# CYCLIZATION REACTIONS OF SULFONAMIDES/ EPOXY YNAMIDES AND HALO-ADDITION AND CYCLIZATION REACTIONS OF PHOSPHORUS BASED ALLENES

**A THESIS**

**SUBMITTED FOR THE DEGREE OF**

**DOCTOR OF PHILOSOPHY**

**By**


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**HYDERABAD - 500 046**

**INDIA**


**JUNE 2018**

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## 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 acknowledgements have been made wherever the work described is based on the findings of other investigators.

Hyderabad
June 2018

Mandala Anitha

# DECLARATION

I, **MANDALA ANITHA** hereby declare that this thesis entitled ***"Cyclization Reactions of Sulfonamides/Epoxy-Ynamides and Halo-Addition and Cyclization Reactions of Phosphorus Based Allenes"*** 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 deposited in Shodganga/INFLIBNET.

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## CERTIFICATE

This is to certify that the thesis entitled ***"Cyclization Reactions of Sulfonamides/Epoxy-Ynamides and Halo-Addition and Cyclization Reactions of Phosphorus Based Allenes"*** submitted by **Mrs. Mandala Anitha** bearing registration number **12CHPH01** in partial fulfillment of the requirements for award of Doctor of Philosophy in the School of Chemistry is a bonafide work carried out by her 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 award of any degree or diploma. Further the student has eight publications before the submission of her thesis.

Parts of this thesis have been published in the following five publications:

1. Anitha, M.; Gangadhararao, G.; Kumara Swamy, K. C. *Org. Biomol. Chem.* **2016**, *14*, 3591.
2. Kumara Swamy, K. C.; Phani Pavan, M.; Anitha, M.; Gangadhararao, G. *Phosphorus, Sulfur, and Silicon* 2018, *193*, 81, DOI: 10.1080/10426507.2017.1417302.
3. Anitha, M.; Kumara Swamy, K. C. *Org. Biomol. Chem.* **2018**, *16*, 402.
4. Kumara Swamy, K. C.; Gangadhararao, G.; Anitha, M.; Leela Siva Kumari, A.; Siva Reddy, A.; Kalyani, A.; Allu, S. *J. Chem. Sci*. **2018**, 0000. DOI: 10.1007/s12039-018-1496-2.

She has also made presentations in the following conferences:

1. Poster presentation in the National Symposium on Frontiers in Organic Chemistry (NSFOC), School of Chemistry, University of Hyderabad, INDIA, Oct-**2013**.
2. Oral and Poster presentation in the *Chemfest-2017* (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Mar-**2017**.
3. Poster presentation in the *Chemfest-2018* (annual in-house symposium), School of Chemistry, University of Hyderabad, INDIA, Mar-**2018**.

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

| | Course | Title | Credits | Pass/Fail |
|---|---|---|---|---|
| 1. | CY-801 | Research Proposal | 3 | Pass |
| 2. | CY-806 | Instrumental Methods B | 3 | Pass |
| 3. | CY-821 | Organic Reactions and Mechanisms | 3 | Pass |
| 4. | CY-851 | Biological Chemistry | 3 | Pass |

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*M. Anitha...* 

# LIST OF PUBLICATIONS

1. $FeCl_3$ catalyzed regioselective allylation of phenolic substrates with (α-hydroxy)allylphosphonates
   **Mandala Anitha**, Ramesh Kotikalapudi, and K. C. Kumara Swamy*
   *J. Chem. Sci*. **2015**, *127*, 1465.
2. Base catalysed intermolecular cyclisation of *N*-protected o-amino benzaldehyde/ acetophenone with phosphorus/ sulphur based allenes: Facile synthesis of substituted quinolines
   **Mandala Anitha**, G. Gangadhararao and K. C. Kumara Swamy*
   *Org. Biomol. Chem.* **2016**, *14*, 3591.
3. Phosphorus-Based Allenes as Scaffolds in Cycloaddition and Cyclization Reactions
   K. C. Kumara Swamy,* R. Rama Suresh, G. Gangadhararao and **Mandala Anitha**.
   *Phosphorus, Sulfur, and Silicon* **2016**, *191*, 1427
4. Exploring Allene Chemistry Using Phosphorus-Based Allenes as Scaffolds
   K. C. Kumara Swamy,* **Mandala Anitha**, G. Gangadhararao and R. Rama Suresh
   *Pure and Applied Chemistry* **2017**, *89*, 367-377.
5. On the NHC/DBU-Mediated Tosyl Group Transfer to Allenes: Is There an Organocatalytic Role for DBU?
   K. C. Kumara Swamy,*R. Rama Suresh, G. Gangadhararao and **Mandala Anitha**
   *Synthesis* **2017**, *49*, 2275–2285
6. New addition and cyclization reactions involving phosphorus based allenes
   K. C. Kumara Swamy,* M. Phani Pavan, **Mandala Anitha**, G. Gangadhararao
   *Phosphorus, Sulfur, and Silicon* **2018**, *193*, 81.
7. Synthesis of thiazolidine-thiones, iminothiazolidines and oxazolidines via base promoted cyclisation of epoxy-sulfonamides and heterocumulenes
   **Mandala Anitha** and K. C. Kumara Swamy*
   *Org. Biomol. Chem.* **2018**, *16*, 402.
8. New reactions of allenes, alkynes, ynamides, enynones and isothiocyanates

K. C. Kumara Swamy,* G. Gangadhararao, **Mandala Anitha**, A. Leela Siva Kumari, Alla Siva Reddy, A. Kalyani and Srinivasarao Allu.

*J. Chem. Sci*. **2018** (*accepted for publication*).

9 Nucleophile (Br/Cl) Assisted Tandem Intramolecular 5-*exo-dig and* 6-*endo-dig* Cyclizations of Epoxy-Ynamides leading to Functionalized 1,3 Oxazolidines and 1,4-Oxazines

**Mandala Anitha**, Mallepalli Shankar, and K. C. Kumara Swamy*

*(to be communicated).*

10 Synthesis of highly functionalized (*γ*-azido/*γ*-fluoro-*β*-iodo)vinyl derivatives from phosphorus based allenes

**Mandala Anitha** and K. C. Kumara Swamy*

*(to be communicated).*

11 $AlCl_3$ as a regio- and stereo-specific hydrochlorinating agent for the ynamides

Alla Siva Reddy, **Mandala Anitha** and K. C. Kumara Swamy*

*(to be communicated).*

## Posters presented in symposia

1. Synthesis of multi-substituted 2-furyl phosphonates and Regioselective allylation of functionalized arenes with (α-hydroxy)allylphosphonates.

   Anasuyamma Uravakilli, **Mandala Anitha**, Ramesh Kotikalapudi and K. C. Kumara Swamy*

   National Symposium on Frontiers in Organic Chemistry (NSFOC), School of Chemistry, University of Hyderabad, Oct-2013 (Poster presentation).

2. Transition metal free- base catalyzed one pot synthesis of 1,3-thiazolidine-2-thiones and thiazolidin-2-ylidenes from sulfonamides

   **Mandala Anitha** and K. C. Kumara Swamy*

   *Chemfest-2017* (Annual in-house symposium), School of Chemistry, University of Hyderabad, March-2017 (Poster & Oral Presentation)

3. Addition and cyclization reactions of allenyl-phosphonates/phosphine oxides

   **Mandala Anitha** and K. C. Kumara Swamy*

   *Chemfest-2018* (Annual in-house symposium), School of Chemistry, University of Hyderabad, March-2018 (Poster Presentation)

*4.* New Catalytic and Noncatalytic Transformations Involving Allenes/Alkynes/Ynamides and Indoles.

   K. C. Kumara Swamy,***Mandala Anitha**, Alla Siva Reddy, A. Leela Siva Kumari and R. N. Prasad Tulichala

   *6$^{th}$ International Collaborative and Cooperative Chemistry Symposium (ICCCS-6)-2015*, Seoul National University, Seoul, Korea, Nov-**2015** (Poster presentation).

## SYNOPSIS

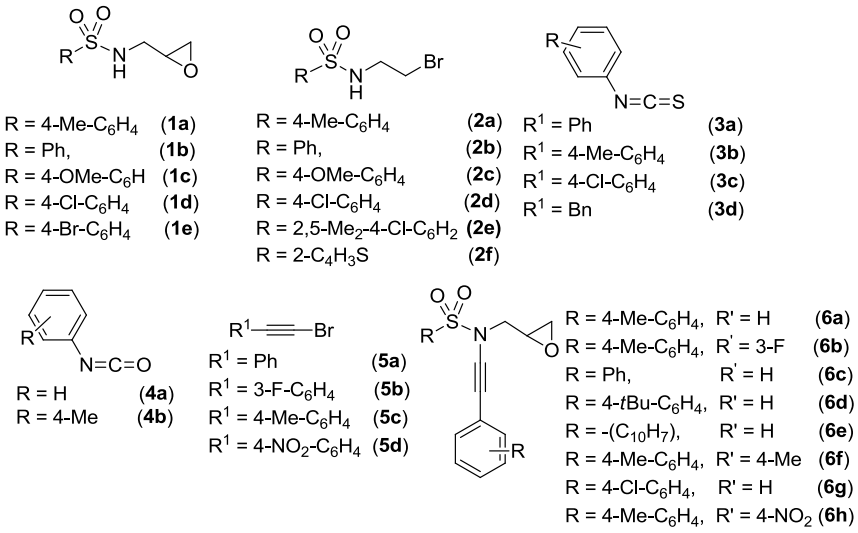
This thesis is divided into two parts: **Part-A** and **Part-B**. **Part-A** deals with the following topics: (i) A transition metal-free, base mediated synthesis of thiazolidine-thiones and imino-thiazolidines/oxazolidines *via* regioselective 5-*exo*-*tet* cyclization by treating epoxy-sulfonamides with carbon disulfide/ isothiocyanates/ isocyanates, (ii) A simple route to thiazolidine-2-thiones and imino-thiazolidines /oxazolidines by insertion of the heterocumulenes into 2-bromoethyl-sulfonamides by dehydrohalogenation, (iii) Nucleophile assisted regio- and stereo-selective 5-*exo*-*dig*/6-*endo*-*dig* cyclization of epoxy ynamides by using CuBr or LiCl as the nucleophilic source for the synthesis of 1,3-oxazolidines or 1,4-oxazines, and (iv) A simple approach for the regio-specific synthesis of (*E/Z*)-*α*-chloro-*β*-iodo-enamides and (*E*)-*α,β*-dibromo-enamide. **Part-B** deals with the following topics: (i) Synthesis of *γ*-azido/*γ*-fluoro-*β*-iodo-vinyl phosphine oxides/ phosphonates/ esters from phosphorus based allenes/ allenyl esters by iodination followed by azidation/fluorination, (ii) Pd-PVP catalyzed addition reactions of allenylphosphonates with 2-iodophenols leading to isomeric (*E/Z*)-vinylphosphonates and synthesis of phosphorus based naphthalenes from a novel self-dimerization-cum-cyclization by [Pd]-catalysis, and (iii) Synthesis of densely substituted phosphorus/ sulfur based quinolines *via* base catalyzed intermolecular cyclization of *N*-protected *o*-amino benzaldehyde with phosphorus/sulfur based allenes.

Each part is subdivided into three chapters: (a) Introduction (literature survey), (b) Results and Discussion and (c) Experimental Section. The compounds synthesized in the present study are, in general, characterized by mp, IR and NMR ($^{1}$H, $^{13}$C & $^{31}$P) techniques followed by HRMS or elemental analysis in conjunction with LC-MS. X-ray structure determination is undertaken wherever required. Summary as well as references are given at the end of each part.

## PART A

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

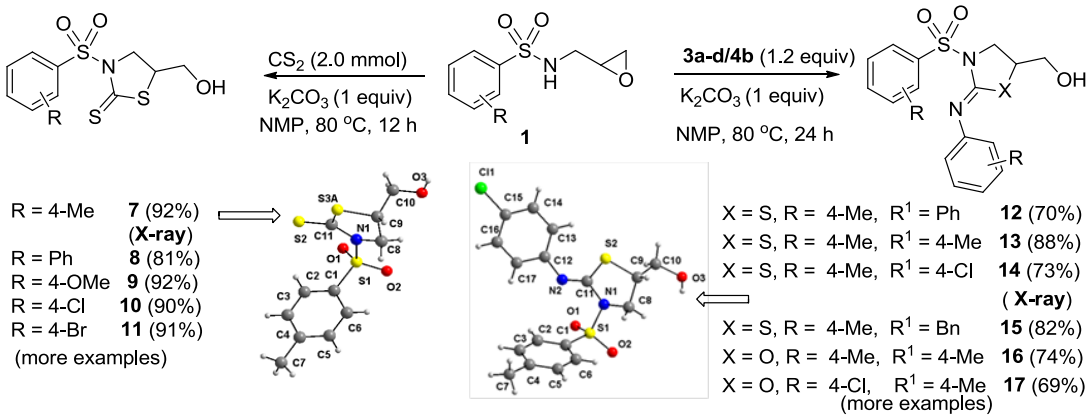
**Chart 1**




## (i) Regioselective 5-*exo-tet* cyclization of epoxy-sulfonamides with $CS_2$/RNCS/RNCO leading to thiazolidine-thiones/iminothiazolidines/oxazolidine

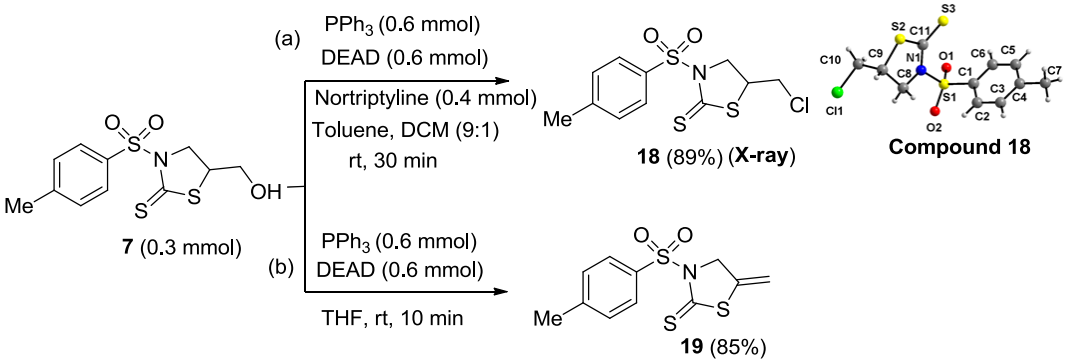
Thiazolidine-thiones **7-11**, imino-thiazolidines **12-15** and imino-oxazolidine **16-17** were obtained by treating epoxy sulfonamides **1** with heterocumulenes ($CS_2$/RNCS/RNCO) in the presence of $K_2CO_3$ as a base with NMP as the solvent at 80 $^oC$ (Scheme 1). This reaction involves nucleophilic attack on *sp*-hybridized cumulene carbon and 5-*exo-tet* cyclization.

**Scheme 1**




Product **7** contains a pendent primary alcohol group that can undergo C-N coupling or dehydration *via* the Mitsunobu reaction. Thus we treated **7** with $Ph_3P$/DEAD/nortriptyline in toluene/DCM (9:1). Surprisingly the chloro-substituted product **18** was obtained in good yield. Here DCM acted as the chlorine source, which is not normal (Scheme 2a). When we performed the reaction in THF as the solvent, the dehydration product **19** was formed in decent yields (Scheme 2b).

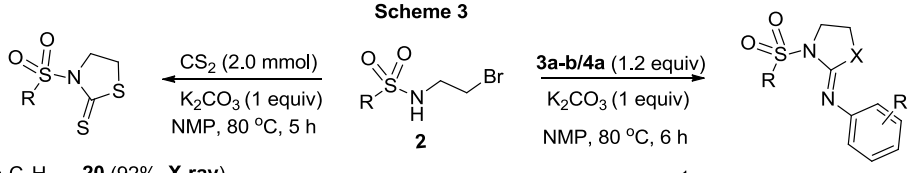
**Scheme 2**




## (ii) Cyclization reaction of *N*-(2-bromoethyl)-sulfonamides with heterocumulenes (carbon disulfide, isothiocyanates or isocyanates)

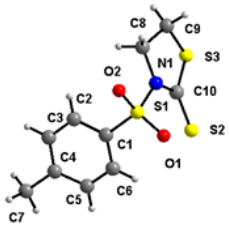
Treatment of *N*-(2-bromoethyl)-sulfonamides **2** with carbon disulfide, isothiocyanates **3a-b**, **3d** or isocyanate **4a** in NMP at 80 $^{o}$C for 5 h afforded thiazolidine-2-thiones **20-24**, imino-thiazolidines **25-27** and imino-oxazolidine **28** in good yields (Scheme 3). These compounds are similar to thiazolidine-thione **8**, but do not contain the primary alcohol group.

**Scheme 3**




R = 4-Me-$C_6H_4$ **20** (92%, **X-ray**)
R = Ph **21** (81%)
R = 4-OMe-$C_6H_4$ **22** (92%)
R = 4-Cl-$C_6H_4$ **23** (90%)
R = 4-Br-$C_6H_4$ **24** (91%)
(more examples)

X = S, R = 4-Me-$C_6H_4$, $R^1$ = H **25** (70%)
X = S, R = 4-OMe-$C_6H_4$, $R^1$ = H **26** (88%)
X = S, R = 4-Cl-2,5-$Me_2$-$C_6H_2$, $R^1$ = 4-Me **27** (73%, **X-ray**)
X = O, R = $C_4H_3S$, $R^1$ = H **28** (69%)
(more examples)

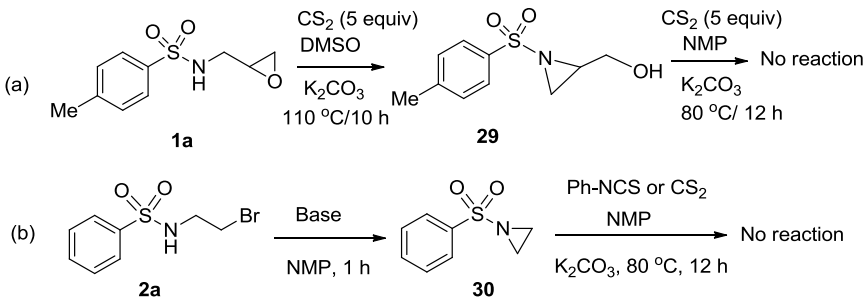


Compound 20

Compound 27

We prepared aziridines **29-30** by the conversion of sulfonamides **1a** and **2a** in the presence of a base in DMSO/NMP solvent. Treatment of aziridines **29-30** with $CS_2$/Ph-NCS/NMP/$K_2CO_3$ showed that they remained unreacted (Scheme 4). These control experiments and the available literature suggest that this base promoted reaction proceeds *via* 5-*exo*-*tet* cyclization, but not through the aziridines.

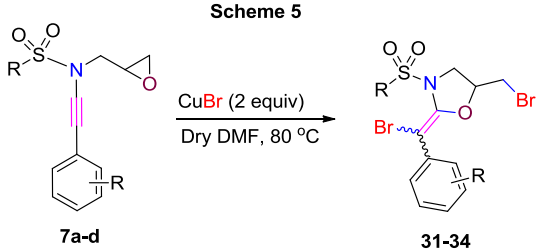
**Scheme 4**



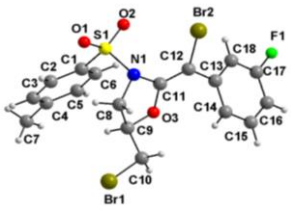

**(iii)(a) CuBr mediated concomitant bromination/cyclization reactions of epoxy ynamides**

Epoxy-ynamides **7a-d** on treatment with CuBr (2 equiv) in dry DMF for 2-4 h at 80 $^{o}$C afforded the ring expanded cyclized products (*E/Z*-1,3-oxazolidines) **31-34** in good yields. Most of these 1,3-oxazolidines except that with alkyne attached to $–C_6H_4Br$ group are *E*-predominant. These are most likely formed *via* epoxide ring opening from the less hindered side by the bromide ion followed by intramolecular 5-*exo-dig* cyclization at *α*-carbon atom of ynamide and bromination at *β*-carbon of ynamide through reductive elimination of copper as $Cu_2O$.

**Scheme 5**




R = 4-Me-$C_6H_4$, R' = H (**31**, 88% E:Z 96:4)
R = 4-Me-$C_6H_4$, R' = 3-F (**32**, 83% E:Z 78:22, **X-ray**)
R = Ph, R' = H (**33**, 80% E:Z 88:12)
R = 4-$^{t}$Bu-$C_6H_4$, R' = H (**34**, 82% E:Z 92:8)
(more examples)



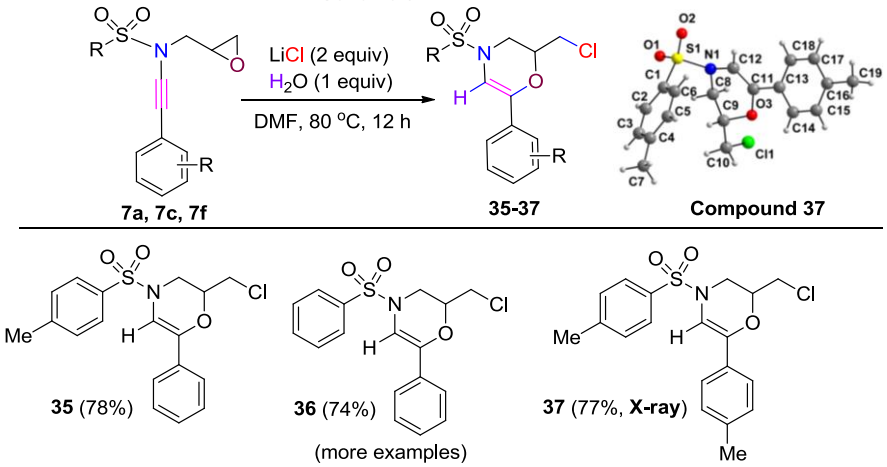

Compound 32

**(iii)(b) Regioselective synthesis of 1,4-oxazines by the tandem 6-*endo-dig* cyclization of epoxy ynamides using LiCl**

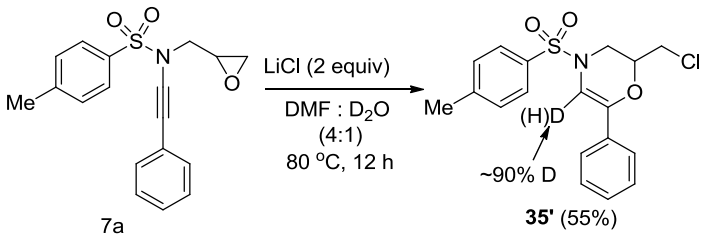
We treated epoxy-ynamides **7a, 7c, 7f** with LiCl (2 equiv) in DMF/$H_2O$ (4:1) for 12 h at 80 $^{o}$C to obtain ring expanded cyclized products 1,4-oxazines **35-37** in good yields (Scheme 6). Involvement of water in this reaction is demonstrated by the incorporation of $^{2}$D at the olefinic site by using $D_2O$ in place of water. Thus the reaction using epoxy ynamide (**7a**; 1.0 equiv) and LiCl (2.0 equiv) in DMF:$D_2O$ (4:1) furnished compound **35'** (Scheme 7). Formation of the deuterium incorporated compound **35'** clearly suggested the

key role of water as a proton source in the cyclization process. This control experiment and the available literature suggest that these 1,4-oxazines are obtained *via* epoxide ring opening from less hindered side by the chloride ion followed by intramolecular 6-*endo-dig* cyclization at the *β*-carbon atom of ynamide and protonation.

**Scheme 6**



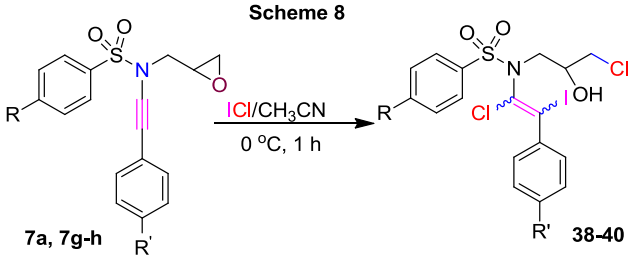

**Scheme 7**




**(iv)(a) ICl addition reactions of epoxy ynamides**

We treated epoxy ynamides **7a**, **7g-7h** with 1M solution of ICl in $CH_3CN$ (0.5 mL) at 0 °C for 10 min to obtain highly regioselective *E/Z*-isomeric mixture (1:1) of *α*-chloro-*β*-iodoenamides **38-40** in good yields. In this transformation, along with addition reaction, intermolecular $S_N2$ nucleophilic ring opening of epoxide part of the ynamide by chloride ion occurs simultaneously (Scheme 8). Here, electrophilic addition reactions are highly favored in contrast to the 5-*exo-dig* and/or 6-*endo-dig* halo-cyclization reactions of epoxy-ynamides with CuBr/LiCl.

Scheme 8

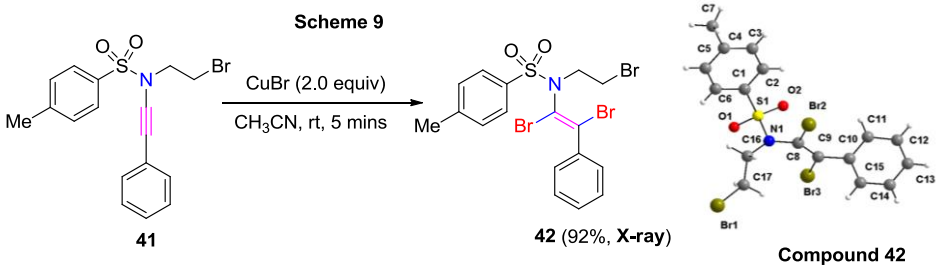



R = 4-Me, R' = H (**38,** 89%, E/Z 53:47, **Xray)**
R = 4-Cl, R' = H (**39,** 85%, E/Z 53:47)
R = 4-Me, R' = 4-$NO_2$ (**40,** 82%, E/Z 51:49, **Xray)**

**(iv)(b) Bromine addition reaction of ynamides using CuBr**

When we treated *N*-(2-bromoethyl)-4-methyl-*N*-(phenylethynyl) benzenesulfonamide **41** with CuBr at 0 °C, rather surprisingly, we obtained (*E*)-*α*,*β*-dibromo-enamide **42** in good yields within 5 min (Scheme 9). This reaction is fairly consistent with the results given above (section iii) for the bromination of epoxy ynamides with CuBr.

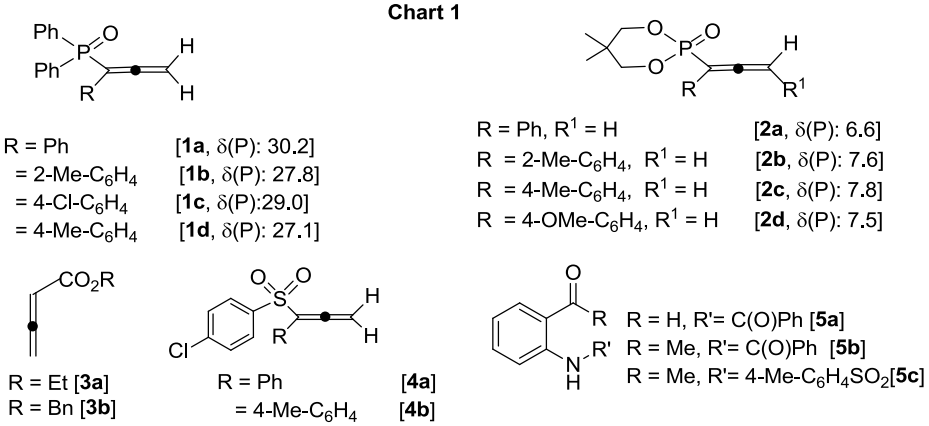
Scheme 9




## PART-B

In this part, allene-based reactions are explored. Chapter 4 deals with a review of literature on halo-addition, cycloaddition and cyclization reactions of allenes. Chapter 5 pertains to the results obtained on these aspects. Chapter 6 is the experimental section for this part. The main precursors are shown in Chart 1. Important results of this part are outlined below:

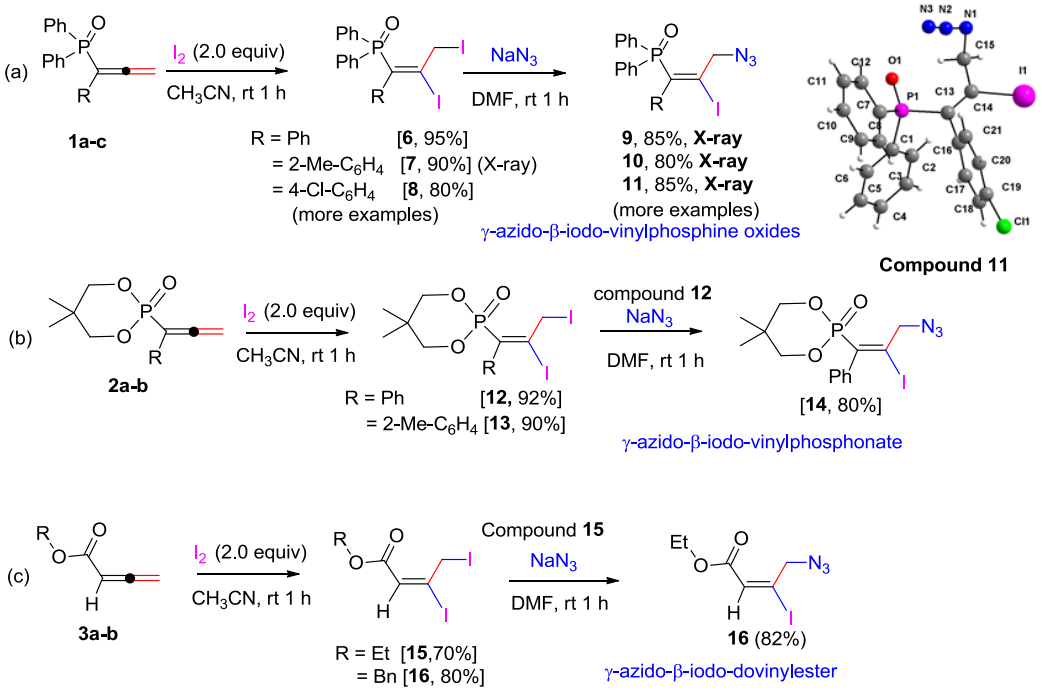
**Chart 1**




## (i)(a) Synthesis of (*γ*-azido-*β*-iodo)vinylphosphine oxides, (*γ*-azido-*β*-iodo)vinylphosphonate and (*γ*-azido-*β*-iodo)vinyl ester

Initially, 2,3-diiodovinyl derivatives were synthesized as single products by treating allenylphosphine oxides /allenylphosphonates /allenoates with $I_2$ in dry acetonitrile (Scheme 1; compounds **6-8**, **12-13**, **16**). All these molecules are highly functionalized (contain vinylic iodine, allylic iodine, ester) and hence we were interested in utilizing such products further. The reaction of 2,3-diiodovinylphosphine oxides **6-8** with $NaN_3$ in dry DMF afforded *γ*-azido-*β*-iodo-vinylphosphine oxides **9-11**. We have continued this azidation reaction with 2,3-diiodovinylphosphonate **12** also and obtained *γ*-azido-*β*-iodo-vinylphosphonate **14**. Similarly *γ*-azido-*β*-iodo-vinyl ester **17** was synthesized by using 2,3-diiodovinylester **12**.

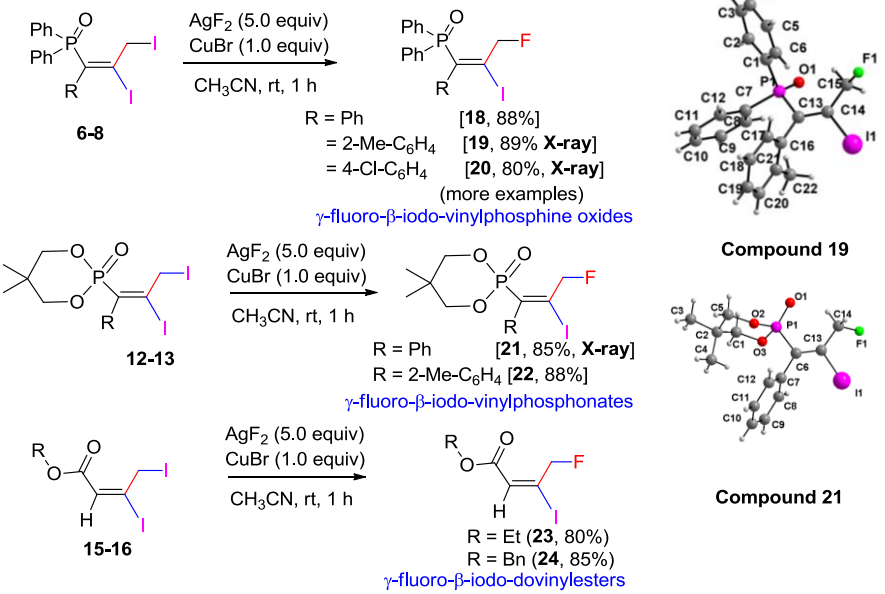
**Scheme 1**



**(i)(b) Fluorination reactions of 2,3-diiodovinyl derivatives**

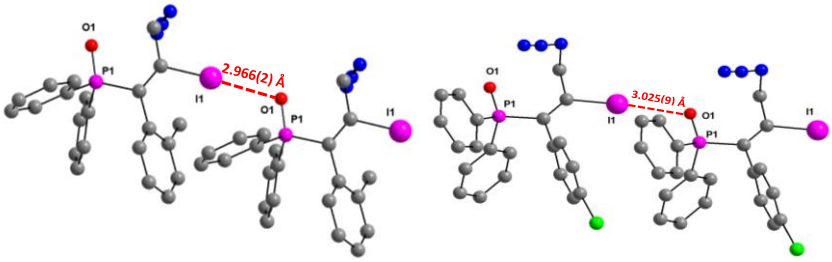
We performed fluorination of compounds **6-8**, **12-13** and **15-16** with $AgF_2$/CuBr in dry $CH_3CN$ at 25 $^oC$ and obtained *γ*-fluoro-*β*-iodo- diiodovinyl derivatives **18-24** in good yields (Scheme 2). All these are highly functionalized molecules. They have vinylic iodine, allylic fluorine, C=C double bond, and ester group (in case of compound **23-24**) which can be utilized for further transformations.

**Scheme 2**

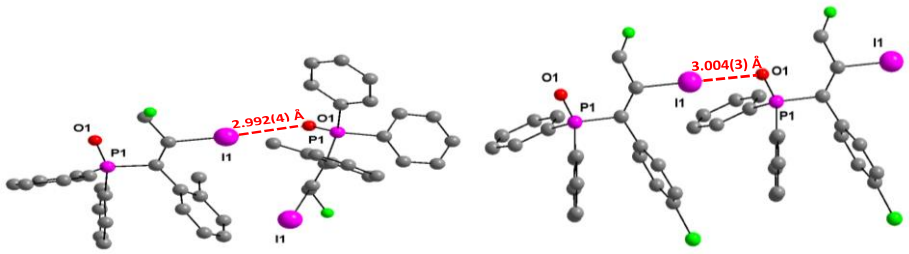



**(i)(c) Halogen bond (I•••O) interactions in *γ*-azido-*β*-iodo-vinylphosphine oxides and *γ*-fluoro-*β*-iodo-vinylphosphine oxides**

In γ-azido-β-iodo-vinylphosphine oxides **10-11** and *γ*-fluoro-*β*-iodo-vinylphosphine oxides **19-20**, iodine attached to *β*-carbon has a high tendency to interact with electron donor like phosphoryl oxygen. Thus, compounds **10-11** and **19-20** (Figure 1) show I•••O halogen bonding interactions. The I•••O distances in compounds **10** and **11** are 2.966(2) Å and 3.025(9) Å respectively; in **19** and **20** the corresponding distances are 2.992(4) Å and 3.004(3) Å, respectively. All these distances are considerably shorter than the sum of the corresponding van der Waals radii of O and I [i.e. <3.50 Å].




(a) (b)



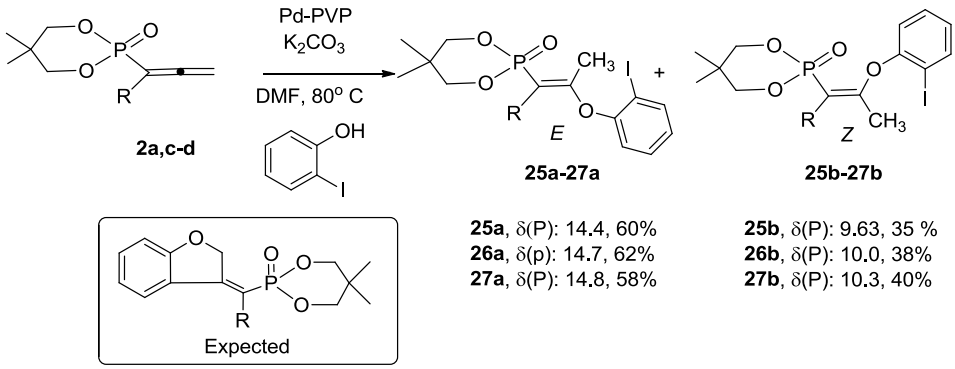

(c) (d)

**Figure 1.** Diagram showing I•••O halogen bonding in (a) **11,** (b) **12**, (c) **19** and (d) **20**.

**(ii)(a) Pd-nanoparticle [Pd-PVP]-catalyzed reaction of allenylphosphine oxides with 2-iodophenol**

In a couple of earlier papers, we have disclosed that the [Pd]-catalyzed reactions of 2-iodophenols with allenylphosphonates readily afford phosphonobenzofurans. In this context, we were wondering whether palladium nanoparticles will be effective in such reactions or not. However, in these cases, we obtained mainly phenol addition products **25-27** (Scheme 3). An interesting point though, is that in the absence of Pd-PVP nanoparticles, the total yield of the addition products is much less (<30%). Only vinylphosphonates are formed with no indication of the allylphosphonates.

**Scheme 3**




**25a**, δ(P): 14.4, 60%
**26a**, δ(p): 14.7, 62%
**27a**, δ(P): 14.8, 58%

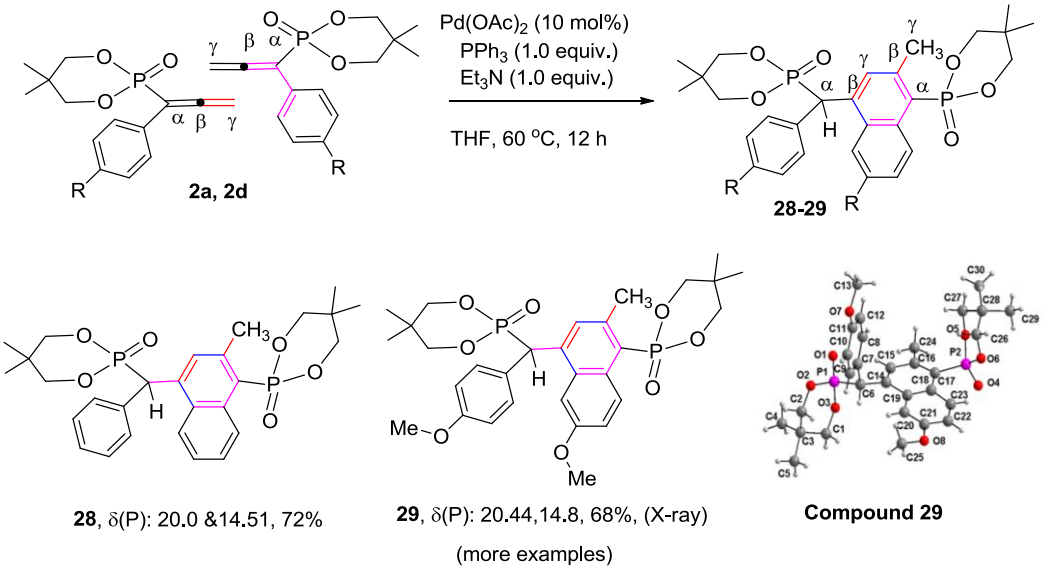
**25b**, δ(P): 9.63, 35 %
**26b**, δ(P): 10.0, 38%
**27b**, δ(P): 10.3, 40%

**(ii)(b) [Pd]-catalyzed dimerization reaction of allenylphosphonates involving [4+2] cycloaddition**

When we treated the allenylphosphonate **2a** with $Pd(OAc)_2/PPh_3/Et_3N$, interestingly, compound **28** (Scheme 4) was obtained. The $^{31}P$ NMR spectrum of **28** showed two peaks of equal intensity at δ 20.0 and 14.5 indicating that two molecules of allenylphosphonate are involved in the reaction. The product was an unsymmetrical dimer in which (*β*,*γ*)-double bond of one allene and (*α*,*β*)-double bond of the second allene are involved in cycloaddition. Here, one of the aryl double bonds is also involved in the [4+2]

cyclization forming a new six-membered ring as shown in Scheme 4. A similar product **29** (X-ray) could also be obtained in good yield.

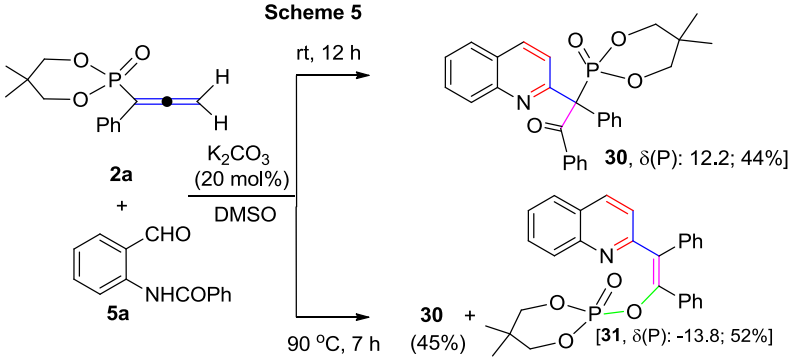
**Scheme 4**




**(iii) Reaction of allenylphosphonates/allenylphosphine oxides/allenylsulfones with protected benzamides: Formation of quinolines**

We treated the allenylphosphonate **2a** with *N*-(2-formyl-phenyl) benzamide **5a** in the presence of $K_2CO_3$ and obtained the benzoyl group rearranged product **30** [δ (P) 12.2]. Rather interestingly, when the same reaction was conducted at 90 °C, the phosphoryl migrated product **31** was obtained along with phosphono-quinoline **30** with the combined yield of the isolated products being 86% (Scheme 5). When we conducted the reaction at 110 °C for 12 h, we obtained compound **31** exclusively. Thus compound **30** underwent rearrangement under thermal conditions leading to phosphoryl group migrated product **31**. We proved this conversion by individually heating compound **30** and monitoring the sample by $^{31}P$ NMR as shown in Figure 2.

**Scheme 5**



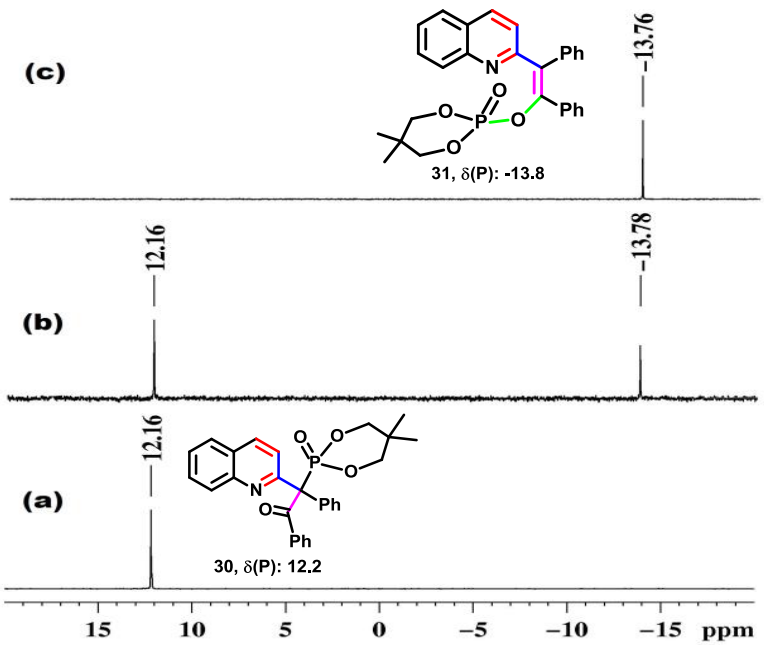
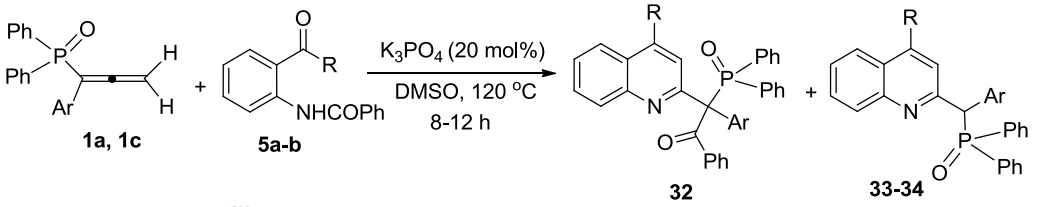


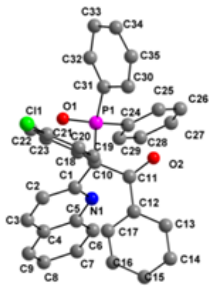

**Figure 2.** Conversion of compound **30** (δ 12.2) to compound **31** (δ-13.8): (a) at rt, (b) at 190 $^{o}$C (after 12 min) and (c) at 200 $^{o}$C (after 12 min).

In contrast to the above, from the reaction of allenylphosphine oxides **1a** or **1c** with benzamides **5a-5b**, we isolated the phosphonoquinolines **32** - **34** (Scheme 6). Here the phosphorus part remained intact.

**Scheme 6**




Ar = 4-Cl-$C_6H_4$, R = H (**32**, δ(P): 37.8, 40%, **X-ray**)
Ar = 4-Cl-$C_6H_4$, R = H (**33**, δ(P): 30.8, 45%)
Ar = Ph, R = Me (**34**, δ(P): 31.0, 80%)

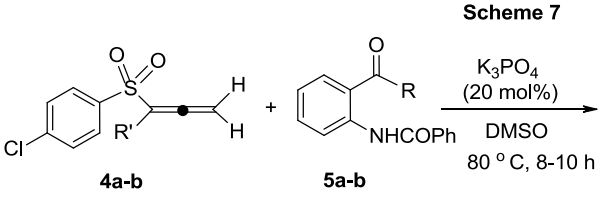


Compound 32

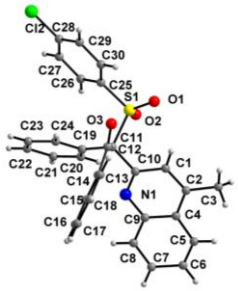
The above reaction was successfully extended to sulfur based allenes **4a-b** by treating them with *N*-(2-formyl phenyl) benzamide **5a** or *N*-(2-acetyl-phenyl) benzamide **5b** at 80 $^{o}$C, affording the sulfur containing quinolines **35-38** (Scheme 7) in moderate to

good yields. Unlike their phosphorus counterparts, we did not observe any rearrangement of the sulfonyl group in these cases.

**Scheme 7**



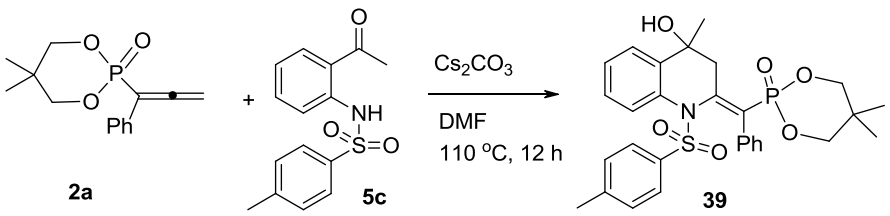

R = H, R' = Ph [**35**, 65%]
R = H, R' = 4-Me-$C_6H_4$ [**36**, 58%]
R = Me, R' = Ph [**37**, 68%, X-ray]
R = Me, R' = 4-Me-$C_6H_4$ [**38**, 62%]

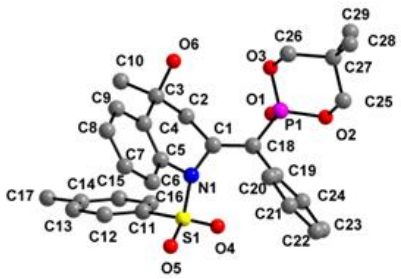


Compound 37

In an effort to see if we can identify any intermediate species in the above reactions, we treated the allenylphosphonate **2a** with *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide **5c** in the presence of $Cs_2CO_3$ in DMF at 110 °C for 12 h (Scheme 8). Interestingly, we obtained the cyclic intermediate **39**. This result shows that in the above reactions an intermediate similar to **39** may be involved.

**Scheme 8**



Compound 39

# INTRODUCTION

## 1.1 General Introduction: Sulfonamides

Sulfonamides are important structural motifs present in numerous pharmaceutically important products. They are widely used as anti-bacterial, anticancer, anti-inflammatory and antiviral agents.[1] Bacteria synthesize folic acid (required for cell growth and metabolism) from dihydropteroate-diphosphate and *p*-aminobenzoic acid (PABA) by using enzyme dihydropteroate synthase. Most of the sulfonamides or sulfa drugs are chemical analogues of PABA, thus antibacterial activity of sulfonamides is mainly due to competitive inhibition of enzyme dihydropteroate synthase. In other words, the structurally similar sulfonamide mimics the PABA, and binds to the active binding site of enzyme inhibiting the enzyme action thereby stopping the folate synthesis. This will inhibit cell growth and proliferation of bacteria due to folate deficiency (Figure 1). Representative sulfonamide drugs are shown in Figure 2.

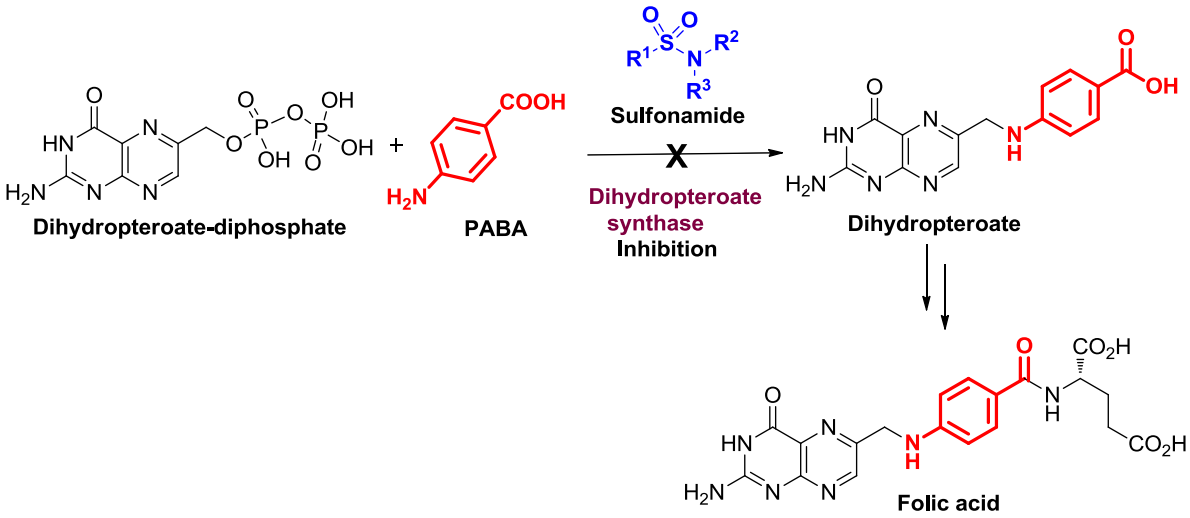



**Figure 1:** Inhibition of dihydropteroate synthase enzyme action by sulfonamide

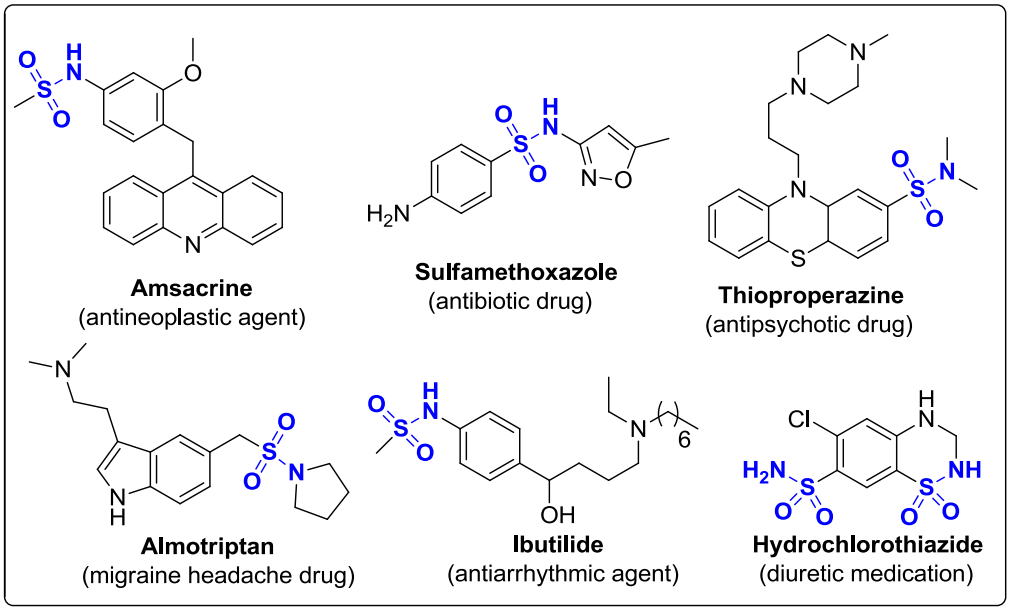



**Figure 2:** Representative sulfonamide drugs

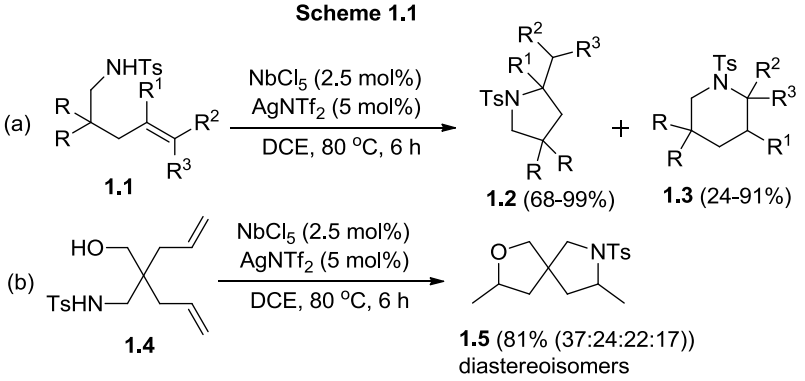
Sulfonamides are also virtuous precursors for constructing *N*-containing heterocyclic compounds and with suitable pendent functionalities, can undergo intramolecular[2] or intermolecular cyclization[3] as well as addition reactions.[4] Sulfonamide bearing an epoxide or any leaving group also facilitates a number of organic transformations to form heterocycles.[5] In this Chapter, literature on the following topics involving sulfonamides as relevant to the present study will be covered: (i) intra/ intermolecular cyclization, (ii) ring expansion reactions of sulfonamides containing epoxide moiety, (iii) synthesis of thiazolidine-thiones, iminothiazolidines and oxazolidines from aziridines/epoxides, and (iv) cyclization and addition reactions of ynamides that contain sulfonamide moiety.

## 1.2 Intramolecular cyclization reactions of sulfonamides

Very recently, Amatore's group developed a novel, atom economic and eco-friendly protocol to synthesize pyrrolidines **1.2** and piperidines **1.3** through $NbCl_5/AgNTf_2$ catalyzed intramolecular hydroamination (C−N bond formation) of alkenes of type **1.1** (Scheme 1.1a).[6] As an extension, using the precursor **1.4** that contains reactive OH and NH functionalities, spirocyclic heterocycles **1.5** could be obtained (Scheme 1.1b). Here, $HNTf_2$ itself was able to catalyze the reaction and gave moderate yields compared to those obtained under niobium catalysis. Therefore, these results do not exclude the possibility of a mechanism involving the

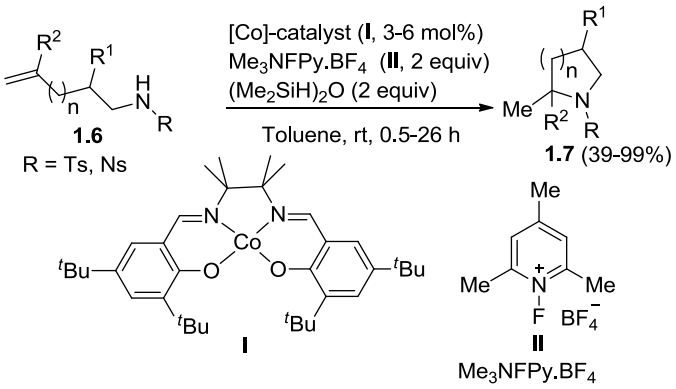
release of $HNTf_2$ in the medium. Control experiments using $PhSiMe_3$ as an efficient noncoordinative proton scavenger did not have any effect, neither in terms of yield nor in terms of regio-selectivity. They suggested a mechanism involving a direct interaction between the metallic complex species and the substrate, but did not explain how the metal complex is involved in the catalysis.

**Scheme 1.1**



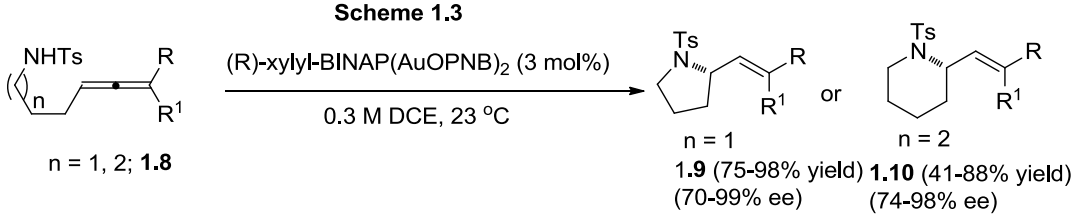

Shigehisa *et al*. reported the synthesis of three-, five-, six-, and seven-membered ring nitrogen- heterocycles **1.7** from unactivated *N*-protected amino-olefins **1.6** by using Co(salen) complex **I**, *N*-fluoropyridinium salt **II**, and a disiloxane as the catalytic system for intramolecular hydroamination (Scheme 1.2).[7] This protocol was compatible with various protecting or functional groups. In this reaction, first [Co]-catalyst strongly and selectively activates an olefin moiety in order to react with weakly nucleophilic nitrogen atom. While the use of Ts group afforded principally 5-membered rings, in the case of Ns protecting group, due to its strong electron-withdrawing nature, 3-, 5-, 6- and 7- membered nitrogen-containing heterocycles could be obtained in good-to-excellent yields.

**Scheme 1.2**



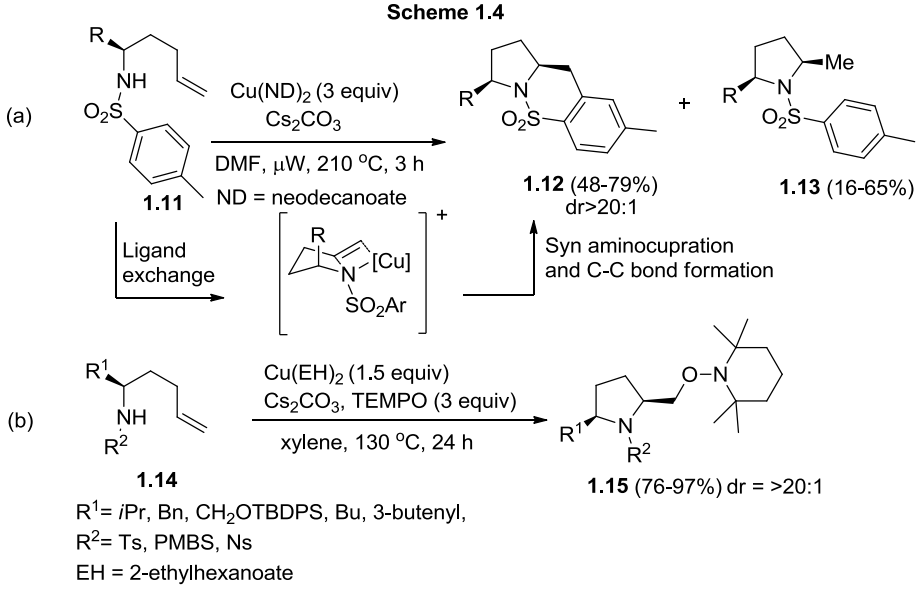
In the year 2007, Toste's group described a significant counter-ion effect on the enantioselectivity of gold-catalyzed intramolecular hydroamination of allenes **1.8** that contain an internal amino group (Scheme 1.3).[8] This discovery led to the development of (phosphine)gold(I)-bis-*p*-nitrobenzoate complexes as catalysts for enantioselective formation of vinyl-substituted pyrrolidines **1.9** and piperidines **1.10** in good yields with excellent enantiomeric excess.

**Scheme 1.3**



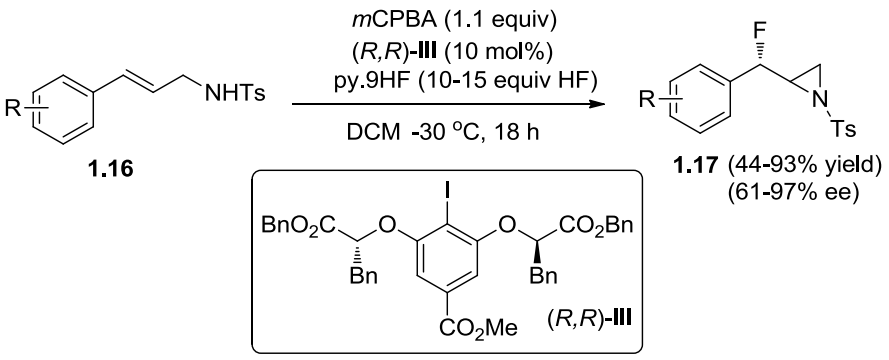

Chemler's group reported copper(II) carboxylate promoted intramolecular oxidative cyclization reaction of alkenyl *N*-arylsulfonamides **1.11** affording *N*-functionalized pyrrolidines **1.12** and **1.13** (Scheme 1.4a).[9a] Both aliphatic and aromatic γ- and δ-alkenyl sulfonamides underwent carboamination and oxidative cyclization. The efficacy of the reaction was enhanced by the use of more organo--soluble copper(II) carboxylates. High levels of diastereoselectivity were observed in the synthesis of 2,5-disubstituted pyrrolidines, wherein the *cis*-substitution pattern predominated. In this reaction, N-C bond is formed *via* intramolecular *syn* aminocupration and the C-C bond is formed *via* intramolecular addition of a primary carbon radical to an aromatic ring. In the year 2009, the same group reported high yielding route for the synthesis of di-substituted pyrrolidines **1.15** by using copper(II) 2-ethylhexanoate as the catalyst for the intramolecular aminooxygenation of alkenes **1.14** (Scheme 1.4b).[9b] TEMPO was used for trapping the radical intermediates. The efficiency of this approach was demonstrated with the formal synthesis of (+)-monomorine.

**Scheme 1.4**




Very recently, Jacobsen's group described chiral aryl-iodide **III** catalyzed fluorination of allylic amines **1.16** that gave highly stereoselective *syn-β*-fluoroaziridines **1.17** in good yields with excellent *ee* (Scheme 1.5).[10] In this protocol, HF-pyridine was used as the nucleophilic fluoride source and *m*CPBA was used as a stoichiometric oxidant. This catalyst-controlled enantioselective method was applied successfully to other classes of multifunctional alkene substrates to generate highly enantioenriched *anti-β*-fluoropyrrolidines as well as a variety of 1,2-oxyfluorinated products with multi-stereocenters.

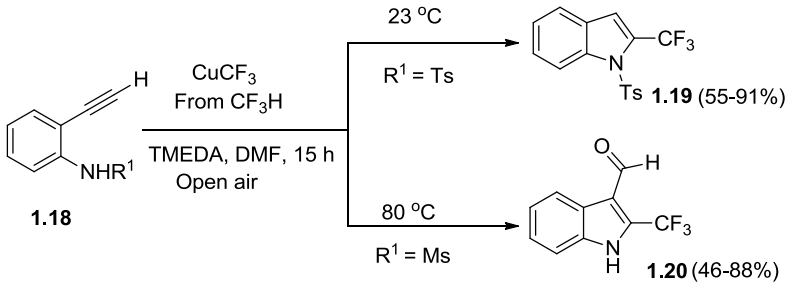
**Scheme 1.5**




Very recently Tsui's group reported the synthesis of trifluoromethylated indoles **1.19** by treating 2-alkynylsulfonamides **1.18** with $CuCF_3$ and tetramethylethylenediamine (TMEDA). The reaction involves trifluoromethylation of terminal alkyne, followed by 5-*endo-dig*

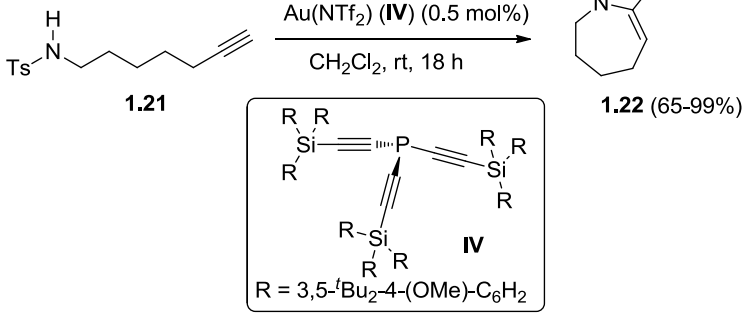
cyclization initiated by the *ortho*-nitrogen nucleophilic attack to the triple bond, to construct the indole core. In the case of mesyl (Ms) as the protecting group, desulfonylation took place and 3-formylated product **1.20** was formed (Scheme 1.6).[11] In this reaction, TMEDA plays a very crucial role as a reagent and a reactant, i.e. it acts as carbon donor for the formylation reaction.

**Scheme 1.6**



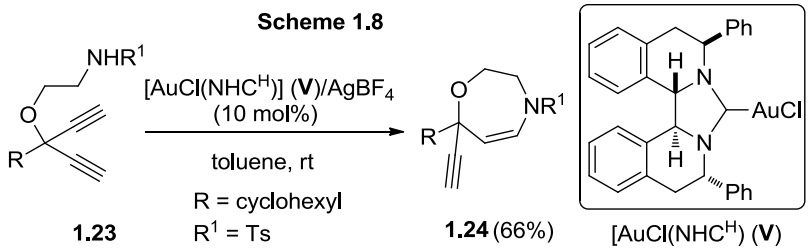

Sawamura's group described gold(I) catalyzed 7-*exo-dig* intramolecular hydroamination of ω-alkynic *N*-alkyl-*N*-sulfonamides **1.21** that led to 4,5,6,7-tetrahydroazepines **1.22** in good yields (Scheme 1.7).[12] Gold(I) complex in coordination with the bulk semi-hollow-shaped triethynylphosphine ligand **IV** is the active catalyst for activating alkyne moiety as well as enhancing the reaction rate, which enforces a nucleophilic center close to a gold-activated alkyne moiety. Alkynic sulfonamides with an acyclic or ring-fused linker chain can undergo this cyclization leading to complex heterocycles.

**Scheme 1.7**



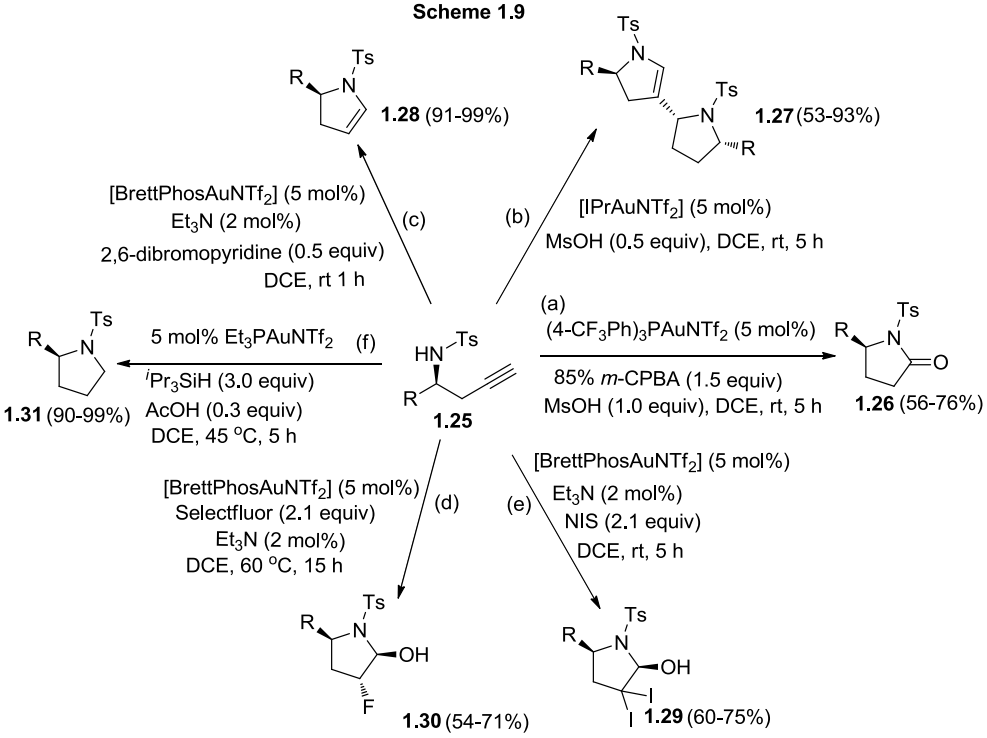

Czekelius's group developed a convenient method for synthesis of tetrahydro-oxazepines **1.24** in moderate yield through [AuCl($PCy_3$)]/$AgBF_4$ catalyzed intramolecular *endo*-cyclization of diyne sulfonamides **1.23** (Scheme 1.8).[13] They obtained a better yield by incorporating a carbene ligand into the complex [AuCl($NHC^H$) (**V**)] that was reported by Herrmann's group.

**Scheme 1.8**



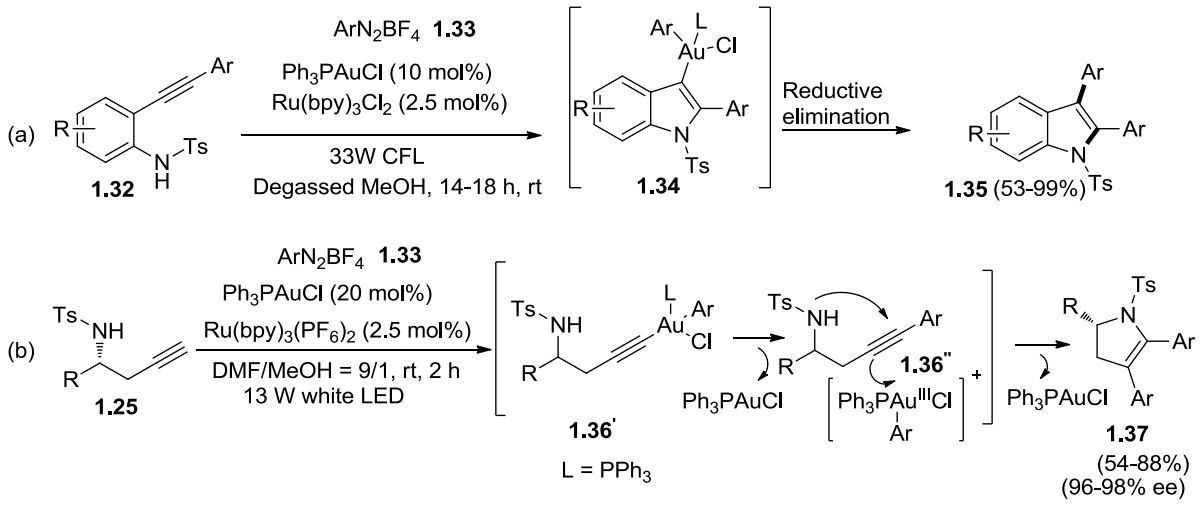

In the year 2013, Long-Wu Ye *et al*. reported that highly enantioselective γ-lactams **1.26** can be synthesized from a gold–catalyzed ($(4\text{-}CF_3Ph)_3PAuNTf_2$) sequential cycloisomerization followed by oxidation (*m*-CPBA) of homopropargyl amides **1.25** (Scheme 1.9a).[14a] Using this methodology, they have synthesized the biologically active compound S-MPP 4 and optically active natural product (−)-bgugaine. In the same year, this group also reported $IPrAuNTf_2$ catalyzed 5-*endo-dig* cyclization followed by gold and acid catalyzed dimerization of homopropargyl sulfonamides **1.25** leading to enantio-enriched pyrrolidines **1.27** under mild reaction conditions (Scheme 1.9b).[14b] By changing the acidic medium (MsOH) to basic medium ($Et_3N$ or 2,6-dibromopyridine) using $BrettPhosAuNTf_2$ as the catalyst, Ye's group effectively synthesized 2,3-dihydropyrroles **1.28** from homopropargyl sulfonamides **1.25** (Scheme 1.9c).[14c] Here, 2,6-dibromopyridine completely inhibits the formation of dimer. Later, they developed two novel gold-catalyzed cycloisomerization-halogenation reactions of chiral homopropargyl sulfonamides **1.25** by using NIS or selectfluor as the halogen source to obtain enantio-enriched 3,3-diiodopyrrolidin-2-ols **1.29** and 3-fluoropyrrolidin-2-ols **1.30** respectively. Prominently, excellent diastereocontrol was achieved in both transformations (Scheme 1.9d-e).[14d] Ye's group also achieved the cycloisomerization followed by hydrogenation by using $Et_3PAuNTf_2$ and triisopropylsilane (as hydride source) to obtain pyrrolidines **1.31** (Scheme 1.9f).[14e] All these transformations followed anti-Markovnikov addition.

**Scheme 1.9**




In the year 2016, Zhu's group reported photoredox and gold catalyzed cyclization and arylation of *o*-alkynylarylsulfonamides **1.32** with aryldiazonium salts **1.33** (Scheme 1.10a).[15a] In this reaction, arylgold(III) species, which is formed *in situ* by photoredox reaction [(Au(I) to Au(II)] followed by SET oxidation [Au(II) to Au(III)], activates the alkyne of *o*-alkynylarylsulfonamide **1.32** for nucleophilic cyclization affording 3-aurated indole intermediate **1.34** which undergoes reductive elimination to give the cross-coupled product **1.35**. Similarly, Ye's group reported dual gold- and photoredox-catalyzed bis-arylative cyclization of homopropargyl sulfonamides **1.25** with aryldiazonium salts **1.33** leading to enantio-enriched 2,3-dihydropyrroles **1.37** (Scheme 1.10b).[15b] This reaction was promoted by formed organogold(III) species which coordinates later with the alkyne substrate. Compound **1.25** gives species **1.36'** which undergoes reductive elimination affording cross-coupled product **1.36"**. Later, one more cationic intermediate also coordinates with **1.36"**, activating it towards the intramolecular cyclization followed by reductive elimination affording the 2,3-dihydropyrroles **1.37**.

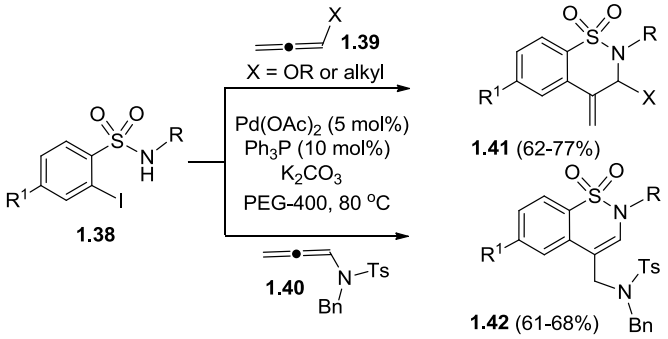
**Scheme1.10**




## 1.3 Intermolecular cyclization reactions of sulfonamides

Our research group reported the palladium catalyzed regiospecific cyclization of 2-iodobenzene sulfonamides **1.38** with allenes **1.39** and **1.40** in PEG-400 medium that gave benzosultams **1.41**-**1.42** (Scheme 1.11).[16] The *O*-substituted or alkyl allenes **1.39** favorably led to the formation of (*β,α*)-cyclized sultams **1.41**, whereas the *N*-substituted allenes **1.40** gave the (*β,γ*)-cyclized sultams **1.42**. In the case of aryl substituted allenes, (*β,γ*)-cyclized sultams were formed as major isomers.

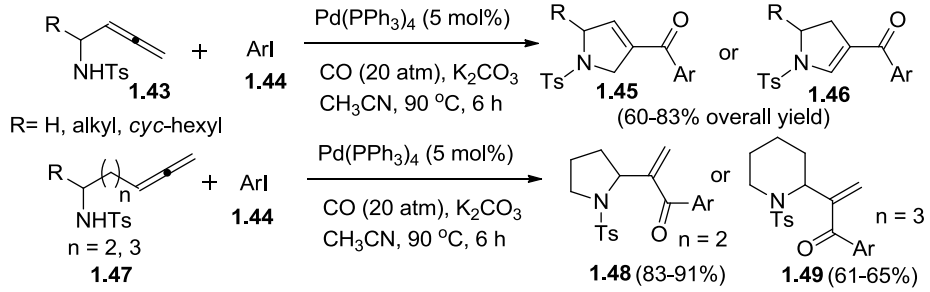
**Scheme 1.11**




Kang *et al*. developed a protocol of Pd(0) catalyzed carbonylation and coupling followed by *endo/exo* mode of cyclization of *α*, *γ* and *δ* allenic-sulfonamides **1.43** and **1.47** with aryl iodide **1.44** and carbon monoxide that afforded the products **1.45**-**1.46** and **1.48**-**1.49**. In this reaction, it is apparent that the formed π-allylpalladium complex by the addition of ArCOPdI to central

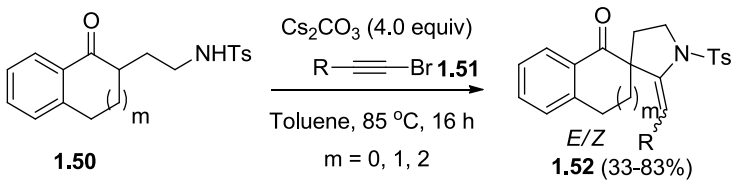
carbon of allene moiety undergoes intramolecular nucleophilic cyclization by the *endo* mode to give the 3-pyrroline enone **1.45** which isomerizes to the thermodynamically stable isomer 3-aroyl-2-pyrroline **1.46** (Scheme 1.12).[17] In the case of $\gamma$ or $\delta$ allenic-sulfonamides, this reaction may occur by addition of an aroylpalladium intermediate to allenic *p*-toluenesulfonamide to produce a $\lambda^3$-allylpalladium species which undergoes nucleophilic attack *via* the *exo*-mode affording pyrrolidine- or piperidine-substituted enones.

**Scheme 1.12**



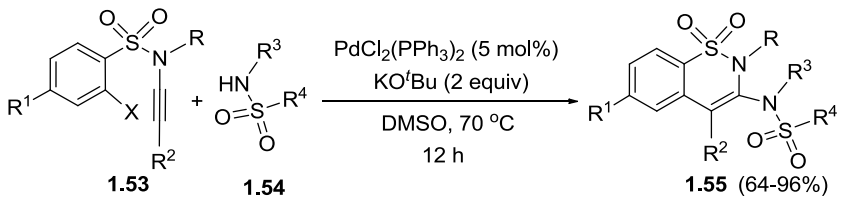

Very recently, Miesch's group reported spirocyclization of keto-sulfonamides **1.50** *via* ynamides through a base catalyzed one-pot reaction leading to spirocyclic scaffolds **1.52**. (Scheme 1.13).[18] At first, they conducted the reaction with $CuSO_4 \cdot 5H_2O$/1,10-phenanthroline/$Cs_2CO_3$; surprisingly they isolated a spirocyclic compound instead of the ynamide. To study whether or not the copper plays a key role in the mechanistic pathway, they performed DFT calculations and found that energy barrier required to achieve this transformation for copper complexed intermediate is high compared to copper-free pathway. Based on this, a plausible mechanism involving 5-*endo*-*dig* addition of keto-ynamide enolate *in situ*, i.e. Michael addition/elimination process, followed by cyclization in basic medium providing the spiro derivative after protonation is proposed. Alkynes containing electron-withdrawing groups favor only the (*E*/*Z*)-spirocyclic compounds in good yields.

**Scheme 1.13**



Very recently, our group has reported intermolecular nucleophilic addition followed by cyclization reaction of various sulfonamides **1.54** with functionalized ynamides **1.53** providing a wide range of hetero-substituted benzosultams (1,2-benzothiazine 1,1-dioxides) **1.55** by using palladium catalysis (Scheme 1.14).[19] Along with sulfonamides, amines, substrates with an active methylene group and phenols as nucleophiles also worked well for this methodology. Generality of this methodology was shown by using medicinally useful compounds like nortriptyline and eugenol as nucleophiles. Depending on the nucleophile source used, base had a significant effect in the cyclization process. DFT studies suggested that the reaction pathway involves a [$Pd^{II}$]-[$Pd^{0}$]-[$Pd^{II}$] cycle.

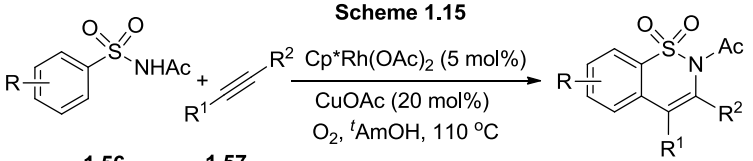
**Scheme 1.14**




**1.53** **1.54** **1.55** (64-96%)

Cramer's group reported an efficient access to benzosultams **1.58** by rhodium(III) catalyzed oxidative C-H functionalization of sulfonamides **1.56** with internal alkynes **1.57** using CuOAc and molecular oxygen which involves the use of *N*-acyl sulfonamide as the directing group (Scheme 1.15).[20] The generality of this method is emphasized by the C-H functionalization of the acylated COX-2 inhibitor, Celecoxib. An important advantage of this method is that the acetyl directing group on the *N*-atom can be easily removed from the sultam under either basic or acidic conditions.

**Scheme 1.15**

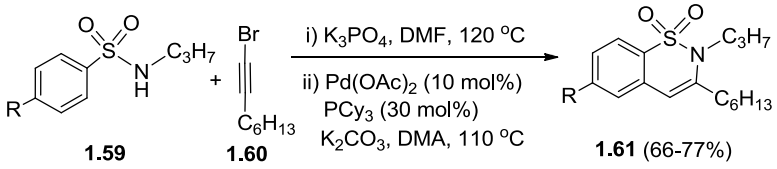



**1.56** **1.57** **1.58** (47-99%)

Urabe *et al*. developed a base mediated nucleophilic addition reaction of sulfonamides **1.59** with 1-bromoalkynes **1.60** that afforded 1,2-benzothiazine 1,1-dioxides **1.61** *via* (*Z*)-2-(*N*-alkyl-*N*-sulfonylamino)-1-bromoalkenes by [Pd]-catalyzed cyclization through the activation of aromatic C-H bond (Scheme 1.16).[21] The same group also described the synthesis of *N*,*N*- or *N* or *O*-heterocycles **1.64** from diamine or ethanolamine precursors **1.62** and bromoacetylenes **1.60'**

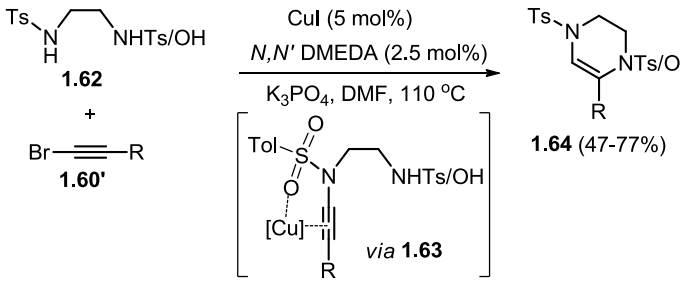
under [Cu]-catalysis (Scheme 1.17).[22] This reaction proceeds *via in situ* generated ynamide intermediate **1.63** which undergoes hydro-amination or hydroalkoxylation in a 6-*endo-dig* fashion (but not in a 5-*exo-dig* fashion) due to the coordination of copper to both the alkyne and the sulfonyl groups, affording the tetrahydropyrazines or oxazines **1.64**.

**Scheme 1.16**




**1.59** **1.60** **1.61** (66-77%)

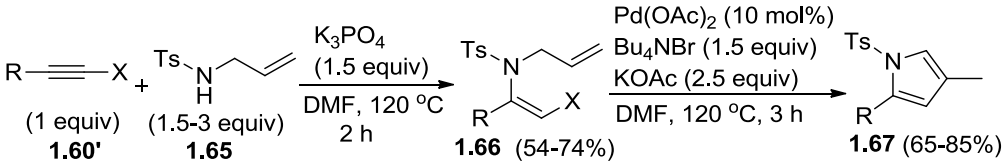
**Scheme 1.17**




**1.62** **1.60'** **1.64** (47-77%)

Urabe and co-workers have reported nucleophilic addition of allylsulfonamides **1.65** with bromoalkynes **1.60'** resulting in vinylbromo-allylsulfonamides **1.66** which undergoes Heck reaction in the presence of $Pd(OAc)_2$ to afford *N*-protected pyrroles **1.67** in good yields (Scheme 1.18).[23] Bromoacetylenes responded well to this reaction to afford the addition product.

**Scheme 1.18**



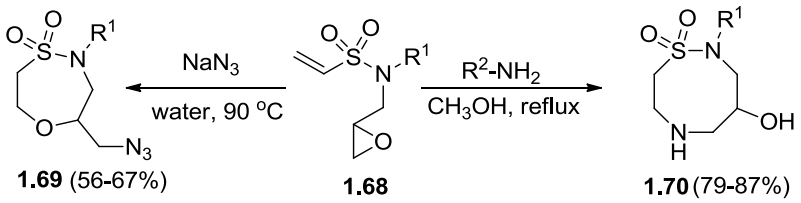

(1 equiv) **1.60'** (1.5-3 equiv) **1.65** **1.66** (54-74%) **1.67** (65-85%)

## 1.4 Ring expansion reactions of sulfonamides containing epoxide moiety

Zhou and Co-workers have synthesized seven/ eight membered ring sultams through a two tandem protocol using epoxy-vinylsulfonamides **1.68** (Scheme 1.19).[24] By treating epoxy vinylsulfonamide **1.68** with $NaN_3$ in water medium, nucleophilic oxygen anionic intermediate is generated from nucleophilic opening of epoxide by $NaN_3$, which initiates an intramolecular 7-

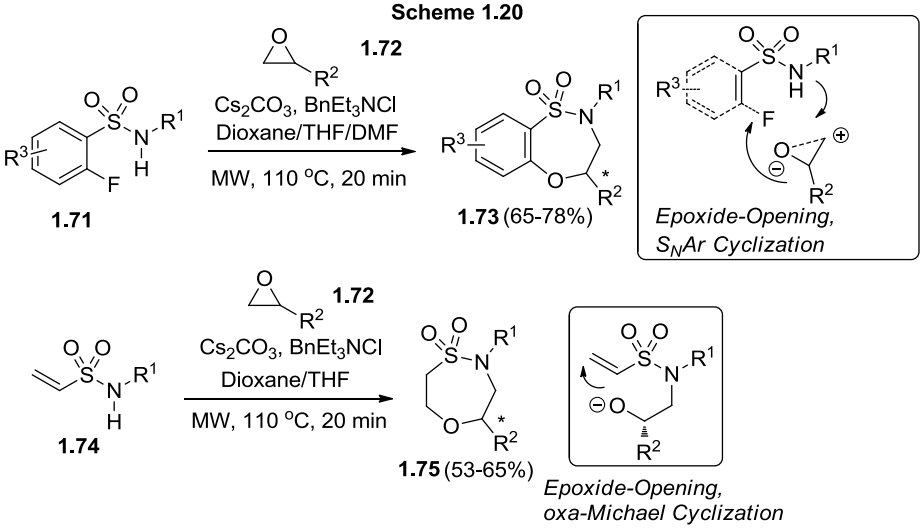
*endo-trig* oxa-Michael reaction to afford seven-membered ring sultams **1.69** in good yields. When primary amine was used as the nucleophile, it first underwent aza-Michael addition to give vinyl sulfonamide epoxides, followed by 8-*endo-tet* intramolecular epoxide ring opening to give eight-membered-ring sultams **1.70** in good yields under mild reaction conditions.

**Scheme 1.19**



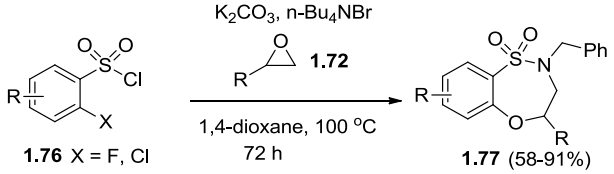

Hanson's group reported the synthesis of benzothiaoxazepine-1,1′-dioxides **1.73** and oxathiazepine-1,1′- dioxides **1.75** from base catalyzed one-pot epoxide ring opening followed by either intramolecular $S_NAr$ cyclization or intramolecular oxa-Michael cyclization of ambiphilic sulfonamides **1.71** and **1.74**, respectively (Scheme 1.20).[25] In this reaction, dioxane for the initial epoxide ring-opening step, DMF for the $S_NAr$ and THF for oxa-Michael ring closing step of the cascade are essential.

**Scheme 1.20**



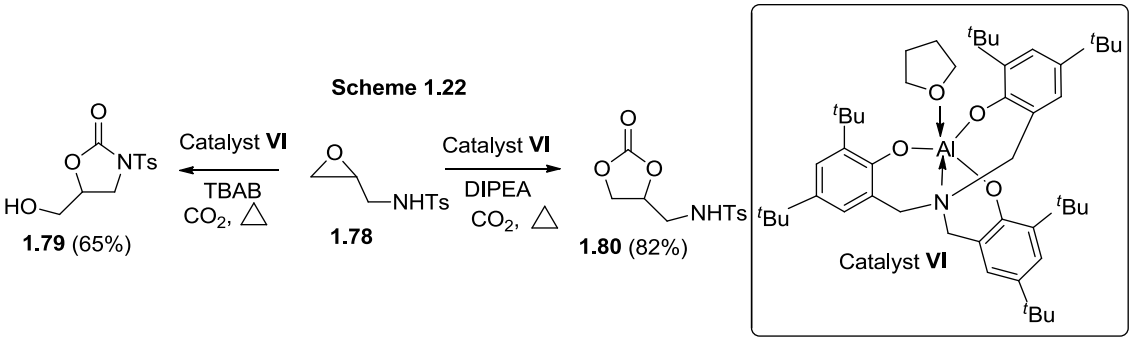

Cleator and co-workers demonstrated the one pot multi-component reaction of *o*-fluorobenzenesulfonamides **1.76** with epoxides **1.72**. Initial ring opening, and then the ensuing $S_NAr$ cyclization gives the corresponding benzoxathiazepines **1.77** (Scheme 1.21).[26]

**Scheme 1.21**



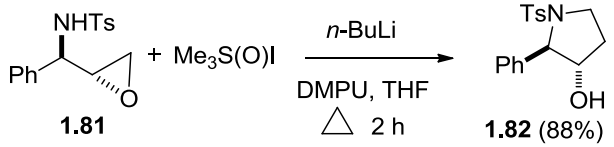

A recent elegant report by Kleij and co-workers delves on the divergent behavior of oxirane appended sulfonamides **1.78** with $CO_2$ under Al(III) (Lewis acid based on aluminium(III)-centered aminotriphenolate complex **VI**) catalyzed ring expansion that affords either oxazolidines **1.79** or cyclic carbonates **1.80** (Scheme 1.22)[27] depending on subtle modifications in the reaction conditions. Various other substrates also have been utilized in this report.

**Scheme 1.22**




Hodgson and co-workers reported highly regioselective and stereodefined synthesis of 3-hydroxypyrrolidines **1.82** *via* 5-*exo*-*tet* intramolecular cyclization of epoxy-sulfonamides **1.81** with *in situ* generated dimethylsulfoxonium methylide by treating $Me_3S(O)I$ with *n*-BuLi (Scheme 1.23).[28] This methodology can be applied to generate highly strained spiro(hydroxyl)pyrrolidines. Either *trans*- or *cis*- 2-substituted-3-hydroxypyrrolidines could be synthesized in good yield, starting from the corresponding *anti*- or *syn*-epoxysulfonamides.

**Scheme 1.23**

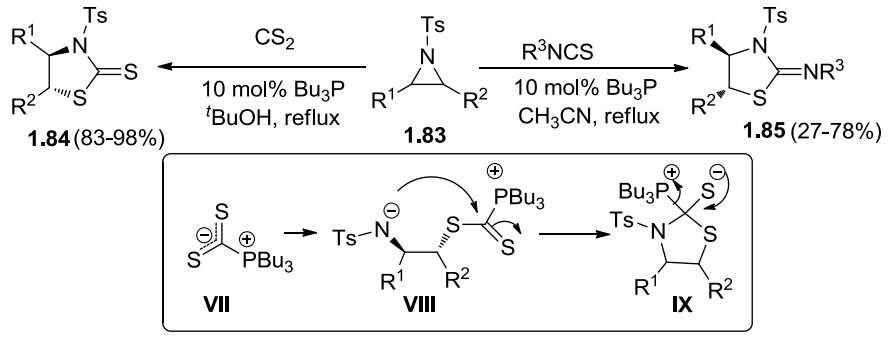



## 1.5 Synthesis of thiazolidine-thiones and imino-thiazolidines

In the year 2008, Hou *et al* reported organophosphine catalyzed ring expansion reaction of aziridines **1.83** with carbon disulfide and aryl isothiocyanates that afforded thiazolidine-thiones

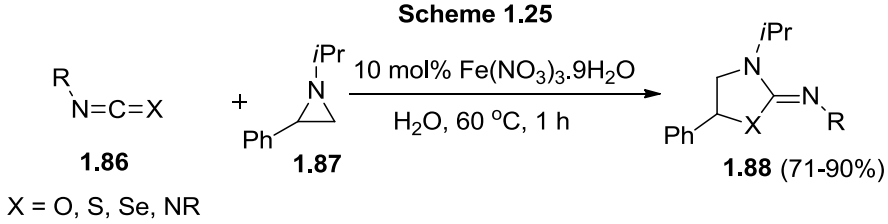
**1.84** and imino thiazolidines **1.85** in good yields (Scheme 1.24).[29] Based on $^{31}P$ NMR data, they proposed that organophosphine attacks $CS_2$ forming the zwitterionic intermediate **VII** that opens up aziridine ring forming intermediate **VIII**. Ring closure to **IX** followed by release of phosphine catalyst affords the desired product.

**Scheme 1.24**



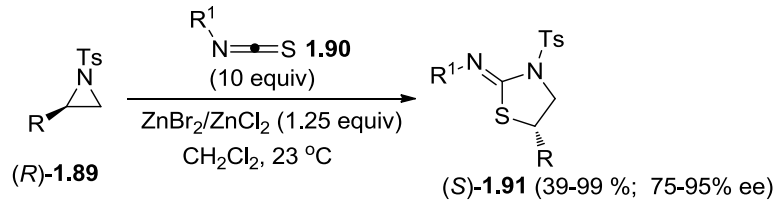

Sengoden and Punniyamurthy described a water medium based route for synthesis of heterocycles **1.88** through the [3+2] cycloaddition of aziridines **1.87** with heterocumulenes **1.86** using iron(III) catalysis in air (Scheme 1.25).[30] Iron salts are soluble in water, while the aziridines and heterocumulenes are hydrophobic in nature so float on the surface of water. Thus, chelation of the iron species with nitrogen of the aziridines may act as the driving force for insertion of heterocumulene in aziridine ring producing the ring expanded products (imino-selenazolidine/imino-thiazolidines/imino-oxazolidines/imino-imidazolidines) in good yields.

**Scheme 1.25**



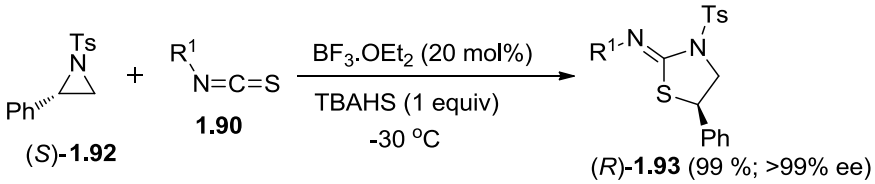

Stoltz's group has developed a Lewis acid mediated chemo-, regio-, and diastereo-selective (3+2) cycloaddition reaction of *N*-H- and *N*-sulfonylaziridines **1.89** with allyl, alkyl, silyl, and aryl heterocumulenes **1.90** that gives enantio-enriched iminothiazolidines **1.91** in excellent yields (Scheme 1.26).[31] They have further derivatized the formed heterocyclic scaffolds successfully by removal of sulfonyl and allyl protecting groups without losing enantiomeric purity.

**Scheme 1.26**



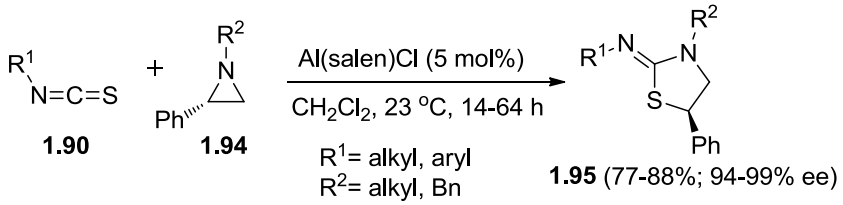

Ghorai and co-worker have described a Lewis acid catalyzed quaternary ammonium salt mediated domino ring-opening cyclization of activated aziridines **1.92** with aryl and alkyl isothiocyanates **1.90** as the nucleophiles affording nonracemic and racemic substituted 2-iminothiazolidines **1.93** in yields up to 99% with excellent stereospecificity (*de*, *ee* up to or >99%) (Scheme 1.27).[32]

**Scheme 1.27**




Punniyamurthy's group reported an atom-economic, [Al]-catalyzed enantiospecific (3+2) cycloaddition of unactivated chiral aziridines **1.94** with one equiv of isothocyanates **1.90** at rt (25 $^{o}$C) that gave iminothiazolidines **1.95** with excellent enantiomeric purities (94−99% ee) (Scheme 1.28).[33] This procedure comprises the advantages of ambient reaction conditions, use of catalytic amount of Al(salen)Cl with no requirement of additives.

