoxy allenoate **12i** containing ethyl group instead of benzyl group afforded the product **21ia** in good yield of 76%, as expected. The scope of acyl benzothiazoles was checked by having -OMe, -CF_3 at the *p*-position of the phenyl moiety in the acyl part (**15b** and **15c**), by replacing the phenyl ring with benzyl (**15d**) or 2-furyl substituent (**15e**). The products **21ab**, **21ic**, **21id**, and **21ae** were obtained in yields of 65-77%. The 5-substituted acyl-benzothiazoles **15f** and **15g** also gave the expected products **21af** and **21ag** in 75-77% yield. To further expand the scope of DBU catalyzed (3 + 3) dearomative cyclization, we checked the reaction of 2-benzothiazolyl-acetonitrile **15h** with **12i** under the optimized condition and the expected product **21ih** was obtained in 72% yield. The relevant C=C distances of *ca* 1.35 Å in **21aa** (Figure 10) clearly indicate the 1,4-dihydropyridine skeleton.

Table 10 Substrate Scope for (3 + 3) Annulation[a]



Entry	*β*-Acetoxy allenoate	Acyl-tethered benzothiazole	1,4-dihydropyridine	Yield (%)[b]
1	 12a	 15a	 21aa	75
2	 12b	 15a	 21ba	73
3	 12c	 15a	 21ca	79

4	 12d	 15a	 21da	68
5	 12e	 15a	 21ea	70
6	 12f	 15a	 21fa	65
7	 12g	 15a	 21ga	69
8	 12h	 15a	 21ha	60
9	 12i	 15a	 21ia	77
10	 12a	 15b	 21ab	77

11	 **12i**	 **15c**	 **21ic**	73
12	 **12i**	 **15d**	 **21id**	65
13	 **12a**	 **15e**	 **21ae**	72
14	 **12a**	 **15f**	 **21af**	77
15	 **12a**	 **15g**	 **21ag**	75
16	 **12i**	 **15j**	 **21ij**	72

[a]Reaction conditions: **12a-i** (0.20 mmol), **15a-g** and **15j** (0.20 mmol), DBU (0.04 mmol) in toluene (2.0 mL) at 100 ºC (oil bath). Isolated yields.

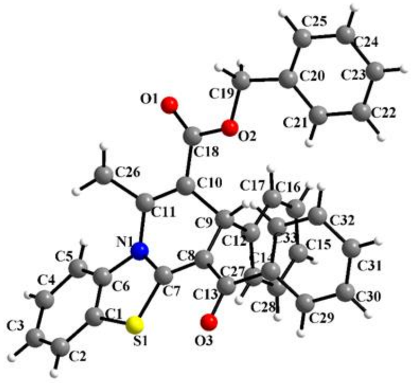


Figure 10. Molecular structure of compound **21aa** (CCDC No. 2348193). Relevant bond distances: N1-C7 1.394(3), C7-C8 1.356(3), C8-C9 1.515(3), C9-C10 1.525(3), C10-C11 1.351(3), C11-N1 1.420(2) Å

It may be noted that our above reaction is chemoselective since pyrans/dihydropyrans of the type **XV/XV'** are not observed in the reaction using **12a** and the enolizable acyl-benzothiazole precursor **15a**.[39] A possible reason is that the enol form of **15a** probably exists more in *syn*-conformation (Figure 11); however, currently, we do not have more data on this aspect.[114]

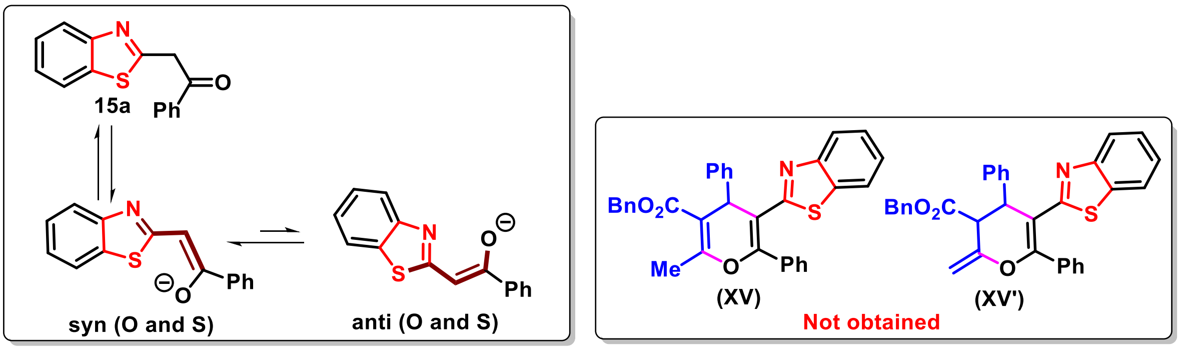
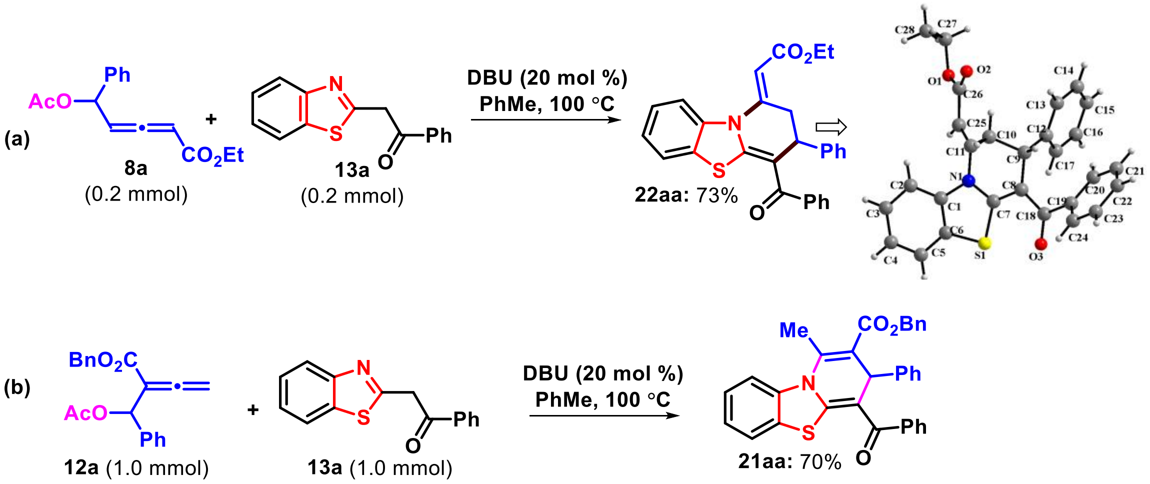


Figure 11: Possible tautomerization in **15a** and the structures of pyrans/dihydropyrans **XV/XV'**

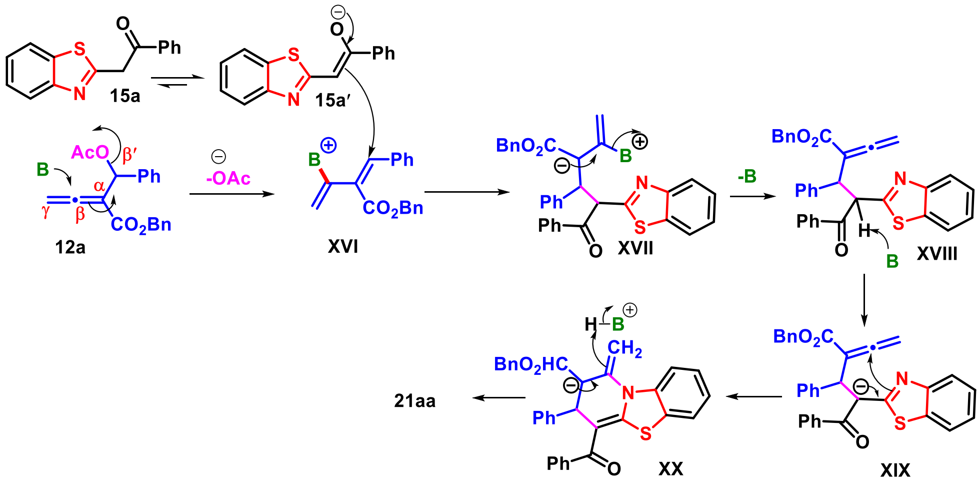
In order to check whether the ester group at the α-carbon poses any steric effect, we performed the reaction between **15a** and δ-acetoxy allenoate **8a** under DBU catalysis using the above-optimized conditions (Scheme 15a). Here also we obtained a similar dearomatized (3 + 3) cyclization product **22aa** (CCDC No. 2348197) in good yield, albeit with an exocyclic double bond, suggesting that the position of the ester group does not have a significant steric effect on the dearomative cyclization. The presence of only one C=C double bond in the newly formed ring in **22a** is clearly shown by X-ray crystallography also (cf. Scheme 15a). A scale-up reaction using 1.0 mmol reactants using the above conditions afforded **21aa** in 70% yields (Scheme 15b).



Scheme 15: Synthesis of **22aa** and scale-up reaction for **21aa.** Relevant bond distances for **22aa**: N1-C7 1.392(2), C7-C8 1.373(2), C8-C9 1.513(2), C9-C10 1.541(2), C10-C11 1.492(2), C11-N1 1.423(2) C11-C25 1.336(2) Å

2.4.3 *Plausible pathways for (3 + 3) annulation*

A plausible pathway for the (3 + 3) dearomative cyclization is depicted in Scheme 16. Initially, the *β'*-acetoxy allenoate **12a** undergoes S_N2' attack with DBU at the *β*-carbon of the allenoate *via* an addition-elimination pathway to deliver the reactive electrophilic diene-ammonium intermediate **XVI**, which upon 1,4-addition with the anion **15a′** provides zwitterionic intermediate **XVII**. Since DBU is an alicyclic tertiary amine, the positive charge on the nitrogen atom is not stabilized; hence, allylic elimination is involved, and **XVII** rapidly undergoes DBU elimination to give allenic intermediate **XVIII**. Proton abstraction from **XVIII**, followed by *aza*-Michael addition and dearomatization, delivers **21aa** *via* **XIX-XX**. The intermediates (**XVI** to **XVIII**) were identified in HRMS using reaction mixture HRMS data in the formation of **21ah.**



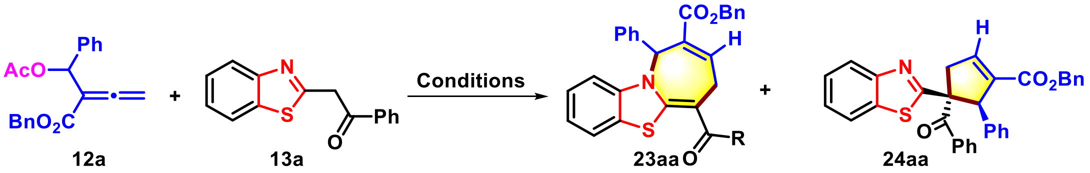
Scheme 16: Plausible mechanistic pathway for the formation of **21aa**

2.4.4. Phosphine catalyzed (4 + 3) or (4 + 1) Annulation reactions of β'-acetoxy allenoates with acyl-tethered benzothiazole: Optimization study

Based on our earlier studies,[14, 32] we expected that the reaction of 2-acyl benzothiazoles **15** and *β'*-acetoxy allenoates **12** under phosphine catalysis could lead to a product different from that using amine catalysis. One possibility is (4 + 3) annulation with the allenoate acting as a 4-C partner. As depicted in Table 11 (entry 1), we performed a reaction between 2-acyl benzothiazoles **15a** (0.20 mmol) and *β'*-acetoxy allenoate **12a** (0.20 mmol) in the presence of Ph_3P (20 mol%). We were able to isolate compound **23aa** in 15% yield and identified it as the (4 + 3) cyclization product formed *via* dearomative cyclization. Unlike **21aa**, this product exhibits a characteristic AB portion of ABX pattern at δ 3.10 for the ring CH_2 protons [AB, connected olefinic C*H* proton (X)] in the ^{1}H NMR spectrum; the ring C*H* connected to the nitrogen and olefinic C*H* appear in the aromatic region. The $^{13}C\{^1H\}$ NMR spectrum exhibits 3 clear aliphatic carbons [δ 67.6, 56.7, 26.8] as expected. Final confirmation is done by single crystal X-ray structure determination (Figure 12a, *vide infra*). Upon lowering the temperature to 50 °C, there was no change in the yield, but at rt (25 °C) the yield of **23aa** increased to 40% (entries 2-3). Rather surprisingly, we also isolated the (4 + 1) product **24aa** in 30% yield (dr >99:1) formed *via* carbo-annulation. The NMR peaks were distinctly different from that of **23aa** with three characteristic peaks in the aliphatic/olefinic region in the ^{1}H NMR [δ 3.46 (m) and 4.17 (m) for ring CH_AH_M, 5.67(s) for C*H*Ph(ring)] and 4 peaks in the aliphatic region in the $^{13}C\{^1H\}$ NMR [δ 68.0, 66.1, 57.2, 42.6] along with other peaks. Use of other phosphines and solvents (entries 4−15) indicated that P(n-Bu)$_3$ in $CHCl_3$ as the solvent gave **23aa** in 85%

yield (^{1}H NMR, entry 11). For the (4 + 1) annulation, P(*n*-Bu)$_3$ in EtOAc was found to be the best giving **24aa** in 50% (^{1}H-NMR, entry 12) yield along with **23aa**.

Table 11. Optimization of Reaction Conditions for 23aa and 24aa[a]



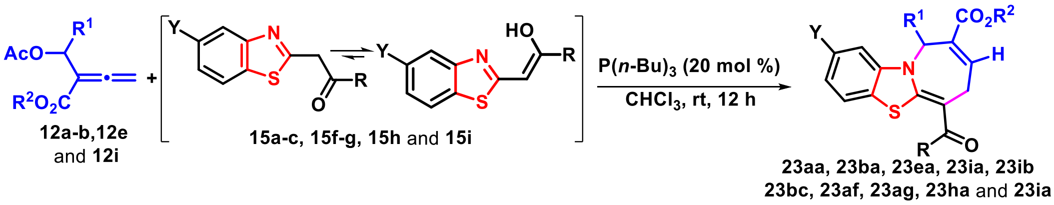
Entry	PR$_3$	Solvent	Temp (oil bath, °C)	**23aa:24aa**[b]
1	PPh$_3$	PhMe	100	100:00 (15:00)
2	PPh$_3$	PhMe	50	100:00 (15:00)
3	PPh$_3$	PhMe	25	60:40 (40:30)
4	(*o*-tolyl)$_3$P	PhMe	25	60:40 (20:15)
5	(*p*-tolyl)$_3$P	PhMe	25	65:35 (30:15)
6	(4-F-C$_6$H$_4$)$_3$P	PhMe	25	65:35 (30:15)
7	PPh$_2$Me	PhMe	25	65:35 (50:30)
8	PPh$_2$Me	THF	25	60:40
9	PPh$_2$Me	PhMe[c]	25	65:35
10	P(*n*-Bu)$_3$	PhMe	25	75:25
11	**P(*n*-Bu)$_3$**	**CHCl$_3$**	**25**	**85:15**
12	**P(*n*-Bu)$_3$**[d]	**CHCl$_3$**	**25**	**55:45**
13	P(*n*-Bu)$_3$	DCM	25	70:30
14	P(*n*-Bu)$_3$	EtOAc	25	50:50
15	P(*n*-Bu)$_3$[e]	CHCl$_3$	100	70:30

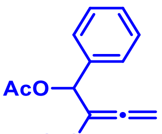
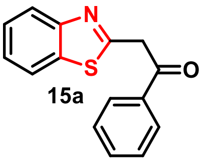
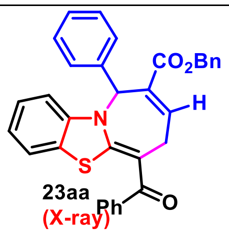
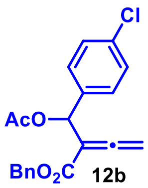
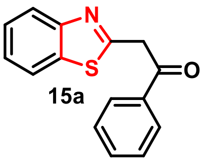
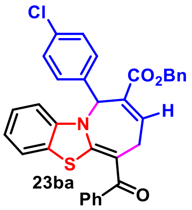
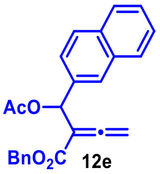
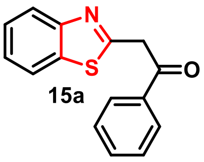
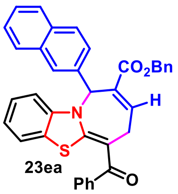
[a] Reaction conditions: **12a** (0.20 mmol), **15a** (0.20 mmol), phosphine (20 mol%) in solvent (2.0 mL). [b] The ratio was determined by ^{1}H NMR (entries 8-15) or tlc (entries 1-7) analysis of the crude reaction mixture after 12h; the values in parentheses for entries 1-7 are percentage yields of **23aa** and **24aa** after isolation. Diastereomeric ratio for **24aa** was >99:1. [c] 4.0 mL of the solvent was used here. [d] Cs$_2$CO$_3$ (0.30 mmol) was used. [e] Reaction was done in a sealed tube.

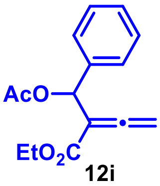
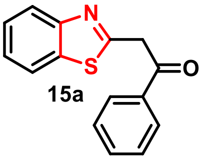
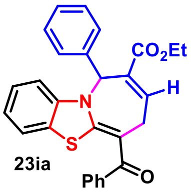
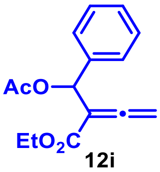
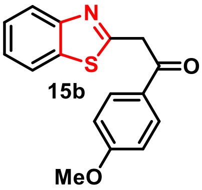
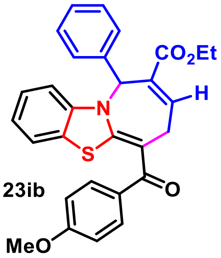
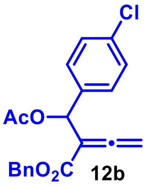
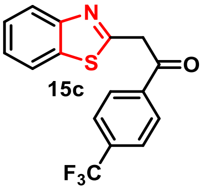
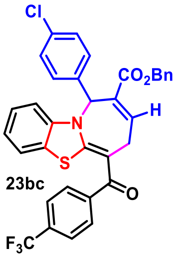
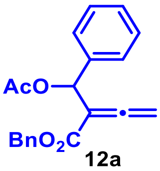
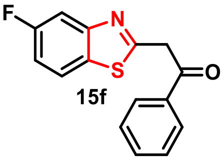
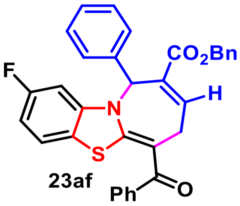
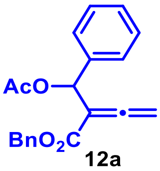
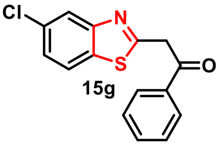
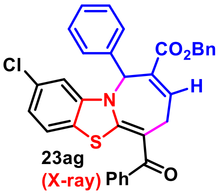
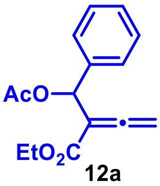
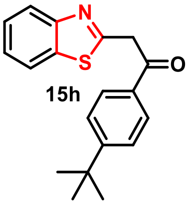
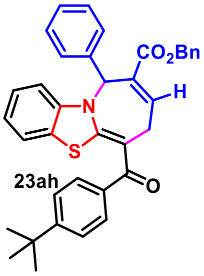
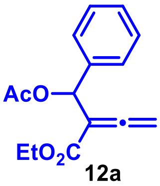
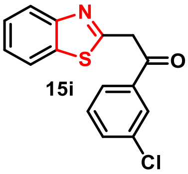
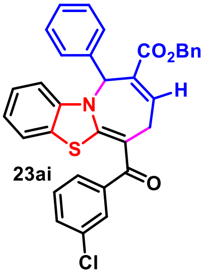
2.4.5 Substrate scope for dearomative (4 + 3) and (4+1) annulation reactions

The substrate scope for P(*n*-Bu)$_3$-catalyzed (4 + 3) annulation between 2-acyl benzothiazoles (**15a-c, 15f-g** or **15i-j**) and *β'*-acetoxy allenoates (**12a-b**, **12e**, or **12h)** under optimized conditions is depicted in Table 11. Although the reaction was complete and the (4 + 3) annulation products **23** were predominant (ca 85%), the yields after isolation were in the range of 55-67% since the (4 + 1) cyclization product was also present as a minor product. For a similar reason, the isolated yields of the (4 + 1) annulation products **24** were lower than the NMR yields (Table 12). The structures of representative (4 + 3) and (4 + 1) annulation products **23aa**, **23ag**, and **24ia** were confirmed by X-ray crystallography (Figures 12-13). The nitrogen atom is essentially planar (Σ√N = 360°) with the 7-membered ring having a tub-like conformation in both **23aa** and **23ga**. Finally, it may be noted that in a recent report, the (4 + 1) product was not observed/isolated.[54]

Table 12. Substrate Scope for (4 + 3) Annulation*^a^*



Entry	*β*-Acetoxy allenoate	Acyl-tethered benzothiazole	Azipines	Yield (%)*^b^*
1	 **12a**	 **15a**	 **23aa** (X-ray)	67
2	 **12b**	 **15a**	 **23ba**	63
3	 **12e**	 **15a**	 **23ea**	58

4	 12i	 15a	 23ia	65
5	 12i	 15b	 23ib	60
6	 12b	 15c	 23bc	55
7	 12a	 15f	 23af	64
8	 12a	 15g	 23ag (X-ray)	61
9	 12a	 15h	 23ah	64
10	 12a	 15i	 23ai	61

[a]Reaction conditions: **12a-b, 12e**, or **12i** (0.20 mmol), **15a-c** or **15f-j** (0.20 mmol), , P(n-Bu)$_3$ (0.04 mmol) in CHCl$_3$ (2.0 mL) at rt. Isolated yields.

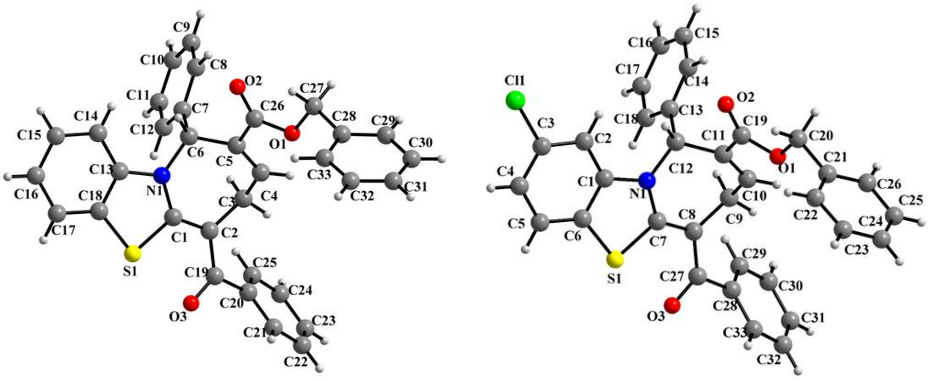
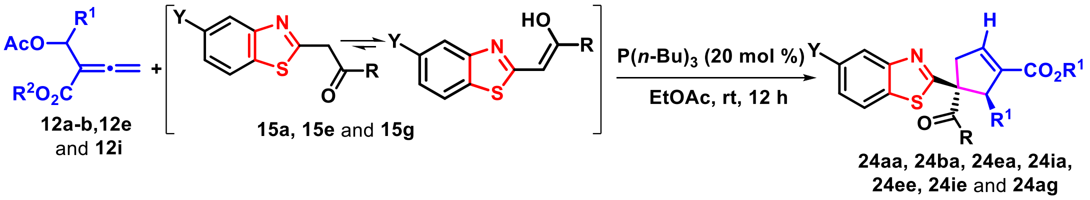
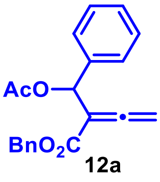
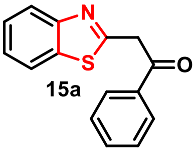
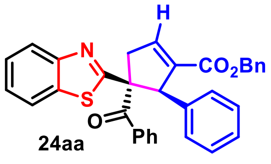
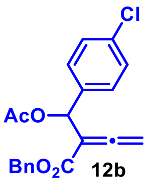
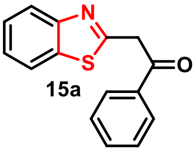
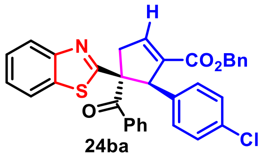
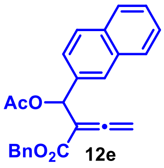
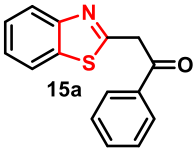
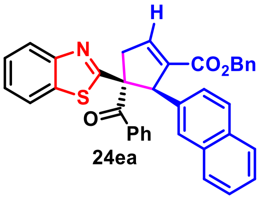
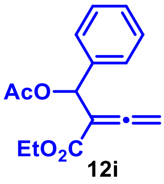
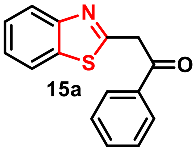
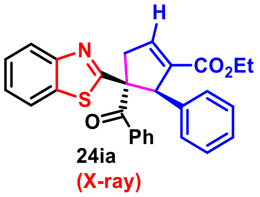
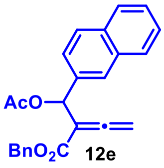
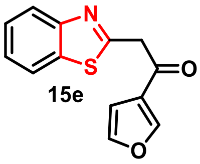
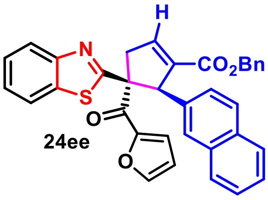
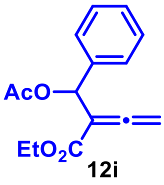
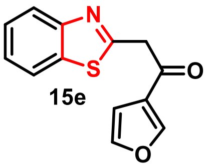
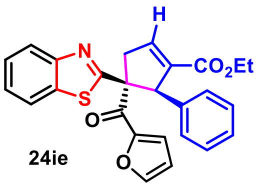
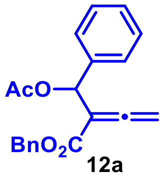
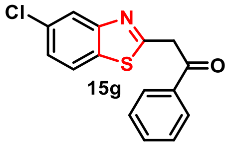
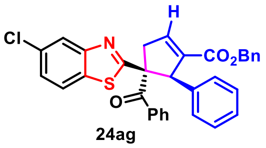


Figure 12. Molecular structures of compounds **23aa** (left, CCDC No. 2348194) and **23ag** (right, CCDC No. 2348195). Relevant bond distances: **23aa** N1-C1 1.378(2), C1-C2 1.382(2), C2-C3 1.517(2), C3-C4 1.499(2), C4-C5 1.318(2), C5-C6 1.526(2), C6-N1 1.480(2) Å. **23ga** N1-C7 1.381(4), C7-C8 1.383(4), C8-C9 1.513(4), C9-C10 1.482(5), C10 C11 1.329(4) C11 C12 1.518(4), C12-N1 1.476(4) Å

Table 13 Substrate Scope for (4 + 1) Annulation[a]



Entry	*β*-Acetoxy allenoate	Acyl-tethered benzothiazole	Cyclopentene	Yield (%)[b]
1	 **12a**	 **15a**	 **24aa**	35
2	 **12b**	 **15a**	 **24ba**	31

3	 12e	 15a	 24ea	28
4	 12i	 15a	 24ia (X-ray)	37
5	 12e	 15e	 24ee	32
6	 12i	 15e	 24ie	30
7	 12a	 15g	 24ag	33

^{a}Reaction conditions: **12a-b, 12e**, or **12i** (0.20 mmol), **15a, 15e**, or **15g** (0.20 mmol), P(n-Bu)$_3$ (0.04 mmol) in EtOAc (2.0 mL) at rt. Isolated yields.

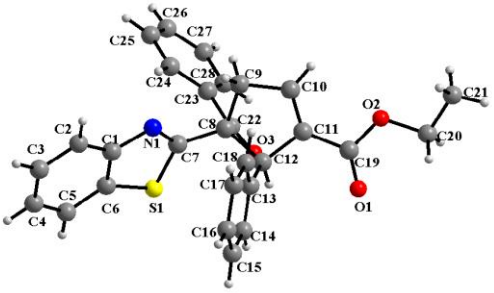
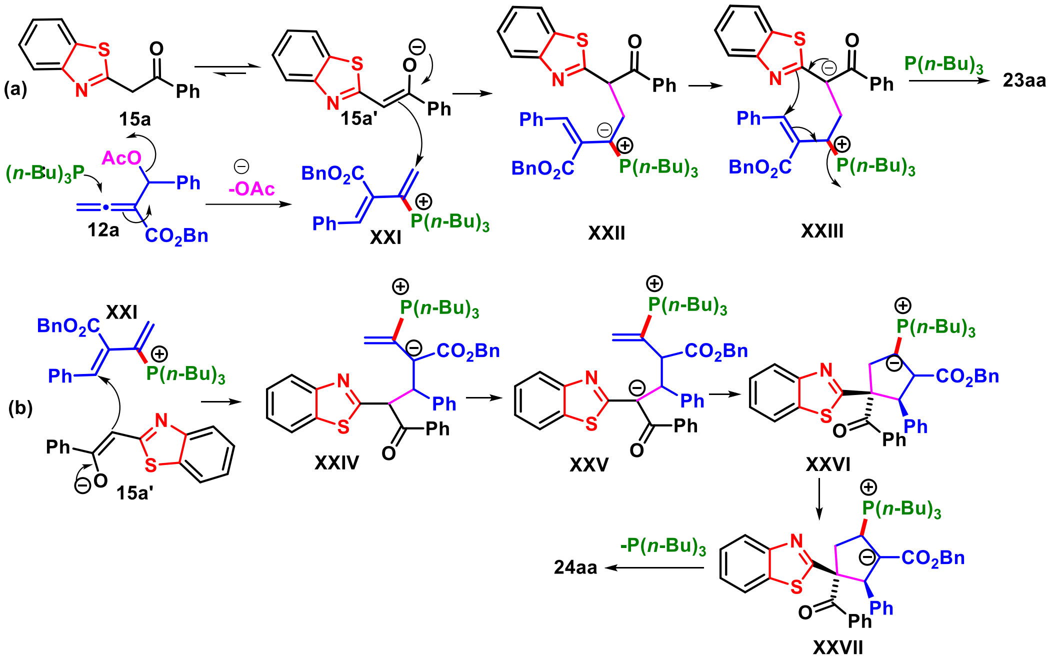


Figure 13. Molecular structure of compound **24ia** (CCDC No. 2348196). Relevant bond distances: C8-C9 1.536(6), C9 C10 1.503(6), C10-C11 1.321(6), C11-C12 1.501(6), C12-C8 1.580(6) Å.

2.4.6 *Plausible pathways for (4 + 3) and (4 + 1) annulations*

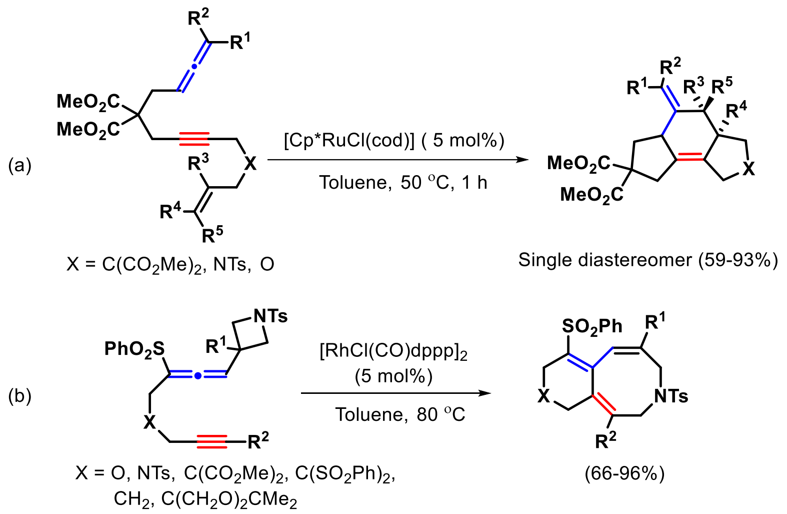
For the (4 + 3) and (4 + 1) annulations, possible mechanistic steps are presented in Scheme 17. Initially, the β'-acetoxy allenoate **12a** undergoes S_N2' attack with P(n-Bu)$_3$ at the β-carbon of the allenoate *via* an addition elimination to deliver the reactive electrophilic diene-phosphonium intermediate **XXI**. Then **XXI** undergoes umpolung addition with the anion **15a′** to provide the ylide **XXII**, which upon proton shift, aza-Michael addition, dearomatization, and phosphine elimination gives **23aa**. In the (4 + 1) annulation, **15a'** adds to **XXI** by 1,4-addition to give zwitterionic intermediate **XXIV**. 1,3-H shift from **XXIV** then gives the cyclic ylide intermediate **XXV**. Then 1,2-H shift, followed by P(n-Bu)$_3$ elimination, gives **24aa**.



Scheme 17: Plausible mechanistic pathways for the formation of **23aa** and **24aa**

2.5 Phosphorylated Allenes as Reactive Substrates or Intermediates in Annulation Reactions: A [Pd]-Catalyzed Domino (4 + 1)/(5 + 1) Annulation and a (4 + 2) Cyclization in the Reaction of Vinylic Propargylic Alcohol with Ph_2PCl

As described in the Introduction (section 1.6), the reaction of P(III)-Cl compounds with normal propargylic alcohols leads to phosphorylated allenes; if the propargylic alcohol possesses additional functional groups (e.g., -CHO, $-NO_2$), the reaction could directly bring about new annulations/cyclizations.[85,86] Two additional reports relevant to the present work are mentioned here. In 2012, Sato and colleagues developed a method for the intramolecular (2 + 2 + 2) cyclization of allene-ene-ynes *via* ruthenium catalysis involving a ruthenacyclopentane intermediate. Here, the allene and alkyne groups of the starting material coordinate with the active site of the catalyst to form an intermediate which undergoes oxidative addition of the alkyne to the internal double bond of the allene, yielding a ruthenacyclopentane species. Subsequent insertion of the alkene generates ruthenacycloheptane, which, through reductive elimination, produces the products (Scheme 18a).[115] In 2016, Mukai's group described the intramolecular hetero-(6 + 2) cycloaddition of an allenylazetidine moiety with an alkyne group in the allene-yne, which was aided by a rhodium catalyst. The mechanism involves metal coordination with the allene and alkyne moieties, followed by the breakage of the C-C bond in the azetidine ring. This results in a (6 + 2) cyclization, furnishing azabicyclo[6.4.0]dodecatrienes (Scheme 18b).[116]



Scheme 18: (a) Intramolecular [Rh]-catalyzed cyclization of allenynes, (b) [Rh]-catalyzed intramolecular (6 + 2) cycloaddition of allene-ynes

In the first set of propargylic alcohols that we used herein, we introduced an *ortho*-iodo-aryl moiety in the propargylic alcohol. These substrates **25a-b** led to the expected allenylphosphine oxides **26a-b** that underwent an efficient [Pd]-catalyzed annulation reaction with terminal alkynes that resulted in novel benzofluorenes. Our initial aim, though, was to synthesize alkyne-tethered allenes for further catalytic reactions. In the second set of propargylic alcohols, we introduced an alkenyl moiety attached to a propargyl-tethered sulfonamide group (intended for further annulations). Interestingly, these second set of propargylic alcohols **28a-d** reacted with Ph_2PCl and directly led a novel annulation process *via* allenylphosphine oxide and involved a (4 + 2) cyclization. The precursors/substrates used in this study and prepared using a procedure developed in our laboratory[87,117] are shown in Figure 14.

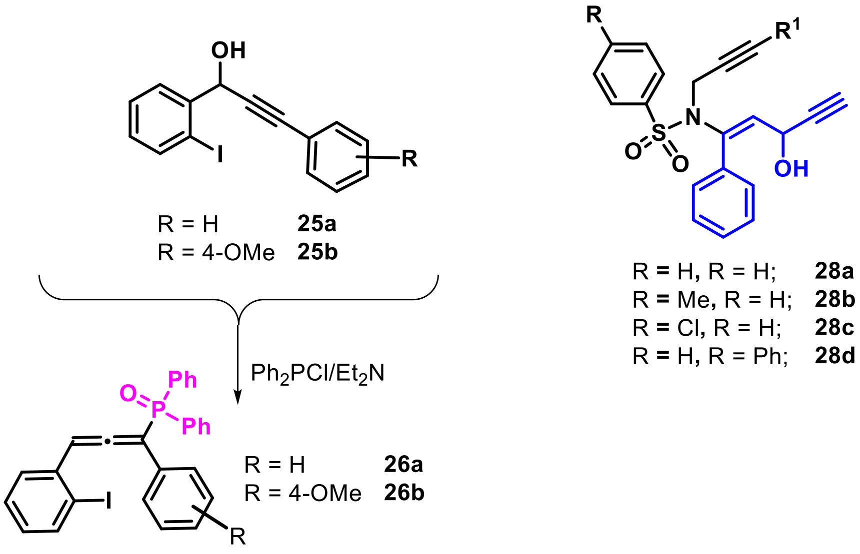
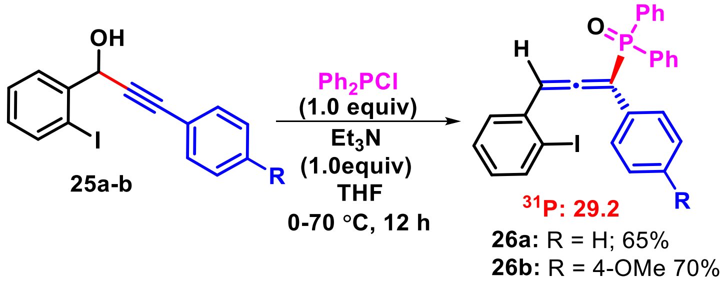


Figure 14: Substrates used in the present study

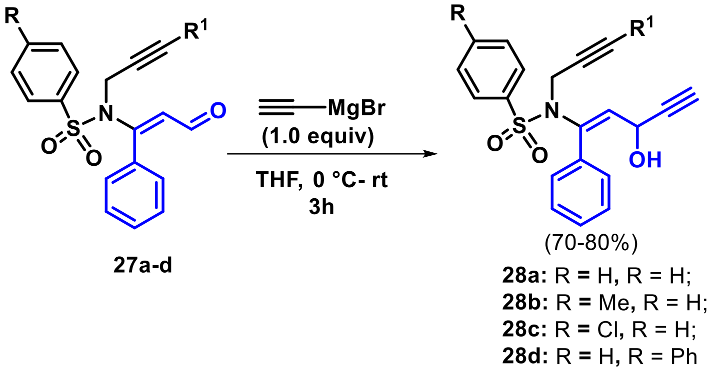
2.5.1 Synthesis of allenylphosphine oxides 26a-b and sulfonamide tethered vinylic propargylic alcohols 28a-d

Following a literature procedure,[83, 87] the reaction of *ortho*-iodo-aryl propargylic alcohol **25** with Ph_2PCl afforded the allenylphosphine oxides **26a-b** (Scheme 19). These allenes are air-stable. The signal for *sp*-hybridized *β*-carbon for these compounds appears around δ 212.6 (d, $J = 5.5$ Hz) ppm in the ^{13}C NMR spectra.



Scheme 19: Synthesis of allenylphosphine oxides **26a-b**

Following a literature procedure,[117] the reaction of sulfonamide tethered aldehyde **27** with Ethynylmagnesium bromide afforded the propargylic alcohol **28a-d** (Scheme 20).

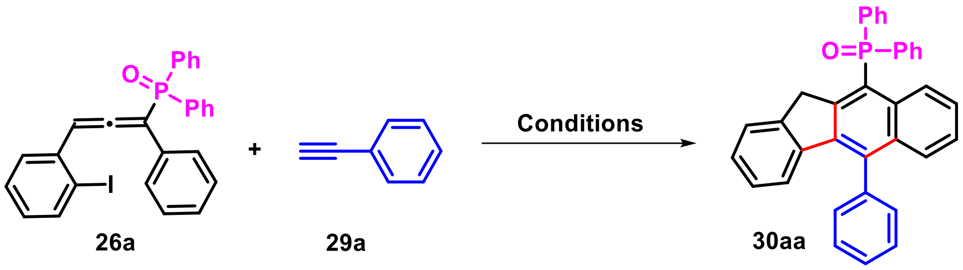


Scheme 20: Synthesis of Sulfonamide tethered vinylic propargylic alcohol **28a-d**

2.5.2 [Pd]-catalyzed cascade annulation reaction of allenylphosphine oxides with terminal alkynes: Optimization study

Initially, we examined a reaction between **26a** (0.20 mmol) and phenylacetylene (**29a**; 0.20 mmol) in the presence of $PdCl_2(PPh_3)_2$ (2.0 mol%) with CuI (4.0 mol%) as a co-catalyst in CH_3CN solvent and Et_3N as a base at rt (25 °C). We observed the formation of 5-phenyl-11*H*-benzo[*b*]fluorene **30aa** after 12 in 45% isolated yield (Table 14, entry 1) [*Note*: The R_f values of both the reactant and the product are the same, but the product is more (blue) fluorescent]. Compound **30aa** exhibited a characteristic singlet in the region δ 3.95-4.00 for the CH_2 protons in the ^{1}H NMR spectrum; in the $^{13}C\{^{1}H\}$ NMR spectrum, $Ph_2P(O)C$ carbon appears as a doublet at δ 122.2 (^{1}J(P-C) = 100.0 Hz). By increasing the reaction temperature to 50 °C, the product yield increased to 77%, and the reaction was completed in 6 h (entry 2). Performing the reaction at 80 °C not only increased the yield of the reaction to 85% but also reduced the reaction time to 2 h. Shifting from $PdCl_2(PPh_3)_2$ to $PdCl_2(CH_3CN)_2$ did not significantly affect the yield of the product. We checked other [Pd]-catalysts like $Pd(OAc)_2$, $Pd(TFA)_2$, and $Pd_2(dba)_3$, and the yield of **30aa** was not higher than that using $PdCl_2(PPh_3)_2$ (entries 5 and 6). Formation of **30aa** was not observed by using $Pd_2(dba)_3$ as the catalyst (entry 7) under same conditions. Next, we checked the scope of the co-catalyst by using CuBr and CuCl which gave **30aa** in 78% and 80% yields, respectively (entries 8 and 9). Solvents like DCE and THF were not better than CH_3CN (entries 10 and 11). When we replaced Et_3N with DIPA, the reaction proceeded smoothly and gave **30aa** in 80% yield (entry 12). There was no reaction in the absence of Et_3N (entry 13).

Table 14. Optimization of Reaction Conditions for 30aa[a]



Entry	Catalyst	Co-catalyst	Solvent	Temp (°C)	Time (h)	Yield of **30aa** (%)[b]
1	$PdCl_2(PPh_3)_2$	CuI	CH_3CN	25	12	45
2	$PdCl_2(PPh_3)_2$	CuI	CH_3CN	50	6	77
3	$PdCl_2(PPh_3)_2$	CuI	CH_3CN	80	2	85
4	$PdCl_2(CH_3CN)_2$	CuI	CH_3CN	80	2	83
5	$Pd(OAc)_2$	CuI	CH_3CN	80	2	40
6	$Pd(TFA)_2$	CuI	CH_3CN	80	2	55
7	$Pd_2(dba)_3$	CuI	CH_3CN	80	2	NR
8	$PdCl_2(PPh_3)_2$	CuBr	CH_3CN	80	2	78
9	$PdCl_2(PPh_3)_2$	CuCl	CH_3CN	80	2	80
10	$PdCl_2(PPh_3)_2$	CuI	THF	80	2	70
11	$PdCl_2(PPh_3)_2$	CuI	DCE	80	2	75
12	$PdCl_2(PPh_3)_2$	CuI[c]	CH_3CN	80	2	80
13	$PdCl_2(PPh_3)_2$	CuI[d]	CH_3CN	80	2	NR

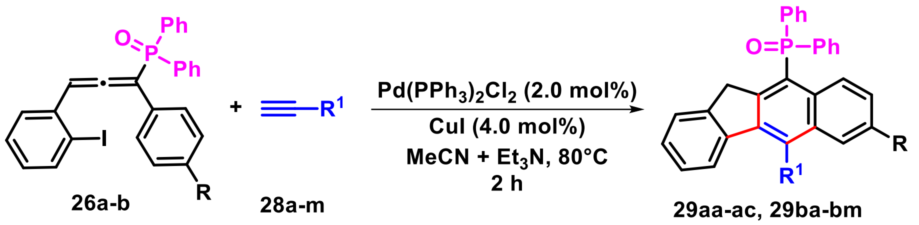
[a]Reaction conditions: **26a** (0.20 mmol), **29a** (0.20 mmol), catalyst (2.0 mol%), Co-catalyst (4.0 mol%), Et_3N (0.5 mL, 0.004 mmol), solvent (0.1 M). [b]Isolated yields. [c]DIPA was used in place of Et_3N. [d]No Et_3N was used.

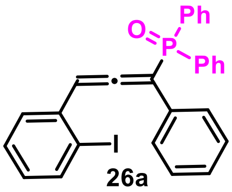
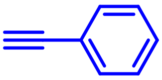
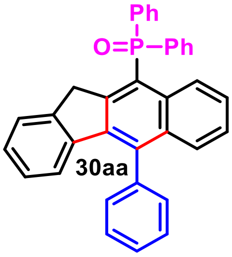
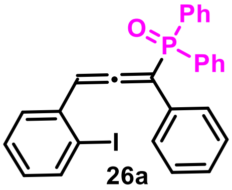
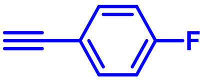
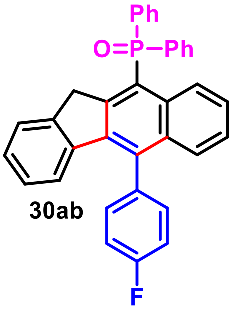
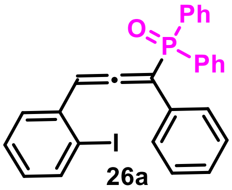
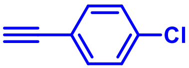
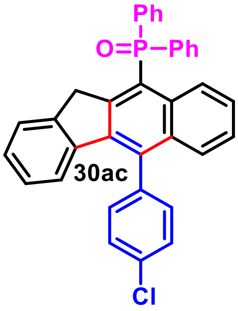
2.5.3 Substrate scope for (4 + 1)/(5 + 1) annulation

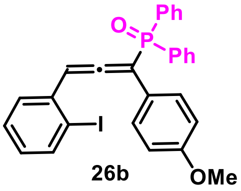
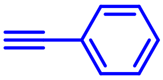
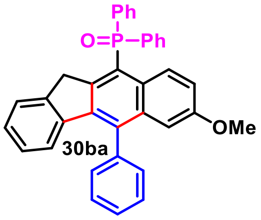
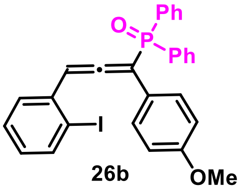
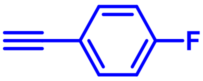
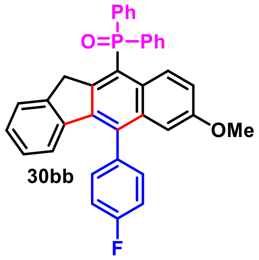
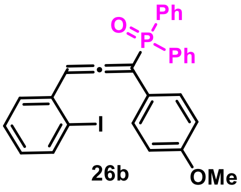
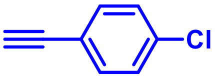
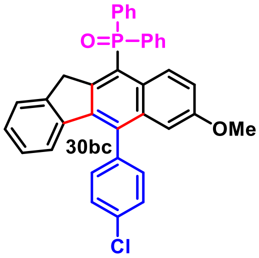
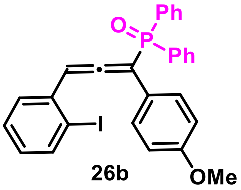
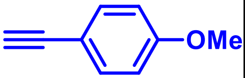
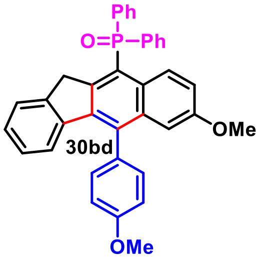
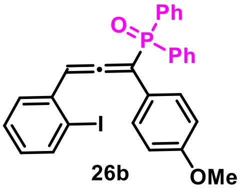
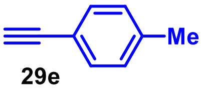
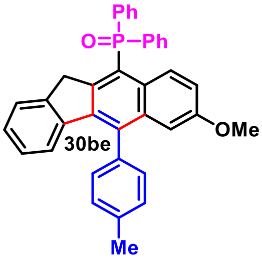
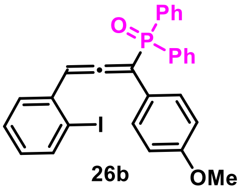
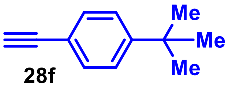
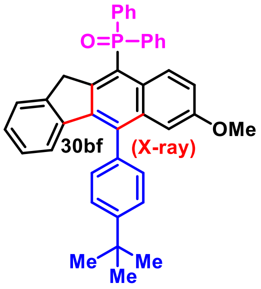
The substrate scope for the $PdCl_2(PPh_3)_2$-catalyzed domino (4 + 1)/ (5 + 1) annulation between allenes **26** and alkynes **29** is presented in Table 15. Different types of alkynes substituted at the *p*-position of the alkyne (H, F, Cl, OMe, Me, and *t*-Bu) reacted well with allenyl phosphine oxides **26a** and **26b** and gave 5-phenyl-11*H*-benzo[*b*]fluorenes **30aa-ac**,

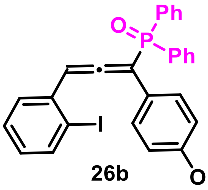
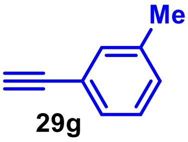
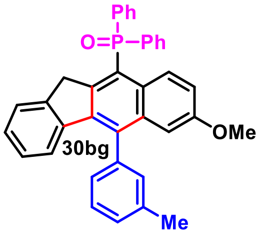
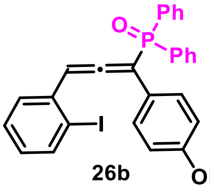
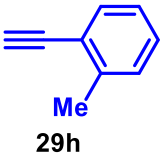
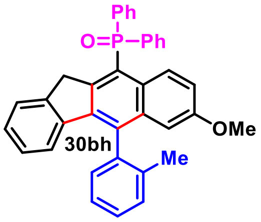
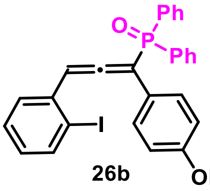
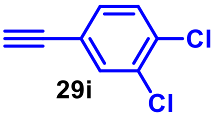
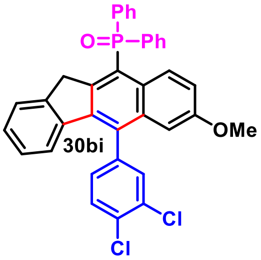
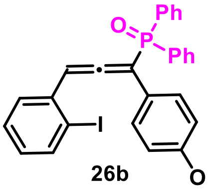
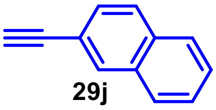
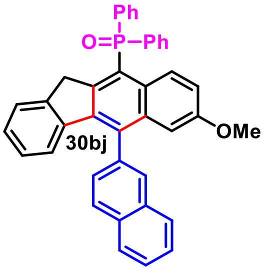
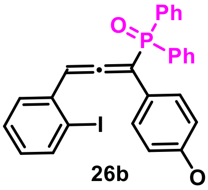
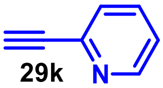
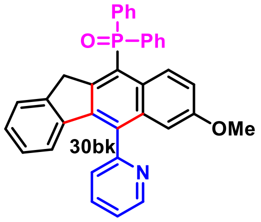
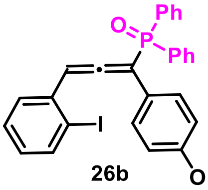
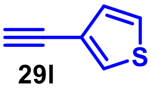
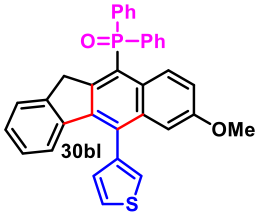
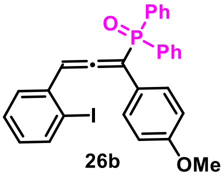
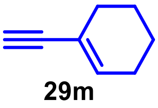
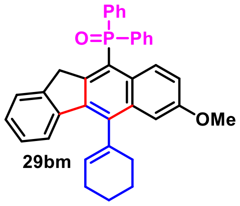
30ba-bf in yields of 74-87%. The *m*- and *o*-substituted alkynes **29g-h** also delivered **30bg** and **30bh** in 81% and 76% yields, respectively. The atropisomers were not distinuished in the ^{1}H-NMR at rt. Disubstituted alkyne **29i** also delivered **30bi** in 77% yield. The polycyclic aromatic and heterocyclic substituted alkynes (**29j-l**) gave products **30bj-bl** in yields of 75%, 71%, and 74%, respectively. We could also obtain product **30bm** in 68% yield using 1-ethynylcyclohex-1-ene **29m**. An X-ray structure determination (Figure 15) for compound **30bf** confirmed the fused tetracyclic structures of these compounds as proposed.

