Investigations on the Reactivity of Acetoxy Allenoates with *N*-Sulfonyl-imines, Azides, and Enolizable Carbonyls

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

By

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NOVEMBER 2023

CONTENTS

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
November 2023


(Signature)

Asif Ali Qurashi

DECLARATION

I, **Asif Ali Qurashi**, hereby declare that this thesis entitled ***"Investigations on the reactivity of acetoxy allenoates with N-sulfonyl-imines, azides, and enolizable carbonyls"*** 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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CERTIFICATE

This is to certify that the thesis entitled ***"Investigations on the reactivity of acetoxy allenoates with N-sulfonyl-imines, azides, and enolizable carbonyls"*** submitted by **Mr. Asif Ali Qurashi** bearing registration number **17CHPH17** in partial fulfillment of the requirements for the award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by him under my supervision and guidance.

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

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

1. Kumar, A. S.; **Qureshi, A. A**.; Kumara Swamy, K. C. Lewis Base-Switched (3 + 3) and (4 + 2) Annulation Reaction of *δ*-Acetoxy Allenoates with *N*-Sulfonyl Ketimines: Divergent Synthesis of Functionalized *α*-Pyridyl Acetates and Teraryl Scaffolds. *J. Org. Chem.* **2020**, *85*, 4130.
2. **Qureshi, A. A**.; Kumar, A. S.; Chauhan, S.; Kumara Swamy, K. C. Stereo-and Regioselective (3 + 2) Cycloaddition of Acetoxy Allenoates with Azides: Metal-Free Synthesis of Multiubstituted Triazoles. *Synthesis*, **2022**, *54*, 965.

The following paper has been communicated:

3. **Qureshi, A. A**.; Kumar, A. S.; Kumara Swamy, K. C. Tertiary-Amine Controlled (3 + 3) and (4 + 2) Annulations of *β′*-Acetoxy Allenoates with N-Sulfonyl Ketimines: An Entry to m-Teraryl and Fused Hydropyridines *(Submitted).*

The following manuscript has to be submitted

4. **Qureshi, A. A**.; Chauhan, S.; Kumara Swamy, K. C. DBU catalyzed (3 + 3) annulation of δ/β′-acetoxy allenoates with benzo-oxathiin-dioxide and phenylthiazolone: Synthesis of fused dihydropyrans. (*to be communicated*).

He has also made presentations in the following conferences:

1. Poster presentation in the *Chemfest-2019* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, February-**2019**.
2. Poster presentation in the *XVI*th JNOST Conference for Research Scholars, IISc Bengaluru, INDIA, Oct-Nov, **2020**.
3. Oral and Poster presentation in the *Chemfest-2022* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, April-**2022**.

Further, the student has passed the following courses towards the fulfilment 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

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I would like to express my heartfelt thanks to my family and friends.

Asif.....

LIST OF PUBLICATIONS

(A) Published papers:

1. Lewis Base-Switched (3 + 3) and (4 + 2) Annulation Reaction of δ-Acetoxy Allenoates with *N*-Sulfonyl Ketimines: Divergent Synthesis of Functionalized α-Pyridyl Acetates and Teraryl Scaffolds.
Sanjeeva K. Arupula, **Asif Ali Qureshi** and K. C. Kumara Swamy*
J. Org. Chem. **2020**, *85*, 4130.

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

3. (3 + 2) Cycloadditions of Vinyl Sulfonyl Fluorides with Ethyl Diazoacetate or Azides: Metal-Free Synthesis of Pyrazole and Triazole Scaffolds via SO_2 Elimination.
Sandeep Kondapati, A. Sanjeeva Kumar, **Asif Ali Qureshi** and K. C. Kumara Swamy*
Synthesis, **2022**, 54, 4111.

4. Tertiary-Amine Controlled (3 + 3) and (4 + 2) Annulations of β'-Acetoxy Allenoates with N-Sulfonyl Ketimines: An Entry to m-Teraryl and Fused Hydropyridines
Asif Ali Qureshi, A. Sanjeeva Kumar, and K. C. Kumara Swamy*
(Submitted).

5. 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*
(To be communicated).

PARTICIPATION IN CONFERENCES/ SYMPOSIA

1. **Asif Ali Qureshi**, A. Sanjeeva Kumar, K. C. Kumara Swamy
   Multi-Substituted Pyridine/Biaryl Scaffolds via (3 + 3)/(2 + 4)-Annulation Protocol of 4-Alkyl Cyclic Sulfamidate Imines with δ-Acetoxy Allenoates
   Poster presentation in the *Chemfest-2019* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, February-**2019**.

2. A. Sanjeeva Kumar, **Asif Ali Qureshi**, K. C. Kumara Swamy
   Lewis Base-Switched (3 + 3) and (4 + 2) Annulation Reaction of δ-Acetoxy Allenoates with *N*-Sulfonyl Ketimines: Divergent Synthesis of Functionalized α-Pyridyl Acetates and Teraryl Scaffolds
   Poster presentation in the *XVI*th JNOST Conference for Research Scholars, IISc Bengaluru, INDIA, Oct-Nov, **2020**.

3. **Asif Ali Qureshi**, A. Sanjeeva Kumar, K. C. Kumara Swamy
   Metal-free Annulations/Cycloaddition Reactions of Acetoxy Allenoates
   Oral and Poster presentation in the *Chemfest-2022* (Annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, April-**2022**.

Synopsis

This thesis is divided into three chapters. Chapter 1 deals with the literature relevant to the present study. Results and Discussion are presented in Chapter 2. The following topics are covered: (i) Lewis's base mediated (3 + 3) and (4 + 2) annulations of acetoxy allenoates and cyclic *N*-sulfonyl ketimines for the synthesis of *α*-pyridyl acetates and *o*-teraaryl motifs, (ii) tertiary amine switched (3 + 3) and (4 + 2) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl imines for the synthesis of fused dihydropyridines and *m*-teraryls, (iii) Thermal (3 + 2) cycloaddition of *δ*/*β′*-acetoxy allenoates with azides for the synthesis of 1,4,5-tri/ 1,5-di-substituted-1,2,3-triazole under metal-free conditions, and (iv) DBU catalyzed (3 + 3) annulations of *β′*-acetoxy allenoates with enolizable carbonyl compounds that lead to the formation of fused pyrans.

The compounds synthesized in the present study are, in general, characterized by melting point, IR, and NMR (^{1}H, ^{13}C, and ^{19}F) techniques in conjunction with LC-MS/ 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 by methodologies available (with modifications where necessary) in the literature.

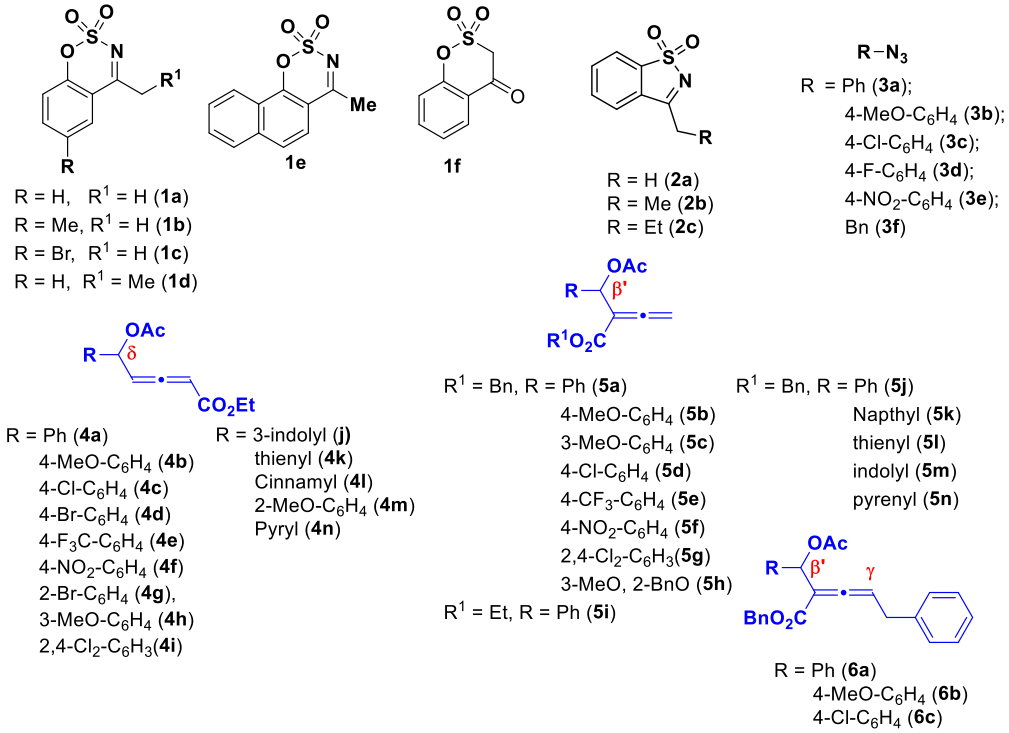
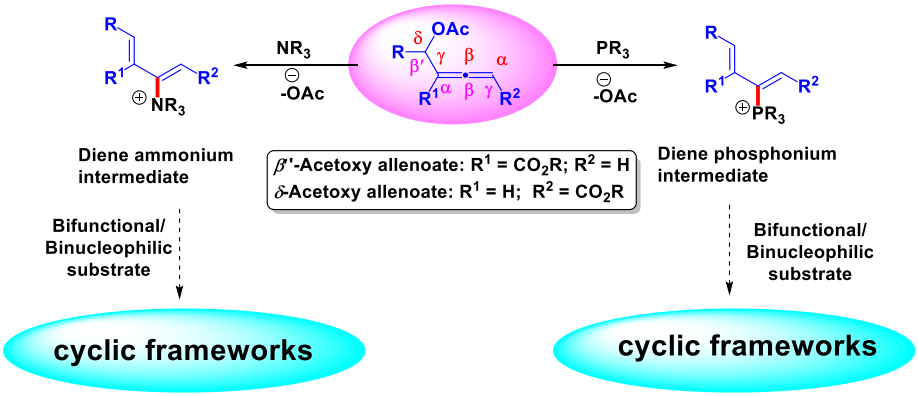


Chart 1. Precursors used in the present study

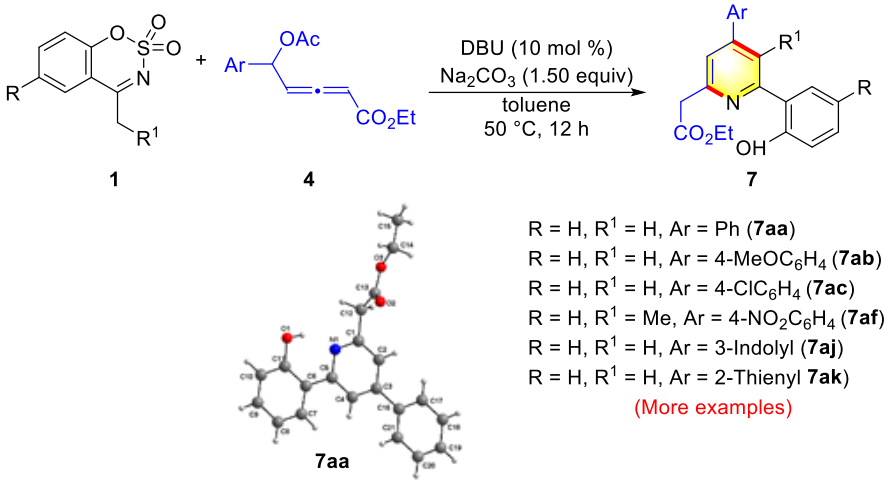
(i) Synthesis of *α*-pyridyl acetates from *δ*-acetoxy allenoates and cyclic *N*-sulfonyl ketimines via [3 + 3] annulation under DBU catalysis/mediation

The introduction of an acetoxy group on the allenoate moiety makes the reactions more fascinating since the –OAc group can be readily eliminated under basic conditions. Two such useful substrates are *δ*-acetoxy allenoates and *β′*-acetoxy allenoates (cf. compounds **4-6**, Chart 1 above). The reactions utilizing these are facilitated by the addition of a Lewis base at the *sp* carbon of allenoate *via* addition-elimination to generate a reactive dienyl-ammonium or dienyl-phosphonium intermediate after the removal of the acetoxy group. Subsequent annulation in the presence of an appropriate bifunctional substrate can lead to the formation of cyclic frameworks (Scheme 1). The other substrates in these reactions act as dinucleophiles.



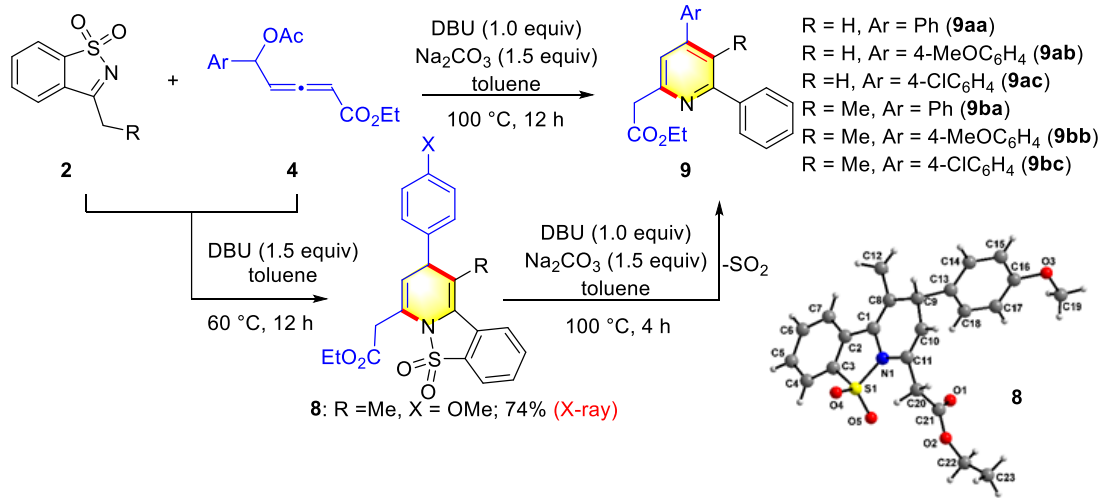
Scheme 1: Synthesis of cyclic frameworks via diene ammonium/phosphonium intermediates generated from acetoxy allenoates

We performed DBU-catalyzed (3 + 3) annulation reaction between 4-methyl cyclic sulfamidate imine (*N*-sulfonyl imine) **1a** and *δ*-acetoxy allenoates (e.g., **4a-c**, **4f**, **4j** and **4k)** that gave *α*-pyridyl acetates (e.g., **7aa-7ac**, **7af**, **7aj** and **7ak**) in good yield by performing the reaction at 50 ºC (Scheme 2). The system was generalized with many more examples. A possible mechanistic pathway involving the dienyl-ammonium intermediate (cf. Scheme 1) has been proposed.



Scheme 2: Synthesis of α-pyridyl acetates from δ-acetoxy allenoates and 4-methyl cyclic sulfamidate imine

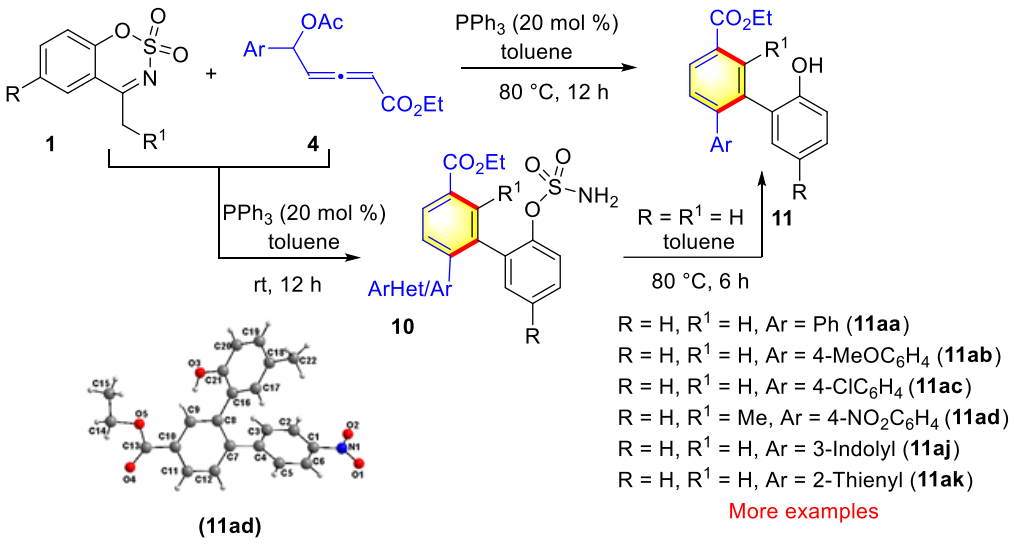
Based on the above successful annulation of acetoxy allenoates with sulfamidate imines **1** containing -OSO_2 moiety, we performed (3 + 3) annulations of acetoxy allenoates with a slightly different sulfonyl imine **2a** having sulfur directly bonded to the arene ring. After using 1 mole equiv of DBU we obtained **9aa** in 71% yield at 100 °C after 12 h. We could generalize this using the sulfonyl imines **2a** and **2b** which showed good reactivity with allenoates **4a-c** and produced α-pyridyl acetates **9aa-ac** and **9ba-bc** in acceptable yields. To know more details about the reaction we even isolated fused dihydropyridine intermediate **8** in 74% yield whose structure was confirmed by X-ray crystallography. This product **8** could be converted to 2-pyridinyl acetate **9bb** in toluene under basic conditions at 100 °C.



Scheme 3: Synthesis of α-pyridyl acetates from δ-acetoxy allenoates and 4-methyl cyclic sulfonyl imine

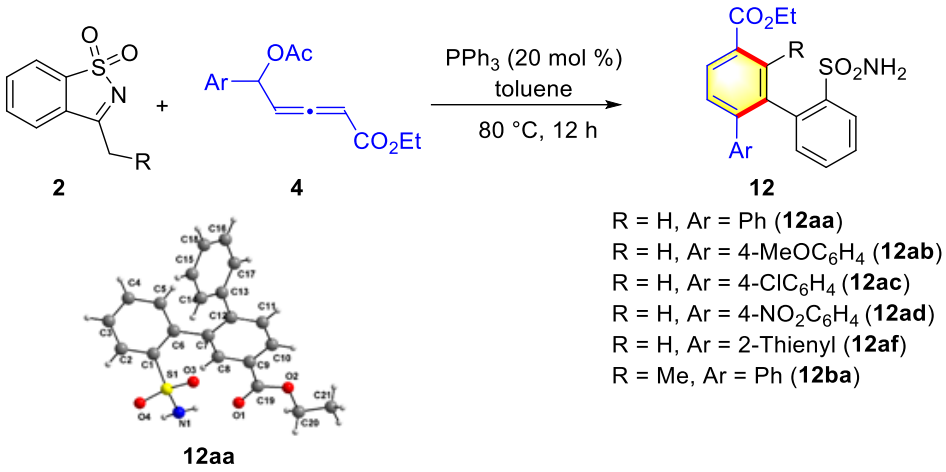
(ii) Synthesis of *o*-teraaryls from *δ*-acetoxy allenoates and cyclic *N*-sulfonyl ketimines via (4 + 2) annulation under phosphine catalysis

In contrast to amine catalysis, phosphine catalysis quite often produces distinctly different products, particularly in allene chemistry. In the current work, phosphine-catalyzed reaction between 4-methyl cyclic sulfamidate imine **1a** and *δ*-acetoxy allenoate **4a** at room temperature in the presence of Ph_3P led to (4 + 2) annulation affording teraryl **10aa**, which upon further heating gave phenolic terphenyl **11aa** by the elimination of -$SO_2(NH_2)$ moiety. Since such phenolic terphenyls of type **11aa** are useful scaffolds in organic synthesis, we prepared the analogous of multi-substituted phenolic terphenyls (e.g., **11aa-11ad**, **11aj, 11a**) in one pot in good to excellent yields (Scheme 4). More examples along with possible mechanistic pathways are discussed.



Scheme 4: Synthesis of *o*-teraaryl scaffolds from sulfamidate imine and *δ*-acetoxy allenoate

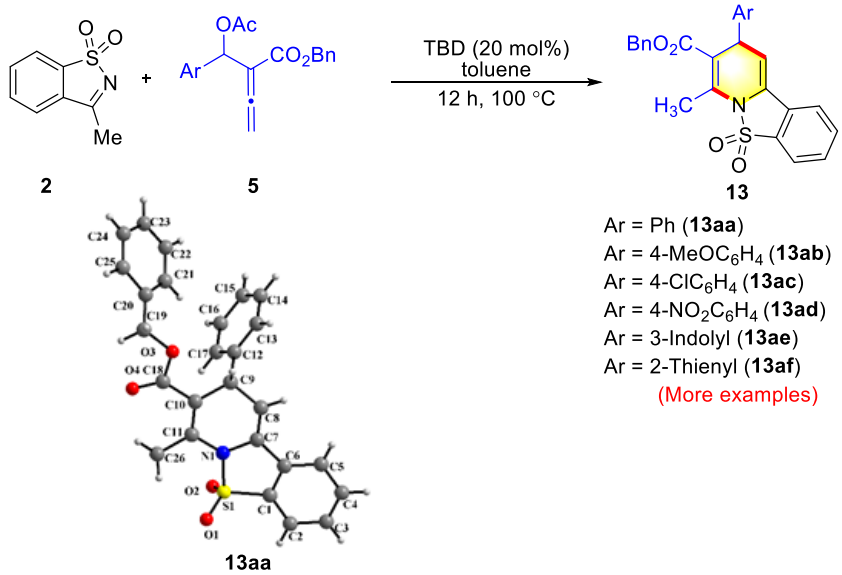
Inspired by the above success with sulfonyl imines in (3 + 3) annulation, we were curious to test this protocol in (4 + 2) annulation reaction of cyclic sulfonyl imines **2a** and **2b** also with *δ*-acetoxy allenoates **4a-d** and **4f**. Thus the Ph_3P-catalyzed reaction was performed in toluene at 80 °C. Pleasingly, terphenyls **12aa-ad**, **12af**, and **12ba** were obtained in high to excellent yields with the retention of sulfonamide group (Scheme 5).



Scheme 5: Synthesis of *o*-teraaryl scaffolds from cyclic *N*-sulfonyl imine and *δ*-acetoxy allenoates

(iii) TBD- catalyzed (3 + 3) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl imines

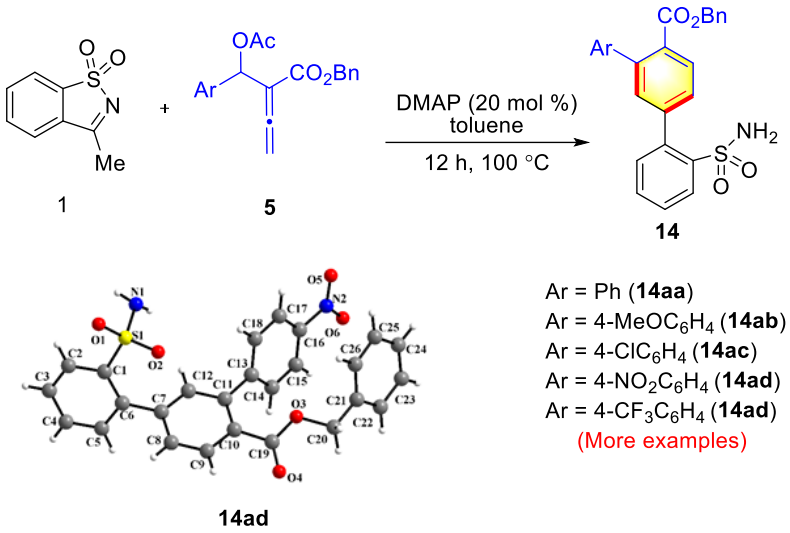
Although both *δ*-acetoxy allenoates and *β'*-acetoxy allenoates have the ester group connected to an allenic carbon, its relative position vis-à-vis the removable acetoxy moiety is different. Hence, in base-catalyzed reactions with bifunctional nucleophiles these subtle differences could lead to somewhat different products. We developed Lewis base dependent (3 + 3) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl imines affording fused hydropyridines with varying substituents under TBD (triazabicyclodecene)-catalysis to obtain fused hydropyridines. The reaction involves 1,2-elimination followed by 6-*endo*-dig cyclization as key steps delivering fused hydropyridines (Scheme 6).



Scheme 6: Synthesis of fused hydropyridines from cyclic *N*-sulfonyl imine and *β'*-acetoxy allenoates

(iv) DMAP catalyzed (4 + 2) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl imines

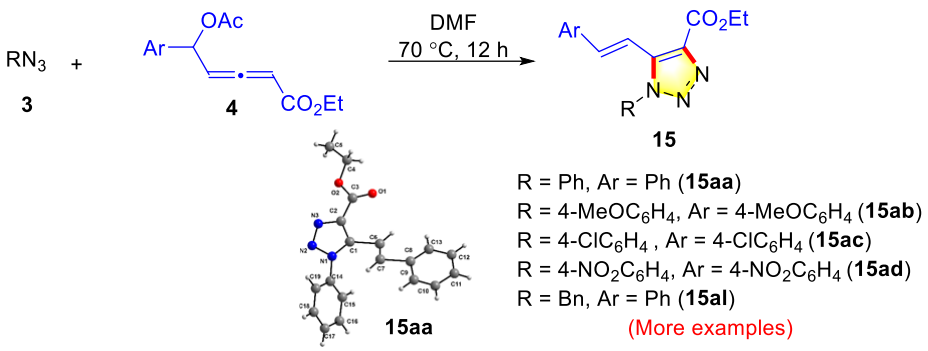
Realizing that even among the amine bases in the course of our studies on allenoate chemistry, we performed the reaction of *β′*-acetoxy allenoates with *N*-sulfonyl imines in the presence of a different amine base, DMAP. Indeed this reaction involved (4 + 2) annulation offering *m*-teraryls **14** in like that deliberated above (section ii). The reaction proceeds *via* Mannich coupling, rather than 1,2-elimination followed by C-N bond cleavage/ aromatization (Scheme 7). The intermediates in this as well as those discussed in section (iii) have been identified by in-process HRMS studies.



Scheme 7: Formation of *m*-teraaryls from cyclic *N*-sulfonyl imines and *β'*-acetoxy allenoates

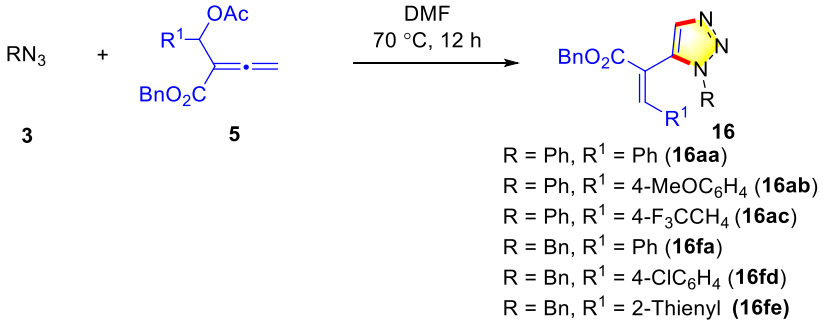
(v) Thermal metal-free (3 + 2) cycloadditions involving acetoxy allenoates and azides

Although numerous azide-alkyne click reactions are reported, the corresponding reaction of azides with allenes is relatively much less explored. Herein regio-and stereo-selective (3 + 2)-thermal cycloaddition involving δ-acetoxy allenoates and azides for the construction of 1,4,5-trisubstituted-1,2,3-triazoles in good to high yields under metal-free conditions is disclosed. In this cycloaddition, the aryl-attached nitrogen atom chemoselectively attacks the β-carbon of acetoxy allenoate and delivers *essentially E-isomer* in all cases (Scheme 8). Interestingly, *β* and *α*-carbons of *δ*-acetoxy allenoate were involved in delivering fully substituted triazole cores.



Scheme 8: Formation of 1,4,5-trisubstituted-1,2,3-triazoles from δ-acetoxy allenoates

Inspired by the results achieved with *δ*-acetoxy allenoates, we conducted a similar thermal (3 + 2) cycloaddition reaction using *β′*-acetoxy allenoates. First, we examined the reaction between **4a** and **1a** using standard reaction conditions. In this case, we isolated product **5aa** in high yield (71%) and assigned it as 1,5-disubstituted 1,2,3-triazole using spectroscopic data. For the substrate scope, we synthesized **16aa-16ac**, **16fa**, **16fd**, and **16fe**. In these reactions involving *β′*-acetoxy allenoates, *β* and *γ*-carbons participated in the (3 + 2) cycloaddition.

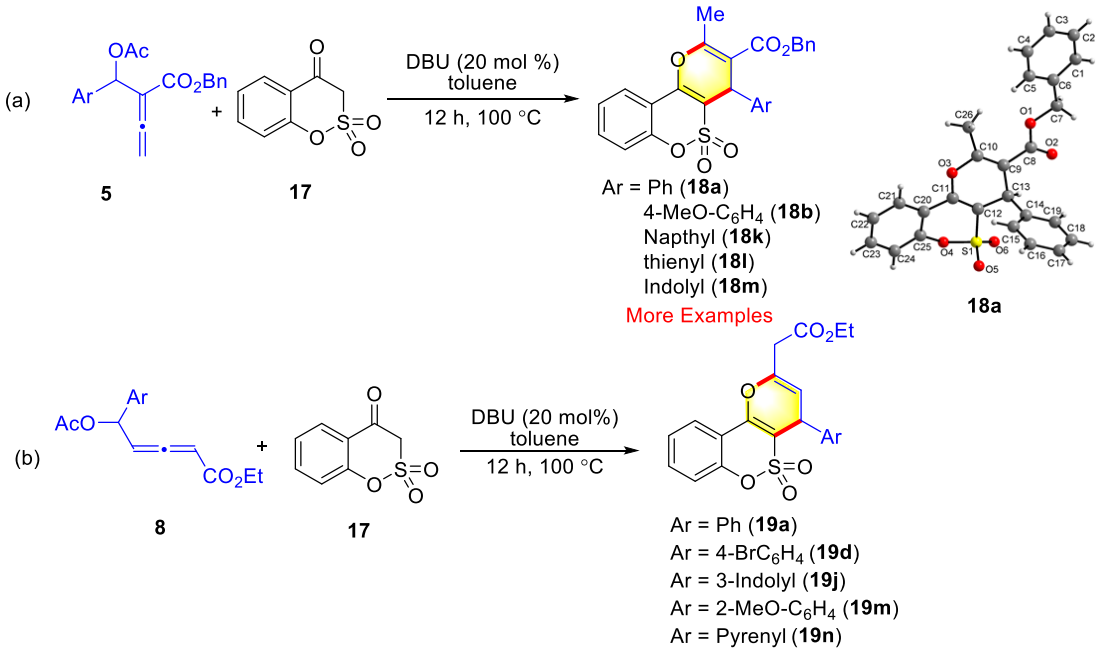


Scheme 9: Formation of 1,5-disubstituted-1,2,3-triazoles from *β′*-acetoxy allenoates

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

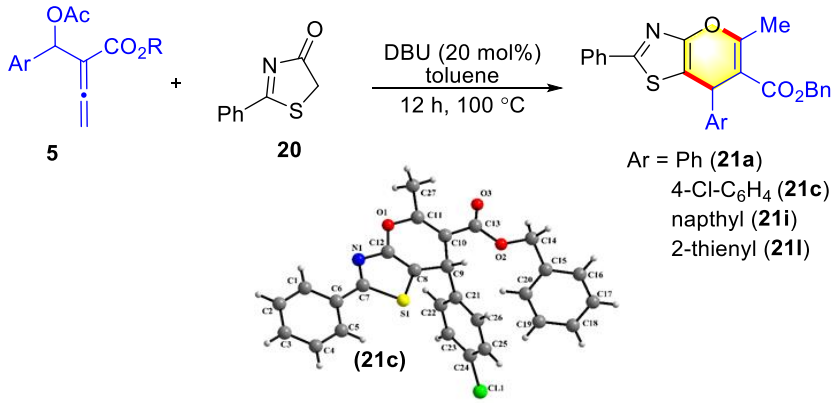
Annulations involving acetoxy allenoates and enolizable carbonylthiocarbonyl or imino substrates, catalyzed by Lewis bases, can be valuable tools to obtain pyrans/dihydropyrans/thiopyrans as well as spirocycles. Since the work described above involved cyclic sulfonyl imines, it was thought prudent to check the reactivity of acetoxy allenoates with bifunctional substrates possessing a sulfonyl group and enolizable carbonyls. Thus DBU catalyzed (3 + 3) annulations of *β′*-acetoxy allenoates with benzo-oxathiin-dioxide and phenylthiazolone has been explored. The products were dihydropyrans. Thus DBU catalyzed (3 + 3) annulation of *β′*-acetoxy allenoates **5a-b** and **5k-m** with benzo-oxathiin-

dioxide **17** afforded fused dihydropyrans **18a-18b** and **18k-18m** (Scheme 10a). We also explored the reactivity of *δ*-acetoxy allenoates with benzo-oxathiin-dioxide **17**. Thus (3 + 3) annulation of *δ*-acetoxy allenoates **8a**, **8d**, **8j**, **8m**, and **8n** with benzo-oxathiin-dioxide **17** afforded dihydropyrano-oxathiines **19a, 19d**, **19j**, **19m**, and **19n** (purity >90%) in decent yields but purification posed some difficulties (Scheme 10b).



Scheme 10: Formation of dihydropyrans from δ/*β′*-acetoxy allenoates

In continuation of the above work, we conducted the reaction of *β′*-acetoxy allenoates **5a**, **5c**, and **5i** with phenylthiazolone **20** with. Pleasingly, this reaction also worked well to afford the products **21a**, **21c**, and **21i** in decent yields (Scheme 11). The annulated product **21c** was characterized by single crystal X-ray diffraction.



Scheme 11: Formation of pyrano-thiazole-carboxylate from *δ*-acetoxy allenoates

Chapter 1

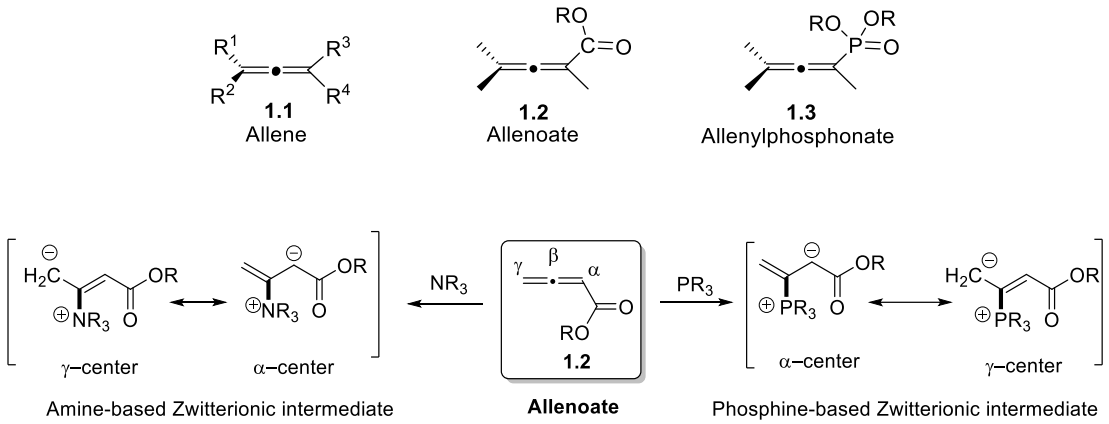
INTRODUCTION

The work embodied in this thesis deals with the chemistry of allenes, more specifically allenoates. The current chapter deals with the literature on the topics that will be discussed in Chapter 2. An Introduction to allene as well as allenoate chemistry is delved into in sections 1.1-1.4. Recent advances in the chemistry of allenoates are deliberated in section 1.4. Since the *N*-sulfonyl-ketimines as well as click (azide + alkyne/allene) chemistry are also used in the current work, literature relevant to these aspects is discussed in sections 1.5-1.6.

1.1 Allenes: From Esoteric Compounds to Valuable Synthons

Allenes possess cumulative double bonds with the central *sp*-hybridized carbon connected to its two adjacent sp^2-hybridized carbon atoms by double bonds (cf. **1.1**). Even during the 1960s, they were viewed as only curiosities with not much synthetic utility.[1] However, in recent decades, allenes have been proven to be not just intermediates but synthetically valuable substrates for numerous organic transformations.[2,3] An industrially important material, MAPP gas, is a mixture of **M**ethyl **A**cetylene [$(H_3C)MeC{\equiv}CH$], **A**llene [Propadiene, $H_2C{=}C{=}CH_2$], and **P**ropane. Numerous synthetic methods are available for allene synthesis.[4] Although multisubstituted allenes show chirality, this feature is most often lost in their reactions and hence is not made use of in a majority of cases. Tethering another functional group to the allene moiety would make the system a more versatile synthon. Allenoates (2,3-butadienoates; **1.2**) possess an ester group attached to a terminal carbon of allenes. Upon reaction with a base, they generate zwitterionic intermediates which may be involved as one-,[3a] two-,[3b] three-,[3c] four-[3d] or five-[3e] C-precursors to obtain varied cyclic scaffolds. In place of the ester group one can also have a phosphonate or sulfonate group; the resulting compounds are allenylphosphonates (cf. **1.3**) whose chemistry has been well-explored in our laboratory.[5] In the work reported in this thesis, the main focus is on allenoate chemistry. The negative charge produced after the Lewis base attacks the C(*sp*) atom of allenoate is stabilized by the electron-withdrawing ester group. This gives rise to a zwitterionic species that can attack an electrophilic reactant (Scheme 1.1). An important point to note is that because of the larger size and some contribution from the available d-orbitals,

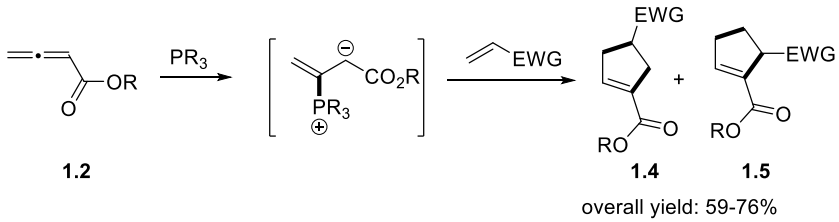
the zwitterionic intermediates are better stabilized by phosphines. This factor in the case of phosphine bases tends to direct the reactivity in a way different from that by amines.



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

1.2. Allenoate (and allenyl-ketone) Chemistry

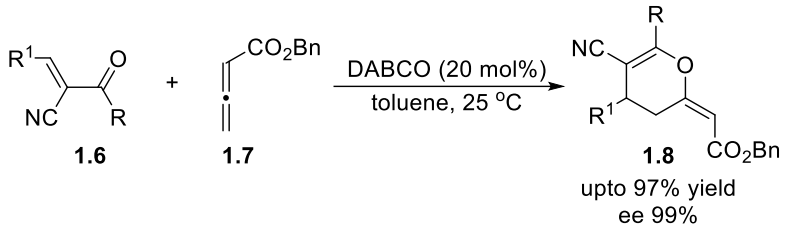
In the year 1995, the research team of Lu published the first (3 + 2) annulation reaction between allenoates (2,3-butadienoates) with activated olefins which gave rise to the cyclopentene products **1.4**-**1.5** under phosphine catalysis (Scheme 1.2)[6] [*Note*: In most of the annulation reactions using allenes in the current work we are concerned with the number of atoms of each substrate involved; hence we have used normal parenthesis for the depicting the type of annulation]. This discovery was the key to a plethora of numerous subsequent reports in allenoate chemistry. Thus allenoates can perform either as dipolarophiles or as dienophiles in the cycloadditions; numerous other annulations are also possible.[7,8] Asymmetric synthesis using appropriate catalysts can lead to transformations that are highly stereoselective. Some of these, with emphasis on recent literature, are presented in this section.



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

In 2011, Tong's group developed the enantioselective (4 + 2) annulations of cyano-oxo-dienes **1.6** with allenoate **1.7**. This process entails a nice route to 2H-pyrans **1.8** with high enantioselectivity. Importantly, both enantiomers were prepared by switching the

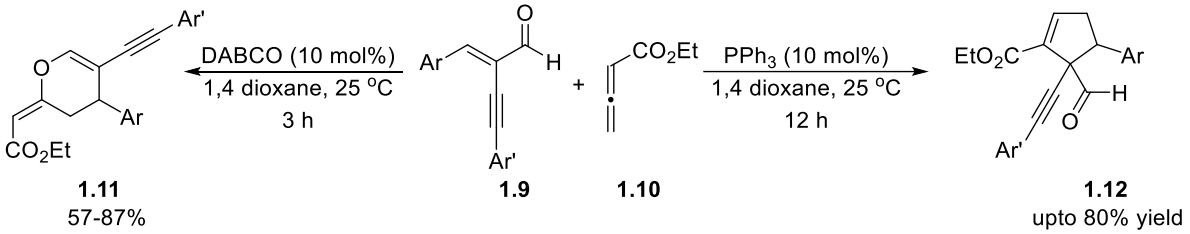
solvent and the catalyst. The cyano substituent in the oxodiene **1.6** (Scheme 1.3), though, is required and hence is a limitation.[9]



1.6 **1.7** **1.8**

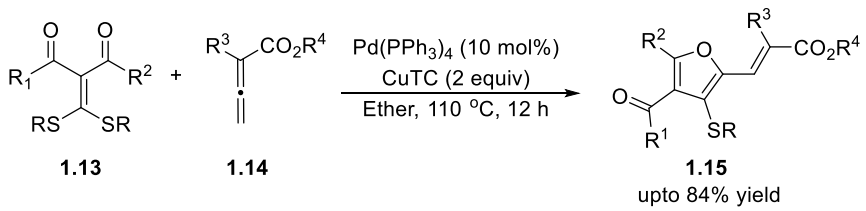
Scheme 1.3: Synthesis of substituted 2H-pyrans **1.8** from allenoate **1.7**.

In the year 2015, Swamy's group developed the regioselective synthesis of novel dihydropyrans **1.11** by (4 + 2) cycloaddition of enynals **1.9** with allenoates **1.10** by using DABCO as the organocatalyst. By contrast, (3 + 2) cycloaddition of enynals with allenoates under phosphine-catalysis provided cyclopentenes **1.12** wherein the electrophiles were enynals (Scheme 1.4).[10]



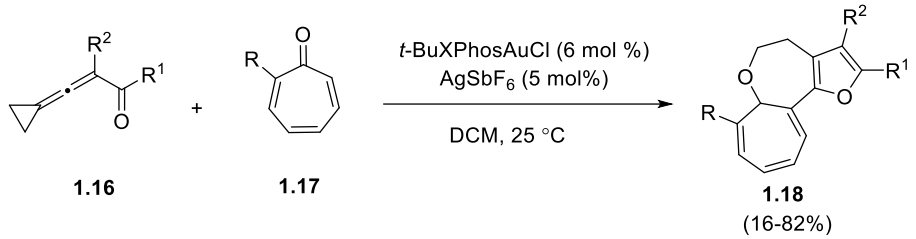
Scheme 1.4: Synthesis of dihydropyrans **1.11** and cyclopentenes **1.12** from allenoate **1.10**.

Yu and co-workers in the year 2018 reported an efficient copper-mediated palladium-catalyzed, (4 + 1) annulation of α-oxo ketene dithioacetals **1.13** with allenoates **1.14** to obtain 2-alkenylfurans **1.15** by employing mild reaction conditions. The reaction involves C-S cleavage of tetrasubstituted internal alkene under palladium-catalysis to give multisubstituted 2-alkenylfurans with high regioselectivity. It must be noted that in this (4 + 1) annulation, allenoates performed their role as C1 synthons (Scheme 1.5).[11]



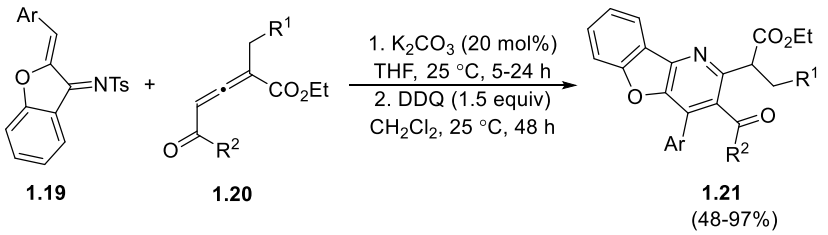
Scheme 1.5: Synthesis of 2-alkenylfurans **1.15** from allenoate **1.14**.

In 2020, Hongjun Ren and co-workers described a cascade cyclization reaction of readily accessible allenyl ketones **1.16** bearing a cyclopropyl moiety with tropone **1.17**. The route involves creation of non-classical 1,4-all-carbon gold-containing dipoles from 1,2-carbene transfer/ cycloisomerization/ring opening. This method involves an unprecedented high-order (8+4) cycloaddition to deliver 7,7,5-tricycles **1.17** in good yields (Scheme 1.6).[12]



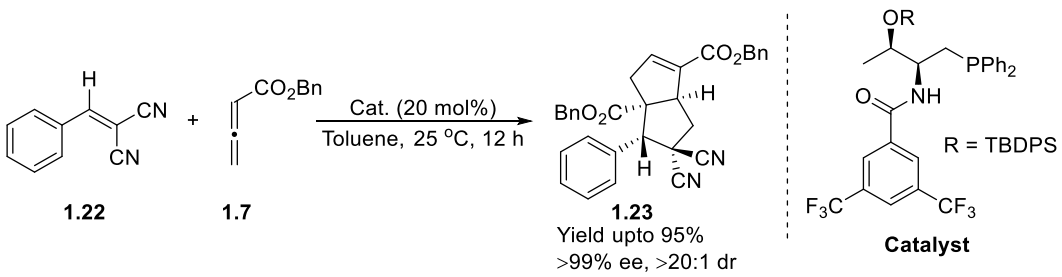
Scheme 1.6: Synthesis of 7,7,5-tricycles **1.18** from allenyl ketones **1.16**.

Guo and co-workers reported an effective and concise 1,4-addition followed by intramolecular cyclization and aromatization incorporating trisubstituted allenoates **1.20** with azadienes **1.19** mediated by K_2CO_3 furnishing a new class of benzofuro[3,2-b]pyridines **1.21** in moderate to excellent yields. They successfully carried out the reaction in air in the absence of transition metal catalysts. This procedure offers an interesting route to benzofuro-pyridines (Scheme 1.7).[13]



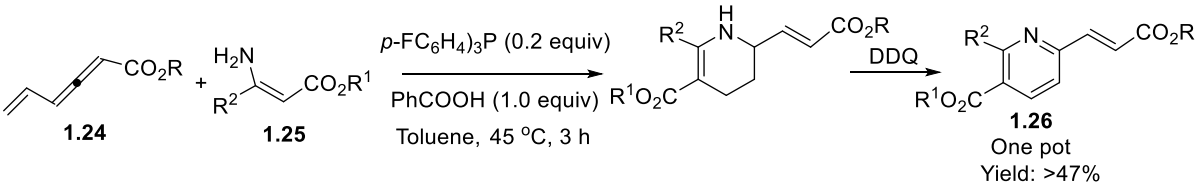
Scheme 1.7: Synthesis of benzofuro[3,2-b]pyridines **1.21** from allenoate **1.20**.

Yixin Lu and co-workers explored a highly enantio- and diastereo-selective sequential (3 + 2)/(3 + 2) annulation of allenoate **1.7** with arylidenemalononitriles **1.22** under phosphine catalysis to prepare multifunctionalized bicyclic-octenes **1.23** containing one quaternary carbon center with three consecutive stereogenic centers, in a one-step operation from readily available materials (Scheme 1.8).[14]



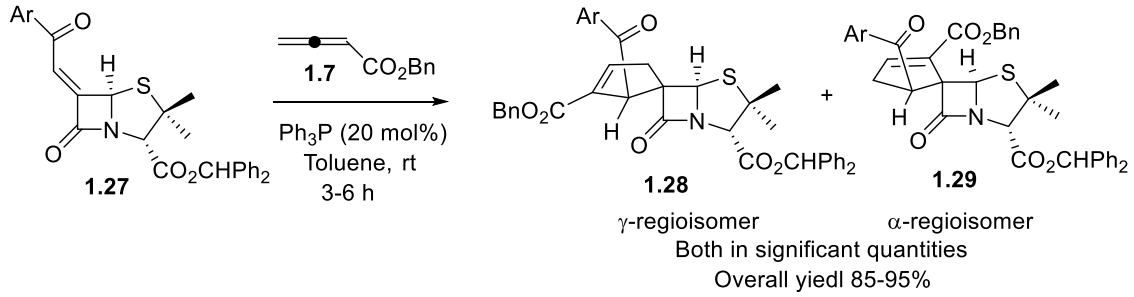
Scheme 1.8: Synthesis of *cis*-fused bicyclic[3,3,0]octene scaffolds **1.23** from allenoate **1.7**.

Huang's group developed one-pot route to prepare trisubstituted pyridine scaffolds **1.26** by (p-$FC_6H_4)_3P$--catalyzed cyclization and oxidative aromatization (DDQ) from enamino esters **1.25** and γ-vinyl allenoates **1.24** under metal-free conditions (Scheme 1.9).[15]



Scheme 1.9: Synthesis of trisubstituted pyridines **1.26** from vinyl allenoate **1.24**.

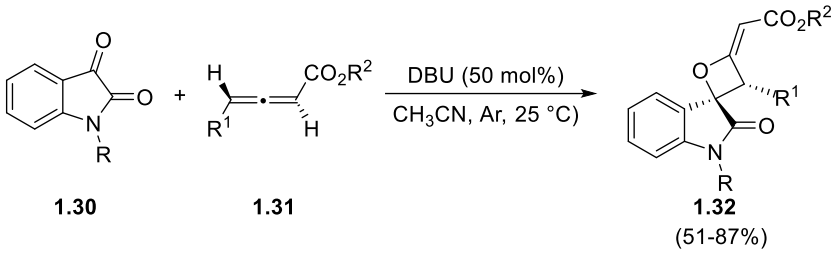
Phosphine catalyzed synthesis of pharmaceutically significant spirocyclopentene-β-lactams **1.28-1.29** was accomplished by Taveira, Melo, and co-workers by starting with the allenoate **1.7** and the lactam **1.27** (Scheme 1.10).[16] Excellent yields were obtained in this reaction. Most of these products were checked for inhibition of HIV-2 with some of them exhibiting excellent activity.



Scheme 1.10: Synthesis of spiro-β-lactams **1.28-1.29** from allenoate **1.7**.

In 2023, a highly efficient process to synthesize highly functionalized spiro-oxetane oxindoles **1.32** using DBU-catalyzed reaction was developed by Somappa and co-workers. This process proceeds *via* spiro-annulation of isatins **1.30** with allenoates **1.31** and is compatible with a large number of isatins having electron-donating or electron-withdrawing groups and various allenoates furnishing the relevant products in good yields. This is the first

protocol for constructing highly functionalized spiro-oxetane oxindoles of medicinal importance (Scheme 1.11).[17]

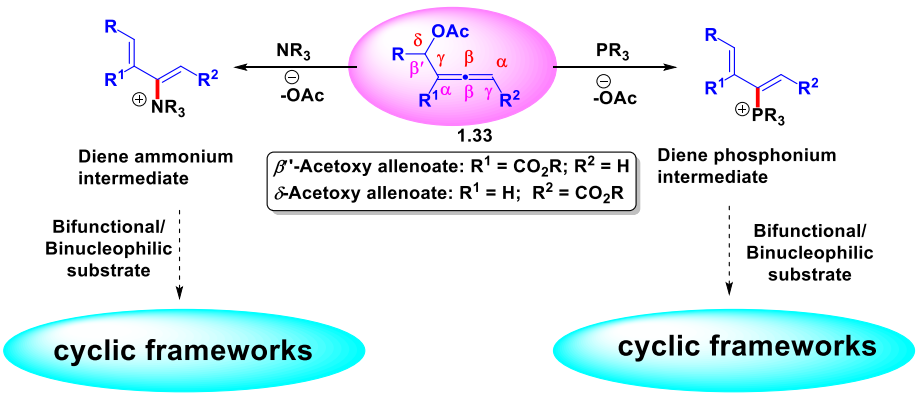


Scheme 1.11: Synthesis of spiro-oxetane oxindoles **1.32** from allenoate **1.31**.

A recent review by Hajinasiri summarizes the recent contributions on this topic.[2m]

1.3. *δ*-Acetoxy Allenoate Chemistry

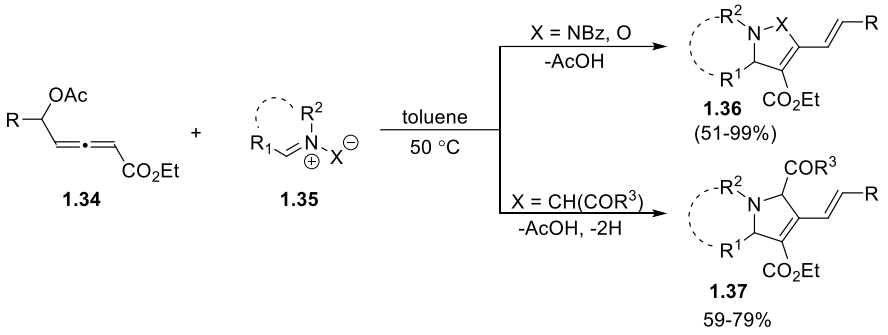
The introduction of an acetoxy group on the allenoate moiety makes the reactions more fascinating since the –OAc group can be readily eliminated under basic conditions. Two such useful substrates are *δ*-acetoxy allenoates and *β′*-acetoxy allenoates (cf. **1.33**). The reactions utilizing these are facilitated by adding Lewis base at the *sp* carbon of allenoate *via* addition-elimination to generate a reactive ammonium or phosphonium dienyl-intermediate after the removal of the acetoxy group. Subsequent annulation in the presence of an appropriate bifunctional substrate can lead to the formation of cyclic frameworks (Scheme 1.12). Relevant work on this topic is delineated below.



Scheme 1.12: Synthesis of cyclic frameworks *via* diene ammonium/phosphonium intermediates generated from acetoxy allenoates

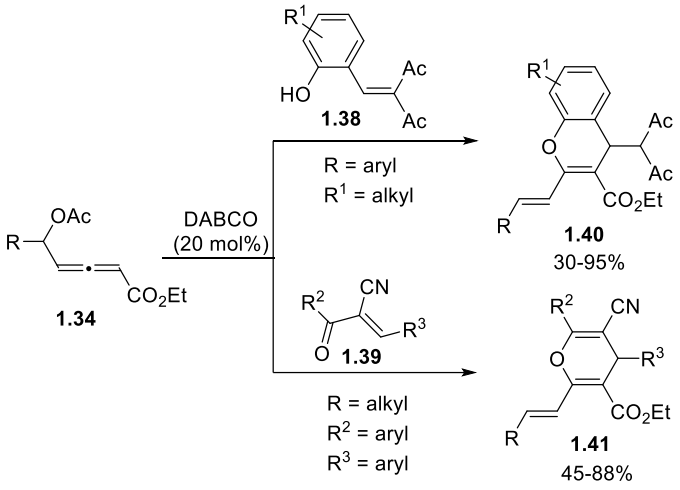
Tong and coworkers reported thermal 1,3-dipolar cycloaddition of various azomethine imines **1.35** with *δ*-acetoxy allenoates **1.34** to obtain 2,3-dihydropyrazoles **1.36** and 2,3-

dihydroisoxazoles **1.37**, respectively. These reactions take place *via* thermal 1,3-dipolar cycloaddition followed by the removal of AcOH (Scheme 1.13).[18]



Scheme 1.13: Synthesis of 2,3-dihydropyrazoles **1.36** and 2,3-dihydroisoxazoles **1.37** from *δ*-acetoxy allenoates **1.34**.

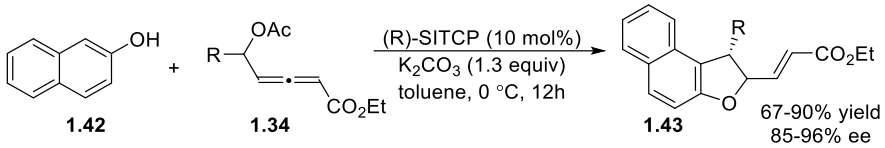
Tong and coworkers also reported a (4 + 2) annulation reaction of *δ*-acetoxy allenoates **1.34** with substituted salicylaldehydes **1.38** or *α*-cyano carbonyl compounds **1.39** in the presence of DABCO catalyst to generate 4*H*-chromenes **1.40** or 4*H*-pyrans **1.41** under mild reaction conditions. Allenoates with an aromatic group at *δ*-C favored the formation of 4H-chromenes by reacting with salicylaldehydes while the alkyl group tethered allenoates at δ-C afforded 4H-pyrans by reacting with oxo-dienes (Scheme 1.14).[19]



Scheme 1.14: Synthesis of 4*H*-chromenes and 4*H*-pyrans *via* acetoxy allenoates

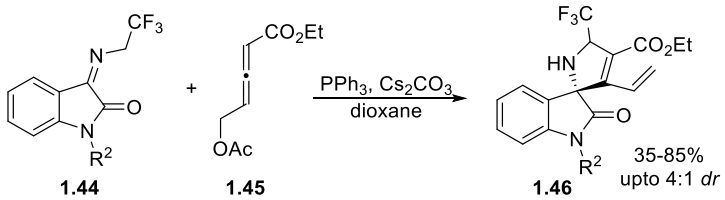
Wang *et al.* developed a $PPhMe_2$ catalyzed (3 + 2) cyclization of *δ*-acetoxy allenoates **1.34** and 2-naphthols **1.42** for the synthesis of 1,2-dihydronaphthofurans **1.43** in decent yields. The mechanistic study revealed that the *α-C* of 2-naphthol attacked *δ-C* of allenoate *via* the Friedel-Crafts type process to form the C-C bond while a C-O bond was formed *via* oxa-Michael addition between the 2-naphthol hydroxyl group and the *γ-C* of allenoate. They

also developed the asymmetric version with the use of (*R*)-SITCP as the chiral phosphine catalyst (Scheme 1.15).[20]



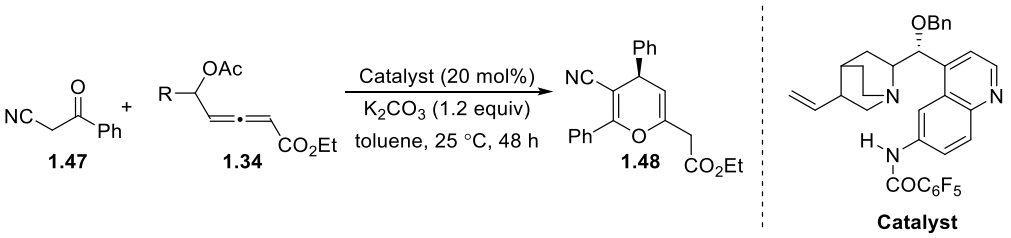
Scheme 1.15: Synthesis of 1,2-dihydronaphtho[2,1-*b*]furans *via* acetoxy allenoates

Min Shi's research team developed a Ph_3P-catalyzed (3 + 2) annulation of *N*-2,2,2-trifluoroethyl isatin-based ketimines **1.44** and *δ*-acetoxy allenoate **1.45** to synthesize spirooxindoles **1.46** in decent yields. The technique could be applied exclusively for making spirooxindoles with a CF_3 moiety. This process is amenable to a vast range of allenoate precursors and affords the products under mild reaction conditions in good yields (Scheme 1.16).[21]



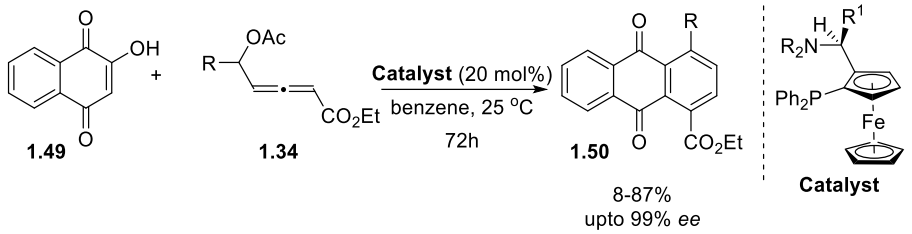
Scheme 1.16: Synthesis of spirooxindoles **1.46** from acetoxy allenoate **1.45**

In 2017, a highly facile route for the construction of 4*H*-pyran **1.36** was reported by Tong and coworkers. This bifunctional amine catalyzed reaction proceeded by asymmetric (3 + 3) annulation of δ-acetoxy allenoates **1.34** with 1*C*,3*O*-bisnucleophiles **1.47** for the construction of 4*H*-pyran scaffolds **1.48** with good enantioselectivity. This method can be utilized with allenoates which contain electron-donating (EDG) or electron-withdrawing (EWG) groups furnishing the products in good yields under mild reaction conditions (Scheme 1.17).[22]



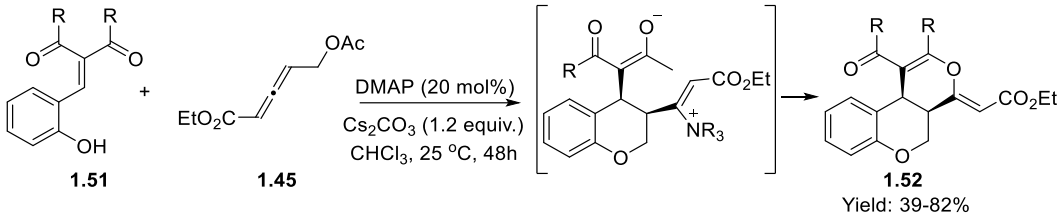
Scheme 1.17: Synthesis of 4*H*-pyran **1.48** from acetoxy allenoates **1.34**

Tong and coworkers also developed chiral phosphine catalyzed atroposelective (4 + 2) annulation of *δ*-acetoxy allenoates **1.34** with 2-hydroxy-quinone **1.49** featuring the *de novo* construction of a aryl ring with concomitant formation of axial chirality to give aryl-naphthoquinone atropisomers **1.50** in good enantioselectivities. The key (4 + 2) cycloaddition in a *pseudo*-intramolecular form is well-known for its broad efficiency and substrate variety (Scheme 1.18).[23]



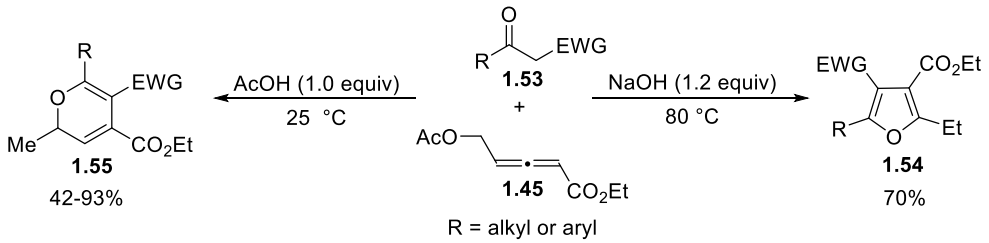
Scheme 1.18: Synthesis of aryl naphtha-quinones **1.50** from acetoxy allenoate **1.34**

Tong's group described a simple DMAP-catalyzed (4 + 2) domino annulation reaction of oxadiene **1.51** with *δ*-acetoxy allenoate **1.45** that gave polycyclic frameworks **1.52**. The authors proposed that 3-ammonium-dienoate played a role in an addition-elimination reaction involving an allenoate and a catalyst, that could add to either an O- or N-nucleophile and undergo subsequent (4 + 2) annulation with oxadiene. The process utilized commonly available reactants and mild conditions. It provides a straightforward and quick method for creating polycyclic products (Scheme 1.19).[24]



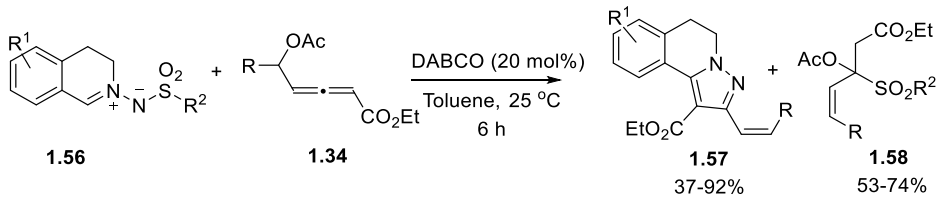
Scheme 1.19: Synthesis of hetero-polycyclic frameworks **1.52** from *δ*-acetoxy allenoate **1.45**

In 2012, Tong and co-workers reported the formation of tetrasubstituted furans **1.54** and dihydropyrans **1.55** from *δ*-acetoxy allenoate **1.45** and carbonyl compounds **1.53** having active methylene group which behave as 1C-3O binucleophiles. This phosphine-catalyzed (3 + 2) annulation requires basic conditions whereas, in (3 + 3) annulation, the reaction worked well under acidic conditions (Scheme 1.20).[25]



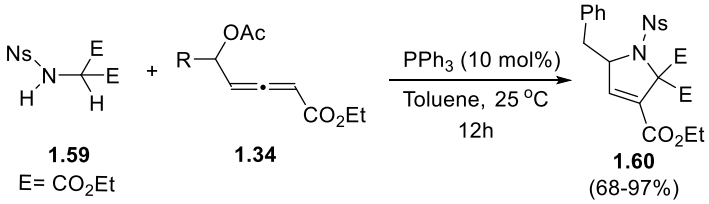
Scheme 1.20: Synthesis of furans **1.54** and dihydropyrans **1.55** from acetoxy allenoate **1.45**

Min Shi and his colleagues demonstrated a one-pot, (3 + 2) annulation of C,N-cyclic azomethine imine **1.56** with *δ*-acetoxy allenoate **1.34** catalyzed by DABCO to yield 5,6-dihydropyrazolo [5,1-a]isoquinoline **1.57** and ethyl (*Z*)-3-acetoxy-3-tosylpent-4-enoate **1.58** in moderate to good yields under mild conditions. This approach facilitates the simultaneous synthesis of heterocycles **1.57** and ethyl acetoxy-tosylpentenoates **1.58** (Scheme 1.21).[26]



Scheme 1.21: Synthesis of 5,6-dihydropyrazolo [5,1-a]isoquinolines **1.57** and ethyl (*Z*)-3-acetoxy-3-tosylpent-4-enoates **1.58** using δ-acetoxy allenoates **1.34**

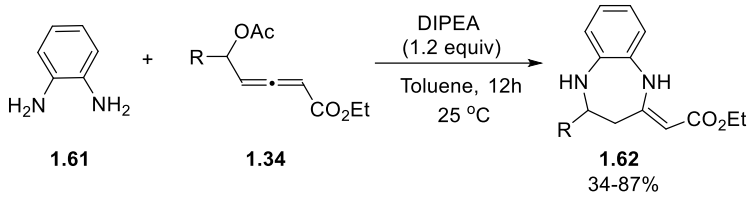
In the year 2018, Tong and co-workers developed a novel synthetic protocol for the highly substituted 3-pyrrolines **1.60** by Ph_3P-catalyzed (3 + 2) annulation of *δ*-acetoxy allenoates **1.34** with 2-sulfonamidomalonate **1.59** under mild reaction conditions. Using phosphine (*R*)-SITCP as the catalyst, the asymmetric variant (up to 83% ee) was also obtained. The mechanistic studies showed that the associated deprotonation of amide NH and aza-addition to vinyl phosphonium may occur in a concerted manner (Scheme 1.22).[27]



Scheme 1.22: Synthesis of 3-pyrrolines **1.60** from *δ*-acetoxy allenoates **1.34**.

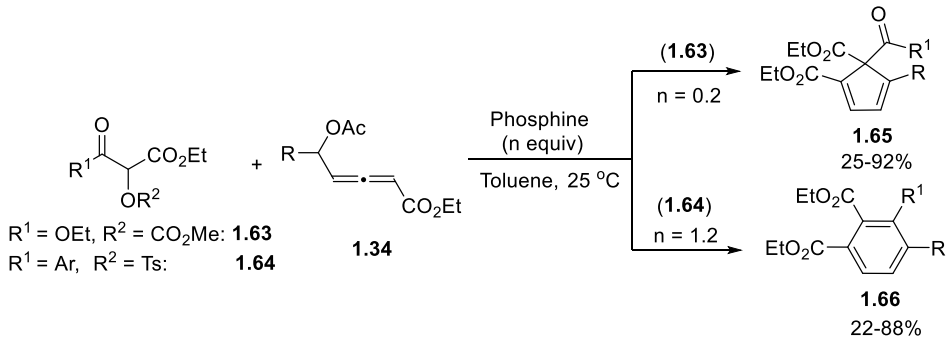
Tong and coworkers discovered a novel technique for the synthesis of 1,5-benzodiazepines **1.62** *via* (3+4) annulation of *δ*-acetoxy allenoates **1.34** with *o*-diaminobenzenes **1.61**. This (3 + 4) annulation probably occurs *via* the aza-Michael addition

of diaminobenzene to allenoate, followed by acetate group removal, and 1,6-addition. This approach has a wide substrate scope, widely available starting materials, moderate reaction conditions, and a high reaction efficiency (Scheme 1.23).[28]



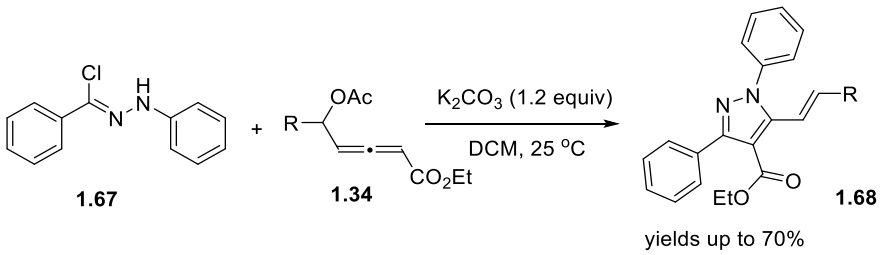
Scheme 1.23: Synthesis of 1,5-benzodiazepines **1.62** from δ-acetoxy allenoates **1.34**

Tong *et al.* demonstrated the synthesis of highly substituted cyclopentadienes **1.65** by PPh_3-catalyzed (4+1) annulation reaction of unsymmetrical malonate **1.63** with δ-acetoxy allenoates **1.34**. However, using 1.2 equiv phosphine and another base, similar starting materials **1.64** underwent (4 + 2) annulation, yielding tetrasubstituted benzenes **1.66**. The protocol allowed the authors to generate a significant number of products **1.65-1.66** in high-yields (Scheme 1.24).[29]



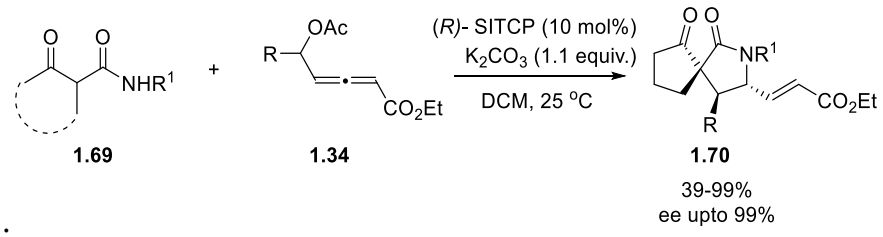
Scheme 1.24: Synthesis of cyclopentadienes **1.65** and tetrasubstituted aryls **1.66** from acetoxy allenoates **1.34**

Zhou *et al.* developed an important protocol for synthesizing 1,3,5-trisubstituted pyrazoles **1.68** from nitrilimines **1.67** and *δ*-acetoxy allenoates **1.34** with K_2CO_3 as a base. The reaction proceeds *via* 1,3-dipolar cycloaddition. The authors further reported that the presence of the electron-withdrawing nitro group on the benzene ring of nitrilimines reduced the yield of the product, whereas the presence of a methoxy group boosted the yield (Scheme 1.25).[30]



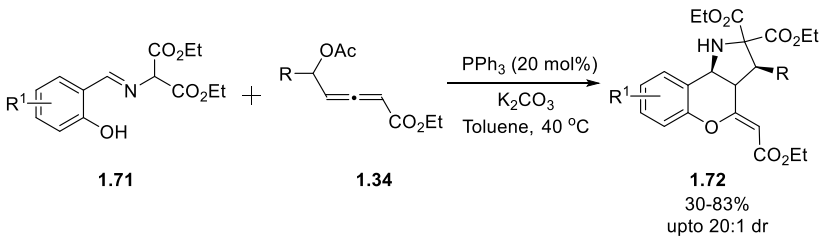
Scheme 1.25: Synthesis of trisubstituted pyrazoles **1.68** from δ-acetoxy allenoates **1.34**

Zhou and coworkers also described an unusual asymmetric (3 + 2) annulation of *δ*-acetoxy allenoates **1.34** with *β*-carbonyl amides **1.69** by using chiral phosphine (*R*)-SITCP as catalyst. The δ-C and γ-C positions of allenoate acted as two electrophilic sites engaging in the annulation with the α-C and N of the amide, respectively. This technique has a broad substrate scope in terms of allenoate and β-carbonyl amide, resulting in a robust method for the synthesis of different γ-lactams **1.70** with strong stereoselectivity (up to 97% ee and >20:1 dr; Scheme 1.26).[31]



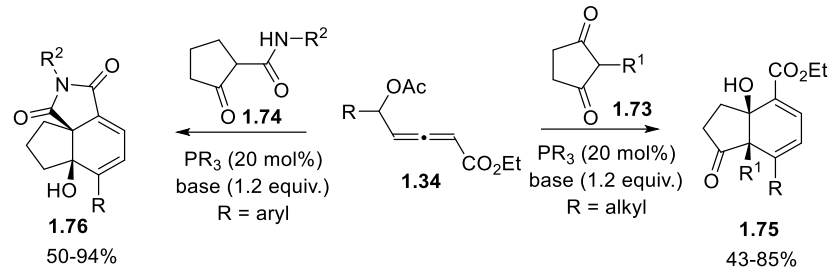
Scheme 1.26: Synthesis of γ-lactams **1.70** from *δ*-acetoxy allenoates **1.34**

Zhou's research group published a tandem cyclization process catalyzed by phosphine to generate a series of chromeno[4,3-b]pyrroles **1.72** with three successive asymmetric centers by using aldimine esters **1.71** and *δ*-acetoxy allenoates **1.34**. The reaction gives high yield as well as outstanding *Z/E* selectivity (Scheme 1.27).[32] The novel approach is straightforward, needs only mild conditions, and is suitable for substrates with a wide range of functional groups. Similarly, to accomplish asymmetric synthesis, this reaction can be catalyzed by a chiral phosphine catalyst.