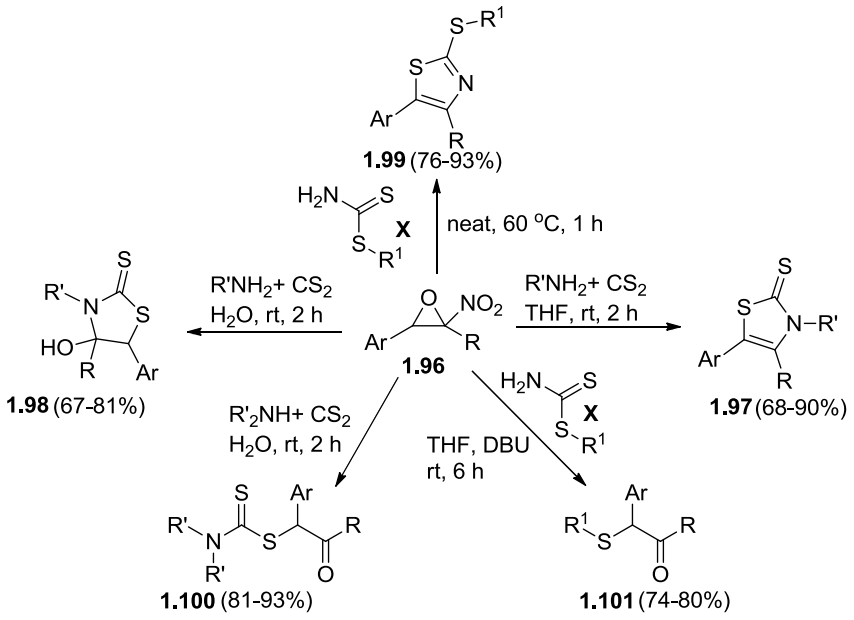
**Scheme 1.28**




Very recently, Halimehjani *et al*. have developed several efficient and highly practical methods for the synthesis of *N*, *S*-heterocycles like thiazole-2(3H)-thiones **1.97** (THF as solvent), thiazolidine-2-thiones **1.98** (water as solvent) and 2-(alkylsulfanyl)thiazoles **1.99** (neat conditions) from nitro-epoxides **1.96** and *in situ* generated dithiocarbamic acids or *S*-alkyl dithiocarbamates **X** (Scheme 1.29).[34] A novel dithiocarbamate-substituted aryl-2-propanone **1.100** was thus obtained by a facile and ecofriendly reaction of secondary amines, $CS_2$, and nitro-

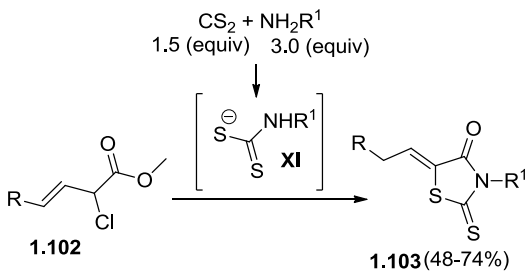
epoxides **1.96** in water. Moreover, the reaction of *S*-alkyldithiocarbamates **X** with nitro-epoxides **1.96** in the presence of DBU afforded 1-(alkylsulfanyl)-1-aryl-2-propanones **1.101**. All these reactions were performed under mild reaction conditions in short reaction times, with good to excellent yields of the products.

**Scheme 1.29**




Jacobine and Posner have reported a one pot multicomponent sequential transformation of *in situ* generated dithiocarbamates **XI** with racemic α-chloro-β,γ-alkenoate esters **1.102** to obtain sulfur/nitrogen heterocycles such as 5-(*Z*)-alkylidene-2-thioxo-1,3-thiazolidin-4-ones **1.103** (rhodanine derivatives) (Scheme 1.30).[35] Using this simple process, they have prepared an analogue of the drug epalrestat, an aldose reductase inhibitory rhodanine.

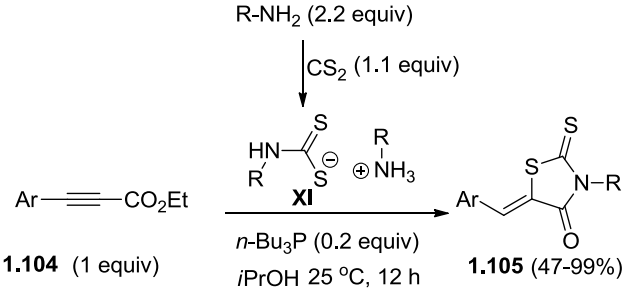
**Scheme 1.30**




Taran's group has developed a simple and practical method for the preparation of S/N-containing heterocycles **1.105** (rhodanine derivatives) *via* *n*-$Bu_3P$-catalyzed tandem α-*S*-addition and intramolecular cyclization of dithiocarbamates **XI** with aryl propiolates **1.104** (Scheme

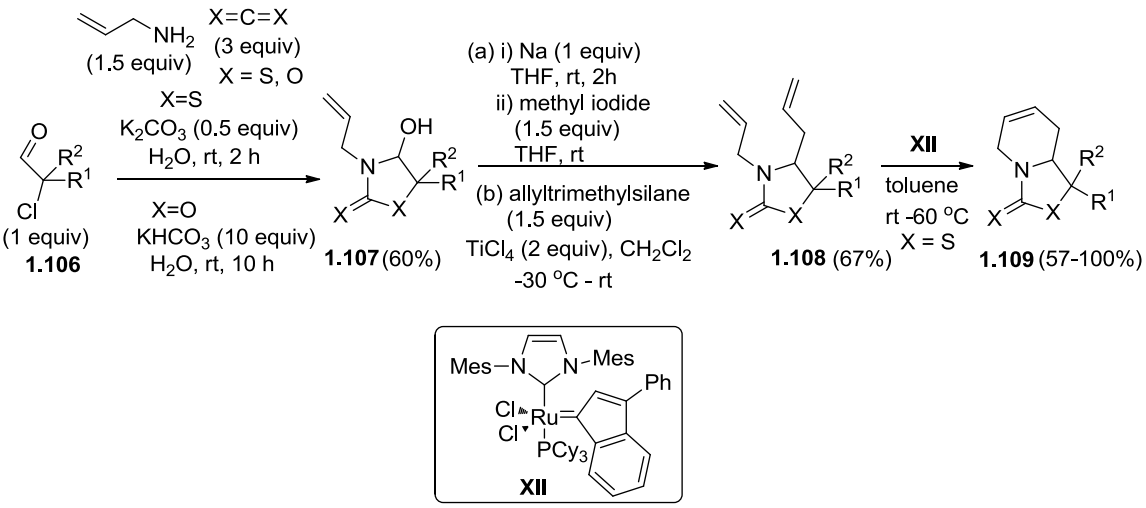
1.31).[36] This strategy offers a forthright way for constructing heterocycles that are present in many biologically active products.

**Scheme 1.31**




Martens's group developed one-pot multicomponent reaction (MCR) of $CO_2/CS_2$, allylamine and α-chloroacetaldehyde **1.106** in water to afford hydroxy-thiazolidine-thiones and oxazolidinones **1.107** under mild reaction conditions, using principles of "green chemistry" (Scheme 1.32).[37] These hydroxy-thiazolidine-thiones and oxazolidinones **1.107** were further derivatized to different dienes **1.108** containing terminal C–C double bonds that underwent ring-closing metathesis (RCM) using the catalyst **XII** to give unsaturated bicycles **1.109.**

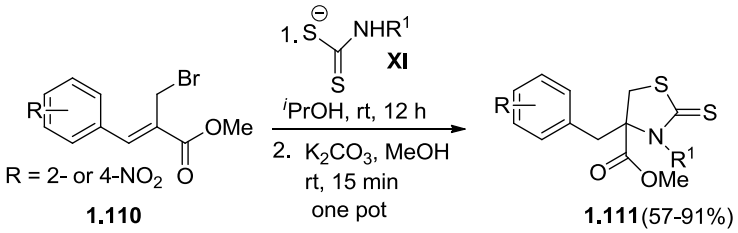
**Scheme 1.32**




Batra's group has reported the base-mediated intramolecular cyclization of *in situ* generated allyldithiocarbamates from allylbromo-alkanoates **1.110** to give substituted 2-

thioxothiazolidine-4-alkanoates **1.111** instead of substituted 1,3-thiazines (Scheme 1.33).[38] But the reaction was restricted to 2- or 4-nitrophenyl bearing substrates.

**Scheme 1.33**

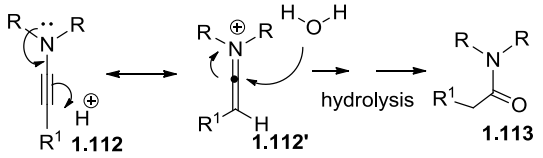



**1.110** **1.111** (57-91%)

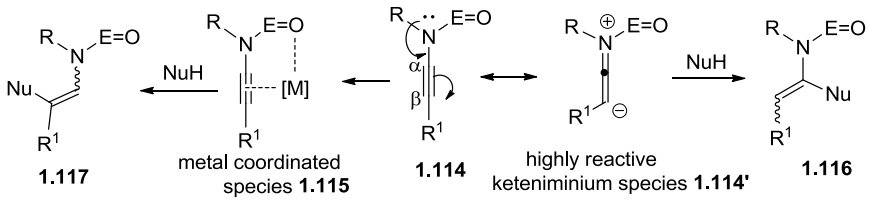
## 1.6 Ynamide reactivity

Ynamines belong to the subgroup of alkynes (heteroatom-substituted alkynes) incipient as highly useful and versatile building blocks for the synthesis of numerous heterocycles.[39] The synthetic efficacy of ynamines is because of their predictable regioselectivity and innately high reactivity.[39a, 39e] Ynamines are very sensitive towards hydrolysis (Scheme 1.34). This limitation hindered the development of ynamine chemistry. This problem was alleviated by replacing one of the alkyl/aryl groups by an electron withdrawing group, which led to the relatively more stable ynamides. In the year 1972, the first ynamide was synthesized by Viehe and co-workers from $\alpha$-chloro-enamide.[40] After this report, several functionalized ynamides were explored for many organic transformations.[41] The binding affinity of the electron-withdrawing carbonyl/sulfonamide protecting group of the ynamide nitrogen atom to the electrophilic metal catalyst influences the reactivity as well as the regioselectivity (Scheme 1.35).

**Scheme 1.34.** Hydrolysis of ynamines




**Scheme 1.35.** Reactivity of ynamides

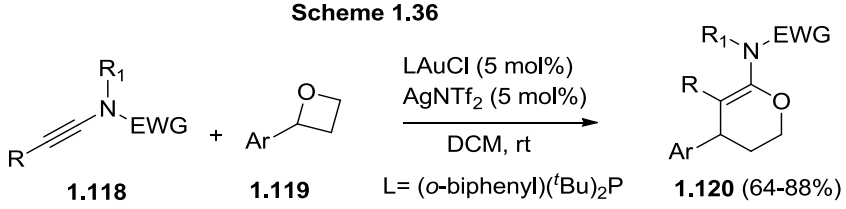



[E=O or EWG means Electron Withdrawing Group]

## 1.7 Inter/intramolecular cyclization and cycloaddition reactions of ynamides

Shung Liu's group described the gold catalyzed [4+2] cycloaddition of ynamides **1.118** with oxetanes **1.119** to obtain 6-amino-3,4-dihydro-2H-pyrans **1.120** with excellent regioselectivity. (Scheme 1.36).[42] Here, oxetanes act as nucleophiles whereas gold-π-ynamides behave as electrophiles.

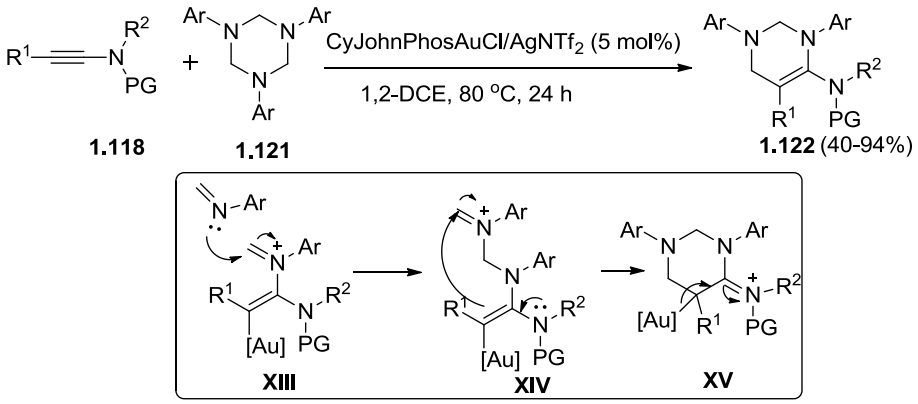
**Scheme 1.36**




**1.118** **1.119** **1.120** (64-88%)

Very recently, Hashmi's group reported a regioselective cyclocarboamination of ynamides **1.118** with 1,3,5-triazinanes **1.121** that afforded 5-aminotetrahydropyrimidines **1.122** through gold-catalysis in good to excellent yields. It established a unique yet challenging annulation of ynamides with unstrained saturated heterocycles. In this method, first *in situ* generated formaldimines (nucleophile) from 1,3,5-triazinanes reacts with the gold-activated ynamides regiospecifically at the α-position and forms intermediate **XIII** which is attacked rapidly by another formaldimine giving the iminium species **XIV**. Then intramolecular cyclization affords **XV**; later, proto-deauration takes place to provide the final products **1.122** regenerating the active gold catalyst (Scheme 1.37).[43]

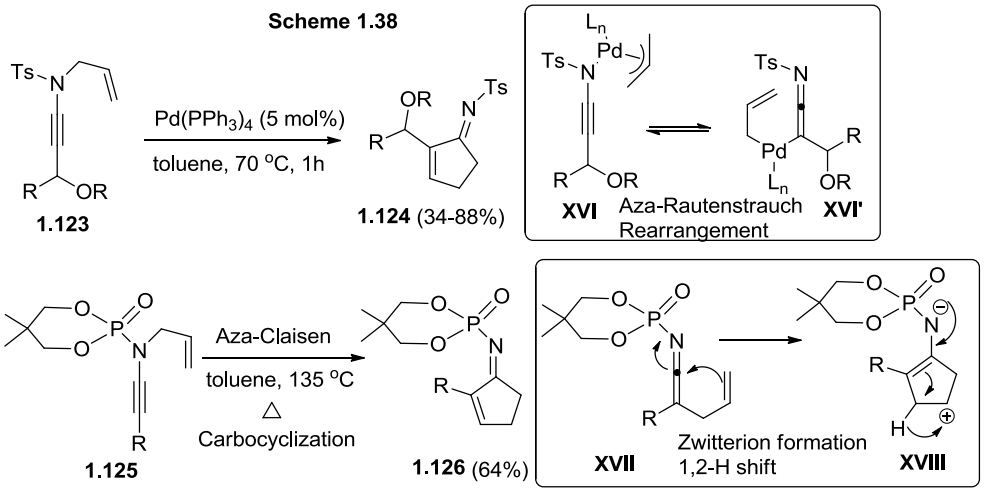
**Scheme 1.37**




**1.118** **1.121** **1.122** (40-94%)

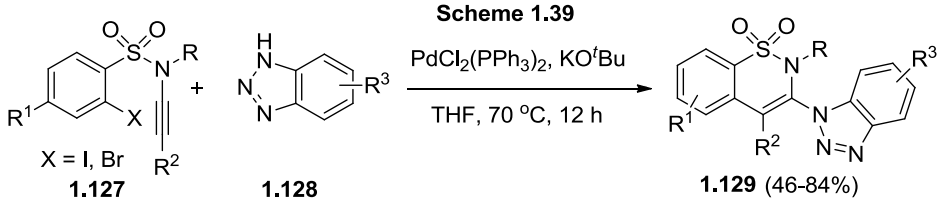
DeKorver's group reported the synthesis of *α,β*-unsaturated cyclopentenimines **1.124** and **1.126** by Pd-catalyzed, thermal aza-Claisen-carbocyclization of *N*-sulfonyl-allyl and *N*-phosphoryl-allyl ynamides **1.123** and **1.125** (Scheme 1.38).[44] In the case of *N*-sulfonyl-allyl ynamides **1.123**, carbocyclization occurs through Pd-π-allyl complexes (**XVI**-**XVI'**) *via* a Rautenstrauch rearrangement, so the use of palladium catalysis is compulsory. In the case of *N*-phosphoryl ynamides **1.125**, thermal conditions may be employed to obtain allyl-ketenimine **XVII** that undergoes carbocyclization to yield cyclopentenimines **1.126** *via N*-promoted 1,2-H shift through zwitterionic intermediate **XVIII**. Alternatively, more complex fused bi- and tri-cyclic scaffolds could be generated by employing ynamides bearing tethered carbon nucleophiles through capture of the zwitterionic intermediate.

**Scheme 1.38**



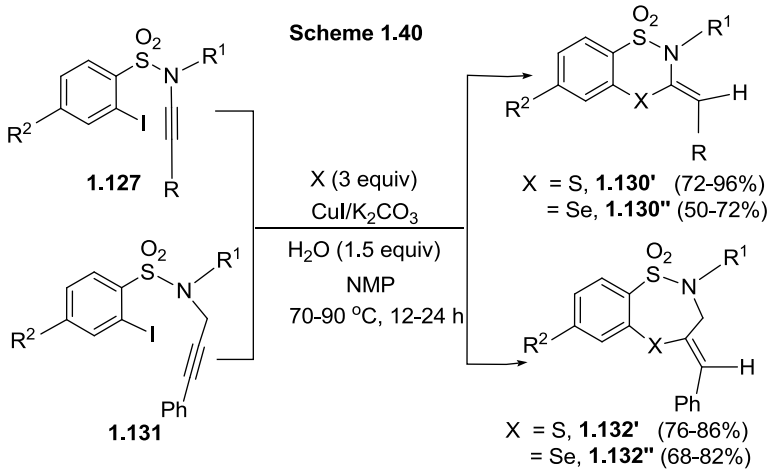

Very recently, our group has reported highly regioselective [Pd]-catalyzed intermolecular cyclization of functionalized ynamides **1.127** and benzotriazoles **1.128** leading to benzotriazole appended benzosultams **1.129** in good yields (Scheme 1.39).[45] Coordinating solvents appear to enhance the yield of the products. This methodology could be extended to synthesize triazole/tetrazole appended benzosultams also.

**Scheme 1.39**



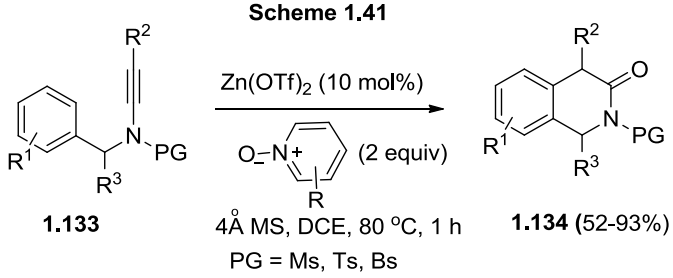
Our group has also described a novel [Cu]-catalyzed one-pot regio- and stereo-specific synthesis of benzo[1,4,2]dithiazine 1,1-dioxides **1.130'** and benzo[1,4,2]thiaselenazine 1,1-dioxides **1.130"** by the cyclization of functionalized ynamides **1.127** with elemental sulfur or selenium (Scheme 1.40).[46] This methodology was elegantly extended for the synthesis of benzodithiazepines **1.132'** and benzothiaselenazepines **1.132"** by using *N*-propargyl-sulfonamides **1.131**. Here, water acts as proton source; this was proven by incorporation of $^2$D at the olefinic site by using $D_2O$ in place of water.

**Scheme 1.40**




Long-Wu Ye's group developed a convenient method for site-selective synthesis of isoquinolones **1.134** through non-noble metal catalyzed intermolecular alkyne oxidation and C-H functionalization of ynamides **1.133** (Scheme 1.41).[47] This methodology was applicable to intra-/inter-molecular oxidative C-H functionalization. Prominently, this oxidative zinc catalysis could considerably inhibit over-oxidation (undesired diketone formation). On the basis of both mechanistic studies and DFT calculations, the authors proposed a Lewis acid catalyzed Friedel–Crafts-type pathway.

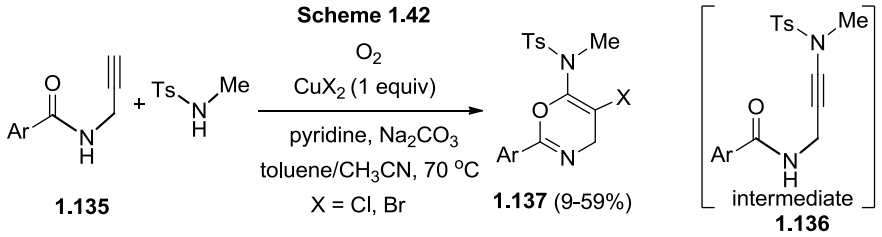
**Scheme 1.41**



## 1.8 Halocyclization of ynamides

Hashmi *et al.* reported the $CuX_2$ catalyzed one pot sequential tandem cyclization of propargyl amides **1.135** with sulfonamides that produced 5-halo-4*H*-1,3-oxazine-6-amines **1.137** under aerobic conditions (Scheme 1.42).[48] In this method, initially ynamide intermediate **1.136** is formed *via N*-alkynylation process, which is followed by 6-*endo-dig* halo-cyclization to provide the 5-halo-1,3-oxazines. Both $CuCl_2$ and $CuBr_2$ worked well in this cyclization process.

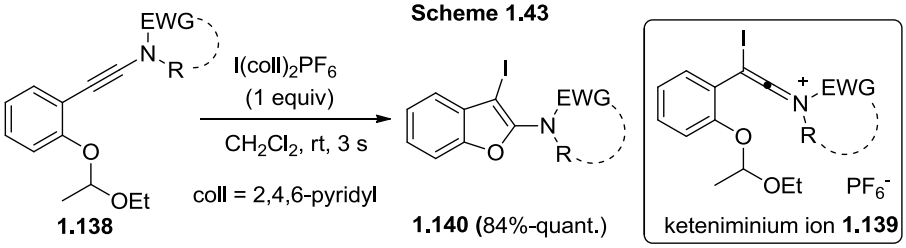
**Scheme 1.42**




**1.135** **1.137** (9-59%) **1.136**

Okitsu's group described an effective and fast electrophilic iodocyclization of ynamides containing ethoxyethyl ether group **1.138** that gives 3-iodo-benzo[*b*]furans **1.140** in good yields (Scheme 1.43).[49] In the presence of iodinating reagent $I(coll)_2PF_6$, electrophilic iodonium ion attacks at the *β*-position of ynamide to form keteniminium ion **1.139**. Later, nucleophilic attack of oxygen of the ethoxyethyl ether group on keteniminium ion species followed by the loss of the ethoxyethyl group affords the 3-iodo-benzo[*b*]furan **1.140**.

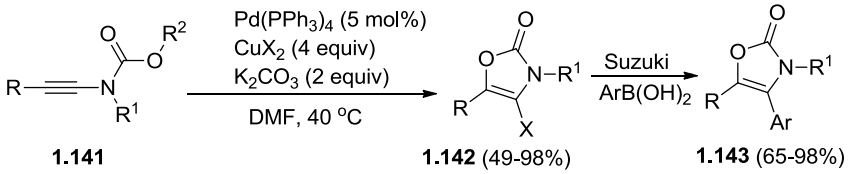
**Scheme 1.43**




**1.138** **1.140** (84%-quant.) keteniminium ion **1.139**

Zhu *et al* developed a mild and efficient method for the synthesis of 4-halo-oxazolones **1.142** by $Pd(PPh_3)_4$-catalyzed intramolecular halocyclization of *N*-alkynyl alkyloxycarbamates **1.141** with $CuCl_2$ or $CuBr_2$ (Scheme 1.44).[50] The resulting 4-halo-oxazolones **1.142** were utilized further in the preparation of highly substituted oxazolones **1.143** *via* a [Pd]-catalyzed cross-coupling reaction.

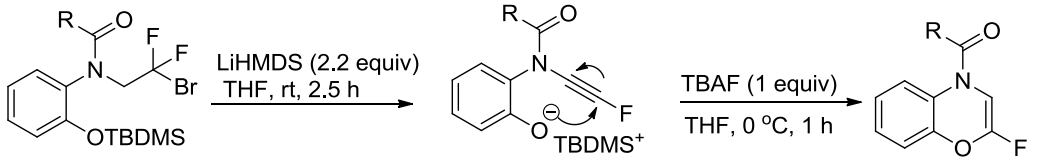
**Scheme 1.44**




**1.141** **1.142** (49-98%) **1.143** (65-98%)

Mangelinckx's group developed a method to prepare fluoro-benzoxazines **1.146** from *β*-bromo-*β,β*-difluoro-benzamides **1.144** *via* terminal fluoroynamide intermediate **1.145**. This intermediate was treated with TBAF in THF to afford benzoxazines **1.146** in good yields (Scheme 1.45).[51] The reaction proceeds through a ynamide intermediate. Generally, *β*-position of ynamide is nucleophilic, but the presence of a fluorine substituent at the *β*-position of the ynamide and the electron-withdrawing group at nitrogen make *β*-position electrophilic (umpolung), so nucleophilic alkoxide ion attacks *β*-position of alkyne regioselectively affording benzoxazines **1.146** without the need of a metal catalyst.

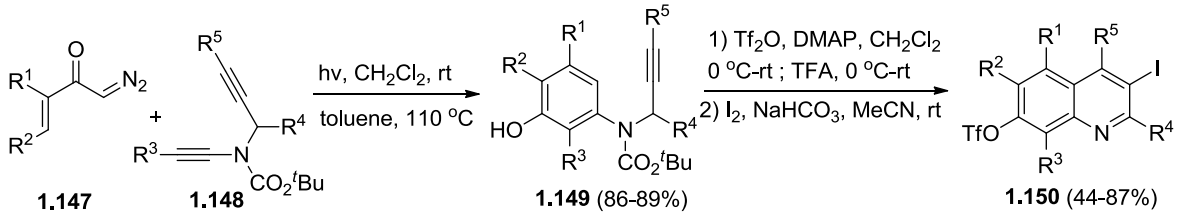
**Scheme 1.45**




**1.144** **1.145** (83-97%) **1.146** (70-86%)

Densely substituted quinolines **1.150** were synthesized from an efficient tandem chemoselective and regiocontrolled thermal or photochemical benzannulation followed by iodocyclization of *N*-propargyl ynamides **1.148** with diazoketone **1.147** as reported by Danheiser's group (Scheme 1.46).[52] Initially, diazoketones **1.147** react with *N*-propargyl-substituted ynamides **1.148** *via* a cascade of several pericyclic reactions or thermal [2+2] cycloaddition chemoselectively to generate highly substituted aniline derivatives **1.149**. In the second step, triflate derivatives of the phenolic benzannulation products undergo Larock cyclization upon addition of iodine to obtain 3-iodo-quinolines **1.150.**

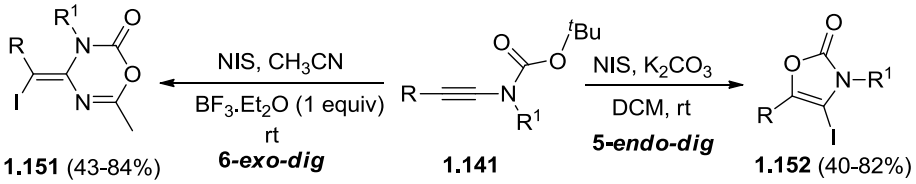
**Scheme 1.46**




**1.147** **1.148** **1.149** (86-89%) **1.150** (44-87%)

Zhu's group has developed solvent dependent protocols for the synthesis of 1,3,5-oxadiazin-2-ones **1.151** and oxazolones **1.152** from electrophilic iodocyclization of ynamides **1.141** (Scheme 1.47).[53] In this methodology, electrophilic iodine attacks at alkyne moiety of ynamide that will increase the electrophilicity of *α*-position; acetonitrile-*N* then attacks the *α*-position which is followed by intramolecular 6-*exo-dig* cyclization on nitrile-*C* atom to afford *E*-1,3,5-oxadiazin-2-ones **1.151**. In DCM as the solvent (without $CH_3CN$) oxazolones **1.152** were obtained through intramolecular 5-*endo-dig* cyclization under transition-metal-free conditions.

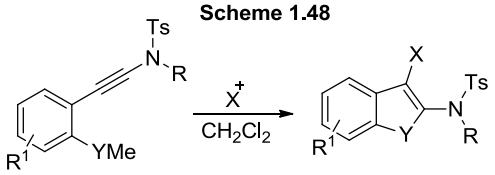
**Scheme 1.47**




**1.151** (43-84%) **1.141** **1.152** (40-82%)

Cao's group described the electrophilic iodo-cyclization reaction of *o*-anisole- and *o*-thioanisole- substituted ynamides **1.153** with $I_2$, NBS, and NCS to obtain 2-amido-3-halobenzofurans and 2-amido-3-halobenzothiophenes **1.154** in moderate to good yields (Scheme 1.48).[54] The 3-iodo-2-amidobenzofurans were utilized further to synthesize 3-aryl-, 3-alkynyl- and 3-vinyl-2-amidobenzofurans *via* Pd-catalyzed Suzuki–Miyaura and Sonogashira cross-coupling reactions.

**Scheme 1.48**

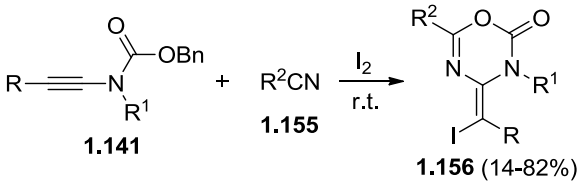



**1.153**
Y = O, S

**1.154** (39-92%)
X = I, Br, Cl

Zhao' group developed a simple and convenient method for synthesizing 1,3,5-oxadiazin-2-ones **1.156** through intermolecular cyclization of ynamides **1.141** with nitriles **1.155** mediated by inexpensive molecular iodine (Scheme 1.49).[55]

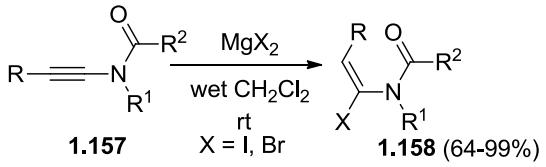
**Scheme 1.49**




## 1.9 Halo-addition reactions of ynamides

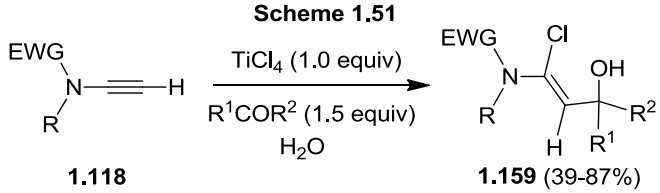
In the year 2003, Hsung and co-workers reported the synthesis of *E*-*α*-halo-enamides **1.158** in good yields with excellent stereoselectivity from hydrohalogenation of ynamides **1.157** by treatment with $MgBr_2$ or $MgI_2$ (Scheme 1.50).[56] In this hydrohalogenation reaction water played a vital role because reactive species HX is generated *in situ* from the reaction of magnesium salt with wet $CH_2Cl_2$.

**Scheme 1.50**




Matsuo *et al.* described the synthesis *α*-halo-*γ*-hydroxyenamides **1.159** from the titanium tetrachloride mediated addition of carbonyl compounds to terminal ynamides **1.118** (Scheme 1.51).[57] The products were utilized in additional synthetic applications including either Suzuki coupling or intramolecular direct cyclization by using [Pd]-catalysis.

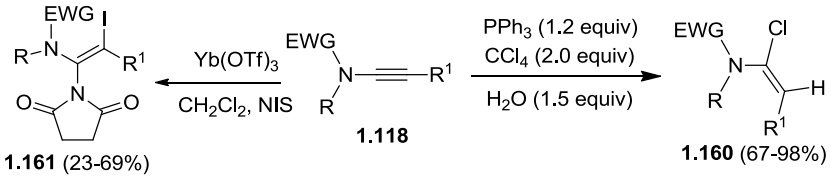
**Scheme 1.51**




Sahoo and co-workers developed a simple protocol to synthesize *α*-chloroenamides **1.160** through a metal-free triphenylphosphine promoted regio- and stereo-selective hydrohalogenation of ynamides **1.118** (*syn* addition) using carbon tetrahalides as the halogen source (Scheme 1.52).[58a] The role of water in the reaction was elucidated by deuterium labelling experiment.

Very recently, the same group reported Yb(III) catalyzed iodo-imidation (*anti*-addition) of NIS to ynamides **1.118** by treating NIS affording *β*-iodo-enamides **1.161** in good to excellent yields.[58b]

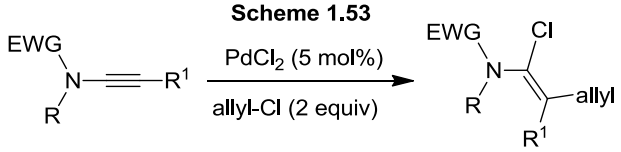
**Scheme 1.52**




**1.161** (23-69%) **1.118** **1.160** (67-98%)

A report from Zhu *et al*. involved [Pd] catalyzed atom economic approach to synthesize stereo-defined multisubstituted enamides **1.162** by the chloro-allylation (*syn*-addition) of allyl chlorides to ynamides **1.118** (Scheme 1.53).[59] It is important to note that the reaction was performed at rt (25 $^{o}$C) by using 5 mol% of $PdCl_2$.

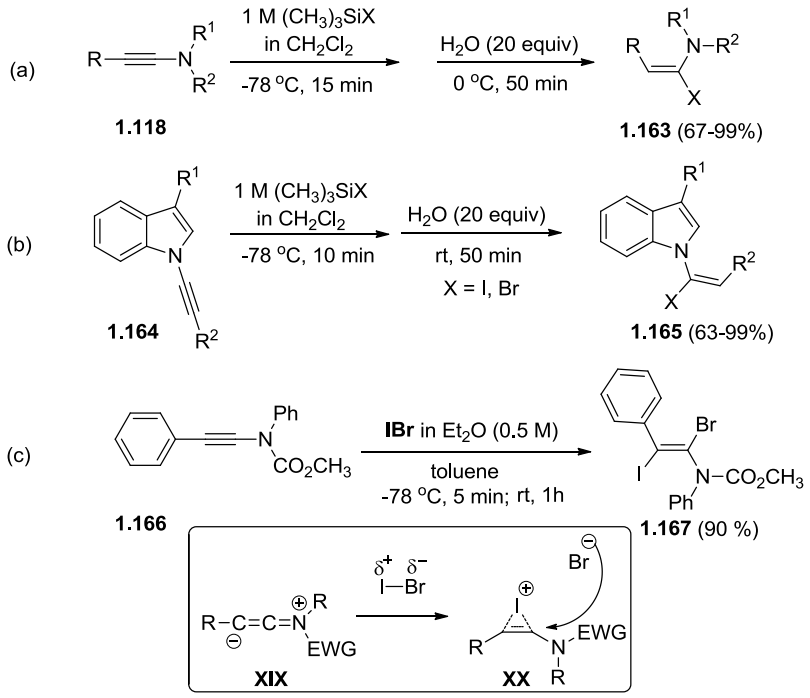
**Scheme 1.53**




**1.118** **1.162** (60-85%)

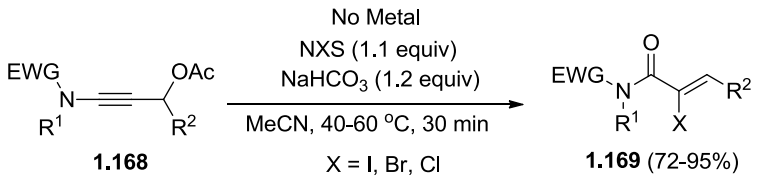
In the year 2013, Iwasawa *et al.* reported the regio- and stereo-specific hydrohalogenation reaction of ynamides **1.118** by using bromo- or iodo-trimethylsilane to obtain (*E*)-*α*-bromo/chloroenamides **1.163** (Scheme 1.54a).[60a] This method showed tremendous substrate compatibility and afforded a variety of (*E*)-*α*-haloenamides **1.163**. Later, the same group described the synthesis of diverse 1-(1-halovinyl)-1H-indoles **1.165** from 1-ethynyl-1-H-indoles **1.164** with TMSI/TMSBr by following a simple protocol (Scheme 1.54b).[60b] Mechanistically, nitrogen of indole likely coordinates to silicon, involving the *syn*-addition of HI. Later the same group synthesized (*E*)-2-bromo-1-iodoenamides **1.167** from iodobromination of ynamides **1.166** (Scheme 1.54c) by using IBr. The *in situ* IBr generated by the reaction of TMSBr with NIS, added to the ynamide according to the nature of the keteniminium resonance forms **XIX**-**XX**.[60c]

**Scheme 1.54**



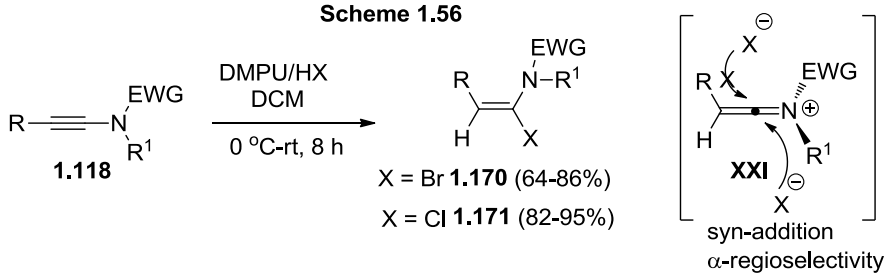

Skrydstrup's group has demonstrated a metal-free procedure to synthesize $\alpha$- iodo, bromo, and chloro acrylamides and acrylimides **1.169** from 3-acetoxy ynamides **1.168** through electrophile addition at $\beta$ position of ynamide followed by acetate shift to $\alpha$ position (Scheme 1.55).[61]

**Scheme 1.55**



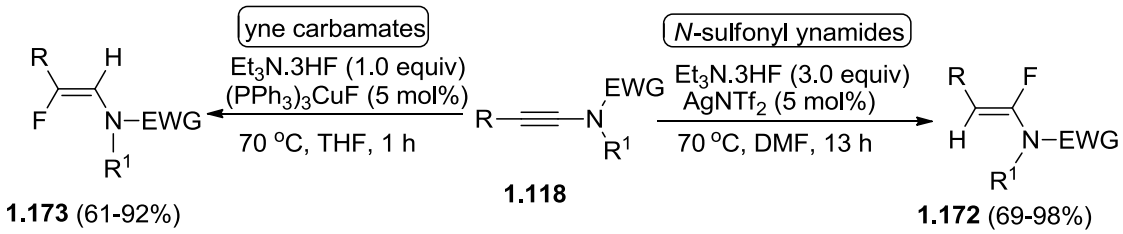

Hammond *et al*. developed an atom-economical and metal-free protocol for the regio- and stereo-selective hydrohalogenation of ynamides **1.118** using easy to handle DMPU/HX (X = Br or Cl) reagents to obtain *syn*-$\alpha$-haloenamides **1.170** and **1.171** in good yields (Scheme 1.56).[62] The reaction operates under mild conditions and a range of functional groups is well tolerated. The hydrohalogenation of ynamides operates *via* a cationic keteniminium intermediate **XXI**.

**Scheme 1.56**



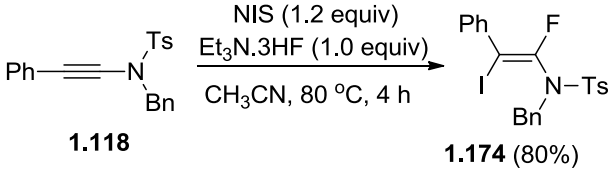

Zhu *et al*. have reported a novel, withdrawing group dependent, Ag(I)- or Cu(I)- catalyzed *trans*-hydrofluorination of alkynamides **1.118** to obtain *α/β*-fluorinated enamides **1.172** and **1.173** in good to excellent yields with high regio- and stereo-selectivity (Scheme 1.57).[63] In this reaction, $Et_3N{\cdot}3HF$ acts as the fluorinating agent and tolerates a variety of functional groups such as -$NO_2$, -Ac, -Br, and -OMe.

**Scheme 1.57**




Zhu and co-workers reported the synthesis of (*E*)-*α*-fluoro-*β*-iodoenamides **1.174** through a metal-free, regio- and stereo-selective *trans*-iodofluorination of ynamides **1.118** with NIS and $Et_3N{\cdot}3HF$ in moderate to good yields. The reaction proceeds under mild reaction conditions and exhibits good functional group tolerance (Scheme 1.58).[64]

**Scheme 1.58**

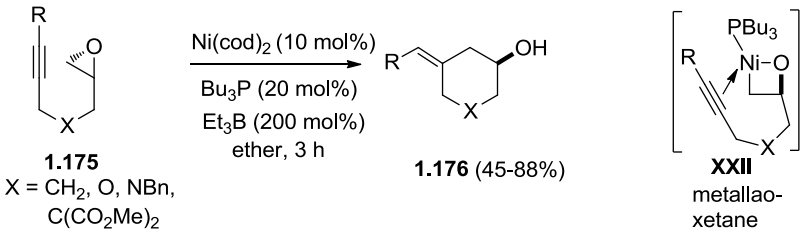



## 1.10 Ring expansion reactions of epoxide and alkyne containing substrates

Jamison's group developed a novel [Ni]-catalyzed reductive coupling of epoxides **1.175** containing alkyne functionalities that gives carbo-/hetero-cycles **1.176** (Scheme 1.59).[65] This is the first catalytic method for the reductive coupling of substrates having both alkyne and epoxide moieties. The reaction proceeds through regioselective oxidative addition of a $Bu_3P$-Ni(0)

complex onto the less hindered side of the epoxide resulting in metallaoxetane **XXII**, which then undergoes *exo-dig* cyclization with the alkyne, *β*-H elimination, and finally reductive elimination to afford the cyclized product **1.176**.

**Scheme 1.59**



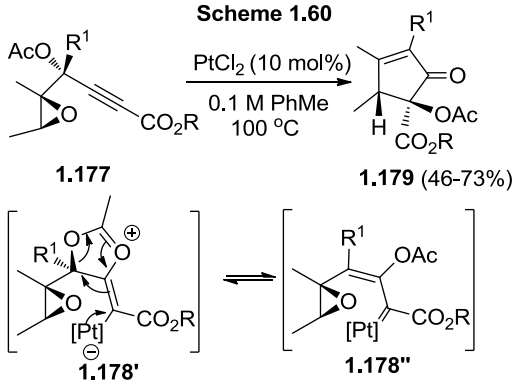

**1.175**
X = $CH_2$, O, NBn, $C(CO_2Me)_2$

**1.176** (45-88%)

**XXII**
metallao-xetane

A report by Sarpong's group delves on an efficient protocol for pentannulation of epoxy appended propargylic esters **1.177** through platinum catalysis leading to pentannulated products **1.179** (Scheme 1.60).[66] In this methodology, first the [Pt]-catalyst activates the alkyne moiety; later oxygen of the ester group attacks the alkyne in an 5-*exo-dig* fashion to produce the zwitterion **1.178'** which is in equilibrium with the metallocarbenoid **1.178''**. Nucleophilic attack of epoxide oxygen to metallocarbenoid **1.178''** through oxa-6*π* electrocyclization affords the pentannulated product.

**Scheme 1.60**




**1.177**

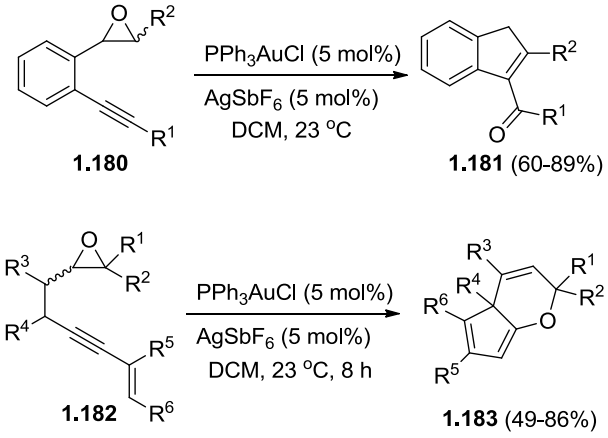
**1.179** (46-73%)

**1.178'**

**1.178"**

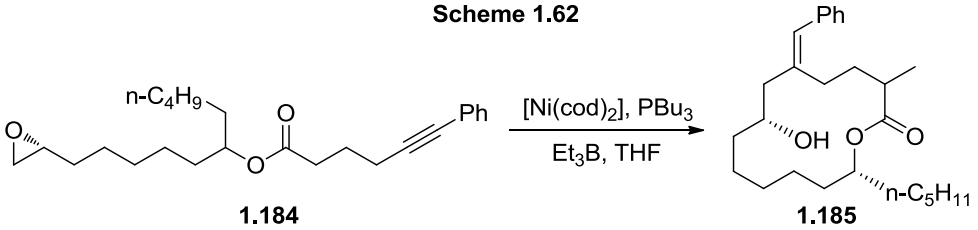
Liu's group reported the [Au]/[Ag]-catalyzed cycloisomerization of aromatic and nonaromatic epoxide-alkynes **1.180** and **1.182** to give 3-1*H*-indenyl ketones **1.181** and polycyclic 2*H*-pyrans **1.183**, respectively. (Scheme 1.61).[67] The cycloisomerization proceeds *via* 6-*exo-dig* attack of the epoxide on the alkyne that generates the gold-carbenoid intermediate, which undergoes Nazarov-type cyclization in the presence of [Au]/[Ag] catalytic system. The gold-carbenoid intermediate was identified by a series of trapping experiments using $Ph_2SO$ oxidation.

**Scheme 1.61**



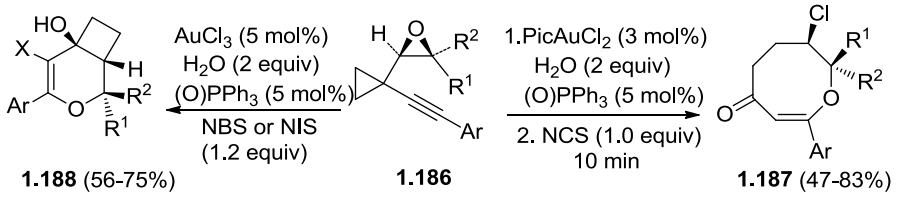

Jamison and co-workers developed a [Ni]-catalyzed reductive coupling of alkynyl epoxides **1.184** that led to macrocycles **1.185** with high regioselectivity (Scheme 1.62).[68] This methodology was applied for the synthesis of (−)-gloeosporone in 10 steps with an overall yield of 6% by using 20 mol% catalyst loading.

**Scheme 1.62**



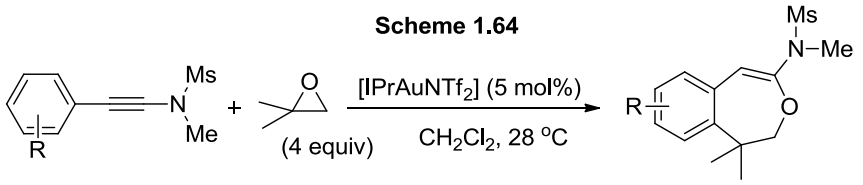

Liu's group reported the [Au]-catalyzed ring expanded halocyclization of *cis*-1-oxiranyl-1-alkynylcyclopropanes **1.186** and *N*-halosuccinimides producing heterocyclic compounds **1.187** and **1.188** (Scheme 1.63).[69] In this methodology, two different sequential ring opening reactions ensued resulting in the eight-membered ether **1.187** *via* oxacyclization/ring expansion in the presence of (Pic)$AuCl_2$ and *N*-chlorosuccinimide (NCS). In contrast, divergent ring expansion reaction with $AuCl_3$ and NBS or NIS provided the bicyclic-compound **1.188**.

**Scheme 1.63**



Liu's group developed a gold catalyzed [4+3] cycloaddition reaction of arenynamides **1.118** with epoxides **1.189** that gave 7-membered cycloadduct **1.190** in good yields (Scheme 1.64).[70] This reaction involves $S_N2$-type retention i.e. front-side attack of phenyl at the oxiranyl ring for the formation of [4+3] cycloadducts.

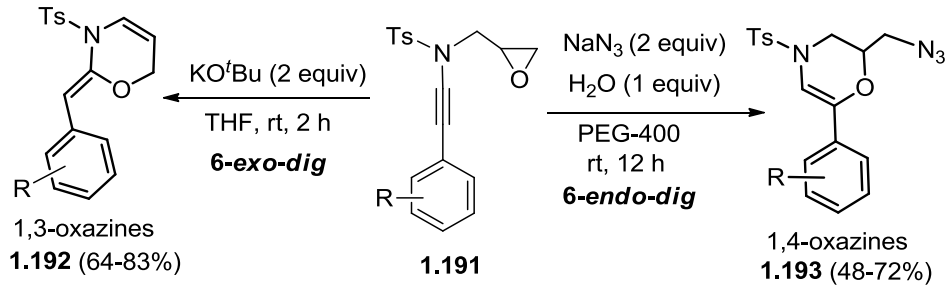
**Scheme 1.64**




**1.118** **1.189** **1.190** (45-85%)

Recently, our research group developed a novel protocol to synthesize 1,3- and 1,4-oxazines from transition metal-free, base or $NaN_3$ mediated cyclization of epoxy tethered ynamides **1.191** (Scheme 1.65).[71] This regio- and stereo-selective atom economic synthesis of 1,3-oxazines **1.192** involved the base mediated cyclization of epoxy ynamides **1.191** in a 6-*exo*-*dig* fashion. A highly regioselective synthesis of 1,4-oxazines **1.193** was achieved by the 6-*endo*-*dig* cyclization of epoxy ynamides **1.191** using sodium azide as the nucleophile. In the formation of 1,4-oxazines, water acts as proton donor; this was proven by using $D_2O$ in place of $H_2O$.

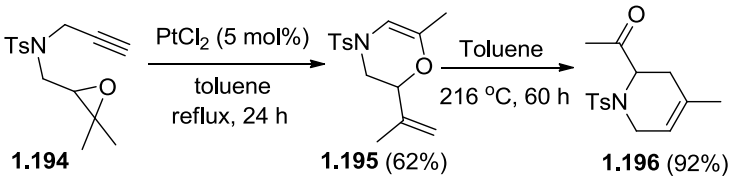
**Scheme 1.65**




## 1.11 Synthesis of 1,4-oxazines and 1,3-oxazolidines

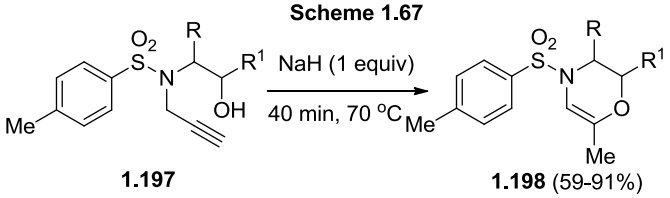
Fang and co-workers described Pt(II) catalyzed concomitant ring expansion-isomerization of alkynyl epoxides **1.194** to obtain 1,4-oxazines **1.195** (Scheme 1.66).[72] Hydrolysis of these allyl vinyl ethers affords 2-hydroxymorpholine derivatives in excellent yields. However, thermal Claisen rearrangement of 1,4-oxazines **1.195** led to piperidine derivatives **1.196**.

**Scheme 1.66**



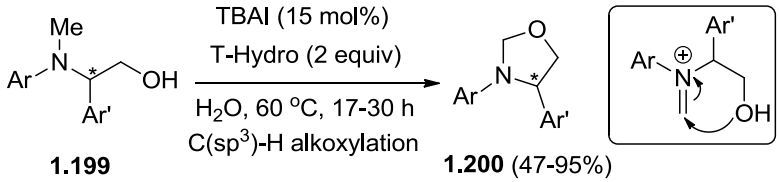

Wang's group developed a base mediated, metal-free, intramolecular cyclization of alkynyl alcohols **1.197** in the presence of NaH at 70 $^{o}$C to get 1,4-oxazine **1.198** (Scheme 1.67).[73] This is an atom economic approach. The induced stereoselectivity was studied by application of Cram's rule and density functional theory (DFT) calculations. The reaction involves nucleophilic alkoxide obtained from alkynyl alcohol **1.197** attacking the alkyne motif in an *exo-dig* fashion to form the 1,4-oxazine **1.198**.

**Scheme 1.67**



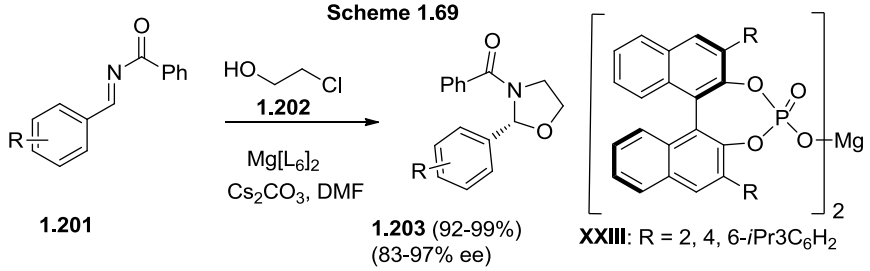

Punniyamurthy *et al*. described a metal-free, regioselective, intramolecular oxidative cross-coupling of *N*-aryl substituted alcohols **1.199** by using TBAI as the catalyst and T-Hydro as the oxidant to obtain functionalized oxazolidines **1.200** in good yields (Scheme 1.68).[74] The reaction proceeds through cross-coupling of *N*-alkyl C-H bond with alkyl O-H bond (C($sp^3$)-H alkoxylation).

**Scheme 1.68**




Antilla's group described magnesium salt **XXIII** of chiral BINOL phosphate catalyzed, base mediated enantioselective addition of chloro-ethanol **1.202** to imines **1.201** to afford chiral 1,3-oxazolidines **1.203** in high yields and excellent enantioselectivities *via* 5-*exo-tet* cyclization in one-pot (Scheme 1.69).[75]

**Scheme 1.69**




In the above context, it may be noted that 1.3-thiazolidine-thiones, imino-thiazolides, 1,4-oxazines and 1,3-oxazolidines constitute important classes of heterocycles due to their extensive range of biological activities (cf. Figure 4).[74, 76] Thus from the above literature, it is clear that sulfonamides show a diverse array of reactions and it is a worthwhile exercise to explore their chemistry in order to generate new classes of, hopefully, medicinally relevant systems.

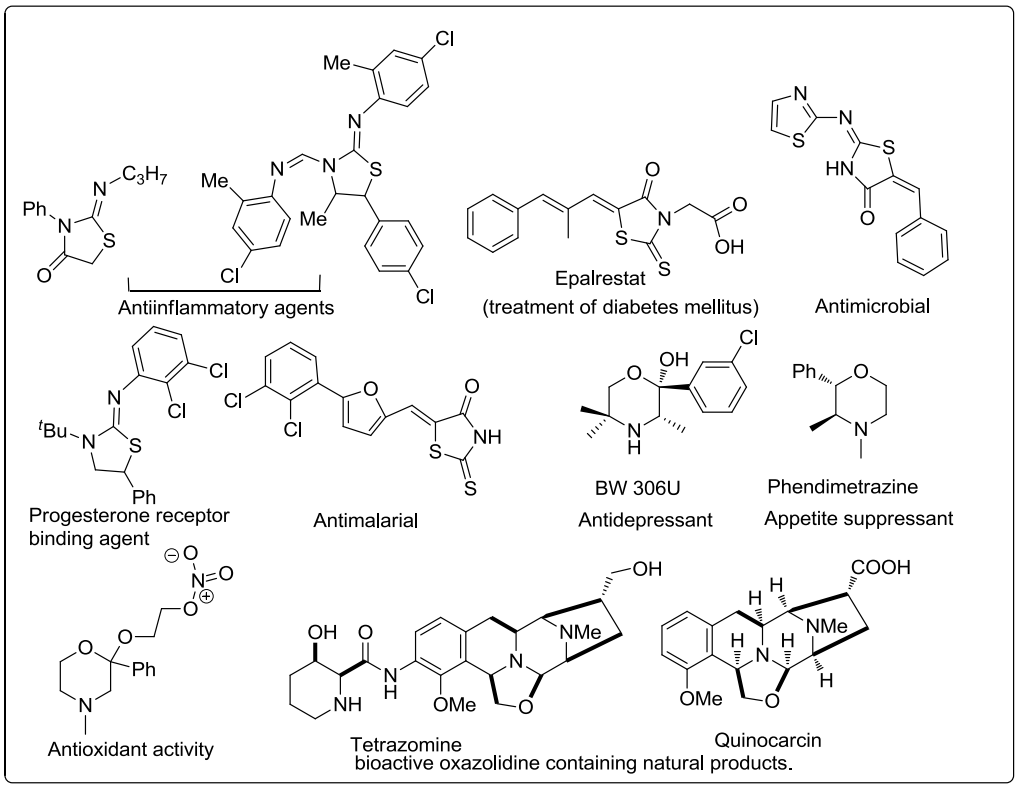



**Figure 3.** Biologically important 1,3-thiazolidine-thione, imino-thiazolidine, 1,4-oxazine and 1,3-oxazolidine derivatives

## OBJECTIVES OF THE PRESENT WORK - PART A

The main aim of this part of the present work was to explore the cyclization and addition reactions of sulfonamides. Specifically, it was intended

(i) To synthesize various thiazolidine-thiones, iminothiazolidines and oxazolidines from base mediated reactions of epoxy sulfonamides or *N*-(2-bromoethyl)-sulfonamides with heterocumulenes (as substrates), and

(ii) To study the intermolecular reaction of epoxy tethered ynamides with CuBr and LiCl in an effort to synthesize 1,3-oxazolidines and 1,4-oxazines, and addition reactions of functionalized ynamides with ICl and CuBr.

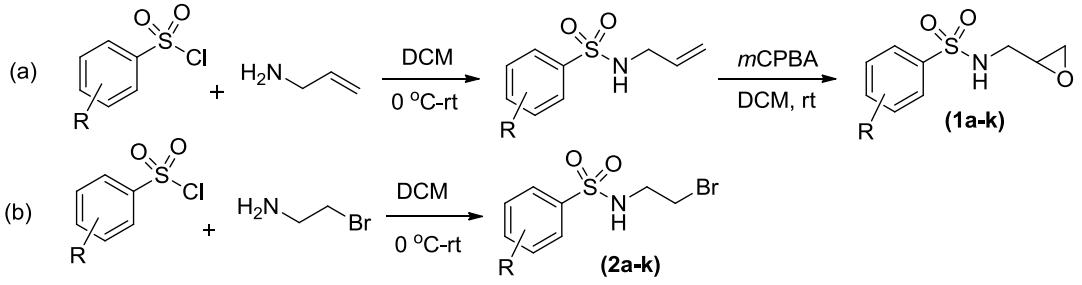
# RESULTS AND DISCUSSION

This chapter deals with the results on cyclization and addition reactions of sulfonamides, ynamides and related substrates leading to thiazolidine-thiones, imino-thiazolidines, 1,3-oxazolidines and 1,4-oxazines. Details on the precursors that are utilized in the present study are presented in sections 2.1-2.2. After this, base catalyzed cyclization reactions of epoxy-sulfonamides/ *N*-(2-bromoethyl)-sulfonamides with carbon disulfide and isothicyanates/ isocyanates are discussed. Later, reaction of *N*-(2-bromoethyl)-sulfonamide with a P(III) isothiocyanate, that afforded an unexpectedly different non-cyclized product, is described. After this, the Mitsunobu reaction of 5-(hydroxymethyl)-3-tosylthiazolidine-2-thione **9** with $Ph_3P$/DEAD/nortriptyline and addition reaction with allenylphosphonate are deliberated. Subsequently, Br/Cl assisted intramolecular 5-*exo-dig*/6-*endo-dig* regio- and stereo-specific cyclization of functionalized ynamides is described. 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 based on X-ray crystallographic studies of illustrative compounds.

## 2.1 Synthesis of epoxy sulfonamide precursors 1a-k and *N*-(2-bromoethyl)-sulfonamides 2a-k

The epoxy sulfonamides **1a-k** and *N*-(2-bromoethyl)-sulfonamides **2a-k** were synthesized from the corresponding sulfonyl chlorides and allylamine/2-bromoethylamine hydrobromide by following literature procedures (Scheme 1).[77a-b] Compound **1j** is new. Remaining compounds are known [27, 71, 77c-d] or are commercially available.

**Scheme 1**



Isothiocyanates **3a-h** and isocyanates **4a-b** are commercially available. P(III) isothiocyanate [**3i**; δ(P) 105.5 (t, *J*(PN) ~ 66.0 Hz) ][78a] and allenylphosphonate [**5**; δ(P) 6.6][78b] were prepared by following literature procedures. 1-Bromo alkynes **6a-f** were also prepared by following a literature method.[79] All these precursors are shown in Figure 1.

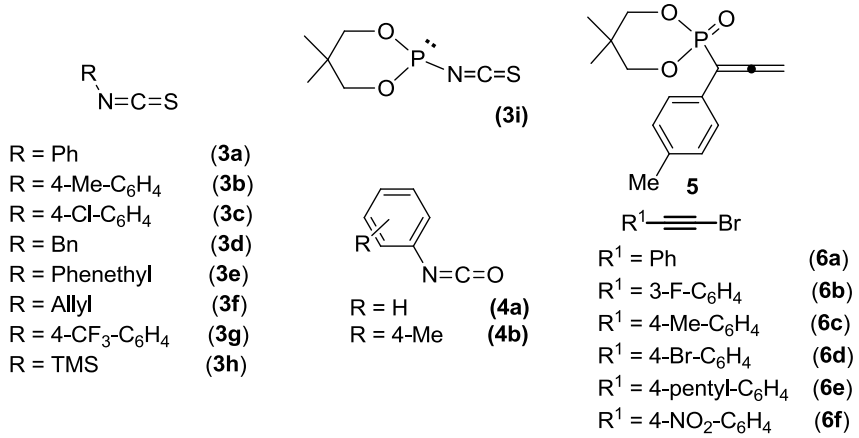
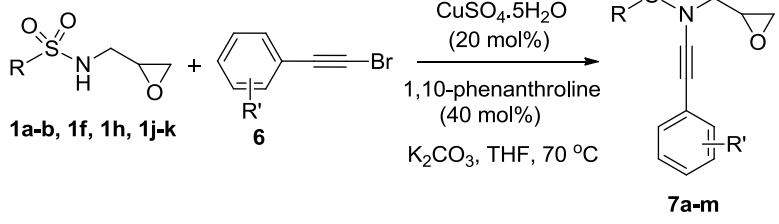



**Figure 1.** Isothiocyanates, isocyanates, allene and bromoalkynes used in the present study

## 2.2 Synthesis of epoxy ynamides 7a-m

Our research group reported the synthesis of epoxy ynamides **7a-f** and **7l** by known protocol with slight modification.[71] In addition, in the current work, the new compounds **7g-k** and **7m** have been prepared (Scheme 2). The identities of all these substrates **7a-m** were confirmed by IR and NMR spectra. IR spectra are particularly useful in identifying these compounds because the alkyne *C*≡*C* group shows a strong band at ~ 2200 $cm^{-1}$. In the $^{13}C$ NMR spectra, two peaks at δ ~ 80 and ~ 70 due to the presence of -*C*≡*C*- group are observed.

**Scheme 2**




R = 4-Me-$C_6H_4$, R' = H (**7a**)
R = 4-Me-$C_6H_4$, R' = 3-F (**7b**)
R = Ph, R' = H (**7c**)
R = 4-$^t$Bu-$C_6H_4$, R' = H (**7d**)
R = -($C_{10}H_7$), R' = H (**7e**)
R = 4-Me-$C_6H_4$, R' = 4-Me (**7f**)
R = 4-Me-$C_6H_4$, R' = 4-Br (**7g,** 84%)
R = Bn, R' = H (**7h**, 90%)
R = 2,5-$Me_2$-4-Cl-$C_6H_2$, R' = H (**7i**, 86%)
R = 4-Me-$C_6H_4$, R' = 4-pentyl (**7j,** 90%)
R = 2-$C_4H_3S$, R' = H (**7k**, 78%)
R = 4-Cl-$C_6H_4$, R' = H (**7l**)
R = 4-Me-$C_6H_4$, R' = 4-$NO_2$ (**7m**, 60%)

## 2.3 Base catalyzed cyclization reactions of epoxy-sulfonamides

From the literature reports presented in Chapter 1, it is clear that sulfonamides are highly useful precursors for the synthesis of heterocyclic compounds. Heterocycles possessing both nitrogen and sulfur/oxygen in the core structure are present in numerous pharmaceutically active compounds.[76] This section is devoted to a new reaction leading to thiazolidine-2-thiones and imino-thiazolidines.

### 2.3.1 Reaction of epoxy-sulfonamides with carbon disulfide

Sulfonamides appended with epoxide functionality are interesting substrates, since such epoxide attached sulfonamide substrates **1a-h** can generate multitudes of nitrogen and oxygen containing heterocycles regio-/stereo-specifically. In the presence of a base, sulfonamide forms aza-anionic intermediate that may attack electrophiles or open epoxide ring regio-specifically to form cyclized products. We discuss herein a simple base catalyzed regio- and stereo-selective intermolecular 5-*exo*-*tet* cyclization of epoxy sulfonamides with heterocumulenes for the generation of thiazolidine-thiones, imino-thiazolines and oxazolidines in the absence of any transition metal catalyst. We started with the reaction of epoxy-sulfonamide **1a** with $CS_2$ in the presence of DMAP with $K_3PO_4$ or $K_2CO_3$ as the base in EtOH solvent (Table 1, entries 1-3). However, we observed only the ring rearrangement from *epoxide* **1a** to the *aziridine* product **8**. Such a reaction, although interesting, has been reported before.[80] When we performed the reaction in DMF with $K_2CO_3$ as the base (entry 7), apart from **8**, we obtained the *ring modified/expanded* product **9** in 10% yield (cf. Scheme 3). The presence of C=S (δ 196.9) and -

OH (band at 3401 $cm^{-1}$) groups in the product **9** were readily inferred by $^{13}C$ NMR and IR spectra, respectively. While the absence of NH moiety was indicated by $^{1}H$ NMR spectrum. HRMS data suggested the incorporation of $CS_2$ (*vide infra* for X-ray structure). In solvents like DMSO or $H_2O$ (entries 5-6), we obtained only the aziridine **8** (IR, NMR, HRMS). In the solvents THF, dioxane, toluene, acetonitrile and PEG-400 (entries 7-11) again, traces of **8** (but not **9**) were observed. Pleasingly, with NMP as the solvent and by using the inexpensive $K_2CO_3$ as the base (entry 12), we obtained the desired product **9** in 92% yield. Bases like $K_3PO_4$, $Cs_2CO_3$, NaOH, KOH (entries 13-16) did not enhance the yield. Thus the optimized conditions are: **1a** (0.4 mmol), $CS_2$ (2.0 mmol), $K_2CO_3$ (0.4 mmol) in NMP (1 mL) at 80 $^{o}C$ for 12 h. These conditions were utilized to obtain the desired thiazolidine-2-thiones **9-16** in good to excellent yields by starting with epoxy-sulfonamides **1a-h** (Table 2). The structure of compound **9** was further proven by single crystal X-ray analysis (Figure 2). In view of the reactions of aziridines with isothiocyanates,[29-33] we treated the (isolated) aziridine **8** with $CS_2$/NMP/$K_2CO_3$ (Scheme 4) and observed that this compound **8** remained unreacted. Thus our reaction leading to product **9** from **1a** follows a pathway different from that shown in Scheme 1.24-1.28 in Chapter 1 (i.e. not from aziridines).

**Scheme 3**

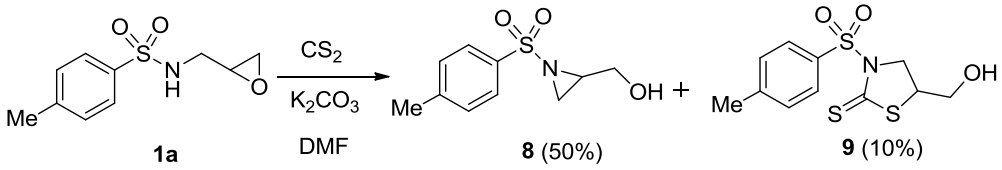
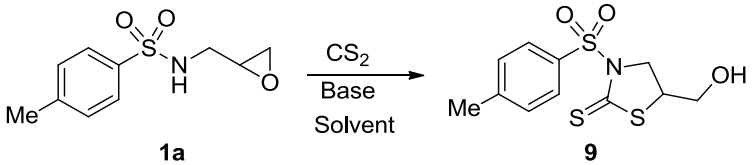



**Table 1.** Optimization of the conditions for the regioselective 5-*exo*-*tet* cyclization of **1a** with $CS_2$[a]




| Entry | Base | Solvent | Temp ($^{o}C$)/ time (h) | Yield of **9** (%)[b] |
|---|---|---|---|---|
| 1 | DMAP | EtOH | 80/12 | -[c] |

| | | | | |
|---|---|---|---|---|
| 2 | $K_3PO_4$ | EtOH | 80/12 | -[c] |
| 3 | $K_2CO_3$ | EtOH | 80/12 | -[c] |
| 4 | $K_2CO_3$ | DMF | 110/ 10 | 10 |
| 5 | $K_2CO_3$ | DMSO | 110/ 10 | -[d] |
| 6 | $K_2CO_3$ | $H_2O$ | 100/ 12 | -[d] |
| 7 | $K_2CO_3$ | THF | 65/ 10 | -[c] |
| 8 | $K_2CO_3$ | Dioxane | 110/ 12 | -[c] |
| 9 | $K_2CO_3$ | Toluene | 110/ 12 | -[c] |
| 10 | $K_2CO_3$ | Acetonitrile | 80/ 15 | -[c] |
| 11 | $K_2CO_3$ | PEG-400 | 110/ 12 | -[c] |
| **12** | **$K_2CO_3$** | **NMP** | **80/ 12** | **92** |
| 13 | $K_3PO_4$ | NMP | 80/ 12 | 85 |
| 14 | $Cs_2CO_3$ | NMP | 80/ 12 | 60 |
| 15 | NaOH | NMP | 80/ 12 | 84 |
| 16 | KOH | NMP | 80/ 12 | 85 |

[a] Reaction conditions: **1a** (0.4 mmol), $CS_2$ (2.0 mmol), Base (0.4 mmol) in solvent (1 mL) at the specified oil bath temperature for 10-12 h. [b]Isolated yields. [c]A small amount of aziridine **8** was noticed. [d]In these cases, the main product obtained was the aziridine **8** (see Scheme 4; yield: 40-50% after isolation).

**Scheme 4**

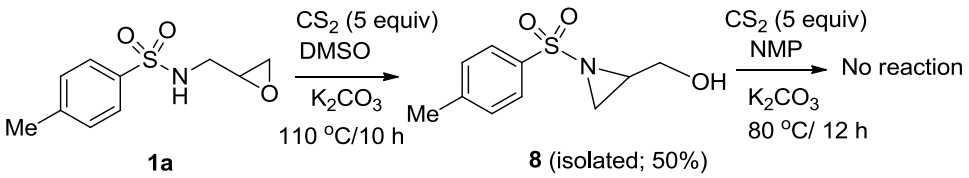
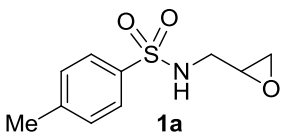
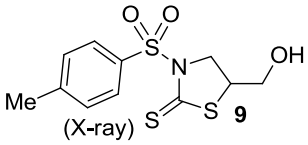
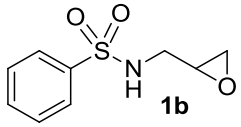
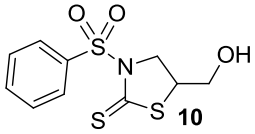
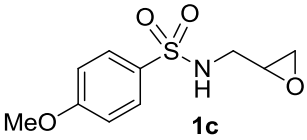
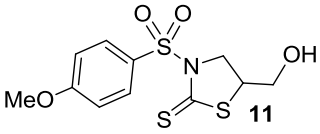
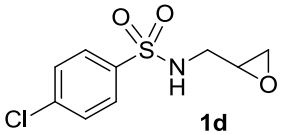
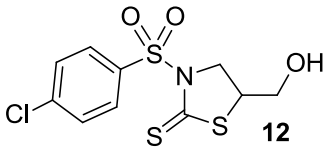
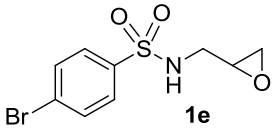
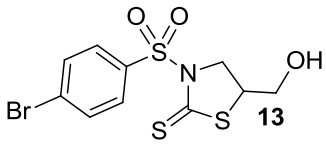
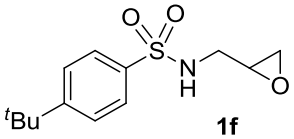
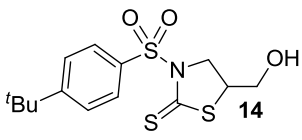
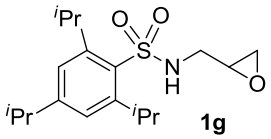
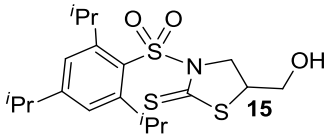
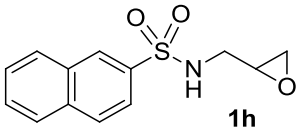
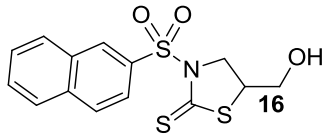


**Table 2.** Regioselective 5-*exo*-*tet* cyclization of epoxy-sulfonamides **1a-h** with $CS_2$ leading to thiazolidine-thiones **9**-**16**[a]

| Entry | Epoxy-sulfonamide | 1,3-Thiazolidine-2-thione derivatives | yield (%)[b] |
|---|---|---|---|
| 1 |  **1a** |  (X-ray) **9** | 92 |
| 2 |  **1b** |  **10** | 81 |
| 3 |  **1c** |  **11** | 92 |
| 4 |  **1d** |  **12** | 90 |
| 5 |  **1e** |  **13** | 91 |
| 6 |  **1f** |  **14** | 85 |

| | | | |
|---|---|---|---|
| 7 |  1g |  15 | 90 |
| 8 |  1h |  16 | 70 |

[a]Standard conditions: Epoxy sulfonamide (0.4 mmol) in NMP (1 mL), $CS_2$ (2.0 mmol) and $K_2CO_3$ (0.6 mmol) at 80 $^oC$ (oil bath) for 10-12 h. [b]Isolated yields.

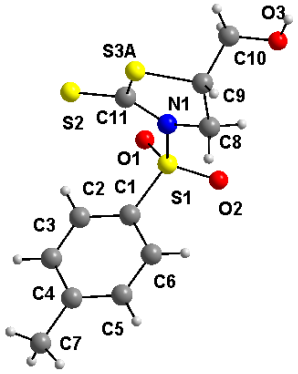



**Figure 2**. Molecular structure of compound **9**. The disordered S3B atom is not shown. Selected bond lengths [Å] with esds in parentheses: S1-N1 1.679(3), S2-C11 1.634(5), S3A-C11 1.751(5), C9-S3A 1.817(7), N1-C11 1.378(5), C8-C9 1.520(7).

### 2.3.2 Reaction of epoxy-sulfonamides with isothiocyanates and isocyanates

By extending the above conditions to the reaction of epoxy-sulfonamides with aryl-isothiocyanates/isocyanates (heterocumulenes), the expected thiazolidines/oxazolidines are obtained, but in addition, small quantities of products in which the terminal –OH group undergoes an addition reaction with isocyanate/ isothiocyanate are also formed. This problem could be readily alleviated by conducting the reaction at 80 °C for 24 h wherein the desired products **17–24** are almost exclusively formed (Scheme 5, Table 3; the yields shown are after isolation). Only in the reaction with $Me_3SiNCS$, the yield of the final product **24** was slightly lower probably because of the removal of the TMS group. The structure of compound **19** was

proven by single crystal X-ray analysis (Figure 3). A ready extension to the use of isocyanates was possible as demonstrated by the isolation of oxazolidines **25**–**26** (Table 3).

**Scheme 5**

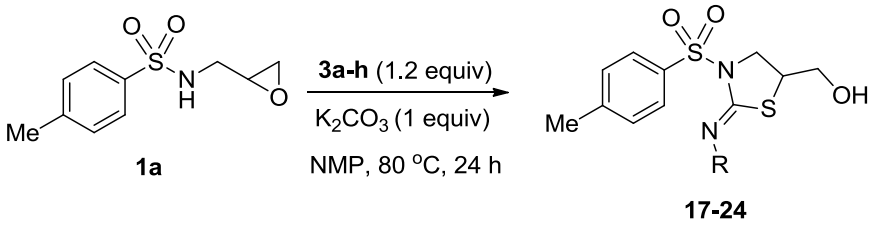
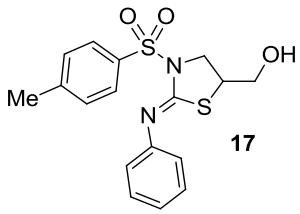
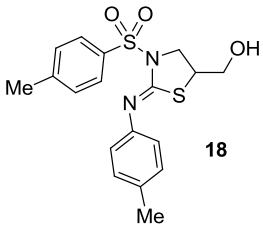
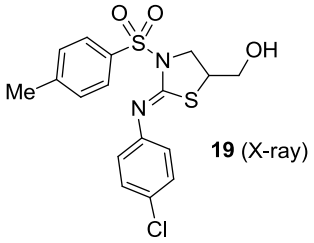
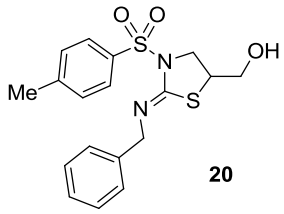
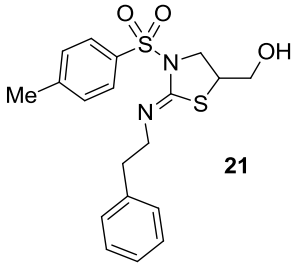
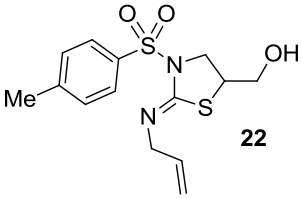
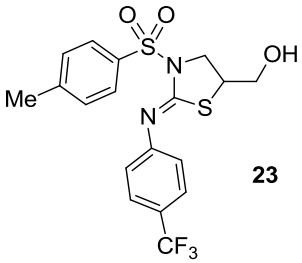
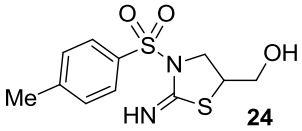
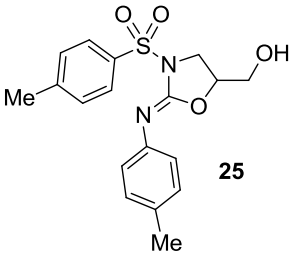
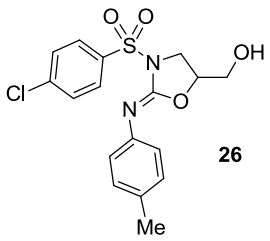



**Table 3.** Regioselective 5-*exo-tet* cyclization of epoxy-sulfonamides with isothiocyanates/ isocyanates leading to thiazolidines/oxazolidines **17-26**[a]

| Entry | Epoxy-sulfonamide | Isothocynate /isocyanate | Imino-thiazolidine/ oxazolidines derivatives | yield (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | **3a** |  **17** | 70 |
| 2 | **1a** | **3b** |  **18** | 88 |
| 3 | **1a** | **3c** |  **19** (X-ray) | 73 |

| | | | | |
|---|---|---|---|---|
| 4 | **1a** | **3d** |  **20** | 82 |
| 5 | **1a** | **3e** |  **21** | 83 |
| 6 | **1a** | **3f** |  **22** | 89 |
| 7 | **1a** | **3g** |  **23** | 80 |
| 8 | **1a** | **3h** |  **24** | 61 |
| 9 | **1a** | **4b** |  **25** | 74 |

| | | | | |
|---|---|---|---|---|
| 10 | **1c** | **4b** |  **26** | 69 |

[a]Standard conditions: Epoxy-sulfonamide **1a** (0.4 mmol) in NMP (1 mL), R-NCS **3a-h** or R-NCO **4b** (0.5 mmol) and $K_2CO_3$ (0.6 mmol) at 80 $^oC$ (oil bath) for 24 h. [b]Isolated yields.

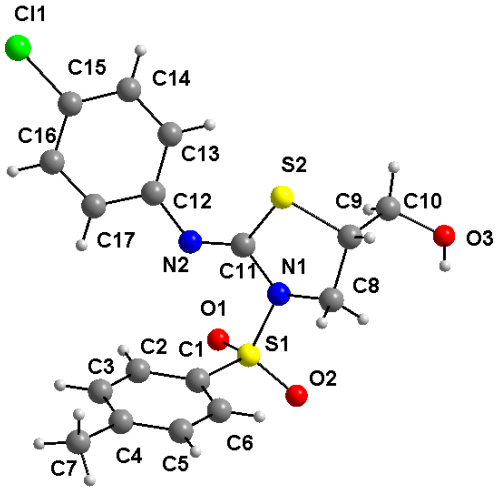



**Figure 3.** Molecular structure of **19**. Selected bond lengths [Å] with esds in parentheses: N1-C11 1.413(7), N2- C11 1.271(7), N2- C12 1.402(7), S2- C11 1.787(6), S2 C9 1.7948(18), O3-C10 1.419(9), S1 N1 1.679(5).

When the above reaction was conducted at rt (25 $^oC$) for only 10 h by increasing the stoichiometry of isocyanate or isothiocyanate, imino-thia/oxazolidine carbamates **27-30**, in which the terminal -OH group underwent addition, were obtained in moderate yields (Scheme 6). It can be noted that in compounds **27-29**, hydrolysis of the C=S to C=O also had taken place.[81] Since this was not the main theme of the present work, we did not proceed further.

**Scheme 6**

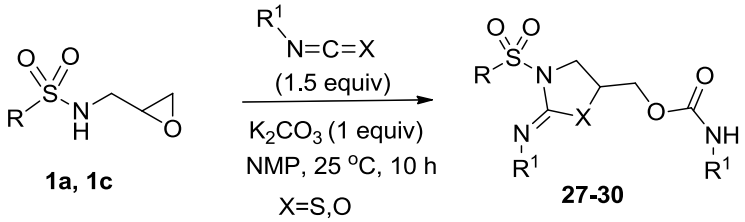
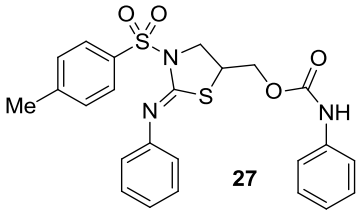
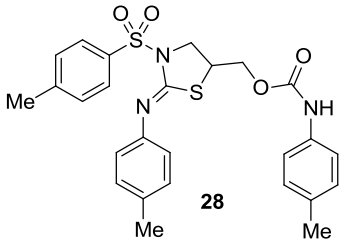
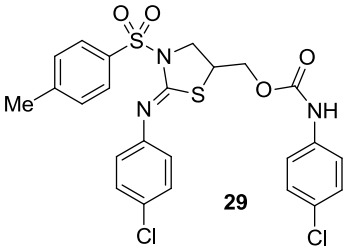
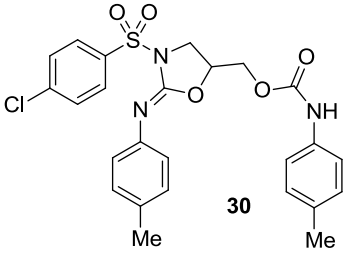


**Table 4.** Formation of imino-thiazolidine/oxazolidine carbamates **27-30**[a]

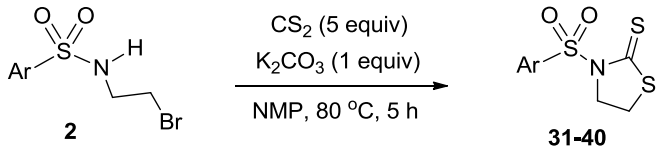
| Entry | Epoxy sulfonamide | Isothiocynate /isocyanate | Imino-thiazolidine/oxazolidine carbamates | yield (%)[b] |
|---|---|---|---|---|
| 1 | **1a** | **3a** |  **27** | 56 |
| 2 | **1a** | **3b** |  **28** | 60 |
| 3 | **1a** | **3c** |  **29** | 67 |
| 4 | **1c** | **4b** |  **30** | 62 |

[a]Standard conditions: Epoxy sulfonamide **1a/1c** (0.4 mmol) in NMP (1 mL), R-NCS/R-NCO (0.6 mmol) and $K_2CO_3$ (0.6 mmol) at rt (25 $^oC$) for 10 h. [b]Isolated yields.

### 2.3.3 Cyclization reaction of *N*-(2-bromoethyl)-sulfonamides with heterocumulenes (carbon disulfide, isothiocyanate or isocyanate)

We envisaged another viable route to the above class of compounds (but without substitution at the five-membered ring) by insertion of the heterocumulenes into bromoethyl-sulfonamides. Thus, treatment of *N*-(2-bromoethyl)-sulfonamides **2a-k** with carbon disulfide in NMP at 80 $^{o}$C for 5 h afforded thiazolidine-2-thiones **31-41** in good yields (Scheme 7; Table 5). These compounds are similar to thiazolidine-thione **9**, but do not contain the primary alcohol group. In this reaction, steric or electronic effects did not seem to affect the overall yield significantly. Interestingly, the 4-nitrophenyl sulfonyl group was cleaved to form the unsubstituted thiazolidine-thione **41**. The method could be conveniently extended to the synthesis of imino-thiazolidines and imino-oxazolidine **42-49** (Scheme 8; Table 6). The structures of compounds **32** (Figure 4 left) and **45** (Figure 4 right) were confirmed by X-ray crystallography.

**Scheme 7**



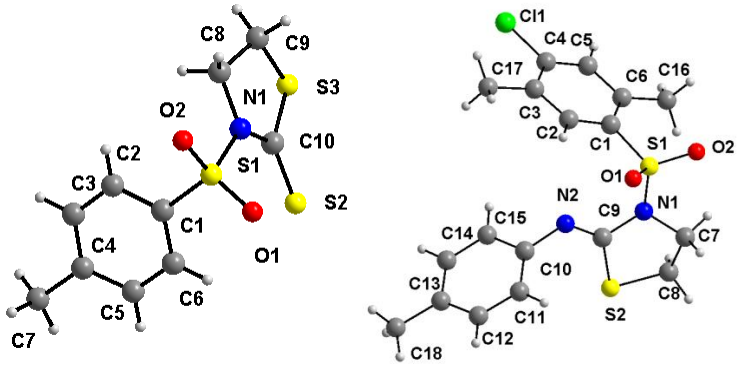
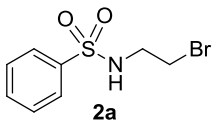
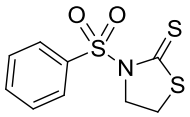
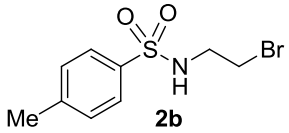
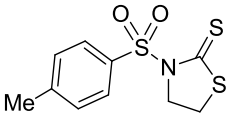
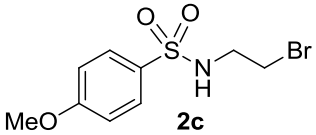
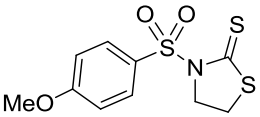
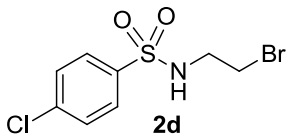
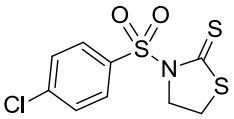
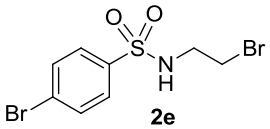
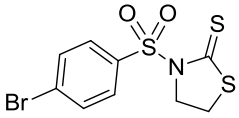
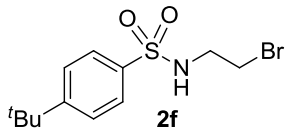
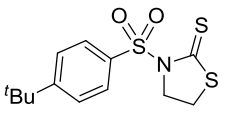
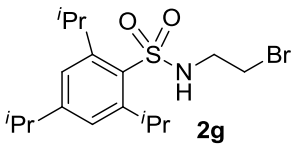
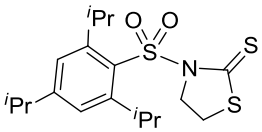
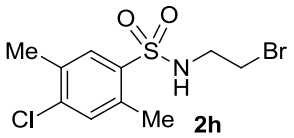
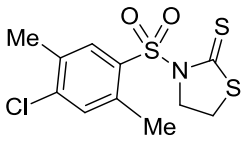
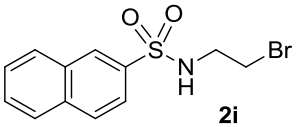
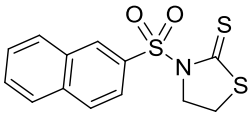
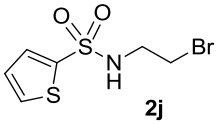
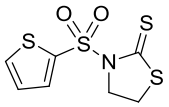
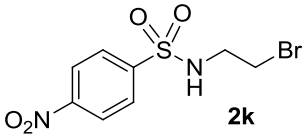
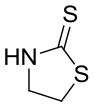




**Figure 4.** Molecular structures of compounds **32** and **45.** Selected bond lengths [Å] with esds in parentheses: Compound **32** S1-N1 1.693(3), S2-C10 1.618(3), S3-C10 1.745(3), S3-C9 1.786(4), C10-N1 1.365(4), C9-C8 1.492(6). Compound **45** N2-C9 1.269(4), N2- C10 1.407(4), S2-C9 1.742(3), N1-C7 1.470(4), S2-C8 1.795(4), N1-C9 1.412(4), S1-N1 1.661(3).

**Table 5.** Synthesis of thiazolidine-thiones **31-41** by HBr elimination/ heterocumulene insertion

| Entry | *N*-Bromoethyl-sulfonamides | 1,3-Thiazolidine-2-thione derivatives | yield (%)[a] |
|---|---|---|---|
| 1 |  **2a** |  **31** | 88 |
| 2 |  **2b** |  **32** (X-ray) | 85 |
| 3 |  **2c** |  **33** | 93 |
| 4 |  **2d** |  **34** | 88 |
| 5 |  **2e** |  **35** | 87 |
| 6 |  **2f** |  **36** | 82 |
| 7 |  **2g** |  **37** | 90 |

| | | | |
|---|---|---|---|
| 8 |  **2h** |  **38** | 80 |
| 9 |  **2i** |  **39** | 80 |
| 10 |  **2j** |  **40** | 88 |
| 11 |  **2k** |  **41** | 65 |

[a]Isolated yields

**Scheme 8**

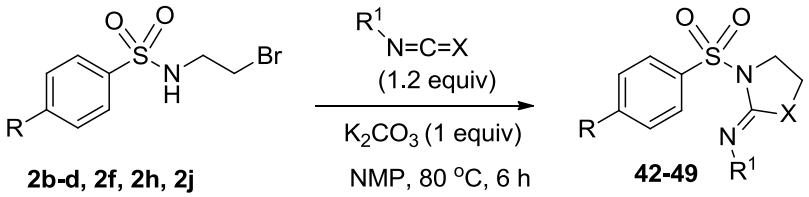
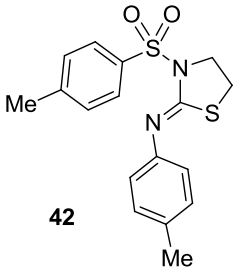
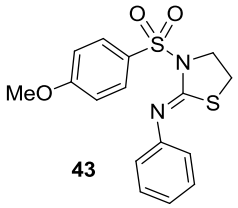
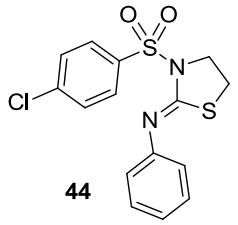
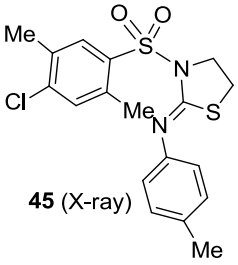
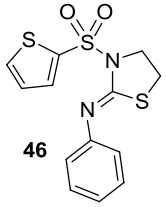
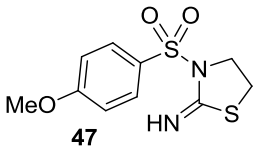
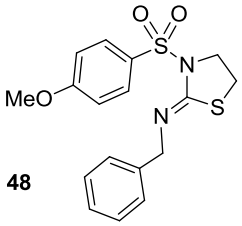
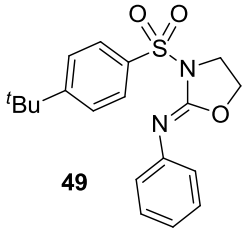


**Table 6.** Cyclization of *N*-(2-bromoethyl)-sulfonamides with R'NCS/ PhNCO leading to iminothiazolidines/iminooxazolidines **42-49**

| Entry | *N*-(Bromoethyl)-sulfonamides | Isothiocyanate/ Isocyanate | Imino-Thiazolidine/ oxazolidine derivatives | yield (%)[a] |
|---|---|---|---|---|
| 1 | **2b** | **3b** |  **42** | 82 |
| 2 | **2c** | **3a** |  **43** | 85 |
| 3 | **2d** | **3a** |  **44** | 79 |
| 4 | **2h** | **3b** |  **45** (X-ray) | 89 |
| 5 | **2j** | **3a** |  **46** | 87 |

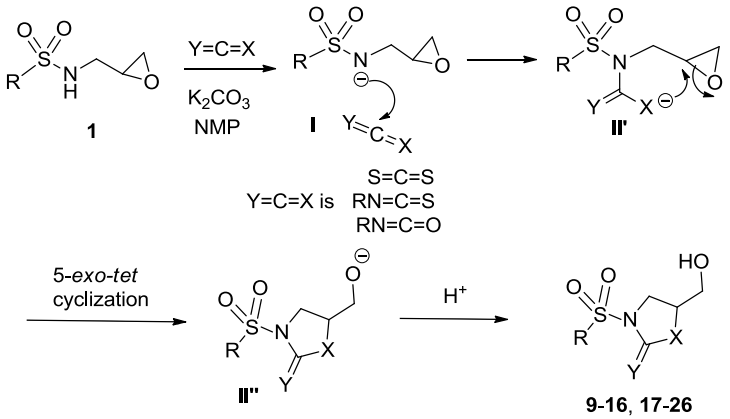
| | | | | |
|---|---|---|---|---|
| 6 | **2c** | **3h** |  **47** | 82 |
| 7 | **2c** | **3d** |  **48** | 86 |
| 8 | **2f** | **3a** |  **49** | 78 |

[a]Isolated yields

### 2.3.4 Possible pathway for the ring modification/expansion of epoxy-sulfonamides and thiazolidine-thiones/ imino-thiazolidines/oxazolidines from bromoethyl-sulfonamides

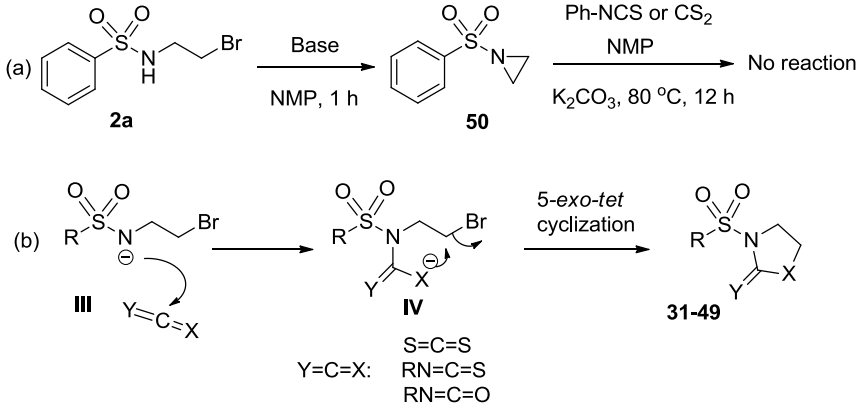
To conclusively establish that our reaction does not take place *via* the aziridine **8**, we treated it with Ph-NCS/NMP/$K_2CO_3$ and observed that it remained unreacted. Even with Ph-NCS/$Fe(NO_3)_3.9H_2O/H_2O$,[30] no significant reaction occurred. Thus our reaction leading to product **9-16** from **1** follows a pathway different from that of aziridines.[29-33] Based on the literature,[3c, 27, 82a] a plausible pathway for the formation of thiazolidine-2-thiones **9-16** and imino-thiazolidines/oxazolidines **17-26** is shown in Scheme 9. Initially, the base abstracts proton from epoxy-sulfonamide **1** generating intermediate **I** which attacks the central carbon atom of the $CS_2$/RNCS/RNCO affording thio/oxo anionic intermediate **II'**[3c, 82a] which will attack at the $2^o$ carbon atom of epoxide regioselectively, affording 5-*exo*-*tet* cyclized[27] alkoxide intermediate **II''**. This species upon protonation affords hydroxymethyl-thiazolidines-thiones/ iminothiazolidines/ iminooxazolidines **9-16** and **17-26**.