Table 15. Substrate Scope for (4 + 1)/(5 + 1) Annulation[a]



Entry	Allenyl phosphine oxide	Alkyne	Benzo[b]fluorene	Yield (%)[b]
1	 **26a**	 **29a**	 **30aa**	85
2	 **26a**	 **29b**	 **30ab**	83
3	 **26a**	 **29c**	 **30ac**	80

4	 26b	 29a	 30ba	87
5	 26b	 29b	 30bb	81
6	 26b	 29c	 30bc	82
7	 26b	 29d	 30bd	85
8	 26b	 29e	 30be	85
9	 26b	 28f	 30bf (X-ray)	83

10	 26b	 29g	 30bg	81
11	 26b	 29h	 30bh	76
12	 26b	 29i	 30bi	77
13	 26b	 29j	 30bj	75
14	 26b	 29k	 30bk	71
15	 26b	 29l	 30bl	74
16	 26b	 29m	 29bm	68

[a]Reaction conditions: **26a-b** (0.10 mmol), **29a-m** (0.10 mmol), $PdCl_2(PPh_3)_2$ (0.004 mmol), CuI (0.008 mmol), CH_3CN (0.1 M) and Et_3N (0.5 mL). [b]Isolated yields.

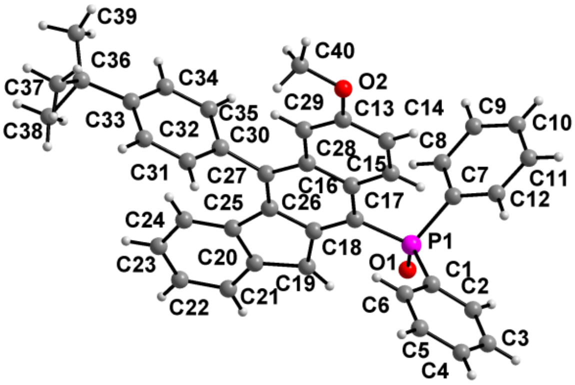
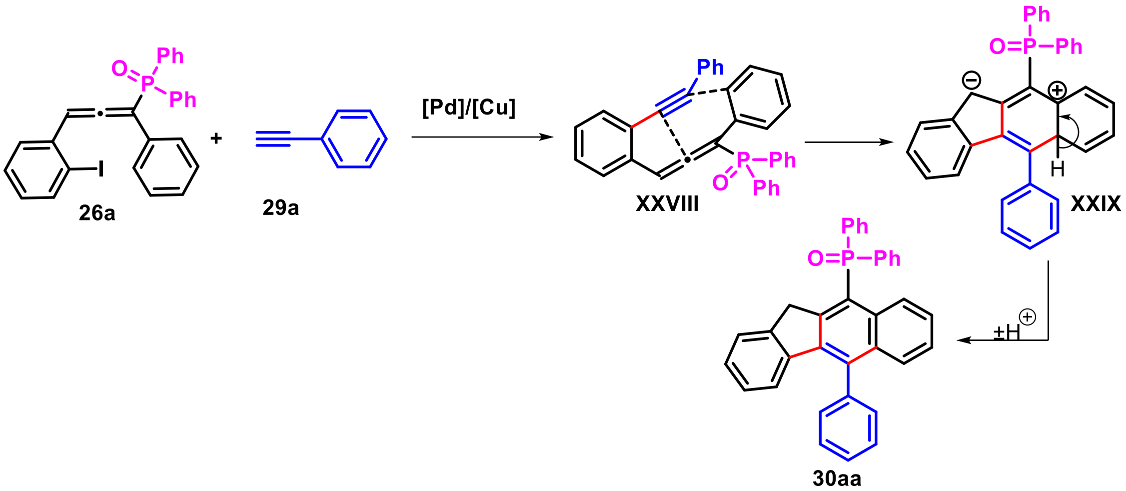


Figure 15: Molecular structure of compound **30bf.** Relevant bond parameters: P1-C17 1.813(3), C17-C18 1.384(3), C18-C19 1.508(3), C19-C20 1.494(4), C20-C25 1.408(4), C25-C26 1.476(3), C18-C26 1.428(3), C26-C27 1.378(3), C27-C28 1.427(3), C28-C16 1.432(3) Å

2.5.4 Plausible pathways of the [Pd]-catalyzed cascade annulation

Possible mechanistic steps for the above cascade annulation are presented in Scheme 19. Initially, allenyl phosphine oxide **26a** undergoes Sonogashira coupling[118] in the presence of [Pd]/[Cu]-catalyst to give allene-yne[119] intermediate **XXVIII**. Then **XXVIII** undergoes cyclization to give zwitterionic intermediate **XXIX,** which, upon aromatization affords **30aa**.

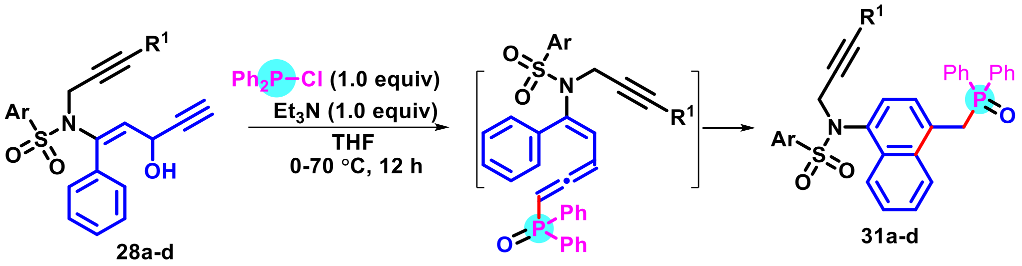


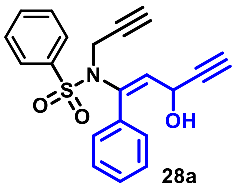
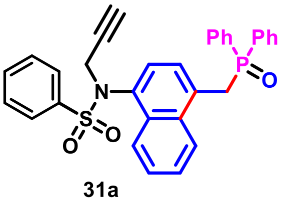
Scheme 21: [Pd]-Catalyzed intramolecular annulation of allene-ynes

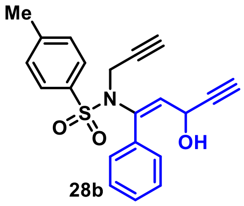
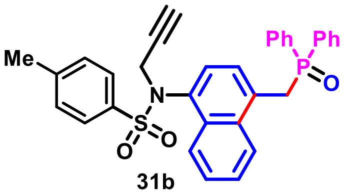
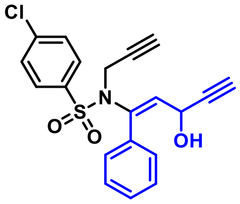
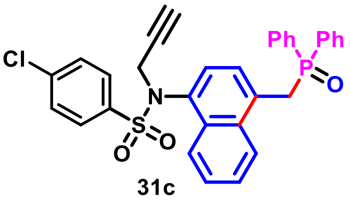
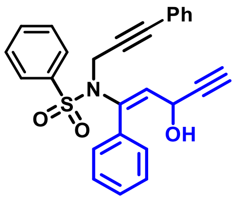
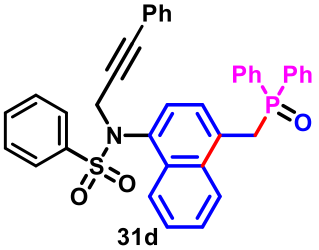
2.5.5 Direct formation of 4-amino-naphthalenyl diphenylphosphine oxides 31a-d via allenic species using vinylic propargyl alcohols 28a-d

In the previous section, we aimed to synthesize allene-tethered alkynes but unexpectedly obtained the domino annulated benzo[*b*]fluorenes. Hence, in continuation of this work, we first synthesized sulfonamide-tethered vinylic propargyl alcohol **28a** and treated it with Ph_2PCl (Scheme 20). Surprisingly, we obtained 4-amino-naphthalenyl diphenylphosphine oxide **31a** by intramolecular (4 + 2) annulation utilizing an allenic intermediate and a benzene ring double bond. These compounds show a characteristic multiplet (two dd→t) in the region δ 4.00-4.20 (J ~ 14.0 Hz) for the PCH_2 protons in the ^1H NMR spectra; correspondingly, PCH_2 carbon appears as a doublet around δ 35.1 (^1J(P-C) ~ 65.0 Hz). Table 16 summarizes the results of this reaction, and single crystal XRD confirmed the structure of **31b** (Figure 16**)**. Previously, our group reported the cyclization reaction of *o*-substituted (NO_2, CHO, or alkylidene) propargyl alcohols with P^{III}-Cl precursors[85,86] but those cycloadditions did not involve the benzene ring as observed here; in the allene dimerization reported by us recently, however, involvement of benzene as a part of diene was noticed.[87] It may be noted here that the sulfonamide-alkyne part does not take part in the cycloadddition; hence it is planned to pursue this part with vinyl-tethered propargyl alcohols devoid of the sulfonamide-alkyne moiety.

Table 16. Substrate Scope for Direct (4 + 2) Annulation *via* Allenic Intermediates[a]



Entry	Propargyl alcohol	Alkyne	4-Amino-naphthalene	Yield (%)[b]
1	 **28a**	**Ph_2PCl**	 **31a**	77

2	 **28b**	**Ph$_2$PCl**	 **31b**	78
3	 **28c**	**Ph$_2$PCl**	 **31c**	75
4	 **28d**	**Ph$_2$PCl**	 **31d**	71

[a] Reaction conditions: **28a-d** (0.55 mmol), **Ph$_2$PCl** (0.55 mmol), Et$_3$N (0.55 mmol) in THF at 70 °C [b] Isolated yield.

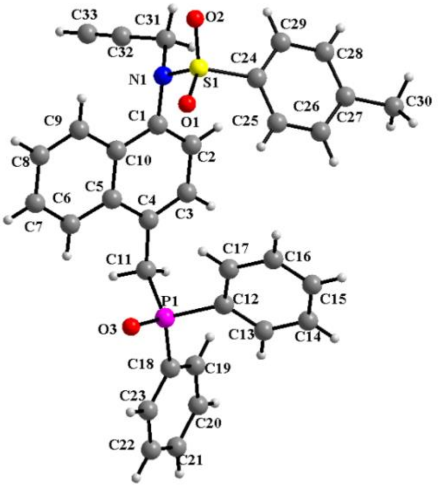
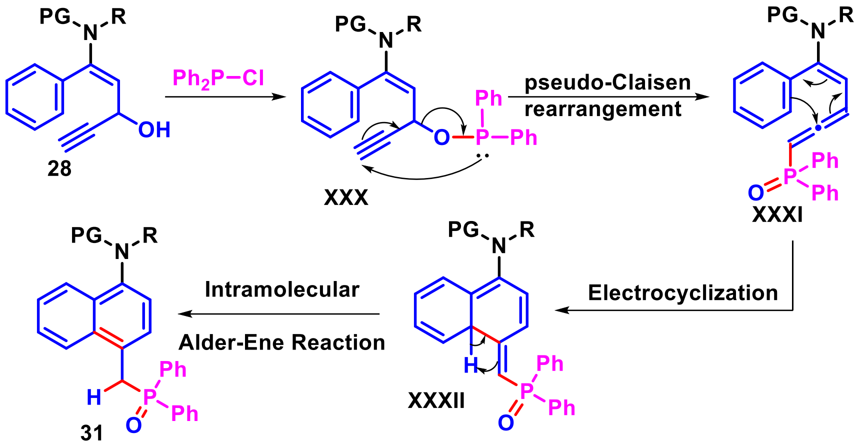


Figure 16. Molecular structure of compound **31b**. Relevant bond parameters: P1-C11 1.816(2), C11-C4 1.516(2), C1-C2 1.362(2), C2-C3 1.408(2), C3-C4 1.365(2), C4-C5 1.425(2), C5-C10 1.433(2) Å

2.5.5 *Plausible pathways for the electrocyclization*

Based on our previous studies,[120] it is very likely that the allene **XXXI** is formed initially. Then 6π-electrocyclization results in the intermediate **XXXII** which leads to one of the 4-aminonaphthalene products **31**.



Scheme 22: Possible pathway for the formation of 4-amino-naphthalenes **31**.

Summary

(1) A new tertiary amine switched (4 + 2) annulation strategy involving cyclic *N*-sulfonamide imines and *δ*-acetoxy allenoates for the synthesis of spirocyclic sultams and *m*-terphenyls respectively is reported. The DABCO/$MeCO_2H$ combination leads to an essentially single diastereomer *via* chemo- and regio-specific (4 + 2)-carboannulation and a new hydroxyl group is introduced. In contrast, DMAP-catalyzed benzannulation using the same reactants affords unsymmetrical *m*-teraryls *via* Mannich coupling, sequential proton transfers, and C−N bond cleavage. Here, *δ*-acetoxy allenoate serves as a *4C*-synthon and the carboannulation is completely base-dependent and mutually exclusive.

(2) A DMAP-catalyzed sequential benzannulation and lactonization strategy in which *δ*-acetoxy allenoate functions as a *5C*-synthon in its reaction with cyclic sulfamidate imines has been discovered. This platform delivers π-extended coumarin frameworks under metal-free conditions *via* allylic elimination followed by Mannich coupling, proton shifts, C−N bond cleavage, and lactonization as key steps. The driving force for this domino reaction is the formation of the diene-ammonium intermediate and O−S bond cleavage. ESI-HRMS has been useful in gaining insights into the reaction pathway.

(3) Dearomative annulation reaction of acyl-tethered benzothiazole bisnucleophiles with *β′*-acetoxy allenoates by switching the Lewis base is developed. The DBU-catalyzed reaction gives benzothiazole-fused 1,4-dihydropyridine carboxylates by (3+ 3) annulation chemoselectively. By contrast, the PR_3-catalyzed reaction gives benzothiazole-fused azepines by (4 + 3) annulation and cyclopentene carboxylates by (4 + 1) annulation; the ratio of the latter two products depends on the solvent. A possible rationale for the difference in the reactivity, based on the 1,4/1,5-addition of the 2-acyl−tethered benzothiazole to the key phosphonium intermediate, is provided.

(4) A [Pd]-catalyzed domino annulation reaction of *o*-iodoaryl substituted allenylphosphine oxides with terminal alkynes that involves (4 + 1)/(5 + 1) annulations was developed for the synthesis of benzo[*b*]fluorenes. Reaction of sulfonamide tethered vinylic propargyl alcohols with Ph_2PCl results in the direct formation of 4-aminonaphthalenyl-diphenylphosphine oxides *via* an allenic intermediate.

Chapter 3

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.[121]

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

Infrared spectroscopy: IR spectra were recorded on a *J*ASCO FT/IR 5300 spectrophotometer.

NMR spectroscopy: ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded using 5 mm tubes on a Bruker 400 MHz and 500 MHz spectrometer [operating at field strengths: 400, 100, 376, and 162 MHz (for 400 MHz NMR spectrometer) and 500, 125, 470, and 202 MHz (for 500 MHz NMR spectrometer) respectively] in $CDCl_3$ solution (unless specified otherwise) with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C), $CFCl_3$ (^{19}F) and ext. 85% H_3PO_4 (^{31}P) ($\delta = 0$), respectively. All *J* values are in Hz.

HRMS: Mass spectra were recorded using HRMS (ESI-TOF and ESI-EXACTIVE ORBITRAP analyzer) equipment.

3.1 Synthesis of Starting Materials

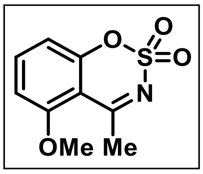
3-Alkyl-substituted *N*-sulfonylketimines (**2a-c**),[90] cyclic sulfamidate imines (**5a-4m**),[91] δ-acetoxy allenoates (**8a-8t**), [32, 92] β'-acetoxy allenoates (**12a-12i**),[50] 2-acyl tethered benzothiazole (**15a-15i**)[93] allenylphosphine oxides **(26a-26b)**[83-87] and sulfonamide tethered vinylic propargylic alcohols (**28a-d**)[117] were synthesized using literature procedures. Precursors **4h**, **4i**, **8j**, **8m**, **8o**, **15d**, **15f**, and **15g** are new.

3.1.1 Procedure for the synthesis of cyclic sulfamidate imines 5h and 5i:

Following a literature procedure,[91] in a 100 mL round-bottom flask containing chlorosulfonyl isocyanate (2.0 equiv), anhydrous formic acid (2.0 equiv) was added drop-wise (5 min) *via* syringe at 0 °C. Vigorous gas evolution ensued and a white solid was formed. The viscous reaction mixture was stirred for 2 h until gas evolution ceased. To the resulting sulfamoyl chloride was added 2-hydroxyketone (1.0 equiv) drop-wise *via* syringe at rt, the mixture was stirred further for 10 min, and then cooled to 0 °C. Anhydrous dimethylacetamide

(7 mL) was slowly added, the reaction mixture was warmed to rt and stirred further for 10 min. Sodium hydride (1.2 equiv; 60% dispersion in mineral oil) was then added, followed by one more portion (1.2 equiv) after 30 min. The reaction mixture was stirred for 1 h at rt, then warmed to 50 °C and stirring continued for 12 h. The reaction was quenched with H_2O **(**10 mL) and extracted with EtOAc (2 x 20 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The product was purified by flash column chromatography using silica gel with ethyl acetate/hexane (1:4) as the eluent.

Compound 5h



Yield: [using 1.60 g (10.0 mmol) of 2′-hydroxy-6′-methoxy acetophenone] 1.50 g (66%), White solid

Mp: 123 °C.

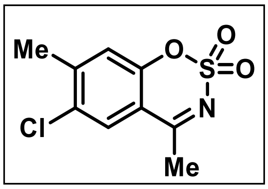
IR (neat): ν_{max} 2978, 1601, 1583, 1475, 1368, 1178, 1083, 938, 809, 756 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.62-7.58 (m, 1H), 6.88-6.86 (m, 2H), 3.99 (s, 3H), 2.77 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.7, 159.9, 154.6, 137.2, 111.2, 108.8, 108.6, 56.6, 29.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): *m/z* $[M + Na]^+$ calcd for $C_9H_9O_4SNNa$ 250.0144, found 250.0152.

Compound 5i



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.40 g (57%), White solid

Mp: 187 °C.

IR (neat): ν_{max} 2925, 1595, 1538, 1425, 1375, 1196, 1091, 905, 827, 727 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.74 (s, 1H), 7.19 (s, 1H), 2.69 (s, 3H), 2.50 (s, 3H) ppm.

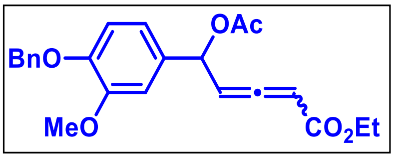
^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 176.4, 151.7, 147.3, 131.7, 128.4, 121.1, 115.4, 23.7, 21.2 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): *m/z* [M + Na]$^+$ calcd for $C_9H_8O_3SClNNa$ 267.9806, found 267.9808.

3.1.2 Procedure for synthesis of δ-acetoxy allenoates 8j, 8m and 8o

Following a literature procedure,[32,92] to a solution of ethyl 5-hydroxy-5-aryl penta-2,3-dienoate (10.0 mmol, 1.0 equiv) in dry dichloromethane (20 mL) at 0 °C was added triethylamine (20.0 mmol, 2.0 equiv), and then the mixture stirred for 30 min at the same temperature. After that, acetyl chloride (12.0 mmol, 1.2 equiv) was slowly added into the mixture over 5 min, and the contents were stirred for 40 min at 0 °C. After completion of the reaction (TLC), the aqueous layer was extracted with dichloromethane (3 × 25 mL). Then, the combined organic layer was washed with brine (2 × 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. [In the ^{1}H NMR spectrum for the second isomer, corresponding protons are indicated by the prime (′) symbol]

Compound 8j (*dr* = 1:1)



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.98 g (50%), gummy liquid

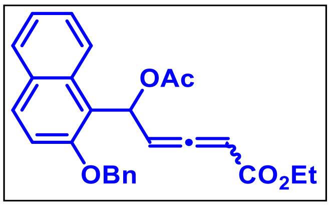
IR (neat): ν_{max} 3054, 2986, 2305, 1712, 1514, 1422, 1265, 1161, 1029, 737 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.45-7.43 (m, 4H), 7.39-7.36 (m, 4H′), 7.32-7.30 (m, 1H + 1H′), 7.05 (d, *J* = 1.5 Hz, 1H′), 7.00 (d, *J* = 1.5 Hz, 1H), 6.97 (dd, *J* = 8.5, 1.5 Hz, 1H′), 6.92 (dd, *J* = 8.5, 1.5 Hz, 1H), 6.88-6.85 (m, 1H + 1H′), 6.35 (dd, *J* = 6.0, 2.5 Hz, 1H), 6.32-6.30 (m, 1H′), 5.91-5.88 (m, 1H + 1H′), 5.77-5.73 (m, 1H + 1H′), 5.17-5.16 (m, 2H + 2H′), 4.25-4.16 (m, 2H + 2H′), 3.93 (s, 3H′), 3.92 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H′), 1.32-1.26 (m, 3H + 3H′) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ (1st isomer) 212.4, 169.9, 165.1, 149.7, 148.7, 137.0, 130.9, 128.6, 128.0, 127.3, 119.7, 113.6, 111.0, 97.0, 91.1, 72.2, 71.1, 61.1, 56.1, 21.2, 14.3; (2nd isomer) 211.8, 169.8, 165.2, 149.8, 148.6, 137.0, 130.7, 128.6, 128.0, 127.3, 120.1, 113.7, 111.5, 97.1, 91.4, 71.8, 71.1, 61.1, 56.2, 21.2, 14.3

HRMS (ESI- EXACTIVE ORBITRAP): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{24}NaO_6$, 419.146, found, 419.200.

Compound 8m (*dr* = 1:0.8)



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.95 g (47%), gummy liquid

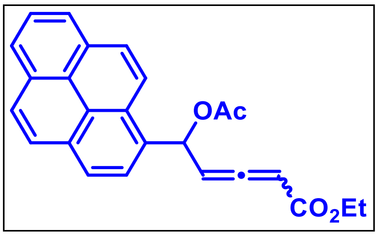
IR (neat): ν_{max} 2946, 2364, 2335, 2253, 1738, 1371, 1241, 1174, 1022, 909, 736 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42-8.37 (m, 1H + 1H′), 8.27-8.15 (m, 5H + 5H′), 8.11-8.02 (m, 3H + 3H′), 7.44-7.41 (m, 1H + 1H′), 6.17-6.14 (m, 1H + 1H′), 5.71 (dd, *J* = 6.0, 3.0 Hz, 1H + 1H′), 4.20-4.07 (m, 2H + 2H′), 2.18 (s, 3H′), 2.17 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H′) ppm.

NMR (125 MHz, $CDCl_3$): δ (major isomer) 211.8, 169.9, 165.4, 154.0, 137.0, 132.3, 131.2, 130.0, 128.7, 128.1, 127.5, 126.7, 125.3, 124.0, 119.5, 115.2, 97.0, 91.3, 72.1, 65.6, 61.1, 21.1, 14.4; (minor isomer) 212.3, 169.9, 165.0, 154.1, 137.1, 132.2, 131.1, 129.9, 128.8, 128.1, 127.5, 126.6, 125.2, 124.0, 119.5, 115.1, 96.6, 91.1, 72.0, 66.1, 60.9, 21.2, 14.2 ppm

HRMS (ESI- EXACTIVE ORBITRAP): *m/z* [M + Na]$^+$ calcd for $C_{26}H_{24}NaO_5$, 439.152, found, 439.200.

Compound 8o (*dr* = 1:0.8)



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.88 g (49%), gummy liquid

IR (neat): ν_{max} 3155, 2984, 2374, 2254, 1744, 1468, 1231, 1096, 906, 730 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): 8.42-8.37 (m, 1H + 1H′), 8.27-8.15 (m, 5H + 5H′), 8.11-8.02 (m, 3H + 3H′), 7.44-7.41 (m, 1H + 1H′), 6.17-6.14 (m, 1H + 1H′), 5.71 (dd, *J* =

6.0, 3.0 Hz, 1H + 1H′), 4.20-4.07 (m, 2H + 2H′), 2.18 (s, 3H′), 2.17 (s, 3H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.0 Hz, 3H′) ppm.

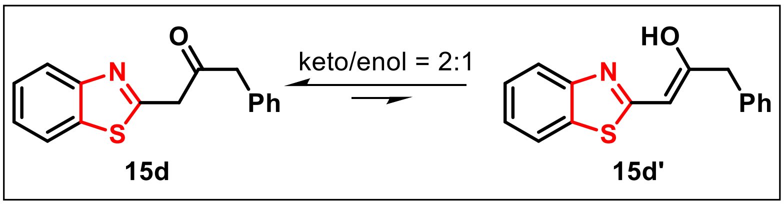
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ (major isomer) 212.5, 170.0, 165.0, 131.9, 131.4, 131.0, 130.7, 128.4, 128.1, 127.5, 126.3, 125.8, 125.6, 125.1, 125.0, 122.9, 97.2, 91.7, 69.8, 61.2, 21.3, 14.3; (minor isomer) 212.1, 170.0, 165.2, 131.2, 131.4, 131.1, 130.7, 128.5, 128.4, 128.1, 127.5, 126.3, 125.8, 125.6, 125.0 (2s), 122.8, 97.4, 91.5, 70.1, 61.2, 21.2, 14.2 ppm

HRMS (ESI- EXACTIVE ORBITRAP):): *m/z* [M + Na]$^+$ calcd for $C_{25}H_{20}NaO_4$, 407.125, found, 407.200.

3.1.3 Procedure for the synthesis of 2-acyl tethered benzothiazoles 15d, 15f, and 15g:

A modified literature procedure was used.[93] To a 100 mL round-bottom flask containing 2-methylbenzothiazole (1.0 equiv) in dry THF (10.0 mL) NaH (3 equiv) was added at 0 °C under N_2 atmosphere. Vigorous gas evolution ensued and a white solid was formed. The viscous reaction mixture was stirred for 10 min until gas evolution ceased. To the resulting mixture methyl benzoate (1.3 equiv) was added drop-wise via syringe at 0 °C, the contents warmed to rt and stirred for 10 min. After that, the mixture was warmed to 60 °C (oil bath) and stirring continued for 6 h. The reaction was quenched with cold 1M H_2SO_4 **(**10 mL) and the contents extracted with EtOAc (2 x 20 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The product was purified by flash column chromatography using silica gel and ethyl acetate/hexane mixture (5:95) as the eluent.

Compound 15d



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.87 g (70%), Yellow solid

Mp: 153-155 °C.

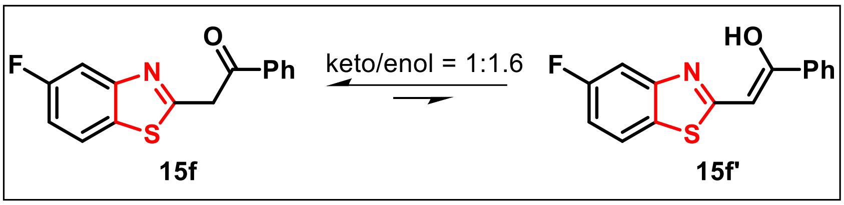
IR (neat): ν_{max} 2902, 1738, 1650, 1490, 1341, 1272, 1181, 1098, 916, 713 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): Keto form δ 8.00 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.72-7.68 (m, 1H), 7.35-7.32 (m, 3H), 7.29-7.22 (m, 3H), 4.25 (s, 2H), 3.89 (s, 2H); Enol form: δ 13.53 (br s, 1H), 7.49-7.45 (m, 2H), 7.40-7.36 (m, 4H), 7.29-7.22 (m, 3H), 5.56 (s, 1H,), 3.65 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): Keto form: δ 202.1, 172.3, 162.8, 152.8, 133.2, 129.6, 128.9, 127.4, 126.1, 125.2, 122.9, 121.6, 49.9, 46.6; Enol form: 176.7, 149.6, 136.6, 135.8, 130.7, 129.4, 128.6, 126.9, 126.4, 124.0, 121.4, 119.3, 92.7, 42.7 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{14}NOS$ 268.0791; Found 268.0796.

Compound 15f



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.15 g (85%), Yellow solid

Mp: 169-172 °C.

IR (neat): ν_{max} 2602, 1693, 1593, 1452, 1256, 1150, 1057, 954, 744 cm^{-1}

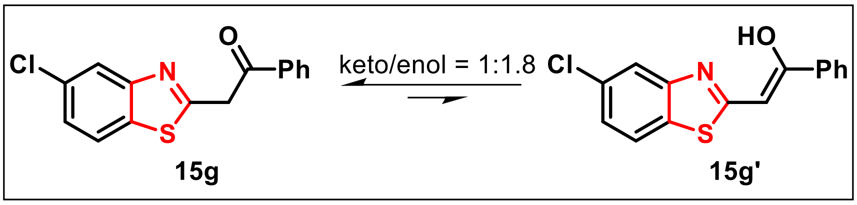
^1H NMR (500 MHz, $CDCl_3$): Keto form δ 8.12 (d, J = 7.5 Hz, 1H), 7.79 (dd, J_1 = 9.0, J_2 = 5.0 Hz, 1H), 7.63-7.59 (m, 1H), 7.52-7.47 (m, 2H), 7.45-7.44 (m, 2H), 7.18-7.14 (m, 1H), 4.83 (s, 2H); Enol form: δ 13.40 (br s, 1H), 8.08 (d, J = 7.5 Hz, 1H), 7.87-7.86 (m, 2H), 7.70-7.68 (m, 1H), 7.52-7.47 (m, 1H), 7.45 (m, 2H), 7.08-7.04 (m, 1H), 6.35 (s, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): Keto form: δ 193.9, 165.3, 161.7 (d, $^1J_{C\text{-}F}$ = 242.5 Hz), 153.4 (d, $^3J_{C\text{-}F}$ = 12.5 Hz), 135.7, 134.0, 129.5, 128.7, 128.6, 122.3 (d, $^3J_{C\text{-}F}$ = 12.5 Hz), 113.9 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 109.0 (d, $^2J_{C\text{-}F}$ = 23.7 Hz), 43.8; Enol form: 170.5, 166.2, 162.1 (d, $^1J_{C\text{-}F}$ = 242.5 Hz), 151.9 (d, $^3J_{C\text{-}F}$ = 12.5 Hz), 134.4, 131.3, 130.5, 128.5, 125.9, 122.0 (d, $^3J_{C\text{-}F}$ = 10.0 Hz), 112.5 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 106.7 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 91.1 ppm.

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.41, -116.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{11}FNOS$ 272.0540; Found 272.0544.

Compound 15g



Yield: [using 1.85 g (10.0 mmol) of 5′-chloro-2′-hydroxy-4′-methylacetophenone] 1.2 g (87%), Yellow solid

Mp: 174-176 °C.

IR (neat): ν_{max} 2956, 1688, 1544, 1399, 1255, 1130, 735, 569 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): Keto form δ 7.99 (br s, 1H), 7.88-7.82 (m, 2H), 7.79 (d, J = 8.5 Hz, 1H), 7.64-7.61 (m, 1H), 7.46-7.44 (m, 2H), 7.37-7.35 (m, 1H), 4.83 (s, 2H); Enol form: δ 13.67 (br s, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.88-7.82 (m, 2H), 7.69 (d, J = 8.5 Hz, 1H), 7.53-7.50 (m, 1H), 7.46-7.44 (m, 2H), 7.29-7.26 (m, 1H), 6.36 (s, 1H) ppm.

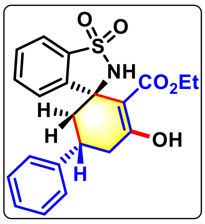
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): Keto form: δ 194.0, 165.7, 153.7, 135.9, 134.5, 134.4, 132.2, 129.1, 126.1, 122.9, 122.4, 120.3, 43.9; Enol form: 170.1, 165.4, 152.1, 134.2, 132.7, 130.7, 130.2, 128.8, 128.7, 125.8, 124.7, 122.2, 91.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): *m/z*: [M+H]$^+$ Calcd for $C_{15}H_{11}ClNOS$ 288.0244; Found 288.0247.

3.2 Synthesis of Compounds 16aa-ac, 16ae, 16ag, 16ai, 16aj, 16al-am, 16ap-16ar, 16ba-16bc, 16be, 16bl, 16bo, and 16bq: Representative Procedure for 16aa

A Schlenk tube was charged with δ-acetoxy allenoate **8a** (64.2 mg, 0.24 mmol), DABCO (22.4mg, 0.20 mmol), Na_2CO_3 (oven dried at 110 °C for 12 h, 32.0 mg, 0.30 mmol) and 1.5 mL of toluene. Subsequently, 3-alkylbenzo[*d*]isothiazole 1,1-dioxide **2a** (36.2 mg, 0.20 mmol) and acetic acid (23.0 µL, 0.40 mmol) in 0.5 mL of toluene was added, and the mixture stirred at 110 °C (oil bath) for the 12 h, and progress of the reaction was monitored using TLC. After completion of the reaction, 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 (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 (10:90) as the eluent. All other compounds were prepared by using the same molar quantities.

Compound 16aa (*dr* 97:3)



Yield: 56.6 mg (71%), White solid

Mp: 204-206 °C.

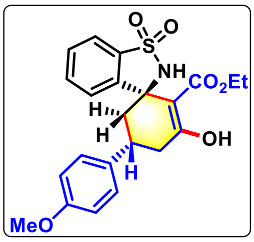
IR (neat): ν_{max} 3263 (br), 2923, 2853, 1734, 1453, 1276, 1260, 1173, 1027, 753 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 13.01 (s, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.59-7.56 (m, 1H), 7.51-7.48 (m, 1H), 7.32-7.29 (m, 2H), 7.27-7.25 (m, 1H), 7.24-7.21 (m, 3H), 4.85 (s, 1H), 4.00-3.84 (m, 2H), 3.40 (m, *J* = 12.0, 5.0, 2.0 Hz, 1H), 2.79 (ddd, *J* = 18.5, 5.0, 2.0 Hz, 1H), 2.67 (dd, *J* = 18.5, 12.5 Hz, 1H), 2.47 (dt, *J* = 13.0, 2.0 Hz, 1H), 1.95-1.90 (m, 1H), 0.71 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 179.2, 170.7, 147.6, 142.6, 136.4, 133.3, 128.9, 128.8, 127.2, 126.9, 122.7, 121.3, 99.3, 64.3, 61.2, 46.2, 37.4, 35.8, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{21}H_{22}NO_5S$ $[M + H]^+$ *m/z* 400.1213, found 400.1219.

Compound 16ab (*dr* 97:3)



Yield: 62.6 mg (73%), White solid.

Mp: 195-197 °C.

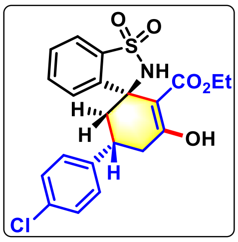
IR (neat): ν_{max} 3326, 3005, 2987, 1721, 1513, 1276, 1260, 1173, 1035, 752 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 13.00 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.58-7.56 (m, 1H), 7.50-7.47 (m, 1H), 7.26-7.24 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 4.83 (s, 1H), 3.98-3.83 (m, 2H), 3.78 (s, 3H), 3.37-3.32 (m, 1H), 2.76 (dd, *J* = 18.5, 3.5 Hz, 1H), 2.62 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.44 (d, *J* = 13.5 Hz, 1H), 1.88 (t, *J* = 13.5 Hz, 1H), 0.71 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 179.3, 170.7, 158.7, 147.6, 136.4, 134.7, 133.3, 128.8, 127.8, 122.7, 121.2, 114.3, 99.2, 64.4, 61.2, 55.4, 46.4, 37.6, 35.0, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{24}NO_6S$ $[M + H]^+$ *m/z* 430.1319, found 430.1309

Compound 16ac (*dr* 98:2)



Yield: 59.0 mg (68%), White solid.

Mp: 149-151 °C.

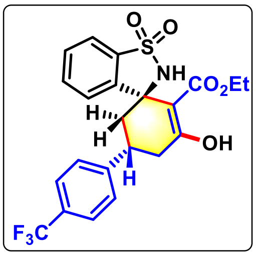
IR (neat): ν_{max} 3456, 3234, 2969, 1739, 1647, 1369, 1274, 1215, 1170, 1037, 757 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 13.00 (s, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.59-7.56 (m, 1H), 7.51-7.48 (m, 1H), 7.28-7.24 (m, 3H), 7.16 (d, *J* = 8.5 Hz, 2H), 4.87 (s, 1H), 3.98-3.83 (m, 2H), 3.41-3.36 (m, 1H), 2.76 (ddd, *J* = 18.5, 5.0, 2.0 Hz, 1H), 2.62 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.44-2.42 (m, 1H), 1.88 (t, *J* = 13.0 Hz, 1H), 0.71 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.7, 170.6, 147.3, 141.0, 136.3, 133.3, 132.9, 129.0, 128.9, 128.2, 122.7, 121.2, 99.2, 64.1, 61.3, 46.0, 37.2, 35.2, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{21}H_{21}ClNO_5S$ $[M + H]^+$ *m/z* 434.0823, found 434.0817.

Compound 16ae (*dr* 99:1)



Yield: 60.7 mg (65%), White solid.

Mp: 204-260 °C.

IR (neat): ν_{max} 3276, 2922, 2852, 1740, 1644, 1463, 1323, 1277, 1165, 1068, 763 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): 13.00 (s, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.60-7.56 (m, 3H), 7.52-7.49 (m, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 4.86 (s, 1H), 3.99-3.84 (m, 2H), 3.51-3.46 (m, 1H), 2.78 (dd, *J* = 5.0, 2.0 Hz, 1H), 2.67 (dd,

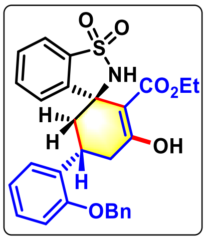
J = 18.5, 12.5 Hz, 1H), 2.47 (dt, J = 13.5, 2.5 Hz, 1H), 1.96-1.90 (m, 1H), 0.71 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 178.5, 170.6, 147.3, 146.5, 136.4, 133.4, 129.6 (q, $^2J_{C-F}$ = 32.5 Hz), 129.0, 127.4, 125.9 (q, $^3J_{C-F}$ = 4.0 Hz), 124.2 (q, $^1J_{C-F}$ = 270.1 Hz), 122.7, 121.3, 99.3, 64.1, 61.4, 45.8, 37.0, 35.7, 13.3 ppm.

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

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{21}F_3NO_5S$ $[M + H]^+$ *m/z* 468.1087, found 468.1062.

Compound 16ag (*dr* 96:4)



Yield: 60.6 mg (60%), White solid.

Mp: 150-152 °C.

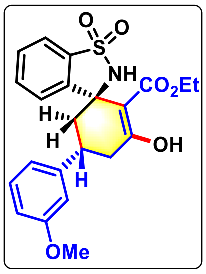
IR (neat): ν_{max} 3005, 2987, 2922, 2853, 1735, 1620, 1453, 1276, 1176, 1022, 753 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 12.99 (s, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.57-7.54 (m, 1H), 7.50-7.46 (m, 3H), 7.43-7.40 (m, 2H), 7.37-7.34 (m, 1H), 7.20-7.16 (m, 2H), 7.13 (d, J = 7.5 Hz, 1H), 6.93-6.89 (m, 2H), 5.15-5.06 (m, 2H), 4.81 (s, 1H), 3.96-3.78 (m, 2H), 3.81-3.75 (m, 1H), 2.80 (ddd, J = 18.5, 5.0, 1.5 Hz, 1H), 2.68 (dd, J = 18.5, 12.5 Hz, 1H), 2.42-2.39 (m, 1H), 2.11 (t, J = 13.0 Hz, 1H), 0.70 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ): δ 179.8, 170.8, 156.6, 147.7, 137.1, 136.3, 133.2, 131.0, 128.8, 128.7, 128.1 (1s) 127.7, 127.2, 122.8, 121.1, 112.3, 99.2, 70.5, 64.4, 61.1, 44.6, 36.0, 30.7, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{28}H_{28}NO_6S$ $[M + H]^+$ *m/z* 506.1632, found 506.1610.

Compound 16ai (*dr* 98:2)



Yield: 56.6 mg (66%), White solid.

Mp: 159-161 °C.

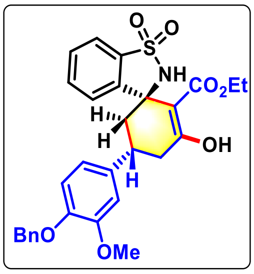
IR (neat): ν_{max} 3457, 3250, 3002, 2969, 2935, 1738, 1636, 1603, 1369, 1216, 1273, 1155, 1042, 778 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 13.00 (s, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.59-7.56 (m, 1H), 7.51-7.48 (m, 1H), 7.25-7.21 (m, 2H), 6.82 (d, *J* = 7.5 Hz, 1H), 6.76_3-6.76_0 (m, 2H), 4.85 (s, 1H), 3.98-3.83 (m, 2H), 3.79 (s, 3H), 3.40-3.34 (m, 1H), 2.78 (dd, *J* = 18.5, 3.0 Hz, 1H), 2.66 (dd, *J* = 18.5, 12.5 Hz, 1H), 2.47-2.45 (m, 1H), 1.91 (t, *J* = 13.0 Hz, 1H), 0.71 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 179.1, 170.7, 160.0, 147.5, 144.2, 136.3, 133.3, 129.9, 128.8, 122.7, 121.2, 119.2, 113.0, 112.3, 99.2, 64.3, 61.2, 55.4, 46.1, 37.4, 35.8, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{24}NO_6S$ $[M + H]^+$ *m/z* 430.1319, found 430.1307.

Compound 16aj (*dr* 97:3)



Yield: 70.6 mg (66%), White solid.

Mp: 155-157 °C.

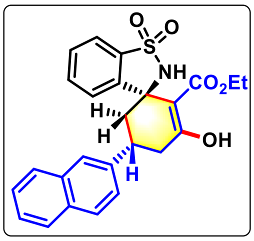
IR (neat): ν_{max} 3456, 3282, 3004, 2969, 2943, 1738, 1604, 1369, 1264, 1228, 1171, 1023, 734 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 12.99 (s, 1H), 7.75 (d, *J* = 7.0 Hz, 1H), 7.59-7.56 (m, 1H), 7.51-7.48 (m, 1H), 7.41 (d, *J* = 7.5 Hz, 2H), 7.36-7.33 (m, 2H), 7.29 (d, *J* = 7.0 Hz, 1H), 7.24 (s, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.68 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.12 (s, 2H), 4.81 (s, 1H), 3.98-3.93 (m, 1H), 3.90-3.84 (m, 4H), 3.36-3.30 (m, 1H), 2.79 (ddd, *J* = 18.5, 5.0, 2.5 Hz, 1H), 2.67-2.60 (m, 1H), 2.46-2.44 (m, 1H), 1.86 (t, *J* = 12.5 Hz, 1H), 0.71 (d, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 179.2, 170.7, 150.0, 147.6, 147.3, 137.3, 136.3, 135.9, 133.3, 128.9, 128.7, 127.9, 127.4, 122.7, 121.3, 118.6, 114.5, 111.1, 99.2, 71.3, 64.4, 61.3, 56.3, 46.4, 37.6, 35.4, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{29}H_{30}NO_7S$ $[M + H]^+$ *m/z* 536.1737, found 536.1734.

Compound 16al (*dr* 97:3)



Yield: 54.8 mg (61%), White solid.

Mp: 190-192 °C.

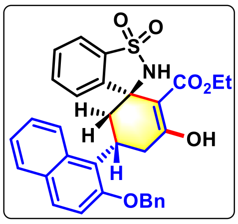
IR (neat): ν_{max} 3456, 3240, 3014, 2969, 2932, 1739, 1605, 1369, 1228, 1251, 1092, 764 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 13.03 (s, 1H), 7.81-7.75 (m, 4H), 7.66 (s, 1H), 7.61-7.57 (m, 1H), 7.52-7.49 (m, 1H), 7.48-7.42 (m, 2H), 7.38 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 4.88 (s, 1H), 4.00-3.85 (m, 2H), 3.61-3.55 (m, 1H), 2.88 (ddd, , *J* = 18.5, 5.0, 2.0 Hz, 1H), 2.78 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.58 (dt, , *J* = 13.5, 2.0 Hz, 1H), 2.05-2.00 (m, 1H), 0.73 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 179.1, 170.7, 147.5, 139.9, 136.3, 133.6, 133.3, 132.6, 128.9, 128.6, 127.8 (1s), 126.4, 125.9, 125.5, 125.1, 122.8, 121.3, 99.3, 64.4, 61.3, 46.1, 37.3, 35.8, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{25}H_{24}NO_5S$ $[M + H]^+$ *m/z* 450.1370, found 450.1360.

Compound 16am (*dr* 99:1)



Yield: 66.6 mg (60%), White solid.

Mp: 201-203 °C.

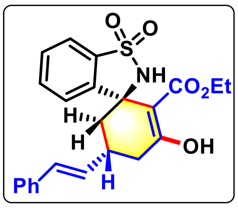
IR (neat): ν_{max} 3250, 2983, 2951, 1700, 1639, 1597, 1408, 1382, 1238, 1215, 1167, 1012, 763 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): 13.00 (s, 1H), 8.20 (d, *J* = 7.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.70-7.68 (m, 1H), 7.55-7.54 (m, 1H), 7.45-7.37 (m, 8H), 7.30 (d, *J* = 9.0 Hz, 1H), 6.78 (s, 1H), 5.22 (d, *J* = 11.0 Hz, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.87 (s, 1H), 4.30 (s, 1H), 3.95-3.82 (m, 2H), 3.45 (dd, *J* = 19.0, 12.5 Hz, 1H), 2.78 (t, *J* = 12.5 Hz, 1H), 2.58 (dd, , *J* = 19.0, 3.5 Hz, 1H), 2.24 (d, *J* = 13.5 Hz, 1H), 0.70 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 180.7, 170.9, 155.1, 147.9, 136.9, 136.2, 133.1, 133.0, 129.7, 129.3, 128.9 (1s), 128.5, 128.3, 128.1, 127.3, 123.8, 122.9, 122.7, 122.5, 121.0, 114.6, 99.3, 71.4, 64.8, 61.1, 42.7, 33.9, 29.5, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{32}H_{30}NO_6S$ $[M + H]^+$ *m/z* 556.1788, found 556.1781.

Compound 16ap (*dr* 95:5)



Yield: 48.5 mg (63%), White solid.

Mp: 217-219 °C

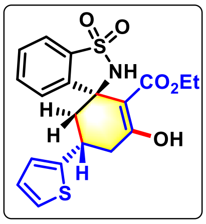
IR (neat): ν_{max} 3005, 2987, 2923, 1735, 1609, 1454, 1276, 1260, 1155, 753 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 12.99 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.58-7.55 (m, 1H), 7.51-7.48 (m, 1H), 7.33-7.27 (m, 4H), 7.22-7.21 (m, 2H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.14 (dd, *J* = 16.0, 6.5 Hz, 1H), 4.76 (s, 1H), 3.97-3.82 (m, 2H), 3.06-3.00 (m, 1H), 2.71 (ddd, *J* = 18.5, 5.0, 2.0 Hz, 1H), 2.47 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.42-2.39 (m, 1H), 1.66 (t, *J* = 12.5 Hz, 1H), 0.71 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 178.9, 170.7, 147.5, 137.0, 136.2, 133.3, 131.1, 130.4, 128.9, 128.7, 127.7, 126.3, 122.8, 121.3, 99.3, 64.0, 61.2, 45.3, 35.8, 33.1, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{23}H_{24}NO_5S$ $[M + H]^+$ *m/z* 426.1370, found 426.1361.

Compound 16aq (*dr* 96:4)



Yield: 48.6 mg (60%), White solid.

Mp: 136-138 °C.

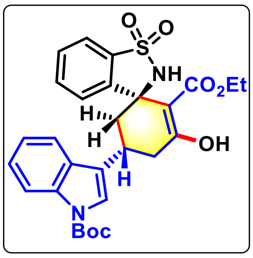
IR (neat): ν_{max} 3456, 3234, 3014, 2969, 2951, 1739, 1614, 1369, 1277, 1216, 1056, 767 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 12.98 (s, 1H), 7.76 (d, *J* = 7.5 Hz, 1H), 7.60-7.56 (m, 1H), 7.52-7.49 (m, 1H), 7.26-7.24 (m, 1H), 7.17 (dd, *J* = 5.0, 1.0 Hz, 1H), 6.93 (dd, *J* = 5.0, 1.5 Hz, 1H), 6.88 (d, *J* = 3.5 Hz, 1H), 4.80 (s, 1H), 3.98-3.83 (m, 2H), 3.73-3.67 (m, 1H), 2.92 (ddd, *J* = 18.5, 5.0, 2.0 Hz, 1H), 2.69 (dd, *J* = 18.5, 12.0 Hz, 1H), 2.60 (dt, *J* = 14.0, 2.0 Hz, 1H), 1.95-1.89 (m, 1H), 0.71 (t, *J* = 7.5 Hz, 3H)ppm.

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 178.3, 170.6, 147.2, 146.4, 136.3, 133.4, 129.0, 127.0, 123.7 (1s), 122.8, 121.3, 99.3, 64.1, 61.3, 47.0, 38.3, 31.7, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{19}H_{20}NO_5S_2$ $[M + H]^+$ *m/z* 406.0777, found 406.0776.

Compound 16ar (*dr* 98:2)



Yield: 67.8 mg (63%), White solid.

Mp: 136-138 °C.

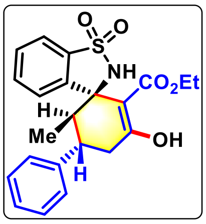
IR (neat): ν_{max} 3005, 2987, 2923, 1735, 1609, 1454, 1276, 1260, 1155, 753 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 13.01 (s, 1H), 8.10 (s, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.58-7.55 (m, 1H), 7.50-7.47 (m, 1H), 7.35-7.29 (m, 3H), 7.24 (d, *J* = 7.5 Hz, 1H), 4.89 (s, 1H), 3.99-3.86 (m, 2H), 3.71-3.65 (m, 1H), 2.97-2.92 (m, 1H), 2.80-2.72 (m, 2H), 1.82 (t, *J* = 13.0 Hz, 1H), 1.66 (s, 9H), 0.72 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 179.1, 170.7, 149.9, 147.5, 136.5, 135.9, 133.3, 129.4, 128.9, 124.9, 123.0, 122.7, 122.4, 121.3, 121.2, 119.5, 115.5, 99.4, 83.9, 64.3, 61.3, 45.3, 35.6, 28.4, 27.7, 13.3 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{28}H_{31}N_2O_7S$ $[M + H]^+$ *m/z* 539.1846, found 539.1849.

Compound 16ba (*dr* 99:1)



Yield: 57.0 mg (69%), White solid

Mp: 219-221°C.

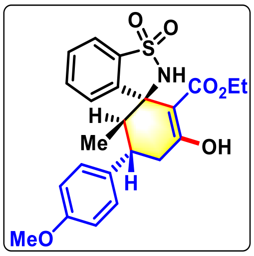
IR (neat): ν_{max} 3457, 3210, 2970, 2941, 1739, 1615, 1409, 1370, 1281, 1165, 1048, 789 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 13.21 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.60 (td, *J* = 7.5, 1.0 Hz, 1H), 7.51 (td, *J* = 7.5, 1.0 Hz, 1H), 7.34-7.26 (m, 3H), 7.24-7.12 (m, 3H), 4.53 (s, 1H), 4.02-3.94 (m, 1H), 3.87-3.79 (m, 1H), 2.98-2.91 (m, 1H), 2.83-2.70 (m, 2H), 2.20-2.13 (m, 1H), 0.70 (t, *J* = 7.0 Hz, 3H), 0.43 (d, *J* = 6.5 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 177.6, 171.0, 145.2, 142.1, 136.6, 133.4, 129.0, 128.9, 127.2, 122.5, 121.3, 101.5, 68.0, 61.2, 47.1, 42.5, 38.7, 13.3, 13.1 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{24}NO_5S$ $[M + H]^+$ *m/z* 414.1370, found 414.1365.

Compound 16bb (*dr* 98:2)



Yield: 62.0 mg (70%), White solid

Mp: 178-180°C.