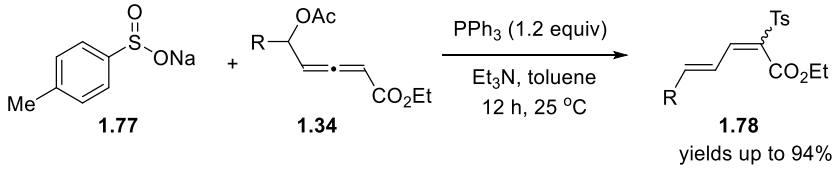
Scheme 1.27: Synthesis of compounds **1.72** from *δ*-acetoxy allenoates **1.34**

Tong and his colleagues discovered an elegant route to access 1,3-cyclohexadienes **1.75** and **1.76** by coupling acetoxy allenoates **1.34** with ketones in phosphine-catalyzed substrate-dependent (4 + 2) annulations. Allenoates with an alkyl group at the *δ*-carbon show *δ*-C electrophilicity and *α*-C nucleophilicity when exposed to cyclic 1,3-diketones **1.73**, whereas aryl-containing allenoates exhibit the reverse reactivity when exposed to cyclic *β*-carbonyl amides **1.74**. The catalytic cycle is based on 1,3-diene isomerization, and is new in the area of phosphine-catalyzed annulations (Scheme 1.28).[33]



Scheme 1.28: Synthesis of fused 1,3-cyclohexadienes **1.75-1.76** from acetoxy allenoates **1.34**

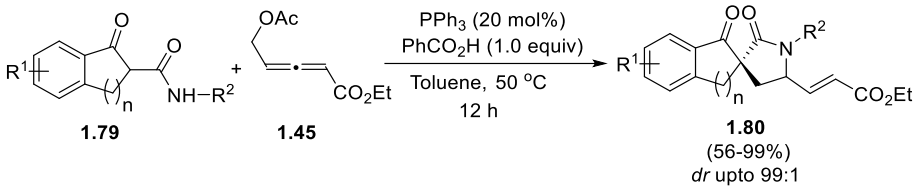
Tong and coworkers reported the Ph_3P-catalyzed α-umpolung addition of sodium *p*-tolylsulfinate **1.77** to *δ*-acetoxy allenoates **1.34**, resulting in conjugated *trans*-diene product **1.78** with good to exceptional stereoselectivity. The mechanistic study revealed that the reaction proceeded *via* 3-phosphonium-2,4-dienoate, which was stabilized by the electrophilicity of the acetoxy allenoate's α-carbon atom. The presence of an electron-withdrawing chloro substituent on the phenyl ring of sodium benzenesulfinate enhanced the product yield. By contrast, electron-donating substituents like methoxy lowered the product yield (Scheme 1.29).[34]



Scheme 1.29: Synthesis of conjugated *trans*-dienes **1.78** from *δ*-acetoxy allenoates **1.34**

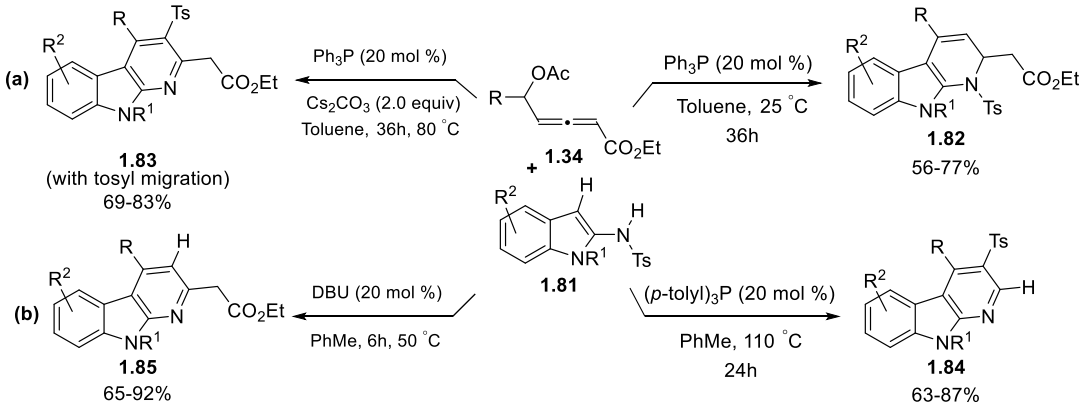
Min Shi and co-workers developed a diastereoselective Ph_3P-catalyzed (3 + 2) spiroannulation of *α*-substituted *β*-ketoamides **1.79** with *δ*-acetoxy allenoates **1.45** affording five-membered *N*-heterocycles **1.80** with a quaternary stereocenter in decent to excellent yields and under mild conditions. In this spiroannulation reaction, the bis-nucleophilic partner

was β-ketoamide while the γ,δ-carbon of 5-acetoxypenta-2,3-dienoate acted as a C2 synthon (Scheme 1.30).[35]



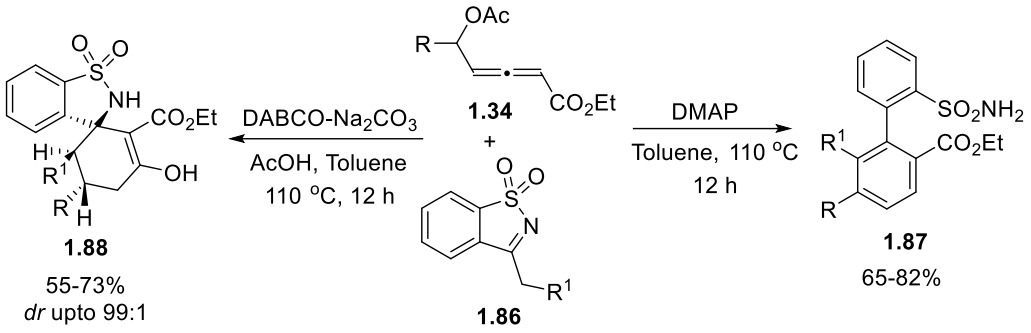
Scheme 1.30: Synthesis of spiro-heterocycles **1.80** from acetoxy allenoate **1.45**

Very recently, our group developed phosphine-catalyzed divergent annulations by using *δ*-acetoxy allenoates **1.34** and 2-sulfonamidoindoles **1.81**. The temperature-dependent phosphine catalyzed (3 + 3) annulation between *δ*-acetoxy allenoates **1.34** and 2-sulfonamidoindoles **1.81** resulted in the formation of 1,2-dihydro-carbolines **1.82** in the presence of Ph_3P at room temperature and *α*-carboline motifs **1.83** with tosyl functionality at the γ-carbon at higher temperature (80 ºC, Scheme 1.31a).[36] As an extension of this work, in the year 2022, our research team reported Lewis base directed (3 + 3) annulations of *δ*-acetoxy allenoates **1.34** with iminoindolines **1.81** offering the synthesis of tosyl-migrated α-carbolines **1.84** and α-carbolines **1.85**. The phosphine-catalyzed annulation involves diene-phosphonium ion intermediate in the formation of tosyl-migrated α-carbolines **1.84**. By contrast, DBU-catalyzed (3 + 3) annulations using the same starting materials delivered α-carbolines **1.85** *via* C-H and N-S bond cleavage (Scheme 1.31b).[37] Thus subtle changes in the conditions alter the nature of products in these reactions.



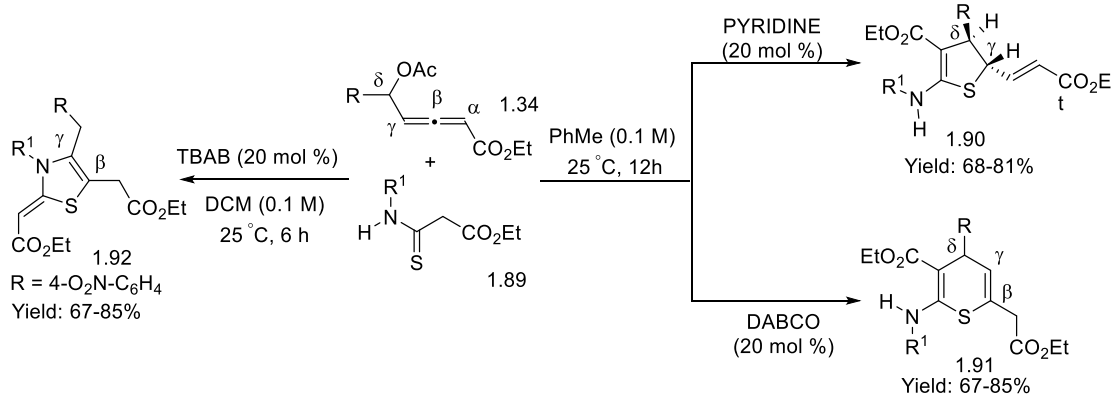
Scheme 1.31: Synthesis of 1,2-dihydro carbolines **1.82/1.84** and α-carbolines **1.83/1.85** from acetoxy allenoates **1.34**

In 2021, our research group reported the synthesis of spirocyclic sultams **1.88** as essentially single diastereomers *via* chemo- and regio-specific (4 + 2)-carbo-annulation involving *δ*-acetoxy allenoates **1.34** and *N*-sulfonyl ketimines **1.86** in the presence of DABCO. On the other hand, DMAP-catalyzed benzannulation with the same reactants produced unsymmetrical *m*-teraryls **1.87** *via* Mannich coupling where the *δ*-acetoxy allenoate **1.34** served as a 4-carbon precursor (Scheme 1.32).[38]



Scheme 1.32: Synthesis of spirocyclic sultams **1.88** and *m*-teraryls **1.87** from δ-acetoxy allenoates **1.34**

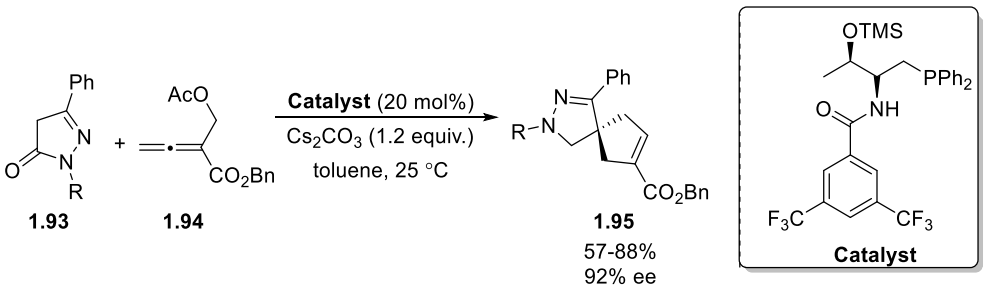
In another work from our group, DABCO, pyridine, or tetra-*n*-butyl ammonium bromide (TBAB) catalyzed the reaction of *δ*-acetoxy allenoates **1.34** with thioamides **1.89** to furnish different types of products. When pyridine was used, dihydrothiophenes **1.90** were formed by (3 + 2) annulation. The use of DABCO as the base led to the formation of thiopyran motifs **1.91**. In a third pathway, tetra-*n*-butyl ammonium bromide (TBAB) facilitated addition-elimination and (3 + 2) annulation giving thiazoles **1.92**.[39]



Scheme 1.33: Synthesis of dihydrothiophenes, thiopyrans and thiazoles from δ-acetoxy allenoates **1.34**

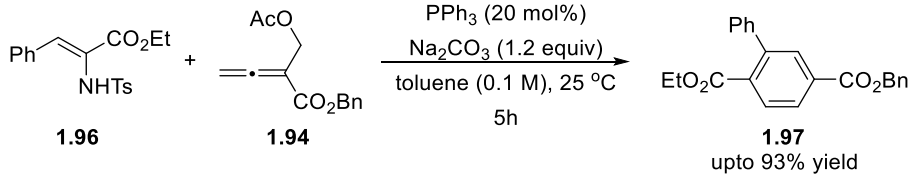
1.4 *β′*-Acetoxy Allenoate Chemistry

These substrates do not differ much from the *δ*-acetoxy allenoates, but since the removable acetoxy group is positioned closer to the electron with-drawing CO_2R group connected to the α-carbon, some differences in the reactivity may be observed. Relevant details are highlighted here. In the year 2014, Lu and coworkers developed phosphine-mediated (4+1) spiroannulation for enantioselective synthesis of spiropyrazolones **1.95** from pyrazolones **1.93** and allenoates **1.94**. Significantly, this is the first report describing the use of substituted allenoates in asymmetric (4+1) annulation, as well as the first use of substituted pyrazolones in cycloaddition. This is also the first asymmetric phosphine catalysed process where a substituted allenoate was used as a C4 synthon for (4+1) annulation (Scheme 1.34).[40]



Scheme 1.34: Synthesis of spiropyrazolones **1.95** from acetoxy allenoate **1.94**

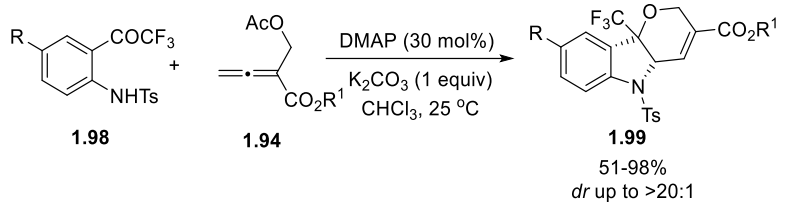
Huang and coworkers reported the preparation of substituted terephthalates **1.97** by domino benzannulation of *β′*-acetoxy allenoates **1.94** with enamines **1.96**. This method to get substituted terephthalates *via* domino benzannulation of *β'*-acetoxy allenoates **1.94** and enamines **1.96** utilizes environmentally benign conditions and easily available phosphine catalyst. This protocol has a fairly broad substrate scope in terms of *β*-carbonyl amides, resulting in a robust method for the synthesis of different terephthalates under mild conditions (Scheme 1.35).[41]



Scheme 1.35: Synthesis of terephthalates **1.97** from acetoxy allenoates **1.94**

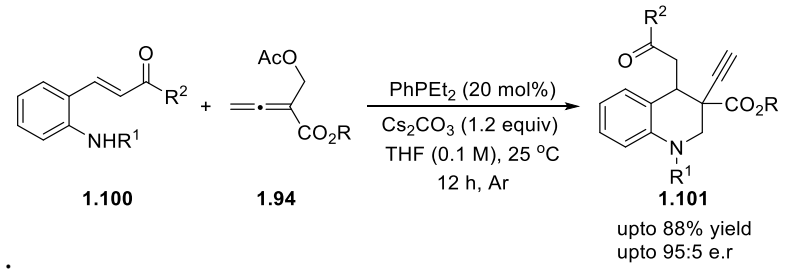
Huang and coworkers developed a diastereoselective (4 + 1)/ (3 + 3) domino sequential annulation between *o*-aminotrifluoroacetophenones **1.98** and *β′*-acetoxy allenoates **1.94** by DMAP catalysis for the synthesis of tetrahydropyrano[3,2-*b*]indoles **1.99** containing

the CF_3 moiety in high to excellent yields under mild reaction conditions. The reaction proceeds through an ammonium ylide intermediate resulting in consecutive formation of one each of C-N, C-C, and C-O bonds (Scheme 1.36).[42]



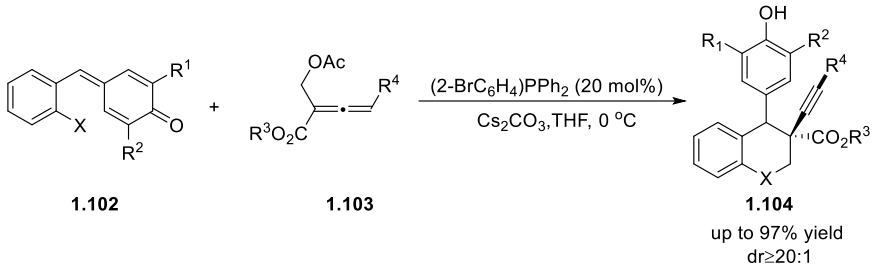
Scheme 1.36: Synthesis of tetrahydropyrano[3,2-*b*]indoles **1.99** from acetoxy allenoates **1.94**

In 2019, Huang and coworkers discovered a novel enantioselective (4 + 2) annulation reaction between *β′*-acetoxy allenoate **1.94** and 2-aminochalcones **1.100** for the synthesis of 3-ethynyl tethered tetrahydroquinolines **1.101**. It should be noted that *β′*-acetoxy allenoates **1.94** were used as C2 precursors (α−β′, 1,2-dipole) for the first time. A novel approach for constructing 3-ethynyl substituted tetrahydroquinolines **1.101** in good yields with high *ee* is provided by this reaction, which uses a phosphine sequential catalytic procedure. In all reactions, only one isomer was separated (Scheme 1.37).[43]



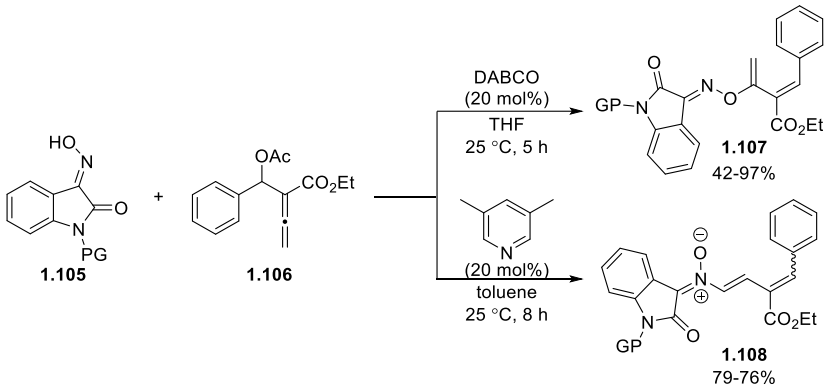
Scheme 1.37: Synthesis of tetrahydroquinolines **1.101** from acetoxy allenoates **1.94**

Huang and coworkers developed a new domino (4 + 2) cycloaddition of *p*-quinone methides (*p*-QMs) **1.102** and *β′*-acetoxy allenoates **1.103**, under phosphine-catalysis affording a new class of chroman and tetrahydroquinolines that have an alkynyl-substituted quaternary carbon **1.104**. 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 of the products could be synthesized (Scheme 1.38).[44]



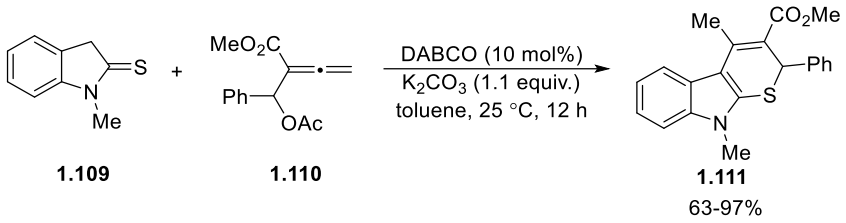
Scheme 1.38: Synthesis of tetrahydroquinolines **1.104** from acetoxy allenoates **1.103**

Min Shi and co-workers established novel routes for the synthesis of oxime ethers **1.107** or nitrones **1.108** in good to high yields with high regio- and stereoselectivities by reacting *β*'-acetoxy allenoate **1.106** with isatin-derived oximes **1.105** catalyzed by different nitrogen-containing Lewis bases. The yield and stereoselectivity of products are better for the substrates with electron-donating groups compared to those with electron-withdrawing groups (Scheme 1.39).[45]



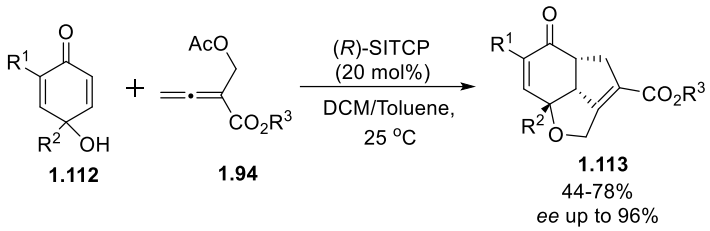
Scheme 1.39: Synthesis of oxime ethers **1.107** and nitrones **1.108** from acetoxy allenoate **1.106**

Tong and coworkers developed facile DABCO catalyzed (3 + 3) annulation of indoline-2-thione **1.109** with *β*'-acetoxy allenoate **1.110** to obtain thiopyrano[2,3-*b*] indole **1.111** under mild reaction conditions with a broad substrate scope and good efficiency. In this case, indoline-2-thione **1.109** was used as 1*C*-3*S* bis-nucleophile. The mechanistic investigation revealed that the reaction proceeded by S_N2' – S_N2' -type process between indole-2-thiolate **1.109** and *β'*-acetoxy allenoate using catalytic DABCO (along with K_2CO_3 as the additive), and subsequent intramolecular Friedel-Crafts reaction at the the allene central carbon and indole 3-position (Scheme 1.40).[46] It should be noted here that the substrate **1.109** acts as a binucleophile and there should be an enormous opportunity to explore many other similar binucleophiles, which is one of the objectives of the present work.



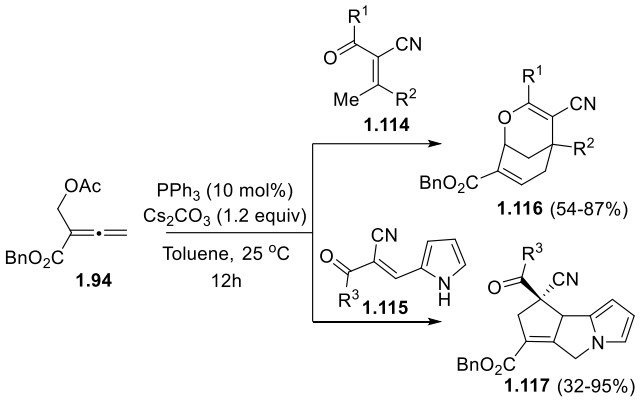
Scheme 1.40: Synthesis of thiopyrano[2,3-*b*]indole **1.111** from *β*'-acetoxy allenoate **1.110**

Min Shi and coworkers discovered a one-step phosphine catalyzed highly diastereoselective cascade annulation reaction between *p*-quinols **1.112** and *β′*-acetoxy allenoates **1.94** to obtain multiple ring-fused hexahydroindeno furans **1.113** containing three consecutive stereogenic carbon centers. The important points in this phosphine-catalyzed process are excellent tolerance for the functional group, vast substrate scope, asymmetric version, mild conditions, ease of scale-up to gram scale, good yields, and subsequent reactions (Scheme 1.41).[47]



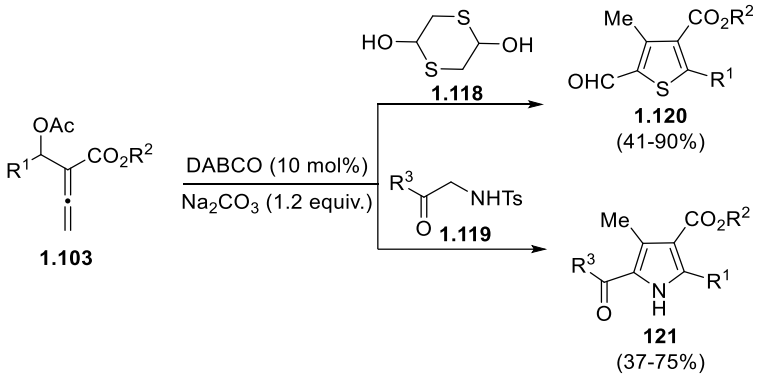
Scheme 1.41: Synthesis of hexahydroindeno derivatives **1.113** from *β′*-acetoxy allenoate **1.94**

Tong's group developed two types of addition/cycloaddition domino reactions of acrylonitriles with *β′*-acetoxy allenoates. Thus *β′*-acetoxy allenoate **1.94** underwent reaction with 2-acyl-3-methyl-acrylonitriles **1.114** to yield 2-oxabicyclo[3.3.1]nonanes **1.115** *via β′*-addition/(4 + 4) cycloaddition. The same *β′*-acetoxy allenoate **1.94** reacted with 2-acyl-3-(2-pyrrole)-acrylonitriles **1.116** to give cyclopenta[*a*]pyrrolizines **1.117** *via γ*-addition/(3 + 2) cycloaddition. Furthermore, both of these asymmetric forms were obtained in up to 93% ee (Scheme 1.42).[48]



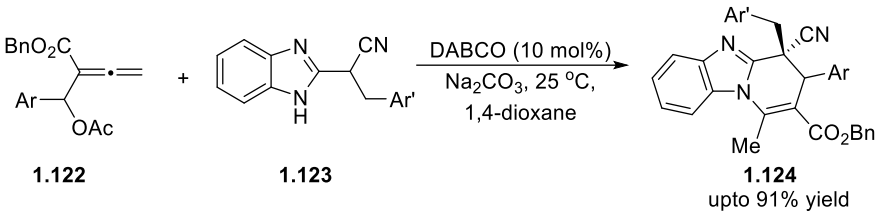
Scheme 1.42: Synthesis of 2-oxabicyclo[3.3.1]nonanes **1.116** and cyclopenta[*a*]pyrrolizines **1.117** from *β*'-acetoxy allenoate **1.94**

In the year 2016, Tong and coworkers discovered DABCO catalyzed cascade (3 + 2) annulation followed by aromatization of *β'*-acetoxy allenoates with 1,2-bisnucleophiles. The amine-catalyzed (3 + 2) annulation reaction of 1,4-dithane-2,5-diol **1.118** with *β*'-acetoxy allenoates **1.103** produced fully substituted thiophene-2-carbaldehydes **1.120**. The reaction is also amenable to 2-tosylamino-carbonyl bisnucleophile substrates **1.119** with tosyl group elimination followed by isomerization to produce 1*H*-pyrroles **1.121** (Scheme 1.43).[49]



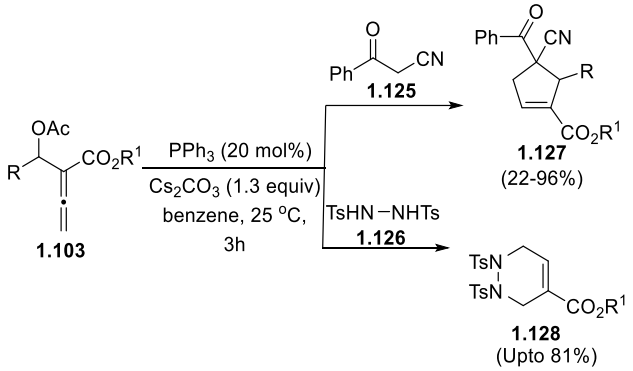
Scheme 1.43: Synthesis of thiophene-2-carbaldehydes **1.120** and 1*H*-pyrroles **1.121** from *β'*-acetoxy allenoates

Qin and coworkers established an amine-catalyzed (3 + 3) annulation of *β'*-acetoxy allenoates **1.122** with 1C,3N-bisnucleophiles **1.123** 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 **1.124** in good yields. Additionally, the asymmetric version of this reaction have been checked by using cinchona alkaloid-based tertiary amines by the authors (Scheme 1.44).[50]



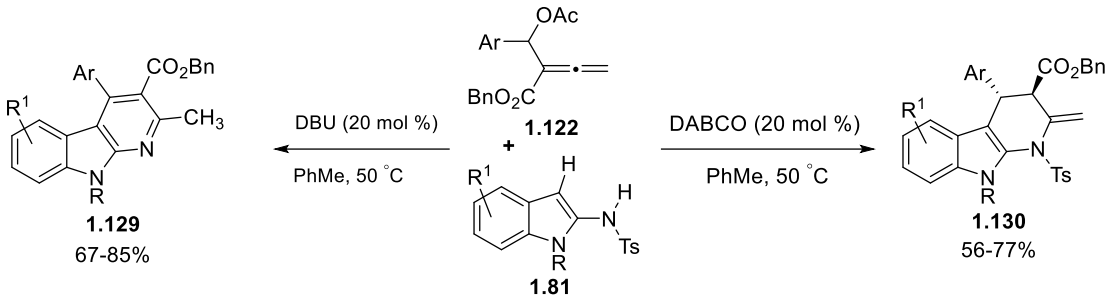
Scheme 1.44: Synthesis of 1,2-fused benzimidazoles from *β′*-acetoxy allenoates

Tong and coworkers reported PPh_3-catalyzed (4 + 1) and (4 + 2) annulations of *β′*-acetoxy allenoates **1.103** and 1,n-bisnucleophiles (n = 1, 2). Thus while the reaction of **1.103** with 3-oxo-3-phenylpropanenitrile **1.125** resulted in the formation of cyclopentenes **1.127**, that with 4-methyl-*N*'-tosylbenzenesulfonohydrazide **1.126** gave tetrahydropyridazines **1.128**. The difference in the 2,3-butadienoate's typical phosphine-catalyzed reaction modes depends critically on the acetate group being present at the *β′*-position (Scheme 1.45).[51]



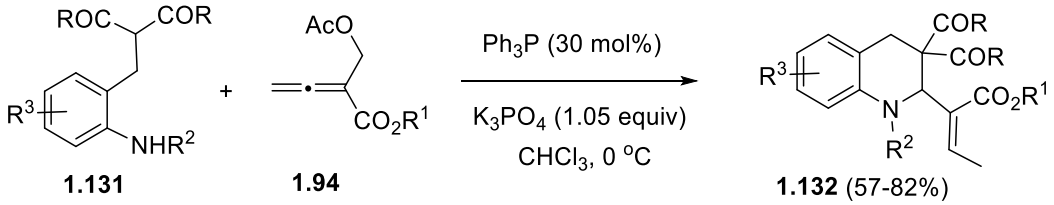
Scheme 1.45: Synthesis of cyclopentenes **1.127** and tetrahydropyridazines **1.128** from acetoxy allenoate **1.103**

Our research group also developed Lewis base dependent (3 + 3) annulations of *β′*-acetoxy allenoates **1.122** with iminoindolines offering α-carbolines with varying substituents depending on the base used as well as subtle changes in the reaction conditions. Thus the reaction of **1.122** with iminoindolines **1.81** is completely tertiary amine dependent; the use of DBU offers substituted α-carbolines **1.129**, while DABCO affords tetrahydro-α-carbolines **1.130** (that are distinct from those using DBU) exclusively with excellent stereoselectivity (Scheme 1.46).[37] Several control experiments and HRMS studies have been done in support of a plausible reaction mechanism.



Scheme 1.46: Synthesis of substituted α-carbolines **1.129** and tetrahydro-α-carbolines **1.130** from acetoxy allenoate **1.122**

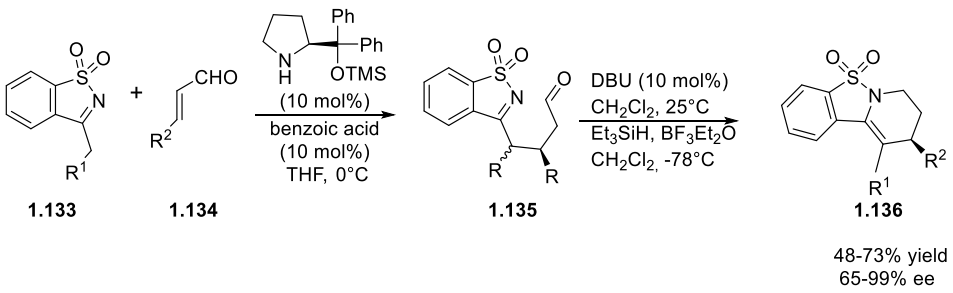
A very interesting (5+1) annulation involving *β′*-acetoxy allenoates **1.94** and 1,5-dinucleophiles **1.131** under phosphine-catalysis has been very recently developed by Wan and coworkers. This method provides a novel route to tetrahydroquinolines **1.132** in decent yields under mild reaction conditions using catalytic PPh_3 with K_3PO_4 as an additive. Thus in this reaction, *β′*-acetoxy allenoates behave as 1C synthon (Scheme 1.47).[52]



Scheme 1.47: Synthesis of tetrahydroquinolines from acetoxy allenoates

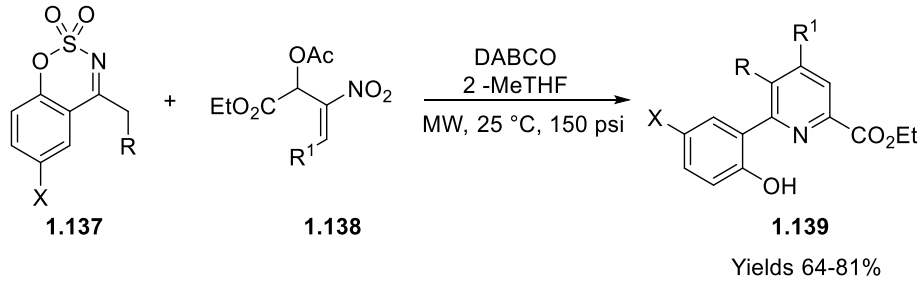
1.5. Reaction Chemistry of Cyclic *N*-Sulfonyl-ketimines

Sulfonyl-imines {3-alkylbenzo[*d*]-isothiazole 1,1-dioxides} of the type **1.133** with a pendant alkyl moiety on the imino-carbon are useful synthons and the work involved in this thesis utilizes this feature. Hence selected recent developments in their chemistry are summarized below. Chen and coworkers reported the synthesis of tricyclic tetrahydropyridines **1.136** from saccharin-derived isothiazolo dioxide-**1.133** and substituted acroleins **1.134** in THF solvent, utilizing diphenylprolinolsilyl ether along with benzoic acid as the catalytic system. The process generated a variety of Michael adducts **1.135** that effectively transform into tricyclic fused tetrahydro-pyridines **1.136** by retaining the enantioselectivity by tautomerization and hemiaminal formation and subsequent dehydroxylation via DBU-catalysis using Et_3SiH/BF_3-OEt_2. This gentle reaction produced tetrahydropyridines **1.136** in moderate to high yields (48-73%; Scheme 1.48).[53]



Scheme 1.48: Synthesis of tetrahydropyridines **1.136** from isothiazolo dioxides **1.133**

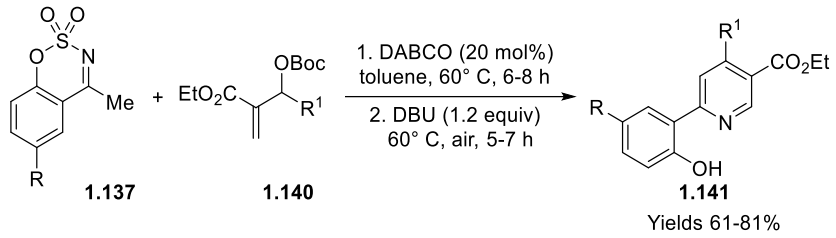
Samanta and co-workers described an environmentally friendly metal-free domino approach for the rapid synthesis of functionalized tri- and tetra-substituted pyridines **1.139** with ester/ aroyl and phenolic moieties at the C2 and C6 positions, respectively. Under MW irradiation, the reaction took place *via* a (3 + 3) annulation involving cyclic *N*-sulfonyl ketimines **1.137** and Morita-Baylis-Hillman acetates of nitroalkenes **1.138** with DABCO or DBU as the organo-base. The distinguishing characteristics of annulation include a broad substrate scope, good functional group tolerance, mild reaction conditions, and high yields (Scheme 1.49).[54]



Scheme 1.49: Synthesis of tetrasubstituted pyridines **1.139** from *N*-sulfonyl ketimines **1.137**

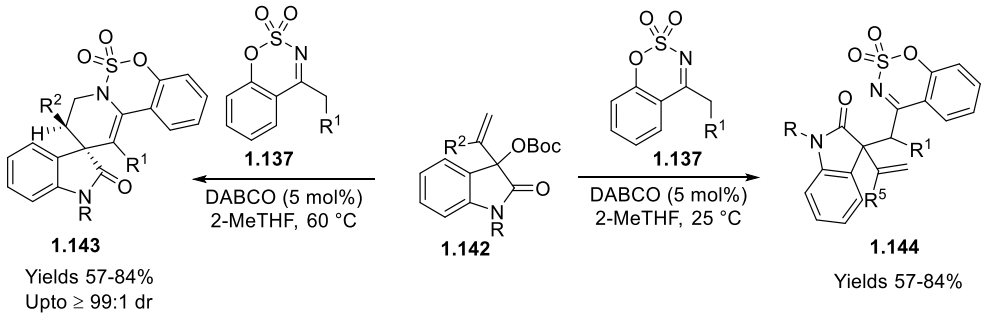
In 2018, Samanta and his colleagues developed an effective procedure for the synthesis of highly substituted pyridines **1.141** by using ketimines {4-alkylbenzo[*e*]-[1,2,3]oxathiazine-2,2-dioxides} **1.137** and Morita-Baylis-Hillman carbonates of acrylate or acrylonitrile **1.140**. Under moderate reaction conditions, the one-pot, two-step domino (3 + 3) annulation reaction of ketimines **1.137** with MBH carbonates **1.140** catalyzed by DABCO and aromatization by DBU gave 2-hydroxyarylnicotinates **1.141** in excellent yields (61-79%) using mild reaction parameters. The generation of C-N and C-C bonds was a regioselective allylic alkylation and aza-Michael reaction between *N*-sulfonyl ketimines (as C,N-binucleophiles) and MBH carbonates under DABCO catalysis; this was followed by SO_2

elimination under the influence of DBU and subsequent aromatization in an open atmosphere (Scheme 1.50).[55]



Scheme 1.50: Synthesis of 2-hydroxyarylnicotinates **1.141** from *N*-sulfonyl ketimines **1.137**

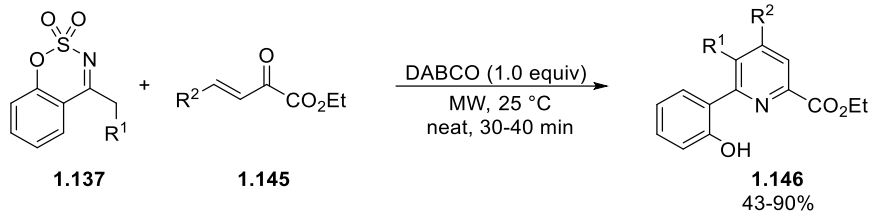
Samanta and co-workers reported temperature dependent DABCO catalyzed one pot synthetic protocol between ketimines **1.137** and isatin-based Morita-Baylis-Hillman carbonates **1.142**. The allylic alkylation of ketimines with **1.142** took place quickly in the presence of nucleophilic organo-base DABCO affording oxindoles **1.143** at room temperature with excellent diastereoselectivity (dr ~96:4). At 60 °C, the (3 + 3) annulation reaction between cyclic ketimines and MBH carbonates produced polycyclic spirooxindoles **1.144** with exceptional diastereoselectivity (dr ~99:1) and an all-carbon quaternary center (Scheme 1.51).[56]



Scheme 1.51: Formation of spirooxindoles **1.143** and polycyclic oxindoles **1.144** from *N*-sulfonyl ketimines **1.137**

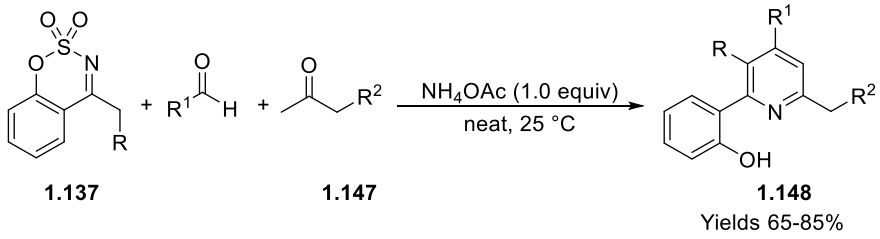
From the reaction of *N*-sulfonyl ketimines **1.137** with *α*-ketocarbonyls **1.145** under neat conditions at 70 ^{o}C, Samanta and coworkers discovered a one-pot MW-assisted DABCO promoted approach to access diversely functionalized pyridines. Under metal-free conditions, this novel Michael elimination-cum-cyclization (formation of C-N and C-C bonds) procedure provides several medicinally important multisubstituted pyridines **1.146** with a benzoyl, carboxylate, or cinnamoyl group at C-2 position in good yields. The operational simplicity, broad substrate scope, high to exceptional yields, compatibility with a wide range of

functional groups on aryl rings, less reaction time, and environmentally benign nature of this approach makes it a viable alternative to the previously described methods (Scheme 1.52).[57]



Scheme 1.52: Synthesis of tetrasubstituted pyridines **1.146** from *N*-sulfonyl ketimines **1.137**

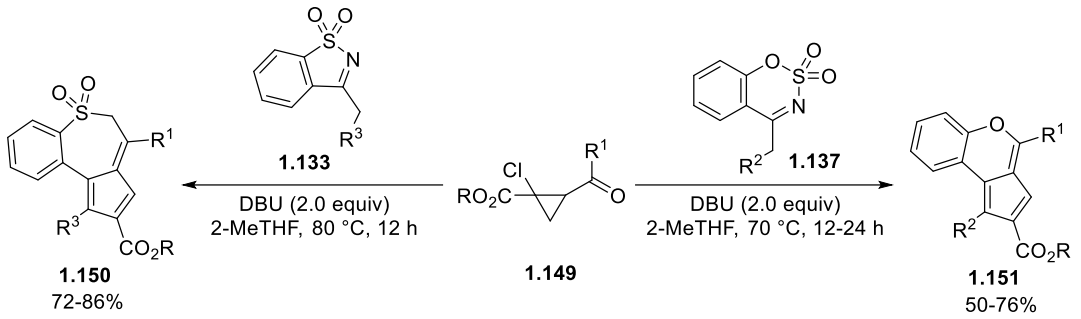
Samanta and coworkers recently reported an intriguing procedure for the synthesis of multisubstituted pyridines using *N*-sulfonyl ketimines **1.137**, aromatic/heteroaromatic aldehydes, and acyclic/cyclic enolizable ketones **1.147** promoted by NH_4OAc without using any solvent. This oxidant-free, solvent-free, and metal-free technique provides a potent alternative to synthesize a diverse range of multi-substituted pyridines **1.148** in high to outstanding yields (65-85%). Control tests revealed that NH_4OAc promoted the formation of an aza-diene species from benzaldehyde and *N*-sulfonyl ketimine. The aza-diene was then (4 + 2) cyclized with acetophenone, aided by NH_4OAc, to provide the required pyridine derivatives (Scheme 1.53).[58]



Scheme 1.53: Synthesis of tetrasubstituted pyridines **1.148** using cyclic *N*-sulfonyl ketimines **1.137**.

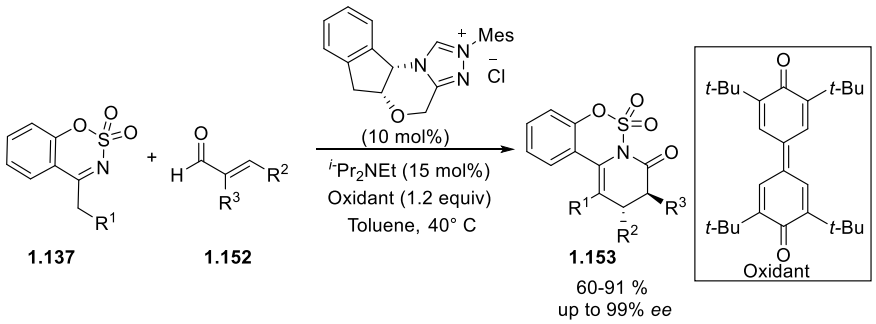
Samanta's research group developed substrate-controlled and DBU-promoted annulation reaction between *N*-sulfonyl ketimines **1.133** or **1.137** and chloro-aroylcycloproanecarboxylates **1.149**. This reaction gave two different sets of 6/7-membered pentafulvenes having carboxylate moiety on the fulvene part. The reaction of 3-alkyl *N*-sulfonyl ketimines **1.133** saccharin-derived with 1-chloro-2-aroylcycloproanecarboxylates **1.149** afforded benzo[f]cyclopenta[d][1,2]thiazepine 5,5-dioxides **1.150** *via* formation of one C-N and two C-C bonds. On the other hand, the Michael-initiated ring-expansion reaction by employing 4-alkyl *N*-sulfonyl ketimines **1.137** as nucleophiles provided fused

cyclopentachromenes **1.151** in decent yields by the formation of one C-O and two C-C bonds (Scheme 1.54).[59]



Scheme 1.54: Annulation of cyclic *N*-sulfonyl imines with electron-deficient cyclopropanes **1.149**

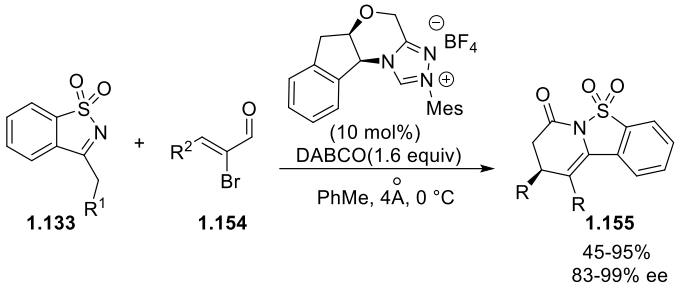
In 2012, Bode and co-workers reported highly enantioselective (3 + 3) annulation of cyclic sulfamidate imine **1.137** with *α,β*-unsaturated aldehyde **1.152** for synthesizing an interesting class of medicinally significant dihydropyridinones **1.153** in high yields and excellent enantioselectivity of up to 99% ee using catalytic *N*-heterocyclic carbene (NHC), $^{i}Pr_2NEt$ as a base with 1.2 equiv of an oxidant. The mechanistic study revealed that the reaction proceeded *via* catalytic generation of *α,β*-unsaturated acyl azoliums (Scheme 1.55).[60] The authors further coupled *N*-sulfonyl ketimines with substituted acroleins and tri-substituted enals under the same conditions to deliver expected tricyclic scaffolds. The reaction was compatible with a wide range of functional groups.



Scheme 1.55: Synthesis of dihydropyridinones **1.153** using cyclic *N*-sulfonyl ketimines **1.137**

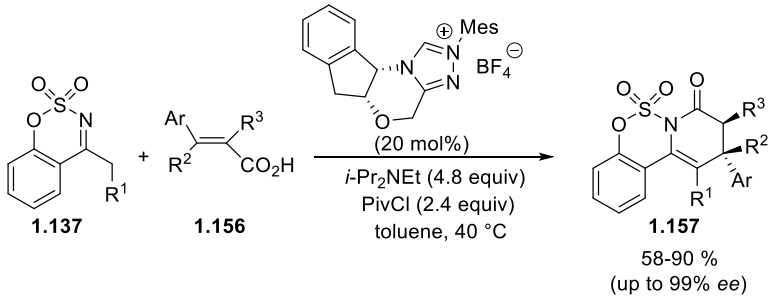
A similar annulation concept was adopted by Ye and coworkers for the enantioselective synthesis of tricyclic fused dihydropyridinone scaffolds **1.155**. The authors reported that in the absence of any oxidant, the chiral NHC catalyst reacted with *α*-bromoenal **1.154** to generate a chiral acyl azolium intermediate, which then underwent annulation with

isothiazolo-dioxide **1.133** to give the chiral product **1.155**. This (3 + 3) annulationn procedure produced good to high yields (45-95%) of the respective dihydropyridinones **1.155** with varying enantiomeric excess (83-99% ee; Scheme 1.56).[61]



Scheme 1.56: Synthesis of fused dihydropyridinones **1.155** using cyclic *N*-sulfonyl ketimines **1.133**

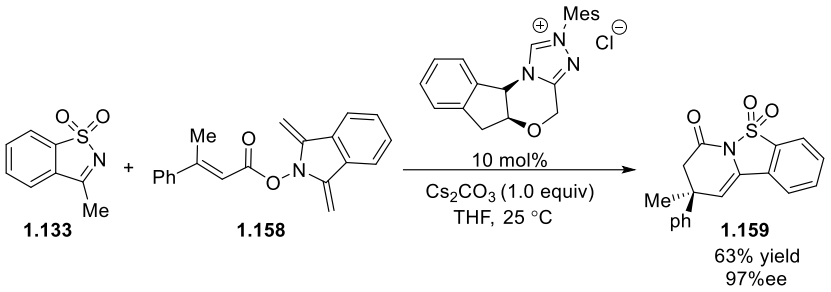
The same group, in the year 2014, developed an asymmetric (3 + 3) annulation reaction of *N*-sulfonyl ketimines **1.137** with *α,β*-unsaturated carboxylic acids **1.156** under NHC-catalysis for the synthesis of a series of substituted fused dihydropyridinones **1.157** in good to high yields with excellent enantioselectivities (up to 99% *ee*). In this case, the reaction between **1.137** and **1.156** proceeded efficiently in the presence of excess base and PivCl *via* Michael addition and subsequent lactamization to provide the dihydropyridinones **1.157** (Scheme 1.57).[62]



Scheme 1.57: Synthesis of fused dihydropyridinones **1.157** using cyclic *N*-sulfonyl ketimines **1.137**

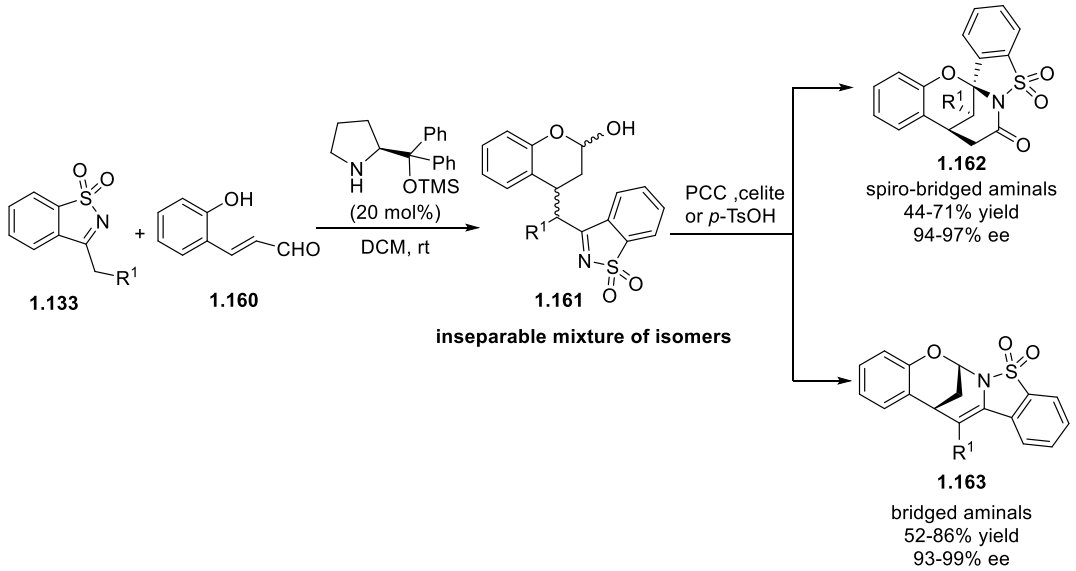
In 2015, Zhong and co-workers reported carbene-catalyzed (3 + 3) cyclization of isothiazolo-dioxide **1.133** with ***N*-h**ydroxy**p**hthal**i**mide acrylate **1.158** (NHPI ester) for the synthesis of fused dihydropyridinone **1.159** possessing an all carbon quaternary chiral center in decent yield (63%) with excellent enantioselectivity (97%). The authors proposed that NHPI, without any oxidant, favored the generation of acyl azolium intermediate. The reaction proceeded *via* 1,2-addition with the *in situ* generated enamine intermediate from isothiazolo-

dioxide **1.133** and subsequent sequential *aza*-Claisen rearrangement, tautomerization and lactam formation (Scheme 1.58).[63]



Scheme 1.58: Annulation of cyclic *N*-sulfonyl ketimines **1.133** with *N*-hydroxyphthalimide ester **1.158**

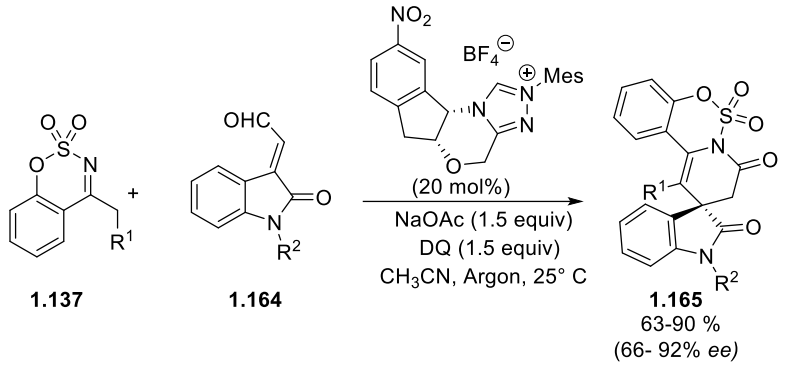
In 2019, Liu *et al.* reported the synthesis of spiro-bridged **1.162** and chiral bridged benzofused aminals **1.163** from saccharin-derived isothiazolo dioxides **1.133** and 2-hydroxy cinnamaldehydes **1.160** by utilizing diphenylprolinolsilyl ether as a catalyst. The reaction proceeded by conjugate addition-cyclization reaction between **1.133** and **1.160** *via* amine-catalysis affording an inseparable mixture of cyclic hemiacetals **1.161**. The procedure generated a variety of spiro-bridged and chiral bridged benzo-fused aminals (**1.162-1.163**) with good regio- and stereoselectivity (single diastereomers; 93-99% *ee*; Scheme 1.59).[64]



Scheme 1.59: Organocatalyzed synthesis spiro-bridged and chiral bridged benzofused aminals **1.162-1.163** from *N*-sulfonyl imines **1.133**.

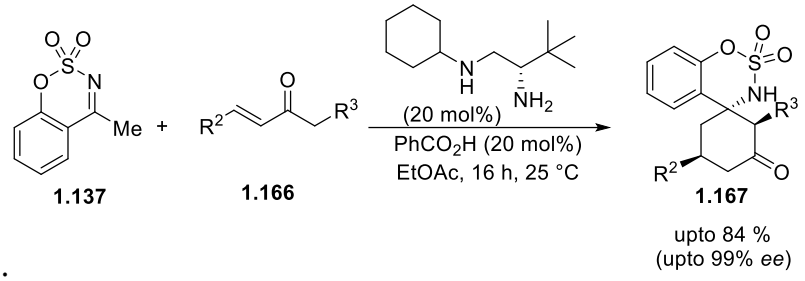
In 2019, Ender's group published a highly enantioselective (3 + 3) cyclization of isothiazolo-dioxides **1.137** and isatin-derived acroleins **1.164** for the synthesis of pentacyclic

spirooxindoles **1.165** with an all carbon quaternary spiro-stereocenter in good to high yields (63-90%) with ee of 66-92% using a chiral (NHC) as a catalyst along with diphenoquinone (DQ; oxidant) and NaOAc. The mechanistic study revealed that the reaction proceeded *via* catalytic generation of azolium intermediate followed by lactamization to provide the targeted spirooxindole scaffold. A wide range of functional groups were compatible with the reaction (Scheme 1.60).[65]



Scheme 1.60: Synthesis of spirooxindoles **1.165** from cyclic *N*-sulfonyl imines **1.137**.

In 2015, Ye and colleagues developed an effective protocol for the synthesis of spiro-cyclohexanones **1.167** by using *N*-sulfonyl ketimines **1.137** and enones **1.166** using a chiral amine catalyst using *tert*-leucine. The catalyst exhibited good activity in the enantioselective (4 + 2) cyclization yielding decent yields of spiro-cyclohexanones with excellent ee of 99%. This reaction proceeded *via* the sequence of Michael addition, followed by intramolecular Mannich reaction and hydrolysis (Scheme 1.61).[66]



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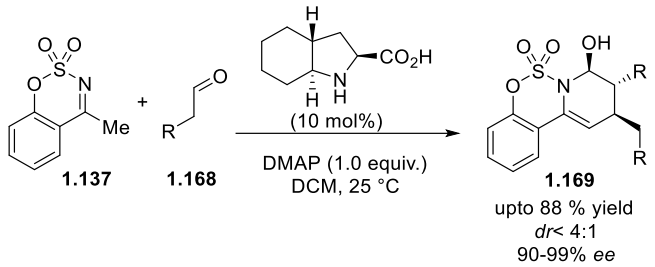
Scheme 1.61: Synthesis of spiro-cyclohexanone **1.167** by annulation involving cyclic sulfamidate imines **1.137** and enones **1.166**

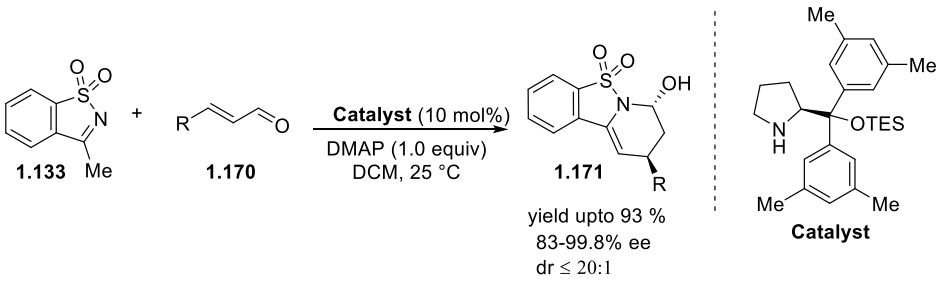
In the year 2014, Zhang's group reported an enantioselective approach to fused tetrahydropyridine **1.169** bearing three contiguous stereogenic centers by using *N*-sulfonyl ketimines **1.137** with various α-unsubstituted aldehydes **1.168**. This (4 + 2) annulation of **1.165** with **1.134** was catalyzed by *trans*-perhydroindolic acid using DMAP base affording

fused tetrahydopyridines in high yields, excellent *ee* of 90-99%, and good dr (4:1; Scheme 1.62).[67]



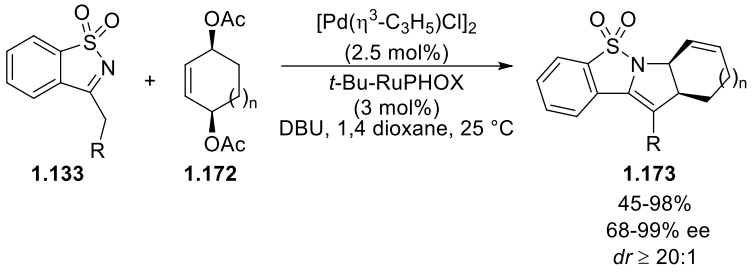
Scheme 1.62: Synthesis of fused tetrahydropyridine**1.169** by annulation using cyclic sulfamidate imines **1.137**

Another protocol for the synthesis of tricyclic fused tetrahydropyridine derivatives **1.171** by employing *N*-sulfonyl ketimines **1.133** and *α,β*-unsaturated aldehydes **1.170** in the presence of catalytic diarylprolinolsilyl ether was established by the same Zhang's group. Thus condensation of **1.170** with diarylprolinolsilyl ether is followed by Michael addition and hydrolysis to give Michael adducts that cyclizes in the presence of a base, yielding tetrahydropyridines. This reaction was compatible with various alkyl/aryl/heteroaryl-substituted acroleins. The tetrahydropyridines **1.171** were obtained in good yields (70-93%) and excellent *ee* (99.7%; Scheme 1.63).[68]



Scheme 1.63: Synthesis of tricyclic tetrahydropyridines **1.171** from *N*-sulfonylimines **1.133**

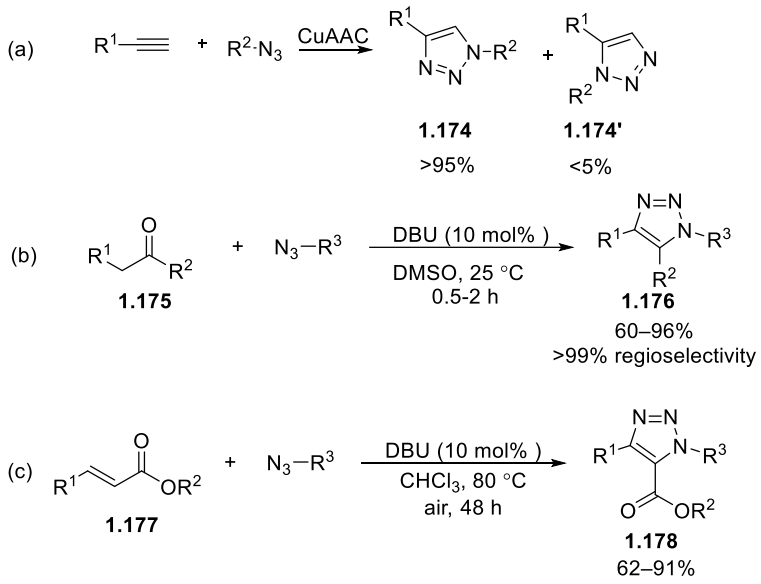
In 2017, Zhang *et al*. reported the asymmetric synthesis of fused dihydropyrrole scaffolds **1.173** by using *N*-sulfonyl ketimines **1.133** and *cis*-cyclic allyl diacetates **1.172**. This reaction occurs in the presence of DBU and the ligand ^{t}Bu-RuPHOX in 1,4-dioxane at ambient temperature. The reaction proceeds *via* the generation of an allyl-Pd-intermediate from the *cis*-cyclic allyl diacetate which undergoes nucleophilic attack by *N*-sulfonyl ketimine to generate alkylated an allylic species which upon allylic amination gives the fused dihydropyrrole. The dihydropyrrole scaffolds were obtained in high yields but with variable *ee* (68-99.8%; Scheme 1.64).[69]



Scheme 1.64: [Pd]-catalyzed allylic alkylation of cyclic *N*-sulfonyl ketimines with cyclic allyl diacetates

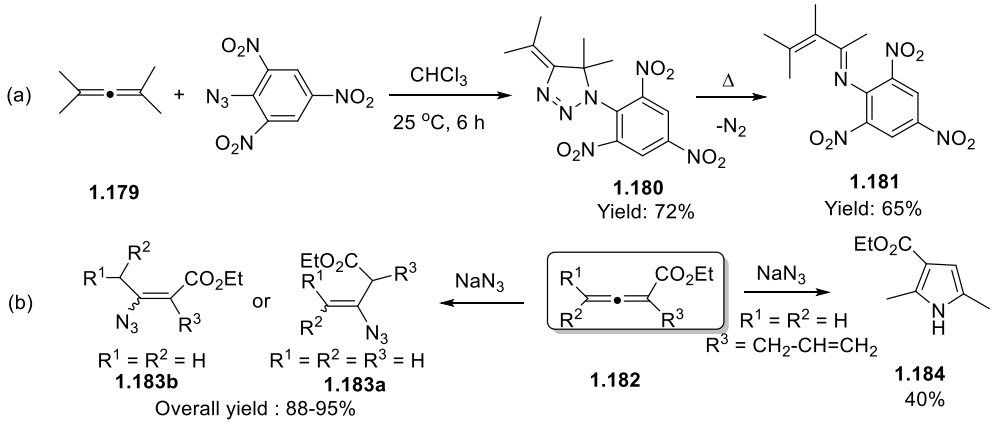
1.6. Reaction of Azides with Alkynes/Allenes (Click Reaction)

In recent years, click chemistry involving the reaction of an alkyne with an azide has emerged as a very popular tool in drug discovery, chemical biology, and proteomic applications.[70] The strategies on [Cu]-catalyzed azide−alkyne cycloaddition (CuAAC) from Sharpless and Meldal have involved the concept of "click" chemistry and regiospecific assembly of 1,4-disubstituted 1,2,3-triazoles (cf. **1.174-1.174'**; Scheme 1.65a).[71] Our group also has contributed to this type of azide-alkyne reaction previously.[72] Since there are numerous reports of this type and since all of these do not involve allenes, we are not discussing them further. An alternative to reaction using alkynes is the use of DBU catalyzed (3 + 2)-cycloaddition between aldehydes (with an active methylene group) **1.175** and azides affording 1,4-disubtituted 1,2,3-triazoles **1.176** developed by Ramachary's group (Scheme 1.65b); extension of this type of reaction to other substrates has also been developed by the same group.[73] As reported by Li and Wang, it is also known that electron-deficient olefins **1.177** can also undergo a reaction with azides to afford 1,2,3-triazoles **1.178** (Scheme 1.65c) under organocatalytic conditions.[74] Although allenes also have an *sp*-hybridized carbon center, their reactivity with azides is not explored in any great detail. Some aspects of these are discussed below.



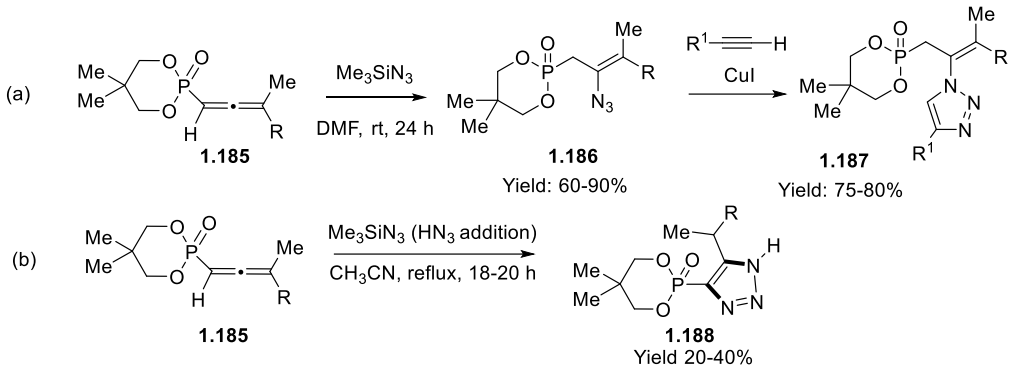
Scheme 1.65: (a) [Cu]-catalyzed (3 + 2) cycloaddition of alkynes and azides, (b) Ramachary group's organocatalytic reaction to produce 1,2,3-triazoles, and (c) Reaction of an activated alkene with an azide.

Earlier work on the reaction of the allene **1.179** with azide was reported by Bleiholder and Shechter. They obtained alkylidenetriazoles **1.180** and allyl-imines **1.181** (Scheme 1.66a).[75] In a reaction of perfluoropropadiene with phenyl azide, only a small quantity of triazole could be isolated, but the structural elucidation could not be fully done.[76] A more recent work by Molteni and Ponti indeed showed that tetramethylallene and tetrafluoroallene showed distinctly different reactivities although both of these gave the triazole products.[77] Another work by Huang *et al.* showed that allenyl esters **1.182** reacted with sodium azide to give *E*-vinyl azides **1.183** and polysubstituted pyrroles **1.184** (Scheme 1.66b).[78]



Scheme 1.66: (a) Earlier work on the reaction of tetramethyl allene with an azide; (b) Reaction of allenyl esters with sodium azide

Our group reported that the vinyl azides **1.186**, prepared from allenylphosphonates **1.185**, undergo 1,3-dipolar cycloaddition reactions with phenyl acetylene in the presence of CuI to form phosphonotriazoles **1.187** stereoselectively in high yields. In the second type of reaction reported in the same paper, Me_3SiN_3 directly reacted with allenylphosphonates **1.185** to generate phosphono-1,2,3-triazoles **1.188**, albeit in low yields (Scheme 1.67).[5h] Apart from these, to our knowledge, there is currently no other report on the reactions of allenes/allenoates with azides.



Scheme 1.67: Reactivity of allenylphosphonates with azides

OBJECTIVES OF THE PRESENT WORK

The major objective of the work was to explore the reactivity of acetoxy allenoates with *N*-sulfonyl ketimines (and related binucleophiles) and azides. More specifically, it was intended

(i) To explore the Lewis base mediated (3 + 3) and (4 + 2) annulation reactions of *δ*- and *β*'-acetoxy allenoates with *N*-sulfonyl

(ii) ketimines that could lead to the formation of *α*-pyridyl acetates and *o*-teraaryl motifs,

(iii) To study tertiary amine catalyzed (3 + 3) and (4 + 2) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl imines in the presence of Lewis bases that could lead to the formation of fused dihydropyridines and *m*-teraryls,

(iv) To investigate transition metal-free (3 + 2) cycloadditions of *δ*- and *β*'-acetoxy allenoates with azides for the construction of 1,4,5-tri/ 1,5-di-substituted-1,2,3-triazoles, and

(v) To explore the Lewis base mediated (3 + 3) annulation reaction of *δ/β*'-acetoxy allenoates with enolizable carbonyls (which may function as binucleophiles) that could lead to the formation of dihydropyrans.

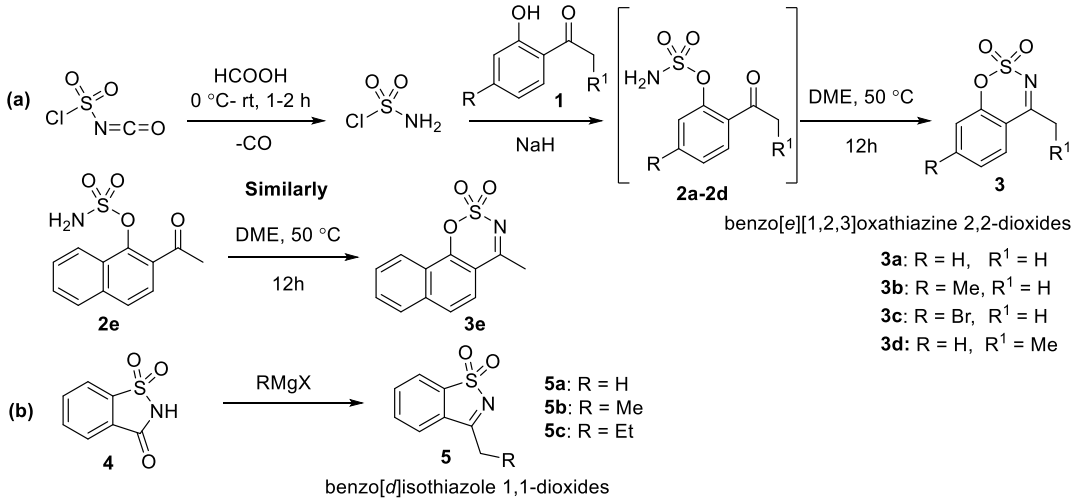
RESULTS AND DISCUSSION

This chapter deals with the results on various transformations involving acetoxy allenoates and sulfonyl ketimines leading to *α*-pyridyl acetates, fused dihydropyridines and *o/m*-teraaryl motifs. It also deals with the reactivity of acetoxy allenoates with azides to give triazoles. The last topic of discussion is on the reaction of acetoxy allenoates with the binucleophiles benzo-oxathiin-dioxide and phenylthiazolone. All the products are well characterized by using IR, NMR, LCMS/CHN, or HRMS and Mp (for solids); the assigned regio- or stereo-chemistry of the products is generally based on X-ray crystallographic studies of illustrative compounds.