**Scheme 9**




We treated aziridine **50**[82b] (prepared from **2a**) with $CS_2$/NMP/$K_2CO_3$ as well as Ph-NCS/NMP/$K_2CO_3$ (Scheme 10a) and observed that this compound remained unreacted. So the plausible pathway for the formation of thiazolidine-thiones and imino-thiazolidines/oxazolidines does not involve aziridine, but instead follows a different pathway (Scheme 10b). Initially, as we explained before, the base abstracts proton from sulfonamide **2** and generates aza-anionic intermediate **III**. The species **III** attacks the central carbon atom of the $CS_2$/RNCS/RNCO affording thio/oxo anionic intermediate **IV**[3c, 82a] that subsequently leads to 5-*exo-tet* cyclized thiazolidine-thiones and imino-thiazolidines/oxazolidine **31-49**.

**Scheme 10**

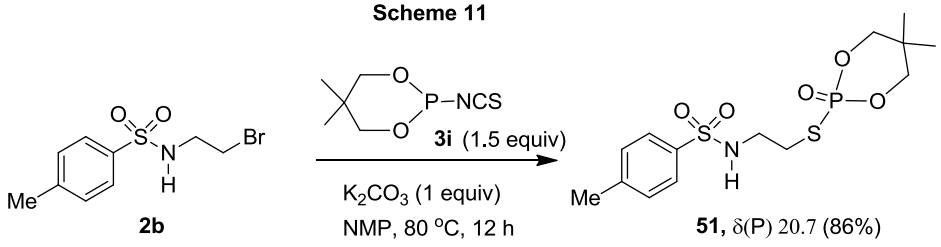



### 2.3.5 Reaction of *N*-(2-bromoethyl)-sulfonamide 2b with the isothiocyanatophosphite 3i

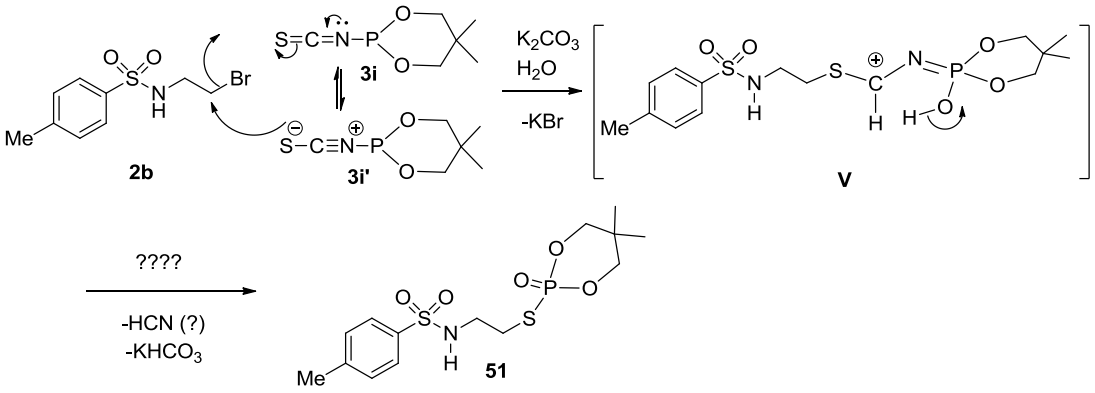
In our earlier work on P(III) compounds, we had noted that P(III) azides react in a manner different from organic azides.[78b, 83] Hence to know whether a P(III) isothiocyanate will react in a manner similar to the traditional organic isothiocyanates, we treated the precursor **3i** with the bromoethyl-sulfonamide **2b**. This reaction did take place, but in a direction entirely

different from the above, leading to the cyanogen bromide eliminated addition product **51**. IR, NMR ($^{1}$H and $^{13}$C) and HRMS data are consistent with the structure shown below (Scheme 11). A tentative pathway for its formation is shown in Scheme 11. Compound **3i** is in equilibrium with **3i'**, which will undergo substitution with bromoethyl-sulfonamide **2b** in the presence of adventitious moisture to afford intermediate **V**. This is followed by formation of P-S bond with the elimination of HCN to form **51** (Scheme 12). Clearly, this formulation looks far-fetched, but at the moment we do not have an alternative rationalization. In this case, new P-S and C-S bonds have been formed in addition to the oxidation at the phosphorus center. The structure of compound **51** was also confirmed by X-ray crystallography (Figure 5).

**Scheme 11**




**Scheme 12**



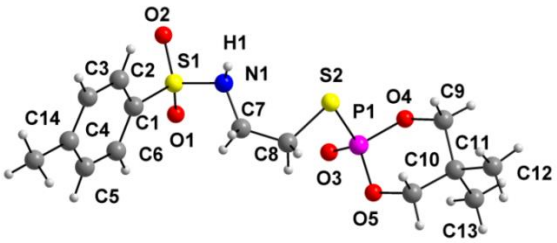
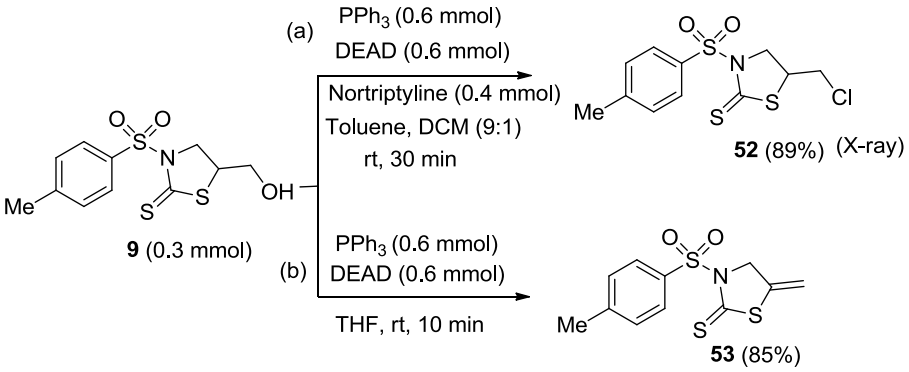



**Figure 5.** Molecular structure of compound **51**. The data quality was only moderate in this case. Selected bond lengths [Å] with esds in parentheses: N1-C7 1.404(8), C8-C7 1.398(9), S2-C8 1.777(7), P1-S2 2.052(4), P1-O3 1.427(7), N1-H1 0.751(11), S1-N1 1.583(10).

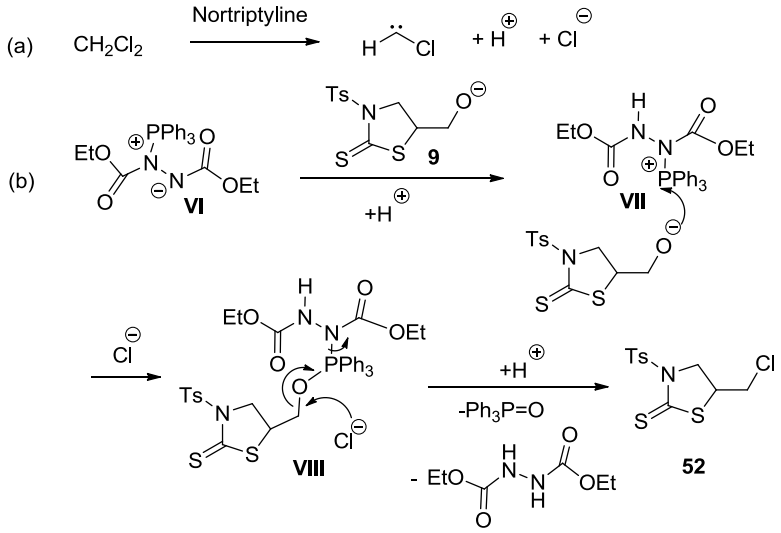
### 2.3.6 Mitsunobu reaction of 5-(hydroxymethyl)-3-tosylthiazolidine-2-thione 9 with $Ph_3P$/DEAD/nortriptyline

Product **9** (cf. Table 2) contains a pendent primary alcohol group that can undergo C-N coupling or dehydration *via* the Mitsunobu reaction.[84] Thus we treated **9** with $Ph_3P$/DEAD/nortriptyline in toluene/dichloromethane (9:1). Surprisingly, the chloro-substituted product **52** was obtained in good yield. Here, dichloromethane (DCM) acted as the chlorine source, which is not normal (Scheme 13a). Structure of **52** was further confirmed by single crystal X-ray analysis (Figure 6). In this reaction nortriptyline, most likely, acted as base and abstracted proton from dichloromethane to afford carbene and $H^+Cl^-$. This is consistent with the observation that when we conducted blank reaction of compound **9** with $Ph_3P$/DEAD/nortriptyline in toluene or THF without adding DCM, we did not observe any chlorinated product formation. The Mitsunobu redox system generates **VI** followed by **VII** (Scheme 14). The attack of alkoxide ion at the oxyphosphonium ion **VII** gives **VIII** that upon nucleophilic attack by chloride ion affords compound **52**, along with the byproducts $Ph_3P(O)$ and $EtO_2CNH\text{-}NHCO_2Et$. It is interesting to note that when we performed the reaction in THF as the solvent, the dehydration product **53** was formed in decent yields (Scheme 13b). Both the products **52-53** are amenable to further functionalization.

**Scheme 13**




**Scheme 14**



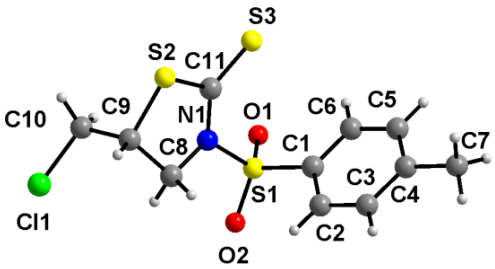
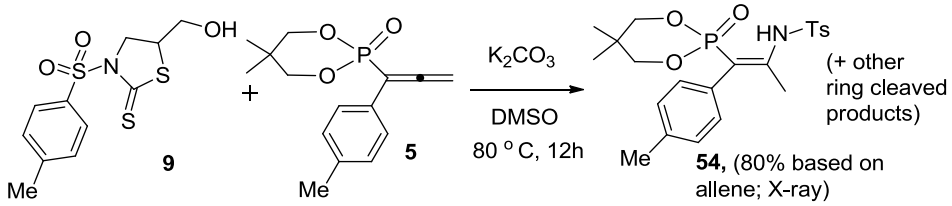




**Figure 6**: Molecular structure of **52** Selected bond lengths [Å] with esds in parentheses: S1-N1 1.705(5), S2-C11 1.733(6), S3-C11 1.635(6), C9-S2 1.808(6), N1-C11 1.367(8), C8-C9 1.527(8), Cl1-C10 1.776(6).

### 2.3.7 Reaction of 5-(hydroxymethyl)-3-tosylthiazolidine-2-thione 9 with allenylphosphonate 5

The central carbon of allenes is *sp*-hybridized and hence can readily undergo nucleophilic attack. We wanted to see if the double bonded sulfur or OH can act as a nucleophile in such a reaction. Thus when we treated allenylphosphonate **5**[78b] (0.3 mmol) with compound **9** in the presence of $K_2CO_3$ in DMSO solvent at 80 $^oC$ for 12 h, the NHTs addition product **54** was formed most likely by cleavage of the five-membered ring (Scheme15). Single crystal X-ray structure of compound **54** (Figure 7) confirms its identity. This result is consistent with the nucleophilicity of the allenic central carbon, but the fate of the thiazolidine ring could not be ascertained because of the formation of other products.

**Scheme 15**



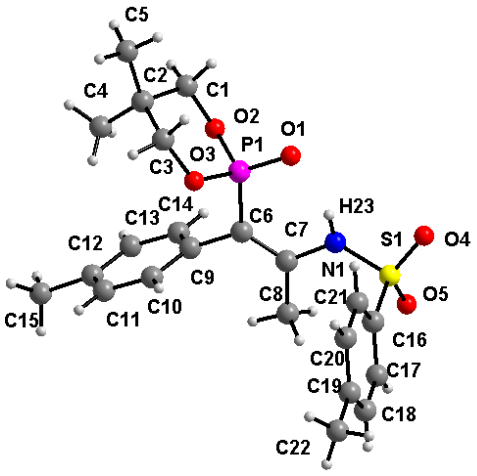




**Figure 7.** Molecular structure of **54**. Selected bond lengths [Å] with esds in parentheses: C7-C8 1.491(4), N1-C7 1.398(4), S1-N1 1.630(3), N1-H23 0.80(4), C7-C6 1.349(4), C9-C6 1.498(4), P1-C6 1.775(3).

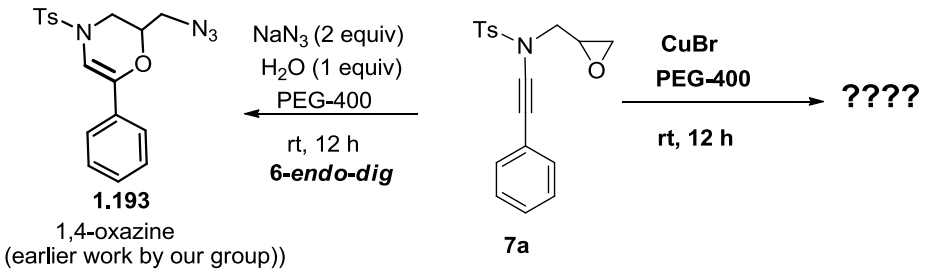
## 2.4 Cyclization reactions of epoxy-ynamides

From the literature reports presented in Chapter 1, it is clear that ynamides are highly useful precursors for the synthesis of heterocyclic compounds. Due to the presence of activated alkyne moiety and epoxide ring, epoxy-ynamides are interesting precursors for generating nitrogen and oxygen containing heterocycles. This section is devoted to a new reaction leading to 1,3-oxazolidines and 1,4-oxazines.

### 2.4.1 CuBr mediated concomitant bromination/cyclization reactions of epoxy-ynamides

In continuation of our interest in the reactivity of functionalized ynamides,[19, 45-46, 71] in this section we discuss CuBr mediated bromination and concomitant intramolecular 5-*exo*-*dig* cyclization of epoxy ynamides to obtain 1,3-oxazolidines. Our initial aim was to open up the epoxide ring and then cyclization as shown in Scheme 16, because in an earlier example our group had shown that sodium azide reacts with such ynamides to afford 1,4-oxazines at 25 $^{o}$C.[71]

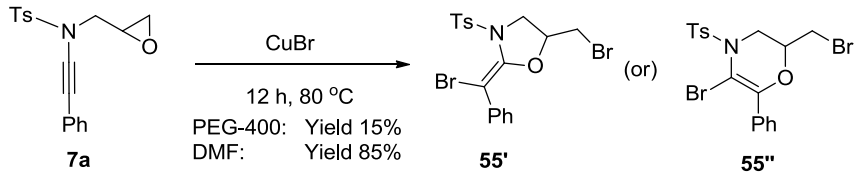
**Scheme 16**




In the above context, when we treated 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-(phenylethynyl) benzenesulfonamide **7a** with CuBr (2 equiv) in PEG-400 for 12 h at rt (25 $^{o}$C), we did not observe any product formation. Interestingly though, when the reaction was conducted at 80 $^{o}$C (oil bath temperature), we isolated ring expanded cyclized product **55** in 15% yield (Scheme 17). Absence of υ(*C*≡*C*) stretch in the IR spectrum and disappearance of peaks due to *C*≡*C* bond in the $^{13}$C NMR spectra indicated that the alkyne part of ynamide was involved in the reaction. Moreover, we did not observe (i) alkenyl =C-*H* proton at δ ~ 5.5-7.0 in the $^{1}$H NMR spectrum and (ii) peak at δ ~93 in the $^{13}$C spectrum. These features suggested that a compound similar to **1.193** was not formed. HRMS data indicated that the product contained two

bromine atoms (1:2:1 pattern). A possible structure for the product is ring expanded cyclized derivative **55'** or **55''**, both of which have the same molar mass. When we checked the reaction by changing the solvents from PEG-400 to toluene, DMSO, $(EtO)_2CO$, THF, NMP, 1,4-dioxane or DCM, we did not observe any product formation, with the starting material remaining unreactive. Surprisingly, when we tried this reaction in dry DMF with 2 equiv of CuBr at 80 $^oC$, within 2 h total starting material was consumed and we obtained product **55'/55"** in 85% yield. Further, we checked the reaction with other polar solvents like MeOH, DMA and acetonitrile, but no product was observed. When we changed the nucleophile source to $CuBr_2$ or $Br_2$ or AgBr, again product formation was not detected. Thus the optimal reaction conditions for this cyclization are: **7a** (1.0 equiv) in dry DMF (1 mL) as the solvent and CuBr (2 equiv) as mediator/reactant (Br donor) at 80 $^oC$ (oil bath temperature) for 2 h.

**Scheme 17**




We then explored the substrate scope for this bromination/ cyclization of epoxy-ynamides (Scheme 18; Table 7). When we treated *N*-((3-fluorophenyl)ethynyl)-4-methyl-*N*-(oxiran-2-ylmethyl)benzenesulfonamide **7b** with CuBr, we obtained ring expanded cyclized product **56** in 83% yield as a solid with *E/Z* ratio of 78:22. Fortunately, we could obtain single crystals from ethyl acetate and hexane solvent mixture (1:2). Based on the single crystal X-ray analysis (Figure 8), we confirmed that the formed ring expanded cyclized product is 5 membered *E*-1,3-oxazolidine, but not the 6 membered 1,4-oxazine i.e. oxide ion attacks regio-selectively at *α*-position of alkyne part of ynamide. Sulfonyl attached phenyl or 4-*t*-butylphenyl and naphthyl groups **57-59** gave good yields with almost entirely *E*-selectivity. But in the case of tolyl, and 4-bromophenyl substituents on alkyne attached aryl group of the epoxy ynamide, 1,3-oxazolidines **60-61** in 80-84% yields with *E/Z* ratio 86:14 and 54:46, respectively in a regioselective manner. Benzyl sulfonyl-epoxy ynamide also underwent this cyclization to afford 1,3-oxazolidine **62** in

highly regio- and stereo-selective manner. In compound **56**, the C11-C12 distance of 1.326(6) Å establishes the presence of a double bond between these two atoms. Three single bonds Br(1)-C(10), O(3)-C(11) and C(12)-Br(2) are newly formed.

**Scheme 18**

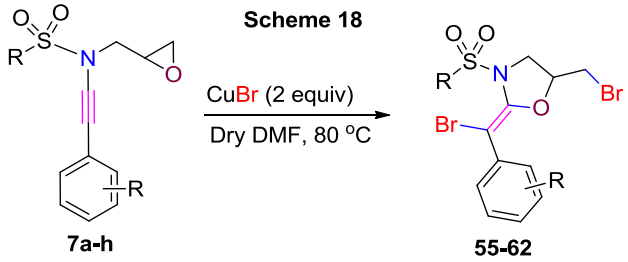
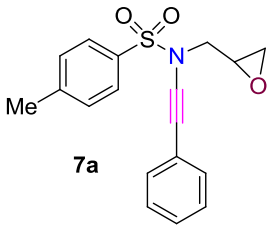
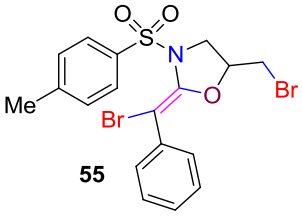
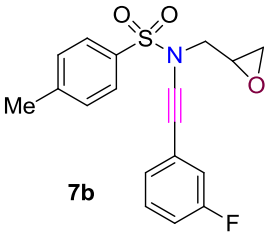
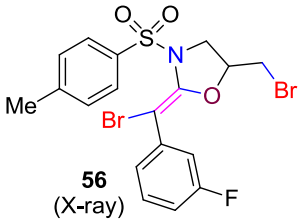
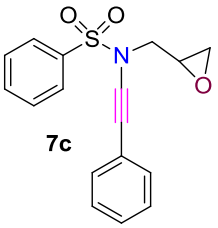
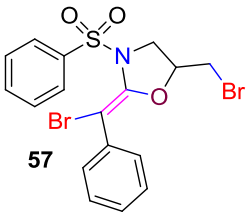
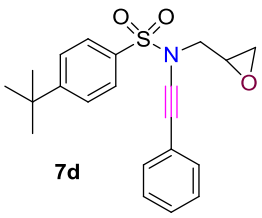
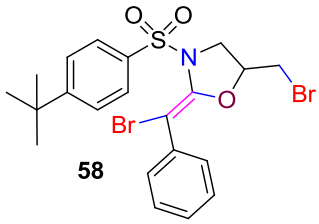
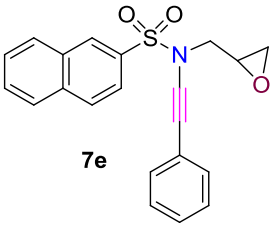
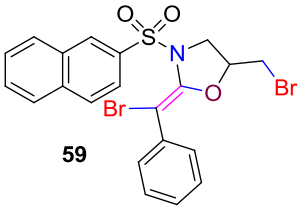
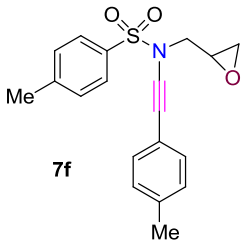
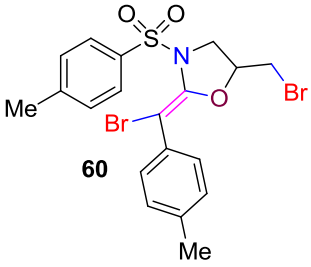
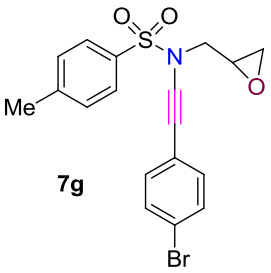
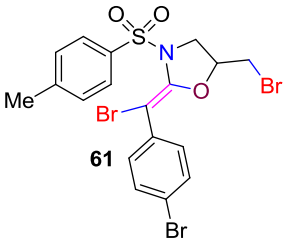
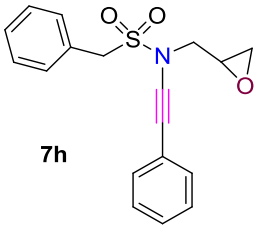
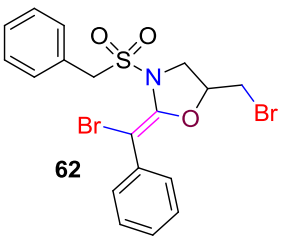



**Table 7.** Regio-selective synthesis of 1,3-oxazolidines **55-62** from epoxy-ynamides **7a-h**[a]

| Entry | Epoxy-ynamide | 1,3-Oxazolidine derivatives | yield (%)[b] |
|---|---|---|---|
| 1 |  **7a** |  **55** | 88 *E*:*Z* 96:4 |
| 2 |  **7b** |  **56** (X-ray) | 83 *E*:*Z* 78:22 |
| 3 |  **7c** |  **57** | 80 *E*:*Z* 88:12 |

| | | | |
|---|---|---|---|
| 4 |  **7d** |  **58** | 82<br>*E:Z* 92:8 |
| 5 |  **7e** |  **59** | 78<br>*E:Z* 96: 4 |
| 6 |  **7f** |  **60** | 86<br>*E:Z* 86:14 |
| 7 |  **7g** |  **61** | 78<br>*E:Z* 54:46 |
| 8 |  **7h** |  **62** | 85<br>*E:Z* 94:6 |

[a]Standard conditions: Epoxy-ynamides **7a-h** (0.3 mmol) in dry DMF (1 mL), CuBr (0.6 mmol) at 80 $^{o}$C for 2-4 h. [b]Isolated yields.

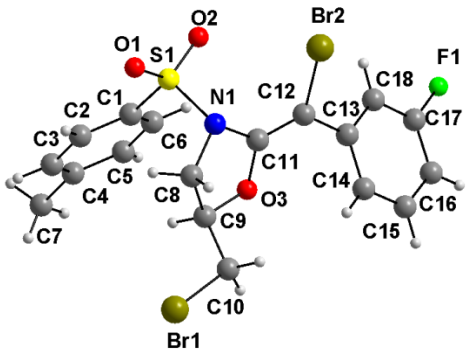
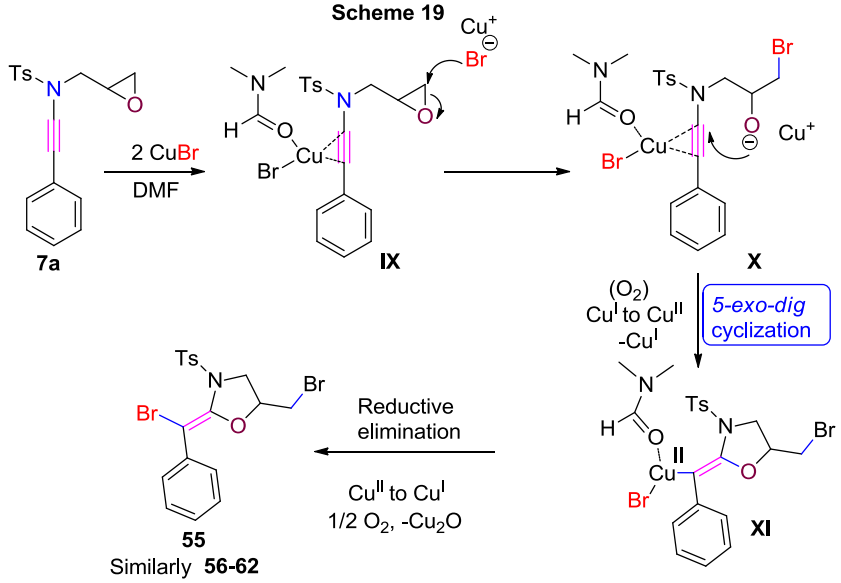



**Figure 8**. Molecular structure of compound **56**. Selected bond lengths [Å] with esds in parentheses: S1-N1 1.694(4), N1-C8 1.479(6), O3-C9 1.441(5), O3-C11 1.358(5), C11-C12 1.326(6), Br2-C12 1.899(4), Br1-C10 1.928(5), C9-C10 1.491(7), C12-C13 1.477(5).

### 2.4.2 Possible pathway for 5-*exo*-*dig* cyclization of epoxy-ynamide with CuBr

Based on the single crystal X-ray analysis and literature reports,[85] we propose the following pathway for the formation of 1,3-oxazolidine **55** (Scheme 19). Initially, CuBr co-ordinates with alkyne of the ynamide and DMF. This is followed by opening of epoxide ring by the attack of bromide ion [from one more CuBr] on epoxide ring from less hindered side of the epoxide group leading to intermediates **IX**-**X**. Later, the formed oxide ion will undergo intramolecular **5-*exo*-*dig*** cyclization involving the $\alpha$-position of the ynamide resulting in intermediate **XI**. This is followed by reductive elimination and bromination at $\beta$-carbon delivering the cyclized product **55**. In this process, we suspect that at the intermediate level, water may be coordinated to Cu(II), but in the overall process, oxygen may be involved. This aspect needs to be investigated further.

Scheme 19




The striking features of the above reaction is the highly regio-selective ring expansion of epoxide ring and dibromination by using CuBr to afford functionalized ***1,3-oxazolidines***. Most of the 1,3-oxazolidines except that with alkyne attached to $-C_6H_4Br$ group are *E*-predominant. In continuation of this study, we discuss below one more interesting reaction involving intermolecular nucleophilic attack of $Cl^-$ on epoxy-ynamides that leads to ***1,4-oxazines.***

### 2.4.3 Regioselective synthesis of 1,4-oxazines by the tandem 6-*endo-dig* cyclization of epoxy-ynamides using LiCl

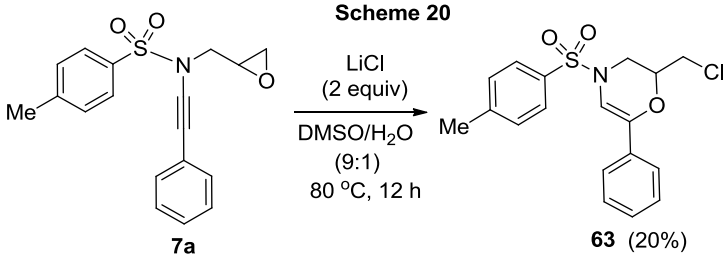
Due to the presence of electron withdrawing group on nitrogen atom of ynamide, the $\alpha$-position of alkyne moiety is more electropositive in nature, thus mostly nucleophiles will attack at this position,[86] whereas the electrophiles attack the $\beta$-position.[49, 54-55] Attack of nucleophile at the $\beta$-position of ynamides (umpolung) is rarely explored.[71, 87] In this context, a transition metal free, regioselective synthesis of 1,4-oxazines by tandem-cyclization of epoxy ynamides in their reaction with LiCl is discussed below.

### 2.4.4 Reaction of epoxy ynamide 7a with LiCl

Lithium chloride is a typical ionic compound, but even with the small size of $Li^+$ ion, this salt is highly soluble in polar solvents and is fairly hygroscopic. Its function as a chloride transfer agent is not particularly common, but in this study, as descried below, we have encountered this

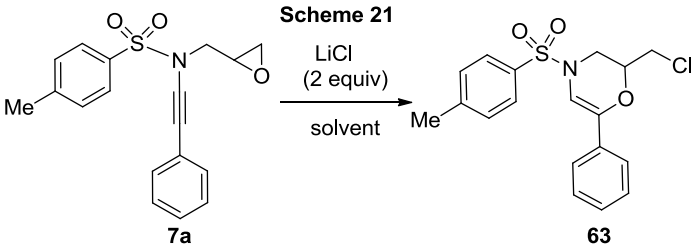
fascinating observation. At first, we did the reaction between 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-(phenylethynyl) benzene sulfonamide **7a** and LiCl (2 equiv) in DMSO/$H_2O$ mixture (9:1) at 80 $^oC$ for 12 h. Surprisingly, the cyclized product **63** was isolated in 20% yield in the absence of any transition metal catalyst (Scheme 20). Based on the disappearance of alkyne band at ~ 2200 $cm^{-1}$ in the IR spectrum, absence of alkyne peaks in $^{13}C$ NMR spectrum and appearance of alkenyl C-H peak at $\delta$ 6.7 in $^1H$ NMR spectra, we assumed that the formed product is epoxide ring expanded cyclized one (cf. Scheme 20) analogous to an earlier report on the reaction of epoxy-ynamides with $NaN_3$ from our research group.[71]

**Scheme 20**




**7a** **63** (20%)

To increase the yield of the cyclized product **63**, we checked several reaction conditions by varying the solvent system (Scheme 21). When we performed the reaction in NMP and PEG-400 the product was formed in traces; in solvents like toluene, chlorobenzene, THF, DMA, acetonitrile, dioxane, EtOAc, MeOH, or water also we did not observe any product formation. One equivalent of water that is required for the transformation was also added to the solvent in all these cases. But when we used DMF as the solvent, pleasingly, we obtained the product in 78% yield with excellent regio-selectivity. The reaction with the same solvent did not occur at rt (25 $^oC$). Increasing the amount of $H_2O$ to 2 equiv decreased the yield due to the formation of byproducts which were not isolated. There was no reaction using $AlCl_3$ or CuCl and use of $FeCl_3$ in place of LiCl gave a mixture of products. Thus the optimal reaction conditions for this cyclization reaction were: **7a** (1.0 equiv), LiCl (2.0 equiv), and $H_2O$ (1 equiv) in DMF solvent at 80 $^oC$ (oil bath temperature) for 12 h.




After having optimized conditions in hand, we explored the substrate scope for the cyclization reaction of epoxy-ynamides with LiCl (Scheme 22; Table 8). Substrates possessing phenyl or naphthyl group attached to -$SO_2$ moiety also offered the corresponding ring expanded cyclized product **64** or **65** in 74 or 69% yield respectively. But sulfonyl attached electron withdrawing group (4-chloro-2,5-dimethyphenyl; cf. **68**) marginally reduced the yield to 65%. The scope of this method could be extended by changing the substituents on alkyne attached aryl group of the epoxy ynamide. Electron withdrawing groups attached aryl group of alkyne gave slightly lower yield (cf. **67**; ~62%). Electron releasing groups attached aryl group of alkynes gave good yields of **66** and **69** (74-77%). The reaction was clean and afforded dihydro-1,4-oxazine **70** in 69% when thiophene group attached to -$SO_2$ moiety used. The structures of cyclized product **67** (Figure 9) was further confirmed by single crystal X-ray diffraction. In compound **66**, The C12-C11 distance 1.332(3) Å establishes the presence of a double bond between these two atoms. Two single bonds C(10)-Cl(1) and O(3)-C(11) are newly formed.

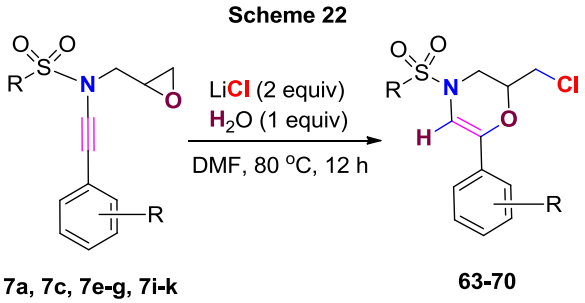
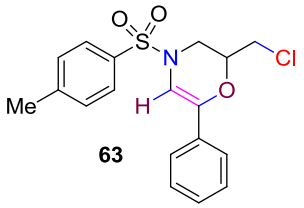
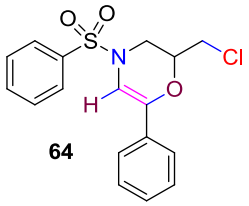
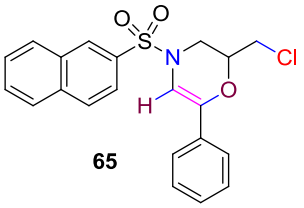
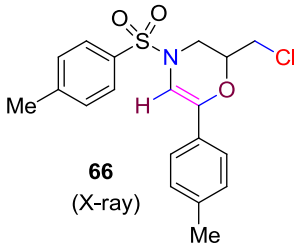
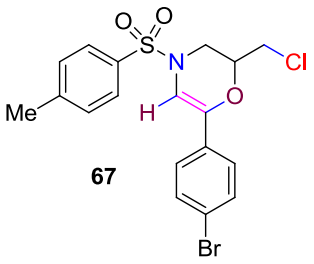
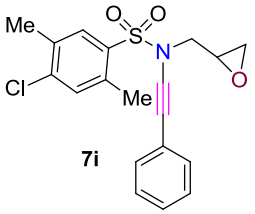
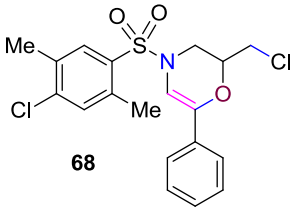
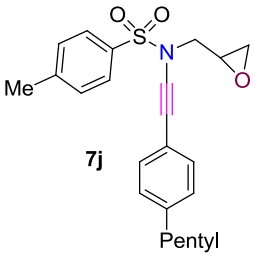
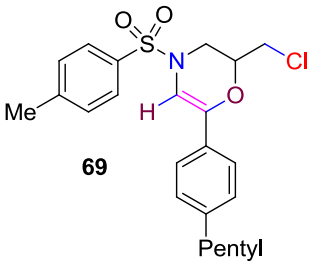
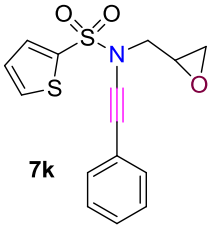
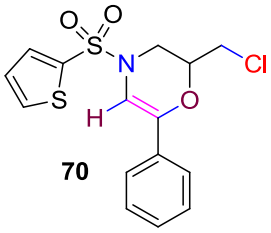


**Table 8.** Regio selective synthesis of 1,4-oxazine derivatives from epoxy ynamides and LiCl

| Entry | Epoxy ynamide | 1,4-Oxazine | Yield (%)[b] |
|---|---|---|---|
| 1 | **7a** |  **63** | 78 |
| 2 | **7c** |  **64** | 74 |
| 3 | **7e** |  **65** | 69 |
| 4 | **7f** |  **66** (X-ray) | 77 |
| 5 | **7g** |  **67** | 62 |

| | | | |
|---|---|---|---|
| 6 |  **7i** |  **68** | 65 |
| 7 |  **7j** |  **69** | 74 |
| 8 |  **7k** |  **70** | 69 |

[a]Standard conditions: Epoxy ynamide **7a**, **7c, 7e-g**, **7i-k** (0.3 mmol) in dry DMF (1 mL), LiCl (0.6 mmol) at 80 $^{o}$C (oil bath temperature) for 12 h. [b]Isolated yields.

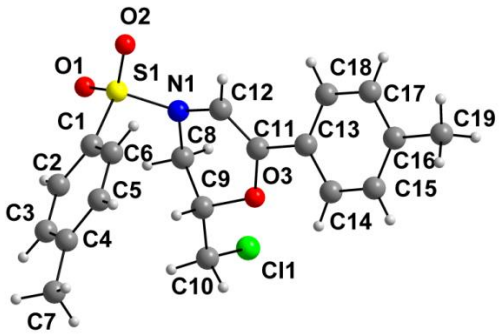
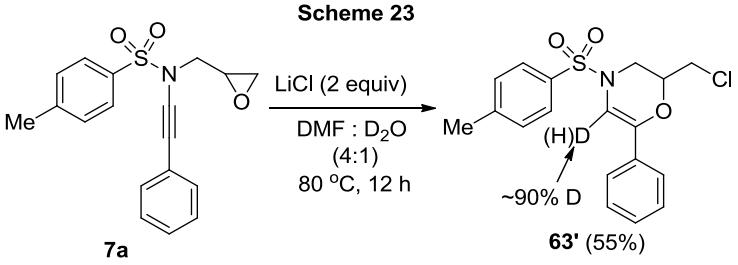



**Figure 9**. Molecular structure of compound **66**. Selected bond lengths [Å] with esds in parentheses: S1-N1 1.6563(19), N1-C8 1.470(3), N1-C12 1.419(3), C12-C11 1.332(3), C13-C11 1.471(3), O3-C11 1.377(2), O3-C9 1.436(3), Cl1-C10 1.770(3), C9-C8 1.504(3), C9-C10 1.514(3).

### 2.4.5 Control experiment

To understand the plausible pathway of the above chlorination/ cyclization reaction, we have performed deuterium-labelling experiment. Thus the reaction using epoxy ynamide (**7a**; 1.0 equiv) and LiCl (2.0 equiv) in DMF:$D_2O$ (4:1) furnished compound (**63'**; Scheme 23). Notably, ~90% deuterium incorporation was observed at the alkenyl C-*H* position of **63'**. Formation of the deuterium incorporated compound **63'** clearly suggests the key role of water as a proton source in the cyclization process.

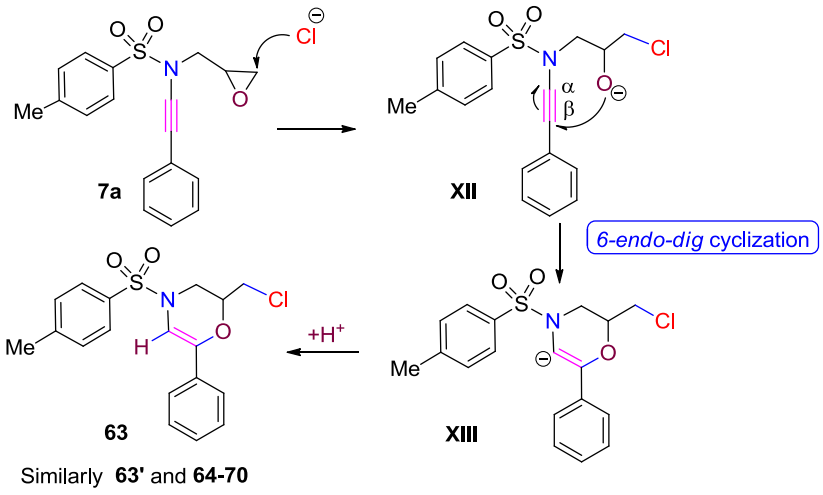
**Scheme 23**




### 2.4.6 Possible pathway for the formation of 1,4-oxazine 63

On the basis of the control experiment, and our group earlier report[71] we propose the following possible pathway for the formation of 1,4-oxazine **63** (Scheme 24). Initially, chloride ion will attack epoxide ring from less hindered side (intermolecular nucleophilic attack) of epoxide group of epoxy ynamide leading to intermediate **XII**. Thus formed oxide ion will undergo intramolecular **6-*endo-dig*** cyclization at the *β*-position of the ynamide resulting in intermediate **XIII**. This is followed by the protonation which delivers the cyclized product **63**.

**Scheme 24**



The noteworthy features of the above reaction are (i) the intermolecular nucleophilic ring opening of epoxide and intramolecular 6-*endo-dig* and (ii) highly regioselective cyclization at *β*-position of alkyne part of ynamide by alkoxide ion, to afford functionalized ***1,4-oxazines***.

## 2.5 Addition reactions of ynamides

From the literature reports presented in Chapter 1, ynamides are flawless precursors for the synthesis of enamides which are highly useful scaffolds in many organic transformations.[88] Hence we discuss two more interesting reactions below, one involving intermolecular haloaddition reaction of epoxy ynamides with ICl that leads to functionalized enamides and the other, dibromination of ynamides with CuBr.

### 2.5.1 ICl addition reactions of epoxy ynamides

We treated epoxy ynamides **7a**, **7l-7m** with 1M solution of ICl in $CH_3CN$ (0.5 mL) at 0 $^oC$ for 10 min and obtained highly regioselective *E/Z*-isomeric mixture (1:1) of *α*-chloro-*β*-iodoenamide derivatives **71-73** in good yields. In this transformation, along with addition reaction, intermolecular $S_N2$ nucleophilic ring opening of epoxide part of the ynamide by chloride ion occurs simultaneously (Scheme 25). Both electron -releasing and -withdrawing groups attached to sulfonyl/alkyne group of ynamide underwent addition reactions in a facile manner to give good yields of the products. A band due to OH group is observed at ~ 3534 $cm^{-1}$ in the IR spectra as expected. Also $^{13}C$ NMR spectra showed the absence of alkyne peaks. Here, electrophilic addition reactions are highly favorable in contrast with the corresponding 5-*exo-dig* and/or 6-*endo-dig* halo-cyclization reactions of epoxy-ynamides with CuBr/LiCl. The structures of the addition products **71** and **73** (Figure 10) were confirmed by single crystal X-ray diffraction (due to the low quality of the crystals and weakly diffracting nature we could not get good data). In compound **71**, the C8-C9 distance [1.340(10) Å] proved the presence of a double bond between these two atoms. Three single bonds Cl(1)-C(8), C(l2)-C(18) and I(1)-C(9) are newly formed. Similar structural features are observed in compound **73** also. Crystal structures of the compound **71** and **73** show I•••O halogen bonding interactions. (Figure 11).[89]

Scheme 25

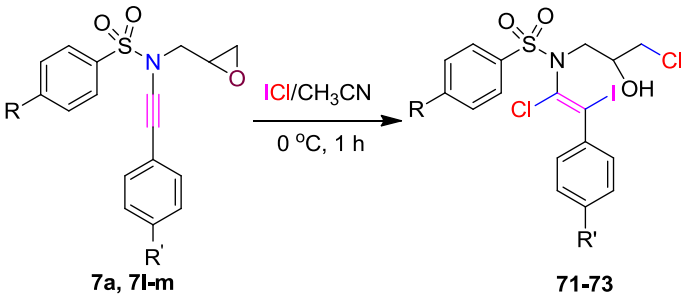
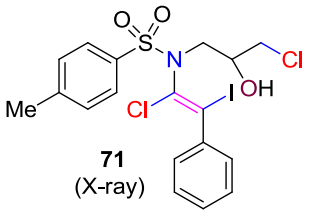
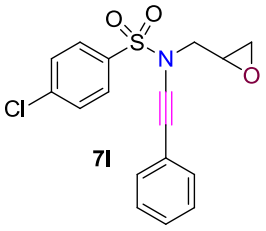
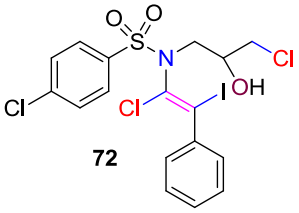
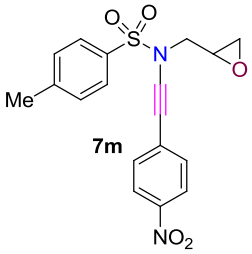
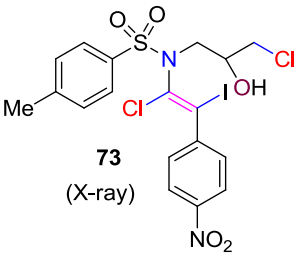



**Table 9:** Regioselective synthesis of *α*-chloro-*β*-iodoenamide derivatives from reaction of epoxy-ynamides with ICl

| Entry | Epoxy-ynamide | *α*-chloro-*β*-iodoenamide derivatives | yield (%)[a] |
|---|---|---|---|
| 1 | **7a** |  **71** (X-ray) | 89 *E*/*Z* 53:47 |
| 2 |  **7l** |  **72** | 85 *E*/*Z* 53:47 |
| 3 |  **7m** |  **73** (X-ray) | 82 *E*/*Z* 51:49 |

[b]isolated yields.

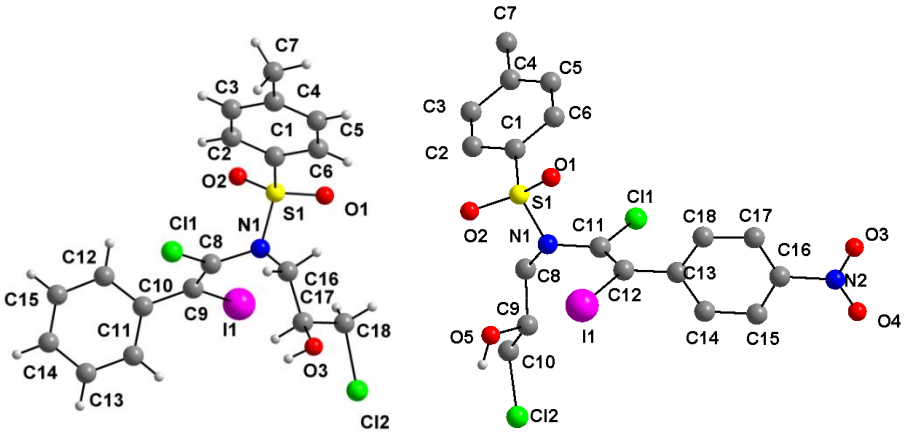



**Figure 10**: Molecular structure of compound **71** (left) Selected bond lengths [Å] with esds are given in parentheses: I1-C9 2.099(7), C9-C8 1.340(10), Cl1-C8 1.754(8), C16-C17 1.494(15), C18-C17 1.44(2), O3-C17 1.550(18), Cl2-C18 1.908(15); compound **73.** $CH_2Cl_2$ (right, solvent molecule is omitted): I1-C12 2.116(10), C11-C12 1.315(13), C12-C13 1.447(13), Cl1-C11 1.747(10), Cl2-C10 1.789(15), O5-C9 1.464(16), N1-C11 1.411(12).

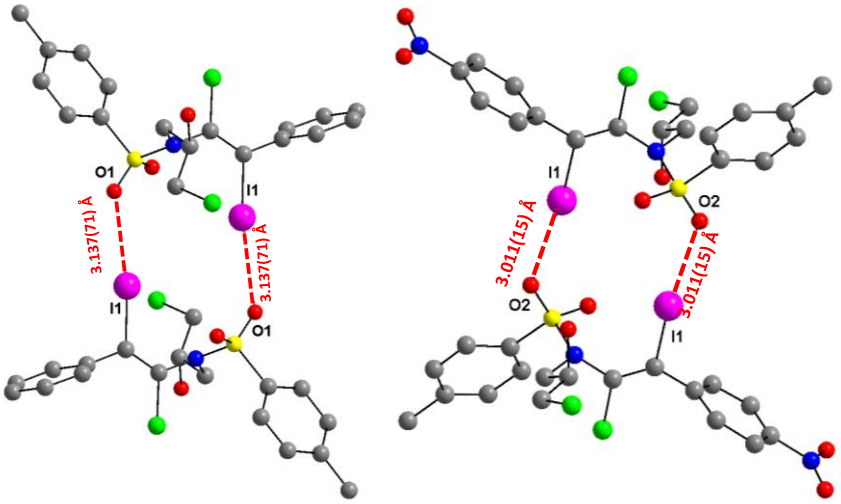



**Figure 11:** I•••O distances in compounds **71** and **73** are 3.137(71) Å and 3.011(15) Å, respectively. These are considerably shorter than the sum of the corresponding van der Waals radii of O (1.52 Å) and I (1.98 Å) i.e. they are <3.50 Å. [Note: Average I-O covalent bond distance: 2.14 Å].

### 2.5.2 Addition reaction of ynamides with CuBr

When we treated *N*-(2-bromoethyl)-4-methyl-N-(phenylethynyl)benzenesulfonamide **74** with CuBr at 0 $^{o}$C, rather surprisingly, we obtained exclusively *E*-*α*,*β*-dibromo-enamide **75** in good yields within a very short period of time (5 min, Scheme 26). A band due to alkyne group at 2200 cm$^{-1}$ was not observed in the IR spectrum as expected. Also, $^{13}$C NMR spectrum showed the absence of alkyne peaks and appearance of alkene peaks at δ 114; absence of alkenyl C*H* peak in the $^{1}$H NMR spectrum indicated that dibromination may have occurred on alkyne moiety. The structure of addition product **75** was confirmed by single crystal x-ray analysis (Figure 12a, left). The C8-C9 distance 1.309(6) Å proved the presence of a double bond between these two atoms. Two single bonds Br(2)-C(8) and Br(3)-C(9) are newly formed. Crystal structure of the compound **75** have bromine to carbon halogenic bonding interactions (Br•••(C4; π-system)). The distance between (Br•••(C4; π-system)) is 3.414(4) Å.( Figure 12b, right).

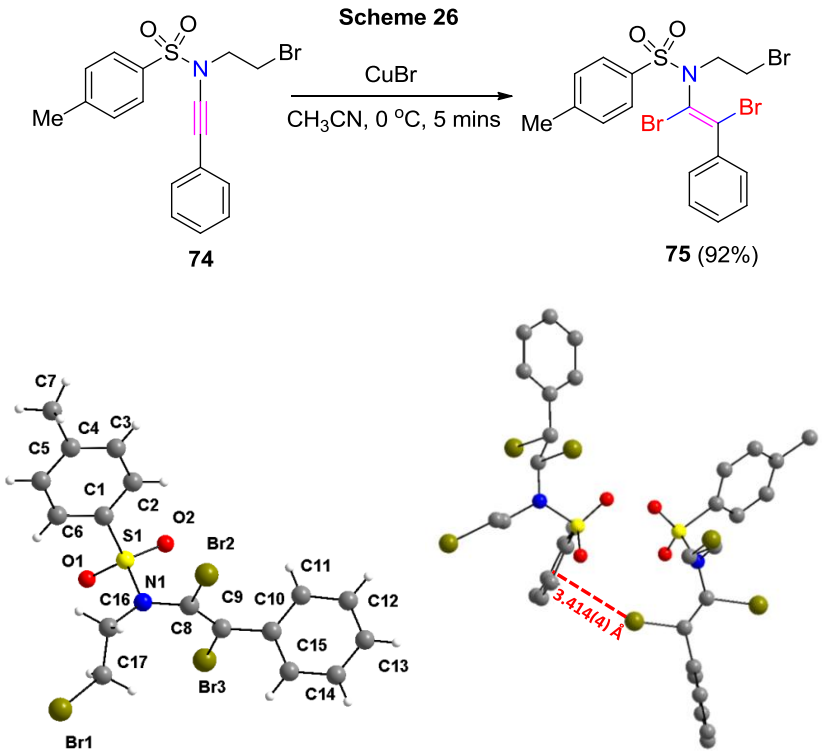



**Figure 12:** (a) Molecular structure of compound **75.** Selected bond lengths [Å] with esds are given in parentheses: Br2-C8 1.931(4), Br3-C9 1.890(4), C8-C9 1.309(6), N1-C8 1.394(5), C10-C9 1.488(5), Br1-C17 1.919(6). (b) A diagram of two individual crystallographic structures of the compound **75** showing weak halogen bonding interaction [Br•••C4 (π-system) 3.414(4) Å].

## Summary of PART-A

**1.** We have developed a simple and new transition metal-free, base mediated synthesis of thiazolidine-thiones and iminothiazolidines/oxazolidines *via* regioselective 5-*exo-tet* cyclization by treating epoxy-sulfonamides with heterocumulenes like carbon disulfide, isothiocyanates or isocyanates. We have shown that this ring expansion/cyclization occurs through a thio/oxo anionic intermediate *but not though aziridine intermediate*. A second but equally simple route to thiazolidine-2-thiones and imino-thiazolidines /oxazolidines by insertion of the heterocumulenes into 2-bromoethyl-sulfonamides after dehydrohalogenation is also described. Compound **9** could be derivatized further as shown by the isolation of compounds **52-54**.

2. Nucleophile assisted regio- and stereo-selective 5-*exo-dig*/6-*endo-dig* cyclization of epoxy ynamides by using CuBr or LiCl as the nucleophile source for the synthesis of 1,3-oxazolidines and 1,4 oxazines has been developed. Most of the 1,3-oxazolidines except those with alkyne phenyl group substituents are *E*-selective. Deuterium-labeling experiment supported the important role of water as the proton source in latter cyclization process.

3. An elegant and operationally simple approach for the regio-specific synthesis of (*E/Z*)-$\alpha$-chloro-$\beta$-iodo-enamides by the halo-addition reaction of epoxy ynamides using ICl as the iodo-chlorinating agent is developed. An interesting stereo-specific dibromination of functionalized ynamides with CuBr lead to *E*-$\alpha,\beta$-dibromo-enamide has been developed.

# EXPERIMENTAL SECTION

**General information**: Chemicals and solvents were procured from Aldrich/ Fluka or local manufacturers. Further purification was done according to standard procedures wherever required.[90] All operations, unless otherwise specified, were carried out under dry nitrogen atmosphere using standard vacuum line techniques.[91]

**Thin layer chromatography (TLC):** Glass micro slides or aluminum plates were coated with silica-gel-GF254 (mesh size 75 μ) and spots were identified using iodine or UV chamber as appropriate.

**Column chromatography** was performed on silica gel 100-200 mesh, using ethyl acetate and hexane mixture as eluent.

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

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

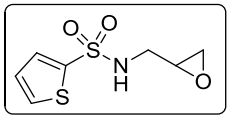
**Infrared spectroscopy**: IR spectra were recorded neat or by using KBr pellets on a JASCO FT/IR 5300 spectrophotometer.

**NMR spectroscopy**: $^{1}H$, $^{13}C$, $^{31}P$ and $^{19}F$ NMR spectra were recorded using 5 mm tubes on a Bruker 400 MHz and 500 NMR spectrometer [field strengths: 400, 100, 162 and 376 MHz (for 400 MHz NMR spectrometer) and 500, 125, 202 and 470 MHz (for 500 MHz NMR spectrometer) respectively] in $CDCl_3$, DMSO-$D_6$ solutions (unless specified otherwise) with shifts referenced to $SiMe_4$ ($^{1}H$, $^{13}C$: $\delta = 0$), ext. 85% $H_3PO_4$ ($^{31}P$: $\delta = 0$) or $CFCl_3$ ($^{19}F$: $\delta = 0$). 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 analyzer) equipment.

Epoxy-sulfonamides **1a-k** and *N*-(2-bromoethyl)-sulfonamides **2a-k** were synthesized based on the literature procedures.[77] Isothiocyanates **3a-h** and isocyanates **4a-b** are commercially available. The P(III) isothiocyanate **3i**,[78a] allenylphosphonate 5,[78b] 1-bromo-alkynes **6a-f**,[79] ynamide precursors **7a-m**,[71] (1-tosylaziridin-2-yl)methanol **8**[80] and 1-(phenylsulfonyl)aziridine **50**[82b] were prepared by following known procedures.

**Compound 1j**



Yield: 0.97 g (90%, gummy liquid, $R_f$ = 0.54 (9:1 hexane/ethyl acetate)).

IR (neat): 3307, 3026, 2924, 2854, 1737, 1703, 1657, 1489, 1351, 1161, 1090, 980, 752 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.63-7.60 (m, 2H), 7.11-7.10 (m, 1H), 5.32 (s, 1H), 3.44-3.41 (m, 1H), 3.13-3.10 (m, 2H), 2.79 (t, *J* = 4.3 Hz, 1H), 2.67-2.65 (m, 1H).

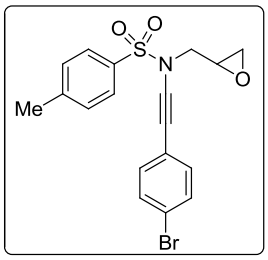
$^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 140.7, 132.3, 132.1, 127.5, 50.3, 45.3, 44.7.

HRMS (ESI): Calcd for $C_7H_9NO_3S_2Na$ ($M^+$+Na) *m/z* 241.9922. Found: 241.9921.

### 3.1 Synthesis of epoxy ynamide precursors 7a-m

To a mixture of 4-methyl-*N*-(oxiran-2-ylmethyl)benzenesulfonamide **1a** (1.00 g, 4.40 mmol), $CuSO_4 \cdot 5H_2O$ (0.220 g, 0.88 mmol), 1,10-phenanthroline monohydrate (0.349 g, 1.76 mmol) and $K_2CO_3$ (1.520 g, 11.0 mmol) in dry THF (20 mL), (bromoethynyl)benzene **6a** (0.956 g, 5.28 mmol) was added. The vessel was stoppered under nitrogen atmosphere and heated overnight on an oil-bath maintained at 70 $^oC$. The mixture was filtered and concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain the pure epoxy ynamide **7a** by using hexane-ethyl acetate (8:2) as the eluent. Compounds **7b-m** were prepared following the same procedure and by using the same molar quantities. Compounds **7g-k** and **7m** are new.

**Compound 7g**




Yield: 1.50 g (84%, gummy liquid, $R_f$ = 0.60 (9:1 hexane/ethyl acetate)).

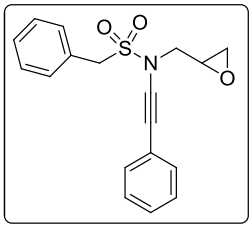
IR (KBr): 3064, 2999, 2925, 2237, 1596, 1488, 1367, 1171, 940, 819, 711 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.87-7.86 (m, 2H), 7.46-7.43 (m, 2H), 7.39 (m, 2H), 7.25-7.22 (m, 2H), 3.62 (d, $J$ = 5.0 Hz, 2H), 3.24-3.21 (m, 1H), 2.85-2.83 (m, 1H), 2.66-2.65 (m, 1H), 2.48 (s, 3H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 145.1, 134.3, 132.8, 131.6, 129.9, 127.8, 122.1, 121.6, 83.4, 69.8, 53.9, 49.3, 45.5, 21.7.

HRMS (ESI): Calcd for $C_{18}H_{17}BrNO_3S$ ($M^+$+H), ($M^+$+H+2) *m/z* 406.0112, 408.0092. Found: 406.0111, 408.0090.

**Compound 7h**




Yield: 1.29 g (90%, gummy liquid, $R_f$ = 0.58 (9:1 hexane/ethyl acetate)).

IR (KBr): 3062, 2999, 2929, 2237, 1495, 1361, 1258, 1202, 1158, 1135, 1007, 937, 796, 695 $cm^{-1}$.

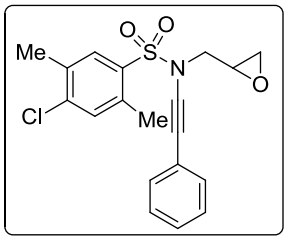
$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.53 (m, 2H), 7.42 (m, 5H), 7.36-7.34 (m, 3H), 4.64 (AB multiplet, 2H), 3.40-3.30 (m, 2H), 3.10 (m, 1H), 2.81 (m, 1H), 2.63 (m, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 131.7, 131.0, 129.4, 129.0, 128.4, 128.3, 127.7, 122.3, 81.8, 71.0, 57.5, 54.8, 49.4, 45.6.

LC-MS: *m/z* 328 $[M+1]^+$.

Anal.Calcd. for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 66.15; H, 5.18; N, 4.32.

**Compound 7i**




Yield: 1.21 g (86%, gummy liquid, $R_f$ = 0.62 (9:1 hexane/ethyl acetate)).

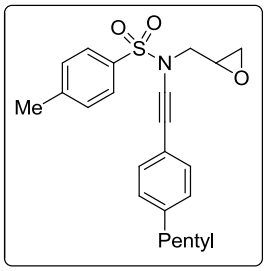
IR (KBr): 3059, 2997, 2926, 2858, 2236, 1599, 1543, 1479, 1370, 1169, 940, 755 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.92 (s, 1H), 7.36 (s, 1H), 7.34-7.29 (m, 5H), 3.72-3.68 (m, 1H), 3.64-3.60 (m, 1H), 3.32-3.28 (m, 1H), 2.87 (t, *J* = 4.3 Hz, 1H), 2.70 (d, *J* = 2.5 Hz, 1H), 2.69 (s, 3H), 2.42 (s, 3H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 140.2, 137.3, 134.5, 134.1, 133.2, 132.8, 131.2, 128.3, 128.1, 122.4, 81.9, 71.6, 53.5, 49.3, 45.7, 20.4, 19.6.

HRMS (ESI): Calcd for $C_{19}H_{18}ClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2) *m/z* 398.0594, 400.0564. Found: 398.0589, 400.0565.

**Compound 7j**




Yield: 1.71 g (90%, gummy liquid, $R_f$ = 0.68 (9:1 hexane/ethyl acetate)).

IR (KBr): 2955, 2927, 2857, 2236, 1597, 1366, 1170, 1114, 841, 745 $cm^{-1}$.

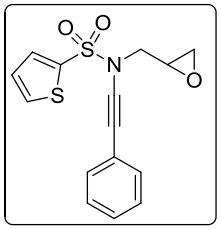
$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.89-7.87 (m, 2H), 7.38-7.36 (m, 2H), 7.32-7.30 (m, 2H), 7.12 (m, 2H), 3.68-3.64 (m, 1H) and 3.58-3.54 (m, 1H) [as AB system], 3.24-3.21 (m, 1H), 2.81 (t, *J* = 4.3 Hz, 1H), 2.66-2.64 (m, 1H), 2.59 (t, *J* = 7.7 Hz, 2H), 2.46 (s, 3H), 1.64-1.58 (m, 2H), 1.38-1.32 (m, 4H), 0.91 (t, *J* = 7.0 Hz, 3H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 144.9, 143.3, 134.4, 131.6, 129.8, 128.4, 127.8, 119.6, 81.6, 70.7, 54.0, 49.2, 45.6, 35.8, 31.4, 31.0, 22.5, 21.7, 14.0.

LC-MS: *m/z* 398 $[M+1]^+$.

Anal.Calcd. for $C_{23}H_{27}NO_3S$: C, 69.49; H, 6.85; N, 3.52. Found: C, 69.36; H, 6.81; N, 3.58.

**Compound 7k**



Yield: 1.136 g (78%, gummy liquid, $R_f$ = 0.55 (9:1 hexane/ethyl acetate)).

IR (KBr): 3099, 3059, 3000, 2927, 2238, 1401, 1371, 1228, 1171, 1017, 856, 757 $cm^{-1}$.

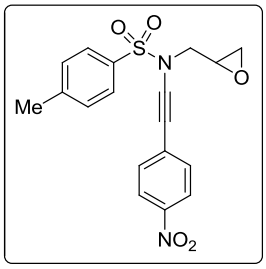
$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 7.78-7.77 (m, 1H), 7.72-7.70 (m, 1H), 7.43-7.41 (m, 2H), 7.31-7.30 (m, 3H), 7.17-7.15 (m, 1H), 3.68-3.58 (m, 2H), 3.26-3.23 (m, 1H), 2.82 (dd→t, $J$ = 4.5 Hz, 1H), 2.66-2.65 (m, 1H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): $\delta$ 136.4, 134.1, 134.0, 131.5, 128.4, 128.3, 127.8, 122.3, 81.8, 71.6, 54.4, 49.2, 45.5.

LC-MS: *m/z* 320 $[M+1]^+$.

Anal.Calcd. for $C_{15}H_{13}NO_3S_2$: C, 56.41; H, 4.10; N, 4.39. Found: C, 56.32; H, 4.15; N, 4.31

**Compound 7m**



Yield: 1.07 g (60%, gummy liquid, $R_f$ = 0.62 (9:1 hexane/ethyl acetate)).

IR (KBr): 2937, 2833, 2235, 1605, 1512, 1468, 1364, 1293, 1260, 1162, 1079, 1041, 838, 668 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.18-8.15 (m, 2H), 7.88-7.86 (m, 2H), 7.49-7.47 (m, 2H), 7.41 (m, 2H), 3.78-3.74 (m, 1H), 3.60-3.54 (m, 1H), 3.26-3.22 (m, 1H), 2.86 (t, $J$ = 4.4 Hz, 1H), 2.67-2.65 (m, 1H).

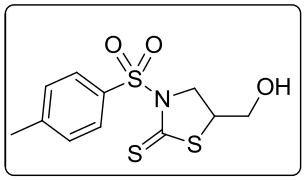
$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 146.4, 145.5, 134.1, 131.0, 130.1, 130.0, 127.8, 123.7, 88.1, 70.4, 54.0, 49.3, 45.2, 21.7.

HRMS (ESI): Calcd for $C_{18}H_{17}N_2O_5S$ ($M^+$+H) *m/z* 373.0858. Found: 373.0859.

### 3.2 Synthesis of thiazolidine-thiones 9-16: Representative procedure for the synthesis of compound 9

To a solution of epoxy-sulfonamide **1a** (100 mg, 0.46 mmol) and $CS_2$ (0.167 g, 2.1 mmol) in NMP (1 mL) was added anh. $K_2CO_3$ (60 mg, 0.8 mmol) and the reaction mixture heated with stirring at 80 $^o$C for 12 h. After the completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 2:1) afforded compound **9**. Compounds **9-16** were prepared following same procedure using the same molar quantities.

**Compound 9**




Yield: 0.122 g (92%, light yellow solid, $R_f$ = 0.38 (9:1 hexane/ethyl acetate)).

Mp: 98-100 $^o$C.

IR (KBr): 3401, 2920, 1650, 1593, 1464, 1366, 1242, 1175, 1097, 1056, 808 $cm^{-1}$.

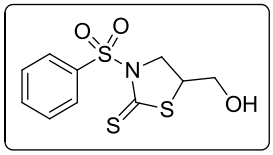
$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, *J* = 8.0 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.87-4.83 (m, 1H), 4.64-4.59 (m, 1H), 3.83-3.78 (m, 3H), 2.47 (s, 3H), 2.27 (br, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 196.9, 146.1, 133.5, 129.5, 129.2, 63.2, 58.5, 45.5, 21.8.

HRMS (ESI): Calcd. for $C_{11}H_{14}NO_3S_3$ ($M^+$+H) *m/z* 304.0136. Found: 304.0138.

This compound was crystallized from DCM/ethyl acetate/hexane (2:1:1) mixture at 25 $^o$C. X-ray structure was determined for this sample.

**Compound 10**



Yield: 0.109 g (81%, $R_f$ = 0.35 (9:1 hexane/ethyl acetate)).

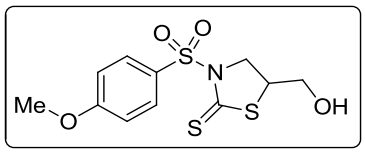
IR (neat): 3387, 2928, 2875, 1463, 1447, 1361, 1235, 1169, 1022, 809, 752 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.08-8.06 (m, 2H), 7.72-7.68 (m, 1H), 7.60-7.55 (m, 2H), 4.87-4.84 (m, 1H), 4.65-4.60 (m, 1H), 3.84-3.78 (m, 3H), 2.34 (br, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 196.7, 136.5, 134.7, 129.2, 128.9, 63.3, 58.5, 45.6.

HRMS (ESI): Calcd for $C_{10}H_{11}NO_3S_3Na$ ($M^+$+Na) *m/z* 311.9799. Found: 311.9797.

**Compound 11**



Yield: 0.120 g (92%, $R_f$ = 0.30 (9:1 hexane/ethyl acetate)).

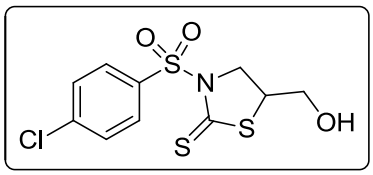
IR (neat): 3530, 2936, 2838, 1722, 1587, 1494, 1463, 1412, 1360, 1314, 1267, 839, 740 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02-7.98 (m, 2H), 7.03-7.00 (m, 2H), 4.84-4.80 (m, 1H), 4.61-4.56 (m, 1H), 3.90 (s, 3H), 3.81-3.76 (m, 3H), 2.73 (br, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 195.5, 163.2, 130.3, 126.2, 112.7, 61.9, 57.2, 54.5, 44.1.

HRMS (ESI): Calcd for $C_{11}H_{14}NO_4S_3$ ($M^+$+H) *m/z* 320.0085. Found: 320.0086.

**Compound 12**



Yield: 0.117 g (90%, light yellow solid, $R_f$ = 0.4 (9:1 hexane/ethyl acetate)).

Mp: 76-78 $^oC$.

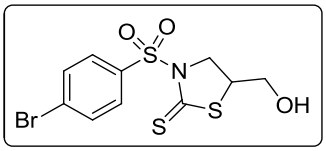
IR (KBr): 3365, 3096, 2931, 2874, 1582, 1474, 1360, 1231, 1164, 1092, 1066, 1009, 813, 756, 699, 617 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.01(d, $J$ = 8.4 Hz, 2H), 7.54 (d, $J$ = 8.8 Hz, 2H), 4.86-4.83 (m, 1H), 4.64-4.60 (m, 1H), 3.83 (br, 3H), 2.46 (br, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.4, 141.5, 134.7, 130.6, 129.3, 63.2, 58.6, 45.7.

HRMS (ESI): Calcd for $C_{10}H_{11}ClNO_3S_3$ ($M^+$+H) and ($M^+$+H+2) *m/z* 323.9589, 325.9560. Found 323.9590 and 325.9563.

**Compound 13**




Yield: 0.114 g (91%, light yellow solid, $R_f$ = 0.41 (9:1 hexane/ethyl acetate)).

Mp: 98-100 $^oC$.

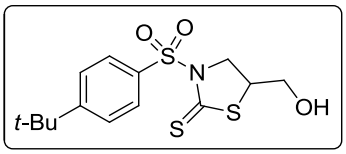
IR (KBr): 3530, 3354, 3091, 2931, 1567, 1469, 1391, 1366, 1231, 1169, 1071, 1009, 823, 735, 699 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.91 (d, $J$ = 8.8 Hz, 2H), 7.69 (d, $J$ = 8.8 Hz, 2H), 4.81 (d, $J$ = 10.8 Hz, 1H), 4.62-4.59 (m, 1H), 3.80 (br, 3H), 3.08 (br, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.3, 135.3, 132.3, 130.6, 130.2, 63.2, 58.6, 45.7.

HRMS (ESI): Calcd for $C_{10}H_{11}BrNO_3S_3$ ($M^+$+H) & ($M^+$+H +2) *m/z* 367.9084, 369.9064. Found: 367.9082 and 369.9062.

**Compound 14**




Yield: 108 g (85%, gummy liquid, $R_f$ = 0.42 (9:1 hexane/ethyl acetate)).

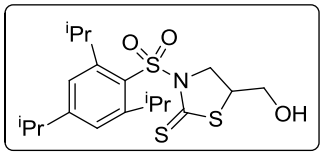
IR (neat): 3411, 2962, 2869, 1588, 1459, 1366, 1242, 1169, 1082, 828, 803, 751, 622 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.00-7.78 (m, 2H), 7.58-7.55 (m, 2H), 4.87-4.84 (m, 1H), 4.64-4.59 (m, 1H), 3.86-3.78 (m, 3H), 1.36 (s, 9H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 196.7, 158.9, 133.3, 129.1, 125.9, 63.2, 58.5, 45.5, 35.4, 31.0.

HRMS (ESI): Calcd for $C_{14}H_{20}NO_3S_3$ ($M^+$+H) *m/z* 346.0605. Found: 346.0606.

**Compound 15**




Yield: 0.108 g (90%, white solid, $R_f$ = 0.43 (9:1 hexane/ethyl acetate)).

Mp: 96-98 $^oC$.

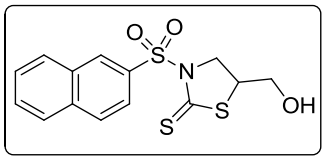
IR (KBr): 3437, 2957, 2931, 2864, 1598, 1562, 1469, 1428, 1371, 1340, 1247, 1169, 1066, 880 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.18 (s, 2H), 4.75-4.61 (m, 2H), 4.00-3.86 (m, 5H), 2.95-2.88 (m, 2H), 1.30-1.24 (m, 18H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.1, 154.7, 151.6, 131.2, 124.0, 63.2, 56.5, 46.0, 34.2, 29.7, 24.6, 24.3, 23.5.

HRMS (ESI): Calcd for $C_{19}H_{30}NO_3S_3$ ($M^+$+H) *m/z* 416.1388. Found: 416.1391.

**Compound 16**




Yield: 0.090 g (70%, yellow solid, $R_f$ = 0.38 (9:1 hexane/ethyl acetate)).

Mp: 104-106 $^oC$.

IR (KBr) 3411, 3055, 2926, 1619, 1583, 1500, 1459, 1355, 1242, 1164, 1071, 860, 658 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.71 (d, $J$ = 1.2 Hz, 1H), 8.04-7.93 (m, 4H), 7.73-7.64 (m, 2H), 4.96-4.92 (m, 1H), 4.72- 4.67 (m, 1H), 3.85-3.79 (m, 3H), 2.22-2.06 (br, 1H).

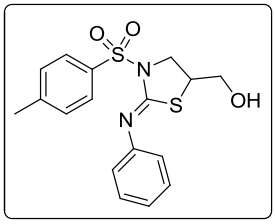
$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 196.7, 135.7, 133.1, 132.1, 131.6, 129.9, 129.8, 129.2, 128.0, 122.9, 63.3, 58.7, 45.6.

HRMS (ESI): Calcd for $C_{14}H_{14}NO_3S_3$ ($M^+$+H) *m/z* 340.0136. Found: 340.0133.

### 3.3 Synthesis of imino-thiazolides 17-24 and imino-oxazolidines 25-26

The procedure was similar to that for **9** using epoxy sulfonamide **1a** (0.4 mmol), RNCS/RNCO (0.5 mmol) and $K_2CO_3$ (0.6 mmol) in NMP (1 mL) at 80 $^oC$ for 24 h.

**Compound 17**



Yield: 0.091 (70%, gummy liquid, $R_f$ = 0.48 (9:1 hexane/ethyl acetate)).

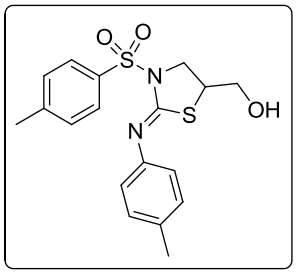
IR (neat): 3411, 3049, 2915, 2874, 1634, 1587, 1494, 1360, 1262, 1169, 1081, 1040, 766, 694 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 8.5 Hz, 2H), 7.36 (d, $J$ = 8.5 Hz, 2H), 7.27 (t, $J$ = 7.8 Hz, 2H), 7.09 (t, $J$ = 7.5 Hz, 1H), 6.75 (d, $J$ = 7.0 Hz, 2H), 4.36-4.33 (m, 1H), 4.12-4.09 (m, 1H), 3.73-3.65 (m, 3H), 2.48 (s, 3H), 2.46 (br, 1H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 151.9, 150.0, 145.1, 134.4, 129.3, 129.1, 124.4, 120.8, 63.5, 51.4, 43.8, 21.8.

HRMS (ESI): Calcd for $C_{17}H_{19}N_2O_3S_2$ ($M^+$+H) *m/z* 363.0837. Found: 363.0840.

**Compound 18**



Yield: 0.144 g (88%, gummy liquid, $R_f$ = 0.50 (9:1 hexane/ethyl acetate)).

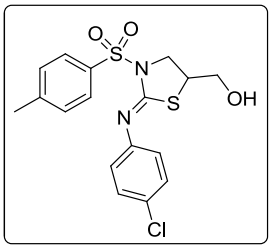
IR (neat): 3426, 2920, 2848, 1634, 1505, 1458, 1355, 1169, 1081, 1040, 808, 668 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 8.4 Hz, 2H), 7.36 (d, $J$ = 8.0 Hz, 2H), 7.08 (d, $J$ = 7.6 Hz, 2H), 6.66 (d, $J$ = 8.4 Hz, 2H), 4.36-4.32 (m, 1H), 4.13-4.09 (m, 1H), 3.76-3.65 (m, 3H), 2.48 and 2.31 (2s, 6H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 151.2, 147.4, 144.9, 134.5, 133.9, 129.5, 129.2, 129.1, 120.5, 63.5, 51.3, 43.8, 21.7, 20.9.

HRMS (ESI): Calcd for $C_{18}H_{21}N_2O_3S_2$ ($M^+$+H) *m/z* 377.0993. Found: 377.0992.

**Compound 19**



Yield: 0.104 g (73%, white solid, $R_f$ = 0.52 (9:1 hexane/ethyl acetate)).

Mp: 126-128 $^oC$.

IR (KBr): 3434, 2957, 2874, 1638, 1591, 1484, 1354, 1262, 1170, 1085, 1034, 865, 812, 663 $cm^{-1}$.

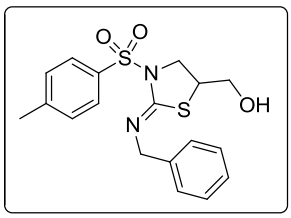
$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.07 (d, *J* = 7.6 Hz, 2H), 6.46 (d, *J* = 8.0 Hz, 2H), 6.32 (d, *J* = 8.4 Hz, 2H), 5.79 (d, *J* = 8.0 Hz, 2H), 3.45 (d, *J* = 10.0 Hz, 1H), 3.23-3.19 (m, 1H), 2.80 (d, *J* = 7.6 Hz, 3H), 1.58 (s, 4H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 151.3, 147.3, 144.1, 133.2, 128.5, 128.2, 128.0, 127.9, 121.1, 62.3, 50.4, 42.8, 20.6.

HRMS (ESI): Calcd for $C_{17}H_{18}ClN_2O_3S_2$ ($M^+$+H), ($M^+$+H+2) *m/z* 397.0447, 399.0417. Found: 397.0449, 399.0405.

This compound was crystallized from ethyl acetate/hexane (2:1) mixture 25 $^oC$. X-ray structure was determined for this sample.

**Compound 20**



Yield: 0.135 g (82%, white solid, $R_f$ = 0.53 (9:1 hexane/ethyl acetate)).

Mp: 108-110 $^oC$.

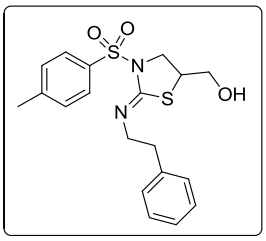
IR (KBr): 3306, 3029, 2925, 1699, 1645, 1597, 1519, 1159, 1086, 812, 751 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.85 (d, $J$ = 6.6 Hz, 2H), 7.27-7.23 (m, 3H), 7.19 (d, $J$ = 4.0 Hz, 2H), 7.11-7.10 (m, 2H), 4.42-4.29 (m, 3H), 4.04-4.01 (m, 1H), 3.77-3.70 (m, 3H), 2.41 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 150.8, 144.5, 139.3, 134.7, 129.2, 128.8, 128.1, 127.4, 126.6, 63.4, 59.4, 51.1, 44.0, 21.6.

HRMS (ESI): Calcd for $C_{18}H_{21}N_2O_3S_2$ ($M^+$+H) *m/z* 377.0993. Found: 377.0996.

**Compound 21**




Yield 0.142 g (83%, gummy liquid, $R_f$ = 0.54 (9:1 hexane/ethyl acetate))

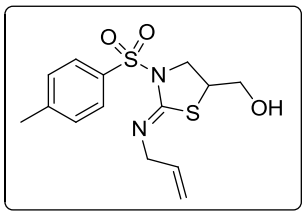
IR (neat): 3369, 3025, 2926, 2872, 1704, 1651, 1598, 1454, 1350, 1160, 1088, 813, 748 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.86 (d, $J$ = 8.4 Hz, 2H), 7.27-7.20 (m, 5H), 7.07 (d, $J$ = 6.4 Hz, 2H), 4.25-4.22 (m, 1H), 3.94-3.91 (m, 1H), 3.69-3.59 (m, 3H), 3.40-3.35 (m, 2H), 2.82 (t, $J$ = 7.2 Hz, 2H), 2.44 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 149.8, 144.5, 140.0, 134.8, 129.1, 129.0, 128.9, 128.2, 126.0, 63.4, 57.5, 50.8, 43.8, 36.9, 21.6.

HRMS (ESI): Calcd for $C_{19}H_{23}N_2O_3S_2$ ($M^+$+H) *m/z* 391.1150. Found: 391.1151.

**Compound 22**




Yield: 0.127 g (89%, gummy liquid, $R_f$ = 0.52 (9:1 hexane/ethyl acetate)).

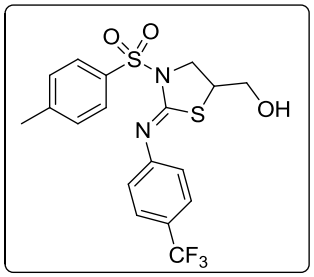
IR (neat): 3398, 2927, 1698, 1354, 1214, 1159, 745, 665 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.89-7.70 (m, 2H), 7.28 (d, $J$ = 6.0 Hz, 2H), 5.82-5.76 (m, 1H), 5.02-4.97 (m, 2H), 4.25 (d, $J$ = 8.4 Hz, 1H), 3.98-3.95 (m, 1H), 3.81-3.67 (m, 5H), 2.42 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 151.0, 144.7, 134.8, 134.6, 129.2, 128.8, 115.2, 63.3, 57.9, 51.1, 43.8, 21.6.

HRMS (ESI): Calcd for $C_{14}H_{19}N_2O_3S_2$ ($M^+$+H) *m/z* 327.0837. Found: 327.0840.

**Compound 23**




Yield: 0.151 g (80%, white solid, $R_f$ = 0.51 (9:1 hexane/ethyl acetate)).

Mp: 118-120 $^{o}$C.

IR (KBr): 3397, 3015, 2919, 1642, 1604, 1356, 1321, 1163, 1104, 1063, 846 $cm^{-1}$.

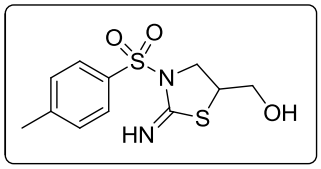
$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.0 Hz, 2H), 7.52 (d, $J$ = 8.4 Hz, 2H), 7.38 (d, $J$ = 8.0 Hz, 2H), 6.83 (d, $J$ = 8.0 Hz, 2H), 4.40-4.37 (m, 1H), 4.18-4.14 (m, 1H), 3.79-3.70 (m, 3H), 2.49 (s, 3H), 1.98 (br, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 152.8 (d, $J$ = 16.5 Hz), 145.3, 134.2, 129.4, 129.0, $126.3_0$, $126.2_6$, 126.1, 122.9, 121.1, 63.3, 51.6, 43.9, 21.7.

$^{19}$F NMR (470 MHz, $CDCl_3$): $\delta$ -61.9.

HRMS (ESI): Calcd for $C_{18}H_{17}F_3N_2O_3S_2Na$ ($M^+$+Na) *m/z* 453.0531. Found: 453.0528.

**Compound 24**




Yield: 0.076 g (61%, white solid, $R_f$ = 0.43 (9:1 hexane/ethyl acetate)).

Mp: 118-120 $^{o}$C.

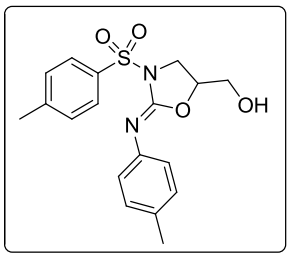
IR (KBr): 3466, 3279, 2923, 1790, 1704, 1598, 1454, 1327, 1158, 1091, 814, 754 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$D_6$): $\delta$ 7.72-7.68 (m, 2H), 7.40 (d, $J$ = 7.6 Hz, 2H), 4.90-4.83 (m, 1H), 3.70 (t, $J$ = 10.0 Hz, 1H), 3.47-3.42 (m, 1H), 3.01-2.98 (m, 3H), 2.38 (s, 3H).

$^{13}C$ NMR (100 MHz, DMSO-$D_6$): $\delta$ 188.2, 143.3, 137.8, 130.2, 127.0, 80.7, 46.3, 45.1, 21.4.

HRMS (ESI): Calcd for $C_{11}H_{14}N_2O_3S_2Na$ ($M^+$+Na) *m/z* 309.0344. Found: 309.0341.

**Compound 25**




Yield: 0.117 g (74%, white solid, $R_f$ = 0.48 (9:1 hexane/ethyl acetate)).

Mp: 144-146$^o$C.

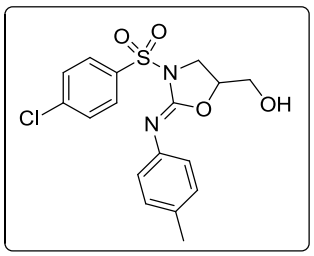
IR (KBr): 3496, 2922, 1597, 1404, 1333, 1164, 1093, 815, 662 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 8.4 Hz, 2H), 7.34 (d, $J$ = 8.0 Hz, 2H), 7.23 (d, $J$ = 8.4 Hz, 2H), 7.15 (d, $J$ = 8.4 Hz, 2H), 4.32-4.28 (m, 2H), 4.07-4.03 (m, 2H), 3.74-3.72 (m, 1H), 3.68-3.66 (m, 1H), 2.44 and 2.32 (2s, 6H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 152.2, 144.9, 135.9, 135.0, 133.6, 129.9, 129.6, 128.3, 122.6, 60.8, 54.7, 44.2, 21.7, 20.9.

HRMS (ESI): Calcd for $C_{18}H_{21}N_2O_4S$ ($M^+$+H) 361.1222. Found: 361.1223.

**Compound 26**




Yield: 0.102 g (69%, white solid, $R_f$ = 0.49 (9:1 hexane/ethyl acetate)).

Mp: 152-154$^o$C.

IR (KBr): 3486, 2922, 1515, 1335, 1162, 1085, 819, 753, 618 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.71 (d, $J$ = 7.2 Hz, 2H), 7.45 (d, $J$ = 6.8 Hz, 2H), 7.29 (s, 1H), 7.27 (s, 1H), 7.18 (d, $J$ = 6.4 Hz, 2H), 5.07 (t, $J$ = 5.0 Hz, 2H), 4.60-4.53 (m, 2H), 4.42-4.39 (m, 1H), 3.22-3.07 (m, 2H), 2.36 (s, 3H).

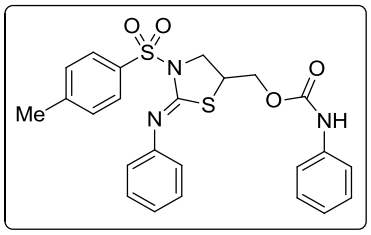
$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 155.6, 139.7, 137.8, 135.9, 133.2, 130.1, 129.6, 128.4, 121.7, 64.6, 55.7, 42.9, 20.9.

HRMS (ESI): Calcd for $C_{17}H_{17}ClN_2O_4SNa$ ($M^+$+Na) and ($M^+$+Na+2) *m/z* 403.0496, 405.0465. Found: 403.0497, 405.0449.

### 3.4 Synthesis of imino-thiazolidine/oxazolidine carbamates 27-30

The procedure was similar to that for **9** using epoxy sulfonamide **1a** (0.4 mmol), RNCS (0.6 mmol) and $K_2CO_3$ (0.6 mmol) in NMP (1 mL) at rt for 10 h.

**Compound 27**




Yield: 0.095g (56%, gummy liquid, $R_f$ = 0.70 (9:1 hexane/ethyl acetate)).

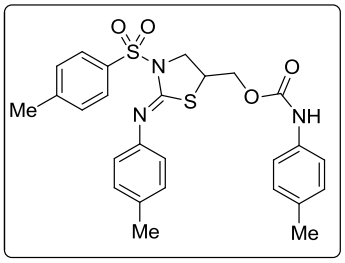
IR (neat): 3347, 3060, 2924, 1736, 1644, 1596, 1537, 1445, 1356, 1314, 1215, 1089, 813, 761 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.03 (d, $J$= 8.0 Hz, 2H), 7.42-7.31 (m, 8H), 7.11 (br, 3H), 6.76 (d, $J$ = 8.0 Hz, 2H), 4.43 (d, $J$ = 8.0 Hz, 1H), 4.30 (br, 1H), 4.23-4.14 (m, 2H), 3.83 (br, 1H), 2.48 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 152.7, 151.2, 149.9, 145.1, 137.9, 134.6, 129.4, $129.1_3$, $129.1_0$, 129.0, 124.5, 123.8, 120.7, 118.8, 65.1, 51.7, 40.8, 21.7.

HRMS (ESI): Calcd for $C_{24}H_{24}N_3O_4S_2$ ($M^+$+H) *m/z* 482.1208. Found: 482.1209.

**Compound 28**




Yield: 0.133g (60%, white solid, $R_f$ = 0.71 (9:1 hexane/ethyl acetate)).

Mp: 74-76 $^{o}$C.

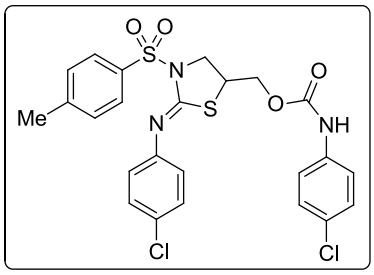
IR (KBr): 3349, 2920, 2848, 1720, 1643, 1505, 1463, 1360, 1236, 1164, 1092, 1030, 818 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): $\delta$ 8.01 (d, $J$ = 8.0 Hz, 2H), 7.36 (d, $J$ = 8.0 Hz, 2H), 7.27 (br, 2H), 7.14 (d, $J$ = 8.5 Hz, 2H), 7.07 (d, $J$ = 8.0 Hz, 2H), 6.83 (br, 1H), 6.65 (d, $J$ = 8.0 Hz, 2H), 4.42-4.39 (m, 1H), 4.31-4.28 (m, 1H), 4.21-4.13 (m, 2H), 3.85-3.80 (m, 1H), 2.47 (s, 3H), 2.33 (s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 152.8, 150.9, 147.4, 145.0, 134.9, 134.7, 133.9, 133.3, 129.6, 129.3, 129.1, 120.5, 118.9, 64.9, 51.6, 40.7, 21.7, 20.9, 20.8.

HRMS (ESI): Calcd for $C_{26}H_{28}N_3O_4S_2$ ($M^+$+H) *m/z* 510.1521. Found: 510.1522.

**Compound 29**




Yield: 0.131 g (67%, gummy liquid, $R_f$ = 0.72 (9:1 hexane/ethyl acetate)).

IR (neat: 3351, 2922, 1736, 1642, 1596, 1533, 1489, 1402, 1357, 1307, 1214, 1090, 824 $cm^{-1}$.

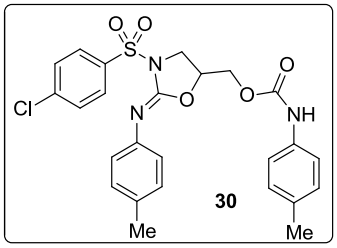
$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.98 (d, $J$ = 6.8 Hz, 2H), 7.38-7.21 (m, 7H), 7.06 (br, 1H), 6.68-6.66 (m, 2H), 4.48-4.45 (m, 1H), 4.34-4.24 (m, 2H), 4.15-4.11 (m, 1H), 3.86-3.83 (m, 1H), 2.48 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 152.5, 151.6, 148.2, 145.2, 136.0, 134.7, 129.7, 129.3, 129.1$_5$, 129.1$_3$, 129.0, 128.9, 122.1, 119.9, 65.4, 51.7, 41.0, 21.7.

HRMS (ESI): Calcd for $C_{24}H_{22}Cl_2N_3O_4S_2$ ($M^+$+H) and ($M^+$+H+2) *m/z* 550.0429, 552.0399. Found: 550.0428, 552.0396.

**Compound 30**

The procedure was similar to that for **9** using epoxy sulfonamide **1c** (0.4 mmol), RNCO **4b** (0.6 mmol) and $K_2CO_3$ (0.6 mmol) in NMP (1 mL) at rt for 10 h.



**30**

Yield: 0.126 g (62%, white solid, $R_f$ = 0.71 (9:1 hexane/ethyl acetate)).

Mp: 188-190 $^o$C.

IR (KBr): 3339, 2922, 1711, 1514, 1405, 1206, 1171, 1085, 814, 756, 621 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.05-8.03 (m, 2H); 7.50-7.48 (m, 2H), 7.28-7.12 (m, 8H), 6.85 (br, 1H), 4.46 (t, *J* = 3.4 Hz, 1H), 4.32 (t, *J* = 4.6 Hz, 1H), 4.12-4.02 (m, 3H), 2.33 and 2.31 (2s, 6H).

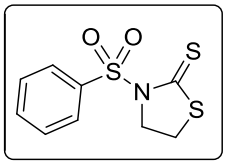
$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 152.7, 151.9, 140.6, 136.4, 136.3, 134.6, 133.2, 130.0, 129.7, 129.6, 129.4, 128.1, 122.9, 118.9, 63.0, 53.2, 44.4, 20.9, 20.7.

HRMS (ESI): Calcd for $C_{25}H_{24}ClN_3O_5SNa$ ($M^+$+Na) and ($M^+$+Na+2) *m/z* 536.1023, 538.0993. Found 536.1024, 538.0979.

## 3.5 Synthesis of thiazolidine-thiones 31-41 by HBr elimination/ heterocumulene insertion

The procedure was similar to that for **9**. *N*-(2-Bromoethyl)-sulfonamide **2** (0.38 mmol) and $CS_2$ (1.9 mmol) were used.

**Compound 31**



Yield: 0.086 g (88%, yellow solid, $R_f$ = 0.75 (9:1 hexane/ethyl acetate)).

Mp: 102-104 $^oC$.

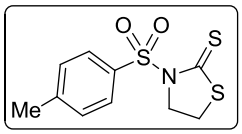
IR (KBr): 3065, 2930, 1691, 1572, 1448, 1360, 1283, 1179, 1086, 968, 875, 689 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.08-8.06 (m, 2H), 7.72-7.60 (m, 1H), 7.59-7.55 (m, 2H), 4.72 (t, $J$ = 7.4 Hz, 2H), 3.42 (t, $J$ = 7.4 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.8, 136.6, 134.6, 129.1, 128.8, 56.9, 29.2.

HRMS (ESI): Calcd for $C_9H_9NO_2S_3Na$ ($M^+$+Na) *m/z* 281.9693. Found: 281.9690.

**Compound 32**



Yield: 0.083 g (85%, light yellow solid, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

Mp: 110-112 $^oC$.

IR (KBr): 2956, 2920, 1593, 1360, 1257, 1164, 1086, 1024, 808, 673 $cm^{-1}$.

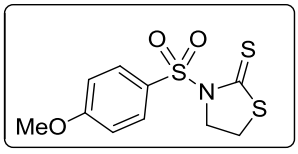
$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.0 Hz, 2H), 7.36 (d, $J$ = 8.0 Hz, 2H), 4.71 (t, $J$ = 7.2 Hz, 2H), 3.41 (t, $J$ = 7.4 Hz, 2H); 2.47 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.9, 145.9, 133.5, 129.5, 129.2, 57.0, 29.1, 21.8.

HRMS (ESI): Calcd for $C_{10}H_{11}NO_2S_3Na$ ($M^+$+Na) *m/z* 295.9850. Found: 295.9858.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^oC$. X-ray structure was determined for this sample.

**Compound 33**



Yield: 0.091 g (93%, gummy liquid, $R_f$ = 0.73 (9:1 hexane/ethyl acetate)).

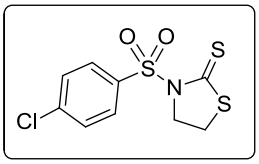
IR (neat): 3101, 1680, 1603, 1494, 1365, 1257, 1159, 1019, 802, 694 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.03-8.01 (m, 2H), 7.02-7.00 (m, 2H), 4.70 (t, $J$ = 5.8 Hz, 2H), 3.91 (s, 3H), 3.40 (t, $J$ = 6.0 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.7, 164.5, 131.6, 127.8, 114.0, 57.0, 55.8, 29.0.

HRMS (ESI): Calcd for $C_{10}H_{11}NO_3S_3Na$ ($M^+$+Na) *m/z* 311.9799. Found: 311.9797.

**Compound 34**




Yield: 0.086 g (88%, light yellow solid, $R_f$ = 0.77 (9:1 hexane/ethyl acetate)).

Mp: 118-120 $^oC$.

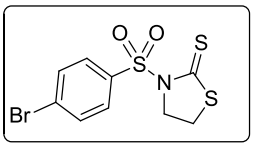
IR (KBr): 3091, 2936, 1701, 1582, 1474, 1371, 1288, 1179, 1086, 756 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.02-8.00 (m, 2H), 7.55-7.53 (m, 2H), 4.71 (t, $J$ = 7.2 Hz, 2H), 3.44 (t, $J$= 7.4 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 198.0, 141.4, 130.6, 129.9, 129.2, 56.9, 29.2.

HRMS (ESI): Calcd for $C_9H_8ClNO_2S_3Na$ ($M^+$+Na) and ($M^+$+Na+2) *m/z* 315.9304, 317.9273. Found: 315.9304, 317.9267.

**Compound 35**




Yield: 0.085 g (87%, yellow solid, $R_f$ = 0.77 (9:1 hexane/ethyl acetate)).

Mp: 124-126 $^oC$.