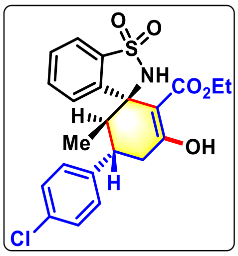
IR (neat): ν_{max} 3267, 2976, 2938, 2835, 1734, 1610, 1245, 1168, 762 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 13.19 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.61-7.58 (m, 1H), 7.53-7.50 (m, 1H), 7.27-7.26 (m, 1H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 2H), 4.42 (s, 1H), 4.01-3.95 (m, 1H), 3.86-3.81 (m, 4H), 2.92-2.87 (m, 1H), 2.78-2.68 (m, 2H), 2.13-2.07 (m, 1H), 0.71 (t, *J* = 7.0 Hz, 3H), 0.43 (d, *J* = 6.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 177.7, 171.0, 158.7, 145.2, 136.5, 134.0, 133.4, 129.0, 122.4, 121.2, 114.3, 101.5, 68.0, 61.3, 55.4, 47.3, 41.6, 38.8, 13.3, 13.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{23}H_{26}NO_6S$ $[M + H]^+$ *m/z* 444.1475, found 444.1463.

Compound 16bc (*dr* 98:2)



Yield: 58.0 mg (65%), White solid.

Mp: 161-163 °C.

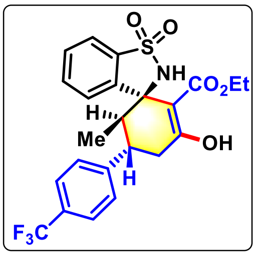
IR (neat): ν_{max} 3220, 2923, 2853, 1738, 1614, 1452, 1276, 1168, 1052, 753 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 13.20 (s, 1H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.62-7.59 (m, 1H), 7.54-7.51 (m, 1H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.27-7.25 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 4.54 (s, 1H), 4.01-3.95 (m, 1H), 3.86-3.80 (m, 1H), 2.97-2.91 (m, 1H), 2.73-2.71 (m, 2H), 2.16-2.09 (m, 1H), 0.70 (t, *J* = 7.0 Hz, 3H), 0.42 (d, *J* = 6.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 177.2, 170.9, 144.9, 140.5, 136.5, 133.5, 132.9, 129.2, 129.1, 122.4, 121.3, 101.5, 67.8, 61.2, 47.0, 41.9, 38.5, 13.3, 13.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{23}ClNO_5S$ $[M + H]^+$ *m/z* 448.0980, found 448.0977.

Compound 16be (*dr* 99:1)



Yield: 60.0 mg (62%), White solid.

Mp: 100-102 °C.

IR (neat): ν_{max} 3466, 3237, 3014, 2969, 1739, 1618, 1368, 1229, 1171, 1067, 761 cm^{-1}

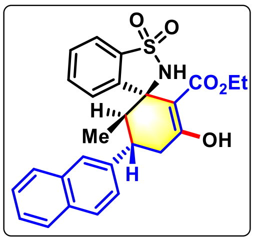
^{1}H NMR (400 MHz, $CDCl_3$): 13.23 (s, 1H), 7.75 (d, *J* = 9.5 Hz, 1H), 7.62 (dd, *J* = 9.5, 1.5 Hz, 1H), 7.58 (d, *J* = 10.0 Hz, 2H), 7.55-7.51 (m, 1H), 7.34 (d, *J* = 10.0 Hz, 2H), 7.28 (d, *J* = 9.5 Hz, 1H), 4.68 (s, 1H), 4.03-3.95 (m, 1H), 3.87-3.79 (m, 1H), 3.09-3.01 (m, 1H), 2.81-2.69 (m, 2H), 2.23-2.17 (m, 1H), 0.70 (t, *J* = 7.0 Hz, 3H), 0.43 (d, *J* = 6.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 176.9, 170.9, 146.2, 144.8, 136.6, 133.6, 129.3 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 129.2, 128.4, 125.9 (q, $^3J_{C\text{-}F}$ = 3.4 Hz), 124.2 (q, $^1J_{C\text{-}F}$ = 270.5 Hz), 122.4, 121.3, 101.6, 67.7, 61.3, 46.8, 42.4, 38.4, 13.3, 13.1ppm.

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

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{23}H_{23}F_3NO_5S$ $[M + H]^+$ *m/z* 482.1244, found 482.1232.

Compound 16bl (*dr* 99:1)



Yield: 53.0 mg (57%), White solid.

Mp: 215-217 °C.

IR (neat): ν_{max} 3207, 2922, 1736, 1607, 1453, 1276, 1167, 1053, 752 cm^{-1}

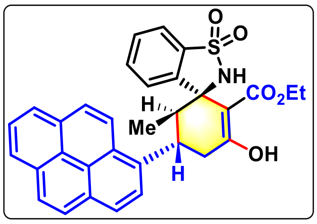
^{1}H NMR (500 MHz, $CDCl_3$): δ 13.23 (s, 1H), 7.83-7.79 (m, 3H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.68 (s, 1H), 7.63-7.60 (m, 1H), 7.54-7.44 (m, 3H), 7.35-7.31 (m, 2H), 4.47 (s, 1H), 4.03-3.97 (m, 1H), 3.88-3.82 (m, 1H), 3.14 (td, *J* = 11.5, 5.5 Hz, 1H), 2.92

(dd, J = 19.0, 12.0 Hz, 1H), 2.79 (dd, J = 19.0, 5.0 Hz, 1H), 2.31-2.25 (m, 1H), 0.72 (t, J = 7.0 Hz, 3H), 0.46 (d, J = 6.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 177.6, 171.0, 145.1, 139.3, 136.6, 133.7, 133.5, 132.8, 129.0, 128.8, 127.7 (1s), 126.5, 126.0, 122.5, 121.3, 101.6, 68.0, 61.2, 47.0, 42.6, 38.6, 13.3, 13.2 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{26}H_{26}NO_5S$ $[M + H]^+$ m/z 464.1526, found 464.1517.

Compound 16bo (*dr* 99:1)



Yield: 59.0 mg (55%), White solid.

Mp: 251-253 °C.

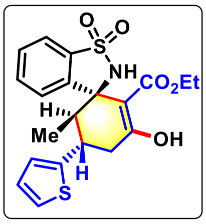
IR (neat): ν_{max} 3250, 2983, 2951, 1700, 1639, 1597, 1408, 1382, 1238, 1215, 1167, 1012, 3294, 3005, 2987, 2921, 2852, 1739, 1606, 1460, 1276, 1172, 747 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): 13.30 (s, 1H), 8.45 (d, J = 9.0 Hz, 1H), 8.20-8.14 (m, 4H), 8.08-7.99 (m, 3H), 7.94 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.65-7.62 (m, 1H), 7.55-7.52 (m, 1H), 7.38 (d, J = 8.0 Hz, 1H), 4.77 (s, 1H), 4.28 (td, J = 11.5, 5.0 Hz, 1H), 4.07-4.01 (m, 1H), 3.93-3.86 (m, 1H), 3.06 (dd, J = 19.0, 12.0 Hz, 1H), 2.88 (dd, J = 19.0, 5.0 Hz, 1H), 2.55-2.49 (m, 1H), 0.76 (t, J = 7.0 Hz, 3H), 0.47 (d, J = 6.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 177.7, 171.1, 145.1, 136.6, 135.9, 133.5, 131.6, 130.9, 130.1, 129.6, 129.1, 128.3, 127.5, 127.4, 126.2, 125.4, 125.3, 125.2, 125.0, 123.7, 122.5, 122.4, 121.3, 101.7, 68.3, 61.2, 47.9, 39.1, 35.7, 13.3, 12.7 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. for $C_{32}H_{28}NO_5S$ $[M + H]^+$ m/z 538.1683, found 538.1694.

Compound 16bq (*dr* 99:1)



Yield: 48.6 mg (58%), White solid.

Mp: 145-147 °C.

IR (neat): ν_{max} 3265, 2923, 2852, 1737, 1637, 1452, 1371, 1281, 1170, 1051, 764 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 13.19 (s, 1H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.62-7.59 (m, 1H), 7.54-7.50 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.20 (d, *J* = 4.5 Hz, 1H), 6.94 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.90 (dd, *J* = 3.5, 1.0 Hz, 1H), 4.50 (s, 1H), 4.01-3.95 (m, 1H), 3.86-3.79 (m, 1H), 3.34-3.28 (m, 1H), 2.91-2.79 (m, 2H), 2.09-1.98 (m, 1H), 0.70 (t, *J* = 7.0 Hz, 3H), 0.52 (d, *J* = 6.5 Hz, 3H) ppm.

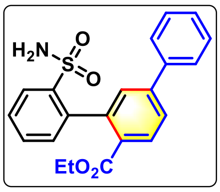
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 176.9, 170.9, 145.6, 144.9, 136.5, 133.5, 129.1, 126.9, 125.6, 124.1, 122.5, 121.3, 101.5, 67.8, 61.2, 48.6, 39.7, 38.0, 13.3, 13.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{20}H_{22}NO_5S_2$ $[M + H]^+$ *m/z* 420.0934, found 420.0935.

3.3 Synthesis of Compounds 17aa-ac, 17ae, 17ag, 17aj, 17al-am, 17ao, 17aq-ar, 17ba-bc, 17bm, 17bo, 17bq-br, and 17ca: Representative Procedure for 17aa

A Schlenk tube was charged with 3-alkylbenzo[*d*]isothiazole 1,1-dioxide **2a** (36.2 mg, 0.20 mmol), *δ*-acetoxy allenoate **8a** (62.4 mg, 0.24 mmol) in toluene (2.0 mL). Subsequently, 4-dimethylaminopyridine (5.0 mg, 0.04 mmol) was added at 110 °C (oil bath), and the mixture stirred at the same temperature for 12 h, and progress of the reaction was monitored using TLC. After completion of the reaction, 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 (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. All other compounds were prepared by using the same molar quantities.

Compound 17aa



Yield: 59.5 mg (78%), White solid.

Mp: 166-168 °C.

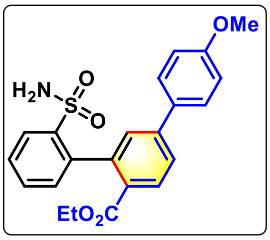
IR (neat): ν_{max} 3330, 3257, 2987, 1699, 1602, 1506, 1469, 1286, 1161, 1045, 696cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.15 (d, *J* = 7.0 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.73 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65-7.64 (m, 3H), 7.59-7.56 (m, 1H), 7.54-7.51 (m, 1H), 7.46-7.43 (m, 2H), 7.40-7.37 (m, 1H), 7.26-7.24 (m, 1H), 4.54 (s, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 1.09 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 167.2, 144.2, 140.2$_4$, 140.1$_7$, 139.9, 139.3, 132.1, 131.2, 130.8, 130.7, 129.1 (1s), 128.5, 128.1, 128.0, 127.5, 127.0, 61.3, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{21}H_{19}NNaO_4S$ [M + Na]$^+$ *m/z* 404.0927, found 404.0923.

Compound 17ab



Yield: 67.5 mg (82%), White solid.

Mp: 177-179 °C.

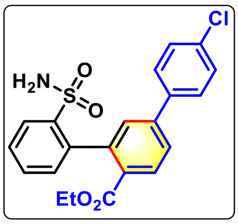
IR (neat): ν_{max} 3323, 3253, 2924, 1697, 1603, 1518, 1446, 1290, 1162, 1045, 829 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.17 (d, *J* = 7.5 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.69 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.60-7.52 (m, 5H), 7.26-7.24 (m, 1H), 6.97 (d, *J* = 9.0 Hz, 2H), 4.46 (s, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 3.84 (s, 3H), 1.10 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 167.3, 160.2, 143.8, 140.3, 140.1, 139.9, 132.1, 131.6, 131.2, 130.9, 130.2, 128.7, 128.2, 128.1, 128.0, 126.5, 114.6, 61.3, 55.5, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{21}NNaO_5S$ [M + Na]$^+$ *m/z* 434.1033, found 434.1029.

Compound 17ac



Yield: 62.3 mg (75%), White solid.

Mp: 189-191 °C.

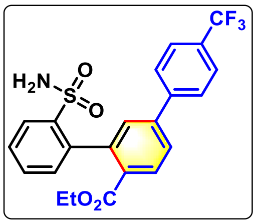
IR (neat): ν_{max} 3323, 3253, 2924, 1697, 1603, 1518, 1446, 1290, 1162, 1045, 829 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.19-8.17 (m, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.69 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.61 (d, *J* = 2.0 Hz, 1H), 7.59-7.53 (m, 4H), 7.43-7.40 (m, 2H), 7.24-7.23 (m, 1H), 4.49 (s, 2H), 4.13 (qd, *J* = 7.0, 1.0 Hz, 2H), 1.12 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 167.2, 142.9, 140.3, 140.0, 139.9, 137.8, 134.8, 132.2, 131.2, 130.9, 130.8, 129.3, 128.8, 128.2, 128.1, 126.8, 61.4, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{21}H_{19}ClNO_4S$ [M + H]$^+$ *m/z* 416.0718, found 416.0717.

Compound 17ae



Yield: 64.0 mg (71%), White solid.

Mp: 189-191 °C.

IR (neat): ν_{max} 3333, 3258, 2923, 2859, 1700, 1605, 1467, 1325, 1293, 1164, 1041, 763 cm^{-1}

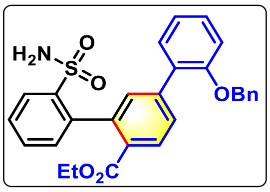
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.19-8.17 (m, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.76-7.22 (m, 3H), 7.71-7.69 (m, 2H), 7.65 (d, *J* = 1.5 Hz, 1H), 7.61-7.54 (m, 2H), 7.25-7.24 (m, 1H), 4.54 (s, 2H), 4.19-4.10 (m, 2H), 1.13 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 167.2, 142.8, 142.6, 140.4, 139.9, 139.8, 132.3, 131.2, 130.9, 130.6 (q, $^2J_{C\text{-}F}$ = 32.4 Hz), 129.8, 128.4, 128.2, 127.9, 127.2, 126.1 (q, $^3J_{C\text{-}F}$ = 3.6 Hz), 124.2 (q, $^1J_{C\text{-}F}$ = 270.5 Hz), 61.5, 14.0 ppm.

^{1}H NMR (376 MHz, CDCl$_3$): δ -62.6 ppm

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{18}F_3NNaO_4S$ [M + Na]$^+$ *m/z* 472.0801, found 472.0803.

Compound 17ag



Yield: 68.0 mg (70%), White solid.

Mp: 188-190 °C.

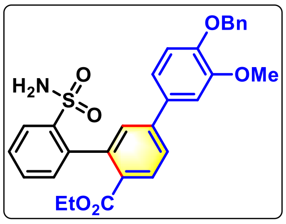
IR (neat): ν_{max} 3352, 3240, 2989, 1698, 1607, 1463, 1276, 1159, 1052, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13-8.07 (m, 2H), 7.67-7.65 (m, 2H), 7.59-7.56 (m, 1H), 7.53-7.50 (m, 1H), 7.45 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.38-7.32 (m, 2H), 7.26-7.25 (m, 5H), 7.11-7.06 (m, 2H), 5.06-4.98 (m, 2H), 4.11-4.05 (m, 2H), 3.74 (s, 2H), 1.02 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ): δ 166.7, 155.8, 141.7, 140.8, 139.6, 138.8, 136.5, 132.5, 132.0, 131.2, 131.0, 130.6, 129.9, 129.5, 128.9, 128.6, 128.1, 127.7, 127.6, 121.7, 112.9, 70.9, 61.0, 13.9 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{28}H_{29}N_2O_5S$ [M + NH_4]$^+$ *m/z* 505.1792, found 505.1777.

Compound 17aj



Yield: 75.6 mg (73%), White solid.

Mp: 180-182 °C.

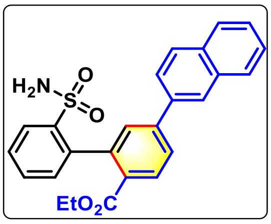
IR (neat): ν_{max} 3352, 3240, 2989, 1698, 1607, 1463, 1276, 1159, 1052, 699 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 7.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.67 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.60-7.51 (m, 3H), 7.45-7.43 (m, 2H), 7.38-7.35 (m, 2H), 7.31-7.29 (m, 1H), 7.25-7.23 (m, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.14 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.93 (d, *J* = 8.5 Hz, 1H), 5.19 (s, 2H), 4.52 (s, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 3.94 (s, 3H), 1.09 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.2, 150.2, 148.9, 143.9, 140.2, 140.1, 140.0, 137.0, 132.6, 132.1, 131.2, 130.8, 130.4, 128.7, 128.5, 128.0_3, 127.9_6, 127.4, 126.6, 120.0, 114.5, 111.3, 71.2, 61.2, 56.3, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{29}H_{27}NNaO_6S$ $[M + Na]^+$ *m/z* 540.1451, found 540.1464.

Compound 17al



Yield: 62.1 mg (72%), White solid.

Mp: 181-183 °C.

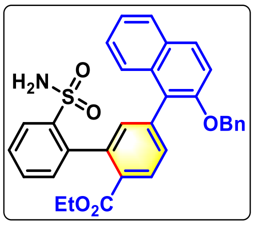
IR (neat): ν_{max} 3222, 2922, 2852, 1699, 1602, 1437, 1275, 1158, 1105, 696 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.19 (d, *J* = 8.0 Hz, 1H), 8.14-8.11 (m, 2H), 7.93-7.85 (m, 4H), 7.78-7.77 (m, 2H), 7.61-7.50 (m, 4H), 7.29 (d, *J* = 7.0 Hz, 1H), 4.53 (s, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 1.12 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.3, 144.2, 140.3, 140.2, 139.9, 136.5, 133.7, 133.2, 132.2, 131.3, 131.0, 130.9, 129.0, 128.9, 128.5, 128.2, 128.0, 127.8, 127.2, 126.7 (1s), 125.3, 61.4, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{25}H_{21}NNaO_4S$ $[M + Na]^+$ *m/z* 454.1083, found 454.1092.

Compound 17am



Yield: 76.3 mg (71%), White solid.

Mp: 193-195 °C.

IR (neat): ν_{max} 3409, 3308, 2922, 2852, 1714, 1618, 1589, 1398, 1247, 1164, 1016, 752 cm^{-1}

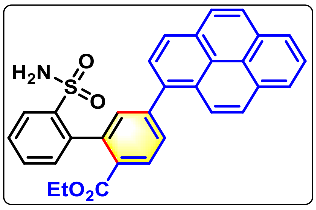
^1H NMR (500 MHz, $CDCl_3$): **major isomer**: δ 8.22 (d, *J* = 8.0 Hz, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.86 (d, *J* = 9.5 Hz, 1H), 7.84-7.79 (m, 1H), 7.59-7.55 (m, 1H), 7.53-7.47 (m, 2H), 7.42-7.34 (m, 5H), 7.28-7.26 (m, 4H), 7.19 (d, *J* = 7.0 Hz, 2H), 5.10

(s, 2H), 4.19-4.06 (m, 4H), 1.01 (t, *J* = 7.0 Hz, 3H) ppm. **minor isomer**: δ 8.15 (d, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 8.0 Hz, 1H), 7.84-7.79 (m, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.59-7.55 (m, 1H), 7.53-7.47 (m, 2H), 7.42-7.34 (m, 5H), 7.28-7.26 (m, 4H), 7.23-7.21 (m, 2H), 5.13 (s, 2H), 4.65 (s, 1H), 4.19-4.06 (m, 3H), 1.15 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): **major isomer:** δ 166.7, 152.8, 140.6, 140.2, 140.0, 139.6, 136.5, 134.4, 133.4, 131.9, 131.2, 131.0, 130.0, 129.6, 128.9, 128.6, 128.2, 128.0, 127.6, 127.3, 127.0, 125.3, 125.1, 124.3, 115.9, 72.4, 61.3, 14.1 ppm. **minor isomer**: 167.6, 152.8, 140.5 (1s), 139.9, 139.8, 137.2, 133.3, 133.1, 132.0, 131.4, 131.3, 130.1, 129.5, 128.8, 128.6, 128.0, 127.9, 127.7, 127.2, 127.0, 125.3, 125.0, 124.7, 115.4, 71.2, 61.0, 14.0.

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{32}H_{27}NNaO_5S$ $[M + Na]^+$ 560.1502, found 560.1503.

Compound 17ao



Yield: 70.0 mg (69%), White solid.

Mp: 221-223 °C.

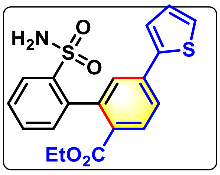
IR (neat): ν_{max} 3409, 3308, 2922, 2852, 1714, 1618, 1589, 1398, 1247, 1164, 1016, 752 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): 8.29 (d, *J* = 9.0 Hz, 1H), 8.22-8.16 (m, 5H), 8.11-8.07 (m, 3H), 8.03-8.00 (m, 2H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.68 (s, 1H), 7.59-7.56 (m, 1H), 7.54-7.51 (m, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 4.71 (s, 2H), 4.20 (q, *J* = 7.0 Hz, 2H), 1.17 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.5, 144.7, 140.2, 140.0, 135.6, 134.3, 132.2, 131.5, 131.3, 131.2, 131.1, 130.7, 130.3, 128.9, 128.6, 128.3, 128.2, 128.1, 128.0, 127.6, 127.5, 126.3, 125.5, 125.3, 125.1, 124.9, 124.8, 61.5, 14.1 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{31}H_{23}NNaO_4S$ $[M + Na]^+$ 528.1240, found 528.1251.

Compound 17aq



Yield: 55.0 mg (71%), White solid.

Mp: 170-172 °C.

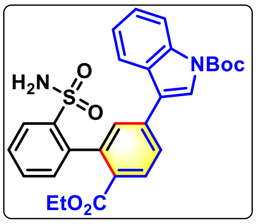
IR (neat): ν_{max} 3356, 3262, 3118, 2976, 1688, 1599, 1404, 1364, 1290, 1166, 1015, 760 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): **major isomer**: δ 8.16 (dd, *J* = 8.0, 1.0 Hz, 1H), 8.08 (d, *J* = 8.5 Hz, 1H), 7.72 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.60-7.53 (m, 2H), 7.43-7.42 (m, 1H), 7.36 (d, *J* = 4.5 Hz, 1H), 7.24 (d, *J* = 1.0 Hz, 1H), 7.10 (dd, *J* = 5.0, 4.0 Hz, 1H), 4.50 (s, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 1.10 (t, *J* = 7.0 Hz, 3H) ppm. **minor isomer**: δ 8.14-8.10 (m, 2H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.59-7.53 (m, 2H), 7.31-7.29 (m, 2H), 7.22 (dd, *J* = 1.3, 5.0Hz, 1H), 6.90-6.89 (m, 2H), 4.42-4.35 (m, 2H), 4.23 (s, 2H), 1.39 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): **major isomer**: δ 167.0, 142.4, 140.7, 140.1, 139.9, 137.5, 132.2, 131.2, 131.1, 128.9 (1s), 128.6, 128.2, 128.1, 126.8, 125.5, 125.2, 61.3, 14.0 ppm. **minor isomer**: 167.0, 142.4, 140.7, 140.1, 139.9, 137.5, 133.2, 132.6, 132.3, 130.0, 129.4, 129.0, 128.7, 127.9, 127.6, 127.5, 61.4, 14.5 ppm

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{19}H_{17}NNaO_4S_2$ $[M + Na]^+$ 410.0491, found 410.0495.

Compound 17ar



Yield: 72.0 mg (69%), White solid.

Mp: 159-161 °C.

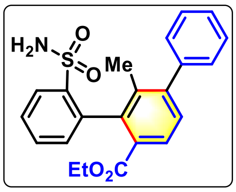
IR (neat): ν_{max} 3344, 3257, 2980, 2928, 2859, 1733, 1690, 1599, 1452, 1368, 1287, 1156, 1029, 768 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): 8.22 (d, *J* = 7.5 Hz, 1H), 8.18 (d, *J* = 7.5 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.82 (s, 1H), 7.79 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.71 (s, 1H), 7.60-7.53 (m, 2H), 7.39-7.36 (m, 1H), 7.32-7.28 (m, 2H), 4.57 (s, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 1.69 (s, 9H), 1.12 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.2, 149.7, 140.4, 140.2, 139.9, 137.6, 136.1, 132.2, 131.2_4, 131.1_7, 130.9, 128.7, 128.4, 128.1, 128.0, 127.6, 125.1, 124.3, 123.5, 120.6, 120.1, 115.6, 84.4, 61.3, 28.3, 14.0 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{28}H_{29}N_2O_6S$ $[M + H]^+$ 521.1741, found 521.1740.

Compound 17ba



Yield: 58.5 mg (74%), White solid.

Mp: 147-149 °C.

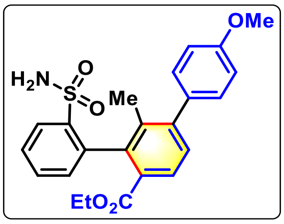
IR (neat): ν_{max} 3351, 3256, 2922, 2852, 1696, 1559, 1445, 1320, 1288, 1158, 1023, 762 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.62-7.59 (m, 1H), 7.56-7.53 (m, 1H), 7.44-7.41 (m, 2H), 7.38-7.33 (m, 4H), 7.19 (d, *J* = 7.5 Hz, 1H), 4.71 (s, 2H), 4.15-4.09 (m, 2H), 1.89 (s, 3H), 1.16 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.3, 146.6, 141.2, 140.2, 139.7, 139.4, 136.9, 132.7, 130.9, 129.9, 129.4, 129.2, 128.5, 128.4, 128.3, 127.6, 126.7, 61.4, 19.0, 14.1ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{21}NNaO_4S$ $[M + Na]^+$ *m/z* 418.1083, found 418.1072.

Compound 17bb



Yield: 65.5 mg (77%), White solid.

Mp: 177-179 °C.

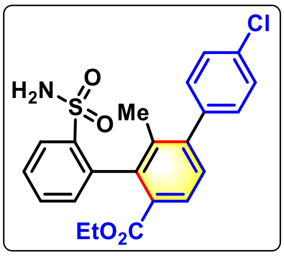
IR (neat): ν_{max} 3412, 3267, 3005, 2988, 1703, 1609, 1514, 1464, 1276, 1260, 1165, 1030, 747 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.18 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.62-7.59 (m, 1H), 7.56-7.52 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.28-7.26 (m, 2H), 7.18 (dd, *J* = 7.5, 1.0 Hz, 1H), 6.96 (d, *J* = 8.5 Hz, 2H), 4.67 (s, 2H), 4.14-4.08 (m, 2H), 3.85 (s, 3H), 1.90 (s, 3H), 1.15 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.4, 159.2, 146.4, 140.2, 139.7, 139.6, 137.0, 133.5, 132.7, 130.9, 130.5, 130.1, 129.1, 128.5, 128.3, 126.9, 113.8, 61.4, 55.5, 19.1, 14.1 ppm

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{23}H_{24}NO_5S$ $[M + H]^+$ *m/z* 426.1370, found 426.1358

Compound 17bc



Yield: 62.0 mg (72%), White solid.

Mp: 193-195 °C.

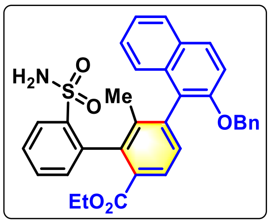
IR (neat): ν_{max} 3386, 3280, 2988, 1694, 1554, 1493, 1368, 12765, 1196, 1086, 751cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.18 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.62-7.59 (m, 1H), 7.57-7.54 (m, 1H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 2H), 7.17 (dd, *J* = 7.5, 1.0 Hz, 1H), 4.73 (s, 2H), 4.16-4.07 (m, 2H), 1.87 (s, 3H), 1.16 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.3, 145.3, 140.2, 139.9, 139.6, 139.2, 137.0, 133.8, 132.8, 130.8, 130.6, 129.7, 128.6$_4$, 128.5$_7$, 128.4, 126.9, 61.5, 19.0, 14.1 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{22}H_{21}ClNO_4S$ $[M + H]^+$ *m/z* 430.0874, found 430.0864.

Compound 17bm



Yield: 75.0 mg (68%), White solid.

Mp: 204-206 °C.

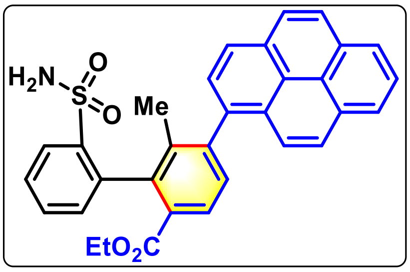
IR (neat): ν_{max} 3390, 3255, 2922, 1744, 1702, 1619, 1586, 1461, 1344, 1295, 1188, 1067, 733 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$, **isomers not distinguished** δ 8.12 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.88-7.83 (m, 2H), 7.62-7.59 (m, 1H), 7.52-7.49 (m, 1H), 7.40-7.36 (m, 3H), 7.35-7.29 (m, 6H), 7.24-7.23 (m, 2H), 5.14-5.09 (m, 2H), 4.15-4.06 (m, 4H), 1.68 (s, 3H), 1.07 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): **major isomer:** δ 167.3, 152.5, 141.3, 139.8, 139.4, 138.9, 137.7, 136.8, 133.0, 132.2, 131.2, 130.8, 129.7, 129.3, 129.0, 128.4, 128.2, 127.9, 127.8, 126.9, 124.8, 124.2, 115.3, 71.7, 61.1, 18.0, 14.0 ppm **minor isomer**: 152.6, 140.0, 139.0, 133.1, 132.1, 130.8, 129.7 (shoulder), 129.4$_4$, 128.9, 128.4, 126.9 (shoulder), 124.7, 124.5, 115.4, 71.8, 61.0, 18.0 (other peaks were buried in those due to the major isomer) ppm.

HRMS (ESI- EXACTIVE ORBITRAP): calcd $C_{33}H_{30}NO_5S$ [M + H]$^+$ 552.1839, found 552.1842.

Compound 17bo



Yield: 67.5 mg (65%), White solid.

Mp: 135-137 °C.

IR (neat): ν_{max} 3409, 3308, 2922, 2852, 1714, 1618, 1589, 1398, 1247, 1164, 1016, 752 cm^{-1}

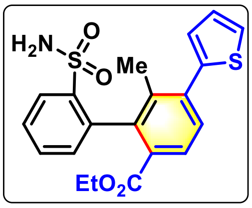
^{1}H NMR (500 MHz, CDCl$_3$): **Major isomer**: δ 8.25-8.17 (m, 5H), 8.12-8.11 (m, 2H), 8.04-8.00 (m, 1H), 7.95-7.92 (m, 1H), 7.90-7.85 (m, 2H), 7.57-7.52 (m, 3H), 7.26-

7.25 (m, 1H), 4.97 (s, 2H), 4.22-4.14 (m, 2H), 1.69 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H) ppm. **Minor isomer:** 8.25-8.17 (m, 5H), 8.10-8.09 (m, 1H), 8.04-8.00 (m, 1H), 7.95-7.92 (m, 1H), 7.90-7.85 (m, 2H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.66-7.61 (m, 3H), 7.34 (d, *J* = 7.5 Hz, 1H), 4.82 (s, 2H), 4.22-4.14 (m, 2H), 1.73 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ **Major isomer**: δ 168.7, 145.7, 140.3, 139.8, 139.4, 138.6, 136.3, 132.8, 131.5, 131.0, 130.8, 129.5, 129.2, 128.6, 128.5, 128.4, 127.8, 127.6, 127.4, 126.8, 126.3, 125.6, 125.5, 125.3, 61.6, 18.8, 14.2 ppm. Major isomer: δ 168.7, 145.7, 140.3, 139.8, 139.4, 138.6, 136.3, 132.8, 131.5, 131.0, 130.8, 129.5, 129.2, 128.6, 128.5, 128.4, 127.8, 127.6, 127.4, 126.8, 126.3, 125.6, 125.5, 125.3, 61.6, 18.8, 14.2 ppm. **Minor isomer**: δ 168.5, 145.4, 140.2, 139.9, 139.3, 138.5, 136.2, 132.8, 131.6, 131.2. 130.1, 129.8, 129.2, 128.6, 128.5, 128.4, 127.9, 127.7, 127.6, 127.4, 126.9, 126.3, 125.5 (1s), 125.2, 61.6, 18.9, 14.2: δ 168.5, 145.4, 140.2, 139.9, 139.3, 138.5, 136.2, 132.8, 131.6, 131.2. 130.1, 129.8, 129.2, 128.6, 128.5, 128.4, 127.9, 127.7, 127.6, 127.4, 126.9, 126.3, 125.5 (1s), 125.2, 61.6, 18.9, 14.2 ppm.

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{32}H_{29}N_2O_4S$ $[M + NH_4]^+$ 537.1843, found 537.1836.

Compound 17bq



Yield: 54.5 mg (68%), White solid.

Mp: 139-141 °C °C.

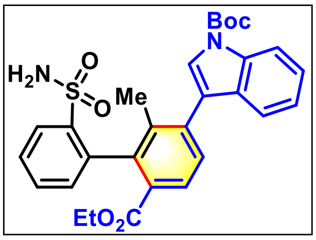
IR (neat): ν$_{max}$ 3005, 2987, 2853, 1739, 1461, 1276, 1164, 752 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.18-8.17 (m, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.62-7.59 (m, 1H), 7.56 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 1H), 7.34 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.17 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.12-7.09 (m, 2H), 4.69 (s, 2H), 4.14-4.08 (m, 2H), 2.05 (s, 3H), 1.15 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 168.1, 141.9, 140.2, 140.1, 139.3, 138.9, 137.5, 132.7, 130.9, 130.7, 129.9, 128.5, 128.4, 127.9, 127.4, 127.0, 126.3, 61.5, 19.3, 14.1 ppm

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{20}H_{20}NO_4S_2$ $[M + H]^+$ 402.0828, found 402.0818.

Compound 17br



Yield: 70.5 mg (66%), White solid.

Mp: 128-130 °C.

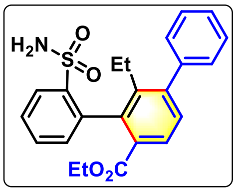
IR (neat): ν_{max} 3396, 3257, 2925, 2859, 1701, 1585, 1458, 1335, 1286, 1160, 1022, 761 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.62-7.60 (m, 2H), 7.55 (td, *J* = 7.5, 1.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.37-7.33 (m, 1H), 7.25-7.23 (m, 1H), 7.20 (dd, *J* = 7.5, 1.0 Hz, 1H), 4.74 (s, 2H), 4.17-4.11 (m, 2H), 1.91 (s, 3H), 1.69 (s, 9H), 1.18 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.4, 149.9, 140.2, 139.9, 139.4, 138.7, 138.0, 135.2, 132.8, 130.8, 130.0, 129.7, 128.5, 128.4, 127.0, 124.8, 124.1, 123.3, 121.5, 120.7, 115.4, 84.1, 61.5, 28.4, 19.1, 14.1 ppm

HRMS (ESI- EXACTIVE ORBITRAP): calcd for $C_{29}H_{31}N_2O_6S$ $[M + H]^+$ 535.1897, found 535.1889.

Compound 17ca



Yield: 58.1 mg (71%), White solid.

Mp: 140-142 °C.

IR (neat): ν_{max} 3323, 3235, 3107, 2926, 1680, 1586, 1454, 1326, 1291, 1153, 1027, 761 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, *J* = 7.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.59-7.53 (m, 2H), 7.43-7.31 (m, 6H), 7.26-7.24 (m, 1H), 4.68 (s, 2H), 4.11 (q, *J* = 7.0

Hz, 2H), 2.66-2.59 (m, 1H), 2.20-2.13 (m, 1H), 1.16 (t, *J* = 7.0 Hz, 3H), 0.56 (t, *J* = 7.5 Hz, 3H) ppm.

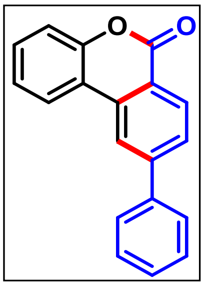
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): **Major isomer** δ 168.4, 143.1, 141.2, 140.3, 138.5_5, 138.5_1, 132.1, 131.4, 130.6, 129.9, 129.1, 128.3 (1s)127.5, 126.7, 61.5, 24.3, 14.4, 14.1; **Minor isomer** δ 168.4, 146.5, 143.1, 141.2, 140.2, 138.4, 132.1, 131.4, 130.5, 129.9, 128.4 (2s), 127.5, 126.7, 61.4, 24.3, 14.4, 14.1ppm.

HRMS (ESI- EXACTIVE ORBITRAP): Calcd. For $C_{23}H_{24}NO_4S$ $[M + H]^+$ *m/z* 410.1421, found 410.1410.

3.4 Synthesis of Compounds 18aa-ar, 18bk-ka, 18fo, 18js, 18la, 18ld, 18ll, 18lr, 18ma, 18ml, 18mn, and 18mo : Representative Procedure for 18aa

A Schlenk tube was charged with *δ*-acetoxy allenoate **8a** (52.0 mg, 0.20 mmol), 4-dimethylaminopyridine (5.0 mg, 0.04 mmol), K_2CO_3 (oven dried at 110 °C for 12 h, 0.40 mmol) and 2.0 mL of toluene. Subsequently, 4-alkylbenzo[*e*][1,2,3]oxathiazine 2,2-dioxide **5a** (39.4 mg, 0.20 mmol) was added at 130 °C (oil bath), and the mixture stirred at the same temperature for 6-8 h and progress of the reaction was monitored using TLC. After completion of the reaction, 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 (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **18aa** was then purified by silica gel column chromatography using ethyl acetate/hexane (1:19) as the eluent. All other compounds were prepared by using the same molar quantities.

Compound 18aa



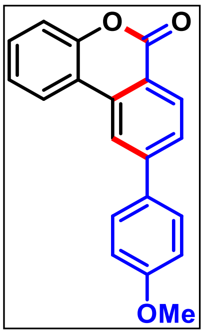
Yield:	46.0 mg (85%), White solid
Mp:	160 °C.
IR (neat):	ν_{max} 3018, 2925, 1729, 1613, 1407, 1276, 1214, 1081, 752 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.47 (d, *J* = 8.5 Hz, 1H), 8.30 (d, *J* = 1.5 Hz, 1H), 8.16 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 7.80 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.73-7.71 (m, 2H), 7.56-7.46 (m, 4H), 7.41-7.35 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.3, 151.7, 148.0, 139.8, 135.3, 131.3, 130.7, 129.3, 129.0, 128.1, 127.7,124.7, 122.9, 120.3, 120.1, 118.3, 118.0 ppm.

HRMS (ESI- TOF): Calcd. For $C_{19}H_{13}O_2$ $[M + H]^+$ *m/z* 273.0910, found 273.0911.

Compound 18ab



Yield: 53.1 mg (88%), White solid

Mp: 197.7 °C.

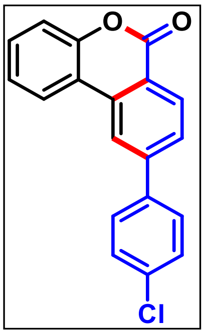
IR (neat): ν_{max} 3014, 2969, 1739, 1605, 1438, 1367, 1228 1216, 1092, 768 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.39 (d, *J* = 8.5 Hz, 1H), 8.20 (s, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.36-7.32 (m, 2H), 7.04 (d, *J* = 8.5 Hz, 2H), 3.89 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.3, 151.7, 148.0, 139.8, 135.3, 131.3, 130.7, 129.3, 129.0, 128.1, 127.7,124.7, 122.9, 120.3, 120.1, 118.3, 118.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{15}O_3$ $[M + H]^+$ *m/z* 303.1016, found 303.1016.

Compound 18ac



Yield: 49.6 mg (81%), White solid

Mp: 286 °C.

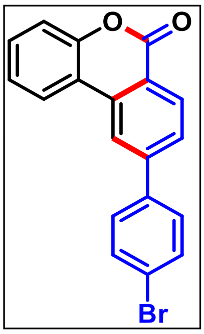
IR (neat): ν_{max} 3014, 2969, 1738, 1437, 1367, 1228, 1216, 1092, 899, 752 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.48 (d, *J* = 8.5 Hz, 1H), 8.27 (d, *J* = 1.0 Hz, 1H), 8.16 (d, *J* = 7.0 Hz, 1H), 7.77 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.54-7.50 (m, 3H), 7.42- 7.36 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.2, 151.7, 146.7, 138.3, 135.5, 135.3, 131.5, 130.9, 129.5, 128.9, 127.9, 124.8, 122.9, 120.4, 120.2, 118.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{12}ClO_2$ $[M + H]^+$ *m/z* 307.0520, found 307.0525.

Compound 18ad



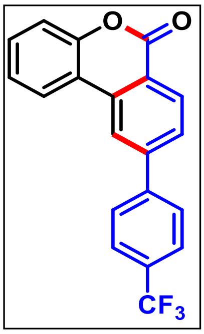
Yield:	56.6 mg (78%), White solid
Mp:	286 °C.
IR (neat):	ν_{max} 3014, 2969, 2945, 1738, 1437, 1367, 1216, 1092, 899, 772 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.47 (d, *J* = 8.0 Hz, 1H), 8.26 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.76 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.54-7.51 (m, 1H), 7.42-7.36 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.2, 151.7, 146.7, 138.7, 135.5, 132.5, 131.5, 130.9, 129.2, 127.8, 124.8, 123.5 122.9, 120.4, 120.1, 118.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{11}BrNaO_2$ $[M + Na]^+$, $[M + Na + 2]^+$: *m/z* 372.9835, 374.9814 found 372.9831, 374.9810.

Compound 18ae



Yield:	48.3 mg (71%), White solid
Mp:	265 °C.
IR (neat):	ν_{max} 3014, 2969, 2945, 1738, 1437, 1367, 1216, 1092, 899, 772 cm^{-1}

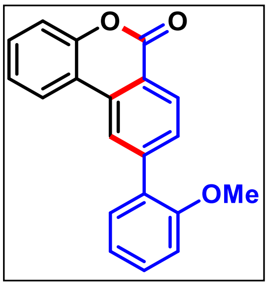
^{1}H NMR (500 MHz, CDCl$_3$): 8.48 (d, J = 8.0 Hz, 1H), 8.28 (d, J = 1.5 Hz, 1H), 8.14 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.83-7.77 (m, 5H), 7.54-7.50 (m, 1H), 7.40 -7.36 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.0, 151.7, 146.3, 143.3, 135.5, 131.6, 131.0 (q, $^{2}J_{C\text{-}F}$ = 32.5 Hz), 131.0 (s), 128.1, 126.2 (q, $^{3}J_{C\text{-}F}$ = 3.6 Hz), 124.8, 124.2 (q, $^{1}J_{C\text{-}F}$ = 270.6 Hz), 122.9, 120.9, 120.6, 118.1, 118.0ppm.

^{19}F NMR (471 MHz, CDCl$_3$): δ -62.6 ppm

HRMS (ESI-TOF): Calcd. for $C_{20}H_{11}F_3O_2$ [M + H] *m/z* 341.0784, found 341.0786.

Compound 18af



Yield: 45.3 mg (75%), White solid

Mp: 211 °C.

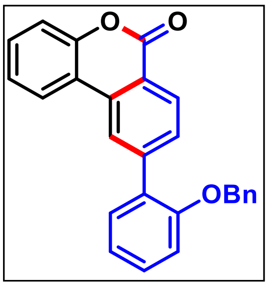
IR (neat): ν_{max} 3016, 2969, 1738, 1436, 1367, 1215, 1093, 899, 750 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.45 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 1.5 Hz, 1H), 8.14 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 7.78 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.52 – 7.48 (m, 1H), 7.46-7.43 (m, 1H), 7.40-7.34 (m, 2H), 7.29 (dq, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.23-7.22 (m, 1H), 7.01 (ddd, J_1 = 7.5, J_2 = 2.5 Hz, J_3 = 1.0 Hz 1H), 3.91 (s, 3H) ppm.

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 161.3, 160.3, 151.7, 147.8, 141.3, 135.3, 131.3, 130.7, 130.3, 128.1, 124.7, 122.9, 120.3, 120.2, 120.1, 118.2, 118.0, 114.1, 113.6, 55.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{15}O_3$ $[M + H]^+$ *m/z* 303.1016, found 303.1015.

Compound 18ag



Yield: 53.0 mg (70%), White solid

Mp: 198 °C.

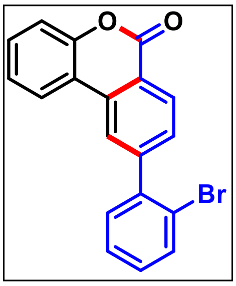
IR (neat): ν_{max} 3014, 2969, 1739, 1436, 1367, 1216, 1092, 899, 768 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.37 (d, *J* = 8.5 Hz, 1H), 8.33 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.75- 7.73 (m, 1H), 7.43 - 7.42 (m, 2H), 7.40-7.32 (m, 2H), 7.30 - 7.29 (m, 2H), 7.27 – 7.22 (m, 4H), 7.10-7.07 (m, 2H), 5.10 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.4, 155.8, 151.6, 145.4, 136.7, 134.5, 131.0, 130.5, 130.4, 130.3, 130.2, 129.5, 128.7, 128.1, 127.2, 124.5, 122.9 (2s), 121.7, 119.7, 118.4, 117.9, 113.4, 70.7ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{19}O_3$ $[M + H]^+$ *m/z* 379.1329, found 379.1331.

Compound 18ah



Yield: 51.0 mg (73%), White solid

Mp: 198 °C.

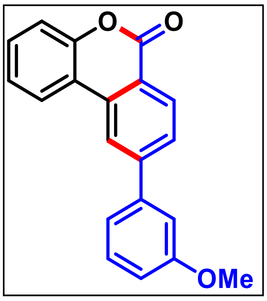
IR (neat): ν_{max} 3014, 2969, 1738, 1438, 1367, 1216, 1091, 898, 753 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.40 – 8.39 (m, 1H), 8.10 (s, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.45-7.42 (m, 1H), 7.40-7.37 (m, 1H), 7.35-7.32 (m, 2H), 7.29-7.20 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.1, 151.6, 147.7, 141.2, 134.7, 133.6, 131.1, 130.7, 130.5, 130.3, 130.0, 127.9, 124.7, 123.0, 122.9, 122.3, 120.4, 118.1, 118.0 ppm.

HRMS (ESI-TOF): Calcd. for $C_{19}H_{11}BrO_2$ $[M + H]^+$, $[M + H + 2]^+$ *m/z* 351.0015, 352.9995 found 351.0000, 352.9984.

Compound 18ai



Yield: 48.3 mg (80%), White solid

Mp: 213 °C.

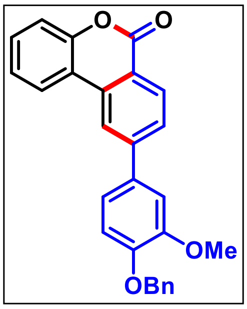
IR (neat): ν_{max} 3014, 2969, 1738, 1437, 1367, 1216, 1092, 900, 769 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46-8.42 (m, 1H), 8.27 (d, *J* = 11.5 Hz, 1H), 8.15-8.12 (m, 1H), 7.79-7.75 (m, 1H), 7.52-7.47 (m, 1H), 7.46-7.42 (m, 1H), 7.40-7.33 (m, 2H), 7.29-7.27 (m, 1H), 7.22 (q, *J* = 1.5 Hz, 1H), 7.01-7.00 (m, 1H), 3.91 (d, *J* = 2.4 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 161.1, 160.2, 151.5, 147.6, 141.1, 135.1, 131.1, 130.6, 130.2, 127.9, 124.6, 122.8, 120.2, 120.1, 119.9, 118.1, 117.9, 114.0, 113.4, 55.5 ppm.

HRMS (ESI-TOF): Calcd. for $C_{20}H_{14}NaO_3$ $[M + Na]^+$ *m/z* 325.0835, found 325.0836.

Compound 18aj



Yield: 64.5 mg (79%), White solid

Mp: 167 °C.

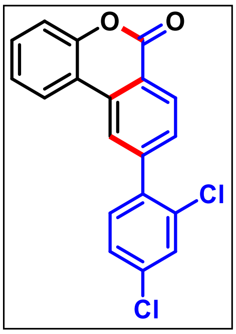
IR (neat): ν_{max} 3014, 2969, 1739, 1437, 1367, 1092, 900, 771 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, *J* = 8.5 Hz, 1H), 8.22 (s, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.50-7.47 (m, 3H), 7.41-7.33 (m, 5H), 7.23-7.20 (m, 2H), 7.02 (d, *J* = 8.5 Hz, 1H), 5.24 (s, 2H), 4.01 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 161.3, 151.7, 150.3, 149.2, 147.7, 137.0, 135.2, 133.1, 131.2, 130.6, 128.8, 128.1, 127.7, 127.4, 124.6, 122.9, 120.3, 119.7, 119.6, 118.3, 118.0, 114.5, 111.4, 71.2, 56.5 ppm.

HRMS (ESI-TOF): Calcd. for $C_{27}H_{21}O_4$ [M + H]$^+$ *m/z* 409.1434, found 409.1435.

Compound 18ak



Yield: 55.7 mg (82%), White solid

Mp: 228 °C.

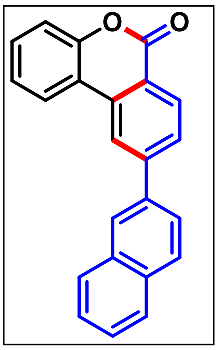
IR (neat): ν_{max} 3015, 2969, 1738, 1441, 1368, 1216, 1088, 906, 786 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.48 (d, *J* = 8.0 Hz, 1H), 8.16 (d, *J* = 1.5 Hz, 1H), 8.08 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.63 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.58 (d, *J* = 1.5, 1H), 7.53-7.50 (m, 1H), 7.42-7.34 (m, 4H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.0, 151.7, 145.0, 137.8, 135.3, 134.9, 133.3, 132.0, 130.9, 130.8, 130.3, 130.2, 127.7, 124.8, 123.0, 122.9, 120.8, 118.1, 118.0 ppm.

HRMS (ESI-TOF): Calcd. for $C_{19}H_{11}Cl_2O_2$ [M + H]$^+$ *m/z* 341.0131, found 341.0132.

Compound 18al



Yield: 47.0 mg (73%), White solid

Mp: 203 °C.

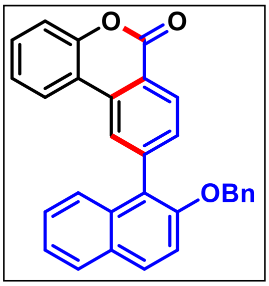
IR (neat): ν_{max} 3015, 2969, 1725, 1610, 1443, 1367, 1215, 1080, 899, 748 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.50 (d, *J* = 8.5 Hz, 1H), 8.41 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 8.17 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.97-7.95 (m, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.57-7.56 (m, 2H), 7.53-7.50 (m, 1H), 7.41-7.36 (m, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.3, 151.7, 147.8, 137.0, 135.3, 133.6, 133.4, 131.3, 130.7, 129.1, 128.6, 128.2, 127.9, 127.0, 126.9, 125.2, 124.7, 123.0, 120.4, 120.1, 118.2, 118.0 ppm.

HRMS (ESI-TOF): Calcd. for $C_{23}H_{15}O_2$ $[M + H]^+$ *m/z* 323.1067, found 323.1068.

Compound 18am



Yield: 59.9 mg (70%), White solid

Mp: 247.6°C.

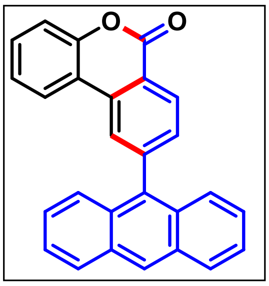
IR (neat): ν_{max} 3015, 2969, 1739, 1438, 1368, 1216, 1092, 900, 752 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 0.5 Hz, 1H)), 7.95-7.93 (m, 2H), 7.89-7.87 (m, 1H), 7.61 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.51-7.46 (m, 2H), 7.45-7.63 (m, 4H), 7.29-7.26 (m, 1H), 7.22-7.17 (m, 5H), 5.15 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 152.8, 151.6, 144.1, 136.8, 134.7, 133.1, 132.2, 130.5, 130.4, 130.3, 129.4, 128.6, 128.3, 128.0, 127.2, 127.1, 124.8 (2s) 124.6 (2s) 124.3, 123.1, 120.1, 118.3, 117.9, 115.6, 71.6 ppm.

HRMS (ESI-TOF): Calcd. for $C_{30}H_{21}O_3$ $[M + H]^+$ *m/z* 429.1485, found 429.1483.

Compound 18an



Yield: 52.8 mg (71%), White solid

Mp: 228°C.