2.1 Synthesis of Precursors

2.1.1 *Cyclic N-sulfonyl ketimines 3a-d, 3e and 5a-c*

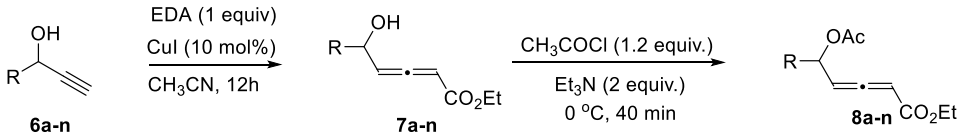
Cyclic *N*-sulfonyl ketimines used in this study have been prepared by using one of the two available methods.[79] Thus treating sulfamoyl chloride H_2NSO_2Cl, generated *in situ* from $ClSO_2NCO$ and HCO_2H, with α-hydroxyl ketone/ *ortho*-hydroxy arylketone **1** in the presence of a base affords O-sulfamyl intermediates **2**. Intermediates **2** are then cyclized upon heating to produce *N*-sulfonyl ketimines **3** (Scheme 1a).[79] For the synthesis of 3-alkyl-substituted *N*-sulfonyl ketimine **5**, the reaction involves addition of alkylmagnesium bromide to saccharin **4** (Scheme 1b).[80]



Scheme 1: Synthesis of cyclic *N*-sulfonyl ketimines **3a-e** and **5a-c**

2.1.2 *δ-Acetoxy allenoates 8a-n*

Propargylic alcohols **6a-n** were reacted with ethyl diazoacetate in the presence of CuI and triethylamine in acetonitrile to deliver *δ*-hydroxy allenoates **7a-n**.[81] The hydroxyl group of *δ*-hydroxy allenoates **7a-n** was converted to the easily removable acetoxy group in the presence of acetyl chloride and triethylamine (Scheme 2).

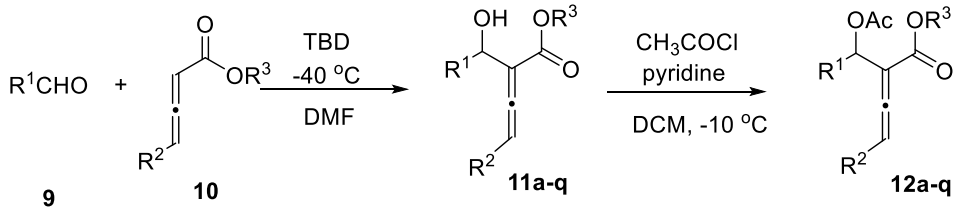


R^1 = Ph (**8a**); 4-MeO-C_6H_4 (**8b**);
4-Cl-C_6H_4 (**8c**); 4-NO_2-C_6H_4 (**8d**);
3-Indolyl (**8e**); 2-Thienyl (**8f**);
4-Br-C_6H_4 (**8g**); 4-CF_3-C_6H_4 (**8h**);
3-$MeOC_6H_4$ (**8i**); 2-Br-C_6H_4 (**8j**);
2,4-Cl_2-C_6H_3 (**8k**); Cinnamyl(**8l**);
2-MeO-C_6H_4 (**8m**); Pyryl (**8n**)

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

2.1.3 *β′-Acetoxy allenoates 12a-q*

Allenic esters **10** were synthesized at the first stage for the synthesis of *β′*-acetoxy allenoates utilizing a literature approach.[82] These allenic esters were then treated with various aldehydes **9** in the presence of triazabicyclodecene (TBD) in DMF solvent at -40 °C for the synthesis of *β′*-hydroxy allenoates **11a-q**. These *β′*-hydroxy allenoates **11a-p** were then acetylated with acetyl chloride and pyridine in DCM solvent at -10 °C to yield *β′*-acetoxy allenoates **12a-q** (Scheme 3).

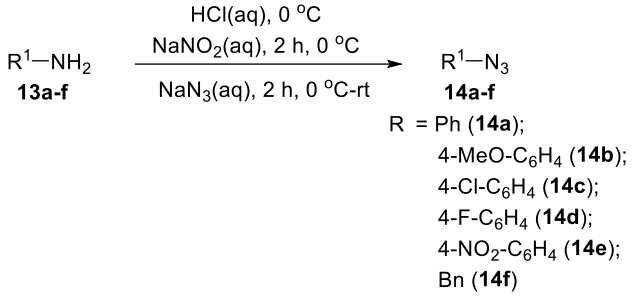


R^2 = H, R^3 = Bn
R^1 = Ph **(12a);** 4-MeO-C_6H_4 (**12b**);
4-Cl-C_6H_4 (**12c**); 4-NO_2-C_6H_4 (**12d**);
4-CF_3-C_6H_4 (**12e**); 2,4-Cl-C_6H_4 (**12f**);
3-MeO-C_6H_4 (**12g**); vanilyl (**12h**); napthyl (**12i**);
thienyl (**12j**); indolyl (**12k**); pyrenyl (**12l**); Bn_2syringyl (**12m**)
R^2 = H, R^3 = Et
R^1 = Ph (**12n**)
R^2 = R^3 = Bn
R^1 = Ph **(12o);** 4-MeO-C_6H_4 (**12p**); 4-Cl-C_6H_4 (**12q**)

Scheme 3: Synthesis of *β′*-acetoxy allenoates **12a-q**

2.1.4 *Aryl azides 14a-f*

Aryl azides **14a-f** were prepared from the anilines **13a-f** by following a literature procedure (Scheme 4).[83]

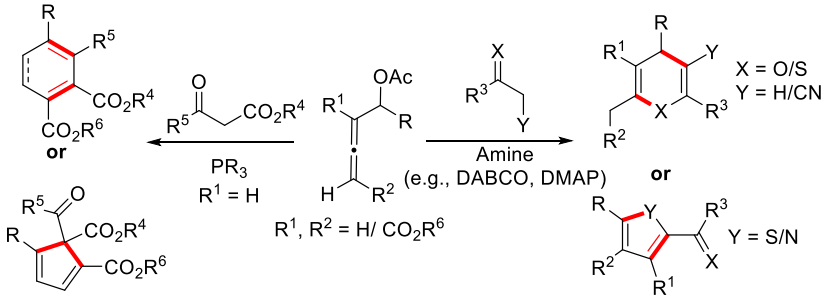


Scheme 4: Synthesis of azides **14a-f**

2.2. Lewis Base Switched (3 + 3) and (4 + 2) Annulation Reactions of *δ*-Acetoxy Allenoates with *N*-Sulfonyl Ketimines: Access to *α*-Pyridyl Acetates and *o*-Teraaryl Scaffolds

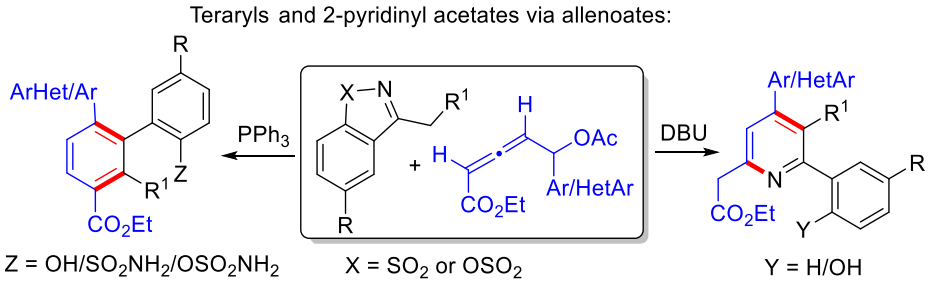
As mentioned in Chapter 1, the (4 + 2), (3 + 3)* and other annulation reactions of allenoates have been reported for the construction of numerous oxygen or nitrogen heterocycles.[9] Thus the β′/δ-acetoxy allenoates are aslo important annulation partners under Lewis base catalysis as shown by the groups of Tong and others (cf. Scheme 5).[10] An essential point in these organocatalytic reactions is the distintion between phosphines and amines leading to vastly different products.[11]

[*Note: The term ‘annulation’ {transformation involving fusion of a new ring to a molecule via two new bonds is used sometimes “interchangeably with cycloaddition {two or more unsaturated molecules, or parts of the same molecule, combine with the formation of a cyclic adduct involving a net reduction of the bond multiplicity”}.[84] In this chapter, the use of square brackets for cycloadditions/annulations is avoided. Also, the term annulation is used interchangeably with cyclization].



Scheme 5: Reactions of δ-acetoxy allenoates leading to carbo- and heterocycles

Despite substantial progress made on acetoxy allenoates,[16] there was no report of annulation reaction between δ-acetoxy allenoates and bi-nucleophilic cyclic *N*-sulfonyl imines prior to our work. It may be noted that sulfamidate imines/ sulfonyl imines (cf. Scheme 1 above) can act as nucleophiles (using active methylene group) as well as electrophiles (imine moiety). A combination of acetoxy allenoates and cyclic *N*-sulfonyl imines (benzoxathiazines) of type **3** with a pendant active methylene moiety may lead to 2-pyridinyl acetates and unsymmetrical *o*-teraryls with hydroxyl, sulfonamide or sulfamoyloxy unit, which are otherwise difficult to obtain by reported procedures. The α-pyridyl acetates as well as teraryl scaffolds with hydroxyl/sulfonamide functionality have been found in a variety of natural and pharmaceutical compounds.[12] These scaffolds are also explored as versatile intermediates to construct complex molecules.[13] A fair amount of research is focused on α-pyridyl acetates[14] and teraryls.[15] The work reported herein embodies divergent annulations of δ-acetoxy allenoates with cyclic *N*-sulfonyl imines (sulfamidate imines/ sulfonyl imines) under metal-free conditions and involves a simple Lewis base switch to afford (i) a new class of α-pyridyl acetates (2-pyridinyl acetates) by (3 + 3) annulation *via* SO_2 elimination, and (ii) functionalized *o*-teraryls by (4 + 2)-benzannulation through C-N bond cleavage (Scheme 6). While the reaction with sulfamidate imines involves O-S bond cleavage, the one with sulfonyl imines entails C-S bond cleavage. Details are presented below.



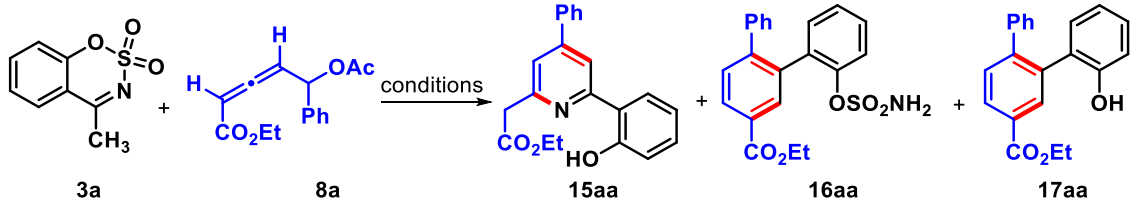
Scheme 6: Lewis base switched reactivity of *δ*-acetoxy allenoates with cyclic *N*-sulfonyl imines

2.2.1 *Reaction of δ-acetoxy allenoates with N-sulfamidate imines: Optimization study*

Initially, we tested the reaction of 4-methyl cyclic sulfamidate imine **3a** with *δ*-acetoxy allenoate **8a**. As shown in Table 1, we reacted **3a** with **8a** in the presence of DABCO (20 mol %) in toluene at rt (25 ^{o}C). However, only a trace amount of desired *α*-pyridyl acetate **15aa** was observed (entry 1). The yield could be enhanced to 31% by using 50 mol% DABCO (entry 2). The ^{1}H NMR spectrum of this compound exhibited characteristic peak for

the -C*H*$_2$ protons at δ 3.93 and a phenolic –O*H* peak at δ 13.98 along with those due to CO_2Et and aromatic protons; the $^{13}C\{^1H\}$ NMR spectrum also showed an aliphatic signal at δ 43.4 in addition to those corresponding to the CO_2Et group. These are consistent with the structure as assigned; for unambiguous confirmation, an X-ray structure was determined for this compound (*vide infra*). The addition of Na_2CO_3 increased the yield of **15aa** to 43% (entry 3); running the reaction at 50 °C for 12 h increased the yield to 56% (entry 4). The addition of more (1.5 or 2.0 equiv) Na_2CO_3 increased the yield to 62% (entries 5 and 6). Among the bases tested (DBU, Et_3N, DIPEA, and DMAP), DBU proved to be the best. In the absence of Na_2CO_3, the addition of K_2CO_3 and *t*-BuOK produced **15aa** with a significantly lower yield (entries 8 and 9). Toluene was the best among screened solvents yielding the intended product **15aa** in 79% yield (entry 7). There was no noticeable variation in isolated yields as time passed (entry 10). Interestingly, substituting PPh_3 (TPP) for DBU resulted in a completely different product **16aa** in 53% yield (entry 11). This product exhibited a moderately broad peak at δ 4.65 and the phenolic –O*H* peak was absent in the ^1H NMR spectrum. Also, the characteristic –*C*H$_2$(Ar) peak in the $^{13}C\{^1H\}$ NMR that was observed for **15aa** was absent in this case. These data are consistent with the assigned structure; an X-ray structure for analogous compound was also obtained (*vide infra*). We performed the reaction between **3a** and **8a** at different temperatures to increase the yield of the latter product **16aa**. Surprisingly, the S-O bond cleaved product **17aa** was produced in 73% yield at 80 °C (entry 12); the yield of this product could be increased further by excluding Na_2CO_3 (entry 13). Compound **17aa** exhibited the phenolic –O*H* peak at *ca* δ 4.86 in the ^1H NMR spectrum; an X-ray structural analysis confirmed its structure unambiguously. Pleasingly, we obtained the sulfomoyloxy carboxylate **16aa** solely at rt, with an isolated yield of 73% (entry 14); prolonging the reaction time was not required here also (entry 15). In the absence of TPP and Na_2CO_3, we did not observe any reaction even after 24 h.

Table 1. Optimization of reaction conditions for 15aa, 16aa and 17aa[a]



3a 8a 15aa 16aa 17aa

Entry	Base	Additive	Solvent	Temperature (°C)	Yield

					15aa	16aa	17aa
1	DABCO		PhMe	25	5	00	00
2	DABCO		PhMe	25	31	00	00
3	DABCO	Na_2CO_3	PhMe	25	43	00	00
4	DABCO	Na_2CO_3	PhMe	50	56	00	00
5	DABCO	Na_2CO_3	PhMe	50	62	00	00
6	DABCO	Na_2CO_3	PhMe	50	62	00	00
7	DBU	K_2CO_3	PhMe	50	79	00	00
8	DBU	*t*-BuOK	PhMe	50	72	00	00
9	DBU	Na_2CO_3	PhMe	50	75	00	00
10	DBU	Na_2CO_3	PhMe	50	79	00	00
11	PPh_3	Na_2CO_3	PhMe	50	00	53	00
12	PPh_3		PhMe	80	00	00	73
13	PPh_3		PhMe	80	00	00	81
14	PPh_3		PhMe	25	00	73	00
15	PPh_3		PhMe	80	00	00	81

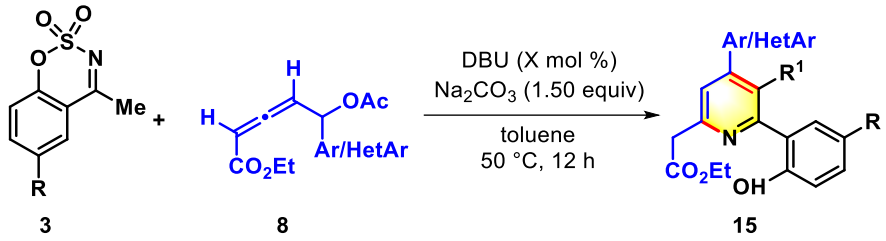
[a]Reaction conditions: **3a** (0.20 mmol), **8a** (0.24 mmol), with base (20 mol % for entries 1 and 13-15; 50 mol % for entries (2-12) and additive (1.0 equiv for entries 1 and 2 and 1.5 equiv for entries 5-10) in toluene (2.0 mL); temperature is that of oil bath. [b]Isolated yield (after 12 h for entries 1-9 and 11-14; after 24 h for entries 10 and 15).

2.2.2 *Reaction of δ-acetoxy allenoates with N-sulfamidate imines: Substrate scope*

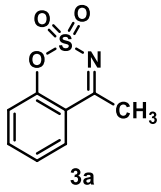
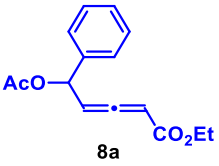
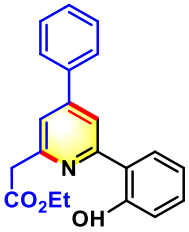
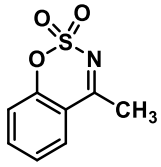
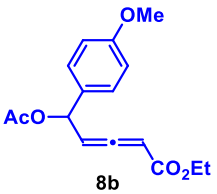
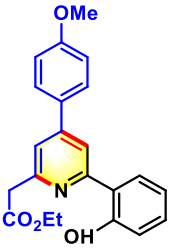
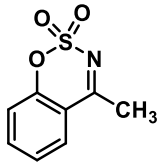
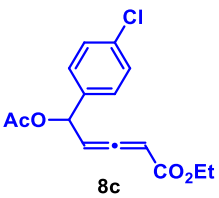
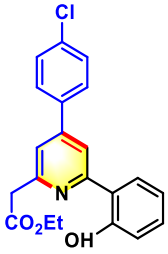
As depicted in Table 2, *δ*-acetoxy allenoates with various functionalities (OMe, Cl, and NO_2) on the phenyl ring furnished 2-pyridinyl acetates **15aa-15ad** in good to high yields (71-80 %). Heterocyclic allenoates **8e** and **8f** easily underwent (3 + 3) annulation with **3a**, yielding the required pyridyl acetates **15ae** and **15af** in yields of 67% and 69%, respectively. The allenoate **8b** with the electron-donating group (4-OMe) on the phenyl ring yielded the product **15ab** in significantly more quantities (80%) than the allenoate **8d** that has an electron-withdrawing NO_2 group (**15ad**, 71%). The interaction of nucleophilic partners possessing electron-poor (-Br; **3c**) as well as electron-rich (Me; **3b**) functionalities with the allenoates **8a-8d** yielded the corresponding *α*-pyridyl acetates (**15ba-15bd**, **15ca-15cc**) in yields of 67-83%. In the case of precursor **3d**, we had to use 1 mole equivalent of DBU to get the best yields of **15da-15dc** (72-76%). It is remarkable that the cyclic sulfamidate imine **3e**

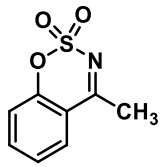
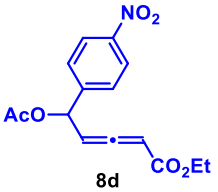
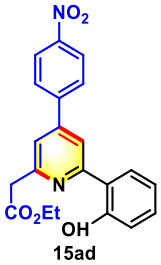
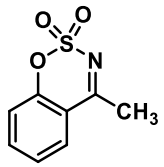
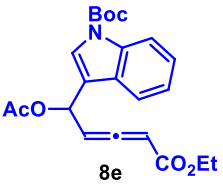
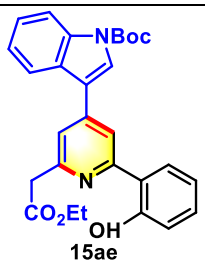
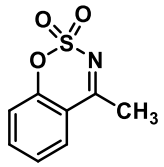
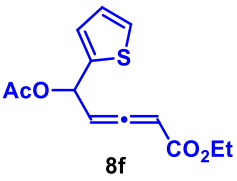
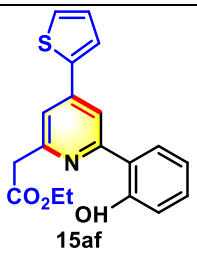
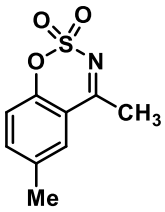
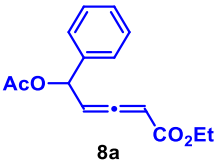
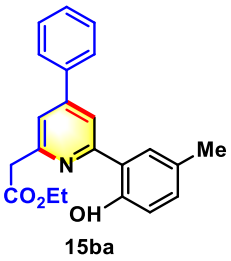
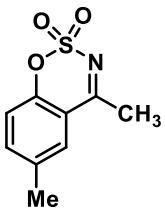
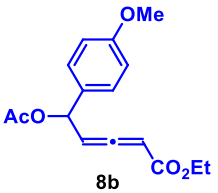
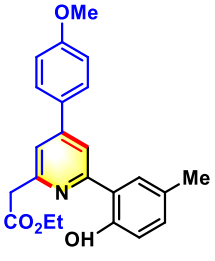
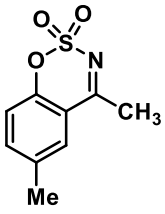
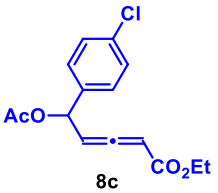
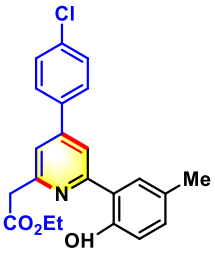
with a naphthyl group also enabled us to obtain the corresponding acetate **15ea** in 69% yield under our protocol. The structures of compounds **15aa** and **15db** as revealed by single crystal X-ray diffraction studies are shown in Figure 1.

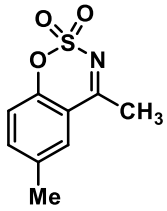
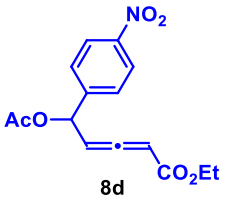
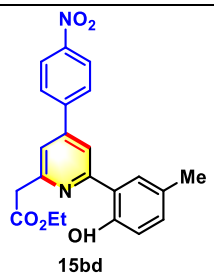
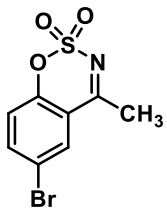
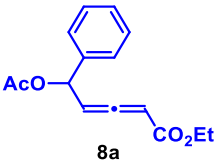
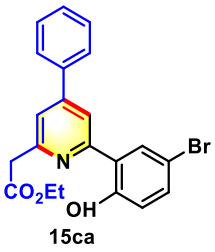
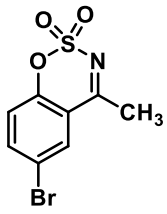
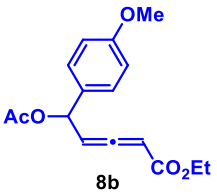
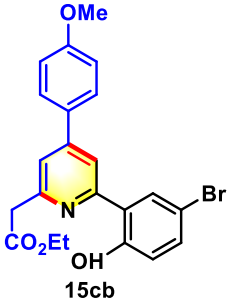
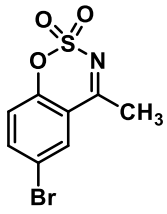
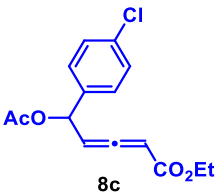
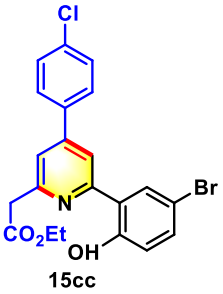
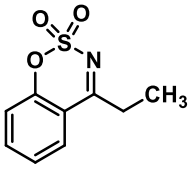
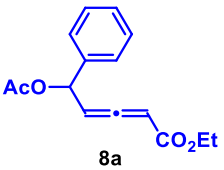
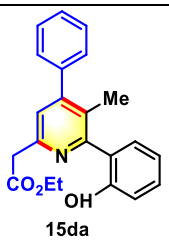
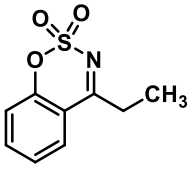
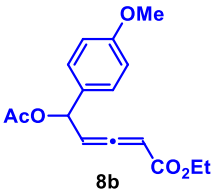
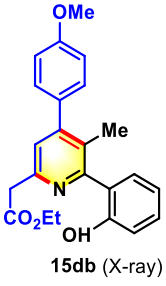
Table 2. Substrate scope for the synthesis of *α*-pyridyl acetates from *N*-sulfamidate imines and *δ*-acetoxy allenoates[a]

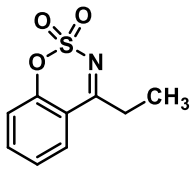
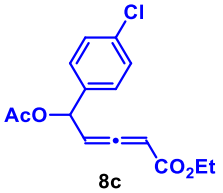
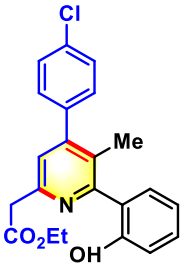
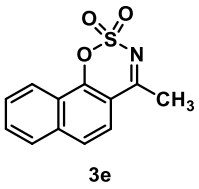
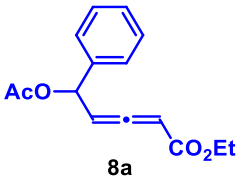
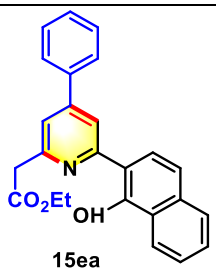


3 8 15

Entry	*N*-Sulfamidate imines	*δ*-Acetoxy allenoate	α-Pyridyl acetates	Yield (%)[b]
1	 3a	 8a	 **15aa** (X-ray)	79
2	 3a	 8b	 **15ab**	73
3	 3a	 8c	 **15ac**	80

4	 3a	 8d	 15ad	71
5	 3a	 8e	 15ae	67
6	 3a	 8f	 15af	69
7	 3b	 8a	 15ba	81
8	 3b	 8b	 15bb	75
9	 3b	 8c	 15bc	83

10	 3b	 8d	 15bd	72
11	 3c	 8a	 15ca	74
12	 3c	 8b	 15cb	67
13	 3c	 8c	 15cc	70
14	 3d	 8a	 15da	75
15	 3d	 8b	 15db (X-ray)	72

16	 3d	 8c	 15dc	76
17	 3e	 8a	 15ea	69

[a]Reaction conditions: (i) **3a-c** or **3e** (0.20 mmol), **8a-f** (0.24 mmol), DBU (0.10 mmol), and Na_2CO_3 (0.30 mmol) in toluene (2.0 mL) at 50 °C; (ii) **3d** (0.20 mmol), **8a-c** (0.24 mmol), DBU (0.20 mmol), and Na_2CO_3 (0.30 mmol) in toluene (2.0 mL) at 50 °C. Yields given are after isolation.

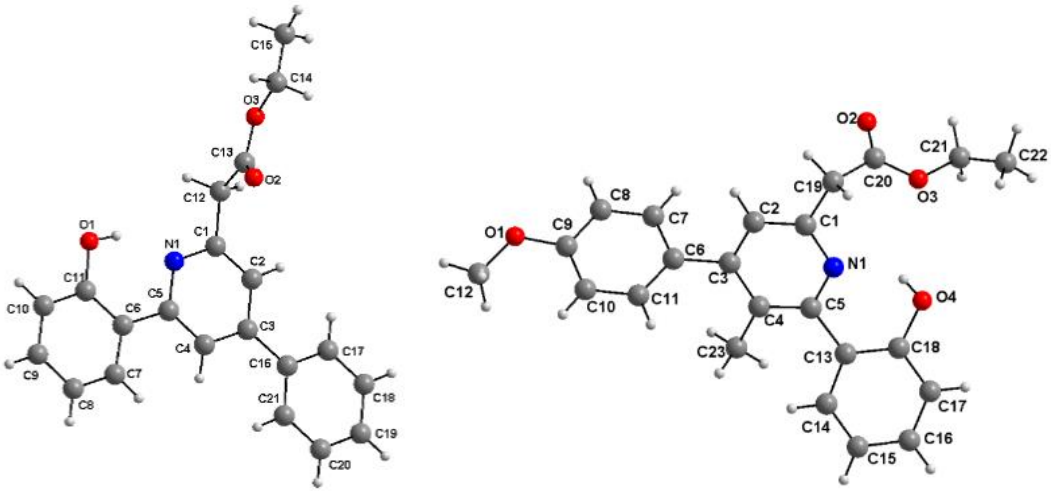
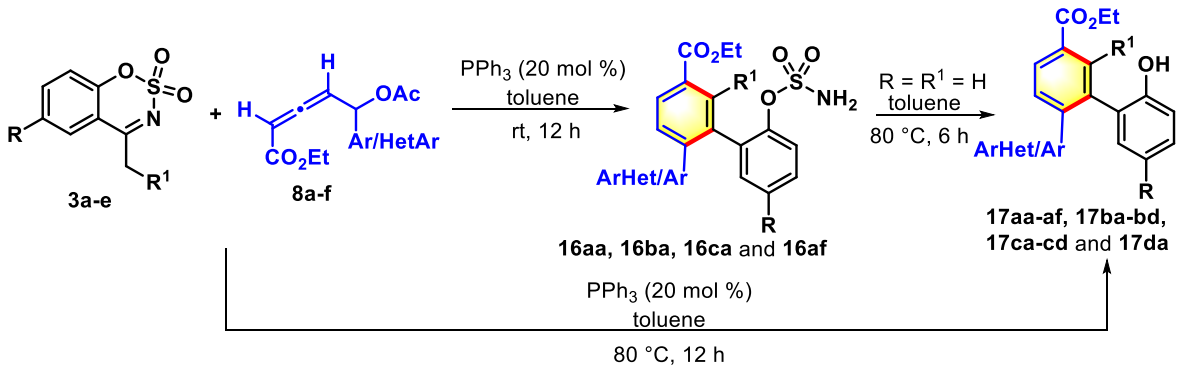


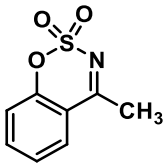
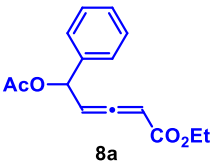
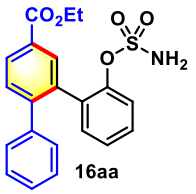
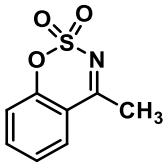
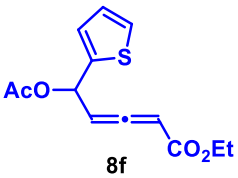
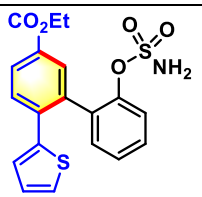
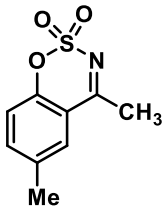
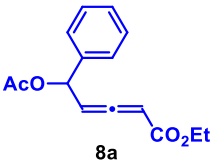
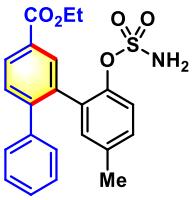
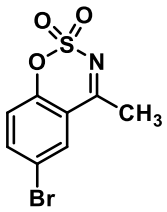
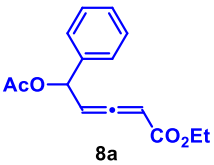
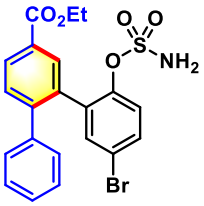
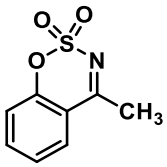
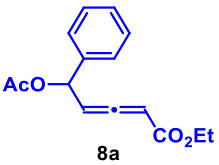
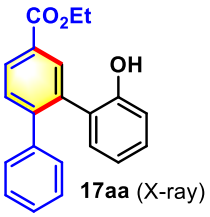
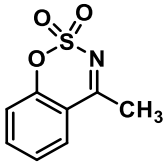
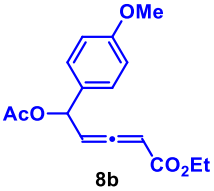
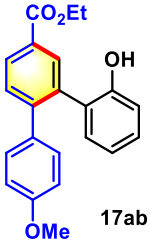
Figure 1. Molecular structures of compounds **15aa** (left, CCDC No. 1952241) and **15db** (right, CCDC No. 1952242). Selected bond distances (Å; pyridine ring): **15aa** N1-C1 1.349(3), C1-C2 1.372(3), C2- C3 1.388(3), C3-C4 1.385(3), C4-C5 1.384(3), C5-N1 1.357(3) Å. **15db** N1-C1 1.336(3), C1-C2 1.376(4), C2-C3 1.387(3), C3-C4 1.403(3), C4-C5 1.413(3), C5-N1 1.347(3) Å.

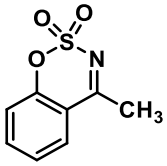
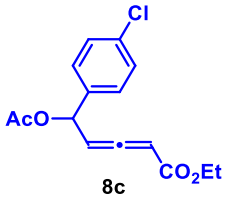
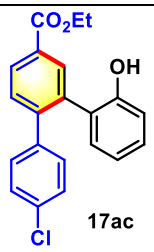
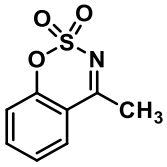
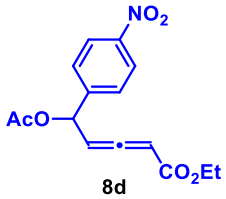
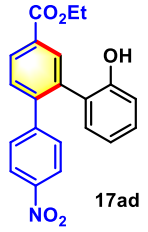
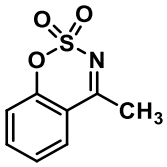
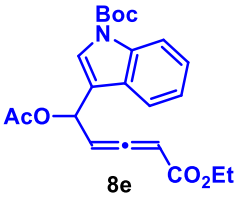
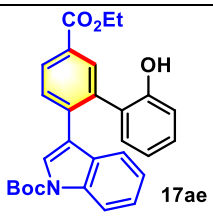
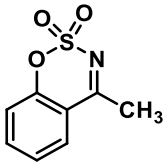
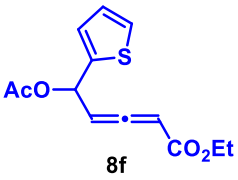
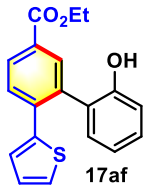
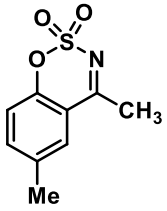
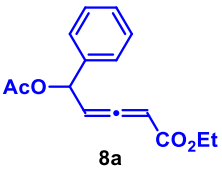
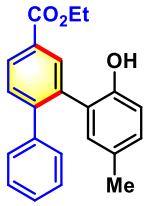
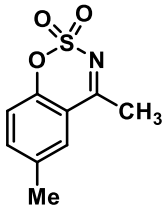
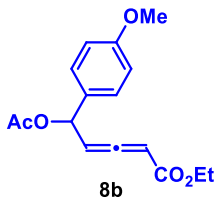
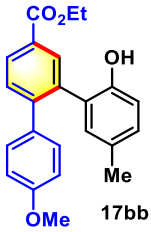
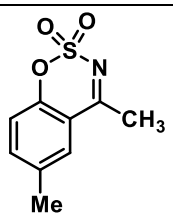
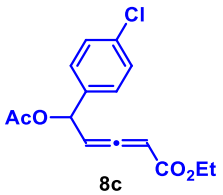
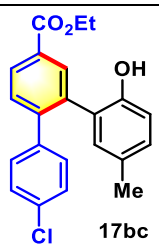
Next, we explored the substrate scope involving δ-acetoxy allenoates and cyclic sulfamidate imines in (4 + 2) annulation leading to the terphenyl products **16**. As indicated in Table 3, by conducting the reaction of **3a** with **8a** at rt (25 ^{o}C) in the presence of Ph_3P (TPP), the (4 + 2) annulation product, the terphenyl sulfomoyloxy carboxylate **16aa**, was obtained in good yield (cf. Table 3, entry 14). Using the same conditions and cyclic sulfamidate imines **3b** and **3c**, we were able to synthesize sulfomoyloxy carboxylates **16ba** and **16ca** in good yields (Table 3). The annulated product **16af** was obtained in a decent yield of 65% from the heterocyclic allenoate **8f**. The phenolic terphenyl **17aa** must have formed by the elimination of -SO_2NH_2 moiety from **16aa**. This could be proven readily by heating compound **16aa** in toluene, which yielded **17aa** quantitatively by the S-O bond cleavage. Because such phenolic teraryls are important scaffolds in organic synthesis.[85] we synthesized multisubstituted phenolic teraryls **17aa-17ad** in 75-85% yields in one-pot. Precursors **3b** and **3c** also provided the (4 + 2) annulation products **17ba-17bd** and **17ca-17cd** in good yields. Even the ethyl substituted precursor **3d** delivered the product **17da** in 72% yield. Heterocyclic allenoates **8e** and **8f** also participated efficiently to afford the products **17ae** and **17af**. The structures of compounds **16af**, **16ca**, **17aa** and **17bd** as revealed by single crystal X-ray diffraction are shown in Figures 2-3.

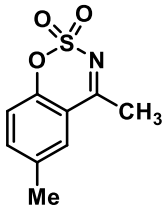
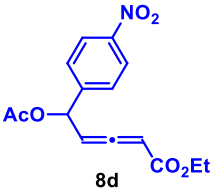
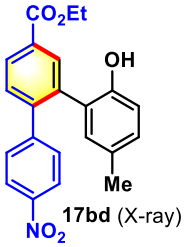
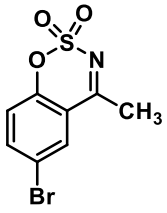
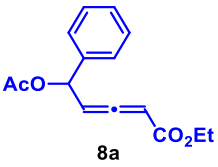
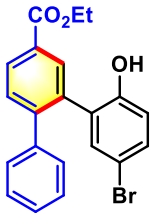
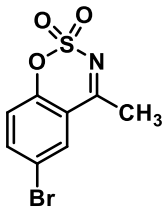
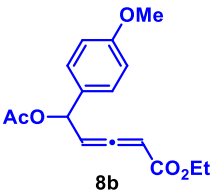
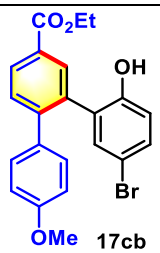
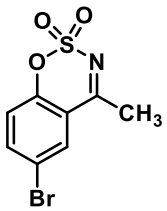
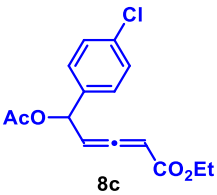
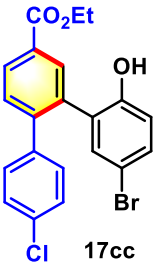
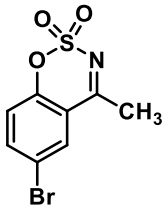
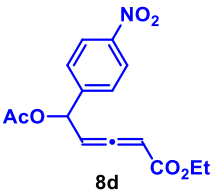
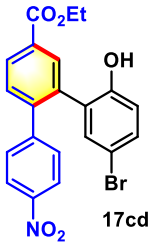
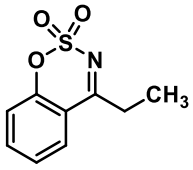
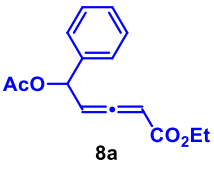
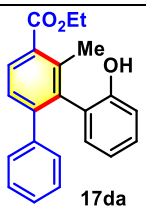
Table 4. Substrate scope for the synthesis of terphenyls from cyclic sulfamidate imines and δ-acetoxy allenoates[a]



Entry	*N*-sulfamidate imines	δ-Acetoxy allenoate	Terphenyls	Yield (%)[b]

1	 3a	 8a	 16aa	75
2	 3a	 8f	 **16af** (X-ray)	70
3	 3b	 8a	 16ba	78
4	 3c	 8a	 **16ca** (X-ray)	73
5	 3a	 8a	 **17aa** (X-ray)	68
6	 3a	 8b	 **17ab**	64

7	 3a	 8c	 17ac	72
8	 3a	 8d	 17ad	68
9	 3a	 8e	 17ae	76
10	 3a	 8f	 17af	65
11	 3b	 8a	 17ba	74
12	 3b	 8b	 17bb	77
13	 3b	 8c	 17bc	75

14	 3b	 8d	 17bd (X-ray)	77
15	 3c	 8a	 17ca	74
16	 3c	 8b	 17cb	74
17	 3c	 8c	 17cc	74
18	 3c	 8d	 17cd	74
19	 3d	 8a	 17da	74

Reaction conditions: **3a-d** (0.20 mmol), **8a-f** (0.24 mmol), and PPh_3 (0.04 mmol) in toluene (2.0 mL) at rt/12 h for 4 and 80 °C/12 h for 5. Yields given are after isolation

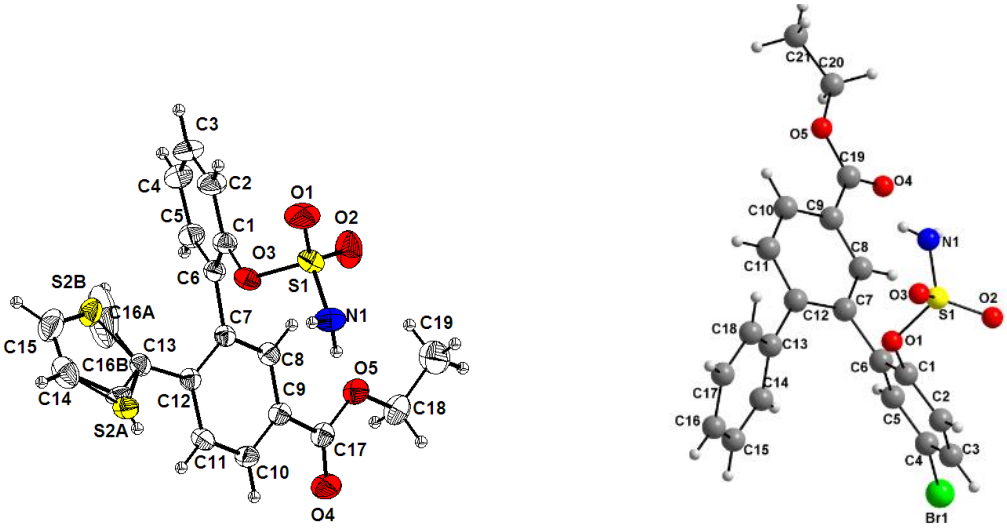


Figure 2. Molecular structures of compounds **16af** (left, CCDC No. 1952243) and **16ca** (right, CCDC No. 1952244). Selected bond distances (newly formed benzene ring): **16af** C7-C8 1.387(3), C8-C9 1.388(3), C9-C10 1.384(3), C10-C11 1.374(3), C11-C12 1.396(3), C12-C7 1.408(3) Å. **16ca** C7-C8 1.389(5), C8-C9 1.381(6), C9-C10 1.384(5-, C10-C11 1.371(5), C11-C12 1.391(6), C12-C7 1.407(5) Å.

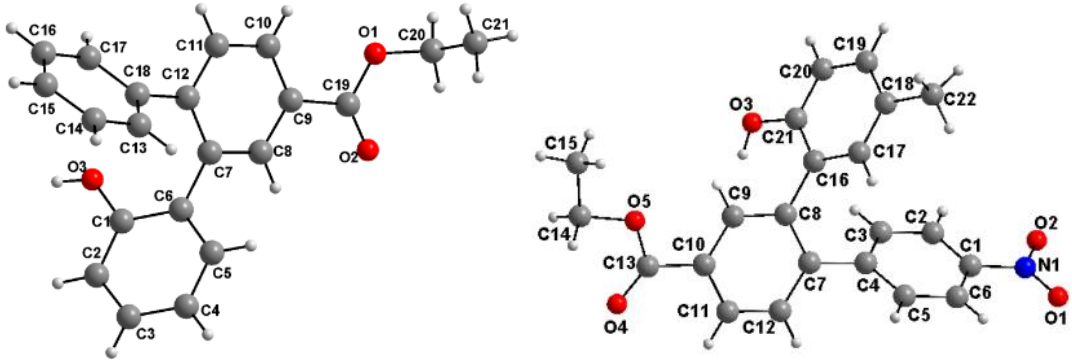


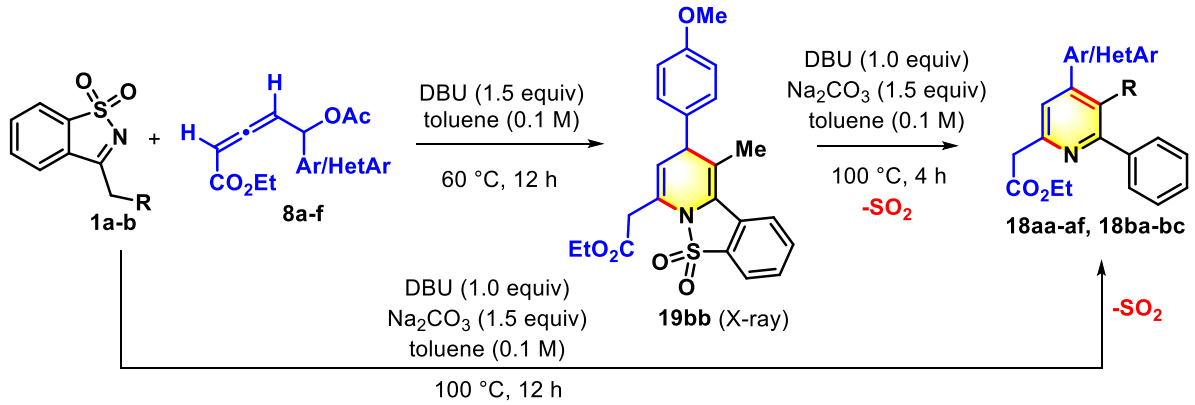
Figure 3. Molecular structures of compounds **17aa** (left, CCDC No. 1952245) and **17bd** (right, CCDC No. 1952246). Selected bond distances (newly formed benzene ring): **17aa** C7-C8 1.382(5), C8-C9 1.392(5), C9-C10 1.385(5), C10-C11 1.389(5), C11-C12 1.408(5), C12-C7 1.426(5) Å. **17bd** C7-C8 1.400(3), C8-C9 1.395(3), C9-C10 1.389(3), C10-C11 1.375(3), C11-C12 1.387(3), C12-C7 1.387(3) Å.

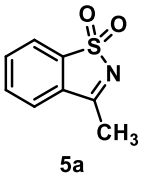
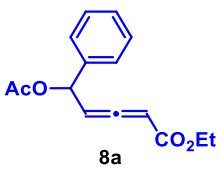
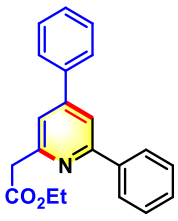
2.2.3 *Formation of α-pyridyl acetates from N-sulfonyl imines 5 and δ-acetoxy allenoates 8 via DBU catalysis*

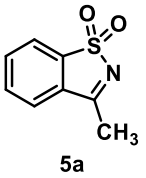
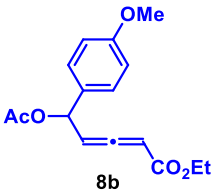
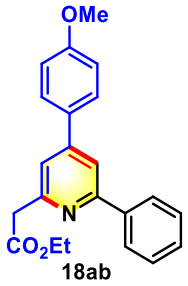
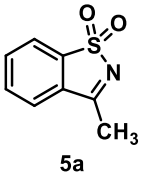
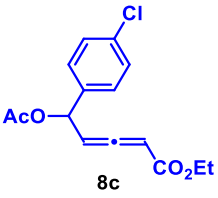
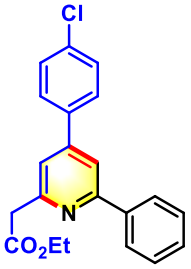
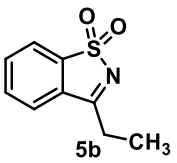
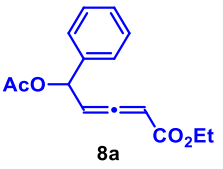
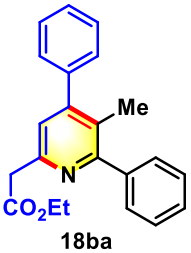
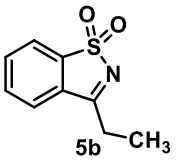
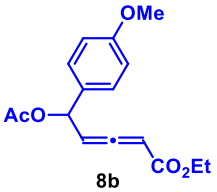
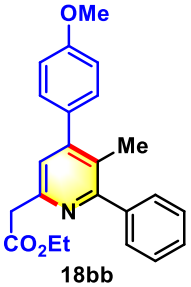
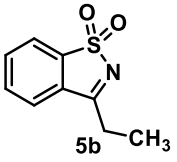
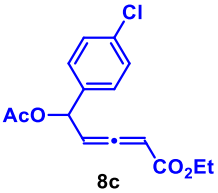
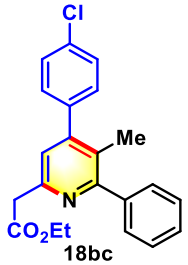
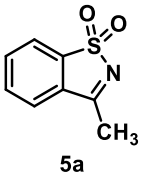
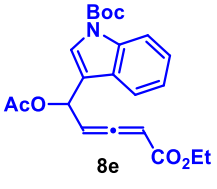
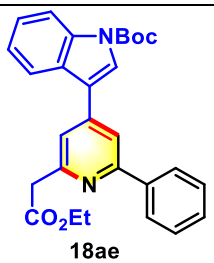
Taking a cue from the reactivity of *δ*-acetoxy allenoates and sulfamidate imines for the synthesis of *α*-pyridyl acetates as described above, we expected the formation of *α*-pyridyl acetates **18** from sulfonyl imines. Thus, as depicted in Table 4, based on our previous successful annulation of acetoxy allenoates with sulfamidate imines containing OSO_2 moiety,

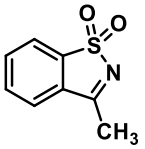
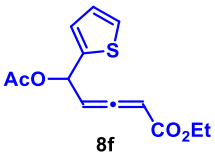
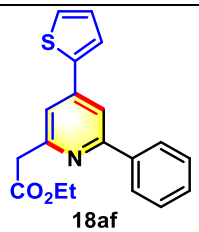
we tried (3 + 3) annulations with the slightly different sulfonyl imine **5** possessing benzo-isothiazole skeleton and the sulfur directly bonded to the arene ring. Initially, we faced some difficulties but after using 1 mole equiv of DBU we obtained **18aa** in 71% yield at 100 °C after 12 h. The sulfonyl imines **5a** and **5b** showed good reactivity with allenoates **8b-8c** and produced 2-pyridinyl acetates **18ab-18ac** and **18ba-18bc** in acceptable yields. The heterocyclic acetoxy allenoates **18e-18f** also participated efficiently in this (3 + 3) annulation to produce **18ae-18af** in decent yields. The expected C*H*$_2$Ar signal in the ^{1}H NMR spectrum was observed around 4.0 ppm for these compounds; the corresponding carbon appeared around 44.0 ppm in the ^{13}C{^{1}H} NMR spectrum. To know more details about this reaction, we even isolated fused dihydropyridine intermediate **19bb** in 74% yield whose structure was confirmed by X-ray crystallography. A point to be noted here is that this product **19bb** is different from the pyridyl acetates **18bb**; the 1H NMR spectrum exhibits a characteristic doublet at δ 4.96 for C*H*Ar proton in the ^{1}H NMR spectrum. Compound **19bb** could be converted to 2-pyridinyl acetate **18bb** in toluene under basic conditions at 100 °C.

Table 5. Substrate scope for the synthesis of *α*-pyridyl acetates from *N*-sulfonyl imines and *δ*-acetoxy allenoates



Entry	*N*-Sulfonyl Imine	*δ*-Acetoxy Allenoate	*α*-Pyridyl Acetate	Yield (%)[b]
1	 5a	 8a	 18aa	71

2	 5a	 8b	 18ab	69
3	 5a	 8c	 18ac	73
4	 5b	 8a	 18ba	69
5	 5b	 8b	 18bb	64
6	 5b	 8c	 18bc	70
7	 5a	 8e	 18ae	57

8	 5a	 8f	 18af	62

[a]Reaction conditions for one pot reaction to give **17aa-17bc**: **5a-b** (0.20 mmol), **8a-f** (0.24 mmol), DBU (0.20 mmol) and Na_2CO_3 (0.30 mmol) in toluene (2.0 mL) at 100 °C (oil bath). [b]Conditions: **5b** (0.20 mmol), **8b** (0.24 mmol) and DBU (0.30 mmol) in toluene (2.0 mL) at 60 °C. [c]Conditions: 1**9bb** (0.10 mmol), DBU (0.10 mmol) and Na_2CO_3 (0.15 mmol) in toluene (1.0 mL) at 100 °C (oil bath). [d]Isolated yield.

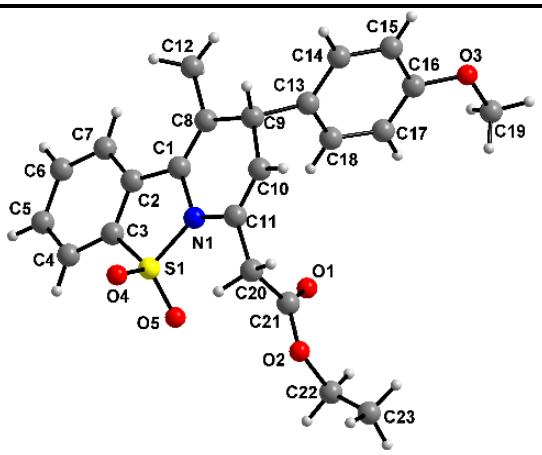


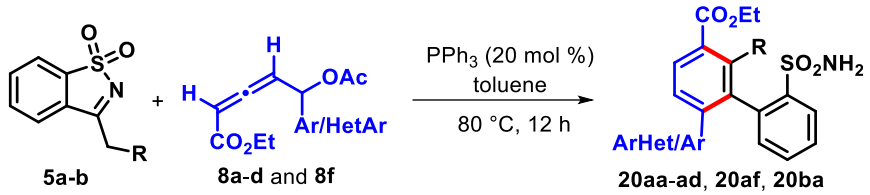
Figure 4. Molecular structure of compound **19bb** (CCDC No. 1952247). Selected bond distances: S1-N1 1.652(5), N1-C1 1.438(6), C1-C2 1.479(8), C2-C3 1.380(7), C3-S1 1.733(6), N1-C11 1.419(8), C11-C10 1.310(9), C10-C9 1.492(8), C9-C8 1.513(9), C8-C1 1.328(8) Å.

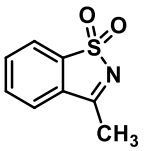
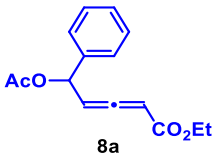
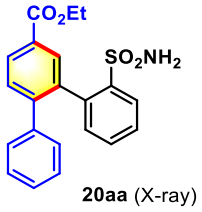
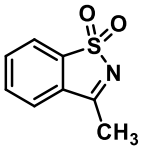
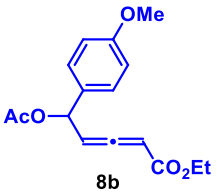
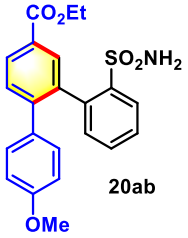
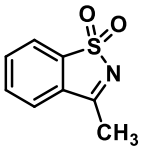
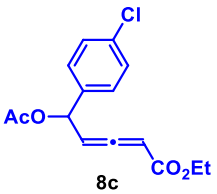
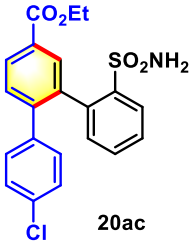
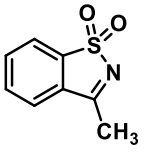
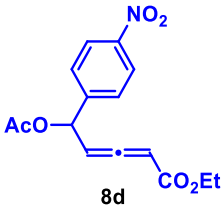
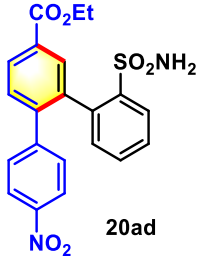
2.2.4 *Formation of teraryls from N-sulfonyl imines 5 and δ-acetoxy allenoates 8 via phosphine catalysis*

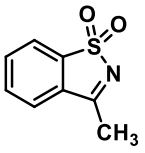
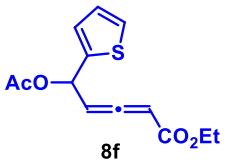
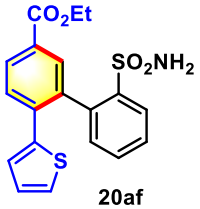
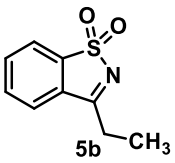
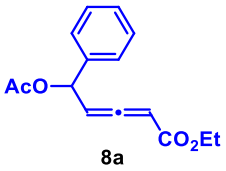
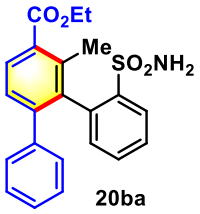
Inspired by the above success with sulfonyl imines in (3 + 3) annulation, we were curious to test this protocol in (4 + 2) annulation reaction of sulfonyl imines **5a** and **5b** with *δ*-acetoxy allenoates **8a-8d** and **8f** under phosphine catalysis. This Ph_3P-catalyzed reaction was performed in toluene at 80 °C. Pleasingly, terphenyls **20aa-20ad**, **20af**, and **20ba** were obtained in high to excellent yields with retention of sulfonamide group. In these compounds also, the SO_2NH_2 proton was clearly discernible in the ^{1}H NMR spectrum at δ ~4.3. Although in a compound like **20ba** there is a possibility of hindered rotation leading to enantiomers, we

have not explored this aspect in the current study. An X-ray structure determination for **20aa** (Figure 5) clearly established the authenticity of these teraryls.

Table 6. Substrate scope for the synthesis of terphenyls from cyclic sulfonyl imines and *δ*-acetoxy allenoates[a]



Entry	*N*-Sulfonyl imine	*δ*-Acetoxy allenoate	Teraryl	Yield (%)[b]
1	 5a	 8a	 20aa (X-ray)	71
2	 5a	 8b	 20ab	69
3	 5a	 8c	 20ac	73
4	 5a	 8d	 20ad	69

5	 5a	 8f	 20af	64
6	 5b	 8a	 20ba	70

[a]Reaction conditions: **5a-b** (0.20 mmol), **8a-d** and **8f** (0.24 mmol), PPh_3 (0.04 mmol) in toluene (2.0 mL), at 80 °C. [b]Isolated yield.

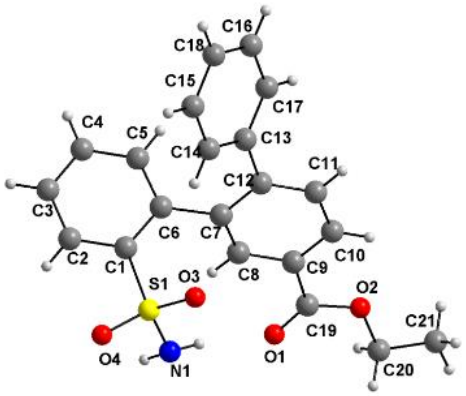
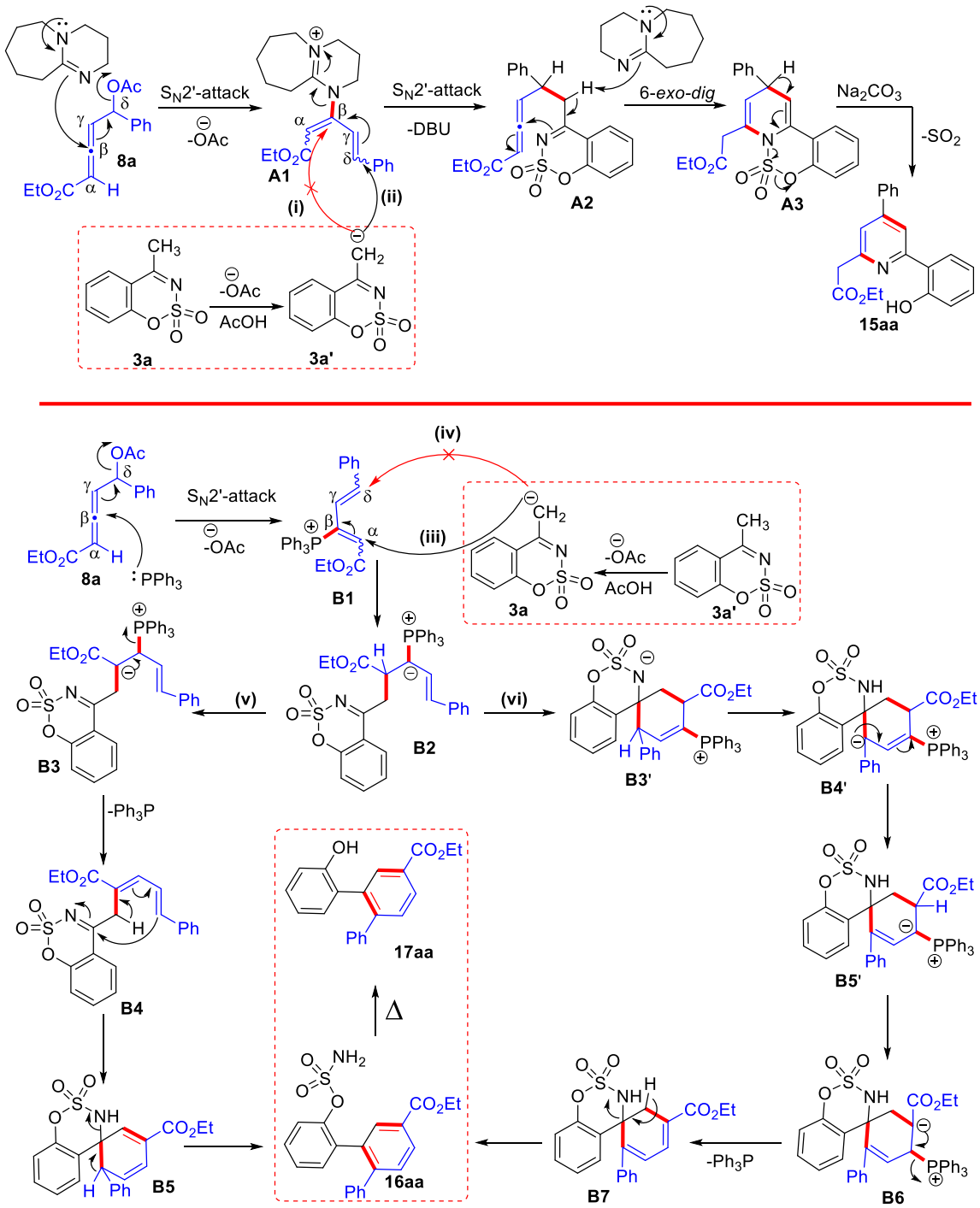


Figure 5. Molecular structure of compound **20aa** (CCDC No. 1952248). Selected bond distances (newly formed benzene ring): C7-C8 1.389(3), C8-C9 1.391(3), C9-C10 1.390(3), C10-C11 1.379(3), C11-C12 1.394(3), C12-C13 1.488(3) Å.

2.2.5 *Proposed pathways for (3 + 3) and (4 + 2) annulations*

Based partly on previous literature,[86] plausible pathways for the above (3 + 3) and (4 + 2) annulations are shown in Scheme 7. Initially, the *δ*-acetoxy allenoate **8a** undergoes SN_2'-attack with Lewis base (DBU[86d] or TPP) to deliver the electrophilic intermediate **A1** or **B1** by the elimination of acetate anion. Similar facile removal of acetate group is quite common in the reactions using propargylic acetates as well as Baylis-Hillman acetates.[87] In our reaction, though, the resulting species is the diene-ammonium or diene-phosphonium ion. In the (3 + 3) annulation, **A1** is likely to be less electrophilic (at *β*-carbon) rendering Michael addition (route i) less favorable than DBU elimination. Hence the cationic intermediate **A1** undergoes a second S_N2' attack (route ii) rapidly with carbanion **3a'** generated by deprotonation of **3a** to

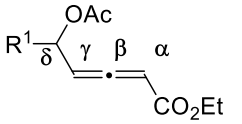
afford intermediate **A2**. Subsequently, ring closure of **A2** via *6-exo-dig* cyclization leading to **A3** followed by SO_2 elimination/aromatization, offers 2-pyridinyl acetate **15aa**. The likely role of Na_2CO_3 in this reaction is to scavenge the acetic acid formed and to facilitate SO_2 elimination.[88] In the (4 + 2) annulation, the α-carbon in the intermediate **B1** is more electrophilic. The driving force for Michael addition is ylide formation with **3a'** to give **B2** *via* route iii (more favorable than route iv). This is followed by 1,2-proton shift to afford **B3** that undergoes TPP elimination leading to the diene **B4** via route v. Then **B4** undergoes intramolecular vinylogous Mannich coupling[89] followed by C-N bond cleavage/aromatization affording sulfamoyloxy-terphenyl-carboxylate **16aa**. Finally, **16aa** produces **17aa** by the cleavage of O-S bond upon heating. Obviously, if this is the process leading to **17aa**, adventitious moisture may be involved. Another pathway, which involves more number of steps, is also possible for the phosphine catalysis. Thus, ylide **B2** may involve in Mannich coupling *via* route vi to afford **B3'** that undergoes 1,3-proton shift leading to the **B4'**. Then, **B4'** undergoes isomerization followed by 1,2-proton shift and TPP elimination affording the spirocyclic diene **B7**. This in turn will give the products **16aa** and **17aa**. We could observe peaks assignable to intermediates of types **A1**, **A2/A3**, **B1** and **B2** by checking crude reaction mixtures using ESI-HRMS.



Scheme 7: Plausible mechanistic pathway for the formation of **15aa**, **16aa** and **17aa**

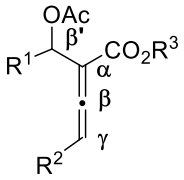
2.3 Tertiary Amine Controlled (3 + 3) and (4 + 2) Annulations of *β'*-Acetoxy Allenoates with *N*-Sulfonyl Ketimines: Formation of *m*-Teraryl and Fused Dihydropyridines

Although both *δ*-acetoxy allenoates and *β'*-acetoxy allenoates have the ester group connected to an allenic carbon, the relative position of the ester group *vis-à-vis* the removable acetoxy moiety is different. Hence, in base-catalyzed reactions with bifunctional nucleophiles these subtle differences could lead to somewhat different products.



δ–acetoxy allenoate

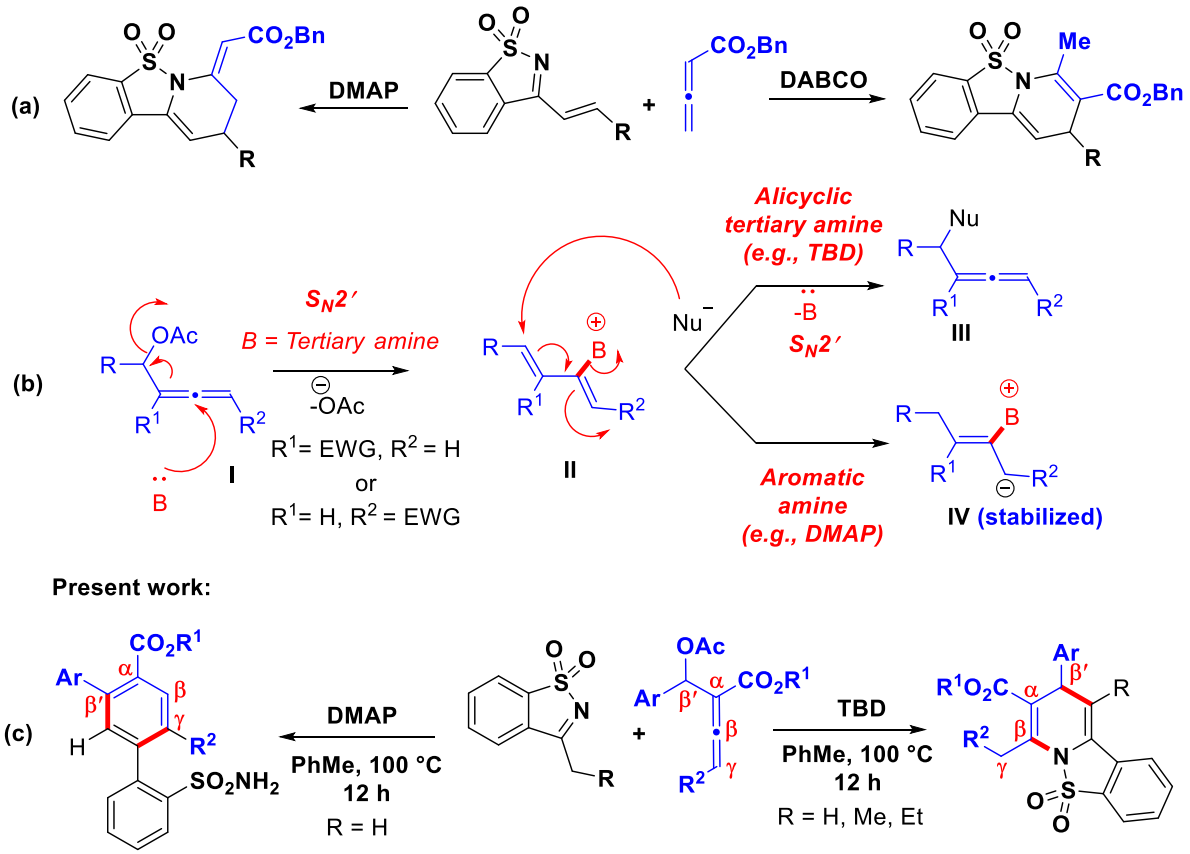
8



β'-acetoxy allenoate

12

It is also important to note that even alicyclic tertiary amines (e.g., DABCO) and aromatic amines (e.g., DMAP) show markedly distinct pathways in reactions involving allenoates as shown earlier by Huang and co-workers in the reaction of allenoates with sulfonyl-substituted α,β-unsaturated ketimines (Scheme 7a).[90] As described in the previous section, the *β'*-acetoxy allenoates that we planned to use in the present study under amine catalysis lead to diene-ammonium intermediates and hence could lead to other important heterocyclic compounds with a sulfomadite moiety. Alicyclic tertiary amines (e.g., TBD, DABCO) and aromatic amines (e.g., pyridine, DMAP) may show distinct pathways in reactions involving allenoates (Scheme 7b). In the reaction using aromatic amines, positive charge on the nitrogen atom is dissipated by the attached ring. This type of stabilization is not possible in the case of alicyclic tertiary amines and hence allylic elimination is involved. Since both TBD [pK_a(MeCN) of the conjugate acid 26.0] and DMAP [pK_a(MeCN) of the conjugate acid 17.9] are explored as nucleophilic organocatalysts in numerous reactions, we believe that the distinction observed may be significant. This is a point that we intended to explore in greater detail by using *β′*-acetoxy allenoates wherein the ester group is positioned on the allenic *α*-carbon that could introduce additional electronic factors like rendering the *γ*-carbon in *β′*-acetoxy allenoate nucleophilic. Herein, the results of tertiary-amine controlled (3 + 3)/ (4 + 2) annulations involving *β′*-acetoxy allenoates with isothiazole dioxides (*N*-sulfonyl ketimines) are discussed. These include (i) TBD catalyzed annulation of *β′*-acetoxy allenoates delivering fused 1,4-dihydropyridines *via* sequential S_N2'-attack and 6-*endo*-dig cyclization, and (ii) DMAP catalyzed annulation of *β′*-acetoxy allenoates giving *m*-teraryls *via* S_N2'-attack followed by proton shifts, Mannich-coupling and C-N bond cleavage (Scheme 7c). A large numer of 1,4-dihydropyridines are well known drugs (cf. Figure 6) in the market and hence these compounds are pharmaceutically very important.