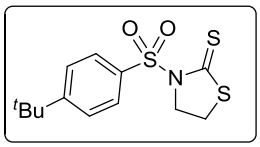
IR (KBr): 3090, 2941, 1696, 1567, 1469, 1365, 1329, 1272, 1164, 1086, 1004, 968, 823, 746, 694 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.94-7.92 (m, 2H), 7.72-7.70 (m, 2H), 4.70 (t, $J$ = 7.4 Hz, 2H), 3.43 (t, $J$ = 7.4 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.8, 135.6, 132.2, 130.6, 130.1, 56.9, 29.2.

HRMS (ESI): Calcd for $C_9H_8BrNO_2S_3Na$ ($M^+$+Na) and ($M^+$+Na+2) *m/z* 359.8799, 361.8778. Found: 359.8795, 361.8775.

**Compound 36**




Yield: 0.080 g (82%, light yellow solid, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

Mp: 158-160 $^oC$.

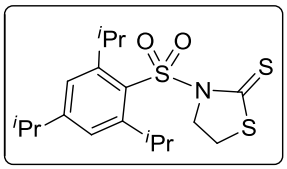
IR (KBr): 2961, 2863, 1696, 1593, 1463, 1371, 1226, 1179, 1081, 632 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.99 (d, *J* = 8.4 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 2H), 4.73-4.70 (m, 2H), 3.43-3.40 (m, 2H), 1.37 (s, 9H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.9, 158.7, 133.4, 129.1, 125.9, 57.0, 35.4, 31.0, 29.1.

HRMS (ESI): Calcd for $C_{13}H_{18}NO_2S_3$ ($M^+$+H) *m/z* 316.0499. Found 316.0504.

**Compound 37**




Yield: 0.088 g (90%, light yellow solid, $R_f$ = 0.77 (9:1 hexane/ethyl acetate)).

Mp: 134-136 $^oC$.

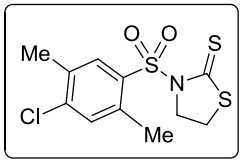
IR (KBr): 2956, 2925, 2868, 1706, 1593, 1453, 1422, 1371, 1334, 1278, 1236, 1164, 1076, 1030, 968, 771 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.18 (s, 2H), 4.73-4.26 (m, 2H), 4.08-3.97 (m, 2H), 3.45-3.38 (m, 2H), 2.94-2.89 (m, 1H), 1.31-1.25 (m, 18H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 197.4, 154.6, 151.6, 130.9, 123.9, 55.2, 34.2, 29.7, 24.4, 23.5;

HRMS (ESI): Calcd for $C_{18}H_{27}NO_2S_3Na$ ($M^+$+Na) *m/z* 408.1102. Found: 408.1104.

**Compound 38**




Yield: 0.078 g (80%, yellow solid, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

Mp: 128-130 $^{o}$C.

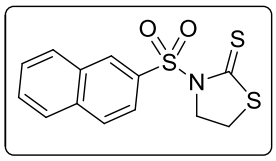
IR (KBr): 2925, 1593, 1541, 1484, 1365, 1231, 1164, 1076, 937, 627 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.01 (s, 1H), 7.31 (s, 1H), 4.78 (t, *J* = 7.6 Hz, 2H), 3.47 (t, *J* = 7.4 Hz, 2H), 2.55 and 2.42 (2s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 197.3, 140.7, 136.3, 134.8, 134.3, 133.9, 132.6, 56.1, 29.2, 19.6, 19.5.

HRMS (ESI): Calcd for $C_{11}H_{12}ClNO_2S_3$ ($M^+$+Na) and ($M^+$+Na+1) *m/z* 343.9617, 345.9586. Found 343.9617, 345.9570.

**Compound 39**




Yield: 0.078 g (80%, yellow solid, $R_f$ = 0.75 (9:1 hexane/ethyl acetate)).

Mp: 112-114 $^{o}$C.

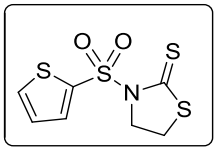
IR (KBr): 2956, 2930, 2863, 1587, 1551, 1458, 1360, 1236, 1169, 1066, 937, 833, 802, 746 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.71-8.65 (m, 1H), 8.05-7.94 (m, 3H), 7.72-7.66 (m, 2H), 4.80 (t, *J* = 7.4 Hz, 2H), 3.44 (t, *J* = 7.4 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 197.9, 135.7, 133.2, 132 0, 131.6, 129.8, 129.7, 129.2, 127.9, 127.8, 122.8, 57.1, 29.2.

HRMS (ESI): Calcd for $C_{13}H_{11}NO_2S_3$ ($M^+$+H) *m/z* 310.0030. Found: 310.0029.

**Compound 40**



Yield: 0.086 g (88%, light yellow solid, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

Mp: 134-136 $^{o}$C.

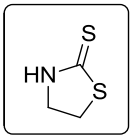
IR (KBr): 3096, 1510, 1402, 1324, 1221, 1154, 1097, 1019, 849, 740 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.01-7.99 (m, 1H), 7.77-7.76 (m, 1H), 7.19-7.17 (m, 1H), 4.66 (t, $J$ = 7.4 Hz, 2H), 3.42 (t, $J$ = 7.4 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 197.7, 136.7, 135.5, 134.9, 127.3, 56.9, 28.7.

HRMS (ESI): Calcd for $C_7H_7NO_2S_4$ ($M^+$+H) *m/z* 265.9438. Found: 265.9437.

**Compound 41**



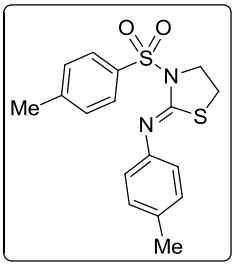
Yield: 0.025 g (65%, white solid, $R_f$ = 0.58 (9:1 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[92]

### 3.6 Synthesis of imino-thiazolidines/imino-oxazolidines 42-49

The procedure was similar to that for **9**. *N*-(2-Bromoethyl)-sulfonamide **2** (0.38 mmol) and R-NCS/RNCO (0.54 mmol) were used.

**Compound 42**



Yield: 0.102 g (82%, white solid, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

Mp: 114-116 $^{o}$C.

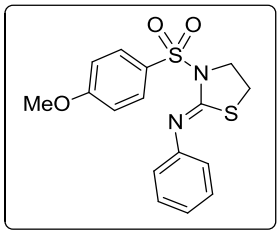
IR (KBr): 3028, 2923, 2858, 1642, 1503, 1442, 1358, 1170, 1131, 1093, 1018, 801, 671 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.00 (d, $J$ = 6.0 Hz, 2H), 7.36 (d, $J$ = 7.2 Hz, 2H), 7.08 (d, $J$ = 7.2 Hz, 2H), 6.65 (t, $J$ = 4.0 Hz, 2H), 4.21 (br, 2H), 3.20 (br, 2H), 2.48 and 2.31 (2s, 6H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 152.6, 147.8, 144.9, 134.5, 133.8, 130.1, 129.6, 129.2, 129.1, 125.5, 120.5, 50.1, 27.1, 21.7, 20.9.

HRMS (ESI): Calcd for $C_{17}H_{19}N_2O_2S_2$ ($M^+$+H) *m/z* 347.0888. Found: 347.0887.

**Compound 43**




Yield: 0.100 g (85%, white solid, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

Mp: 108-110 $^oC$.

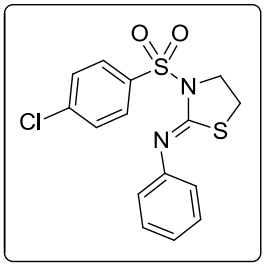
IR (KBr): 3064, 1634, 1587, 1546, 1494, 1355, 1267, 1159, 1092, 1014, 833, 792, 761, 694 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 8.05 (d, $J$ = 7.2 Hz, 2H), 7.29-7.26 (m, 2H), 7.08 (t, $J$ = 6.0 Hz, 1H), 7.03-7.01 (m, 2H), 6.77-6.75 (m, 2H), 4.20 (t, $J$ = 5.3 Hz, 2H), 3.91 (s, 3H), 3.18 (t, $J$ = 5.3 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 163.9, 152.8, 150.3, 131.4, 128.9, 124.2, 120.7, 113.7, 55.7, 50.1, 27.0.

HRMS (ESI): Calcd for $C_{16}H_{17}N_2O_3S_2$ ($M^+$+H) *m/z* 349.0680. Found: 349.0687.

**Compound 44**



Yield: 0.093 g (79%, white solid, $R_f$ = 0.79 (9:1 hexane/ethyl acetate)).

Mp: 168-170 $^{o}$C.

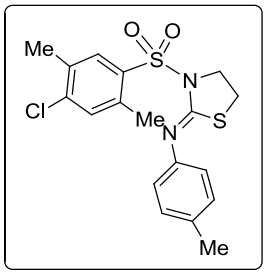
IR (KBr): 2957, 1650, 1593, 1402, 1361, 1237, 1170, 1118, 829, 762 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.04 (d, $J$ = 8.8 Hz, 2H), 7.52 (d, $J$ = 8.4 Hz, 2H), 7.26 (t, $J$ = 7.8 Hz, 2H), 7.09-7.06 (m, 1H), 6.73 (d, $J$ = 8.0 Hz, 2H), 4.19 (t, $J$ = 6.6 Hz, 2H), 3.20 (t, $J$ = 6.6 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 151.5, 148.8, 139.4, 134.9, 129.5, 127.9, 127.8, 123.4, 119.5, 48.9, 26.1.

HRMS (ESI): Calcd for $C_{15}H_{14}ClN_2O_2S_2$ ($M^+$+H), ($M^+$+H+2) *m/z* 353.0185, 355.0155. Found: 353.0188, 355.0146.

**Compound 45**



Yield: 0.107 g (89%, white solid, $R_f$ = 0.80 (9:1 hexane/ethyl acetate)).

Mp: 158-160 $^{o}$C.

IR (KBr): 2951, 2924, 2855, 1643, 1603, 1505, 1439, 1363, 1336, 1279, 1218, 1167, 1137, 1087, 861 cm$^{-1}$.

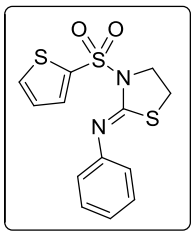
$^{1}$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.02 (s, 1H), 7.32 (s, 1H), 7.05 (d, $J$ = 8.0 Hz, 2H), 6.55-6.53 (m, 2H), 4.35 (t, $J$ = 6.6 Hz, 2H), 3.28-3.24 (m, 2H), 2.61, 2.40 and 2.30 (3s, 9H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 151.4, 147.1, 139.6, 136.7, 135.2, 134.3, 133.9, 133.8, 132.3, 129.5, 120.5, 49.1, 27.3, 20.9, 19.9, 19.5.

HRMS (ESI): Calcd for $C_{18}H_{20}ClN_2O_2S_2$ ($M^+$+H), ($M^+$+H+2) *m/z* 395.0654, 397.0625. Found: 395.0655, 397.0627.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^oC$. X-ray structure was determined for this sample.

**Compound 46**



Yield: 0.104 g (87%, white solid, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

Mp: 120-122 $^oC$.

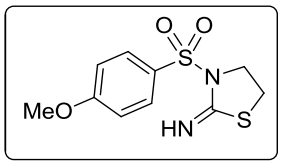
IR (KBr): 3085, 1639, 1587, 1536, 1494, 1365, 1221, 1164, 1133, 1097, 1019, 859, 735 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95-7.94 (m, 1H), 7.75-7.73 (m, 1H), 7.33-7.29 (m, 2H), 7.19-7.17 (m, 1H), 7.14-7.09 (m, 1H), 6.87-6.84 (m, 2H), 4.19 (t, *J* = 6.6 Hz, 2H), 3.23 (t, *J* = 6.6 Hz, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 152.9, 150.2, 135.3, 134.0, 129.0, 127.0, 124.5, 120.8, 50.2, 26.9.

HRMS (ESI): Calcd for $C_{13}H_{12}N_2O_2S_3$ ($M^+$+H) *m/z* 325.0139. Found: 325.0133.

**Compound 47**



Yield: 0.092 g (82%, white solid, $R_f$ = 0.68 (9:1 hexane/ethyl acetate)).

Mp: 122-124 $^oC$.

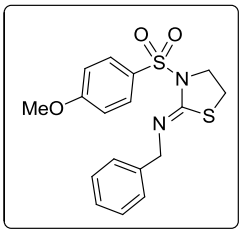
IR (KBr): 3255, 3058, 2915, 1640, 1583, 1484, 1435, 1230, 1160, 1106, 1104, 895 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.83-7.80 (m, 2H), 7.02-7.00 (m, 2H), 5.59 (br m, *J* = 8.0 Hz, 2H), 3.88 (s, 3H), 3.35-3.37 (m, 2H), 3.08 (t, *J* = 8.0 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 163.2, 130.8, 129.2, 114.5, 111.6, 55.7, 42.3, 33.8.

HRMS (ESI): Calcd for $C_{10}H_{13}N_2O_3S_2$ ($M^+$+H) *m/z* 273.0367. Found: 273.0366.

**Compound 48**




Yield: 0.105 g (86%, white solid, $R_f$ = 0.70 (9:1 hexane/ethyl acetate)).

Mp: 126-128 $^o$C.

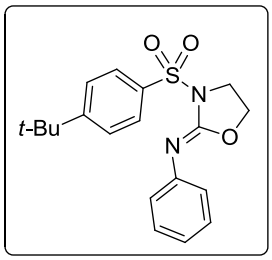
IR (KBr): 3018, 1697, 1353, 1214, 1159, 745, 665 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.92-7.90 (m, 2H), 7.28-7.23 (m, 3H), 7.13 (d, *J* = 5.2 Hz, 2H), 6.83-6.81 (m, 2H), 4.15 (t, *J* = 5.2 Hz, 2H), 3.84 (s, 3H), 3.25 (t, *J* = 5.2 Hz, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 163.6, 152.1, 139.4, 131.1, 128.8, 128.1, 127.5, 126.6, 113.7, 59.6, 55.6, 49.8, 27.2.

HRMS (ESI): Calcd for $C_{17}H_{19}N_2O_3S_2$ ($M^+$+H) *m/z* 363.0837. Found: 363.0838.

**Compound 49**




Yield: 0.087 g (78%, white solid, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

Mp: 194-196 $^o$C.

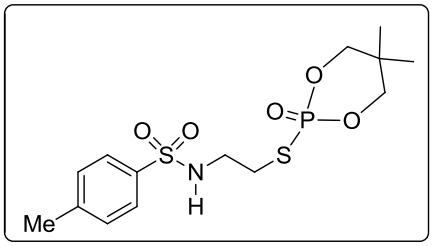
IR (KBr): 2910, 2843, 1706, 1644, 1593, 1474, 1402, 1360, 1309, 1267, 1226, 1174, 1081, 735 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.04 (d, *J* = 6.8 Hz, 2H), 7.57 (d, *J* = 6.8 Hz, 2H), 7.47 (d, *J* = 6.8 Hz, 2H), 7.34 (t, *J* = 6.4 Hz, 2H), 7.12 (t, *J* = 5.8 Hz, 1H), 4.05-4.01 (m, 2H), 3.91-3.88 (m, 2H), 1.35 (s, 9H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 157.9, 151.7, 138.4, 134.8, 129.0, 128.1, 126.1, 124.4, 118.6, 42.3, 41.2, 35.3, 31.0.

HRMS (ESI): Calcd for $C_{19}H_{22}N_2O_3S$ ($M^+$+Na) *m/z* 381.1249. Found: 381.1253.

**Compound 51**




Yield: 0.118 g (86%, white solid, $R_f$ = 0.42 (9:1 hexane/ethyl acetate)).

Mp: 136-138 $^o$C.

IR (KBr): 3175, 2974, 1324, 1262, 1155, 1092, 1050, 1000, 835, 782, 732 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 7.71-7.69 (m, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.19 (br, 1H), 4.08 (d, *J* = 12.0 Hz, 2H), 3.90-3.83 (m, 2H), 3.20-3.18 (m, 2H), 2.95-2.92 (m, 2H), 2.36 (s, 3H), 1.21 (s, 3H), 0.83 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 143.2, 137.1, 129.7, 127.0, 78.1 (*J* = 5.5 Hz), 43.6 (*J* = 2.1 Hz), 32.4 (*J* = 6.0 Hz), 29.4, 21.8, 21.4, 20.2.

$^{31}$P NMR (162 MHz, $CDCl_3$): $\delta$ 20.74.

HRMS (ESI): Calcd for $C_{14}H_{22}NO_5PS_2Na$($M^+$+Na) 402.0575. Found: 402.0575.

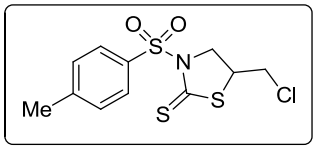
This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^o$C. X-ray structure was determined for this sample.

### 3.7 Mitsunobu reaction of 5-(hydroxymethyl)-3-tosylthiazolidine-2-thione 9 with $Ph_3P$/DEAD/nortriptyline

To an oven dried 10 mL RBF (round bottom flask) thiazolidine thione **9** (0.3 mmol) in toluene/DCM (9+1 mL), PPh3 (0.6 mmol), DEAD (diethyl azodicarboxylate) (0.6 mmol) and nortriptyline (0.4 mmol) was added at room temperature for 30 mins. After completion of the reaction as monitored by TLC, solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 9:1) afforded compound **52**. Compound **53** was prepared

following the same procedure and by using the same molar quantities of $PPh_3$, DEAD in THF solvent.

**Compound 52**




Yield: 0.094 g (89%, White solid, $R_f$ = 0.81 (9:1 hexane/ethyl acetate)).

Mp: 98-100 $^oC$.

IR (KBr): 2957, 2917, 1592, 1459, 1436, 1366, 1232, 1169, 1091, 1060, 807, 705 $cm^{-1}$

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ (ppm) 7.96 (d, $J$ = 8.4 Hz, 2H), 7.38 (d, $J$ = 8.0 Hz, 2H), 4.99-4.95 (m, 1H), 4.63-4.58 (m, 1H), 3.86-3.80 (m, 1H), 3.74-3.63 (m, 2H), 2.48 (s, 3H).

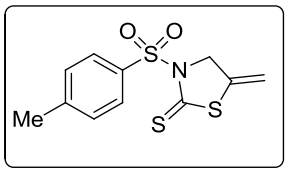
$^{13}C$ NMR (400 MHz, $CDCl_3$): $\delta$ 195.3, 146.4, 133.5, 129.8, 129.4, 59.2, 45.2, 44.4, 22.0.

LC/MS: *m/z* 322 $[M+1 (^{35}Cl)]^+$.

Anal. Calcd. for $C_{11}H_{12}ClNO_2S_3$: C, 41.05; H, 3.76; N, 4.35. Found: C, 41.13; H, 3.79; N, 4.28.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at room temperature. X-ray structure was determined for this sample.

**Compound 53**




Yield 0.079 g (85%, white solid, $R_f$ = 0.82 (9:1 hexane/ethyl acetate)).

Mp: 134-136 $^oC$.

IR (KBr): 3094, 3050, 2921, 1627, 1595, 1454, 1363, 1235, 1167, 1071, 874 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.95 (d, $J$ = 8.4 Hz, 2H), 7.36 (d, $J$ = 8.4 Hz, 2H), 5.32-5.30 (m, 1H), 5.28-5.09 (m, 3H), 2.46 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 194.6, 146.3, 134.8, 133.5, 129.6, 129.3, 106.3, 62.2, 21.8.

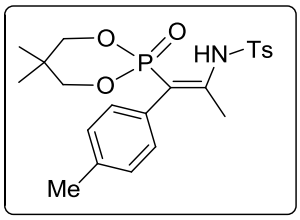
LC/MS: *m/z* 286 $[M+1]^+$.

Anal. Calcd. for $C_{11}H_{11}NO_2S_3$: C, 46.29; H, 3.88; N, 4.91. Found: C, 46.15; H, 3.83; N, 5.02.

### 3.8 Reaction of 5-(hydroxymethyl)-3-tosylthiazolidine-2-thione 9 with allenylphosphonate 5: Synthesis of compound 54

The method involves straightforward reaction using 0.32 mmol each of **9/5** in DMSO (ca 1 mL) and $K_2CO_3$ (1 equiv), stirred at 80 $^oC$ for 12 h. After completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 9:1) afforded compound **54**.

**Compound 54**




Yield: 0.118 g (80%, white solid, $R_f$ = 0.53 (9:1 hexane/ethyl acetate).

Mp: 152-154 $^oC$.

IR (KBr): 2966, 2887, 1600, 1471, 1441, 1380, 1342, 1304, 1163, 1051, 1004, 816 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 11.4 (br, 1H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 6.97-6.95 (m, 2H), 4.15-4.12 (m, 2H), 3.53-3.47 (m, 2H), 2.42 (s, 3H), 2.33 (s, 3H), 1.80 (d, *J* = 1.0 Hz, 3H), 0.87 (s, 3H), 0.50 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 153.0 (d, *J* = 7.1 Hz), 143.8, 137.5 (d, *J* = 20.3 Hz), 137.4, 131.3 (d, *J* = 4.6 Hz), 131.3, 131.2, 129.8, $129.1_1$, $129.1_0$, 127.3, 104.0 (d, *J* = 149.1 Hz), 75.6 (d, *J* = 5.1 Hz), 32.1 (d, *J* = 5.6 Hz), 21.6, 21.4, 21.2, 20.9, 17.4 (d, *J* = 11.4 Hz).

$^{31}P$ NMR (162 MHz, $CDCl_3$): $\delta$ 15.16.

LC/MS: *m/z* 450 $[M+1]^+$.

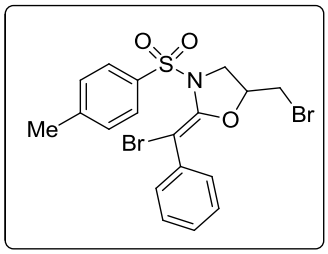
Anal. Calcd. For $C_{22}H_{28}NO_5PS$: C, 58.78; H, 6.28; N, 3.12. Found: C, 58.76; H, 6.28; N, 3.12.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^oC$. X-ray structure was determined for this sample.

### 3.9 Synthesis of 1,3 oxazolidines 55-62 from epoxy ynamides

To an oven dried RBF (10 mL), 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-(phenylethynyl)benzenesulfonamide (**7a**; 0.100 g, 0.3 mmol) in dry DMF (1 mL), CuBr (0.088 g, 0.6 mmol) was added. The mixture was heated with stirring at 80 $^{o}$C for 1-2 h. After completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL). The aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 9:1) afforded 1,3-oxazolidine **55**. Compounds **56-62** were prepared following the same procedure and by using the same molar quantities.

**Compound 55**




Yield: 0.131g (88% with *E:Z* in 96:4, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

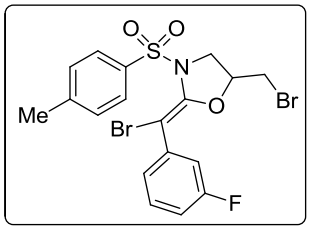
IR (KBr): 3054, 3030, 2959, 2923, 2852, 1649, 1596, 1490, 1443, 1367, 1346, 1165, 1088, 1052, 1018, 753 $cm^{-1}$.

$^{1}$H NMR (400 MHz, DMSO-$D_6$): $\delta$ 7.91 (d, *J* = 8.0 Hz, 2H), 7.54 (m, 4H), 7.38 (dd→t, *J* ~ 7.4 Hz, 2H), 7.29 (t, *J* ~ 7.4 Hz, 1H), 4.24-4.20 (m, 1H), 3. 97 (br m, 1H), 3.62-3.56 (m, 2H), 3.53-3.49 (m, 1H), 2.46 (s, 3H).

$^{13}$C NMR (125 MHz, DMSO-$D_6$): $\delta$ 146.4, 145.8, 136.6, 134.8, 130.7, 130.2, 129.8, 129.4, 128.6, 128.4, 128.2, 127.0, 93.6, 77.7, 51.8, 33.2, 21.6.

HRMS (ESI): Calcd. for $C_{18}H_{18}Br_2NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4) *m/z* 485.9374, 487.9354, 489.9334. Found: 485.9376, 487.9356, 489.9338.

**Compound 56**



Yield: 0.121 g (83% with *E:Z* in 78:22, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

Mp: 118-120 $^oC$

IR (KBr): 3068, 3033, 2958, 1648, 1608, 1582, 1487, 1434, 1348, 1265, 1165, 1088, 1054, 1019, 953, 779, 680 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$D_6$): Major isomer: δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.45-7.42 (m, 2H), 7.37-7.32 (m, 2H), 4.25-4.20 (m, 1H), 4.03-3.97 (m, 1H), 3.66-3.62 (m, 2H), 3.56-3.53 (m, 1H), 2.45 (s, 3H).

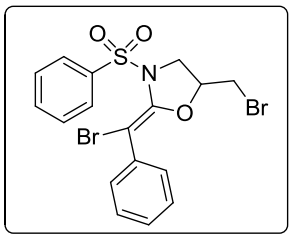
$^{13}C$ NMR (100 MHz, DMSO-$D_6$): Major isomer: δ 162.0 (d, *J* = 241.4 Hz), 147.3, 145.9, 138.8 (d, *J* = 8.3 Hz), 134.7, $130.7_4$, $130.6_8$, 128.2, 127.8, 126.9 (d, *J* = 3.3 Hz), 125.6 (d, *J* = 2.8 Hz), 115.9 (d, *J* = 23.3 Hz), 115.1 (d, *J* = 20.8 Hz), 91.8, 78.1, 51.8, 33.2, 21.6.

$^{19}F$ NMR: -113.30 (major isomer); -114.06 (minor isomer).

HRMS (ESI): Calcd. for $C_{18}H_{17}Br_2FNO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4): *m/z* 503.9280, 505.9260, 507.9240. Found: 503.9281, 505.9263, 507.9250.

This compound was crystallized from hexane/ethyl acetate (2:1) mixture at 25 $^oC$. X-ray structure was determined for the *E*-isomer.

**Compound 57**




Yield: 0.121g (80% with *E:Z* in 88:12, $R_f$ = 0.66 (9:1 hexane/ethyl acetate)).

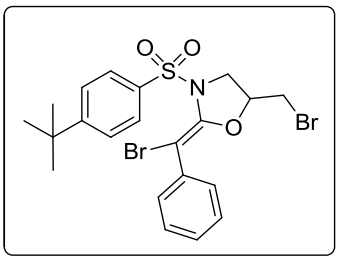
IR (KBr): 3061, 2955, 2926, 2854, 1651, 1446, 1367, 1348, 1168, 1088, 1053, 1023, 754, 726, 689 $cm^{-1}$.

$^1H$ NMR (400 MHz, DMSO-$D_6$): Major isomer: *δ* 8.04-8.02 (m, 2H), 7.86-7.82 (m, 1H), 7.75-7.72 (m, 2H), 7.56-7.54 (m, 2H), 7.39-7.36 (m, 2H), 7.31-7.27 (m, 1H), 4.26-4.22 (m, 1H), 4.01-3.96 (m, 1H), 3.64-3.58 (m, 2H), 3.52-3.49 (m, 1H).

$^{13}C$ NMR (100 MHz, DMSO-$D_6$): Major isomer: *δ* 146.3, 137.8, 136.6, 135.0, 130.3, 129.4, 128.6, 128.4, 128.2, 127.7, 93.6, 77.8, 51.9, 33.1.

HRMS (ESI): Calcd. for $C_{17}H_{16}Br_2NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4): *m/z* 471.9217, 473.9197, 475.9177. Found: 471.9218, 473.9195, 475.9178.

**Compound 58**




Yield: 0.117 g (82% with *E:Z* in 92:8, $R_f$ = 0.72 (9:1 hexane/ethyl acetate)).

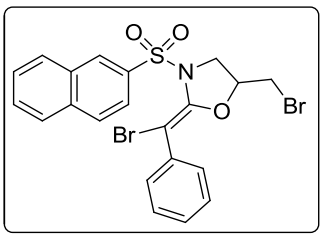
IR (KBr): 2925, 2870, 2854, 1752, 1596, 1496, 1399, 1331, 1267, 1164, 1113, 1088, 1027, 837, 753, 629 $cm^{-1}$.

$^1$H NMR (400 MHz, DMSO-$D_6$): Major isomer: δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.38 (dd→t, *J* ~ 7.4 Hz, 2H), 7.29 (t, *J* ~ 7.4 Hz, 1H), 4.22-4.17 (m, 1H), 4.03-3.98 (m, 1H), 3.61-3.55 (m, 2H), 3.49-3.45 (m, 1H), 1.34 (s, 9H).

$^{13}$C NMR (100 MHz, DMSO-$D_6$): Major isomer: δ 158.4, 146.4, 136.6, 134.7, 129.5, 128.6, 128.4, 128.2, 127.1, 93.6, 78.0, 51.8, 35.6, 33.1, 31.2.

HRMS (ESI): Calcd. for $C_{21}H_{24}Br_2NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4): *m/z* 527.9843, 529.9823, 531.9803. Found: 527.9842, 529.9824, 531.9801.

**Compound 59**




Yield: 0.112 g (78% with *E:Z* in 96: 4, $R_f$ = 0.70 (9:1 hexane/ethyl acetate)).

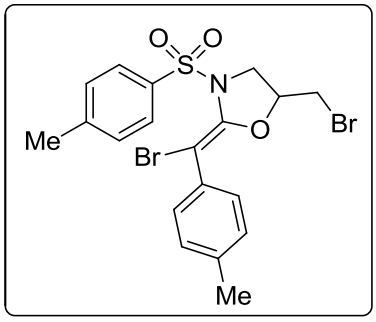
IR (KBr): 3058, 2923, 2853, 1748, 1591, 1504, 1455, 1444, 1336, 1260, 1157, 1131, 1073, 1027, 900, 814, 749, 659 $cm^{-1}$.

$^{1}$H NMR (500 MHz, DMSO-$D_6$): Major isomer: δ 8.75 (s, 1H), 8.28-8.24 (m, 2H), 8.12 (d, *J* = 8.0 Hz, 1H), 8.02-8.00 (m, 1H), 7.81-7.72 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.37 (dd→t, *J* ~ 7.7 Hz, 2H), 7.28 (t, *J* = 7.5 Hz, 1H), 4.34-4.30 (m, 1H), 4.01-3.97 (m, 1H), 3.68-3.64 (m, 1H), 3.59-3.56 (m, 1H), 3.51-3.50 (m, 1H).

$^{13}$C NMR (125 MHz, DMSO-$D_6$): Major isomer: δ 146.4, 136.6, 135.4, 134.8, 132.1, 130.4, 130.2, 130.1, 130.0, 129.5, 128.6, $128.5_3$, $128.4_6$, 128.4, 122.8, 93.6, 77.8, 52.0, 33.2.

HRMS (ESI): Calcd. for $C_{21}H_{17}Br_2NO_3SNa$ ($M^+$+Na), ($M^+$+Na+2), ($M^+$+Na+4): *m/z* 543.9194, 545.9174, 547.9154. Found: 543.9193, 545.9180, 547.9155.

**Compound 60**




Yield: 0.126 g (86% with *E:Z* in 86:14, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

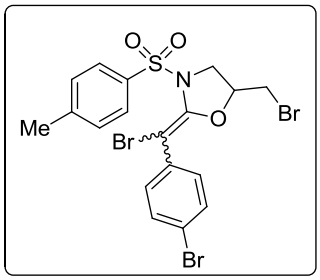
IR (KBr): 2960, 2923, 2855, 1747, 1597, 1513, 1422, 1330, 1260, 1159, 1090, 1018, 811, 752 $cm^{-1}$.

$^{1}$H NMR (500 MHz, DMSO-$D_6$): Major isomer: δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 4.21-4.17 (m, 1H), 3.93-3.90 (m, 1H), 3.59-3.53 (m, 2H), 3.50-3.47 (m, 1H), 2.44 (s, 3H), 2.30 (1s, 3H).

$^{13}$C NMR (125 MHz, DMSO-$D_6$): Major isomer: δ 146.0, 145.7, 137.9, 134.8, 133.8, 130.7, 129.3, 129.1, 128.2, 127.7, 93.9, 77.6, 51.8, 33.2, 21.6, 21.2.

HRMS (ESI): Calcd. for $C_{19}H_{20}Br_2NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4): *m/z* 499.9530, 501.9500, 503.9480. Found: 499.9523, 501.9504, 503.9484.

**Compound 61 (two isomers)**




Yield: 0.108 g (78% with *E:Z* in 54:46, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

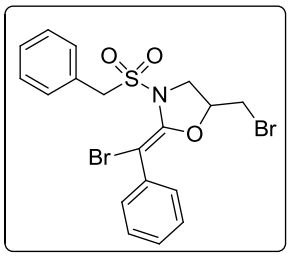
IR (KBr): 2956, 2925, 2854, 1748, 1657, 1596, 1488, 1338, 1163, 1090, 1011, 814, 756, 669 $cm^{-1}$.

$^1H$ NMR (500 MHz, DMSO-$D_6$): Isomer 1: δ 7.89 (d, *J* = 8.5 Hz, 2H), 7.53-7.48 (m, 6H), 4.23-4.19 (m, 1H), 4.00-3.94 (m, 1H), 3.59-3.56 (m, 2H), 3.52-3.49 (m, 1H), 2.44 (s, 3H). Isomer 2: δ 7.59-7.57 (m, 2H), 7.45-7.41 (m, 4H), 7.38-7.36 (m, 2H), 4.34-4.30 (m, 1H); 4.00-3.94 (m, 1H), 3.82-3.78 (m, 1H); 3.64-3.60 (m, 2H), 2.43 (s, 3H).

$^{13}C$ NMR (125 MHz, DMSO-$D_6$): Isomer 1: δ 146.9, 145.8, 135.9, 134.8, 132.0, 131.4, 130.7, 130.3, 128.2, 121.3, 92.1, 77.9, 51.9, 33.1, 21.6. Isomer 2: 146.5, 145.7, 137.2, 134.3, 131.5, 131.3, 130.6, 127.7, 121.0, 88.9, 76.9, 52.9, 32.8, 21.6.

HRMS (ESI): Calcd. for $C_{18}H_{17}Br_3NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4), ($M^+$+H+6): *m/z* 563.8479, 565.8459, 567.8439, 569.8419. Found: 563.8479, 565.8447, 567.842, 569.8403.

**Compound 62**




Yield: 0.126 g (85% with *E:Z* in 94:6, $R_f$ = 0.80 (9:1 hexane/ethyl acetate)).

IR (KBr): 2929, 1745, 1495, 1455, 1327, 1212, 1127, 1029, 830, 751, 695 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.68-7.65 (m, 2H), 7.59-7.57 (m, 2H), 7.48-7.46 (m, 3H), 7.38-7.34 (m, 2H), 7.29-7.25 (m, 1H), 4.77 (AB pattern, 2H), 4.49-4.42 (m, 1H), 3.43-3.33 (m, 3H), 3.27-3.23 (m, 1H).

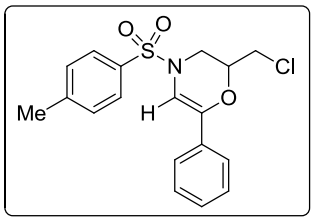
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 146.2, 135.9, 131.4, 129.3, 128.9, 128.1, 128.0, 127.9, 92.1, 78.1, 60.7, 52.5, 30.0.

HRMS (ESI): Calcd. for $C_{18}H_{18}Br_2NO_3S$ ($M^+$+H), ($M^+$+H+2), ($M^+$+H+4): *m/z* 485.9374, 487.9354, 489.9334. Found: 485.9368, 487.9353, 489.9331.

### 3.10 Synthesis of 1,4-oxazines 63-70 from epoxy ynamides

To an oven dried 10 mL RBF, 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-(phenylethynyl)benzenesulfonamide (**7a**; 0.1 g, 0.3 mmol) in DMF/$H_2O$(0.9+0.1 mL), anhy. LiCl (0.024 g, 0.6 mmol) was added. The mixture was heated with stirring at 80 $^{o}$C for 12 h. After completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 9:1) afforded compound 1,4-oxazine **63**. Compounds **63'** and **64-70** were prepared following the same procedure and by using the same molar quantities.

**Compound 63**




Yield: 0.086 g (78%, $R_f$ = 0.80 (9:1 hexane/ethyl acetate)).

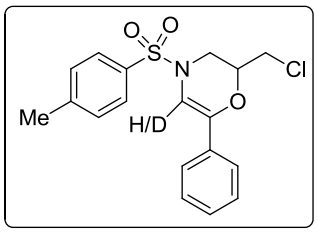
IR (KBr): 3112, 3059, 3028, 2960, 2924, 2872, 1651, 1597, 1494, 1353, 1306, 1164, 1005, 755 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.51-7.48 (m, 2H), 7.37-7.30 (m, 5H), 6.75 (s, 1H), 4.03-4.00 (m, 1H), 3.70-3.64 (m, 2H), 3.53-3.48 (m, 1H), 3.26-3.21 (m, 1H), 2.45 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 1.44.4, 139.8, 133.1, 130.1, 128.4, 128.2, 127.4, 123.8, 101.8, 71.9, 45.1, 42.4, 21.6.

HRMS (ESI): Calcd. for $C_{18}H_{19}ClNO_3S$ ($M^+$+H), ($M^+$+H+2): *m/z* 364.0774, 366.0744. Found: 364.0772, 366.0747.

**Compound 63'**




Yield: 0.061 g (55%, $R_f$ = 0.79 (9:1 hexane/ethyl acetate)).

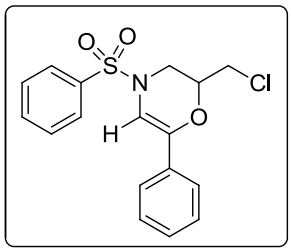
IR (KBr): 2957, 2925, 2855, 1725, 1637, 1598, 1494, 1356, 1167, 1089, 760 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.5 Hz, 2H), 7.50-7.48 (m, 2H), 7.37-7.34 (m, 4H), 7.32-7.30 (m, 1H), 6.75 (s, *0.1*H), 4.02-4.00 (m, 1H), 3.70-3.64 (m, 2H), 3.52-3.49 (m, 1H), 3.26-3.22 (m, 1H), 2.45 (s, 3H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ 144.3, 139.7, 133.7, 133.2, 130.0, 128.4, 128.2, 127.4, 123.8, 101.8, 101.4 (d, *J* = 28.4 Hz), 72.0, 45.0, 42.4, 21.6.

HRMS (ESI): Calcd. for $C_{18}H_{17}DClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 387.0657, 389.0627. Found: 387.0654, 389.0628.

**Compound 64**




Yield: 0.082 g (74%, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

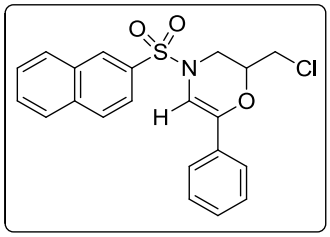
IR (KBr): 3027, 2960, 2925, 2873, 1652, 1446, 1354, 1309, 1166, 1088, 1007, 749, 688 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): *δ* 7.85 (d, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.58 (dd→t, *J* ~ 7.6 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.39-7.30 (m, 3H), 6.77 (s, 1H), 4.03 (d, *J* = 13.2 Hz, 1H), 3.70-3.63 (m, 2H), 3.52-3.48 (m, 1H), 3.29-3.24 (m, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 139.9, 136.5, 133.5, 133.1, 129.5, 128.5, 128.3, 127.3, 123.8, 101.6, 72.0, 45.1, 42.4.

HRMS (ESI): Calcd. for $C_{17}H_{17}ClNO_3S$ ($M^+$+H), ($M^+$+H+2): *m/z* 350.0617, 352.0587. Found: 350.0616, 352.0584.

**Compound 65**




Yield: 0.076 g (69%, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

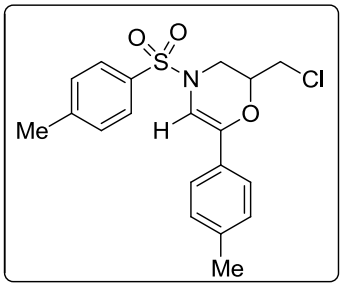
IR (KBr): 3027, 2959, 2926, 1653, 1498, 1448, 1350, 1308, 1164, 1133, 1074, 1007, 858, 751 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): $\delta$ 8.43 (s, 1H), 8.02-7.99 (m, 2H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.82-7.80 (m, 1H), 7.71-7.63 (m, 2H), 7.50-7.48 (m, 2H), 7.37-7.30 (m, 3H), 6.84 (s, 1H), 4.12-4.09 (m, 1H), 3.68-3.62 (m, 2H), 3.50-3.46 (m, 1H), 3.33-3.29 (m, 1H).

$^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ 139.9, 135.1, 133.6, 133.1, 132.2, 129.8, 129.4, 129.3, 128.9, 128.5, 128.3, 128.0, 127.9, 123.9, 122.3, 101.7, 72.0, 45.1, 42.4.

HRMS (ESI): Calcd. for $C_{21}H_{18}ClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 422.0594, 424.0564. Found: 422.0595, 424.0559.

**Compound 66**




Yield: 0.085 g (77%, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

Mp: 124-126 $^o$C.

IR (KBr): 3111, 3031, 2957, 2922, 2871, 1655, 1597, 1514, 1354, 1308, 1165, 1089, 1007, 818, 758 $cm^{-1}$.

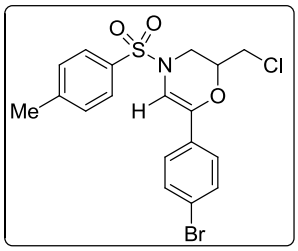
$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.70 (s, 1H), 4.02-4.00 (m, 1H), 3.68-3.60 (m, 2H), 3.51-3.48 (m, 1H), 3.25-3.20 (m, 1H), 2.45 and 2.40 (2s, 6H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 144.3, 140.0, 138.2, 133.7, 130.4, 130.0, 129.1, 127.4, 123.8, 101.1, 72.0, 45.1, 42.4, 21.6, 21.2.

HRMS (ESI): Calcd. for $C_{19}H_{20}ClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 400.0750, 402.0720. Found: 400.0743, 402.0714.

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

**Compound 67**




Yield: 0.067 g (62%, $R_f$ = 0.80 (9:1 hexane/ethyl acetate)).

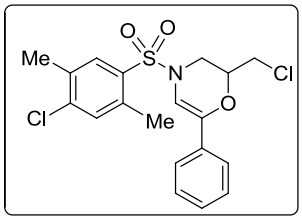
IR (KBr): 3110, 3028, 2960, 2924, 1651, 1596, 1490, 1355, 1308, 1166, 1088, 1006, 752 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 2H), 7.48-7.45 (m, 2H), 7.36-7.34 (m, 4H), 6.75 (s, 1H), 4.01-3.98 (m, 1H), 3.68-3.64 (m, 2H), 3.52-3.50 (m, 1H), 3.25-3.21 (m, 1H), 2.45 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 143.5, 137.7, 132.7, 131.1, 130.5, 129.1, 126.3, 124.2, 121.0, 101.2, 71.0, 44.0, 41.3, 20.6.

HRMS (ESI): Calcd. for $C_{18}H_{17}BrClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2), ($M^+$+Na+4): *m/z* 463.9699, 465.9679, 467.9659. Found: 463.9702, 465.9681, 467.9657.

**Compound 68**




Yield: 0.068 g (65%, $R_f$ = 0.79 (9:1 hexane/ethyl acetate)).

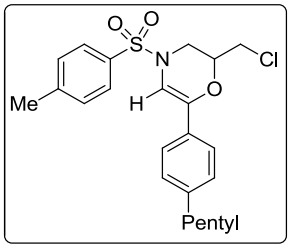
IR (KBr): 2961, 2926, 2870, 2857, 1724, 1658, 1599, 1448, 1365, 1341, 1165, 1087, 1016, 758 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.51-7.50 (m, 2H), 7.38-7.30 (m, 4H), 6.75 (s, 1H), 3.95-3.90 (m, 2H), 3.77-3.73 (m, 1H), 3.60-3.56 (m, 1H), 3.29-3.25 (m, 1H), 2.62 and 2.42 (2 s, 6H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ 139.8, 139.1, 136.7, 134.8, 133.8, 133.4, 133.1, 132.4, 128.5, 128.2, 123.8, 101.6, 72.4, 44.6, 42.3, 20.5, 19.6.

HRMS (ESI): Calcd. for $C_{19}H_{19}Cl_2NO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 434.0361, 436.0331. Found: 434.0363, 436.0329.

**Compound 69**




Yield: 0.081 g (74%, $R_f$ = 0.81 (9:1 hexane/ethyl acetate)).

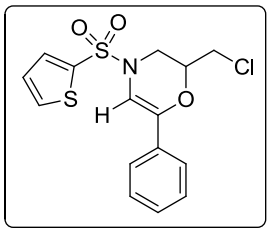
IR (KBr): 3112, 3029, 2956, 2927, 2856, 1658, 1597, 1356, 1310, 1261, 1218, 1167, 1124, 1055, 1009, 813, 770 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.70 (s, 1H), 4.01-3.98 (m, 1H), 3.68-3.59 (m, 2H), 3.51-3.47 (m, 1H), 3.24-3.20 (m, 1H), 2.61 (t, *J* = 7.7 Hz, 2H), 2.45 (s, 3H), 1.64-1.58 (m, 2H), 1.36-1.30 (m, 4H), 0.90 (t, *J* = 7.0 Hz, 3H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ 144.3, 143.3, 140.0, 133.7, 130.6, 130.0, 128.5, 127.4, 123.8, 101.1, 71.9, 45.1, 42.4, 35.6, 31.4, 31.0, 22.5, 21.6, 14.0.

HRMS (ESI): Calcd. for $C_{23}H_{28}ClNO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 456.1376, 458.1346. Found: 456.1375, 458.1350.

**Compound 70**




Yield: 0.076 g (69%, $R_f$ = 0.70 (9:1 hexane/ethyl acetate)).

IR (KBr): 3110, 3028, 2958, 2926, 1652, 1448, 1403, 1360, 1310, 1226, 1165, 1092, 1014, 757, 724 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ 7.66-7.65 (m, 1H), 7.64-7.63 (m, 1H), 7.53-7.51 (m, 2H), 7.38-7.32 (m, 3H), 7.18-7.16 (m, 1H), 6.71 (s, 1H), 4.08-4.05 (m, 1H), 3.74-3.67 (m, 2H), 3.58-3.55 (m, 1H), 3.30-3.26 (m, 1H).

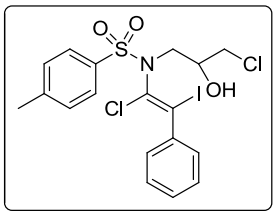
$^{13}C$ NMR (125 MHz, $CDCl_3$): δ 140.7, 136.6, 133.0, $132.8_4$, $132.8_0$, 128.5, 128.4, 127.9, 123.9, 101.1, 72.0, 45.2, 42.4.

HRMS (ESI): Calcd. for $C_{15}H_{15}ClNO_3S_2$ ($M^+$+H), ($M^+$+H+2): *m/z* 356.0182, 358.0152. Found: 356.0187, 358.0160.

### 3.11 Synthesis of *α*-chloro, *β*-iodo enamides 71-73 from epoxy ynamides

To an oven dried 10 mL RBF, 4-methyl-*N*-(oxiran-2-ylmethyl)-*N*-(phenylethynyl)benzenesulfonamide (**7a**; 0.100 g, 0.3 mmol), 1M ICl in acetonitrile (1 mL) solution was added at 0 $^oC$. The mixture was stirred at 0 $^oC$ to rt for 1 h. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure and purification by column chromatography (hexane/ethyl acetate 9:1) afforded compound **71**. Compounds **71-73** were prepared following the same procedure and by using the same molar quantities.

**Compound 71**



Yield: 0.143 g (89% with *E:Z* in 53:47, $R_f$ = 0.68 (9:1 hexane/ethyl acetate)).

Mp: 124-126 $^{o}$C.

IR (KBr): 3534, 2926, 1595, 1490, 1441, 1353, 1167, 1090, 1025, 816, 701, 658 cm$^{-1}$.

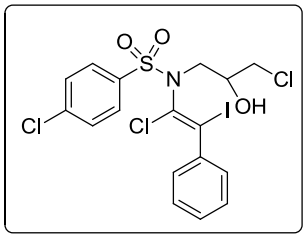
$^{1}$H NMR (400 MHz, $CDCl_3$): Isomer 1: δ 7.89-7.86 (m, 4H), 7.41-7.40 (m, 5H), 4.22-4.18 (m, 1H), 3.76-3.73 (m, 1H), 3.69-3.66 (m, 1H), 3.59-3.54 (m, 1H), 3.44-3.40 (m, 1H), 2.47 (s, 3H). Isomer 2: 7.39-7.36 (m, 9H), 4.28-4.26 (m, 1H), 4.05-4.02 (m, 1H), 3.85-3.81 (m, 1H), 3.66-3.62 (m, 1H), 3.37-3.33 (m, 1H), 2.47 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): Isomer 1: δ 145.3, 141.3, 134.3, 129.9, 129.2, 129.0, 128.5, 128.5, 128.4, 128.2, 103.6, 68.6, 52.2, 46.1, 21.7. Isomer 2: 145.2, 141.1, 134.3, 129.8, 129.1, 128.9, 128.5, 128.4, 127.7, 102.9, 69.3, 51.3, 47.9, 21.7.

HRMS (ESI): Calcd. for $C_{18}H_{19}Cl_2INO_3S$ ($M^+$+H), ($M^+$+H+2): *m/z* 525.9507, 527.9477, 529.9447. Found: 525.9506, 527.9475, 529.9429.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^{o}$C. X-ray structure was determined for *E*-isomer.

**Compound 72**



Yield: 0.134 g (85% with *E:Z* in 53:47, $R_f$ = 0.70 (9:1 hexane/ethyl acetate)).

Mp: 102-104 $^{o}$C.

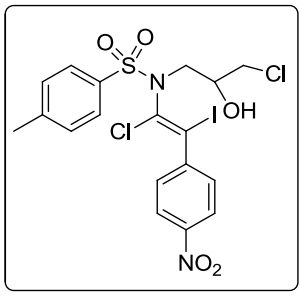
IR (KBr): 3523, 3063, 2921, 1753, 1600, 1490, 1441, 1359, 1227, 1167, 1085, 1041, 822, 707 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): Isomer 1: δ 7.95-7.92 (m, 4H), 7.58-7.52 (m, 5H), 4.23-4.19 (m, 1H), 3.77-3.74 (m, 1H), 3.60-3.55 (m, 1H), 3.47-3.43 (m, 1H), 3.40-3.35 (m, 1H). Isomer 2: δ 7.42-7.35 (m, 9H), 4.31-4.27 (m, 1H), 4.03-4.00 (m, 1H), 3.86-3.82 (m, 1H), 3.70-3.63 (m, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): Isomer 1: δ 140.9, $140.8_6$, 135.9, 130.3, 129.6, 129.3, 128.5, 128.4, 127.3, 104.1, 68.6, 52.3, 46.1. Isomer 2: 141.1, $140.7_8$, 135.8, 130.3, 129.5, 129.2, 128.5, 128.3, 127.7, 103.5, 69.2, 51.5, 47.8.

HRMS (ESI): Calcd. for $C_{17}H_{15}Cl_3INO_3SNa$ ($M^+$+Na), ($M^+$+Na+2): *m/z* 567.8781, 569.8751. Found (major peaks): 567.8782, 569.8754.

**Compound 73**




Yield: 0.125 g (82% with *E:Z* in 51:49, $R_f$ = 0.69 (9:1 hexane/ethyl acetate)).

Mp: 128-130 $^{o}$C.

IR (KBr): 3535, 3103, 3068, 2963, 1744, 1599, 1522, 1403, 1348, 1261, 1165, 1014, 814, 711 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): Isomer 1: δ 8.30-8.26 (m, 4H), 7.88-7.85 (m, 4H), 4.21-4.16 (m, 1H), 3.79-3.77 (m, 1H), 3.70-3.67 (m, 1H), 3.59-3.53 (m, 1H), 3.46-3.41 (m, 1H), 2.48 (s, 3H). Isomer 2: 7.59-7.55 (m, 4H), 7.40-7.37 (m, 4H), 4.29-4.25 (m, 1H), 4.01-3.97 (m, 1H), 3.82-3.80 (m, 1H), 3.66-3.62 (m, 1H), 3.36-3.31 (m, 1H), 2.48 (s, 3H).

$^{13}$C NMR (125 MHz, $CDCl_3$): Isomer 1: δ 147.8, 147.5, 145.5, 134.1, 130.1, 129.9, 129.6, 128.9, 127.0, 124.1, 123.9, 99.0, 69.5, 52.1, 46.3, 21.7. Isomer 2: 147.7, 147.4, 145.6, 134.0, 130.0, 129.7, 129.6, 127.0, 124.0, 123.8, 99.5, 68.9, 51.3, 47.7, 21.7.

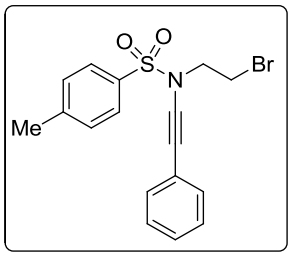
HRMS (ESI): Calcd. for $C_{18}H_{21}Cl_2IN_3O_5S$ ($M^+$+$NH_4^+$), ($M^+$+$NH_4^+$+2), ($M^+$+$NH_4^+$+4): *m/z* 587.9624, 589.9594, 591.9564. Found: 587.9625, 589.9598, 591.9575.

This compound was crystallized from DCM/hexane (2:1) mixture at room temperature. X-ray structure was determined for this sample (*E* isomer).

### 3.12 Synthesis of ynamide 74

To a mixture of N-(2-bromoethyl)-4-methylbenzenesulfonamide **2a** (1.00 g, 3.62 mmol), $CuSO_4 \cdot 5H_2O$ (0.180 g, 0.72 mmol), 1,10-phenanthroline monohydrate (0.287 g, 1.44 mmol) and $K_2CO_3$ (1.25 g, 9.0 mmol) in dry THF (20 mL), (bromoethynyl)benzene **6a** (0.786 g, 4.34 mmol) was added. The vessel was stoppered under nitrogen atmosphere and heated overnight on an oil-bath maintained at 70 $^oC$. The mixture was filtered and concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain the pure ynamide **74** by using hexane-ethyl acetate (8:2) as the eluent.

**Compound 74**




Yield: 1.03 g (76%, $R_f$ = 0.67 (9:1 hexane/ethyl acetate)).

IR (KBr): 3061, 2925, 2855, 2235, 1730, 1704, 1597, 1493, 1367, 1289, 1168, 1119, 1089, 1020, 958, 813, 755 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): $\delta$ 7.89 (d, $J$ = 8.4 Hz, 2H), 7.40 -7.33 (m, 7H), 3.83 (t, $J$ = 7.4 Hz, 2H), 3.58 (t, $J$ = 7.4 Hz, 2H), 2.49 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): $\delta$ 145.2, 134.3, 131.6, 129.9, 128.4, 128.2, 127.8, 122.3, 81.4, 71.2, 52.7, 27.5, 21.7.

HRMS (ESI): Calcd for $C_{17}H_{17}BrNO_2S$ ($M^+$+H), ($M^+$+H+2) *m/z* 378.0163, 380.0143. Found 378.0164, 380.0145.

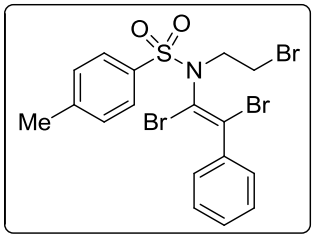
Anal.Calcd. for: C, 53.98; H, 4.26; N, 3.70. Found: C, 53.86; H, 4.22; N, 3.65.

### 3.13 Synthesis of *α,β*-dibromo enamide 75 from ynamide 74

To an oven dried 10 mL RBF (round bottom flask) N-(2-bromoethyl)-4-methyl-N-(phenylethynyl)benzenesulfonamide **74** (0.3 mmol) in dry acetonitrile (1 mL), CuBr (0.6 mmol)

was added at 25 $^{o}$C for 5 min. After completion of the reaction as monitored by TLC, the contents were passed through a pad of celite, washed with ethyl acetate (2 x 20 mL) and concentrated *in vacuo*. Purification by column chromatography (hexane/ethyl acetate 9:1) afforded compound **75**.

**Compound 75**




Yield: 0.131 g (92%, white solid, $R_f$ = 0.76 (9:1 hexane/ethyl acetate)).

Mp: 132-134 $^{o}$C.

IR (KBr): 2954, 2923, 2853, 1597, 1492, 1445, 1361, 1165, 1087, 967, 899, 813, 695 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.92-7.89 (m, 2H), 7.47-7.37 (m, 7H), 3.92-3.86 (m, 1H), 3.76-3.70 (m, 1H), 3.61-3.47 (m, 2H), 2.48 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 145.1, 138.8, 134.6, 130.0, 129.8, 129.6, 128.9, 128.8, 128.5, 128.3, 126.9, 116.2, 50.4, 27.2, 21.7.

HRMS (ESI): Calcd. for $C_{17}H_{16}Br_3NO_2SNa$ ($M^+$+Na), ($M^+$+Na+2), ($M^+$+Na+2): *m/z* 557.8350, 559.8330, 561.8310. Found: 557.8352, 559.8336, 561.8316.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at 25 $^{o}$C. X-ray structure was determined for this sample.

### 3.14 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **9**, **19, 32, 45, 51, 52, 54, 56, 66, 71, 73** and **75**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer using Mo-$K_\alpha$ radiation (λ = 0.71073 Å) or Cu- $K_\alpha$ (λ = 1.54184 Å). Structures were solved and refined using standard methods.[93] Absorption corrections were done using SADABS program, where applicable. All non-hydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier and refined isotropically. Crystal data are summarized in Tables 10-13.

**Table 10**: Crystal data for compounds **9**, **19**, **32** and **45**[a]

| Compound | **9** | **19** | **32** | **45** |
|---|---|---|---|---|
| Emp. formula | $C_{11}H_{13}NO_3S_3$ | $C_{17}H_{17}ClN_2OS_2$ | $C_{10}H_{11}NO_2S_3$ | $C_{18}H_{19}ClN_2O_2S_2$ |
| Formula weight | 303.40 | 396.90 | 273.38 | 394.92 |
| Crystal system | Triclinic | Monoclinic | Monoclinic | Monoclinic |
| Space group | *P-1* | *P 21/c* | *P 21/c* | *P 21/c* |
| *a* /Å | 6.0374(7) | 10.9934(13) | 6.1417(8) | 17.218(7) |
| *b* /Å | 9.0824(10) | 15.541(2) | 9.6650(13) | 7.657(3) |
| *c* /Å | 13.2438(15) | 10.7812(15) | 20.803(3) | 14.611(6) |
| $\alpha$/deg | 71.460(2) | 90 | 90 | 90 |
| $\beta$/deg | 92.682(6) | 99.582(4) | 97.498(2) | 103.225(12) |
| $\gamma$/deg | 78.837(2) | 90 | 90 | 90 |
| *V* /Å$^3$ | 674.86(13) | 1816.2(4) | 1224.3(3) | 1875.2(13) |
| *Z* | 2 | 4 | 4 | 4 |
| *D*calc /g cm$^{-3}$] | 1.493 | 1.452 | 1.483 | 1.399 |
| $\mu$ /mm$^{-1}$ | 0.548 | 0.459 | 0.589 | 0.440 |
| *F*(000) | 316.0 | 824.0 | 568.0 | 824.0 |
| Data/ restraints/ parameters | 2370/0/174 | 3193/0/226 | 2161/0/146 | 3274 /0/229 |
| S | 1.060 | 1.057 | 1.182 | 1.009 |
| R1 [I>2σ(I)] | 0.0703 | 0.0885 | 0.056 | 0.0547 |
| wR2 [all data] | 0.2115 | 0.2073 | 0.1351 | 0.1277 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.784/-0.505 | 1.346/-0.753 | 0.357/-0.262 | 0.299/-0.334 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 11**: **Crystal data for compounds 51, 52 and 54**[a]

| Compound | **51** | **52** | **54** |
|---|---|---|---|
| Emp. formula | $C_{14}H_{22}NO_5PS_2$ | $C_{11}H_{12}ClNO_2S_3$ | $C_{22}H_{28}NO_5PS$ |
| Formula weight | 379.42 | 321.85 | 449.48 |
| Crystal system | Triclinic | Monoclinic | Monoclinic |
| Space group | *P-1* | *P2(1)/c* | *P2(1)/c* |
| *a* /Å | 6.8296(8) | 8.2234(8) | 15.4813(7) |
| *b* /Å | 7.4875(8) | 8.3596(7) | 13.2156(6) |
| *c* /Å | 18.4067(19) | 20.6229(18) | 11.7370(4) |
| $\alpha$/deg | 80.149(5) | 90 | 90 |
| $\beta$/deg | 81.744(5) | 93.712(9) | 98.0030(10) |
| $\gamma$/deg | 82.580(4) | 90 | 90 |
| *V* /Å$^3$ | 912.47(17) | 1414.7(2) | 2377.94(17) |
| *Z* | 2 | 4 | 4 |
| *D*calc /g cm$^{-3}$] | 1.381 | 1.511 | 1.256 |
| $\mu$ /mm$^{-1}$ | 0.401 | 6.483 | 0.235 |
| *F*(000) | 400.0 | 664.0 | 952.0 |
| Data/ restraints/ parameters | 3205 /4/214 | 2700/0/164 | 4165/0/280 |
| S | 1.088 | 1.024 | 1.051 |
| R1 [I>2σ(I)] | 0.1064 | 0.0724 | 0.0625 |
| wR2 [all data] | 0.2825 | 0.2268 | 0.1792 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.760/-0.558 | 0.989/-0.336 | 0.798/-0.617 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 12**: **Crystal data for compounds 56, 66 and 71**[a]

| Compound | **56** | **66** | **71** |
|---|---|---|---|
| Emp. formula | $C_{18}H_{16}Br_2FNO_3S$ | $C_{19}H_{20}ClNO_3S$ | $C_{18}H_{18}Cl_2INO_3S$ |
| Formula weight | 505.20 | 377.87 | 526.19 |
| Crystal system | Triclinic | Monoclinic | Triclinic |
| Space group | *P-1* | *C2/c* | *P-1* |
| *a* /Å | 6.9921(3) | 18.258(2) | 8.1350(16) |
| *b* /Å | 11.2113(6) | 13.0810(13) | 10.516(2) |
| *c* /Å | 12.4434(7) | 15.4466(14) | 13.286(3) |
| $\alpha$/deg | 96.443(2) | 90 | 75.18(3) |
| $\beta$/deg | 95.376(2) | 91.845(3) | 82.70(3) |
| $\gamma$/deg | 95.626(2) | 90 | 69.77(3) |
| *V* /Å$^3$ | 959.19(9) | 3687.2(6) | 1030.1(4) |
| *Z* | 2 | 8 | 2 |
| *D*calc /g cm$^{-3}$] | 1.749 | 1.361 | 1.696 |
| $\mu$ /mm$^{-1}$ | 4.361 | 0.338 | 1.932 |
| *F*(000) | 500.0 | 1584.0 | 520.0 |
| Data/ restraints/ parameters | 3377/0/237 | 3227/0/229 | 3604 /0/240 |
| S | 0.897 | 1.123 | 1.046 |
| R1 [I>2$\sigma$(I)] | 0.0479 | 0.0488 | 0.0674 |
| wR2 [all data] | 0.1485 | 0.1434 | 0.1750 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.947/-1.082 | 0.717/-0.320 | 1.401/-0.907 |

[a]R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 13**: **Crystal data for compounds 73 and 75**[a]

| Compound | **73** | **75** |
|---|---|---|
| Emp. formula | $C_{17}H_{15}Cl_2IN_2O_5S$ | $C_{17}H_{16}Br_3NO_2S$ |
| Formula weight | 557.18 | 538.10 |
| Crystal system | Triclinic | Monoclinic |
| Space group | *P-1* | *P2(1)/c* |
| *a* /Å | 8.2369(9) | 8.2985(3) |
| *b* /Å | 10.5969(15) | 12.4303(6) |
| *c* /Å | 15.273(2) | 19.4432(8) |
| $\alpha$/deg | 78.483(7) | 90 |
| $\beta$/deg | 85.906(7) | 101.3220(10) |
| $\gamma$/deg | 80.176(7) | 90 |
| *V* /Å$^3$ | 1286.2(3) | 1966.59(14) |
| *Z* | 2 | 4 |
| *D*calc /g cm$^{-3}$] | 1.658 | 1.817 |
| $\mu$ /mm$^{-1}$ | 1.772 | 6.269 |
| *F*(000) | 632.0 | 1048.0 |
| Data/ restraints/ parameters | 4578/0/294 | 3431/0/218 |
| S | 1.038 | 1.047 |
| R1 [I>2σ(I)] | 0.0759 | 0.0394 |
| wR2 [all data] | 0.1987 | 0.1036 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.799/-0.982 | 0.669/-0.826 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

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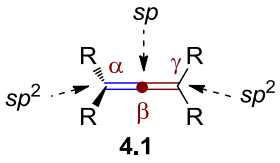
# INTRODUCTION

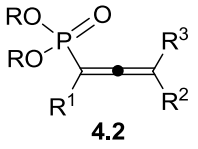
## 4.1 General Introduction: Allenes

Allenes **4.1** have always engrossed the minds of chemists because of their interesting feature of having two cumulative C=C double bonds and three reactive carbon centers. They exhibit unique reactivity and constitute building blocks for many precursors for highly complex and strained molecules including natural products, pharmaceuticals and molecular materials.[1] They can undergo reactions with nucleophiles as well as electrophiles.[2] Allenylphosphonates **4.2** and allenylphosphine oxides **4.3** constitute a special class of allenes containing one of the substituents as -P(O)(OR)$_2$ and -P(O)R$_2$ group, respectively. Due to the relative stability and low cost of preparation, these are valuable precursors for exploring allene chemistry. In general, changing the substituents on the allene can alter the reactivity preferences as shown in Chart 1 for compounds **4.4**-**4.7**.



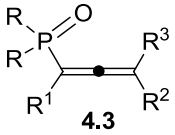

**4.1**

**Three reactive carbon centers: Allene**




**4.2**

**Allenylphosphonate**




**4.3**

**Allenylphosphine oxide**

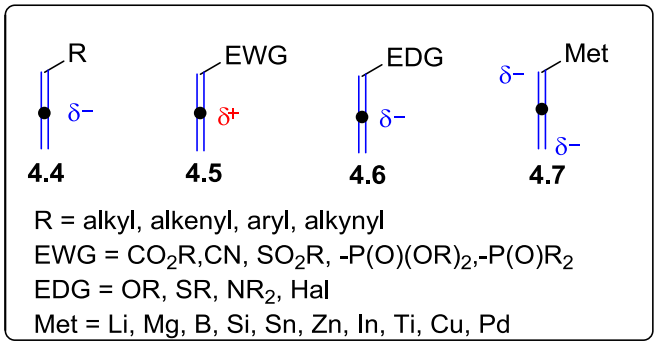


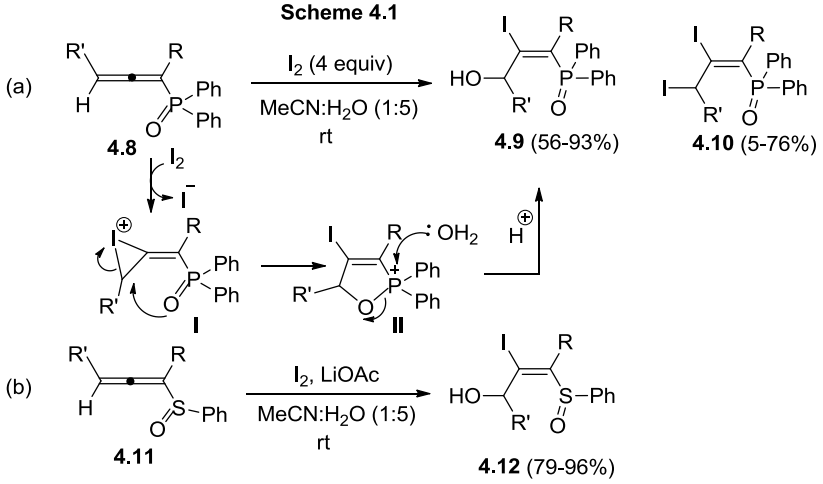

**Chart 1. Reactivity preferences of allenes based on the substituents on one of the C($sp^2$) centers.**

In the past decade, by using phosphorus based allenes, various phosphorus substituted heterocycles/homocycles like isocoumarins, benzofurans,[3a] pyrazoles, triazoles,[3b] tetrahydrofurans,[3c] indenes, indenones, isochromenes,[3d] indolo-pyrane-1-ones,[3e] pyrazines, pyrroles,[3f] indolinones, indoles,[3g-3h] dihydro[1,2]oxaphospholes,[3i] pyrrolines,[3j] tetrahydropyridines,[3j] cyclopentenes,[3j] substituted vinylphosphonates/allylphosphonates[3k-p] and β-amino-phosphonates[3q-r] have been synthesized. In this chapter, literature on the following topics involving allenes as relevant to the present study will be covered: (i) Halogen addition, (ii) Inter-/intra-molecular cyclization, (iii) Cycloaddition and (iv) Nucleophilic addition.

## 4.2 Halogen addition reactions on allenes

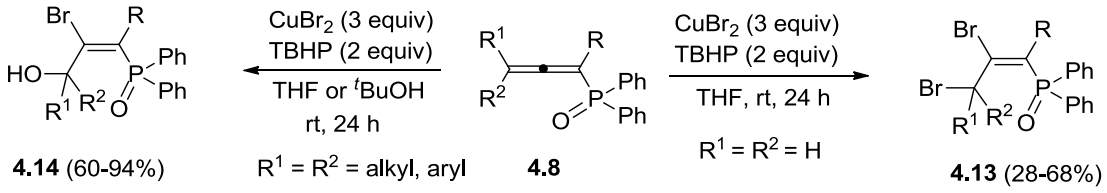
A number of methods are reported for the addition of halogen to alkenes and alkynes,[4] whereas halogen additions related to allenes are less investigated.[5-13a] Ma *et al.* explored the iodohydroxylation of allenylphosphine oxides (Scheme 4.1).[6a] Thus, *β*-iodo-*γ*-hydroxy-vinyl phosphine oxides **4.9** were synthesized by treating allenyl diphenylphosphine oxide **4.8** with iodine at rt (25 $^{o}$C) in acetonitrile-water (1:5) mixture. In this protocol, first $I^{+}$ ion attacks the electron rich C=C double bond (*β* and *γ*) forming cyclic iodonium intermediate **I**. Later, five membered cyclic intermediate **II** is formed by neighboring-group participation of the diphenylphosphinoyl oxygen group. Subsequently, water molecule attacks at the positively charged diphenylphosphonium ion to cleave the P-O bond of intermediate **II**. This is followed by protonation affording *β*-iodo-*γ*-hydroxy-vinyl phosphine oxides **4.9**. In some cases *β,γ*-diiodo-vinyl phosphine oxides **4.10** are also formed as byproducts. Later, the same group also reported the iodohydroxylation of allenyl phenyl sulfoxides **4.11** using iodine and lithium acetate in MeCN:$H_2O$ that afforded *β*-iodo-*γ*-hydroxy-vinyl sulfoxides **4.12** (Scheme 4.1b).[6b-c]

**Scheme 4.1**




Very recently, Zhou's group developed a co-operative $CuBr_2$/TBHP mediated protocol to synthesize *β, γ*-dibromo-vinyl-diphenylphosphine oxides **4.13** and *β*-bromo-*γ*-hydroxy-vinyldiphenylphosphine oxides **4.14** from allenylphosphine oxides **4.8** (Scheme 4.2).[7] In this transformation, bromohydroxylated product was formed due to neighboring-group participation of the diphenylphosphoryl group of allenylphosphine oxide.

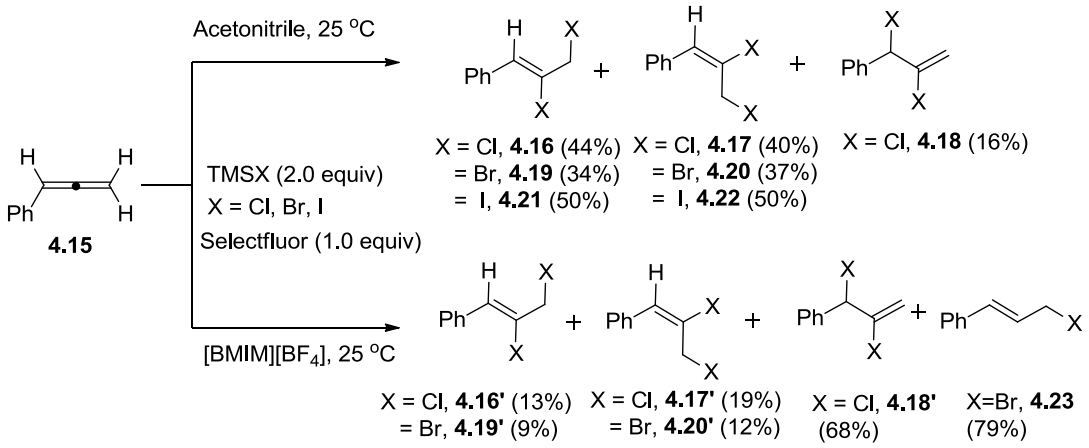
**Scheme 4.2**




Laali's group explored a dihalogenation reaction of phenylallenes with TMSX (X = Cl, Br, I) using selectfluor as the oxidant in acetonitrile or in the ionic liquid [BMIM][$BF_4$] (Scheme 4.3).[8] In acetonitrile, preference for *β,γ*-dihalogenation was observed with TMSCl leading to isomeric *β,γ*-dichloroalkenes **4.16** (44%) - **4.17** (40%), whereas 1,2-addition was preferred in [BMIM][$BF_4$] and led to *α,β*-dichloroalkene **4.18'** as the major product in 68% yield. With TMSBr or TMSI in acetonitrile, only products corresponding to *β,γ*-addition [**4.19** (34%) + **4.20** (37%) or **4.21** + **4.22** (1:1)] were observed. Interestingly, reactions carried out using TMSBr in

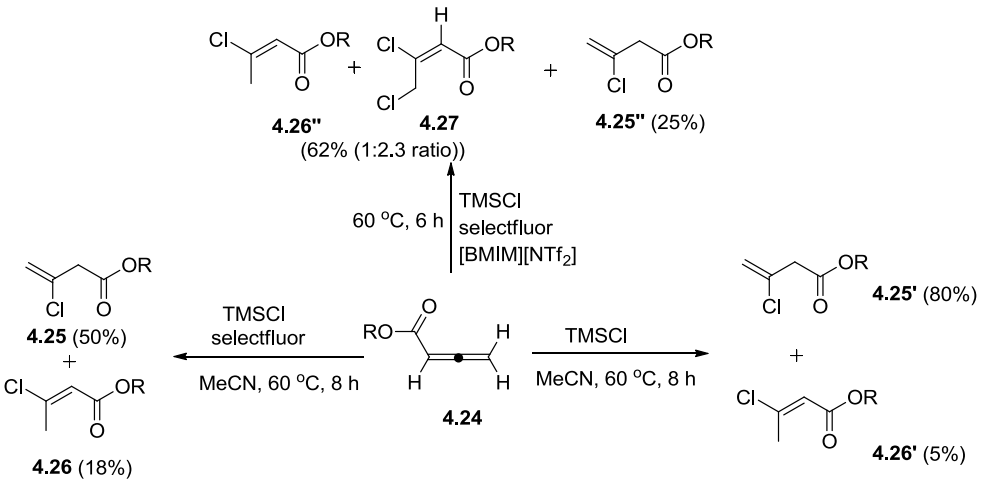
[BMIM][$BF_4$] gave the corresponding $\gamma$-monobromoalkenes **4.23** as major products in ~79% yield along with the isomeric dibromo-alkenes [**4.19'** + **4.20'** (9:12)].

**Scheme 4.3**



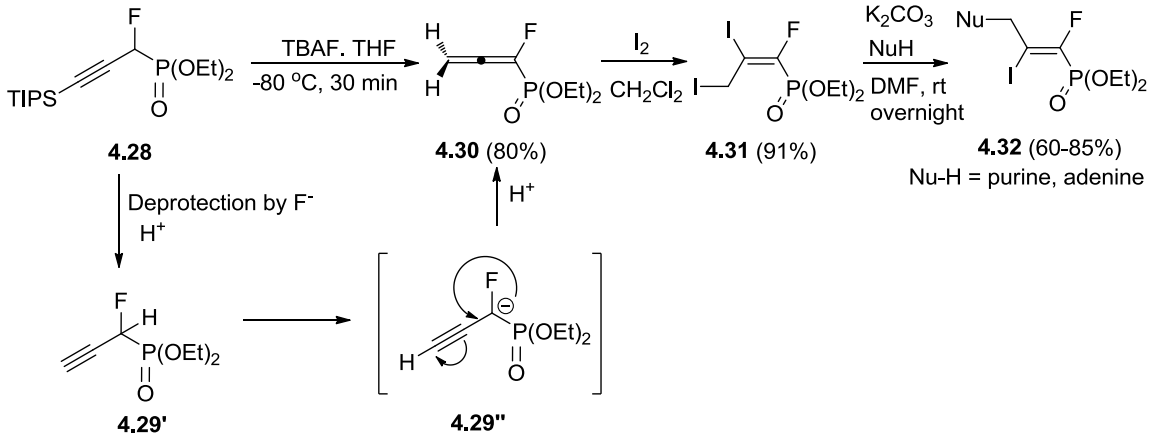

In the year 2015, the above group has performed comparative product analysis studies as shown in Scheme 4.3 by using alkyl allenoates and TMSX (X = I, Br, Cl) in MeCN, DMF and imidazolium ionic liquids like [BMIM][$NTf_2$] or [BMIM][$PF_6$] in the presence/ absence of selectfluor. Results suggested that the capability of selectflour to promote dihalogenation with TMSX is reduced in allenoates, most significantly in reactions with TMSCl. Instead of dihalogenation, hydrochlorination occurred (Scheme 4.4).[9] Thus when allenoate **4.24** was treated with TMSCl in the presence of selectfluor in MeCN, hydrochlorinated isomeric products **4.25** and **4.26** were obtained in 50 and 18% yield respectively. When the same reaction was conducted in the absence of selectfluor, hydrochlorinated product **4.25'** formed as the major product in 80% yield. Interestingly, when the reaction was performed with TMSCl/selectfluor in [BMIM][$NTf_2$], in addition to the hydrochlorinated products, dichloro-addition product **4.27** was also observed. These competing pathways are influenced by the nature of the anion, allene structure, and the choice of solvent.

**Scheme 4.4**



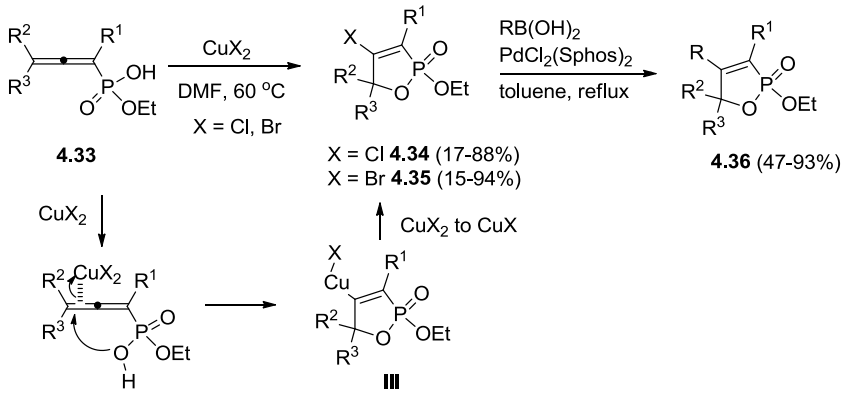

Hammond *et al.* reported the synthesis of novel α-fluoro allenylphosphonate from silylfluoropropargylphosphonate **4.28** by treating the latter with TBAF in THF at -80 °C for 30 min (Scheme 4.5).[10] In this reaction, first TBAF de-protects **4.28** by cleaving the C-Si bond leading to fluoropropargylphosphonate intermediate **4.29**. Due to the basic nature of TBAF, it abstracts proton from *α*-carbon of phosphonate **4.29** forming intermediate **4.29'** which isomerizes to *α*-fluoro-allenylphosphonate **4.30**. From this allene, *β,γ*-diiodo-*α*-fluoro-vinylphosphonate was synthesized by treating with iodine in DCM solvent at 25 °C. The diiodovinylphosphonate **4.31** further undergoes nucleophilic substitution reaction with nucleoside bases such as purine and adenine affording fluorinated acyclic phosphono-nucleosides (which show *in vitro* anti-HIV activity) in good yields.

**Scheme 4.5**



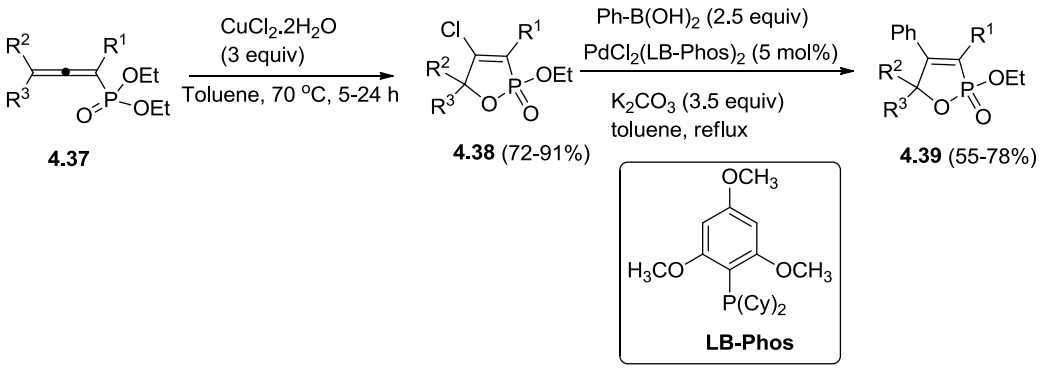
Ma *et al.* developed a protocol for the synthesis of phosphono-heterocycles **4.34-4.35**, by the reaction of monoesters of 1,2-allenyl phosphonic acids **4.33** with $CuX_2$ (X = Cl, Br) (Scheme 4.6).[11] A plausible pathway for this halolactonization reaction involves the attack of $CuX_2$ at *β, γ* C=C double bond followed by attack of oxygen from the back side to generate the five-membered ring containing intermediate **III**, which undergoes C-X bond formation in the presence of another molecule of $CuX_2$ to afford product **4.34** or **4.35**. The Suzuki cross-coupling reaction of these 4-halo-2,5-dihydro[1,2]oxaphosphole 2-oxides **4.34** or **4.35** with arylboronic acids by using $PdCl_2(Sphos)_2$ afforded 4-substitueted-2,5-dihydro[1,2]oxaphosphole-2-oxides **4.36** in good yields.

**Scheme 4.6**




Ma *et al*. have also reported the synthesis of 4-chloro-2,5-dihydro-1,2-oxaphosphole 2-oxides **4.38** by a $CuCl_2$-mediated halocyclization of diethyl 1,2-allenylphosphonates **4.37** and the subsequent Suzuki cross-coupling of the resulting compounds **4.38** with boronic acids by using $PdCl_2(LB\text{-}Phos)_2$ (Scheme 4.7).[12] Comparison of this transformation with the results described in Scheme 4.6 shows that in this case there is better functional group tolerance and less number of steps. Also the reaction is easier to perform.

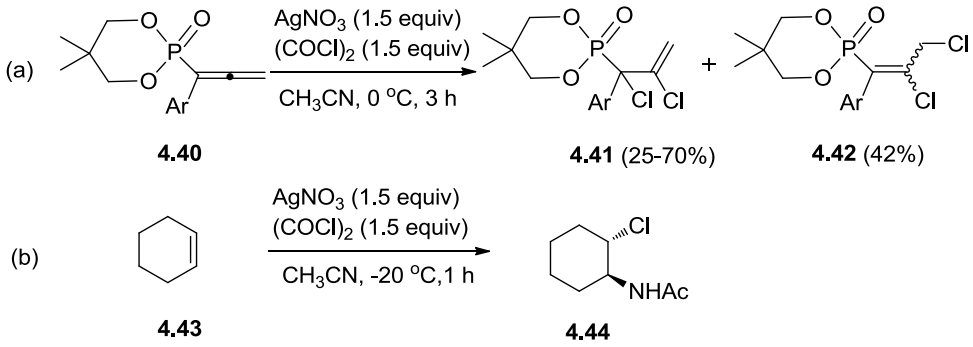
**Scheme 4.7**




**4.37** **4.38** (72-91%) **4.39** (55-78%)

Very recently our group reported the dichloro-addition on allenylphosphonates **4.40** by treating them with $AgNO_3$ and oxalyl chloride. From this reaction, *α,β*-vicinal dichloro-vinylphosphonates **4.41** as major products and an isomeric mixture of *β,γ*-vicinal dichloro vinylphosphonates **4.42** as minor products were obtained (Scheme 4.8).[13a] These reactions are in contrast to the reaction of $AgNO_3$/oxalyl chloride with normal olefins **4.43** wherein chloroamidated product **4.44** was formed.[13b]

**Scheme 4.8**



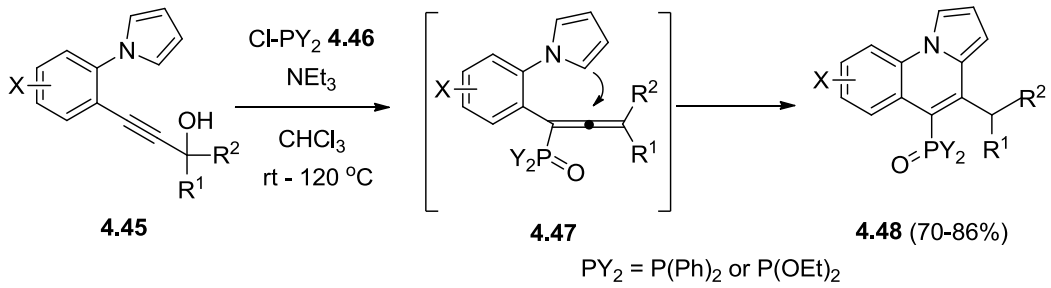

**4.40** **4.41** (25-70%) **4.42** (42%)

**4.43** **4.44**

## 4.3 Inter/intramolecular cyclization reactions of allenes

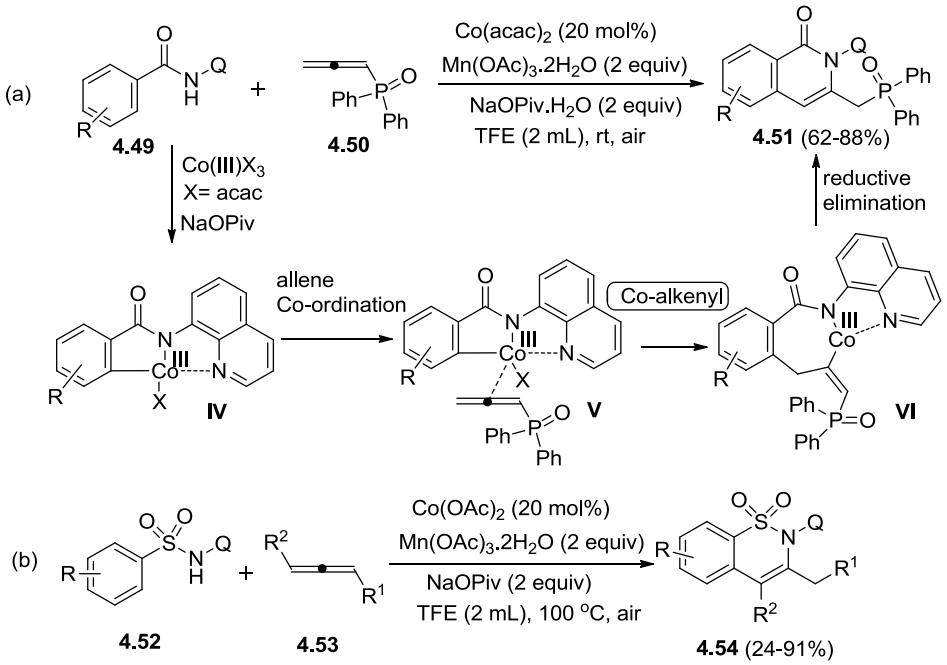
Baumann and Baxendale have developed an efficient protocol for synthesis of phosphorus based pyrrolo[1,2-a]quinolines **4.48** by the reaction of 2-pyrrol-phenyl propargylic alcohols **4.45** with chlorodiphenylphosphine or diethyl chlorophosphite **4.46** in the presence of $Et_3N$ in $CHCl_3$ (Scheme 4.9).[14] In this reaction, first transient allenes **4.47** is formed *in situ via* [2,3]-sigmatropic rearrangement; after that trapping of the resulting allenes by an adjacent pyrrole leads to pyrrolo[1,2-a]quinolines **4.48**.

**Scheme 4.9**



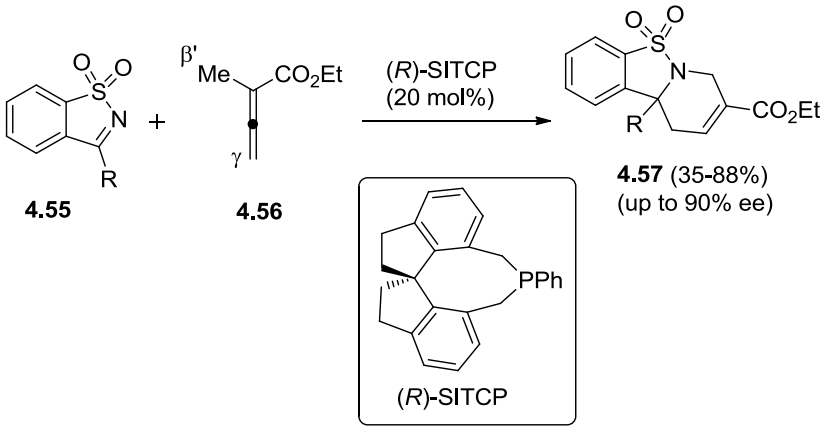

Thrimurtulu *et al.* have developed the C-*H* functionalization reaction of allenylphosphine oxides **4.50** and *N*-quinoline benzamides **4.49** in the presence of $Co(acac)_2$ catalyst in combination with the oxidant $Mn(OAc)_3$ and $NaOPiv{\cdot}H_2O$ in TFE to obtain dihydroisoquinolin-1(2H)-one **4.51** in good yield (Scheme 4.10).[15a] In this reaction, first $Mn(OAc)_3{\cdot}H_2O$ oxidizes the Co(II) to Co(III) that will coordinate with amide and quinoline *N* atoms. Subsequently, C-Co bond is formed in the presence of NaOPiv leading to the 5-membered intermediate **IV**. Coordinative insertion of allene from less hindered side in between C-Co bond of **IV** gives **V,** which subsequently affords the 7-membered ring containing intermediate **VI**. This species undergoes reductive elimination to afford dihydroisoquinolin-1(2H)-one **4.51**. In the year 2017, the same group reported the C-H functionalization reaction of more substituted allenyl phosphine oxides **4.53** and *N*-quinoline sulfonamides **4.52** that led to phosphano-benzosultams **4.54** in good yields (Scheme 4.9b).[14b] In this latter reaction, instead of $Co(acac)_2$, $Co(OAc)_2$ was used as the catalyst. Quinoline acted as the directing group for C-*H*-functionalization.

**Scheme 4.10**




Sasai's group has reported the novel cyclization reaction of saccharin-derived ketimines **4.55** and *α*-methyl allenoate **4.56** to afford six-membered tetrahydropyridines **4.57** bearing a chiral carbon stereogenic center in good yields with excellent regioselectivities and up to 93% ee (Scheme 4.11).[16] In this enantioselective organocatalytic reaction, spiro-type monoaryl phosphine (*R*)-SITCP is used as the catalyst. Here, *β'* and *γ* positions of allene take part in the reaction.

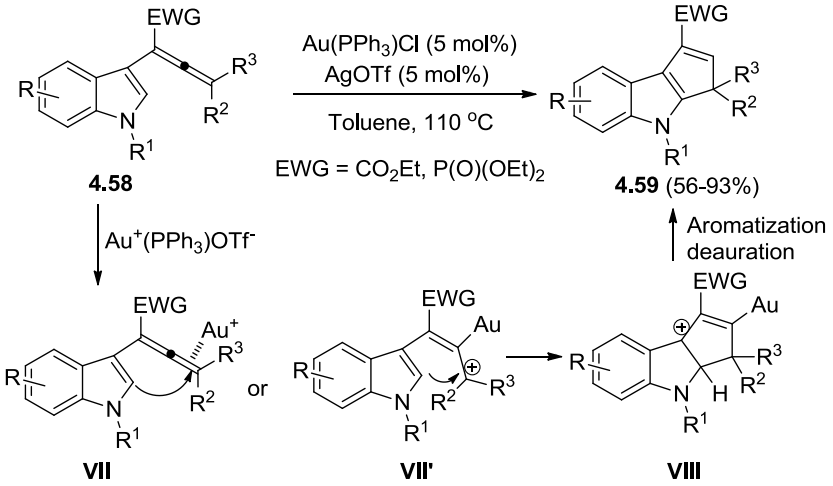
**Scheme 4.11**




Ma *et al.* have reported gold catalyzed intramolecular cyclization and C2-*H* bond functionalization reaction of 3-allenyl-indoles **4.58** to obtain dihydrocyclopenta[b]indole

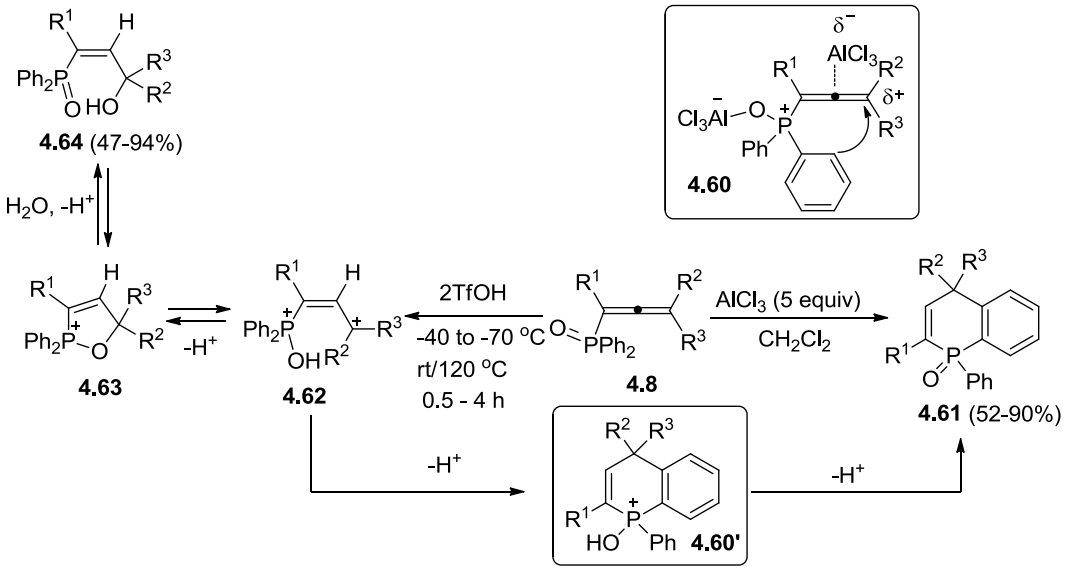
derivatives **4.59** in good yields (Scheme 4.12).[17] Electronic withdrawing group on allene moiety is mandatory for this reaction. In this transformation, first $[Au]^+$ coordinates with ($\beta$, $\gamma$) C=C double bond of allene moiety to form intermediate **VII** or **VII'**; later, **VII'** undergoes cyclization between C2 carbon and $\gamma$-carbon of allene. This is followed by dearomatization giving intermediate **VIII** that undergoes aromatization and deauration affording dihydrocyclopenta[b]indole **4.59**.