IR (neat): ν_{max} 3015, 2969, 1739, 1437, 1367, 1228, 1216, 1092, 899, 771 cm^{-1}

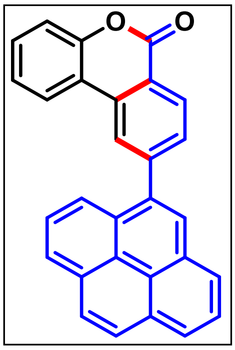
^1H NMR (500 MHz, $CDCl_3$): δ 8.64 (d, *J* = 8.0 Hz, 1H), 8.59 (s, 1H), 8.23 (d, *J* = 1.5Hz, 1H), 8.10 (d, *J* = 8.5Hz, 2H), 7.98 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.70 (dd, J_1 = 8.0,

J_2 = 1.5 Hz, 1H), 7.60 (dd, J_1 = 8.5, J_2 = 1.0 Hz, 2H), 7.52-7.49 (m, 3H), 7.45 (dd, J_1 = 8.5, J_2 = 1.0 Hz, 1H), 7.41-7.37 (m, 2H), 7.30-7.28 (m, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.3, 151.8, 146.5, 135.2, 135.0, 132.3, 131.4, 131.0, 130.8, 129.9, 128.7, 127.8, 126.3, 126.2, 125.5, 124.8, 124.7, 123.2, 120.7, 118.1 (2s) ppm.

HRMS (ESI-TOF): Calcd. for $C_{27}H_{17}O_2$ $[M + H]^+$ *m/z* 373.1223, found 373.1226.

Compound 18ao



Yield: 54.6 mg (69%), White solid

Mp: 269.5°C.

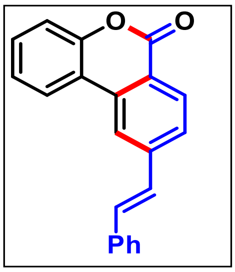
IR (neat): ν_{max} 3016, 2969, 1738, 1436, 1367, 1215, 1092, 900, 747 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, J = 8.0 Hz, 1H), 8.39 (d, J = 1.0 Hz, 1H), 8.30 (d, J = 7.5 Hz, 1H), 8.26 (d, J = 7.5 Hz, 1H), 8.22 (d, J = 7.5 Hz, 1H), 8.18-8.14 (m, 2H), 8.12-8.04 (m, 5H), 7.87 (dd, J_1 = 7.0, J_2 = 1.5 Hz, 1H), 7.54-7.51 (m, 1H), 7.46-7.44 (m, 1H), 7.35-7.32 (m, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 151.8, 148.4, 135.9, 135.1, 131.6 (2s), 131.5, 131.0, 130.9, 130.8, 128.6, 128.5, 128.3, 127.5, 127.4, 126.5, 125.8, 125.5, 125.1, 124.9, 124.8, 124.5, 123.9, 123.1, 120.2, 118.3, 118.1 ppm.

HRMS (ESI-TOF): Calcd. for $C_{29}H_{17}O_2$ $[M + H]^+$ *m/z* 397.1223, found 397.1221.

Compound 18ap



Yield: 38.7 mg (65%), White solid

Mp: 166-168°C.

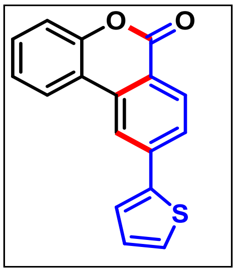
IR (neat): ν_{max} 3016, 2969, 1738, 1436, 1367, 1215, 1092, 900, 747 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.38 (d, *J* = 8.5 Hz, 1H), 8.16-8.13 (m, 2H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 7.0 Hz, 2H), 7.51-7.48 (m, 1H), 7.43-7.40 (m, 2H), 7.39-7.35 (m, 4H), 7.24 (d, *J* = 15.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.2, 151.7, 143.9, 136.5, 135.4, 133.1, 131.1, 130.7, 129.1, 128.9, 127.2 (2s), 126.6, 124.7, 122.9, 120.0, 119.8, 118.2, 118.0 ppm.

HRMS (ESI-TOF): Calcd. for $C_{21}H_{15}O_2$ $[M + H]^+$ *m/z* 299.1067, found 299.1069.

Compound 18aq



Yield: 41.1 mg (74%), White solid

Mp: 172.3°C.

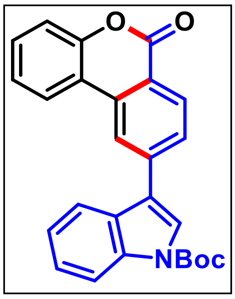
IR (neat): ν_{max} 3016, 2969, 1738, 1436, 1367, 1215, 1092, 900, 747 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.37 (d, *J* = 8.5 Hz, 1H), 8.25 (d, *J* = 1.5 Hz, 1H), 8.11-8.09 (m, 1H), 7.77-7.80 (m, 1H), 7.55-7.54 (m, 1H), 7.51-7.48 (m, 1H), 7.46-7.45 (m, 1H) 7.37-7.34 (m, 2H), 7.18-7.17 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.0, 151.7, 143.6, 140.7, 135.5, 131.5, 130.8, 128.7, 127.4, 126.4, 125.6, 124.7, 122.9, 119.9, 118.3, 117.9 (2s) ppm.

HRMS (ESI-TOF): Calcd. for $C_{17}H_{11}O_2S$ $[M + H]^+$ *m/z* 279.0474, found 279.047.

Compound 18ar



Yield: 56.7 mg (69%), White solid

Mp: 155.8°C.

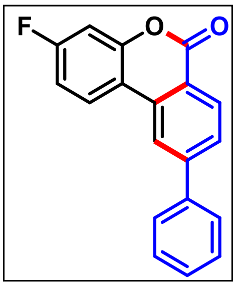
IR (neat): ν_{max} 3014, 2969, 1739, 1436, 1367, 1228, 1216, 1092, 898, 767 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.49 (d, *J* = 8.5 Hz, 1H), 8.39 (s, 1H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.15 (d, *J* = 7.5 Hz, 1H), 7.92 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.87 (d, *J* = 8.5 Hz, 1H), 7.54-7.51 (m, 1H), 7.45-7.36 (m, 4H), 1.73 (s, 9H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.0, 152.0, 149.7, 141.2, 136.5, 135.6, 131.4, 130.7, 128.6 (2s), 125.3, 124.7, 124.6, 123.7, 123.0, 121.2, 120.6, 120.2, 119.8, 118.4, 118.1, 116.0, 84.7, 28.5 ppm.

HRMS (ESI-TOF): Calcd. for $C_{26}H_{22}O_4N$ [M + H]$^+$ *m/z* 412.1543, found 412.1546.

Compound 18ba



Yield: 43.5 mg (75%), White solid

Mp: 203 °C.

IR (neat): ν_{max} 3014, 2969, 1738, 1436, 1367, 1215, 1092, 898, 772 cm^{-1}

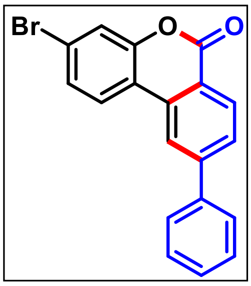
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.20 (s, 1H), 8.12 (dd, J_1 = 9.5, J_2 = 6.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.70 (d, *J* = 7.0 Hz, 2H), 7.55-7.52 (m, 2H), 7.49-7.46 (m, 1H), 7.11-7.08 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 164.0 (d, $^1J_{C\text{-}F}$ = 250.0 Hz), 160.7, 153.0 (d, $^3J_{C\text{-}F}$ = 12.4 Hz), 148.4, 140.0, 135.0, 131.5, 129.4, 129.1, 128.0, 127.7, 124.6 (d, $^3J_{C\text{-}F}$ = 12.3 Hz), 120.2, 119.7, 115.1 (d, $^4J_{C\text{-}F}$ = 3.6 Hz), 112.5 (d, $^2J_{C\text{-}F}$ = 28.3 Hz), 105.4 (d, $^2J_{C\text{-}F}$ = 21.3 Hz) ppm.

^{19}F NMR (471 MHz, CDCl$_3$): δ -108.2 ppm

HRMS (ESI- TOF): Calcd. for $C_{19}H_{12}FO_2$ [M + H]$^+$ *m/z* 291.0816, found 291.0818.

Compound 18ca



Yield: 49.2 mg (70%), White solid

Mp: 225 °C.

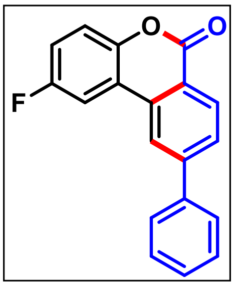
IR (neat): ν_{max} 3056, 2923, 1720, 1477, 1392, 1266, 1071, 859, 758cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.43 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 1.5 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.81 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 7.71-7.69 (m, 2H), 7.55-7.52 (m, 3H), 7.50-7.46 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 160.6, 151.9, 148.2, 139.5, 134.5, 131.5, 129.3, 129.1, 128.4, 128.0, 127.6, 124.1, 124.0, 121.1, 120.2, 119.8, 117.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{19}H_{11}BrNaO_2$ [M + Na]$^+$, [M + Na + 2]$^+$: m/z 372.9835, 374.9814 found 372.9836, 374.9816.

Compound 18da



Yield: 42.3 mg (73%), White solid

Mp: 225 °C.

IR (neat): ν_{max} 3056, 2923, 1720, 1477, 1392, 1266, 1071, 859, 758cm^{-1}

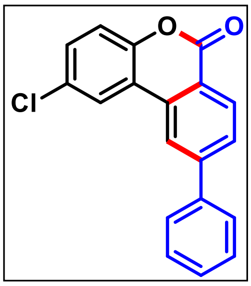
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.43 (d, J = 8.5 Hz, 1H), 8.14 (s, 1H), 7.81 (d, J = 8.0 Hz, 1H), 7.76 (dd, J_1 = 9.0, J_2 = 2.5 Hz, 1H), 7.69 (d, J = 7.0 Hz, 2H), 7.55-7.46 (m, 3H), 7.35-7.32 (m, 1H), 7.21-7.17 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 160.8, 159.4 (d, $^1J_{C\text{-}F}$ = 242.0 Hz), 148.1, 147.7 (d, $^5J_{C\text{-}F}$ = 1.4 Hz) , 139.4, 134.3 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 131.4, 129.4, 129.3, 128.9 (d, $^1J_{C\text{-}F}$ = 242.0 Hz), 127.6, 120.3, 119.9, 119.4 (2d, $^3J_{C\text{-}F}$ = 8.6, 8.8 Hz), 117.9 (d, $^2J_{C\text{-}F}$ = 24.1 Hz), 108.9 (d, $^2J_{C\text{-}F}$ = 24.6 Hz) ppm.

^{19}F NMR (471 MHz, CDCl$_3$): δ -117.1 ppm

HRMS (ESI- TOF): Calcd. for $C_{19}H_{12}FO_2$ [M + H]$^+$ m/z 291.0816, found 291.0820.

Compound 18ea



Yield: 46.0 mg (75%), White solid

Mp: 215 °C.

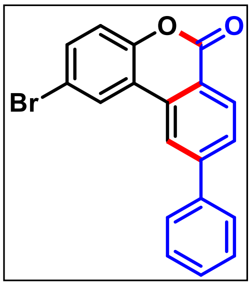
IR (neat): ν_{max} 3017, 2924, 1738, 1450, 1369, 1229, 1213, 757 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.45 (d, *J* = 7.5 Hz, 1H), 8.19 (d, *J* = 1.5 Hz, 1H), 8.08 (d, *J* = 2.5 Hz, 1H), 7.83 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.72-7.71 (m, 2H), 7.69-7.53 (m, 2H), 7.50-7.47 (m, 1H), 7.44 (dd, J_1 = 8.5, J_2 = 2.5 Hz, 1H), 7.32 (d, *J* = 9.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 160.7, 150.1, 148.2, 139.4, 134.1, 131.5, 130.6, 132.2, 129.4, 129.1, 128.7, 127.6, 122.7, 120.3, 120.0, 119.6, 119.4 ppm.

HRMS (ESI- TOF): Calcd. for $C_{19}H_{12}ClO_2$ $[M + H]^+$ *m/z* 307.0520, found 307.0516.

Compound 18fa



Yield: 49.6 mg (71%), White solid

Mp: 210 °C.

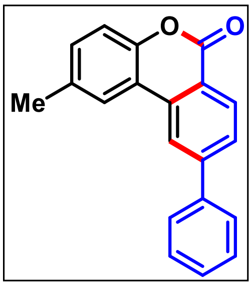
IR (neat): ν_{max} 3014, 2969, 1738, 1436, 1367, 1216, 1092, 899, 770 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.43 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 2.0 Hz, 1H), 8.18 (d, *J* = 1.5 Hz, 1H), 7.81 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.70-7.69 (m, 2H), 7.57 (dd, J_1 = 8.5, J_2 = 2.5 Hz, 1H), 7.54-7.51 (m, 2H), 7.48-7.45 (m, 1H), 7.24 (d, *J* = 0.5 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 160.6, 150.5, 148.2, 139.4, 134.0, 133.5, 131.5, 129.4, 129.1, 128.7, 125.8, 120.3, 120.0 (2s), 119.7, 117.6 ppm.

HRMS (ESI- TOF): Calcd. for $C_{19}H_{11}BrNaO_2$ $[M + Na]^+$, $[M + Na + 2]^+$: *m/z* 372.9835, 374.9814 found 372.9832, 374.9812.

Compound 18ga



Yield: 44.6 mg (78%), White solid

Mp: 181 °C.

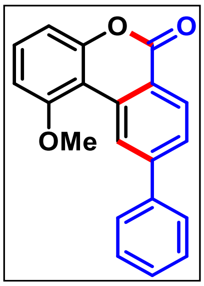
IR (neat): ν_{max} 3014, 2969, 1739, 1437, 1367, 1215, 1078, 899, 796 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (dd, J_1 = 8.0, J_2 = 3.0 Hz, 1H), 8.23 (s, 1H), 7.88 (s, 1H), 7.76-7.74 (m, 1H), 7.71 (d, J = 7.5 Hz, 2H), 7.55-7.52 (m, 2H), 7.48-7.45 (m, 1H), 7.28-7.26 (m, 1H), 7.25-7.23 (m, 1H), 2.46 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 149.7, 147.7, 139.8, 135.3, 134.2, 131.6, 131.2, 129.2, 128.9, 127.8, 127.6, 122.8, 120.1 (2s), 117.8, 117.7, 21.2 ppm.

HRMS (ESI- TOF): Calcd. for $C_{20}H_{15}O_2$ $[M + H]^+$ *m/z* 287.1067, found 287.1072.

Compound 18ha



Yield: 48.9 mg (81%), White solid

Mp: 172 °C.

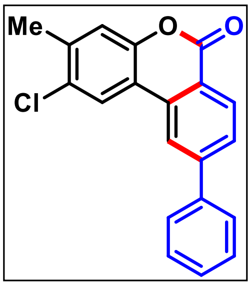
IR (neat): ν_{max} 2964, 2923, 1731, 1607, 1489, 1394, 1239, 1080, 848, 792 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 9.29 (d, J = 1.5 Hz, 1H), 8.49 (d, J = 8.0 Hz, 1H), 7.77 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.73-7.72 (m, 2H), 7.55-7.52 (m, 2H), 7.48-7.40 (m, 2H), 7.05 (dd, J_1 = 8.5, J_2 = 1.0 Hz, 1H), 6.90 (d, J = 8.5 Hz, 1H), 4.07 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.5, 158.7, 153.0, 147.5, 140.6, 135.2, 130.8, 130.1, 129.2, 128.6, 127.7, 127.1, 126.3, 119.8, 110.7, 108.6, 107.1, 56.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{20}H_{14}O_3Na$ [M + Na]$^+$ *m/z* 325.0835, found 325.0839.

Compound 18ia



Yield: 46.1 mg (75%), White solid

Mp: 172 °C.

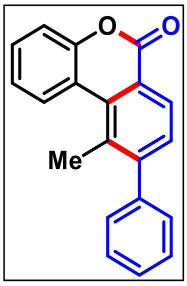
IR (neat): ν_{max} 3061, 2923, 1738, 1611, 1440, 1389, 1271, 1080, 876, 779 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.42 (d, *J* = 7.0 Hz, 1H), 8.15 (d, *J* = 1.5 Hz, 1H), 8.05 (s, 1H), 7.77 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.71-7.69 (m, 2H), 7.55-7.51 (m, 2H), 7.49-7.46 (m, 1H), 7.23 (d, *J* = 0.5 Hz, 1H), 2.46 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.9, 149.9, 148.1, 139.5, 139.2, 134.3, 131.4, 130.6, 129.3, 129.1, 128.2, 127.6, 123.0, 120.0, 119.9, 119.7, 117.3, 20.5 ppm.

HRMS (ESI- TOF): Calcd. for $C_{20}H_{14}ClO_2$ [M + H]$^+$*m/z* 321.0677, found 321.0679.

Compound 18ja



Yield: 45.2 mg (79%), White solid

Mp: 172 °C.

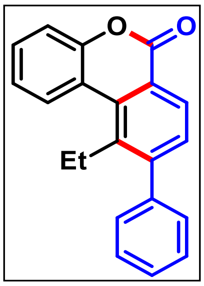
IR (neat): ν_{max} 3014, 2969, 1739, 1436, 1367, 1228, 1093, 898, 768 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.0 Hz, 1H), 8.32 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.51-7.48 (m, 4H), 7.46-7.42 (m, 2H), 7.40-7.38 (m, 2H), 7.35-7.32 (m, 1H), 2.71 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.9, 151.6, 151.0, 141.6, 135.1, 132.9, 130.5, 129.9, 129.3, 128.7, 128.4, 128.0, 127.9, 123.9, 122.1, 119.9, 118.1, 22.9 ppm.

HRMS (ESI- TOF): Calcd. for $C_{20}H_{15}O_2$ [M + H]$^+$*m/z* 287.1067, found 287.1062.

Compound 18ka



Yield: 43.3 mg (75%), White solid

Mp: 172 °C.

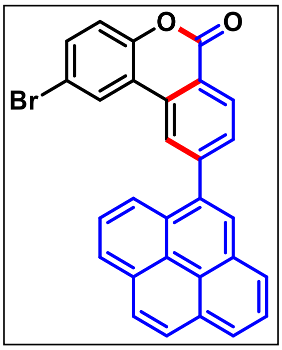
IR (neat): ν_{max} 3027, 2966, 1719, 1465, 1372, 1224, 1099, 854, 753 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.39 (d, J = 8.0 Hz, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.51-7.40 (m, 6H), 7.35-7.31 (m, 3H), 3.16 (q, J = 7.5 Hz, 2H), 1.17 (t, J = 7.5 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.9, 151.4, 150.9, 141.7, 139.2, 133.8, 131.1, 129.9, 128.8, 128.4, 127.7, 127.3, 124.3, 122.6, 119.4, 118.3, 25.1, 14.5 ppm.

HRMS (ESI- TOF): Calcd. for $C_{21}H_{17}O_2$ $[M + H]^+$ m/z 301.1223, found 301.1226.

Compound 18fo



Yield: 59.9 mg (63%), White solid

Mp: 327 °C.

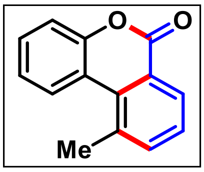
IR (neat): ν_{max} 3030, 2969, 1738, 1455, 1372, 1229, 1099, 848, 757 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, J = 8.0 Hz, 1H), 8.31-8.29 (m, 2H), 8.27 (dd, J_1 = 1.0, J_2 = 8.0 Hz, 1H), 8.23 (dd, J_1 = 7.5, J_2 = 0.5 Hz, 1H), 8.20 (d, J = 2.5 Hz, 1H), 8.18-8.14 (m, 2H), 8.10-8.05 (m, 3H), 8.03 (d, J = 8.0 Hz, 1H), 7.91 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.60 (dd, J_1 = 2.0, J_2 = 9.0 Hz, 1H), 7.32 (d, J = 8.5 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 160.8, 150.7, 148.8, 135.5, 133.8, 133.6, 132.2, 131.7, 131.6, 131. 0 (2s), 128.7, 128.5, 128.4, 127.5, 127.4, 126.5, 125.9 (2s), 125.5, 125.1, 125.0, 124.9, 124.3, 123.9, 120.1 (2s), 119.8, 117.7 ppm.

HRMS (ESI- TOF): Calcd. for $C_{29}H_{16}BrO_2$ $[M + H]^+$, $[M + H + 2]^+$: *m/z* 475.0328, 477.0308 found 475.0324, 477.0309.

Compound 18js



Yield: 59.9 mg (26%), White solid

Mp: 158 °C.

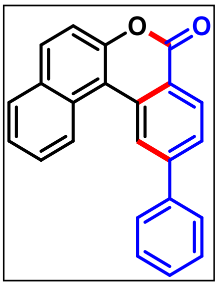
IR (neat): ν_{max} 2956, 2924, 1713, 1444, 1376, 1231, 1091, 846, 750 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 8.39 (d, *J* = 7.5Hz, 1H), 8.33 (d, *J* = 8.5Hz, 1H), 7.66 (d, *J* = 7.5 Hz, 1H), 7.50-7.47 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H); 7.36-7.33 (m, 1H), 2.92 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.9, 151.4, 139.2, 135.2, 133.7, 129.8, 129.4, 128.4, 127.3, 124.1. 123.0, 119.9, 118.1, 25.5 ppm.

HRMS (ESI- TOF): Calcd. for $C_{14}H_{11}O_2$ $[M + H]^+$ *m/z* 211.0754, found 211.0750.

Compound 18la



Yield: 51.0 mg (79%), White solid

Mp: 172 °C.

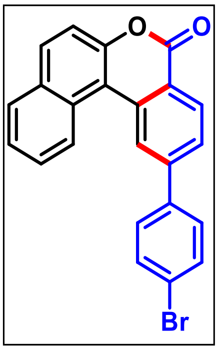
IR (neat): ν_{max} 3018, 2924, 1724, 1460, 1341, 1216, 1067, 848, 749 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.84-8.82 (m, 2H), 8.56 (d, *J* = 8.5 Hz, 1H), 7.98-7.94 (m, 2H), 7.85 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.75-7.73 (m, 2H), 7.71-7.68 (m, 1H), 7.59-7.47 (m, 5H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 150.7, 147.4, 140.0, 136.0, 131.8 (2s), 131.4, 129.7, 129.6, 129.4, 128.9, 128.1, 127.7, 127.4, 125.6, 125.1 (2s), 121.2, 117.8, 112.8 ppm.

HRMS (ESI- TOF): Calcd. for $C_{23}H_{15}O_2$ [M + H]$^+$ *m/z* $C_{23}H_{15}O_2$ 323.1067, found 323.1070.

Compound 18la



Yield: 61.2 mg (75%), White solid

Mp: 222 °C.

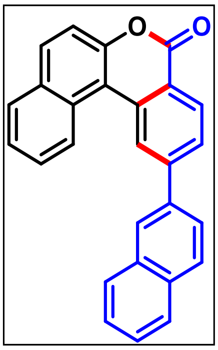
IR (neat): ν_{max} 2958 2922, 1730, 1462, 1368, 1263, 1010, 817, 735 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.80 (s, 1H), 8.79 (d, *J* = 6.5 Hz, 1H), 8.56 (d, *J* = 8.5 Hz, 1H), 7.99-7.95 (m, 2H), 7.80 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.71-7.68 (m, 3H), 7.61-7.57 (m, 3H), 7.52 (d, *J* = 9.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.3, 150.8, 146.2, 138.9, 136.2, 132.6, 132.0, 131.9, 131.6, 129.7 (2s), 129.3, 128.2, 127.1, 125.6, 125.0, 123.5, 121.5, 117.8, 112.7 ppm.

HRMS (ESI- TOF): Calcd. for $C_{23}H_{14}BrO_2$ [M + H]$^+$, [M + H + 2]$^+$: *m/z* 401.0172, 403.0151, found 401.0171, 403.0154.

Compound 18ll



Yield: 54.4 mg (73%), White solid

Mp: 235 °C.

IR (neat): ν_{max} 3055, 2962, 1725, 1458, 1340, 1216, 1052, 848, 750 cm^{-1}

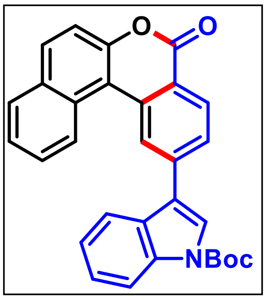
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (s, 1H), 8.86 (d, *J* = 8.5 Hz, 1H), 8.59 (d, *J* = 8.5 Hz, 1H), 8.17 (s, 1H), 8.02 (d, *J* = 8.5 Hz, 1H) 7.98-7.92 (m, 5H), 7.84 (dd, J_1 = 8.5, J_2

= 1.5 Hz, 1H), 7.71-7.68 (m, 1H), 7.59-7.55 (m, 3H), 7.52 (d, *J* = 8.5 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.4, 150.8, 147.4, 137.3, 136.1, 133.7, 133.4, 131.9, 131.8, 131.5, 129.8, 129.6, 129.2, 128.6, 128.1, 127.9, 127.6, 127.0(3s), 125.6, 125.4, 125.3, 125.1, 121.2, 117.8, 112.9 ppm.

HRMS (ESI- TOF): Calcd. for $C_{27}H_{17}O_2$ 373 [M + H]$^+$ *m/z* 373.1223, found 373.1223.

Compound 18lr



Yield: 62.7 mg (68%), White solid

Mp: 242 °C.

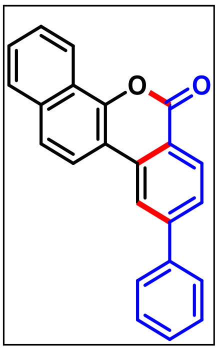
IR (neat): ν_{max} 3006, 2980, 1725, 1455, 1366, 1215, 1064, 840, 764cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.92 (s, 1H), 8.85 (d, *J* = 8.5 Hz, 1H), 8.58 (d, *J* = 8.0 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.99-7.94 (m, 3H), 7.91 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 2H), 7.69-7.65 (m, 1H), 7.58-7.55 (m, 1H), 7.53(d, *J* = 10.0 Hz, 1H), 7.46-7.43 (m, 1H), 7.39-7.35 (m, 1H), 1.73 (s, 9H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.4, 150.8, 149.7, 140.6, 136.2, 136.1, 131.8, 131.5, 129.7, 129.6, 128.5, 128.0, 127.8, 125.6, 125.4, 125.3, 125.1, 124.6, 123.7, 121.1, 120.9, 119.7, 117.9, 115.9, 112.8, 84.7, 28.4 ppm.

HRMS (ESI- TOF): Calcd. for $C_{30}H_{24}O_4N$ [M + H]$^+$ *m/z* 462.1700, found 462.1701.

Compound 18ma



Yield: 47.6 mg (74%), White solid

Mp: 172 °C.

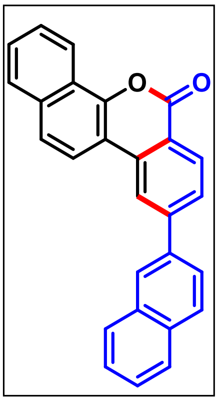
IR (neat): ν_{max} 3015, 2969, 1739, 1436, 1367, 1216, 1092, 899, 772 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.61 (d, *J* = 8.0 Hz, 1H), 8.52 (d, *J* = 8.0 Hz, 1H), 8.37 (d, *J* = 1.0 Hz, 1H), 8.15 (d, *J* = 8.5 Hz, 1H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.81 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.79 (d, *J* = 9.0 Hz, 1H), 7.76-7.74 (m, 2H), 7.66-7.60 (m, 2H), 7.57-7.54 (m, 2H), 7.50-7.47 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.2, 147.9, 147.5, 139.8, 135.8, 134.4, 131.2, 129.3, 128.9, 128.0, 127.7, 127.6, 127.2, 124.5, 124.0, 122.4, 120.5, 119.9, 119.2, 113.1 ppm.

HRMS (ESI- TOF): Calcd. for $C_{23}H_{15}O_2$ [M + H]$^+$ *m/z* 323.1067, found 323.1068.

Compound 18ml



Yield: 52.8 mg (71%), White solid

Mp: 172 °C.

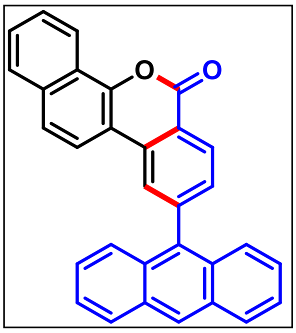
IR (neat): ν_{max} 3014, 2928, 1739, 1442, 1368, 1228, 1212, 898, 802 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.60-8.58 (m, 1H), 8.53 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 1.0 Hz, 1H), 8.19-8.16 (m, 2H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.98-7.97 (m, 1H), 7.93-7.90 (m, 2H), 7.88 (dd, J_1 = 7.0, J_2 = 2.0 Hz, 1H), 7.85 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.65-7.61 (m, 2H), 7.59-7.55 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.3, 147.9, 147.7, 137.1, 136.0, 134.5, 133.7, 133.4, 131.4, 129.1, 128.6, 128.1, 128.0, 127.9, 127.8, 127.3, 127.0 (2s), 126.9, 125.3, 124.6, 124.1, 122.5, 120.8, 120.0, 119.3, 113.2 ppm.

HRMS (ESI- TOF): Calcd. for $C_{27}H_{17}O_2$ [M + H]$^+$ *m/z* 373.1223, found 373.1224.

Compound 18mn



Yield: 58.3 mg (69%), White solid

Mp: 172 °C.

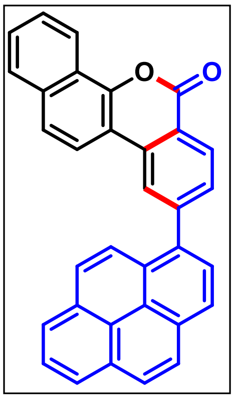
IR (neat): ν_{max} 3015, 2969, 1739, 1436, 1367, 1216, 1092, 899, 772 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.71 (d, J = 8.0 Hz, 1H), 8.68 (d, J = 8.0 Hz, 1H), 8.61 (s, 1H), 8.30 (s, 1H), 8.12 (d, J = 8.5 Hz, 2H), 7.98 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 7.72 (d, J = 8.5 Hz, 2H), 7.68 (d, J = 7.5 Hz, 1H), 7.64 (d, J = 8.5 Hz, 3H), 7.53-7.50 (m, 2H), 7.42-7.39 (m, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 161.4, 147.9, 146.7, 135.8, 135.1, 134.6, 132.0, 131.4, 131.0, 130.0, 128.8, 128.2, 127.9, 127.8, 127.4, 126.3, 126.2 125.5, 125.1, 124.7, 124.1, 122.6, 120.6, 119.5, 113.2 ppm.

HRMS (ESI- TOF): Calcd. for $C_{31}H_{19}O_2$ $[M + H]^+$ m/z 423.1380, found 423.1384.

Compound 18mo



Yield: 52.0 mg (65%), White solid

Mp: 225 °C.

IR (neat): ν_{max} 3017, 2968, 1739, 1440, 1370, 1229, 1215, 845, 752 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.67 (d, J = 8.0 Hz, 2H), 8.45 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.26 (d, J = 7.5 Hz, 1H), 8.22 (d, J = 7.5 Hz, 1H), 8.18-8.16 (m, 3H), 8.11-8.05 (m, 4H), 7.90 (d, J = 8.0 Hz, 2H), 7.76 (d, J = 8.0 Hz, 1H) 7.70-7.62 (m, 2H) ppm.

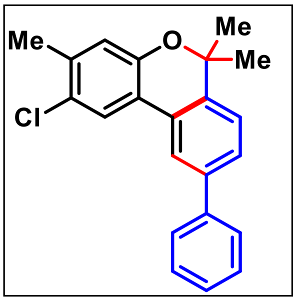
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 161.4, 148.5, 147.8, 136.0, 135.7, 134.5, 131.6 (2s), 131.2, 131.0, 130.9, 128.6, 128.5, 128.3, 128.2, 127.9, 127.5, 127.4, 127.3, 126.5, 125.8, 125.5, 125.1, 124.9, 124.7, 124.6, 124.2, 124.1, 122.6, 120.1, 119.4, 113.2 ppm.

HRMS (ESI- TOF): Calcd. for $C_{33}H_{19}O_2$ $[M + H]^+$ *m/z* 447.1380, found 447.1377.

3.5 Synthesis of 2-Chloro-3,6,6-trimethyl-9-phenyl-6H-benzo[c]chromene (19ia)

A solution of **18ia** (20.0 mg, 0.0625 mmol) in THF (1.0 mL) was added drop-wise to a solution of MeLi (1.6 M in Et_2O, 400 µL, 0.625 mmol) at 0˚C. The mixture was stirred 45 min, warmed to rt, and stirred for 1 h more. The reaction mixture was then cooled to 0˚C and quenched with sat. NH_4Cl solution. The aqueous layer was extracted with Et_2O (3 x 3 mL). The combined organic extract was washed with water (10 mL), then brine (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The crude mixture was taken up in DCM (500 µL), treated with TFA (1µL, 0.012 mmol) and allowed to stir until the reaction was complete (TLC). The reaction mixture was diluted with Et_2O, washed with water (10 mL), then brine (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was purified by silica gel chromatography by eluting with ethyl acetate/hexane (1:49) to give **19ia** as a white solid.

Compound 19ia



Yield: 17.8 mg (85%), White solid

Mp: 190 °C.

IR (neat): ν_{max} 3058, 2973, 2912, 1622, 1575, 1480, 1392, 1282, 1123, 1045, 879, 759 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.0 Hz, 1H), 7.74 (s, 1H), 7.64-7.62 (m, 2H), 7.52 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 7.49-7.46 (m, 2H), 7.40-7.37 (m, 1H) 7.30 (d, *J* = 8.0 Hz, 1H), 6.85 (s, 1H), 2.36 (s, 3H), 1.66 (s, 6H) ppm.

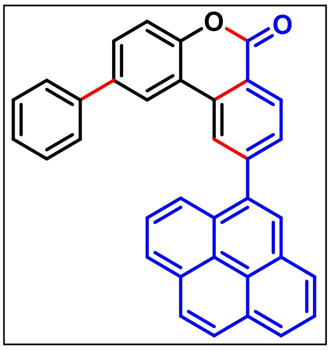
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 151.5, 141.1, 140.9, 138.3, 137.4, 129.0, 128.3, 127.7, 127.3, 127.1, 127.0, 124.0, 123.2, 121.7, 121.0, 120.4, 78.0, 27.8, 20.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{22}H_{20}ClO$ $[M + H]^+$ *m/z* 335.1197, found 335.1198.

3.6 Syntheisis of 2-Phenyl-9-(pyren-4-yl)-6H-benzo[c]chromen-6-one (20fo)

A mixture of **18fo** (20.0 mg, 0.042 mmol), $PhB(OH)_2$ (7.7 mg, 0.063 mmol), $Pd(OAc)_2$ (1.0 mg, 0.0042 mmol), and Na_2CO_3 (0.042 mmol) in DMF/H_2O (2.0 mL, 1:1) was heated to 110 °C and stirring continued at this temperature for 12 h. The reaction mixture was quenched with cold water (5 mL) and extracted with EtOAc 2 x 5 mL). The combined organic extract was washed with brine (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The crude mixture was purified by silica gel chromatography by eluting with ethyl acetate/hexane (1:19) to give **20fo** as off-white solid. The compound probably exists as a mixture of isomers (maybe diastereomers with 2:1 ratio) but we have not checked this point further.

Compound 20fo



Yield: 14.1 mg (71%), White solid

Mp: > 350.

IR (neat): ν_{max} 3043, 2922, 1726, 1459, 1409, 1271, 1138, 844, 759 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ **Major isomer**: δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.45 (d, *J* = 1.5 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.26-8.25 (m, 2H), 8.20 (d, *J* = 7.5 Hz, 1H), 8.18-8.13 (m, 2H), 8.12-8.10 (m, 2H), 8.07 (d, *J* = 6.0 Hz, 1H), 8.06-8.04 (m, 1H), 7.90-7.86 (m, 1H), 7.74 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 7.61-7.59 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.40 (m, 2H), 7.35-7.31 (m, 1H). **Minor isomer**: δ 8.60 (d, *J* = 8.0 Hz, 1H), 8.39 (d, *J* = 1.5 Hz, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.26-8.25 (m, 2H), 8.20 (d, *J* = 7.5 Hz, 1H), 8.18-8.13 (m, 2H), 8.12-8.10 (m, 2H), 8.07 (d, *J* = 6.0 Hz, 1H), 8.06-8.04 (m, 1H), 7.90-7.86 (m, 1H), 7.74 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 7.61-7.59 (m, 2H), 7.54-7.51 (m, 1H), 7.47-7.40 (m, 2H), 7.35-7.31 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ **Major isomer**: δ 161.3, 151.8, 151.2, 148.5, 140.1, 138.2, 135.9, 135.0, 131.6, 131.5, 131.0, 130.9, 129.8, 129.1, 128.6, 128.3, 127.8, 127.5, 127.3 (2s), 126.5, 125.8, 125.5, 125.1, 124.9, 124.8, 124.5, 123.9, 123.1, 121.5, 120.3, 118.4, 118.3 ppm. **Minor isomer** (observed peaks): δ

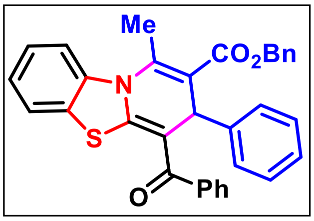
161.4, 151.8, 148.4, 140.2, 135.9, 135.1, 130.8, 128.5, 125.1, 124.5, 123.1, 121.5, 120.2, 118.4, 118.1 ppm.

HRMS (ESI- TOF): Calcd. for $C_{35}H_{21}O_2$ $[M + H]^+$ m/z 473.1536, found 473.1532.

3.7 Synthesis of Compounds 21aa-ia, 21ab, 21ic, 21id, 21ae, 21af-ag, and 21ij: Representative Procedure for 21aa

A Schlenk tube was charged with 2-acyl tethered benzothiazole **15a** (50.7 mg, 0.2 mmol), β-acetoxy allenoate **12a** (64.5 mg, 0.20 mmol) in 2.0 mL of toluene. Subsequently, DBU (6.0 µL, 0.04 mmol) was added at 100 °C (oil bath), and the mixture stirred at the same temperature for 12 h and progress of the reaction was monitored using TLC. After completion of the reaction, 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 (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **21aa** was then purified by silica gel column chromatography using ethyl acetate/hexane (10:90) as the eluent.

Compound 21aa



Yield: 77.4 mg (75%), Yellow solid

Mp: 185 °C.

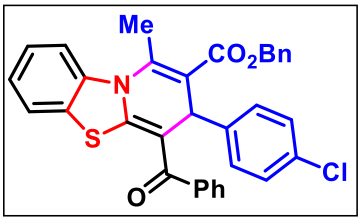
IR (neat): ν_{max} 3045, 1699, 1628, 1470, 1317, 1199, 1094, 904, 719 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.61 (dd, $J_1 = 7.5$, $J_2 = 1.5$ Hz, 1H), 7.44 (dd, $J_1 = 7.5$, $J_2 = 1.5$ Hz, 2H), 7.39-7.36 (m, 2H), 7.33-7.30 (m, 3H), 7.28-7.25$_7$ (m, 3H), 7.25$_5$-7.24 (m, 1H), 7.23-7.21 (m, 2H), 7.06-7.05 (m, 3H), 6.83-6.81 (m, 2H), 5.65 (s, 1H), 5.27 (d, $J = 12.5$ Hz, 1H), 5.20 (d, $J = 12.5$ Hz, 1H), 2.70 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 192.2, 167.2, 155.5, 144.3, 143.8, 139.5, 136.9, 135.9, 130.3, 130.0, 128.8, 128.7, 128.4, 128.3, 128.2, 127.7, 126.9, 126.6, 125.8, 124.8, 123.2, 1167, 115.7, 105.0, 66.9, 40.9, 19.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{33}H_{26}NSO_3$ 516.1628, found 516.1623.

Compound 21ba



Yield: 80.3 mg (73%), Yellow solid

Mp: 181 °C.

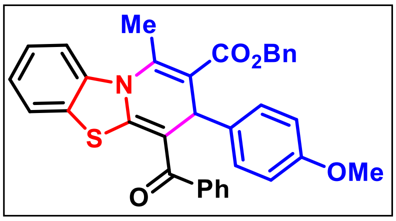
IR (neat): ν_{max} 2924, 1701, 1624, 1477, 1358, 1258, 1198, 1094, 985, 748 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.67 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.43 (d, *J* = 8.5 Hz, 2H), 7.39-7.37 (m, 3H), 7.35-7.29 (m, 6H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.5 Hz, 2H), 5.65 (s, 1H), 5.32-5.25 (m, 2H), 2.75 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 192.0, 167.0, 155.6, 144.5, 142.2, 139.3, 136.7, 136.0, 132.6, 130.4, 130.0, 128.8 (1s), 128.5, 128.4, 128.2, 128.0, 127.5, 126.9, 124.9, 123.2, 116.7, 115.3, 104.6, 67.0, 40.4, 19.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{33}H_{25}NClSO_3$ 550.1238, found 550.1237.

Compound 21ca



Yield: 86.2 mg (79%), Yellow solid

Mp: 201 °C.

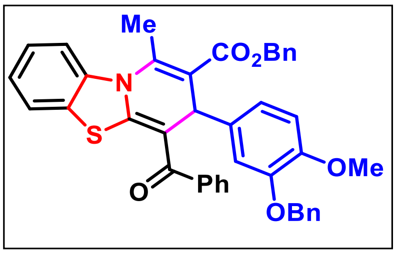
IR (neat): ν_{max} 2924, 1702, 1165, 1458, 1366, 1265, 1175, 1029, 969, 754 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.46 (d, J_1 = 8.0 Hz, 2H), 7.42-7.41 (m, 2H), 7.35-7.34 (m, 3H), 7.32-7.29 (m, 3H), 7.28-7.25 (m, 3H), 6.76 (d, *J* = 8.5 Hz, 2H), 6.62-6.61 (m, 2H), 5.59 (s, 1H), 5.29-5.22 (m, 2H), 3.68 (s, 3H), 2.71 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 192.2, 167.2, 158.5, 155.3, 143.9, 139.5, 136.8, 136.0, 135.9, 130.2, 130.0, 128.7, 128.3 (1s), 128.1, 127.6 (1s), 125.7 (1s), 123.1, 116.7, 116.0, 114.1, 105.3, 66.8, 55.3, 40.1, 19.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{33}H_{26}NSO_3$ 516.1628, found 516.1623.

Compound 21da



Yield: 88.6 mg (68%), Yellow solid

Mp: 214 °C.

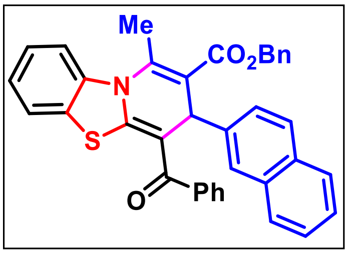
IR (neat): ν_{max} 2923, 1707, 1677, 1462, 1376, 1268, 1150, 1026, 924, 754 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.63 (dd, J_1= 8.0, J_2= 1.0 Hz, 1H), 7.48-7.46 (m, 2H), 7.44-7.40 (m, 2H), 7.36-7.34 (m, 4H), 7.33-7.32 (m, 2H), 7.31-7.30 (m, 3H), 7.29-7.28 (m, 3H), 7.27-7.25 (m 2H), 6.59 (d, J = 8.5 Hz, 1H), 6.37 (dd, J_1= 8.5, J_2= 2.0 Hz, 1H), 6.31 (d, J = 2.0 Hz, 1H), 5.58 (s, 1H), 5.27-5.22 (m, 2H), 5.01 (s, 2H), 3.45 (s, 3H), 2.73 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 192.1, 167.2, 155.3, 149.7, 147.3,144.2, 139.8, 137.5, 137.2, 136.9, 136.0, 130.2, 130.1, 128.9, 128.6, 128.4, 128.3, 128.1, 127.9, 127.7, 127.4, 125.8, 124.7, 123.2, 118.5, 116.6, 116.0, 114.5, 110.8, 105.6, 71.3, 66.8, 55.7, 40.6, 19.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{41}H_{34}NSO_5$ 652.2152, found 652.2159.

Compound 21ea



Yield: 79.2 mg (70%), Yellow solid

Mp: 202 °C.

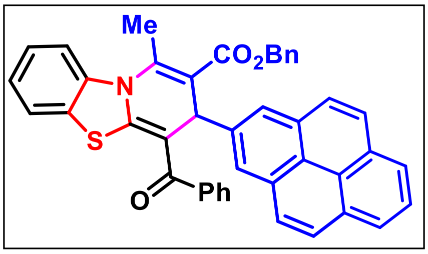
IR (neat): ν_{max} 2929, 1711, 1633, 1454, 1275, 1217, 1151, 1020, 975, 750 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.61-7.60 (m, 1H), 7.56 (d, J = 7.0 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.44-7.43 (m, 1H), 7.40 (d, J = 7.5 Hz, 2H), 7.34-7.29 (m, 2H), 7.28-7.26 (m, 5H), 7.23-7.19 (m, 4H), 7.17-7.16 (m, 2H), 7.09 (br s, 1H), 7.00 (dd, J_1 = 8.5, J_2 = 0.5 Hz, 1H), 5.75 (s, 1H), 5.23-5.17 (m, 2H), 2.65 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 192.2, 167.2, 155.7, 144.5, 141.1, 139.5, 136.8, 135.9, 133.4, 132.5, 130.3, 129.9, 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 127.6, 127.5, 126.0, 1288, 125.7, 125.2, 125.0, 124.8, 123.2, 116.8, 115.5, 104.8, 66.9,41.1, 19.4 ppm.

HRMS (ESI- TOF): Calcd. for $C_{37}H_{28}NSO_3$ 566.1784, found 566.1781.

Compound 21fa



Yield: 83.2 mg (65%), Yellow solid

Mp: 215 °C.

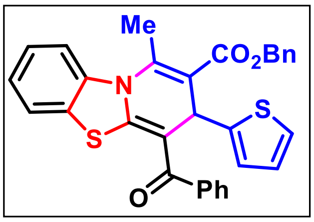
IR (neat): ν_{max} 2925, 1704, 1677, 1462, 1268, 1115, 1016, 754 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 78.19-8.11 (m, 2H), 8.04-7.92 (m, 6H), 7.71 (dd, J_1= 15.5, J_2= 7.5 Hz, 2H), 7.62 (d, J = 8.5 Hz, 1H), 7.51 (d, J = 8.5 Hz, 2H), 7.37-7.36 (m, 2H), 7.30-7.28 (m, 3H), 7.24-7.20 (m, 2H), 7.18-7.14 (m, 3H), 6.56 (s, 1H), 5.17 (d, J = 11.5 Hz, 1H), 5.04 (d, J = 12.0 Hz, 1H), 2.67 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 193.0, 167.6, 155.6, 142.3, 139.8, 138.1, 136.9, 135.6, 131.5, 130.7, 130.5, 130.0, 129.9, 128.6 (2s), 128.4 (2s), 128.0, 127.4, 127.3, 127.2, 127.0, 126.6, 126.0, 125.9, 125.5, 125.1, 124.9 (2s), 124.7 (2s), 123.3, 123.2, 117.4, 116.5, 106.2, 67.1, 37.8, 19.6 ppm.

HRMS (ESI- TOF): Calcd. for $C_{43}H_{30}NO_3S$ 640.1941, found 640.1939.

Compound 21ga



Yield: 77.4 mg (75%), Yellow solid

Mp: 185 °C.

IR (neat): ν_{max} 2957, 1703, 1625, 1471, 1328, 1214, 1105, 1047, 882, 706 cm^{-1}

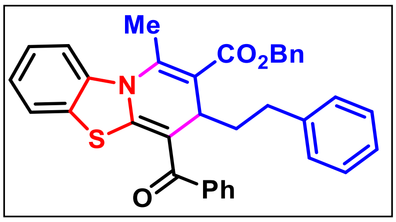
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (dd, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.44 (d, J = 9.5 Hz, 2H), 7.36-7.34 (m, 2H), 7.33-7.28 (m, 2H), 7.27-7.23 (m, 4H), 7.21-7.18 (m, 3H), 6.89 (dd, J_1 = 5.0, J_2 = 1.0 Hz, 1H), 6.66 (dd, J_1 = 4.5, J_2 = 3.5 Hz, 1H), 6.41

(dd, J_1 =2.0, J_2 = 1.0 Hz, 1H), 5.80 (s, 1H), 5.25 (d, J = 12.5 Hz, 1H), 5.16 (d, J = 12.5 Hz, 1H), 2.27 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 191.5, 166.4, 155.8, 148.3, 145.1, 139.2, 136.7, 135.9, 130.4, 130.0, 128.7, 128.3, 128.1, 127.6, 126.9, 125.8, 124.9, 123.9, 123.4, 123.2, 116.8, 115.2, 105.4, 66.9, 36.8, 19.1 ppm.

HRMS (ESI- TOF): Calcd. for $C_{31}H_{24}NO_3S_2$ 522.1192, found 522.1193.

Compound 21ha



Yield: 69.8 mg (77%), Yellow solid

Mp: 202 °C.

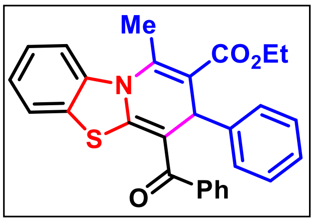
IR (neat): ν_{max} 2957, 1699, 1624, 1475, 1337, 1209, 1099, 1025, 852, 745cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.66 (d, J = 7.5, 1H), 7.56 (d, J = 7.0 Hz, 2H), 7.48-7.46 (m, 1H), 7.44-7.40 (m, 3H), 7.35-7.32 (m, 1H), 7.30-7.28 (m, 1H), 7.15-7.12 (m, 3H), 6.93 (d, J = 6.5 Hz, 2H), 5.67 (s, 1H), 4.34-4.28 (m, 2H), 2.74 (s, 3H) 1.39 (t, J = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 192.2, 167.5, 155.6, 143.9, 143.6, 139.5, 136.9, 130.4, 130.0, 128.7, 128.3, 127.8, 126.8, 126.6, 125.7, 124.7, 123.1, 116.7, 116.1, 104.9, 61.1, 40.9, 19.3, 14.4 ppm.

HRMS (ESI- TOF): Calcd. for $C_{28}H_{24}NO_3S$ 454.1471, found 454.1472.

Compound 21ia



Yield: 69.8 mg (77%), Yellow solid

Mp: 202 °C.

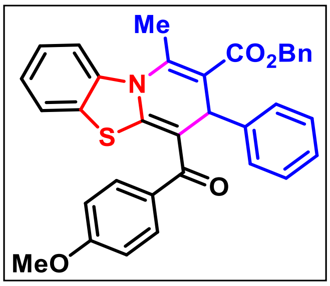
IR (neat): ν_{max} 2957, 1699, 1624, 1475, 1337, 1209, 1099, 1025, 852, 745cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.66 (d, J = 7.5, 1H), 7.56 (d, J = 7.0 Hz, 2H), 7.48-7.46 (m, 1H), 7.44-7.40 (m, 3H), 7.35-7.32 (m, 1H), 7.30-7.28 (m, 1H), 7.15-7.12 (m, 3H), 6.93 (d, *J* = 6.5 Hz, 2H), 5.67 (s, 1H), 4.34-4.28 (m, 2H), 2.74 (s, 3H) 1.39 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 192.2, 167.5, 155.6, 143.9, 143.6, 139.5, 136.9, 130.4, 130.0, 128.7, 128.3, 127.8, 126.8, 126.6, 125.7, 124.7, 123.1, 116.7, 116.1, 104.9, 61.1, 40.9, 19.3, 14.4 ppm.

HRMS (ESI- TOF): Calcd. for $C_{28}H_{24}NO_3S$ 454.1471, found 454.1472.

Compound 21ab



Yield: 84.0 mg (77%), Yellow solid

Mp: 211 °C.

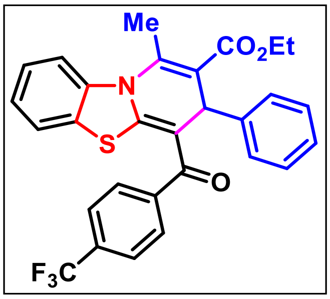
IR (neat): ν_{max} 22920, 1709, 1690, 1478, 1248, 1219, 1182, 1025, 978, 772 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.62 (d, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.36-7.29 (m, 7H), 7.28-7.25 (m, 1H), 7.09 (br s, 3H), 6.91-6.90 (m, 2H), 6.69 (d, *J* = 8.0 Hz, 2H), 5.78 (s, 1H), 5.33 (d, *J* = 12.5 Hz, 1H), 5.25 (d, *J* = 12.5 Hz, 1H), 3. 18 (s, 3H), 2.71 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 191.2, 167.3, 161.5, 155.3, 144.5, 143.7, 136.9, 136.0, 131.8, 130.1, 129.9. 128.8, 128.4. 128.3, 126.8, 126.5, 125.6, 124.7, 123.1, 116.7, 115.2, 113.6, 104.9, 66.9, 55.5, 40.8, 19.3 ppm.