Scheme 7: Reactivity of allenoates and the present work

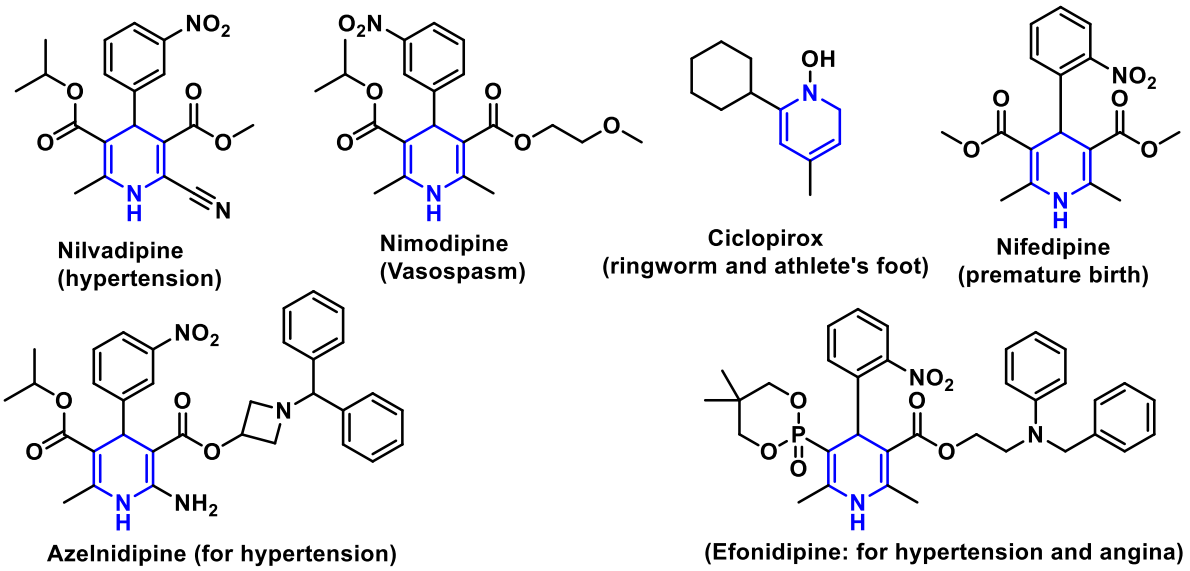
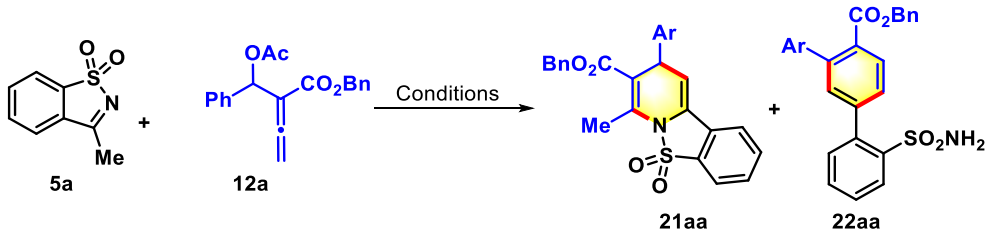


Figure 6: Selected biologically active 1,4-dihydropyridines

2.3.1 *Annulation reactions of β′-acetoxy allenoates with N-sulfonyl ketimines: Optimization study*

Initially, isothiazole dioxide **5a** and *β′*-acetoxy allenoate **12a** were selected as model substrates to test the above reactions. As shown in Table 7, we conducted the reaction of **5a** (0.20 mmol) with **12a** (0.24 mmol) in toluene using DABCO (20 mol %) at rt (25 ^{o}C). After 12 h of reaction, **21aa** was obtained in 45% yield (entry 1). The use of 50 mol% of DABCO in toluene at rt (25 ^{o}C) did not improve the yield of **21aa** (entry 2). The addition of 1.0 equiv Na_2CO_3 or Cs_2CO_3 was ineffective in improving the yield (entries 3 and 4). At a higher temperature of 100 ^{o}C with reaction time of 12 h the yield of **21aa** improved to 66% (entry 9). Use of TBD in place of DABCO enhanced the yield to 71% (entry 10). Longer reaction time did not improve the yield further (entry 11). We then screened the reaction in different solvents like THF, MeCN, and DCE but they were not better than toluene (entries 12-14). No reaction occurred with DBU catalyst (entry 15). Interestingly, use of DMAP in place of TBD under otherwise identical conditions resulted in only the terphenyl product **22aa** in 76% yield (entry 16). At 50 ^{o}C, treating **5a** with **12a** in the presence of DMAP yielded only a very small quantity of **22aa** (5%; entry 17). We then examined various DMAP analogues such as pyridine (PY), 4-PPY, and 4-PiPY. We observed a slightly lower yield of **22aa** in the case of 4-PPY and 4-PiPY (entries 19 and 20) while PY was ineffective (entry 18). Since we observed *o*-teraryl formation by using **5a** and *δ*-acetoxy allenoates in the presence of PPh_3,[10] we attempted a similar reaction of **5a** with **12a** but did not observe any product formation (entry 21). Thus toluene was chosen as the solvent, yielding the anticipated products **21aa** (71%; entry 10) and **22aa** (76%; entry 16).

Table 7. Optimization of reaction conditions for the synthesis of 21aa and 22aa



Entry	Catalyst	Base	Solvent	Temperature (^{o}C)	Yield[b] **21aa**	*dr* of[c] **22aa**[c]
1	DABCO		PhMe	25	45	0
2	DABCO		PhMe	25	45	0
3	DABCO	Na_2CO_3	PhMe	25	45	0

4	DABCO	Cs_2CO_3	PhMe	25	0	0
5	DABCO		PhMe	50	36	0
6	DABCO		PhMe	80	53	0
7	DABCO	Na_2CO_3	PhMe	80	46	0
8	DABCO	Cs_2CO_3	PhMe	80	40	0
9	DABCO		PhMe	100	66	0
10	**TBD**		**PhMe**	**100**	**71**	**0**
11	TBD[d]		PhMe	100	71	0
12	TBD		THF	100	10	0
13	TBD		ACN	80	53	0
14	TBD		DCE	80	0	0
15	DBU		PhMe	100	0	0
16	**DMAP**		**PhMe**	**100**	**0**	**76**
17	DMAP		PhMe	50	0	<5
18	PY		PhMe	100	0	0
19	4-PPY		PhMe	100	0	68
20	4-PiPY		PhMe	100	0	69
21	PPh_3		PhMe	100	0	0

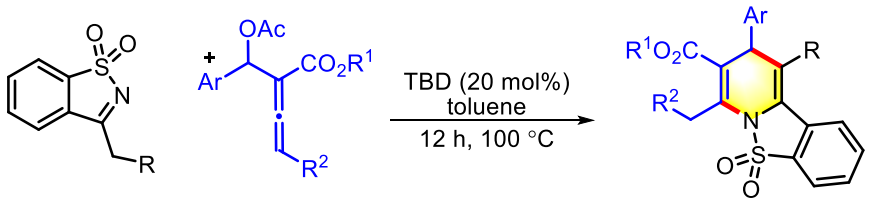
[a]Reaction conditions: **5a** (0.20 mmol; 1.0 equiv), **12a** (0.24 mmol; 1.2 equiv), Lewis base catalyst (20 mol% for entries 1 and 3-21; 50 mol% for entry 2), base (1.0 equiv for entries 3, 4, 7 and 8) in a stoppered Schlenk tube in toluene (2.0 mL). Temperature is that of the oil bath. [b]DABCO = 1,4-Diazabicyclo [2.2.2]octane, DMAP = 4-(Dimethylamino)pyridine, PY = Pyridine, 4-PPY = 4-Pyrrolidinopyridine, 4-PiPY = 4-Piperidinopyridine. [c]Isolated yield. [d]Time = 24 h.

2.3.2 *Formation of fused dihydropyridines: Substrate scope*

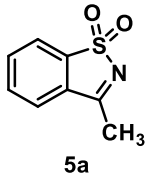
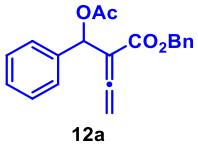
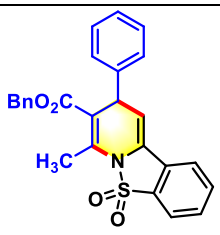
For substrate scope, we explored a range of *β′*-acetoxy allenoates and isothiazole dioxides as shown in Table 8. Thus *β′*-acetoxy allenoates having different functionalities (H, OMe, Cl, NO_2, and CF_3) at the *p*-position of the phenyl ring **12a-e** reacted well and afforded dihydropyridines **21aa-ae** in 63-74% yield. Disubstituted allenoates **12f** and **12h** also delivered the corresponding **21af** and **21ah** in 74% and 69% yield. Polycyclic aromatic and heterocyclic functionalities on the allenoates **12i-k** did not hamper the reactivity in giving the (3 + 3) annulated products **21ai-ak**. As expected, the *β′*-acetoxy allenoate **12n** with ethyl

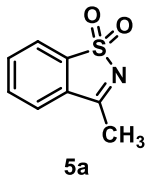
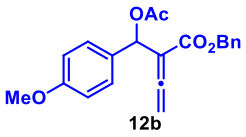
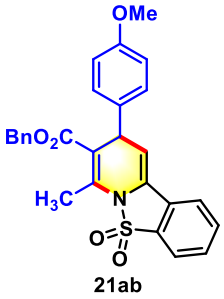
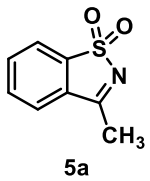
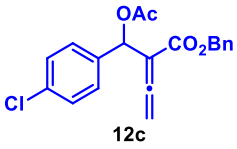
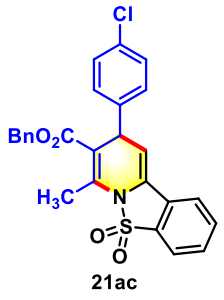
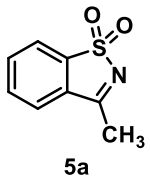
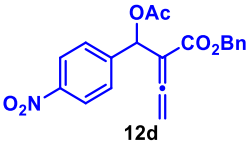
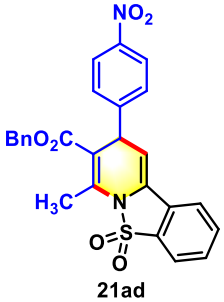
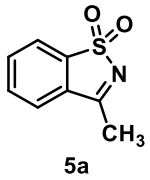
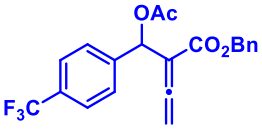
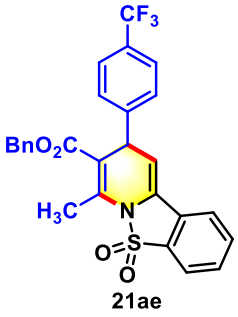
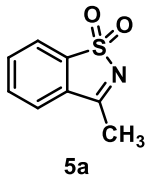
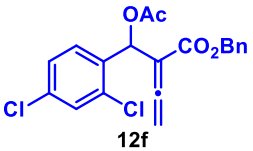
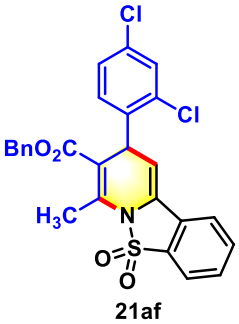
group also afforded the product **21an** in good yield (76%). Other *β′*-acetoxy allenoates **12o-p** afforded products **21ao-ap** in excellent yields. Inspired by these positive results, we explored the reactions of *β′*-acetoxy allenoates **12a**, **12n** and **12o** with isothiazole dioxides **5b** and **5c** and isolated **21ba**, **21bn**, **21bo** and **21ca** in good to excellent yields of 55%-74%. All these compounds show characteristic doublets corresponding to the C*H*(Ar)=C*H* around δ values 4.7and 5.7 ppm in the ^{1}H NMR spectra; the newly generated CH_3 from the allene part in the compounds **21aa-21an** also exhibit a characteristic singlet at δ ~2.9. In the ^{13}C{^{1}H} NMR spectra, a peak at δ ~41.0 ppm ascribable to the *C*H(Ar) carbon is readily discernible in all these compounds. These compounds are resistant to oxidation due to the additional substitution on the nitrogen in the ring, unlike the pyridyl acetate products obtained from *δ*-acetoxy allenoates (*vide supra*, section 2.2). The structural confirmation is provided by single crystal X-ray diffraction studies on compounds **21aa** and **21bk** (Figure 7); the C8-C9 and C9-C10 distances clearly show a single bond between the corresponding atoms. As far as the significance of these compounds is concerned, it is important to note that sultam and dihydropyridine structural frameworks exhibit diverse biological activities.[91, 92]

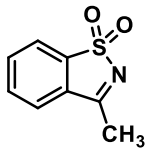
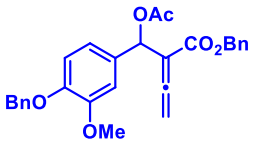
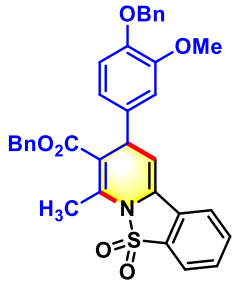
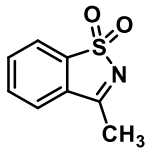
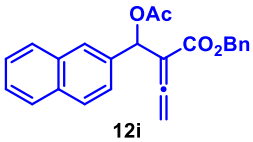
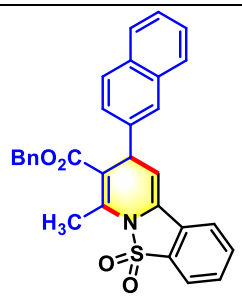
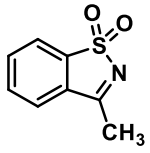
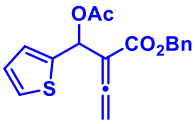
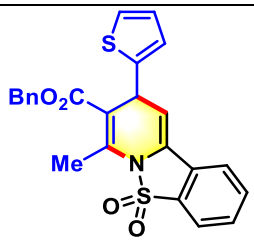
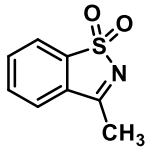
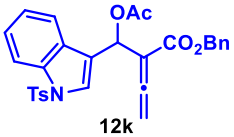
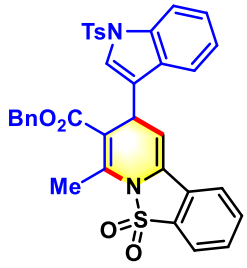
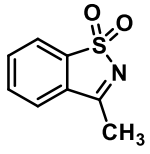
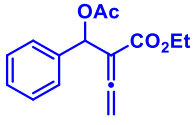
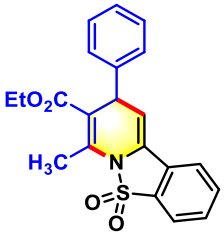
Table 8. Substrate scope for the synthesis of fused dihydropyridines from *N*-sulfonyl ketimines and *β*'-acetoxy allenoates

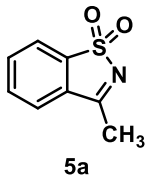
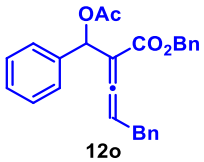
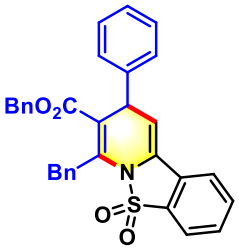
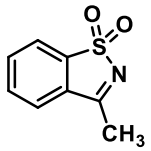
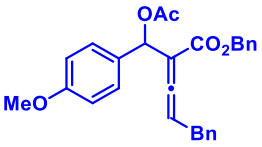
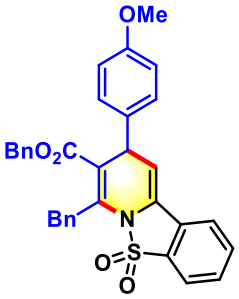
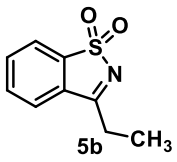
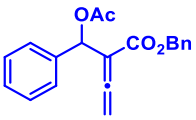
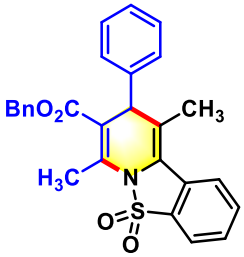
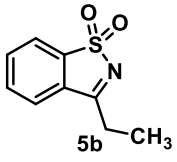
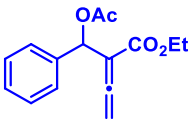
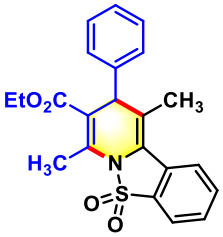
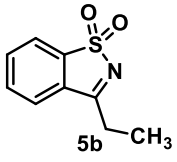
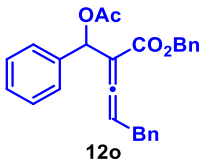
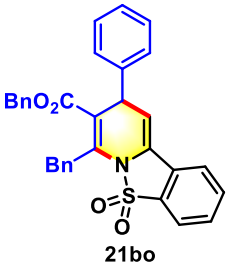


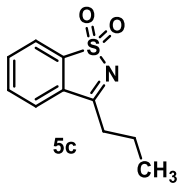
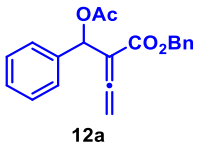
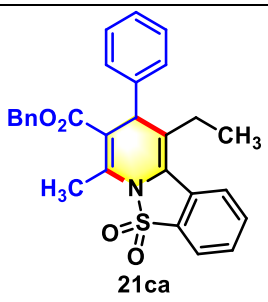
5a-c **12a-q** **21aa-af, 21ah-ak, 21an-ap**

Entry	1C,3O-bisnucleophile	*δ*-Acetoxy Allenoate	Dihydropyran	Yield (%)[b]
1	 **5a**	 **12a**	 **21aa** (X-ray)	71

2	 5a	 12b	 21ab	75
3	 5a	 12c	 21ac	72
4	 5a	 12d	 21ad	63
5	 5a	 12e	 21ae	66
6	 5a	 12f	 21af	74

7	 5a	 12h	 21ah	69
8	 5a	 12i	 21ai	69
9	 5a	 12j	 21aj	63
10	 5a	 12k	 21ak	65
11	 5a	 12n	 21an (X-ray)	76

12	 5a	 12o	 21ao	81
13	 5a	 12p	 21ap	83
14	 5b	 12a	 21ba	65
15	 5b	 12n	 21bn	73
16	 5b	 12o	 21bo	74

17	 5c	 12a	 21ca	55

[a]Reaction conditions: **5a-c** (0.20 mmol; 1.0 equiv), **12a-n** (0.24 mmol; 1.2 equiv), TBD (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 °C. [b]Isolated yield.

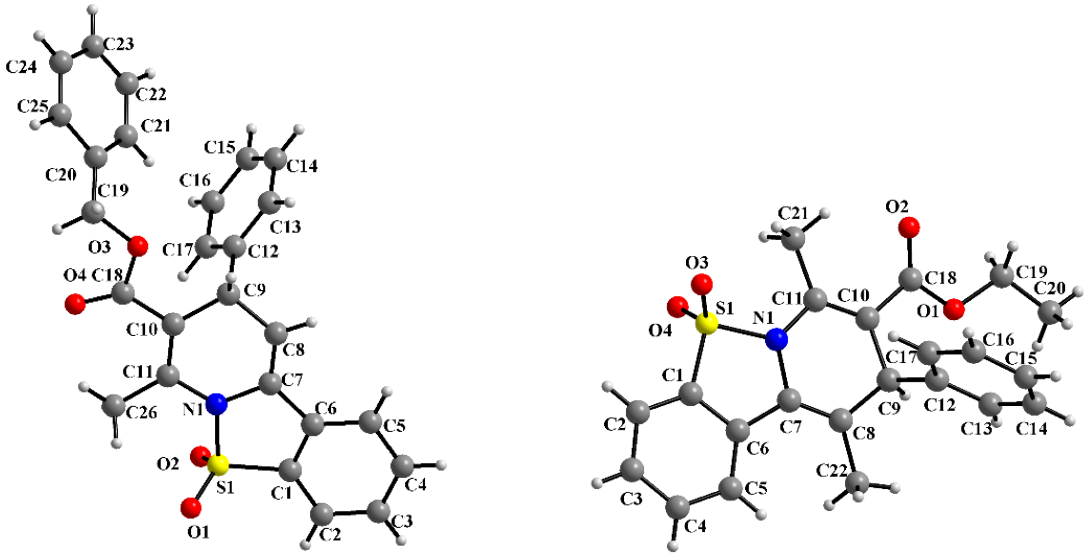


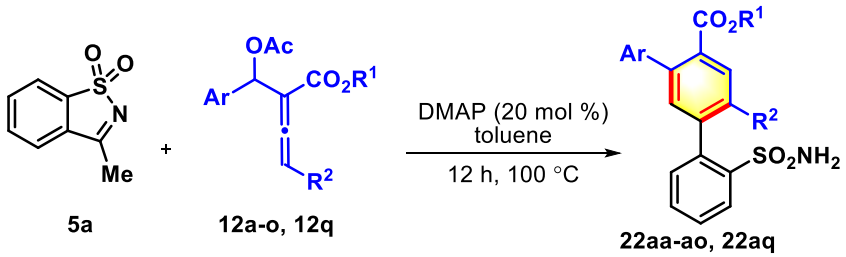
Figure 7: Molecular structures of compounds **21aa** (left, CCDC No. 2298991), and **21bk** (right, CCDC No. 2298992). Selected bond distances: **21aa** S1-N1 1.676(3), N1-C7 1.415(5), C7-C6 1.463(5), C6-C1 1.376(7), C1-S1 1.727(5), C7-C8 1.310(5), C8-C9 1.491(5), C9-C10 1.511(5), C10-C11 1.346(5), C11-N1 1.395(5) Å. **21an** S1-N1 1.686(3), N1-C7 1.436(3), C7-C6 1.466(4), C6-C1 1.392(4), C1-S1 1.733(4), C7-C8 1.326(4), C8-C9 1.514(4), C9-C10 1.524(3), C10-C11 1.339(3), C11-N1 1.402(4) Å.

2.3.3 *Formation of teraryls: Substrate scope*

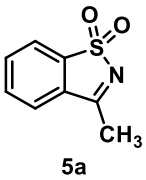
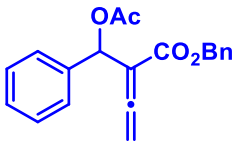
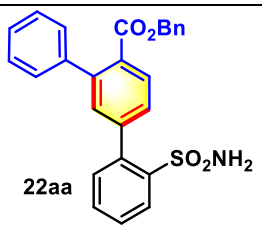
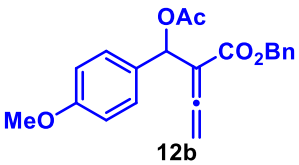
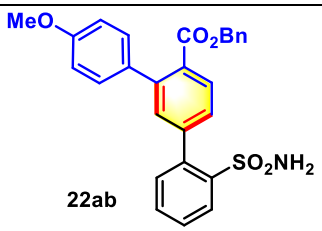
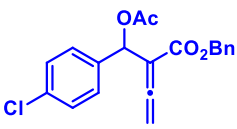
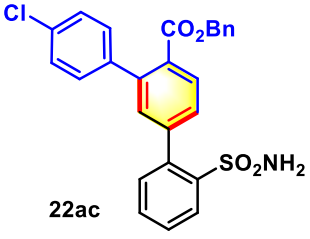
The results in DMAP catalyzed reactions of *β′*-acetoxy allenoates (**12a-o**, **12q**) with *N*-sulfonyl imine **5a** are collated in Table 9. Here also, the substituents at the different positions on the aryl ring of allenoate (**12a-h**) did not show dramatic difference in the reactivity/yield under optimal conditions and furnished (4 + 2) annulated products **22aa-ah** in good to high yields (65%-84% and 70%). Allenoates with polycyclic aromatic functionalities at *β′*-position such as **12i** and **12l** participated well, leading to 72% and 66% yields. The *β′*-

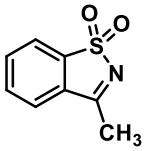
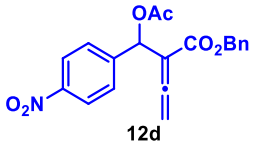
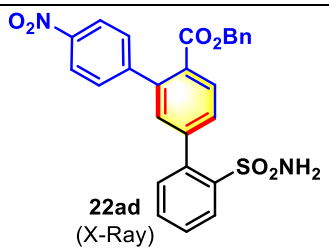
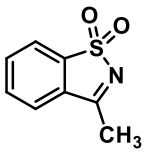
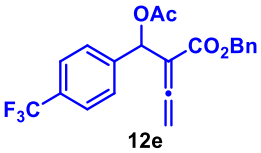
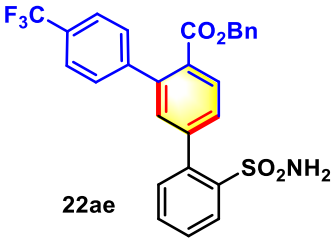
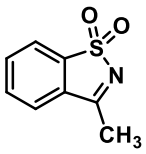
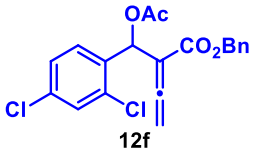
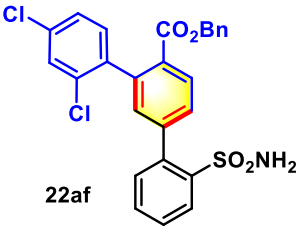
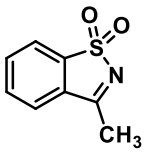
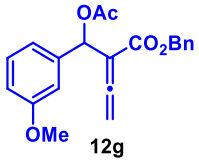
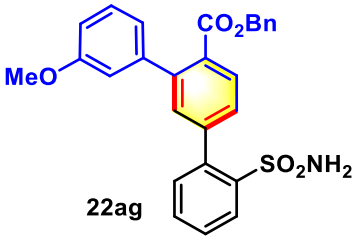
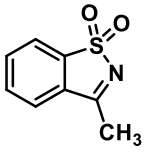
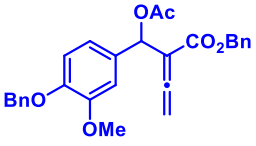
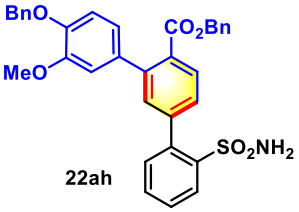
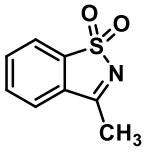
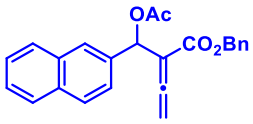
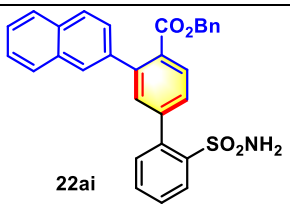
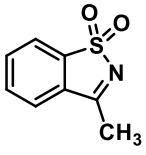
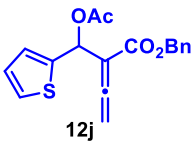
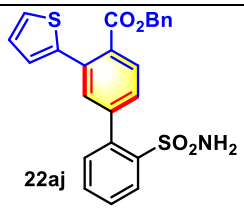
acetoxy allenoate **12n** containing an ethyl group instead of the benzyl group expected afforded the product **22an** in a good yield of 78%. Heterocyclic substituted allenoates **12j** and **12k** also gave the desired products **22aj** and **22ak** in satisfactory yields (65% and 71%). Remarkably, β'-acetoxy allenoates **12o** and **12q** having benzyl (-CH_2Ph) group at the γ-position afforded desired products **22ao** and **22aq** in 70-76% yield. These products are analogous to the teraryls **20** obtained from δ-acetoxy allenoates and the characteristic peak in the ^{1}H NMR spectra is that of the SO_2NH_2 protons at ca 4.4 ppm. Further confirmation of the structures is provided by the single crystal X-ray diffraction study on **22ad**. The terphenyl formation, however, was not observed in the reaction of **5b** or **5c** with **12a** in the presence of DMAP.

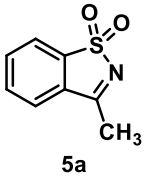
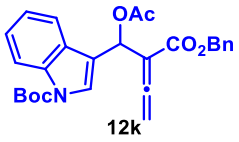
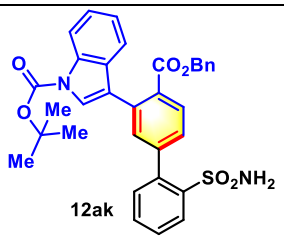
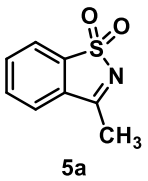
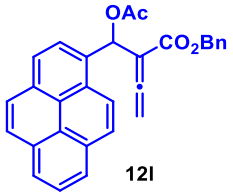
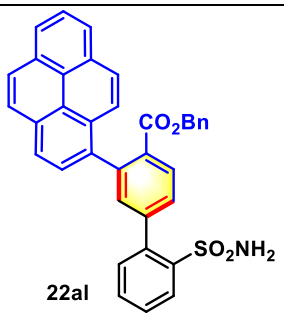
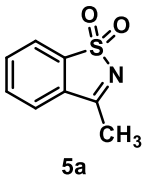
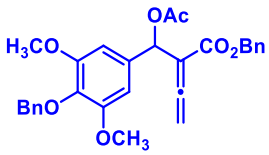
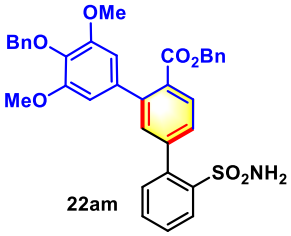
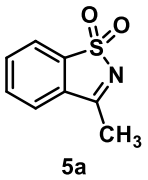
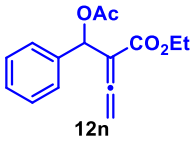
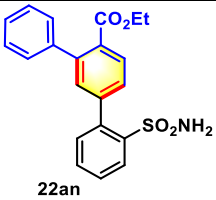
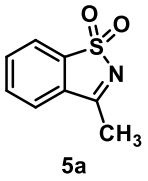
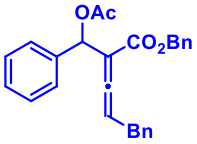
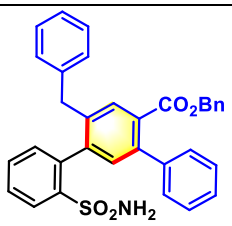
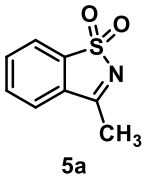
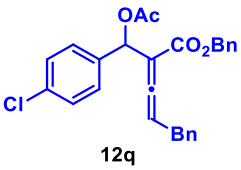
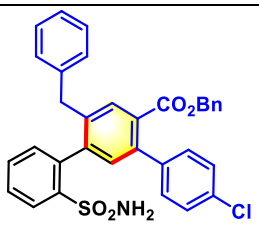
Table 9. Substrate scope for the synthesis of teraryls from *N*-sulfonyl ketimines and *β*'-acetoxy allenoates



5a 12a-o, 12q 22aa-ao, 22aq

Entry	*N*-Sulfonyl Imine	β'-Acetoxy Allenoate	*m*-Teraryl	Yield[b] (%)
1	 5a	 12a	 22aa	76
2	 5a	 12b	 22ab	84
3	 5a	 12c	 22ac	77

4	 5a	 12d	 22ad (X-Ray)	69
5	 5a	 12e	 22ae	71
6	 5a	 12f	 22af	65
7	 5a	 12g	 22ag	78
8	 5a	 12h	 22ah	70
9	 5a	 12i	 22ai	72
10	 5a	 12j	 22aj	65

11	 5a	 12k	 12ak	71
12	 5a	 12l	 22al	66
13	 5a	 12m	 22am	74
14	 5a	 12n	 22an	78
15	 5a	 12o	 22ao	76
16	 5a	 12q	 22aq	70

[a]Reaction conditions: **5a** (0.20 mmol), **12a-i**, **12k-l**, **12n**, **12o-r** (0.24 mmol; 1.2 equiv), DMAP (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 °C. [b]Isolated yield.

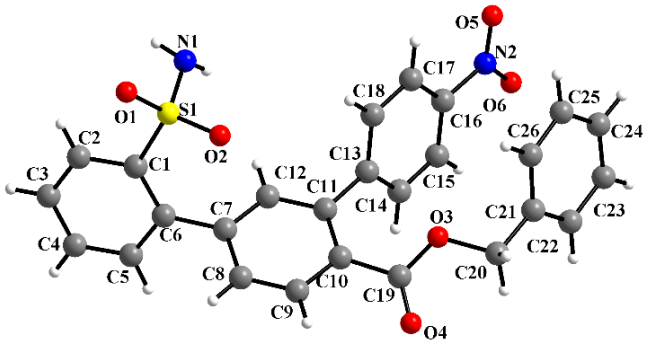
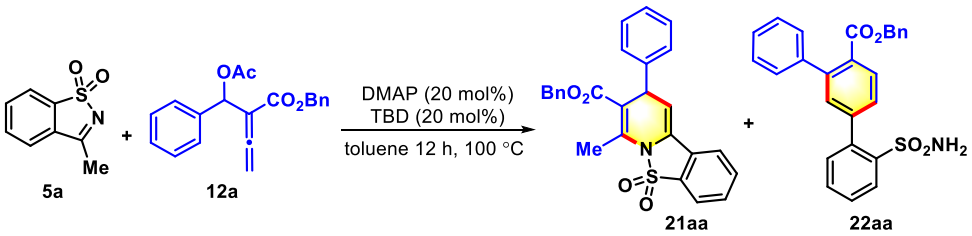


Figure 8: Molecular structure of compound **22ad** (CCDC No. 2298993). Selected bond distances (newly formed benzene ring): C7-C8 1.388(3), C8-C9 1.372(3), C9-C10 1.391(3), C10-C11 1.408(3), C11-C12 1.389(3), C12-C7 1.389(3) Å.

2.3.4 *Control experiments*

To identify the difference between TBD and DMAP catalysis, we performed a reaction between **5a** and **12a** in the presence of both DMAP and TBD in toluene at 100 ^{o}C for 12 h (Scheme 8). Both the products **21aa** and **22aa** were observed to form in ca 2:3 ratio as confirmed by TLC. This observation indicated that there is only marginal difference in the reactivity with no significant preference for either of the products.

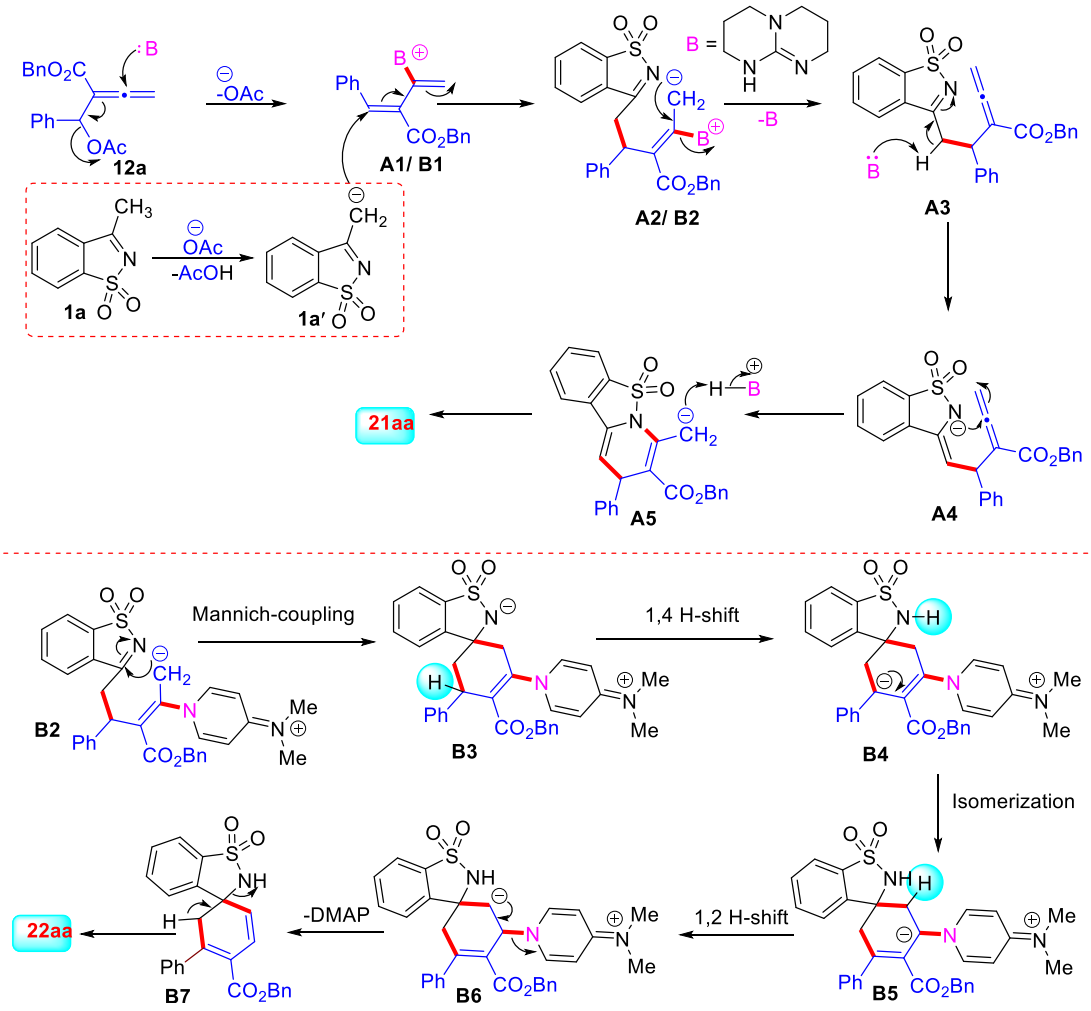


Scheme 8: Control experiments

2.3.5 *Proposed pathways for (4 + 2) and (3 + 3) annulations*

A plausible pathway for (4 + 2) carbo-annulation is proposed in Scheme 9. This annulation reaction is facilitated by the addition of a tertiary amine to the *β*-carbon of the *β′*-acetoxy allenoate **12a** *via* an allylic elimination to deliver the reactive electrophilic intermediate **A1/ B1**. This upon 1,6-addition with the anion **1a′** provides zwitterionic intermediate **A2/ B2**. In the TBD-catalyzed (3 + 3) annulation, **A2** rapidly undergoes 1,2-elimination followed by *6-endo-dig* cyclization and delivers **21aa** *via* allenoate intermediate **A3**. In sharp contrast to this, in the case of DMAP catalysis, the intermediate ylide **B2** is more stable because of the delocalization effect of the attached aromatic ring and dimethylamino group. Thus, the intermediate B2 immediately participates in the Mannich coupling, rather

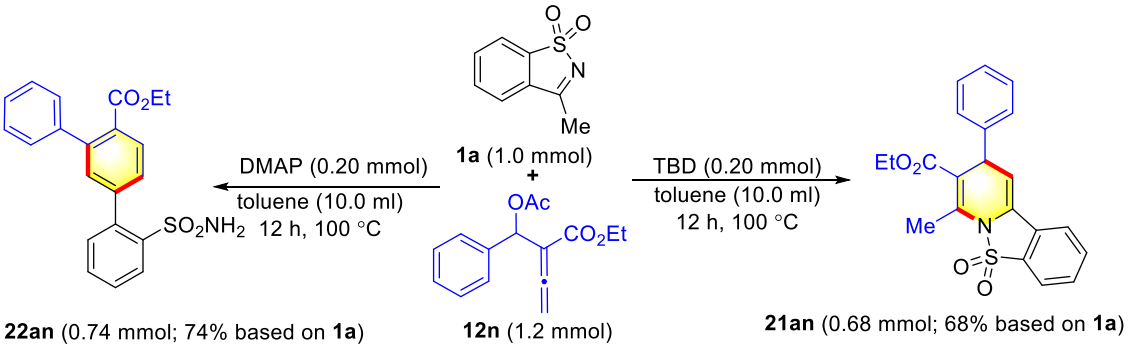
than 1,2-elimination to give spirocyclic zwitterionic specie **B3**. Next, **B3** undergoes 1,4-proton transfer followed by isomerization, 1,2-proton transfer, and DMAP elimination affording the spirocyclic diene **B7**. Finally, C-N bond cleavage and aromatization lead to the unsymmetrical *m*-teraryl **22aa**. Thus, in our analysis, the difference in products formed in the presence of the bases TBD and DMAP might have arisen due to the difference in structure of these bases (that stabilize the intermediates) rather than the basicity. The aforementioned intermediates **A1** {m/z $[M+H]^+$: Calcd. 402.2176; found 402.2180}, **B1** {m/z $[M+H]^+$: Calcd. 385.1911; found 385.1915}, **A2** {m/z $[M+H]^+$: Calcd. 583.2374; found 583.237002.2180} and **B2** {m/z $[M+H]^+$: Calcd. 566.2108; found 566.2111} were identified by an in-process HRMS study.



Scheme 9: Plausible pathways for the formation of **21aa** and **22aa**

To establish the practicality of this reaction, we carried out the 1.0 mmol scale reaction of **1a** with **12n** (1.2 mmol) using standard reaction conditions as shown in Scheme

10. The reactions proceeded nicely to afford the corresponding products **21ak** and **22ak** in yields of 68% and 74%, respectively.



Scheme 10: Scale-up experiment for the synthesis **21an** and **22an**

2.4. Catalyst-free Thermal (3 + 2) Cycloaddition of *δ/β′*-Acetoxy Allenoates with Azides

As mentioned in Chapter 1, although numerous azide-alkyne click reactions are reported, the corresponding reaction of azides with allenes is relatively much less explored. The 1,2,3-triazole products thus obtained by using alkynes have emerged as an important class of aza-heterocycles owing to their possible applications in medicinal chemistry (cf. Figure 9), agrochemical industry, and materials chemistry.[93] Synthesis of 1,4,5-tri/ 1,5-disubstituted 1,2,3-triazoles using acetoxy allenoates had not been reported prior to the current work. Also, in most of the reactions using alkyne-azide click reaction, a transition metal catalyst is utilized. Hence, the development of a metal-free, stereo-and regioselective thermal cycloaddition involving δ/β′-acetoxy allenoate for the synthesis of fully-substituted 1,2,3-triazoles is of some significance. Herein regio-and stereo-selective (3 + 2)-thermal cycloaddition involving δ/β′-acetoxy allenoates and azides for the construction of 1,4,5-tri/ 1,5-di-substituted-1,2,3-triazole under metal-free conditions is disclosed. In this cycloaddition, the aryl attached nitrogen atom chemoselectively attacks at the β-carbon of acetoxy allenoate and delivered *essentially E-isomer* in all cases.

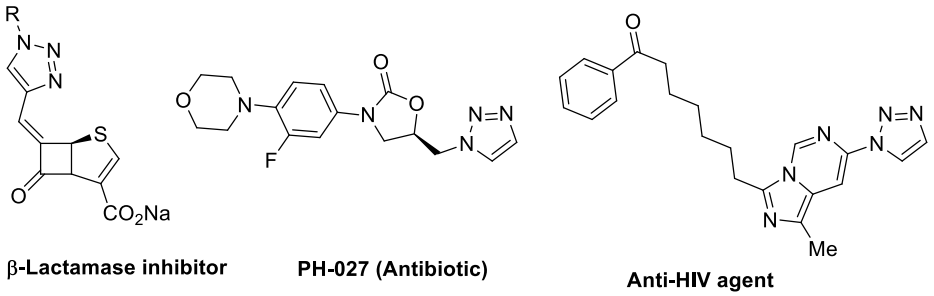
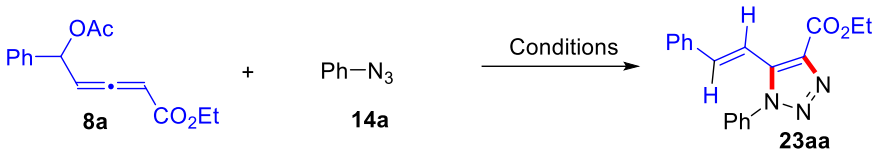


Figure 9. Selected biologically active molecules with triazole functionality

2.4.1 *(3 + 2) Cycloaddition of δ/β'-acetoxy allenoates with azides: Optimization studies*

To realize the optimal reaction conditions, we have used *δ*-acetoxy allenoate **8a** and phenyl azide **14a** as model substrates. As depicted in Table 10, we examined the reaction between **8a** (0.50 mmol) and **14a** (1.5 mmol) in toluene (2.0 mL) at room temperature (25 ^{o}C), but could not isolate any product even after 24 h (entry 1). Pleasingly, we obtained **23aa** in 56% yield at 70 ^{o}C after 12 h (entry 2) and identified it as 1,4,5-tri substituted-1,2,3-triazole (NMR). It meant that this is a thermal cycloaddition and heating is essential for this reaction. Encouraged by this, several solvents such as *N*,*N*-dimethyl formamide (DMF), dimethyl sulfoxide (DMSO), 1,2-dichloroethane (DCE) 1,4-dioxane, methanol, and water were examined (entries 3-8); among these, DMF was the best solvent to deliver **23aa** in higher yield 82% (entry 6). Lowering the temperature to 25 ^{o}C did not lead to the desired product even after 24 h (entry 9). Different mole ratios (1.0 mmol) of **14a** were also checked but failed to give better yields of the product **23aa** (entries 10). The yield even at 100 ^{o}C (entry 11) was essentially the same as that 70 ^{o}C (entry 6).

Table 10. Optimization of reaction conditions



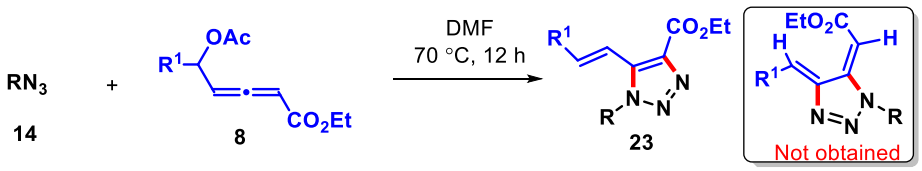
Entry	Solvent	Temperature (^{o}C)	Time	Yield[b]
1	PhMe	25	24	nr
2	PhMe	70	12	56
3	DMSO	25	12	75
4	DCE	70	12	59
5	1,4-Dioxane	70	12	63
6	**DMF**	**70**	**12**	**82**
7	MeOH	70	12	31
8	H_2O	70	12	15
9	DMF	25	24	nr
10	DMF	70	12	61
11	DMF	100	12	82

[a]Reaction conditions: **8a** (0.50 mmol) and **14a** (1.5 mmol for entries 1-9 and 1.0 mmol for entry 10) in solvent (2.0 mL). [b]Isolated yield.

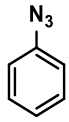
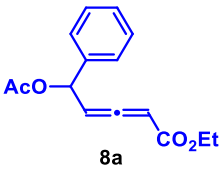
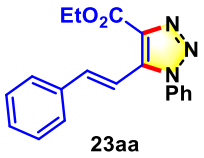
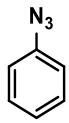
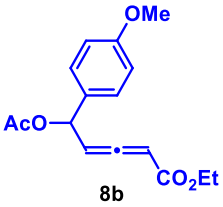
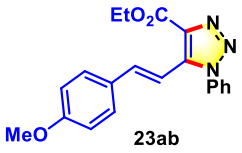
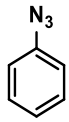
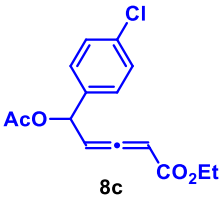
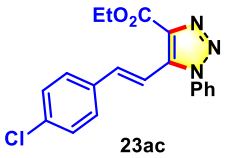
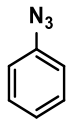
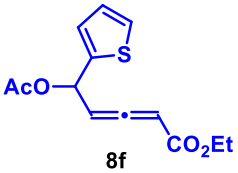
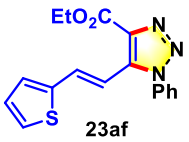
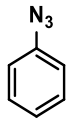
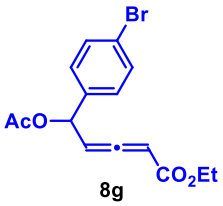
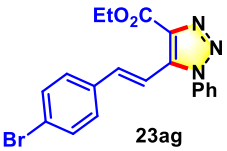
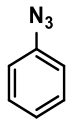
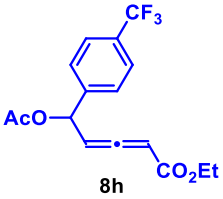
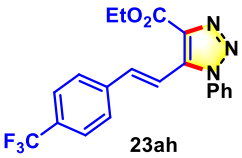
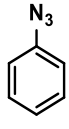
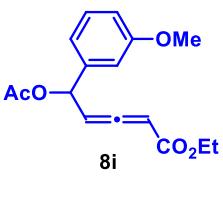
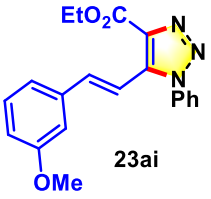
2.4.2 *Substrate scope*

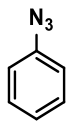
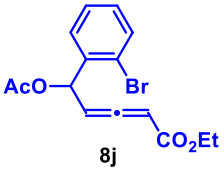
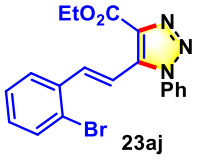
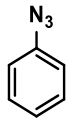
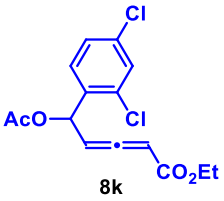
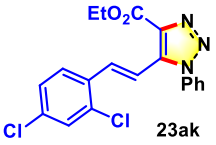
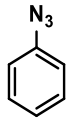
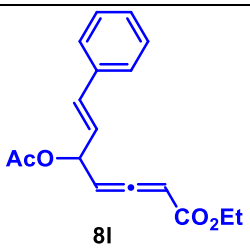
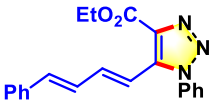
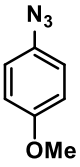
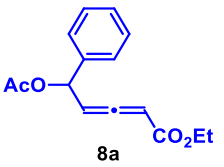
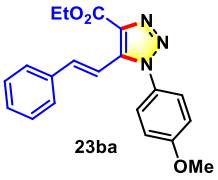
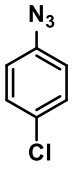
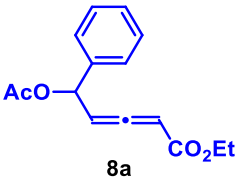
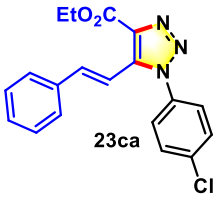
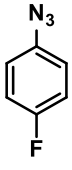
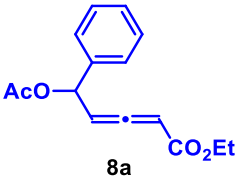
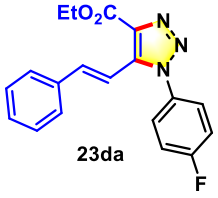
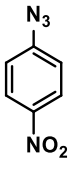
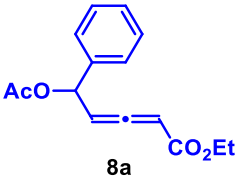
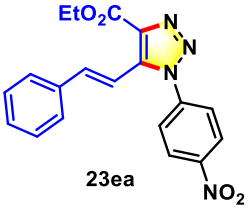
After having optimized conditions in hand (Table 10, entry 6), we explored the substrate scope concerning allenoate and azides to test the generality of this thermal cycloaddition. As shown in Table 11, different substituents such as OMe, Br, Cl, and CF_3 at the *p*-position of the phenyl ring of allenoate **12b-e**, provided the corresponding triazoles **23ab-ae** in 71-82% yields. Substituents at *meta*- and *ortho*-position of allenoates **12f** and **12g** exhibited good tolerance and target products **23af** and **23ag** were generated in high yields 79% and 73%. Likewise, this reaction smoothly proceeded with disubstituted allenoate **12h** to give **23ah** in 70% yield. The *δ*-thienyl substituted allenoate **12i** was also a good substrate in the thermal cycloaddition and delivered **23ai** in 73% yield. A similar trend was observed with **12j**, resulting in the formation of **23aj** in 71% yield. Next, we examined different aryl azides bearing electron-donating and withdrawing functionalities on the phenyl ring **14b-e**. Satisfyingly, all reactions worked well and furnished the fully-substituted triazoles **23ba-ea** in good to high yields 69-79%. This methodology was also compatible with aliphatic azide **14f**, providing triazoles **23fa-fg** and **23fi** in high yields (72-85% and 75%). The other possible product was not formed (Table 11). The chemical shifts of the olefinic -C*H*=C*H*- protons in most cases were close or merged with the aromatic protons in the ^{1}H NMR spectra. The relative configuration and structure of all compounds is corroborated by the X-ray crystallographic data on **23fi** (Figure 10).

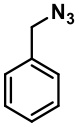
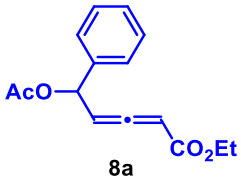
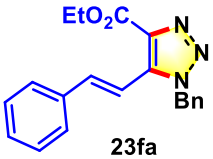
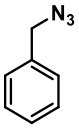
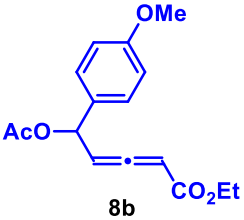
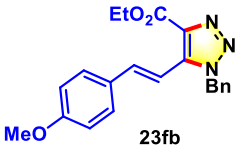
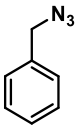
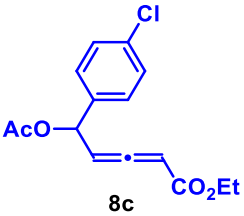
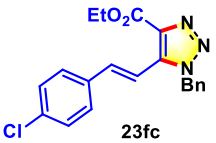
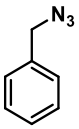
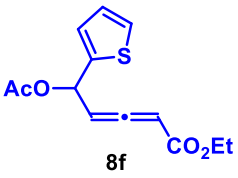
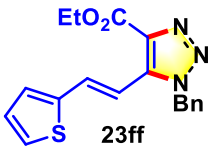
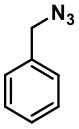
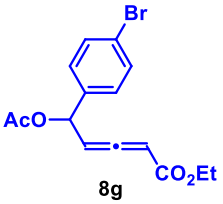
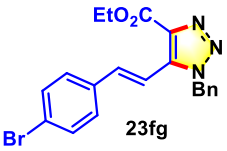
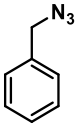
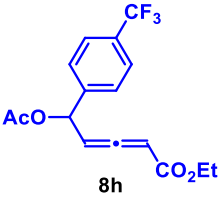
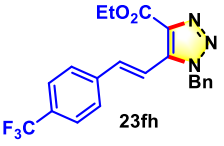
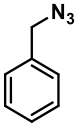
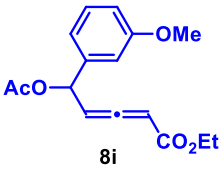
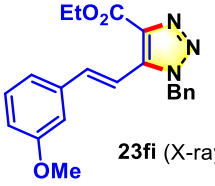
Table 11. Substrate scope for the reaction of aryl azides with *δ*-acetoxy allenoates

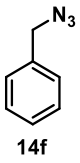
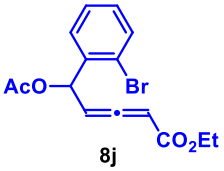
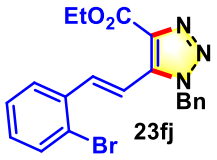


Entry	2-Sulfonamido indole	*δ*-Acetoxy allenoate	Triazoles	Yield[b] (%)

1	 14a	 8a	 23aa	82
2	 14a	 8b	 23ab	77
3	 14a	 8c	 23ac	73
4	 14a	 8f	 23af	73
5	 14a	 8g	 23ag	75
6	 14a	 8h	 23ah	71
7	 14a	 8i	 23ai	79

8	 14a	 8j	 23aj	73
9	 14a	 8k	 23ak	70
10	 14a	 8l	 23al	71
11	 14b	 8a	 23ba	79
12	 14c	 8a	 23ca	73
13	 14d	 8a	 23da	70
14	 14e	 8a	 23ea	69

15	 14f	 8a	 23fa	85
16	 14f	 8b	 23fb	80
17	 14f	 8c	 23fc	76
18	 14f	 8f	 23ff	75
19	 14f	 8g	 23fg	79
20	 14f	 8h	 23fh	72
21	 14f	 8i	 **23fi** (X-ray)	82

22	 14f	 8j	 23fj	74

[a]Reaction conditions: **14a-f** (1.5 mmol) and **8a-j** (0.50 mmol) in DMF (2.0 mL) at 70 [o]C (oil bath). [b]Isolated yield.

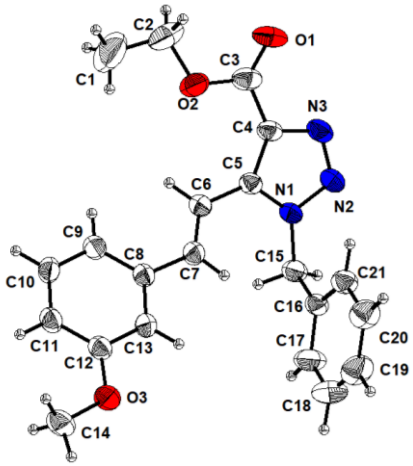
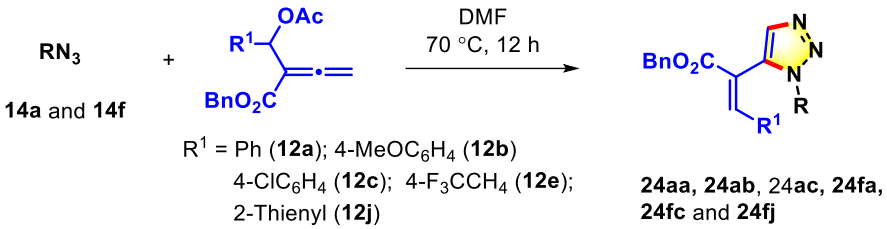


Figure 10. Molecular structure of compound **23fi** (CCDC 2097131). Selected bond distances: N1-N2 1.358(2), N2-N3 1.298(3), N3-C4 1.364(3), N1-C5 1.356(3), C4-C5 1.379(3), C5-C6 1.455(3), C6-C7 1.319(3) Å.

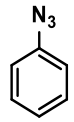
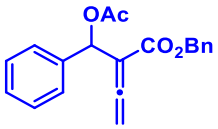
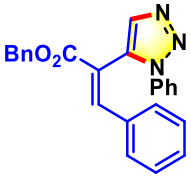
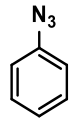
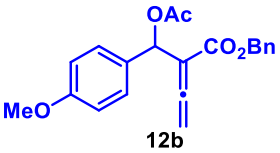
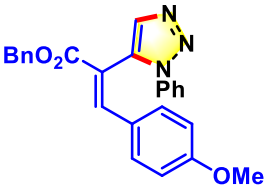
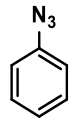
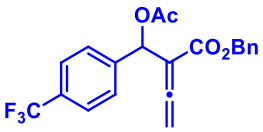
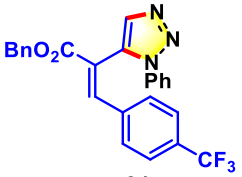
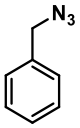
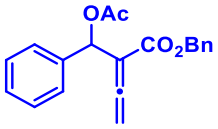
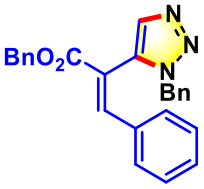
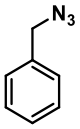
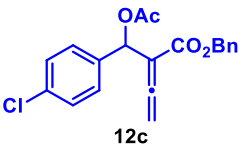
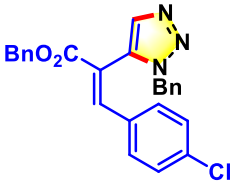
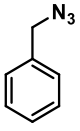
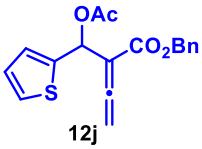
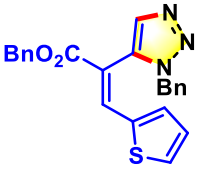
Inspired by the results achieved with *δ*-acetoxy allenoate, we conducted similar thermal (3 + 2) cycloaddition reaction using *β′*-acetoxy allenoate as shown in Table 12. To this end, we examined the reaction between **12a** and **14a** using standard reaction conditions (Table 10, entry 6). In this case, we isolated product **24aa** in high yield 71% and assigned it as 1,5-disubstituted 1,2,3-triazole using spectroscopic data; assignment of relative configuration of -CO_2Bn and R^1 is tentative at the moment. Other *β′*-acetoxy allenoates **12b** and **12c** also delivered triazole motifs **24ab** and **24ac** with **14a** in acceptable yields 69% and 67%. Similarly, **14f** reacted nicely with **12a**, **12c**, and **12e** to deliver corresponding triazoles **24fa**, **24fd**, and **24fe** in 76%, 72%, and 64% yields, respectively.

Table 12. Substrate scope for the reaction of aryl azides with *β'*-acetoxy allenoates



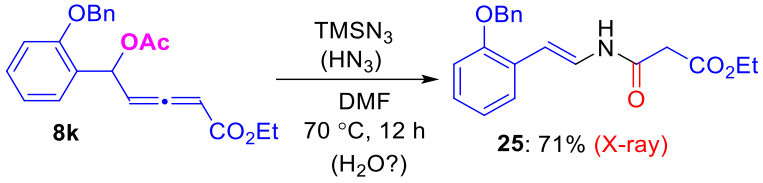
R^1 = Ph (**12a**); 4-$MeOC_6H_4$ (**12b**)
4-ClC_6H_4 (**12c**); 4-F_3CCH_4 (**12e**);
2-Thienyl (**12j**)

24aa, 24ab, 24**ac, 24fa, 24fc** and **24fj**

Entry	Azides	β'-Acetoxy Allenoate	1,2,3-Triazole	Yield[b] (%)
1	 **14a**	 **12a**	 **24aa**	71
2	 **14a**	 **12b**	 **24ab**	69
3	 **14a**	 **12e**	 **24ae**	67
4	 **14f**	 **12a**	 **24fa**	76
5	 **14f**	 **12c**	 **24fc**	72
6	 **14f**	 **12j**	 **24fj**	64

[a]Reaction conditions: **14a** and **14f** (1.5 mmol) and **12a-c, 12e, 12j** (0.50 mmol) in DMF (2.0 mL) at 70 °C (oil bath). [b]Isolated yield.

Next, we examined a reaction between trimethylsilyl azide and δ-acetoxy allenoate (**8k**) to test whether this will give the cycloaddition product or not (Scheme 11). Interestingly, we obtained nitrogen inserted product **25** (X-ray, Figure 11) *via* elimination of nitrogen molecule, possibly due to the presence of adventitious moisture. Such an observation has been made only in a gold catalyzed reaction of $TMSN_3$ with allene.[94] Since the present work is on cycloadditions, we have not studied this aspect further.



Scheme 11: Reaction of $TMSN_3$ with δ-acetoxy allenoate

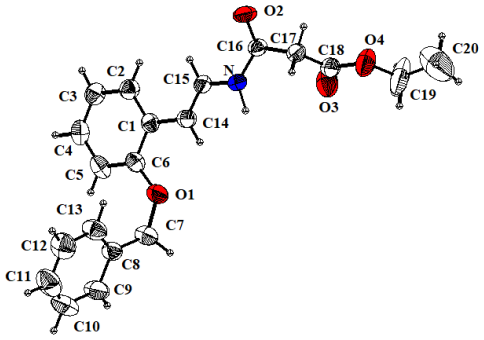
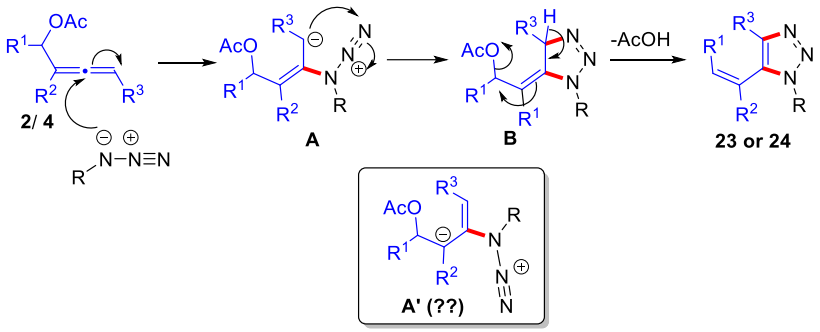


Figure 11. ORTEP of compound **25** (CCDC 2097132). Selected bond distances: C14-C15 1.315(6), C15-N 1.378(6), N-C16 1.361(6), C16-C17 1.481(7) Å.

2.4.3 *Proposed mechanistic pathway for (3 + 2) cycloaddition*

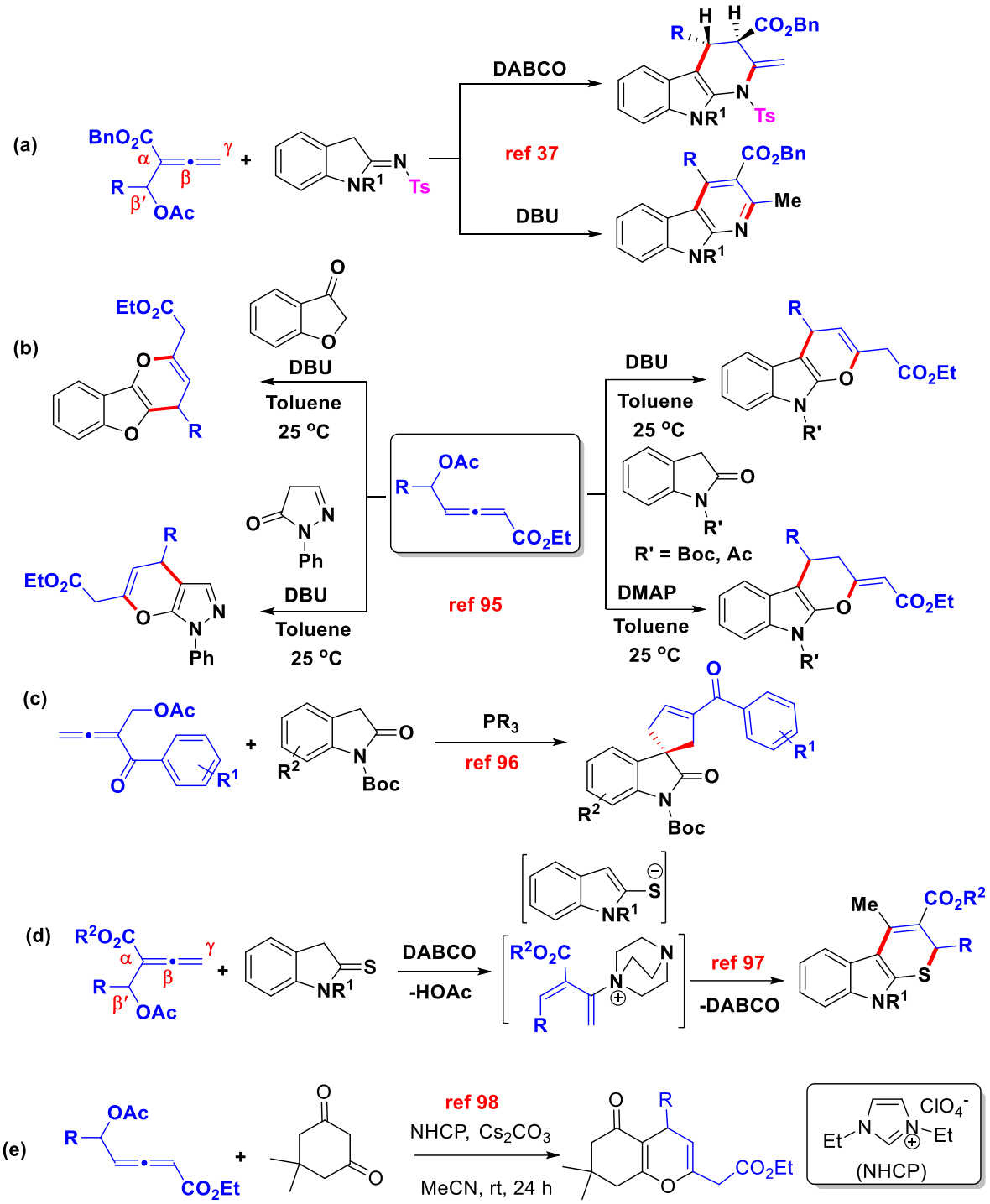
A plausible pathway for the formation of **23** and **24** is shown in Scheme 12. This cycloaddition is initiated by the addition of an aryl/ alkyl attached nitrogen atom at the β-position of allenoate in a chemoselective fashion to give zwitterionic intermediate **A**. Although an intermediate of type **A'** is feasible, at least in the case of β′-acetoxy allenoates, we have not observed the corresponding product. Next, **A** undergoes an intramolecular addition reaction to form cycloaddition adduct **B**. Finally, the elimination of acetic acid moiety from intermediate **B** results in the formation of **23/24.**



Scheme 12: Plausible pathway for the formation of **23** and **24**

2.5 DBU Catalyzed (3 + 3) Annulation of β′-Acetoxy Allenoates with Benzo-oxathiin-dioxide and Phenylthiazolone: Synthesis of Dihydropyrans

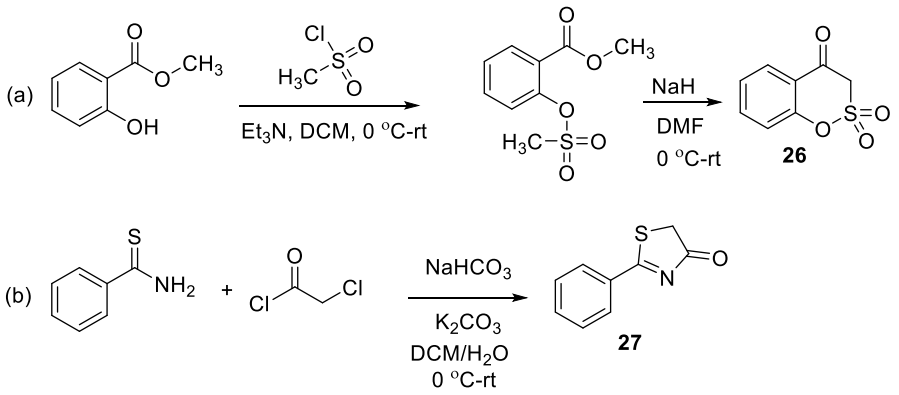
Annulations involving acetoxy allenoates and enolizable carbonyl/thiocarbonyl or imino substrates, catalyzed by Lewis bases, can be valuable tools to obtain pyrans/dihydropyrans/thiopyrans as well as spirocycles (Scheme 12).[37, 95-98] Most of the reactions reported to date take place *via* (3 +3) annulations. Since the work described earlier in this thesis involved cyclic sulfonyl imines, it was thought prudent to check the reactivity of bifunctional reagents possessing a sulfonyl group (or sulfur moiety in the ring) with enolizable carbonyls with acetoxy allenoates. Thus DBU catalyzed (3 + 3) annulations of *β′*-acetoxy allenoates with benzo-oxathiin-dioxide is explored in this section. The results are discussed below.



Scheme 12: Reactivity of acetoxy allenoates with enolizable substrates

2.5.1 (3 + 3) Annulation of β′-acetoxy allenoates with benzo-oxathiin-dioxide and phenylthiazolone: Optimization study

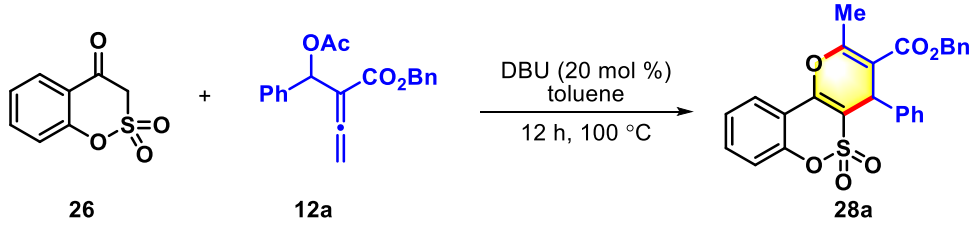
The precursors, enolizable carbonyls **26-27** with sulfur as a part of the ring, were prepared by using literature procedures (Scheme 13).[99,100]



Scheme 13: Synthesis of bisnucleophiles **26-27**

As shown in Table 13, we conducted the reaction of **26** (0.20 mmol) with **12a** (0.20 mmol) in toluene using DBU (20 mol %) at rt (25 °C). No reaction was observed after 12 h (entry 1). At 50 °C, compound **28a** was obtained in 30% yield (entry 2). The addition of 1.0 equiv K_2CO_3 was ineffective in improving the yield (entries 3). At 100 °C with a reaction time of 12 h the yield of **28a** improved to 76% (entry 4). Use of TBD, DABCO, DMAP and pyridine in place of DBU did not enhance the yield of **28a** (entry 5-8). We then screened the reaction in different solvents like MeCN, THF and DCE but they were not better than toluene (entries 9-11). Thus toluene was chosen as the solvent, yielding the anticipated products **28a**. No reaction occurred with Ph_3P as the catalyst (entry 12). Similar conditions were used for reaction between benzo-oxathiin-dioxide and *δ*-acetoxy allenoates, as well as that between phenylthiazolone *β′*-acetoxy allenoates.