**Scheme 4.12**



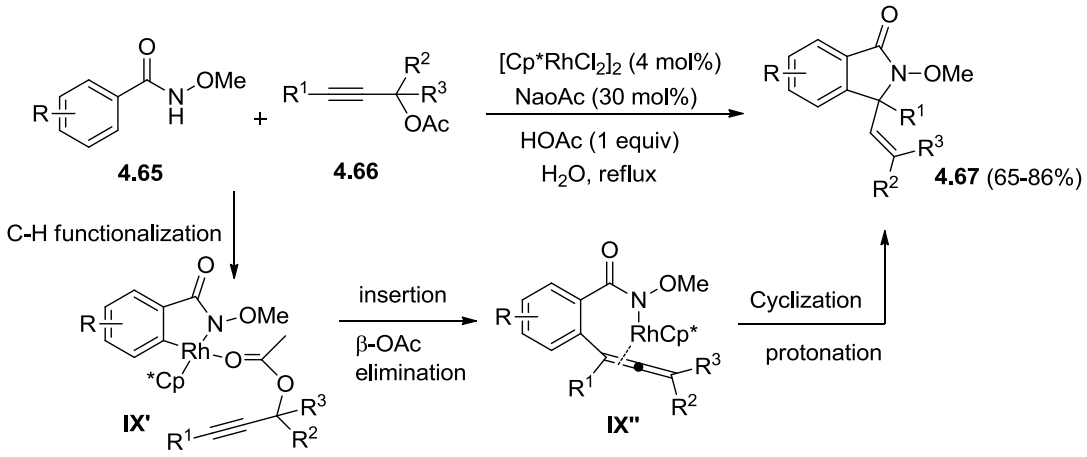

Vasilyev's group has developed a novel method for synthesis of 1-phenyl-1,4-dihydrophosphinoline 1-oxides **4.61** (phospha-heterocycles) by treating allenylphosphine oxides **4.8** with the Lewis acid $AlCl_3$ at 25 $^oC$ for 10-120 min (Scheme 4.13).[18a] In this reaction, first $AlCl_3$ coordinates with $\beta,\gamma$-C=C bond, and creates positive charge on the $\gamma$-carbon atom to give **4.60**. The authors proposed that this species is attacked by carbon of the phenyl ring of the diphenyl phosphoryl group affording **4.61**. However, it is difficult to say whether **4.60** is the exact intermediate or not. In contrast, the reaction of allenylphosphine oxides **4.8** on treatment with Brønsted acids (TfOH, $FSO_3H$, and $H_2SO_4$) gave (3-hydroxyalk-1-en-1-yl)diphenylphosphine oxides **4.64** as the major products. After prolonging the reaction times from 0.30 h to 4 h, these alcohols **4.64** convert to phosphaheterocycles **4.61**. In this reaction, first 1,2-oxaphosphol-3-enium ion **4.62** is formed. The cation is attacked by neighboring oxygen atom of phosphoryl group to give intermediate **4.63**, which upon hydrolysis affords **4.64**. The cations further converted into O-protonated forms of 1-phenyl-1,4-dihydrophosphinoline-1-oxides **4.60'**; upon deprotonation, **4.60'** gave phospha-heterocycles **4.61**. Later, they have provided evidence for the mechanism of this reaction by NMR studies and DFT calculations.[18b]

**Scheme 4.13**



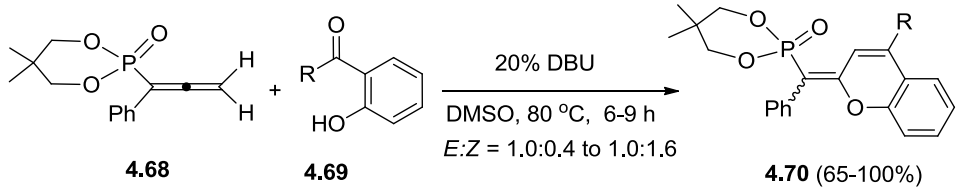

Very recently Ma *et al*. have developed a novel green approach for the efficient synthesis of isoindolin-1-ones **4.67** from *N*-protected benzamides **4.65** and propargylic-acetates **4.66** *via* Rh(III) catalyzed C−H functionalization and allene formation followed by intramolecular cyclization pathway (Scheme 4.14).[19] In this methodology, water was used as the solvent; functional groups such as Br, $CO_2Me$, and $CF_3$ were well tolerated. Plausible pathway for this reaction involves C-H bond cleavage, insertion of Rh(III) in between N and Ar-*C* and subsequent regio-specific insertion of the alkyne moiety of propargylic acetates induced by the coordination of the carbonyl group with [Rh] to afford carbonyl oxygen-coordinated intermediate **IX'**. This species undergoes *β*-OAc elimination to form the allene product **IX"** [Rh(III) coordinate to the formed allene moiety]. After that, cyclization followed by protonolysis by AcOH relieves the catalytically active Rh(III) species and finishes the catalytic-cycle to afford isoindolin-1-ones **4.68**.

**Scheme 4.14**



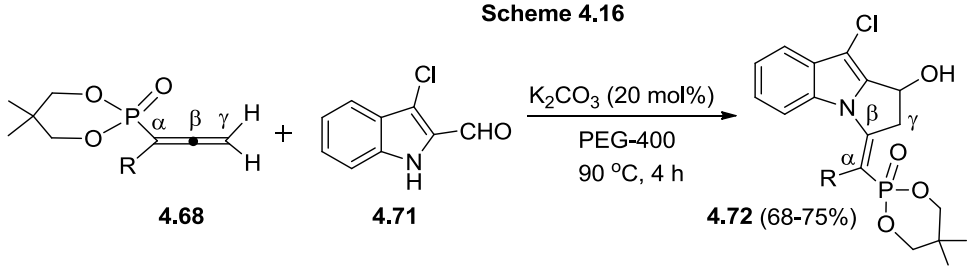

Synthesis of phosphono-chromenes **4.70** by base catalyzed intermolecular cyclization of allenylphosphonates **4.68** with salicylaldehydes or hydroxyaceto-/benzo-phenones **4.69** in the presence of DBU (20 mol%) has been reported from our laboratory (Scheme 4.15).[20] This reaction involves a nucleophilic attack of phenoxide ion at the β-position of allene followed by the cyclization and dehydration to afford **4.70**.

**Scheme 4.15**




In another report, base catalyzed domino cyclization of allenylphosphonates **4.68** with 3-chloro-2-formylindole **4.71** in the environmentally friendly PEG-400 solvent that gives (*β, γ*)-cyclized pyrrolo[1,2-a]indoles **4.72** has also been reported from our group (Scheme 4.16).[21]

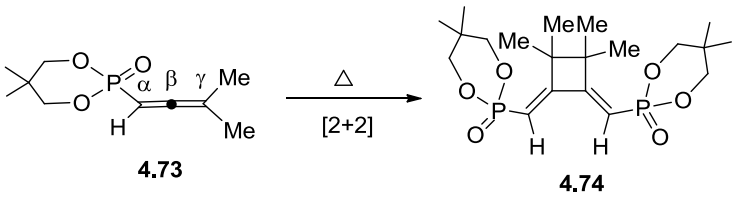
**Scheme 4.16**



## 4.4 Cycloaddition reactions of allenes

Allenes are excellent partners for the [2+2] and [4+2] cycloaddition with alkenes and alkynes, affording the cyclobutane/ cyclobutene or cyclohexane/ cyclohexene skeletons under thermal, photochemical or microwave induced conditions.[2d-e] Due to two cumulative and reactive double bonds, allenylphosphonates **4.73** undergo thermally activated [2+2] cycloaddition (dimerization) leading to the phosphonocyclobutane **4.74** has been reported from our group (Scheme 4.17).[22] In this cycloaddition reaction, [*β,γ*]-C=C double bonds of two molecules of allenylphosphonate (self-dimerization) are involved.

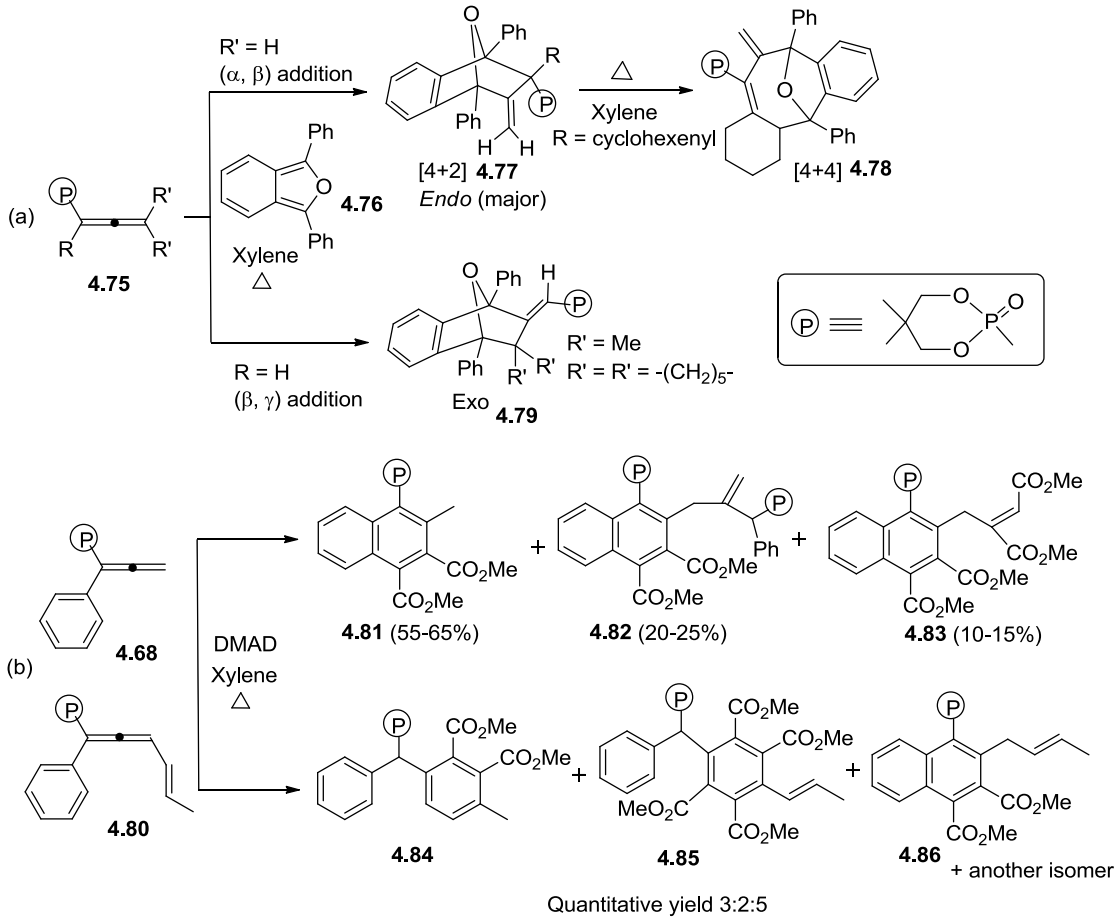
**Scheme 4.17**




**4.73** **4.74**

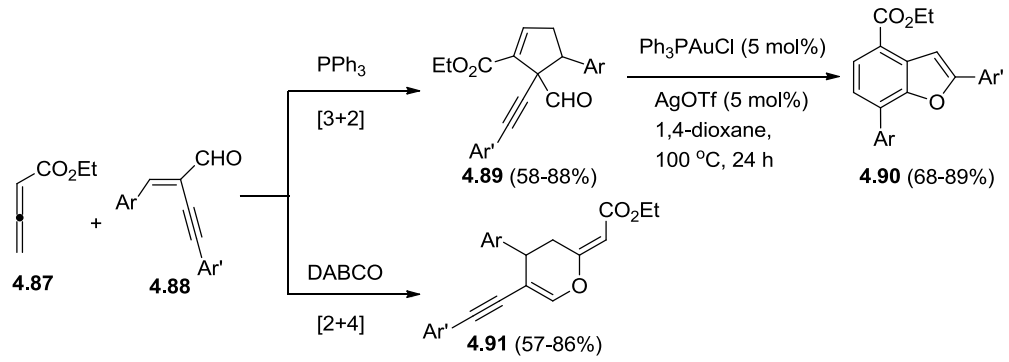
Cycloaddition reactions of allenylphosphonates **4.75**, **4.68** and **4.80** with 1,3-diphenylisobenzofuran **4.76** and dialkyl acetylenedicarboxylates have been investigated in our laboratory (Scheme 4.18).[23] While the reaction of $=CH_2$ terminal allenylphosphonates **4.75** with 1,3-diphenylisobenzofuran **4.76** afforded preferentially *endo*-[4+2] cycloaddition products **4.77** *via* [*α, β*] attack. This endo-[4+2] cyclo-adduct **4.77** converted into unusual [4+4] or [4+2+2] cycloaddition product **4.78** under thermal conditions (R = cyclohexenyl; Scheme 4.18a). Under similar conditions, allenylphosphonates with a terminal $=CR_2$ group gave only [*β,γ*]-cycloaddition products **4.79**. Allenylphosphonates like **4.68** with an α-aryl group preferentially undergo [4+2] cycloaddition with DMAD under thermal activation, but in addition to the expected 1:1 (allene **4.68**:DMAD) cyclo-adduct **4.81**, the reaction also leads to 2:1 as well as 1:2 cycloaddition products **4.82** and **4.83** in moderate yields (Scheme 4.18b). In this, *α*-carbon atom of aryl group also participates in cycloaddition. In case of *γ*-vinyl-allenylphosphonate **4.80**, [4+2] cycloaddition takes place by utilizing either the vinylic or the aryl end, but additionally a novel cyclization wherein complete opening of the [*β,γ*] carbon-carbon double bond of the allene **4.80** takes place to afford **4.84**, **4.85** and **4.86** (isomers) in quantitative yields (3:2:5 ratio).

**Scheme 4.18**




Our research group has also reported $PPh_3$ catalyzed [3+2] cycloaddition of allenoates **4.87** with enynals **4.88** to afford 1,1-alkyne (aldehyde)-substituted cyclopentenes **4.89**. Here, enynals act as electrophiles (Scheme 4.19).[24] These alkyne-tethered cyclopentenes **4.89** upon [Au]/[Ag] catalysis lead to substituted benzofurans **4.90** *via* 1,2-alkyl migration and dehydrogenation (aromatization). In contrast, the reaction of allenoates **4.87** with enynals **4.88** in the presence of DABCO takes place by [2+4] cycloaddition to form functionalized dihydropyrans **4.91** in good yields.

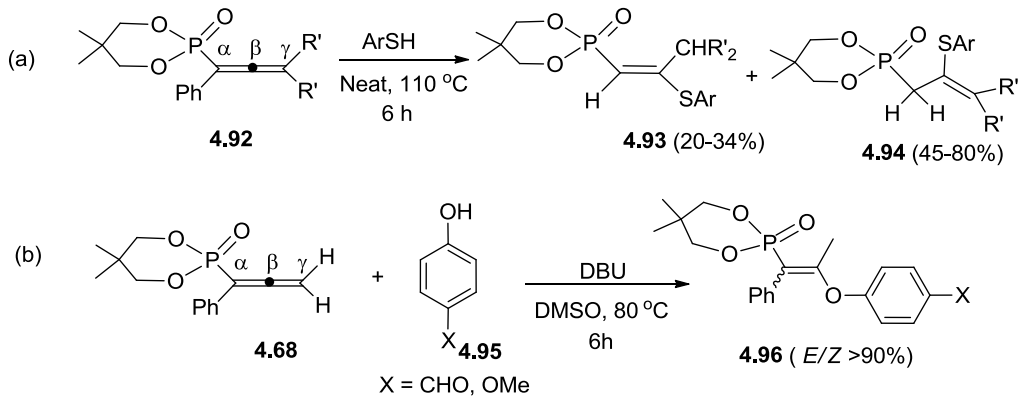
**Scheme 4.19**




## 4.5 Nucleophilic addition reactions on allenes

Due to the presence of the electron withdrawing group, allenylphosphonates and allenylphosphine oxides undergo nucleophilic addition at *β*-carbon of allene moiety. Our research group has reported nucleophilic addition reactions of allenylphosphonate **4.92** with various thiophenols under neat conditions that lead to vinyl phosphonates **4.93** (minor) and allyl-phosphonates **4.94** (major), respectively (Scheme 4.20a).[25] Similarly, base mediated nucleophilic addition of substituted phenols **4.95** at the *β*-carbon of the allenylphosphonate **4.68** affords vinyl-phosphonates **4.96** (Scheme 4.20b).[20]

**Scheme 4.20**



## OBJECTIVES OF THE PRESENT WORK – PART B

The main aim of this part of the present work was to explore the addition and cyclization reactions of phosphorus based allenes and sulfur based allenes. Specifically, it was intended

(i) To synthesize *γ*-azido/fluoro, *β*-iodovinylphosphine oxides/phosphonates and their utility in cycloaddition reactions- To study I•••O nonbonding interactions, if any, in *γ*-azido, *β*-iodovinylphosphine oxides and *γ*-fluoro, *β*-iodovinylphosphine oxides,

(ii) To explore nucleophilic addition and cyclization reactions of allenylphosphonates by using [Pd]-catalysis, and

(iii) To explore base mediated intermolecular cyclization of phosphorus/sulfur based allenes with *N*-protected *o*-amino benzaldehydes/acetophenones.

## RESULTS AND DISCUSSION

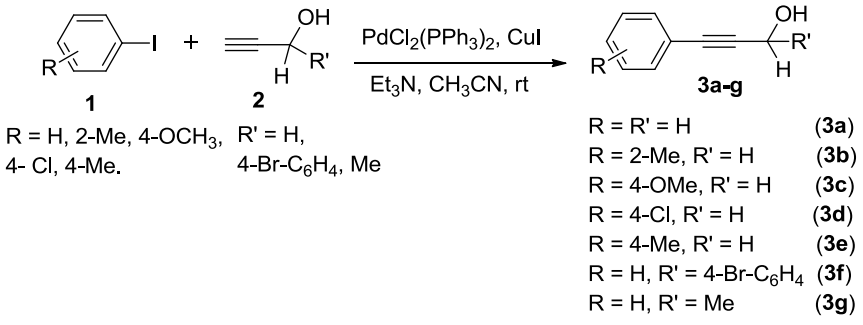
In this chapter, we begin with the discussion on addition and cyclization reactions of phosphorus based allenes. Details on the precursors used in the present work will be presented in sections 5.1-5.2. After this, azidation and fluorination reactions of 2,3-diiodo-vinyl phosphine oxides/ phosphonates/esters are described. Subsequently, Pd-PVP catalyzed addition reactions of allenylphosphonates with 2-iodophenols are discussed. Later, [Pd] catalyzed cyclization reactions of allenylphosphonates are presented. In the last section, base catalyzed cyclization reaction of phosphorus/sulfur based allenes with *N*-protected benzamides/ *N*-protected acetamides is described. Characterization of the products is generally done by using mp (for solids), IR, NMR, LCMS, and HRMS/CHN analyses along with single crystal X-ray structure determination for illustrative compounds.

### 5.1 Synthesis of precursors

#### 5.1.1 Aryl substituted propargylic alcohol precursors 3a-g

The aryl substituted propargylic alcohol precursors **3a-g** were prepared by Sonogashira cross-coupling of aryl iodides **1** with propargylic alcohols **2** (Scheme 1) following a literature procedure.[26]

**Scheme 1**




**1** R = H, 2-Me, 4-$OCH_3$, 4- Cl, 4-Me.

**2** R' = H, 4-Br-$C_6H_4$, Me

**3a-g**

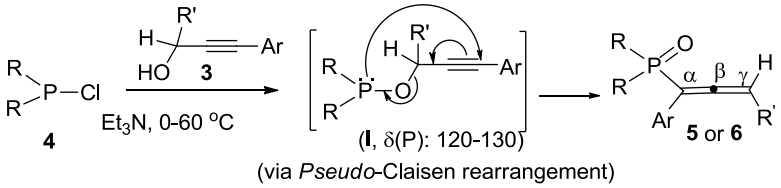
| | |
|---|---|
| R = R' = H | (**3a**) |
| R = 2-Me, R' = H | (**3b**) |
| R = 4-OMe, R' = H | (**3c**) |
| R = 4-Cl, R' = H | (**3d**) |
| R = 4-Me, R' = H | (**3e**) |
| R = H, R' = 4-Br-$C_6H_4$ | (**3f**) |
| R = H, R' = Me | (**3g**) |

#### 5.1.2 Synthesis of allenylphosphine oxides 5a-e and allenylphosphonates 6a-g

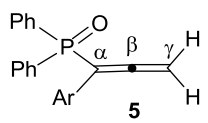
Allenylphosphine oxides **5a-e** and allenylphosphonates **6a-g** are prepared by following a method previously reported from our laboratory (Scheme 2).[3b, 6a, 22, 27] The reaction involves, the

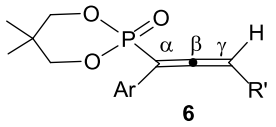
reaction of $P^{III}$-Cl precursor $R_2PCl$ [R = Ph (**4a**) or $R_2$ = ($OCH_2CMe_2CH_2O$) (**4b**)] [28] with the appropriate aryl propargylic alcohols **3** in the presence of triethylamine *via* a *pseudo*-Claisen rearrangement of the initially formed $P^{III}$ intermediate **I**. These allenes are quite stable in air in the solid state. In the IR spectra, they show a characteristic strong band at 1920-1975 $cm^{-1}$ due to $\nu_{asym}$(C=C=C).[29] The $^{31}P$ NMR spectra of allenylphosphine oxides **5a-e** show a peak in the range δ 27-30, whereas allenylphosphonates **6a-g** show a signal in the range δ 5-7. The PC=*C* signal for all these compounds appears as a doublet in the region δ 206-214 [$^2J$(P-C) ~ 6-7 Hz] in the $^{13}C$ NMR spectra.

**Scheme 2**




(via *Pseudo*-Claisen rearrangement)



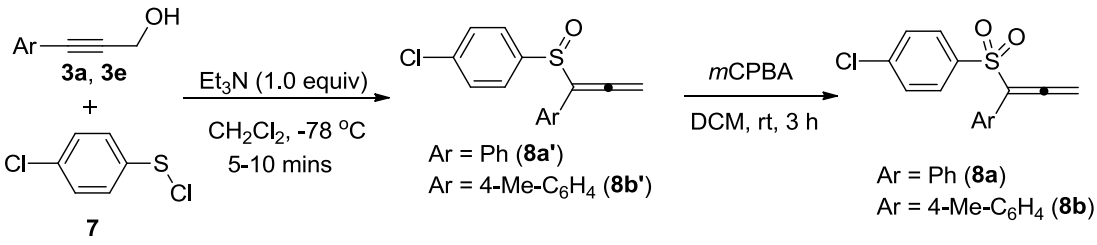

| | |
|---|---|
| Ar = Ph | [**5a**, δ(P): 30.2] |
| =2-Me-$C_6H_4$ | [**5b**, δ(P): 27.1] |
| = 4-OMe-$C_6H_4$ | [**5c**, δ(P):29.3] |
| = 4-Cl-$C_6H_4$ | [**5d**, δ(P):29.0] |
| =4-Me-$C_6H_4$ | [**5e**, δ(P): 27.1] |

| | |
|---|---|
| Ar = Ph, R' = H | [**6a**, δ(P): 6.6] |
| Ar = 2-Me-$C_6H_4$, R' = H | [**6b**, δ(P): 7.8] |
| Ar = 4-OMe-$C_6H_4$, R' = H | [**6c**, δ(P): 7.5] |
| Ar = 4-Cl-$C_6H_4$, R' = H | [**6d**, δ(P): 6.8] |
| Ar = 4-Me-$C_6H_4$, R' = H | [**6e**, δ(P): 7.8] |
| Ar = Ph, R' = 4-Br-$C_6H_4$ | [**6f**, δ(P): 5.7] |
| Ar = Ph, R' = Me | [**6g**, δ(P): 8.2] |

### 5.1.3 Synthesis of allenylsulfones 8a and 8b

The reaction of 4-chlorophenylsulfenylchloride **7** with the appropriate propargyl alcohols **3a** or **3e** in the presence of $Et_3N$ led to the allenylsulfoxides **8a'-b'**; compounds **8a'-b'** are oxidized by *m*-chloroperbenzoic acid (*m*CPBA) to give allenylsulfones **8a** and **8b** (Scheme 3).[21, 30] The allenylsulfoxides **8a'-b'** and allenylsulfones **8a-8b** are crystalline solids and are stable under nitrogen for several months at <4 °C.

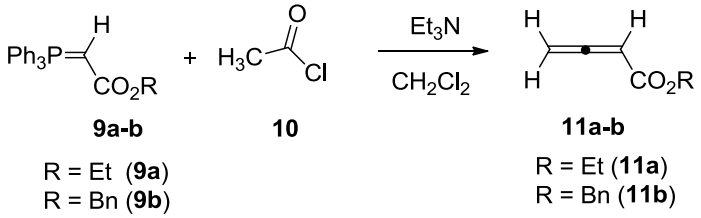
**Scheme 3**




### 5.1.4 Synthesis of 1,2-alkadienoates 11a-b

The main approach to prepare allenyl esters **11a-b** is the treatment of *α*-phosphoranylidene esters **9a-b** with acetyl chloride **10** in the presence of a base (Scheme 4).[24, 31] For purification, this compound has to be distilled at 70 $^{o}$C/ 15 mm of Hg.

**Scheme 4**




*N*-(2-formyl phenyl)benzamide **12a**,[32a] *N*-(2-acetyl-phenyl) benzamide **12b**[32b] and *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide **12c**[33] were synthesized by following literature procedures.[32-33] 2-Iodophenol (**13**) is commercially available. All these compounds are shown in Chart 1.

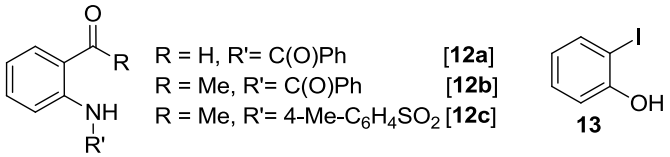


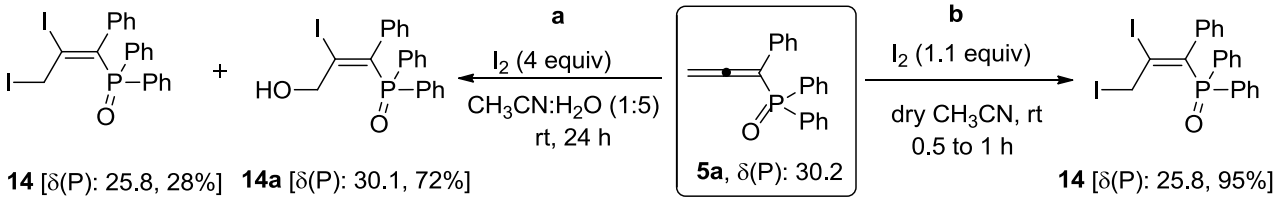

**Chart 1.** Structures of the precursors **12a-c** and **13**.

## 5.2 Synthesis of 2,3-diiodovinylphosphine oxides 14-18, 2,3-diiodovinylphosphonates 19-20 and 2, 3-diiodovinylesters 21-22

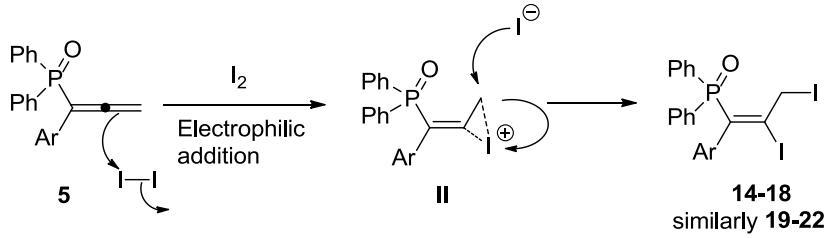
2,3-Diiodovinylphosphine oxides were synthesized in low yields by Ma *et al.* as byproducts in the reaction of iodohydroxylation of allenylphosphine oxides by using $I_2$ (4 equiv.) in $CH_3CN$:$H_2O$ (1:5) solvent system (Scheme 5a).[6a] By considering the above reaction, some

initial experiments (slight modification in reaction conditions) were done by Swamy and Karaghiosoff to obtain 2,3-diiodovinylphosphine oxides as single products by treating allenylphosphine oxide **5a** with $I_2$ in dry acetonitrile;[34] this route afforded crystals of 2,3-diiodovinylphosphine oxide **14** (Scheme 5b). The $^{31}P$ NMR spectrum of the reaction mixture exhibited a peak at $\delta = 25.8$, whereas allenylphosphine oxide **5a** showed a characteristic peak at $\delta = 30.2$. We were interested in utilizing such products further; however, full characterization (HRMS/IR/$^1H$ and $^{13}C$ NMR) was not done on compound **14** and hence this is included in the present work. It should be noted that the other possible ($\alpha,\beta$)-diiodination product is not observed in this reaction. In general, $I_2$ adds on to 1,1-disubstituted allenes regio-selectively across the C2-C3 ($\beta,\gamma$) double bond to afford the highly substituted olefin.[35] Based on the literature[10] a plausible pathway for the formation of diiodovinylphosphine oxide is shown in Scheme 6. Electrophile would approach the allenylphosphine oxide **5a** at C2-C3 double bond, on the less hindered aryl group side to afford intermediate **II**. The intermediate **II** has a stronger, shorter bond to C2 and a weaker, longer bond to C3 due to the added stability conferred by the $sp^2$ allylic character of the latter (versus an *sp* vinylic character in C2). Therefore, the C3-I bond would be expected to open up by iodide attack on the iodonium intermediate to afford compound **14.**

**Scheme 5**



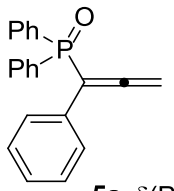
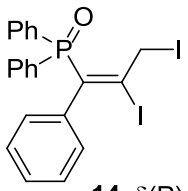
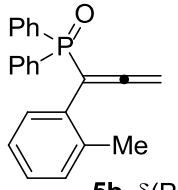
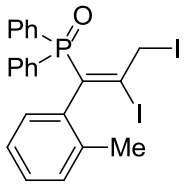
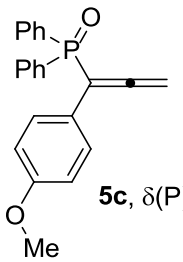
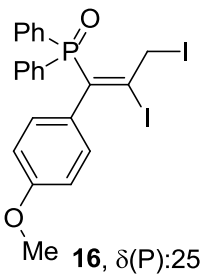

**Scheme 6**

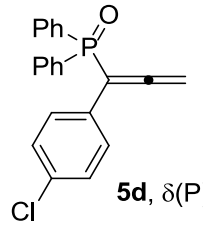
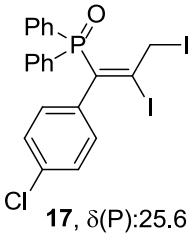
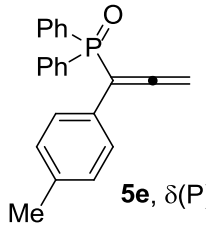
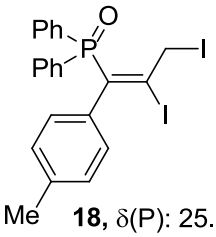
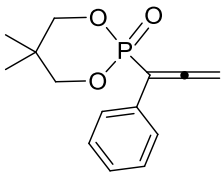
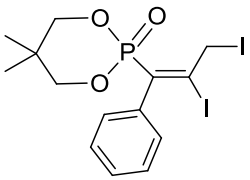
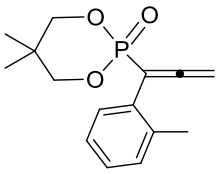
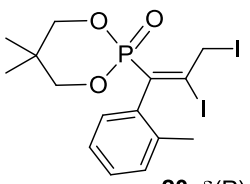
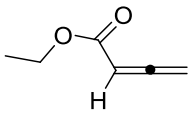
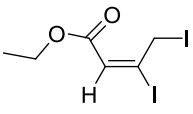
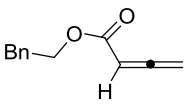
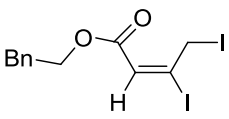



By using the above modified method, we synthesized 2,3-diiodo vinyl phosphine oxides **15-18** from allenylphosphine oxides **5b-e**. These compounds show a characteristic peak in the $^{31}P$ NMR spectra at $\delta$ 25.3-25.9. All these compounds show a doublet at $\delta$ 5.6 [$^3J$~ 2.0 Hz] in the

$^{1}$H NMR spectra indicating the presence of two allylic protons (C$H_2$). They also show a doublet at δ 15-16 [$^{3}J$(PC) ~ 4.5 Hz] in the $^{13}$C NMR spectra that suggests the presence of $CH_2$ attached to iodine. In the $^{13}$C NMR spectra, the P-*C* carbon appears in the range δ ~130.1 [$^{1}J$(P-C) ~ 104-110 Hz]. The structure of 2,3-diiodovinylphosphine oxide **15** was further confirmed by single crystal X-ray analysis (Figure 1); the C13-C21 distance 1.318(8) Å establishes the presence of a double bond between these two atoms and C21-C22 distance of 1.488(9)Å shows the presence of a single bond. Two bonds, I(1)-C(21) and I(2)-C(22), are newly formed. The above reaction was successfully extended to allenylphosphonates **6a-b** and allenoates **11a-b**, affording 2,3-diiodovinylphosphonates **19-20** and 2,3-diiodovinylesters **21-22**, respectively. In the $^{13}$C NMR spectra, the P-*C* carbon appears at δ ~138 [$^{1}J$ ~ 164.3 Hz] (Table 1).

**Table 1.** Synthesis of 2, 3-diiodovinylderivatives **14-22** from allenes **5a-e**, **6a-b** and **11a-b**[a]

| Entry | Allene derivative | 2, 3-diiodovinyl derivatives | yield (%)[b] |
|---|---|---|---|
| 1 |  **5a**, δ(P): 30.2 |  **14**, δ(P): 25.8 | 95 |
| 2 |  **5b**, δ(P): 27.3 |  **15**, δ(P): 25.3 | 95 |
| 3 |  **5c**, δ(P): 29.3 |  **16**, δ(P):25.9 | 85 |

| | | | |
|---|---|---|---|
| 4 |  **5d**, δ(P): 29.0 |  **17**, δ(P):25.6 | 80 |
| 5 |  **5e**, δ(P): 27.1 |  **18,** δ(P): 25.3 | 96 |
| 6 |  **6a**, δ(P): 6.6 |  **19**, δ(P): 0.44 | 92 |
| 7 |  **6b**, δ(P): 7.8 |  **20**, δ(P): 0.78 | 90 |
| 8 |  **11a** |  **21** | 60 |
| 9 |  **11b** |  **22** | 55 |

[a]Standard conditions: One of the allenes **5a-e**, **6a-b** or **11a-b** (0.3 mmol) in dry $CH_3CN$ (1 mL), $I_2$ (0.34 mmol) at 25 $^oC$ for 0.5-1 h. [b]Isolated yields.

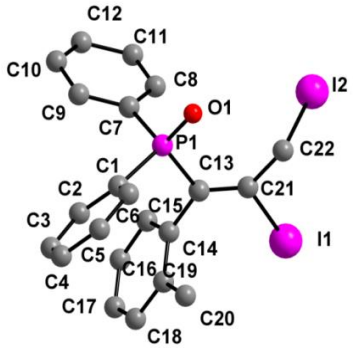



**Figure 1**: Molecular structure of Compound **15.** Selected bond lengths [Å] with esds are given in parentheses**:** P1-C13 1.840(6), C13-C21 1.318(8), C21-C22 1.488(9), I2-C22 2.138(7), I1-C21 2.124(6), C13-C14 1.505(7), P1-O1 1.486(4).

### 5.3 Substitution reactions of 2,3-diiodo-vinyl phosphine oxides, phosphonates and esters

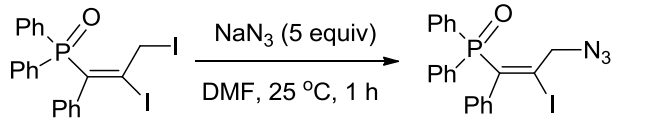
Due to the presence of iodine at allylic position these 2,3- diiodo vinyl derivatives can easily undergoes nucleophilic substitution reactions.[10] This section is devoted to the synthesis of *γ*-azido-*β*-iodo-vinyl derivatives by a simple and convenient method.

#### 5.3.1 Synthesis of *γ*-azido-*β*-iodo-vinylphosphine oxides, *γ*-azido-*β*-iodo-vinylphosphonates and *γ*-azido-*β*-iodo-vinyl ester

The reaction of 2,3-diiodovinylphosphine oxide **14** with $NaN_3$ in dry DMF afforded (*γ*-azido-*β*-iodo)vinylphosphine oxide **23** as one of the products (Scheme 7). We intended to utilize this product in a later work. The $^{31}$P NMR spectrum of this compound showed a single peak at δ = 25.4, whereas 2,3-diiodovinylphosphine oxide **14** gave a characteristic peak at δ = 25.8. A strong band due to $N_3^-$group was observed at ~ 2094 $cm^{-1}$ in the IR spectrum as expected. This compound shows a doublet at δ 5.2 [$^3J$~ 2.0 Hz] in the $^1$H NMR spectrum indicating the presence of allylic protons ($CH_2$) and a doublet at δ 58.2 [$^3J$(PC) ~ 5.0 Hz] in the $^{13}$C NMR showing the presence of $C(sp^3)H_2$ attached to $N_3$ moiety. In the $^{13}$C NMR spectrum, the P-*C* carbon appears at δ ~130.1-132.5 [$^1J$(P-C) ~ 81.5-85.5 Hz]. In a similar manner, compounds **24-26** were also synthesized. The structures of compounds **23-26** were determined by single crystal X-ray analysis (Figures 2-3) in an effort to delineate the factors governing the interesting I···O 'halogen bonding' (section 5.5). We have also continued this azidation reaction with 2,3-diiodovinylphosphonate **19** and obtained *γ*-azido-*β*-iodo-vinylphosphonate **28**. Similarly *γ*-azido-

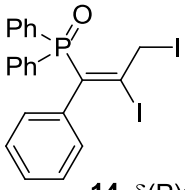
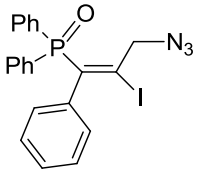
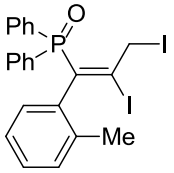
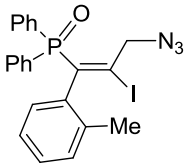
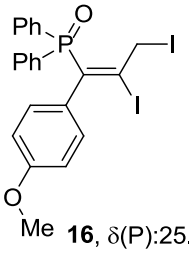
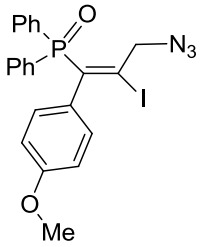
*β*-iodo-vinyl ester **29** was synthesized by using the 2,3-diiodovinylester **21**. In compound **23** (similarly in **24-26**), the C19-C20 [1.336(7) Å], N2-N1 [1.17(2) Å] and N2-N3 [1.18(3) Å] distances establish the presence of double bond between the corresponding atoms.

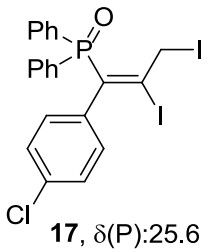
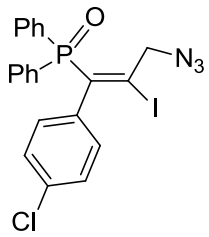
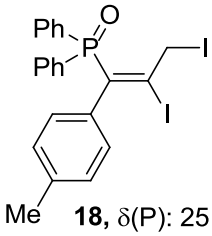
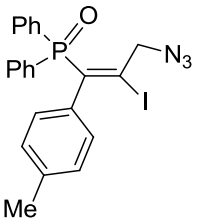
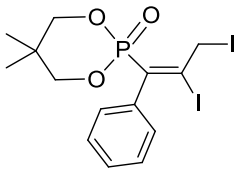
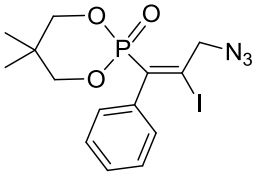
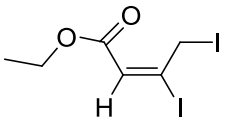
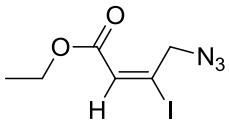
**Scheme 7**




**14** **23** [δ(P):25.4, 85%]

**Table 2.** *γ*-Azido-*β*-iodo-vinylphosphine oxides/phosphonates/esters **23-29**[a]

| Entry | 2,3-diiodovinyl derivatives | *γ*-azido-*β*-iodo-vinyl derivatives | yield (%)[b] |
|---|---|---|---|
| 1 |  **14**, δ(P): 25.8 |  **23**, δ(P): 25.4 (X-ray) | 85 |
| 2 |  **15**, δ(P): 25.3 |  **24**, δ(P): 25.5 (X-ray) | 90 |
| 3 |  **16**, δ(P):25.9 |  **25**, δ(P):25.8 (X-ray) | 95 |

| | | | |
|---|---|---|---|
| 4 |  **17**, δ(P):25.6 |  **26**, δ(P): 25.9 (X-ray) | 85 |
| 5 |  **18,** δ(P): 25.3 |  **27**, δ(P): 26.4 | 88 |
| 6 |  **19**, δ(P): 0.44 |  **28**, δ(P): 9.6 | 80 |
| 7 |  **21** |  **29** | 82 |

[a]Standard conditions: One of 2,3-diiodovinyl precursors **14-22** (0.18 mmol) in dry DMF (1 mL), $NaN_3$ (0.87 mmol) at 25 $^oC$ for 1 h. [b]Isolated yields.

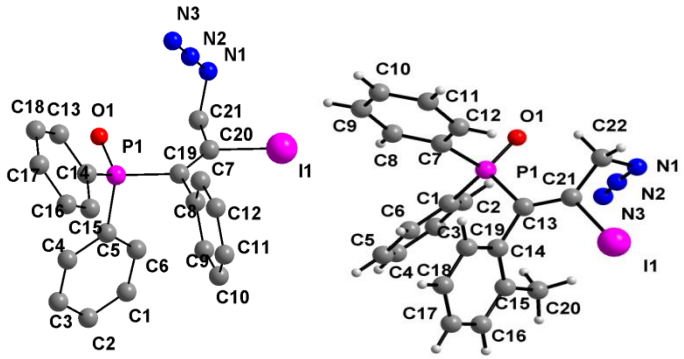



**Figure 2**: Molecular structures of compounds **23** (left) and **24** (right)**.** Selected bond lengths [Å] with esds are given in parentheses: Compound **23** (left): P1-C19 1.833(5), C19-C20 1.336(7), C20-C21 1.500(8), C21-N1 1.432(16), N2-N1 1.17(2), N2-N3 1.18(3), I1-C20 2.114(5), C19-C8 1.493(6). Compound **24** (right): P1-C13 1.835(3), C13-C14 1.341(3), C14-C15 1.499(3), C15-N1 1.473(4), N1-N2 1.226(4), N2-N3 1.125(4), C14-I1 2.110.

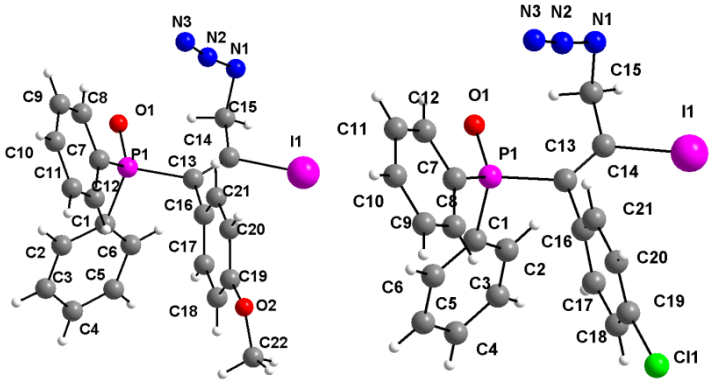


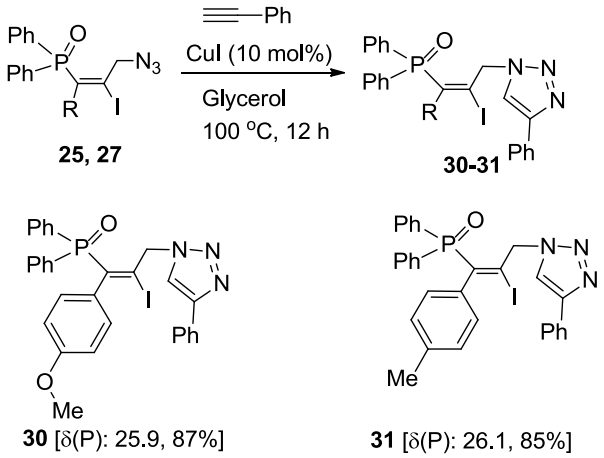

**Figure 3**: Molecular structures of compounds **25** (left) and **26** (right)**.** Selected bond lengths [Å] with esds are given in parentheses: Compound **25** (left): P1-C13 1.844(6), C13-C14 1.329(8), C14-C15 1.516(9), N1-C15 1.485(10), N1-N2 1.244(11), N2-N3 1.119(12), I1-C14 2.112(5), C13-C16 1.488(8). Compound **25** (right): P1-C13 1.822(13), I1-C14 2.102(12), C13-C14 1.315(18), N1-C15 1.50(2), N1-N2 1.23(2), N2-N3 1.12(2), C16-C13 1.521(19).

### 5.3.2 Click reaction of *γ*-azido-*β*-iodo-vinylphosphine oxides with phenyl acetylene

We performed the atom economical click reaction between *γ*-azido-*β*-iodo-vinylphosphine oxides **25** and **27** and phenyl acetylene in the presence of copper iodide (10 mol%) in glycerol at 100 $^{o}$C (oil bath temperature) for 12 h to obtain 1,2,3-triazoles **30-31** in good yields (Scheme 8). In the IR spectra, the band due to $N_3^-$group at ~ 2094 cm$^{-1}$ is absent as expected. In $^{1}$H NMR spectra, presence of a new peak at δ 8.14-8.15 indicates the formation of

triazole. The structure of compound **31** was determined by single crystal X-ray analysis (cf. Figure 4) to know more about I···O 'halogen bonding' (see later). In compound **31**, the C13-C21 [1.336(3) Å], N2-N1 [1.170(2) Å] and C23-C24 [1.363(3) Å] distances establish the presence of double bond between the corresponding atoms.

**Scheme 8**



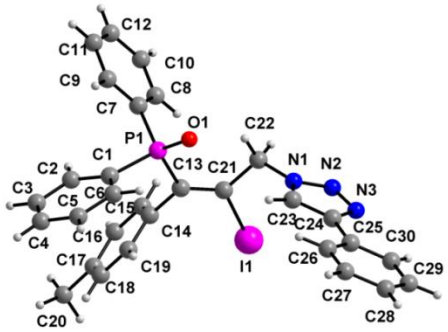




**Figure 4:** Molecular structures of Compound **31**. Selected bond lengths [Å] with esds are given in parentheses: P1-C13 1.8374(19), C13-C21 1.336(3), C21-C22 1.502(3), N1-C22 1.454(3), N1-N2 1.344(3), N3-N2 1.310(3), N1-C23 1.336(3), N3-C24 1.364(3), C23-C24 1.363(3), C24-C25 1.464(3), I1-C21 2.115(2).

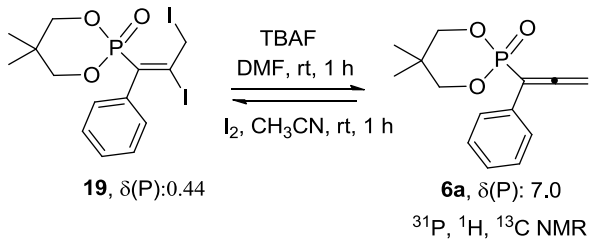
### 5.4 Fluorination reactions of 2, 3-diiodovinyl derivatives 14-22

The presence of fluorine in organic molecules has profound consequences on the physical, chemical, and biological activity of the resulting organofluoro compounds.[36] Thus we were interested in introducing fluorine at the *γ*-position of 2,3 diiodovinyl motifs. In this section, we discuss the synthesis of *γ*-fluoro-*β*-iodo-vinylphosphine oxides, *γ*-fluoro-*β*-iodo-vinylphosphonates and *γ*-fluoro-*β*-iodo-vinyl esters.

### 5.4.1 Attempted fluorination reactions of 2,3-diiodovinylphosphonate 19 with TBAF/ CsF

We were curious to know whether any of the iodine atoms can be exchanged for fluorine in compound **19**. Interestingly though, attempted fluorination of diiodovinylphosphonate **19** with tetra-*n*-butylammonium fluoride (TBAF) in $CH_3CN$ at rt (25 $^oC$), showed that it was converted back to allenylphosphonate **6a!** The $^{31}P$ NMR spectrum of the reaction mixture exhibits one major peak at δ = 7.0 (cf. Figure 5) corresponding to the allenylphosphonate **6a**. After isolation, the $^1H$ NMR and $^{13}C$ NMR spectra of the resultant compound proved that the product formed is indeed allenylphosphonate **6a** (Scheme 9). Previously, Hammond and co-workers have made a somewhat similar observation elsewhere but details are not available.[10] TBAF here acts as a scavenger for iodine.

**Scheme 9**



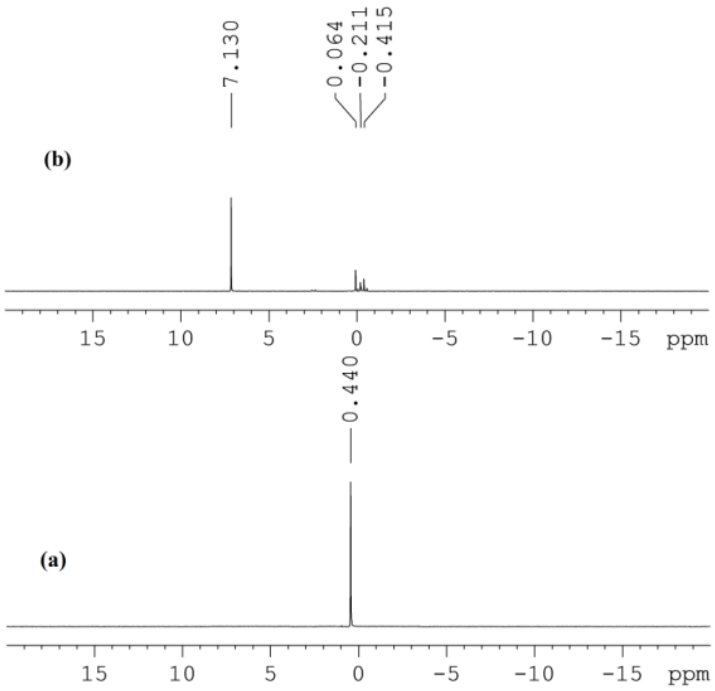
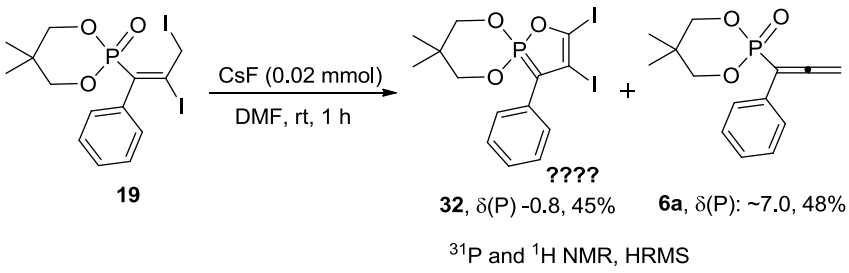




**Figure 5.** $^{31}P$ NMR spectra showing conversion of compound **19** (δ 0.44) back to compound **6a** (δ-7.13). (a) $^{31}P$ NMR spectrum of compound **19**, (b) $^{31}P$ NMR spectrum of reaction mixture corresponding to Scheme 9.

Later, we attempted fluorination of **19** with CsF in $CH_3CN$ at rt (25 $^oC$) but in this case an unexpected product **32** was obtained along with the allenylphosphonate **6a**. The $^{31}P$ NMR spectrum of the reaction mixture contains mainly three peaks (Figure 6). The one at δ(P) 5.7 [solvent DMF; δ 7.0 in $CDCl_3$), after isolation, is assigned to **6a** ($^1H$/ $^{13}C$/ $^{31}P$ NMR). The second one with δ(P) -0.91, labeled as compound **32**, exhibited peaks assignable to 5 Ar*H* (unsaturated) and the 1,3,2-dioxaphosphorinane ring protons in the $^1H$ NMR spectrum, with the signals due to C*H*$_2$I protons missing. The $^{13}C$ NMR spectrum was not clear (we could not unequivocally identify the C-I/P-C peaks), but *C*$H_2$I carbon is absent. Based on HRMS ([M+H] = 516.8926]), we believe that product **32** may have the structure shown in Scheme 10. We are still trying to obtain single crystals for this compound. A plausible pathway for formation of compound **32** is shown in Scheme 11. At first, base (CsF) will abstract one proton from allylic *γ-C*-atom generating the carbanion intermediate **III** that is in equilibrium with oxide ion intermediate **III'.** Thus formed oxide ion attacks at *γ-C*-atom and eliminates hydride ion to obtained compound **32.**

**Scheme 10**



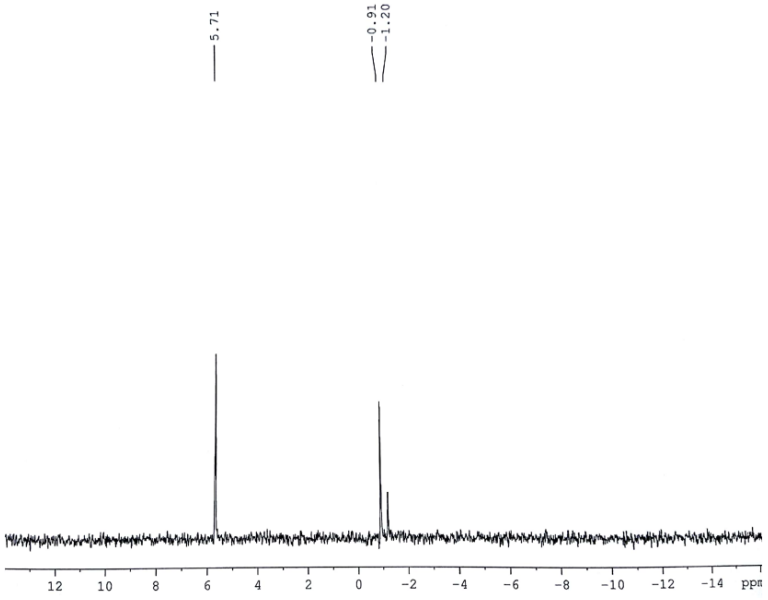
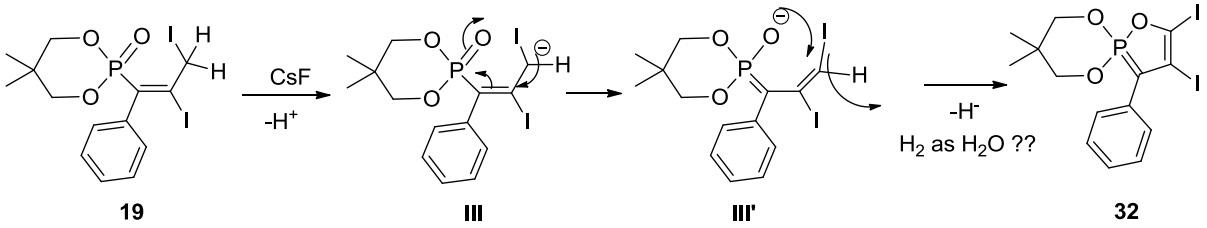




**Figure 6.** $^{31}P$ NMR spectrum of the reaction mixture corresponding to Scheme 10.

Scheme 11

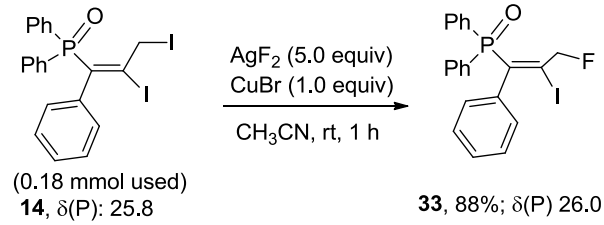



19 III III' 32

### 5.4.2 Fluorination of 2,3-diiodovinylphosphine oxides 14-17, 2,3-diiodovinylphosphonates 19-20 and 2,3-diiodovinylesters 21-22

In our next attempt, we tried fluorination of **14** with $AgF_2$/CuBr in dry $CH_3CN$ at 25 $^oC$ and obtained *γ*-fluoro-*β*-iodo-vinylphosphine oxide **33** as the major product (Scheme 12).[36] The $^{31}P$ NMR spectrum exhibits only one peak at δ = 26.5, whereas the 2,3-diiodovinylphosphine oxide **14** gives a signal at δ = 25.8. Appearance of triplet of doublet peak range -196.3 to -196.6 in $^1H$-coupled $^{19}F$ NMR spectrum suggests the presence of $CH_2F$ moiety (cf. Figure 7a). In the $^1H$-NMR spectrum, this compound shows a broad doublet at δ 5.89 [$^2J$ = 47.6 Hz; cf. Figure 7b]. In $^{13}C$ NMR spectrum, a doublet of doublet at δ 84.6 [$J$ = 168.2, 4.6 Hz] is seen (cf. Figure 7c). In a similar manner, *γ*-fluoro-*β*-iodo)vinylphosphine oxides **34-36** were synthesized (Scheme 12). The structures of compounds **34-36** were determined by single crystal X-ray analysis (Figure 8) to check for I···O interactions (see later).

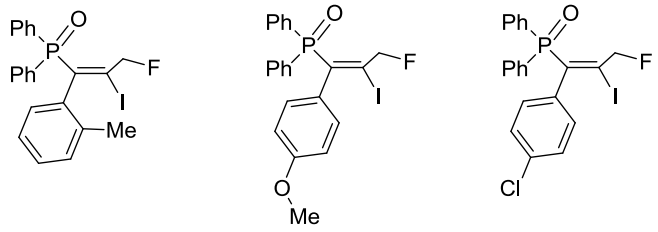
Scheme 12




(0.18 mmol used)
**14**, δ(P): 25.8

**33**, 88%; δ(P) 26.0

**Similarly**



**34** (X-ray), 89%; δ(P) 26.0 **35** (X-ray), 90%; δ(P) 26.6 **36** (X-ray), 80%; δ(P) 26.3

The ease of fluorination in the above examples suggests that the reaction iodination of allenes followed by reaction with $AgF_2$/CuBr could be utilized for other allenic systems.

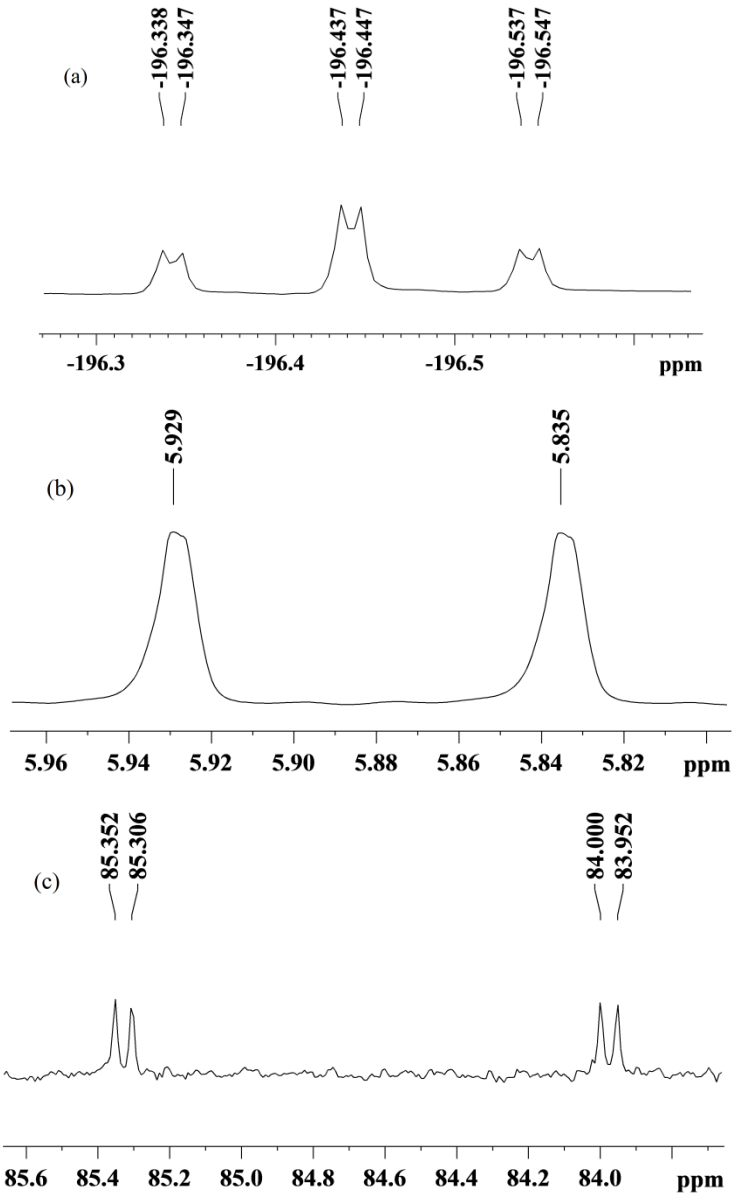



**Figure 7**. (a) $^{1}H$ coupled $^{19}F$-NMR spectrum of compound **33** showing triplet of doublet; (b) partial $^{1}H$ NMR of compound **33** showing broad doublet at 5.83-5.92; (c) Partial $^{13}C$ NMR spectrum of compound **33** showing doublet of doublet in the region 85.35-83.95.

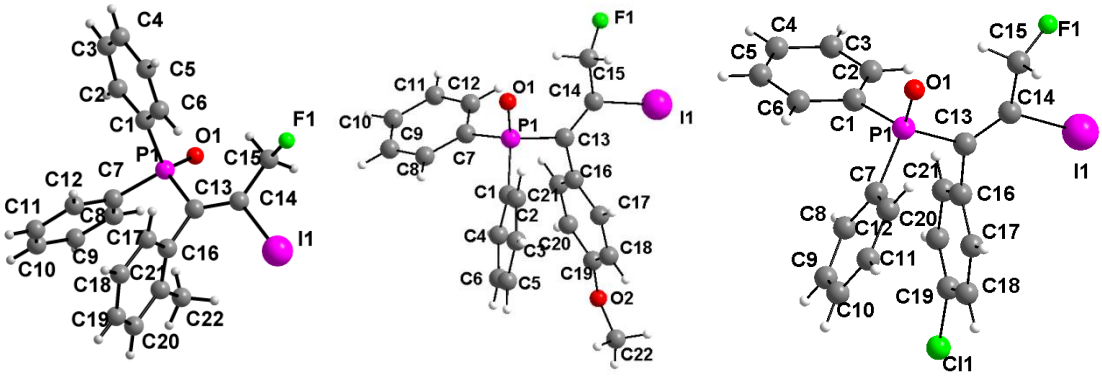
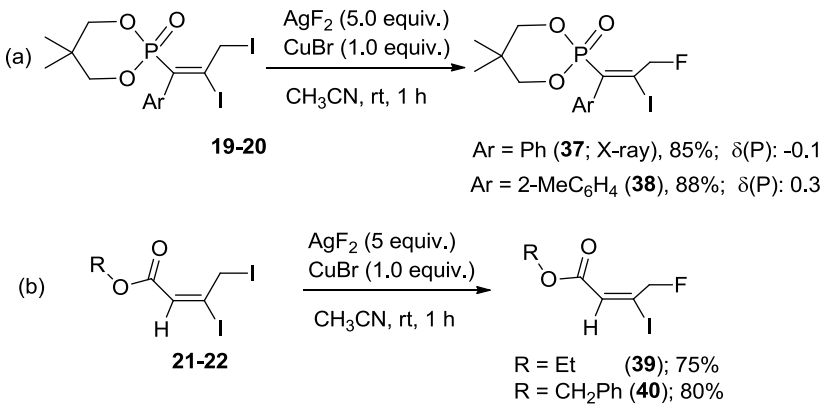



**Figure 8.** Molecular structure of Compound **34** (left), compound **35** (middle) and compound **36** (right). Selected bond lengths [Å] with esds are given in parentheses: Compound **34** (left) C13-P1 1.827(4), C13-C14 1.341(7), C13-C16 1.485(6), C14-C15 1.520(7), C15-F1 1.350(7), I1-C14 2.106(4). Compound **35** (middle): P1-C13 1.836(10), C14-C13 1.347(15), C14-C15 1.480(16), I1-C14 2.120(12), C15-F1 1.358(14), C16-C13 1.465(15). Compound **36** (right): P1-C13 1.832(5), C14-C13 1.331(6), C14-C15 1.503(7), F1-C15 1.298(6), I1-C14 2.120(4), C13-C16 1.496(6).

The above reaction was successfully extended to 2,3-diiodovinylphosphonates **19-20** and 2,3-diiodovinylesters **21-22** to afford the *γ*-fluoro-*β*-iodo-vinylphosphonates **37-38** and *γ*-fluoro-*β*-iodo-vinyl esters **39-40** (Scheme 13) in good yields. In the $^{13}$C NMR spectra, the P-*C* carbon appears as doublet in the range δ 140.7-141.1 [$^{1}J$(P-C) ~ 165.0-172.5 Hz]. The *C*H$_2$F carbon appears as a doublet at 84.8 [$J$ = 175.0 Hz] for **37**, but as a doublet of doublet at 84.4 [$J$ = 169.0 Hz, $J$ = 5.0 Hz] in **38**. In the $^{1}$H NMR spectra, C*H*$_2$F protons appears as doublet of doublet in compound **37** [δ 5.72, $J$ = 47.2 Hz, $J$ = 3.0 Hz], whereas in compound **38** these two protons show nonequivalence and appear as two quartet of doublets centered at [δ 5.83, $J$ = 24.0, 12.0 Hz] and [δ 5.71, $J$ = 24.0, 12.0 Hz] (Figure 9). The structure of compound **37** was also proven by X-ray crystallography (Figure 10). Analytical data for compounds **39-40** are also consistent with the structures shown in Scheme 13.

**Scheme 13**



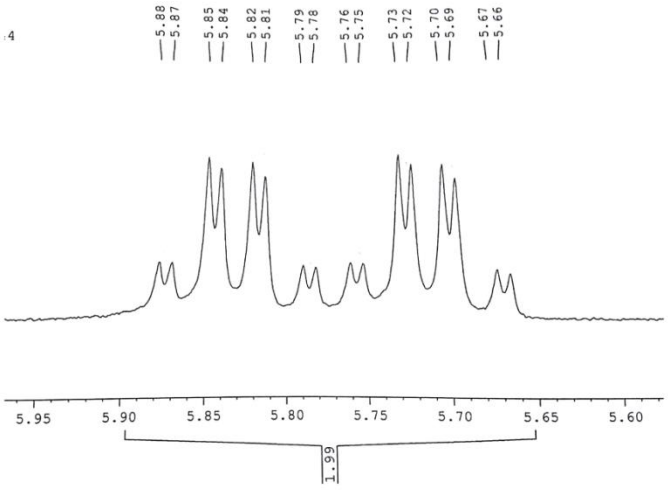




**Figure 9.** $^{1}$H NMR spectrum of compound **38** showing two quartet of doublets (2qd) pattern for C*H*$_2$F protons.

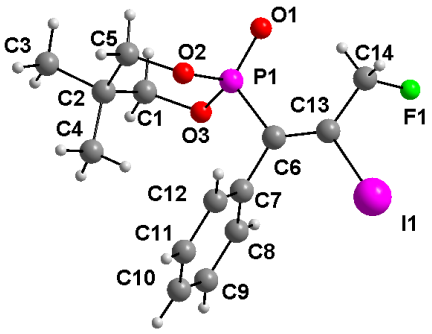
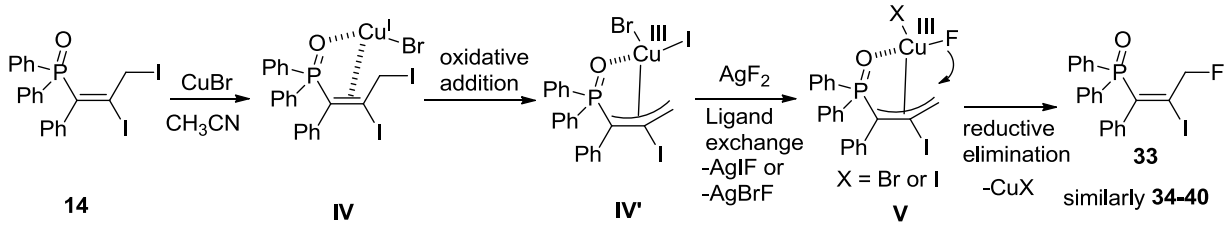



**Figure 10.** Molecular structure of compound **37.** Selected bond lengths [Å] with esds are given in parentheses**:** P1 C6 1.811(6), C6-C13 1.315(9), C13-C14 1.508(9), C14-F1 1.360(8), C13-I1 2.075(6), C6-C7 1.471(8).

### 5.4.3 Plausible pathway for the fluorination of 2,3-diiodovinylphosphine oxide 14

When we treated 2,3-diiodovinylphosphine oxide **14** with $AgF_2$ in $CH_3CN$ at 25 $^oC$ without adding CuBr, we did not observe any fluorinated product formation. Based on this observation, and literature reports,[36] we propose the following pathway for the formation of *γ*-fluoro-*β*-iodo)vinylphosphine oxide **33** (Scheme 14). Initially, CuBr co-ordinates with oxygen atom of phosphine oxide (functional group) to form intermediate **IV** and could promote oxidative addition of the allylic iodide to copper(I) to give the allyl$Cu^{III}$ complex **IV'**.[37] Ligand exchange affords the allyl$Cu^{III}$ fluoride intermediate **V**, and the final reductive elimination gives the fluorination product.

**Scheme 14**




## 5.5 Halogen bond (I•••O) interactions in *γ*-azido-*β*-iodo-vinylphosphine oxides 24-26 and *γ*-fluoro-*β*-iodo-vinylphosphine oxides 34-36

Halogen bonding is the non-covalent interaction between halogen atoms (Lewis acids) and neutral or anionic Lewis bases (N, O, S).[38] The strength of the halogen bond depends on the withdrawing moiety attached to halogen atom, stronger the withdrawing group the stronger is the halogen bond.[39] Increased electron density on the donor site also results in stronger interactions.[40] Due to the more electropositive nature, iodine acts as an electron acceptor and oxygen acts as donor. In *γ*-azido-*β*-iodo-vinylphosphine oxides **24-26** and *γ*-fluoro-*β*-iodo-vinylphosphine oxides **34-36**, iodine is attached to *β*-carbon and has high tendency to interact with electron donor like phosphoryl oxygen. Thus, compounds **24-26** (Figure 11) and **34-36** (Figure 12) show I•••O halogen bonding interactions. The I•••O distances in compounds **24**, **25** and **26** are 2.966(2) Å, 3.003(4) Å and, 3.025(9) Å respectively.; in compounds **34**, **35** and **36** the corresponding distances are 2.992(4) Å, 3.044(9) Å and 3.004(3) Å, respectively. All these are considerably shorter than the sum of the corresponding van der Waals radii of O (1.52 Å) and I (1.98 Å) [i.e. <3.50 Å]. [*Note*: Average I-O covalent bond distance is 2.14 Å]. However, such

I•••O interactions were not observed in compounds **15**, **23**, **31** and **37**. As yet we do not have a ready explanation for this difference, but it should be noted that they are weak interactions. However, the $CH_2I$ appears to have some weak interactions with a phenyl ring in compound **37** [I•••C4 (π-system) 3.632(12) Å] (Figure 13).

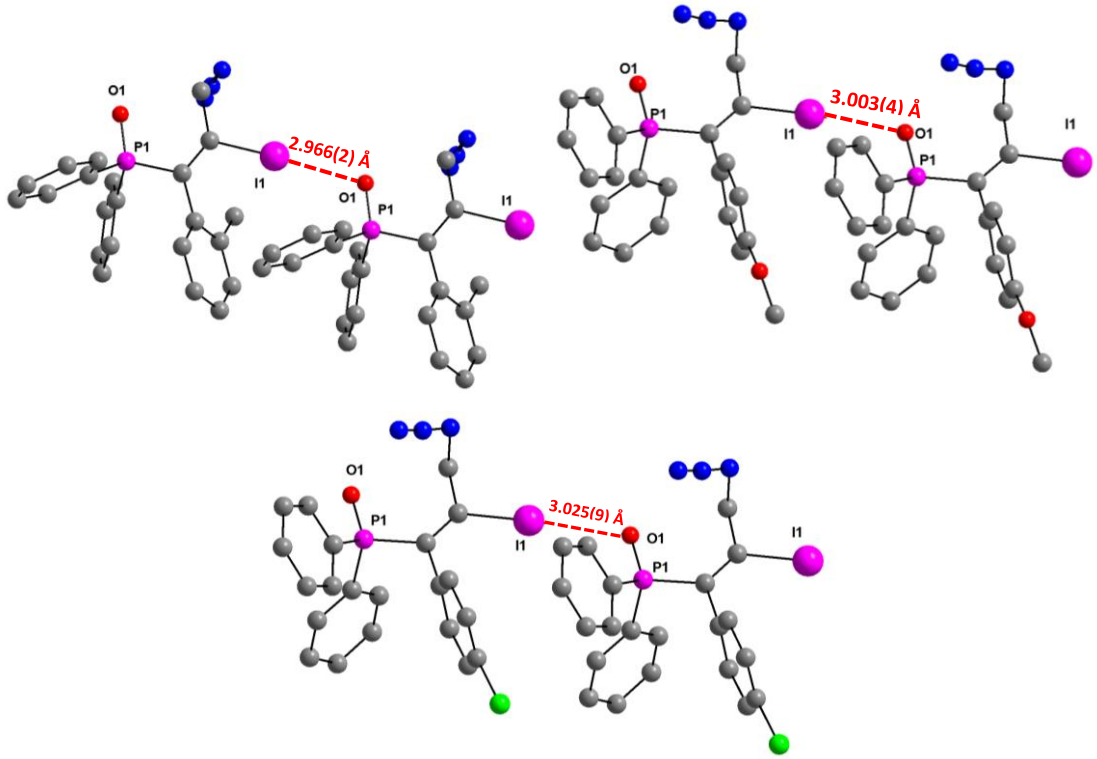
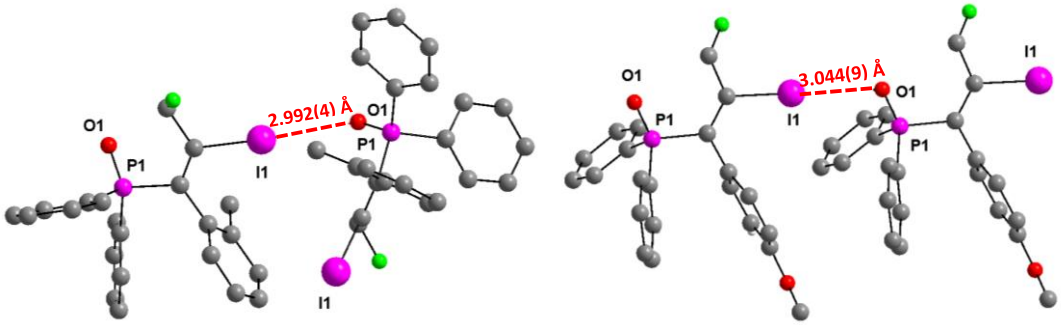



**Figure 11.** Diagrams showing I•••O halogen bonding interactions in compounds **24** (top-left), **25** (top-right) and **26** (bottom).



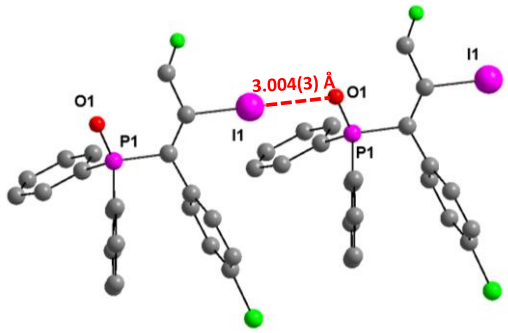



**Figure 12:** Diagrams showing I•••O halogen bonding interactions in compounds **34** (top-left), **35** (top-right) and **36** (bottom).

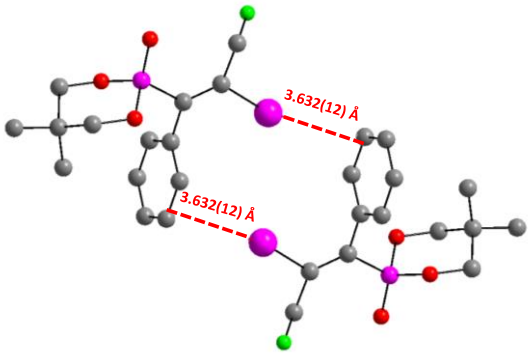


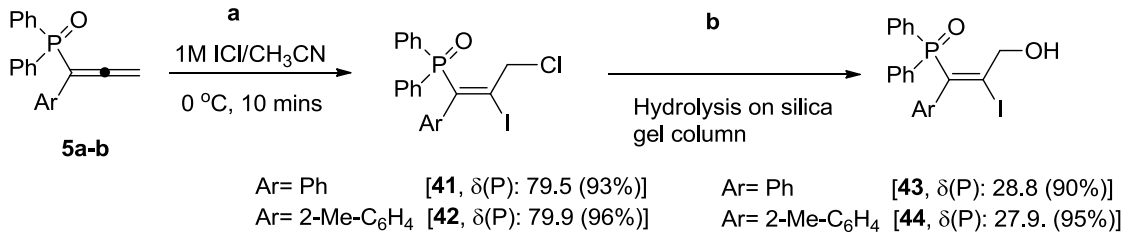

**Figure 13.** Diagram of two individual crystallographic structures of the compound **37** showing weak halogen bonding interaction [I•••C4 (π-system) 3.632(12) Å].

### 5.6 ICl addition reactions of allenylphosphine oxides 5a-b

In the interhalogen ICl, we can assign a partial positive charge on iodine and hence if the attack is electrophilic with an intermediate having the three-membered ring, iodine is supposed to be on the *β*-carbon and hence the chlorine will go to the terminal carbon of the allene. Thus we treated allenylphosphine oxides **5a-b** with 1M solution of ICl in $CH_3CN$ at 0 $^oC$ and obtained *γ*-chloro-*β*-iodo-vinylphosphine oxides **41 -42** in good yields (Scheme 15a). In the $^{31}P$ NMR spectrum of compound **41** shows peak at δ 79.5 and in $^{13}C$ NMR spectrum, this compound shows doublet at δ 118.0 [$^1J$(P*C*=C) = 102.6 Hz] indicating the presence of a P-*C*=C moiety. A surprising point here is that the $^{31}P$ NMR chemical shifts of compounds **41-42** are unusually downfield. Presence of chlorine in the molecule was also confirmed by HRMS data. These compounds could be purified by recrystallization from DCM/hexane (1:2) mixture, but when we tried silica gel column chromatography, the hydrolyzed products **43-44** were obtained in good

yields (Scheme 15b). In the $^1$H NMR spectra, the $OCH_2$ protons appear as a singlet in **43** but a doublet of doublet in **44**. The structure of compound **44** was confirmed by single crystal X-ray analysis (Figure 14a). Compound **44** exhibits H-bonding involving the $–CH_2OH$ group and the phosphoryl group (Figure 14b); this factor together with the presence of 2-methyl group on the aromatic ring at the $\alpha$-position may be the reason for the observation of separate signals for the two C$H_2$ protons in the $^1$H NMR spectrum.

**Scheme 15**



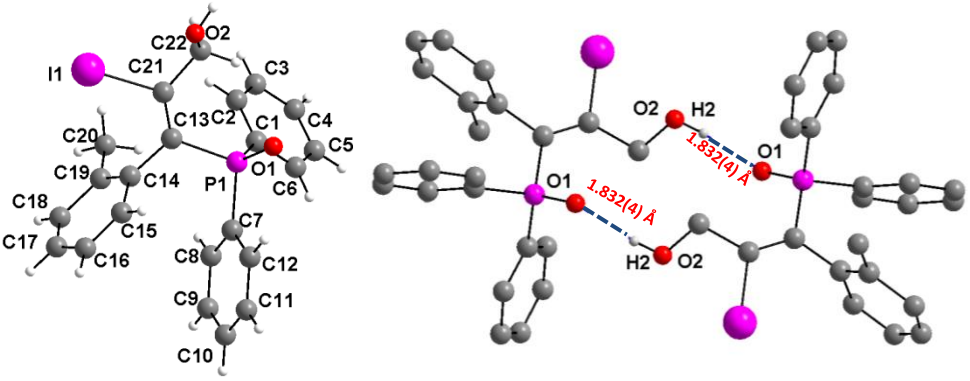



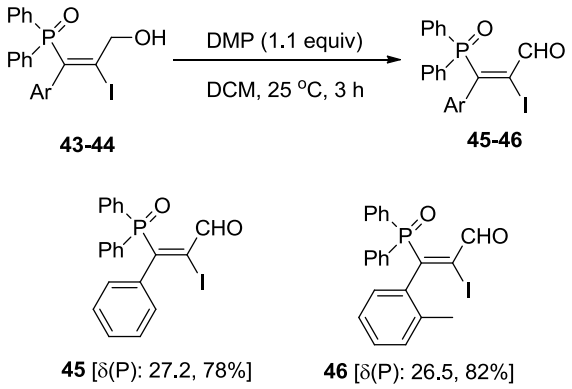

**Figure 14:** (a) Molecular structure of Compound **44** (left). Selected bond lengths [Å] with esds are given in parentheses: P1 C13 1.846(5), C21 C13 1.324(7), I1 C21 2.113(5), C21 C22 1.507(7), O2 C22 1.393(6), C13 C14 1.490(7); (b) Molecular structure of compound **44** (right) showing H-bonding O1•••H2O2 (1.832(4) Å).

## 5.7 Oxidation of $\gamma$-hydroxy-$\beta$-iodo-vinylphosphine oxides 43-44 with Dess–Martin periodinane (DMP)

We treated $\gamma$-hydroxy-$\beta$-iodovinylphosphine oxides **43-44** with Dess–Martin periodinane in DCM to obtain the corresponding functionalized aldehydes **45-46** in good yields (Scheme 16). Absence of allylic protons at δ 4.9-5.2 and appearance of aldehyde proton at δ 10.11 [$^3J$ = 1.2 Hz] in the $^1$H NMR in addition to *C*HO signal at δ 187.2 [$J$ = 6.4 Hz] in the $^{13}$C NMR confirm

that the primary alcohol is readily converted into aldehyde without affecting other bonds. These compounds have geminal functionalities (iodo, aldehyde and alkene) that could be gainfully employed later.

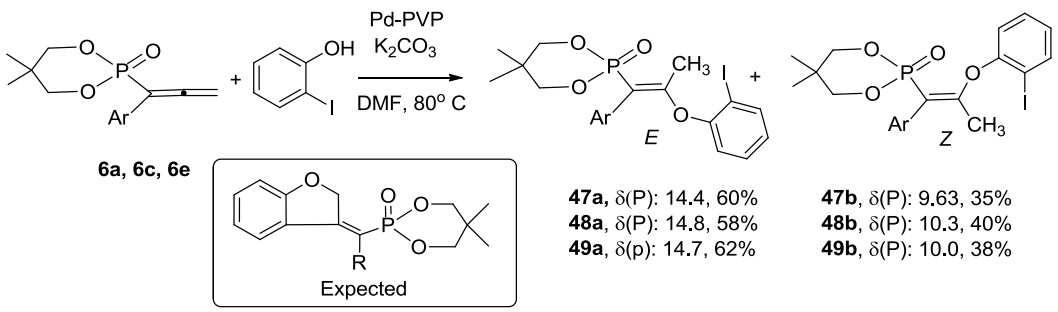
**Scheme 16**




## 5.8 Pd-nanoparticle [Pd-PVP]-catalyzed reaction of allenylphosphonates with 2-iodophenol

In a couple of earlier papers, we have disclosed that the [Pd]-catalyzed reactions of 2-iodophenols with allenylphosphonates readily afford phosphonobenzofurans.[3a, 41] In this context, we were wondering whether palladium nanoparticles will be effective in such reactions or not. However, in these cases, we obtained mainly phenol addition products **47-49** (Scheme 17). An interesting point though, is that in the absence of the Pd-PVP nanoparticles, the total yield of the addition products is much less (<30%). Only vinylphosphonates are formed with no indication of the allylphosphonates. In all the cases, the yields were good and the two isomers could be readily separated. The assignment of *Z* or *E* stereochemistry for these products is based on the $^{4}J$(P-H) coupling constants but at the moment, is tentative. Since cyclization did not take place in these cases, we did not proceed further.

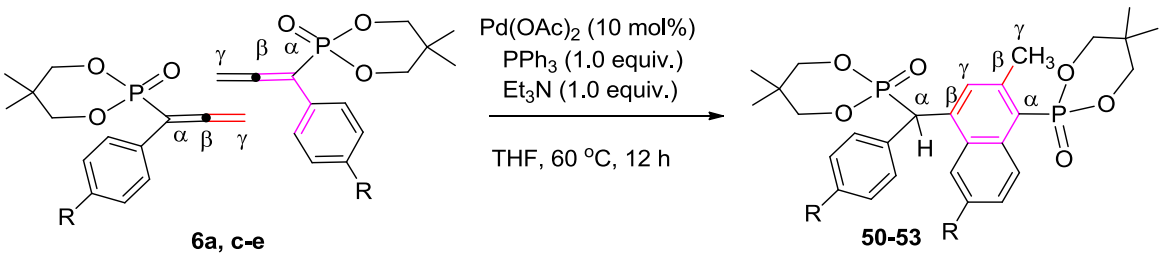
**Scheme 17**



## 5.9 [Pd]-catalyzed cyclization reactions of allenylphosphonates

Based on literature reports on cyclization and C-H-functionalization reactions of allenes,[3a, 3e, 14-18, 41] we were very much interested to check whether allenylphosphonate will dimerize/cyclize in the presence of a [Pd] catalyst in a way different from that reported earlier.[3a, 3e, 3q, 41] For this purpose, we treated allenylphosphonate **6a** with $Pd(OAc)_2/PPh_3/Et_3N$. Interestingly, this reaction afforded compound **50** (Scheme 18). The $^{31}P$ NMR spectrum of **50** showed two peaks of equal intensity at δ 20.0 and 14.5 indicating that two molecules of allenylphosphonate are involved in the reaction. In the $^{1}H$ NMR spectrum, a doublet at δ 5.41 [$J$ = 26.4 Hz] due to the PC*H* proton and another doublet at δ 2.87 [$^{3}J$ = 2.0 Hz] are observed. In the $^{13}C$ NMR spectrum, a doublet for PC carbon at δ 46.5 [$^{1}J$(P*C*) = 137.4 Hz] indicates a phosphorus is attached to $sp^3$ carbon atom. One more doublet at δ 121.4 [$^{1}J$(PC) = 172.8 Hz] clearly indicates one of the phosphorus atoms attached to alkenyl carbon. Based on these NMR data, we ascertained that the formed product was an unsymmetrical dimer in which (*β,γ*)-double bond of one allene and (*α,β)*-double bond of another allene are involved. Similar products **51-53** could also be obtained in good yields (Table 3). Fortunately we could obtain single crystal structure of compound **51** crystallized from ethyl acetate/chlorobenzene (2:1) mixture (Figure 15). Here, one of the aryl double bonds is also involved in the cyclization forming a new six-membered ring as shown in Scheme 18. The C6-C14 distance of 1.529(9) Å establishes the presence of a single bond; the C14-C19 [1.452(9) Å] and C15-C16 [1.428(10) Å] bond lengths confirm the presence of single bonds between these atoms. It may be noted that unlike the literature reports,[2d, 22] cyclobutane products of the type shown in Scheme 19 are not observed in our reaction.

**Scheme 18**



Scheme 19

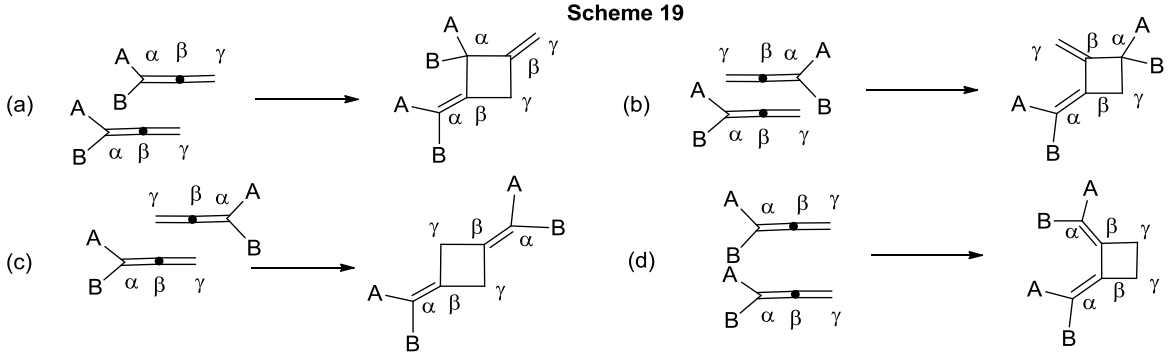
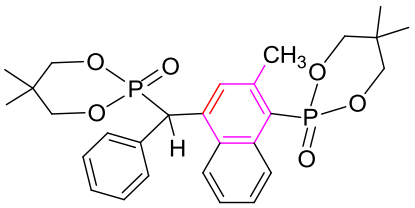
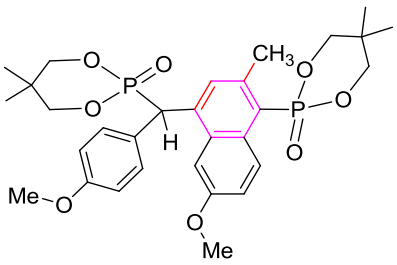
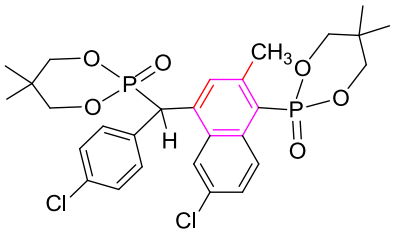
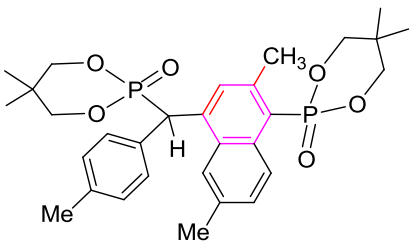


**Table 3.** Synthesis of phosphorus based naphthalenes from allenylphosphonates[a]

| Entry | Allenylphosphonate | Phosphorus based naphthalenes | yield (%)[b] |
|---|---|---|---|
| 1 | **6a** |  **50**, δ(P): 20.0, 14.5 | 72 |
| 2 | **6c** |  **51**, δ(P): 20.44,14.8 (X-ray) | 68 |
| 3 | **6d** |  **52**, δ(P): 19.37 &13.46 | 45 |

| | | | |
|---|---|---|---|
| 4 | **6e** |  **53**, δ(P): 20.41 & 14.88 | 75 |

[a]Standard conditions: allenylphosphonate (0.38 mmol) in dry THF, $Pd(OAc)_2$ (0.038 mmol), $PPh_3$ (0.38 mmol) and $Et_3N$ (0.38 mmol) at 60 $^oC$ (oil bath) for 12 h. [b]Isolated yields.

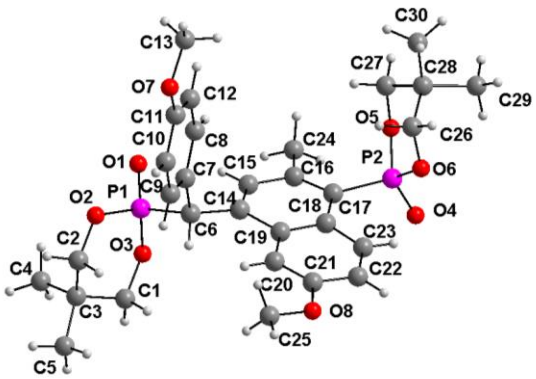


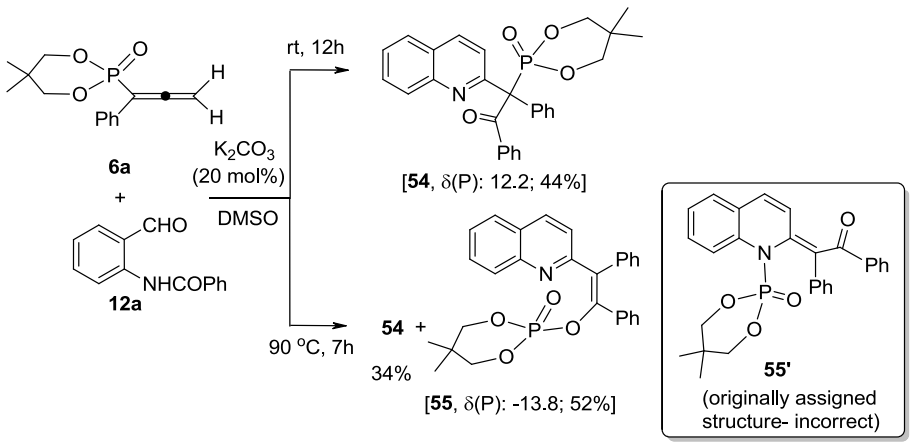

**Figure 15:** Molecular structure of Compound **51.** Selected bond lengths [Å] with esds are given in parentheses: P1 C6 1.813(7), P2 C17 1.791(8), C6 C14 1.529(9), C19 C14 1.452(9), C19 C18 1.411(9), C17 C18 1.427(10), C17 C16 1.363(10), C16 C24 1.504(11), C15 C16 1.428(10), C15 C14 1.357(9).

### 5.10 Reaction of allenylphosphonates 6a, 6c, and 6e-g with protected benzamides 12a-b

In a previous work from our laboratory, we have conducted the reaction of allenylphosphonates with aryl aldehydes/ ketones bearing protected *amide* functionality at the *ortho*-position. However, while continuing the work, it was noticed that the structure **55'** assigned in the thesis was incorrect (Scheme 20).[42] Hence there was a necessity to explore this aspect further. Thus, we treated the allenylphosphonate **6a** with *N*-(2-formyl-phenyl) benzamide **12a** in the presence of $K_2CO_3$ and obtained the benzoyl group rearranged product **54**[43] [δ (P) 12.2]. Rather interestingly, when the same reaction was conducted at 90 $^oC$, the phosphoryl migrated product **55** was obtained along with phosphono-quinoline **54** with the combined yield

of the isolated products being 86%. The δ(P) value of -13.8 for compound **55** is much up-field to that for **54** indicating that the phosphorus atom in **55** is linked to either oxygen or nitrogen but not to carbon.[3g,44] Consistent with this, the P*C* signal was absent in the $^{13}$C NMR spectrum (*vide infra*; Figure 17 for X-ray structure of analogous compound **57**). Thus we surmised that compound **54** underwent rearrangement under thermal conditions leading to phosphoryl group migrated product **55**. We have proven this conversion by individually heating compound **54** and monitoring the sample by $^{31}$P NMR as shown in Figure 16.

**Scheme 20**



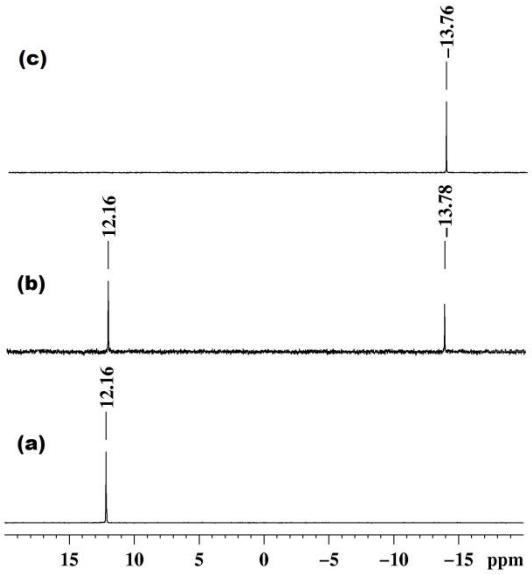
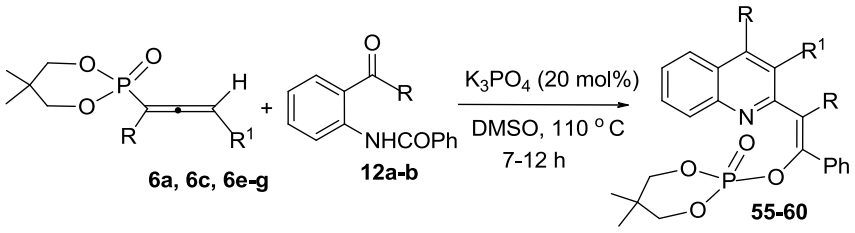




**Figure 16:** $^{31}$P NMR spectra showing conversion of compound **54** (δ 12.16) to compound **55** (δ-13.78): (a) at r.t, (b) at 190 °C (after 12 min), (c) at 200 °C (after 12 min).

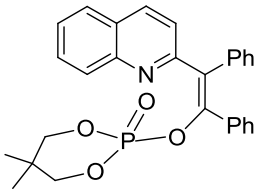
To check the effect of bases and solvents on the yield of compound **55**, different reaction conditions were employed. In the presence of $K_2CO_3$ and DMSO at 110 $^oC$, the expected phosphoryl group migrated product **55** was formed in 90% yield. It was found that this reaction leads exclusively to the desired quinoline **55** [98%, $^{31}P$ NMR evidence] using $K_3PO_4$ (20 mol%)/ DMSO. Based on these optimized conditions, we then treated various allenylphosphonates **6a, 6c, 6e-g** with *N*-(2-formyl phenyl) benzamide **12a** or *N*-(2-acetyl-phenyl) benzamide **12b** to obtain the desired *O*-phosphorylated quinolines **55-60** in good to excellent yields (Scheme 21; Table 4). The $^{31}P$ NMR spectra of *O*-phosphorylated-quinolines show signals in the range δ -13.7 – -15.0. We obtained the crystal structure of compound **57** in which phosphoryl group being migrated to oxygen as shown in Figure 17.