HRMS (ESI- TOF): Calcd. for $C_{34}H_{28}NO_4S$ 546.1734, found 546.1737.

Compound 21ic



Yield: 76.2 mg (73%), Yellow solid

Mp: 195 °C.

IR (neat): ν_{max} 2950, 1706, 1628, 1472, 1369, 1281, 1164, 1065, 908, 749 cm^{-1}

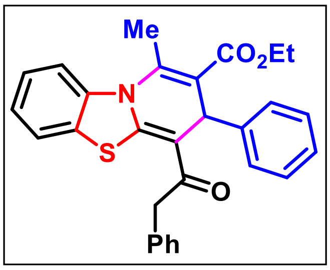
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.68-7.63 (m, 3H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.36-7.30 (m, 2H), 7.14-7.13 (m, 3H), 6.89 (d, *J* = 6.0 Hz, 2H), 5.50 (s, 1H), 4.30 (q, *J* = 7.0 Hz, 2H), 2.70 (s, 3H) 1.33 (t, *J* = 7.0 Hz, 3H) (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 190.5, 167.4, 156.5, 143.6, 143.2, 143.0, 136.8, 132.0 (q, $^2J_{C-F}$ = 33.5 Hz), 129.7, 128.9, 128.0, 127.1, 126.5, 126.0, 125.3 (q, $^3J_{C-F}$ = 4.0 Hz), 124.9, 124.0 (q, $^1J_{C-F}$ = 271.0 Hz), 123.3, 116.8, 116.6, 104.5, 61.3, 40.8, 19.4, 14.4 ppm.

^{19}F NMR (471 MHz): -62.8.

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{29}H_{23}F_3NO_3S$ 522.1345, found 522.1344.

Compound 21id



Yield: 60.8 mg (65%), Yellow solid

Mp: 193 °C.

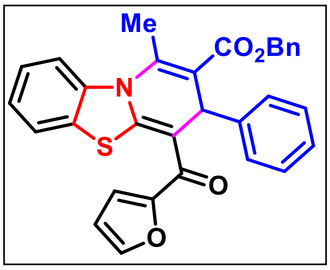
IR (neat): ν_{max} 2923, 1704, 1646, 1489, 1372, 1216, 1108, 1026, 943, 706 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.60 (d, *J* = 7.5, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.32-7.28 (m, 3H), 7.25-7.23 (m, 4H), 7.22-7.21 (m, 3H), 7.71 (d, *J* = 7.0 Hz, 2H), 5.58 (s, 1H), 4.39-4.26 (m, 2H), 3.99 (d, *J* = 15.0 Hz, 1H), 3.72 (d, *J* = 15.5 Hz, 1H) 2.64 (s, 3H) 1.40 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 193.3, 167.5, 154.1, 143.8, 143.1, 136.7, 135.3, 130.1, 129.6, 129.0, 128.6, 127.2, 127.1, 126.8, 125.7, 124.4, 123.1, 116.7, 116.3, 105.7, 61.1, 45.2, 40.6, 19.5, 14.5 ppm.

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{29}H_{26}NO_3S$ 468.1628, found 468.1629.

Compound 21ae



Yield: 73.8 mg (72%), Yellow solid

Mp: 205 °C.

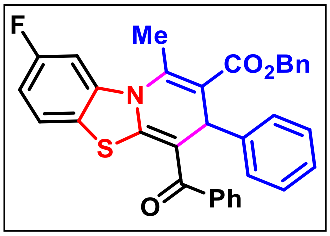
IR (neat): ν_{max} 2925, 1700, 1625, 1473, 1382, 1227, 1103, 1056, 975, 755 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 7.5, 1H), 7.47 (d, J = 7.0 Hz, 2H), 7.44-7.39 (m, 4H), 7.33-7.28 (m, 3H), 7.15-7.08 (m, 6H), 6.47-6.42 (m, 2H), 5.42-5.33 (m, 2H), 2.72 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 176.0, 167.3, 156.9, 153.5, 144.9, 144.0, 143.9, 136.8, 136.0, 130.3, 128.8, 128.7, 128.4, 128.3, 126.8, 126.6, 125.7, 124.6, 123.0, 117.1, 116.5, 116.3, 112.0, 105.0, 67.0, 39.1, 19.4 ppm.

HRMS (ESI- TOF): m/z $[M + H]^+$ calcd. for $C_{31}H_{24}NO_4S$ 506.1421, found 506.1426.

Compound 21af



Yield: 81.2 mg (77%), Yellow solid

Mp: 218 °C.

IR (neat): ν_{max} 3021, 1698, 1623, 1478, 1384, 1210, 1125, 1058, 975, 761 cm^{-1}

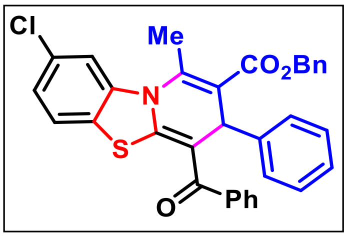
^1H NMR (500 MHz, $CDCl_3$): δ 7.57 (dd, J_1 = 8.5, J_2 = 5.0 Hz, 1H), 7.49 (d, J = 7.0 Hz, 2H) 7.47-7.43 (m, 1H), 7.39-7.38 (m, 3H), 7.35-7.34 (m, 2H), 7.31-7.28 (m, 2H), 7.18-7.16 (m, 1H), 7.13-7.12 (m, 3H), 7.05-7.02 (m, 1H), 6.88-6.87 (m, 2H), 5.70 (s, 1H), 5.34-5.26 (m, 2H), 2.74 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 192.1, 167.0, 161.1 (d, $^1J_{C-F}$ = 243.0 Hz) 152.2, 143.5 (d, $^3J_{C-F}$ = 9.1 Hz), 139.2, 137.8, 137.7, 135.8, 130.4, 128.8 (2s), 128.4, 128.3, 128.2, 127.6, 127.0, 126.5, 125.2 (d, $^4J_{C-F}$ = 2.0 Hz), 123.7 (d, $^3J_{C-F}$ = 9.8 Hz), 116.3, 112.1 (d, $^2J_{C-F}$ = 23.1 Hz), 105.4, 104.8 (d, $^2J_{C-F}$ = 28.5 Hz), 67.0, 40.9, 19.1 ppm.

^{19}F NMR (471 MHz): 114.3 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{33}H_{25}FNO_3S$ 534.1534, found 534.1537.

Compound 21ag



Yield: 82.5 mg (75%), Yellow solid

Mp: 208 °C.

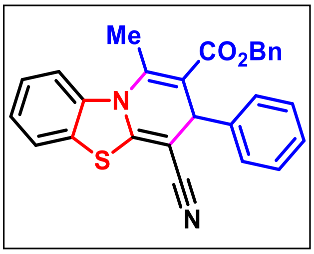
IR (neat): ν_{max} 2936, 1702, 1627, 1478, 1361, 1215, 1102, 1052, 995, 754 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 1H) 7.49-7.47 (m, 2H), 7.45-7.42 (m, 1H) 7.41-7.38 (m, 4H), 7.34-7.32 (m, 2H), 7.31 (s, 1H), 7.29-7.25 (m, 2H), 7.13-7.12 (m, 3H), 6.86-6.85 (m, 2H), 5.70 (s, 1H), 5.33-5.25 (m, 2H), 2.73 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 192.3, 167.0, 155.5, 143.7, 143.4, 139.1, 137.8, 135.8, 131.8, 130.4, 128.8 (2s), 128.5, 128.4 (2s), 128.2, 127.6, 127.0, 126.5, 124.9, 123.7, 116.8, 116.3, 105.4, 67.0, 40.9, 19.3 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1243.

Compound 21ij



Yield: 53.9 mg (72%), Yellow solid

Mp: 196 °C.

IR (neat): ν_{max} 2980, 2191, 1630, 1597, 1492, 1344, 1262, 1096, 1054, 961, 744 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41 (dd, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.29-7.25 (m, 3H), 7.23-7.20 (m, 3H), 7.19-7.17 (m, 1H), 5.03 (s, 1H), 4.20 (dq, J_1 = 7.0, J_2 = 2.0 Hz, 2H), 2.72 (s, 3H) 1.26 (t, *J* = 7.0 Hz, 3H) ppm.

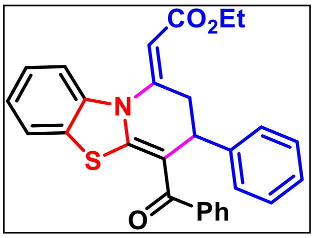
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.9, 152.7, 143.9, 142.5, 138.1, 129.0, 127.6, 126.9, 126.1, 125.8, 124.6, 122.9, 119.0, 116.3, 112.4, 79.4, 61.1, 42.1, 19.2, 14.3 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{22}H_{19}N_2O_2S$ 375.1162, found 375.1157.

3.8 Synthesis of Compounds 22aa

Following the general procedure (section 3.7) for the DBU catalyzed reaction, the reaction of **15a** (50.7 mg, 0.20 mmol, 1.0 equiv) with **8a** (52.0 mg, 0.20 mmol, 1.0 equiv) in the presence of DBU (6.0 µL, 0.04 mmol, 0.2 equiv) afforded **22aa** as a yellow solid.

Compound 22aa



Yield: 66.2 mg (73%), Yellow solid

Mp: 202 °C.

IR (neat): ν_{max} 2931, 1702, 1677, 1467, 1384, 1232, 1100, 1026, 850, 757 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.39-7.36 (m, 1H), 7.33-7.30 (m, 1H), 7.28-7.27 (m, 1H), 7.23-7.16 (m, 7H), 7.00 (d, *J* = 7.5 Hz, 2H), 6.16 (s, 1H), 4.32-4.28 (m, 2H), 4.02-4.00 (m, 2H). 2.74 (dd, J_1 = 12.5, J_2 = 5.0 Hz, 1H), 1.12 (t, *J* = 7.0 Hz, 3H) ppm.

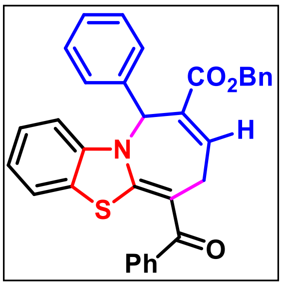
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 190.6, 165.8, 155.6, 147.4, 143.6, 140.6, 136.9, 129.5, 128.8, 128.4, 127.9, 127.7, 127.0, 126.7, 126.6, 124.3, 123.0, 112.7, 110.8, 104.6, 60.4, 40.6, 31.7, 14.2 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{28}H_{24}NO_3S$ 454.1471, found 454.1467.

3.9 Synthesis of Compounds 23aa, 23ba, 23ea, 23ia, 23ib, 23bc, 23af, 23ag, 23ah and 23ai: Representative Procedure for 23aa

A 5.0 mL round bottom flask was charged with 2-acyl benzothiazole **15a** (50.7 mg, 0.2 mmol), P(*n*-Bu)$_3$ (20.0 µL, 50 mol% in EtOAc, 0.04 mmol) in $CHCl_3$ (1.0 mL). Subsequently, *β′*-acetoxy allenoate **12a** (64.5 mg, 0.20 mmol) in $CHCl_3$ (1.0 mL) was added portion-wise at room temperature (25 °C), the mixture stirred for 12 h and progress of the reaction was monitored using TLC. After completion of the reaction, the mixture was quenched by adding water (10 mL). The whole mixture was extracted with $CHCl_3$ (3 × 5 mL). Then the combined organic layer was washed with brine (10 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 (10:90) as the eluent [Note: R_f values for **23** (~ 0.43) is lower than the R_f values of **24** (~ 0.49). All other compounds were prepared by using the same molar quantities.

Compound 23aa



Yield: 69.1 mg (67%), Yellow solid

Mp: 201 °C.

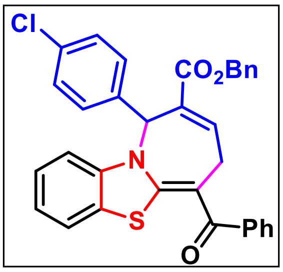
IR (neat): ν_{max} 2939, 1699, 1627, 1463, 1377, 1200, 1095, 903, 725 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.70-7.68 (m, 1H), 7.47 (dd, J_1 = 9.0, J_2 = 7.0 Hz, 1H), 7.39-7.38 (m, 3H), 7.36-7.34 (m, 3H), 7.32-7.29 (m, 7H), 7.27-7.24 (m, 3H), 7.15-7.13 (m, 3H), 5.31-5.24 (m, 2H), 3.17 (dd, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 3.05 (dd, J_1 = 15.0, J_2 = 9.5 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 189.8, 166.2, 159.8, 145.0, 141.1, 141.0, 139.3, 135.7, 131.1, 129.4, 129.1, 128.8, 128.6, 128.4, 128.2, 127.9, 127.5, 127.4, 126.9, 125.0, 123.6, 122.2, 110.7, 97.6, 67.6, 56.7, 26.8 ppm.

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{33}H_{26}NO_3S$ 516.1628, found 516.1631.

Compound 23ba



Yield: 69.3 mg (63%), Yellow solid

Mp: 195 °C.

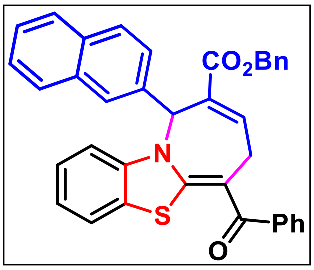
IR (neat): ν_{max} 2968, 1707, 1652, 1490, 1378, 1247, 1093, 946, 731 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.69 (d, J = 7.5 Hz, 1H), 7.48-7.45 (m, 1H) 7.39-7.38 (m, 4H), 7.37-7.35 (m, 6H), 7.33-7.28 (m, 3H), 7.25-7.21 (m, 2H), 7.09-7.08 (m, 3H), 5.30-5.24 (m, 2H), 3.14 (dd, J_1 = 15.3, J_2 = 7.0 Hz, 1H), 3.08 (dd, J_1 = 15.5, J_2 = 9.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.9, 166.1, 159.6, 145.1, 140.9, 140.8, 137.8, 135.5, 133.9, 130.7, 129.5, 129.3, 128.8, 128.7, 128.5, 128.3, 127.5, 127.4, 127.0, 126.5, 123.8, 122.3, 110.5, 97.5, 67.8, 56.3, 26.7 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1239.

Compound 23ea



Yield: 65.6 mg (58%), Yellow solid

Mp: 197 °C.

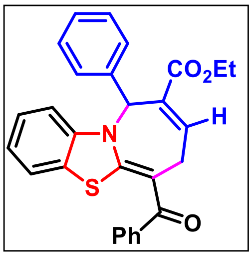
IR (neat): ν_{max} 2950, 1703, 1594, 1430, 1380, 1240, 1042, 943, 739 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, $J = 8.5$ Hz, 2H), 7.72 (d, $J = 7.5$ Hz, 2H), 7.54 (s, 1H), 7.52-7.45 (m, 3H), 7.42-7.35 (m, 5H), 7.32-7.31 (m, 5H), 7.30-7.27 (m, 4H), 7.25 (s, 1H), 5.34-5.8 (m, 2H), 3.24 (dd, $J_1 = 15.5$, $J_2 = 6.5$ Hz, 1H), 3.03 (dd, $J_1 = 15.0$, $J_2 = 9.0$ Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.8, 166.3, 159.9, 145.3, 141.1, 140.0, 136.6, 135.6, 133.2, 132.9, 130.7 (2s), 129.4, 129.3, 128.8, 128.7, 128.5, 128.2, 127.8, 127.5, 126.9 (2s), 126.6, 124.0, 123.7, 122.8, 122.2, 110.8, 97.7, 67.9, 57.0, 26.6 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{37}H_{28}NO_3S$ 566.1784, found 566.1782.

Compound 23ia



Yield: 58.9 mg (65%), Yellow solid

Mp: 190 °C.

IR (neat): ν_{max} 2960, 1705, 1645, 1448, 1378, 1263, 1018, 910, 731 cm^{-1}

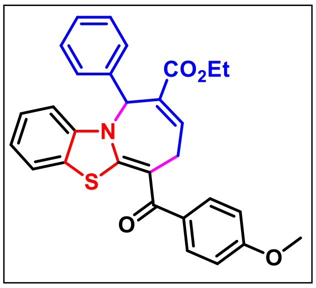
^1H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, $J = 7.5$ Hz, 1H), 7.45-7.41 (m, 1H), 7.36-7.33 (m, 7H), 7.31-7.24 (m, 4H), 7.16-7.214 (m, 3H), 4.31 (q, $J = 7.0$ Hz, 2H), 3.17 (dd, J_1

= 15.0, J_2 = 6.5 Hz, 1H), 3.05 (dd, J_1 = 15.0, J_2 = 9.0 Hz, 1H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.7, 166.4, 159.8, 144.4, 141.1 (2s), 139.4, 131.3, 129.4, 129.1, 128.2, 127.9, 127.5, 127.4, 126.9, 125.0, 123.6, 122.2, 110.7, 97.7, 61.9, 56.7, 26.7, 14.4 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{28}H_{24}NO_3S$ 454.1471, found 454.1474.

Compound 23ib



Yield: 57.9 mg (60%), Yellow solid

Mp: 223 °C.

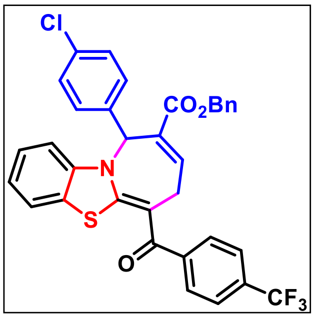
IR (neat): ν_{max} 2925, 1701, 1677, 1433, 1377, 1251, 1101, 945, 759 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 7.5 Hz, 1H), 7.45-7.41 (m, 1H), 7.36-7.30 (m, 6H), 7.25-7.22 (m, 2H), 7.16 (d, J = 7.5 Hz, 2H), 7.12 (s, 1H), 6.87 (d, J = 8.5 Hz, 2H), 4.32-4.29 (m, 2H), 3.82 (s, 3H), 3.22 (dd, J_1 = 15.5, J_2 = 6.5 Hz, 1H), 3.13 (dd, J_1 = 15.0, J_2 = 9.0 Hz, 1H) 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.3, 166.5, 160.7, 159.5, 144.4, 141.2, 139.4, 131.4 (2s), 129.6, 129.1, 127.9, 127.4, 126.8, 125.0, 123.5, 122.1, 113.5, 110.6, 97.8, 61.8, 56.6, 55.5, 26.9, 14.4 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{29}H_{26}NO_4S$ 484.1577, found 484.1575.

Compound 23bc



Yield: 68.0 mg (55%), Yellow solid

Mp: 176 °C.

IR (neat): ν_{max} 2925, 1701, 1677, 1433, 1377, 1251, 1101, 945, 759 cm^{-1}

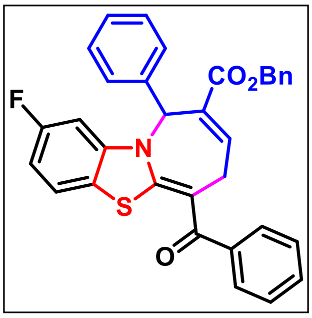
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.71 (d, J = 7.5 Hz, 1H), 7.66-7.62 (m, 2H), 7.46-7.42 (m, 3H), 7.37-7.36 (m, 6H), 7.32-7.30 (m, 3H), 7.28-7.27 (m, 1H), 7.12 (s, 1H), 7.07 (d, J = 8.0 Hz, 2H), 5.30-5.24 (m, 2H), 3.15 (dd, J_1 = 15.5, J_2 = 6.5 Hz, 1H), 2.95 (dd, J_1 = 15.5, J_2 = 9.5 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 188.0, 166.0, 160.3, 144.7, 144.5, 140.6, 137.6, 135.4, 134.1, 131.2 (q, $^{2}J_{C\text{-}F}$ = 31.6 Hz), 131.0, 129.4, 128.9, 128.7, 128.5, 127.3, 127.2, 126.4, 125.4 (q, $^{3}J_{C\text{-}F}$ = 4.0 Hz), 124.1, 124.0 (q, $^{1}J_{C\text{-}F}$ = 270.4 Hz), 122.4, 110.8, 97.1, 67.9, 56.4, 26.5 ppm.

^{19}F NMR (471 MHz, CDCl$_3$): -62.7 ppm

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{34}H_{24}ClF_3NO_3S$ 618.1112, found 618.1114.

Compound 23af



Yield: 68.3 mg (64%), Yellow solid

Mp: 215 °C.

IR (neat): ν$_{max}$ 2922, 1707, 1686, 1490, 1370, 1285, 1096, 961, 729 cm^{-1}

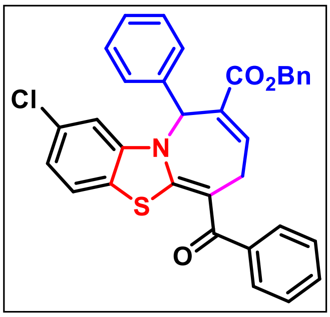
^{1}H NMR (500 MHz, CDCl$_3$): δ 7.59 (dd, J_1 = 9.0, J_2 = 5.5 Hz, 1H), 7.47 (dd, J_1 = 8.5, J_2 = 7.5 Hz, 1H) 7.39-7.38 (m, 4H), 7.37-7.35 (m, 3H), 7.34-7.31 (m, 6H), 7.13 (d, J = 7.5 Hz, 2H), 7.00-6.96 (m, 3H), 5.32-5.25 (m, 2H), 3.17 (dd, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 3.06 (dd, J_1 = 15.5, J_2 = 9.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 189.9, 166.1, 162.6 (d, $^{1}J_{C\text{-}F}$ = 242.6 Hz), 160.6, 145.1, 142.3 (d, $^{3}J_{C\text{-}F}$ = 11.0 Hz), 140.8, 138.7, 135.5, 131.1, 129.5, 129.2, 128.9, 128.7, 128.5, 128.2, 128.1, 127.5, 124.9, 123.0 (d, $^{3}J_{C\text{-}F}$ = 9.5 Hz), 122.5 (d, $^{4}J_{C\text{-}F}$ = 2.0 Hz), 111.2 (d, $^{2}J_{C\text{-}F}$ = 23.5 Hz), 98.8 (d, $^{1}J_{C\text{-}F}$ = 28.5 Hz), 98.3, 67.7, 57.0, 26.7 ppm.

^{19}F NMR (471 MHz, CDCl$_3$): -114.0 ppm

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{33}H_{25}FNO_3S$ 534.1534, found 534.1536.

Compound 23ag



Yield: 67.1 mg (61%), Yellow solid

Mp: 225 °C.

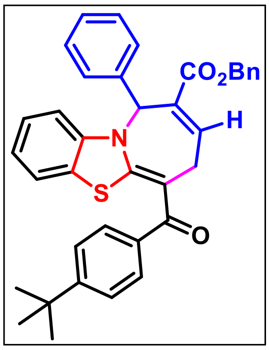
IR (neat): ν_{max} 2923, 1701, 1650, 1494, 1372, 1245, 1079, 957, 753 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.57 (d, J = 9.0 Hz, 1H), 7.46 (dd, J_1 = 8.5, J_2 = 6.5 Hz, 1H) 7.39-7.38 (m, 4H), 7.37-7.35 (m, 3H), 7.34-7.33(m, 6H), 7.22-7.20 (m, 2H), 7.13 (d, J = 7.0 Hz, 2H), 7.02 (s, 1H), 5.32-5.26 (m, 2H), 3.16 (dd, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 3.05 (dd, J_1 = 15.5, J_2 = 9.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 190.2, 166.1, 159.8, 145.1, 142.2, 140.7, 138.7, 135.5, 133.1, 131.2, 129.6, 129.2, 128.9, 128.7, 128.4, 128.3, 128.1, 127.5, 126.0, 124.9, 123.9, 122.9, 110.9, 98.4, 67.8, 56.9, 26.7 ppm.

HRMS (ESI- TOF): m/z [M + H]$^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1237.

Compound 23ah



Yield: 74.3 mg (64%), Yellow solid

Mp: 197 °C.

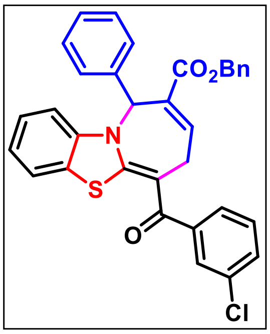
IR (neat): ν_{max} 2922, 1717, 1646, 1458, 1375, 1263, 1028, 968, 737 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.67 (d, J = 7.5 Hz, 1H), 7.48 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 7.38-7.37 (m, 4H), 7.36-7.33 (m, 3H), 7.33-7.32 (m, 2H), 7.31-7.29 (m, 3H), 7.28 (s, 1H), 7.25-7.22 (m, 2H), 7.15-7.14 (m, 3H), 5.31-5.24 (m, 2H), 3.18 (dd, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 3.11 (dd, J_1 = 15.5, J_2 = 9.0 Hz, 1H), 1.29 (s, 9H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 189.9, 166.3, 159.5, 152.7, 145.1, 141.1, 139.3, 138.1, 135.7, 131.0, 129.1, 128.8, 128.6, 128.4, 127.9, 127.5, 127.4, 126.8, 125.1, 125.0, 123.5, 122.2, 110.6, 97.7, 67.6, 56.7, 34.9, 31.4, 26.9 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{37}H_{34}NO_3S$ 572.2254, found 572.2249.

Compound 23ai



Yield: 67.1 mg (61%), Yellow solid

Mp: 220 °C.

IR (neat): ν_{max} 2919, 1705, 1693, 1493, 1379, 1249, 1079, 968, 744 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 7.5 Hz, 1H), 7.46 (dd, J_1 = 8.5, J_2 = 7.0 Hz, 1H), 7.39-7.38 (m, 4H), 7.33-7.31 (m, 7H), 7.29-7.26 (m, 3H), 7.20-7.17 (m, 2H), 7.13 (d, J = 7.5 Hz, 2H), 5.31-5.25 (m, 2H), 3.17 (dd, J_1 = 15.5, J_2 = 7.0 Hz, 1H), 2.98 (dd, J_1 = 15.0, J_2 = 15.5 Hz, 1H) ppm.

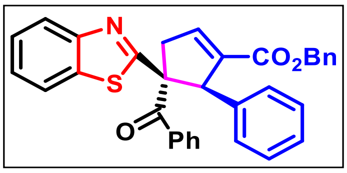
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 187.7, 166.2, 160.3, 144.8, 142.9, 140.9, 139.1, 135.6, 134.3, 131.2, 129.5, 129.3, 129.2, 128.8, 128.7, 128.5, 128.0, 127.7, 127.3, 127.0, 125.5, 124.9, 128.8, 122.3, 110.9, 97.3, 67.7, 56.8, 26.6 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1237.

3.10 Synthesis of Compounds 24aa, 24ba, 24ea, 24ia, 24ee, 24ie, and 24ag: Representative Procedure for 24aa

A 5.0 mL round bottom flask was charged with 2-acyl benzothiazole **15a** (50.7 mg 0.2 mmol) and P(*n*-Bu)$_3$ (20.0 μL, 50 mol% in EtOAc, 0.04 mmol) in EtOAc (1.0 mL). Subsequently, *β'*-acetoxy allenoate **12a** (64.5 mg, 0.20 mmol) in EtOAc (1.0 mL) was added in portion-wise at rt (25 °C), the mixture stirred for 12 h and progress of the reaction was monitored using TLC. After completion of the reaction, the mixture was quenched by adding water (10 mL). The contents were extracted with EtOAc (3 × 5 mL). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **24** was then purified by silica gel column chromatography using ethyl acetate/hexane (10:90) as the eluent. [Note: R_f values for **24** is higher than the R_f values of **23** (R_f values for **23** (lower R_f) = 0.43 and R_f values for **24** (higher R_f) = 0.49]. All other compounds were prepared by using the same molar quantities.

Compound 24aa



Yield: 36.1 mg (35%), White solid

Mp: 163 °C.

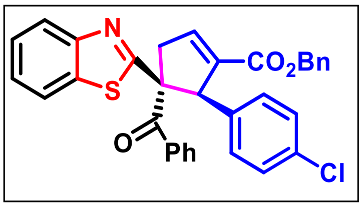
IR (neat): ν_{max} 3062, 1713, 1692, 1495, 1314, 1262, 1098, 957, 861, 758 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.86 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.41-7.38 (m, 1H), 7.36-7.3 (m, 1H), 7.87-7.25 (m, 2H), 7.24-7.22 (m, 4H), 7.06-7.05 (m, 2H), 7.01-7.00 (m, 3H), 6.97-6.93 (m, 3H), 5.67 (s, 1H), 5.31-5.24 (m, 2H), 4.17 (dt, J_1 = 19.0, J_2 = 2.0 Hz, 1H), 3.47 (dd, J_1 = 19.0, J_2 = 3.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 196.1, 170.1, 163.6, 152.4, 140.3, 139.1, 137.4, 136.0, 135.6, 134.4, 132.7, 130.1, 129.5, 128.6, 128.5, 127.9, 127.6, 127.0, 126.0, 125.1, 123.3, 121.4, 68.0, 66.1, 57.2, 42.6 ppm.

HRMS (ESI- TOF): m/z $[M + H]^+$ calcd. for $C_{33}H_{26}NO_3S$ 516.1628, found 516.1628.

Compound 24ba



Yield: 34.1 mg (31%), Yellow solid

Mp: 167 °C.

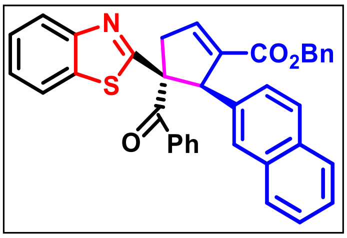
IR (neat): ν_{max} 2924, 1711, 1698, 1500, 1358, 1275, 1091, 956, 826, 751 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 8.5 Hz, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.62 (d, J = 8.0 Hz, 1H), 7.40-7.35 (m, 2H), 7.27-7.24 (m, 6H), 7.01-6.97 (m, 5H), 6.95-6.89 (m, 2H), 5.647 (s, 1H), 5.15 (d, J = 12.5 Hz, 1H), 4.95 (d, J = 12.5 Hz, 1H), 4.20-4.16 (m, 1H), 3.43 (d, J = 19.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 196.3, 170.1, 163.9, 152.9, 141.0, 139.2, 136.8, 136.2, 135.9, 134.7, 133.3, 133.2, 131.2, 130.5, 129.1, 128.9, 128.5 (2s), 128.2, 126.6, 125.8, 123.7, 122.0, 68.4, 66.7, 57.0, 43.1 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1242.

Compound 24ea



Yield: 31.7 mg (28%), Yellow solid

Mp: 217 °C.

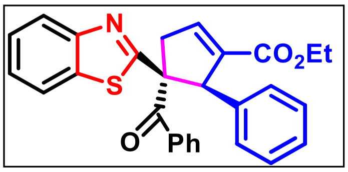
IR (neat): ν_{max} 3060, 1712, 1683, 1498, 1314, 1260, 1096, 960, 858, 755 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.5 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 7.62-7.57 (m, 3H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.41-7.37 (m, 2H), 7.34-7.31 (m, 2H), 7.29-7.25 (m, 3H), 7.15-7.10 (m, 3H), 7.07 (br s, 1H), 7.01-6.99 (m, 2H), 6.86 (d, *J* = 8.0 Hz, 2H), 5.84 (s, 1H), 5.11 (d, *J* = 12.5 Hz, 1H), 4.92 (d, *J* = 13.0 Hz, 1H), 4.25 (dt, J_1 = 18.5, J_2 = 2.0 Hz, 1H), 3.52 (dd, J_1 = 19.0, J_2 = 3.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 196.1, 169.9, 163.7, 152.3, 140.5, 139.1, 135.8, 135.5, 135.3, 134.4, 133.2, 132.7, 132.6, 130.1, 128.6, 128.3, 128.0, 127.9, 127.6, 127.5 (2s), 125.9, 125.7, 125.5, 125.1, 123.2, 121.4, 68.1, 66.2, 57.2, 42.8 ppm.

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{37}H_{28}NO_3S$ 566.1784, found 566.1784.

Compound 24ia



Yield: 33.6 mg (37%), White solid

Mp: 185 °C.

IR (neat): ν_{max} 2988, 1707, 1674, 1445, 1372, 1261, 1185, 1024, 937, 752 cm^{-1}

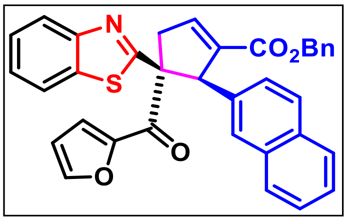
^1H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.71 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.40-7.38 (m, 1H), 7.36-7.32 (m, 1H), 7.28 (s, 1H), 7.26-7.21 (m, 2H), 7.05-7.04 (m, 2H), 6.96-6.88 (m, 4H), 5.62 (s, 1H), 4.15 (dt, J_1 = 19.0, J_2

= 2.0 Hz, 1H), 4.10-4.02 (m, 2H), 3.46 (dd, J_1 = 19.0, J_2 = 3.0 Hz, 1H), 1.10 (t, J = 7.5 Hz; 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 196.2, 170.2, 163.8, 152.4, 139.5, 139.3, 137.5, 135.6, 134.4, 132.7, 130.1, 129.3, 128.5, 127.8, 126.9, 125.9, 125.1, 123.2, 121.4, 68.0, 60.5, 57.2, 42.6, 14.1 ppm.

HRMS (ESI- TOF): m/z $[M + H]^+$ calcd. for $C_{28}H_{24}NO_3S$ 454.1471 found 454.1470.

Compound 24ee



Yield: 35.5 mg (32%), White solid

Mp: 195 °C.

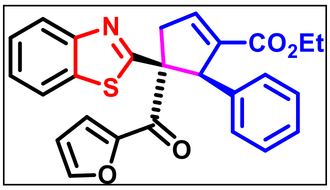
IR (neat): ν_{max} 2934, 1705, 1677, 1458, 1385, 1267, 1163, 1016, 975, 754 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 6.5 Hz, 1H), 7.58-7.54 (m, 2H), 7.47-7.45 (m, 2H), 7.39-7.37 (m, 3H), 7.27 (s, 1H), 7.21-7.09 (m, 1H), 7.13-7.09 (m, 4H), 7.00 (d, J = 7.5 Hz, 2H), 6.73 (d, J = 3.5 Hz, 1H), 6.14 (d, J = 1.5 Hz, 1H), 5.72 (s, 1H), 5.16 (d, J = 13.0 Hz, 1H), 5.00 (d, J = 12.5 Hz, 1H), 4.45 (dt, J_1 = 19.5, J_2 = 2.0 Hz, 1H), 3.00 (dd, J_1 = 20.0, J_2 = 3.0 Hz, 1H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 183.6, 174.2, 163.5, 152.8, 151.7, 145.4, 141.3, 138.6, 135.9, 135.2, 135.0, 133.3, 132.8, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 126.3, 126.2, 125.9, 125.4, 123.6, 121.7, 118.9, 112.3, 68.3, 66.3, 58.8, 43.9 ppm.

HRMS (ESI- TOF): m/z $[M + H]^+$ calcd. for $C_{35}H_{26}NO_4S$ 556.1577, found 556.1578.

Compound 24ie



Yield: 26.6 mg (30%), White solid

Mp: 183 °C.

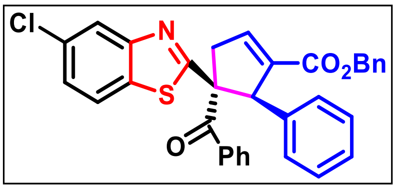
IR (neat): ν_{max} 3062, 1712, 1674, 1494, 1331, 1262, 1092, 979, 864, 759 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.98 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.47-7.43 (m, 1H), 7.39-7.36 (m, 1H), 7.28-7.27 (m, 1H), 7.06-7.04 (m, 3H), 7.00-6.97 (m, 2H), 6.94-6.93 (m, 1H), 6.83-6.82 (m, 1H), 6.23-6.22 (m, 1H), 5.47 (s, 1H), 4.36 (dq, J_1 = 19.0, J_2 = 2.0 Hz, 1H), 4.19-4.07 (m, 2H), 2.94 (dq, J_1 = 19.5, J_2 = 2.0 Hz, 1H) 1.19 (td, J_1 = 7.0, J_2 = 2.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 183.8, 174.4, 163.7, 152.9, 151.7, 145.3, 140.1, 139.0, 137.6, 135.1, 128.4, 128.1, 127.4, 126.2, 125.4, 123.6, 121.6, 118.6, 112.3, 68.1, 60.6, 58.9, 43.8, 14.2 ppm.

HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{26}H_{22}NO_4S$ 444.1264, found 444.1260.

Compound 24ag



Yield: 36.3 mg (33%), White solid

Mp: 171 °C.

IR (neat): ν_{max} 2923, 1713, 1693, 1494, 1318, 1261, 1096, 918, 869, 740 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.85 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 7.5 Hz, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.41-7.38 (m, 1H), 7.36-7.33 (m, 1H), 7.28-7.25 (m, 1H), 7.25-7.22 (m, 4H), 7.06-7.04 (m, 2H), 7.01-7.00 (m, 3H), 6.97-6.92 (m, 3H), 5.67 (s, 1H), 5.15 (d, J = 12.5 Hz, 1H), 4.98 (d, J = 13.0 Hz, 1H), 4.16 (dt, J_1 = 19.5, J_2 = 2.5 Hz, 1H), 3.46 (dd, J_1 = 19.0, J_2 = 3.0 Hz, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 195.7, 172.3, 163.6, 153.2, 140.1, 139.0, 137.3, 136.0, 134.1, 133.8, 132.8, 132.1, 130.3, 130.1, 128.6, 128.5, 128.0 (2s), 127.7, 127.1, 125.7, 123.1, 122.1, 68.1, 66.2, 57.3, 42.6 ppm.

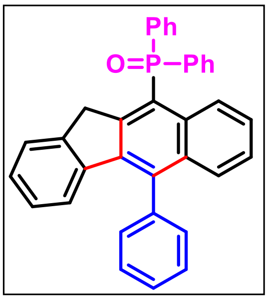
HRMS (ESI- TOF): *m/z* [M + H]$^+$ calcd. for $C_{33}H_{25}ClNO_3S$ 550.1238, found 550.1234.

3.11 Synthesis of Compounds 30aa-ac, 30ba-bm: Representative Procedure for 30aa

A Schlenk tube was charged with **26a** (51.8 mg, 0.1 mmol), alkynes **29a** (11.0 µl, 0.10 mmol) in the presence of $PdCl_2(PPh_3)_2$ (1.4 mg, 0.002 mmol), with CuI (1.0 mg, 0.004 mmol), as a co-catalyst in CH_3CN (1.0 mL, 0.1 M) as a solvent and Et_3N (0.5 mL) as a base at 80 °C (oil bath) and the mixture stirred at the same temperature for 2 h and progress of the reaction was monitored using TLC. After completion of the reaction, the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 5 mL). Then the organic portions were combined, washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using (100-200 mesh) and ethyl acetate/hexane (30:70) as the eluent. All other compounds were prepared by using the same molar quantities.

[Note: In these products, in the $^{13}C\{^1H\}$ NMR spectra, several ^{31}P-^{13}C couplings are there in the overlapping aromatic region and hence the number of signals may be more; a detailed analysis was difficult]

Compound 30aa



Yield: 41.8 mg (85%), gummy liquid

IR (neat): ν_{max} 3054, 2990, 1617, 1503, 1463, 1230, 1178, 1037, 907, 726 cm^{-1}

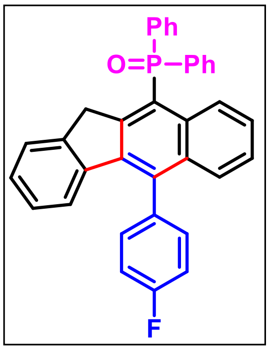
^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, *J* = 8.5 Hz, 1H), 7.82-7.78 (m, 4H), 7.65-7.60 (m, 3H), 7.59-7.56 (m, 3H), 7.50-7.41 (m, 4H), 7.41 (d, *J* = 6.0 Hz, 2H), 7.32-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.20-7.17 (m, 1H), 7.00-6.97 (m, 1H), 6.33 (d, *J* = 8.0 Hz, 1H), 4.07 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 149.9 (d, *J* = 8.3 Hz), 144.4, 139.5, 138.7, 138.6 (d, *J* = 2.9 Hz), 138.2 (d, *J* = 11.9 Hz), 135.8, 134.4 (d, *J* = 102.3 Hz), 133.4 (d, *J* = 8.8 Hz), 133.0 (d, *J* = 9.5 Hz), 132.1 (3 s), 129.7, 129.4, 129.0, 128.3, 127.6 (2 s), 127.3, 126.6, 125.9, 125.5, 124.6, 123.7, 122.2 (d, *J* = 99.6 Hz), 39.1 (d, *J* = 2.6 Hz) ppm.

$^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$): δ 30.9

HRMS (ESI- TOF): *m/z* $[M + H]^+$ calcd. for $C_{35}H_{26}OP$ 493.1716 found 493.1717.

Compound 30ab



Yield: 42.4 mg (purity ca 95%, 83%), white solid.

Mp: 201-203 °C.

IR (neat): ν_{max} 3054, 2990, 1617, 1503, 1463, 1230, 1178, 1037, 907, 726 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, J = 8.0 Hz, 1H), 7.81-7.77 (m, 4H), 7.59-7.54 (m, 3H), 7.50-7.48 (m, 4H), 7.41-7.31 (m, 6H), 7.24-7.20 (m, 2H), 7.04-7.01 (m, 1H), 6.38 (d, J = 7.5 Hz, 1H), 4.07 (s, 2H) ppm.

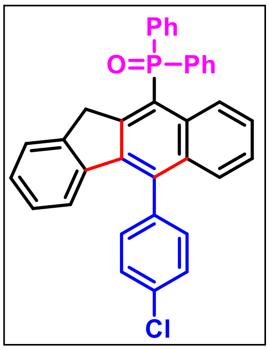
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 162.9 (d, $^1J_{C-F}$ = 246.0 Hz), 149.8 (d, J_{P-C} = 8.6 Hz), 144.5, 143.8 (d, $^3J_{C-F}$ = 7.0 Hz), 139.3, 138.5 (d, J_{P-C} = 12.9 Hz), 137.4, 134.7, (d, J_{P-C} = 102.6 Hz), 134.5, 133.5 (d, J_{P-C} = 8.9 Hz), 133.0 (d, J_{P-C} = 9.5 Hz), 132.1, 132.0, 131.5 (d, J_{P-C} = 8.0 Hz), 129.0 (d, J_{P-C} = 12.2 Hz), 127.8, 127.7 (2 s), 127.0, 126.7, 125.7, 124.7, 123.6, 122.6 (d, J_{P-C} = 99.2 Hz), 116. (d, $^2J_{C-F}$ = 21.2 Hz), 39.1 ppm.

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 30.8 ppm.

^{19}F NMR (476 MHz, $CDCl_3$): δ -113.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{35}H_{25}FOP$ 511.1622 found 511.1621.

Compound 30ac



Yield: 42.2 mg (80%), white solid.

Mp: 201-203 °C.

IR (neat): ν_{max} 3054, 2990, 1617, 1503, 1463, 1230, 1178, 1037, 907, 726 cm^{-1}

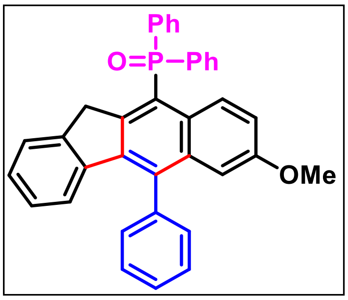
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.33 (d, J = 8.0 Hz, 1H), 7.80-7.77 (m, 4H), 7.63-7.57 (m, 4H), 7.52-7.48 (m, 4H), 7.37-7.33 (m, 5H), 7.23-7.21 (m, 2H), 7.05-7.03 (m, 1H), 6.43 (d, J = 7.0 Hz, 1H), 4.07 (s, 2H) ppm.

^{13}C{^{1}H} NMR (100 MHz, CDCl$_3$): δ 149.7 (d, *J* = 8.6 Hz), 144.4, 139.1, 138.1 (d, *J* = 12.0 Hz), 137.0, 136.9 (d, *J* = 3.4 Hz), 134.5 (d, *J* = 102.3 Hz), 134.3, 133.1 (d, *J* = 8.6 Hz), 132.8 (d, *J* = 9.7 Hz), 132.1 (d, *J* = 2.6 Hz), 132.0 (d, *J* = 10.2 Hz), 131.2, 129.7, 128.9 (d, *J* = 12.0 Hz), 127.7, 127.6 (d, *J* = 6.0 Hz), 126.8, 126.6, 125.9, 125.6, 124.6, 123.5, 122.6 (d, *J* = 96.1 Hz), 38.9 (d, *J* = 2.9 Hz) ppm.

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{35}H_{25}ClOP$ 527.1326 found 527.1326.

Compound 30ba



Yield: 45.5 mg (87%), white solid.

Mp: 211-214 °C.

IR (neat): ν_{max} 3054, 2990, 1617, 1503, 1463, 1230, 1178, 1037, 907, 726 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.32 (d, *J* = 9.5 Hz, 1H), 7.81-7.77 (m, 4H), 7.65-7.56 (m, 5H), 7.50-7.47 (m, 4H), 7.41 (d, *J* = 6.5 Hz, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.18-7.15 (m, 1H), 6.98-6.95 (m, 1H), 6.92 (dd, J_1= 9.5, J_2= 2.5 Hz, 1H), 6.87 (bs, 1H), 6.31 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 2H), 3.64 (s, 3H) ppm.

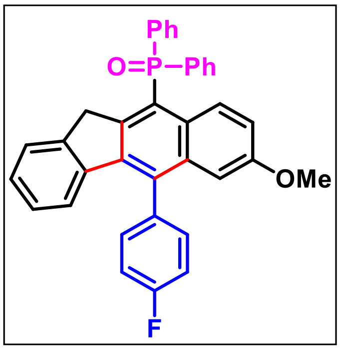
^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 157.0, 147.2 (d, *J* = 8.3 Hz), 144.6, 139.6, 138.9, 138.5 (d, *J* = 12.0 Hz), 137.5 (d, *J* = 2.8 Hz), 135.1 (d, *J* = 8.8 Hz), 134.9 (d, *J* = 102 Hz), 132.2, 132.1, 129.6 (d, *J* = 16.8 Hz), 129.1, 129.0 (d, *J* = 12.3 Hz), 128.5 (d, *J* = 9.5 Hz), 127.9, 126.5, 124.6, 123.7, 122.2 (d, *J* = 99.8 Hz), 117.6, 106.4, 55.1, 38.8 (d, *J* = 2.5 Hz)

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{28}O_2P$ 523.1821 found 523.1822

.

Compound 30bb



Yield: 43.7 mg (81%), white solid.

Mp: 210-212 °C.

IR (neat): ν_{max} 3054, 2990, 1617, 1503, 1463, 1230, 1178, 1037, 907, 726 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.32 (d, J = 9.5 Hz, 1H), 7.80-7.76 (m, 4H), 7.58-7.55 (m, 2H), 7.49-7.46 (m, 4H), 7.41-7.30 (m, 5H), 7.20-7.17 (m, 1H), 7.02-7.00 (m, 1H), 6.93 (dd, J_1 = 9.0, J_2 = 2.5 Hz, 1H), 6.82 (br s, 1H), 6.34 (d, J = 7.5 Hz, 1H), 3.95 (s, 2H), 3.65 (s, 3H) ppm.

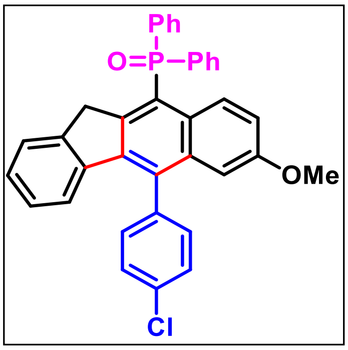
^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 162.8 (d, $^1J_{C\text{-}F}$ = 246.0 Hz), 157.0, 147.1 (d, $J_{P\text{-}C}$ = 8.2 Hz), 144.6, 139.4, 138.8 (d, $^3J_{C\text{-}F}$ = 12.0 Hz), 136.2, (d, $J_{P\text{-}C}$ = 2.7 Hz), 135.2, 135.1, 134.7 (d, $J_{P\text{-}C}$ = 3.3 Hz), 134.3, 132.2 (d, $J_{P\text{-}C}$ = 2.5 Hz), 132.1 132.0, 131.5 (d, $J_{P\text{-}C}$ = 7.6 Hz), 129.0 (d, $J_{P\text{-}C}$ = 12.0 Hz), 127.7, 126.6, 124.7 123.5 122.5 (d, $J_{P\text{-}C}$ = 99.2 Hz), 117.6, 116.7 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 106.0, 55.1, 38.8 (d, $J_{P\text{-}C}$ = 2.7 Hz) ppm.

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

^{19}F NMR (476 MHz, CDCl$_3$): δ -113.6 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{27}FO_2P$ 541.1727 found 541.1727.

Compound 30bc



Yield: 45.7 mg (82%), white solid.

Mp: 225-226°C.

IR (neat): ν_{max} 2920, 2853, 1616, 1501, 1436, 1230, 1178, 1036, 904, 724 cm^{-1}

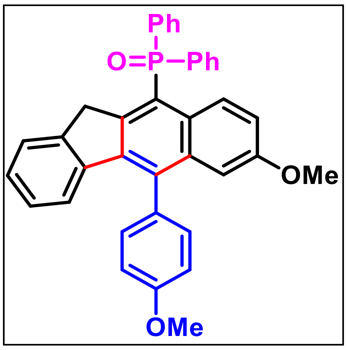
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.32 (d, J = 9.5 Hz, 1H), 7.77 (dd, J_1= 11.5, J_2= 7.5 Hz, 4H), 7.62 (d, J = 8.5 Hz, 2H), 7.58-7.55 (m, 2H), 7.49-7.46 (m, 4H), 7.37 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.0 Hz, 1H), 7.22-7.17 (m, 1H), 7.04-7.01 (m, 1H), 6.92 (dd, J_1= 9.5, J_2= 2.5 Hz, 1H), 6.80 (br s, 1H), 6.40 (d, J = 8.0 Hz, 1H), 3.95 (s, 2H), 3.66 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 157.1, 147.1 (d, J = 8.5 Hz), 144.7, 139.3, 138.6 (d, J = 12.3 Hz), 137.4, 135.9 (d, J = 2.5 Hz), 134.9 (d, J = 9.0 Hz), 134.8 (d, J = 102.1 Hz), 132.1 (2 s), 131.3, 129.9, 129.2 (d, J = 5.6 Hz), 129.1, 129.0, 128.4 (d, J = 10.1 Hz), 127.8, 126.7, 124.7, 123.5, 122.7 (d, J = 99.5 Hz), 117.7, 106.1, 55.2, 38.8 (d, J = 2.9 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 31.0 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for C$_{35}$H$_{25}$O$_2$P 575.1432 found 557.1432.

Compound 30bd



Yield: 46.9 mg (85%), white solid.

Mp: 225-226°C.

IR (neat): ν_{max} 2920, 2853, 1616, 1501, 1436, 1230, 1178, 1036, 904, 724 cm^{-1}

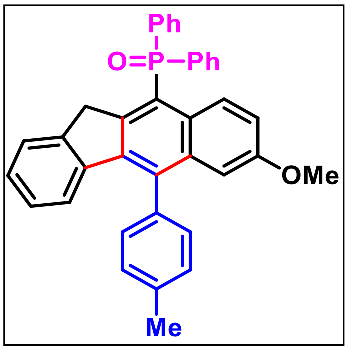
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.32-8.29 (m, 1H), 7.80-7.76 (m, 4H), 7.57-7.53 (m, 2H), 7.48-7.45 (m, 4H), 7.33-7.31 (m, 2H), 7.31-7.29 (m, 1H), 7.18-7.15 (m, 3H), 7.01-6.98 (m, 1H), 6.92-6.90 (m, 2H), 6.44 (d, J = 8.0 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 2H), 3.65 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 159.5, 157.9, 147.1 (d, J = 8.4 Hz), 144.5, 139.7, 138.9 (d, J = 12.0 Hz), 137.3 (d, J = 2.5 Hz), 135.5 (d, J = 8.9 Hz), 135.3, 134.4, 132.1, 132.0, 130.9, 130.8, 129.0, 128.9 (d, J = 12.10 Hz), 127.5, 126.5, 124.5, 123.7, 120.0 (d, J = 99.5 Hz), 117.5, 114.9, 106.4, 55.5, 51.1, 38.8 (d, J = 2.6 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 31.0 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{37}H_{30}O_3P$ 553.1927 found 553.1927.