Table 13: Optimization study for the formation of pyrano-oxathiines



Entry	Catalyst	Base	Solvent	Temperature (°C)	Yield[b] **28a**
1	DBU		PhMe	25	0
2	DBU		PhMe	50	30
3	DBU	K_2CO_3	PhMe	50	30
4	**DBU**		**PhMe**	**100**	**76**

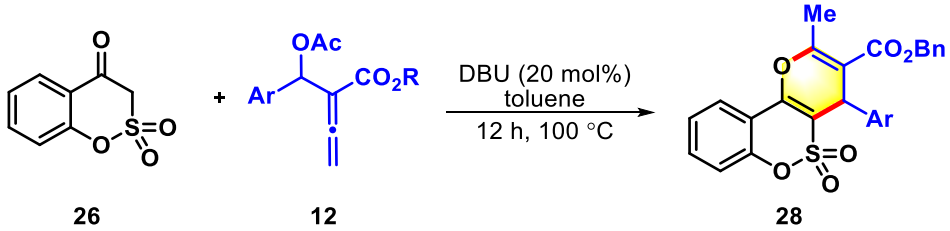
5	TBD	PhMe	100	68
6	DABCO	PhMe	100	64
7	DMAP	PhMe	100	60
8	Pyridine	PhMe	100	48
9	DBU	MeCN	100	65
10	DBU	THF	100	41
11	DBU	DCE	100	54
12	Ph_3P	PhMe	100	0

[a]Reaction conditions: **26** (0.20 mmol; 1.0 equiv), **12a** (0.20 mmol; 1.0 equiv), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 °C. [b]Isolated yield.

2.5.2 *(3 + 3) Annulation of β′-acetoxy allenoates with benzo-oxathiin-dioxide and phenylthiazolone: Substrate Scope*

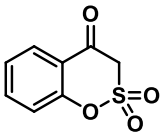
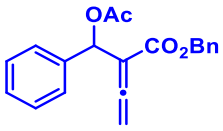
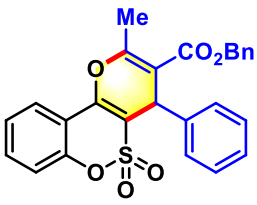
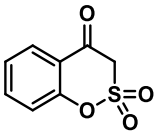
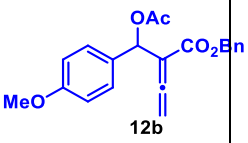
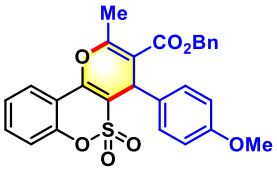
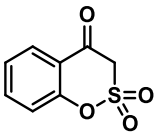
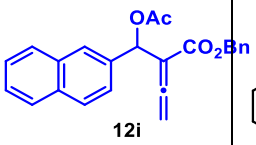
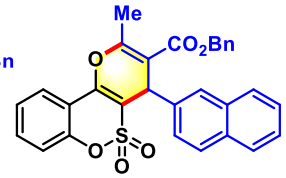
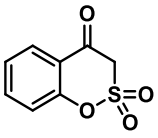
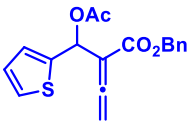
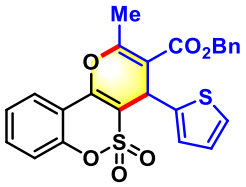
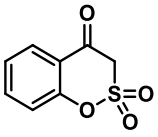
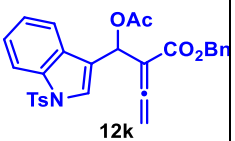
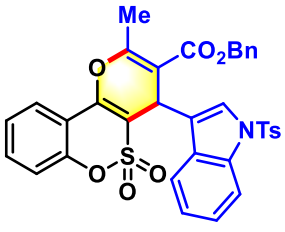
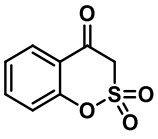
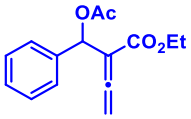
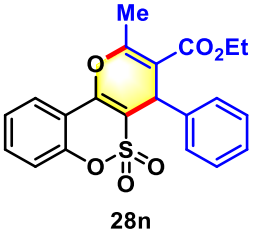
The *β′*-acetoxy allenoates having different functionalities (H, OMe, Cl,) at the *p*-position of the phenyl ring **12a-c** reacted well with benzo-oxathiin-dioxide **26** and afforded pyrano-oxathiines **28a-c** in 69-76% yield (Table 14). Polycyclic aromatic and heterocyclic functionalities on the allenoates **12i-k** did not hamper the reactivity in giving the (3 + 3) annulated products **28i-k**. As expected, the *β′*-acetoxy allenoate **12n** with ethyl group also afforded the product **28n** in good yield (71%). These compounds show a characteristic C*H*$_3$ peak at δ ~2.6 and C*H*(pyrano) peak at δ ~5.3 in the ^{1}H NMR spectra; correspondingly, the ^{13}C{^{1}H} peaks are observed in the δ range 18-19 and 32-36 ppm, respectively. A single crystal X-ray structure determination for compound **28a** (Figure 13) confirmed the structural assignment.

Table 14: Substrate scope for the formation of pyrano-oxathiines from *β′*-acetoxy allenoates



26 12 28

Entry	Benzo-oxathiin-dioxide	*β′*-Acetoxy Allenoate	Pyrano-oxathiines	Yield (%)[b]

1	 **26**	 **12a**	 **28a** (X-ray)	76
2	 **26**	 **12b**	 **28b**	84
3	 **26**	 **12i**	 **28i**	77
4	 **26**	 **12j**	 **28j**	69
5	 **26**	 **12k**	 **28k**	65
6	 **26**	 **12n**	 **28n**	71

[a]Reaction conditions: **26** (0.20 mmol; 1.0 equiv), **12a-c, 12i-k, 12n** (0.20 mmol; 1.0 equiv), DBU(0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 °C. [b]Isolated yield.

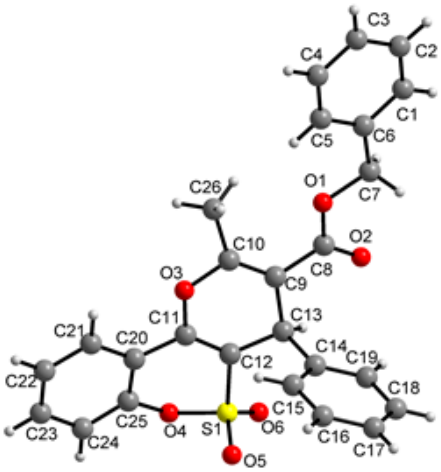
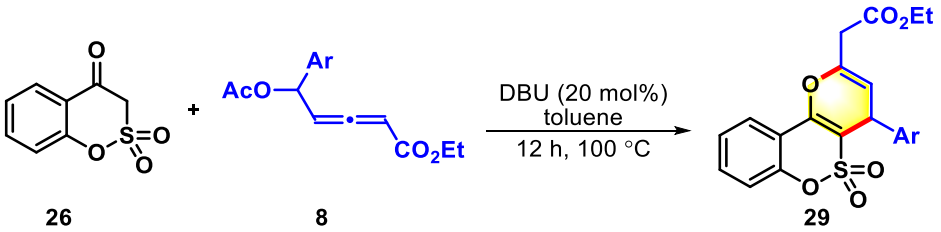
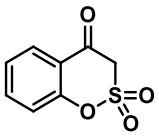
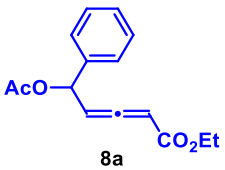
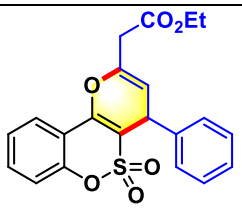


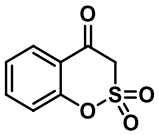
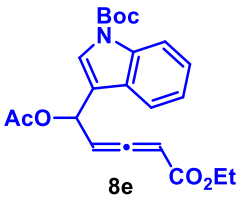
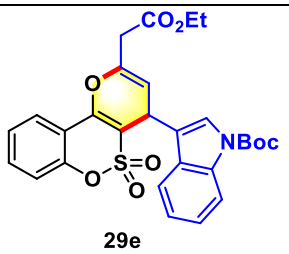
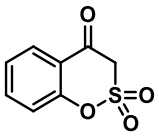
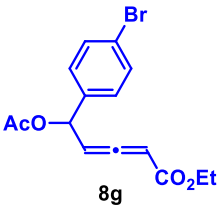
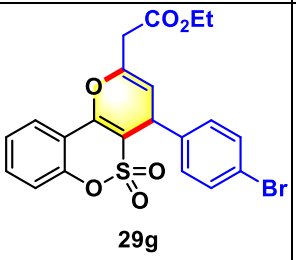
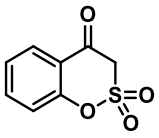
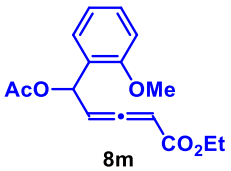
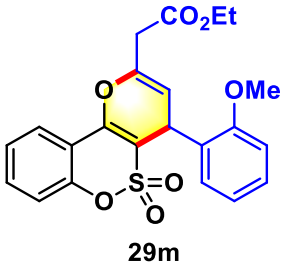
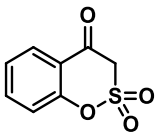
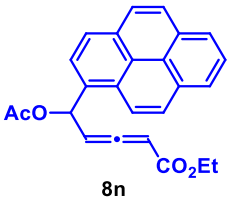
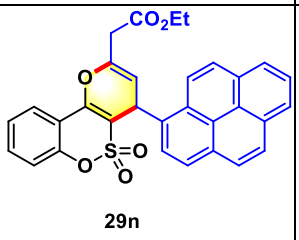
Figure 12: Molecular structure of compound **28a** (unpublished). Selected bond parameters (dihydropyran ring): O3-C10 1.387(2), C10-C9 1.337(3), C9-C13 1.524(2), C13-C12 1.508(2), C12-C11 1.331(2), C11-O3 1.364(2) Å

By following the above procedure, we could synthesize pyrano-oxathiines **29a, 29e, 29g**, **29m**, and **29n** from the corresponding δ-acetoxy allenoates **8a**, **8e**, **8g**, **8m** and **8n** ((Table 15). However, in these cases purification posed some problems and we could achieve a purity of only 90-95% for oxathiines **29a, 29e, 29g**, and **29n**.

Table 15. Substrate scope pyrano-oxathiines acetate using *δ*-acetoxy allenoates[a]



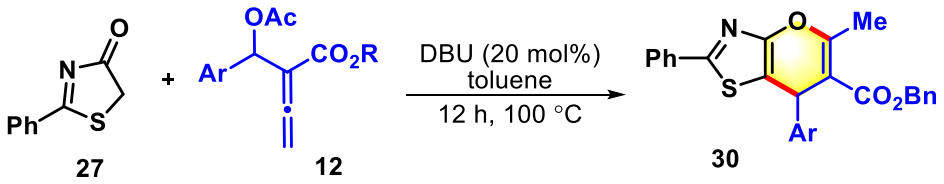
Entry	Benzo-oxathiin-dioxide	*δ*-Acetoxy Allenoate	Pyrano-oxathiines	Yield (%)[b]
1	 26	 8a	 29a	71

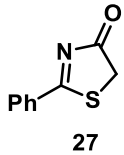
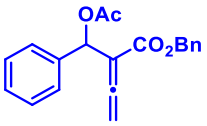
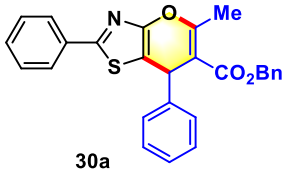
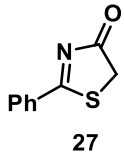
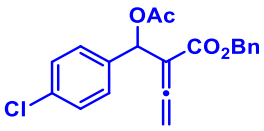
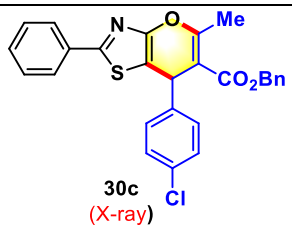
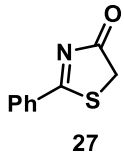
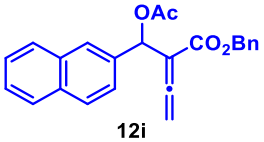
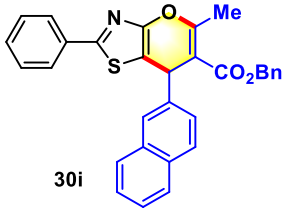
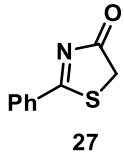
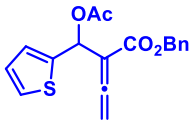
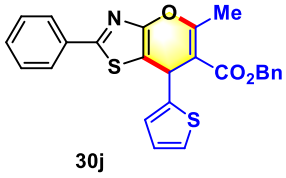
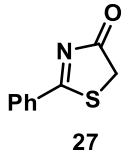
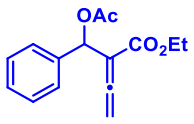
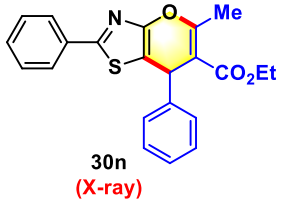
2	 26	 8e	 29e	63
3	 26	 8g	 29g	72
4	 26	 8m	 29m	72
5	 26	 8n	 29n	71

[a]Reaction conditions: **26** (0.20 mmol; 1.0 equiv), **8a, 8e, 8g, 8m** and **8n** (0.20 mmol; 1.0 equiv), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 ºC. [b]Isolated yield; Purity was ca 95% for **29a, 29e, 29g** and **29n**.

In continuation of the above studies, we conducted the reaction of phenylthiazolone **27** with *β′*-acetoxy allenoates **12a**, **12c**, **12i**, **12j** and **12n** pleasingly, this reaction also worked well to afford the products **30a**, **30c**, **30i** (purity ca 95%) **30j** and **30n** were obtained in decent yields (Table 16). The annulated product **30c** was characterized by single crystal X-ray diffraction (Figure 13). Currently this work is still being pursued to obtain more examples.

Table 16. Substrate scope for the synthesis of fused dihydropyrans from phenylthiazolone and β′-acetoxy allenoates



Entry	phenylthiazolone	β′-Acetoxy Allenoate	Pyrano-thiazole-carboxylate	Yield (%)[b]
1	 27	 12a	 30a	78
2	 27	 12c	 30c (X-ray)	75
3	 27	 12i	 30i	72
4	 27	 12j	 30j	79
5	 27	 12n	 30n (X-ray)	81

[a]Reaction conditions: **27** (0.20 mmol; 1.0 equiv), **12a**, **12c**, **12i, 12j** or **12n** (0.20 mmol; 1.0 equiv), DBU (0.04 mmol; 0.2 equiv.) in toluene (2.0 mL; 0.1 M) at 100 °C. [b]Isolated yield. [c]Purity ca 95%.

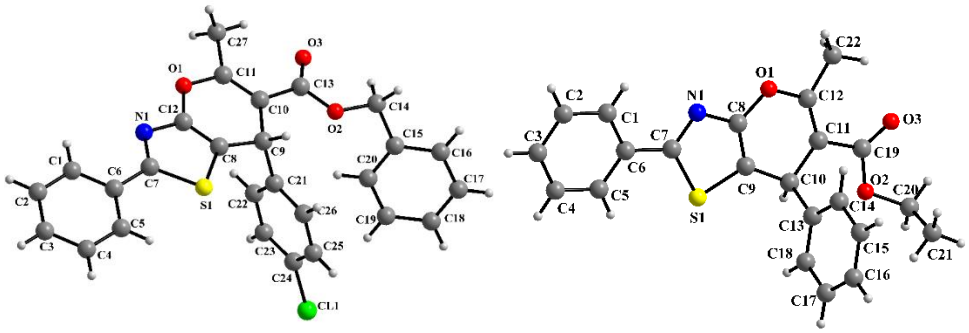
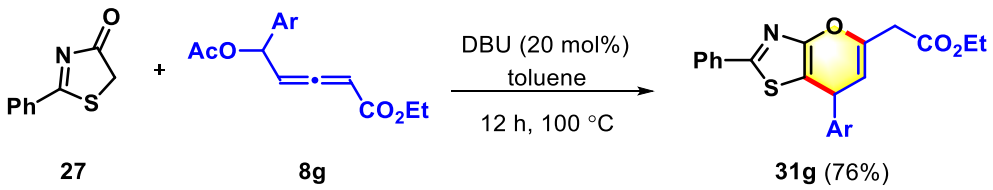


Figure 13: Molecular structure of compound **30c** (left, unpublished) and **30n** (right unpublished). Selected bond parameters (dihydropyran ring): **30c** O1-C11 1.372(2), C11-C10 1.341(3), C10-C9 1.527(3), C9-C8 1.500(2), C8-C12 1.338(3), C12-O1 1.372(2) Å. **30n** O1-C12 1.375(4), C12-C11 1.339(5), C11-C10 1.527(5), C10-C9 1.491(5), C9-C8 1.347(5), C8-O1 1.374(4) Å.

We utilized the above protocol for the reaction of δ-acetoxy allenoate **8g** phenylthiazolone **27** pleasingly, this reaction also worked well to afford the products **31g** in decent yields (Scheme 14). Currently this work is still being pursued to obtain more examples.

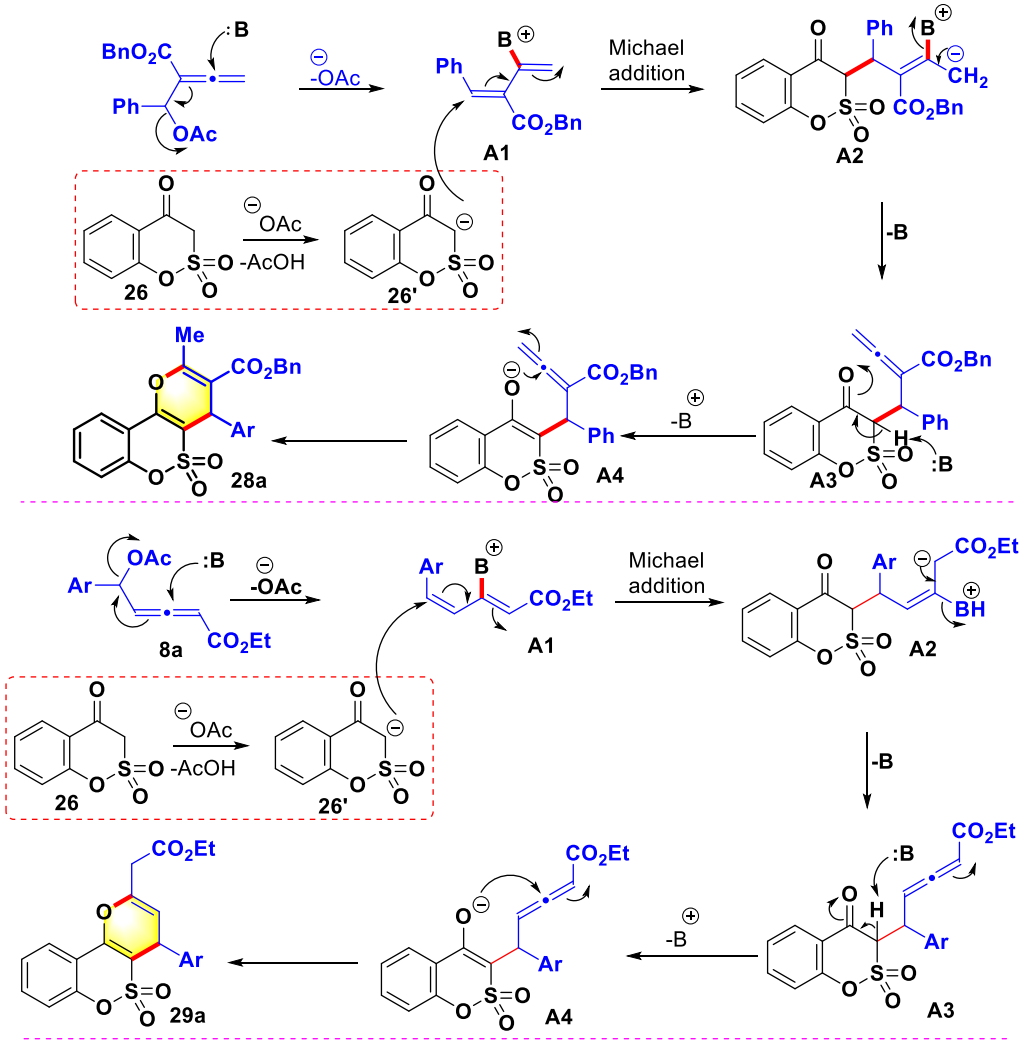


27 **8g** **31g** (76%)

Scheme 14: Synthesis of compound **31g**.

2.5.3 Possible mechanistic pathways for the formation of pyrano-oxathiines

Plausible pathways for the (3 + 3) annulations are shown in Scheme 15. These hetero-annulations may be initiated through the formation of diene-ammonium intermediate **A1** *via* the addition-elimination process between Lewis base (tertiary amine) and allenoates **8a** and **12a** {**A1**: B = DBU}. Next, the addition of **26'** or **27'** (*in situ* generated from **26** or **27**) to **A1** at the *β*-carbon gives zwitterionic intermediate **A2** {**A2**: B = DBU}. Then the base will be eliminated leading to the formation of allenic intermediate **A3**. 1,3-Proton shift followed by cyclization will occur to form the final compounds **28a** and **30a**. In the case of *δ*-acetoxy allenoates, addition of **26′** to **A1** leads to product **29a** *via* cyclization.



Scheme 15: Plausible mechanistic pathways for the formation of **28a** and **29a**

Summary

(1) A new Lewis base switched (3 + 3) and (4 + 2) annulation protocol involving *N*-sulfonyl ketimines and δ-acetoxy allenoates under metal-free conditions to generate functional pyridinyl acetates and terphenyls, respectively, has been disclosed. While in the amine mediated (3 + 3) annulation, *N*-sulfonyl ketimines act as C/N donors and afford 2-pyridyl acetates *via* double $S_N2'-S_N2'$ attack followed by *aza*-Michael addition and SO_2 elimination/aromatization, in the Ph_3P catalyzed (4 + 2) annulation, *N*-sulfonyl ketimines act as C/C donors and deliver terphenyl scaffolds *via* a S_N2'-attack followed by Michael addition, intramolecular direct vinylogous Mannich coupling and C-N bond cleavage/aromatization.

(2) A valuable Lewis base catalyzed scalable synthetic protocol involving *β′*-acetoxy allenoates and isothiazole dioxide to generate functionalized 1,4-dihydropyridine and teraryl scaffolds in good to excellent yields has been developed. Thus Lewis base dependent (3 + 3) and (4 + 2) annulations of *β′*-acetoxy allenoates with *N*-sulfonyl ketimines offer *m*-teraryl and fused dihydropyridines with varying substituents depending on the tertiary amine as well as subtle changes in the reaction conditions. The triazabicyclodecene (TBD)-catalyzed (3 + 3) annulation involves 1,2-elimination followed by 6-*endo*-dig cyclization as key steps in delivering fused hydropyridines. The same reactants under DMAP catalysis offer *m*-teraryls *via* Mannich coupling, rather than 1,2-elimination followed by C-N bond cleavage/ aromatization. Many of the itnermediates were identified by in-process HRMS studies.

(3) Regio-and stereo-selective (3 + 2) thermal cycloaddition involving δ/β′-acetoxy allenoates and azides for the construction of 1,4,5-tri/ 1,5-di-substituted-1,2,3-triazoles has been developed under metal-free conditions. In this cycloaddition, the aryl attached nitrogen atom chemoselectively attacks the β-carbon of acetoxy allenoates and delivers essentially the *E*-isomer in all the cases.

(4) A new DBU catalyzed (3 + 3) annulation reaction of enolizable carbonyls, benzo-oxathiin-dioxide or phenylthiazolone, with δ/β′-acetoxy allenoates that furnishes a novel class of dihydropyrans has been discovered.

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.[101]

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

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

3.1 Synthesis of Starting Materials

3.1.1 Synthesis of cyclic N-sulfonyl ketimines 3a-d, 3e and 5a-c: General procedure

The treatment of sulfamoyl chloride $(NH_2)SO_2Cl$, prepared *in situ* from a mixture of $ClSO_2NCO/HCO_2H$) with a-hydroxyl ketone or *ortho*-hydroxy aryl ketone **1** using a base to afford *O*-sulfamyl intermediate **2**, which is then cyclized under heating conditions to produce *N*-sulfonylketimine **3**.[81] The addition of alkylmagnesium bromide to saccharin **4** leads to *N*-sulfonyl ketimine **5**.[82]

3.1.2 Synthesis of δ-acetoxy allenoates 8a-n: General procedure

Following a literature procedure,[83] to a solution of ethyl 5-hydroxy-5-(3-nitrophenyl)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.

3.1.3 Synthesis of allenoates 6a-d, and 6g-i: General procedure

A literature procedure was followed.[84] To a solution of benzyl 2-(hydroxy-4-aryl/heteroaryl)buta-2,3-dienoate (10.0 mmol, 1.0 equiv) in dry dichloromethane (20 mL) at -5 °C was added pyridine (15.0 mmol, 1.5 equiv), and then the mixture stirred for 5.0 min at the same temperature. After that, acetyl chloride (15.0 mmol, 1.5 equiv) was slowly added into the mixture over 5 min, and the contents were stirred for 45 min. After completion of the reaction (TLC), the aqueous layer was extracted with dichloromethane (3 × 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 purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as the eluent.

3.1.4 Synthesis of azides 14a-f: General procedure

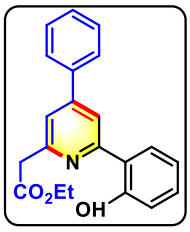
Aryl azides **14a-f** were prepared by following a literature procedure.[85] One of the anilines **13a-f** (20 mmol) was added to conc. HCl (20 mL) at 0 °C. To this, a solution of $NaNO_2$ (1.2 equiv) in water was added portion-wise, and the contents were stirred at 0 °C for 2 h. Then a solution of NaN_3 (1.5 equiv) in water was added drop-wise at 0 °C and the reaction was stirred for 2 h and allowed to warm to room temperature. The aqueous layer was extracted twice with diethyl ether and the combined organic layer was washed with water, sodium bicarbonate, and brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to obtain the corresponding pure aryl azide.

3.2 Synthesis of Compounds 15aa-ea: Representative Procedure for 15aa

A Schlenk tube was charged with cyclic sulfamidate imine **3a** (39.0 mg, 0.20 mmol), *δ*-acetoxy allenoate **8a** (62.4 mg, 0.24 mmol), Na_2CO_3 (31.5 mg 0.30 mmol) and 1.5 mL of toluene. Subsequently, DBU (15.2 mg, 0.10 mmol) in toluene (1.5 mL) was added, and the mixture stirred at 50 °C for the 12 h, and reaction progress 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. Other compounds were prepared similarly using the same mmol quantities.

Compound 15aa



Yield: 53.0 mg (79%), White solid.

Mp: 100-102 °C.

IR (neat): ν_{max} 3438 (w), 3059, 2978, 1727, 1607, 1554, 1416, 1322, 1191, 1025, 746, 678 cm^{-1}

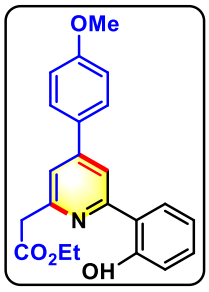
^1H NMR (500 MHz, $CDCl_3$): δ 13.98 (s, 1H), 8.00 (d, *J* = 1.0 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.70-7.67 (m, 2H), 7.54-7.43 (m, 3H), 7.43 (d, *J* = 1.5 Hz, 1H), 7.34-7.31 (m, 1H), 7.04 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.95-6.91 (m, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.93 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.0, 160.0, 158.2, 151.8, 151.2, 138.2, 131.7, 129.6, 129.3, 127.3, 126.5, 120.1, 119.1, 119.0, 118.8, 116.0, 61.6, 43.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{20}NO_3$ $[M + H]^+$ *m/z* 334.1438. Found 334.1439.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 15ab



Yield: 53.0 mg (73%), White solid.

Mp: 99-101 °C

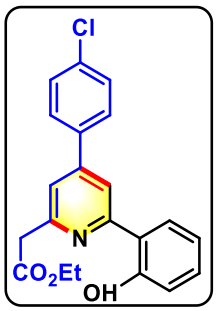
IR (neat): ν_{max} 3444 (w), 2928, 2835, 1723, 1605, 1508, 1410, 1325, 1173, 1033, 767, 655 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 14.03 (s, 1H), 7.96 (d, *J* = 0.5 Hz, 1H), 7.88 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.66-7.64 (m, 2H), 7.39 (d, *J* = 1.0 Hz, 1H), 7.33-7.29 (m, 1H), 7.04-7.02 (m, 3H), 6.94-6.91 (m, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.91 (s, 2H), 3.88 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.0, 161.0, 160.0, 158.0, 151.7, 150.6, 131.6, 130.4, 128.5, 126.5, 119.5, 119.2, 118.9, 118.7, 115.3, 114.7, 61.5, 55.5, 43.4, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_4$ $[M + H]^+$ *m/z* 364.1543. Found 364.1545.

Compound 15ac



Yield: 59.0 mg (80%), White solid

Mp: 149-151 °C

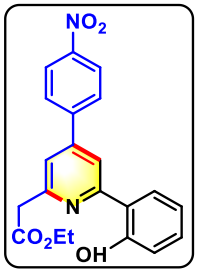
IR (neat): ν_{max} 3441 (w), 2974, 2942, 1726, 1651, 1496, 1186, 1026, 794, 648 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 13.87 (s, 1H), 7.93 (d, *J* = 1.0 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.62-7.60 (m, 2H), 7.50-7.47 (m, 2H), 7.38 (d, *J* = 1.5 Hz, 1H), 7.34-7.30 (m, 1H), 7.04 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 6.94-6.91 (m, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.92 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.9, 160.0, 158.3, 152.1, 149.9, 136.7, 135.9, 131.8, 129.6, 128.6, 126.5, 119.8, 119.0, 118.8, 115.7, 61.6, 43.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{19}ClNO_3$ $[M + H]^+$ *m/z* 368.1048, 370.1018. Found 368.1049, 370.1019.

Compound 15ad



Yield: 54.0 mg (71%), Light brown solid,

Mp: 176-178 °C

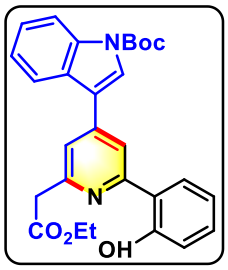
IR (neat): ν_{max} 3444 (w), 2986, 2919, 2846, 1729, 1610, 1594, 1444, 1187, 1022, 749, 688 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 13.69 (s, 1H), 8.40-8.37 (m, 2H), 7.99 (d, *J* = 1.0 Hz, 1H), 7.88-7.83 (m, 3H), 7.45 (d, *J* = 1.0 Hz, 1H), 7.36-7.33 (m, 1H), 7.05 (dd, J_1 = 8.5, J_2 = 1.0 Hz, 1H), 6.96-6.93 (m, 1H), 4.25 (q, *J* = 7.0 Hz, 2H) 3.97 (s, 2H), 1.32 (t, *J* = 7.0 Hz, 3H) ppm

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.8, 160.0, 158.7, 152.6, 148.8, 148.6, 144.6, 132.2, 128.4, 126.6, 124.6, 120.1, 119.2, 119.0, 118.8, 116.2, 61.7, 43.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{19}N_2O_5$ $[M + H]^+$ *m/z* 379.1288. Found 379.1289.

Compound 15ae



Yield: 63.2 mg (67%), White solid

Mp: 131-133 °C

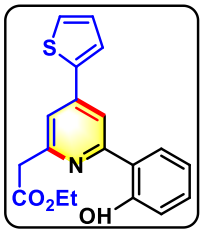
IR (neat): ν_{max} 3059, 2974, 2923, 2856, 1730, 1608, 1453, 1369, 1152, 1061, 761, 645 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): ^1H NMR (500 MHz, $CDCl_3$): δ 13.94 (s, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 8.07 (s, 1H), 7.94 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 2H), 7.49 (s, 1H), 7.45-7.42 (m, 1H), 7.39-7.32 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.95-6.92 (m, 1H), 4.26 (q, *J* = 7.0 Hz, 2H), 3.94 (s, 2H), 1.73 (s, 9H), 1.32 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.0, 160.1, 158.3, 151.9, 149.5, 144.5, 136.2, 131.7, 128.0, 126.5, 125.4, 124.9, 123.7, 120.5, 119.7, 119.5, 119.0, 118.8, 116.3, 115.9, 84.8, 61.6, 43.5, 28.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{28}H_{29}N_2O_5$ $[M + H]^+$ *m/z* 473.2071. Found 473.2074.

Compound 15af



Yield: 46.7 mg (69%) White solid

Mp: 144-146 °C

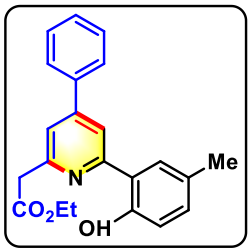
IR (neat): ν_{max} 3430 (w), 3069, 2983, 2904, 1726, 1607, 1555, 1432, 1201, 1178, 755, 621 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 13.85 (s, 1H), 7.96 (d, *J* = 1.0 Hz, 1H), 7.85 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.59-7.58 (m, 1H), 7.47 (dd, J_1 = 5.0, J_2 = 1.0 Hz, 1H), 7.41-7.40 (m, 1H), 7.34-7.30 (m, 1H), 7.17 (dd, J_1 = 5.0, J_2 = 3.5 Hz, 1H), 7.03 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.95-6.92 (m, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.89 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.9, 160.1, 158.4, 152.1, 144.0, 141.0, 131.8, 128.7, 127.9, 126.5, 126.2, 119.0 (2 s), 118.8, 118.2, 114.1, 61.6, 43.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{18}NO_3S$ $[M + H]^+$: *m/z* 340.1002. Found 340.1006.

Compound 15ba



Yield: 56.2 mg (81%), White solid.

Mp: 101-103 °C

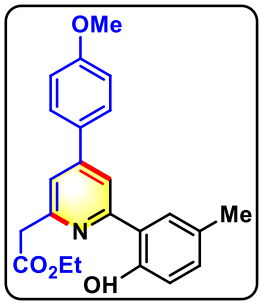
IR (neat): ν_{max} 3447 (w), 3034, 2983, 2903, 1722, 1601, 1545, 1372, 1215, 1023, 761, 691 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 13.73 (s, 1H), 7.97 (s, 1H), 7.69 (d, *J* = 7.0 Hz, 2H), 7.65 (s, 1H), 7.54-7.47 (m, 3H), 7.41 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 1H), 6.95 (d, *J* = 8.5 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.92 (s, 2H), 2.35 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 170.0, 158.2, 157.7, 151.8, 151.1, 138.3, 132.5, 129.5, 129.3, 127.9, 127.3, 126.6, 120.0, 118.7, 118.5, 115.9, 61.5, 43.4, 20.9, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_3$ $[M + H]^+$ *m/z* 348.1594. Found 348.1593.

Compound 15bb



Yield: 56.5 mg (75%), White solid.

Mp: 113-115 °C

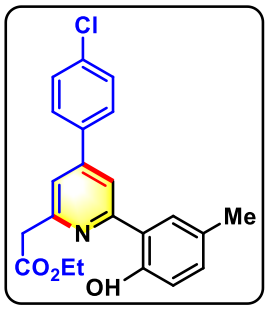
IR (neat): ν_{max} 3434 (w), 2996, 2913, 2839, 1722, 1604, 1515, 1496, 1180, 1030, 766, 671 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 13.77 (s, 1H), 7.94 (s, 1H), 7.67-7.65 (m, 3H), 7.37 (s, 1H), 7.12 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.05-7.02 (m, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.90 (s, 2H), 3.88 (s, 3H), 2.35 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 170.1, 160.9, 158.1, 157.8, 151.7, 150.5, 132.4, 130.5, 128.6, 127.8, 126.6, 119.4, 118.8, 118.5, 115.2, 114.7, 61.5, 55.6, 43.5, 20.9, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{24}NO_4$ $[M + H]^+$ *m/z* 378.1700. Found 378.1703.

Compound 15bc



Yield: 63.2 mg (83%), White solid.

Mp: 130-132 °C

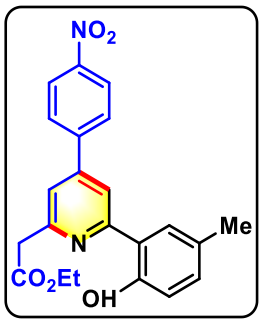
IR (neat): ν_{max} 3426 (w), 2978, 2867, 1723, 1606, 1497, 1180, 1029, 772, 664 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 13.60 (s, 1H), 7.92 (s, 1H), 7.63-7.61 (m, 3H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.37 (s, 1H), 7.14-7.12 (m, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.91 (s, 2H), 2.35 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.9, 158.4, 157.7, 152.1, 149.8, 136.7, 135.8, 132.7, 129.5, 128.6, 127.9, 126.6, 119.7, 118.5 (2 s), 115.7, 61.6, 43.4, 20.9, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}ClNO_3$ $[M + H]^+$ *m/z* 382.1204, 384.1175. Found 382.1205, 384.1178.

Compound 15bd



Yield: 56.4 mg (72%), Pale yellow solid

Mp: 179-181 °C

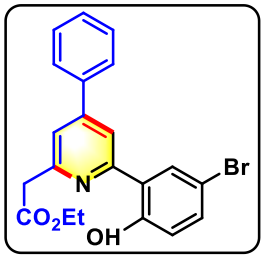
IR (neat): ν_{max} 3428 (w), 2987, 2920, 2849, 1723, 1609, 1500, 1193, 791, 688 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 13.45 (s, 1H), 8.40-8.38 (m, 2H), 7.98 (d, *J* = 1.0 Hz, 1H), 7.86-7.85 (m, 2H), 7.64 (d, *J* = 1.5 Hz, 1H), 7.44 (d, *J* = 1.0 Hz, 1H), 7.16 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 4.25 (q, *J* = 7.0 Hz, 2H) 3.96 (s, 2H), 2.36 (s, 3H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 169.8, 158.8, 157.8, 152.6, 148.8, 148.6, 144.7, 133.1, 128.5, 128.2, 126.6, 124.6, 119.9, 118.7, 118.4, 116.2, 61.7, 43.4, 20.9, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}N_2O_5$ $[M + H]^+$ *m/z* 393.1445. Found 393.1446.

Compound 15ca



Yield: 61.0 mg (74%), White solid.

Mp: 137-139 °C

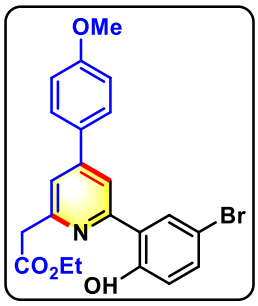
IR (neat): ν_{max} 3434 (w), 3061, 2972, 2930, 1729, 1603, 1543, 1475, 1153, 1027, 760, 683 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 14.02 (s, 1H), 7.95 (s, 1H), 7.91 (s, 1H), 7.68 (d, *J* = 7.0 Hz, 2H), 7.54-7.48 (m, 3H), 7.46 (s, 1H), 7.38 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.93 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.8, 159.1, 156.7, 152.0, 151.5, 137.8, 134.2, 129.7, 129.4, 128.9, 127.3, 120.7, 120.6, 116.0, 110.7, 61.6, 43.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{19}BrNO_3$ $[M + H]^+$ *m/z* 412.0543, 414.0522. Found 412.0539, 414.0523.

Compound 15cb



Yield: 59.1 mg (67%), White solid.

Mp: 149-151 °C

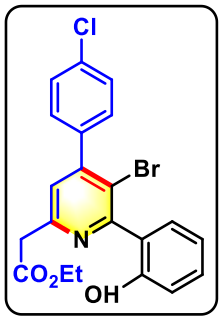
IR (neat): ν_{max} 3444 (w), 3093, 2977, 2931, 1726, 1602, 1516, 1389, 1172, 1028, 769, 672 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 14.05 (s, 1H), 7.95 (d, *J* = 2.4 Hz, 1H), 7.88 (d, *J* = 1.2 Hz, 1H), 7.67-7.63 (m, 2H), 7.42 (d, *J* = 1.2 Hz, 1H), 7.37 (dd, J_1 = 8.8, J_2 = 2.4 Hz, 1H), 7.06-7.02 (m, 2H), 6.92 (d, *J* = 8.8 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.91 (s, 2H), 3.89 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.9, 161.1, 159.1, 156.6, 151.8, 150.9, 134.1, 130.0, 128.9, 128.6, 120.8, 120.6, 120.1, 115.3, 114.8, 110.7, 61.6, 55.6, 43.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}BrNO_4$ $[M + H]^+$ *m/z* 442.0648, 444.0628. Found 442.0648, 444.0631.

Compound 15cc



Yield: 62.3 mg (70%), White solid.

Mp: 145-147 °C

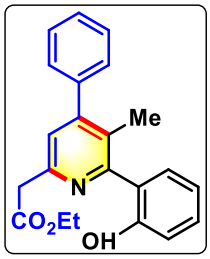
IR (neat): ν_{max} 3429 (w), 2986, 2900, 1722, 1607, 1472, 1290, 1165, 1027, 823, 767, 663 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 13.88 (s, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 7.87 (d, *J* = 1.0 Hz, 1H), 7.63-7.61 (m, 2H), 7.52-7.49 (m, 2H), 7.42 (d, *J* = 1.0 Hz, 1H), 7.38 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 4.24 (q, *J* = 7.0 Hz, 2H), 3.92 (s, 2H), 1.31 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 169.8, 159.1, 157.0, 152.3, 150.3, 136.3, 136.1, 134.4, 129.7, 129.0, 128.7, 120.7_3, 120.6_6, 120.5, 115.8, 110.8, 61.7, 43.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{17}ClBrNNaO_3$ $[M + Na]^+$ *m/z* 467.9973, 469.9952, 471.9948. Found 467.9974, 469.9955, 471.9930.

Compound 15da



Yield: 52.0 mg (75%), Gummy liquid.

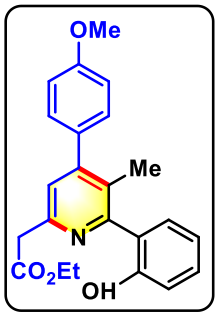
IR (neat): ν_{max} 3423 (w), 3063, 2983, 2935, 2853, 1731, 1595, 1420, 1151, 1032, 733, 700 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): ^1H NMR (500 MHz, $CDCl_3$): δ 11.08 (s, 1H), 7.52 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.49-7.46 (m, 2H), 7.44-7.41 (m, 1H), 7.38-7.36 (m, 2H), 7.30-7.27 (m, 1H), 7.13 (s, 1H), 7.09 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 6.94-6.90 (m, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 3.87 (s, 2H), 2.34 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 170.4, 157.2, 157.1, 154.2, 149.5, 139.8, 130.6, 130.4, 128.8, 128.7, 128.4, 128.2, 123.3, 122.8, 118.7, 118.2, 61.5, 42.8, 19.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_3$ $[M + H]^+$ *m/z* 348.1594. Found 348.1597.

Compound 15db



Yield: 54.3 mg (72%), White solid.

Mp: 114-116 °C

IR (neat): ν_{max} 3441 (w), 2958, 2838, 1727, 1609, 1513, 1425, 1173, 1029, 836, 762, 654 cm^{-1}.

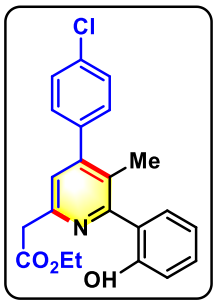
^{1}H NMR (500 MHz, $CDCl_3$): ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.17 (s, 1H), 7.52 (d, *J* = 7.5 Hz, 1H), 7.32-7.27 (m, 3H), 7.12 (s, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.93-6.90 (m, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 3.87-3.86 (m, 5H), 2.36 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 170.5, 159.8, 157.2 (2 s), 153.9, 149.4, 132.1, 130.5 (2 s), 30.2, 128.2, 123.3, 122.8, 118.6, 118.1, 114.1, 61.5, 55.5, 42.8, 19.5, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{24}NO_4$ $[M + H]^+$ *m/z* 378.1700. Found 378.1702.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 15dc



Yield: 58.0 mg (76%), Pale yellow solid.

Mp: 81-83 °C

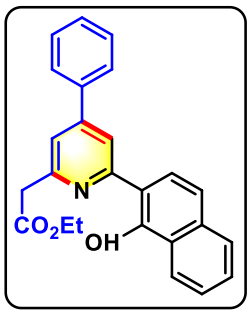
IR (neat): ν_{max} 3390 (w), 2979, 2932, 1731, 1595, 1491, 1151, 1027, 754, 645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 11.03 (s, 1H), 7.50 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1H), 7.47-7.44 (m, 2H), 7.33-7.27 (m, 3H), 7.10-7.08 (m, 2H), 6.92 (td, J = 7.6, 1.2 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 3.87 (s, 2H), 2.33 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.4, 157.3, 157.2, 152.9, 149.7, 138.1, 134.6, 130.7, 130.4, 130.2, 128.9, 128.0, 123.0, 122.6, 118.7, 118.2, 61.5, 42.7, 19.3, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}ClNO_3$ $[M + H]^+$ *m/z* 382.1204, 384.1175. Found 382.1206, 384.1174.

Compound 15ea



Yield: 53.0 mg (69%), Light brown solid.

Mp: 127-129 °C

IR (neat): ν_{max} 3447 (w), 3066, 2983, 2932, 1727, 1605, 1544, 1328, 1187, 1023, 799, 697 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 15.45 (s, 1H), 8.51-8.49 (m, 1H), 8.06 (m, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.78-7.77 (m, 1H), 7.73-7.71 (m, 2H), 7.56-7.48 (m, 5H), 7.42 (d, J = 2.0 Hz, 1H), 7.37 (d, J = 8.5 Hz, 1H), 4.28 (q, J = 7.0 Hz, 2H), 3.98 (s, 2H), 1.35 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 170.0, 158.6, 157.7, 151.6, 151.3, 138.4, 135.4, 129.6, 129.3, 127.8, 127.4, 127.3, 126.6, 125.4, 123.9, 123.0, 119.6, 118.3, 115.9, 111.7, 61.6, 43.5, 14.3 ppm.

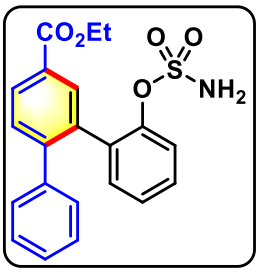
HRMS (ESI-TOF): Calcd. For $C_{25}H_{22}NO_3$ $[M + H]^+$ *m/z* 384.1594. Found 384.1595.

3.3 Synthesis of Compounds 16aa-af: General Procedure

A Schlenk tube was charged with cyclic sulfamidate imine **3** (0.20 mmol), triphenylphosphine (0.04 mmol), and toluene (1.0 mL). Subsequently, *δ*-acetoxy allenoate **8** (0.24 mmol) in toluene (1.0 mL) was added gradually over 30 min, the mixture was stirred at

rt (25 ^{o}C) for the stipulated time, and the 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 (30:70) as the eluent.

Compound 16aa



Yield: 57.9 mg (73%) using **3a** (39.0 mg, 0.20 mmol) and **8a** (64.5 mg, 0.20 mmol); White solid.

Mp: 61-63 °C

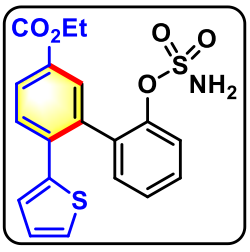
IR (neat): ν_{max} 3390, 3255, 3061, 2982, 2847, 1698, 1601, 1444, 1370, 1241, 1168, 1049, 756, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.11-8.09 (m, 2H), 7.55-7.53 (m, 1H), 7.39-7.37 (m, 1H), 7.34-7.30 (m, 1H), 7.29-7.22 (m, 5H), 7.19-7.17 (m, 2H), 4.49 (s, 2H), 4.40 (q, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.7, 147.6, 146.1, 140.4, 135.7, 133.6, 132.5_3, 132.4_9, 130.7, 129.4 (4 s), 128.2, 127.5, 126.7, 121.4, 61.5, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{23}N_2O_5S$ $[M + NH_4]^+$ *m/z* 415.1322. Found 415.1329.

Compound 16af



Yield: 52.4 mg (65%) using **3a** (39.0 mg, 0.20 mmol) and **8f** (63.9 mg, 0.24 mmol); White solid.

Mp: 154-156 °C

IR (neat): ν_{max} 3374, 3225, 3113, 2999, 2920, 2856, 1699, 1601, 1566, 1244, 1190, 1025, 768, 620 cm^{-1}.

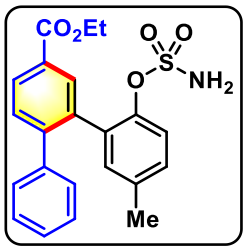
^1H NMR (500 MHz, $CDCl_3$): δ 8.07-8.03 (m, 2H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 1H), 7.44-7.40 (m, 1H), 7.35-7.30 (m, 2H), 7.25-7.24 (m, 1H), 6.90-6.89 (m, 1H), 6.81-6.80 (m, 1H), 4.56 (s, 2H), 4.38 (q, *J* = 7.0 Hz, 2H), 1.39 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 148.1, 141.9, 138.4, 135.3, 133.4, 132.8, 132.4, 130.1, 129.9, 129.6, 129.4, 127.6 (2 s), 127.0 (2 s), 121.9, 61.5, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{29}H_{17}NNaO_5S_2$ $[M + Na]^+$ *m/z* 426.0440. Found: 426.0439.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 16ba



Yield: 62.5 mg (76%) using **3b** (42.2 mg, 0.20 mmol) and **8a** (64.5 mg, 0.24 mmol); White solid.

Mp: 135-137 °C

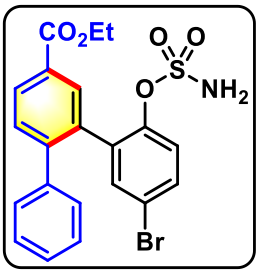
IR (neat): ν_{max} 3361, 3256, 3218, 2929, 2853, 1689, 1605, 1363, 1186, 1047, 839, 755, 695 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.10 (m, 1H), 8.09-8.07 (m, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.25-7.22 (m, 4H), 7.21-7.17 (m, 2H), 7.12-7.10 (m, 2H), 4.40 (q, *J* = 7.0 Hz, 2H), 4.35 (s, 2H), 2.31 (s, 3H), 1.41(t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.6, 146.0, 145.4, 140.5, 136.8, 135.8, 133.2, 132.9, 132.4, 130.6, 129.9, 129.4(2 s), 128.2, 127.5, 121.0, 61.5, 20.9, 14.5 ppm.

HRMS (ESI-TOF): **C**alcd. For $C_{22}H_{25}N_2O_5S$ $[M + NH_4]^+$ *m/z* 429.1479. Found: 429.1482.

Compound 16ca



Yield: 67.4 mg (71%) using **3c** (55.2 mg, 0.20 mmol) and **8a** (64.5 mg, mmol); White solid.

Mp: 162-164 °C

IR (neat): ν_{max} 3390, 3244, 3072, 2910, 2862, 1698, 1468, 1372, 1170, 1049, 857, 758, 699 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.12 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.45-7.43 (m, 2H), 7.28-7.23 (m, 4H), 7.19-7.17 (m, 2H), 4.48 (s, 2H), 4.40 (q, *J* = 7.0, 2H), 1.42 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.5, 146.6, 146.0, 140.0, 135.5, 135.1, 134.3, 132.3, 130.8, 129.9, 129.6, 129.4, 128.4, 127.8, 122.9, 119.8, 61.6, 14.5 ppm.

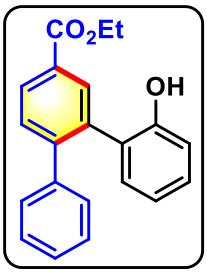
HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}BrN_2O_5S$ $[M + NH_4]^+$ *m/z* 493.0427, 495.0407. Found: 493.0426, 495.0406.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

3.4 Synthesis of Compounds 17aa-da: Representative Procedure for 17aa

A Schlenk tube was charged with cyclic sulfamidate imine **3a** (39.0 mg, 0.20 mmol), triphenylphosphine (10.5 mg, 0.04 mmol), and toluene (1.0 mL). Subsequently, *δ*-acetoxy allenoate **8a** (64.5 mg, 0.24 mmol) in toluene (1.0 mL) was added gradually over a period of 30 min at 80 °C, and the reaction mixture was stirred at the same temperature for the stipulated time, 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 layers were 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. Other compounds were prepared by using the same molar quantities.

Compound 17aa



Yield: 51.5 mg (81%), White solid.

Mp: 182-184 °C

IR (neat): ν_{max} 3421, 3075, 2986, 2931, 2861, 1686, 1600, 1446, 1197, 1028, 749, 695 cm^{-1}.

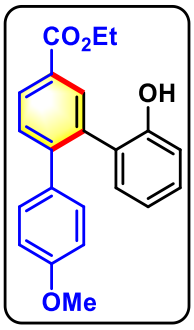
^1H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.10 (d, J = 2.0 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.25-7.16 (m, 6H), 7.06 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 6.87 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 6.79 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 4.86 (s, 1H), 4.40 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 152.5, 146.2, 139.9, 135.8, 132.7, 131.4, 130.8, 130.1, 129.7, 129.4, 129.1, 128.2, 127.7, 127.4, 120.8, 115.9, 61.3, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}NO_3$ $[M + NH_4]^+$ *m/z* 336.1594. Found: 336.1590.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 17ab



Yield: 52.2 mg (75%), White solid.

Mp: 147-149 °C

IR (neat): ν_{max} 3390, 3075, 2992, 2934, 2839, 1706, 1607, 1445, 1175, 1033, 772, 688 cm^{-1}.

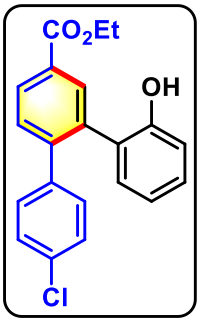
^1H NMR (500 MHz, $CDCl_3$): δ 8.11 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.07 (d, J = 1.5 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.19 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.13-7.11 (m, 2H), 7.09 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 6.90 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H),

6.80 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 6.77-6.75 (m, 2H), 4.81-4.78 (m, 1H), 4.39 (q, J = 7.0 Hz, 2H), 3.76 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 159.3, 152.4, 145.6, 135.5, 132.9, 132.0, 131.3, 130.6, 130.3, 129.7, 129.6, 129.4, 127.5, 120.9, 116.0, 113.8, 61.3, 55.3, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}O_4$ $[M + H]^+$ *m/z* 349.1434. Found: 349.1432.

Compound 17ac



Yield: 58.4 mg (83%), White solid.

Mp: 114-116 °C

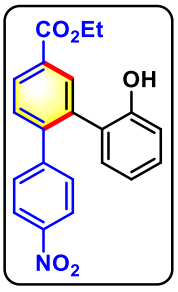
IR (neat): ν_{max} 3412, 3072, 2990, 2924, 2852, 1691, 1604, 1453, 1164, 1046, 769, 677 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.13 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.09 (d, J = 1.5 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.21-7.18 (m, 3H), 7.12-7.09 (m, 2H), 7.04 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 6.88 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 6.79 (dd, J_1 = 8.5, J_2 = 1.0 Hz, 1H), 4.95 (s, 1H), 4.39 (q, J = 7.0 Hz, 2H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 152.5, 145.0, 138.5, 135.9, 133.8, 132.7, 131.3, 130.6, 130.4, 130.3, 129.7, 129.6, 128.4, 127.0, 120.9, 116.0, 61.4, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{21}ClNO_3$ $[M + NH_4]^+$ *m/z* 370.1204, 372.1175. Found 370.1204, 372.1179.

Compound 17ad



Yield: 62.0 mg (85%), White solid.

Mp: 194-196 °C

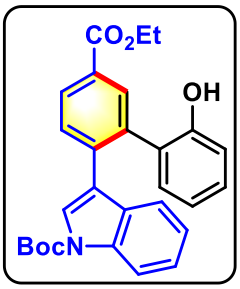
IR (neat): ν_{max} 3442, 3057, 2987, 2849, 1697, 1594, 1515, 1489, 1189, 1046, 776, 699 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 8.12$_4$-8.12$_1$ (m, 1H), 8.06-8.04 (m, 2H), 7.55-7.53 (m, 1H), 7.35-7.32 (m, 2H), 7.20-7.17 (m, 1H), 7.04 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 6.88 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 6.76 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 4.98 (s, 1H), 4.40 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.2, 152.4, 147.2, 147.0, 144.0, 136.4, 132.7, 131.3, 131.0, 130.4, 130.0, 129.9, 129.6, 126.5, 123.3, 121.1, 116.0, 61.6, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{21}N_2O_5$ $[M + NH_4]^+$ *m/z* 381.1445. Found: 381.1442.

Compound 17ae



Yield: 59.4 mg (65%), Gummy liquid.

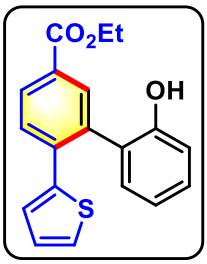
IR (neat): ν_{max} 3418, 2980, 2926, 2856, 1716, 1604, 1451, 1369, 1237, 1155, 1070, 749 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.18 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.15-8.14 (m, 2H), 7.81 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.32-7.29 (m, 1H), 7.22-7.14 (m, 4H), 6.90 (td, J = 7.5, 1.0 Hz, 1H), 6.81 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 4.78 (s, 1H), 4.42 (q, J = 7.0 Hz, 2H), 1.58 (s, 9H), 1.41 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 152.5, 149.4, 138.0, 136.3, 135.5, 132.9, 131.1, 130.7, 129.9, 129.6, 129.5, 129.1, 127.5, 125.6, 124.7, 123.1, 120.9, 119.7, 118.9, 115.9, 115.4, 83.9, 61.3, 28.2, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{28}H_{31}N_2O_5$ $[M + NH_4]^+$ *m/z* 475.2227. Found: 475.2233.

Compound 17af



Yield: 44.0 mg (68%), Pale yellow solid.

Mp: 141-143 °C

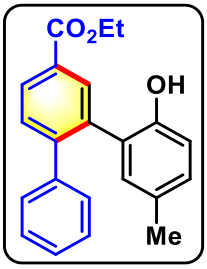
IR (neat): ν_{max} 3403, 3117, 3078, 2984, 2922, 2848, 1684, 1445, 1304, 1253, 1198, 1027, 771, 692 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.03 (d, J = 1.5 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.32-7.29 (m, 1H), 7.26-7.24 (m, 1H), 7.17 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 6.99 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 6.92-6.88 (m, 3H), 4.72 (d, J = 4.0 Hz, 1H), 4.39 (q, J = 7.0 Hz, 2H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 153.0, 141.1, 138.6, 134.7, 133.2, 131.3, 130.0, 129.8 (3 s), 127.5 (2 s), 127.4, 127.1, 121.1, 116.0, 61.4, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}O_3$ $[M + H]^+$ *m/z* S 325.0839. Found: 325.0896.

Compound 17ba



Yield: 49.1 mg (74%), White solid.

Mp: 143-145 °C

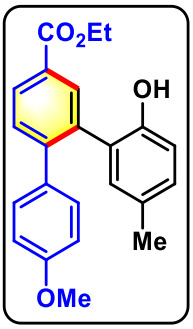
IR (neat): ν_{max} 3365, 3060, 3024, 2972, 2921, 2859, 1692, 1601, 1471, 1264, 1126, 1044, 757, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.08 (d, J = 1.5 Hz, 1H), 7.56 (d, J = 8.5 Hz, 1H), 7.26-7.20 (m, 5H), 6.97 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 6.91 (d, J = 2.0 Hz, 1H), 6.65 (d, J = 7.5 Hz, 1H), 4.53-4.52 (m, 1H), 4.40 (q, J = 7.0 Hz, 2H), 2.23 (s, 3H), 1.41 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 150.2, 146.0, 140.0, 136.1, 132.8, 131.7, 130.7, 130.1, 130.0, 129.9, 129.5, 129.1, 128.3, 127.7, 127.2, 115.8, 61.3, 20.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{24}NO_3$ $[M + NH_4]^+$ *m/z* 350.1751. Found: 350.1750.

Compound 17bb



Yield: 50.7 mg (70%), White solid.

Mp: 139-141 °C

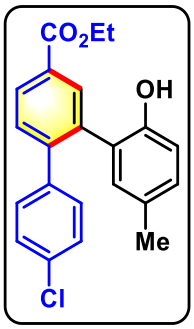
IR (neat): ν_{max} 3430, 2925, 2854, 1707, 1602, 1557, 1459, 1241, 1171, 1032, 768, 687 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$):): δ 8.10 (d, *J* = 8.0 Hz, 1H), 8.05 (s, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.95 (s, 1H), 6.77 (d, *J* = 8.5 Hz, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 4.48 (s, 1H), 4.39 (q, *J* = 7.0 Hz, 2H), 3.77 (s, 3H), 2.26 (s, 3H), 1.40 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 159.4, 150.1, 145.4, 135.8, 133.0, 132.1, 131.6, 130.5, 130.3, 130.1, 129.9, 129.7, 129.6, 127.4, 115.9, 113.9, 61.2, 55.3, 20.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{26}NO_4$ $[M + NH_4]^+$ *m/z* 380.1856. Found: 380.1857.

Compound 17bc



Yield: 55.0 mg (75%), White solid.

Mp: 155-157 °C

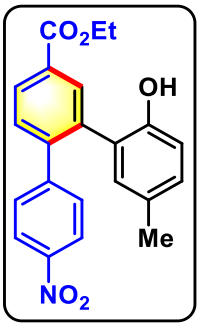
IR (neat): ν_{max}3382, 3063, 2988, 2867, 1691, 1603, 1471, 1273, 1090, 1048, 774, 679 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.10 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 8.07 (d, J = 1.5 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.21-7.18 (m, 2H), 7.14-7.12 (m, 2H), 6.98 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 4.74-4.72 (m, 1H), 4.39 (q, J = 7.0 Hz, 2H), 2.24 (s, 3H), 1.40 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 150.1, 144.9, 138.6, 136.1, 133.8, 132.8, 131.6, 130.5, 130.4, 130.3, 130.1(2 s), 129.6, 128.4, 126.8, 115.8, 61.4, 20.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{23}ClNO_3$ $[M + NH_4]^+$ *m/z* 384.1361, 386.1331. Found: 84.1362, 386.1339.

Compound 17bd



Yield: 58.0 mg (77%), White solid.

Mp: 217-219 °C

IR (neat): ν_{max}3423, 3120, 3045, 2988, 2851, 1698, 1596, 1492, 1295, 1189, 1046, 751, 696 cm^{-1}.

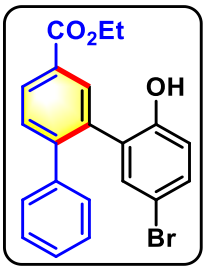
^1H NMR (500 MHz, $CDCl_3$): δ 8.13 (dd, J_1 = 8.0, J_2 =1.5 Hz, 1H), 8.10 (m, 1H), 8.06 (d, J = 8.5 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 8.5 Hz, 2H), 6.98 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 6.89 (s, 1H), 6.62 (d, J = 8.0 Hz, 1H), 4.69 (s, 1H), 4.40 (q, J = 7.0 Hz, 2H), 2.23 (s, 3H), 1.41 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 150.1, 147.3, 147.1, 143.9, 136.6, 132.8, 131.6, 131.0, 130.3 (3 s), 130.0, 129.5, 126.4, 123.3, 115.8, 61.5, 20.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{20}NO_5$ $[M + H]^+$ *m/z* 378.1336. Found: 378.1337.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 17ca



Yield: 58.0 mg (73%), White solid.

Mp: 182-184 °C

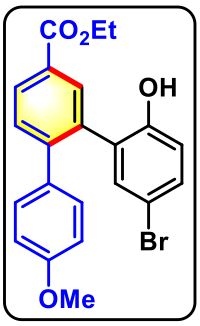
IR (neat): ν_{max} 3335, 3063, 3024, 2981, 2931, 2869, 1687, 1600, 1561, 1462, 1201, 1041, 756, 702 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.04 (d, J = 1.5 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.28-7.25 (m, 5H), 7.20-7.18 (m, 2H), 6.64 (d, J = 9.0 Hz, 1H), 4.77 (s, 1H), 4.40 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H); ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 151.7, 146.1, 139.4, 134.4, 133.7, 132.6, 132.2, 130.9, 130.3, 130.1, 129.5, 129.0, 128.5, 128.1, 117.8, 112.7, 61.4, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{18}BrO_3$ $[M + H]^+$ *m/z* 397.0434, 399.0413. Found: 397.0436, 399.0418.

Compound 17cb



Yield: 59.0 mg (69%), Gummy liquid.

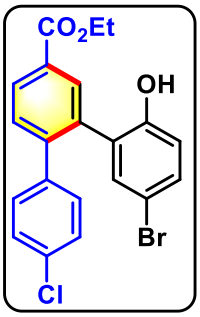
IR (neat): ν_{max} 3457, 3063, 2964, 1725, 1601, 1515, 1464, 1264, 1172, 731, 703 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.12 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 8.01 (d, J = 1.5 Hz, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.29-7.27 (m, 2H), 7.14-7.12 (m, 2H), 6.80-6.78 (m, 2H), 6.67-6.65 (m, 1H), 4.81 (s, 1H), 4.39 (q, J = 7.0 Hz, 2H), 3.78 (s, 3H), 1.40 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.2, 159.6, 151.6, 145.5, 134.2, 133.6, 132.8, 132.2, 131.6, 130.7, 130.2, 130.1, 129.8 (2 s), 117.9, 114.0, 112.8, 61.4, 55.3, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{23}BrNO_4$ $[M + NH_4]^+$ *m/z* 444.0805, 446.0785. Found 444.0812, 446.0795.

Compound 17cc



Yield: 63.0 mg (73%), White solid.

Mp: 179-181 °C

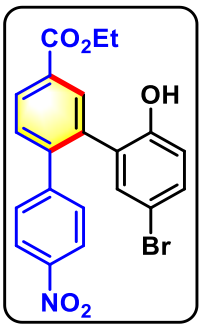
IR (neat): ν_{max} 3310, 3072, 2977, 2933, 2864, 1683, 1601, 1473, 1275, 1191, 1041, 772, 684 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.11 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.02 (d, J = 2.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.28 (dd, J_1 = 8.5, J_2 = 2.0 Hz, 1H), 7.23-7.21 (m, 3H), 7.12-7.10 (m, 2H), 6.65 (d, J = 9.0 Hz, 1H) 5.05 (s, 1H), 4.38 (q, J = 7.0 Hz, 2H), 1.40 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 151.7, 144.9, 138.1, 134.6, 134.1, 133.6, 132.6, 132.4, 130.6, 130.4, 130.3, 130.1, 129.2, 128.6, 117.8, 112.8, 61.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{17}ClBrO_3$ $[M + H]^+$ *m/z* 431.0044, 433.0024, 434.9990. Found 431.0048, 433.0031, 434.9999.

Compound 17cd



Yield: 67.0 mg (76%), Pale yellow solid.

Mp: 154-156 °C

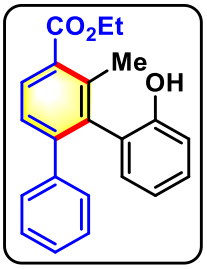
IR (neat): ν_{max} 3452, 3071, 2985, 2936, 2840, 1698, 1595, 1257, 1186, 1041, 746, 695 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 8.10-8.06 (m, 3H), 7.53 (d, J = 8.0 Hz, 1H), 7.35 (d, J = 9.0 Hz, 2H), 7.29 (dd, J_1 = 9.0, J_2 = 2.5 Hz, 1H) 7.25 (d, J = 2.5 Hz, 1H), 6.63 (d, J = 9.0 Hz, 1H), 5.05 (s, 1H), 4.40 (q, J = 7.0 Hz, 2H), 1.41 (t, J = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 166.0, 151.6, 147.3, 146.7, 143.9, 135.0, 133.7, 132.7, 132.6, 131.2, 130.5, 130.1, 129.9, 128.7, 123.5, 117.8, 113.0, 61.7, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{20}BrN_2O_5$ $[M + NH_4]^+$ *m/z* 459.0550, 461.0530. Found 459.0549, 461.0540.

Compound 17da



Yield: 48.0 mg (72%), White solid.

Mp: 113-115 °C

IR (neat): ν_{max} 3420, 3063, 2980, 2929, 2853, 1714, 1585, 1490, 1170, 1070, 755, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.17-7.15 (m, 3H), 7.13-7.11 (m, 1H), 7.09-7.07 (m, 2H), 6.83-6.81 (m, 2H), 6.79-6.76 (m, 1H), 4.68 (s, 1H), 4.41 (q, J = 7.0 Hz, 2H), 2.23 (s, 3H), 1.42 (t, J = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.3, 152.9, 146.5, 140.8, 139.3, 136.0, 131.3, 131.2, 130.1, 129.3, 129.0, 127.9, 127.8, 127.2, 126.2, 120.6, 115.3, 61.2, 18.2, 14.5 ppm.

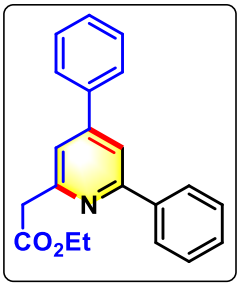
HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}O_3$ $[M + H]^+$ *m/z* 333.1485. Found: 333.1483.

3.5 Synthesis of Compounds 18aa-bc: Representative Procedure for 18aa

A Schlenk tube was charged with cyclic sulfonyl imine **5a** (36.2 mg, 0.20 mmol), *δ*-acetoxy allenoate **8a** (64.5 mg, 0.24 mmol), Na_2CO_3 (31.5 mg, 0.30 mmol) and toluene (1.5 mL). Subsequently, DBU (30.4 mg, 0.20 mmol) in toluene (0.5 mL) was added, the mixture was stirred at 100 °C for the stipulated time, and the 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 **18aa** was then purified by silica gel column chromatography using ethyl acetate/hexane (5:95) as the eluent. All the other products were prepared by using the same molar quantities.

Compound 18aa



Yield: 45.0 mg (71%), Gummy liquid.

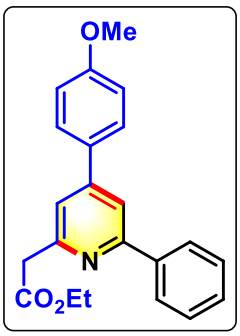
IR (neat): ν_{max} 3069, 2920, 2856, 1733, 1596, 1550, 1436, 1251, 1154, 1030, 762, 694 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.06-8.04 (m, 2H), 7.83 (d, *J* = 1.5 Hz, 1H), 7.70-7.69 (m, 2H), 7.52-7.41 (m, 7H), 4.23 (q, *J* = 7.0 Hz, 2H), 3.99 (s, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 171.0, 157.9, 155.1, 150.1, 139.6, 138.8, 129.2, 129.1 (2 s), 128.8, 127.3 (2 s), 120.4, 117.3, 61.1, 44.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{20}NO_2$ $[M + H]^+$ *m/z* 318.1489. Found: 318.1494.

Compound 18ab



Yield: 48.0 mg (69%), Gummy liquid.