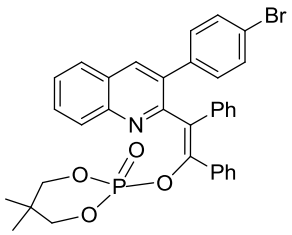
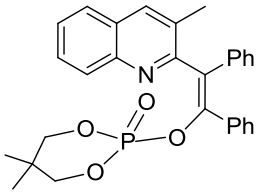
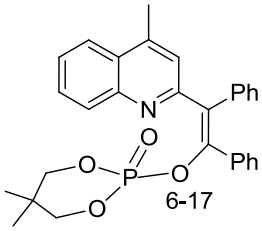
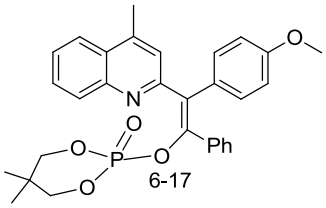
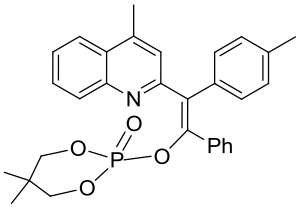
**Scheme 21**




**6a, 6c, 6e-g** **12a-b** **55-60**

**Table 4:** *O*-phosphorylated quinolines **55-60**

| Entry | Allenylphosphonates/ *N*- protected benzamides | *O*-phosphorylated quinolines | yield (%)[a] |
|---|---|---|---|
| 1 | **6a/12a** |  **55**, δ(P): -13.8 | 90 |

| | | | |
|---|---|---|---|
| 2 | **6f/12a** |  <br>**56**, δ(P): -14.7 | 56 |
| 3 | **6g/12a** |  <br>**57**, δ(P): -14.4 (X-ray) | 78 |
| 4 | **6a/12b** |  <br>**58**, δ(P): -13.9 | 74 |
| 5 | **6c/12b** |  <br>**59**, δ(P): -13.7 | 75 |
| 6 | **6e/12b** |  <br>**60**, δ(P): -13.8 | 77 |

[a]Isolated yields

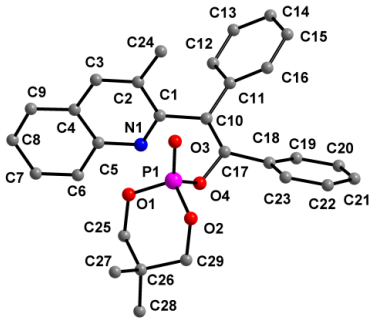
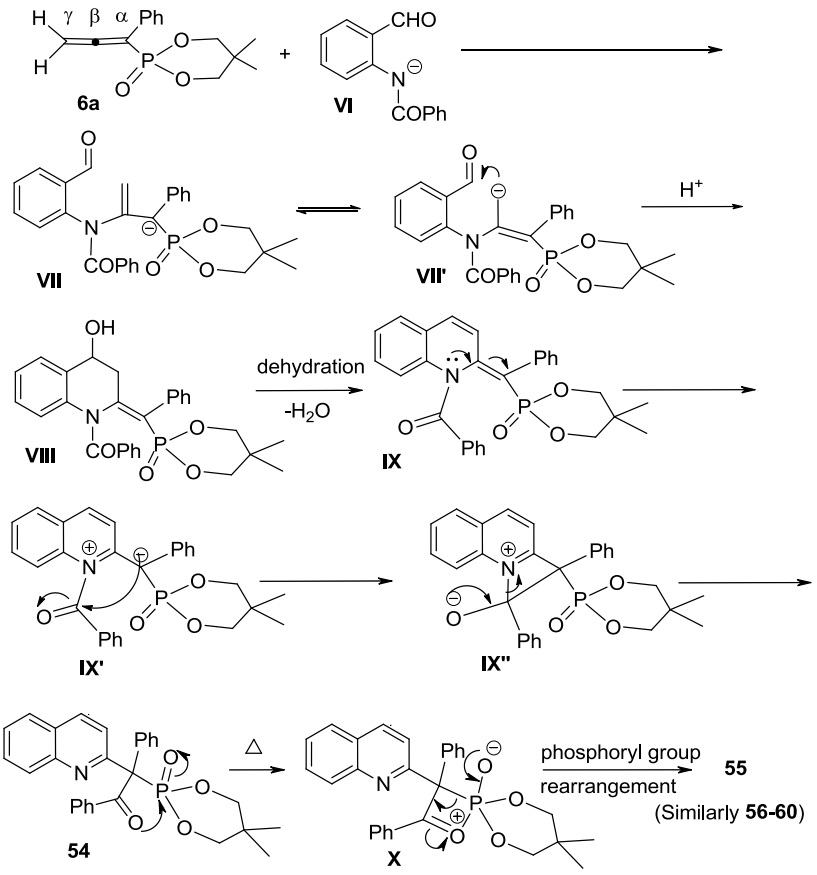



**Figure 17:** Molecular structure of compound **57**. Hydrogen atoms are omitted for clarity. Selected bond parameters: N1-C5 1.367(2), N1-C1 1.319(2), C1-C10 1.500(2), C10-C17 1.337(2), C17-O4 1.404(2), P1-O4 1.5831(12), P1-O3 1.4446(15), C17-C18 1.476(2), C10-C11 1.495(2) (Å).

### 5.11 A plausible pathway for the formation of phosphono-quinoline 54 and *O*-phosphorylated quinoline 55

A plausible pathway for the formation of phosphono-quinoline **54** and *O*-phosphorylated quinoline **55** is shown in Scheme 22. Initially, the base abstracts proton from *N*-(2-formylphenyl) benzamide **12a** and generates aza-anionic intermediate **VI** which reacts with allenylphosphonate **6a** at the *β*- position[20] to give **VII**. Species **VII** is in equilibrium with **VII'**. Intermediate **VII'** undergoes intramolecular aldol reaction followed by proton abstraction to afford **VIII**, which upon dehydration leads to the intermediate **IX**.[20] Benzoyl group in the intermediate **IX** undergoes 1,3-migration to afford **54**.[43] Upon heating, the oxygen of benzoyl group may attack the phosphoryl phosphorus to form the intermediate **X** with a four-membered ring. This is followed by phosphoryl group rearrangement leading to product **55**. Intermediates analogous to **X** are envisaged in Horner-Wadsworth reaction.[45]

**Scheme 22**




## 5.12 Reaction of allenylphosphine oxides 5a and 5c-e with protected benzamides

In contrast to the above, from the reaction of allenylphosphine oxides **5a**, **5c-e** with *N*-(2-formyl phenyl) benzamide **12a** or *N*-(2-acetyl-phenyl) benzamide **12b**, we have isolated the phosphonoquinolines **62** and benzoyl group eliminated phosphonoquinolines **61** and **63-65** (Scheme 23, Table 5). The latter compounds were the major products. In the case of allenylphosphine oxides **5c** and **5e**, we could isolate only benzoyl group eliminated phosphonoquinolines **61** and **64**, but compounds similar to **62** were also present. The overall yields of the isolated products in all the cases were, however, good. It may be noted that compound **62** is analogous to **54**. Compounds **61** and **63-65** most likely arise due to hydrolysis of compounds of type **62**. We attempted thermal rearrangement of **62** (neat, 185-190 $^{o}$C/ 2 min); although there was an additional peak at $\delta$(P) 30.0 (ca 50%) which is probably the rearranged product, we could not isolate it. Hydrolysis of compound **62** (in DMSO with adventitious water at 120 $^{o}$C/ 12 h) leading to phosphono quinolone **63** under thermal conditions could, however, be

conveniently monitored by $^{31}P$ NMR spectroscopy (Figure 18). Structure of compound **62** was confirmed by single crystal X-ray analysis (cf. Figure 19).

**Scheme 23**

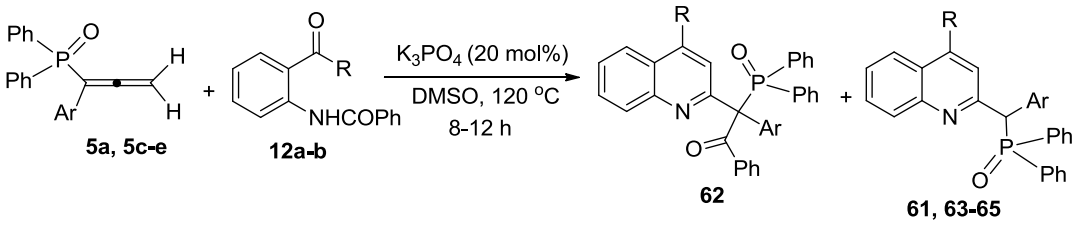
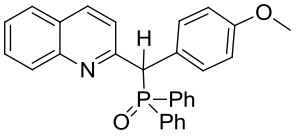
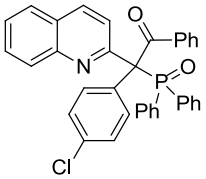
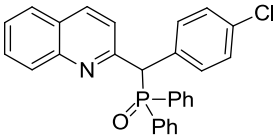
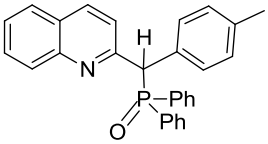
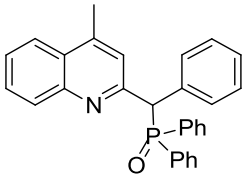



**Table 5:** Reaction of allenylphosphine oxides **5a, 5c-e** with protected benzamides

| Entry | Allenylphosphine oxide/ *N*- protected benzamides | Phosphono-quinolines | Benzoyl group eliminated phosphonoquinolines |
|---|---|---|---|
| 1 | **5c/12a** | - |  **61**, δ(P): 32.1, 63% |
| 2 | **5d/12a** |  **62**, δ(P):37.8, 40% (X-ray) |  **63**, δ(P):30.8, 45% |
| 3 | **5e/12a** | - |  **64**, δ(P):31.2, 66% |
| 4 | **5a/12b** | - |  **65**, δ(P):31.0, 80% |

[a]Standard conditions: allenylphosphine oxides **5a, 5c-e** (0.38 mmol) in dry DMSO, $K_3PO_4$ (0.076 mmol) at 120 $^oC$ (oil bath) for 12 h.

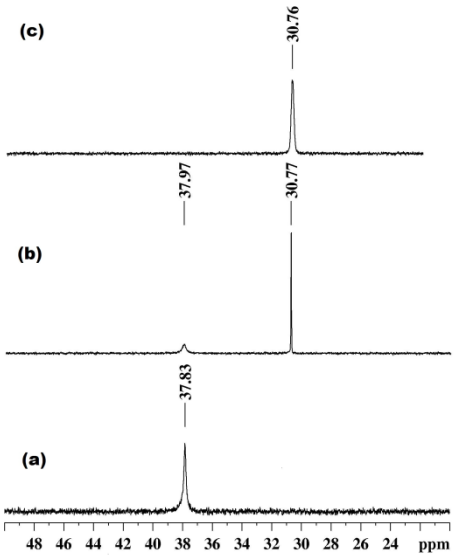



**Figure 18:** $^{31}$P NMR spectra showing conversion of compound **62** (δ 37.83) to compound **63** (δ 30.76): (a) at rt, (b) after 8 h (120 $^{o}$C), (c) after 12 h (120 $^{o}$C).

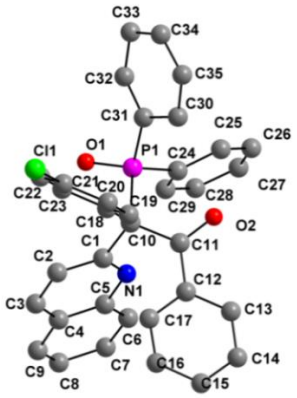



**Figure 19:** Molecular structure of compound **62**. Hydrogen atoms are omitted for clarity. Selected bond parameters: N1-C1 1.31(5), C1-C10 1.54(6), C10-C11 1.53(6), C18-C10 1.55(6), P1-C10 1.91(4), C1-C2 1.40(6), O2-C11 1.22(5) (Å).

### 5.13 Reaction of sulfur based allenes 8a-b with protected benzamides 12a-b

The above reaction was successfully extended to sulfur based allenes **8a-b** by treating them with *N*-(2-formyl phenyl) benzamide **12a** or *N*-(2-acetyl-phenyl) benzamide **12b** at 80 $^{o}$C, affording the sulfur containing quinolines **66-69** (Scheme 24, Table 6) in moderate to good yields. These compounds are similar to the phosphonoquinoline **54**. IR, NMR ($^{1}$H and $^{13}$C) and HRMS data are consistent with the structures shown. The structure of compound **68** was further

proven by X-ray crystallography (cf. Figure 20). Unlike their phosphorus counterparts, we did not observe any rearrangement of the sulfonyl group in these cases.

**Scheme 24**

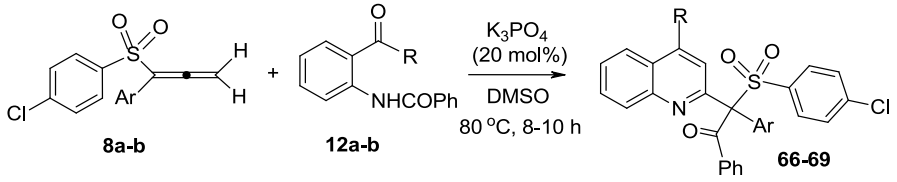
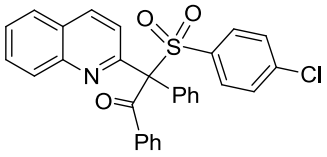
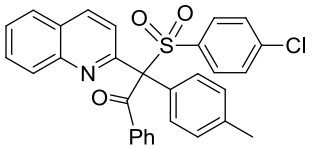
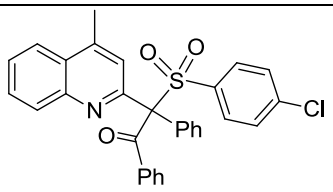
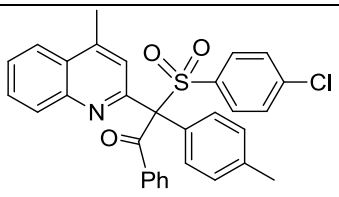



**Table 6**: Reaction of sulfur based allenes **8a-b** with protected benzamides **12a-b** lead to sulfur based quinolines **66-69**[a]

| Entry | Sulfur based allenes | *N*- protected benzamides | Sulfur based quinolines | yield (%)[b] |
|---|---|---|---|---|
| 1 | **8a** | **12a** |  **66** | 65 |
| 2 | **8b** | **12a** |  **67** | 58 |
| 3 | **8a** | **12b** |  **68** (X-ray) | 68 |
| 4 | **8b** | **12b** |  **69** | 62 |

[a]Standard conditions: Sulfur based allenes (0.32 mmol) in dry DMSO, $K_3PO_4$ (0.076 mmol) at 80 $^oC$ (oil bath) for 8-10 h. [b]Isolated yields.

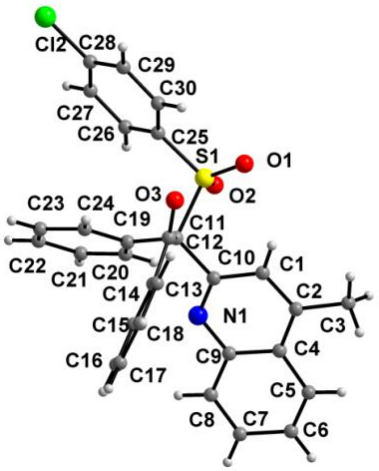
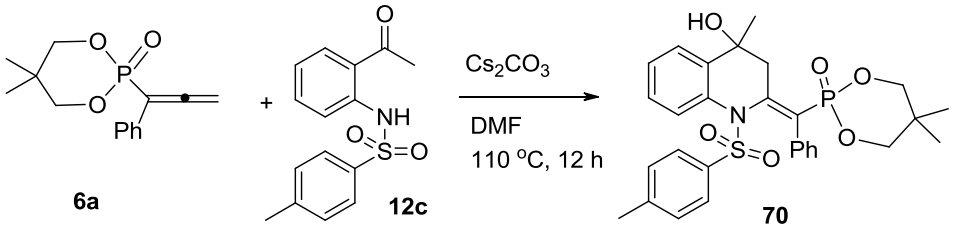



**Figure 20:** Molecular structure of compound **68**. Hydrogen atoms are omitted for clarity. Selected bond parameters: S1-O2 1.430(4), S1-O1 1.435(4), S1-C25 1.786(4), S1-C11 1.891(5), N1-C10 1.288(6), N1-C9 1.368(5), C12-O3 1.208(6), C12-C11 1.548(5) (Å).

## 5.14 Reaction of allenylphosphonate 6a with *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide 12c

In an effort to see if we can identify any intermediate species in the above reactions, we treated the allenylphosphonate **6a** with *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide **12c** in the presence of $Cs_2CO_3$ in DMF at 110 $^oC$ for 12 h (Scheme 25). Interestingly, we obtained the cyclic intermediate **70**. IR, NMR ($^1H$ and $^{13}C$) and HRMS data are consistent with the structure shown. Gratifyingly, a crystal suitable for X-ray structure determination (cf. Figure 21) could be found. This result proves the intermediacy of a species like **XIII** in the above reactions.

**Scheme 25**



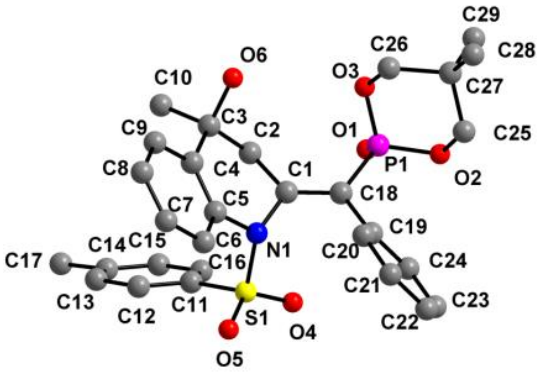



**Figure 21:** Molecular structure of compound **70**. Hydrogen atoms are omitted for clarity. Selected bond parameters: S1-N1 1.671(4), C18-C1 1.343(5), C1-C2 1.494(5), C2-C3 1.533(5), C3-O6 1.433(5), C3-C10 1.521(5), C4-C3 1.527(6), C4-C5 1.368(7), P1-O1 1.455(3) (Å).

## Summary of PART-B

1. *γ*-Azido/*γ*-fluoro-*β*-iodo-vinyl phosphine oxides, phosphonates and esters were synthesized from phosphorus based allenes and allenyl esters by using simple and convenient iodination followed by azidation/fluorination. Surprisingly, attempted fluorination of (*γ*,*β)*-diiodo-vinyl-phosphine oxides with TBAF [*n*-$Bu_4NF$] led to the corresponding allenylphosphine oxide! However, $AgF_2$/CuBr could be used to obtain the *γ*-fluoro-*β*-iodo-vinyl phosphine oxides and relate phosphorus-free *γ*-fluoro-*β*-iodo-vinylesters. In some cases, I•••O halogen to oxygen non-covalent bond interactions ('halogen bonding') is observed. In continuation of this study, allenylphosphine oxides have been treated with ICl to afford *γ*-chloro-*β*-iodo-vinylphosphine oxides and *γ*-hydroxy-*β*-iodo-vinylphosphine oxides in good yields.
2. Use of palladium nanoparticles (Pd-PVP) in the reaction of allenylphosphonates with 2-iodophenols affords only isomeric (*E/Z*)-vinylphosphonates with no indication of the allylphosphonates. These isomeric products were successfully separated. The assignment of *Z* or *E* stereochemistry for these products is based on the $^4J$(P-H) coupling constants.
3. Phosphorus based naphthalenes were synthesized from a novel self-dimerization-cum-cyclization of two molecules of allenylphosphonates by using [Pd]-catalysis. In this interesting [4+2] cycloaddition, the (*β*,*γ*) double bond of one allene, (*α*,*β)* double bond of the second allene and double bond of the aryl group at the *α*-position are involved; in addition a proton shift is also involved.
4. We have synthesized densely substituted phosphorus/ sulfur based quinolines *via* base catalyzed intermolecular cyclization of *N*-protected *o*-amino benzaldehyde or acetophenone with allenylphosphonates or allenylphosphine oxides or sulfur based allenes. We could obtain phosphorus based quinolines in good to excellent yields, whereas sulfur based quinolines were obtained in moderate yields. We have also found a novel benzoyl group rearrangement followed by phosphoryl group migration under thermal conditions. Finally, one of the intermediate species proposed in the reaction pathway has been characterized by X-ray crystallography by utilizing a sulfonamide.

# EXPERIMENTAL SECTION

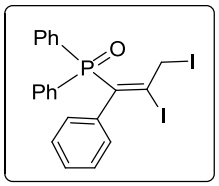
Details of instruments, standards etc. are already given in Chapter 3.

Aryl substituted propargylic alcohol precursors **3a-g**,[26] allenylphosphine oxides **5a-e**,[6a] allenylphosphonates**6a-g**,[3b, 22, 27] 4-chlorophenylsulfenylchloride**7**,[21, 30] sulphur based allenes **8a-b**,[21,30] phosphoranylidene esters **9a-b**,[24,31] ethyl/benzyl allenoate **11a-b**,[24,31] *N*-(2-formyl phenyl) benzamide **12a**,[32a,b] *N*-(2-acetyl-phenyl) benzamide **12b**,[32c,d] and *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide **12c**[33] were synthesized by following literature procedures. Aryl iodides **1**, propargylic alcohols **2**, acetylchloride **10**, 2-iodophenol **13** are commercially available.

## 6.1 Synthesis of 2,3-diiodovinylphosphine oxides, 2,3-diiodovinylphosphonates and 2,3-diiodovinylesters

To a solution of allenylphosphine oxide **5a** (100 mg, 0.32 mmol) in dry acetonitrile was added iodine (88 mg, 0.34 mmol) with continuous stirring, within 0.5 to 1 h, crystals of 2,3 diiodovinylphosphine oxide **14** were formed. They were separated from acetonitrile and used for further studies without any further purification. Compounds **15-22** were prepared following same procedure using the same molar quantities. But in the case of compounds **19-22**, purification was done using column chromatography (hexane/ethyl acetate 2:1).

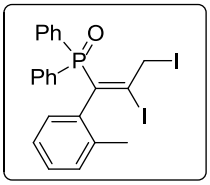
**Compound 14**




Yield: 0.171 g (95%, light yellow solid, $R_f$ = 0.43 (8:2 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[6a]

**Compound 15**




Yield: 0.167 g (95%, light yellow solid, $R_f$ = 0.46 (8:2 hexane/ethyl acetate)).[34]

Mp: 150-154 $^{o}$C.

IR (KBr): 2915, 2849, 1600, 1507, 1436, 1255, 1167, 1118, 1030 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ7.87-7.82 (m, 2H), 7.63-7.60 (m, 1H), 7.56-7.51 (m, 2H), 7.42-7.39 (m, 1H), 7.31-7.26 (m, 2H), 7.22-7.17 (m, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.02 (t, *J* = 7.4 Hz, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.4 Hz, 1H), 5.96-5.93 (m, 1H), 5.43-5.40 (m, 1H), 1.74 (s, 3H).

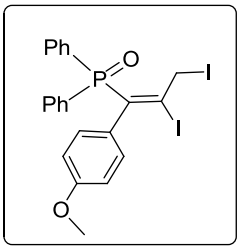
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 142.6 (d, *J* = 8.5 Hz), 142.2 (d, *J* = 58.5 Hz), 137.2 (d, *J* ~ 4.0 Hz), 133.0, 132.7, 132.6, 132.5, 132.4, 131.9 (d, *J* = 3.0 Hz), 131.6, 131.1 (d, *J* = 110.2 Hz), 129.8, 128.8 (d, *J* = 12.4 Hz), 128.5, 128.1, 127.7, 127.5 (d, *J* = 12.2 Hz), 125.5, 19.1, 16.2 (d, *J* = 5.6 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 25.3.

HRMS (ESI): Calcd. for $C_{22}H_{20}I_2OP$ ($M^+$+H): *m/z* 584.9341. Found: 584.9343.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at rt (25 $^{o}$C). X-ray structure was determined for this sample.[34]

**Compound 16**




Yield: 0.147 g (85%, $R_f$ = 0.40 (8:2 hexane/ethyl acetate)).

IR (neat): 3055, 2926, 2853, 1603, 1505, 1433, 1288, 1252, 1175, 1113, 1025, 694 cm$^{-1}$.

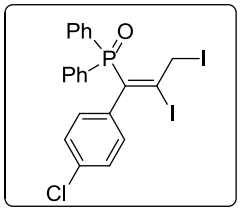
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.62-7.57 (m, 4H), 7.55-7.50 (m, 2H), 7.42-7.37 (m, 4H), 6.62-6.55 (m, 4H), 5.66 (d, *J* = 1.6 Hz, 2H), 3.73 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.2, 135.9, 132.2, 132.1 (d, *J* = 3.0 Hz), 132.0$_8$, 131.1 (d, *J* = 104.9 Hz), 130.5 (d, *J* = 3.1 Hz), 128.4, 128.3, 113.4, 55.2, 16.2 (d, *J* = 5.8 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 25.8.

HRMS (ESI): Calcd. for $C_{22}H_{20}I_2O_2P$ ($M^+$+H): *m/z* 600.9297. Found: 600.9290.

**Compound 17**




Yield: 0.137 g (80%, $R_f$ = 0.46 (8:2 hexane/ethyl acetate)).

Mp: 142-146 $^o$C (white solid).

IR (KBr): 3056, 3026, 1693, 1590, 1486, 1437, 1184, 1117, 1092, 1014, 750, 727 cm$^{-1}$.

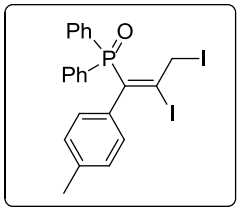
$^1$H NMR (500 MHz, $CDCl_3$): δ 7.59-7.57 (m, 4H), 7.55-7.52 (m, 2H), 7.43-7.40 (m, 4H), 7.07-7.06 (m, 2H), 6.61-6.59 (m, 2H), 5.63 (d, *J* = 1.5 Hz, 2H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ 142.6, 142.1 (d, *J* = 10.0 Hz), 134.1, 132.3 (d, *J* = 2.6 Hz), 132.1, 132.0, 131.8 (d, *J* = 9.7 Hz), 130.8 (d, *J* = 104.9 Hz), 130.5 (d, *J* = 3.0 Hz), 128.5, 128.4, 128.3, 127.9 (d, *J* = 9.8 Hz), 15.9 (d, *J* = 5.6 Hz).

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 25.6.

HRMS (ESI): Calcd. for $C_{21}H_{16}ClI_2OPNa$ ($M^+$+Na): *m/z* 626.8615, 628.8585. Found: 626.8617, 628.8577.

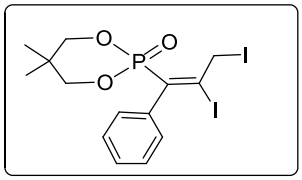
**Compound 18**




Yield 0.169 g (96%, white solid, $R_f$ = 0.44 (8:2 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[6a]

**Compound 19**



Yield: 0.182 g (92%, white solid, $R_f$ = 0.42 (8:2 hexane/ethyl acetate)).

Mp: 132-136 $^{o}$C.

IR (KBr): 3031, 2964, 2926, 2892, 2854, 1598, 1574, 1470, 1268, 1057, 1004, 911, 829, 787, 700 $cm^{-1}$.

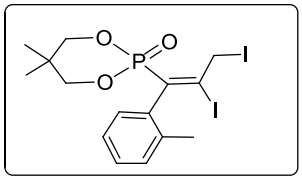
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.43-7.37 (m, 3H), 7.18 (d, *J* = 6.4 Hz, 2H), 5.36 (d, *J* = 2.4 Hz, 2H), 3.97 (t, *J* = 12.0 Hz, 2H), 3.56 (t, *J* = 10.2 Hz, 2H), 1.07 and 0.62 (2s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 142.4 (d, *J* = 7.4 Hz), 138.4 (*J* = 163.0 Hz), 128.6 (d, *J* = 4.2 Hz), 128.4, 128.1 (d, *J* = 18.0 Hz), 76.7, 32.4 (d, *J* = 7.0 Hz), 21.7, 20.8, 15.9 (d, *J* = 6.0 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 0.44

HRMS (ESI): Calcd. for $C_{14}H_{17}I_2O_3P$ ($M^+$+H): *m/z* 518.9083. Found: 518.9086.

**Compound 20**



Yield: 0.172 g (90%, white solid, $R_f$ = 0.44 (8:2 hexane/ethyl acetate)).

Mp: 138-144 $^{o}$C.

IR (KBr): 2962, 2915, 2853, 1712, 1598, 1541, 1474, 1366, 1283, 1232, 1170, 1087, 942 $cm^{-1}$.

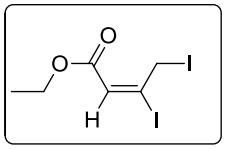
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.32-7.05 (m, 4H), 5.60-5.57 (m, 1H), 5.33-5.30 (m, 1H), 4.10-3.94 (m, 2H), 3.71-3.36 (m, 2H), 2.30 (s, 3H), 1.05 and 0.60 (2s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.6 (d, *J* = 5.2 Hz), 138.0 (d, *J* = 164.3 Hz), 136.8 (d, *J* = 3.0 Hz), 130.7, 129.3 (d, *J* = 16.4 Hz), 128.8 (d, *J* = 2.3 Hz), 125.7, 76.5 (2d, *J* = 6.0 Hz), 32.4 (d, *J* = 5.8 Hz), 21.7, 20.8, 19.3, 15.4 (d, *J* = 4.5 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 0.82

HRMS (ESI): Calcd. for $C_{15}H_{20}I_2O_3P$ ($M^+$+H): *m/z* 532.9239. Found: 532.9239.

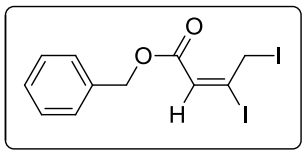
**Compound 21**



Yield 0.195 g (60%, $R_f$ = 0.86 (9:1 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[9]

**Compound 22**



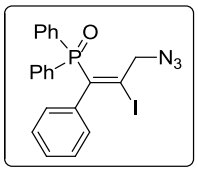
Yield 0.135 g (55%, $R_f$ = 0.85 (9:1 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[9]

## 6.2 Synthesis of *γ*-azido-*β*-iodo-vinylphosphine oxides 23-27, *γ*-azido-*β*-iodovinylphosphonate 28 and *γ*-azido-*β*-iodovinylester 29

To a solution of 2,3-diiodovinylphosphine oxide **14** (100 mg, 0.18 mmol) in DMF (1 mL) was added $NaN_3$ (0.057 g, 0.87 mmol) and the mixture was stirred at 25 $^oC$ for 1 h. After the completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 2:1) afforded compound **23**. Compounds **24-29** were prepared following same procedure using the same molar quantities.

**Compound 23**



Yield: 0.072 g (85%, white solid, $R_f$ = 0.38 (8:2 hexane/ethyl acetate)).

Mp: 180-186 $^{o}$C.

IR (KBr): 3008, 2926, 2853, 2094, 1583, 1479, 1433, 1340, 1268, 1164, 1113, 1066, 994, 875, 762, 694 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.58-7.49 (m, 6H), 7.40-7.36 (m, 4H), 7.18-7.14 (m, 1H), 7.12-7.09 (m, 2H), 6.70-6.68 (m, 2H), 5.21 (d, *J* = 2.0 Hz, 2H).

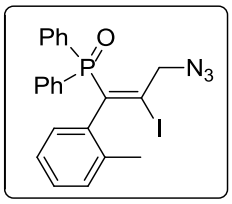
$^{13}$C NMR (125 MHz, $CDCl_3$): δ 145.7 (d, *J* = 75.0 Hz), 142.2 (d, *J* = 8.8 Hz), 131.2 (d, *J* = 2.6 Hz), 131.0, 130.9, 130.1 (d, *J* = 104.9 Hz), 127.9 (d, *J* = 3.4 Hz), 127.4, 127.3, 127.2, 126.8 (d, *J* ~ 2.0 Hz), 122.8 (d, *J* = 10.4 Hz), 58.2 (d, *J* = 5.8 Hz).

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.1.

HRMS (ESI): Calcd. for $C_{21}H_{18}IN_3OP$ ($M^+$+H): *m/z* 486.0232. Found: 486.0231.

This compound was crystallized from ethyl acetate/hexane (1:2) mixture at rt. X-ray structure was determined for this sample.

**Compound 24**



Yield: 0.077 g (90%, white solid, $R_f$ = 0.39 (8:2 hexane/ethyl acetate)).

Mp: 110-112 $^{o}$C.

IR (KBr): 3075, 3055, 3029, 2099, 1572, 1490, 1438, 1335, 1268, 1226, 1180, 1113, 1056, 994, 880, 756, 694 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.79-7.75 (m, 2H), 7.63-7.60 (m, 1H), 7.55-7.52 (m, 2H), 7.42-7.39 (m, 1H), 7.30-7.26 (m, 2H), 7.22-7.18 (m, 2H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.04

(t, *J* = 7.5 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.72 (d, *J* = 7.5 Hz, 1H), 5.45-5.42 (m, 1H), 5.07-5.04 (m, 1H), 1.79 (s, 3H).

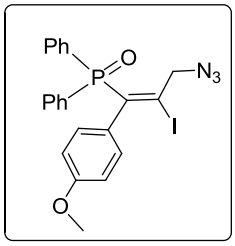
$^{13}$C NMR (125 MHz, $CDCl_3$): δ 145.6 (d, *J* = 76.1 Hz), 142.1 (d, *J* = 9.6 Hz), 136.4 (d, *J* = 3.1 Hz), 132.7, 132.6, 132.5 (d, *J* = 101.9 Hz), 132.4 (d, *J* = 2.4 Hz), 131.9 (d, *J* = 2.8 Hz), 131.6, 131.5, 130.5, 129.6, 129.0, 128.9, 128.7, 128.5, 128.2 (d, *J* = 2.8 Hz), 127.6, 127.5, 125.8, 124.2 (d, *J* = 10.7 Hz), 59.2 (d, *J* = 5.1 Hz), 19.3.

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 25.4.

HRMS (ESI) Calcd. for $C_{22}H_{20}IN_3OP$ ($M^+$+H): *m/z* 500.0388. Found: 500.0389.

This compound was crystallized from ethyl acetate/hexane (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 25**




Yield: 0.082 g (95%, white solid, $R_f$ = 0.35 (8:2 hexane/ethyl acetate)).

Mp: 128-130 $^oC$.

IR (KBr): 3058, 2970, 2904, 2844, 2099, 1611, 1512, 1441, 1244, 1178, 1118, 1025, 827, 740, 690 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ 7.56-7.47 (m, 6H), 7.39-7.35 (m, 4H), 6.62-6.54 (m, 4H), 5.21 (d, *J*= 2.0 Hz 2H), 3.70 (s, 3H).

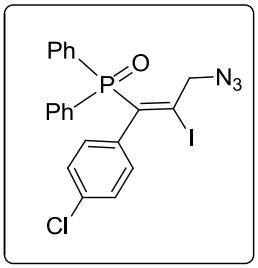
$^{13}$C NMR (125 MHz, $CDCl_3$): δ 159.2, 146.3 (d, *J* = 76.3 Hz), 135.4 (d, *J* = 10.0 Hz), 132.2 (d, *J* = 2.1 Hz), 132.1, 132.0, 131.2 (d, *J* = 104.5 Hz), 130.4 (d, *J* = 3.0 Hz), 128.4, 128.3, 124.6 (d, *J* = 12.7 Hz), 113.6, 59.1 (d, *J* = 5.4 Hz), 55.2.

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.0.

HRMS (ESI): Calcd. for $C_{22}H_{20}IN_3O_2P$ [$M^+$+H] *m/z* 516.0338. Found: 516.0339.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 26**




Yield: 0.073 g (85%, white solid, $R_f$ = 0.40 (8:2 hexane/ethyl acetate)).

Mp: 138-144 $^{o}$C.

IR (KBr): 3055, 2921, 2094, 1572, 1479, 1433, 1185, 1113, 1097, 906, 741 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.57-7.51 (m, 6H), 7.42-7.38 (m, 4H), 7.08-7.06 (m, 2H), 6.61-6.59 (m, 2H), 5.17 (d, *J* = 2.0 Hz, 2H).

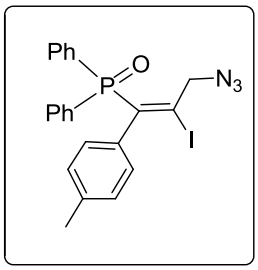
$^{13}$C NMR (125 MHz, $CDCl_3$): δ 145.7 (d, *J* = 76.0 Hz), 145.4 (d, *J* = 10.0 Hz), 134.1, 132.5, 132.0, 131.9, 130.8 (d, *J* = 104.5 Hz), 130.4 (d, *J* = 3.1 Hz), 128.6, 128.5, 124.6 (d, *J* = 10.5 Hz), 59.1 (d, *J* = 5.5 Hz).

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 25.9.

HRMS (ESI): Calcd. for $C_{21}H_{17}ClIN_3OP$ [$M^{+}$+H] *m/z* 519.9842, 521.9812. Found: 519.9841, 521.9805.

This compound was crystallized from ethyl acetate/hexane (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 27**




Yield: 0.133 g (88%, white solid, $R_f$ = 0.39 (8:2 hexane/ethyl acetate)).

Mp: 106-112 $^{o}$C.

IR (KBr): 3112, 3062, 2927, 2101, 1651, 1447, 1357, 1315, 1170, 1090, 756, 719 $cm^{-1}$.

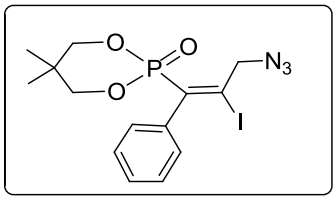
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.62-7.48 (m, 6H), 7.40-7.36 (m, 4H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.57-6.55 (m, 2H), 5.19 (d, *J* ~ 2.0 Hz, 2H), 2.25 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 146.5 (d, *J* = 76.4 Hz), 140.0 (d, *J* = 9.7 Hz), 137.9 (d, *J* = 2.0 Hz), 132.2 (d, *J* = 2.7 Hz), 132.1, 131.9, 131.5, 130.0 (d, *J* = 105.0 Hz), 129.6, 129.0, 128.9 (d, *J* ~ 4.0 Hz), 128.4 (d, *J* = 12.4 Hz), 127.5, 124.1 (d, *J* = 12.0 Hz), 59.2 (d, *J* = 5.5 Hz), 21.2.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 26.4.

HRMS (ESI): Calcd. for $C_{22}H_{20}IN_3OP$ [$M^+$+H] *m/z* 500.0388. Found: 500.0387.

**Compound 28**




Yield: 0.067 g (80%, white solid, $R_f$ = 0.36 (8:2 hexane/ethyl acetate)).

Mp: 102-104 $^{o}$C.

IR (KBr): 3050, 2967, 2879, 2099, 1583, 1474, 1273, 1056, 834 $cm^{-1}$.

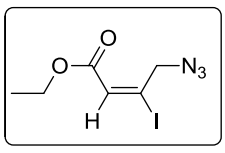
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.43- 7.27 (m, 5H), 4.83 (br, 2H), 4.09 (t, *J* ~ 12.4 Hz, 2H), 3.57 (t, *J* = 12.4 Hz, 2H), 0.97 and 0.60 (2s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 142.3 (d, *J* = 163.0 Hz), 142.0 (d, *J* = 7.4 Hz), 130.1 (d, *J* = 4.6 Hz), 128.8 (d, *J* = 4.0 Hz), 128.6, 128.3, 124.8 (d, *J* = 20.3 Hz), 76.7 (d, *J* = 7.0 Hz), 59.7 (d, *J* = 5.3 Hz), 32.3 (d, *J* = 7.3 Hz), 21.6, 20.8.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 9.6.

HRMS (ESI): Calcd. for $C_{14}H_{18}IN_3O_3P$ [$M^+$+H] *m/z* 434.0130. Found: 434.0130.

**Compound 29**




Yield: 0.064 g (82%, $R_f$ = 0.77 (9:1 hexane/ethyl acetate)).

IR (KBr): 2983, 2084, 1733, 1350, 1268, 1164, 1015, 813 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ 5.77 (s, 1H), 4.25-4.20 (m, 2H), 3.12 (s, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.9, 120.5, 115.9, 61.7, 36.8, 14.1.

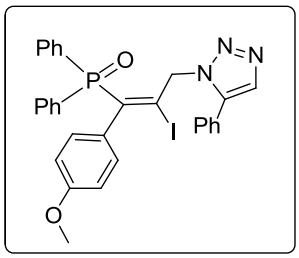
LC-MS: *m/z* 282 $[M+1]^+$.

Anal.Calcd. for $C_6H_8IN_3O_2$: C, 25.64; H, 2.87; N, 14.95; Found: C, 25.71; H, 2.83; N, 14.87.

### 6.3 Click reaction of *γ*-azido-*β*-iodovinylphosphine oxides with phenyl acetylene

To a solution of *γ*-azido,*β*-iodovinylphosphine oxide **25** (100 mg, 0.22 mmol) and phenyl acetylene (0.020 g, 0.22 mmol) in glycerol (1 mL) was added CuI (0.004 g, 0.02 mmol) and the mixture heated with stirring at 100 $^o$C (oil bath) for 12 h. After the completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portions were dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 2:1) afforded compound **30**. Compound **31** was prepared following same procedure using the same molar quantities.

**Compound 30**




Yield: 0.106 g (87%, white solid, $R_f$ = 0.35 (8:2 hexane/ ethyl acetate)).

Mp: 208-210$^o$C.

IR (KBr): 3127, 3055, 2926, 2833, 1603, 1510, 1433, 1288, 1252, 1180, 1113, 1040, 896, 700 $cm^{-1}$.

$^1$H NMR (500 MHz, $CDCl_3$): δ 8.15 (s, 1H), 7.90-7.89 (m, 2H), 7.65-7.61 (m, 4H), 7.55-7.52 (m, 2H), 7.46-7.41 (m, 6H), 7.36-7.33 (m, 1H), 6.63-6.58 (m, 4H), 6.38 (d, *J* = 2.0 Hz, 2H), 3.72 (s, 3H).

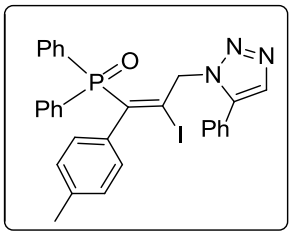
$^{13}$C NMR (125 MHz, $CDCl_3$): δ 159.3, 147.9, 147.1 (d, *J* = 76.1 Hz), 135.2 (d, *J* = 10.8 Hz), 132.4, 132.1, 132.0, 131.1 (d, *J* = 104.6 Hz), 130.7, 130.3 (d, *J* = 3.1 Hz), 128.8,

128.6, 128.5, 128.1, 125.8, 122.9 (d, *J* = 10.8 Hz), 120.8, 113.7, 58.2 (d, *J* = 5.6 Hz), 55.2.

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.5.

HRMS (ESI): Calcd. for $C_{30}H_{25}IN_3O_2PNa$ [$M^+$+Na] *m/z* 640.0627. Found: 640.0623.

**Compound 31**




Yield: 0.102 g (85%, white solid, $R_f$ = 0.37 (8:2 hexane/ ethyl acetate)).

Mp: 168-174 $^oC$.

IR (KBr): 3127, 3055, 2983, 2921, 1572, 1485, 1428, 1340, 1263, 1232, 1180, 1123, 896, 700 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.91-7.89 (m, 2H), 7.66-7.61 (m, 4H), 7.57-7.52 (m, 3H), 7.48-7.41 (m, 6H), 7.38-7.34 (m, 1H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.59-6.57 (m, 2H), 6.37 (d, *J* = 2.0 Hz, 2H), 2.25 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 147.9, 147.2, 139.9 (d, *J* = 9.0 Hz), 138.1, 132.4 (d, *J* = 3.0 Hz), 132.1, 132.0, 130.9 (d, *J* = 104.0 Hz), 130.7, 129.8, 129.0, 128.8 (d, *J* = 4.0 Hz), 128.6, 128.5, 128.1, 127.7, 125.8, 122.3 (d, *J* = 10.0 Hz), 120.8, 58.3 (d, *J* = 6.0 Hz), 21.2.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 26.6.

HRMS (ESI): Calcd. for $C_{30}H_{26}IN_3OP$ [$M^+$+H] *m/z* 602.0858. Found: 602.0854.

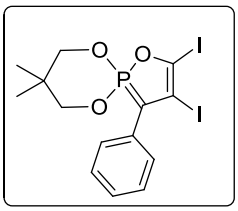
This compound was crystallized from ethyl acetate/hexane (2:1) mixture at rt (25 $^oC$). X-ray structure was determined for this sample.

### 6.4 Reaction of 2,3 diiodovinylphosphonate 19 with CsF

To a solution of 2,3-diiodovinylphosphonate **19** (100 mg, 0.20 mmol) in DMF (1 mL) was added CsF (0.03 g, 0.02 mmol) and the mixture was stirred at 25 $^oC$ for 1 h. After the completion of the reaction as monitored by TLC, ethyl acetate (25 mL) was added and the

solution was washed with water (3 x 30 mL); the aqueous layer was extracted with ethyl acetate (3x 20 mL). The combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 2:1) afforded compound **32**.

**Compound 32**



Yield: 0.044 g (45%, $R_f$ = 0.40 (8:2 hexane/ ethyl acetate)).

IR (KBr): 2957, 2879, 1717, 1257, 1056, 1004, 932, 793, 700 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.64-7.61 (m, 2H), 7.46-7.35 (m, 3H), 4.23 (d, *J* = 11.2 Hz, 2H), 4.05-4.00 (m, 2H), 1.37 and 0.98 (2s, 6H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 129.5, 129.1, 129.0, 128.9, 127.4 (d, *J* = 5.5 Hz), 77.7 (d, *J* = 5.5 Hz), 32.8 (d, *J* = 6.0 Hz), 21.9, 20.6. We could not identify the C-I peaks clearly (low intensity) as there was also coupling to phosphorus.

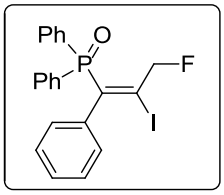
$^{31}$P NMR (162 MHz, $CDCl_3$): δ -0.8.

HRMS (ESI): Calcd. for $C_{14}H_{16}I_2O_3P$ [$M^+$+Na] *m/z* 516.8926. Found: 516.8926.

## 6.5 Synthesis of *γ*-fluoro-*β*-iodovinylphosphine oxides 33-36, *γ*-fluoro-*β*-iodovinylphosphonates 37-38 and *γ*-fluoro-*β*-iodovinylesters 39-40

To an oven dried RBF (10 mL), 2,3-diiodovinylphosphine oxide (**14**; 0.100 g, 0.18 mmol) in dry acetonitrile (1 mL), CuBr (0.03 g, 0.18 mmol) and $AgF_2$ (0.127 g, 0.88 mmol) were added. The mixture was stirred at 25 $^oC$ for 1-2 h. After completion of the reaction as monitored by TLC, the mixture was filtered and the filtrate concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain the pure *γ*-fluoro-*β*-iodovinylphosphine oxides **33** by using hexane-ethyl acetate (8:2) as the eluent. Compounds **34-40** were prepared following the same procedure and by using the same molar quantities.

**Compound 33**



Yield: 0.072 g (88%, white solid, $R_f$ = 0.52 (9:1 hexane/ ethyl acetate)).

Mp: 184-186 $^{o}$C.

IR (KBr): 3050, 1572, 1485, 1438, 1356, 1242, 1175, 1097, 1020, 989, 917, 891, 756 cm$^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.56-7.49 (m, 6H), 7.39-7.36 (m, 4H), 7.17-7.09 (m, 3H), 6.69 (d, *J* = 7.5 Hz, 2H), 5.89 (br d, $^{2}J$ = 47.0 Hz 2H).

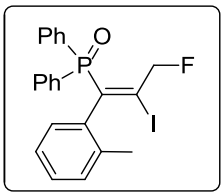
$^{13}$C NMR (125 MHz, $CDCl_3$): δ.147.0 (d, *J* = 4.9 Hz), 146.4 (d, *J* = 5.3 Hz), 142.8 (d, *J* = 10.0 Hz), 132.2 (d, *J* = 2.6 Hz), 132.0, 131.9, 131.1 (d, *J* = 104.5 Hz), 128.7 (d, *J* = 2.5 Hz), 128.4, 128.3, 127.8, 123.8 (d, *J* = 10.4 Hz), 123.7 (d, *J* = 10.1 Hz), 84.6 (dd, *J* = 169.1, 5.8 Hz).

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.5.

$^{19}$F NMR (470 MHz, $CDCl_3$):-196.3 to -196.6 (td) [$^{1}$H Coupled].

HRMS (ESI): Calcd. for $C_{21}H_{18}FIOP$ [$M^{+}$+H] *m/z* 463.0124. Found: 463.0127.

**Compound 34**



Yield: 0.073 g (89%, white solid, $R_f$ = 0.54 (9:1 hexane/ ethyl acetate)).

Mp: 162-168 $^{o}$C.

IR (KBr): 3060, 3019, 2921, 2853, 1578, 1479, 1433, 1356, 1309, 1247, 1169, 1118, 1092, 1015, 989, 901, 756 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.78-7.73 (m, 2H), 7.63-7.40 (m, 4H), 7.31-7.21 (m, 3H), 7.14-7.04 (m, 2H), 6.90 (d, *J* = 6.4 Hz, 1H,), 6.72 (d, *J* = 6.4 Hz, 1H), 6.35-6.20 (dd, *J* = 11.8, 47.6 Hz, 1H), 5.76-5.61 (dd, *J* = 11.8, 46.8 Hz, 1H), 1.79 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ.146.4 (d, *J* = 6.0 Hz), 145.6 (d, *J* = 5.2 Hz), 141.9 (d, *J* = 9.3 Hz), 136.2, 132.7, 132.6, 132.5 (d, *J* = 2.8 Hz), 132.0 (d, *J* = 2.8 Hz), 131.7, 131.5 (d, *J* = 10.7 Hz), 129.1 (d, *J* = 106.5 Hz), 129.0 (d, *J* = 12.4 Hz), 128.5 (d, *J* = 2.0 Hz), 128.1, 127.5 (d, *J* = 12.4 Hz ), 125.8, 124.0 (d, *J* = 10.2 Hz), 123.8 ( d, *J* = 10.2 Hz), 84.7 (dd, *J* = 168.3, 5.6 Hz), 19.2.

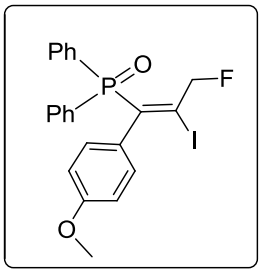
$^{31}$P NMR (162 MHz, $CDCl_3$): δ 26.04.

$^{19}$F NMR (470 MHz, $CDCl_3$): -196.5 (d, *J* = 2.8 Hz).

HRMS (ESI) Calcd. for $C_{22}H_{20}FIOP$ ($M^+$+H): *m/z* 477.0280. Found: 477.0280.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 35**




Yield: 0.072 g (90%, white solid, $R_f$ = 0.50 (9:1 hexane/ ethyl acetate)).

Mp: 158-160 $^{o}$C.

IR (KBr): 3044, 2957, 2926, 2838, 1603, 1583, 1500, 1433, 1278, 1252, 1180, 1118, 1092, 1025, 901, 829 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.55-7.53 (m, 3H), 7.52-7.48 (m, 3H), 7.40-7.36 (m, 4H), 6.63 (d, *J* = 7.2 Hz, 2H), 6.59-6.57 (m, 2H), 5.89 (dd, *J* = 47.0, 2.0 Hz, 2H), 3.73.

$^{13}$C NMR(125 MHz, $CDCl_3$): δ 159.2, 146.6 (d, *J* = 5.4 Hz), 146.0 (d, *J* = 6.0 Hz), 135.2 (d, *J* = 9.8 Hz), 132.2 (d, *J* = 2.6 Hz), 132.1, 131.9, 131.2 (d, *J* = 104.5 Hz), 130.1, 128.4, 128.3, 124.7 (d, *J* = 12.2 Hz), 124.6 (d, *J* = 12.1 Hz), 113.7, 84.6 (dd, *J* = 168.8, 5.6 Hz), 55.2.

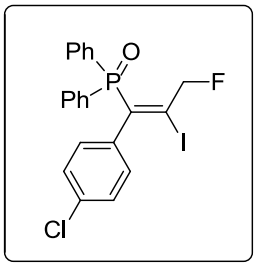
$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.57.

$^{19}$F NMR (470 MHz, $CDCl_3$): -196.1 to -196.4 (td) [$^{1}$H Coupled].

HRMS (ESI): Calcd. for $C_{22}H_{20}FIO_2P$ [$M^+$+H] *m/z* 493.0229. Found: 493.0229.

This compound was crystallized from ethyl acetate at rt. X-ray structure was determined for this sample.

**Compound 36**




Yield: 0.065 g (80%, white solid, $R_f$ = 0.56 (9:1 hexane/ ethyl acetate)).

Mp: 168-170 $^{o}$C.

IR (KBr): 3052, 2926, 1573, 1485, 1430, 1249, 1184, 1085, 1019, 893, 816 $cm^{-1}$.

$^{1}$H NMR (500 MHz, $CDCl_3$): δ 7.56-7.52 (m, 6H), 7.42-7.39 (m, 4H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.63-6.61 (m, 2H), 5.85 (dd, *J* = 47.0, *J* = 2.0 Hz, 2H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ.145.9 (d, *J* =. 5.1 Hz), 145.4 (d, *J* = 5.2 Hz), 141.2 (d, *J* = 9.6 Hz), 134.0 (d, *J* = 2.4 Hz), 132.4 (d, *J* = 2.6 Hz), 132.0 (d, *J* = 10.0 Hz), 130.7 (d, *J* = 104.9 Hz), 130.1, 128.6$_4$, 128.5$_9$, 128.5, 124.7 (d, *J* = 10.0 Hz), 124.5 (d, *J* = 10.0 Hz), 85.1 (dd, *J* = 169.4 Hz, 5.6 Hz).

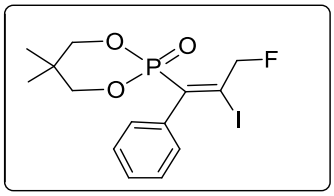
$^{31}$P NMR (202 MHz, $CDCl_3$): δ 26.3.

$^{19}$F NMR (470 MHz, $CDCl_3$): -195.1.

HRMS (ESI) Calcd. for $C_{21}H_{17}ClFIOP$ ($M^+$+H): *m/z* 496.9734, 498.9704. Found: 496.9737, 498.9694.

This compound was crystallized from DCM/ethyl acetate (1:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 37**




Yield: 0.067 g (85%, white solid, $R_f$ = 0.52 (9:1 hexane/ ethyl acetate)).

Mp: 132-134 $^{o}$C.

IR (KBr): 2964, 1595, 1375, 1266, 1238, 1058, 997, 827 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ. 7.44-7.40 (m, 3H), 7.22- 7.19 (m, 2H), 5.72 (dd, *J* = 47.2 Hz, *J* = 3.0 Hz, 2H), 3.98 (t, *J* = 11.6 Hz, 2H), 3.59 (t, *J* = 11.6 Hz, 2H), 1.05 and 0.62 (2s, 6H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 141.8, 141.1 (d, *J* = 172.5 Hz), 128.7 (d, *J* = 13.7 Hz), 126.0 (d, *J* = 24.6 Hz), 84.8 (d, *J* = 175.0 Hz), 76.6, 32.3 (d, *J* = 7.0 Hz), 21.7, 20.8.

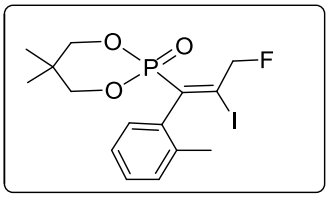
$^{31}P$ NMR (162 MHz, $CDCl_3$): δ -0.11 (d, *J* = 7.0 Hz).

$^{19}F$ NMR (470 MHz, $CDCl_3$): δ -197.0 (d, *J* = 5.0 Hz).

HRMS (ESI): Calcd. for $C_{14}H_{18}FIO_3P$ $[M^+ + H]$ *m/z* 411.0024. Found: 411.0024.

This compound was crystallized from ethyl acetate/hexane (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 38**




Yield: 0.070 g (88%, white solid, $R_f$ = 0.53 (9:1 hexane/ ethyl acetate)).

Mp: 98-100 $^{o}C$.

IR (KBr): 2921, 2874, 1696, 1593, 1459, 1361, 1237, 1164, 1108, 1077, 808, 741 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.35-7.25 (m, 3H), 7.08 (d, *J* = 8.0 Hz, 1H), 5.83 (qd, *J* = 24.0 Hz, *J* = 12.0 Hz, 1H), 5.71 (qd, *J* = 24.0 Hz, *J* = 12.0 Hz, 1H), 4.08 (t, *J* ~ 10.0 Hz, 1H), 3.96 (t, *J* = 10.0 Hz, 1H), 3.70 (t, *J* = 10.0 Hz, 1H), 3.34 (t, *J* = 10.0 Hz, 1H), 2.29 (s, 3H), 1.04 and 0.61 (2s, 6H).

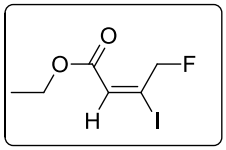
$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 141.0 (d, *J* = 6.0 Hz), 140.7 (d, *J* = 165.0 Hz), 136.3, 130.7, 128.9 (d, *J* = 7.0 Hz), 127.5 (t, *J* = 20.0 Hz), 126.0, 84.4 (dd, *J* = 169.0 Hz, *J* = 5.0 Hz), 76.5 (d, *J* = 7.0 Hz), 32.4 (d, *J* = 8.0 Hz), 21.6, 20.8, 19.5.

$^{31}P$ NMR (162 MHz, $CDCl_3$): δ 0.32 (d, *J* = 7.0 Hz).

$^{19}F$ NMR (470 MHz, $CDCl_3$):-196.6 (d, *J* = 6.1 Hz).

HRMS (ESI): Calcd. for $C_{15}H_{20}FIO_3P$ $[M^+ + H]$ *m/z* 425.0179. Found: 425.0177.

**Compound 39**



Yield: 0.052 g (75%, $R_f$ = 0.89 (9:1 hexane/ethyl acetate)).

IR (KBr): 2983, 2939, 2906, 1713, 1613, 1370, 1325, 1195, 1059, 1024, 871 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ.6.83 (t, *J* ~ 4.0 Hz, 1H), 5.52-5.37 (m, 2H), 4.22-4.17 (qrt, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H).

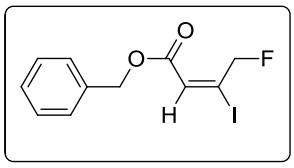
$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 163.7, 132.7 (d, *J* = 4.0 Hz), 120.8 (d, *J* = 22.0 Hz), 81.9 (d, *J* = 169.0 Hz), 61.1, 14.1.

$^{19}F$ NMR (470 MHz, $CDCl_3$):-197.8.

LC-MS: *m/z* 259 $[M+1]^+$.

Anal. Calcd. for $C_6H_8IFO_2$: C, 27.93; H, 3.13; Found: C, 27.85; H, 3.18.

**Compound 40**



Yield: 0.059 g (80%, $R_f$ = 0.90 (9:1 hexane/ethyl acetate)).

IR (KBr): 3066, 3034, 2951, 1713, 1612, 1454, 1378, 1324, 1179, 1060, 1003, 745 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ 7.43-7.37 (m, 5 H), 6.88 (t, *J* = 2.0 Hz, 1H), 5.51 (d, *J* = 2.0 Hz, 1H), 5.39 (d, *J* = 2.0 Hz, 1H), 5.18 (s, 2H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 163.4 (d, *J* = 2.1 Hz), 135.2, 132.2 (d, *J* ~ 4.0 Hz), 128.7, 128.6, 128.4, 121.8 (d, *J* = 22.4 Hz), 81.9 (d, *J* = 170.0 Hz), 66.9.

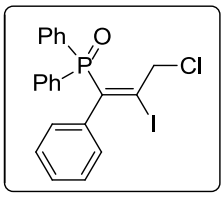
$^{19}F$ NMR (470 MHz, $CDCl_3$):δ -197.0

HRMS (ESI) Calcd. for $C_{11}H_{14}FIO_2N$ ($M^+$+$NH_4$): *m/z* 338.0054. Found: 338.0048.

## 6.6 Synthesis of *γ*-chloro-*β*-iodovinylphosphine oxides 41-42, *γ*-hydroxy-*β*-iodovinylphosphine oxides 43-44 and aldehydes 45-46

To an oven dried 10 mL RBF, allenylphosphine oxide (**5a**; 0.100 g, 0.31 mmol) and 1M ICl in acetonitrile (1 mL) solution were added at 0 $^{o}$C. The mixture was stirred at 0 $^{o}$C – 25 $^{o}$C for 10 min. After completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure and the solid upon recrystallization from DCM/hexane (1:2) afforded compound **41**. Compound **42** was prepared following the same procedure and by using the same molar quantities. When purification by silica gel column chromatography (hexane/ethyl acetate 9:1) was attempted, compound **41** and **42** converted to *γ*-hydroxy-*β*-iodovinylphosphine oxides **43** and **44**, respectively.

**Compound 41**




Yield: 0.140 g (93%, white solid, $R_f$ = 0.47 (9:1 hexane/ ethyl acetate)).

Mp: 130-134 $^{o}$C.

IR (KBr): 3057, 3026, 2992, 1586, 1506, 1437, 1340, 1313, 1233, 1114, 968, 746 cm$^{-1}$.

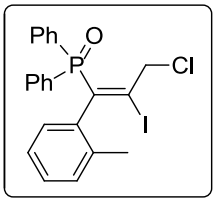
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.98-7.20 (m, 15H), 5.76 (br, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 137.8 (d, *J* = 2.4 Hz), 133.4 (d, *J* = 12.6 Hz), 131.2, 131.1, 131.0, 130.3, 129.8, 129.0, 128.6, $128.5_7$, 128.5, 128.4, 118.4, 118.1, 118.0 (d, *J* = 102.6 Hz), 86.9.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 79.5.

HRMS (ESI) Calcd. for $C_{21}H_{18}ClIOP$ ($M^+$+H), ($M^+$+H+2): *m/z* 478.9828, 480.9798. Found: 478.9829, 480.9796.

**Compound 42**




Yield: 0.143 g (96%, light yellow solid, $R_f$ = 0.49 (9:1 hexane/ ethyl acetate)).

Mp: 142-144 $^{o}$C.

IR (KBr): 3058, 2922, 2850, 1722, 1687, 1586, 1487, 1438, 1117, 969, 751, 695 $cm^{-1}$.

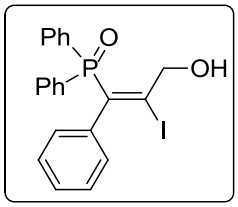
$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 7.98-7.71 (m, 11H), 7.40 (t, *J* ~ 7.4 Hz, 1H), 7.23 (t, *J* ~ 7.4 Hz, 1H), 6.88 (t, *J* ~ 7.4 Hz, 1H), 5.86 (d, *J* ~ 4.0 Hz, 2H), 1.87 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 137.5 (d, *J* = 66.1 Hz), 137.0 (d, *J* = 4.5 Hz), 132.9 (d, *J* = 171.3 Hz), 131.9, 131.6, 131.0, 130.9 (d, *J* = 2.0 Hz), 130.9, 129.0 (d, *J* = 3.2 Hz), 127.2, 127.1, 121.3 (d, *J* = 30.0 Hz), 118.5 (d, *J* = 103.5 Hz), 117.5, 116.5, 86.9, 19.6.

$^{31}P$ NMR (162 MHz, $CDCl_3$): δ 79.9.

HRMS (ESI) Calcd. for $C_{22}H_{20}ClIOP$ ($M^+$+H), ($M^+$+H+2): *m/z* 492.9985, 494.9955. Found: 492.9987, 494.9956.

**Compound 43**




Yield: 0.131 g (90%, white solid, $R_f$ = 0.35 (8:2 hexane/ ethyl acetate)).

Mp: 166-172 $^{o}C$.

IR (KBr): 3249, 3055, 2874, 1568, 1485, 1437, 1358, 1166, 1088, 1042, 999, 696 $cm^{-1}$.

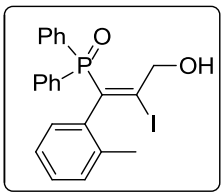
$^{1}H$ NMR (500 MHz, $CDCl_3$): δ 7.54-7.35 (m, 10H), 7.11-6.65 (m, 5H), 5.49 (br, 1H), 5.00 (s, 2H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ 143.6, 142.8, 132.3, 132.2, 132.1, 130.8 (d, *J* = 132.4 Hz), 129.0, 128.4, 128.3, 127.7, 72.5.

$^{31}P$ NMR (202 MHz, $CDCl_3$): δ 28.8.

HRMS (ESI) Calcd. for $C_{21}H_{19}IO_2P$ ($M^+$+H): *m/z* 461.0167. Found: 461.0169.

**Compound 44**



Yield: 0.136 g (95%, white solid, $R_f$ = 0.40 (8:2 hexane/ ethyl acetate)).

Mp: 140-144 $^oC$.

IR (KBr): 3241, 3054, 2918, 1586, 1483, 1435, 1377, 1314, 1240, 1161, 1116, 1096, 1053, 1035, 896 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ.7.84-7.79 (m, 2H), 7.61-7.50 (m, 2H), 7.38 (t, *J* ~ 8.0 Hz, 1H), 7.26 (t, *J* = 9.8 Hz, 2H), 7.19-7.01 (m, 4H), 6.86 (d, *J* ~ 7.0 Hz, 1H), 6.77 (d, *J* ~ 7.0 Hz, 1H), 5.82 (br, 1H), 5.22 (d, *J* = 14.4 Hz, 1H), 4.88 (d, *J* = 14.4 Hz, 1H), 1.77 (s, 3H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ.142.6 (d, *J* = 5.0 Hz), 142.5, 141.8, 136.6 (d, *J* = 4.0 Hz), 132.7 (d, *J* ~ 10.0 Hz), 132.6, 132.0 (d, *J* = 3.0 Hz), 131.8 (d, *J* = 10.8 Hz), 131.6, 131.0, 130.5, 130.2 (d, *J* = 134.5 Hz), 128.8 (d, *J* = 12.0 Hz), 128.4, 128.0 (d, *J* = 3.0 Hz), 127.4 (d, *J* = 12.0 Hz), 125.8, 72.6 (d, *J* = 5.4 Hz), 19.2.

$^{31}P$ NMR (162 MHz, $CDCl_3$): δ 27.9.

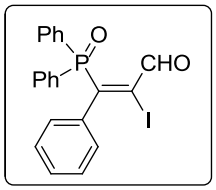
HRMS (ESI) Calcd. for $C_{22}H_{20}IO_2PNa$ ($M^+$+Na): *m/z* 497.0144. Found: 497.0145.

This compound was crystallized from DCM/ethyl acetate (2:1) mixture at room temperature. X-ray structure was determined for this sample.

## 6.7 Oxidation of *γ*-hydroxy-*β*-iodovinylphosphine oxides 43-44 with Dess–Martin periodinane (DMP)

To an oven dried 10 mL RBF, *γ*-hydroxy-*β*-iodovinylphosphine oxide **43** (0.100 g, 0.22 mmol), DMP (0.138 g, 0.32 mmol) in DCM (1 mL) solution was added at 0 $^oC$. The mixture was brought to to 25 $^oC$ and stirred for 3 h. After completion of the reaction as monitored by TLC, the reaction mixture was quenched with saturated sodium thiosulphate solution. The crude product was extracted with DCM (30 mL) and the organic portion was washed with saturated sodium bicarbonate solution (2 x 30 mL) followed by brine solution (1x 30 mL); the combined organic portion was dried over anh. $Na_2SO_4$ and the solvent removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate 2:1) afforded compound **45**. Compound **46** was prepared following same procedure using the same molar quantities.

**Compound 45**




Yield: 0.077 g (78%, white solid, $R_f$ = 0.56 (9:1 hexane/ ethyl acetate)).

Mp: 146-148 $^{o}$C.

IR (KBr): 3026, 2957, 2927, 2856, 1659, 1596, 1368, 1259, 1163, 1016, 800, 674 $cm^{-1}$.

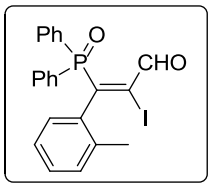
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 10.11 (d, *J* = 1.2 Hz, 1H), 7.57-7.53 (m, 6H), 7.43-7.38 (m, 4H), 7.22-7.14 (m, 3H), 6.68-6.66 (m, 2H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 187.2 (d, *J* = 6.4 Hz), 141.6 (d, *J* = 8.7 Hz), 132.7, 132.6, 132.2, 132.1, 130.2 (d, *J* = 105.5 Hz), 129.4 (d, *J* = 9.0 Hz), 128.7, 128.5, 128.4, 127.6 (d, *J* = 3.3 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 27.2.

HRMS (ESI) Calcd. for $C_{21}H_{16}IO_2P$ ($M^+$+H): *m/z* 459.0011. Found: 459.0013.

**Compound 46**




Yield: 0.081 g (82%, white solid, $R_f$ = 0.59 (9:1 hexane/ ethyl acetate)).

Mp: 162-164 $^{o}$C.

IR (KBr): 3059, 3021, 2957, 2924, 2854, 1691, 1437, 1189, 1115, 1081, 725, 710, 695 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 10.11 (d, *J* = 1.2 Hz, 1H), 7.65-7.70 (m, 2H), 7.66-7.61 (m, 1H), 7.56-7.46 (m, 3H), 7.36-7.30 (m, 2H), 7.27-7.24 (m, 2H), 7.20-7.16 (m, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.96 (d, *J* ~ 7.6 Hz, 1H), 6.63 (d, *J* = 7.6 Hz, 1H), 1.74 (s, 3H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 187.1 (d, *J* = 6.2 Hz), 158.7 (d, *J* = 69.8 Hz), 140.7 (d, *J* = 7.7 Hz), 135.4 (d, *J* = 3.5 Hz), 132.9, 132.8, 132.5 (d, *J* = 3.0 Hz), 132.3, 131.7, 131.6, 131.2, 130.7, 130.0 (d, *J* ~ 10.0 Hz), 129.2, 129.1, 128.9, 127.9 (d, *J* = 106.9 Hz), 127.9, 127.8, 126.6 (d, *J* = 3.0 Hz), 125.8, 19.2.

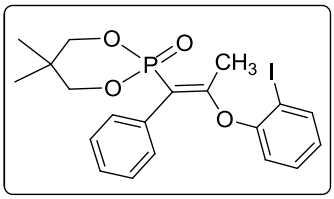
$^{31}$P NMR (162 MHz, $CDCl_3$): δ 26.5.

HRMS (ESI) Calcd. for $C_{22}H_{19}IO_2P$ ($M^+$+H): *m/z* 473.0167. Found: 473.0167.

### 6.8 Reaction of allenylphosphonates with 2-iodophenol

To a solution of allenylphosphonate **6a** (0.100 g, 0.38 mmol) and 2-iodophenol **13** (0.083 g, 0.38 mmol) in DMF (1 mL) was added $K_2CO_3$ (0.052 g, 0.38 mmol) and Pd-PVP (5 mg). The mixture was heated with stirring at 110 $^oC$ for 12 h. The contents were washed with water (2 x 20 mL) and extracted with ethyl acetate (2 x 20 mL). The solvent was removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate; 2:1) afforded compounds **47a** and **47b** which had slightly different $R_f$ values. Compounds **48-49** were prepared similarly using the same molar quantities.

**Compound 47a**




Yield: 0.109 g (60%, white solid, $R_f$ = 0.45 (2:1 hexane +ethyl acetate)).

Mp: 170-172 $^oC$.

IR (neat): 3055, 2961, 2879, 1624, 1572, 1463, 1438, 1376, 1231, 1061, 1009, 895 $cm^{-1}$.

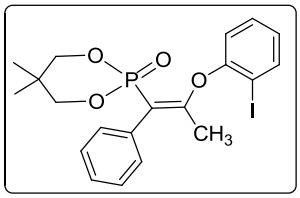
$^1$H NMR (400 MHz, $CDCl_3$): δ 7.73-7.72 (m, 1H, Ar*H*), 7.46-7.44 (m, 2H, Ar*H*), 7.32 (t, *J* = 6.0 Hz, 2H, Ar*H*), 7.28-7.25 (m, 2H, Ar*H*), 6.91-6.82 (m, 2H, Ar*H*), 4.07 (t, *J* = 8.6 Hz, 2H, -OC$H_2$), 3.65-3.61 (m, 2H, -OC$H_2$), 2.36 (d, *J* = 2.0 Hz, 3H, =CC$H_3$), 1.00 and 0.66 (2s, 6H, -C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 164.6 (d, *J* = 26.1 Hz), 153.8, 139.5, 134.0, 133.9, 130.6$_5$, 130.6$_1$, 129.5, 127.9, 127.2, 126.2, 120.7, 110.7 (d, *J* = 154.2 Hz), 89.8, 75.4 (d, *J* = 4.9 Hz), 32.2 (d, *J* = 5.0 Hz), 21.7, 21.0, 17.9 (d, *J* = 1.0 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 14.4.

HRMS (ESI): Calcd. for $C_{20}H_{23}IO_4P$ ($M^+$+H): *m/z* 485.0378. Found: 485.0379.

**Compound 47b**



Yield: 0.073 g (35%, white solid, $R_f$ = 0.40 (2:1 hexane +ethyl acetate)).

Mp: 162-164 $^{o}$C.

IR (neat): 3049, 2967, 2884, 1629, 1572, 1469, 1443, 1371, 1267, 1221, 1055, 1009, 942, 828 cm$^{-1}$.

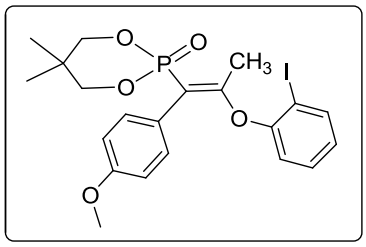
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.83-7.82 (m, 1H, Ar*H*), 7.44-7.34 (m, 6H, Ar*H*), 7.16-7.14 (m, 1H, Ar*H*), 6.92-6.88 (m, 1H, Ar*H*), 3.94-3.86 (m, 4H, -OC$H_2$), 1.81 (d, *J* = 4.0 Hz, 3H, =CC$H_3$), 1.18 and 0.88 (2s, 6H, C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.6, 154.3, 139.6, 134.9 (d, *J* = 5.1 Hz), 130.2, 130.1, 129.8, 128.6, 127.7$_2$, 127.7$_1$, 125.9, 119.5, 114.9 (d, *J* = 138.9 Hz), 88.8, 76.2 (d, *J* = 5.0 Hz) 32.3 (d, *J* = 5.0 Hz), 22.0, 21.1, 17.5 (d, *J* = 8.5 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 9.63.

HRMS (ESI): Calcd. for $C_{20}H_{23}IO_4P$ ($M^+$+H): *m/z* 485.0378. Found: 485.0383.

**Compound 48a**



Yield: 0.101g (58%, white solid, $R_f$ = 0.45 (2:1 hexane +ethyl acetate)).

Mp: 148-150$^{o}$C.

IR (neat): 2955, 2920, 2853, 1613, 1582, 1489, 1443, 1293, 1262, 1123, 1081, 1019, 926, 818 cm$^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 1H, Ar*H*), 7.36-7.34 (m, 2H, Ar*H*), 7.26-7.22 (m, 1H, Ar*H*), 6.88-6.80 (m, 4H, Ar*H*), 4.03 (t, *J* = 9.0 Hz, 2H, -OC$H_2$), 3.78 (s, 3H,

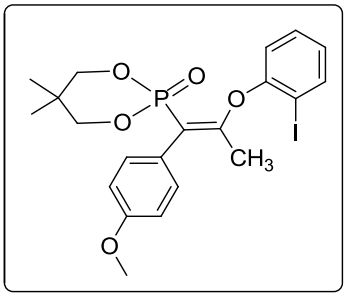
OC$H_3$), 3.63 (t, $J$ = 9.2 Hz, 2H, -OC$H_2$), 2.31 (d, $J$ = 2.0 Hz, 3H, =CC$H_3$), 1.00 and 0.68 (2s, 6H, -C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 164.4 (d, $J$ = 33.7 Hz), 158.6, 153.9, 139.5, 131.7 (d, $J$ = 4.8 Hz), 129.4, 126.1, 120.5, 113.4, 110.6 (d, $J$ = 191.4 Hz), 89.7, 75.4 (d, $J$ = 6.2 Hz), 55.1, 32.2 (d, $J$ = 6.0 Hz), 21.7, 21.1, 17.8 (d, $J$ = 1.7 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 14.8

HRMS (ESI): Calcd. for $C_{21}H_{25}IO_5P$ ($M^+$+H): *m/z* 515.0484. Found: 515.0480.

**Compound 48b**




Yield: 0.069 g (40%, white solid, $R_f$ = 0.40 (2:1 hexane +ethyl acetate)).

Mp: 136-138 $^o$C.

IR (neat): 2968, 2924, 2870, 1623, 1602, 1566, 1515, 1468, 1375, 1267, 1230, 1174, 1065, 941, 827, 765 cm$^{-1}$.

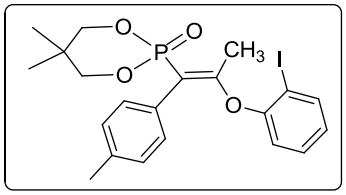
$^1$H NMR (400 MHz, $CDCl_3$): δ 7.82-7.80 (m, 1H, Ar$H$), 7.36-7.32 (m, 3H, Ar$H$), 7.13-7.11 (m, 1H, Ar$H$), 6.93-6.87 (m, 3H, Ar$H$), 3.91-3.88 (m, 4H, -OC$H_2$), 3.83 (s, 3H, -OC$H_3$), 1.80 (d, $J$ = 1.2 Hz, 3H, =CC$H_3$), 1.17 and 0.87 (2s, 6H, C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.5, 159.1, 154.4, 139.6, 131.3 (d, $J$ = 5.0 Hz), 129.7, 127.0, 126.9, 125.8, 119.4, 114.4 (d, $J$ = 139.0 Hz), 114.0, 88.7, 76.2 (d, $J$ = 5.0 Hz), 32.3 (d, $J$ = 5.0 Hz), 22.0, 21.1, 17.4 (d, $J$ = 8.6 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 10.3.

HRMS (ESI): Calcd. for $C_{21}H_{25}IO_5P$ ($M^+$+H): *m/z* 515.0484. Found: 515.0485.

**Compound 49a**



Yield: 0.111 g (62%, white solid, $R_f$ = 0.45 (2:1 hexane +ethyl acetate)).

Mp: 178-180 $^{o}$C.

IR (neat): 2961, 2879, 1618, 1577, 1505, 1463, 1433, 1252, 1226, 1055, 1004, 988, 895, 818 $cm^{-1}$.

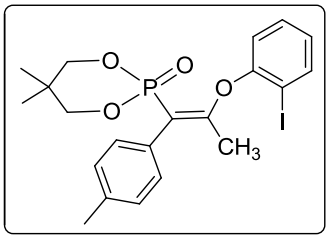
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.72-7.69 (m, 1H, Ar*H*), 7.34-7.32 (m, 2H, Ar*H*), 7.26-7.22 (m, 1H, Ar*H*), 7.12 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.89-6.80 (m, 2H, Ar*H*), 4.03 (t, *J* = 11.4 Hz, 2H, -OC$H_2$), 3.63 (t, *J* = 11.4 Hz, 2H, -OC$H_2$), 2.31 (d, *J* = 2.8 Hz, 3H, =CC$H_3$), 1.01 and 0.68 (2s, 6H, -C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 164.3 (d, *J* = 33.2 Hz), 153.9, 139.5, 136.8, 136.7, 130.9, 130.8, 130.4, 130.3, 129.4, 128.7, 128.6, 120.8, 110.7 (d, *J* = 190.5 Hz), 89.9, 75.5 (d, *J* = 6.2 Hz), 32.3 (d, *J* = 6.0 Hz), 21.7, 21.2, 21.1, 17.9 (d, *J* = 1.5 Hz).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 14.7.

HRMS (ESI): Calcd. for $C_{21}H_{23}IO_4PNa$ ($M^+$+Na): *m/z* 521.0355. Found: 521.0360.

**Compound 49b**



Yield: 068 g (38%, white solid, $R_f$ = 0.40 (2:1 hexane +ethyl acetate))

Mp: 164-166 $^{o}$C.

IR (neat): 2967, 2925, 2874, 1634, 1577, 1510, 1469, 1371, 1231, 1055, 833 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.6 Hz, 1H, Ar*H*), 7.34-7.30 (m, 3H, Ar*H*), 7.18 (d, *J* = 7.6 Hz, 2H, Ar*H*), 7.11 (d, *J* = 8.0 Hz, 1H, Ar*H*), 6.86 (t, *J* = 7.6 Hz, 1H, Ar*H*),

3.90-3.84 (m, 4H, -OC$H_2$), 2.35 (s, 3H, ArC$H_3$), 1.78 (s, 3H, =CC$H_3$), 1.16 and 0.85 (2s, 6H, C(C$H_3$)$_2$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.4, 154.4, 139.6, 137.4 (d, *J* = 2.0 Hz), 131.9 (d, *J* = 6.6 Hz), 130.0, 129.9, 129.7, 129.3, 125.8, 119.4, 114.9 (d, *J* = 173.7 Hz), 88.7, 76.2 (d, *J* = 6.2 Hz), 32.3 (d, *J* = 6.3 Hz), 22.0, 21.2, 21.1, 17.4 (d, *J* = 10.7 Hz).

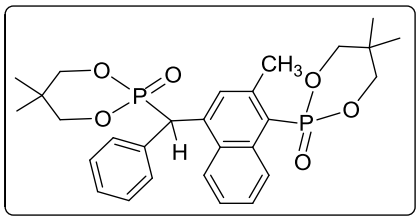
$^{31}$P NMR (162 MHz, $CDCl_3$): δ 10.0.

HRMS (ESI): Calcd. for $C_{21}H_{25}IO_4P$ ($M^+$+H): *m/z* 499.0535. Found: 499.0556.

## 6.9 Cycloaddition reactions of allenylphosphonates: Synthesis of compounds 50-53

To an oven dried 10 mL RBF, allenylphosphonate **6a** (0.100 g, 0.38 mmol), $Pd(OAc)_2$ (0.008 g, 0.038 mmol), $PPh_3$ (0.099 g, 0.38 mmol) and $Et_3N$ (0.038 g, 0.38 mmol) in dry THF (1 mL) were added. The vessel was stoppered under nitrogen atmosphere and heated overnight on an oil-bath maintained at 70 $^o$C. The mixture was filtered and concentrated in vacuum. The crude product was purified by using silica gel column chromatography to obtain compound **50** by using hexane-ethyl acetate (6:4) as the eluent. Compounds **51-53** were prepared following the same procedure and by using the same molar quantities.

**Compound 50**




Yield: 0.144 g (72%, white solid, $R_f$ = 0.30 (2:1 hexane +ethyl acetate)).

Mp: 158-160 $^o$C.

IR (KBr): 2969, 2933, 2885, 1473, 1263, 1060, 1007, 755 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* ~ 8.8 Hz, 1H), 8.09-8.07 (m, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.51-7.40 (m, 4H), 7.32-7.24 (m, 3H), 5.41 (d, *J* = 26.4 Hz, 1H), 4.27-4.18 (m, 2H), 4.07-3.97 (m, 2H), 3.80-3.73 (m, 2H), 3.70-3.61 (m, 2H), 2.87 (d, *J* = 2.0 Hz, 3H), 1.36, 1.00, 0.79 and 0.72 (4s, 12 H).

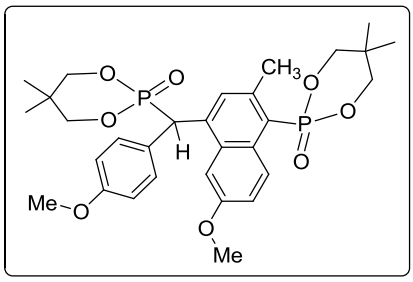
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 142.4 (d, *J* = 8.5 Hz), 136.5 (d, *J* = 4.0 Hz), 135.4 (d, *J* = 7.6 Hz), 134.6, 134.5, 132.2 ( d, *J* = 6.8 Hz), 132.0 (d, *J* = 6.8 Hz), 130.4 (t, *J* = 12.5 Hz), 129.6 (d, *J* = 6.4 Hz), 128.7 (d, *J* = 2.2 Hz), 127.6 (d, *J* = 3.0 Hz), 127.1,

126.9 (d, *J* = 5.0 Hz), 126.1, 123.5, 121.4 (d, *J* = 172.8 Hz), 76.2 (d, *J* = 6.0 Hz), 75.9 (d, *J* = 6.7 Hz), 46.5 (d, *J* = 137.4 Hz), 32.6 (d, *J* = 6.5 Hz), 32.2 (d, *J* = 6.0 Hz), 23.9 (d, *J* = 4.5 Hz), 22.1, 21.5, 21.1, 20.7.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 20.0, 14.5.

HRMS (ESI) Calcd. for $C_{28}H_{35}O_6P_2$ ($M^+$+H): *m/z* 529.1909. Found: 529.1913.

**Compound 51**




Yield: 0.136 g (68%, white solid, $R_f$ = 0.28 (2:1 hexane +ethyl acetate)).

Mp: 208-212 $^{o}$C.

IR (KBr): 3065, 2941, 2879, 1686, 1578, 1454, 1366, 1283, 1226, 1175, 1092, 1009, 973 751 $cm^{-1}$.

$^{1}$H NMR(500 MHz, $CDCl_3$): δ 8.61 (d, *J* ~ 10.0 Hz, 1H), 8.01-7.99 (m, 1H), 7.35-7.32 (m, 2H), 7.23-7.21 (m, 1H), 7.16-7.13 (m, 1H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.22 (d, *J* = 26.4 Hz, 1H), 4.30-4.21 (m, 2H), 4.07-3.95 (m, 2H), 3.81 (s, 3H), 3.77 (s, 3H), 3.74-3.62 (m, 4H), 2.83 (d, *J* = 2.4 Hz, 3H), 1.36, 1.01, 0.79 and 0.77 (4s, 12H).

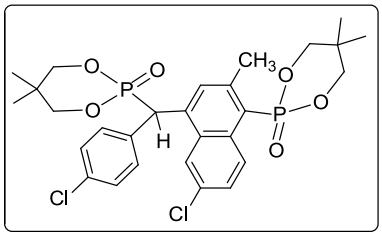
$^{13}$C NMR(125 MHz, $CDCl_3$): δ 159.0, 157.2, 139.5 (d, *J* = 9.5 Hz), 135.5 (d, *J* = 4.0 Hz), 132.4 (d, *J* = 10.0 Hz), 131.9 (d, *J* = 13.0 Hz), 131.8, 130.7 (d, *J* = 6.4 Hz), 129.8 (t, *J* = 10.1 Hz), 128.4 (d, *J* = 4.1 Hz), 127.3 (d, *J* ~ 8.0 Hz), 121.2 (d, *J* = 172.3 Hz), 118.6, 114.1, 103.3, 76.2 (d, *J* = 6.0 Hz), 75.8 (d, *J* = 7.0 Hz), 55.3, 55.1, 46.3 (d, *J* = 137.7 Hz), 32.6 (d, *J* = 6.5 Hz), 32.2 (d, *J* = 5.6 Hz), 23.5 (d, *J* = 4.3 Hz), 22.2, 21.5, 21.3, 20.7.

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 20.5, 14.8.

HRMS (ESI) Calcd. for $C_{30}H_{39}O_8P_2$ ($M^+$+H): *m/z* 589.2120. Found: 589.2122.

This compound was crystallized from ethyl acetate/chlorobenzene (2:1) mixture at rt. X-ray structure was determined for this sample.

**Compound 52**



Yield: 0.091g (45%, white solid, $R_f$ = 0.35 (2:1 hexane +ethyl acetate)).

Mp: 142-144 $^{o}$C.

IR (KBr): 2954, 2923, 2854, 1745, 1491, 1463, 1264, 1060, 1008, 831, 776 $cm^{-1}$.

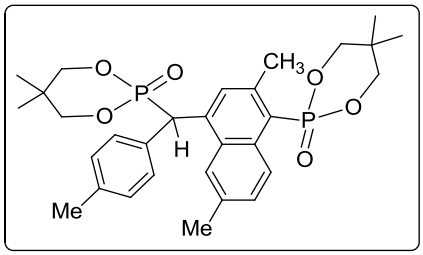
$^{1}$H NMR(500 MHz, $CDCl_3$): δ 8.67 (d, *J* = 9.0 Hz, 1H), 8.05-8.04 (m, 1H), 7.89-7.88 (m, 1H), 7.46-7.44 (m, 1H), 7.39-7.37 (m, 2H), 7.31-7.28 (m, 2H), 5.23 (d, *J* = 26.0 Hz, 1H), 4.31-4.23 (m, 2H), 4.11-4.03 (m, 2H), 3.81-3.67 (m, 4H), 2.84 (d, *J* = 2.0 Hz, 3H), 1.33 (s, 3H), 0.99 (s, 3H), 0.83 (s, 6H).

$^{13}$C NMR (125 MHz, $CDCl_3$): δ 142.5 (d, *J* ~ 10.0 Hz), 135.2, 133.9 (d, *J* ~ 4.0 Hz), 133.6 (d, *J* = 7.3 Hz), 133.2 (d, *J* = 6.5 Hz), 133.0 (d, *J* ~ 6.5 Hz), 132.7 (d, *J* = 13.0 Hz), 132.5, 131.3 (t, *J* = 12.5 Hz), 130.8 (d, *J* = 6.5 Hz), 129.0 (d, *J* = 2.0 Hz), 128.8 (d, *J* ~ 5.0 Hz), 127.8, 122.5, 122.1 (d, *J* = 175.0 Hz), 76.2 (d, *J* = 6.3 Hz), 75.8 (d, *J* = 4.6 Hz), 45.5 (d, *J* = 138.0 Hz), 32.7 (d, *J* = 6.3 Hz), 32.2 (d, *J* = 5.5 Hz), 23.8 (d, *J* = 4.5 Hz), 22.0, 21.4, $21.3_6$, 20.8.

$^{31}$P NMR (202 MHz, $CDCl_3$): δ 19.4, 13.5.

HRMS (ESI) Calcd. for $C_{28}H_{36}Cl_2NO_6P_2$ ($M^+$+$NH_4^+$), ($M^+$+$NH_4^+$+2), ($M^+$+$NH_4^+$+4) : *m/z* 614.1395, 616.1365, 618.1335. Found: 614.1402, 616.1373, 618.1337.

**Compound 53**



Yield: 0.150 g (75%, white solid, $R_f$ = 0.31 (2:1 hexane +ethyl acetate)).

Mp: 218-220 $^{o}$C.

IR (KBr): 2967, 2930, 2884, 1511, 1472, 1260, 1056, 1005, 945, 746 $cm^{-1}$.

$^1H$ NMR (500 MHz, $CDCl_3$): δ 8.57 (d, *J* = 9.0 Hz, 1H), 8.02-8.01 (m, 1H), 7.74 (br, 1H), 7.35-7.31 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 2H), 5.35 (d, *J* = 26.0 Hz, 1H), 4.25-4.17 (m, 2H), 4.04-3.95 (m, 2H), 3.76-3.62 (m, 4H), 2.83 (d, *J* = 2.0 Hz, 3H), 2.44 (s, 3H), 2.30 (s, 3H), 1.35, 1.00, 0.78 and 0.77 (4s, 12H).

$^{13}C$ NMR (125 MHz, $CDCl_3$): δ 141.2 (d, *J* = 10.0 Hz), 137.3 (d, *J* = 3.1 Hz), 136.0, 135.6, 132.7 (d, *J* = 12.7 Hz), 132.3 (d, *J* = 7.2 Hz), 132.0 (d, *J* = 6.4 Hz), 131.9 (d, *J* = 6.8 Hz), 130.6 (t, *J* = 12.1 Hz), 129.5 (d, *J* = 6.9 Hz), 129.4 (d, *J* = 2.5 Hz), 129.1, 126.7 (d, *J* = 4.6 Hz), 122.7, 120.9 (d, *J* = 172.5 Hz), 76.1 (d, *J* = 5.0 Hz), 75.8 (dd, *J* = 6.8 Hz, *J* = 2.6 Hz), 45.8 (d, *J* = 137.3 Hz), 32.6 (d, *J* = 6.7 Hz), 32.2 (d, *J* = 5.4 Hz), 23.7 (d, *J* = 4.5 Hz), 22.1, 21.8, 21.5, 21.3, 21.0, 20.7.

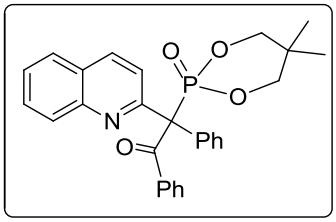
$^{31}P$ NMR (202 MHz, $CDCl_3$): δ 20.4, 14.9.

HRMS (ESI) Calcd. for $C_{30}H_{39}O_6P_2$ ($M^+$+H): *m/z* 557.2222. Found: 557.2222.

### 6.10 Reaction of allenylphosphonates with *N*-(2-formylphenyl)benzamide 12a and *N*-(2-acetyl-phenyl)benzamide 12b

To a solution of allenylphosphonate **6a** (0.100 g, 0.38 mmol) and *N*-(2-formylphenyl)benzamide **12a** (0.085 g, 0.38 mmol) in DMSO (3 mL) was added $K_3PO_4$ (0.016 g, 0.076 mmol) and the mixture heated with stirring at 110 $^oC$ for 12 h. The contents were washed with water and extracted with ethyl acetate (2 x 20 mL). The solvent was removed under reduced pressure. Purification by column chromatography (hexane/ethyl acetate; 2:1) afforded **55**. Compounds **56-60** were prepared following the same procedure and the same molar quantities. Compounds **58-60** prepared by using *N*-(2-acetyl-phenyl)benzamide **12b** (0.081 g, 0.34 mmol).

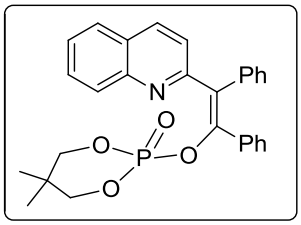
**Compound 54** (isolated from the reaction conducted at rt)




Yield: 0.078 g (44%, white solid, $R_f$ = 0.48 (8:2 hexane/ethyl acetate)).

The spectral data are in accordance with the Ref.[42]

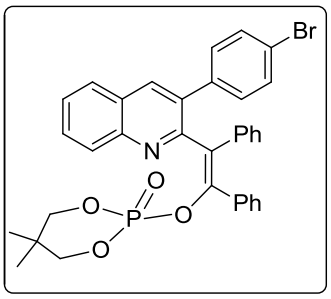
**Compound 55**




Yield: 0.160 g (90%, white solid, $R_f$ = 0.44 (8:2 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[42]

**Compound 56**




Yield: 0.083 g (56 %, white solid, $R_f$ = 0.46 (8:2 hexane/ethyl acetate)).

Mp: 238-240 $^{o}$C.

IR (KBr): 2953, 2920, 2849, 1660, 1485, 1299, 1183, 1052, 992, 844, 751, 696 $cm^{-1}$;

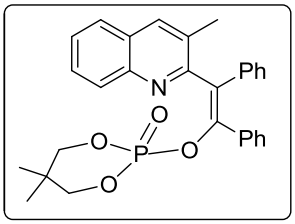
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.04 (s, 1H, Ar-*H*), 7.90 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.80 (t, *J* ~ 7.6 Hz, 1H, Ar-*H*), 7.63 (t, *J* ~ 7.4 Hz, 1H, Ar-*H*), 7.40 (t, *J* ~ 7.8 Hz, 4H, Ar-*H*), 7.26-7.23 (m, 5H, Ar-*H*), 6.96 (t, *J* ~ 7.4 Hz, 1H, Ar-*H*), 6.88 (t, *J* ~ 7.6 Hz, 2H, Ar-*H*), 6.69 (d, *J* = 7.2 Hz, 2H, Ar-*H*), 4.35-3.27 (m, 4H, OC$H_2$), 1.10 and 0.66 (2 s, 6H, $CH_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.3 (*C*O), 146.9, 146.4 (d, *J* = 7.0 Hz), 138.0, 136.9, 135.7, 133.9, 131.0, 130.9, 130.1, 129.6, 129.2, 129.1, $128.5_4$, $128.4_8$, 127.9, 127.8, 127.5, 127.3, 127.0, 126.6, 121.8 (Ar-*C*), 77.8 (d, *J* = 5.0 Hz, O$CH_2$), 31.8 (d, *J* = 5.0 Hz, $C(CH_3)_2$), 21.6 and 19.9 (2 s, $CH_3$).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ -14.67.

HRMS (ESI): Calcd. for $C_{34}H_{30}BrNO_4P$ ($M^+$+H): *m/z* 626.1096. Found: 626.1121.

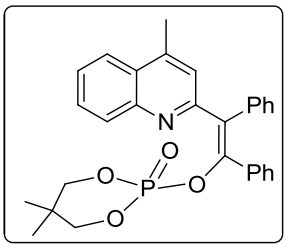
**Compound 57**




Yield 0.136 g (78%, white solid, $R_f$ = 0.45 (8:2 hexane/ethyl acetate)).

The spectral data are in accordance with the literature.[42]

**Compound 58**




Yield: 0.135 g (74 %, white solid, $R_f$ = 0.48 (8:2 hexane/ethyl acetate)).

Mp: 224-226 $^{o}$C.

IR (KBr): 3063, 2964, 2909, 1594, 1545, 1299, 1183, 1052, 1008, 937, 855, 756, 696 $cm^{-1}$;

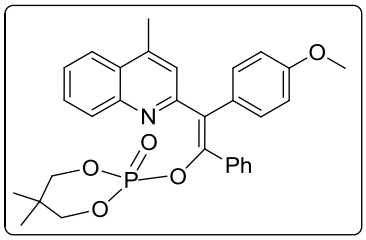
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 8.01 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.73-7.69 (m, 1H, Ar-*H*), 7.60-7.56 (m, 1H, Ar-*H*), 7.49-7.46 (m, 2H, Ar-*H*), 7.38 (s, 1H, Ar*H*), 7.28-7.15 (m, 8H, Ar*H*), 3.90 (d, *J* = 10.4 Hz, 2H, OC$H_2$), 3.50-3.42 (m, 2H, OC$H_2$), 2.69 (s, 3H, ArC$H_3$), 1.10 and 0.65 (2 s, 6H, $CH_3$);

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 158.4 (*C*O), 147.6, 146.1 (d, *J* = 9.2 Hz), 144.4, 138.2, 134.7, 130.7, 130.6, $130.0_6$, $129.9_7$, 129.0, 128.9, 128.1, 127.9, 127.3, 127.2, 126.2, 124.2. 123.8 (Ar-*C*), 77.7 (d, *J* = 7.0 Hz, O*C*$H_2$), 31.8 (d, *J* = 6.0 Hz, *C*$(CH_3)_2$), 21.8 and 20.0 (2 s, *C*$H_3$), 18.7 (s, Ar*C*$H_3$);

$^{31}$P NMR (162 MHz, $CDCl_3$): δ -13.85

HRMS (ESI): Calcd. for $C_{29}H_{29}NO_4P$ ($M^+$+H): *m/z* 486.1834 Found: 486.1860.