Compound 30be



Yield: 45.6 mg (85%), white solid.

Mp: 210-212°C.

IR (neat): ν_{max} 2939, 2904, 1617, 1503, 1470, 1231, 1179, 1037, 907, 726 cm^{-1}

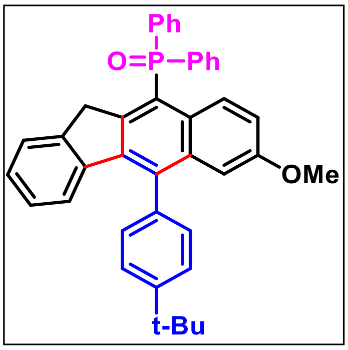
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (d, *J* = 8.5 Hz, 1H), 7.81-7.76 (m, 4H), 7.57-7.54 (m, 2H), 7.49-7.42 (m, 6H), 7.29-7.28 (m, 3H), 7.18-7.15 (m, 1H), 7.00-6.97 (m, 1H), 6.92-6.90 (m, 2H), 6.39 (d, *J* = 7.5 Hz, 1H), 3.95 (s, 2H), 3.65 (s, 3H), 2.55 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 156.9, 147.2 (d, *J* = 8.1 Hz), 144.5, 139.7, 138.6 (d, *J* = 11.9 Hz), 137.9, 137.7 (2 s), 135.7, 135.3 (2 s), 134.4, 132.1, 132.1, 129.8, 129.0, 128.9, 128.5 (d, *J* = 9.5 Hz), 127.5, 126.5, 124.5, 123.8, 121.9 (d, *J* = 99.0 Hz), 117.5, 106.5, 55.1, 38.8 (d, *J* = 2.3 Hz), 21.7 ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 31.0 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{37}H_{30}O_2P$ 537.1978 found 537.1976.

Compound 30bf



Yield: 46.9 mg (81%), white solid.

Mp: 216-218 °C.

IR (neat): ν_{max} 3076, 3018, 1618, 1507, 1473, 1233, 1178, 1033, 907, 728 cm^{-1}

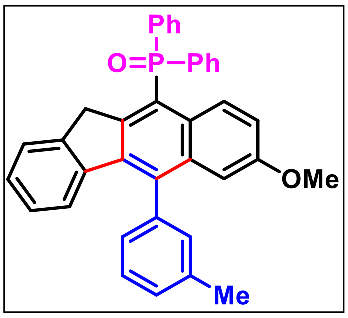
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.33-8.31 (m, 1H), 7.81-7.77 (m, 4H), 7.63 (d, *J* = 8.0 Hz, 2H), 7.58-7.55 (m, 2H), 7.50-7.48 (m, 4H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.17-7.14 (m, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.94-6.91 (m, 2H), 6.29 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 2H), 3.67 (s, 3H), 1.48 (s, 9H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 156.9, 151.3, 147.2 (d, *J* = 8.3 Hz), 144.6, 139.7, 138.7 (d, *J* = 12.0 Hz), 137.7 (d, *J* = 2.9 Hz), 135.7, 134.9 (d, *J* = 102.0 Hz) 135.3, 135.2, 132.2, 132.1 (2 s), 129.2, 129.0 (2 s), 128.9, 128.5 (d, *J* = 9.8 Hz), 127.4, 126.5, 126.4, 124.5, 123.8, 121.9 (d, *J* = 99.9 Hz), 117.2, 106.9, 55.1, 38.8 (d, *J* = 2.8 Hz), 35.0, 31.7ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{28}O_2P$ 579.2447 found 579.2449.

Compound 30bg



Yield: 44.5 mg (83%), white solid.

Mp: 211-214 °C.

IR (neat): ν_{max} 3054, 2992, 1617, 1503, 1463, 1231, 1178, 1037, 908, 727 cm^{-1}

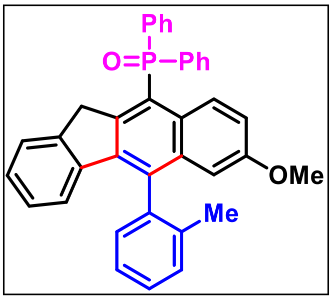
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.31 (d, *J* = 8.5 Hz, 1H), 7.80-7.76 (m, 4H), 7.56 (d, *J* = 6.5 Hz, 2H), 7.52 (d, *J* = 7.0 Hz, 1H), 7.50-7.46 (m, 5H), 7.39 (d, *J* = 7.0 Hz, 1H), 7.30-7.27 (m, 2H), 7.22- 7.20 (m, 1H), 7.19-7.17 (m, 1H), 7.00-6.97 (m, 1H), 6.92-6.90 (m, 1H), 6.35 (d, *J* = 7.5 Hz, 1H), 3.94 (s, 2H), 3.65 (s, 3H), 2.46 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 156.9, 147.2 (d, *J* = 8.5 Hz), 144.6, 139.7, 139.2, 138.7, 138.4 (d, *J* = 12.9 Hz), 137.8 (d, *J* = 2.9 Hz), 135.1 (d, *J* = 9.3 Hz), 134.9 (d, *J* = 102.3 Hz), 132.3, 132.2, 132.1, 130.0, 129.4, 129.0 (2 s), 128.9, 127.1 (d, *J* = 101 Hz), 126.6, 124.6, 123.8, 122.0 (d, *J* = 99.9 Hz), 117.5, 106.6, 55.2, 38.8, 21.7 ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{37}H_{30}O_2P$ 537.1978 found 537.1979.

Compound 30bh



Yield: 40.8 mg (76%), white solid.

Mp: 207-209 °C.

IR (neat): ν_{max} 3056, 2971, 1617, 1505, 1436, 1230, 1177, 1036, 907, 725 cm^{-1}

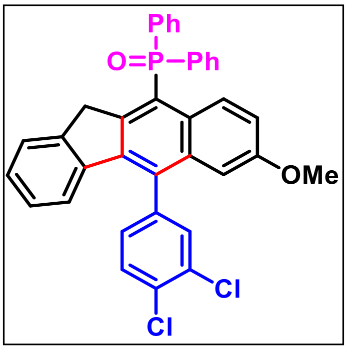
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.37 (d, *J* = 9.0 Hz, 1H), 7.80-7.77 (m, 4H), 7.59-7.55 (m, 2H), 7.49-7.46 (m, 6H), 7.43-7.40 (m, 1H), 7.28-7.27 (m, 1H), 7.24 (s, 1H), 7.17-7.15 (m, 1H), 6.99-6.93 (m, 2H), 6.79 (s, 1H), 6.28 (d, *J* = 8.0 Hz, 1H), 3.86 (s, 2H), 3.63 (s, 3H), 1.97 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 157.2, 147.0 (d, *J* = 8.3 Hz), 143.4, 139.6, 138.4 (d, *J* = 12.1 Hz), 138.0, 136.9, 134.8 (d, *J* = 103.9 Hz), 132.2, 132.1 (2 s), 132.0, 130.8, 129.6, 129.2 (d, *J* = 4.1 Hz), 129.0 (d, *J* = 11.6 Hz), 128.6, 127.2 (d, *J* = 86.8 Hz), 127.0, 124.5, 123.1, 122.1 (d, *J* = 100.0 Hz), 117.6, 105.9, 55.1, 38.8, 19.7 ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{37}H_{30}O_2P$ 537.1978 found 537.1976.

Compound 30bi



Yield: 45.5 mg (77%), white solid.

Mp: 229-232 °C.

IR (neat): ν_{max} 2964, 2932, 1618, 1507, 1473, 1233, 1178, 1033, 910, 728 cm^{-1}

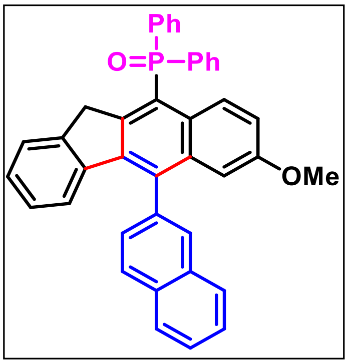
^{1}H NMR (500 MHz, CDCl$_3$): δ 8.33 (d, *J* = 9.0 Hz, 1H), 7.79-7.73 (m, 4H), 7.59-7.56 (m, 3H), 7.50-7.47 (m, 4H), 7.33-7.29 (m, 3H), 7.23-7.21 (m, 1H), 7.08-7.06 (m, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 6.76 (bs, 1H), 6.44 (d, *J* = 7.0 Hz, 1H), 3.95 (s, 2H), 3.69 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 157.3, 147.0 (d, *J* = 8.5 Hz), 144.8, 139.0 (d, *J* = 2.9 Hz), 138.6 (d, *J* = 12.4 Hz), 134.6 (d, *J* = 102.5 Hz), 134.5 (d, *J* = 8.5 Hz), 134.3 (d, *J* = 2.1 Hz), 133.9, 132.7, 132.2, 132.1 (d, *J* = 4.5 Hz), 132.0 (d, *J* = 4.4 Hz), 131.9, 131.7, 129.4, 129.3 (d, *J* = 5.5 Hz), 129.0 (d, *J* = 12.1 Hz), 128.0, 126.8, 124.9, 123.4, 121.9, (d, *J* = 102.1 Hz), 117.6, 106.0, 55.3, 38.7 (d, *J* = 3.1 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 31.0 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{26}Cl_{2}$O2P 591.1042 found 591.1044.

Compound 30bj



Yield: 42.9 mg (75%), white solid.

Mp: 223-225 °C.

IR (neat): ν_{max} 2964, 2932, 1618, 1507, 1473, 1233, 1178, 1033, 910, 728 cm^{-1}

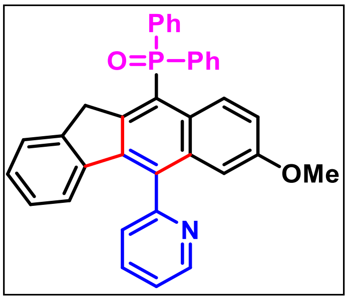
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (d, *J* = 9.5 Hz, 1H), 8.13 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.90 (d, *J* = 7.5 Hz, 1H), 7.83-7.79 (m, 4H), 7.61-7.56 (m, 5H), 7.54-7.50 (m, 4H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.15-7.12 (m, 1H), 6.93 (dd, J_1= 9.5, J_2= 2.5 Hz, 1H), 6.87-6.83 (m, 2H), 6.29 (d, *J* = 8.0 Hz, 1H), 4.00 (s, 2H), 3.56 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 157.0, 147.2 (d, *J* = 4.5 Hz), 144.6, 139.5, 138.7 (d, *J* = 12.3 Hz), 137.3 (d, *J* = 2.4 Hz), 136.3, 135.3, 135.2, 134.9 (d, *J* = 102.6 Hz), 134.4 134.1, 133.2, 132.2, 132.1 (2s), 129.4, 129.1 (2 s), 129.0, 128.9, 128.7, 128.6, 128.4, 128.2, 127.8, 127.6, 126.6 (2 s), 124.6, 123.8, 122.3 (d, *J* = 99.4Hz) 117.6, 106.5, 55.2, 38.8 ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{26}Cl_{2}$O2P 591.1042 found 591.1044.

Compound 30bk



Yield: 37.2 mg (71%), white solid.

Mp: 212-215 °C.

IR (neat): ν_{max} 2969, 2926, 1619, 1508, 1436, 1230, 1170, 1035, 908, 728 cm^{-1}

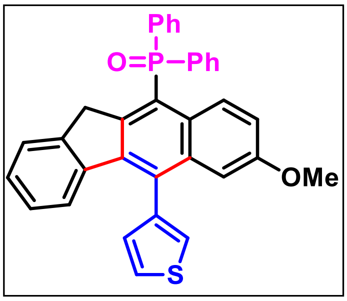
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.31 (d, *J* = 9.0 Hz, 1H), 8.00-7.98 (m, 1H), 7.79-7.75 (m, 4H), 7.69-7.65 (m, 3H), 7.58-7.53 (m, 3H), 7.49-7.44 (m, 3H), 7.31-7.29 (m, 1H), 7.19-7.14 (m, 1H), 6.99-6.96 (m, 1H), 6.91 (d, *J* = 8.5 Hz, 1H), 6.70 (bs, 1H), 6.04 (d, *J* = 8.0 Hz, 1H) 3.95 (s, 2H), 3.65 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 157.2, 147.3 (d, *J* = 8.5 Hz), 144.8, 138.9, 137.4, 134.7 (d, *J* = 102.0 Hz), 132.3 (3 s), 132.2, 132.1, 131.9, 129.2, 128.9 (d, *J* = 4.5 Hz), 128.7 (d, *J* = 12.2 Hz), 127.8, 126.6, 126.7, 125.6, 124.7, 123.3, 123.1, 122.3 (d, *J* = 101.0 Hz), 117.6, 105.9, 55.1, 38.8 (d, *J* = 2.4 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{35}H_{27}NO_2P$ 524.1774 found 527.1777.

Compound 30bl



Yield: 39.1 mg (74%), white solid.

Mp: 202-204 °C.

IR (neat): ν_{max} 3006, 2933, 1618, 1506, 1472, 1232, 1175, 1033, 905, 725 cm^{-1}

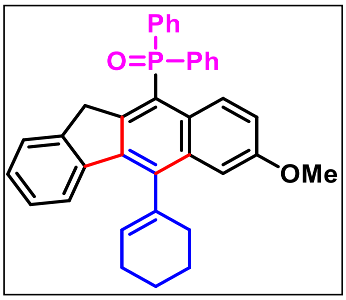
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.29 (d, *J* = 9.5 Hz, 1H), 7.79-7.75 (m, 4H), 7.68 (dd, J_1= 4.5, J_2= 3.0 Hz, 1H), 7.58-7.55 (m, 2H), 7.49-7.47 (m, 4H), 7.35 (dd, J_1= 3.0, J_2= 1.0 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 2H), 7.22-7.19 (m, 1H), 7.08-7.05 (m, 1H), 6.96 (bs, 1H), 6.92 (dd, *J* $_1$= 9.5, *J* $_2$= 3.0 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 3.96 (s, 2H), 3.69 (s, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 157.1, 147.1 (d, *J* = 10.1 Hz), 144.6, 139.5, 139.4, 138.6, 135.6 (d, *J* = 11.0 Hz), 134.7 (d, *J* = 102.2 Hz), 132.4 (d, *J* = 2.0 Hz), 132.1, 132.0, 129.1, 129.0, 128.9, 128.4 (d, *J* = 12.4 Hz), 127.7, 127.3, 126.7, 124.6, 123.9, 123.4, 122.4 (d, *J* = 99.0 Hz), 117.7, 106.0, 55.1, 38.8 (d, *J* = 2.4 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 30.9 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{28}O_2P$ 529.1386 found 529.1380.

Compound 30bm



Yield: 35.8 mg (68%), white solid.

Mp: 202-204 °C.

IR (neat): ν_{max} 2945, 2922, 1617, 1504, 1436, 1228, 1176, 1037, 908, 727 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.26 (d, *J* = 9.5 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.76-7.72 (m, 4H), 7.56-7.53 (m, 2H), 7.47-7.45 (m, 5H), 7.35-7.32 (m, 2H), 7.29-7.27 (m, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 5.91 (br s, 1H), 3.89 (s, 2H), 3.87 (s, 3H), 2.42-2.36 (m, 4H), 2.01-1.09 (m, 4H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ **(major isomer)** 156.9, 147.4 (d, *J* = 8.2 Hz), 144.5, 139.9 (d, *J* = 2.6 Hz), 136.9 (d, *J* = 12.2 Hz), 135.7, 134.9 (d, *J* = 102.1 Hz), 134.1 (d, *J* = 9.0 Hz), 132.1 (d, *J* = 4.1 Hz), 132.0 (d, *J* = 4.0 Hz), 129.6, (d, *J* = 13.5 Hz), 129.2 (2 s), 128.9 (d, *J* = 12.0 Hz), 128.6 (d, *J* = 9.8 Hz), 128.2, 127.5, 126.8, 124.7, 123.8 121.1 (d, *J* = 100.2 Hz), 117.3, 105.6, 55.2, 38.7 (d, *J* = 2.4 Hz), 29.1, 25.7, 23.4, 22.3, **(minor isomer)** 147.1 (d, *J* = 8.3 Hz), 144.6, 139.6, 137.6 (d, *J* = 1.9 Hz), 134.9 (d, *J* = 101.7 Hz), 132.3, 132.2, 129.0, 128.9, 128.3, 127.5, 126.5, 124.6, 123.7, 121.3 (d, *J* = 102.8 Hz), 117.6, 106.4, 55.1, 29.1, 22.5 ppm

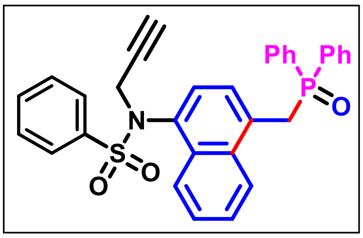
^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 31.0 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{36}H_{32}O_2P$ 527.2134 found 527.2136.

3.12 Synthesis of Compounds 31b-d: Representative Procedure for 31b

A 25.0 mL round-bottomed flask was charged with sulfonamide-tethered vinylic propargyl alcohol **28b** (200 mg, 0.55 mmol) in THF (10.0 mL) to which was added NEt_3 (77.0 µL, 0.55 mmol) followed by Ph_2PCl (94 µL, 0.55 mmol) at 0 °C under N_2-atmosphere. After the addition of Ph_2PCl, the mixture was brought to the room temperature, stirred for 1 h and then heated under reflux overnight. The mixture was quenched by adding water (10 mL) and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). Then the organic layers were combined, washed with brine (10 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography using silica gel (100-200 mesh) with ethyl acetate/hexane (30:70) as the eluent.

Compound 31a



Yield: 226.6 mg (purity ca 95%,77%), yellow solid.

Mp: 203 °C.

IR (neat): ν_{max} 3295, 2963, 2121, 1593, 1488, 1348, 1186, 998, 855, 745 cm^{-1}

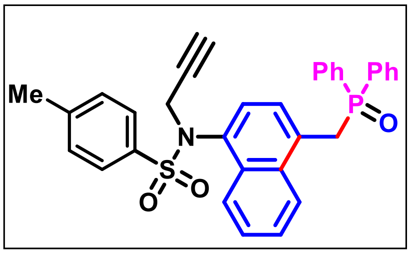
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83-7.73 (m, 7H), 7.60-7.50 (m, 7H), 7.47-7.39 (m, 4H), 7.28-7.24 (m, 2H), 6.90 (d, J = 7.5 Hz, 1H), 4.24-4.14 (m, 2H), 3.45-3.42 (m, 1H), 3.38-3.36 (m, 1H), 2.42-2.20 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 139.8, 136.4, 134.6 (d, J = 3.5 Hz), 133.8 (d, J = 4.4 Hz), 132.7, 132.5 (d, J = 1.5 Hz), 132.4, 132.1 (d J = 3.0 Hz), 131.9, 131.6, 131.3 (3 s), 131.2, 130.3 (d, J = 8.3 Hz), 129.8, 129.1, 128.7 (d, J = 2.6 Hz), 128.6 (d, J = 2.8 Hz), 127.7 (d, J = 6.0 Hz), 127.1, 126.9, 126.4 (d, J = 2.8 Hz), 124.9, 123.9, 77.9, 74.4, 40.7, 38.6 (d, J = 65.3 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 29.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{32}H_{27}NO_3PS$ 536.1444 found 536.1449.

Compound 31b



Yield: 236 mg (78%), yellow solid.

Mp: 207 °C.

IR (neat): ν_{max} 3295, 2963, 2121, 1593, 1488, 1348, 1186, 998, 855, 745 cm^{-1}

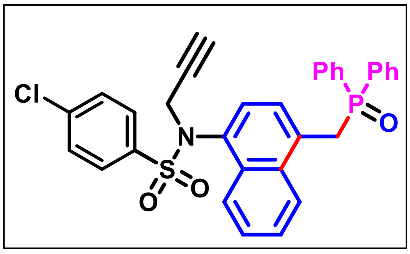
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 1H), 7.92 (d, J = 8.5 Hz, 1H), 7.69-7.65 (m, 3H), 7.64-7.61 (m, 2H), 7.50-7.46 (m, 4H), 7.42-7.38 (m, 5H), 7.24 (d, J = 8.0 Hz, 2H), 7.13 (dd, J_1= 7.5, J_2= 3.0 Hz, 1H), 6.86 (d, J = 7.5 Hz, 1H), 4.73 (dd, J_1= 16.0, J_2= 3.0 Hz, 1H), 4.25 (dd, J_1= 18.0, J_2= 2.5 Hz, 1H), 4.15-4.03 (m, 2H), 2.43 (s, 3H), 2.09-2.08 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 143.9, 136.0, 134.9 (d, J = 3.5 Hz), 133.6 (d, J = 4.4 Hz), 132.8, 132.6, 132.4, 132.0, 131.9, 131.6, 131.3 (d, J = 8.3 Hz), 131.2 (d, J = 8.8 Hz), 129.9 (d, J = 8.2 Hz), 129.5, 128.6 (d, J = 3.4 Hz), 128.5 (d, J = 3.5 Hz), 128.3, 127.7 (d, J = 6.1 Hz), 126.8 (d, J = 2.8 Hz), 126.3, 124.6, 124.2, 78.1, 74.0, 41.8, 35.5 (d, J = 65.7 Hz), 21.7 ppm

^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$): δ 29.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{33}H_{29}NO_3PS$ 550.1600 found 550.1604.

Compound 31c



Yield: 218.1 mg (75%), yellow solid.

Mp: 218°C.

IR (neat): ν_{max} 3222, 3018, 2192, 1592, 1446, 1353, 1163, 989, 825, 743 cm^{-1}

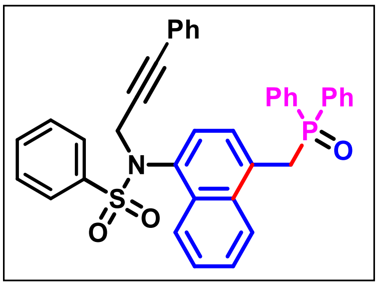
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, J = 8.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.70-7.64 (m, 6H), 7.51-7.46 (m, 3H), 7.45-7.38 (m, 7H), 7.10 (dd, J_1= 8.0, J_2= 3.0 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 4.81 (dd, J_1= 18.0, J_2= 2.5 Hz, 1H), 4.19 (dd, J_1= 18.0, J_2= 2.5 Hz, 1H), 4.14-4.05 (m, 2H), 2.14-2.13 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 139.6, 137.7, 134.6 (d, J = 3.5 Hz), 133.8 (d, J = 4.4 Hz), 132.7, 132.5 (d, J = 1.5 Hz), 132.4, 132.1 (dd→t, J = 3.0 Hz), 131.9, 131.6, 131.3 (3 s), 131.2, 130.3 (d, J = 8.3 Hz), 129.8, 129.1, 128.7 (d, J = 2.6 Hz), 128.6 (d, J = 2.8 Hz), 127.7 (d, J = 6.0 Hz), 127.1, 126.9, 126.4 (d, J = 2.8 Hz), 124.9, 123.9, 77.9, 74.4, 41.9, 35.1 (d, J = 65.6 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 29.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{32}H_{26}ClNO_3PS$ 570.1054 found 570.1057.

Compound 31d



Yield: 204.1 mg (71%), yellow solid.

Mp: 227°C.

IR (neat): ν_{max} 3057, 2969, 2121, 1592, 1488, 1350, 1163, 998, 853, 725 cm^{-1}

^{1}H NMR (500 MHz, CDCl$_3$): δ 8.27 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.5 Hz, 1H), 7.81 (d, J = 7.0 Hz, 2H), 7.69-7.62 (m, 4H), 7.56-7.50 (m, 3H), 7.45-7.42 (m, 3H), 7.39-7.34 (m, 6H), 7.29-7.24 (m, 2H), 7.09-7.06 (m, 3H), 6.89 (d, J = 7.0 Hz, 1H), 5.03 (d, J = 18.0 Hz, 1H), 4.46 (d, J = 18.0 Hz, 1H), 4.19-4.12 (m, 1H), 4.08-4.02 (m, 1H) ppm.

^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$): δ 139.4, 135.0 (d, J = 3.4 Hz), 133.8 (d, J = 4.1 Hz), 133.0, 132.8, 132.4, 132.0 (2 s), 131.6, 131.5, 131.4, 131.3, 131.2, 130.0 (d, J = 8.0 Hz), 128.9, 128.7, 128.6 (3 s), 128.5, 128.4, 128.3, 127.7 (d, J = 6.1 Hz), 127.0, 126.8, 126.4 (d, J = 2.4 Hz), 124.7, 124.3, 122.4, 85.9, 83.6, 42.8, 35.1 (d, J = 65.6 Hz) ppm

^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$): δ 29.7 ppm.

HRMS (ESI- TOF): *m/z* [M + H]+ calcd. for $C_{38}H_{21}CNO_3PS$ 612.1757 found 612.1759.

3.13 X-ray Crystallography

A suitable crystal was mounted on a glass fiber (for **16aa**, **16ab**, **16ai**, **16ba**, **16bb, 16bo, 17aa**, **17bq**, **18aa**, **18an**, **18ga**, **18ll**, **18ml, 21aa, 22aa 23aa, 23ga, 24ai, 30bf** and **31b)** 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.[122] Crystal data are summarized in Tables 17-21.

Table 17: Crystal data for compounds **16aa**, **16ab**, **16ae** and **16ba**

Compound	**16aa**	**16ab**	**16ai**	**16ba**
Emp. formula	$C_{21}H_{21}NO_5S$	$C_{22}H_{23}NO_6S$	$C_{22}H_{23}NO_6S$	$C_{22}H_{23}NO_5S$
Formula weight	399.45	429.47	429.47	413.47
Crystal system	Triclinic	Monoclinic	Triclinic	Monoclinic
Space group	$P\bar{1}$	*P121/n1*	$P\bar{1}$	P121/n1
a /Å	11.4008(4)	11.5288(3)	9.3825(2)	11.9526(4)
b /Å	12.3822(4)	10.2508(3)	11.0897(2)	10.1913(3)
c /Å	16.0543(4)	17.5657(5)	20.4263(4)	18.2238(5)
α/deg	78.679(3)	90	93.499(2)	90
β/deg	89.901(2)	97.490(2)	117.361(6)	107.240(3)
γ/deg	65.999(3)	90	90.127(2)	90
V /Å^3	2022.37(12)	2058.19(10)	2119.71(7)	2120.15(9)
Z	4	4	4	4
Dcalc /g cm^{-3}]	1.312	1.386	1.346	1.295
μ /mm^{-1}	0.192	0.197	0.191	0.185
F(000)	840	904.0	904.0	872
Data/ restraints/ parameters	7132/0/518	3622/0/278	7463/0/551	3724 /1/268
S	0.974	1.100	0.990	1.113
R1 [I>2σ(I)]	0.0602	0.0364	0.0619	0.0587
wR2 [all data]	0.1553	0.1047	0.1761	0.1900
Max./min. residual electron dens. [eÅ^{-3}]	0.205/-0.342	0.205/-0.461	0.433/-0.315	0.653/-0.443
CCDC no.	2047794	2047795	2047796	2047797

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 18: Crystal data for compounds **16bb, 16bo, 17aa**, and **17bq**

Compound	**16bb**	**16bo**	**17aa**	**17bq**
Emp. formula	$C_{21}H_{21}NO_5S$	$C_{33}H_{27}NO_5S$	$C_{21}H_{19}NO4S$	$C_{20}H_{19}NO4S_2$
Formula weight	443.50	537.61	381.43	401.48
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*P121/c1*	*C12/c1*	*P121/c1*	*P121/c1*
a /Å	12.8740(3)	22.4469(4)	16.8403(17)	7.9006(3)
b /Å	13.4187(3)	11.7545(2)	7.9029(6)	30.9881(10)
c /Å	13.0531(3)	20.5837(4)	15.4737(16)	8.0621(4)
α/deg	90	90	90	90
β/deg	102.980(3)	91.608(2)	113.329(12)	105.387(4)
γ/deg	90	90	90	90
V /Å^3	2197.34(9)	5428.91(17)	1891.0(3)	1903.05(13)
Z	4	8	4	4
Dcalc /g cm^{-3}]	1.341	1.315	1.340	1.401
μ /mm^{-1}	0.187	0.162	0.198	0.306
F(000)	936	2256	800.0	840
Data/ restraints/ parameters	3864/0/288	4768/0/356	3332/0/253	3098/0/252
S	1.065	1.107	0.940	1.075
R1 [I>2σ(I)]	0.0414	0.0507	0.0751	0.0509
wR2 [all data]	0.1148	0.1561	0.2177	0.1545
Max./min. residual electron dens. [eÅ^{-3}]	0.164/-0.293	0.488/-0.643	0.400/-0.302	0.435/-0.
CCDC no.	2047798	2047799	2047800	204801

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 19: Crystal data for compounds **18aa, 18an, 18ga**, and **18ll**

Compound	**18aa**	**18an**	**18ga**	**18ll**
Emp. formula	$C_{19}H1_{2}O_{5}$	$C_{27}H_{16}O_{2}$	$C_{20}H_{14}O_{2}$	$C_{27}H_{16}NO_{2}$
Formula weight	272.31	372.43	286.31	372.40
Crystal system	Monoclinic	Monoclinic	Orthorhombic	Monoclinic
Space group	*C12/c1*	*C12/c1*	*P2221*	*P121/n1*
a /Å	23.2769(10)	27.2297(9)	4.0919(1)	5.9323(2)
b /Å	4.0438(2)	7.6813(2)	8.1314(2)	16.5079(5)
c /Å	27.9920(13)	18.4156(5)	42.7388(15)	818.2979(6)
α/deg	90	90	90	90
β/deg	97.935(4)	100.618(3)	90	98.741(4)
γ/deg	90	90	90	90
V /Å^{3}	2609.6(2)	3785.85(19)	1422.04(7)	1771.10(10)
Z	8	8	4	4
Dcalc /g cm^{-3}]	1.3861	1.3067	1.340	1.397
μ /mm^{-1}	0.089	0.0180	0.085	0.087
F(000)	1136.6	1552.7	800.0	776.0
Data/ restraints/ parameters	2732/0/190	3954/0/262	3036/0/200	2948/0/262
S	0.959	1.025	0.940	1.095
R1 [I>2σ(I)]	0.0550	0.0441	0.0723	0.0496
wR2 [all data]	0.1762	0.1252	0.2288	0.1381
Max./min. residual electron dens. [eÅ^{-3}]	0.2578/-0.3023	0.1726/-0.2212	0.400/-0.302	0.195/-0.267
CCDC no.	2258035	2258036	2258037	2264275

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^{2}-Fc^{2})^{2}/\Sigma wFo^{4}]^{0.5}$

Table 20: Crystal data for compounds **18ml, 21aa, 23aa**, and **23ga**

Compound	**18ml**	**21aa**	**22aa**	**23aa**
Emp. formula	$C_{27}H_{16}O_2$	$C_{33}H_{25}NO_3S$	$C_{28}H_{23}NO_3S$	$C_{33}H_{25}NO_3S$
Formula weight	372.40	515.60	453.53	515.60
Crystal system	Monoclinic	Triclinic	Triclinic	Triclinic
Space group	*C12/c1*	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a /Å	18.2658(5)	9.9328(2)	9.432(2)	11.1178(18)
b /Å	7.4703(2)	14.0005(2)	10.639(2)	11.2499(16)
c /Å	27.6329(9)	19.1652(3)	68.627(8)	15.4737(16)
α/deg	90	76.7090(10)	68.627(8)	75.299(6)
β/deg	104.202(3)	88.8420(10)	77.714(9)	71.883(6)
γ/deg	90	88.0750(10)	65.153(9)	63.864(5)
V /Å^3	3655.30(19)	2592.13(8)	1154.0(5)	1297.6(4)
Z	8	4	2	2
Dcalc /g cm^{-3}]	1.341	1.321	1.305	1.320
μ /mm^{-1}	0.084	0.161	0.171	0.161
F(000)	1552.0	1080.0	476.0	540.0
Data/ restraints/ parameters	3835/0/262	10833/0/687	6467/0/299	5979/0/343
S	1.038	1.070	1.068	1.083
R1 [$I>2\sigma(I)$]	0.0475	0.0556	0.0490	0.0478
wR2 [all data]	0.1338	0.1452	0.1419	0.1418
Max./min. residual electron dens. [eÅ^{-3}]	0.162/-0.181	0.223/-0.309	0.411/-0.223	0.387/-0.293
CCDC no.	2258038	2348193	2348197	2348194

^{a}R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

Table 21: Crystal data for compounds **23ga, 24ai, 30bf**, and **31b**

Compound	**23ga**	**24ai**	**30bf**	**30b**
Emp. formula	$C_{33}H_{24}ClNO_3S$	$C_{28}H_{23}NO_3S$	$C_{41}H_{36}ClO_2P$	$C_{33}H_{28}NO_3PS$
Formula weight	550.04	453.53	698.02	549.59
Crystal system	Triclinic	Orthorhombic	Triclinic	Monoclinic
Space group	$P\bar{1}$	*P21212*	$P\bar{1}$	*P121/n1*
a /Å	10.824(4)	20.9950(10)	9.8348(9)	16.0670(6)
b /Å	11.250(3)	18.7983(8)	11.6396(12)	11.3728(6)
c /Å	12.781(4)	6.0806(3)	18.2049(19)	16.9227(8)
α/deg	78.434(12)	90	80.768(4)	90
β/deg	70.596(10)	90	77.932(4)	113.191(2)
γ/deg	66.297(11)	90	65.624(3)	90
V /Å^3	1340.2(8)	2399.83(19)	1849.8(3)	2842.4(2)
Z	2	4	2	4
*D*calc /g cm^{-3}]	1.363	1.255	1.253	1.284
μ /mm^{-1}	0.257	0.164	0.325	0.205
F(000)	572.0	952.0	728.0	572.0
Data/ restraints/ parameters	4911/0/352	4344/0/299	6751/2/446	6527/0/353
S	1.081	0.997	1.025	1.091
R1 [I>2σ(I)]	0.0628	0.0583	0.0666	0.0510
wR2 [all data]	0.1613	0.1530	0.1876	0.1363
Max./min. residual electron dens. [eÅ^{-3}]	0.263/-0.057	0.309/-0.269	0.697/-0.569	0.464/-0.381
CCDC no.	2348195	2348196		

^{a}R1 = Σ‖Fo| - |Fc‖/Σ|Fo| and wR2 = [Σw(Fo^2-Fc^2)^2/ΣwFo^4]$^{0.5}$

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APPENDIX

(A) Copies of $^1H/^{13}C\{^1H\}$ NMR spectra for representative compounds **4h, 8m, 15d, 16aa, 17aa, 18aa, 18la, 18ma, 19ia, 20fo, 21aa, 21ij, 22aa, 23aa, 24aa, 30bf,** and **31b**