IR (neat): ν_{max} 3040, 2920, 2856, 1731, 1599, 1514, 1430, 1249, 1177, 1028, 775, 693 cm^{-1}.

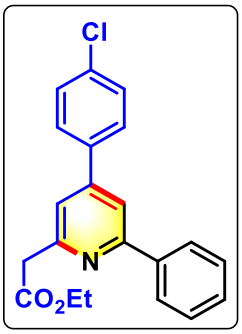
^1H NMR (500 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.0 Hz, 2H), 7.79 (d, *J* = 1.0 Hz, 1H), 7.65 (d, *J* = 9.0 Hz, 2H), 7.49-7.46 (m, 2H), 7.43-7.40 (m, 2H), 7.02 (d, *J* = 9.0 Hz, 2H),

4.23 (q, *J* = 7.0 Hz, 2H), 3.97 (s, 2H), 3.87 (s, 3H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 171.0, 160.7, 157.8, 155.0, 149.5, 139.7, 131.0, 129.0, 128.8, 128.4, 127.3, 119.8, 116.8, 114.7, 61.1, 55.5, 44.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_3$ $[M + H]^+$ *m/z* 348.1594. Found: 348.1596.

Compound 18ac



Yield: 51.2 mg (73%), Gummy liquid.

Mp: 154-156 °C

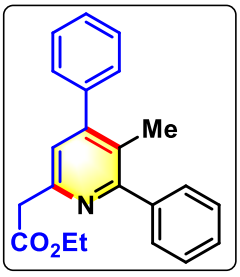
IR (neat): ν_{max} 3031, 2922, 2862, 1733, 1602, 1546, 1255, 1153, 1029, 824, 774, 693 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04-8.02 (m, 2H), 7.77 (d, *J* = 1.5 Hz, 1H), 7.64-7.61 (m, 2H), 7.50-7.46 (m, 4H), 7.44-7.41 (m, 2H), 4.23 (q, *J* = 7.0 Hz, 2H), 3.99 (s, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 171.0, 158.1, 155.2, 148.8, 139.3, 137.2, 135.4, 129.4, 129.2, 128.9, 128.6, 127.3, 120.2, 117.1, 61.2, 44.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{19}ClNO_2$ $[M + H]^+$ *m/z* 352.1099, 354.1069. Found 352.1100, 354.1069.

Compound 18ba



Yield: 45.7 mg (69%), Gummy liquid.

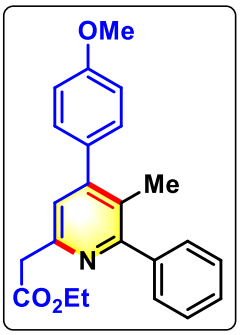
IR (neat): ν_{max} 3069, 2923, 2859, 1733, 1585, 1544, 1264, 1151, 1029, 734, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55-7.53 (m, 2H), 7.47-7.43 (m, 4H), 7.42-7.37 (m, 4H), 7.18 (s, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 2H), 2.17 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 171.2, 159.5, 151.5, 151.1, 141.1, 139.9, 129.3, 128.9, 128.5, 128.3, 128.0, 127.0, 123.5, 61.1, 43.7, 17.9, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_2$ $[M + H]^+$ *m/z* 332.1645. Found: 332.1648.

Compound 18bb



Yield: 46.2 mg (64%), Gummy liquid.

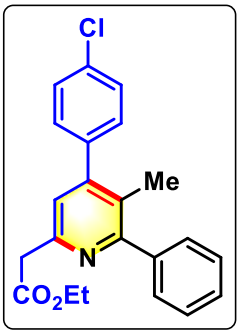
IR (neat): ν_{max}2923, 2853, 1735, 1598, 1511, 1249, 1175, 1032, 845, 714 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54-7.52 (m, 2H), 7.46-7.43 (m, 2H), 7.40-7.36 (m, 1H), 7.33-7.30 (m, 2H), 7.16 (s, 1H), 7.00-6.98 (m, 2H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 2H), 3.87 (s, 3H), 2.18 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 171.2, 159.5, 151.2, 151.0, 132.2, 130.2, 129.3, 128.3, 128.0, 127.2, 123.6, 113.9, 61.1, 55.5, 43.7, 18.0, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{24}NO_3$ $[M + H]^+$ *m/z* 362.1751. Found: 362.1753.

Compound 18bc



Yield: 51.1 mg (70%), Gummy liquid.

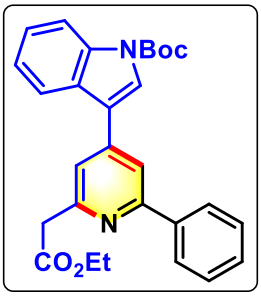
IR (neat): ν_{max} 3058, 2929, 2853, 1732, 1542, 1490, 1383, 1150, 1029, 831, 786, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.5 Hz, 2H), 7.46-7.37 (m, 5H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.14 (s, 1H), 4.19 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 2H), 2.16 (s, 3H), 1.27 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 171.0, 159.8, 151.3, 150.3, 141.0, 138.4, 134.2, 130.3, 129.3, 128.8, 128.3, 128.1, 126.9, 123.2, 61.1, 43.7, 17.8, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{21}ClNO_2$ $[M + H]^+$ *m/z* 366.1255, 368.1226. Found: 366.1259, 368.1232.

Compound 18ae



Yield: 52.0 mg (57%), Gummy liquid.

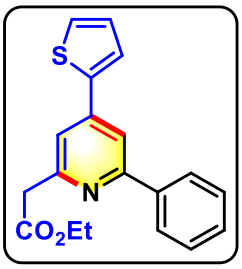
IR (neat): ν_{max} 3066, 2980, 2926, 2853, 1731, 1605, 1451, 1235, 1148, 1028, 765, 694 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (d, *J* = 8.0 Hz, 1H), 8.07-8.05 (m, 2H), 7.91-7.89 (m, 3H), 7.53 (d, *J* = 1.0 Hz, 1H), 7.51-7.48 (m, 2H), 7.45-7.40 (m, 2H), 7.37-7.33 (m, 1H), 4.25 (q, *J* = 7.0 Hz, 2H), 4.01 (s, 2H), 1.72 (s, 9H), 1.32 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 171.0, 157.9, 155.1, 149.6, 143.2, 139.6, 136.2, 129.2, 128.9, 128.3, 127.3, 125.2, 124.5, 123.5, 120.9 (3 s), 117.8, 115.8, 84.6, 61.1, 44.4, 28.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{28}H_{29}N_2O_4$ $[M + H]^+$ *m/z* 457.2122. Found: 457.2126.

Compound 18af



Yield: 40.0 mg (62%), Gummy liquid.

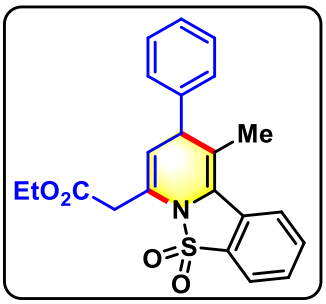
IR (neat): ν_{max} 3078, 2979, 2925, 2850, 1731, 1597, 1551, 1421, 1178, 1028, 733, 694 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.04-8.02 (m, 2H), 7.79 (d, *J* = 1.5 Hz, 1H), 7.56 (dd, *J* = 3.5, 1.0 Hz, 1H), 7.50-7.41 (m, 5H), 7.15 (dd, *J* = 5.0, 3.5 Hz, 1H), 4.23 (q, *J* = 7.0 Hz, 2H), 3.95 (s, 2H), 1.30 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 170.8, 158.1, 155.3, 143.0, 141.7, 139.4, 129.2, 128.8, 128.5, 127.3, 127.1, 125.5, 118.6, 115.6, 61.1, 44.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{18}NO_2S$ $[M + H]^+$ *m/z* 324.1053. Found 324.1055.

Compound 19bb



Yield: 63.0 mg (74%), White solid.

Mp: 136-139 °C

IR (neat): ν_{max} 2967, 2920, 2840, 1734, 1601, 1509, 1293, 1022, 759, 648 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.64-7.61 (m, 1H), 7.54-7.51 (m, 1H), 7.25 (d, *J* = 8.5 Hz, 2H), 6.86 (d, *J* = 9.0 Hz, 2H), 4.96 (d, *J* = 4.0 Hz, 1H), 4.22-4.18 (m, 2H), 4.06 (d, *J* = 4.0 Hz, 1H), 3.78 (s, 3H), 3.76-3.62 (m, 2H), 2.00 (s, 3H), 1.28 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): 169.8, 159.0, 136.0, 133.1, 132.7, 130.0, 129.7, 129.0, 125.2, 124.7, 124.1, 121.4, 117.5, 114.3, 111.8, 61.3, 55.4, 47.7, 37.4, 18.2, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{24}NO_5S$ $[M + H]^+$ *m/z* 426.1370. Found: 426.1352.

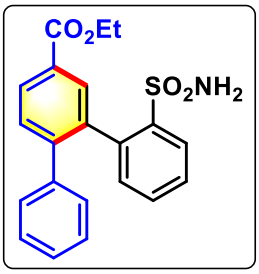
This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

3.6 Synthesis of Compounds 20aa-ba: Representative Procedure for 20aa

A Schlenk tube was charged with cyclic sulfonyl imine **5a** (36.2 mg, 0.20 mmol), triphenylphosphine (10.5 mg, 0.04 mmol), and toluene (1.0 mL). Subsequently, δ-acetoxy allenoate **8a** (64.5 mg, 0.24 mmol) in toluene (1.0 mL) was added gradually over 30 min at 80 °C, and the mixture was stirred at the same temperature for the stipulated time, 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 layers were washed with brine (20 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **20aa** was then purified by silica gel column chromatography using ethyl acetate/hexane (30:70) as the eluent. Other compounds were prepared by using the same molar quantities.

Compound 20aa



Yield: 58.0 mg (76%), White solid.

Mp: 183-185 °C

IR (neat): ν_{max} 3421, 3270, 3078, 2990, 2906, 2360, 1683, 1605, 1364, 1265, 1157, 1037, 757, 688 cm^{-1}.

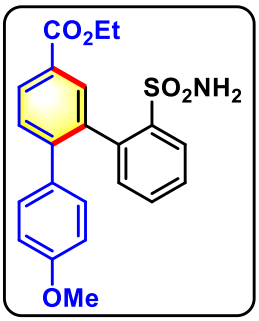
^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.11 (d, J = 2.0 Hz, 1H), 8.06-8.04 (m, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.45-7.41 (m, 2H), 7.25-7.20 (m, 5H), 7.15-7.13 (m, 1H), 4.42-4.36 (m, 2H), 4.31 (s, 2H), 1.39 (t, J = 7.0, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 166.3, 145.2, 140.7, 139.9, 139.2, 138.1, 133.4, 132.1, 131.2, 130.6, 129.7 (2 s), 129.0, 128.5, 128.3, 128.2, 127.6, 61.4, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{23}N_2O_4S$ $[M + NH_4]^+$ *m/z* 399.1373. Found: 399.1376.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 20ab



Yield: 58.4 mg (71%), White solid.

Mp: 148-150 °C

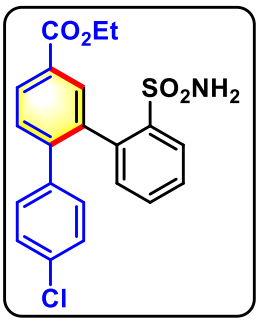
IR (neat): ν_{max}3317, 3218, 3107, 2973, 2908, 2834, 1703, 1609, 1526, 1242, 1166, 1039, 770 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.12 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 8.08-8.05 (m, 2H), 7.54 (d, J = 8.0 Hz, 1H), 7.46-7.41 (m, 2H), 7.16-7.13 (m, 3H), 6.73 (d, J = 8.5 Hz, 2H), 4.41-4.35 (m, 4H), 3.74 (s, 3H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 159.1, 144.8, 140.7, 139.5, 137.9, 133.4, 132.2, 131.3, 130.9, 130.5, 129.8, 128.6, 128.5, 128.2, 113.7, 61.3, 55.3, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{25}N_2O_5S$ $[M + NH_4]^+$ *m/z* 429.1479. Found: 429.1478.

Compound 20ac



Yield: 65.6 mg (79%), White solid.

Mp: 208-210 °C

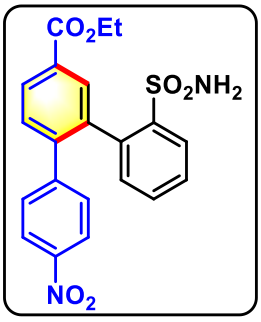
IR (neat): ν_{max} 3431, 3282, 3072, 2993, 2910, 1687, 1607, 1483, 1345, 1262, 1158, 1016, 751, 701 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.14-8.11 (m, 2H), 8.08-8.05 (m, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.44-7.38 (m, 2H), 7.19-7.15 (m, 4H), 7.05-7.02 (m, 1H), 4.63 (s, 2H), 4.41-4.35 (m, 2H), 1.39 (t, J = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.2, 144.4, 141.0, 138.9, 138.4, 138.1, 133.8, 133.2, 132.2, 131.1, 130.9, 130.6, 129.8, 129.3, 128.5, 128.4, 128.3, 61.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}ClN_2O_4S$ $[M + NH_4]^+$ *m/z* 433.0983, 435.0954. Found: 433.0987, 435.0962.

Compound 20ad



Yield: 70.0 mg (82%), Pale yellow solid.

Mp: 197-199 °C

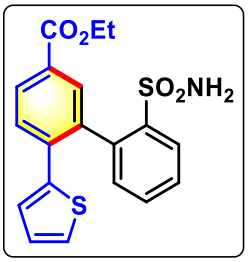
IR (neat): ν_{max} 3336, 3255, 2980, 2850, 1695, 1596, 1516, 1259, 1159, 1032, 775, 697 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.18-8.16 (m, 2H), 8.10-8.09 (m, 1H), 8.04 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.44-7.37 (m, 4H), 7.00 (d, *J* = 7.5 Hz, 1H), 4.78-4.73 (m, 2H), 4.42-4.38 (m, 2H), 1.40 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.1, 147.2, 146.7, 143.5, 141.1, 138.3$_1$, 138.3$_0$, 133.0, 132.2, 131.2, 130.6, 130.5, 130.1, 129.8, 128.6, 128.5, 123.3, 61.6, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{18}N_2NaO_6S$ $[M + Na]^+$ *m/z* 449.0778. Found: 449.0779.

Compound 20af



Yield: 54.2 mg (70%), Gummy liquid.

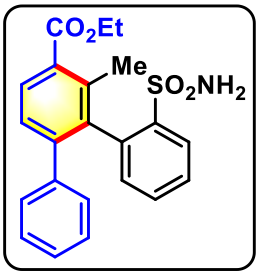
IR (neat): ν_{max}3383, 3256, 2964, 2922, 2862, 1707, 1607, 1307, 1260, 1162, 1029, 768, 701 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.12-8.09 (m, 2H), 8.04 (m, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.58-7.52 (m, 2H), 7.28 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.21 (dd, *J* = 4.5, 1.5 Hz, 1H), 6.89-6.87 (m, 2H), 4.39-4.33 (m, 4H), 1.37 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 166.1, 141.6, 141.0, 138.9, 137.5, 136.9, 133.1, 132.6, 132.2, 129.9, 129.4, 129.0, 128.9, 128.6, 127.8, 127.5$_4$, 127.5$_0$, 61.4, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{21}N_2O_4S_2$ $[M + NH_4]^+$ *m/z* 405.0937. Found: 405.0944.

Compound 20ba



Yield: 54.5 mg (69%), White solid.

Mp: 154-156 °C

IR (neat): ν_{max}3428, 3272, 3081, 2990, 2915, 2876, 1687, 1602, 1301, 1157, 1016, 773, 700 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96-7.94 (m, 2H), 7.56 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.44 (td, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.34-7.32 (m, 2H), 7.18-7.13 (m, 5H), 4.38 (q, J = 7.0 Hz, 2H), 4.10 (s, 2H), 2.25 (s, 3H), 1.41 (t, J = 7.0 Hz, 3H) ppm.

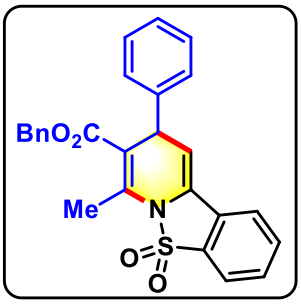
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.1, 144.1, 140.8, 140.4, 138.9, 138.3, 134.0, 132.0, 130.7, 130.3, 129.9, 128.7, 128.5, 128.0, 127.6, 127.4, 61.2, 19.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{25}N_2O_4S$ $[M + NH_4]^+$ *m/z* 413.1530. Found: 413.1533.

3.7 Synthesis of Compounds 21aa-am, 21ba, 21bk, 21bl and 21ca: Representative Procedure for 21aa

A Schlenk tube was charged with isothiazole dioxide **5a** (36.2 mg, 0.20 mmol), *β′*-acetoxy allenoates **12a** (77.4 mg, 0.24 mmol) in toluene (2.0 mL) and TBD (5.5 mg, 0.04 mmol). The mixture was kept stirring at 100 °C for 12h. After completion of the reaction (TLC), the mixture was quenched by adding water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 5 mL). Then, the combined organic layer was washed with brine (2 x 30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **21aa** was then purified by silica gel column chromatography using ethyl acetate/ hexane (15:85) as the eluent. Other compounds were prepared by using the same molar quantities.

Compound 21aa



Yield: 63 mg (71%), White solid.

Mp: 160 °C

IR (neat): ν_{max} 1710, 1595, 1450, 1322, 1220, 1174, 1086, 994, 855, 756 cm^{-1}.

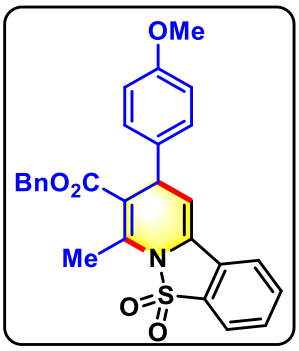
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80-7.78 (m, 1H), 7.62-7.60 (m, 1H), 7.56-7.53 (m, 2H), 7.27-7.24 (m, 5H), 7.22-7.18 (m, 3H), 7.05-7.7.04 (m, 2H), 5.74 (d, J = 5.0 Hz, 1H), 4.99 (s, 2H), 4.72 (d, J = 4.5 Hz, 1H), 2.91 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 167.0, 144.9, 141.5, 135.9, 133.7, 132.0, 130.4, 128.9, 128.5, 128.2, 128.1, 127.3, 127.2, 127.0, 121.1, 121.0, 107.8, 105.8, 66.4, 41.4, 15.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{21}NNaO_4S$ $[M + Na]^+$ m/z 466.1083. Found 466.1082.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 21ab



Yield: 71 mg (75%), White solid.

Mp: 191 °C

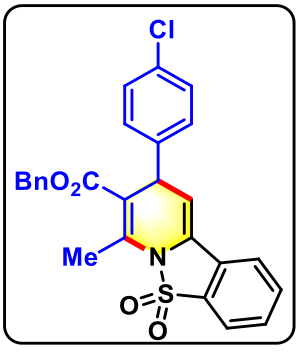
IR (neat): ν_{max} 1706, 1629, 1605, 1454, 1337, 1248, 1137, 1099, 998, 854, 759 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.82-7.80 (m, 1H), 7.64-7.61 (m, 1H), 7.57-7.56 (m, 2H), 7.29-7.26 (m, 3H), 7.11-7.10 (m, 4H), 6.80 (d, *J* = 9.0 Hz, 2H), 5.74 (d, *J* = 5.0 Hz, 1H), 5.02 (s, 2H), 4.68 (d, *J* = 4.5 Hz, 1H), 3.78 (s, 3H), 2.90 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 167.1, 158.8, 140.8, 137.1, 135.9, 133.7, 132.0, 130.3, 129.3, 128.5, 128.3, 128.2, 127.5, 126.8, 121.1, 121.0, 114.3, 108.2, 106.0, 66.4, 55.4, 40.6, 15.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{23}NNaO_4S$ $[M + Na]^+$ m/z 496.1189. Found 496.1193.

Compound 21ac



Yield: 68 mg (72%), White solid.

Mp: 188 °C

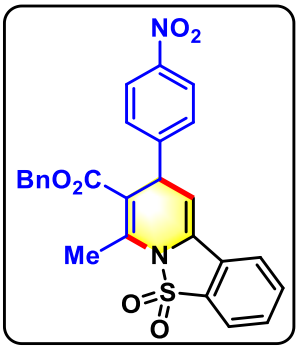
IR (neat): ν_{max} 1700, 1599, 1487, 1318, 1221, 1130, 1091, 994, 851, 759 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 7.5 Hz, 1H), 7.66-7.63 (m, 1H), 7.59-7.56 (m, 2H), 7.30-7.29 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.11-7.07 (m, 4H), 5.70 (d, *J* = 4.5 Hz, 1H), 5.06 (d, *J* = 12.5 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.71 (d, *J* = 4.5 Hz, 1H), 2.92 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 143.4, 141.8, 135.7, 133.8, 133.0, 132.0, 130.6, 129.5, 129.0, 128.6, 128.4, 128.3, 127.2 (2 s), 121.2, 121.0, 107.4, 105.1, 66.5, 40.9, 15.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{20}ClNKO_4S$ $[M + K]^+$ m/z 516.0433. Found: 516.0432.

Compound 21ad



Yield: 61 mg (763%), White solid.

Mp: 160 °C

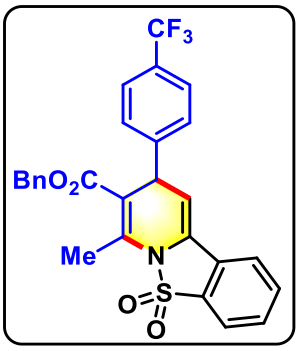
IR (neat): ν_{max} 1702, 1596, 1451, 1319, 1221, 1172, 1092, 993, 854, 754 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.06-8.04 (m, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.68-7.65 (m, 1H), 7.63-7.58 (m, 2H), 7.31-7.27 (m, 4H), 7.25-7.24 (m, 1H), 7.08-7.06 (m, 2H), 5.67 (d, *J* = 5.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.93 (d, *J* = 12.5 Hz, 1H), 4.84 (d, *J* = 4.5 Hz, 1H), 2.96 (d, *J* = 0.5 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 152.1, 147.0, 143.0, 135.5, 134.0, 132.1, 130.9, 128.9, 128.6 (2 s), 128.5, 127.9, 126.9, 124.1, 121.3, 121.1, 106.4, 103.8, 66.6, 41.5, 15.2 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{20}NaN_2O_6S$ $[M + Na]^+$ m/z 511.0934. Found 511.0933.

Compound 21ae



Yield: 61 mg (66%), White solid.

Mp: 160 °C

IR (neat): ν_{max} 1707, 1603, 1455, 1322, 1225, 1125, 1092, 994, 842, 738 cm^{-1}.

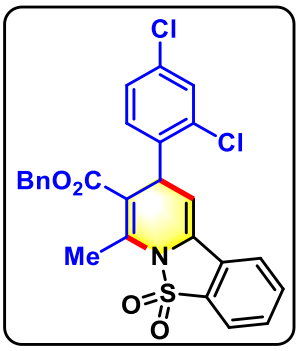
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.67-7.64 (m, 1H), 7.62-7.58 (m, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.30-7.24 (m, 5H), 7.03 (d, *J* = 6.5 Hz, 2H), 5.71 (d, *J* = 4.5 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.96 (d, *J* = 12.0 Hz, 1H), 4.81 (d, *J* = 4.5 Hz, 1H), 2.96 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):): δ 166.6, 148.9, 142.5, 135.6, 133.9, 132.1, 130.7, 129.4 (q, 2*J*C-F = 32.4 Hz), 128.6, 128.5, 128.4 (2 s), 127.5, 127.0, 125.9 (q, 3*J*C-F = 3.8 Hz), 124.2 (q, 1*J*C-F = 271.0 Hz), 121.2, 121.0, 106.9, 104.7, 66.5, 41.4, 15.1 ppm.

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

HRMS (ESI-TOF): Calcd. For $C_{27}H_{24}F_3N_2O_4S$ $[M + H]^+$: m/z 512.1138. Found 512.1137.

Compound 21af



Yield: 75.8 mg (74%), White solid, R_f = 0.53 (9:1 hexane/ethyl acetate))

Mp: 188 °C

IR (neat): ν_{max} 1712, 1468, 1319, 1228, 1173, 1092, 992, 861, 754 cm^{-1}.

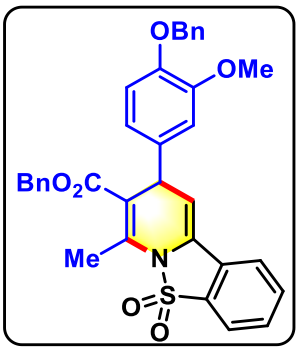
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.77-7.74 (m, 1H), 7.71-7.67 (m, 2H), 7.39-7.34 (m, 5H), 7.26 (s, 1H), 7.12-7.11 (m, 2H), 5.86 (d, *J* = 4.5 Hz,

1H), 5.34 (d, *J* = 4.5 Hz, 1H), 5.22 (d, *J* = 12.5 Hz, 1H), 5.00 (d, *J* = 12.5 Hz, 1H), 3.10 (d, *J* = 0.5 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 143.9, 140.8, 135.6, 133.8, 133.3, 132.8, 131.9, 130.6, 129.4, 128.5, 128.3, 128.2, 128.1, 127.6, 127.1, 121.2, 121.1, 105.7, 103.3, 66.4, 37.7, 15.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{19}Cl_2NNaO_4S$ $[M + Na]^+$ m/z 534.0304. Found 534.0305.

Compound 21ah



Yield: 79.8 mg (69%), White solid.

Mp: 191 °C

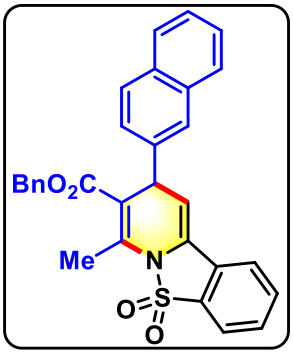
IR (neat): ν_{max} 1737, 1696, 1452, 1330, 1225, 1130, 1091, 985, 853, 763 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 7.5 Hz, 1H), 7.63-7.61 (m, 1H), 7.58-7.55 (m, 2H), 7.43 (d, *J* = 7.5 Hz, 2H), 7.37-7.34 (m, 2H), 7.30-7.26 (m, 4H), 7.09-7.07 (m, 2H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.69-6.66 (m, 2H), 5.75 (d, *J* = 5.0 Hz, 1H), 5.12 (s, 2H), 5.01 (s, 2H), 4.66 (d, *J* = 4.5 Hz, 1H), 3.72 (s, 3H), 2.90 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 167.1, 149.8, 147.4, 141.0, 138.1, 137.3, 135.9, 133.7, 132.0, 130.4, 128.7, 128.5, 128.2 (2 s), 128.0, 127.4 (2 s), 126.8, 121.2, 121.0, 120.4, 114.2, 111.8, 108.0, 105.9, 71.2, 66.4, 55.1, 41.0, 15.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{34}H_{29}NNaO_6S$ $[M + Na]^+$ m/z 602.1608. Found 602.1608.

Compound 21ai



Yield: 70.08 mg (69%), White solid.

Mp: 170 °C

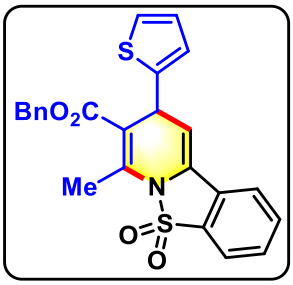
IR (neat): ν_{max} 1704, 1600, 1454, 1324, 1265, 1130, 1092, 992, 860, 735 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.84-7.80 (m, 2H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.74-7.72 (m, 1H), 7.64-7.59 (m, 2H), 7.57-7.55 (m, 2H), 7.47-7.45 (m, 2H), 7.36 (d, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.21-7.18 (m, 1H), 7.12-7.09 (m, 2H), 6.97-6.96 (m, 2H), 5.80 (d, *J* = 5.0 Hz, 1H), 5.0 (s, 2H), 4.91 (d, *J* = 4.5 Hz, 1H), 3.00 (d, *J* = 1.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.0, 142.2, 141.6, 135.7, 133.7 (2 s), 132.8, 132.1, 130.5, 128.8, 128.4, 128.2, 128.1 (2 s), 127.8, 127.4, 127.1, 126.9, 126.4, 126.3, 126.0, 121.2, 121.0, 107.7, 105.6, 66.5, 41.7, 15.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{30}H_{23}NNaO_4S$ $[M + Na]^+$ m/z 516.1240. Found 516.1243.

Compound 21aj



Yield: 56 mg (63%), White solid.

Mp: 215 °C

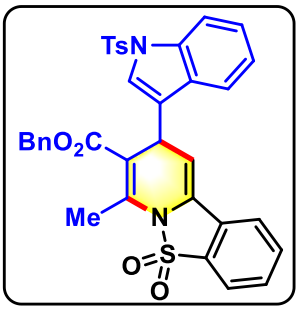
IR (neat): ν_{max} 1703, 1597, 1346, 1220, 1129, 1088, 994, 855, 750 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (d, *J* = 8.0 Hz, 1H), 7.68-7.62 (m, 2H), 7.60-7.57 (m, 1H), 7.33-7.30 (m, 3H), 7.20-7.19 (m, 2H), 7.17 (dd, J_1 = 5.0, J_2 = 1.0 Hz, 1H), 6.90 (dd, J_1 = 5.0, J_2 = 1.5 Hz, 1H), 6.82-6.81 (m, 1H), 5.85 (d, *J* = 5.0 Hz, 1H), 5.14-5.10 (m, 2H), 5.08-5.07 (m, 1H), 2.90 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 148.9, 141.3, 135.9, 133.8, 132.1, 130.6, 128.6, 128.3, 128.2, 127.5, 127.3, 127.2, 124.9 (2 s), 121.2, 121.1, 107.6, 104.6, 66.5, 35.9, 15.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{19}NNaO_4S_2$ $[M + Na]^+$ m/z 472.0648. Found 472.0645.

Compound 21ak



Yield: 83 mg (65%), White solid.

Mp: 167 °C

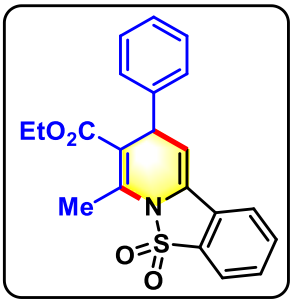
IR (neat): ν_{max} 1707, 1599, 1446, 1326, 1225, 1128, 1092, 968, 812, 737 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.0 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.64-7.57 (m, 2H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.37 (s, 1H), 7.33-7.30 (m, 1H), 7.21-7.17 (m, 2H), 7.13-7.09 (m, 4H), 6.84 (d, *J* = 7.5 Hz, 2H), 5.74 (d, *J* = 5.0 Hz, 1H), 5.03 (d, *J* = 4.5 Hz, 1H), 4.90 (d, *J* = 12.5 Hz, 1H), 4.77 (d, *J* = 12.5 Hz, 1H), 2.92 (s, 3H), 2.23 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 145.0, 141.6, 135.6, 135.5, 135.3, 133.8, 132.1, 130.6, 129.9, 129.3, 128.5, 128.1, 127.8, 127.1, 127.0, 126.1, 125.0, 124.5, 123.6, 121.2, 121.1, 119.6, 114.1, 106.2, 103.8, 66.4, 32.5, 21.6, 15.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{35}H_{28}N_2O_6S_2Na$ $[M + Na]^+$ m/z 659.1281. Found 659.1282.

Compound 21an



Yield: 58 mg (76%), White solid.

Mp: 170 °C

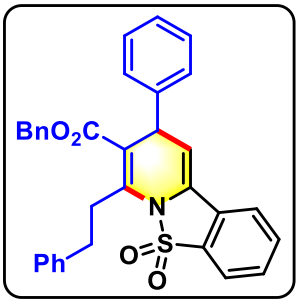
IR (neat): ν_{max} 1703, 1610, 1489, 1386, 1273, 1128, 1091, 981, 846, 754 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.0 Hz, 1H), 7.64-7.61 (m, 1H), 7.58-7.55 (m, 2H), 7.33-7.30 (m, 2H), 7.28-7.27 (m, 2H), 7.24-7.20 (m, 1H), 5.77 (d, *J* = 4.5 Hz, 1H), 4.73 (d, *J* = 4.5 Hz, 1H), 4.07-3.98 (m, 2H), 2.90 (s, 3H), 1.08 (t, *J* = 7.5 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 167.2, 145.0, 140.6, 133.7, 132.1, 130.4, 128.8, 128.2, 127.4, 127.2, 127.1, 121.1, 121.0, 108.3, 105.7, 60.4, 41.6, 14.9, 14.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{20}NO_4S$ $[M + H]^+$ m/z 382.1108. Found 382.1108.

Compound 21ao



Yield: 86 mg (81%), White solid.

Mp: 160 °C

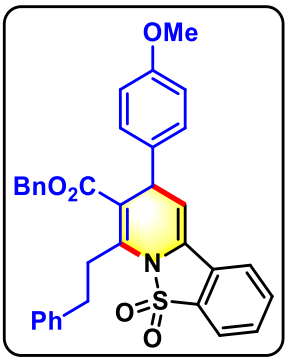
IR (neat): ν_{max} 3027, 1704, 1595, 1453, 1319, 1223, 1131, 1098, 908, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85-7.83 (m, 1H), 7.66-7.62 (m, 1H), 7.59-7.56 (m, 2H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.33-7.30 (m, 7H), 7.25-7.21 (m, 4H), 7.11-7.10 (m, 2H), 5.80 (d, *J* = 4.5 Hz, 1H), 5.04 (s, 2H), 4.80 (d, *J* = 4.5 Hz, 1H), 3.67-3.60 (m, 1H), 3.57-3.53 (m, 1H), 3.24-3.21 (m, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 145.4, 145.0, 141.4, 135.8, 133.7, 132.0, 130.4, 129.0 (2 s), 128.6, 128.5, 128.4, 128.2, 127.5, 127.2, 127.1, 126.2, 121.1, 121.0, 108.1, 106.2, 66.5, 41.4, 35.9, 31.9 ppm.

HRMS (ESI-TOF): Calcd. For $C_{33}H_{28}NO_4S$ $[M + H]^+$ m/z 534.1734. Found 534.1731.

Compound 21ap



Yield: 94 mg (83%), White solid.

Mp: 150 °C

IR (neat): ν_{max} 2894, 1701, 1597, 1454, 1314, 1250, 1131, 1096, 830, 744 cm^{-1}.

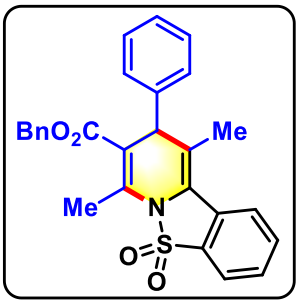
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 7.5 Hz, 1H), 7.66-7.63 (m, 1H), 7.60-7.56 (m, 2H), 7.36-7.35 (m, 2H), 7.31-7.29 (m, 5H), 7.22-7.20 (m, 1H), 7.14-7.12 (m,

4H), 6.82 (d, *J* = 8.0 Hz, 2H), 5.78 (d, *J* = 4.5 Hz, 1H), 5.05 (s, 2H), 4.74 (d, *J* = 4.5 Hz, 1H), 3.80 (s, 3H), 3.63-3.57 (m, 1H), 3.54-3.48 (m, 1H), 3.20 (t, *J* = 8.0 Hz, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.5, 158.8, 144.7, 141.4, 137.2, 135.9, 133.7, 132.0, 130.4, 129.3, 128.9, 128.6, 128.5 (2s), 128.2, 127.6, 127.0, 126.2, 121.1, 120.9, 114.3, 108.6, 106.3, 66.4, 55.4, 40.5, 35.9, 31.9 ppm.

HRMS (ESI-TOF): Calcd. For $C_{34}H_{33}N_2O_5S$ $[M + NH_4]^+$ m/z 581.2105. Found 581.2106.

Compound 21ba



Yield: 55 mg (65%), White solid.

Mp: 188 °C

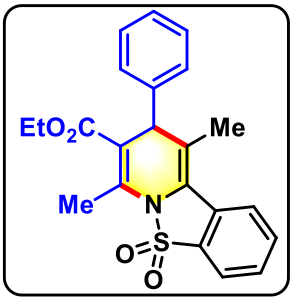
IR (neat): ν_{max} 1708, 1610, 1451, 1383, 1283, 1131, 1088, 964, 842, 759 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): 1H NMR (500 MHz, CDCl3): δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.67-7.64 (m, 1H), 7.58-7.55 (m, 1H), 7.32-7.31 (m, 3H), 7.24-7.19 (m, 5H), 7.17-7.16 (m, 2H), 5.07-5.02 (m, 2H), 4.44 (s, 1H), 2.93 (s, 3H), 2.02 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 143.7, 141.1, 136.0, 133.6, 132.5, 129.2, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 127.3, 124.5, 123.2, 121.6, 119.1, 107.9, 66.4, 49.1, 18.5, 15.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{23}NKO_4S$ $[M + K]^+$ m/z 496.0979. Found: 496.0978.

Compound 21bn



Yield: 58 mg (73%), White solid.

Mp: 198 °C

IR (neat): ν_{max}1701, 1608, 1452, 1389, 1285, 1136, 1091, 971, 860, 760 cm^{-1}.

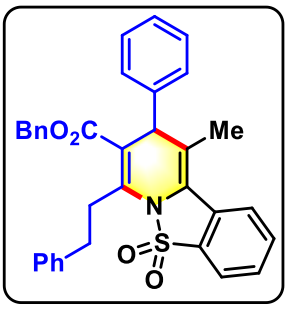
^1H NMR (500 MHz, $CDCl_3$): δ 7.89-7.87 (m, 1H), 7.81-7.79 (m, 1H), 7.68-7.64 (m, 1H), 7.59-7.55 (m, 1H), 7.29-7.27 (m, 4H), 7.24-7.19 (m, 1H), 4.45 (s, 1H), 4.09-4.04 (m, 2H), 2.92 (d, *J* = 3.5 Hz, 3H), 2.04 (d, *J* = 4.5 Hz, 3H), 1.19-1.15 (m, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.1, 143.8, 140.3, 133.6, 132.5, 129.2, 128.7, 128.6, 128.5, 127.3, 124.5, 123.2, 121.5, 119.0, 108.3, 60.4, 49.2, 18.5, 15.0, 14.2 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{22}NO_4S$ $[M + H]^+$ m/z 396.1264. Found 396.1264.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 21bo



Yield: 81 mg (74%), White solid.

Mp: 233 °C

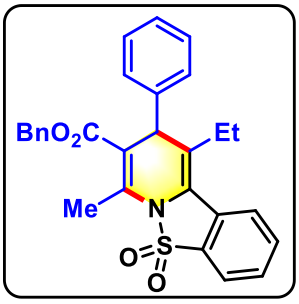
IR (neat): ν_{max} 3027, 2924, 1705, 1599, 1453, 1317, 1249, 1173, 1062, 967, 756 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.67-7.64 (m, 1H), 7.58-7.55 (m, 1H), 7.33-7.31 (m, 5H), 7.29-7.27 (m, 2H), 7.26-7.21 (m, 5H), 7.20-7.18 (m, 3H), 5.10-5.04 (m, 2H), 4.50 (s, 1H), 3.67-3.61 (m, 1H), 3.56-3.49 (m, 1H), 3.18-3.09 (m, 2H), 2.03 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.3, 144.8, 143.7, 141.5, 135.9, 133.6, 132.7, 129.3, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 127.4, 126.1, 124.5, 123.3, 121.6, 119.6, 66.5, 49.0, 35.8, 31.8, 18.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{34}H_{30}NO_4S$ $[M + H]^+$ m/z 548.1890. Found: 548.1891.

Compound 21ca



Yield: 46 mg (55%).

Mp: 176 °C

IR (neat): ν_{max} 1703, 1607, 1453, 1321, 1263, 1133, 1092, 971, 829, 734 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.69-7.66 (m, 1H), 7.59-7.56 (m, 1H), 7.33-7.32 (m, 3H), 7.25-7.21 (m, 5H), 7.20-7.17 (m, 2H), 5.07 (s, 2H), 4.49 (s, 1H), 2.92 (s, 3H), 2.48-2.40 (m, 1H), 2.35-2.28 (m, 1H), 1.02 (t, *J* = 7.5 Hz, 3H) ppm.

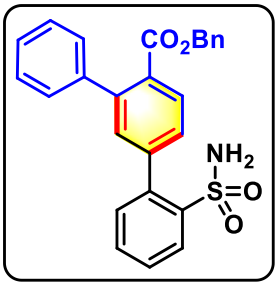
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 167.0, 144.2, 141.2, 136.0, 133.8, 132.5, 129.3, 129.0, 128.6 (2 s), 128.4, 128.2, 127.9, 127.3, 125.9, 124.2, 123.2, 121.6, 108.2, 66.4, 47.1, 24.5, 15.3, 12.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{28}H_{25}NO_4S$ $[M + H]^+$ m/z 472.1577. Found 472.1579. Calcd. For $C_{30}H_{27}N_2O_4S$ $[M + NH_4]^+$ m/z 511.1686. Found 511.1685.

3.8 Synthesis of Compounds 22aa-ai, 22ak, 22al, 22an and 22ao-ar: General Procedure

A Schlenk tube was charged with isothiazole dioxide **5** (0.20 mmol), *β′*-acetoxy allenoates **12** (0.24 mmol) in toluene (2.0 mL), and DMAP (0.04 mmol). Subsequently, DMAP base (0.04 mmol) was added to the reaction mixture and the stirring was continued for 12h. The advancement 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 (2 x 30 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product **22** was then purified by silica gel column chromatography using ethyl acetate/ hexane (20:80) as the eluent.

Compound 22aa



Yield: 67 mg (76%) using **5a** (36.2 mg, 0.20 mmol) and **12a** (77.4 mg, 0.24 mmol); White solid.

Mp: 211 °C

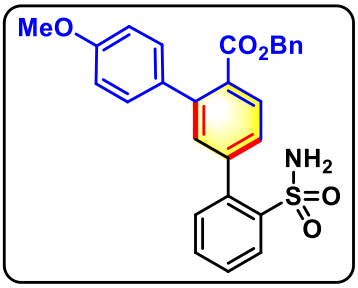
IR (neat): ν_{max} 3408, 3273, 2923, 1710, 1555, 1276, 1077, 760 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (dd, J_1 = 8.0, J_2 = 1.5, 1H), 7.91 (d, J = 8.5 Hz, 1H), 7.60 (td, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 7.54-7.50 (m, 3H), 7.36-7.35 (m, 6H), 7.29-7.25 (m, 3H), 7.05-7.03 (m, 2H), 5.12 (s, 2H), 4.36 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.5, 142.3, 142.2, 140.8, 140.5, 139.2, 135.3, 132.5, 132.3, 132.2, 131.1, 129.9, 128.6, 128.5 (2 s), 128.4 (3 s), 128.3, 128.0, 127.8, 67.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{21}NNaO_4S$ $[M + Na]^+$ m/z 466.1083. Found: 466.1080.

Compound 22ab



Yield: 80 mg (84%) using **5a** (36.2 mg, 0.20 mmol) and **12b** (84.6 mg, 0.24 mmol); White solid.

Mp: 180 °C

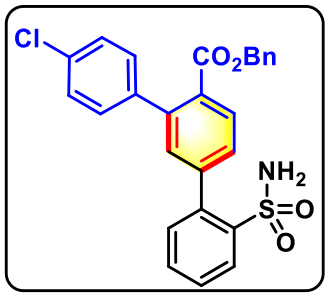
IR (neat): ν_{max} 3400, 3257, 1711, 1608, 1281, 1246, 1078, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.60-7.58 (m, 1H), 7.51-7.46 (m, 3H), 7.34 (d, J = 7.5 Hz, 1H), 7.29-7.25 (m, 5H), 7.10 (d, J = 3.5 Hz, 2H), 6.84 (d, J = 8.5 Hz, 2H), 5.14 (s, 2H), 4.43 (s, 2H), 3.80 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.7, 159.5, 142.1, 141.9, 140.8, 139.3, 135.4, 132.8, 132.4, 132.2 (2 s), 131.0, 129.9, 128.5 (2 s), 128.3, 127.9 (2 s), 113.9, 67.2, 55.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{27}N_2SO_5$ $[M + NH_4]^+$ m/z 491.1634. Found: 491.1632.

Compound 22ac



Yield: 74 mg (77%) using **5a** (36.2 mg, 0.20 mmol) and **12c** (85.6 g, 0.24 mmol); White solid.

Mp: 188 °C

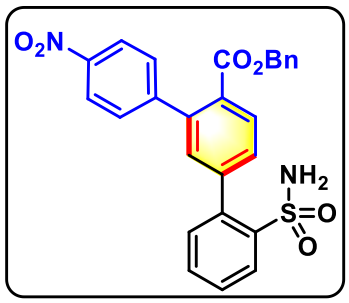
IR (neat): ν_{max} 3406, 3267, 3005, 1708, 1605, 1276, 1090, 748 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 7.5 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.63-7.60 (m, 1H), 7.54-7.52 (m, 2H), 7.48 (s, 1H), 7.35-7.31 (m, 4H), 7.25-7.22 (m, 4H), 7.11-7.09 (m, 2H), 5.14 (s, 2H), 4.35 (s, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.1, 142.4, 141.1, 140.8, 139.1, 139.0, 135.1, 134.0, 132.6, 132.4, 132.2, 130.8, 130.1, 129.9, 128.7, 128.6 (2s), 128.5 (2s), 128.1, 67.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{20}ClNNaSO_4$ $[M + Na]^+$ m/z 500.0694. Found: 500.0692.

Compound 22ad



Yield: 67 mg (69%) using **5a** (36.2 mg, 0.20 mmol) and **12d** (88.2 mg, 0.24 mmol); White solid.

Mp: 205 °C

IR (neat): ν_{max} 3398, 3261, 2922, 1716, 1463, 1346, 1264, 1164, 910, 736 cm^{-1}.

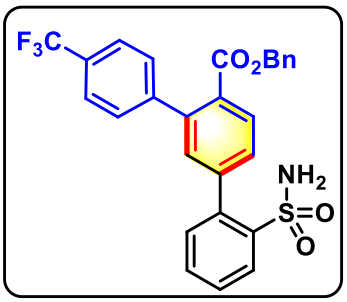
^{1}H NMR (500 MHz, $CDCl_3$):): δ 8.17 (d, *J* = 8.0 Hz, 1H), 8.05 (m, 3H), 7.64 (td, *J*1 = 7.5, *J*2 = 1.0 Hz, 1H), 7.59 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.55 (td, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.50 (d, *J* = 1.5 Hz, 1H), 7.42 (d, *J* = 9.0 Hz, 2H), 7.37 (dd, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.31-7.26 (m, 3H), 7.13 (d, *J* = 6.5 Hz, 2H), 5.14 (s, 2H), 4.44 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.2, 147.4, 147.2, 142.8, 140.7, 140.3, 138.8, 134.8, 132.6, 132.3, 132.1, 130.5, 130.3, 129.5, 129.4, 128.9, 128.8, 128.7, 128.6, 128.2, 123.4, 67.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{20}N_2NaO_6S$ $[M + Na]^+$ m/z 511.0934. Found 511.0933.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 22ae



Yield: 73 mg (71%) using **5a** (36.2 mg, 0.20 mmol) and **12e** (93.7 mg, 0.24 mmol); White solid.

Mp: 170 °C

IR (neat): ν_{max} 3402, 3275, 3062, 1709, 1607, 1279, 1107, 763 cm^{-1}.

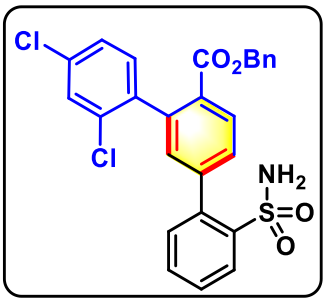
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16-8.15 (m, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.62 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.57-7.51 (m, 4H), 7.49 (d, *J* = 1.5 Hz, 1H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.35 (dd, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.31-7.26 (m, 3H), 7.05 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 2H), 5.12 (s, 2H), 4.40 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.8, 144.2, 142.6, 140.9, 140.7, 138.9, 134.9, 132.6, 132.5, 132.2, 130.6, 130.3, 129.8 (q, $^{2}J_{C-F}$ = 33.3 Hz), 129.0 (2s), 128.6 (3s), 128.1, 125.2 (q, $^{3}J_{C-F}$ = 3.6 Hz), 124.3 (q, $^{1}J_{C-F}$ = 271.0 Hz), 67.5 ppm.

^{19}F NMR (470 MHz, CDCl3): δ -62.4 ppm

HRMS (ESI-TOF): Calcd. For $C_{27}H_{24}F_3N_2O_4S$ $[M + NH_4]^+$ m/z 529.1403. Found: 529.1405.

Compound 22af



Yield: 67 mg (65%) using **5a** (36.2 mg, 0.20 mmol) and **12f** (93.9 mg, 0.24 mmol); White solid.

Mp: 135 °C

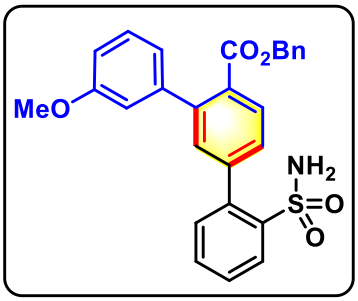
IR (neat): ν_{max} 3402, 3274, 3061, 1709, 1498, 1336, 1283, 1163, 1066, 764 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.17-8.14 (m, 2H), 7.63-7.60 (m, 2H), 7.53 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.37 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.34-7.33 (m, 4H), 7.27-7.26 (m, 1H), 7.18-7.15 (m, 4H), 5.14 (AB q, J = 12.0 Hz, 2H), 4.39 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.4, 143.0, 140.8, 139.2, 138.8, 138.6, 135.0, 134.1, 133.5, 132.5, 132.4, 132.0, 131.0, 130.7, 130.3, 129.6, 129.0, 128.7, 128.6, 128.5, 128.3, 127.0, 67.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{23}Cl_2N_2O_4S$ $[M + NH_4]^+$ m/z 529.0750. Found: 529.0751.

Compound 22ag



Yield: 74 mg (78%) using **5a** (36.2 mg, 0.20 mmol) and **12g** (84.6 mg, 0.24 mmol); White solid.

Mp: 184 °C

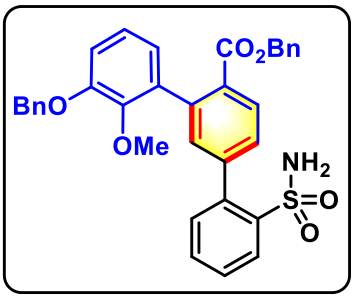
IR (neat): ν_{max} 3398, 3268, 3062, 1710, 1581, 1283, 1162, 1077, 764 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 7.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.63-7.60 (m, 1H), 7.54-7.51 (m, 3H), 7.37 (d, J = 7.0 Hz, 1H), 7.31-7.25 (m, 4H), 7.09-7.07 (m, 2H), 6.95-6.88 (m, 3H), 5.14 (s, 2H), 4.47 (s, 2H), 3.77 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.5, 159.6, 142.1, 142.0, 141.9, 140.7, 139.1, 135.2, 132.4, 132.2, 132.1, 131.0, 129.8, 129.4, 128.5, 128.4 (2 s), 128.3, 128.0, 121.1, 114.0, 113.6, 67.4, 55.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{27}N_2O_5S$ $[M + NH_4]^+$ m/z 491.1635. Found 491.1630.

Compound 22ah



Yield: 68 mg (72%) using **5a** (36.2 mg, 0.20 mmol) and **12h** (110.0 mg, 0.24 mmol); White solid.

Mp: 188 °C

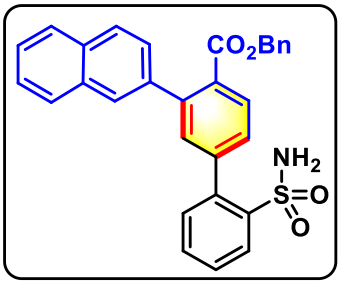
IR (neat): ν_{max} 3398, 3268, 3060, 1712, 1586, 1252, 1207, 1078, 763 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.59-7.56 (m, 1H), 7.51-7.49 (m, 2H), 7.47-7.42 (m, 3H), 7.35-7.32 (m, 3H), 7.28-7.27 (m, 2H), 7.25-7.24 (m, 2H), 7.06 (d, *J* = 4.0 Hz, 2H), 6.89 (s, 1H), 6.79 (s, 2H), 5.13 (s, 2H), 5.10 (s, 2H), 4.35 (s, 2H), 3.77 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.8, 149.5, 148.1, 142.0, 141.7, 140.8, 139.2, 137.2, 135.2, 133.6, 132.5, 132.3, 132.2, 131.2, 129.7, 128.7, 128.5, 128.4 (3 s), 128.0 (2 s), 127.9, 127.4, 120.9, 113.6, 112.5, 71.0, 67.3, 56.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{34}H_{33}N_2O_6S$ $[M + NH_4]^+$ m/z 597.2054. Found: 597.2051.

Compound 22ai



Yield: 71 mg (72%) using **5a** (36.2 mg, 0.20 mmol) and **12i** (89.4 mg, 0.24 mmol); White solid.

Mp: 160 °C

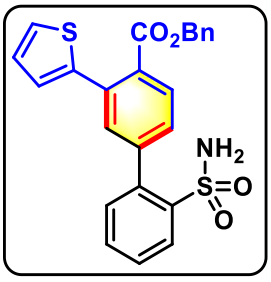
IR (neat): ν_{max} 3398, 3241, 2961, 1715, 1600, 1260, 1089, 799 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.19 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.85-7.83 (m, 2H), 7.81-7.78 (m, 2H), 7.64-7.61 (m, 2H), 7.58 (dd, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 7.54 (td, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.51-7.49 (m, 2H), 7.44 (dd, J_1 = 8.5, J_2 = 1.5 Hz, 1H), 7.40 (dd, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.16-7.14 (m, 1H), 7.05-7.01 (m, 2H), 6.83 (d, J = 7.5 Hz, 2H), 5.08 (s, 2H), 4.32 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.4, 142.4, 142.3, 140.8, 139.2, 138.1, 135.0, 133.4, 132.8, 132.6, 132.2, 131.2, 130.1, 128.5, 128.4, 128.3 (2 s), 128.1, 128.0, 127.9, 127.4, 127.0, 126.5, 126.4, 67.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{30}H_{27}N_2O_4S$ $[M + NH_4]^+$ m/z 511.1686. Found 511.1681.

Compound 22aj



Yield: 58 mg (65%) using **5a** (36.2 mg, 0.20 mmol) and **12j** (78.8 mg, 0.24 mmol); White solid.

Mp: 160 °C

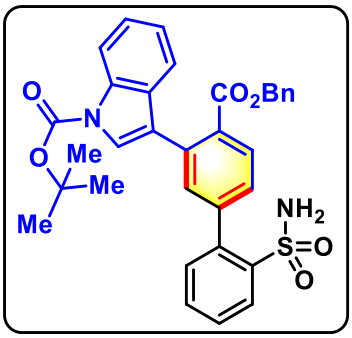
IR (neat): ν_{max} 3398, 3267, 2933, 1709, 1464, 1332, 1280, 1159, 956, 786 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18 (d, J = 7.5 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.63-7.60 (m, 2H), 7.55-7.52 (m, 2H), 7.36-7.31 (m, 5H), 7.21-7.19 (m, 2H), 7.06 (d, J = 3.0 Hz, 1H), 7.01-7.00 (m, 1H), 5.22 (s, 2H), 4.32 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.4, 142.1, 141.2, 140.7, 138.9, 135.3, 134.3, 132.6, 132.4, 132.3, 131.7, 129.6, 129.0, 128.7, 128.6, 128.5 (2s), 128.1, 127.6, 127.1, 126.5, 67.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{24}H_{19}NNaO_4S_2$ $[M + Na]^+$ m/z 472.0648. Found 472.0649.

Compound 22ak



Yield: 68 mg (72%) using **5a** (36.2 mg, 0.20 mmol) and **12k** (110.8 mg, 0.24 mmol); White solid.

Mp: 188 °C

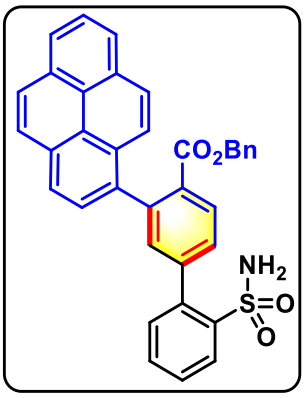
IR (neat): ν_{max} 3408, 3256, 2924, 1709, 1467, 1336, 1289, 1168, 1028, 736 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.18 (dd, J_1 = 7.5, J_2 = 0.5 Hz, 2H), 8.05-8.03 (m, 1H), 7.63-7.58 (m, 4H), 7.53 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.39-7.36 (m, 2H), 7.34-7.31 (m, 1H), 7.24-7.18 (m, 4H), 6.89 (d, J = 7.0 Hz, 2H), 4.97 (s, 2H), 4.33 (s, 2H), 1.65 (s, 9H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.0, 149.6, 142.8, 140.8, 139.1, 135.3, 135.1, 133.9, 132.9, 132.6, 132.2, 131.6, 130.4, 130.0, 128.8, 128.5 (2 s), 128.3 (2 s), 128.1, 124.8, 123.7, 123.2, 121.3, 119.3, 115.7, 84.0, 67.5, 28.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{33}H_{31}N_2O_4S$ $[M + H]^+$ m/z 583.1897. Found 583.1894.

Compound 22al



Yield: 75 mg (66%) using **5a** (36.2 mg, 0.20 mmol) and **12l** (107.2 mg, 0.24 mmol); White solid.

Mp: 100 °C

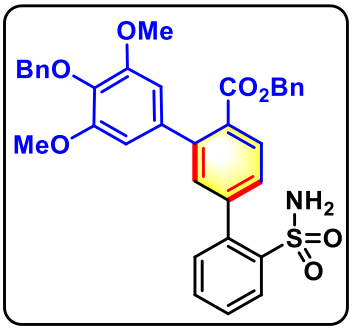
IR (neat): ν_{max} 3415, 3266, 3006, 1707, 1554, 1276, 1261, 1096, 753 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.22-8.19 (m, 2H), 8.15-8.12 (m, 2H), 8.09-8.07 (m, 2H), 8.04-8.00 (m, 2H), 7.94 (d, *J* = 9.5 Hz, 1H), 7.86 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 9.5 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.60-7.58 (m, 2H), 7.51-7.48 (m, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 6.64 (t, *J* = 7.5 Hz, 2H), 6.41 (d, *J* = 7.5 Hz, 2H), 4.73 (s, 2H), 4.49 (s, 2H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.5, 142.7, 141.7, 140.7, 139.2, 136.3, 134.4, 133.6, 132.5, 132.1, 131.9, 131.6, 131.0, 130.9, 130.4, 128.9, 128.8, 128.5, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 126.8, 126.1, 125.3, 125.2, 124.9, 124.7 (2 s), 124.4, 67.2 ppm.

HRMS (ESI-TOF): Calcd. For $C_{36}H_{25}NNaO_4S$ $[M + Na]^+$ m/z 590.1397. Found 590.1395.

Compound 22am



Yield: 90 mg (74%) using **5a** (36.2 mg, 0.20 mmol) and **12m** (117.2 g, 0.24 mmol); White solid.

Mp: 160 °C

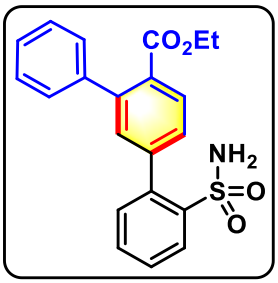
IR (neat): ν_{max} 3405, 3273, 3059, 1713, 1583, 1240, 1066, 758 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.63-7.59 (m, 2H), 7.54-7.49 (m, 4H), 7.37-7.33 (m, 3H), 7.28-7.26 (m, 4H), 7.10 (s, 2H), 6.59 (s, 2H), 5.12 (s, 2H), 5.00 (s, 2H), 4.40-4.39 (m, 2H), 3.75 (s, 6H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.9, 153.5, 142.0, 141.9, 140.8, 139.2, 138.0, 136.9, 136.2, 135.2, 132.5, 132.3, 132.2, 131.4, 129.6, 128.6, 128.5 (2s), 128.4 (2s), 128.3, 128.1 (2s), 128.0, 106.0, 75.2, 67.5, 56.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{35}H_{31}NNaO_7S$ $[M + Na]^+$ m/z 632.1713. Found 632.1716.

Compound 22an



Yield: 60 mg (78%) using **5a** (36.2 mg, 0.20 mmol) and **12n** (62.5 mg, 0.24 mmol); White solid.

Mp: 163 °C

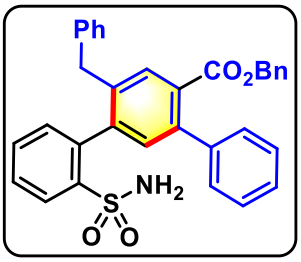
IR (neat): ν_{max} 3409, 3259, 2956, 1707, 1554, 1465, 1335, 1285, 1161, 1045, 901, 760 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 7.5 Hz, 1H), 7.60 (td, J_1 = 7.5 J_2 = 1.5 Hz, 1H), 7.53-7.50 (m, 3H), 7.39-7.33 (m, 6H), 4.43-4.41 (m, 2H), 4.12 (q, *J* = 7.0 Hz, 2H), 1.03 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.6, 142.3, 142.0, 140.8, 140.7, 139.3, 132.4, 132.2, 132.1, 131.4, 129.7, 128.6, 128.3 (2 s), 128.0, 127.6, 61.4, 13.8 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{23}N_2O_4S$ $[M + NH_4]^+$ m/z 399.1373. Found 399.1374.

Compound 22ao



Yield: 68 mg (72%) using **5a** (36.2 mg, 0.20 mmol) and **12o** (99.0 mg, 0.24 mmol); White solid.

Mp: 188 °C

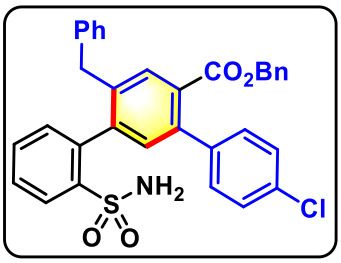
IR (neat): ν_{max} 3400, 3265, 2963, 1711, 1547, 1492, 1337, 1236, 1073, 748 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, *J* = 7.5 Hz, 1H), 7.83 (s, 1H), 7.61-7.54 (m, 2H), 7.41 (s, 1H), 7.31 (s, 6H), 7.25 (s, 2H), 7.17 (s, 4H), 7.00 (d, *J* = 6.0 Hz, 2H), 6.78 (d, *J* = 4.0 Hz, 2H), 5.14-5.08 (m, 2H), 3.98 (d, *J* = 14.5 Hz, 1H), 3.82 (d, *J* = 15.0 Hz, 1H), 3.48 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.6, 141.0, 140.7, 140.1, 140.0, 139.3, 138.7, 137.6, 135.2, 133.4, 132.4, 132.2, 131.6, 131.5, 129.2, 128.7, 128.6 (2s), 128.5, 128.4 (2s), 128.3, 127.7, 126.7, 67.3, 39.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{33}H_{28}NO_4S$ $[M + H]^+$ m/z 534.1734. Found 534.1736.

Compound 22aq



Yield: 80 mg (70%) using **5a** (36.2 mg, 0.20 mmol) and **12q** (107.3 mg, 0.24 mmol); White solid.

Mp: 160 °C

IR (neat): ν_{max} 3409, 3271, 3029, 1708, 1598, 1489, 1336, 1236, 1091, 764 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, *J* = 7.5 Hz, 1H), 7.86 (s, 1H), 7.62-7.55 (m, 2H), 7.37-7.30 (m, 5H), 7.25-7.20 (m, 4H), 7.19-7.17 (m, 3H), 7.07-7.06 (m, 2H), 6.78-6.77 (m, 2H), 5.16-5.11 (m, 2H), 3.98 (d, *J* = 15.0 Hz, 1H), 3.82 (d, *J* = 14.5 Hz, 1H), 3.45 (s, 2H) ppm.

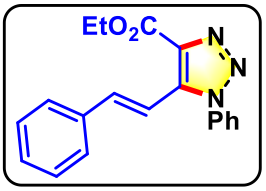
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.1, 141.1, 140.8, 139.2, 139.0, 138.8, 138.6, 137.5, 135.1, 133.8, 133.6, 132.4, 132.1, 131.8, 131.3, 130.0, 129.2, 128.8, 128.7, 128.6, 128.5, 126.8, 67.4, 39.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{33}H_{30}ClN_2O_4S$ $[M + NH_4]^+$: m/z 585.1609. Found 585.1607.

3.9 Synthesis of Compounds 23aa-aj, 23ba-ea, 23fa-fg, 23fi: General Procedure

A Schlenk tube was charged with azide **14** (1.5 mmol) and acetoxy allenoate **8** (0.50 mmol) in DMF (2.0 mL). The mixture was stirred at 70 °C for 12 h, and the 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.

Compound 23aa



Yield: 131.0 mg (82%) using **14a** (137.0 mg, 1.5 mmol) and **8a** (130.2 mg, 0.50 mmol); White solid.

Mp: 265-267 °C.

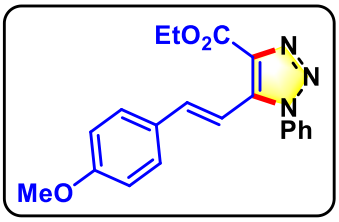
IR (neat): ν_{max} 2923, 2853, 1715, 1635, 1496, 1450, 1375, 1211, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = δ 7.60-7.58 (m, 3H), 7.54-7.52 (m, 2H), 7.37-7.28 (m, 6H), 7.21 (d, *J* = 17.0 Hz, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 139.7, 138.5, 136.4, 136.2, 135.8, 130.5, 130.0, 129.6, 129.0, 127.3, 126.2, 111.2, 61.5, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{18}N_3O_2$ $[M + H]^+$ *m/z* 320.1394. Found: 320.1397.

Compound 23ab



Yield: 134.4 mg (77%) using **14a** (137.0 mg, 1.5 mmol) and **8b** (145.2 mg, 0.50 mmol); White solid.

Mp: 253-255 °C

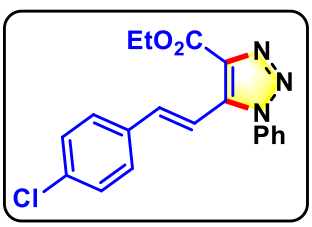
IR (neat): ν_{max} 2927, 1715, 1603, 1535, 1509, 1459, 1251, 1174, 1094, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.60-7.57 (m, 3H), 7.54-7.51 (m, 2H), 7.32-7.30 (m, 2H), 7.27 (d, *J* = 17.0 Hz, 1H), 7.06 (d, *J* = 17.0 Hz, 1H), 6.86-6.84 (m, 2H), 4.51 (q, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 162.0, 160.9, 139.3, 138.9, 136.5, 135.8, 130.4, 129.9, 128.8, 128.5, 126.3, 114.4, 108.8, 61.5, 55.5, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{20}N_3O_3$ $[M + H]^+$ *m/z* 350.1499. Found: 350.1498.

Compound 23ac



Yield: 128.5 mg (73%) using **14a** (137.0 mg, 1.5 mmol) and **8c** (147.4 mg, 0.50 mmol); White solid.

Mp: 269-271 °C.

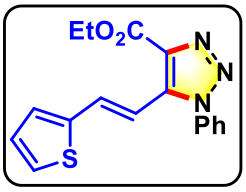
IR (neat): ν_{max} 2980, 1705, 1532, 1251, 1183, 1087, 1027, 765 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.58-7.56 (m, 3H), 7.50-7.47 m, 2H), 7.27-7.23 (m, 5H), 7.14 (d, *J* = 16.5 Hz, 1H), 4.48 (q, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 138.3, 138.2, 136.2$_9$, 136.2$_5$, 135.4, 134.3, 130.5, 130.0, 129.2, 128.5, 126.2, 111.7, 61.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}ClN_3O_2$ $[M + H]^+$ *m/z* 354.1004. Found: 354.1030.

Compound 23af



Yield: 118.7 mg (73%) using **14a** (137.0 mg, 1.5 mmol) and **8f** (133.2 mg, 0.50 mmol); White solid.

Mp: 270-272 °C.

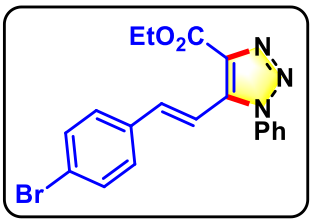
IR (neat): ν_{max} 2920, 1712, 1625, 1541, 1435, 1374, 1248, 1187, 1112, 1017, 766, 690 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.62-7.59 (m, 4H), 7.52-7.51 (m, 2H), 7.29 (d, *J* = 5.0 Hz, 1H), 7.05 (d, *J* = 3.0 Hz, 1H), 7.00-6.98 (m, 1H), 6.94 (d, *J* = 16.5 Hz, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 141.3, 138.2, 136.2, 136.0, 132.7, 130.5, 130.0, 129.3, 128.1, 127.3, 126.2, 110.0, 61.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{17}H_{16}N_3O_2S$ $[M + H]^+$ *m/z* 326.0958. Found: 326.0953.

Compound 23ag



Yield: 149.0 mg (75%) using **14a** (137.0 mg, 1.5 mmol) and **8g** (179.6 mg, 0.50 mmol); Gummy liquid.

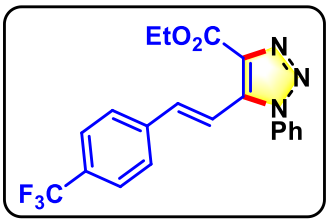
IR (neat): ν_{max} 2981, 1714, 1639, 1537, 1495, 1375, 1246, 1208, 1090, 834, 752 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.58-7.56 (m, 3H), 7.49-7.47 (m, 2H), 7.42 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 2.5 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.15 (d, *J* = 16.5 Hz, 1H), 4.48 (q, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.8, 140.2, 138.5, 136.6, 136.4, 135.6, 134.9, 130.2, 129.8, 129.1, 127.4, 125.8, 110.9, 61.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}BrN_3O_2$ $[M + H]^+$ *m/z* 398.0499. Found: 398.0499.

Compound 23ah



Yield: 137.4 mg (71%) using **14a** (137.0 mg, 1.5 mmol) and **8h** (164.2 mg, 0.50 mmol); Gummy liquid.

IR (neat): ν_{max} 2923, 1727, 1324, 1126, 905, 729 cm^{-1}.

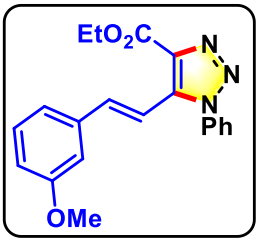
^1H NMR (500 MHz, $CDCl_3$): δ = 7.62-7.61 (m, 3H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.53-7.51 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 16.5 Hz, 1H), 7.27 (d, *J* = 16.5 Hz, 1H), 4.52 (q, *J* = 7.0 Hz, 2H), 1.49 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 139.2, 137.9, 137.8, 136.6, 136.2, 131.1 (q, $^2J_{C-F}$ = 32.7 Hz), 130.7, 130.1, 127.5, 126.2, 125.9 (q, $^3J_{C-F}$ = 3.6 Hz), 124.0 (q, $^1J_{C-F}$ = 270.9 Hz), 113.7, 61.7, 14.5 ppm.

^{19}F NMR (470 MHz, $CDCl_3$): δ = -62.8.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{16}F_3N_3NaO_2$ $[M + Na]^+$ *m/z* 410.1087. Found: 410.1088.

Compound 23ai



Yield: 138.0 mg (79%); using **14a** (137.0 mg, 1.5 mmol) and **8i** (145.2 mg, 0.50 mmol); White solid.

Mp: 220-222 °C.