**Compound 59**



Yield: 0.131 g (75 %, white solid, $R_f$ = 0.42 (8:2 hexane/ethyl acetate)).

Mp: 172-174 $^{o}$C.

IR (KBr): 3063, 3030, 2969, 2887, 2832, 1600, 1512, 1298, 1249, 1172, 1057, 1013, 931, 843, 761 $cm^{-1}$.

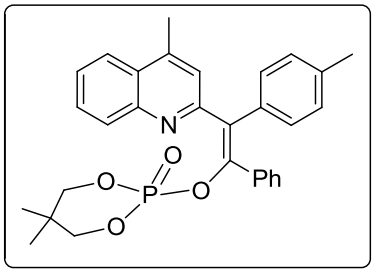
$^{1}$H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.17 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 8.01 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.73-7.69 (m, 1H, Ar-*H*), 7.60-7.55 (m, 1H, Ar-*H*), 7.50-7.48 (m, 2H, Ar-*H*), 7.36 (s, 1H, Ar*H*), 7.28-7.24 (m, 3H, Ar*H*), 7.09-7.06 (m, 2H, Ar-*H*), 6.70-6.68 (m, 2H, Ar-*H*), 3.89 (d, *J* = 8.4 Hz, 2H, OC$H_2$), 3.74 (s, 3H, OC$H_3$), 3.48-3.41 (m, 2H, OC$H_2$), 2.69 (s, 3H, ArC$H_3$), 1.09 and 0.64 (2 s, 6H, $CH_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 158.7 (d, *J* = 9.0 Hz , *C*O), 147.6, 145.4 (d, *J* = 9.0 Hz), 144.3, 134.9, 131.8, 130.5, $130.0_3$, $129.9_6$, 129.8, 129.7, 129.0, 128.7, 128.0, 127.3, 126.2, 124.2, 123.8, 113.6 (Ar-*C*), 77.7 (d, *J* = 7.1 Hz, O*C*$H_2$), 55.1, 31.7 (d, *J* = 6.0 Hz, *C*$(CH_3)_2$), 21.7 and 19.9 (2 s, *C*$H_3$), 18.7 (s, Ar*C*$H_3$).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ-13.74.

HRMS (ESI): Calcd. for $C_{30}H_{31}NO_5P$ ($M^+$+H): *m/z* 516.1940. Found: 516.1971.

**Compound 60**



Yield: 0.138 g (77%, white solid, $R_f$ = 0.46 (8:2 hexane/ethyl acetate)).

Mp: 176-178 $^{o}$C.

IR (KBr): 3057, 2970, 2909, 1638, 1589, 1551, 1512, 1452, 1293, 1178, 1046, 992, 936, 849, 772, 701 $cm^{-1}$.

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 8.01 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.73-7.69 (m, 1H, Ar-*H*), 7.60-7.56 (m, 1H, Ar-*H*), 7.50-7.48 (m, 2H, Ar-*H*), 7.37 (s, 1H, Ar*H*), 7.30-7.25 (m, 4H, Ar*H*), 7.05 (d, *J* = 6.4 Hz, 2H, Ar-*H*), 6.96 (d, *J* = 6.4 Hz, 2H, Ar-*H*), 3.90 (d, *J* = 8.8 Hz, 2H, OC$H_2$), 3.48-3.41 (m, 2H, OC$H_2$), 2.69 (s, 3H, ArC$H_3$), 2.27 (s, 3H, ArC$H_3$), 1.10 and 0.64 (2 s, 6H, $CH_3$).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ 158.6 (*C*O), 147.6, 145.7 (d, *J* = 7.3 Hz), 144.4, 137.0, 135.1, 134.8, 130.5, $130.0_5$, $129.9_6$, 129.0, 128.9, 128.8, 127.9, 127.3, 126.2, 124.2, 123.8 (Ar-*C*), 77.7 (d, *J* = 6.0 Hz, O*C*$H_2$), 31.8 (d, *J* = 4.4 Hz, *C*$(CH_3)_2$), 21.7 and 21.2 (2 s, *C*$H_3$), 19.9 and 18.7 (2s, Ar*C*$H_3$).

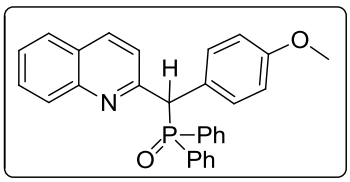
$^{31}P$ NMR (162 MHz, $CDCl_3$): δ -13.80.

HRMS (ESI): Calcd. for $C_{30}H_{31}NO_4P$ ($M^+$+H): *m/z* 500.1991. Found: 500.2011.

### 6.11 Reaction of allenylphosphine oxides 5c-e with *N*-(2-formylphenyl)benzamide 12a and *N*-(2-acetyl-phenyl)benzamide 12b

Procedure was similar to that for compounds **55**. Allenylphosphine oxide **5c-e** (0.100 g, 0.30 mmol) and *N*-(2-formylphenyl)benzamide **12a** or *N*-(2-acetyl-phenyl)benzamide **12b** (0.068 g, 0.30 mmol) were used.

**Compound 61**




Yield: 0.081 g (63%, white solid, $R_f$ = 0.40 (8:2 hexane/ethyl acetate)).

Mp: 194-196 $^{o}$C.

IR (KBr): 3050, 2926, 2831, 1607, 1596, 1511, 1436, 1304, 1253, 1174, 1038, 831, 751 $cm^{-1}$;

$^{1}H$ NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 8.07 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.89 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.80-7.58 (m, 9H, Ar-*H*), 7.49-7.30 (m, 6H, Ar-

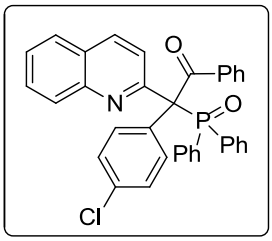
*H*), 6.77 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 5.37 (d, *J* = 8.8 Hz, 1H, PC*H*), 3.73 (s, 3H, Ar-OC$H_3$);

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 158.7, 157.7, 136.8, 132.8, 132.5, 131.8, 131.5, 131.4, 131.3, $131.2_3$, $131.1_6$, 131.1, 129.4, 128.7, 128.4, 128.3, 128.1, 127.5, 127.4, 127.3, 127.0, 126.3, $122.2_0$, $122.1_7$, 114.0, 55.9 (d, *J* = 64.0 Hz, P*C*H), 55.1.

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 31.20;

HRMS (ESI): Calcd. for $C_{29}H_{25}NO_2P$ ($M^+$+H): *m/z* 450.1623. Found: 450.1624.

**Compound 62**




Yield: 0.063 g (40%, white solid, $R_f$ = 0.46 (8:2 hexane/ethyl acetate)).

Mp: 182-184 $^{o}$C.

IR (KBr) 3046, 2926, 2844, 1676, 1589, 1496, 1430, 1232, 1178, 1101, 1019, 728, 684 $cm^{-1}$;

$^1$H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 7.90 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.81 (t, *J* ~ 7.4 Hz, 2H, Ar-*H*), 7.77 (d, *J* = 6.4 Hz, 1H, Ar-*H*), 7.70 (t, *J* ~ 7.6 Hz, 3H, Ar-*H*), 7.64-7.61 (m, 1H, Ar-*H*), 7.54-7.44 (m, 5H, Ar-*H*), 7.41-7.37 (m, 2H, Ar-*H*), 7.31-7.23 (m, 4H, Ar-*H*), 7.20 (t, *J* ~ 6.4 Hz, 3H, Ar-*H*), 7.05 (t, *J* ~ 6.2 Hz, 2H, Ar-*H*);

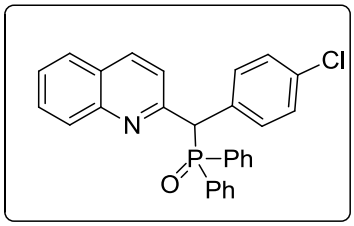
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 198.9 (*C*O), 156.0 (d, *J* = 3.0 Hz), 147.0, 136.9, 135.9, 134.0, 133.9, 133.8, 133.7, 133.1 (d, *J* = 3.0 Hz), 132.5 (d, *J* = 3.0 Hz), 131.9 (d, *J* = 79.0 Hz, P*C*), $131.8_9$, 131.8, 131.4 (d, *J* = 2.0 Hz) , 130.3, 129.5, 129.2, 127.9, 127.8, 127.7, 127.6, $127.5_1$, $127.4_8$, 127.4, 127.0, 126.7, 123.3;

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 37.83;

HRMS (ESI): Calcd. for $C_{35}H_{26}ClNO_2P$ ($M^+$+H): *m/z* 558.1390. Found: 558.1389.

Single crystal X-ray structure was determined for this compound also but the quality of data was only moderate.

**Compound 63**




This compound was isolated along with compound **62**

Yield: 0.058 g (45%, white solid, $R_f$ = 0.42 (8:2 hexane/ethyl acetate)).

Mp: 232-234 $^{o}$C.

IR (KBr): 3057, 2920, 1600, 1556, 1506, 1484, 1435, 1304, 1172, 1117, 1008, 876, 827, 723 $cm^{-1}$.

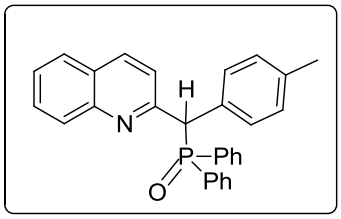
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.10 (t, *J* ~ 8.6 Hz, 2H, Ar-*H*), 7.91 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.80-7.63 (m, 8H, Ar-*H*), 7.49-7.19 (m, 10H, Ar-*H*), 5.40 (d, *J* = 8.4 Hz, 1H, PC*H*).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.0, 147.7, 136.9, 134.0 (d, *J* = 5.0 Hz), 133.4, 132.5, 132.2, $131.7_4$, $131.6_6$, 131.5, 131.4, 131.3, $131.2_5$, $131.1_6$, 129.5, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 127.5, 127.0, 126.4, 122.0, 56.3 (d, *J* = 63.0 Hz, P*C*H).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 30.76.

HRMS (ESI): Calcd. for $C_{28}H_{22}ClNOP$ ($M^+$+H): *m/z* 454.1127. Found: 454.1128.

**Compound 64**




Yield: 0.086 g (66%, white solid, $R_f$ = 0.43 (8:2 hexane/ethyl acetate)).

Mp: 174-176 $^{o}$C.

IR (KBr): 3063, 2942, 2855, 1594, 1501, 1430, 1304, 1265, 1200, 1118, 1030, 827, 723, 695 $cm^{-1}$;

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, *J* = 6.0 Hz, 1H, Ar-*H*), 8.04 (m, 2H, Ar-*H*), 7.84 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.73-7.60 (m, 6H, Ar-*H*), 7.50-7.41 (m, 2H, Ar-*H*), 7.37-7.33

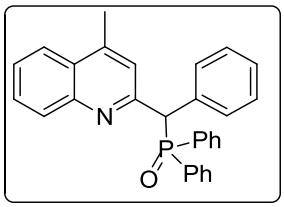
(m, 3H, Ar-*H*), 7.29-7.26 (m, 2H, Ar-*H*) 7.20 (t, *J* ~ 6.0 Hz, 1H, Ar-*H*), 7.10 (t, *J* = 6.0 Hz, 1H, Ar-*H*), 7.04 (d, *J* = 6.0 Hz, 1H, Ar-*H*), 5.62 (d, *J* = 7.6 Hz, 1H, PC*H*), 2.33 (s, 3H, Ar-C$H_3$);

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.1 (d, *J* = 3.0 Hz), 147.5, 137.2, 137.1, 136.6, 134.5 (d, *J* = 3.0 Hz), 132.8, 132.4, 132.0, 131.6$_5$, 131.5$_8$, 131.5, 131.2, 131.1, 130.5, 130.2$_4$, 130.1$_9$, 129.2, 128.9, 128.4, 128.3, 128.2, 128.1, 127.5, 127.4, 126.9, 126.4, 126.2, 122.4$_7$, 122.4$_6$, 52.2 (d, *J* = 51.0 Hz, P*C*H), 20.3;

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 32.16;

HRMS (ESI): Calcd. for $C_{29}H_{25}NOP$ ($M^+$+H): *m/z* 434.1674. Found: 434.1678.

**Compound 65**




Yield: 0.109 g (80%, white solid, $R_f$ = 0.44 (8:2 hexane/ethyl acetate)).

Mp: 198-200 $^oC$.

IR (KBr): 3063, 2915, 2323, 1600, 1561, 1496, 1446, 1172, 1117, 1073, 1030, 865, 761, 712 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 1H, Ar-*H*), 7.91-7.88 (m, 2H, Ar-*H*), 7.80 (t, *J* = 10.0 Hz, 2H, Ar-*H*), 7.71-7.60 (m, 6H, Ar-*H*), 7.49-7.39 (m, 2H, Ar-*H*), 7.36-7.16 (m, 7H, Ar-*H*), 5.37 (d, *J* = 8.0 Hz, 1H, PC*H*).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.1, 147.4, 145.8, 135.6, 135.5, 132.9, 132.6, 131.9, 131.6, 131.5$_6$, 131.5, 131.3, 131.2, 130.1, 130.0, 129.3, 129.0, 128.5, 128.3, 128.2, 128.1$_8$, 128.1, 127.2, 127.1, 126.0, 123.7, 122.7 (Ar-*C*), 56.9 (d, *J* = 63.0 Hz, P*C*H).

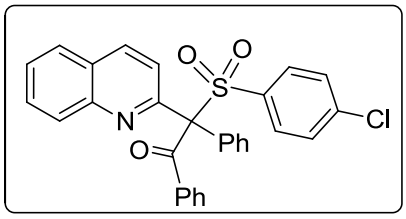
$^{31}$P NMR (162 MHz, $CDCl_3$): δ 31.02.

HRMS (ESI): Calcd. for $C_{29}H_{25}NOP$ ($M^+$+H): *m/z* 434.1674 Found: 434.1674.

## 6.12 Reaction of Sulfonyl allenes 8a-b with *N*-(2-formylphenyl)benzamide 12a and *N*-(2-acetyl-phenyl)benzamide 12b

Procedure was similar to that for compound **55**. Sulfonyl allenes **8a-b** (0.34 mmol) and *N*-(2-formylphenyl)benzamide **12a** or *N*-(2-acetyl-phenyl)benzamide **12b** (0.077 g, 0.34 mmol) were used.

**Compound 66**




Yield: 0.111 g (65%, white solid, $R_f$ = 0.74 (9:1 hexane/ethyl acetate)).

Mp: 100-102 $^{o}$C.

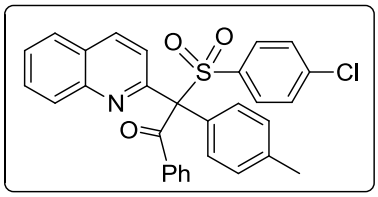
IR(KBr): 3063, 2920, 1688, 1594, 1573, 1496, 1468, 1435, 1315, 1227, 1145, 1090, 1013, 816, 745, 690 $cm^{-1}$;

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 8.04-7.98 (m, 3H, Ar-*H*), 7.83 (d, *J* = 6.4 Hz, 1H, Ar-*H*), 7.74-7.59 (m, 3H, Ar-*H*), 7.52-7.41 (m, 5H, Ar-*H*), 7.36 (t, *J* ~ 5.8 Hz, 2H, Ar-*H*), 7.24-7.18 (m, 3H, Ar*H*), 7.05 (t, *J* ~ 6.2 Hz, 2H, Ar-*H*);

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 193.7, 151.7, 147.3, 140.0, 136.4, 136.3, 135.3, 132.8, 132.5, 131.2, 130.1, 129.9, 129.8, 129.5, 128.0, 127.5, 127.2, 124.4, 90.9;

HRMS (ESI): Calcd. for $C_{29}H_{21}ClNO_3S$ ($M^+$+H): *m/z* 498.0931. Found: 498.0935.

**Compound 67**




Yield: 0.097 g (58%, white solid, $R_f$ = 0.78 (9:1 hexane/ethyl acetate)).

Mp: 182-184$^{o}$C.

IR (KBr): 2920, 2854, 1682, 1589, 1495, 1468, 1320, 1210, 1145, 1090, 1013, 832, 750 $cm^{-1}$.

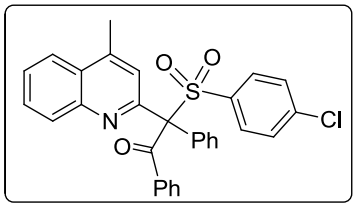
$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 8.03 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.95 (d, *J* = 6.8 Hz, 1H, Ar-*H*), 7.89 (d, *J* = 5.6 Hz, 2H, Ar-*H*), 7.83 (d, *J* = 6.4 Hz, 1H, Ar-*H*), 7.73-7.70 (m, 1H, Ar-*H*), 7.61-7.58 (m, 1H, Ar-*H*), 7.51-7.46 (m,

4H, Ar-*H*), 7.24-7.17 (m, 5H, Ar-*H*), 7.05 (t, *J* = 6.4 Hz, 2H, Ar*H*), 2.40 (s, 3H, ArC$H_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ (ppm) 193.7, 152.1, 147.3, 139.9, 139.6, 136.2, 135.5, 132.8, 132.5, 132.3, 130.3, $129.8_3$, $129.8_0$, 128.7, 128.0, $127.8_2$, $127.7_9$, 127.4, 127.2, 124.3, 90.9, 21.2.

HRMS (ESI): Calcd. for $C_{30}H_{23}ClNO_3S$ ($M^+$+H): *m/z* 512.1087. Found: 512.1089.

**Compound 68**




Yield: 0.119 g (68%, white solid, $R_f$ = 0.77 (9:1 hexane/ethyl acetate)).

Mp: 182-184 $^oC$.

IR (KBr): 3057, 2926, 1687, 1589, 1501, 1468, 1441, 1315, 1221, 1145, 1090, 1013, 821, 750, 695 $cm^{-1}$.

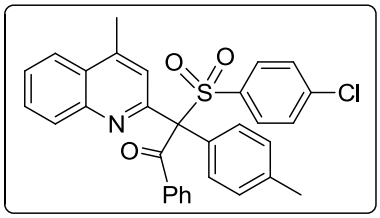
$^1$H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 8.4 Hz, 4H, Ar-*H*), 7.85 (s, 1H, Ar*H*), 7.73-7.69 (m, 1H, Ar-*H*), 7.64-7.60 (m, 1H, Ar-*H*), 7.53 (d, *J* = 7.2 Hz, 2H, Ar-*H*), 7.45 (d, *J* = 8.8 Hz, 2H, Ar-*H*), 7.40 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 7.34 (t, *J* ~ 7.6 Hz, 2H, Ar-*H*), 7.24-7.18 (m, 3H, Ar-*H*), 7.05 (t, *J* ~ 7.8 Hz, 2H, Ar*H*), 2.70 (s, 3H, ArC$H_3$).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 193.7, 151.3, 147.1, 144.9, 139.9, 136.4, 135.3, 132.9, 132.8, 132.4, 131.2, 130.4, 129.5, 129.4, 127.9 (d, *J* = 5.0 Hz), 127.6, 127.5, 124.7, 123.7, 90.8, 19.1.

HRMS (ESI): Calcd. for $C_{30}H_{23}ClNO_3S$ ($M^+$+H): *m/z* 512.1087. Found: 512.1088.

Single crystal X-ray structure was determined for this compound.

**Compound 69**




Yield: 0.107 g (62%, white solid, $R_f$ = 0.79 (9:1 hexane/ethyl acetate)).

Mp: 170-172 $^{o}$C.

IR (KBr): 2926, 2854, 1687, 1649, 1578, 1512, 1446, 1309, 1243, 1150, 1079, 821, 761, 701 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 8.00-7.85 (m, 5H, Ar-*H*), 7.71-7.68 (m, 1H, Ar*H*), 7.62-7.60 (m, 1H, Ar*H*), 7.54-7.52 (m, 2H, Ar-*H*), 7.47 (d, *J* = 7.2 Hz, 2H, Ar-*H*), 7.23-7.13 (m, 5H, Ar-*H*), 7.05 (t, *J* = 6.4 Hz, 2H, Ar*H*), 2.70 and 2.40 (2s, 6H, ArC$H_3$).

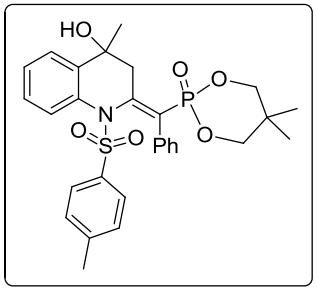
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 193.8, 151.7, 147.1, 144.7, 139.8, 139.5, 136.7, 135.6, 132.8, 132.6, 132.2, 130.4 (d, *J* = 7.4 Hz, Ar*C*), 129.4, 128.6, 128.1, 127.8, 127.7, 127.5, 127.4, 124.7, 123.6, 90.9, 21.1, 18.9.

HRMS (ESI): Calcd. for $C_{31}H_{25}ClNO_3S$ ($M^+$+H): *m/z* 526.1244. Found: 526.1243.

### 6.13 Reaction of allenylphosphonate 6a with *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide 12c

To a solution of allenylphosphonate **6a** (0.100 g, 0.38 mmol) and *N*-(2-acetylphenyl)-4-methylbenzenesulfonamide **12c** (0.108 g, 0.38 mmol) in DMF (3 mL) was added $Cs_2CO_3$ (0.024 g, 0.076 mmol) and the mixture was heated with stirring at 110 $^{o}$C for 12 h. The contents were washed with water and extracted with ethyl acetate (2 x 20 mL). The solvent was removed under reduced pressure. The residue upon purification by column chromatography (hexane/ethyl acetate; 2:1) afforded compound **70** (>80% purity).

**Compound 70**




Yield: 0.062 g (30%, white solid, $R_f$ = 0.44 (9:1 hexane/ethyl acetate)).

Mp: 188-190 $^{o}$C.

IR (KBr): 3326, 2964, 2926, 2345, 1621, 1364, 1249, 1161, 1095, 1063, 947, 761, 701 $cm^{-1}$.

$^{1}$H NMR (400 MHz, $CDCl_3$): δ 7.52-7.49 (m, 4H, Ar*H*), 7.30 (d, *J* = 6.8 Hz, 4H, Ar-*H*), 7.0 (s, 1H, Ar*H*), 6.89-6.87 (m, 2H, Ar*H*), 6.46 (d, *J* = 6.4 Hz, 2H, Ar-*H*), 4.90 (s, 1H, -C(H)*H*), 4.39 (d, *J* = 11.6 Hz, 1H, -C(H)*H*), 3.72-3.56 (m, 2H, -OC$H_2$), 3.40-3.35 (m, 1H, O*H*), 3.01-2.92 (m, 2H, -OC$H_2$), 1.65 (s, 3H, ArC$H_3$), 1.17 (s, 3H, -C$H_3$), 0.44 and 0.19 (2s, 6H, -C$H_3$). $^{1}$H NMR spectrum showed 80% purity and the major peaks corresponded to the compound as shown by the crystal structure.

$^{13}$C NMR (100 MHz, $CDCl_3$): δ 151.0, 150.7, 143.4, 137.97, 136.7, 136.5, 135.1, 135.0, 134.4, 130.91, 129.9, 129.0, 128.4, 128.3, 127.2, 126.6, 124.2, 75.7 (t, *J* = 6.5 Hz, -O*C*H2), 71.1, 43.6, 31.6 (d, *J* = 7.0 Hz, -*C*($CH_3$)$_2$), 20.8, 20.6 and 20.2 (3 s, *C*$H_3$).

$^{31}$P NMR (162 MHz, $CDCl_3$): δ 11.27.

HRMS (ESI): Calcd. for $C_{29}H_{32}NO_6PSNa$ ($M^+$+Na): *m/z* 576.1586 Found: 576.1585.

### 6.14 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **15**, **23, 24, 25, 26, 31, 34, 35, 36, 37, 44, 51, 57, 62, 68** and **70**) and X-ray data were collected at 298 K on a Bruker AXS-SMART or on an OXFORD diffractometer using Mo-$K_\alpha$ radiation (λ = 0.71073 Å) or Cu- $K_\alpha$ (λ = 1.54184 Å) as described in Chapter 3. Structures were solved and refined using standard methods.[46] Crystal data are summarized in Tables 7-10.

**Table 7**: Crystal data for compounds **15**, **23**, **24** and **25**[a]

| Compound | **15** | **23** | **24** | **25** |
|---|---|---|---|---|
| Emp. formula | $C_{22}H_{19}I_2OP$ | $C_{21}H_{17}IN_3OP$ | $C_{22}H_{19}IN_3OP$ | $C_{22}H_{19}IN_3O_2P$ |
| Formula weight | 584.14 | 485.25 | 499.27 | 515.27 |
| Crystal system | Orthorhombic | Monoclinic | Monoclinic | Orthorhombic |
| Space group | *p_n_a_21* | *P 1 21/c 1* | *P2(1)/c* | *P 21 21 21* |
| *a* /Å | 19.5490(16) | 9.1543(3) | 8.209(3) | 8.3026(2) |
| *b* /Å | 9.8719(8) | 10.0610(4) | 16.624(7) | 8.5630(2) |
| *c* /Å | 10.8488(8) | 22.0753(9) | 15.715(6) | 30.1250(8) |
| $\alpha$/deg | 90 | 90 | 90 | 90 |
| $\beta$/deg | 90 | 91.464(3) | 92.215(6) | 90 |
| $\gamma$/deg | 90 | 90 | 90 | 90 |
| *V* /Å$^3$ | 2093.7(3) | 2032.48(13) | 2142.9(14) | 2141.75(10) |
| *Z* | 4 | 4 | 4 | 4 |
| *D*calc /g cm$^{-3}$] | 1.853 | 1.586 | 1.548 | 1.598 |
| $\mu$ /mm$^{-1}$ | 3.089 | 13.245 | 1.586 | 12.643 |
| *F*(000) | 1120.0 | 960.0 | 992.0 | 1024.0 |
| Data/ restraints/ parameters | 3647/1/237 | 3907/0/244 | 3686/0/254 | 3737 /0/263 |
| S | 1.123 | 1.027 | 1.086 | 1.030 |
| R1 [I>2σ(I)] | 0.0347 | 0.0726 | 0.0268 | 0.0476 |
| wR2 [all data] | 0.1021 | 0.1985 | 0.0698 | 0.1264 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.936/-0.931 | 2.388/-2.415 | 0.351/-0.419 | 1.801/-0.933 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 8**: Crystal data for compounds **26**, **31**, **34** and **35**[a]

| Compound | **26** | **31** | **34** | **35** |
|---|---|---|---|---|
| Emp. formula | $C_{21}H_{16}ClIN_3OP$ | $C_{30}H_{25}IN_3OP$ | $C_{22}H_{19}FIOP$ | $C_{22}H_{19}FIO_2P$ |
| Formula weight | 519.69 | 601.40 | 476.24 | 492.24 |
| Crystal system | Orthorhombic | Triclinic | Monoclinic | Monoclinic |
| Space group | *P_21_21_21* | *P-1* | *P2(1)* | *Pn* |
| *a* /Å | 29.548(4) | 8.9643(4) | 9.6921(13) | 8.2948(19) |
| *b* /Å | 8.3033(8) | 11.6596(6) | 9.8549(12) | 26.144(6) |
| *c* /Å | 8.5609(11) | 14.2643(7) | 11.1815(15) | 14.533(3) |
| $\alpha$/deg | 90 | 69.832(2) | 90 | 90 |
| $\beta$/deg | 90 | 71.872(2) | 107.996(4) | 94.408(4) |
| $\gamma$/deg | 90 | 79.193(2) | 90 | 90 |
| *V* /Å$^3$ | 2100.4(4) | 1324.64(11) | 1015.7(2) | 3142.3(12) |
| *Z* | 4 | 2 | 2 | 6 |
| *D*calc /g cm$^{-3}$] | 1.643 | 1.508 | 1.557 | 1.561 |
| $\mu$ /mm$^{-1}$ | 1.745 | 1.297 | 1.671 | 1.627 |
| *F*(000) | 1024.0 | 604.0 | 472.0 | 1464.0 |
| Data/ restraints/ parameters | 3693/0/253 | 6145/0/327 | 3554/1/235 | 11020/2/733 |
| S | 1.121 | 1.137 | 1.141 | 0.960 |
| R1 [I>2σ(I)] | 0.0780 | 0.0293 | 0.0308 | 0.0724 |
| wR2 [all data] | 0.2136 | 0.0875 | 0.0944 | 0.1884 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.784/-0.505 | 0.527/-0.404 | 0.824/-0.993 | 1.476 /-0.566 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 9**: Crystal data for compounds **36**, **37**, **44** and **51**[a]

| Compound | **36** | **37** | **44** | **51** |
|---|---|---|---|---|
| Emp. formula | $C_{21}H_{16}ClFIOP$ | $C_{14}H_{17}FIO_3P$ | $C_{22}H_{20}IO_2P$ | $C_{30}H_{38}O_8P_2$ |
| Formula weight | 496.66 | 410.15 | 474.25 | 588.54 |
| Crystal system | Monoclinic | Monoclinic | Monoclinic | Orthorhombic |
| Space group | *P2(1)/c* | *P21/c* | *P2(1)/c* | *Pbcn* |
| *a* /Å | 8.2639(11) | 16.7231(17) | 9.3892(10) | 27.100(5) |
| *b* /Å | 8.5040(13) | 7.8520(8) | 10.6121(10) | 9.958(2) |
| *c* /Å | 29.114(5) | 12.4005(17) | 20.114(2) | 23.184(5) |
| $\alpha$/deg | 90 | 90 | 90 | 90 |
| $\beta$/deg | 96.974(5) | 103.700(13) | 91.577(3) | 90 |
| $\gamma$/deg | 90 | 90 | 90 | 90 |
| *V* /Å$^3$ | 2030.9(5) | 1582.0(3) | 2003.4(3) | 6257(2) |
| *Z* | 4 | 4 | 4 | 8 |
| *D*calc /g cm$^{-3}$] | 1.624 | 1.722 | 1.572 | 1.250 |
| $\mu$ /mm$^{-1}$ | 1.803 | 2.139 | 1.691 | 0.185 |
| *F*(000) | 976.0 | 808.0 | 944.0 | 2496.0 |
| Data/ restraints/ parameters | 4277/0/235 | 2789/0/183 | 3519/0/237 | 5505/0/368 |
| S | 1.061 | 1.062 | 1.189 | 1.019 |
| R1 [I>2σ(I)] | 0.0516 | 0.0536 | 0.0476 | 0.1275 |
| wR2 [all data] | 0.1046 | 0.1714 | 0.1028 | 0.4026 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.813/-0.547 | 0.741/-1.253 | 1.296/-0.516 | 1.593/-0.325 |

[a]$R1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $wR2 = [\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**Table 10**: Crystal data for compounds **57**, **62**, **67** and **70**[a]

| Compound | **57** | **62** | **67** | **70** |
|---|---|---|---|---|
| Emp. formula | $C_{29}H_{28}NO_4P$ | $C_{35}H_{25}ClNO_2P$ | $C_{30}H_{22}ClNO_3S$ | $C_{29}H_{32}NO_6PS$ |
| Formula weight | 485.49 | 557.98 | 512.01 | 553.59 |
| Crystal system | Triclinic | Monoclinic | Triclinic | Monoclinic |
| Space group | *P-1* | *P2(1)/c* | *P-1* | *C2/c* |
| *a* /Å | 10.4790(9) | 9.6939(19) | 10.626(2) | 34.280(3) |
| *b* /Å | 10.8907(9) | 21.405(4) | 11.358(2) | 17.6184(13) |
| *c* /Å | 12.8985(9) | 27.668(6) | 21.635(4) | 25.486(4) |
| $\alpha$/deg | 68.115(7) | 90 | 104.76(3) | 90 |
| $\beta$/deg | 68.507(7) | 80.83(3) | 91.46(3) | 11548(2) |
| $\gamma$/deg | 89.099(7) | 90 | 90.01(3) | 90 |
| *V* /Å$^3$ | 1258.45(17) | 5667.7(19) | 2524.1(9) | 11548(2) |
| *Z* | 2 | 8 | 4 | 16 |
| *D*calc /g cm$^{-3}$] | 1.281 | 1.308 | 1.347 | 1.274 |
| $\mu$ /mm$^{-1}$ | 1.255 | 0.225 | 0.267 | 0.209 |
| *F*(000) | 512.0 | 2320.0 | 1064.0 | 4672.0 |
| Data/ restraints/ parameters | 4810/0/319 | 9976/26/721 | 5334/0/651 | 9448/0/696 |
| S | 1.045 | 1.125 | 1.107 | 1.058 |
| R1 [I>2σ(I)] | 0.0463 | 0.1094 | 0.0836 | 0.0616 |
| wR2 [all data] | 0.1358 | 0.2583 | 0.2542 | 0.1801 |
| Max./min. residual electron dens. [eÅ$^{-3}$] | 0.312/-0.352 | 0.789/-0.404 | 0.456/-0.524 | 0.369/-0.249 |

[a]R1 = $\Sigma||Fo| - |Fc||/\Sigma|Fo|$ and wR2 = $[\Sigma w(Fo^2-Fc^2)^2/\Sigma wFo^4]^{0.5}$

**References:**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**A) Copies of $^{1}H/^{13}C$ NMR spectra for representative compounds**
**Part A: Compounds 9, 17, 25, 28, 34, 43, 49, 52, 53, 59, 63', 70, 73 and 75.**
**Part B: Compounds 17, 20, 23, 28, 29, 36, 38, 39, 42, 44, 46, 50, 58, 61 and 67.**