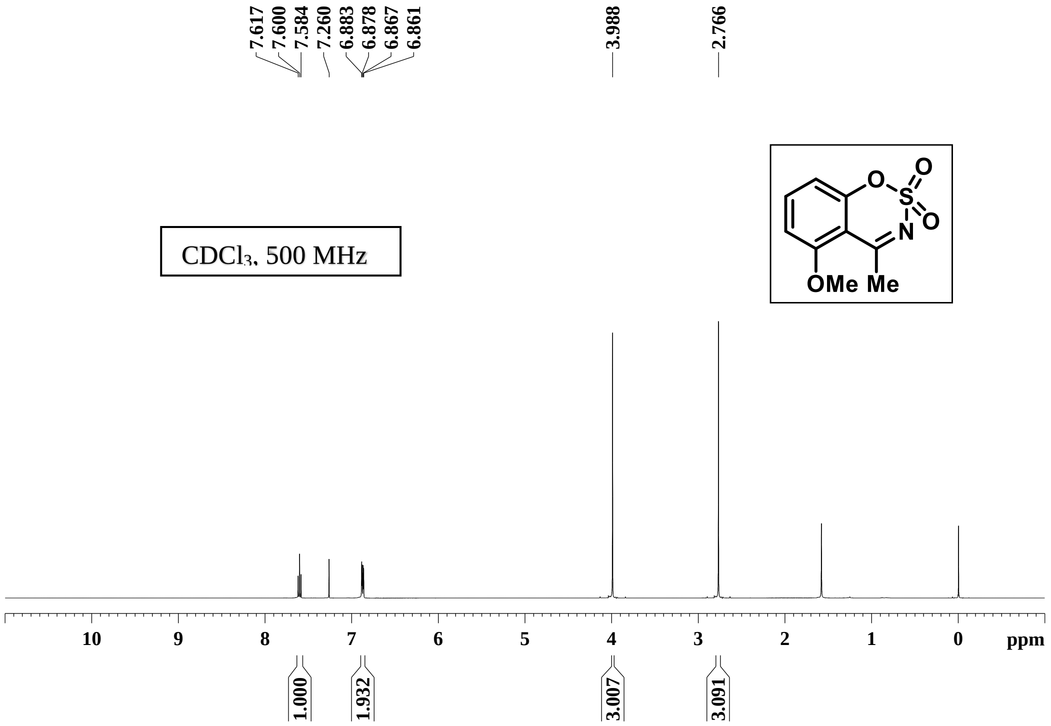


Figure A1: ^1H NMR spectrum of compound 4h

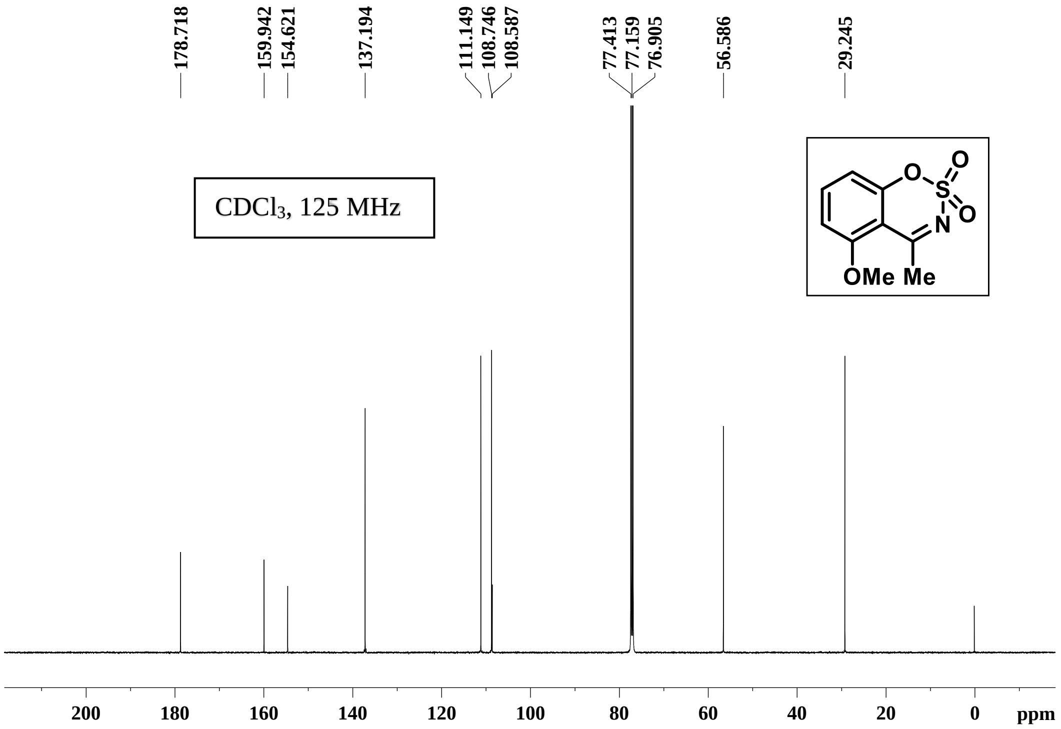


Figure A2: $^{13}C\{^1H\}$ NMR spectrum of compound 4h

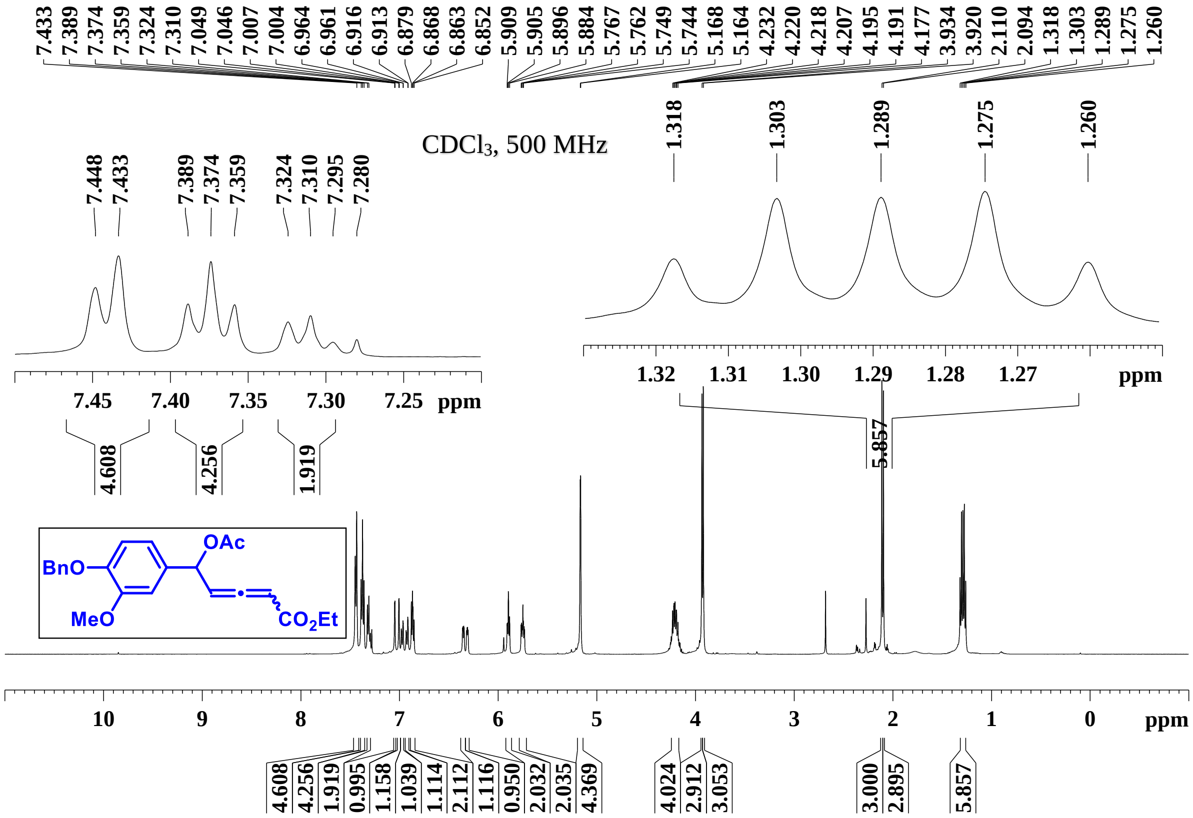


Figure A3: ^{1}H NMR spectrum of compound 8m

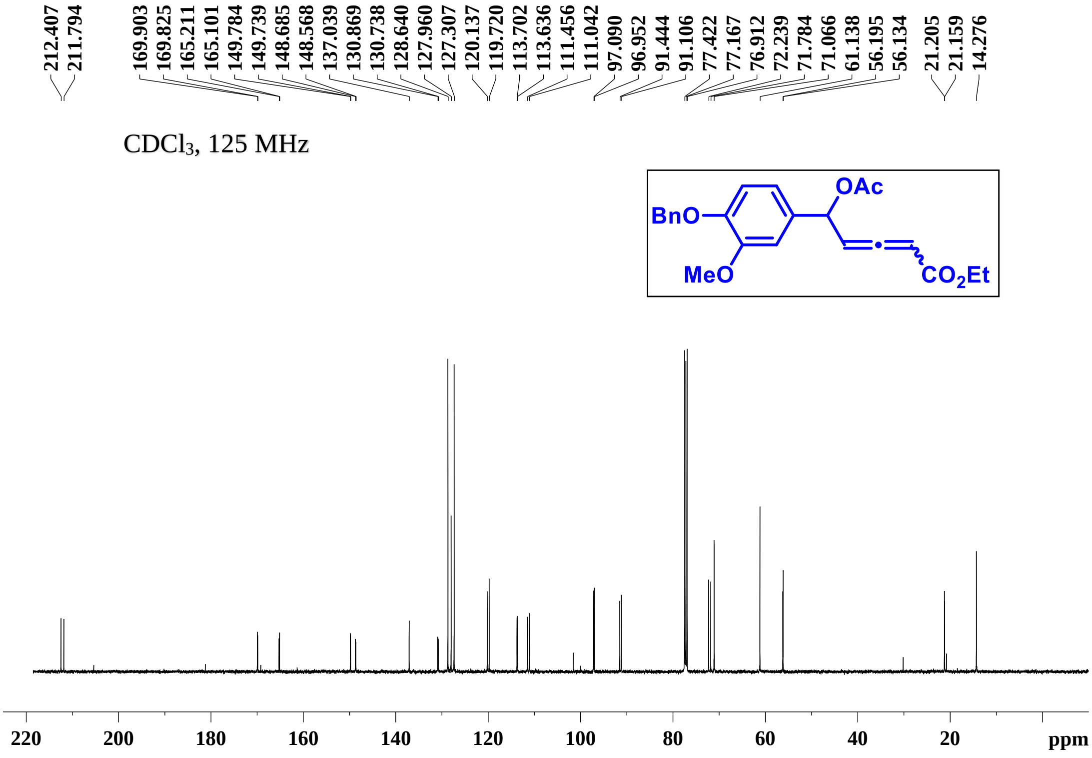


Figure A4: ^{13}C{^{1}H} NMR spectrum of compound 8m

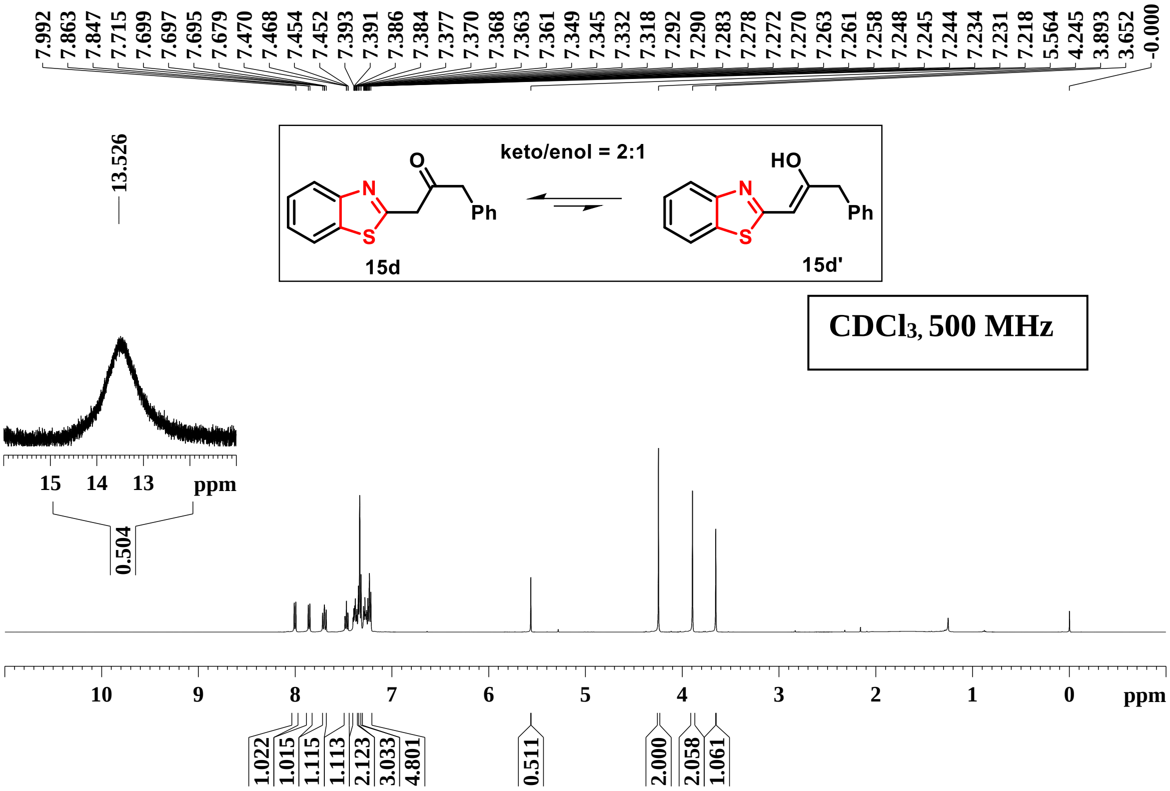


Figure A5: ^{1}H NMR spectrum of compound 15d

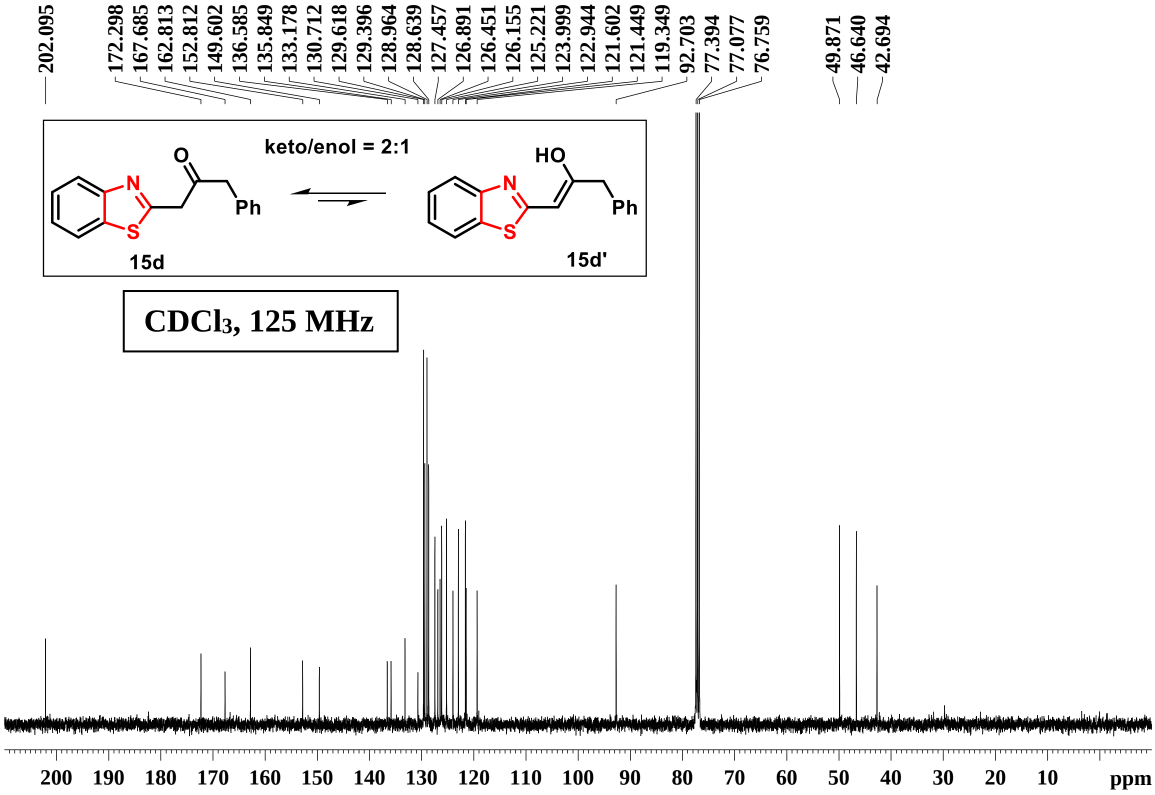


Figure A6: ^{13}C{^{1}H} NMR spectrum of compound 15d

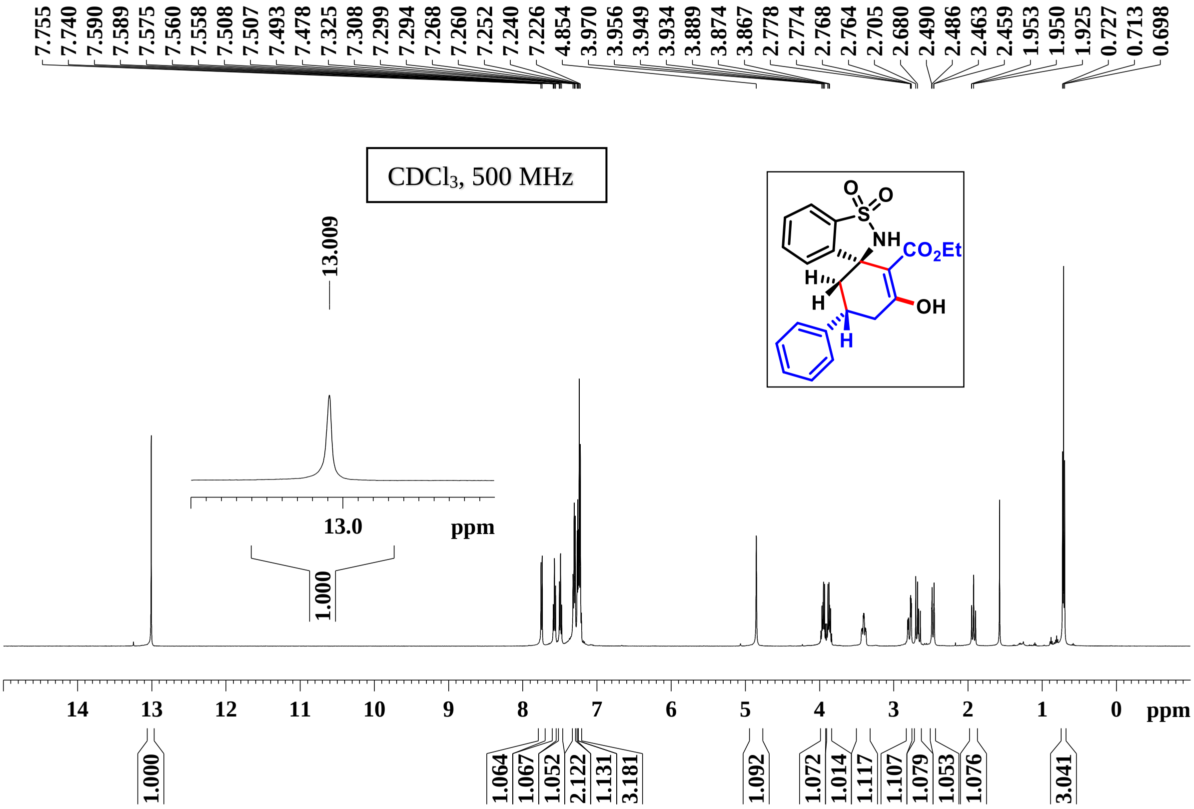


Figure A7: ^{1}H NMR spectrum of compound 16aa

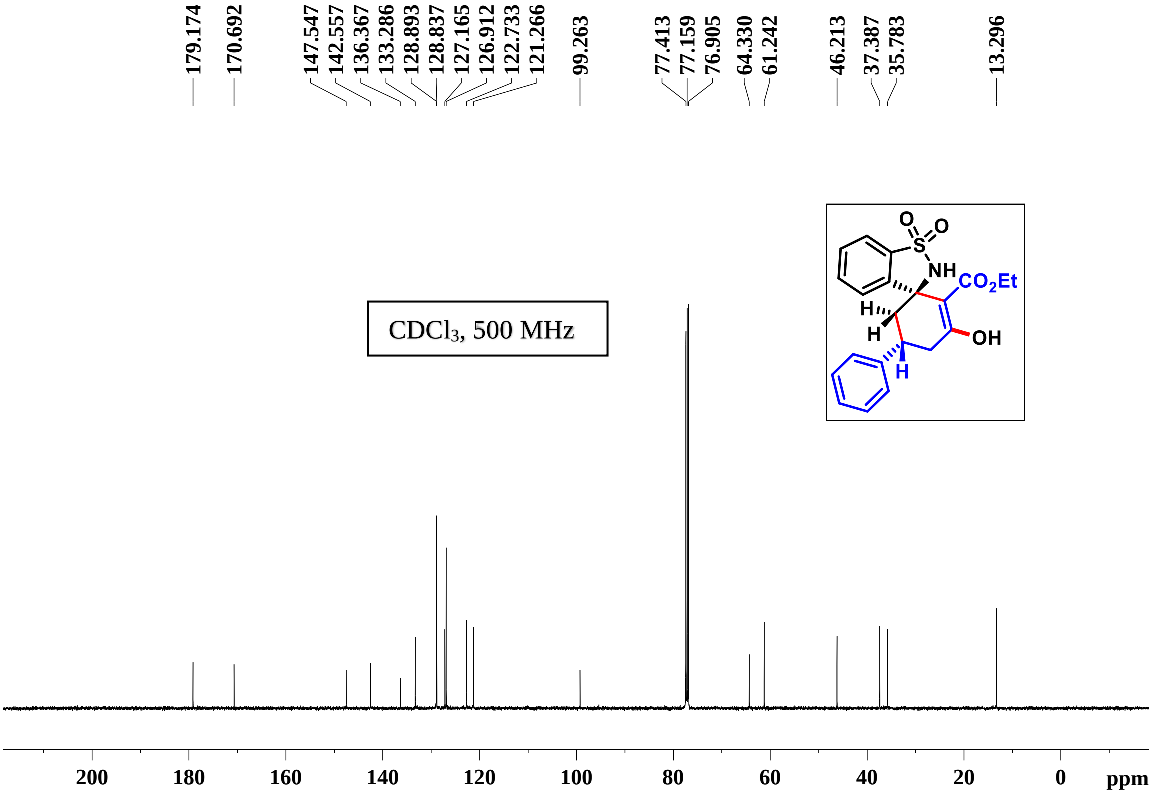


Figure A8: $^{13}C\{^{1}H\}$ NMR spectrum of compound 16aa

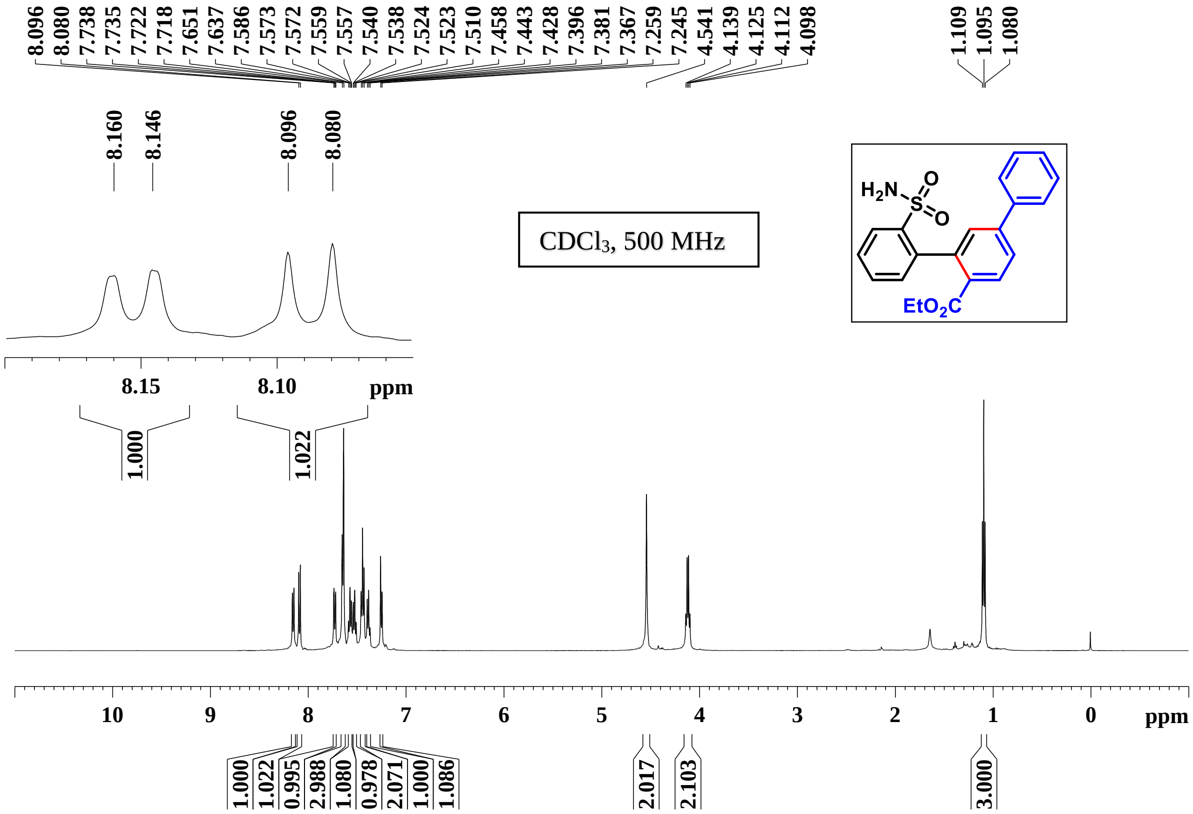


Figure A9: ^{1}H NMR spectrum of Compound 17aa

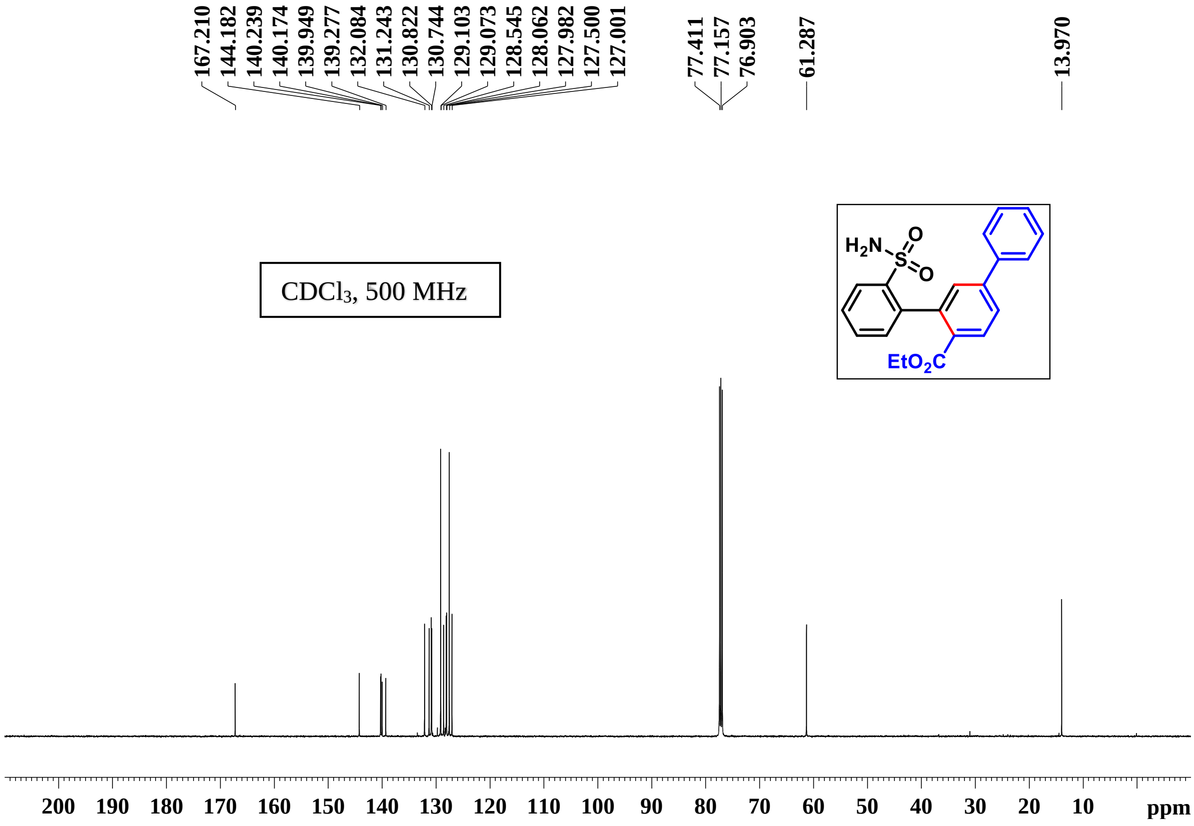


Figure A10: ^{13}C NMR spectrum of compound 17aa

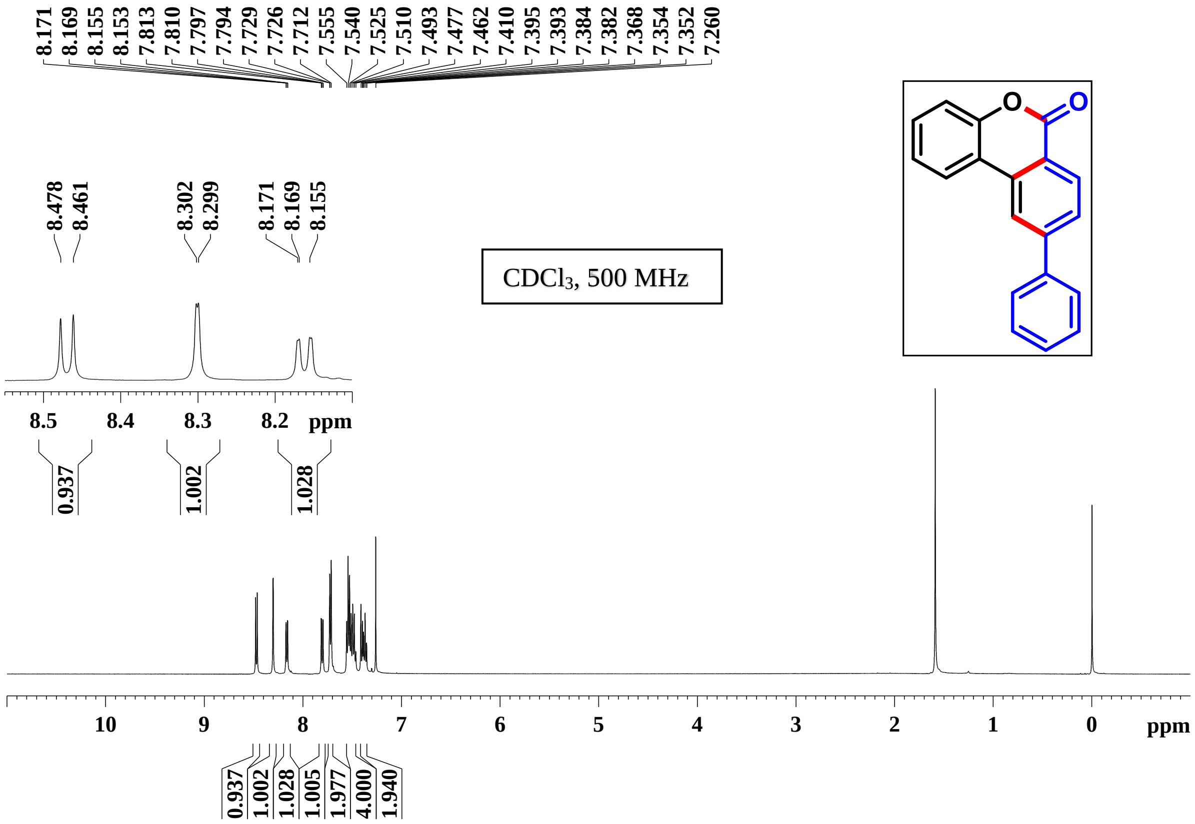


Figure A11: ^{1}H NMR spectrum of compound 18aa

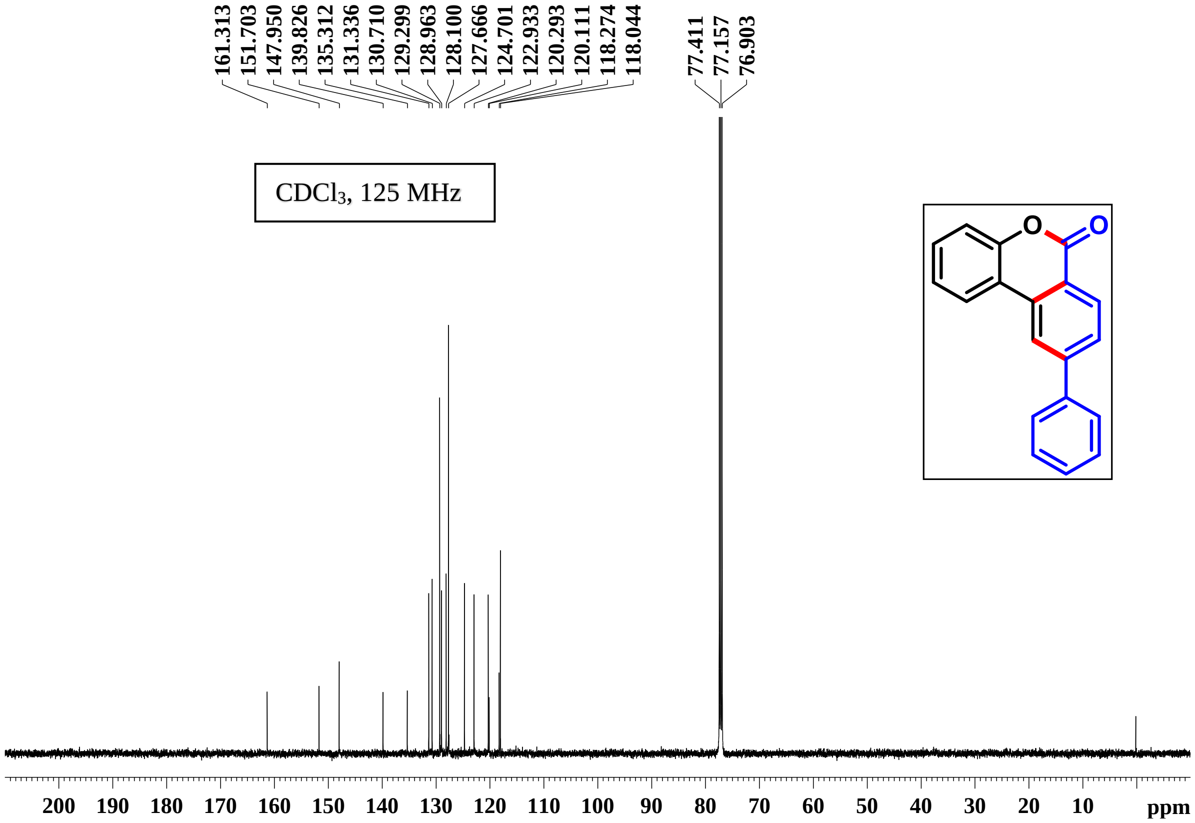


Figure A12: ^{13}C{^{1}H} spectrum of compound 18aa

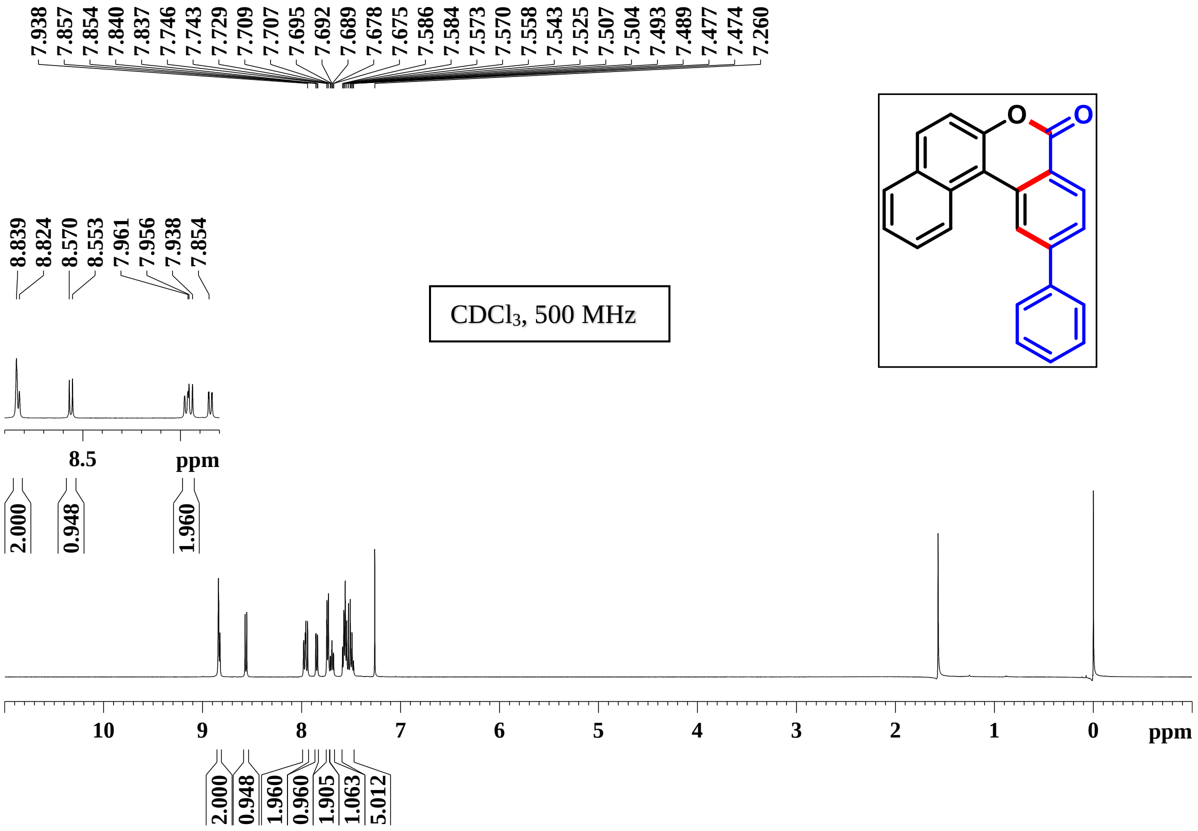


Figure A13: ^{1}H NMR spectrum of compound 18la

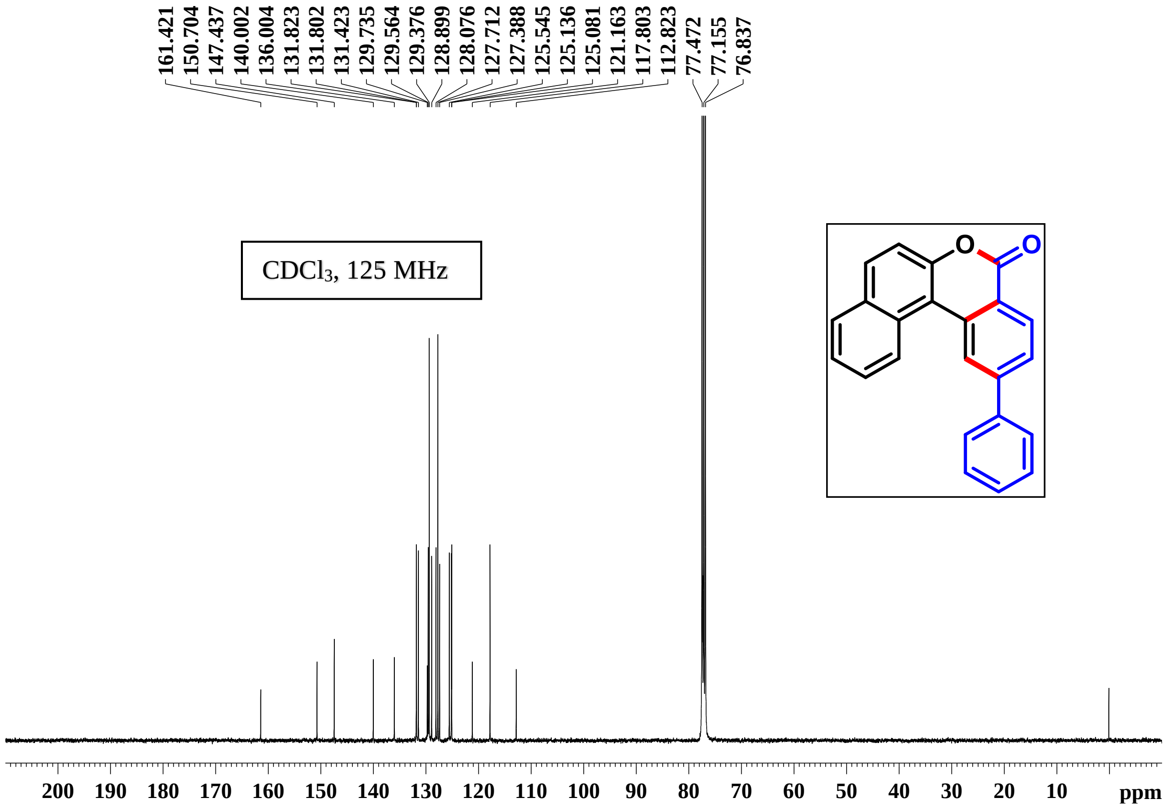


Figure A14: ^{13}C{^{1}H} spectrum of compound 18la

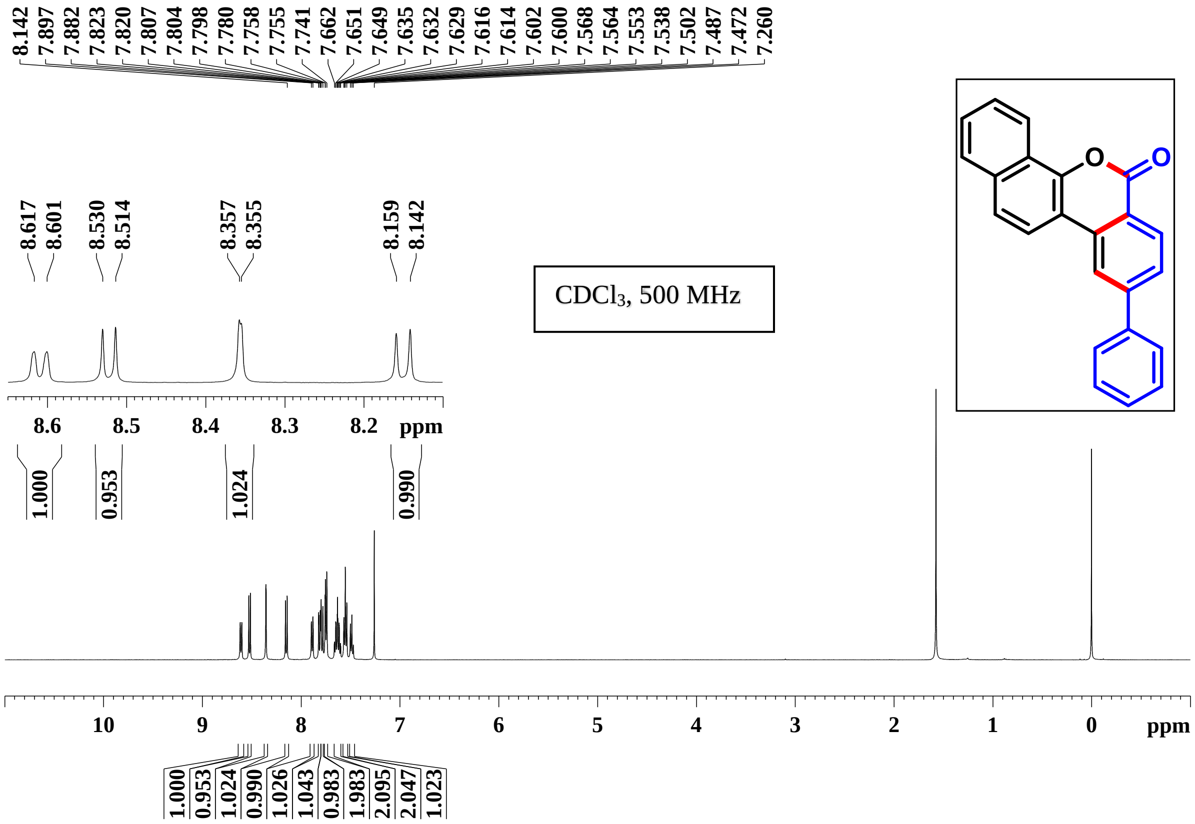


Figure A15: ^{1}H NMR spectrum of compound 18ma

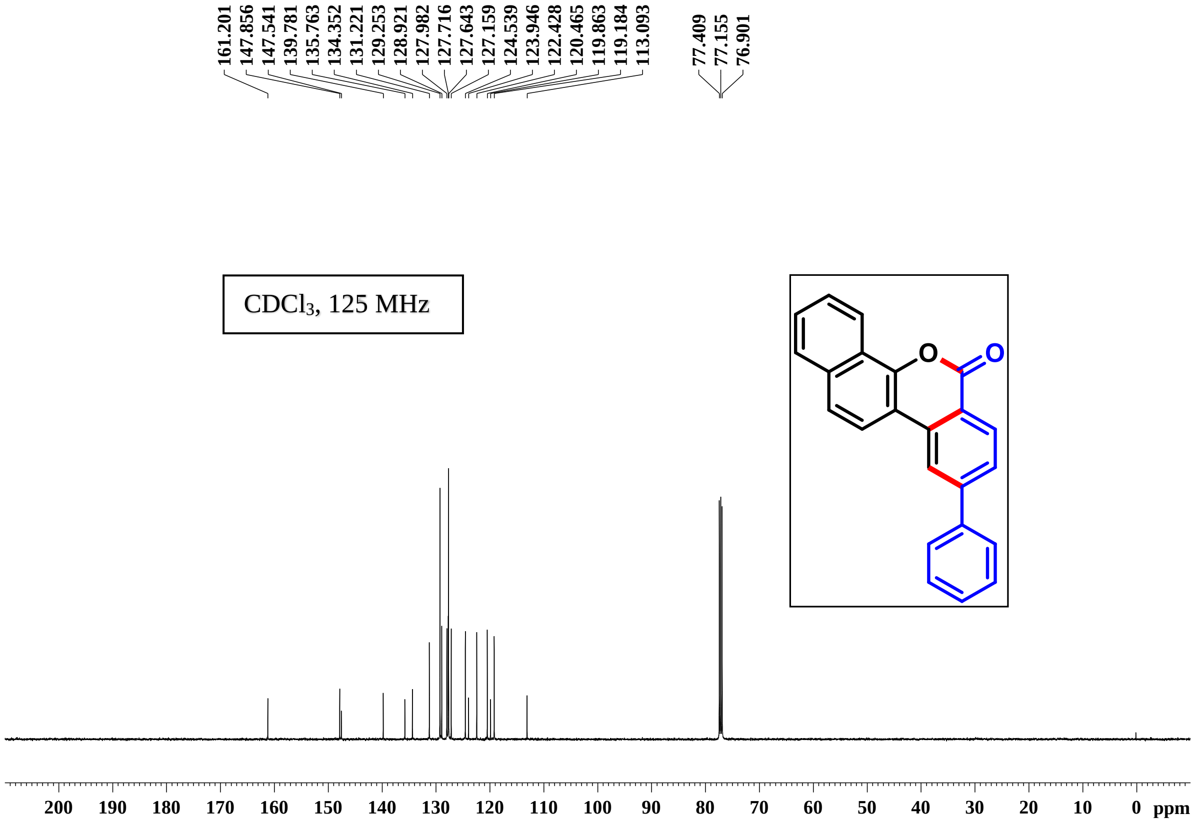


Figure A16: ^{13}C{^{1}H} spectrum of compound 18ma

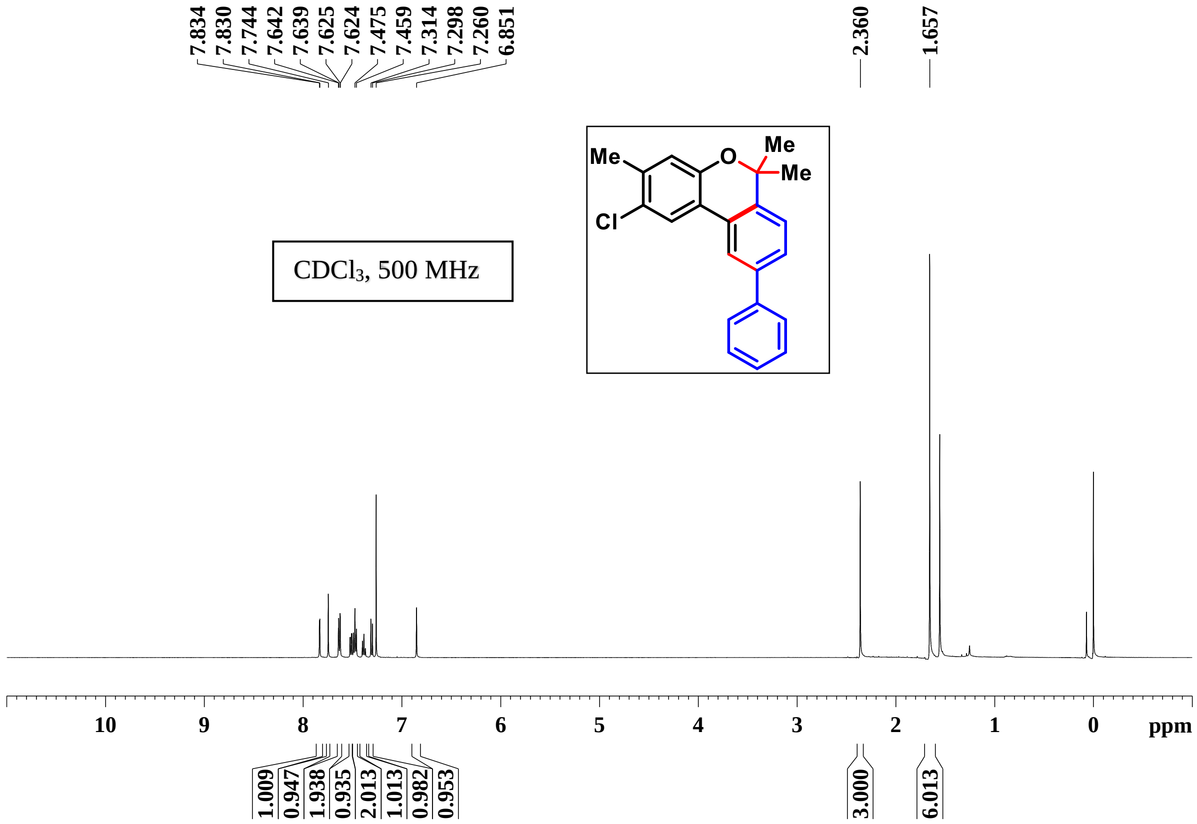


Figure A17: ^{1}H NMR spectrum of compound 19ia

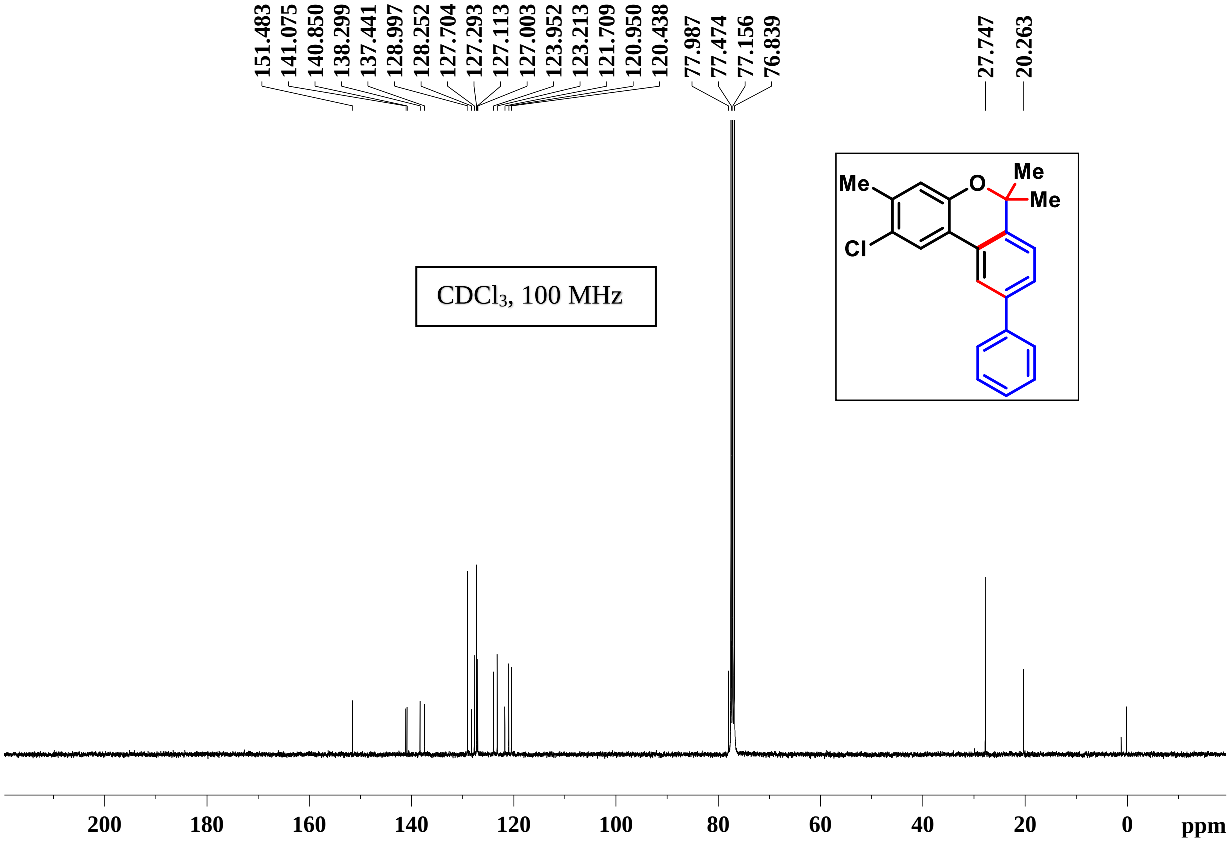


Figure A18: ^{13}C{^{1}H} NMR spectrum of compound 19ia

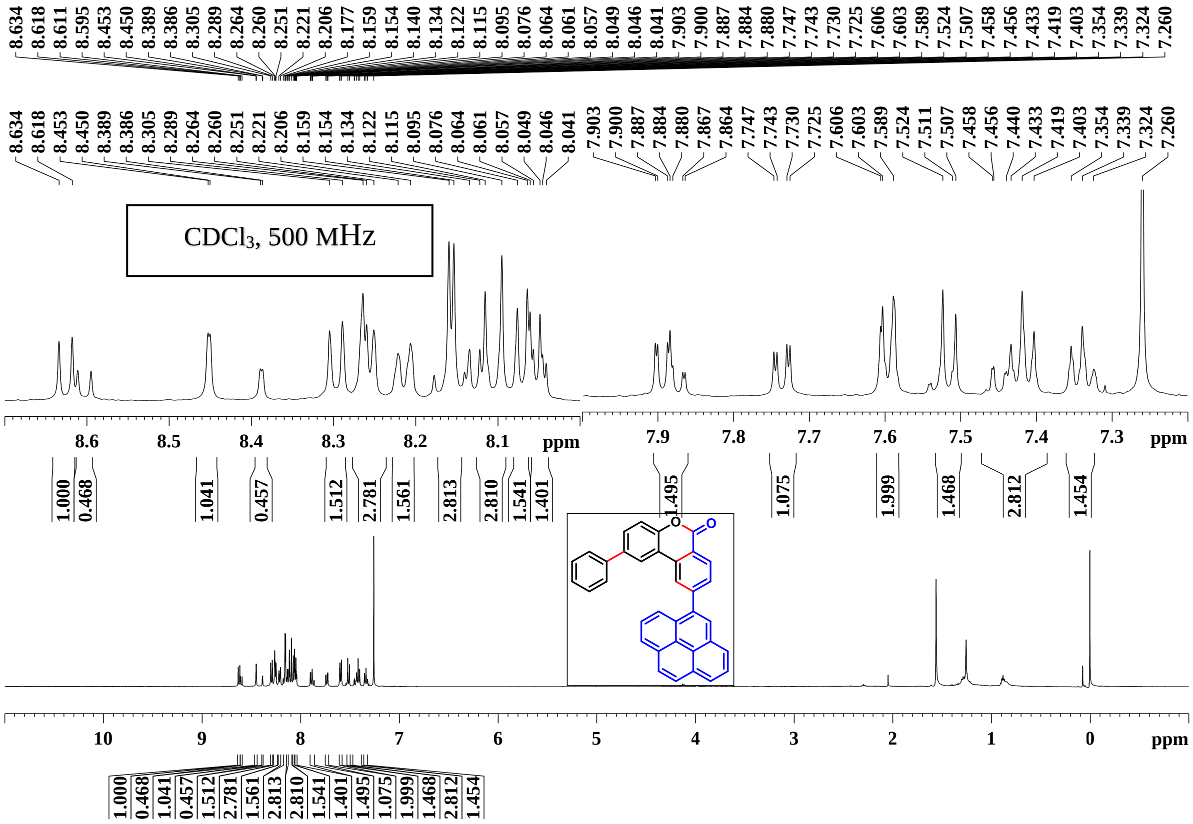


Figure A19: ^{1}H NMR spectrum of compound 20fo

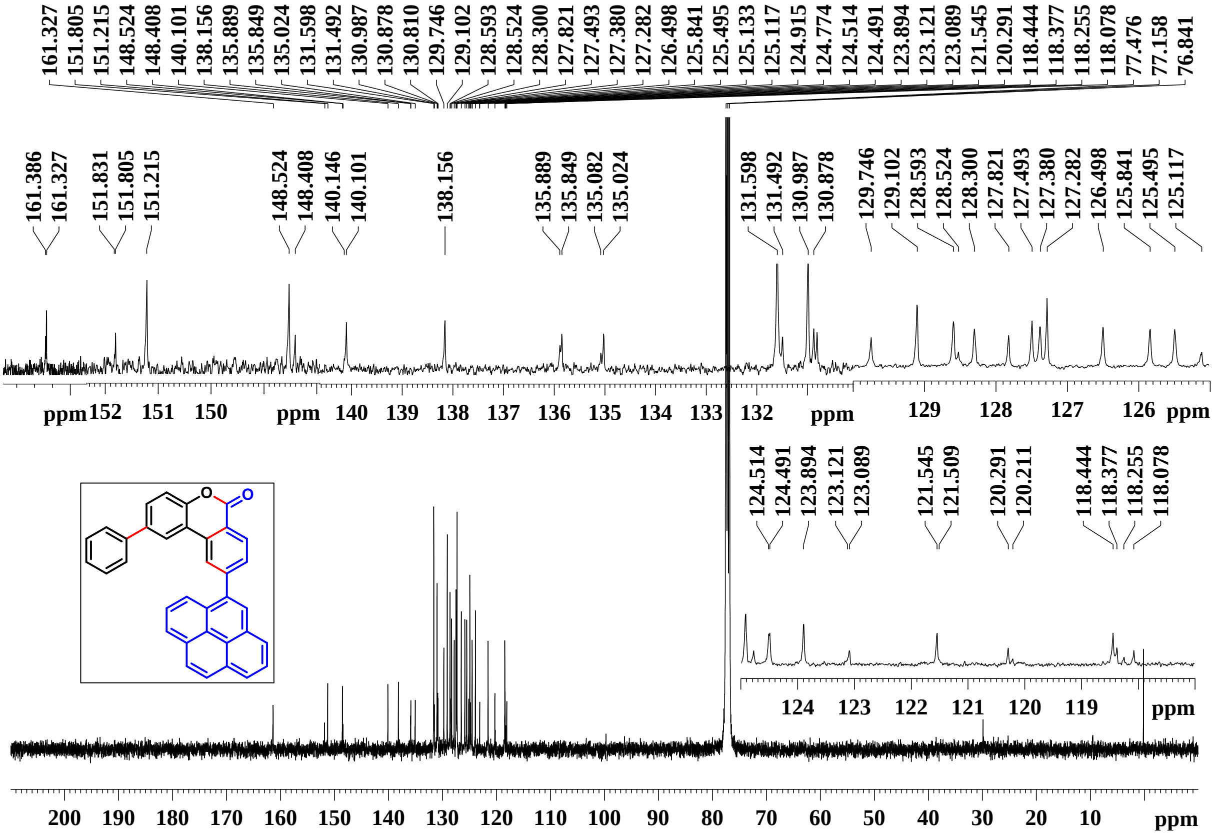


Figure A20: ^{13}C{^{1}H} NMR spectrum of compound 20fo

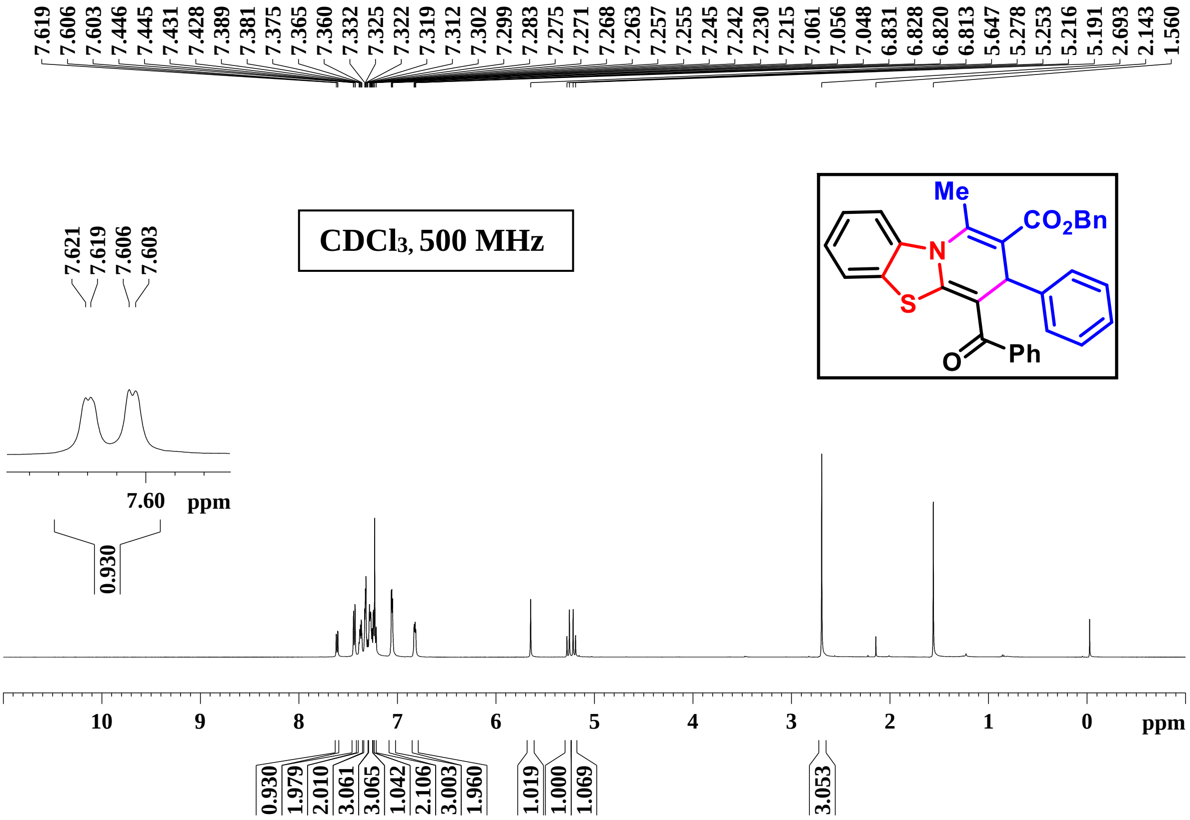


Figure A21: ^{1}H NMR spectrum of compound 21aa

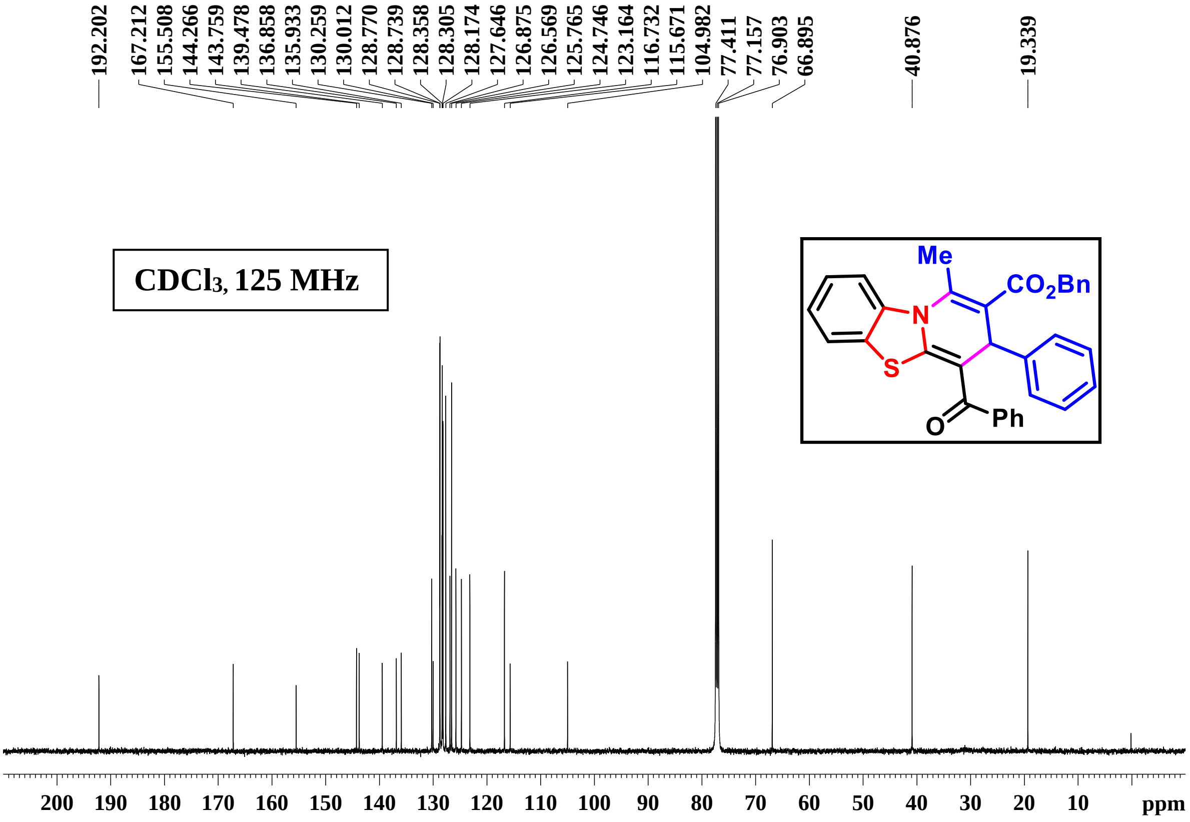


Figure A22: ^{13}C{^{1}H} NMR spectrum of compound 21aa

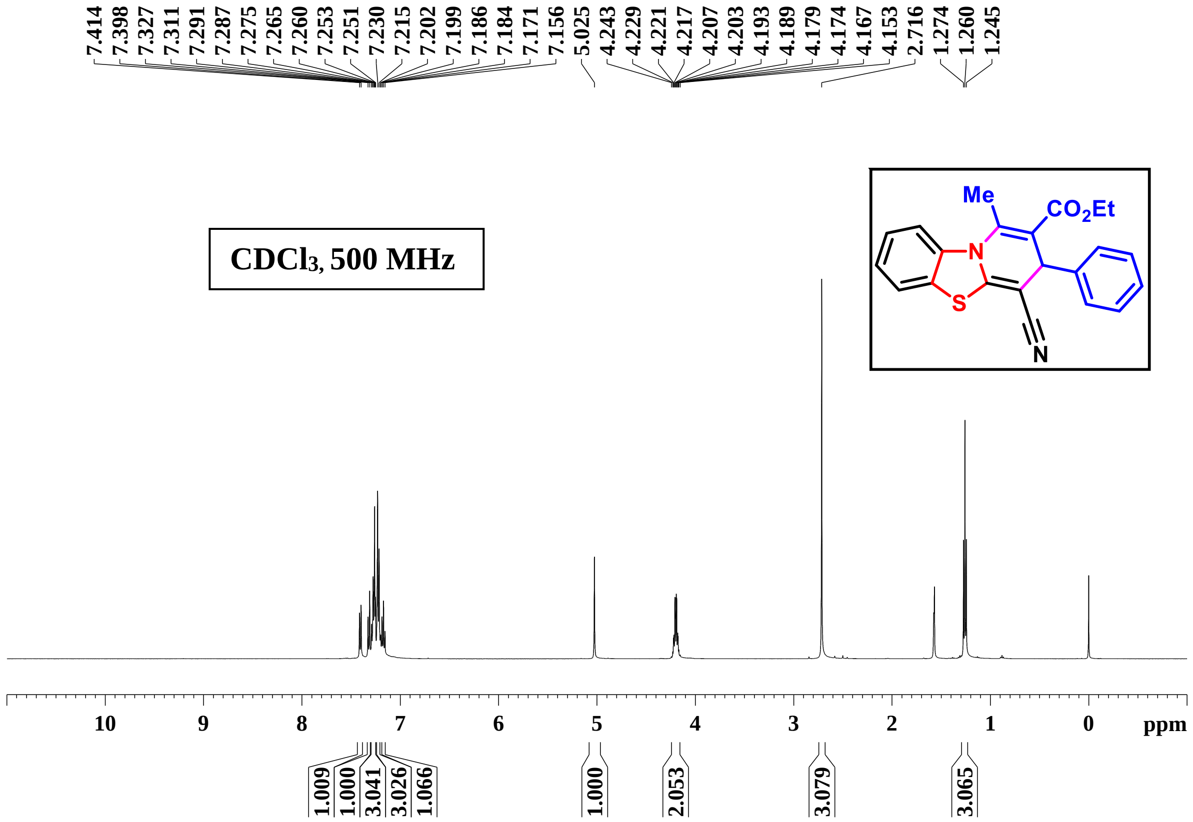


Figure A23: ^{1}H NMR spectrum of compound 21ij

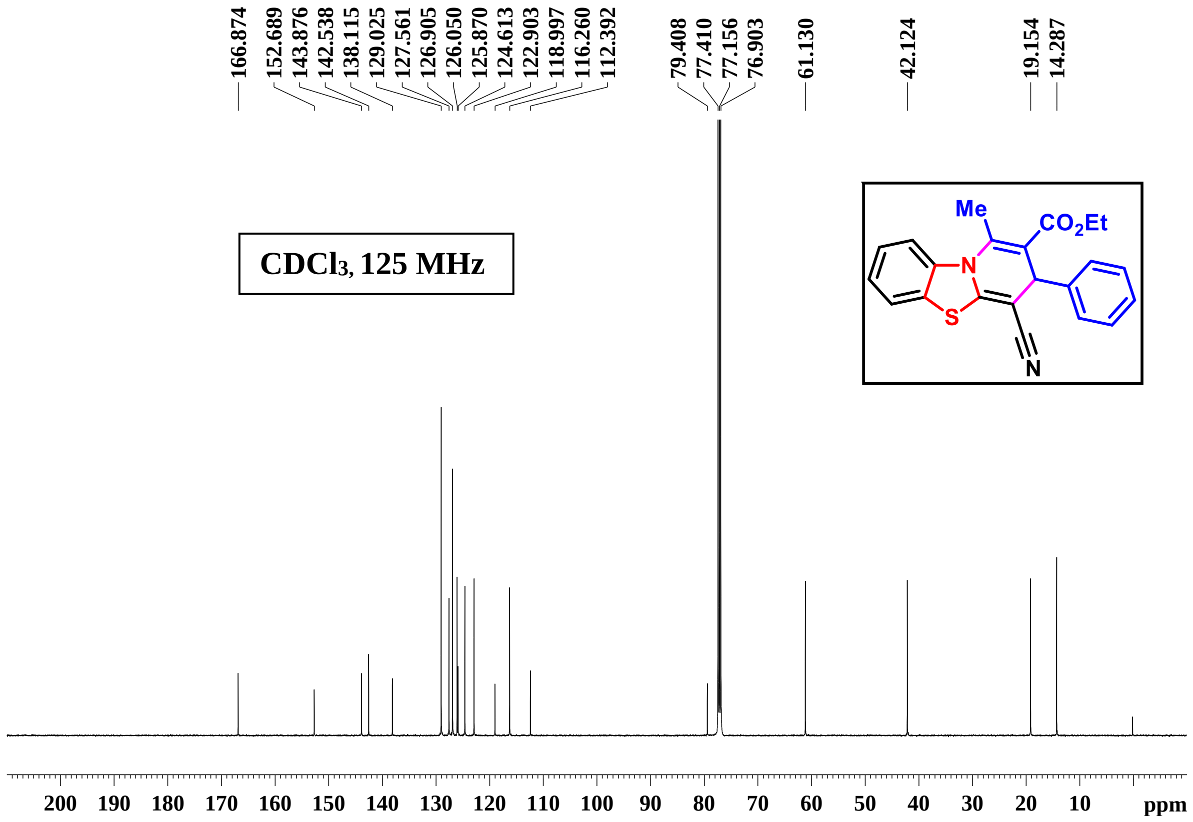


Figure A24: ^{13}C{^{1}H} NMR spectrum of compound 21ij

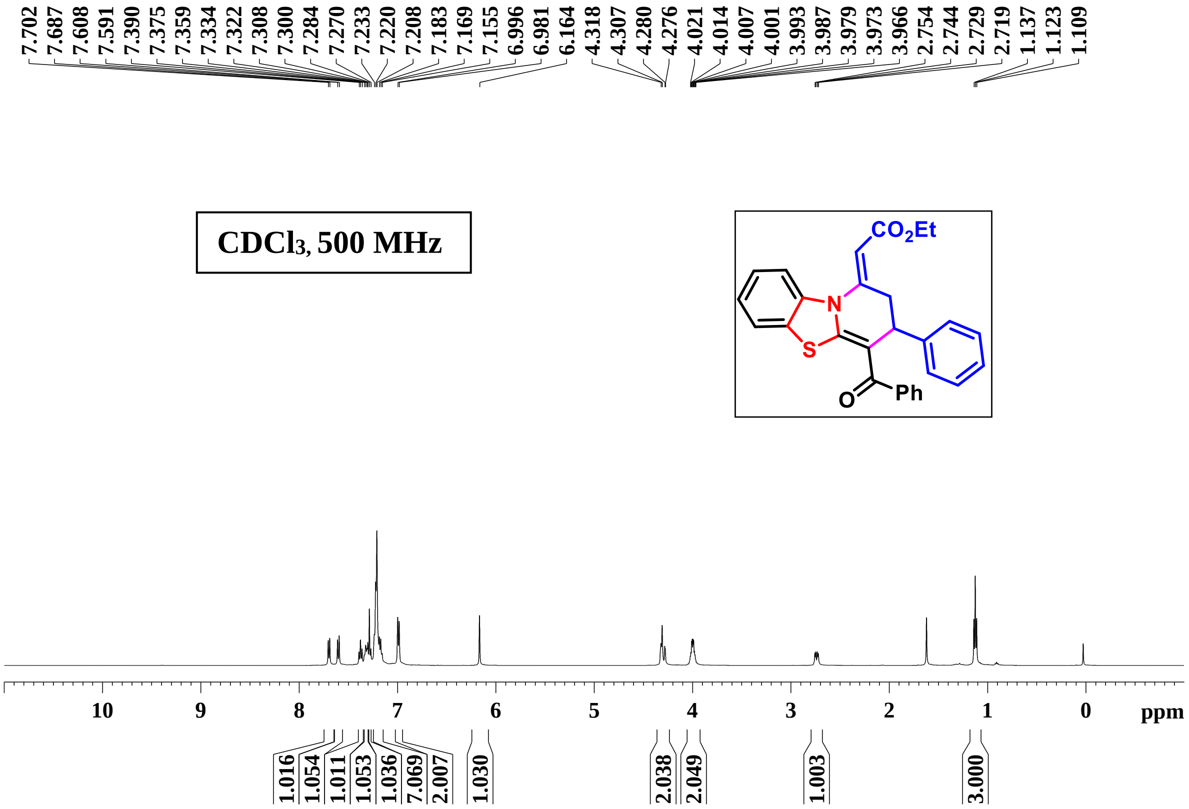


Figure A25: ^{1}H NMR spectrum of compound 22aa

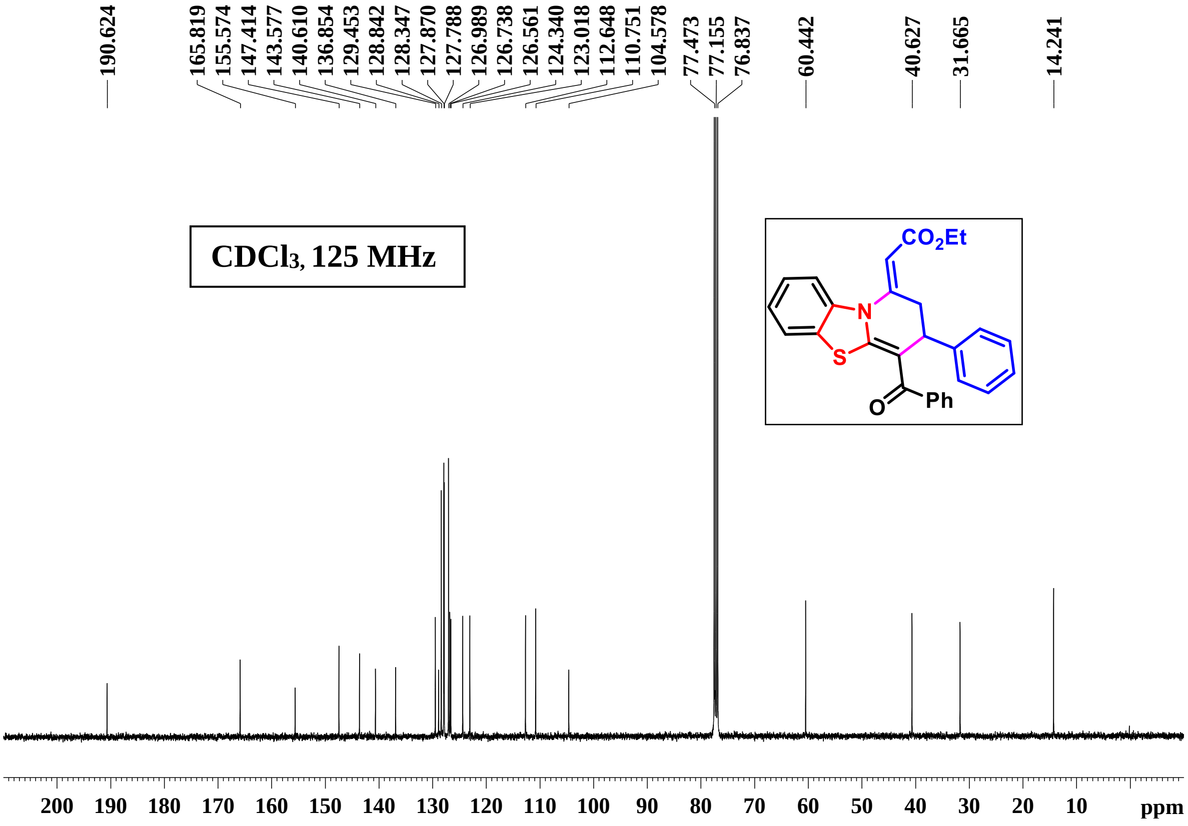


Figure A26: ^{13}C{^{1}H} NMR spectrum of compound 22aa

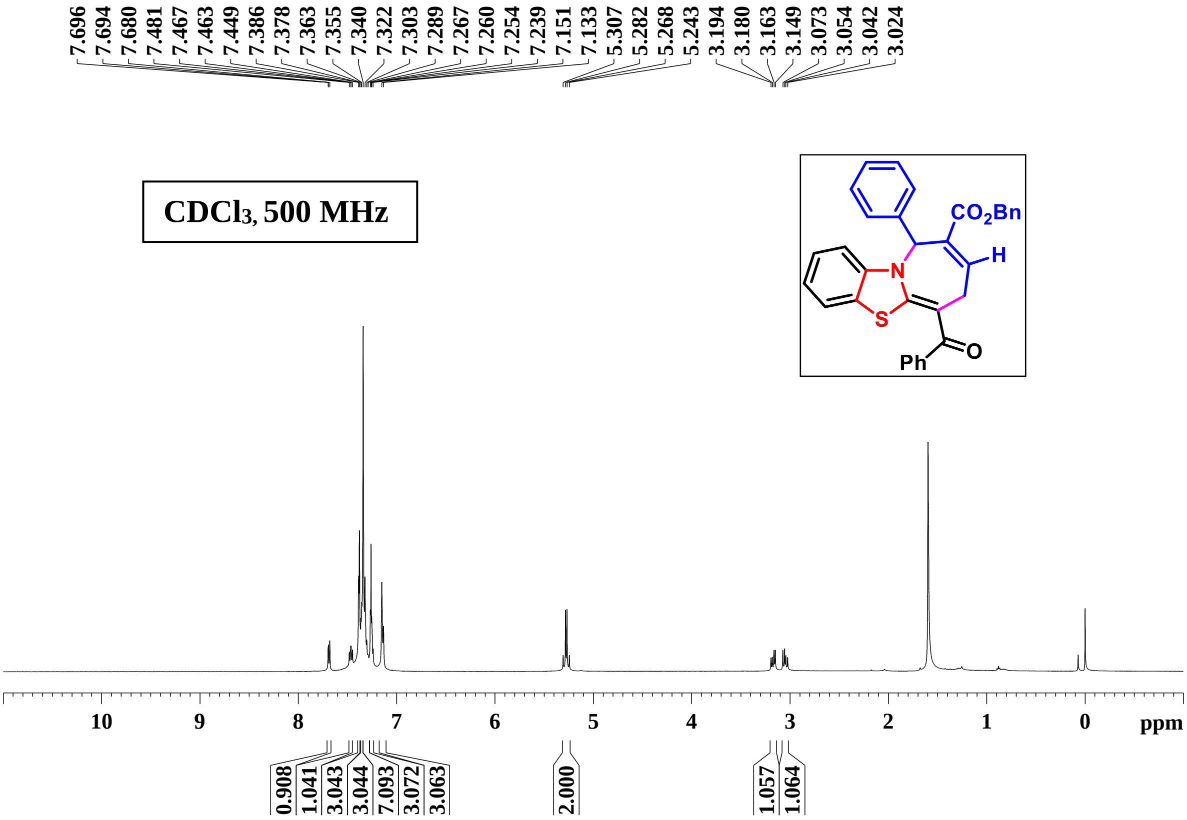


Figure A27: ^{1}H NMR spectrum of compound 23aa

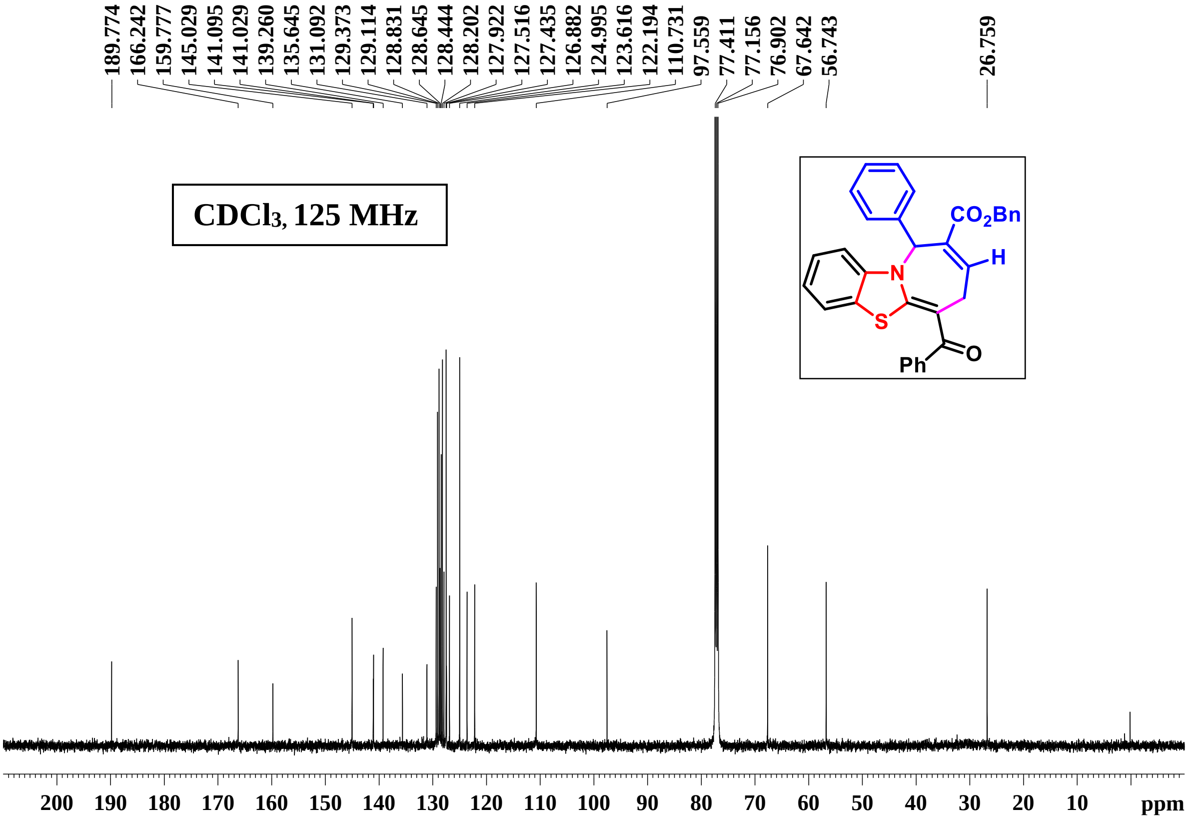


Figure A28: ^{13}C{^{1}H} NMR spectrum of 23aa

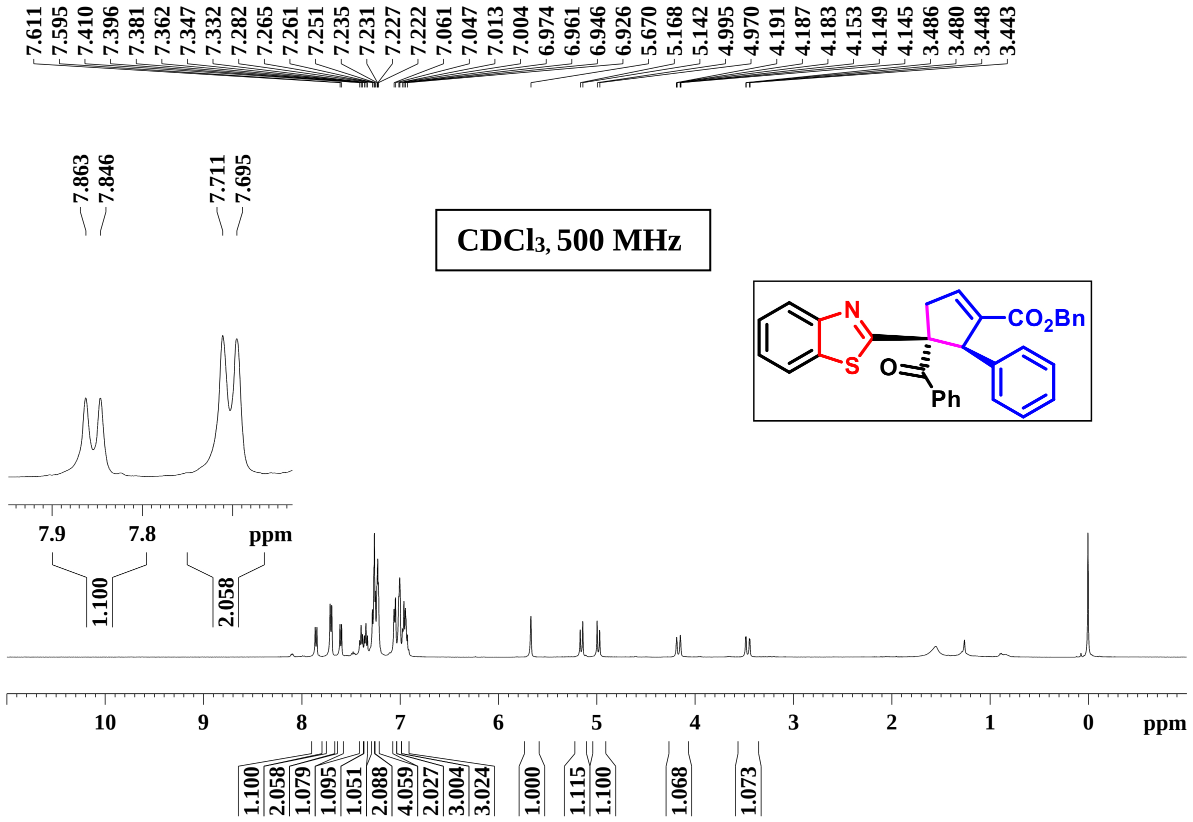


Figure A29: ^{1}H NMR spectrum of compound 24aa

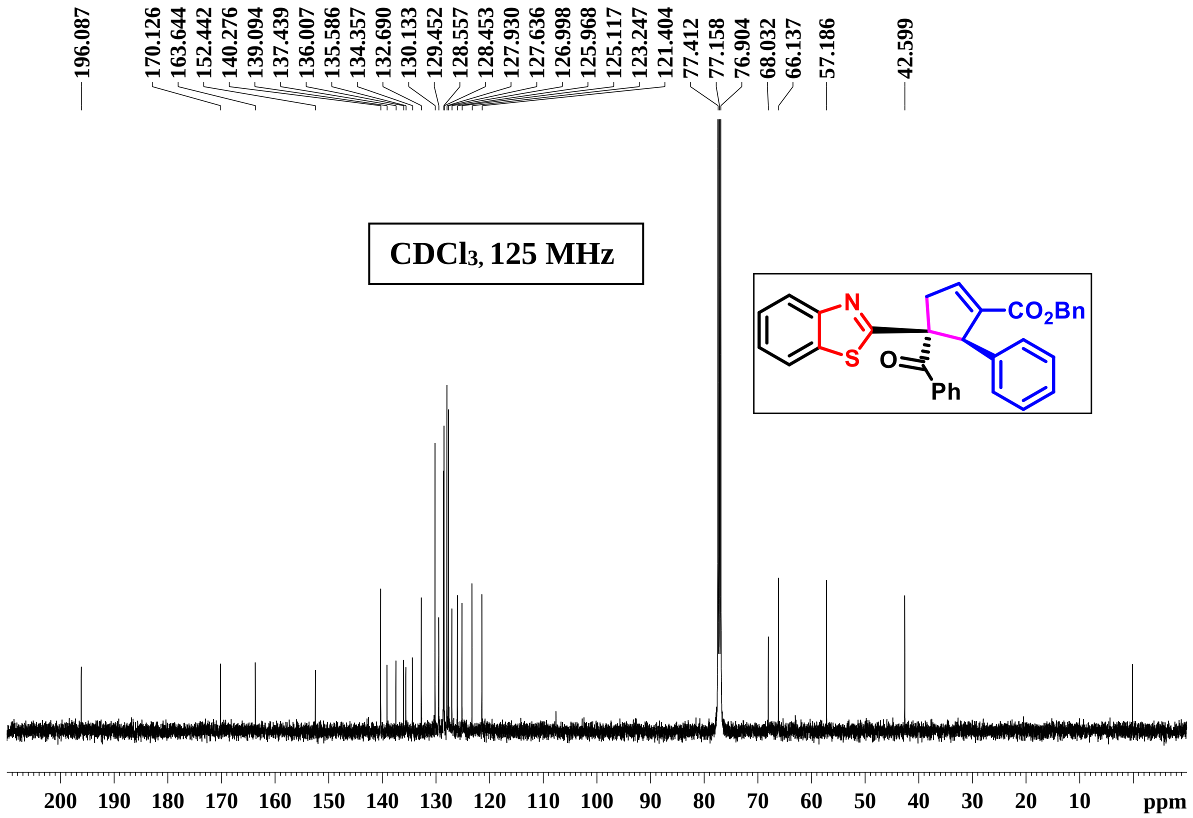


Figure A30: ^{13}C NMR spectrum of compound 24aa

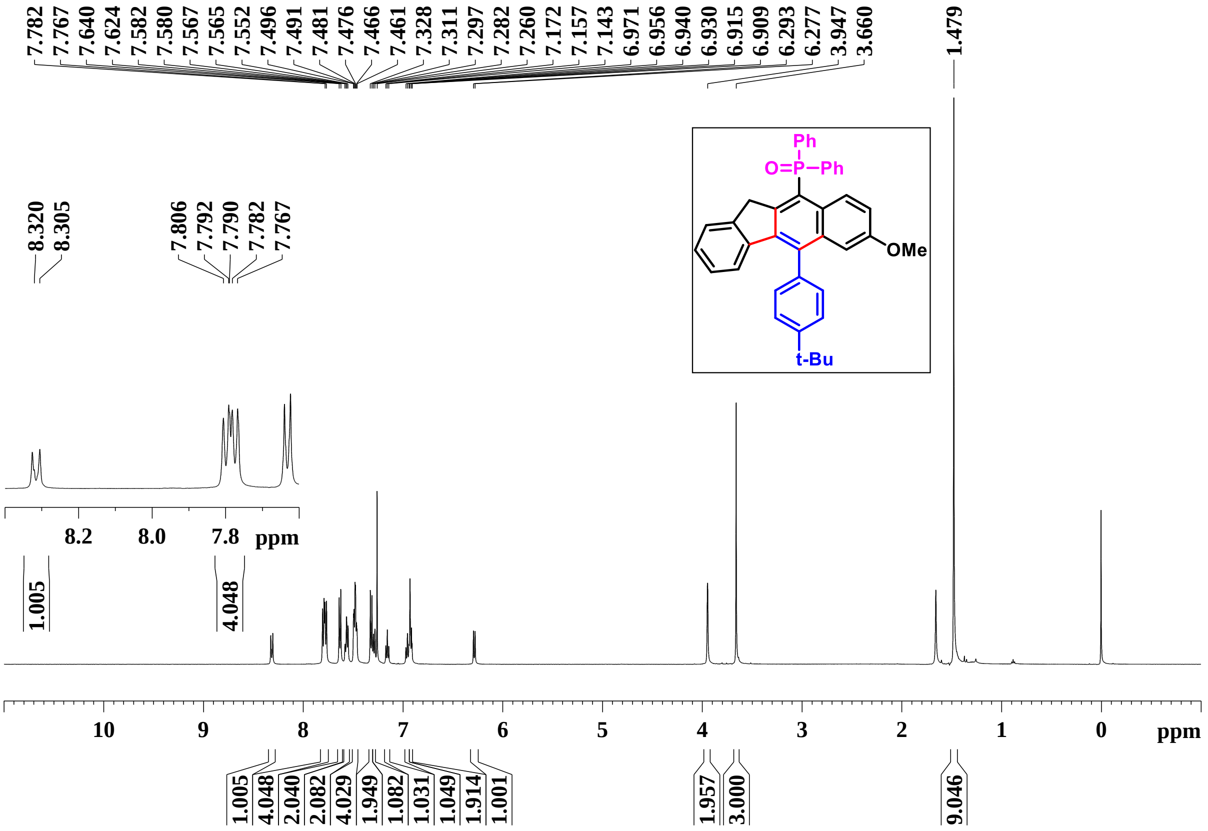


Figure A31: ^{1}H NMR spectrum of compound 30bf

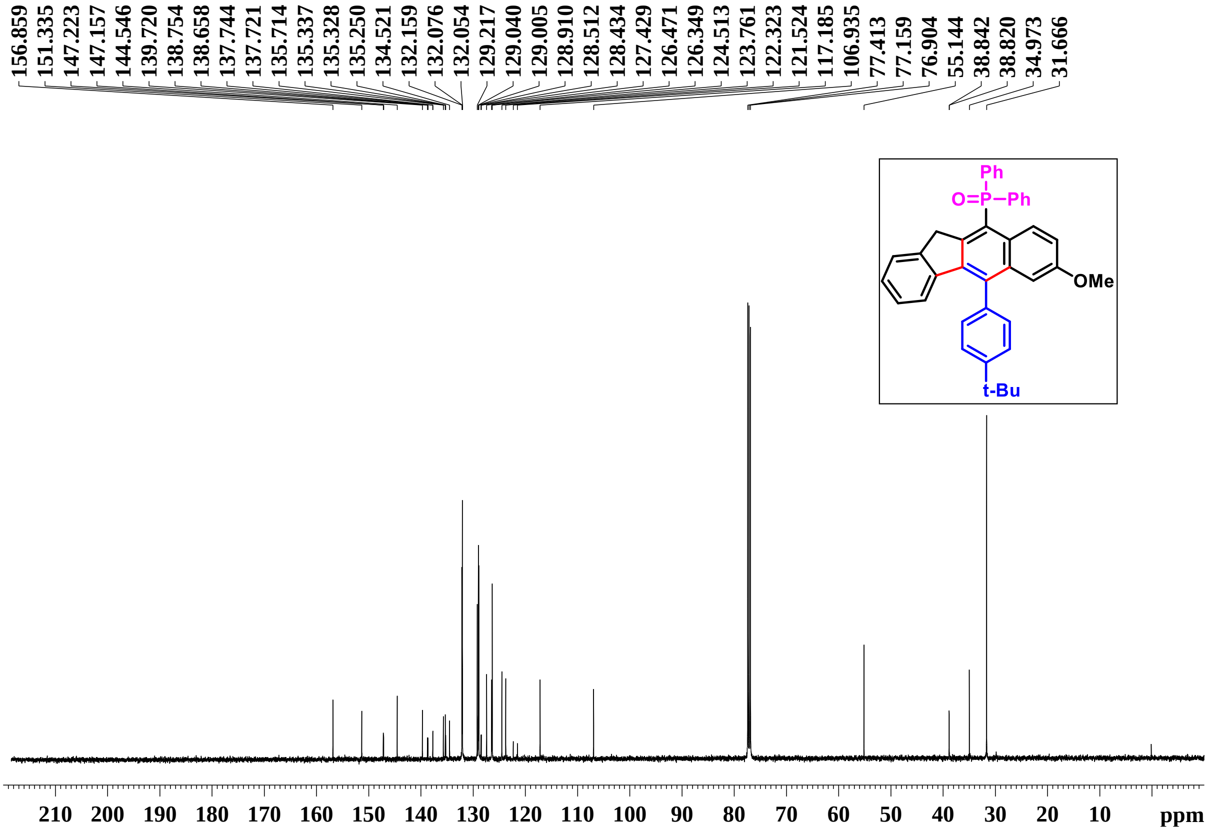


Figure A32: ^{13}C{^{1}H} NMR spectrum of compound 30bf

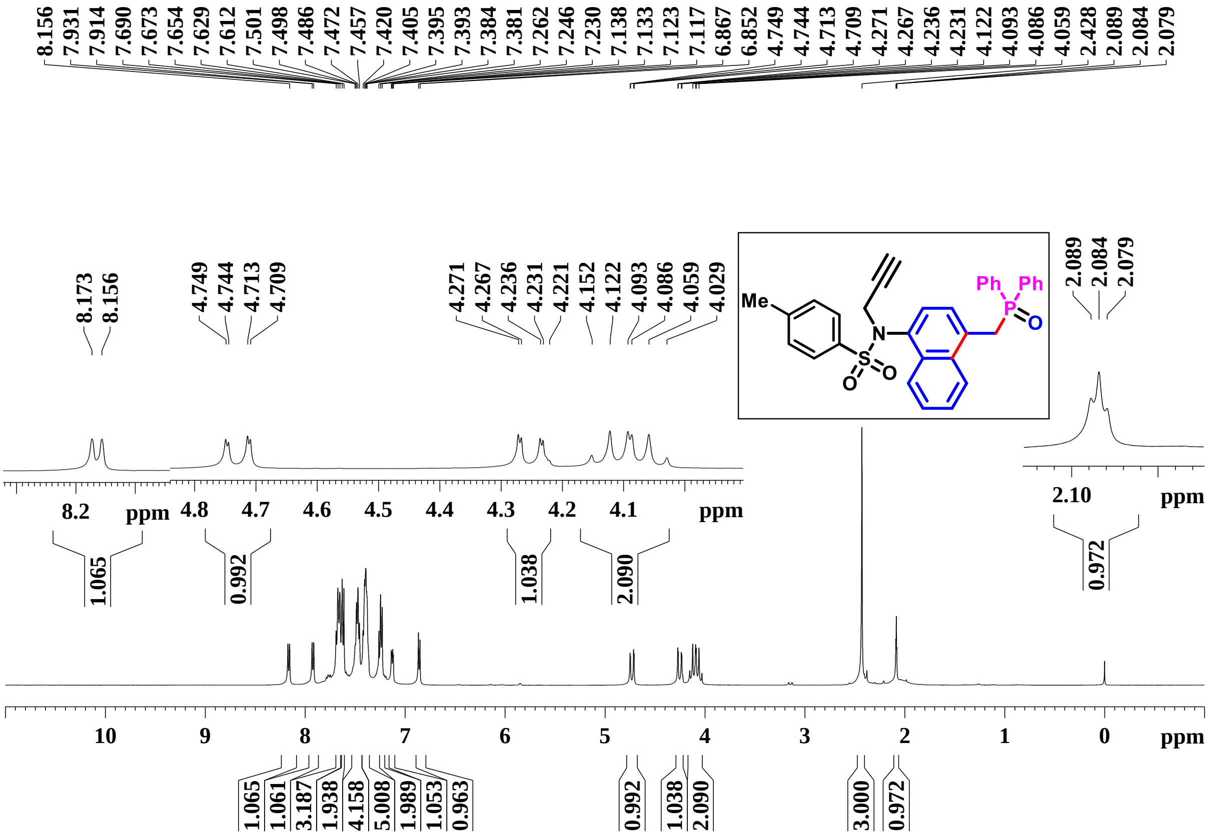


Figure A33: ^{1}H NMR spectrum of compound 31b

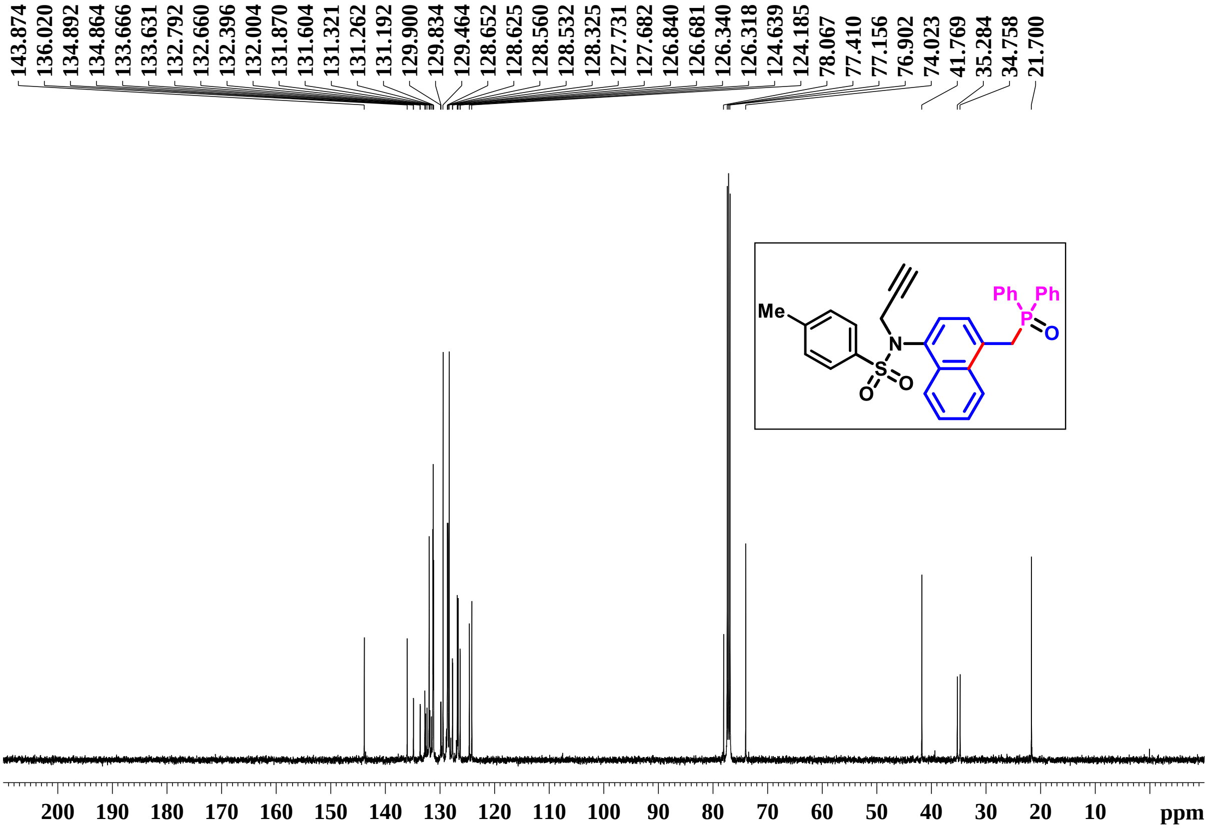
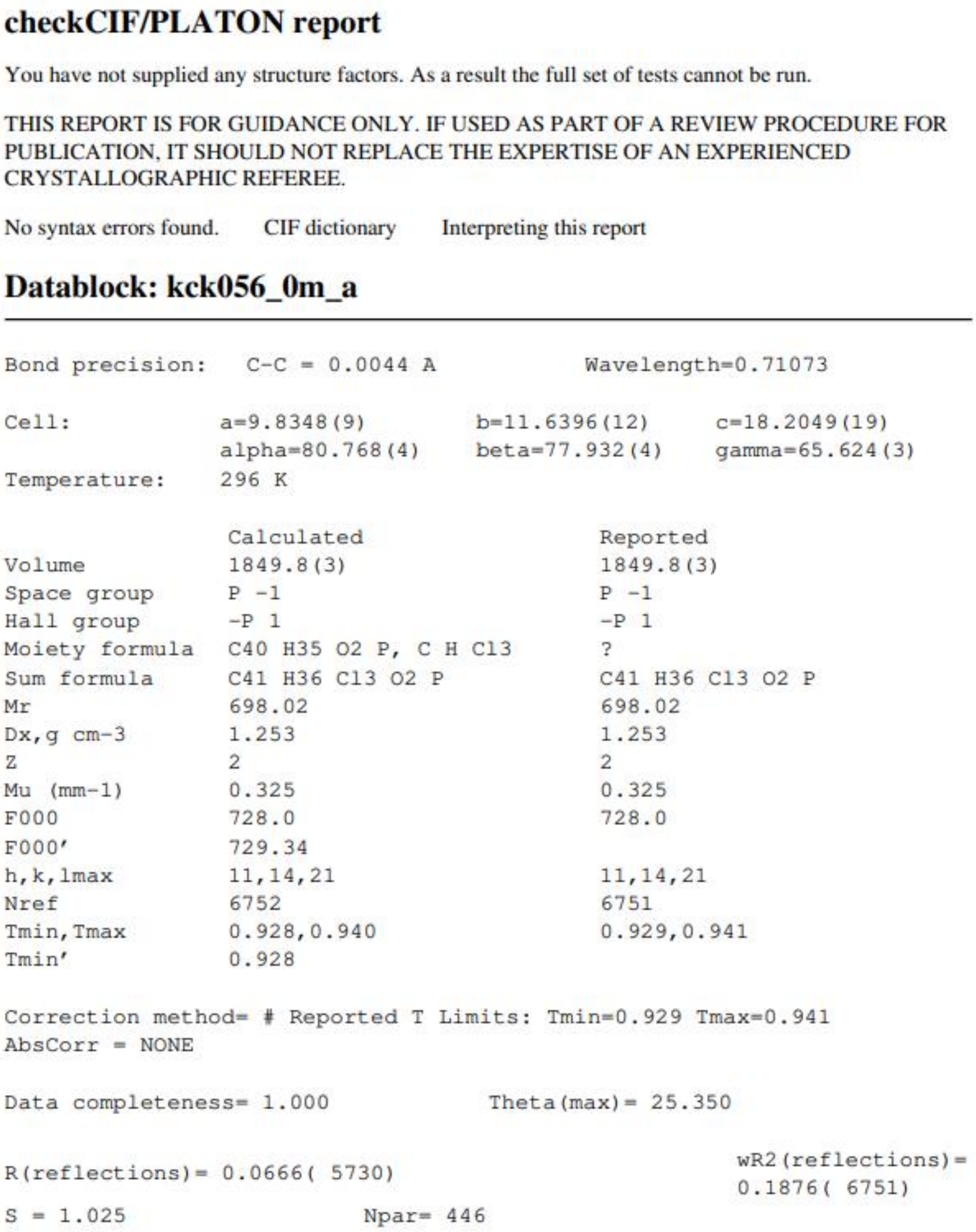


Figure A34: ^{13}C{^{1}H} NMR spectrum of compound 30b

(B) Checkcif copies of unpublished compounds (30bf and 31b)

<u>Compound 30bf</u>



checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck056_0m_a

```
Bond precision:   C-C = 0.0044 A          Wavelength=0.71073

Cell:            a=9.8348(9)        b=11.6396(12)      c=18.2049(19)
                 alpha=80.768(4)    beta=77.932(4)     gamma=65.624(3)
Temperature:     296 K

                  Calculated                  Reported
Volume            1849.8(3)                   1849.8(3)
Space group       P -1                        P -1
Hall group        -P 1                        -P 1
Moiety formula    C40 H35 O2 P, C H Cl3       ?
Sum formula       C41 H36 Cl3 O2 P            C41 H36 Cl3 O2 P
Mr                698.02                      698.02
Dx,g cm-3         1.253                       1.253
Z                 2                           2
Mu (mm-1)         0.325                       0.325
F000              728.0                       728.0
F000'             729.34
h,k,lmax          11,14,21                    11,14,21
Nref              6752                        6751
Tmin,Tmax         0.928,0.940                 0.929,0.941
Tmin'             0.928

Correction method= # Reported T Limits: Tmin=0.929 Tmax=0.941
AbsCorr = NONE

Data completeness= 1.000          Theta(max)= 25.350

                                                        wR2(reflections)=
R(reflections)= 0.0666( 5730)                           0.1876( 6751)

S = 1.025                   Npar= 446
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The following ALERTS were generated. Each ALERT has the format
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Click on the hyperlinks for more details of the test.
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Alert level B
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```

```
Alert level C
PLAT220_ALERT_2_C NonSolvent    Resd 1  C    Ueq(max)/Ueq(min)  Range        5.7 Ratio
PLAT222_ALERT_3_C NonSolvent Resd 1  H    Uiso(max)/Uiso(min) Range        6.7 Ratio
PLAT234_ALERT_4_C Large Hirshfeld Difference C36        --C38       .      0.17 Ang.
PLAT241_ALERT_2_C High   'MainMol' Ueq as Compared to Neighbors of        C11 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of         C7 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C33 Check