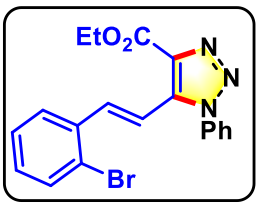
IR (neat): ν_{max} 2986, 2931, 1715, 1596, 1495, 1376, 1256, 1199, 1093, 1045, 764 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.62-7.61 (m, 3H), 7.57-7.55 (m, 2H), 7.33-7.28 (m, 2H), 7.21 (d, *J* = 17.0 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.91-6.88 (m, 2H), 4.54 (q, *J* = 7.0 Hz, 2H), 3.83 (s, 3H), 1.52 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 160.1, 139.6, 138.4, 137.2, 136.4, 136.2, 130.5, 130.0, 126.2, 119.9, 115.1, 112.8, 111.5, 61.5, 55.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{20}N_3O_3$ $[M + H]^+$ *m/z* 350.1499. Found: 350.1499.

Compound 23aj



Yield: 145.0 mg (73%) using **14a** (137.0 mg, 1.5 mmol) and **8j** (169.6 mg, 0.50 mmol); White solid.

Mp: 154-156 °C

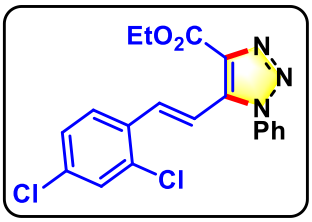
IR (neat): ν_{max} 2974, 1720, 1638, 1494, 1459, 1382, 1196, 1096, 1018, 996, 761 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.63-7.56 (m, 4H), 7.53-7.50 (m, 3H), 7.43-7.33 (m, 2H), 7.30-7.27 (m, 1H), 7.16-7.12 (m, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 161.8, 137.9, 137.4, 136.5, 135.7, 133.3, 130.6, 130.5, 130.2, 127.8, 127.0, 126.3, 124.8, 113.9, 61.6, 14.5.ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}BrN_3O_2$ $[M + H]^+$ *m/z* 398.0499. Found: 398.0500.

Compound 23ak



Yield: 135.5 mg (70%) using **14a** (137.0 mg, 1.5 mmol) and **8k** (169.6 mg, 0.50 mmol); Gummy liquid.

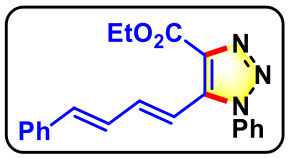
IR (neat): ν_{max} 2924, 1716, 1584, 1468, 1376, 1210, 1101, 1050, 764 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62-7.60 (m, 3H), 7.54-7.50 (m, 3H), 7.42 (d, *J* = 16.5 Hz, 1H), 7.36-7.32 (m, 2H), 7.23 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1H), 4.52 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 161.8, 137.9, 136.7, 136.5, 135.6, 134.9, 133.8, 132.7, 130.7, 130.2, 129.9, 127.7, 127.6, 126.3, 114.1, 61.7, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{16}Cl_2N_3O_2$ $[M + H]^+$ *m/z* 388.0614. Found: 388.0614.

Compound 23al



Yield: 122.5 mg (71%) using **14a** (137.0 mg, 1.5 mmol) and **8l** (143.2 mg, 0.50 mmol); Gummy liquid.

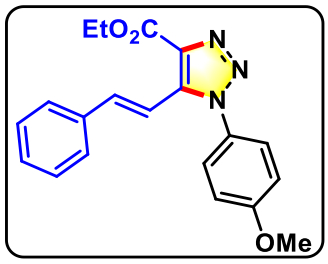
IR (neat): ν_{max} 2921, 1714, 1638, 1535, 1495, 1372, 1203, 1082, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.57-7.56 (m, 3H), 7.47-7.45 (m, 2H), 7.35 (d, *J* = 7.5 Hz, 2H), 7.29-7.26 (m, 2H), 7.24-7.20 (m, 2H), 6.79 (d, *J* = 15.5 Hz, 1H), 6.67 (d, *J* = 15.5 Hz, 1H), 6.61 (d, *J* = 15.5 Hz, 1H), 4.47 (q, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 162.0, 140.3, 138.6, 138.0, 136.4, 136.3, 135.9, 130.5, 129.9, 128.9, 128.8, 128.2, 127.0, 126.3, 114.2, 61.5, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{20}N_3O_2$ $[M + H]^+$ *m/z* 346.1550. Found: 346.1552.

Compound 23ba



Yield: 138.0 mg (79%) using **14b** (223.8 mg, 1.50 mmol) and **8a** (130.2 mg, 0.50 mmol); Gummy liquid.

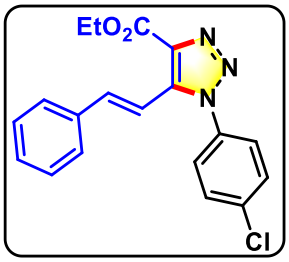
IR (neat): ν_{max} 2924, 1712, 1513, 1448, 1375, 1250, 1208, 1192, 1105, 1019, 735, 695 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44-7.41 (m, 2H), 7.39-7.36 (m, 2H), 7.35-7.30 (m, 4H), 7.19 (d, *J* = 17.0 Hz, 1H), 7.08-7.05 (m, 2H), 4.50 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 162.0, 161.0, 139.4, 138.5, 136.0, 135.9, 129.5, 129.2, 128.9, 127.6, 127.3, 115.0, 111.4, 61.5, 55.8, 14.6 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{20}N_3O_3$ $[M + H]^+$ *m/z* 350.1499. Found: 350.1496.

Compound 23ca



Yield: 129.0 mg (73%) using **14c** (230.4 mg, 1.50 mmol) and **8a** (130.2 mg, 0.50 mmol); White solid.

Mp: 270-272 °C.

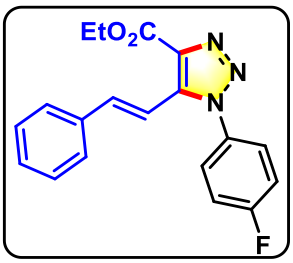
IR (neat): ν_{max} 2980, 2926, 1706, 1642, 1533, 1488, 1204, 1187, 1068, 996, 842, 765 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 9.0 Hz, 2H), 7.49 (d, *J* = 9.0 Hz, 2H), 7.40-7.34 (m, 6H), 7.16 (d, *J* = 16.5 Hz, 1H) 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 138.3, 138.2, 136.3, 134.7, 132.1, 130.5, 130.0, 128.7, 126.2, 123.7, 111.8, 61.6, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{16}ClN_3NaO_2$ $[M + Na]^+$: *m/z* 376.0823. Found: 376.0820.

Compound 23da



Yield: 118.0 mg (70%) using **14d** (205.7 mg, 1.50 mmol) and **8a** (130.2 mg, 0.50 mmol); Gummy liquid.

IR (neat): ν_{max} 2925, 1715, 1633, 1511, 1448, 1209, 1090, 908, 841, 729 cm^{-1}.

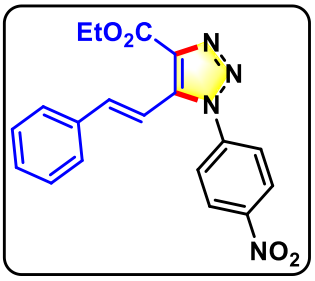
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54-7.51 (m, 2H), 7.39-7.33 (m, 6H), 7.30-7.27 (m, 2H), 7.30-7.27 (m, 3H), 7.17 (d, *J* = 17.0 Hz, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 163.5 (d, $^{1}J_{C\text{-}F}$ = 250.7 Hz), 161.8, 140.0, 138.6, 136.2, 135.6, 132.5, 129.7, 129.0, 128.2 (d, $^{3}J_{C\text{-}F}$ = 8.9 Hz), 127.3, 117.0 (d, $^{2}J_{C\text{-}F}$ = 23.1 Hz), 110.9, 61.6, 14.5 ppm.

^{19}F NMR (470 MHz, $CDCl_3$): δ = -109.2.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}FN_3O_2$ $[M + H]^+$ *m/z* 338.1299. Found: 338.1297.

Compound 23ea



Yield: 125.6 mg (69%) using **14e** (246.2 mg, 1.50 mmol) and **8a** (130.2 mg, 0.50 mmol); White solid.

Mp: 298-300 °C.

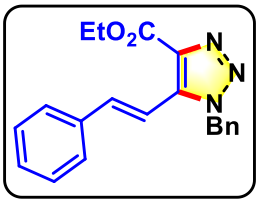
IR (neat): ν_{max} 2934, 1715, 1592, 1519, 1341, 1240, 1191, 1104, 992, 852, 750 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.48-8.45 (m, 2H), 7.82-7.79 (m, 2H), 7.41-7.35 (m, 6H), 7.16 (d, *J* = 16.5 Hz, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.4, 148.5, 141.2, 141.1, 138.6, 136.9, 135.2, 130.1, 129.2, 127.4, 126.7, 125.4, 110.4, 61.8, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{19}H_{17}N_4O_4$ $[M + H]^+$ *m/z* 365.1244. Found: 365.1246.

Compound 23fa



Yield: 141.6 mg (85%) using **14f** (199.8 mg, 1.50 mmol) and **8a** (130.2 mg, 0.50 mmol); Gummy liquid.

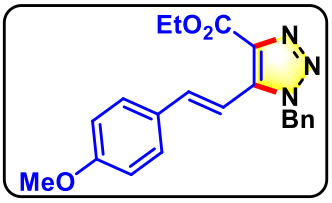
IR (neat): ν_{max} 2980, 1711, 1642, 1539, 1451, 1373, 1174, 1049, 969, 850, 750 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39-7.31 (m, 9H), 7.21-7.20 (m, 2H), 7.17 (d, *J* = 16.5 Hz, 1H), 5.71 (s, 2H), 4.45 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.8, 139.5, 138.4, 136.6, 135.7, 134.7, 129.6, 129.3, 129.0, 128.7, 127.2, 127.0, 111.1, 61.4, 52.9, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{20}N_3O_2$ $[M + H]^+$ *m/z* 334.1550. Found: 334.1552.

Compound 23fb



Yield: 145.3 mg (80%) using **14f** (199.8 mg, 1.50 mmol) and **8b** (145.2 mg, 0.50 mmol); Gummy liquid.

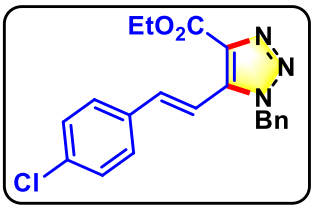
IR (neat): ν_{max} 2979, 2360, 1711, 1602, 1509, 1455, 1248, 970, 820, 726 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38-7.28 (m, 6H), 7.20 (d, *J* = 7.0 Hz, 2H), 7.02 (d, *J* = 16.5 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 5.69 (s, 2H), 4.45 (q, *J* = 7.0 Hz, 2H), 3.82 (s, 3H), 1.44 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.9, 160.8, 139.1, 138.8, 136.3, 134.8, 129.3, 128.7, 128.6, 128.4, 127.0, 114.4, 108.7, 61.3, 55.5, 52.8, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}N_3O_3$ $[M + H]^+$ *m/z* 364.1656. Found: 364.1656.

Compound 23fc



Yield: 139.5 mg (76%) using **14f** (199.8 mg, 1.50 mmol) and **8c** (147.4 mg, 0.50 mmol); White solid.

Mp: 248-250 °C.

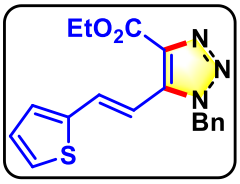
IR (neat): ν_{max} 2980, 1713, 1538, 1490, 1455, 1344, 1185, 1090, 813, 726 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38-7.28 (m, 8H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.11 (d, *J* = 17.0 Hz, 1H), 5.70 (s, 2H), 4.44 (q, *J* = 7.0 Hz, 2H), 1.43 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.7, 138.0 (2 s), 136.7, 135.4, 134.6, 134.2, 129.3, 129.2, 128.8, 128.4, 126.9, 111.6, 61.5, 53.0, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{18}ClN_3NaO_2$ $[M + Na]^+$ *m/z* 390.0980. Found: 390.0992.

Compound 23ff



Yield: 127.2 mg (75%); using **14f** (199.8 mg, 1.50 mmol) and **8f** (133.2 mg, 0.50 mmol); Gummy liquid.

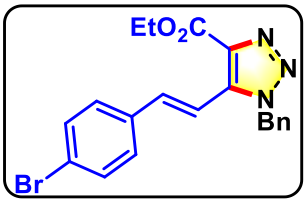
IR (neat): ν_{max} 2981, 1710, 1631, 1496, 1341, 1244, 1096, 1043, 957, 852, 786 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.70 (d, *J* = 16.5 Hz, 1H), 7.38-7.29 (m, 4H), 7.20 (d, *J* = 7.5 Hz, 2H), 7.08 (d, *J* = 3.0 Hz, 1H), 7.00-6.99 (m, 1H), 6.88 (d, *J* = 16.5 Hz, 1H), 5.67 (s, 2H), 4.45 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.7, 141.1, 137.9, 136.3, 134.5, 132.6, 129.2, 128.6, 128.0, 127.1, 109.7, 61.3, 52.8, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{18}H_{18}N_3O_2S$ $[M + H]^+$: *m/z* 340.1114. Found: 340.1123.

Compound 23fg



Yield: 162.4 mg (79%) using **14f** (199.8 mg, 1.50 mmol) and **8g** (169.6 mg, 0.50 mmol); Gummy liquid.

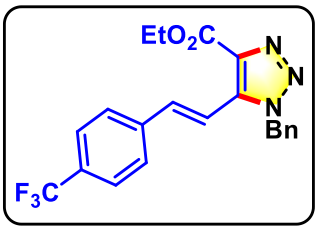
IR (neat): ν_{max} 2981, 1712, 1642, 1486, 1175, 1071, 1050, 855, 725 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.0 Hz, 2H), 7.38-7.33 (m, 3H), 7.30 (d, *J* = 16.5 Hz, 1H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.12 (d, *J* = 16.5 Hz, 1H), 5.70 (s, 2H), 4.44 (q, *J* = 7.0 Hz, 2H), 1.43 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.7, 138.1, 138.0, 136.8, 134.6_3, 134.5_8, 132.2, 129.3, 128.7, 128.6, 126.9, 123.6, 111.8, 61.4, 53.0, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{19}BrN_3O_2$ $[M + H]^+$ *m/z* 412.0655. Found: 412.0650.

Compound 23fh



Yield: 144.4 mg (72%) using **14f** (199.8 mg, 1.50 mmol) and **8h** (164.2 mg, 0.50 mmol); Gummy liquid.

IR (neat): ν_{max} 2982, 1715, 1644, 1455, 1320, 1161, 1110, 1014, 971, 823, 723 cm^{-1}.

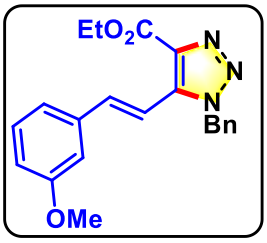
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 7.42-7.33 (m, 4H), 7.23-7.19 (m, 3H), 5.72 (s, 2H), 4.46 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.7, 139.1, 137.8, 137.7, 137.1, 134.5, 131.1 (q, $^{2}J_{C\text{-}F}$ = 32.2 Hz), 129.4, 128.9, 127.4, 127.0, 126.0 (q, $^{3}J_{C\text{-}F}$ = 3.5 Hz), 124.0 (q, $^{1}J_{C\text{-}F}$ = 270.6 Hz), 113.6, 61.6, 53.1, 14.5 ppm.

^{19}F NMR (470 MHz, $CDCl_3$): δ = -62.8.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{19}N_3O_2$ $[M + H]^+$ *m/z* 402.1424. Found: 402.1423.

Compound 23fi



Yield: 149.0 mg (82%) using **14f** (199.8 mg, 1.50 mmol) and **8i** (145.2 mg, 0.50 mmol); White solid.

Mp: 216-218 °C.

IR (neat): ν_{max} 2980, 1715, 1577, 1432, 1377, 1262, 1044, 970, 843, 731 cm^{-1}.

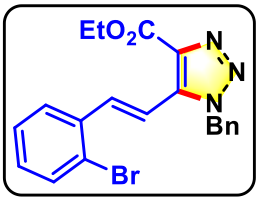
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37-7.28 (m, 4H), 7.24-7.23 (m, 1H), 7.18 (d, *J* = 7.0 Hz, 2H), 7.11 (d, *J* = 16.5 Hz, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.87-6.85 (m, 2H), 5.68 (s, 2H), 4.43 (q, *J* = 7.0 Hz, 2H), 3.79 (s, 3H), 1.42 (t, *J* = 7.0 Hz, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 161.7, 160.0, 139.4, 138.2, 137.1, 136.7, 134.7, 130.0, 129.3, 128.7, 127.0, 119.8, 115.2, 112.5, 111.4, 61.3, 55.4, 52.9, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}N_3O_3$ $[M + H]^+$ *m/z* 364.1656. Found: 364.1659.

This compound was crystallized from an ethyl acetate-hexane (2:1) mixture at room temperature. X-ray structure has been determined for this compound.

Compound 23fj



Yield: 152.1 mg (74%) using **14f** (199.8 mg, 1.50 mmol) and **8j** (169.6 mg, 0.50 mmol); White solid.

Mp: 214-216 ^{o}C.

IR (neat): ν_{max} 2980, 1710, 1538, 1456, 1244, 1185, 1050, 967, 849, 749 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57-7.52 (m, 3H), 7.36-7.29 (m, 4H), 7.26 (d, *J* = 17.0 Hz, 1H), 7.18-7.15 (m, 3H), 5.78 (s, 2H), 4.47 (q, *J* = 7.0 Hz, 2H), 1.44 (t, *J* = 7.0 Hz, 3H) ppm.

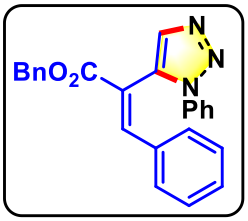
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 161.7, 137.8, 137.2, 135.9, 134.4, 133.3, 130.6, 129.3, 128.6, 127.9, 127.3, 126.8, 124.7, 114.4, 61.5, 53.0, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{20}H_{19}N_3O_2$ $[M + H]^+$ *m/z* 412.0655. Found: 412.0655.

3.10 Synthesis of Compounds 24aa-fe: General Procedure

A Schlenk tube was charged with azide **14** (1.5 mmol) and *β′*-acetoxy allenoate **12** (0.50 mmol) in DMF (2.0 mL). The mixture was stirred at 70 °C for 12 h, and the 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.

Compound 24aa



Yield: 135.3 mg (71%) using **14a** (137.0 mg, 1.5 mmol) and **12a** (161.2 mg, 0.50 mmol); Gummy liquid.

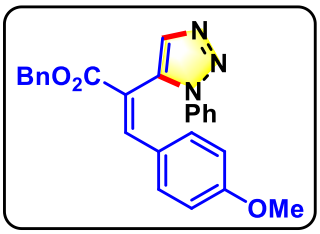
IR (neat): ν_{max} 2889, 1702, 1599, 1507, 1306, 1245, 1166, 1032, 912, 830, 757 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.00 (s, 1H), 7.71 (s, 1H), 7.32-7.29 (m, 5H), 7.24-7.18 (m, 7H), 7.14-7.13 (m, 2H), 6.99 (d, *J* = 7.5 Hz, 1H), 5.09 (s, 2H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 165.3, 147.2, 136.5, 135.4, 134.8, 133.2, 132.1, 130.9, 130.3, 129.3, 129.1, 129.0, 128.7, 128.5, 128.2, 123.9, 118.2, 67.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{24}H_{20}N_3O_2$ $[M + H]^+$ *m/z* 382.1550. Found: 382.1500.

Compound 24ab



Yield: 142.0 mg (69%) using **14a** (137.0 mg, 1.5 mmol) and **12b** (176.2 mg, 0.50 mmol); Gummy liquid.

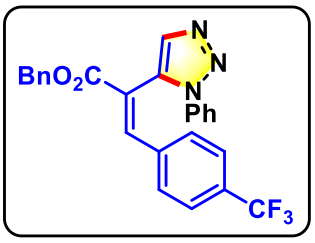
IR (neat): ν_{max} 2889, 1702, 1599, 1507, 1306, 1245, 1167, 1032, 912, 830, 757 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.06 (s, 1H), 8.05 (s, 1H), 7.76 (d, *J* = 7.5 Hz, 2H), 7.52-7.51 (m, 2H), 7.45-7.43 (m, 1H), 7.40-7.37 (m, 3H), 7.35-7.32 (m, 2H), 7.28 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 8.5Hz, 2H), 5.29 (s, 2H), 3.77 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 167.0, 161.1, 144.4, 142.5, 137.1, 136.2, 132.6, 129.9, 128.8, 128.7, 128.3, 128.2, 126.8, 121.9, 120.5, 118.7, 114.0, 67.1, 55.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{25}H_{22}N_3O_3$ $[M + H]^+$ *m/z* 412.1656. Found: 412.1656.

Compound 24ac



Yield: 150.5 mg (67%) using **14a** (137.0 mg, 1.5 mmol) and **12c** (195.2 mg, 0.50 mmol); Gummy liquid.

IR (neat): ν_{max} 2924, 2853, 1713, 1601, 1500, 1324, 1243, 1168, 1067, 838, 759 cm^{-1}.

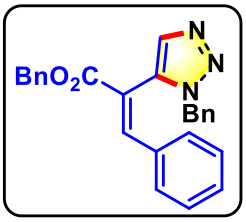
^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (s, 1H), 8.06 (s, 1H), 7.74-7.72 (m, 2H), 7.54-7.525 (m, 4H), 7.45-7.42 (m, 3H), 7.40-7.35 (m, 5H), 5.33 (s, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 166.1, 142.0, 141.4, 138.0, 136.8, 131.0 (q, $^{2}J_{C-F}$ = 31.8 Hz), 130.4, 129.8, 128.9 (2 s), 128.7, 128.5, 128.3, 125.6 (q, $^{3}J_{C-F}$ = 3.4 Hz), 124.0 (q, $^{1}J_{C-F}$ = 271.6 Hz), 123.5, 122.2, 120.4, 67.5 ppm.

^{19}F NMR (470 MHz, $CDCl_3$): δ = -62.9.

HRMS (ESI-TOF): Calcd. For $C_{25}H_{19}F_3N_3O_2$ $[M + H]^+$ *m/z* 450.1424. Found: 450.1425.

Compound 24fa



Yield: 150.2 mg (76%) using **14f** (199.8 mg, 1.50 mmol) and **12a** (161.2 mg, 0.50 mmol); Gummy liquid.

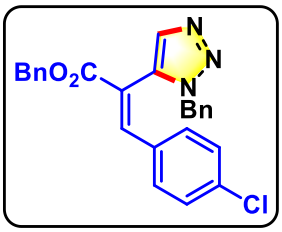
IR (neat): ν_{max} 2879, 1705, 1631, 1496, 1445, 1325, 1237, 1196, 1057, 905, 728 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.03 (s, 1H), 7.42 (s, 1H), 7.37-7.34 (m, 8H), 7.28-7.27 (m, 1H), 7.24-7.21 (m, 6H), 5.57 (s, 2H), 5.28 (s, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 166.8, 144.4, 142.0, 136.1, 134.9, 134.4, 130.5, 129.8, 129.2, 128.8, 128.7, 128.4, 128.3, 127.9, 123.9, 122.0, 67.2, 54.2 ppm.

HRMS (ESI-TOF): Calcd. For $C_{25}H_{22}N_3O_2$ $[M + H]^+$ *m/z* 396.1707. Found: 396.1696.

Compound 24fd



Yield: 154.5 mg (72%) using **14f** (199.8 mg, 1.50 mmol) and **12d** (178.4 mg, 0.50 mmol); White solid.

Mp: 217-219 °C.

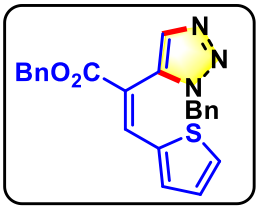
IR (neat): ν_{max} 3054, 2986, 1736, 1422, 1265, 896, 744, 706, 666 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (s, 1H), 7.43 (s, 1H), 7.36-7.33 (m, 8H), 7.22-7.12 (m, 6H), 5.55 (s, 2H), 5.24 (s, 2H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ = 166.5, 142.7, 141.6, 135.9, 135.7, 134.8, 132.9, 131.6, 129.3, 128.9, 128.7$_1$, 128.6$_7$, 128.4, 128.2, 128.0, 124.0, 122.5, 67.3, 54.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{25}H_{21}ClN_3O_2$ $[M + H]^+$: *m/z* 430.1317. Found: 430.1317.

Compound 24fj



Yield: 128.4 mg (64%) using **14f** (199.8 mg, 1.50 mmol) and **12j** (164.2 mg, 0.50 mmol); White solid.

Mp: 201-203 °C.

IR (neat): ν_{max} 2986, 2927, 1709, 1620, 1421, 1265, 1202, 1043, 896, 738 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.18 (s, 1H), 7.53 (s, 1H), 7.36-7.31 (m, 12H), 6.97-6.96 (m, 1H), 5.61 (s, 2H), 5.23 (s, 2H) ppm.

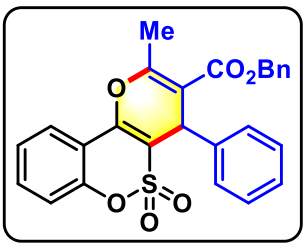
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 166.6, 141.1, 137.9, 137.5, 136.1, 135.1, 134.8, 131.5, 129.2, 128.8, 128.6, 128.2, 128.1, 128.0, 127.0, 124.3, 117.9, 67.0, 54.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{23}H_{20}N_3O_2S$ $[M + H]^+$ *m/z* 402.1271. Found: 402.1279.

3.11 Synthesis of Compounds 28a-b, 28i-k and 28n General Procedure

A Schlenk tube was charged with benzo-oxathiin-dioxide **26**[7] (0.20 mmol) and *β′*-acetoxy allenoate **12** (0.20 mmol) in toluene (2.0 mL). The mixture was stirred at 100 °C for 12 h, and the 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.

Compound 28a



Yield: 67 mg (76%), using **26** (39.6 mg, 0.20 mmol) and **12a** (64.5 mg, 0.20 mmol); White solid.

Mp: 185-187 °C

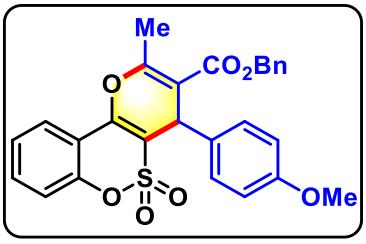
IR (neat): ν_{max} 3057, 1713, 1610, 1486, 1370, 1169, 1067, 820 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.82 (dd, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.51 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.38 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.33-7.26 (m, 8H), 7.25-7.24 (m, 1H), 7.14-7.12 (m, 2H), 5.11-5.03 (m, 3H), 2.56 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.3, 158.7, 149.5, 146.8, 141.7, 135.4, 132.7, 128.8, 128.7, 128.4, 128.0, 126.0, 124.7, 118.9, 116.2, 114.5, 108.3, 67.0, 37.3, 19.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{26}H_{20}NaO_6S$ $[M + Na]^+$ m/z 483.0873. Found: 483.0877.

Compound 28b



Yield: 80 mg (84%), using **26** (39.6 mg, 0.20 mmol) and **12b** (70.5 mg, 0.20 mmol); White solid.

Mp: 192-194 °C

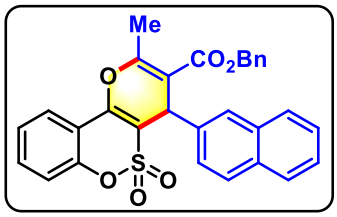
IR (neat): ν_{max} 3062, 1712, 1605, 1490, 1370, 1170, 1071, 836 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (dd, J_1 = 7.5, J_2 = 1.5, 1H), 7.50 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.37 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.33-7.32 (m, 3H), 7.24 (s, 1H) 7.22-7.20 (m, 2H), 7.17-7.16 (m, 2H), 6.80 (d, J = 8.5 Hz, 2H), 5.14-5.02 (m, 3H), 3.77 (s, 3H), 2.55 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.4, 159.2, 158.1, 149.4, 146.5, 135.4, 133.9, 132.6, 129.8, 128.6, 128.4 (2s), 125.9, 124.7, 118.9, 116.2, 114.5, 114.1, 108.4, 66.8, 55.3, 36.5, 18.9 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{26}NO_7S$ $[M + NH_4]^+$ m/z 508.1424. Found: 508.1429.

Compound 28i



Yield: 74 mg (77%), using **26** (39.6 mg, 0.20 mmol) and **12i** (74.5 mg, 0.20 mmol); White solid.

Mp: 179-181 °C

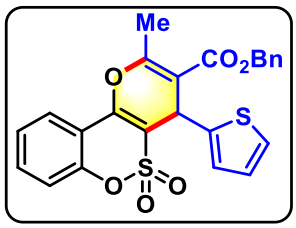
IR (neat): ν_{max} 3058, 1713, 1611, 1486, 1370, 1170, 1068, 854 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.5 Hz, 1H), 7.80 (d, *J* = 10.0 Hz, 2H), 7.75 (s, 2H) 7.54-7.40 (m, 5H), 7.30-7.27 (m, 2H), 7.24-7.21 (m, 2H), 7.10 (d, *J* = 7.0 Hz, 2H), 5.27 (s, 1H), 5.11-5.03 (m, 2H), 2.64 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.3, 158.7, 149.5, 146.9, 138.9, 135.2, 133.4, 133.1, 132.7, 128.8, 128.7, 128.6, 128.4, 128.3, 128.0, 127.8, 127.1, 126.2, 126.1, 126.0, 124.8, 118.9, 116.1, 114.3, 108.2, 67.0, 37.5, 19.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{30}H_{22}NaSO_6$ $[M + Na]^+$ m/z 533.1029. Found: 533.1028.

Compound 28j



Yield: 67 mg (69%) using **26** (39.6 mg, 0.20 mmol) and **12j** (65.7 mg, 0.20 mmol); White solid.

Mp: 194-196 °C

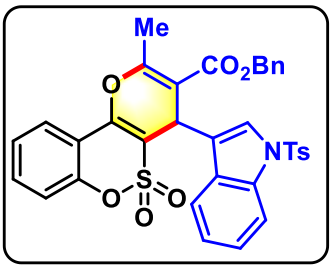
IR (neat): ν_{max} 2969, 1715, 1617, 1452, 1367, 1171, 1053, 855 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$):): δ 7.81 (dd, J_1 = 8.0, J_2 = 1.5, 1H), 7.53 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.38 (td, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.34-7.32 (m, 3H), 7.29-7.27 (m, 1H), 7.22-7.20 (m, 3H), 7.00-6.96 (m, 1H), 6.91-6.89 (m, 1H), 5.43 (s, 1H), 5.20-5.12 (AB m, 2H), 2.55 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.1, 159.0, 149.5, 147.2, 145.6, 135.4, 132.9, 128.7, 128.5, 128.4, 127.2, 126.7, 126.0, 125.8, 124.9, 119.0, 116.2, 113.9, 108.3, 67.0, 32.1, 19.0 ppm.

HRMS (ESI-TOF): Calcd. For $C_{24}H_{22}NO_6S_2$ $[M + NH_4]^+$ m/z 484.0883. Found 484.0881.

Compound 28k



Yield: 67 mg (65%), using **26** (39.6 mg, 0.20 mmol) and **12k** (103.1 mg, 0.20 mmol); White solid.

Mp: 187-189°C

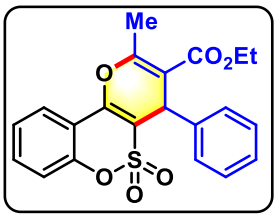
IR (neat): ν_{max} 3033, 1715, 1621, 1446, 1372, 1136, 1065, 810 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.87-7.83 (m, 2H), 7.62-7.58 (m, 3H), 7.53-7.50 (m, 1H), 7.44-7.42 (d, *J* = 7.5 Hz, 1H), 7.41-7.38 (m, 1H), 7.30-7.21 (m, 5H), 7.14-7.12 (m, 3H), 7.07-7.05 (m, 2H), 5.35 (s, 1H), 5.02 (d, *J* = 12.0 Hz, 1H), 5.00 (d, *J* = 12.5 Hz, 1H), 2.57 (s, 3H), 2.26 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.1, 158.6, 149.5, 147.1, 144.9, 135.4, 135.0, 132.8, 129.9, 128.9, 128.8, 128.6, 128.4, 126.9 (2s), 126.1, 124.9, 124.8, 123.7, 122.9, 119.7, 118.9, 116.1, 113.9, 113.1, 107.0, 67.1, 28.6, 21.6, 18.9 ppm.

HRMS (ESI-TOF): Calcd. For $C_{35}H_{31}N_2O_8S_2$ $[M + NH_4]^+$: m/z 671.1516. Found: 671.1515.

Compound 28n



Yield: 73 mg (71%), using **26** (39.6 mg, 0.20 mmol) and **12n** (52.0 mg, 0.20 mmol); White solid.

Mp: 198-200 °C

IR (neat): ν_{max} 2925, 1740, 1602, 1458, 1366, 1148, 1095, 806 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.83 (dd, J_1 = 8.0, J_2 = 1.5, 1H), 7.51 (td, J_1 = 7.5, J_2 = 1.5 Hz, 1H), 7.39 (dd, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.37-7.36 (m, 1H), 7.35 (s, 1H), 7.33-7.30 (m, 2H), 7.27-7.23 (m, 2H), 5.06 (s, 1H), 4.15-4.06 (m, 2H), 2.56 (s, 3H), 1.18 (t, 3H) ppm.

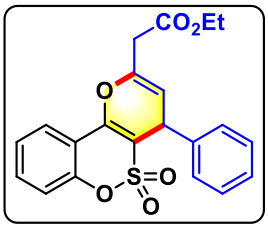
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 165.5, 158.1, 149.5, 146.9, 141.9, 132.7, 128.7, 128.6, 128.0, 126.0, 124.8, 118.9, 116.2, 114.4, 108.6, 61.0, 37.3, 18.8, 14.1 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{22}NO_6S$ $[M + NH_4]^+$ m/z 416.1162. Found: 416.1157.

3.12 Synthesis of Compounds 29a, 29e, 29g, 29m and 29n: General Procedure

A Schlenk tube was charged with benzo-oxathiin-dioxide **26**[99] (0.20 mmol) and *δ*-acetoxy allenoate **8** (0.20 mmol) in toluene (2.0 mL). The mixture was stirred at 100 °C for 12 h, and the 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.

Compound 29a



Yield: 62 mg (61%), using **26** (39.6 mg, 0.20 mmol) and **12a** (52.0 mg, 0.20 mmol); White solid. Purity *ca* 90%.

Mp: 161-163 °C

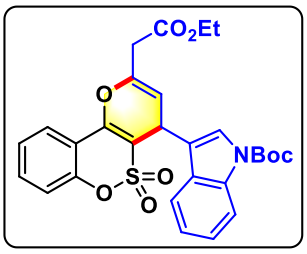
IR (neat): ν_{max} 2984, 1736, 1631, 1487, 1371, 1160, 1061, 907 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): 7.76 (d, *J* = 7.5 Hz, 1H), 7.51-7.48 (m, 1H), 7.44-7.33 (m, 5H), 7.31-7.28 (m, 2H), 5.20 (d, *J* = 4.0 Hz, 1H), 4.68 (d, *J* = 4.0 Hz, 1H), 4.25-4.21 (m, 2H), 3.36-3.29 (m, 2H), 1.30 (t, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 168.7, 149.5, 148.4, 143.5, 141.9, 132.5, 129.0, 128.7, 128.2, 125.9, 125.0, 118.8, 116.8, 112.2, 106.4, 61.6, 39.0, 37.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{21}H_{18}NaO_6S$ $[M + NH_4]^+$ m/z 421.0716. Found: 421.0716.

Compound 29e



Yield: 62 mg (63%), using **26** (39.6 mg, 0.20 mmol) and **12e** (79.9 mg, 0.20 mmol); White solid. Purity *ca* 95%

Mp: 178-180 °C

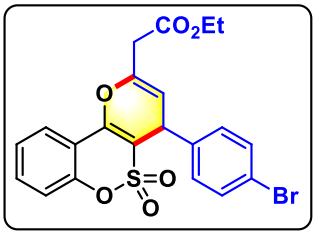
IR (neat): ν_{max} 2981, 1734, 1631, 1452, 1370, 1216, 1157, 1085, 908, 754 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 8.14-8.13 (m, 1H), 7.81 (dd, J_1 = 7.5, J_2 = 1.5, 1H), 7.65-7.63 (m, 2H), 7.51 (td, J_1 = 8.0, J_2 = 1.5 Hz, 1H), 7.37 (td, J_1 = 8.0, J_2 = 1.0 Hz, 1H), 7.31-7.27 (m, 2H), 7.23-7.19 (m, 1H), 5.24 (d, J = 4.0 Hz, 1H), 4.97-4.00 (m, 1H), 4.25-4.21 (m, 2H), 3.36-3.29 (m, 2H), 1.66 (s, 9H), 1.28 (t, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.6, 149.4, 148.9, 143.8, 136.1 (2s), 132.6, 128.6, 125.9, 125.0, 124.7, 122.8, 119.3, 118.9, 115.7, 110.9, 105.5, 84.1, 61.6, 39.0, 28.8, 28.3, 14.4 ppm.

HRMS (ESI-TOF): Calcd. For $C_{28}H_{31}N_2O_8S$ $[M + NH_4]^+$ m/z 555.1796. Found: 555.1795.

Compound 29g



Yield: 62 mg (72%) using **26** (39.6 mg, 0.20 mmol) and **12g** (67.8 mg, 0.20 mmol); White solid. Purity *ca* 90%

Mp: 163-165 °C

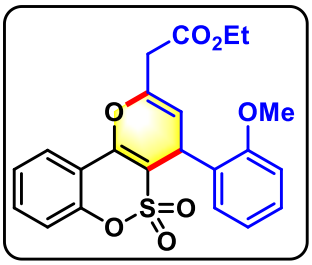
IR (neat): ν_{max} 3028, 1735, 1631, 1486, 1371, 1215, 1159, 1072, 907 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): 7.75 (d, J = 8.0 Hz, 1H), 7.53-7.48 (m, 3H), 7.37-7.25 (m, 4H), 5.17 (d, J = 4.0 Hz, 1H), 4.67 (d, J = 4.0 Hz, 1H), 4.26-4.21 (m, 2H), 3.33 (s, 2H), 1.30 (t, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 168.6, 149.5, 148.6, 143.9, 141.0, 132.7, 132.6, 132.2, 130.4, 129.6, 126.0, 125.1, 122.3, 118.9, 116.6, 111.6, 105.9, 61.7, 39.0 ppm (we were not successful in purifying it further; ca.10% impurities were detected).

HRMS (ESI-TOF): Calcd. For $C_{21}H_{21}NBrO_6S$ $[M + NH_4]^+$ and $[M + 2 + NH_4]^+$ m/z 494.0267 and 496.0247. Found: 494.0269 and 496.0247.

Compound 29m



Yield: 62 mg (72%), using **26** (39.6 mg, 0.20 mmol) and **12m** (58.1 mg, 0.20 mmol); White solid.

Mp: 169-171 °C

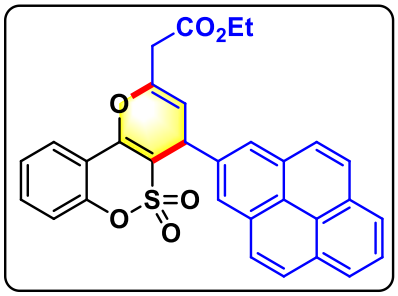
IR (neat): ν_{max} 2982, 1736, 1630, 1453, 1316, 1263, 1167, 1037, 996 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (dd, J_1 = 8.0, J_2 = 1.5, 1H), 7.49 (td, J_1 = 7.5, J_2 = 1.0 Hz, 1H), 7.36-7.33 (m, 1H), 7.30-7.27 (m, 1H), 7.25 (s, 1H), 7.01 (d, J = 7.5 Hz, 1H), 6.97 (s, 1H), 6.83 (dd, J_1 = 8.5, J_2 = 2.5, 1H), 5.20 (d, J = 4.0 Hz, 1H), 4.65 (d, J = 4.0 Hz, 1H), 4.25-7.21 (m, 2H), 3.80 (s, 3H), 3.36-3.28, (m, 2H), 1.30 (t, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.7, 160.1, 149.5, 148.5, 143.5 (2 s), 132.5, 130.0, 125.9, 125.0, 121.0, 118.8, 116.8, 114.6, 113.5, 112.1, 106.3, 61.6, 55.4, 39.0, 37.4, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{24}NO_7S$ $[M + NH_4]^+$: m/z 446.11268. Found: 446.1269.

Compound 29n



Yield: 62 mg (71%), using **26** (39.6 mg, 0.20 mmol) and **12n** (76.9 mg, 0.20 mmol); White solid. Purity ca 95%

Mp: 165-167 °C

IR (neat): ν_{max} 2987, 1733, 1630, 1453, 1368, 1216, 1153, 1068, 996, 751 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.47 (d, J = 9.0 Hz, 1H), 8.19-8.17 (m, 5H), 8.06-7.97 (m, 3H), 7.84 (d, J = 7.0 Hz, 1H), 7.51-7.48 (m, 1H), 7.39-7.36 (m, 1H), 7.24-7.26 (m, 1H), 5.85 (s, 1H), 5.32 (d, J = 3.5 Hz, 1H), 4.21 (d, J = 6.0 Hz, 2H), 3.33-3.25 (m, 2H), 1.27 (t, 3H) ppm.

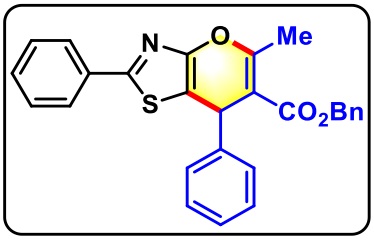
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 168.7, 149.6, 143.2, 132.6, 131.5, 131.1, 130.9, 128.7, 127.8, 127.6, 126.2, 125.9, 125.7, 125.6, 125.3, 125.0, 122.0, 118.9, 116.9, 111.8, 106.7, 61.6, 39.0, 29.8, 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{31}H_{22}NaO_6S$ $[M + Na]^+$ m/z 545.1029. Found: 545.1027.

3.13 Synthesis of Compounds 30a, 30c and 30i: General Procedure

A Schlenk tube was charged with phenylthiazolone **27**[100] (0.20 mmol) and *β′*-acetoxy allenoate **12** (0.20 mmol) in toluene (2.0 mL). The mixture was stirred at 100 °C for 12 h, and the 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.

Compound 30a



Yield: 74 mg (78%), using **27** (35.4 mg, 0.20 mmol) and **12a** (64.5 mg, 0.20 mmol); White solid.

Mp: 178-180 °C

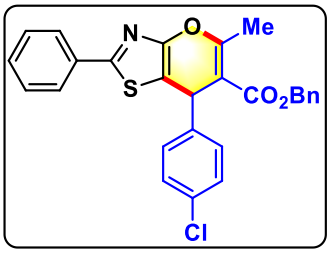
IR (neat): ν_{max} 3027, 1711, 1629, 1566, 1455, 1319, 1217, 1176, 1071, 985 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83-7.82 (m, 2H), 7.38-7.37 (m, 3H), 7.28-7.23 (m, 5H), 7.22-7.20 (m, 3H), 7.06-7.05 (m, 2H), 5.29 (s, 1H) 5.05-4.99 (m, 2H), 2.55 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 164.9, 160.5, 153.8, 145.1, 135.8, 133.1, 130.6, 129.0, 128.9, 128.6, 128.3, 128.2, 127.5, 127.4, 125.9, 111.2, 104.6, 66.6, 40.5, 19.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{22}NO_3S$ $[M + NH_4]^+$ m/z 440.1315. Found 440.1319.

Compound 30c



Yield: 66 mg (75%), using **27** (35.4 mg, 0.20 mmol) and **12i** (71.4 mg, 0.20 mmol); White solid.

Mp: 165-167 °C

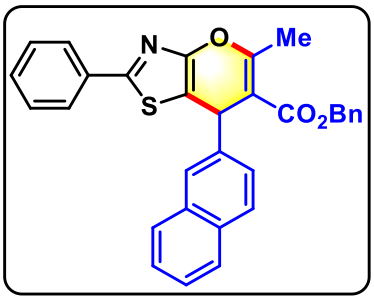
IR (neat): ν_{max} 3018, 1712, 1630, 1567, 1488, 1364, 1217, 1072, 985, 754 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.83-7.82 (m, 2H), 7.39-7.38 (m, 3H), 7.30-7.29 (m, 3H), 7.21-7.19 (m, 2H), 7.12-7.07, (m, 4H), 5.26 (s, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.00 (d, *J* = 12.5 Hz, 1H), 2.54 (s, 3H) ppm.

$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 166.5, 165.1, 160.7, 153.8, 143.6, 135.6, 133.1, 133.0, 130.7, 129.1, 129.0, 128.9, 128.6, 128.4 (2 s), 125.9, 110.5, 104.3, 66.7, 40.0, 19.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{27}H_{21}ClNO_3S$ $[M + H]^+$ m/z 474.0925. Found: 474.0997.

Compound 30i



Yield: 68 mg (72%), using **27** (35.4 mg, 0.20 mmol) and **12i** (74.5 mg, 0.20 mmol); White solid.

Mp: 171-173 °C

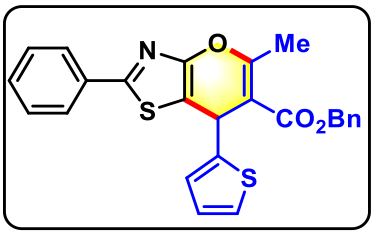
IR (neat): ν_{max} 3069, 1709, 1631, 1567, 1459, 1320, 1217, 1072, 986 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ 7.81-7.80 (m, 3H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.73-7.71 (m, 1H), 7.62 (s, 1H), 7.49-7.44 (m, 2H), 7.37-7.34 (m, 4H), 7.22-7.19 (m, 1H), 7.12-7.09 (m, 2H), 6.97 (d, *J* = 7.5 Hz, 2H), 5.46 (s, 1H), 5.02-4.95 (m, 2H), 2.59 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.8, 165.0, 160.6, 153.8, 142.4, 135.6, 133.5, 133.1, 132.8, 130.6, 129.0, 128.9, 128.4, 128.3, 128.2 (2s), 127.8, 126.3, 126.2, 126.0, 125.9, 125.7, 111.0, 104.6, 66.6, 40.7, 19.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{31}H_{24}NO_3S$ $[M + Na]^+$ m/z 490.1471. Found: 490.1474.

Compound 30j



Yield: 64 mg (79%), using **27** (35.4 mg, 0.20 mmol) and **12j** (65.6 mg, 0.20 mmol); White solid. Purity ca 95%

Mp: 167-169 °C

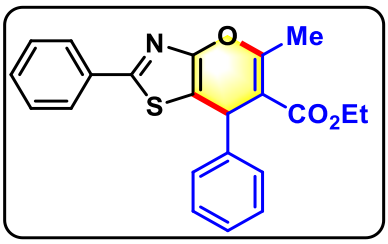
IR (neat): ν_{max} 3062, 1710, 1628, 1566, 1457, 1363, 1215, 1070, 983, 761 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87-7.85 (m, 2H), 7.41-7.38 (m, 3H), 7.32-7.30 (m, 3H), 7.20-7.15 (m, 3H), 6.87 (dd, J_1 = 5.0, J_2 = 3.5 Hz, 1H), 6.83 (d, J = 3.0 Hz, 1H), 5.64 (s, 1H), 5.15-5.01 (m, 2H), 2.52 (s, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.6, 165.0, 160.4, 153.9, 149.3, 135.8, 133.0, 130.7, 129.1, 128.6, 128.4, 128.3, 126.9, 126.0, 124.8, 124.6, 110.4, 104.7, 66.7, 35.3, 19.7 ppm.

HRMS (ESI-TOF): Calcd. For $C_{25}H_{20}NO_3S$ $[M + H]^+$ m/z 446.0879. Found: 446.0870.

Compound 30n



Yield: 74 mg (81%), using **27** (35.4 mg, 0.20 mmol) and **12n** (52.1 mg, 0.20 mmol); White solid.

Mp: 178-180 °C

IR (neat): ν_{max} 2978, 1710, 1632, 1565, 1455, 1363, 1217, 1074, 982, 832 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84-7.83 (m, 2H), 7.39 (s, 3H), 7.30-7.21 (m, 5H), 5.28 (s, 1H), 4.09-4.00 (m, 2H), 2.53 (s, 3H), 1.08 (t, 3H), ppm.

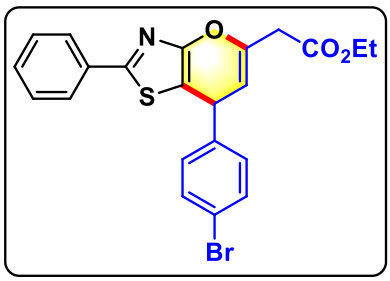
$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 166.9, 164.8, 159.8, 153.9, 145.2, 133.1, 130.5, 129.0, 128.8, 127.6, 127.3, 125.9, 111.1, 105.0, 60.6, 40.5, 19.5, 14.5 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{20}NO_3S$ $[M + H]^+$ m/z 378.1158. Found: 378.1162.

3.14 Synthesis of Compound 31g

The above procedure was adapted by using phenylthiazolone **27** (35.4 mg, 0.20 mmol) and *δ*-acetoxy allenoate **8g** (67.8g, 0.20 mmol) in toluene (2.0 mL). The crude product was then purified by silica gel column chromatography using ethyl acetate/ hexane (1:4) as the eluent.

Compound 31g



Yield: 73 mg (76%); White solid.

Mp: 146-148 °C

IR (neat): ν_{max} 2981, 1736, 1685, 1556, 1484, 1368, 1152, 1051, 967, 823 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 4.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.39-7.38 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 1H), 4.94 (s, 1H), 4.92 (s, 1H), 4.21 (q, *J* = 4.21 Hz, 2H), 5.32 (s, 3H), 1.30 (t, 3H) ppm.

$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$): δ 169.3, 164.5, 155.6, 145.5, 143.9, 133.2, 132.1, 130.5, 129.4, 129.1, 125.9, 121.5, 108.1, 102.4, 61.5, 39.3 (2 s), 14.3 ppm.

HRMS (ESI-TOF): Calcd. For $C_{22}H_{19}BrNO_3S$ $[M + H]^+$ m/z 456.0264 and 458.0243. Found: 456.0261 and 458.0245.

3.15 X-ray Crystallography

A suitable crystal was mounted on a glass fiber (for **15aa**, **15db**, **16af**, **16ca**, **17aa**, **17bd**, **19bb**, **20aa**, **21aa**, **21bk**, **22ad**, **23fi**, **25 28a, 30c** and **30n**) 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.[102] Crystal data are summarized in Tables 17-20.

Table 17: Crystal data for compounds **15aa**, **15db**, **16af** and **16ca**

Compound	**15aa**	**15db**	**16af**	**16ca**
Emp. formula	$C_{21}H_{19}NO_3$	$C_{23}H_{23}NO_4$	$C_{19}H_{17}NO_5S_2$	$C_{21}H_{18}BrNO_5S$
Formula weight	333.37	377.42	403.46	476.33
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	*I*2/a	*P*2(1)/n	*P121/n1*	*P*-1
a /Å	22.8870(8)	14.7401(6)	9.7166(5)	11.45660(18)
b /Å	5.21437(15)	7.7423(3)	22.6956(8)	13.1897(2)
c /Å	29.1121(8)	17.8057(7)	9.8622(5)	14.5799(2)
α/deg	90	90	90	91.9477(14)
β/deg	98.910(3)	101.2327(16)	117.361(6)	105.4986(14)
γ/deg	90	90	90	97.6309(14)
V /Å^3	3432.35(19)	1993.10(14)	1931.55(16)	2098.66(6)
Z	8	4	4	4
*D*calc /g cm^{-3}]	1.290	1.258	1.387	1.508
μ /mm^{-1}	0.086	0.086	0.305	2.090
F(000)	1408.0	800.0	840.0	968.0
Data/ restraints/ parameters	3025/0/228	3501/1/257	3404/2/266	7387/0/550
S	1.070	1.062	1.070	1.030
R1 [I>2σ(I)]	0.0592	0.0700	0.0488	0.0507
wR2 [all data]	0.1916	0.2140	0.1362	0.1143
Max./min. residual electron dens. [eÅ^{-3}]	0.462/-0.204	0.618/-0.423	0.435/-0.376	0.944/-0.542

[a]R1 = Σ||Fo| - |Fc||/Σ|Fo| and wR2 = [Σw(Fo^2-Fc^2)^2/ΣwFo^4]$^{0.5}$

Table 18: Crystal data for compounds **17aa**, **17bd**, **19bb** and **20aa**

Compound	**17aa**	**17bd**	**19bb**	**20aa**

Emp. formula	$C_{21}H_{18}O_3$	$C_{22}H_{19}NO_5$	$C_{23}H_{23}NO_5S$	$C_{21}H_{19}NO_4S$
Formula weight	318.35	377.38	425.48	381.43
Crystal system	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic
Space group	*P2(1)/n*	*P121/n1*	*Pna2(1)*	*P*bca
a /Å	10.445(2)	11.2221(4)	25.6923(19)	15.3107(7)
b /Å	13.422(3)	10.3384(4)	15.3296(9)	7.6551(3)
c /Å	11.971(3)	16.5378(6)	5.3503(5)	33.1427(13)
α/deg	90	90	90	90
β/deg	90.181(8)	90.805(3)	90	90
γ/deg	90	90	90	90
V /Å^3	1678.3(6)	1918.50(12)	2107.2(3)	3884.5(3)
Z	4	4	4	8
*D*calc /g cm^{-3}]	1.260	1.307	1.341	1.304
μ /mm^{-1}	0.083	0.093	0.188	0.193
F(000)	672.0	792.0	896.0	1600.0
Data/ restraints/ parameters	1556/0/215	3376/0/256	3406/2/278	3398/0/253
S	1.780	1.118	0.983	1.098
R1 [I>2σ(I)]	0.1072	0.0498	0.0665	0.0441
wR2 [all data]	0.3498	0.1532	0.1684	0.1167
Max./min. residual electron dens. [eÅ^{-3}]	0.792/-0.402	0.182/-0.200	0.279/-0.240	0.212/-0.321

[a]R1 = Σ||Fo| - |Fc||/Σ|Fo| and wR2 = [Σw(Fo^2-Fc^2)^2/ΣwFo^4]$^{0.5}$

Table 19: Crystal data for compounds **21aa**, **21bk**, **22ad** and **23fi**

Compound	**21aa**	**21bk**	**22ad**	**23fi**
Emp. formula	$C_{26}H_{21}NO_4S$	$C_{22}H_{21}NO_4S$	$C_{24}H_{24}N_2O_3$	$C_{21}H_{21}N_3O_3$
Formula weight	443.50	395.47	488.10	363.41
Crystal system	Triclinic	Monoclinic	Triclinic	Monoclinic
Space group	P-1	C c	P-1	P2(1)

a /Å	9.7856(2)	20.9289(9)	8.21050(10)	11.3445(4)
b /Å	9.8917(2)	9.3814(4)	13.4388(2)	7.2039(3)
c /Å	11.8666(2)	9.9572(4)	21.5135(3)	12.1434(5)
α/deg	100.037(2)	90	78.6300(10)	90
β/deg	105.109(2)	93.143(2)	83.8380(10)	99.778(4)
γ/deg	100.126(2)	90	89.6830(10)	90
V /Å^3	1061.98(4)	1952.08(14)	2313.45(6)	978.00(7)
Z	2	4	4	2
*D*calc /g cm^{-3}]	1.387	1.346	1.403	1.234
μ /mm^{-1}	0.187	0.194	0.186	0.084
F(000)	464.0	832.0	1016.0	384.0
.0Data/ restraints/ parameters	4524/4/284	4322/2/256	9659/540/642	3167/1/247
S	1.112	1.104	1.070	1.064
R1 [I>2σ(I)]	0.0976	0.0626	0.0506	0.0438
wR2 [all data]	0.2856	0.1338	0.1457	0.1193
Max./min. residual electron dens. [eÅ^{-3}]	1.158/-1.277	0.421/-0.625	0.386/-0.326	0.030/ -0.115

[a]R1 = Σ||Fo| - |Fc||/Σ|Fo| and wR2 = [Σw(Fo^2-Fc^2)^2/ΣwFo^4]$^{0.5}$

Table 20: Crystal data for compound **23**, **28a**, **30c** and **30n**

Compound	**25**	**28a**	**30c**	**30n**
Emp. formula	$C_{20}H_{21}NO_4$	$C_{26}H_{20}O_6S$	$C_{27}H_{20}ClNO_3S$	$C_{22}H_{19}NO_3S$
Formula weight	339.38	460.48	473.95	377.44
Crystal system	orthorhombic	Monoclinic	Monoclinic	monoclinic
Space group	*P 21 21 21*	*P 21/n*	*P 1 21/c 1*	*P 1 21/n 1*
a /Å	8.8069(7)	10.6053(3)	5.7479(5)	5.5884(6)
b /Å	9.2345(6)	13.1833(4)	27.840(3)	24.463(3)
c /Å	21.9262(17)	15.5776(5)	14.0482(15)	13.9485(17)
α/deg	90	90	90	90

β/deg	90	92.1990(10)	90.302(3)	95.132(4)
γ/deg	90	90	90	90
V /Å^3	1783.2(2)	2176.34(11)	2247.9(4)	1899.3(4)
Z	4	4	4	4
Dcalc /g cm^{-3}]	1.264	1.405	1.400	1.320
μ /mm^{-1}	0.088	0.191	0.294	0.192
F(000)	720.0	960.0	984.0	792
Data/ restraints/ parameters	3060/2/229	5000/0/299	5260/0/299	3469/0/246
S	1.072	1.078	1.075	1.154
R1 [I>2σ(I)]	0.0760	0.0537	0.0506	0.0745
wR2 [all data]	0.0297	0.1647	0.1418	0.2149
Max./min. residual electron dens. [eÅ^{-3}]	0.422/-0.334	0.635/-0.514	0.521/-0.288	0.744/-0.322

[a]R1 = Σ||Fo| - |Fc||/Σ|Fo| and wR2 = [Σw(Fo^2-Fc^2)^2/ΣwFo^4]$^{0.5}$

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(A) Copies of $^{1}H/^{13}C\{^{1}H\}$ NMR spectra for representative compounds 15aa, 16aa, 17aa, 18aa, 20aa, 21aa, 22aa, 23aa, 24aa, 28n, 29m and **30a**

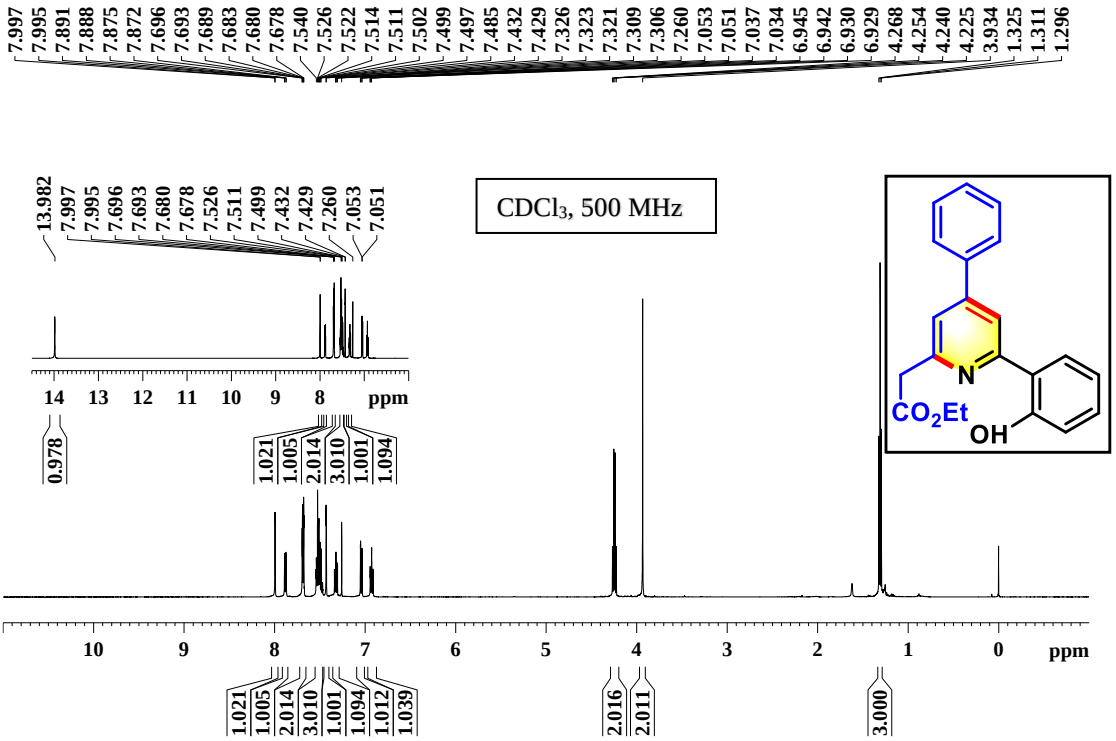

Figure A1: ^{1}H NMR spectrum of compound **15aa**

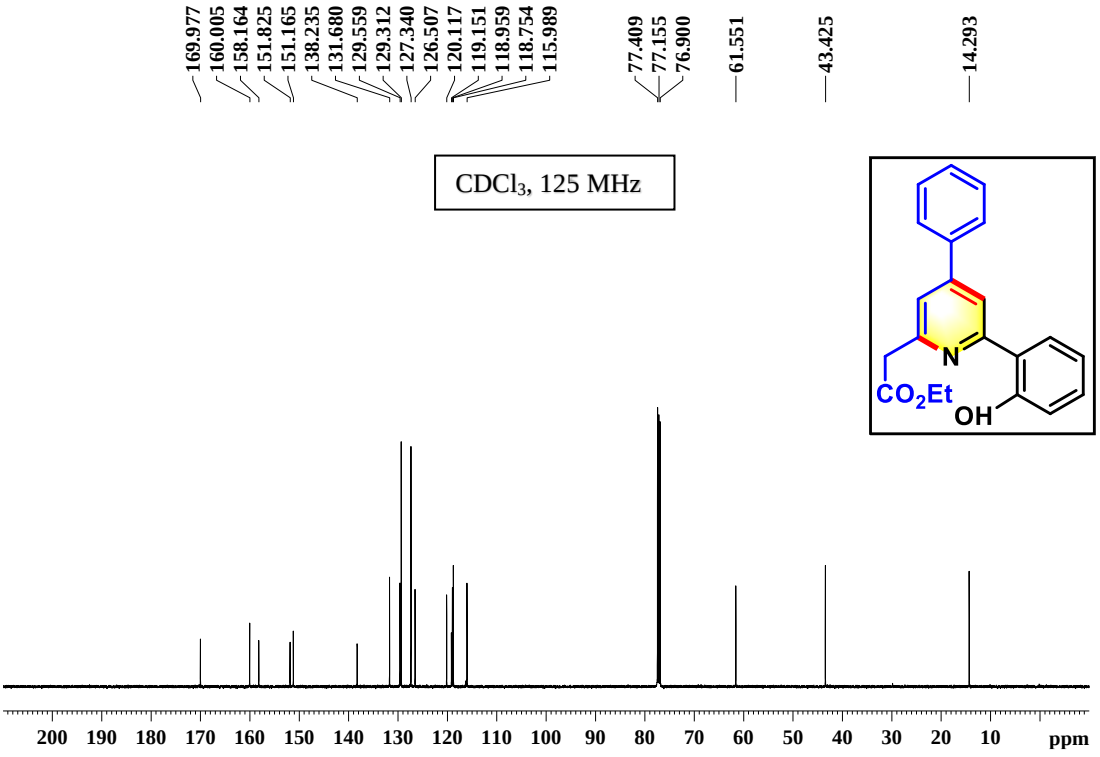

Figure A2: ^{13}C NMR spectrum of compound **15aa**

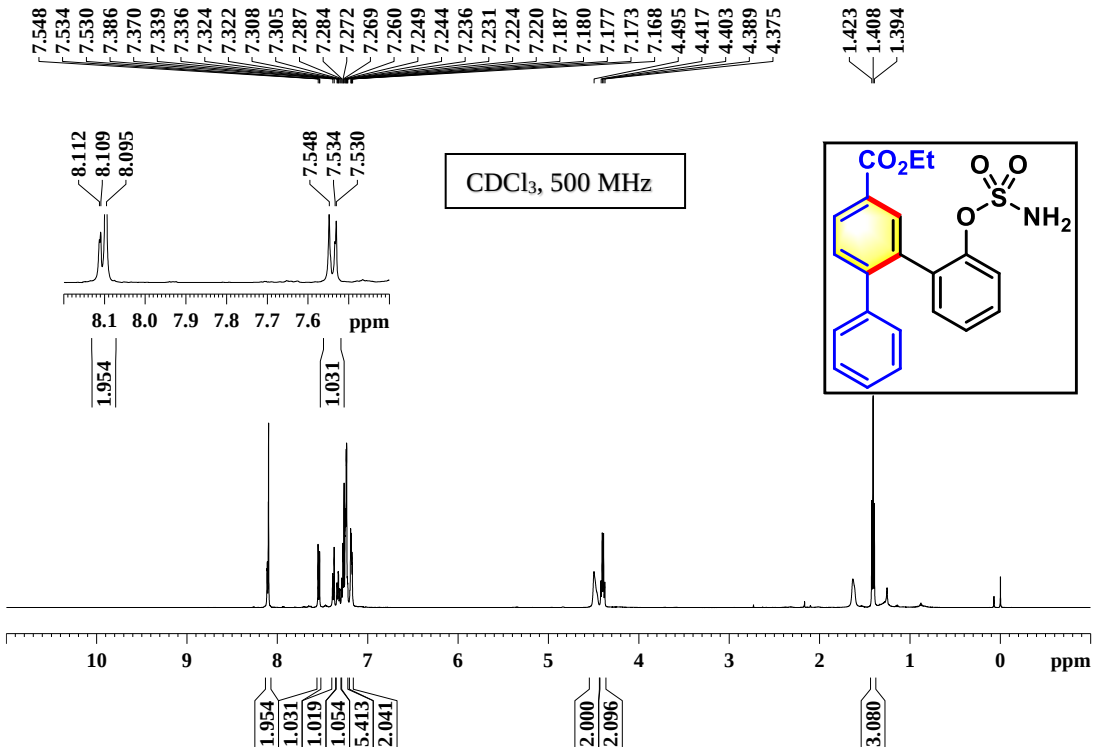

Figure A3: ^{1}H NMR spectrum of compound **16aa**

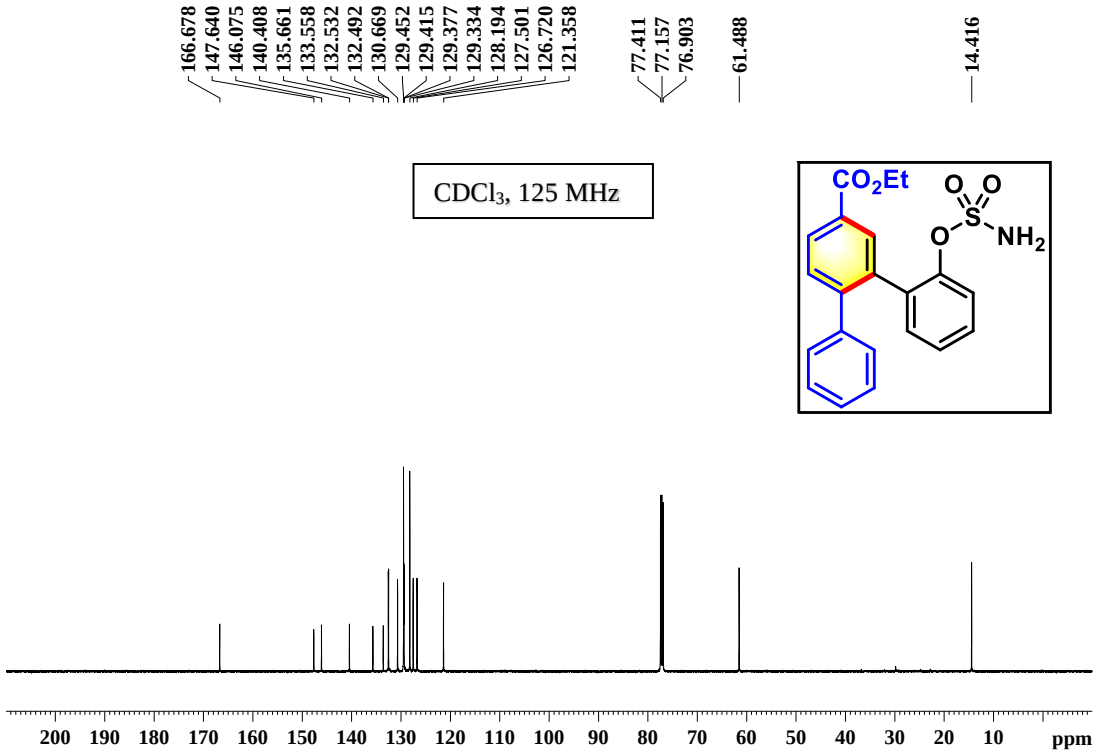

Figure A4: ^{13}C NMR spectrum of compound **16aa**

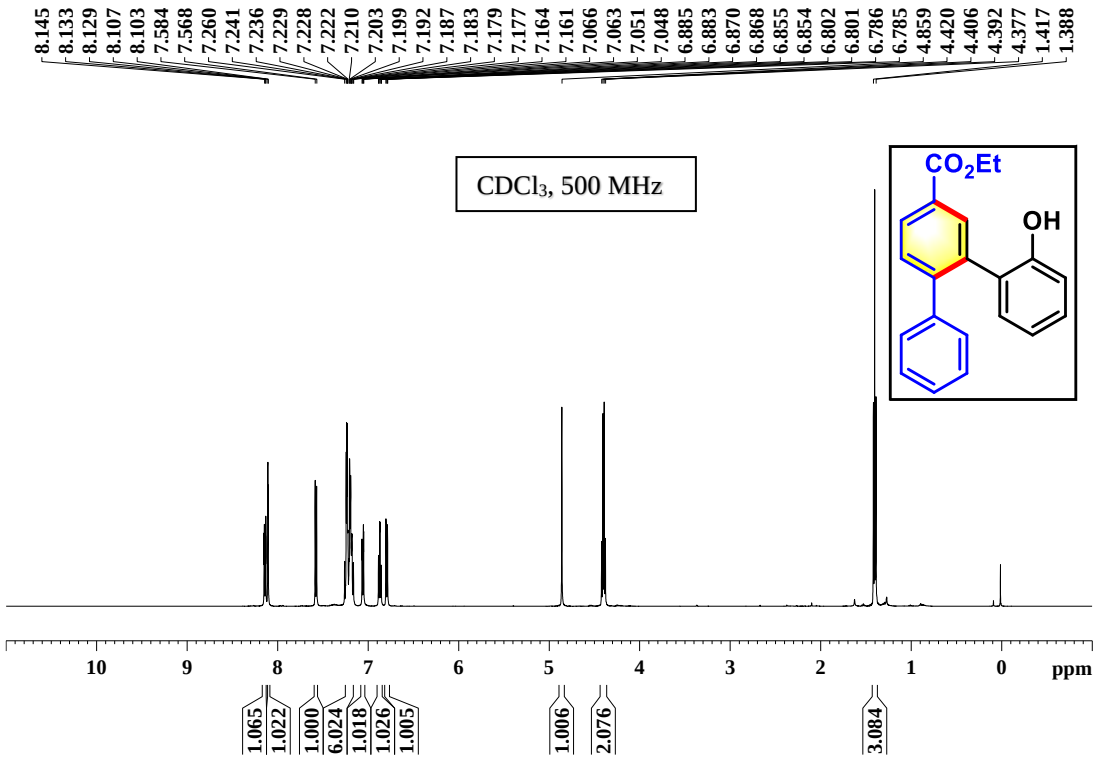

Figure A5: ^{1}H NMR spectrum of compound **17aa**

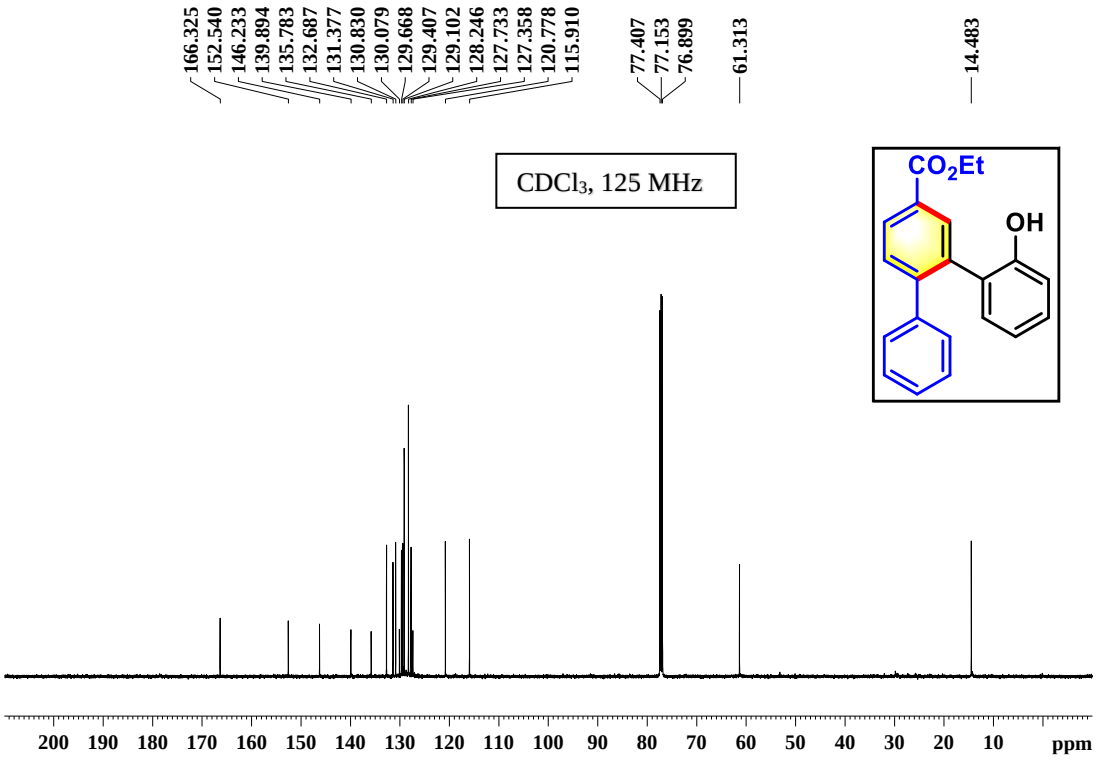

Figure A6: ^{13}C NMR spectrum of compound **17aa**

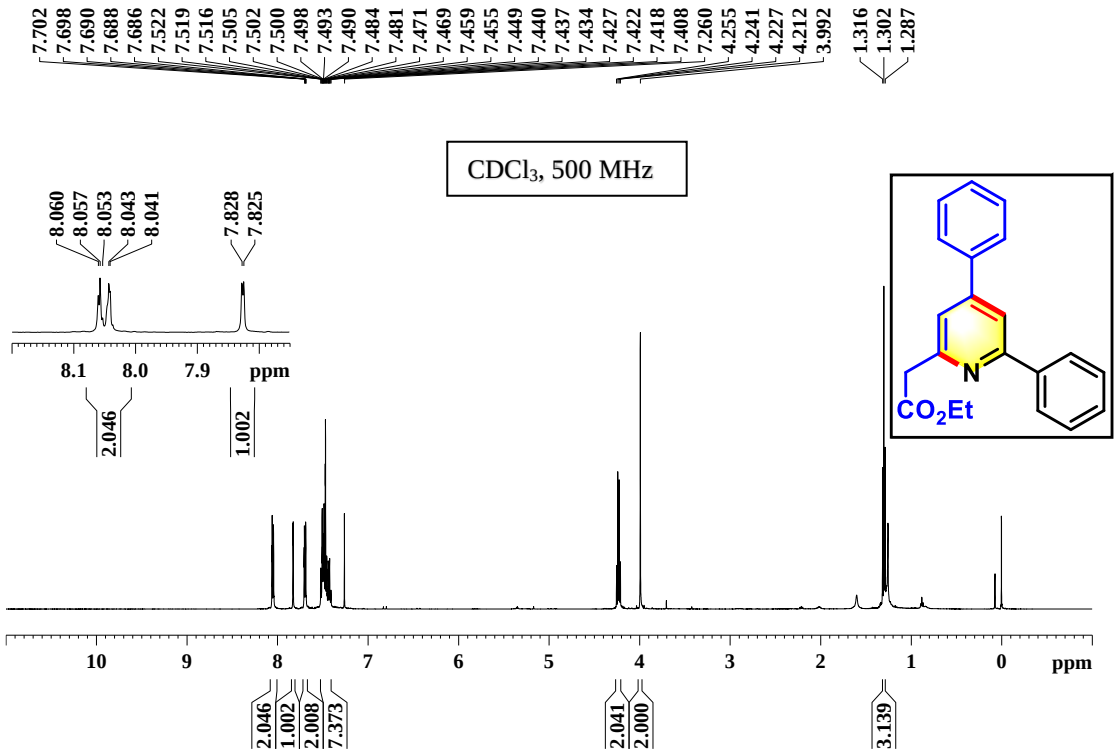

Figure A7: ^{1}H NMR spectrum of compound **18aa**

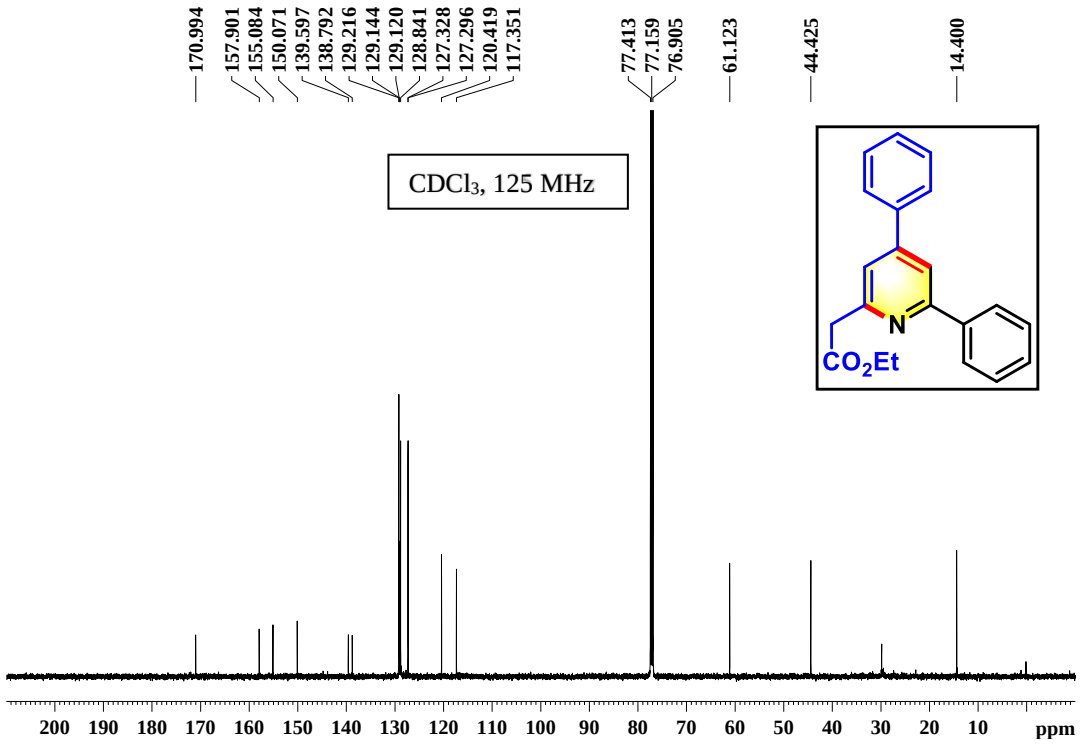

Figure A8: ^{13}C NMR spectrum of compound **18aa**

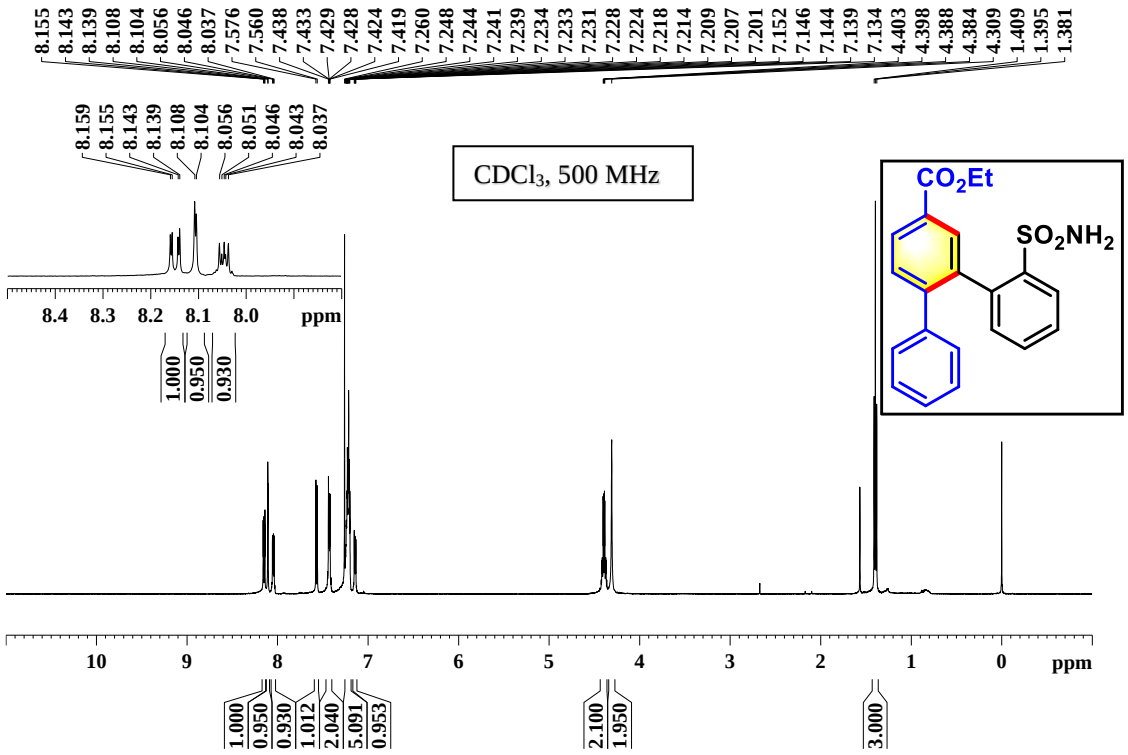

Figure A9: ^{1}H NMR spectrum of compound **20aa**

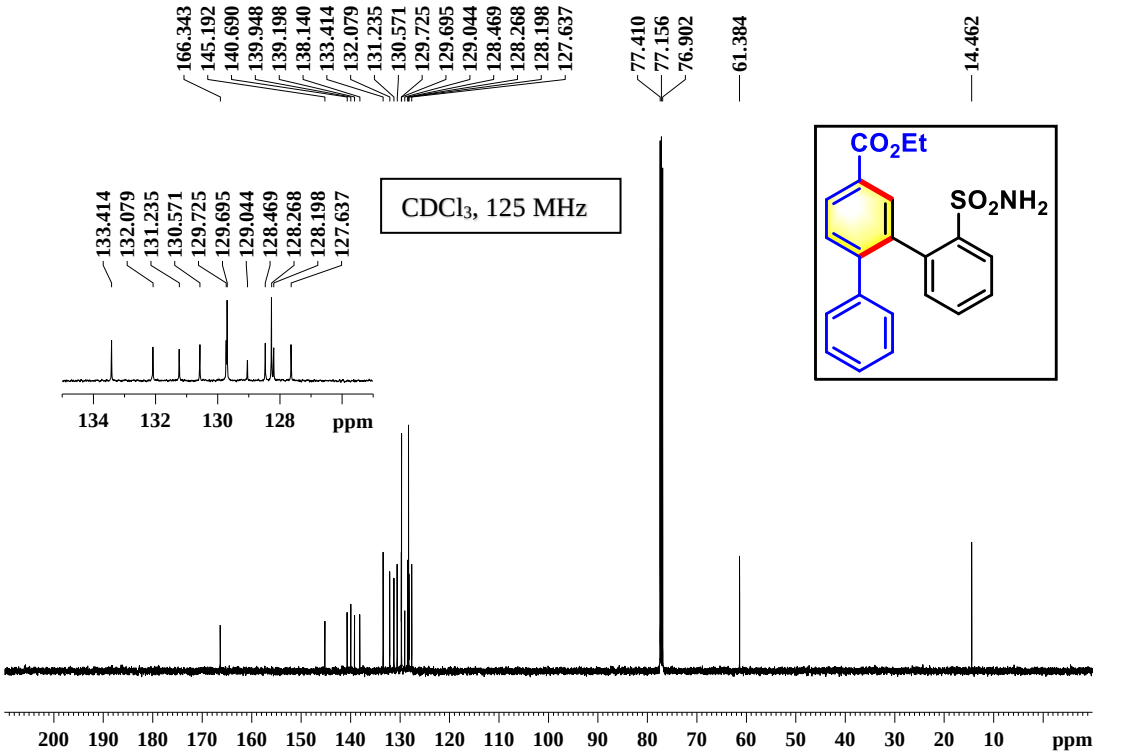

Figure A10: ^{13}C NMR spectrum of compound **20aa**

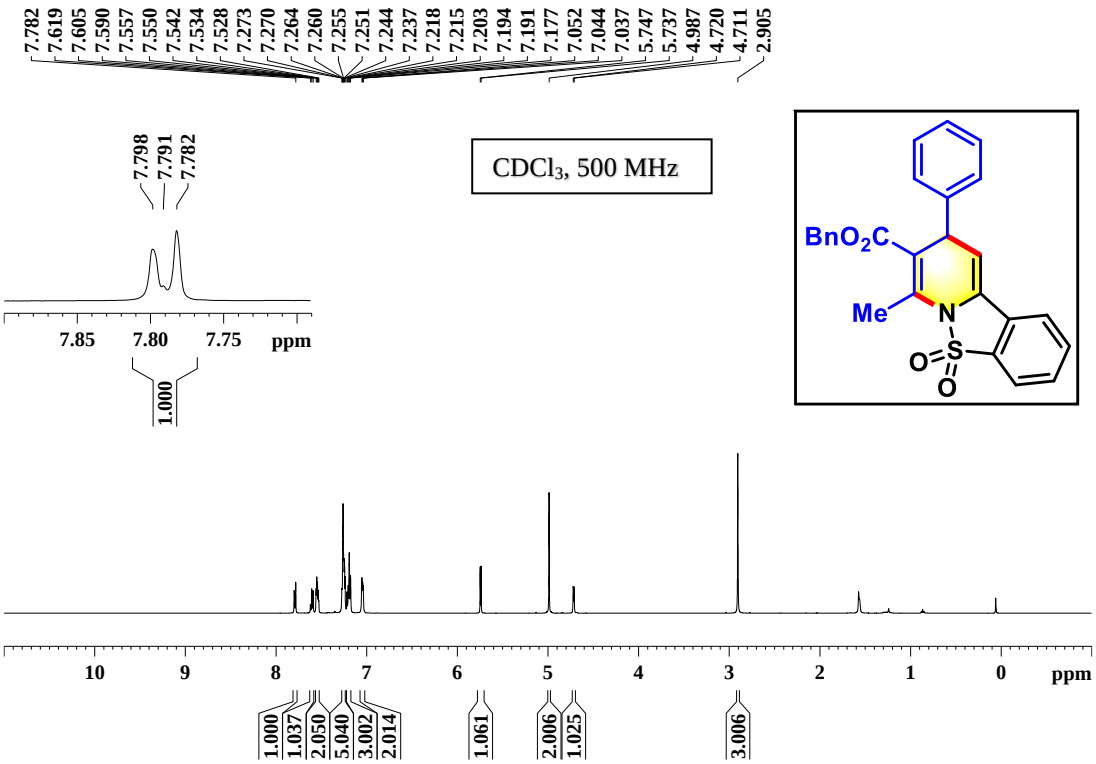

Figure A11: ^{1}H NMR spectrum of compound **21aa**

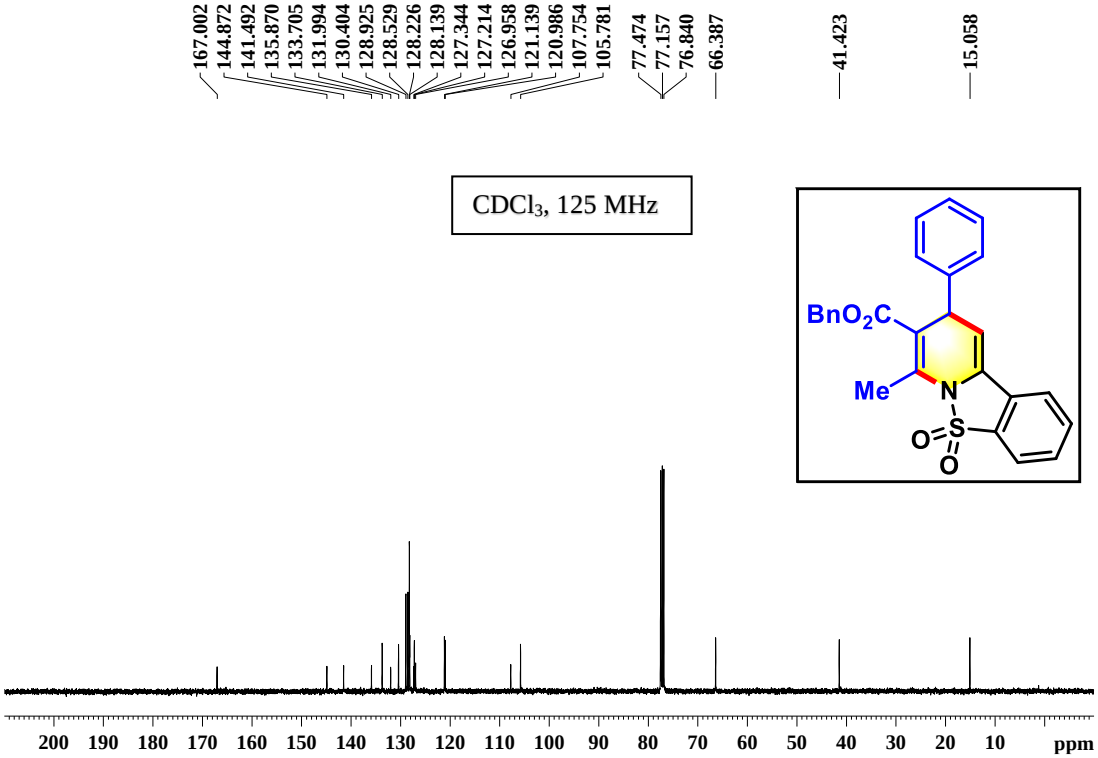

Figure A12: ^{13}C NMR spectrum of compound **21aa**

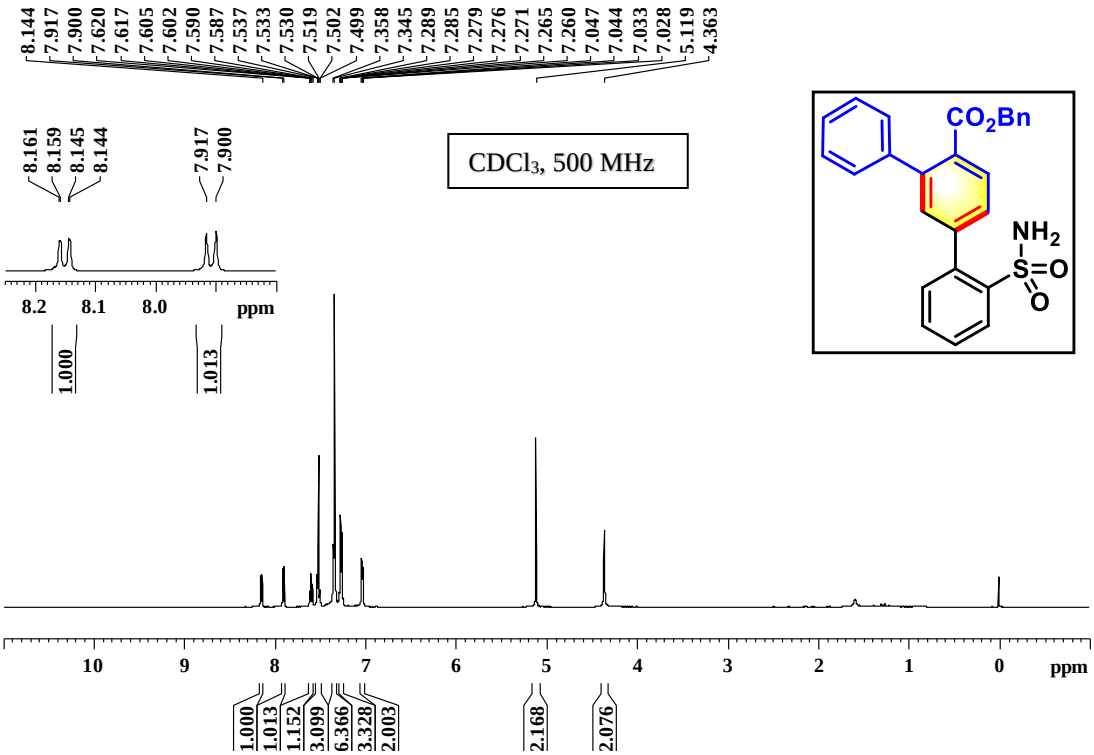

Figure A13: ^{1}H NMR spectrum of compound **22aa**

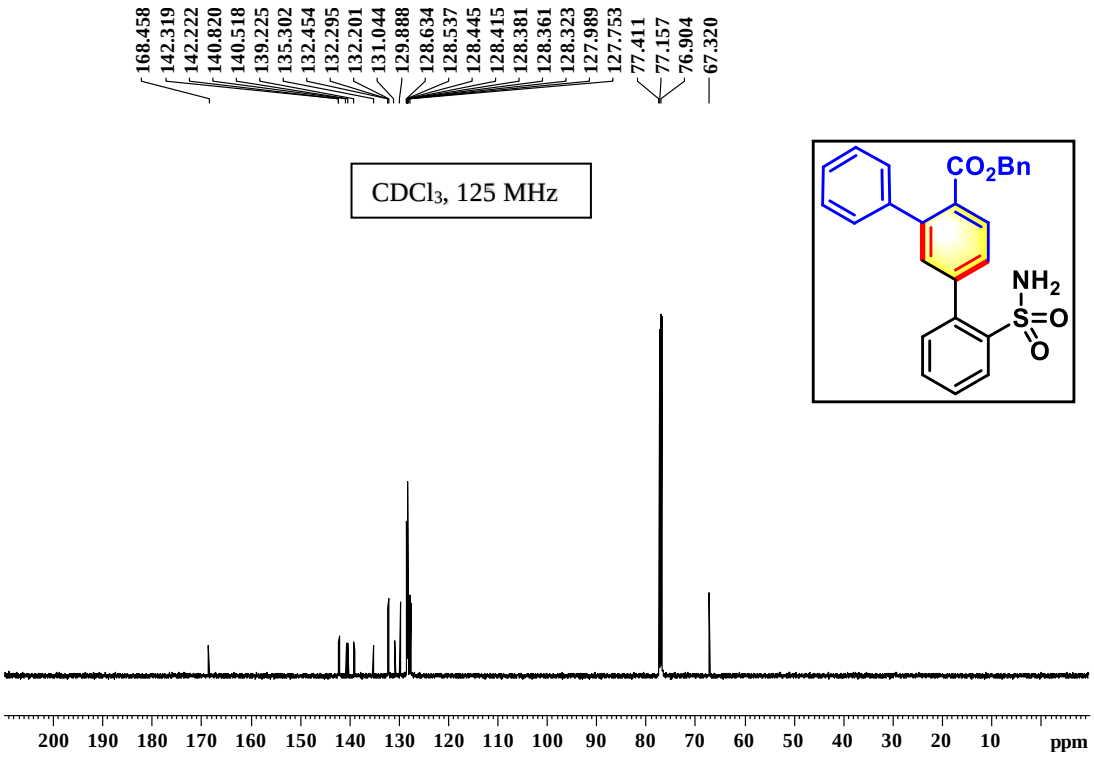

Figure A14: ^{13}C NMR spectrum of compound **22aa**

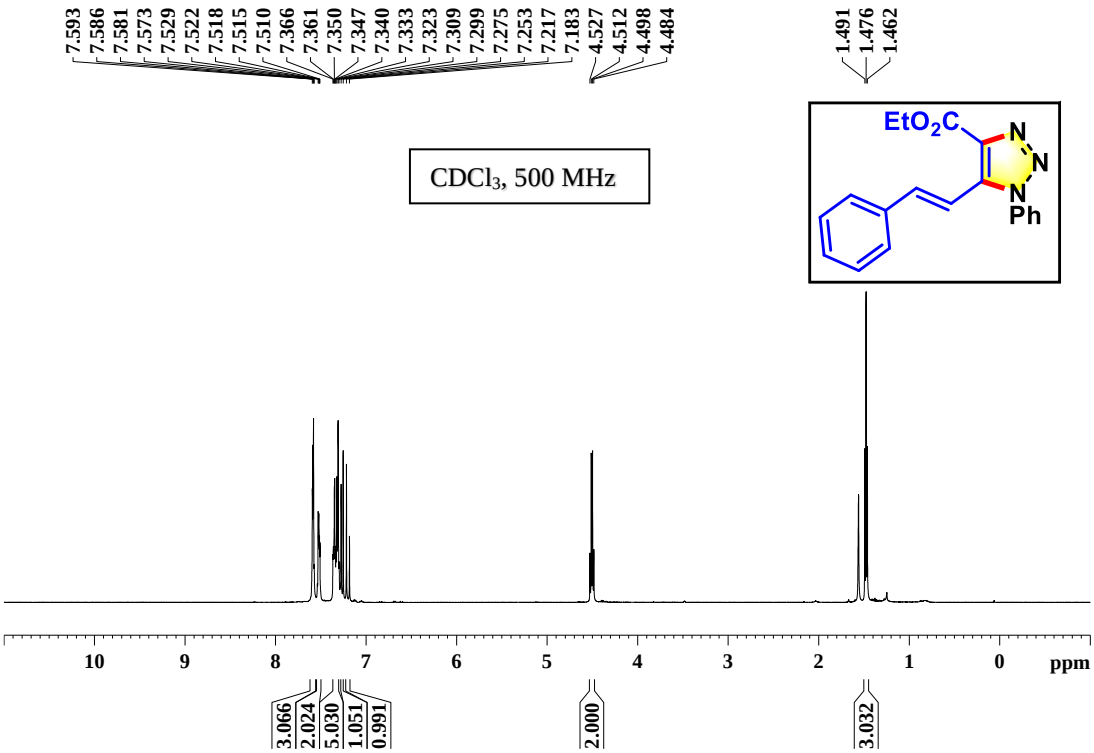

Figure A15: ^{1}H NMR spectrum of compound **23aa**

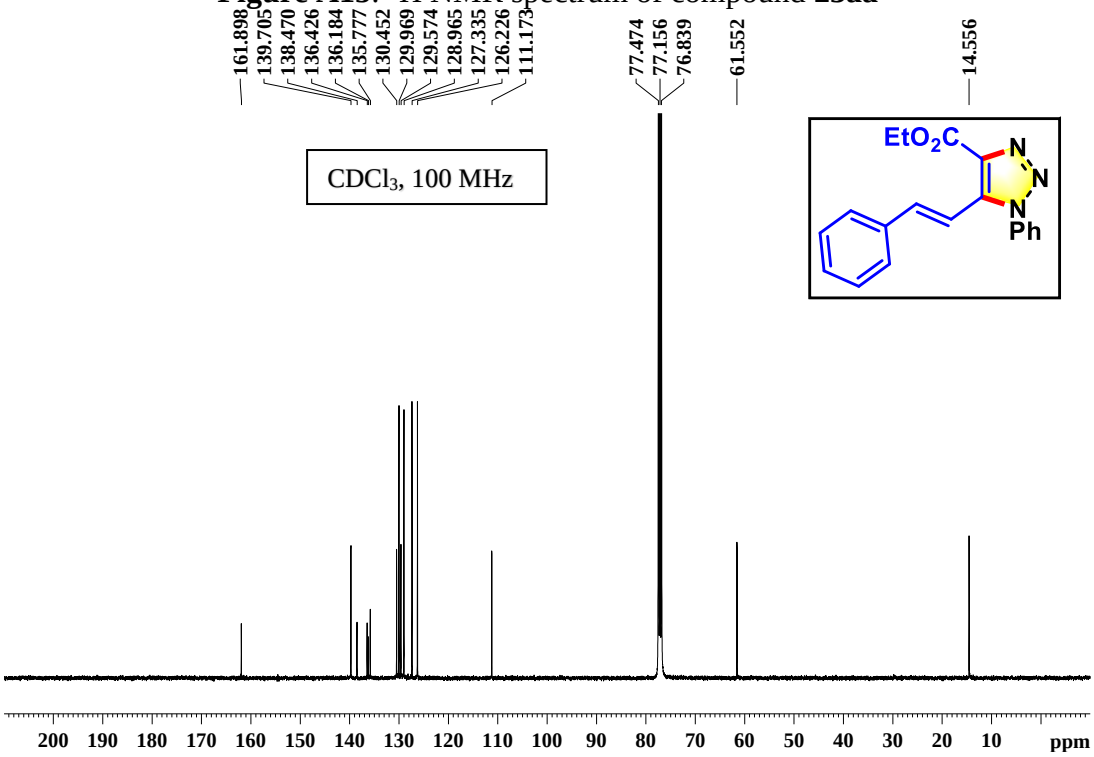

Figure A16: ^{13}C NMR spectrum of compound **23aa**

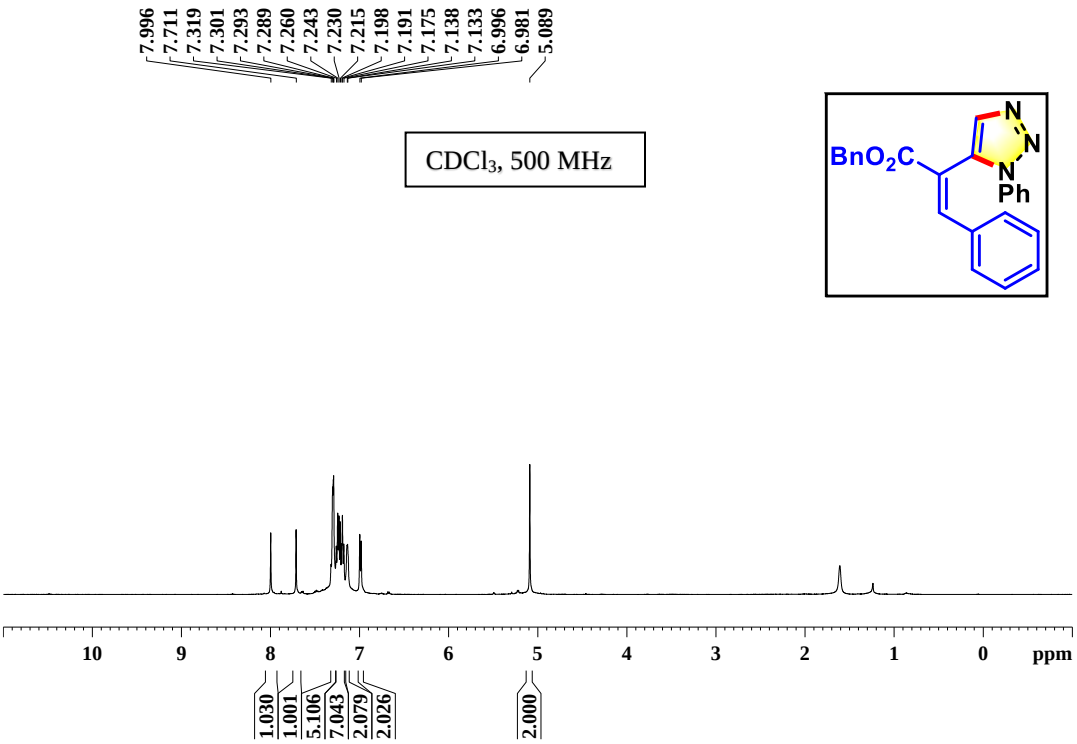

Figure A17: ^{1}H NMR spectrum of compound **24aa**

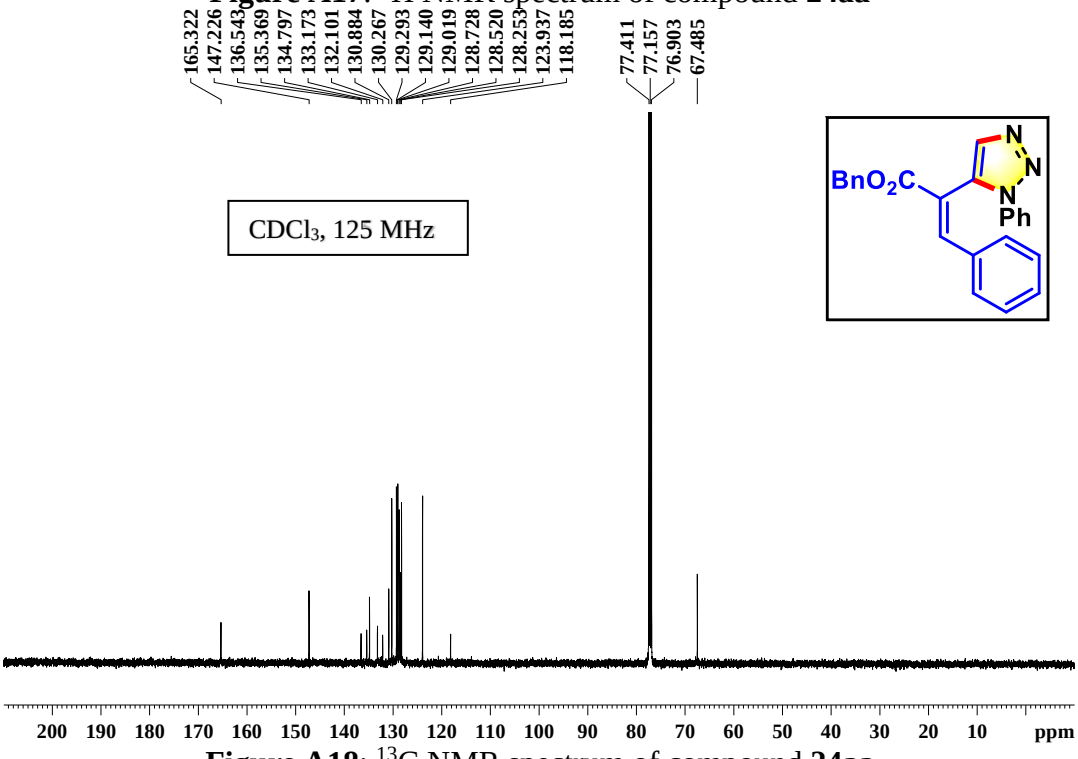

Figure A18: ^{13}C NMR spectrum of compound **24aa**

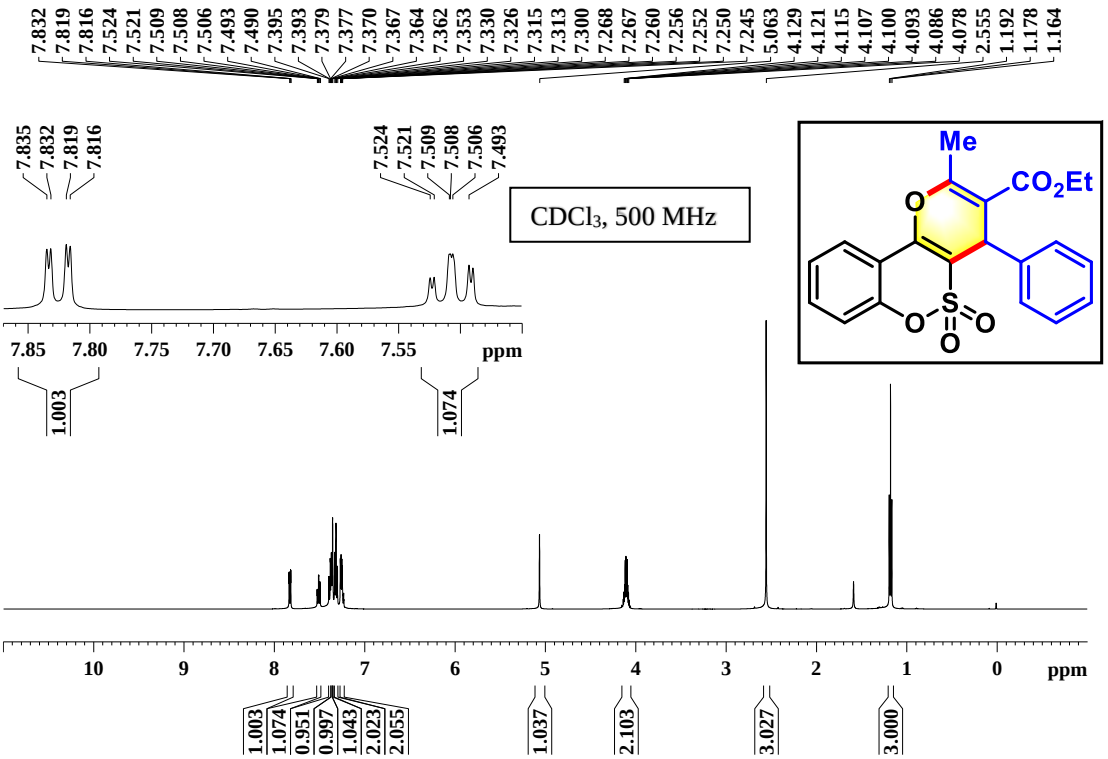

Figure A19: ^{1}H NMR spectrum of compound **28n**

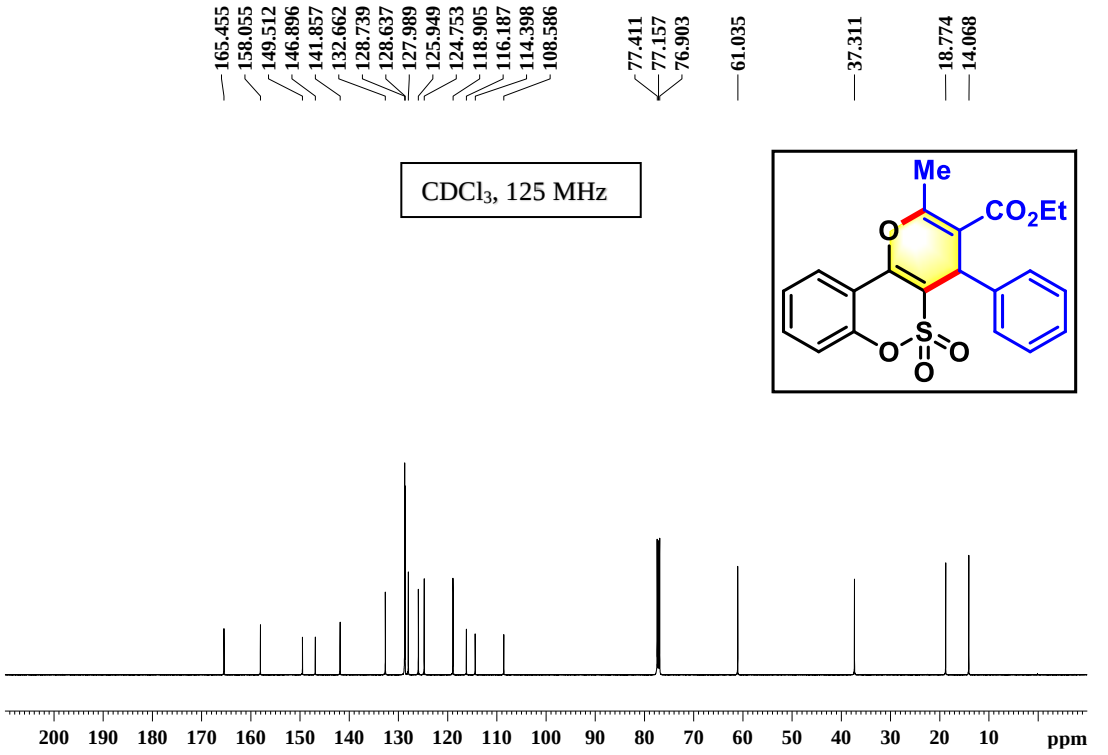

Figure A20: ^{13}C NMR spectrum of compound **28n**

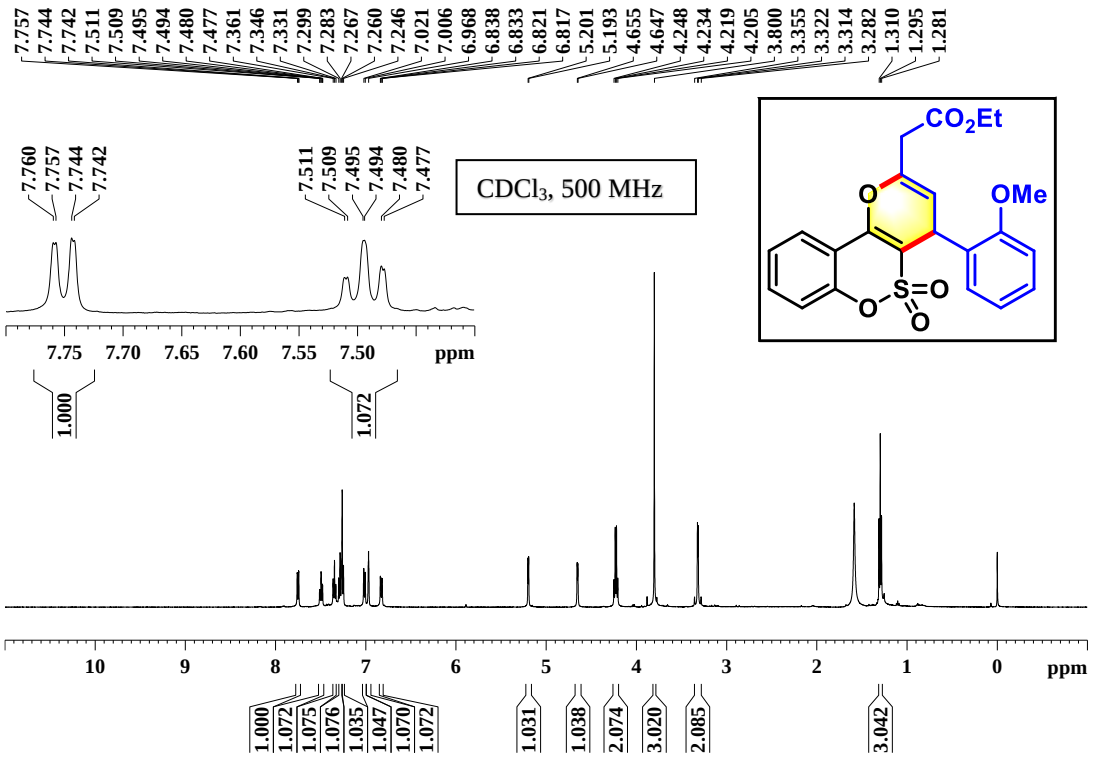

Figure A21: ^{1}H NMR spectrum of compound **29m**

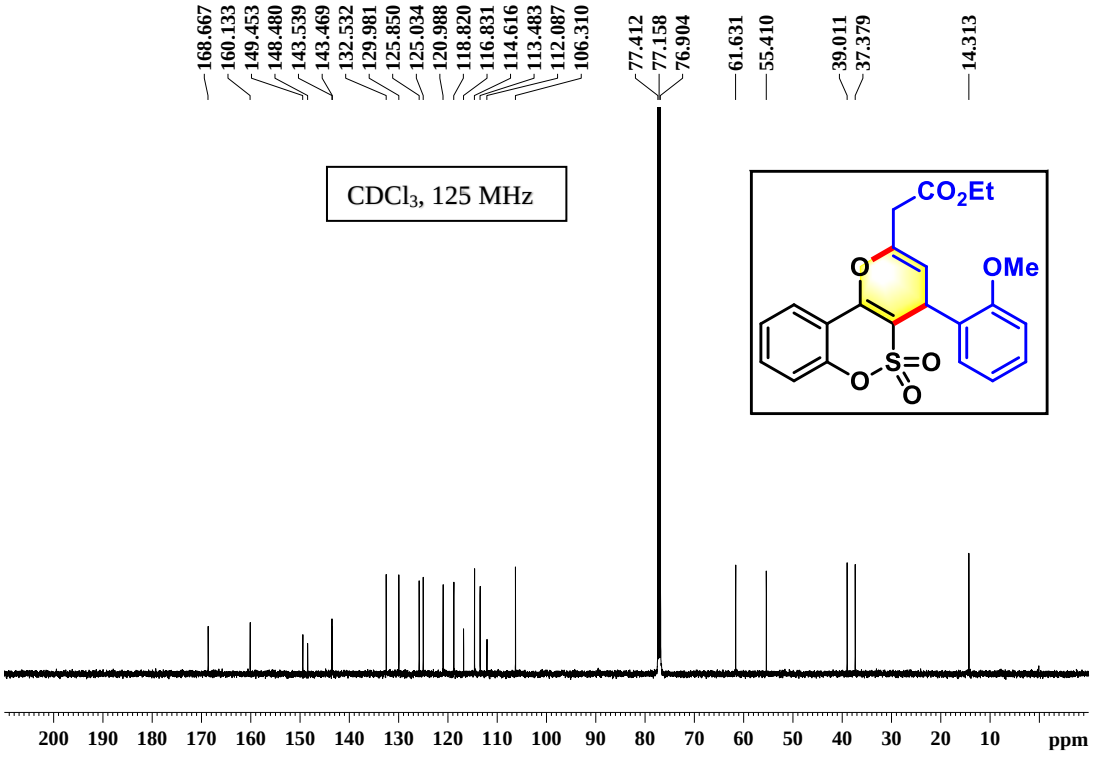

Figure A22: ^{13}C NMR spectrum of compound **29m**

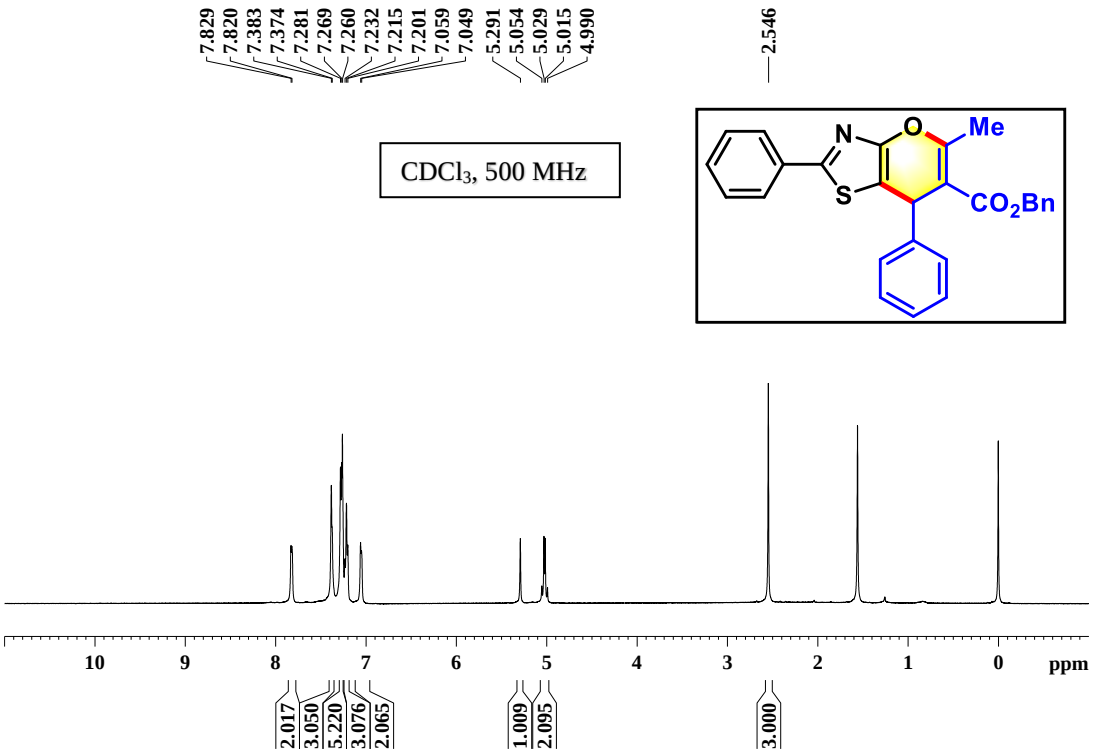

Figure A23: ^{1}H NMR spectrum of compound **30a**

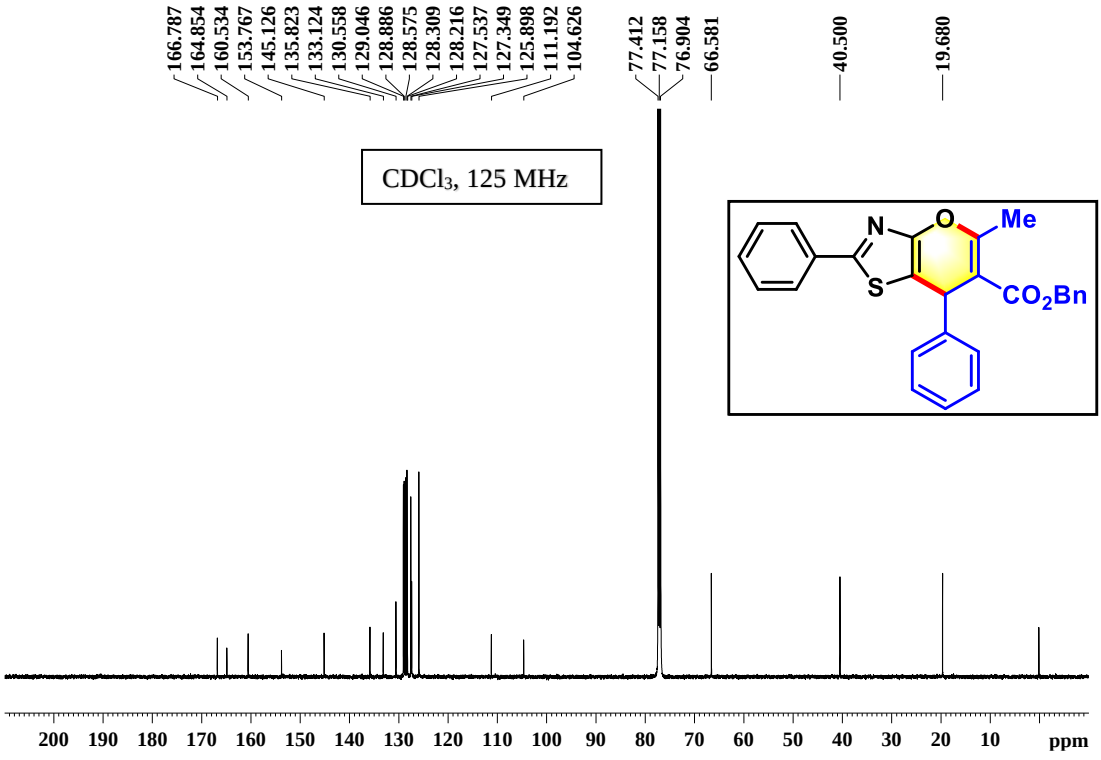

Figure A24: ^{1}H NMR spectrum of compound **30a**

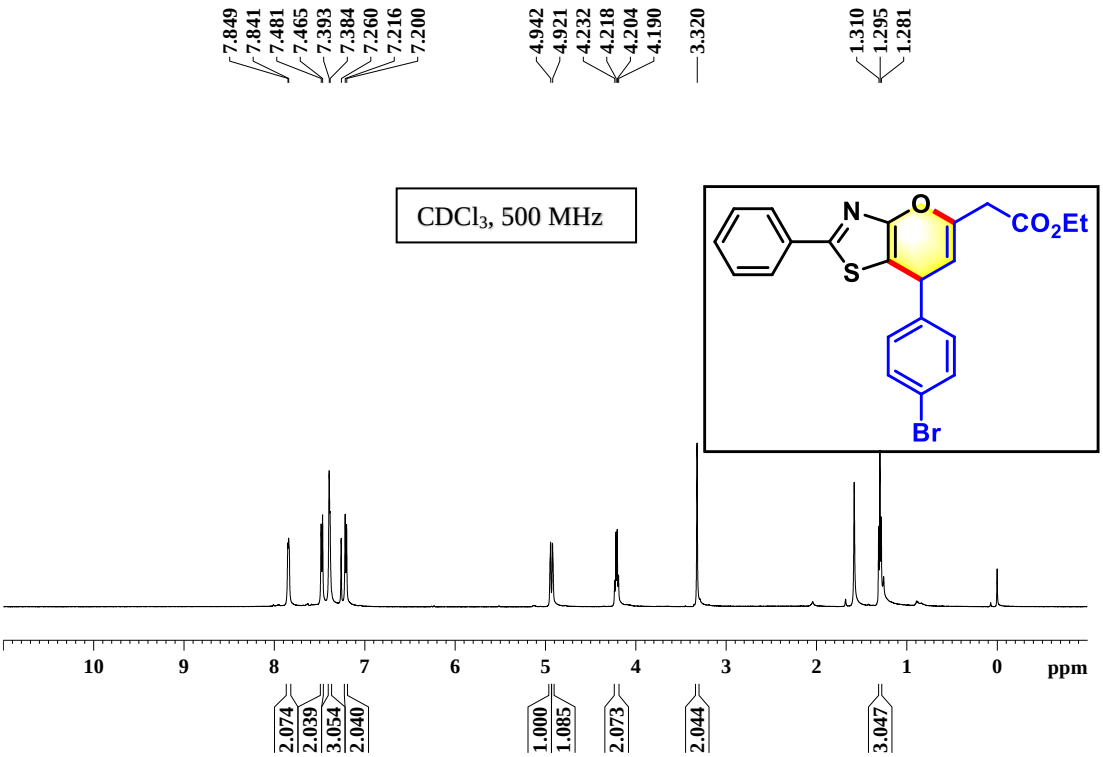

Figure A25: ^{1}H NMR spectrum of compound **31g**

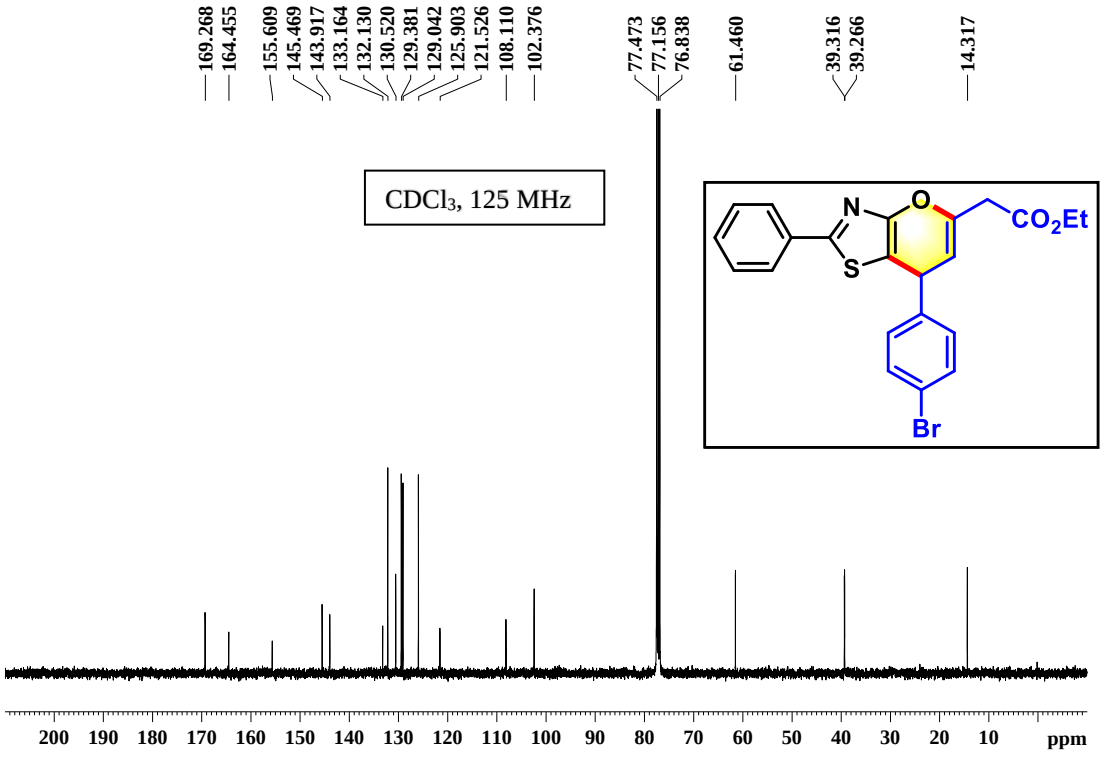

Figure A26: ^{1}H NMR spectrum of compound **31g**

(B) CCDC numbers and atomic coordinates for X-ray structures reported in this thesis

CCDC numbers for the published compounds: 15aa, 15db, 16af, 16ca, 17aa, 17bd, 19bb, 20aa, 21aa, 21bk, 22ad, 23fi and 25 are 1952241, 1952242, 1952243, 1952244, 1952245, 1952246, 1952247, 1952248, 2298991, 2298992, 2298993, 2097131 and 2097132.

Unpublished compounds: 28a, 30c and 30n

Compound 28a

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck052_0m_a

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck052_0m_a

Bond precision: C-C = 0.0028 A Wavelength=0.71073

Cell: a=10.6053(3) b=13.1833(4) c=15.5776(5)
alpha=90 beta=92.199(1) gamma=90
Temperature: 301 K

	Calculated	Reported
Volume	2176.35(11)	2176.34(11)
Space group	P 21/n	P 1 21/n 1
Hall group	-P 2yn	-P 2yn
Moiety formula	C26 H20 O6 S	C26 H20 O6 S
Sum formula	C26 H20 O6 S	C26 H20 O6 S
Mr	460.48	460.48
Dx,g cm-3	1.405	1.405
Z	4	4
Mu (mm-1)	0.191	0.191
F000	960.0	960.0
F000'	960.99	
h,k,lmax	13,17,20	13,17,20
Nref	5011	5000
Tmin,Tmax	0.973,0.979	0.684,0.746
Tmin'	0.961	

Correction method= # Reported T Limits: Tmin=0.684 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.998 Theta(max)= 27.531

R(reflections)= 0.0584(4374) wR2(reflections)= 0.1581(5000)

S = 1.078 Npar= 299

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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 C

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PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600          3 Report
```

Alert level G

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PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .     Please Do !
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          2 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600          7 Note
PLAT933_ALERT_2_G Number of HKL-OMIT Records in Embedded .res File          1 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          4 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   1 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   5 ALERT level G = General information/check it is not something unexpected

   1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   2 ALERT type 2 Indicator that the structure model may be wrong or deficient
   2 ALERT type 3 Indicator that the structure quality may be low
   1 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

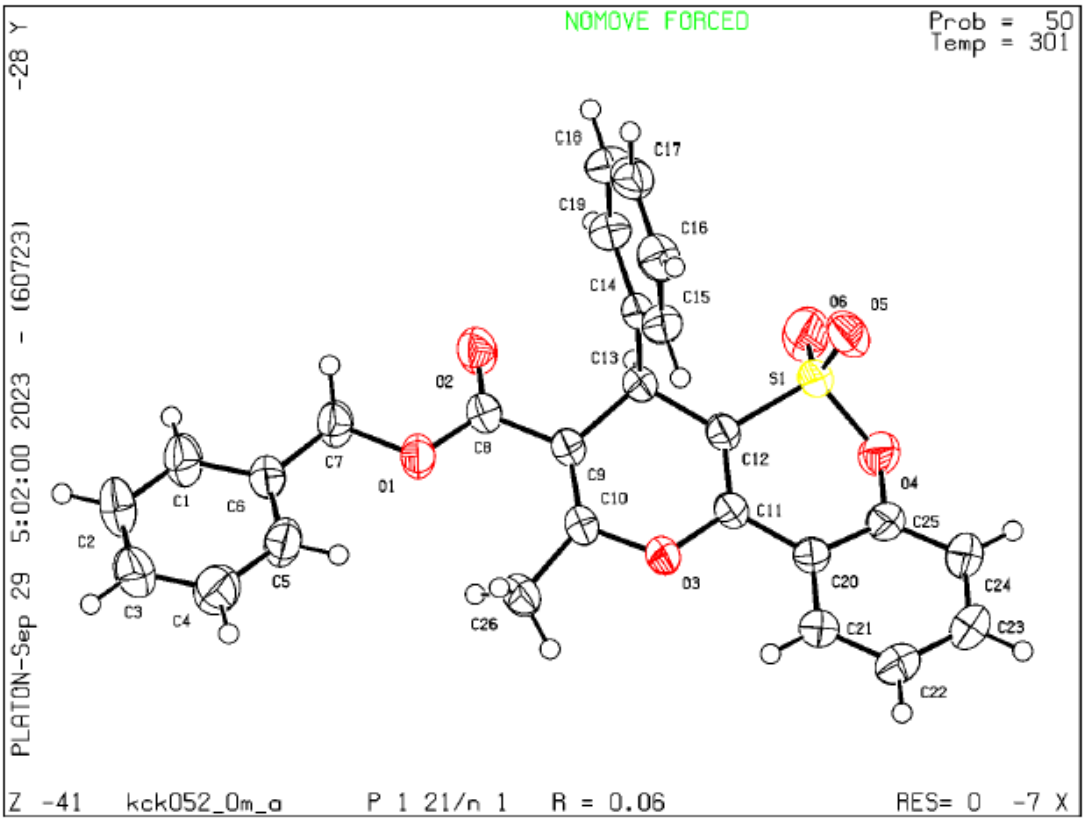
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 06/07/2023; check.def file version of 30/06/2023

Datablock kck052_0m_a - ellipsoid plot



Compound 30c

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck027_0ma_a

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck027_0ma_a

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Bond precision:   C-C = 0.0030 A          Wavelength=0.71073

Cell:             a=5.7479(5)     b=27.840(3)        c=14.0482(15)
                  alpha=90        beta=90.302(3)     gamma=90
Temperature:      297 K

                  Calculated                  Reported
Volume            2248.0(4)                   2247.9(4)
Space group       P 21/c                      P 1 21/c 1
Hall group        -P 2ybc                     -P 2ybc
Moiety formula    C27 H20 Cl N O3 S           C27 H20 Cl N O3 S
Sum formula       C27 H20 Cl N O3 S           C27 H20 Cl N O3 S
Mr                473.95                      473.95
Dx,g cm-3         1.400                       1.400
Z                 4                           4
Mu (mm-1)         0.294                       0.294
F000              984.0                       984.0
F000'             985.48
h,k,lmax          7,36,18                     7,36,18
Nref              5354                        5260
Tmin,Tmax         0.939,0.963                 0.603,0.746
Tmin'             0.939

Correction method= # Reported T Limits: Tmin=0.603 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.982          Theta(max)= 27.854

R(reflections)= 0.0506( 4087)                wR2(reflections)=
                                             0.1418( 5260)
S = 1.075                 Npar= 299
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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.
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Alert level C

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PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of       C13 Check
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......     3.317 Check
```

Alert level G

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PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600        94 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.        13 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
   2 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   2 ALERT type 2 Indicator that the structure model may be wrong or deficient
   1 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
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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Publication of your CIF in other journals

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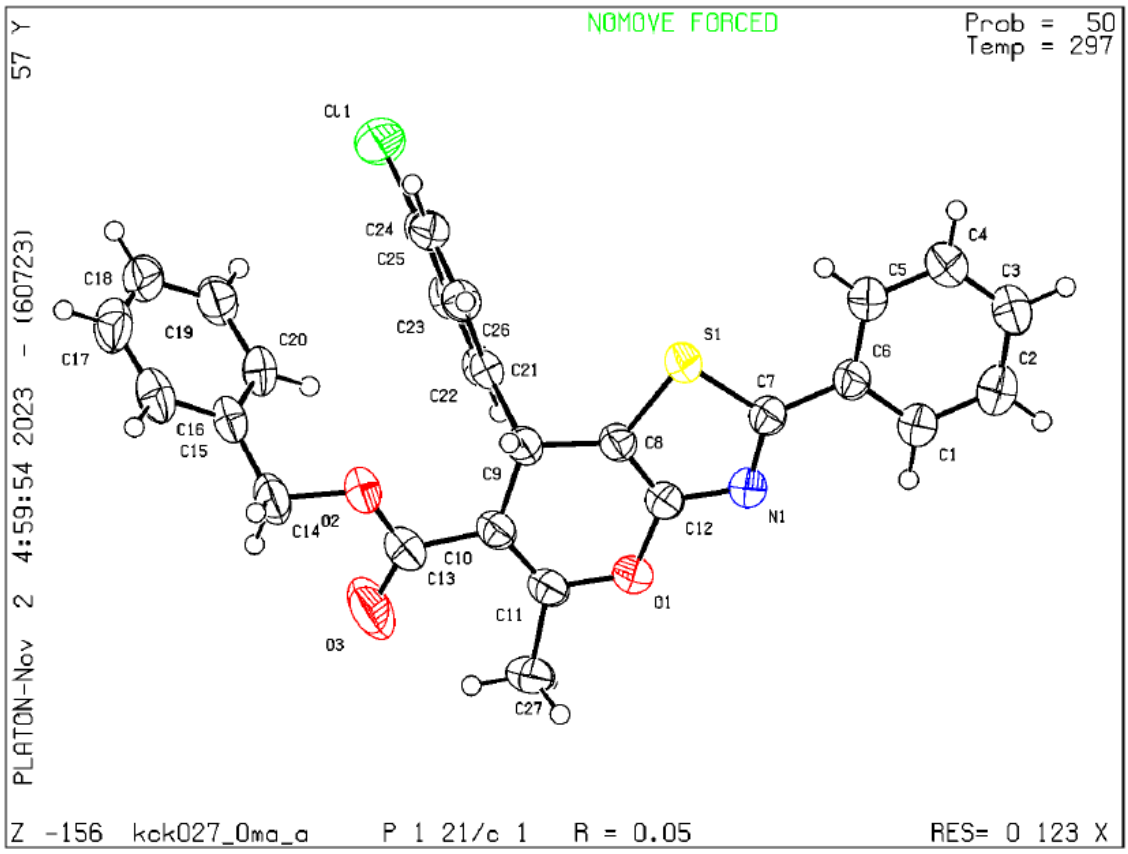
PLATON version of 06/07/2023; check.def file version of 30/06/2023

Datablock kck027_0ma_a - ellipsoid plot



Compound 30n

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) kck060_0m_a

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: kck060_0m_a

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Bond precision:   C-C = 0.0054 A          Wavelength=0.71073

Cell:             a=5.5884(6)     b=24.463(3)        c=13.9485(17)
                  alpha=90        beta=95.132(4)     gamma=90
Temperature:      297 K

                  Calculated                  Reported
Volume            1899.2(4)                   1899.3(4)
Space group       P 21/n                      P 1 21/n 1
Hall group        -P 2yn                      -P 2yn
Moiety formula    C22 H19 N O3 S              C22 H19 N O3 S
Sum formula       C22 H19 N O3 S              C22 H19 N O3 S
Mr                377.44                      377.44
Dx,g cm-3         1.320                       1.320
Z                 4                           4
Mu (mm-1)         0.192                       0.192
F000              792.0                       792.0
F000'             792.84
h,k,lmax          6,29,16                     6,29,16
Nref              3486                        3469
Tmin,Tmax         0.955,0.979                 0.463,0.746
Tmin'             0.955

Correction method= # Reported T Limits: Tmin=0.463 Tmax=0.746
AbsCorr = MULTI-SCAN

Data completeness= 0.995          Theta(max)= 25.346

R(reflections)= 0.0745( 3020)                wR2(reflections)=
                                             0.2149( 3469)
S = 1.154                 Npar= 246
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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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PLAT094_ALERT_2_C Ratio of Maximum / Minimum Residual Density ....       2.31 Report
PLAT242_ALERT_2_C Low    'MainMol' Ueq as Compared to Neighbors of        C19 Check
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00543 Ang.
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      5.105 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600        18 Report
PLAT934_ALERT_3_C Number of (Iobs-Icalc)/Sigma(W) > 10 Outliers ..         1 Check
```

Alert level G

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PLAT930_ALERT_2_G FCF-based   Twin Law ( 0 0 1)         Est.d BASF       0.20 Check
PLAT931_ALERT_5_G CIFcalcFCF  Twin Law ( 0 0 1)         Est.d BASF       0.20 Check
PLAT933_ALERT_2_G Number of HKL-OMIT Records in Embedded .res File          3 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          1 Info
```

```
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   0 ALERT type 4 Improvement, methodology, query or suggestion
   1 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

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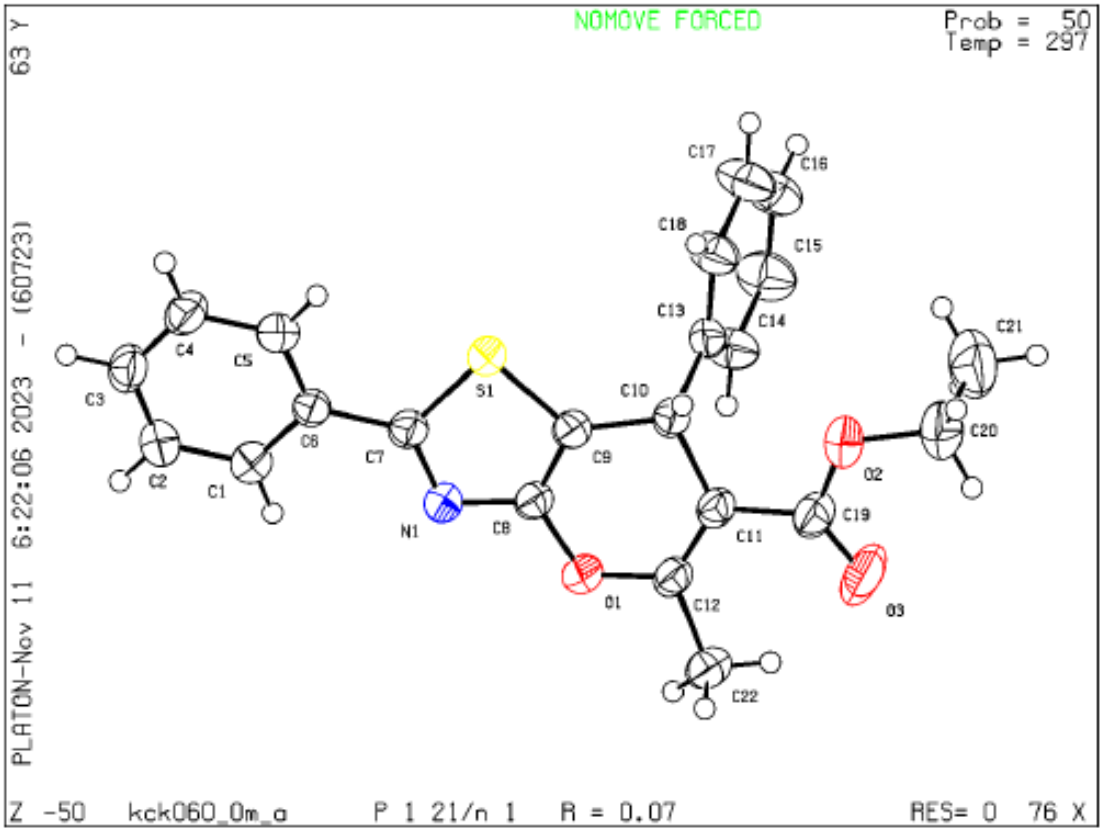

Investigations on the Reactivity of Acetoxy Allenoates with N-Sulfonyl- imines, Azides, and Enolizable Carbonyls

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5 Sanjeeva K. Arupula, Asif Ali Qureshi, K C Kumara Swamy. "Lewis Base Switched [3+3] and [4+2] Annulation Reaction of δ-Acetoxy Allenoates with Cyclic N-Sulfonyl Imines: Divergent Synthesis of Functionalized α-Pyridyl Acetates and Teraryl Scaffolds", The Journal of Organic Chemistry, 2020 — 1 %
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6 Sachin Chauhan, A. Sanjeeva Kumar, K. C. Kumara Swamy. " δ-Acetoxy Allenoate as a -Synthon in Domino-Annulation with Sulfamidate Imines: Ready Access to Coumarins ", The Journal of Organic Chemistry, 2023 — 1 %
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