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C36 Check
PLAT244_ALERT_4_C Low    'Solvent' Ueq as Compared to Neighbors of        C41 Check
PLAT260_ALERT_2_C Large Average Ueq of Residue Including        Cl1      0.184 Check
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ...............     0.00437 Ang.
PLAT410_ALERT_2_C Short Intra H...H Contact  H34          ..H39B     .      1.98 Ang.
                                                   x,y,z  =      1_555 Check
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Alert level G
PLAT002_ALERT_2_G Number of Distance or Angle Restraints on AtSite          3 Note
PLAT005_ALERT_5_G No Embedded Refinement Details Found  in the CIF     Please Do !
PLAT066_ALERT_1_G Predicted and Reported Tmin&Tmax Range Identical          ? Check
PLAT072_ALERT_2_G SHELXL First  Parameter in WGHT  Unusually Large       0.11 Report
PLAT093_ALERT_1_G No s.u.'s on H-positions, Refinement Reported as      mixed Check
PLAT300_ALERT_4_G Atom Site Occupancy of C38          Constrained at        0.6 Check
PLAT300_ALERT_4_G Atom Site Occupancy of C39          Constrained at        0.6 Check
PLAT300_ALERT_4_G Atom Site Occupancy of C38A         Constrained at        0.4 Check
PLAT300_ALERT_4_G Atom Site Occupancy of C39A         Constrained at        0.4 Check
PLAT301_ALERT_3_G Main Residue  Disorder ..............(Resd     1)         5% Note
PLAT367_ALERT_2_G Long?  C(sp?)-C(sp?) Bond  C33         - C36      .      1.53 Ang.
PLAT860_ALERT_3_G Number of Least-Squares Restraints .............          2 Note
PLAT899_ALERT_4_G SHELXL-97  is Deprecated and Succeeded by SHELXL     2019/3 Note
```

```
  0 ALERT level A = Most likely a serious problem - resolve or explain
  1 ALERT level B = A potentially serious problem, consider carefully
 11 ALERT level C = Check. Ensure it is not caused by an omission or oversight
 13 ALERT level G = General information/check it is not something unexpected

  2 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
 11 ALERT type 2 Indicator that the structure model may be wrong or deficient
  4 ALERT type 3 Indicator that the structure quality may be low
  7 ALERT type 4 Improvement, methodology, query or suggestion
  1 ALERT type 5 Informative message, check
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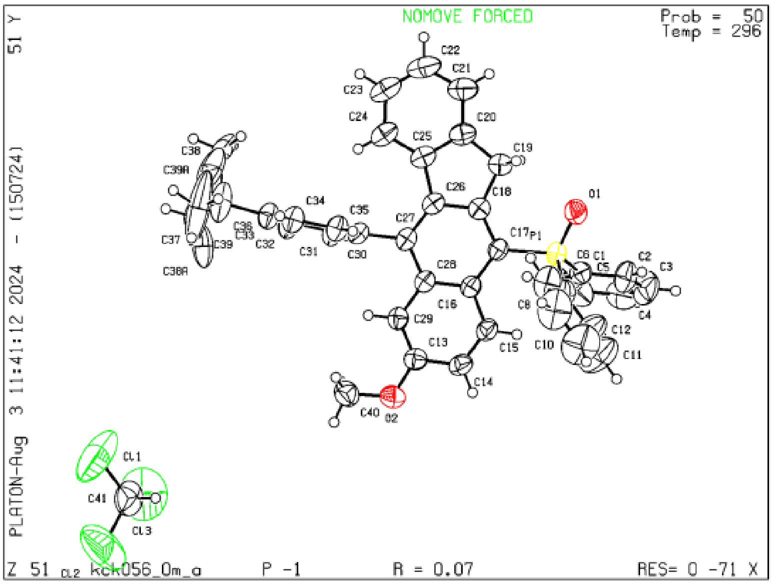
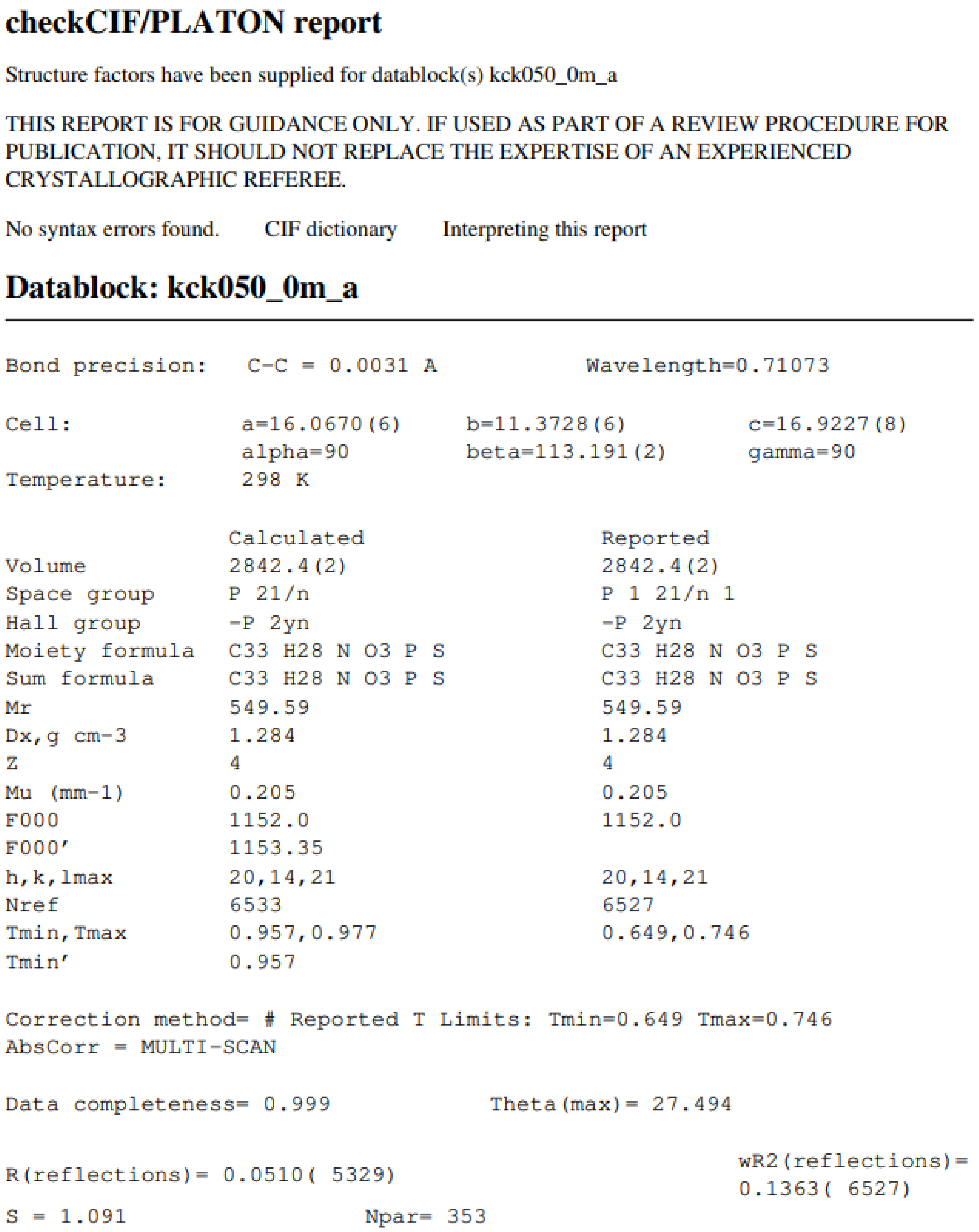
Datablock kck056_0m_a - ellipsoid plot



Compound 31b



checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck050_0m_a

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No syntax errors found.   CIF dictionary   Interpreting this report

Datablock: kck050_0m_a

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Bond precision:    C-C = 0.0031 A           Wavelength=0.71073

Cell:              a=16.0670(6)     b=11.3728(6)       c=16.9227(8)
                   alpha=90         beta=113.191(2)    gamma=90
Temperature:       298 K

                  Calculated                   Reported
Volume            2842.4(2)                    2842.4(2)
Space group       P 21/n                       P 1 21/n 1
Hall group        -P 2yn                       -P 2yn
Moiety formula    C33 H28 N O3 P S             C33 H28 N O3 P S
Sum formula       C33 H28 N O3 P S             C33 H28 N O3 P S
Mr                549.59                       549.59
Dx,g cm-3         1.284                        1.284
Z                 4                            4
Mu (mm-1)         0.205                        0.205
F000              1152.0                       1152.0
F000'             1153.35
h,k,lmax          20,14,21                     20,14,21
Nref              6533                         6527
Tmin,Tmax         0.957,0.977                  0.649,0.746
Tmin'             0.957

Correction method= # Reported T Limits: Tmin=0.649 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.999           Theta(max)= 27.494

                                                      wR2(reflections)=
R(reflections)= 0.0510( 5329)                         0.1363( 6527)

S = 1.091                  Npar= 353
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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

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PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......     2.511 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600         3 Report
```

Alert level G

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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         2 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.        10 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   2 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
   1 ALERT type 2 Indicator that the structure model may be wrong or deficient
   3 ALERT type 3 Indicator that the structure quality may be low
   1 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
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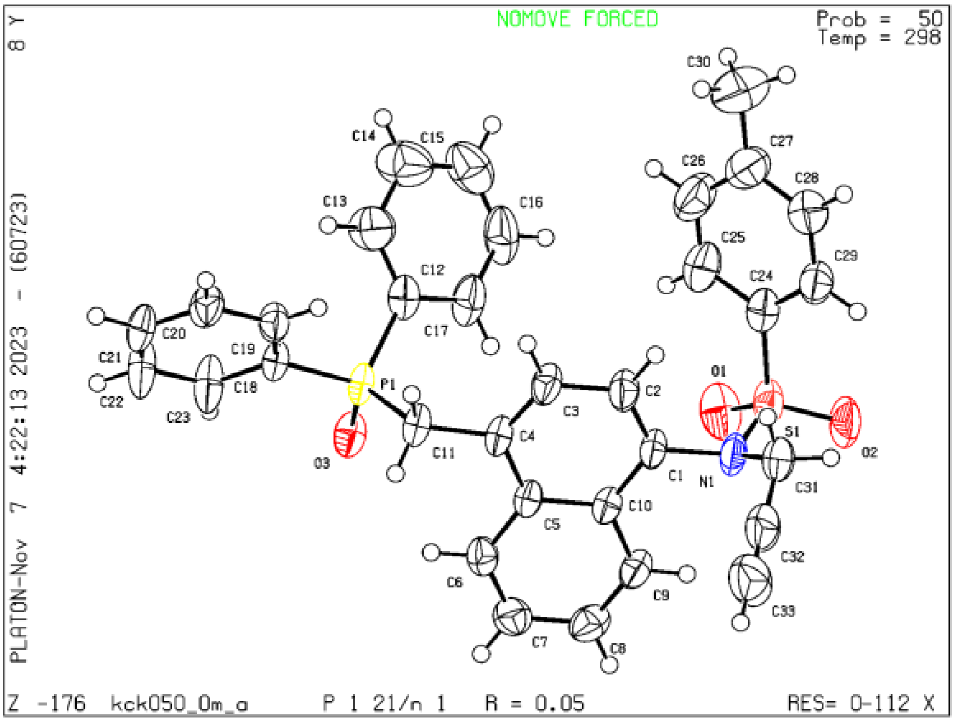
Datablock kck050_0m_a - ellipsoid plot



Reactivity of Acetoxy Allenoates with Bisnucleophiles and Annulation Reactions of Allenylphosphine Oxides

by Sachin Chauhan

Submission date: 04-Sep-2024 04:31PM (UTC+0530)
Submission ID: 2444734320
File name: Sachin_Chauhan.docx (11.79M)
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Reactivity of Acetoxy Allenoates with Bisnucleophiles and Annulation Reactions of Allenylphosphine Oxides

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