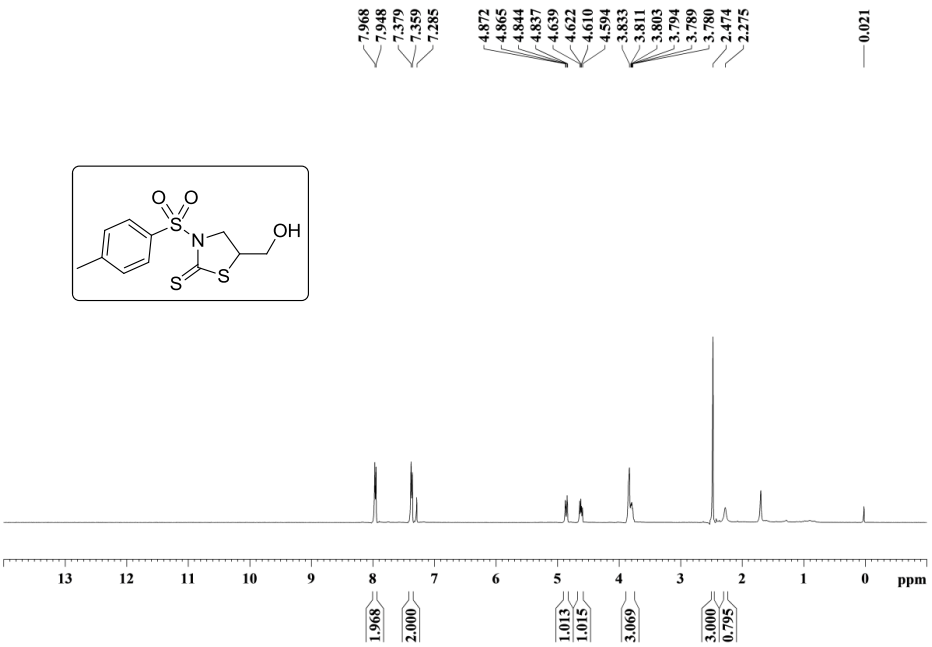


**Figure A1.** $^{1}H$ NMR spectrum of compound **9**

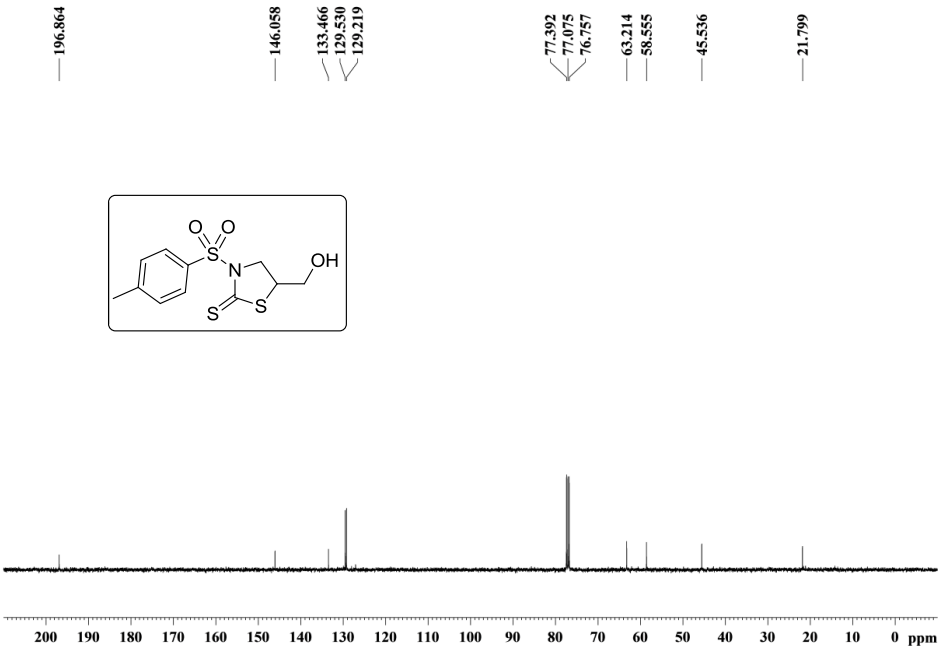


**Figure A2.** $^{13}C$ NMR spectrum of compound **9**

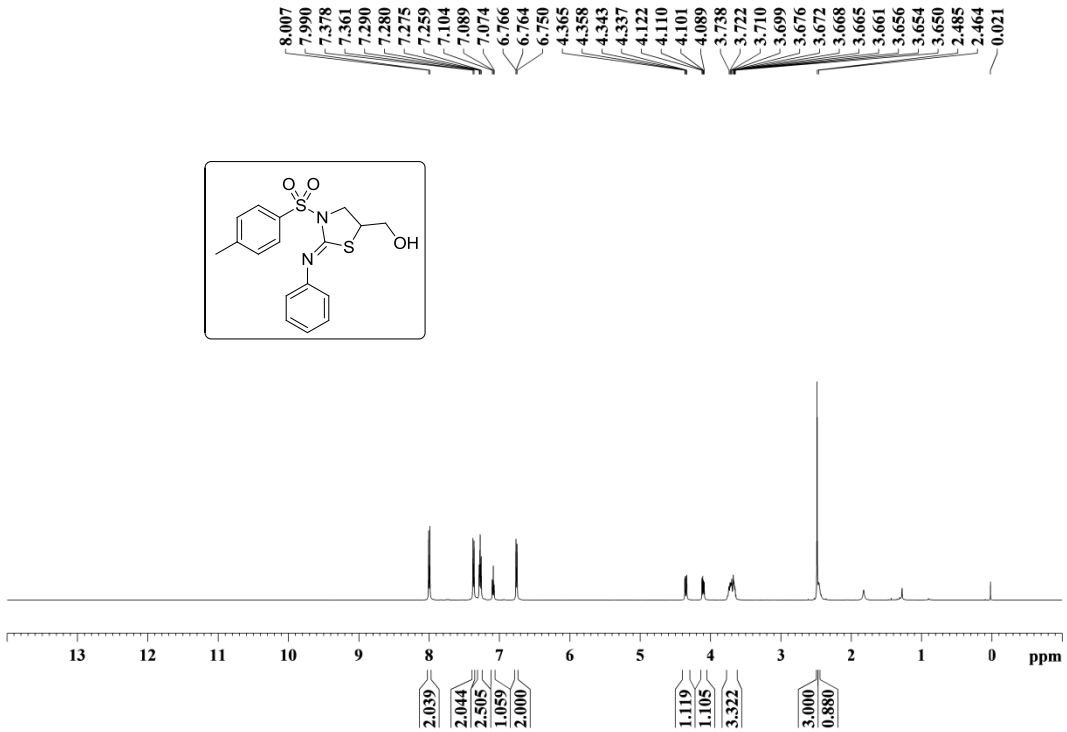


**Figure A3.** $^{1}$H NMR spectrum of compound **17**

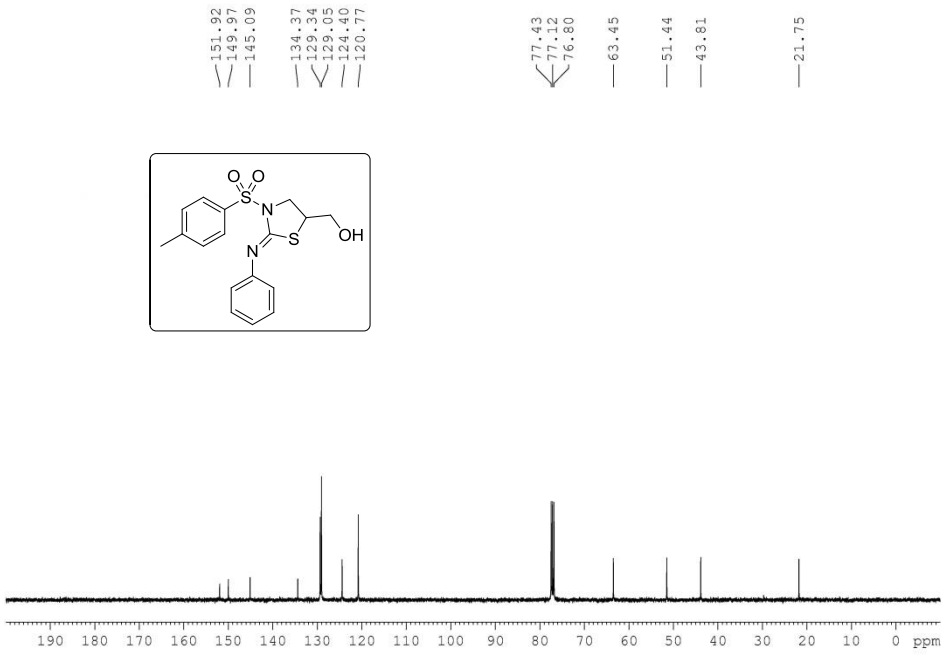


**Figure A4.** $^{13}$C NMR spectrum of compound **17**

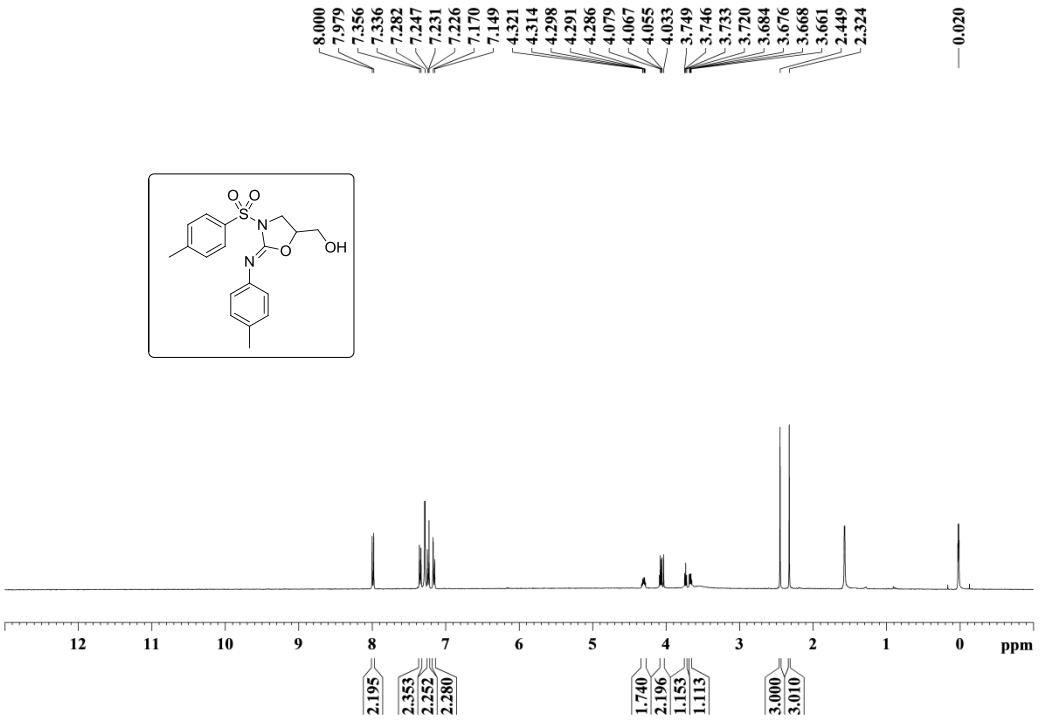


**Figure A5.** $^{1}$H NMR spectrum of compound **25**

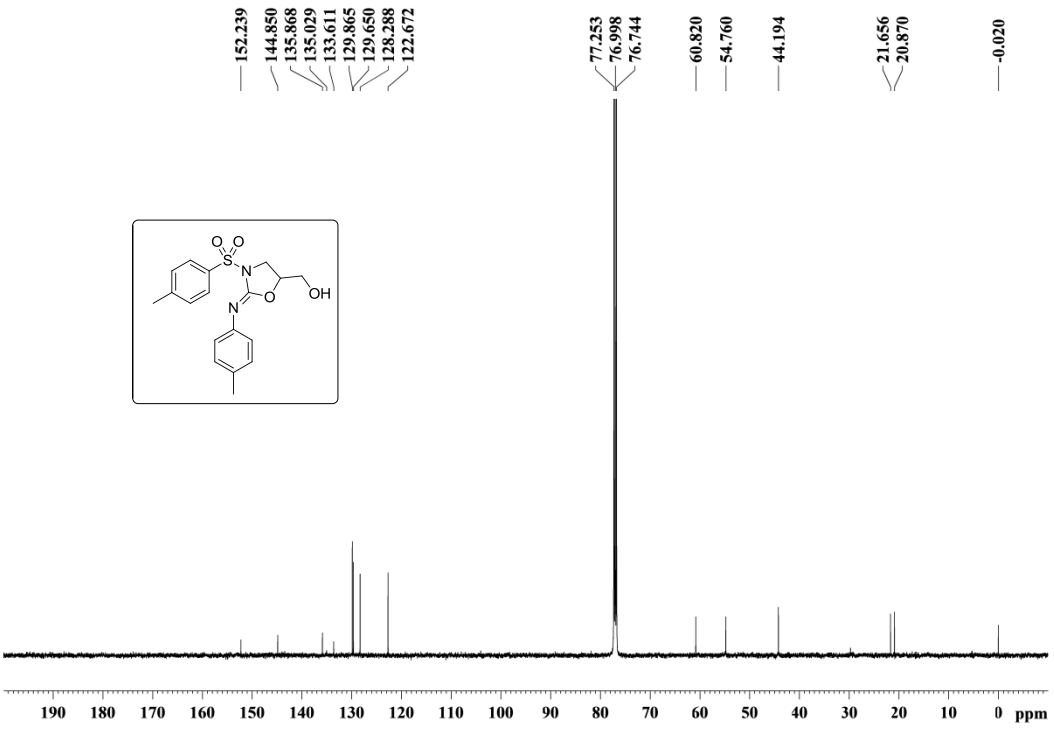


**Figure A6.** $^{13}$C NMR spectrum of compound **25**

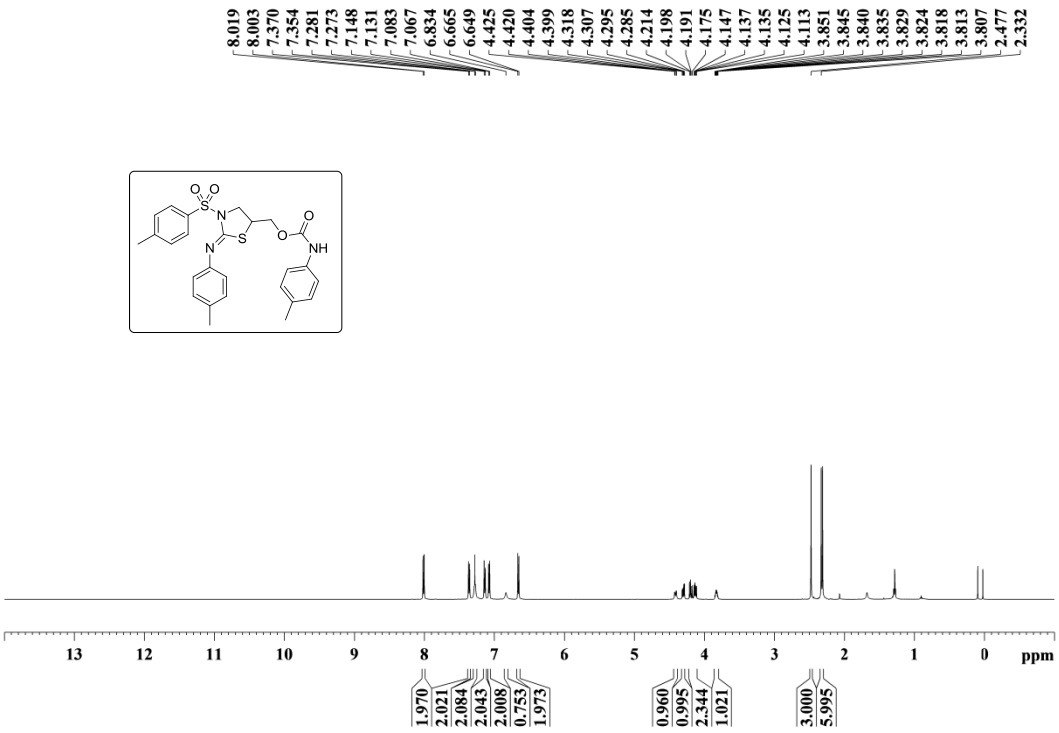


**Figure A7.** $^{1}$H NMR spectrum of compound **28**

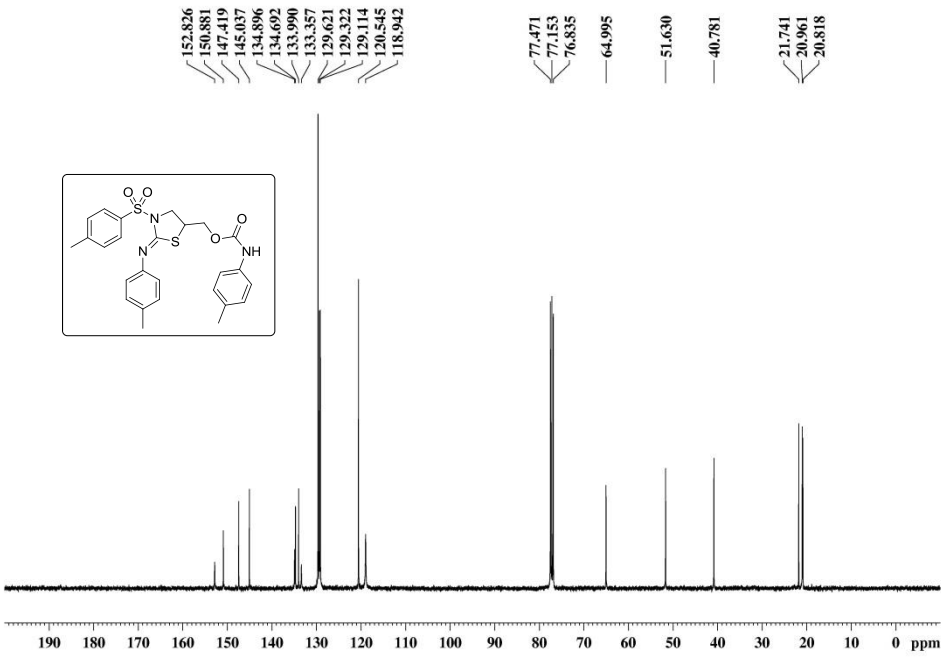


**Figure A8.** $^{13}$C NMR spectrum of compound **28**

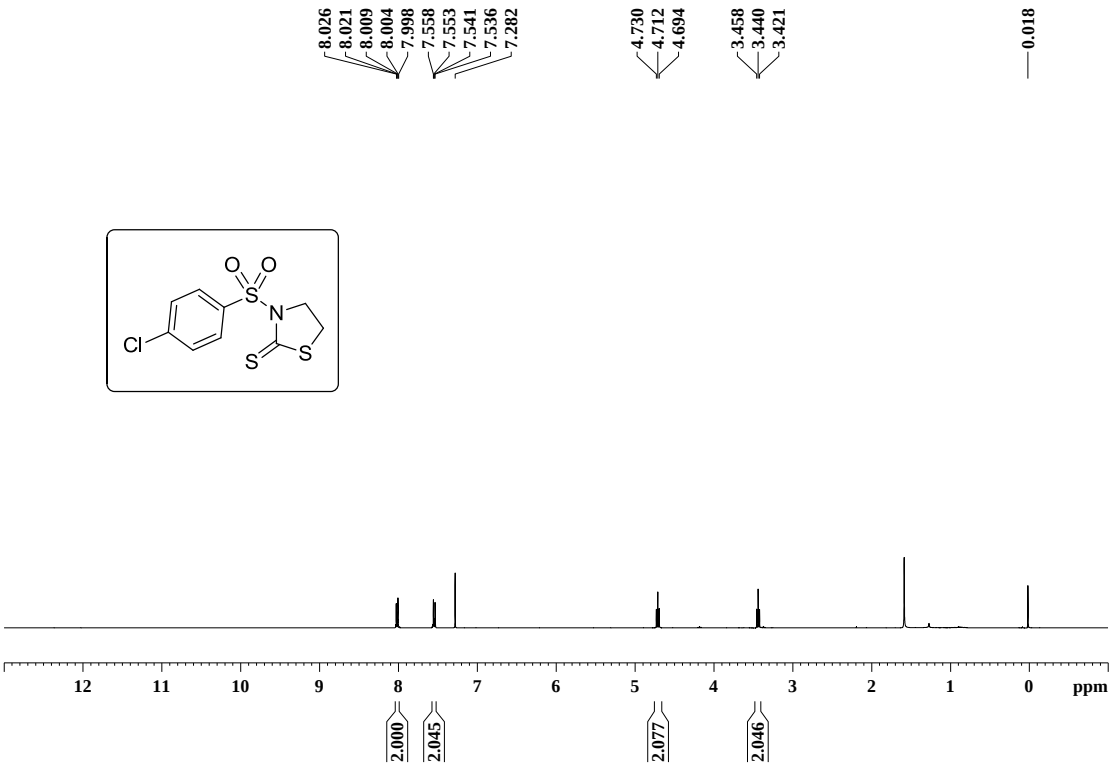


**Figure A9.** $^{1}$H NMR spectrum of compound **34**

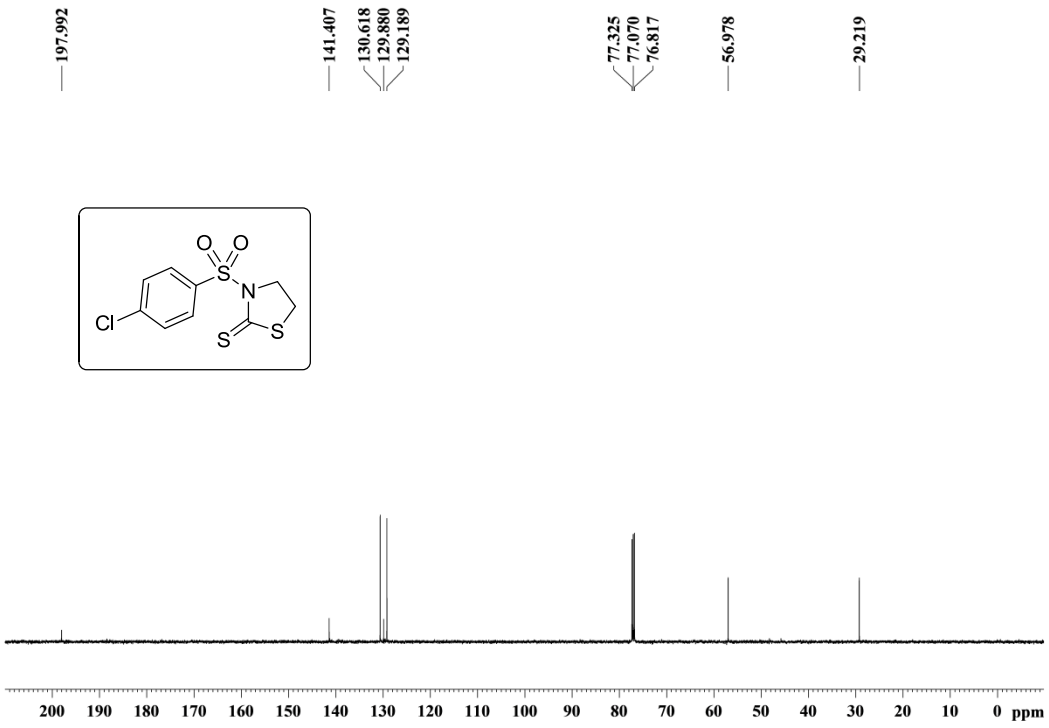


**Figure A10.** $^{13}$C NMR spectrum of compound **34**

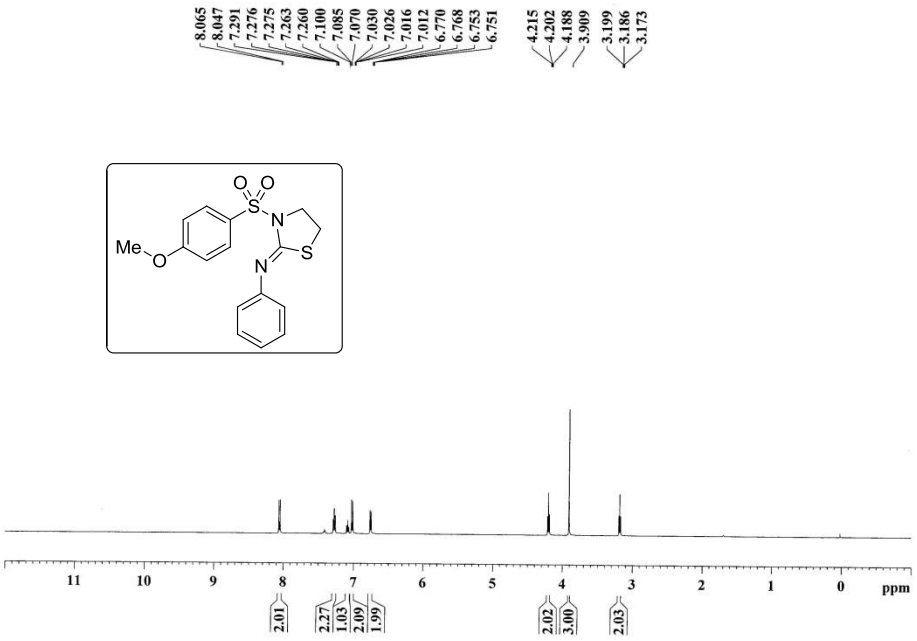


**Figure A11.** $^{1}$H NMR spectrum of compound **43**

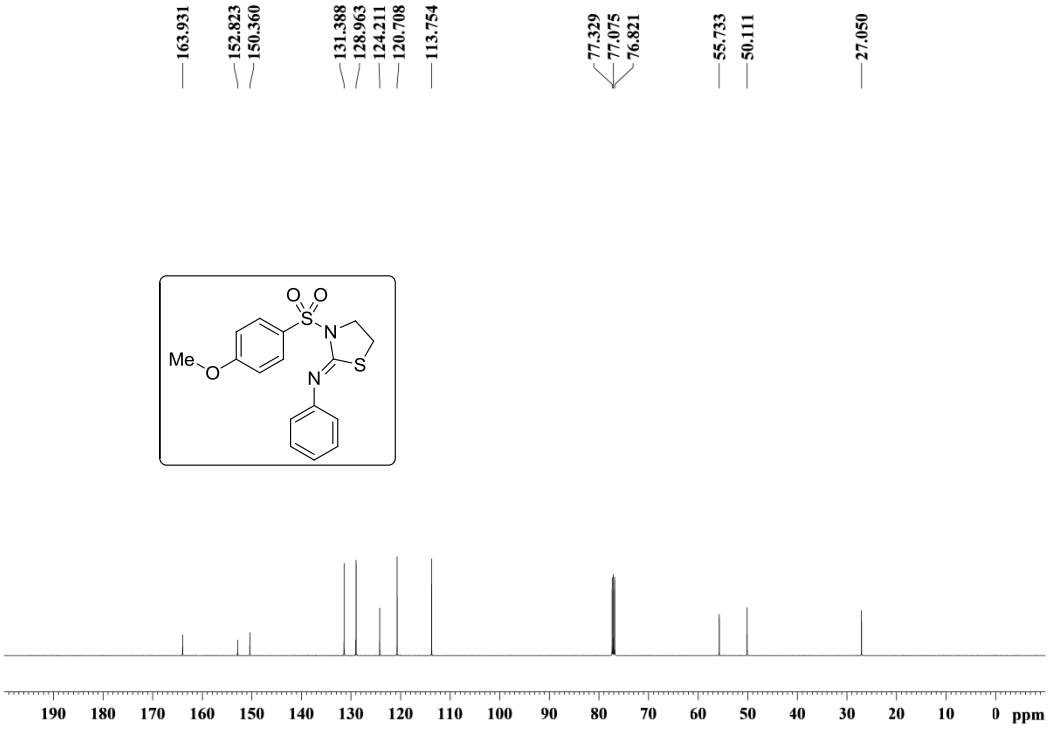


**Figure A12.** $^{13}$C NMR spectrum of compound **43**

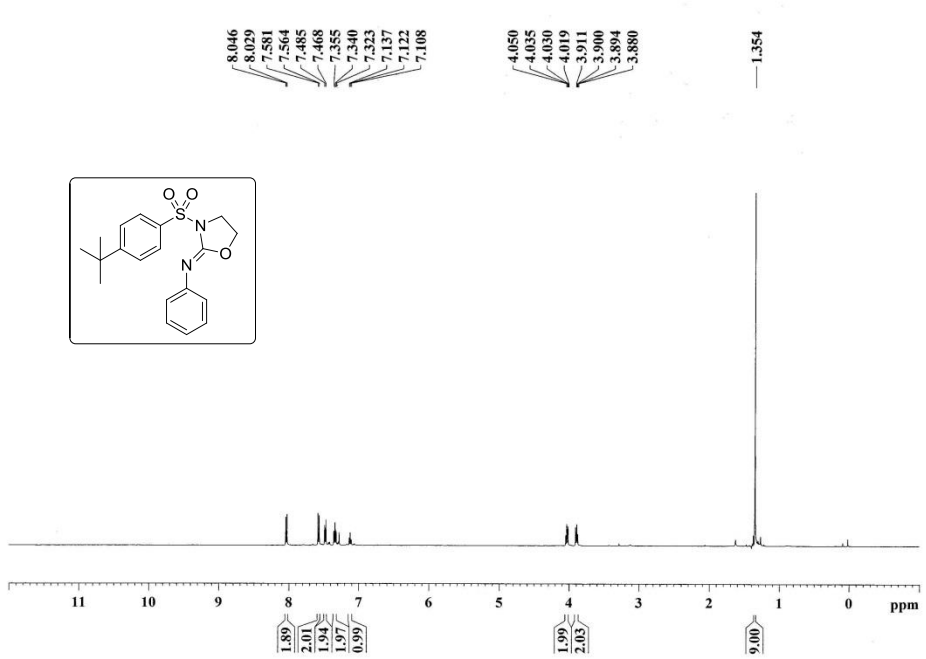


**Figure A13.** $^{1}$H NMR spectrum of compound **49**

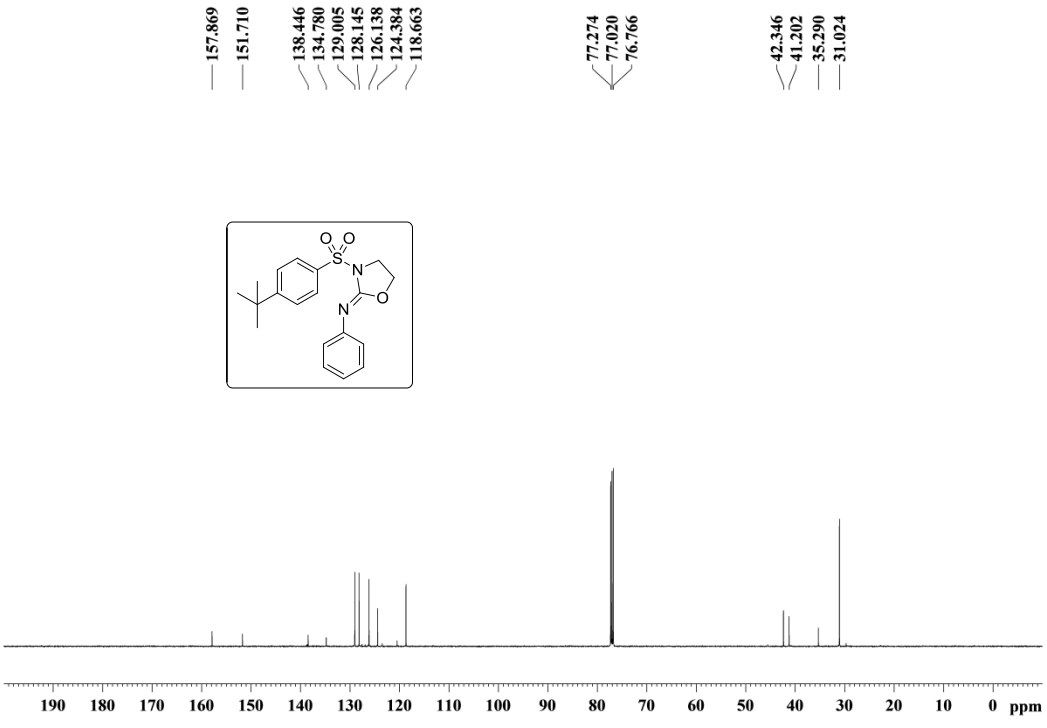


**Figure A14.** $^{13}$C NMR spectrum of compound **49**

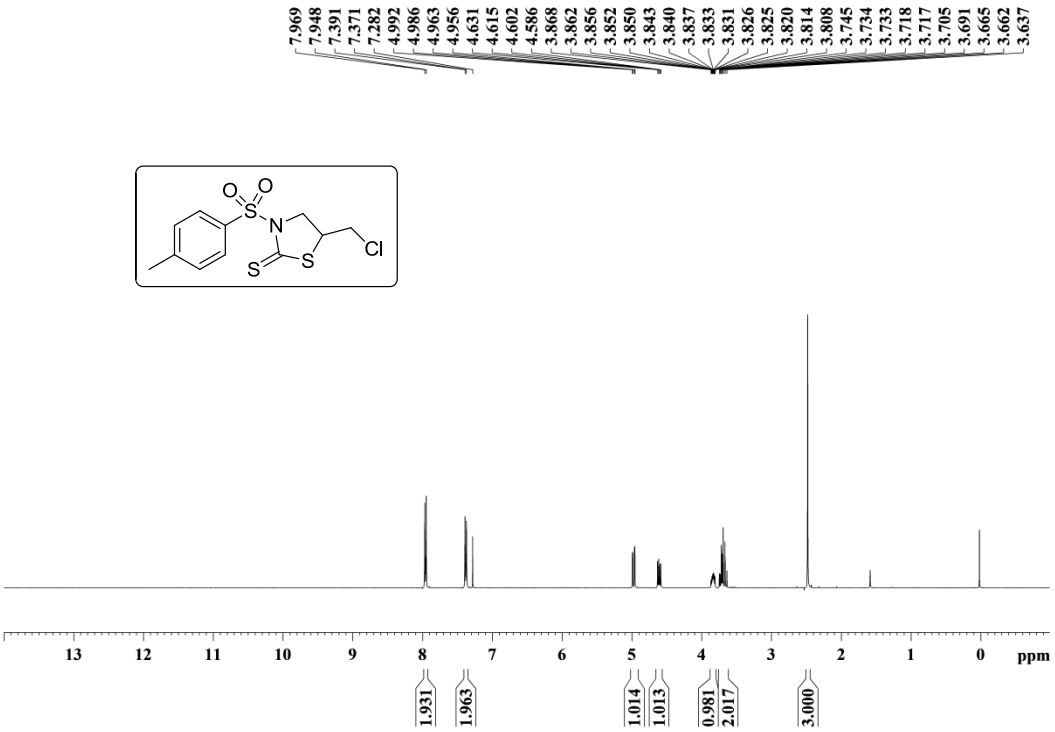


**Figure A15.** $^{1}$H NMR spectrum of compound **52**

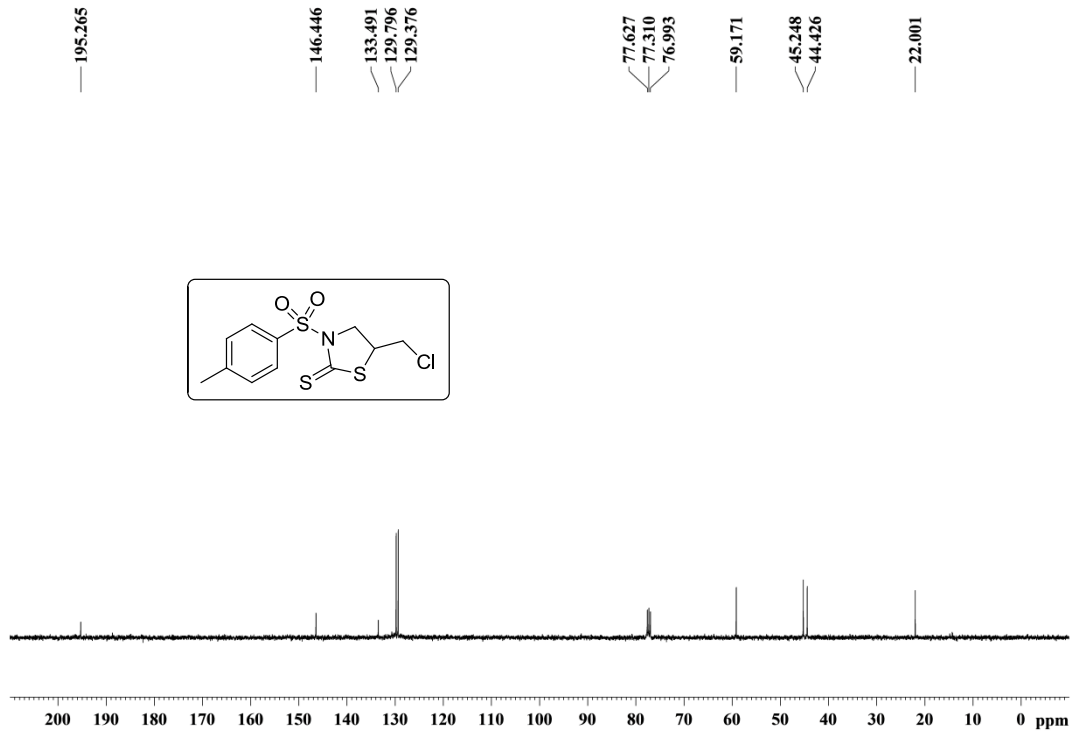


**Figure A16.** $^{13}$C NMR spectrum of compound **52**

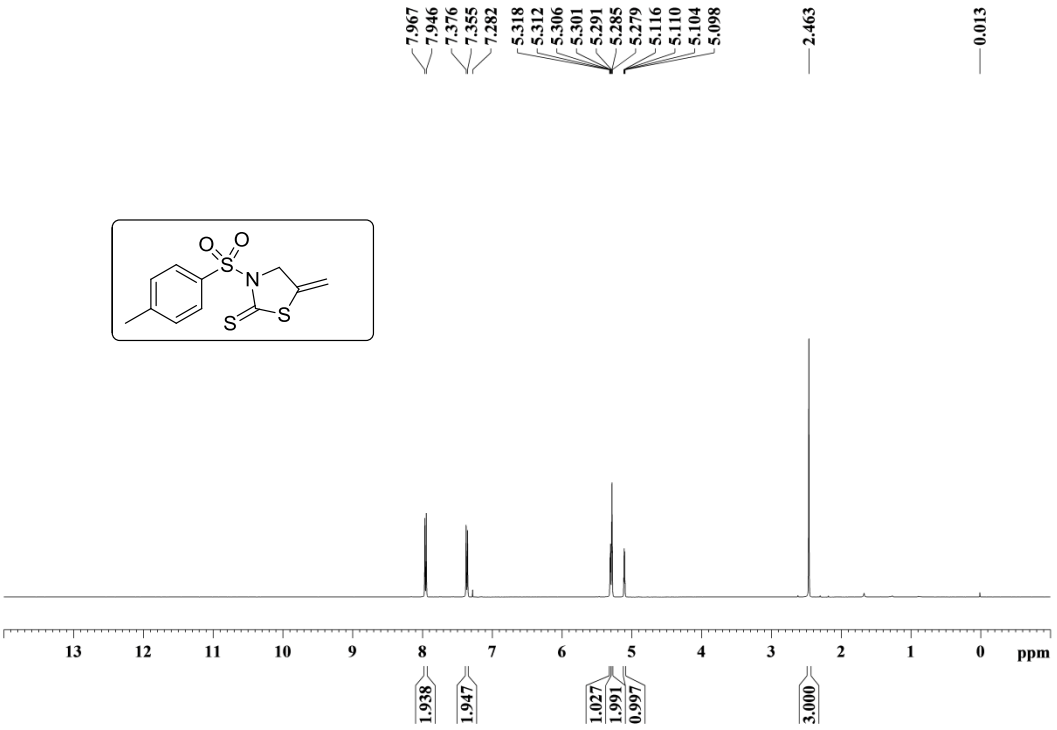


**Figure A17.** $^{1}$H NMR spectrum of compound **53**

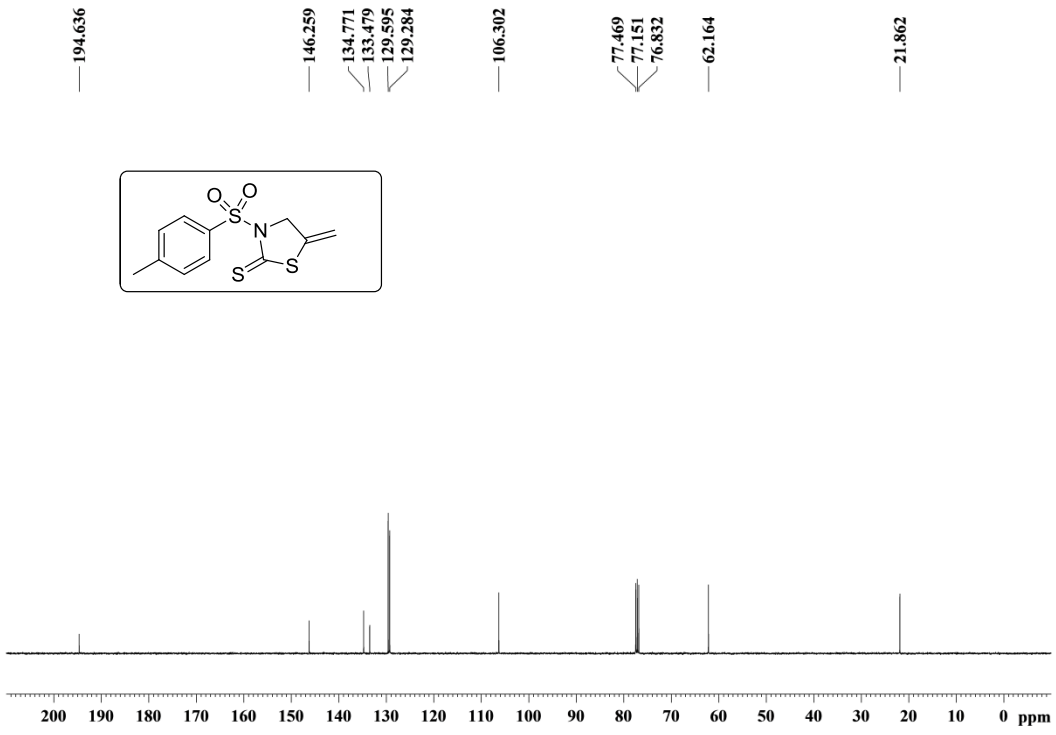


**Figure A18.** $^{13}$C NMR spectrum of compound **53**

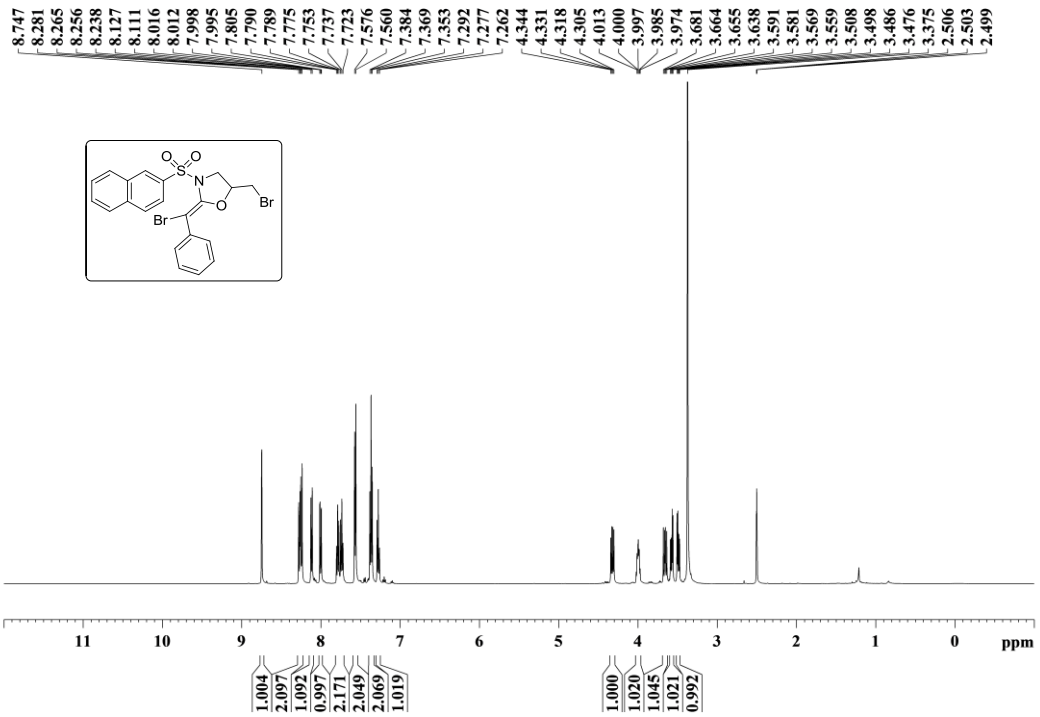


**Figure A19.** $^{1}$H NMR spectrum of compound **59**

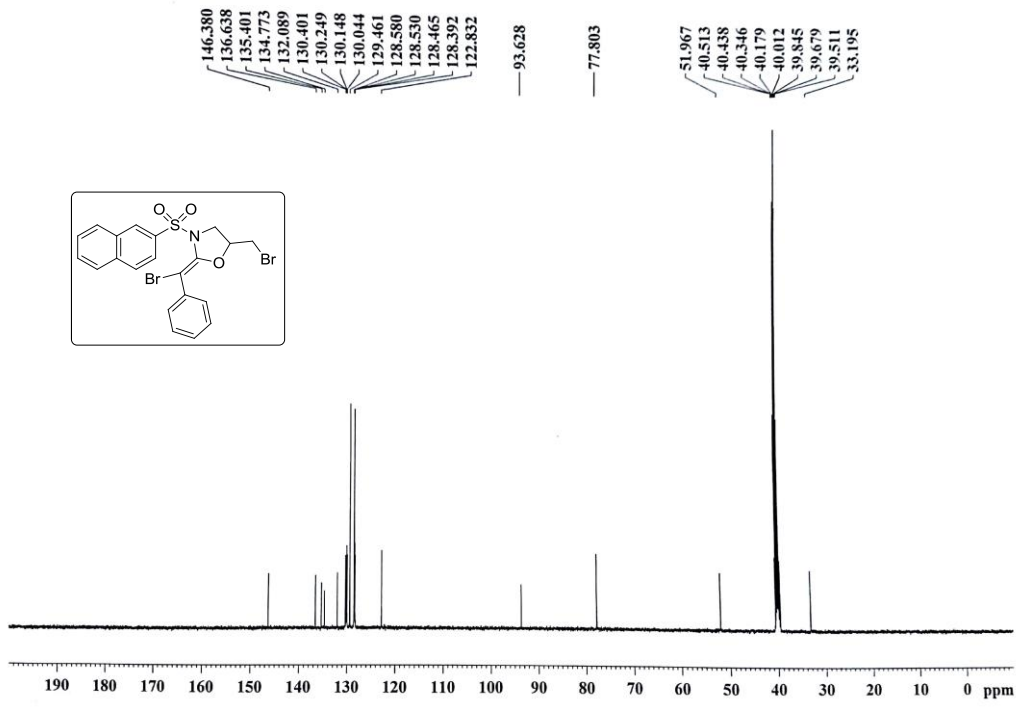


**Figure A20.** $^{13}$C NMR spectrum of compound **59**

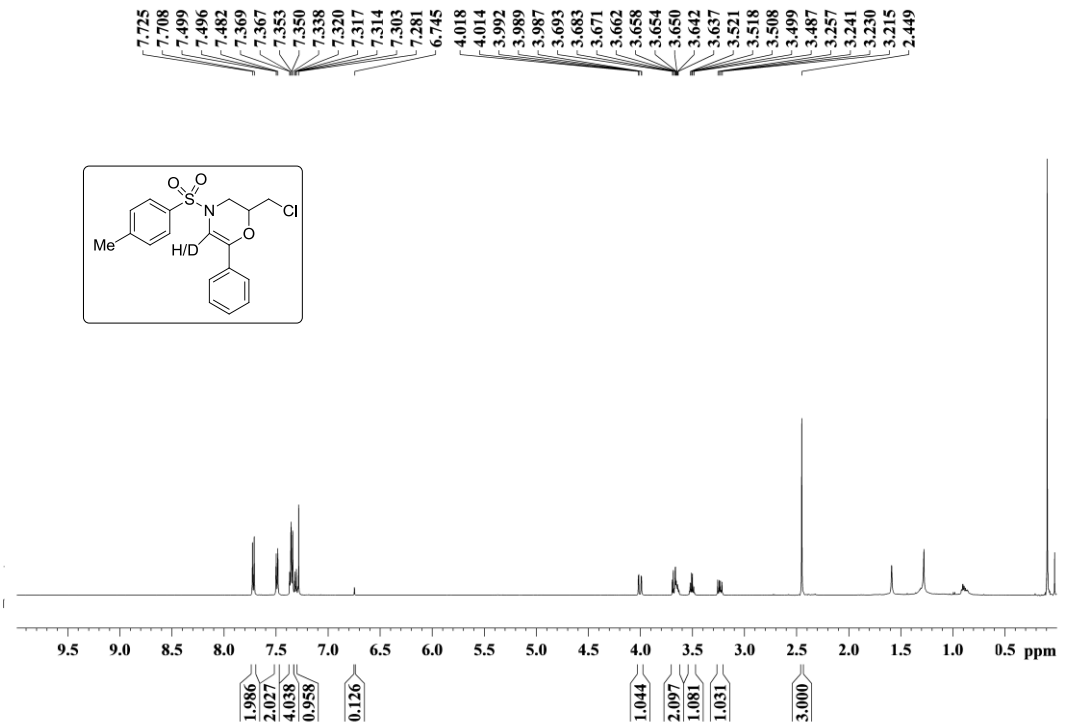


**Figure A21.** $^{1}$H NMR spectrum of compound **63'**

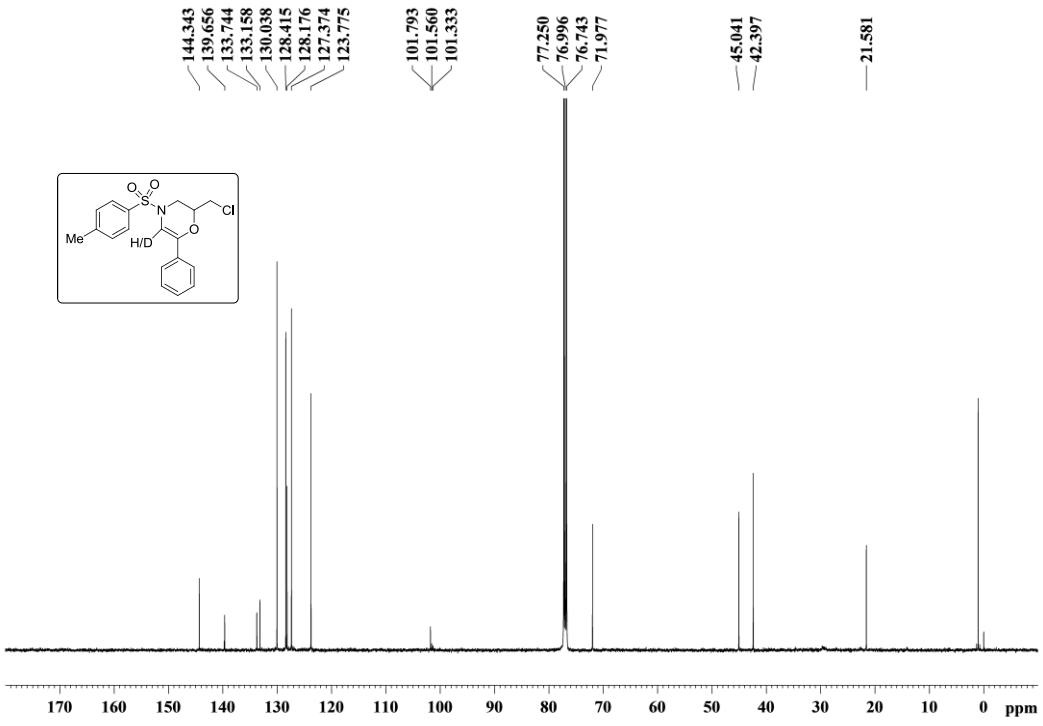


**Figure A22.** $^{13}$C NMR spectrum of compound **63'**

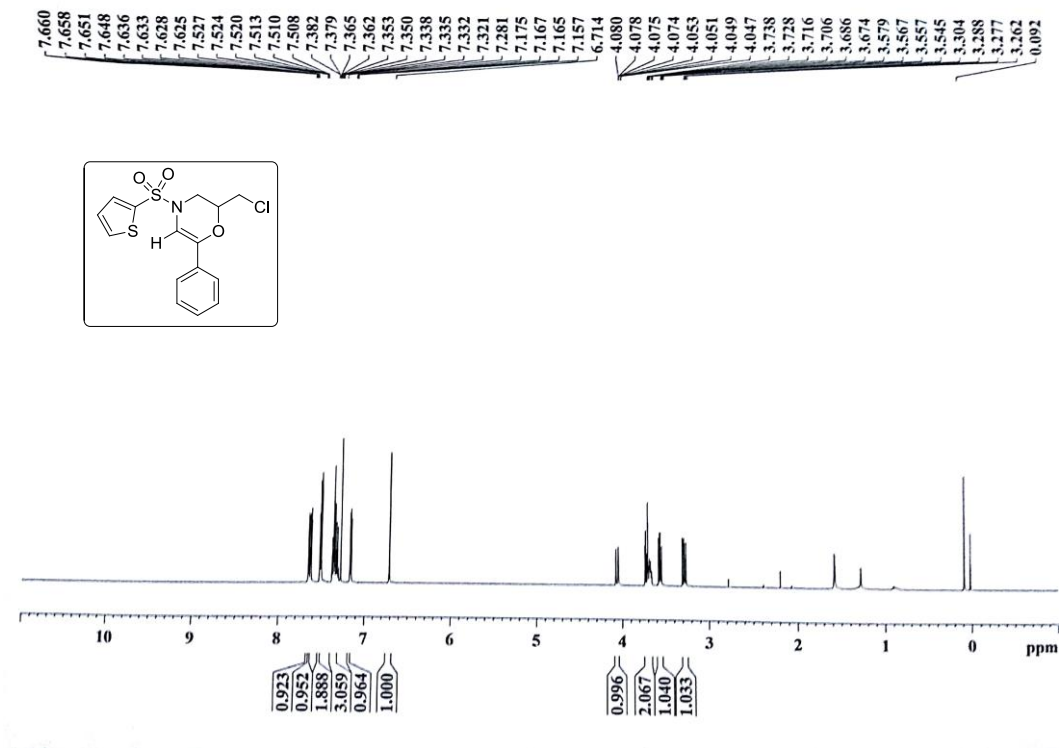


**Figure A23.** $^{1}$H NMR spectrum of compound **70**

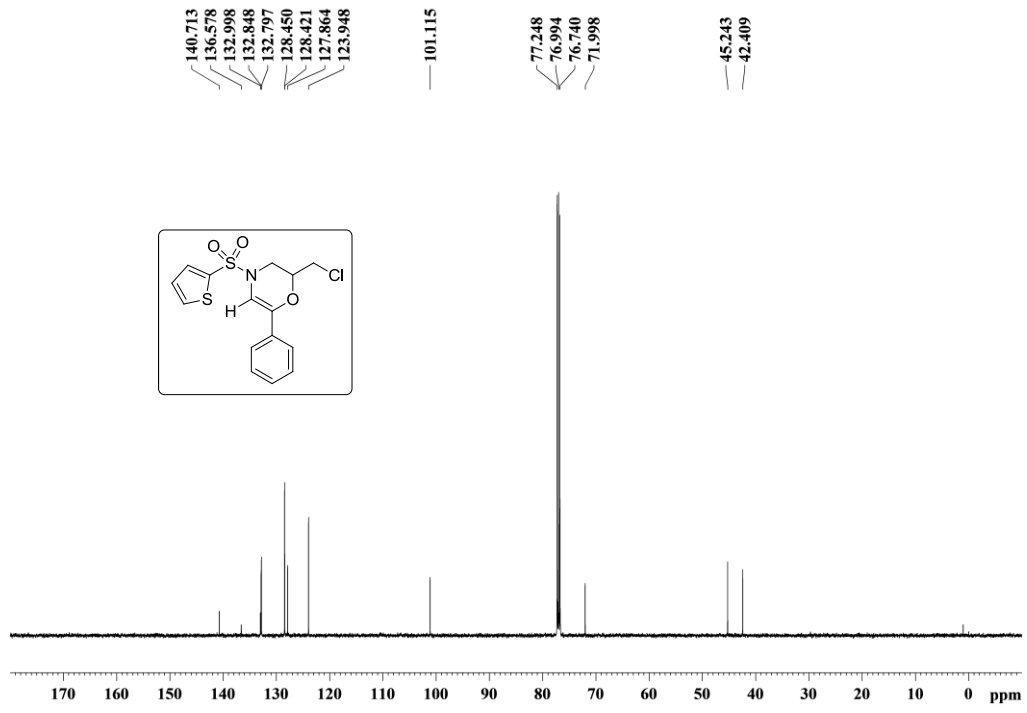


**Figure A24.** $^{13}$C NMR spectrum of compound **70**

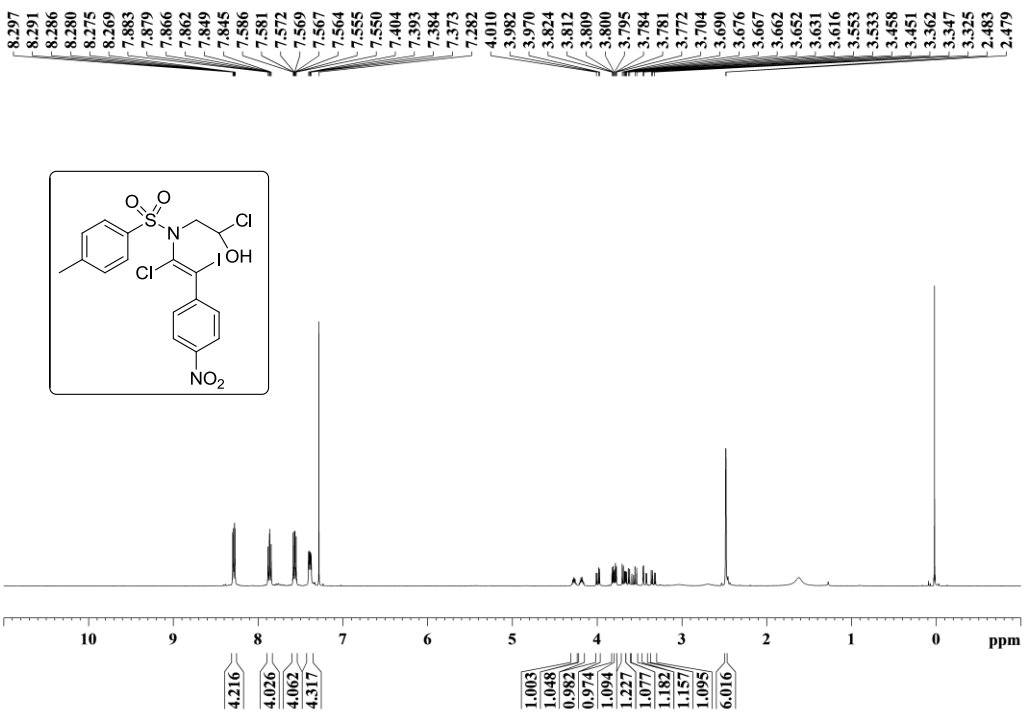


**Figure A25.** $^{1}$H NMR spectrum of compound **73**

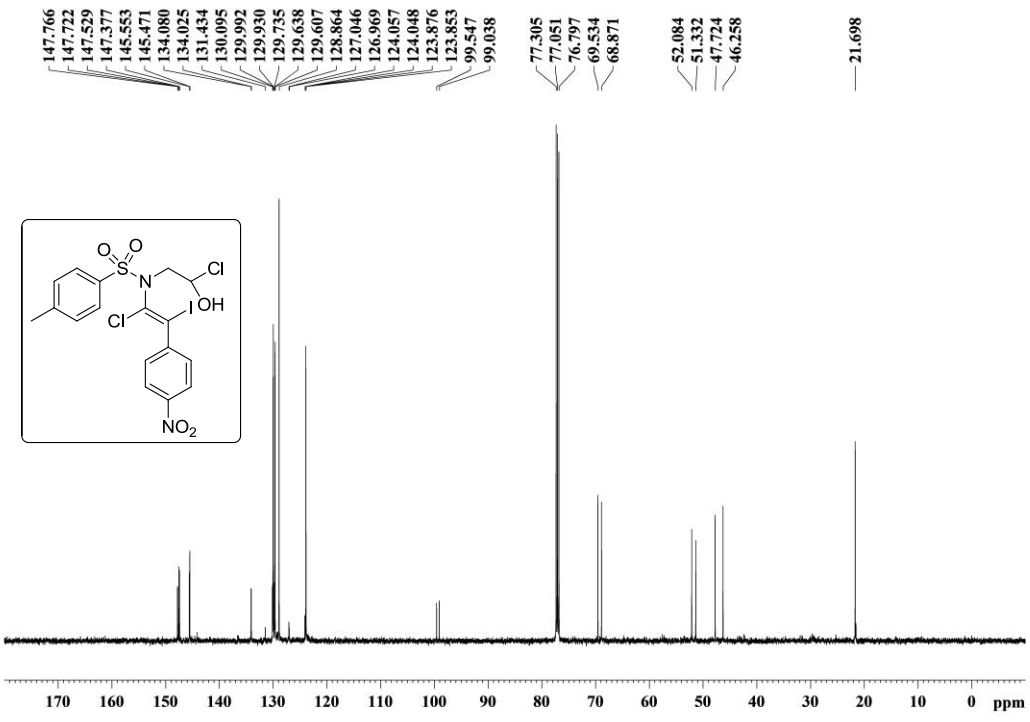


**Figure A26.** $^{13}$C NMR spectrum of compound **73**

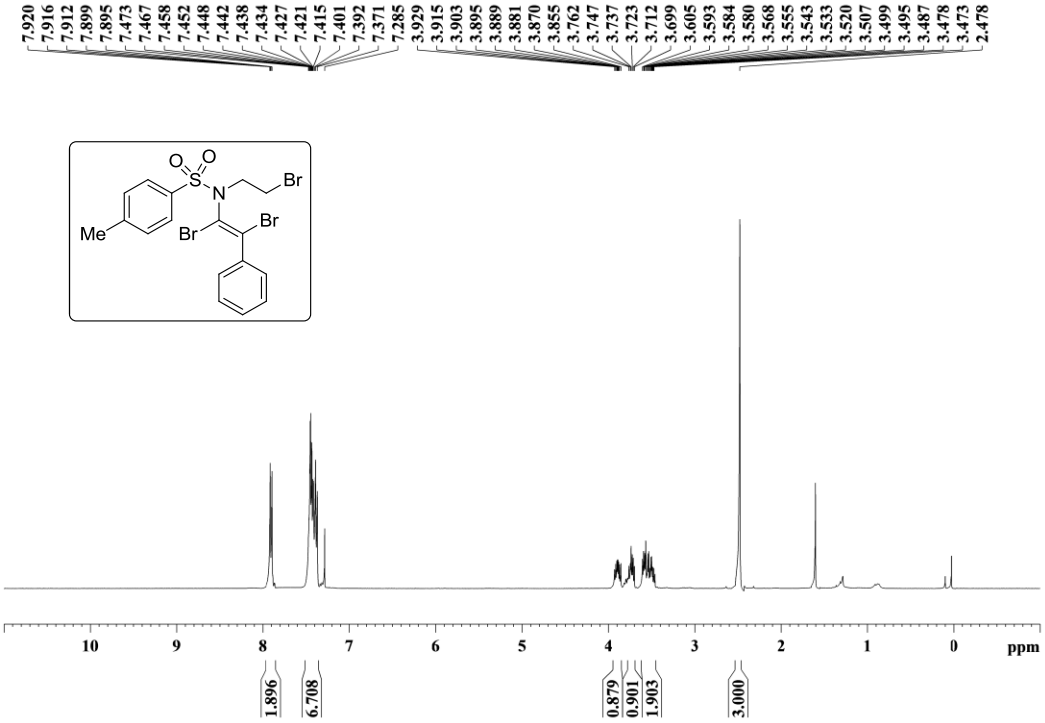


**Figure A27.** $^{1}$H NMR spectrum of compound **75**

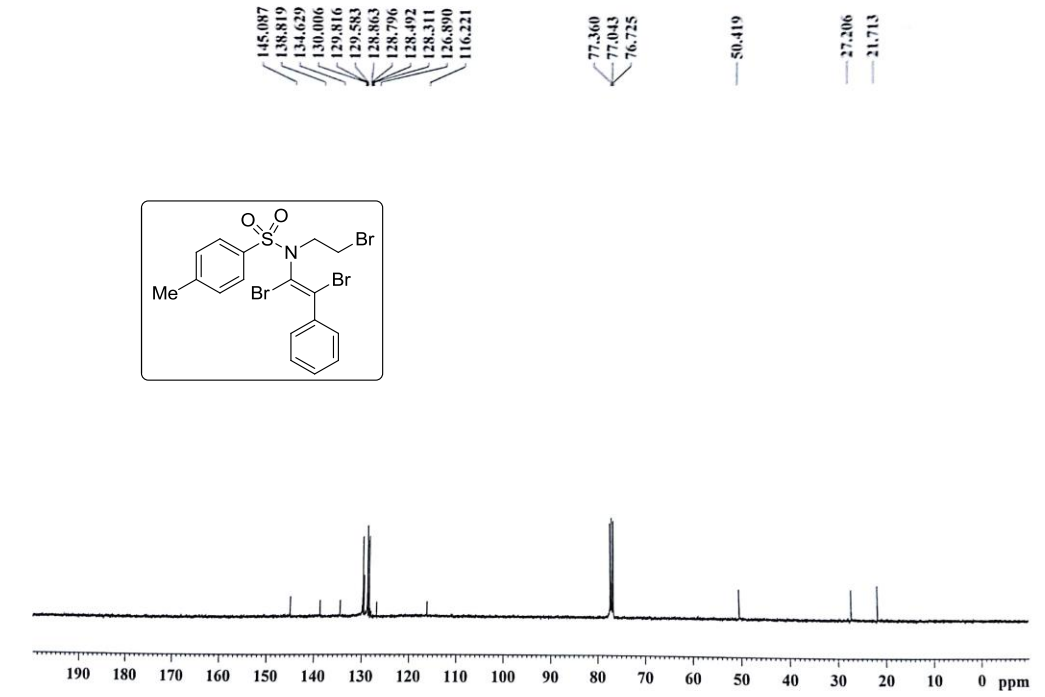


**Figure A28.** $^{13}$C NMR spectrum of compound **75**

**PART B**

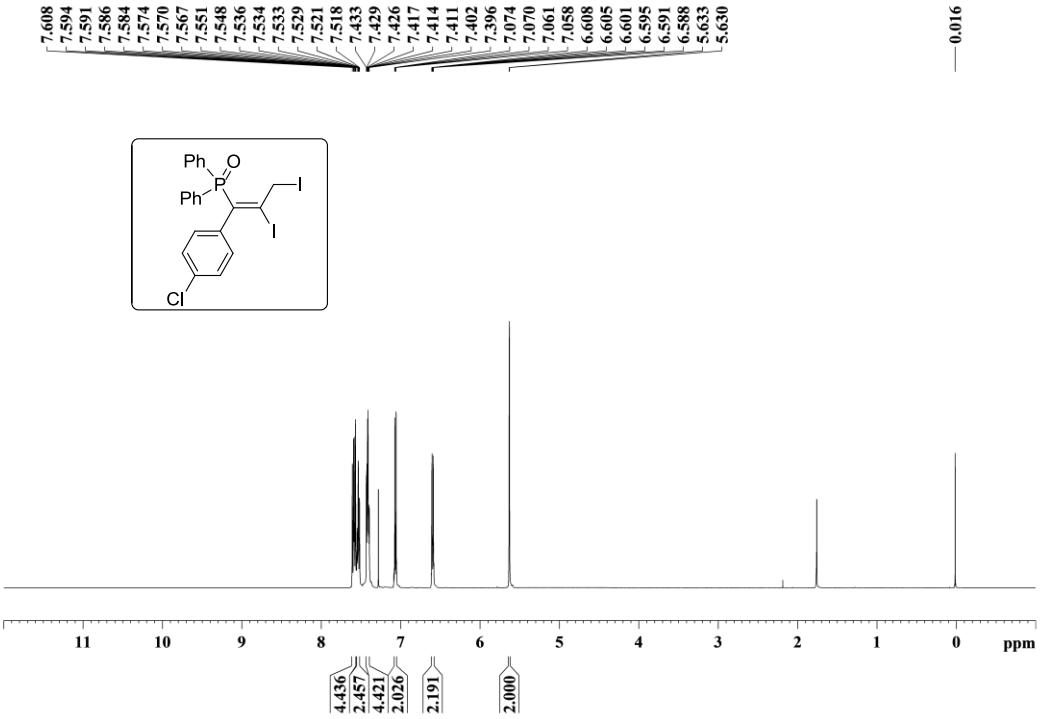


**Figure A29.** $^{1}$H NMR spectrum of compound **17**

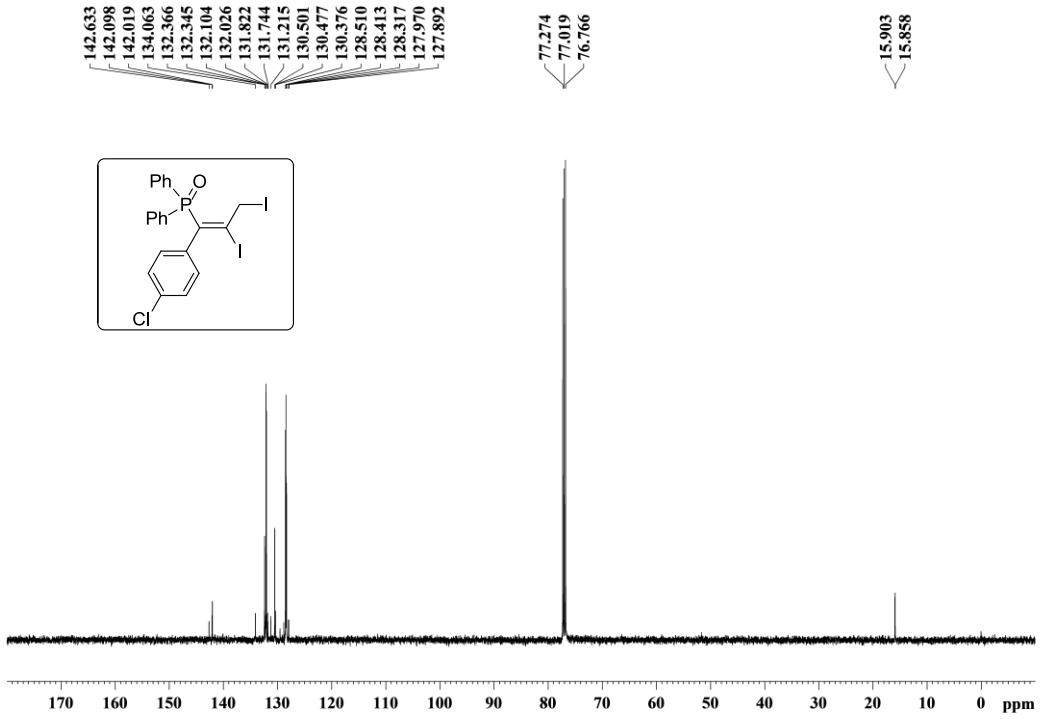


**Figure A30.** $^{13}$C NMR spectrum of compound **17**

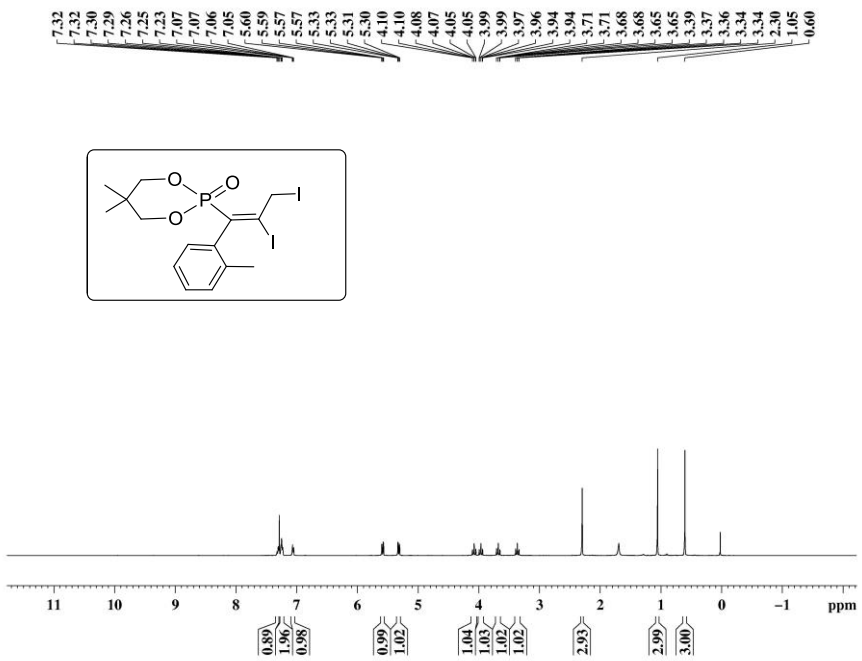

**Figure A31.** $^{1}$H NMR spectrum of compound **20**

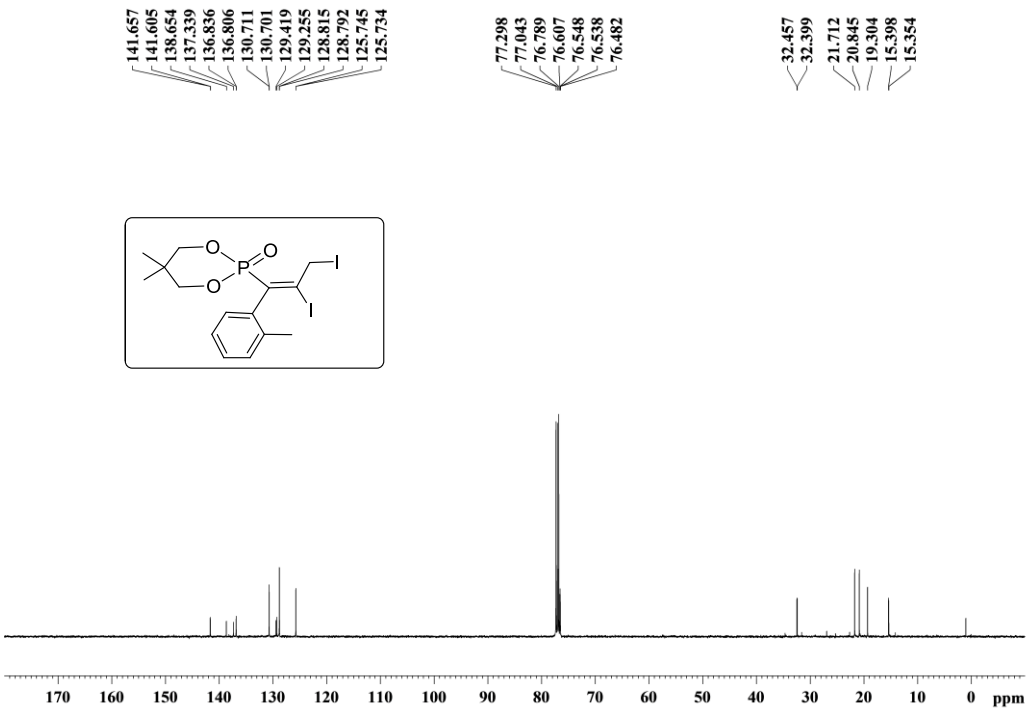

**Figure A32.** $^{13}$C NMR spectrum of compound **20**

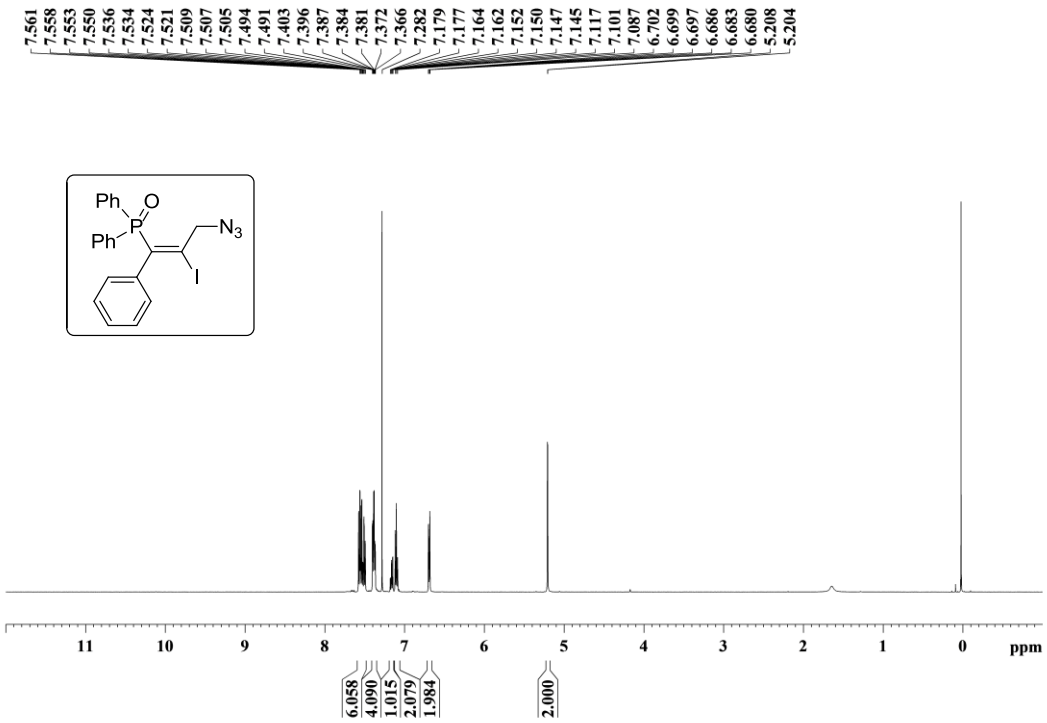


**Figure A33.** $^{1}$H NMR spectrum of compound **23**

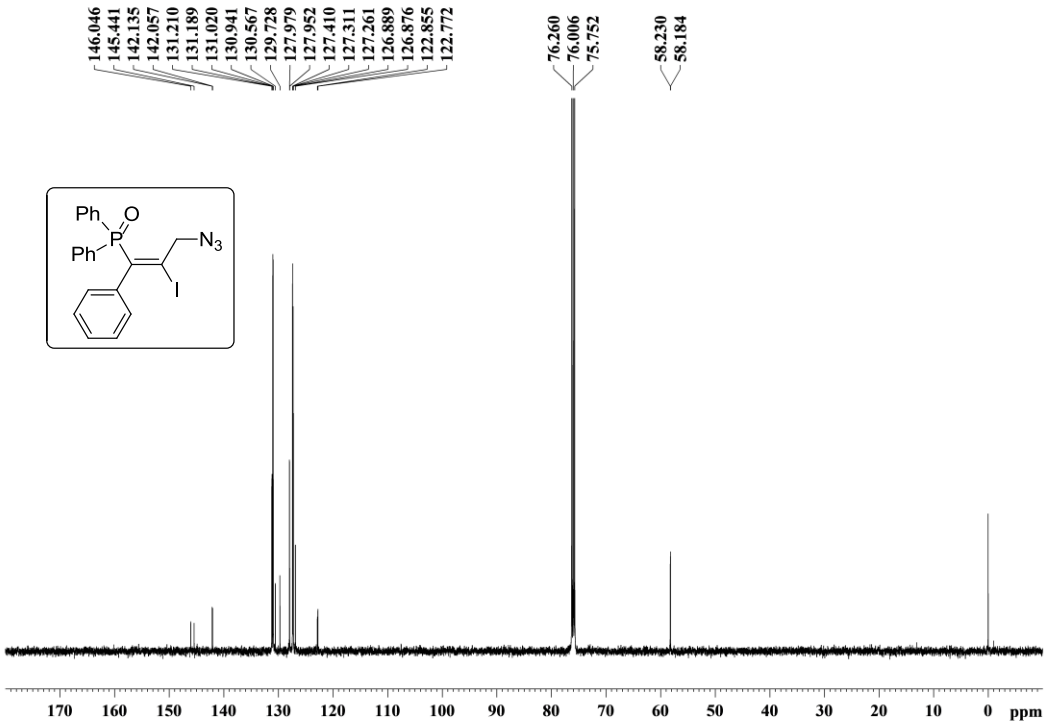


**Figure A34.** $^{13}$C NMR spectrum of compound **23**

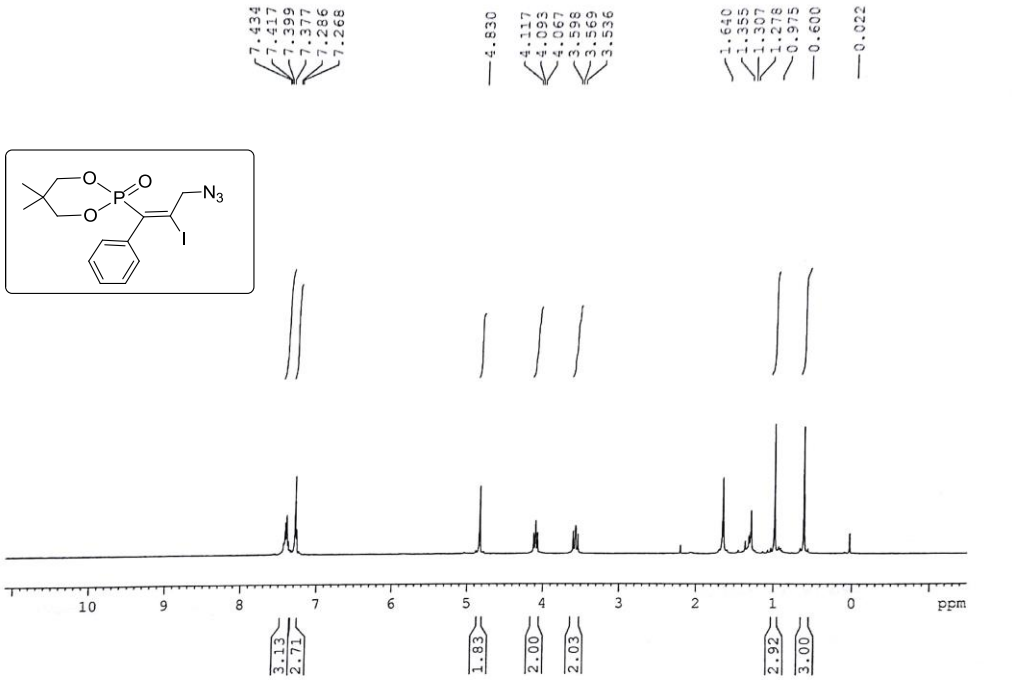


**Figure A35.** $^{1}$H NMR spectrum of compound **28**

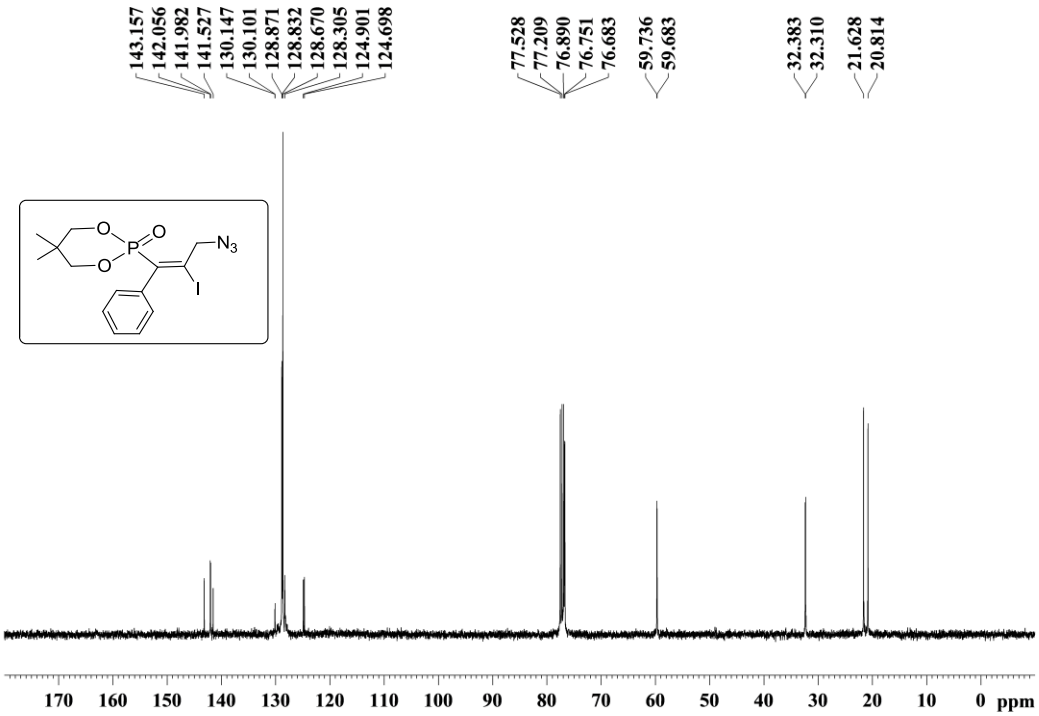


**Figure A36.** $^{13}$C NMR spectrum of compound **28**

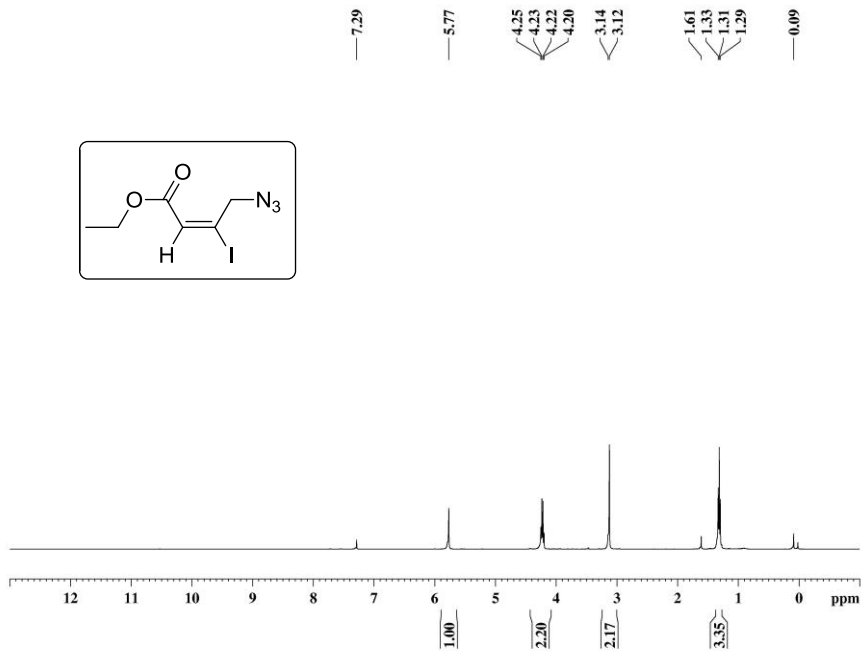


**Figure A37.** $^{1}$H NMR spectrum of compound **29**

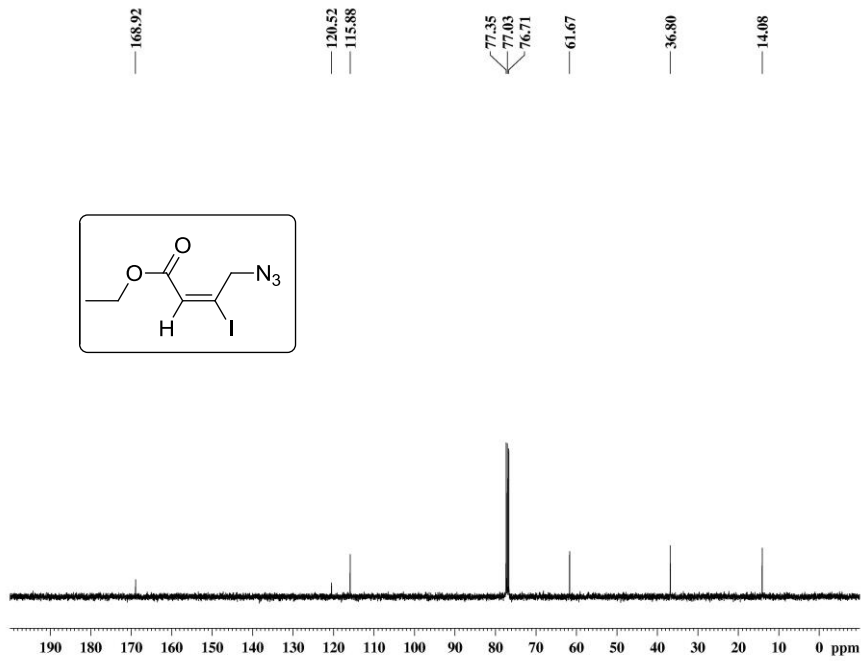


**Figure A38.** $^{13}$C NMR spectrum of compound **29**

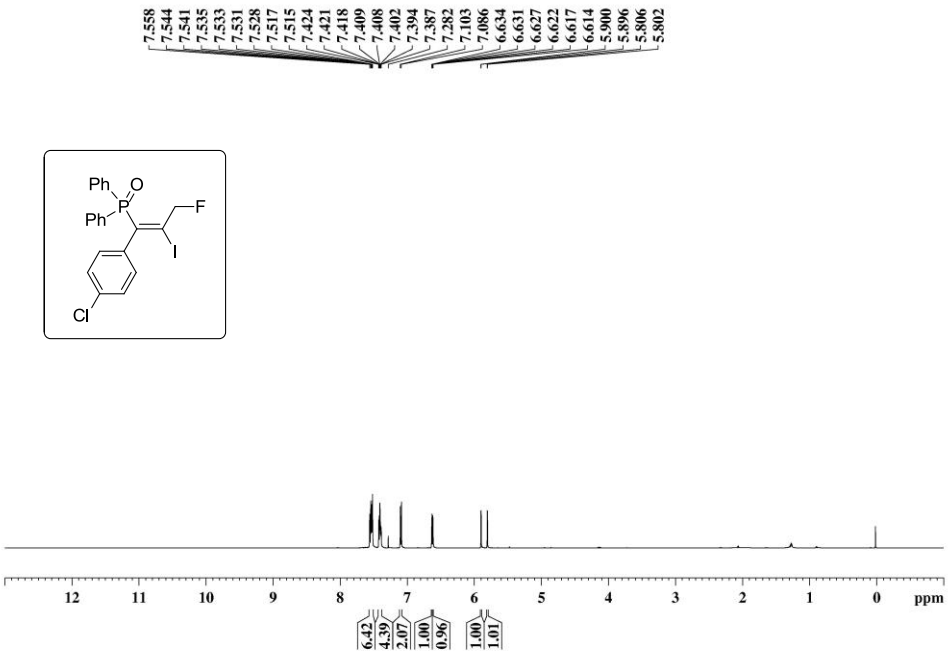


**Figure A39.** $^{1}$H NMR spectrum of compound **36**

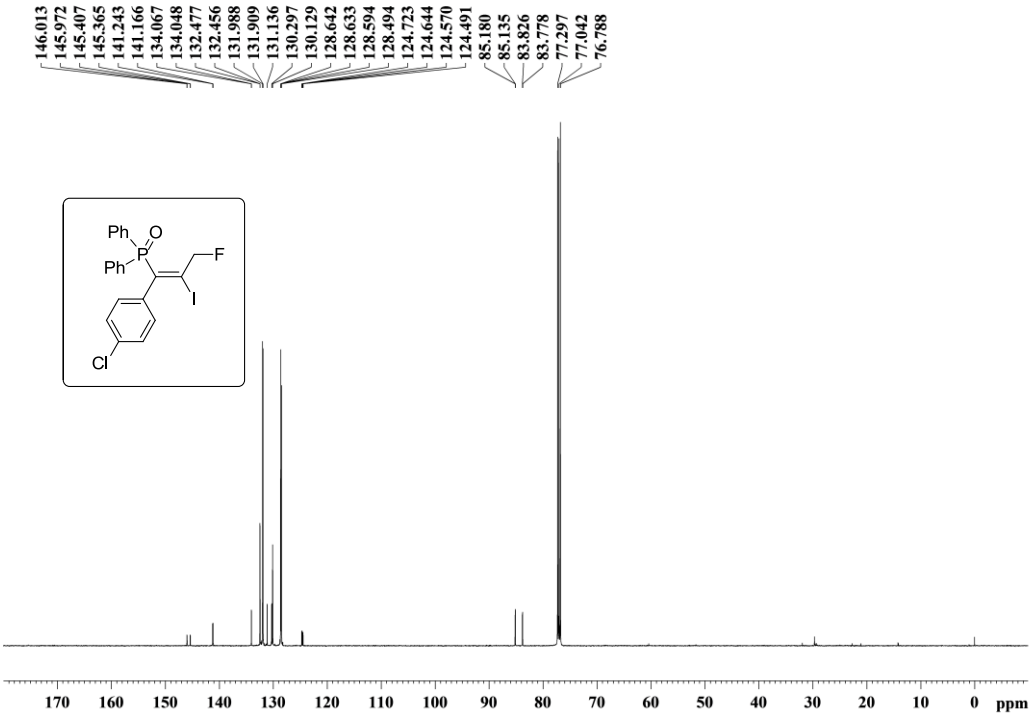


**Figure A40.** $^{13}$C NMR spectrum of compound **36**

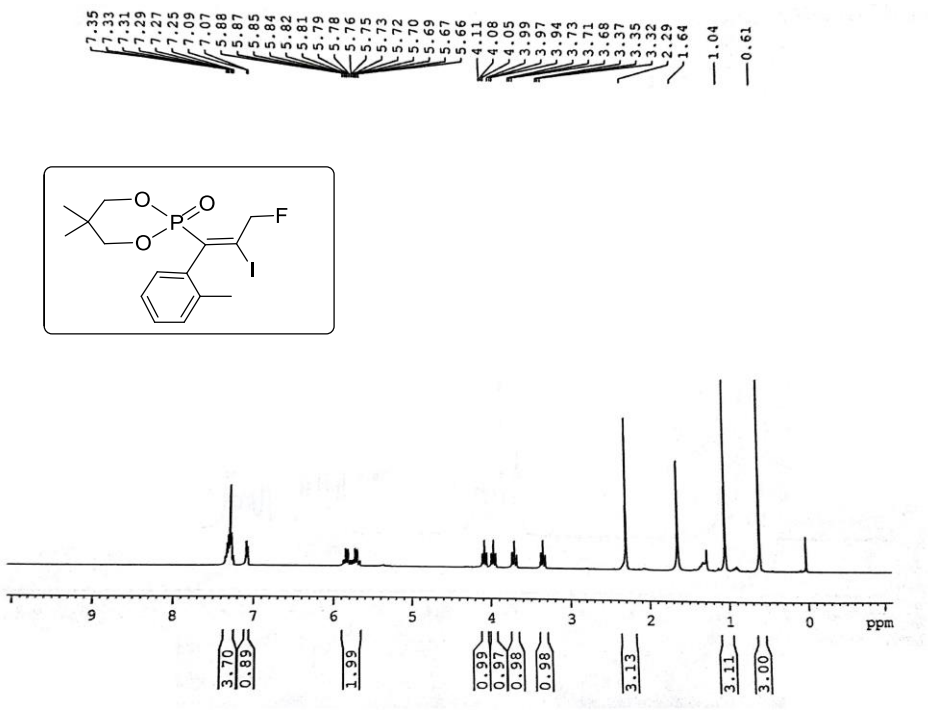


**Figure A41.** $^{1}$H NMR spectrum of compound **38**

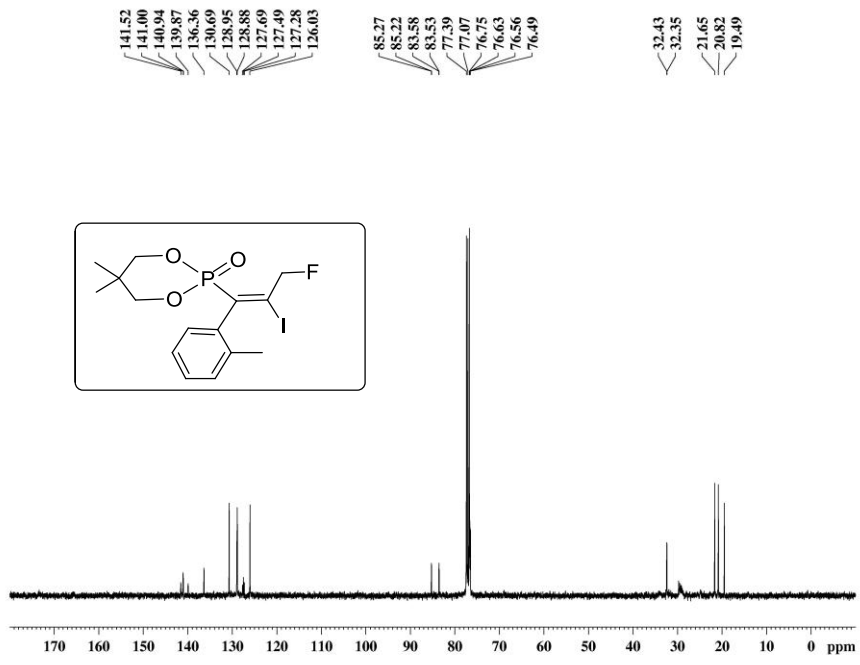


**Figure A42.** $^{13}$C NMR spectrum of compound **38**

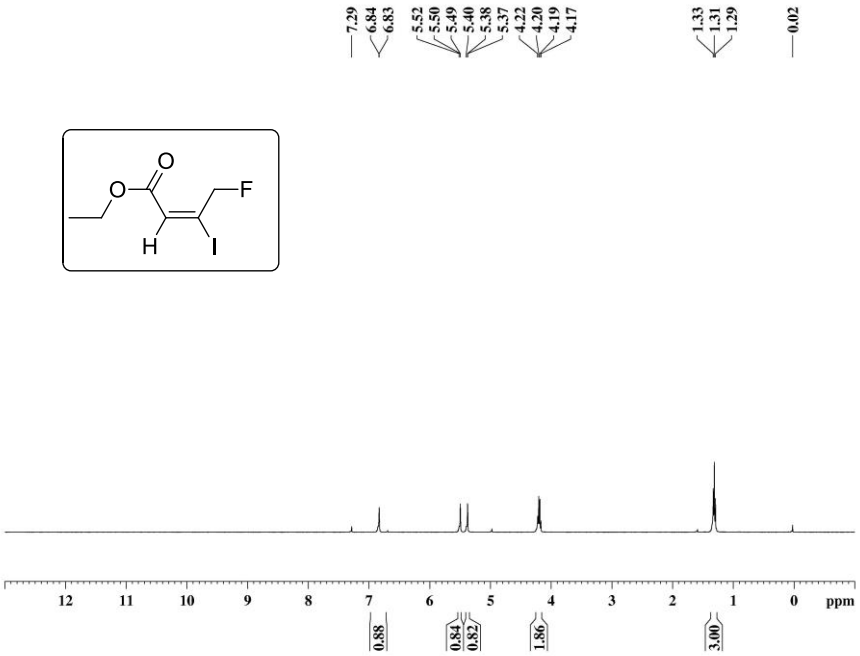


**Figure A43.** $^{1}$H NMR spectrum of compound **39**

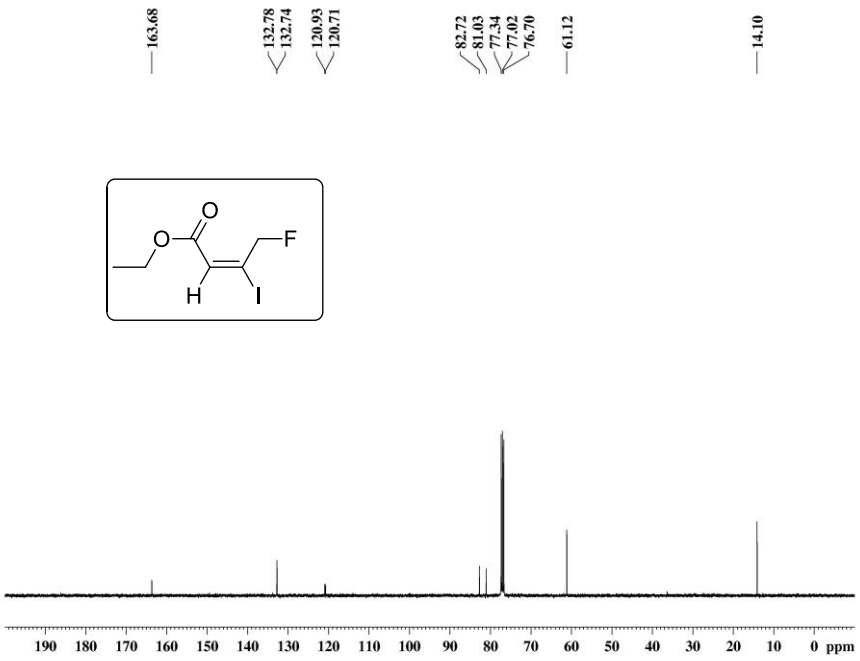


**Figure A44.** $^{13}$C NMR spectrum of compound 3**9**

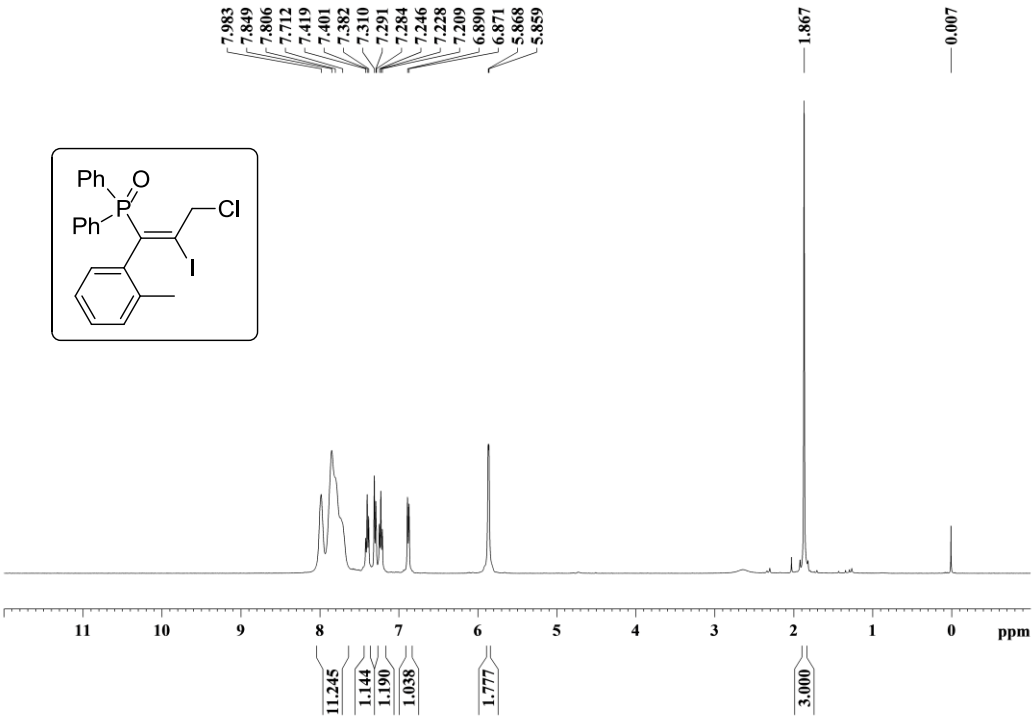


Figure **A45**. $^{1}$H NMR spectrum of compound **42**

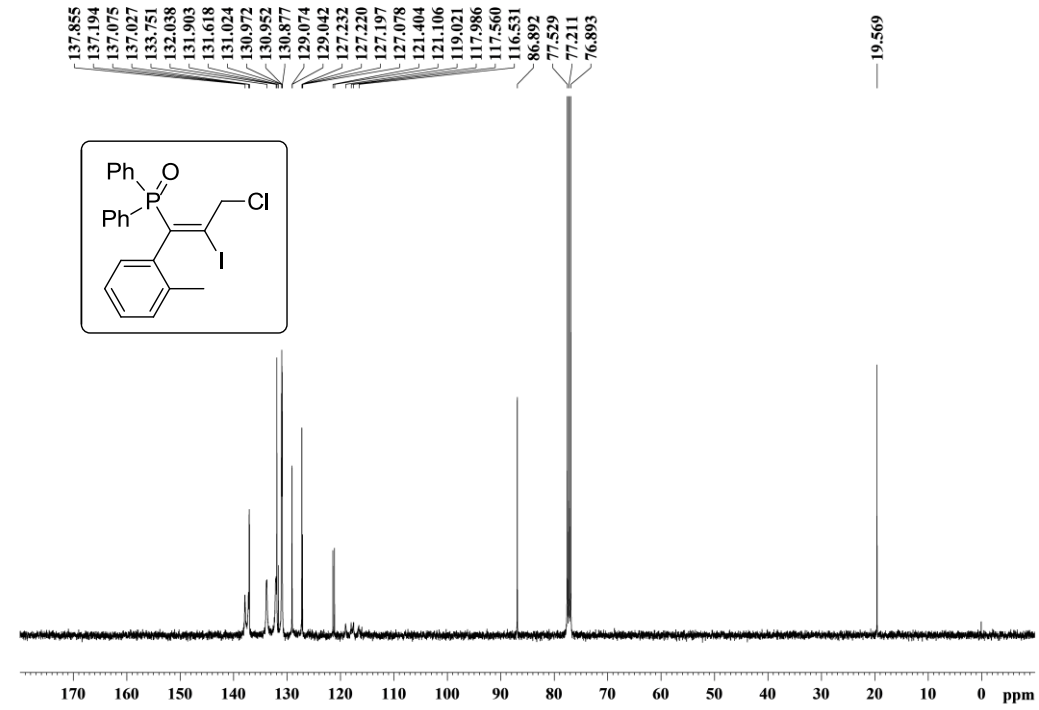


**Figure A46.** $^{13}$C NMR spectrum of compound **42**

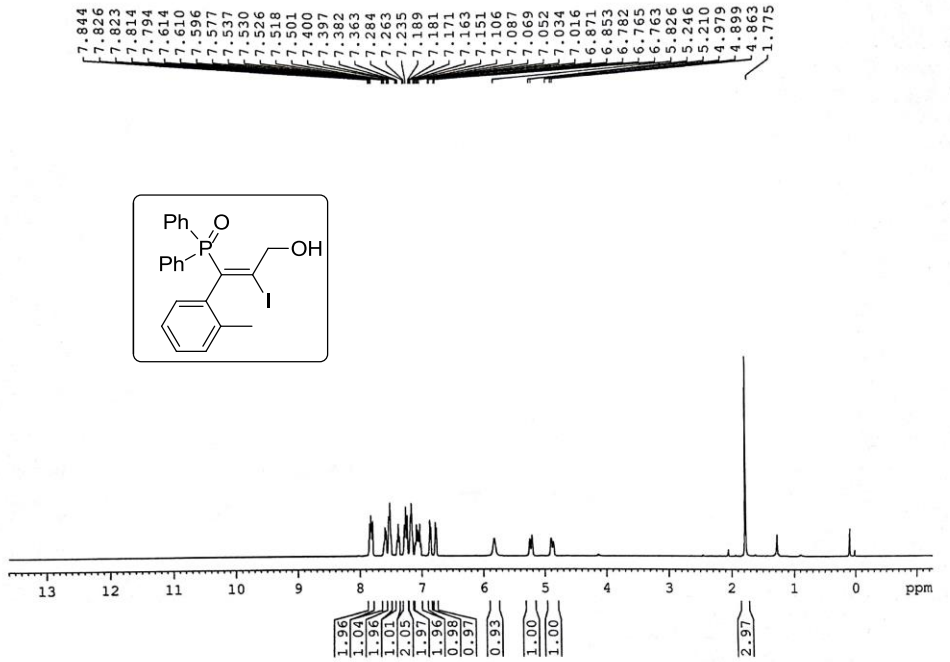


**Figure A47.** $^{1}$H NMR spectrum of compound **44**

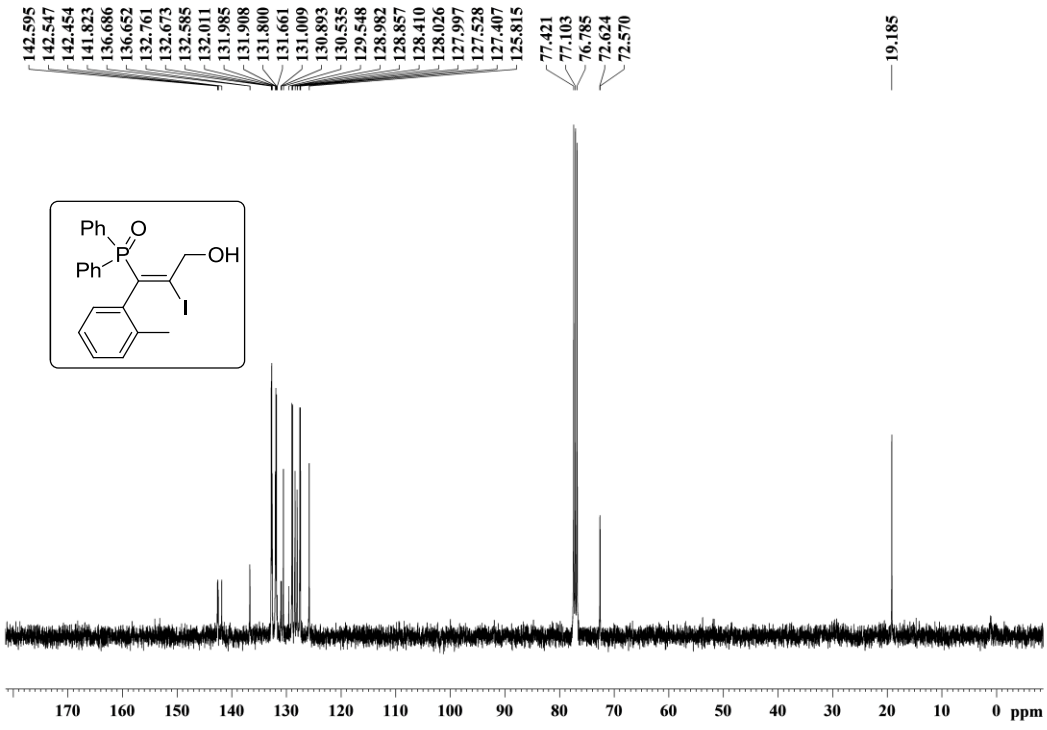


**Figure A48.** $^{13}$C NMR spectrum of compound **44**

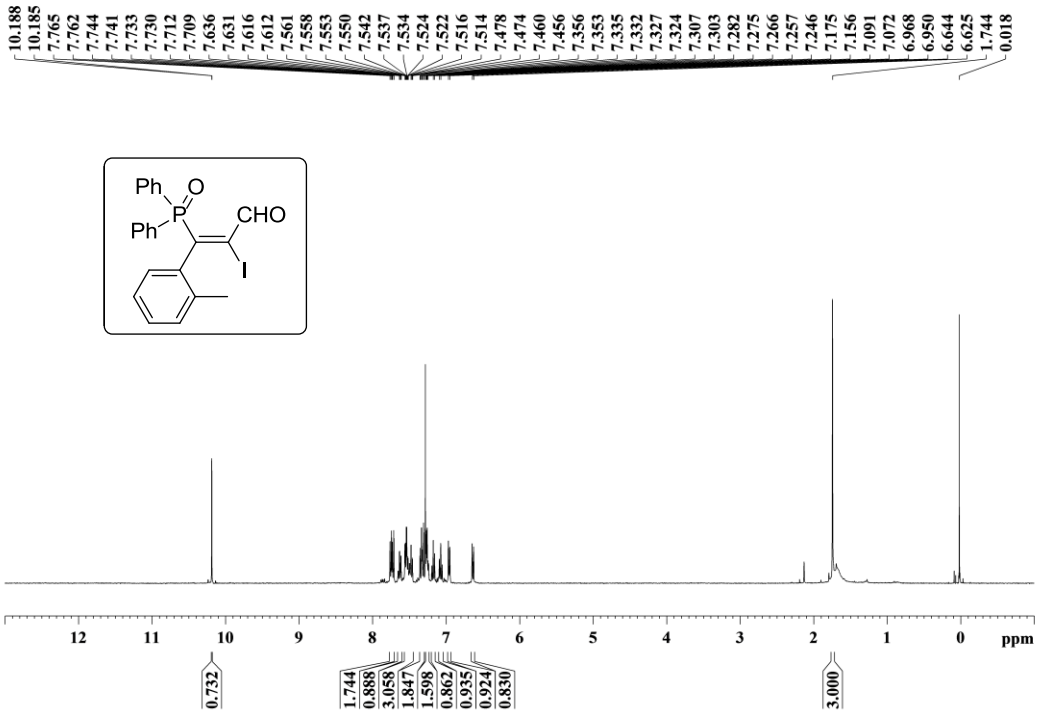


**Figure A49.** $^{1}$H NMR spectrum of compound **46**

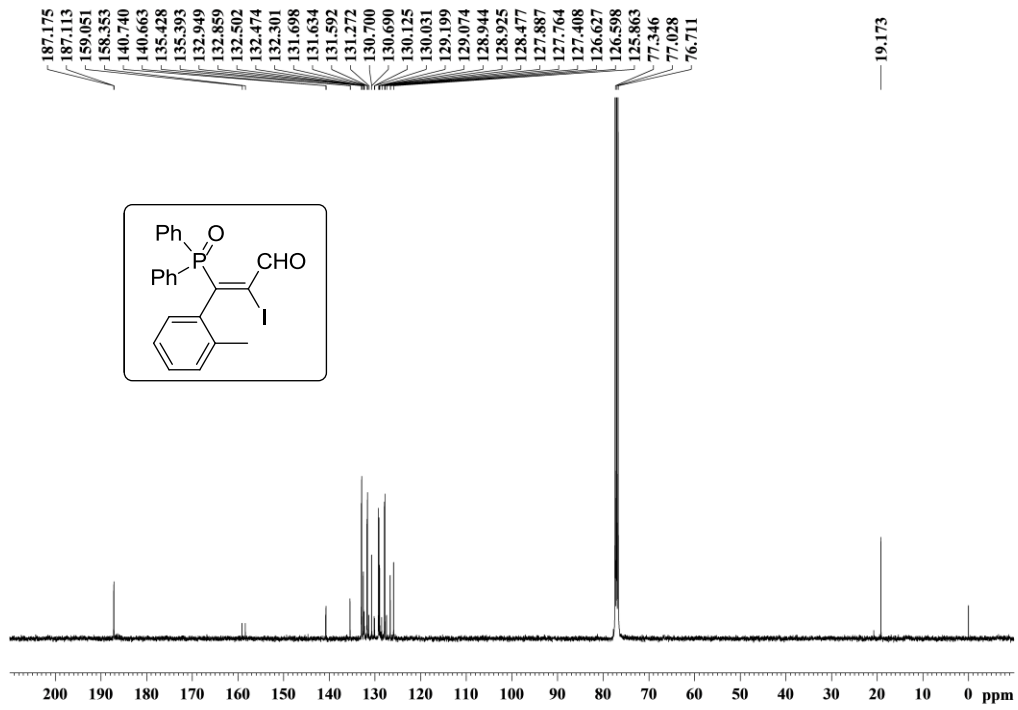


**Figure A50.** $^{13}$C NMR spectrum of compound **46**

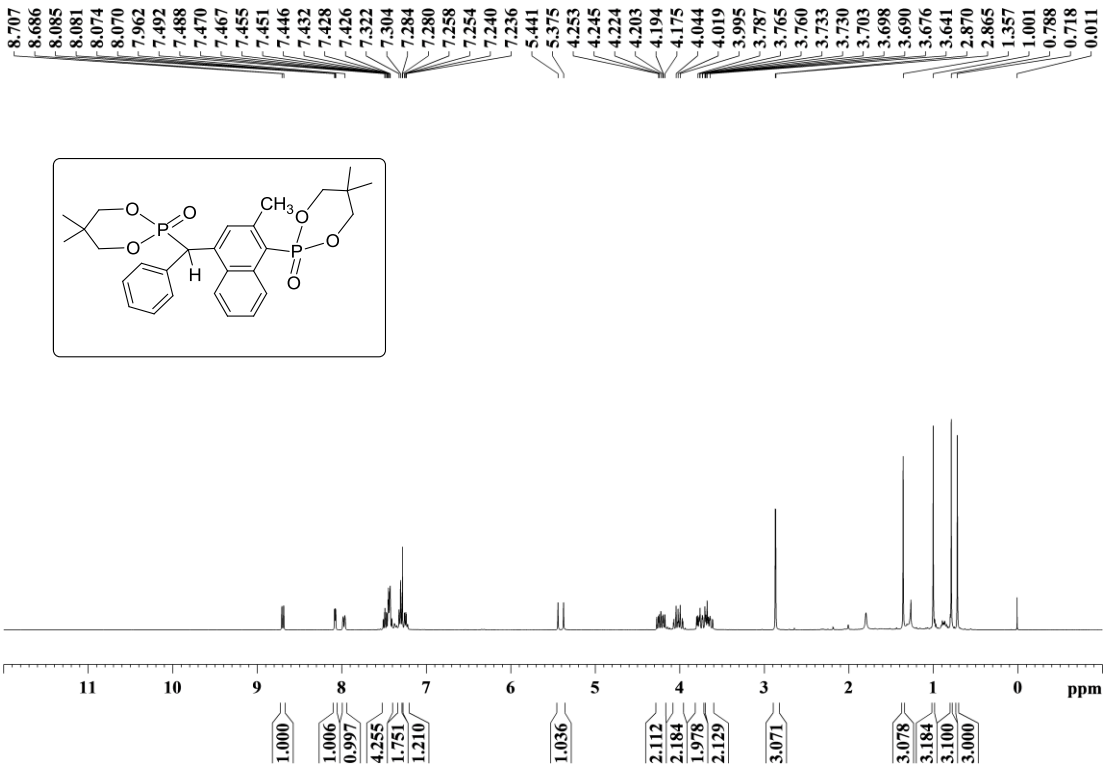


**Figure A51.** $^{1}$H NMR spectrum of compound **50**

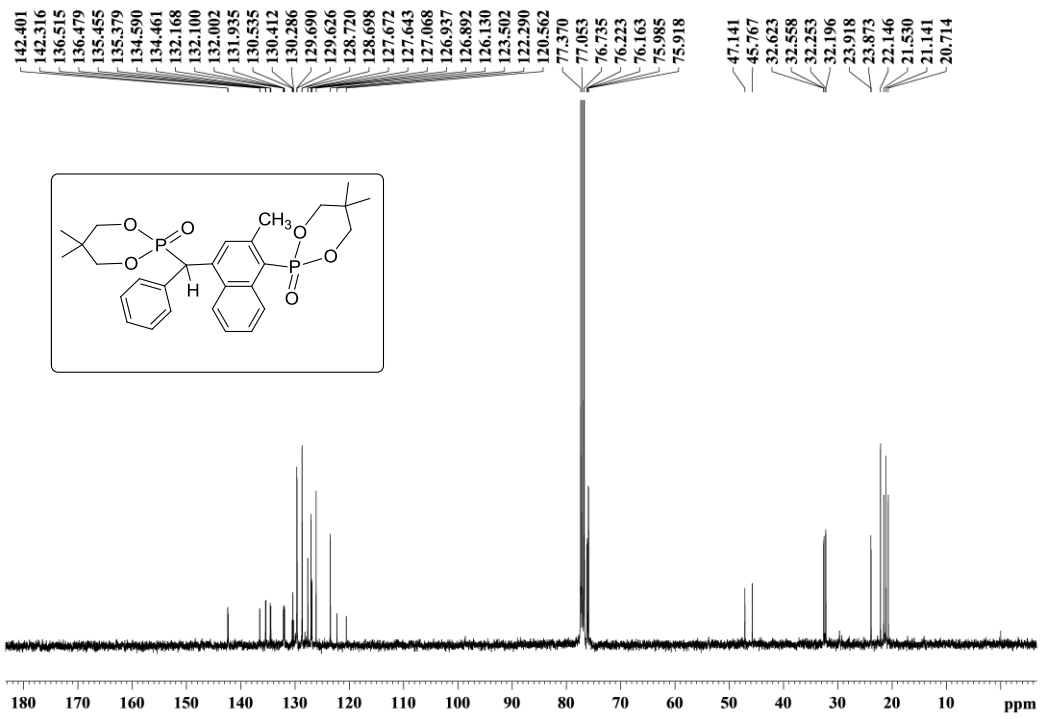


**Figure A52.** $^{13}$C NMR spectrum of compound **50**

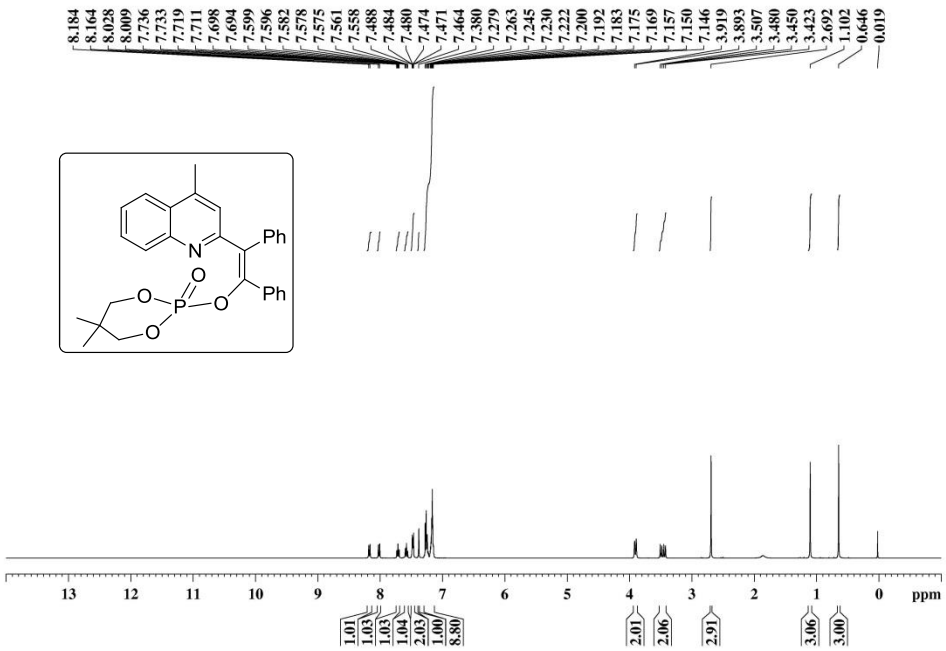


**Figure A53.** $^{1}$H NMR spectrum of compound **58**

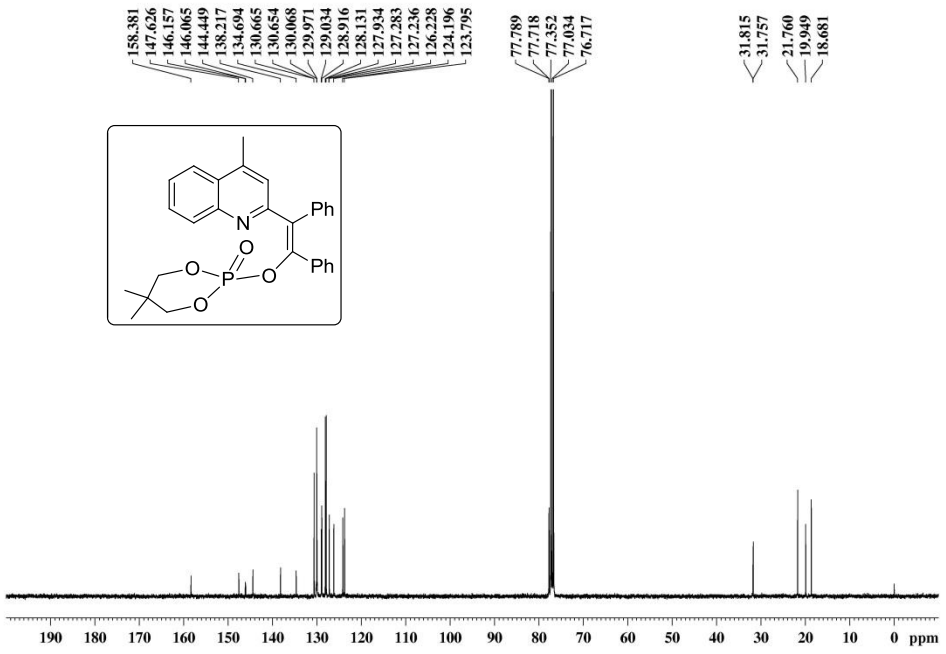


**Figure A54.** $^{13}$C NMR spectrum of compound **58**

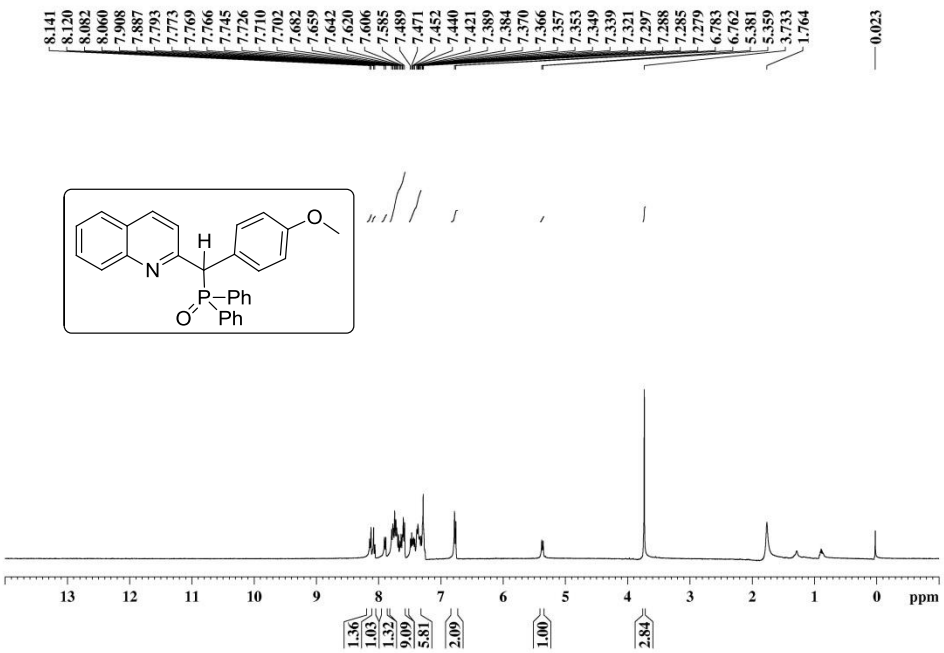


**Figure A55.** $^{1}$H NMR spectrum of compound **61**

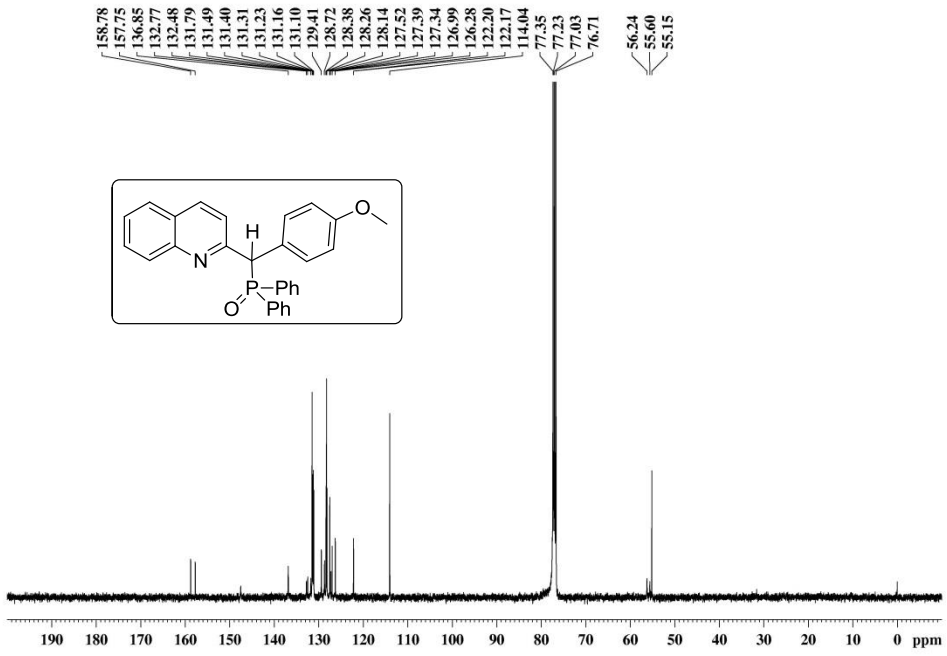


**Figure A56.** $^{13}$C NMR spectrum of compound **61**

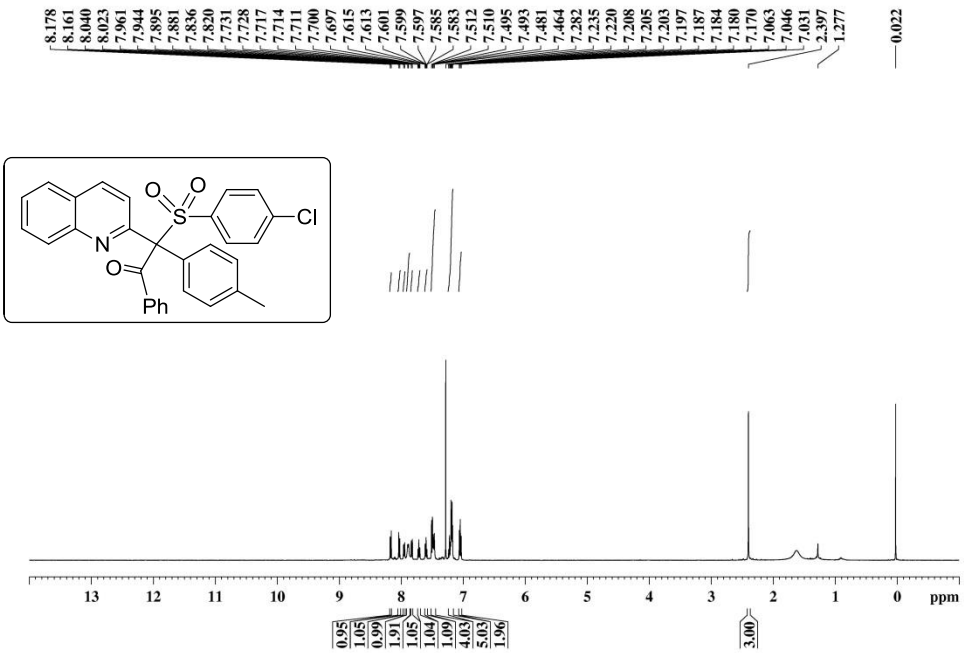


**Figure A57.** $^{1}$H NMR spectrum of compound **67**

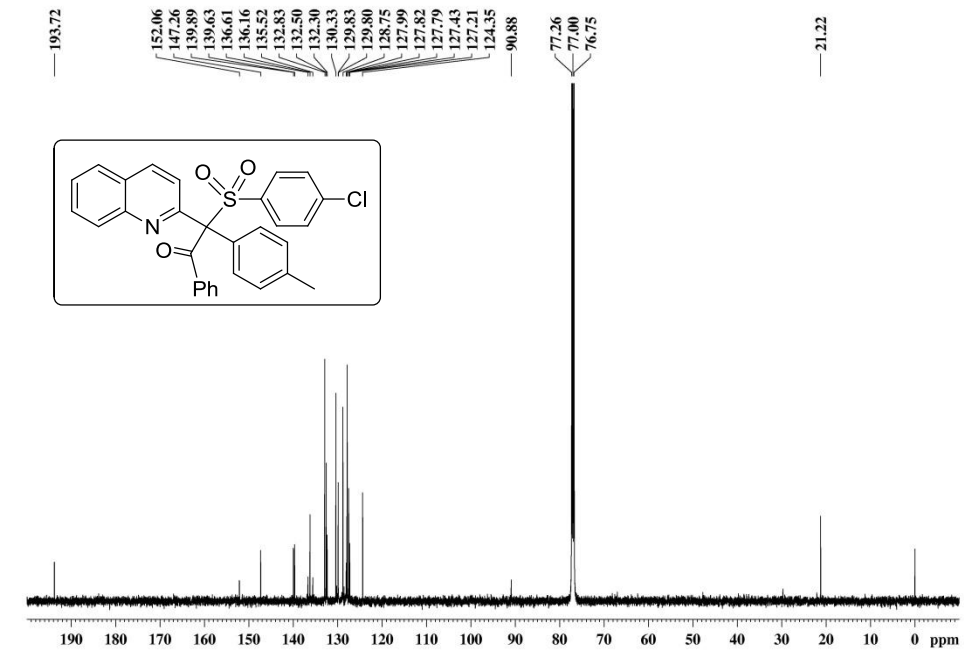


**Figure A58.** $^{13}$C NMR spectrum of compound **67**

**B) Publication numbers and atomic coordinates for X-ray structures reported in this thesis**

**I. Publication numbers for the published compounds**

**PART A: Compounds 9, 19, 32, 45, and 54 Publication no. 3 (Contents, p. xi)**
**Compound 51 Publication no. 4 (Contents, p. xi)**

**PART B: Compounds 57, 62, 68 and 70 Publication no. 1 (Contents, p. xi)**

**II. Selected atomic coordinates for compounds 52, 56, 66, 71, 73 and 75 from PART A and compounds 15, 23, 24, 25, 26, 31, 34, 35, 36, 37, 44 and 51 from PART B.**

Atomic coordinates (x $10^4$) and equivalent isotropic displacement parameters ($Å^2$ x $10^3$) for 4. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.

**PART A**

**Compound 52**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| S(1) | 758(0) | 6231(0) | 6756(0) | 60(0) |
| Cl(1) | 2988(0) | 7968(0) | 9275(0) | 85(1) |
| N(1) | 2510(1) | 6528(1) | 7229(0) | 55(1) |
| O(2) | -371(1) | 5730(1) | 7220(0) | 86(2) |
| O(1) | 460(1) | 7626(1) | 6376(0) | 82(2) |
| S(2) | 5548(0) | 6758(0) | 7573(0) | 70(1) |
| S(3) | 4329(0) | 7450(0) | 6242(0) | 78(1) |
| C(9) | 4208(1) | 6543(1) | 8229(0) | 56(1) |
| C(8) | 2641(1) | 5860(1) | 7900(0) | 59(1) |
| C(11) | 3958(1) | 6938(1) | 6984(0) | 56(1) |
| C(2) | 1187(1) | 3072(1) | 6517(0) | 53(1) |
| C(1) | 1195(1) | 4620(1) | 6257(0) | 48(1) |
| C(6) | 1549(1) | 4860(1) | 5622(0) | 59(1) |
| C(10) | 4007(1) | 8176(1) | 8547(0) | 65(2) |
| C(4) | 1879(1) | 2012(1) | 5492(0) | 62(2) |
| C(3) | 1503(1) | 1801(1) | 6128(0) | 59(1) |
| C(5) | 1903(1) | 3553(1) | 5243(0) | 65(2) |
| C(7) | 2264(1) | 624(1) | 5061(0) | 88(2) |

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**Compound 56**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Br(2) | 1156(0) | 4793(0) | 1783(0) | 47(0) |
| Br(1) | 9620(0) | 9199(0) | 1327(0) | 81(0) |
| S(1) | 3722(0) | 7311(0) | 3907(0) | 40(0) |
| O(3) | 6868(0) | 6130(0) | 2230(0) | 38(1) |
| O(2) | 2622(1) | 6237(0) | 4696(0) | 53(1) |
| O(1) | 2931(1) | 8435(0) | 4003(0) | 56(1) |
| N(1) | 4240(1) | 7094(0) | 2601(0) | 36(1) |
| F(1) | 4163(1) | 630(0) | 1665(0) | 90(1) |
| C(11) | 4918(1) | 5982(0) | 2239(0) | 31(0) |
| C(12) | 3997(1) | 4930(0) | 1876(0) | 32(0) |
| C(13) | 4714(1) | 3818(0) | 1475(0) | 30(1) |
| C(1) | 5942(1) | 7474(0) | 4718(0) | 38(1) |
| C(14) | 6149(1) | 3855(0) | 775(0) | 39(1) |
| C(6) | 6840(1) | 6454(0) | 4903(0) | 45(1) |
| C(9) | 7555(1) | 7394(0) | 2299(0) | 45(1) |
| C(8) | 5688(1) | 8024(0) | 2312(0) | 40(1) |
| C(2) | 6837(1) | 8612(0) | 5140(0) | 52(1) |
| C(18) | 4026(1) | 2707(0) | 1769(0) | 44(1) |
| C(5) | 8622(1) | 6585(0) | 5502(0) | 51(1) |
| C(16) | 6192(1) | 1712(0) | 664(0) | 51(1) |
| C(17) | 4784(1) | 1691(0) | 1358(0) | 50(1) |
| C(15) | 6857(1) | 2814(0) | 3819(0) | 49(1) |
| C(4) | 9520(1) | 7715(1) | 5925(0) | 52(1) |
| C(3) | 8595(1) | 8718(0) | 5743(0) | 58(1) |
| C(10) | 8594(1) | 7537(0) | 1320(0) | 58(1) |
| C(7) | 11473(1) | 7848(1) | 6601(0) | 79(2) |

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**Compound 66**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| S(1) | 1251(0) | 6083(0) | 5411(0) | 41(0) |
| Cl(1) | 1117(0) | 2775(0) | 2890(0) | 81(0) |
| O(3) | 2392(0) | 3816(0) | 4000(0) | 47(0) |
| O(2) | 1691(0) | 6962(0) | 5595(0) | 53(0) |
| O(1) | 479(0) | 6184(0) | 5243(0) | 57(0) |
| N(1) | 1590(0) | 5564(0) | 4531(0) | 40(0) |
| C(13) | 3515(0) | 4338(0) | 4010(0) | 37(0) |
| C(12) | 2364(0) | 5545(0) | 4473(0) | 37(0) |
| C(11) | 2726(0) | 4740(0) | 4177(0) | 37(0) |
| C(1) | 1401(0) | 5166(0) | 6224(0) | 39(0) |
| C(6) | 2103(0) | 5041(0) | 6582(0) | 44(1) |
| C(5) | 2254(0) | 4225(0) | 7124(0) | 49(1) |
| C(9) | 1680(0) | 3715(0) | 4358(0) | 44(1) |
| C(18) | 3889(0) | 5645(0) | 3853(0) | 45(1) |

| | | | | |
|---|---|---|---|---|
| C(14) | 3916(0) | 3835(0) | 4027(0) | 46(1) |
| C(4) | 1716(0) | 3526(0) | 7328(0) | 49(1) |
| C(2) | 849(0) | 4482(0) | 6430(0) | 51(1) |
| C(8) | 1227(0) | 4652(0) | 4163(0) | 45(1) |
| C(16) | 5040(0) | 4745(0) | 3775(0) | 48(1) |
| C(3) | 1013(0) | 3685(0) | 6978(0) | 54(1) |
| C(17) | 4635(0) | 5640(0) | 3738(0) | 52(1) |
| C(10) | 1344(0) | 2733(0) | 4012(0) | 56(1) |
| C(15) | 4665(0) | 3847(0) | 3918(0) | 53(1) |
| C(7) | 1887(0) | 2620(0) | 7891(0) | 68(1) |
| C(19) | 5856(0) | 4760(0) | 3651(0) | 69(1) |

—

**Compound 71**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 4554(0) | 2986(0) | 5589(0) | 71(0) |
| S(1) | 7368(0) | 4109(0) | 7252(0) | 50(0) |
| Cl(1) | 8090(0) | 419(0) | 8396(0) | 67(1) |
| Cl(2) | 9644(1) | 2099(0) | 3381(0) | 138(2) |
| O(2) | 5697(1) | 4252(1) | 7771(1) | 70(2) |
| C(9) | 5725(1) | 1539(1) | 6922(1) | 45(2) |
| N(1) | 7961(1) | 2648(1) | 6831(1) | 50(2) |
| O(1) | 7587(1) | 5149(1) | 6371(1) | 71(2) |
| C(8) | 7120(1) | 1648(1) | 7288(1) | 46(2) |
| C(10) | 4923(1) | 459(1) | 7368(1) | 45(2) |
| C(7) | 12745(2) | 3209(1) | 10332(1) | 88(4) |
| C(1) | 8923(1) | 3864(1) | 8159(1) | 42(2) |
| C(11) | 5216(1) | -625(1) | 6877(1) | 64(3) |
| C(6) | 10338(1) | 4335(1) | 7829(1) | 51(2) |
| C(2) | 8718(1) | 3209(1) | 9174(1) | 52(2) |
| C(5) | 11559(1) | 4123(1) | 8550(1) | 60(2) |
| C(3) | 9960(1) | 3010(1) | 9875(1) | 59(2) |
| C(14) | 3381(1) | -1581(1) | 8164(1) | 70(3) |
| C(12) | 3843(1) | 4913(1) | 8255(1) | 57(2) |
| C(13) | 4456(2) | -1645(1) | 7287(1) | 73(3) |
| O(3) | 11748(1) | 669(1) | 5306(1) | 104(3) |
| C(15) | 3074(1) | -536(1) | 8643(1) | 66(3) |
| C(4) | 11396(1) | 3450(1) | 9567(1) | 55(2) |
| C(18) | 9427(3) | 2874(2) | 4562(1) | 215(14) |
| C(16) | 9767(1) | 2097(1) | 6423(1) | 71(3) |
| C(17) | 9860(2) | 1678(2) | 5419(1) | 110(6) |

—

**Compound 73.$CH_2Cl_2$**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | -1063(0) | 5181(0) | 8666(0) | 64(0) |
| S(1) | 3092(0) | 2817(0) | 9354(0) | 59(1) |
| Cl(1) | 2952(0) | 3026(0) | 6955(0) | 82(1) |
| Cl(2) | 3512(1) | 8727(0) | 7235(0) | 123(1) |
| O(1) | 1729(1) | 2140(1) | 9392(0) | 74(2) |
| O(2) | 3338(1) | 3451(1) | 10061(1) | 84(2) |
| N(1) | 2830(1) | 4008(1) | 8455(1) | 55(2) |
| C(1) | 4943(1) | 1786(1) | 9165(1) | 48(2) |
| C(11) | 1882(1) | 3823(1) | 7770(1) | 55(3) |
| C(12) | 286(1) | 4210(1) | 7695(1) | 56(3) |
| C(4) | 7847(1) | 2066(1) | 8823(1) | 56(3) |
| C(13) | -722(1) | 3997(1) | 7017(1) | 50(2) |
| C(2) | 6394(1) | 1988(1) | 9471(1) | 55(3) |
| C(6) | 4912(1) | 798(1) | 8719(1) | 63(3) |
| C(16) | -2637(1) | 3585(1) | 5718(1) | 79(4) |
| N(2) | -3657(2) | 3384(2) | 5001(1) | 112(5) |
| O(5) | 2621(2) | 6592(1) | 8802(1) | 136(4) |
| C(3) | 7831(1) | 1193(1) | 9291(7) | 65(3) |
| C(5) | 6389(1) | 15(1) | 8558(1) | 65(3) |
| C(8) | 4124(1) | 4844(1) | 8184(1) | 73(3) |
| O(3) | -4301(2) | 2415(2) | 5160(1) | 153(5) |
| C(14) | -1060(2) | 4901(1) | 6268(1) | 105(5) |
| C(17) | -2366(2) | 2673(1) | 6458(1) | 90(4) |
| C(7) | 9489(1) | -621(1) | 8628(1) | 92(4) |
| C(18) | -1377(2) | 2920(1) | 7080(1) | 84(4) |
| C(15) | -2018(2) | 4707(2) | 5593(1) | 126(6) |
| C(9) | 3281(2) | 6251(1) | 7949(1) | 84(4) |
| O(4) | -3737(2) | 4144(1) | 4323(1) | 191(7) |
| C(10) | 4487(2) | 7092(1) | 7644(1) | 130(6) |
| Cl(3) | 8431(1) | 8443(1) | 4668(1) | 276(5) |
| Cl(4) | 8561(2) | 8701(1) | 6370(1) | 345(7) |
| C(19) | 7317(3) | 9104(2) | 5463(2) | 254(17) |

—

**Compound 75**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| Br(3) | 1146(0) | 1042(0) | 6504(0) | 66(0) |
| Br(2) | 3471(0) | 3383(0) | 5154(0) | 70(0) |
| Br(1) | 6855(0) | -627(0) | 5906(0) | 102(0) |

| | | | | |
|---|---|---|---|---|
| S(1) | 4872(0) | 2809(0) | 7119(0) | 54(0) |
| N(1) | 4419(0) | 2119(0) | 6373(0) | 49(1) |
| O(2) | 3415(0) | 3361(0) | 7183(0) | 75(1) |
| O(1) | 5633(0) | 2049(0) | 7633(0) | 84(1) |
| C(1) | 6364(0) | 3754(0) | 7010(0) | 44(1) |
| C(10) | 66(0) | 2349(0) | 5299(0) | 47(1) |
| C(8) | 3049(1) | 2402(0) | 5868(0) | 50(1) |
| C(9) | 1550(0) | 2039(0) | 5823(0) | 49(1) |
| C(15) | -573(1) | 1652(0) | 4765(0) | 59(1) |
| C(6) | 8012(1) | 3491(0) | 7208(0) | 60(1) |
| C(2) | 5912(1) | 4752(0) | 6734(0) | 56(1) |
| C(3) | 7080(1) | 5476(0) | 6638(0) | 69(1) |
| C(4) | 8712(1) | 5227(0) | 6808(0) | 71(2) |
| C(5) | 9176(1) | 4236(0) | 7100(0) | 73(1) |
| C(14) | -1980(1) | 1924(0) | 4287(0) | 70(1) |
| C(16) | 5703(1) | 1432(0) | 6149(0) | 63(1) |
| C(11) | -697(1) | 3313(0) | 5345(0) | 76(1) |
| C(13) | -2750(1) | 2855(1) | 4350(0) | 76(2) |
| C(12) | -2139(1) | 3544(1) | 4865(0) | 90(2) |
| C(17) | 5286(1) | 282(0) | 6227(0) | 88(2) |
| C(7) | 10014(1) | 6022(1) | 6681(0) | 133(4) |

—

**PART B**

**Compound 15**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 4122(0) | 3352(0) | 6394(0) | 45(0) |
| I(2) | 4321(0) | 171(0) | 4252(0) | 74(0) |
| P(1) | 6397(0) | 1838(0) | 5571(0) | 27(0) |
| O(1) | 6334(0) | 345(0) | 5698(0) | 39(1) |
| C(1) | 7035(0) | 2524(1) | 6610(1) | 29(1) |
| C(13) | 5602(0) | 2757(1) | 5927(1) | 25(1) |
| C(14) | 5698(0) | 4254(1) | 6122(1) | 25(1) |
| C(19) | 5778(0) | 4789(1) | 7305(1) | 30(1) |
| C(21) | 5000(0) | 2160(1) | 6006(1) | 31(1) |
| C(15) | 5688(0) | 5123(1) | 5108(6) | 33(1) |
| C(2) | 7291(0) | 3813(1) | 6580(1) | 36(1) |
| C(7) | 6519(0) | 2398(1) | 4030(1) | 35(1) |
| C(22) | 4834(0) | 692(1) | 5927(1) | 45(2) |
| C(8) | 6082(0) | 2402(1) | 3152(1) | 39(1) |
| C(17) | 5836(0) | 7025(1) | 6415(9) | 44(1) |
| C(18) | 5846(0) | 6201(1) | 7407(1) | 38(1) |
| C(16) | 5754(0) | 6519(1) | 5273(1) | 39(2) |
| C(20) | 5806(0) | 3902(1) | 8435(1) | 44(2) |
| C(4) | 7896(0) | 3461(1) | 8443(1) | 53(2) |
| C(11) | 6198(1) | 2762(1) | 1953(1) | 58(2) |

| | | | | |
|---|---|---|---|---|
| C(9) | 7264(0) | 2731(1) | 3678(1) | 42(2) |
| C(5) | 7647(0) | 2170(1) | 8494(1) | 48(2) |
| C(12) | 6876(1) | 3104(1) | 1593(1) | 60(2) |
| C(3) | 7722(0) | 4282(1) | 7499(1) | 48(2) |
| C(6) | 7212(0) | 1676(1) | 7574(1) | 39(1) |
| C(10) | 7387(1) | 3055(1) | 2456(1) | 56(2) |

—

**Compound 23**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 11286(0) | 540(0) | 3962(0) | 46(0) |
| P(1) | 8913(0) | 4434(0) | 3184(0) | 24(0) |
| C(19) | 9461(1) | 2917(0) | 3590(0) | 23(1) |
| C(14) | 8121(1) | 5527(0) | 3738(0) | 26(1) |
| C(20) | 10687(1) | 2261(0) | 3466(0) | 29(1) |
| C(8) | 8442(1) | 2444(0) | 4062(0) | 29(1) |
| C(4) | 6191(1) | 4669(1) | 2595(0) | 38(1) |
| C(15) | 6864(1) | 5260(1) | 4045(0) | 33(1) |
| C(3) | 5134(1) | 4302(1) | 2172(0) | 55(2) |
| C(13) | 8863(1) | 6719(1) | 3851(0) | 38(1) |
| C(5) | 7442(1) | 3894(0) | 2686(0) | 27(1) |
| C(6) | 7612(1) | 2744(1) | 2338(0) | 41(1) |
| C(12) | 7705(1) | 2348(1) | 5091(0) | 55(2) |
| C(7) | 8661(1) | 2808(1) | 4661(0) | 39(1) |
| C(17) | 7097(1) | 7335(1) | 4574(0) | 48(2) |
| C(9) | 7241(1) | 1657(1) | 3889(0) | 48(1) |
| C(21) | 11812(1) | 2610(1) | 3010(0) | 58(2) |
| C(11) | 6531(1) | 1582(1) | 4928(0) | 70(3) |
| C(2) | 5307(1) | 3165(1) | 1835(0) | 63(2) |
| C(16) | 6348(1) | 6153(1) | 4463(0) | 38(1) |
| C(18) | 8335(1) | 7610(1) | 4274(0) | 51(2) |
| N(2) | 13094(1) | 3773(2) | 3664(1) | 112(6) |
| N(1) | 13187(1) | 2956(2) | 3290(1) | 134(6) |
| C(1) | 6540(1) | 2400(1) | 1912(0) | 63(2) |
| C(10) | 6296(1) | 1231(1) | 4331(0) | 67(2) |
| O(1) | 10118(0) | 5107(0) | 2864(0) | 40(1) |
| N(3) | 13026(3) | 4595(2) | 4045(1) | 212(13) |

—

**Compound 24**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | -4384(0) | 7207(0) | 3021(0) | 50(0) |
| P(1) | 1161(0) | 7913(0) | 2600(0) | 36(0) |
| O(1) | 2003(0) | 7556(0) | 2865(0) | 46(0) |

| | | | | |
|---|---|---|---|---|
| C(3) | 2854(0) | 7795(0) | 221(0) | 54(1) |
| C(6) | 1325(0) | 8942(0) | 1179(0) | 43(1) |
| C(1) | 1656(0) | 8195(0) | 1531(0) | 36(1) |
| C(2) | 2430(0) | 7615(0) | 1052(0) | 45(1) |
| C(10) | 2855(0) | 9863(0) | 4481(0) | 81(1) |
| C(7) | 1719(0) | 8742(0) | 3296(0) | 42(1) |
| C(9) | 3549(0) | 9810(0) | 3703(0) | 79(1) |
| C(8) | 3007(0) | 9246(0) | 3114(0) | 58(1) |
| C(5) | 1756(0) | 9113(0) | 355(0) | 50(1) |
| C(4) | 2516(0) | 8537(0) | -117(0) | 52(1) |
| C(11) | 1027(0) | 8809(0) | 4084(0) | 55(1) |
| C(12) | -1068(0) | 7848(0) | 2614(0) | 36(0) |
| C(13) | -1816(0) | 7276(0) | 3057(0) | 38(1) |
| C(17) | -1027(0) | 6614(0) | 3573(0) | 48(1) |
| C(15) | -2267(0) | 9211(0) | 2475(0) | 55(1) |
| C(14) | -1994(0) | 8471(0) | 2109(0) | 42(1) |
| C(16) | -2603(0) | 8306(0) | 1280(0) | 53(1) |
| N(2) | -408(0) | 5873(0) | 2410(0) | 64(1) |
| N(1) | -1034(0) | 5846(0) | 3105(0) | 72(1) |
| N(3) | 109(0) | 5824(0) | 1759(0) | 90(1) |
| C(18) | 1604(0) | 9361(0) | 4674(0) | 70(1) |
| C(19) | -2347(0) | 7522(0) | 850(0) | 69(1) |
| C(20) | -3503(0) | 8907(0) | 861(0) | 68(1) |
| C(22) | -3161(0) | 9801(0) | 2032(0) | 72(1) |
| C(21) | -3779(0) | 96321(0) | 1227(0) | 78(1) |

—

**Compound 25**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | -197(0) | -2063(0) | 755(0) | 32(0) |
| P(1) | 5323(0) | -668(0) | 989(0) | 24(0) |
| O(1) | 6188(1) | -2035(1) | 794(0) | 35(1) |
| C(13) | 3110(1) | -854(1) | 978(0) | 21(1) |
| C(19) | 333(1) | 2307(1) | 1772(0) | 38(1) |
| C(18) | 901(1) | 2796(1) | 1366(0) | 38(1) |
| C(16) | 2202(1) | 286(1) | 1254(0) | 24(1) |
| C(20) | 716(1) | 823(1) | 1921(0) | 39(2) |
| C(17) | 1837(1) | 1764(1) | 1110(0) | 31(1) |
| C(2) | 6797(1) | 2238(1) | 867(0) | 47(2) |
| C(21) | 1643(1) | -164(1) | 1671(0) | 36(1) |
| O(2) | -599(1) | 3181(1) | 2048(0) | 61(2) |
| C(1) | 5724(1) | 1153(1) | 709(0) | 30(1) |
| C(6) | 5027(1) | 1395(1) | 297(0) | 48(2) |
| C(3) | 7081(1) | 3604(1) | 638(0) | 55(2) |
| C(5) | 5333(1) | 2807(1) | 71(0) | 62(2) |
| C(7) | 5846(1) | -404(1) | 1566(0) | 30(1) |
| C(12) | 5442(1) | 9363(1) | 1814(0) | 45(2) |

| | | | | |
|---|---|---|---|---|
| C(8) | 6703(1) | -1613(1) | 1763(0) | 39(2) |
| C(11) | 5913(1) | 1011(1) | 2259(0) | 5701(2) |
| C(4) | 6113(1) | 3899(1) | 242(0) | 53(2) |
| C(10) | 6746(1) | -207(1) | 2451(0) | 64(3) |
| C(14) | 2342(1) | -1927(1) | 740(0) | 25(1) |
| C(9) | 7140(1) | -1509(1) | 2211(0) | 58(2) |
| C(22) | -1241(2) | 4587(2) | 1894(0) | 87(5) |
| N(1) | 3001(1) | -4741(1) | 717(0) | 49(2) |
| C(15) | 3076(1) | -3242(1) | 470(0) | 33(1) |
| N(2) | 3731(1) | -4704(1) | 1077(0) | 49(2) |
| N(3) | 4336(2) | -4842(1) | 1406(0) | 82(3) |

—

**Compound 26**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 5727(0) | 10341(0) | 7232(0) | 38(0) |
| P(1) | 5979(0) | 4809(0) | 5950(0) | 29(1) |
| Cl(1) | 7039(0) | 11121(1) | 1696(1) | 72(2) |
| O(1) | 5731(0) | 3983(1) | 7230(1) | 42(2) |
| C(1) | 5733(0) | 4368(1) | 4054(1) | 35(3) |
| C(7) | 6568(1) | 4254(1) | 5959(1) | 33(3) |
| C(19) | 6740(1) | 9880(1) | 2952(2) | 42(4) |
| N(1) | 5711(1) | 7218(2) | 9957(1) | 49(3) |
| C(6) | 5937(1) | 3424(2) | 2975(2) | 47(4) |
| C(16) | 6250(0) | 7904(1) | 4927(2) | 27(3) |
| C(20) | 6910(0) | 9506(2) | 4371(2) | 47(4) |
| C(21) | 6666(1) | 8531(2) | 5389(2) | 46(4) |
| C(18) | 6328(1) | 9251(1) | 2431(1) | 37(4) |
| C(15) | 5450(1) | 7064(2) | 8455(2) | 393(4) |
| N(2) | 6086(1) | 6569(2) | 9945(2) | 57(4) |
| C(13) | 5965(0) | 6996(2) | 6115(2) | 25(3) |
| C(4) | 5303(1) | 3755(2) | 1264(3) | 67(6) |
| C(2) | 5303(0) | 4976(2) | 3743(2) | 48(4) |
| C(3) | 5094(1) | 4686(2) | 2369(2) | 58(4) |
| C(12) | 6717(1) | 3341(2) | 7229(2) | 41(3) |
| C(8) | 6879(1) | 4639(2) | 4748(2) | 48(4) |
| C(14) | 5719(0) | 7811(1) | 7124(2) | 31(3) |
| C(11) | 7161(1) | 2860(2) | 7335(2) | 48(4) |
| C(17) | 6087(1) | 8254(2) | 3430(2) | 38(3) |
| C(10) | 7457(1) | 3227(2) | 6142(3) | 62(6) |
| C(5) | 5721(1) | 3113(2) | 1577(2) | 64(5) |
| N(3) | 6429(1) | 6117(3) | 10036(3) | 97(7) |
| C(9) | 7327(1) | 4117(2) | 4868(2) | 65(7) |

—

**Compound 31**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 7260(0) | 5663(0) | 5037(0) | 56(0) |
| P(1) | 7986(0) | 5808(0) | 8152(0) | 31(0) |
| O(1) | 7355(0) | 4632(0) | 8866(0) | 44(0) |
| C(13) | 7825(0) | 6133(0) | 6830(0) | 32(0) |
| N(1) | 6868(0) | 3157(0) | 7080(0) | 46(0) |
| C(14) | 7775(0) | 7434(0) | 6176(0) | 34(0) |
| C(21) | 7782(0) | 5222(0) | 6476(0) | 37(0) |
| C(15) | 9084(0) | 7854(0) | 5364(0) | 41(0) |
| C(18) | 6450(0) | 8254(0) | 6329(0) | 43(0) |
| C(1) | 6928(0) | 7091(0) | 8577(0) | 36(0) |
| C(7) | 10026(0) | 5897(0) | 8021(0) | 34(0) |
| N(3) | 5681(0) | 2058(0) | 6667(0) | 64(1) |
| N(2) | 7027(0) | 2514(0) | 6427(0) | 65(1) |
| C(8) | 11209(0) | 5703(0) | 7179(0) | 44(0) |
| C(12) | 13156(0) | 5899(0) | 7926(0) | 52(1) |
| C(17) | 6431(0) | 9446(0) | 5690(0) | 50(1) |
| C(6) | 5439(0) | 6916(0) | 9261(0) | 44(0) |
| C(22) | 8125(0) | 3868(0) | 6955(0) | 46(0) |
| C(23) | 5427(0) | 3110(0) | 7735(0) | 45(0) |
| C(16) | 9053(0) | 9046(0) | 4726(0) | 49(0) |
| C(24) | 4663(0) | 2405(0) | 7478(0) | 47(1) |
| C(9) | 10426(0) | 6091(0) | 8810(0) | 52(1) |
| C(10) | 12776(0) | 5712(0) | 7139(0) | 52(1) |
| C(19) | 7723(0) | 9858(0) | 4870(0) | 51(1) |
| C(2) | 7505(0) | 8232(0) | 8223(0) | 50(1) |
| C(11) | 11992(0) | 6085(0) | 8771(0) | 59(1) |
| C(25) | 3058(0) | 2026(0) | 7926(0) | 51(1) |
| C(5) | 4527(0) | 7897(0) | 9559(0) | 61(1) |
| C(3) | 6565(0) | 9201(0) | 8527(0) | 66(1) |
| C(4) | 5077(0) | 9019(0) | 9187(0) | 70(1) |
| C(20) | 7675(0) | 11166(0) | 4171(0) | 78(0) |
| C(30) | 2497(0) | 1358(0) | 7498(0) | 79(1) |
| C(28) | 37(0) | 1273(0) | 8781(0) | 84(1) |
| C(29) | 990(0) | 972(0) | 7947(0) | 91(1) |
| C(26) | 2073(0) | 2319(0) | 8780(0) | 86(1) |
| C(27) | 581(0) | 1943(0) | 9202(0) | 103(1) |

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**Compound 34**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| C(13) | 8588(1) | 2448(0) | 2982(0) | 33(1) |
| I(1) | 10768(0) | 3628(0) | 5286(0) | 54(0) |

| | | | | |
|---|---|---|---|---|
| P(1) | 7883(0) | 1194(0) | 1740(0) | 28(0) |
| C(14) | 9993(1) | 2410(0) | 3669(0) | 36(0) |
| O(1) | 8468(0) | -196(0) | 2124(0) | 37(1) |
| C(1) | 8295(0) | 1764(0) | 356(0) | 33(1) |
| C(15) | 11173(1) | 1512(1) | 3461(1) | 52(1) |
| C(6) | 9257(1) | 2820(1) | 360(1) | 44(1) |
| C(2) | 7722(1) | 1002(1) | -728(0) | 55(1) |
| C(5) | 9628(1) | 3109(1) | -707(1) | 54(1) |
| C(4) | 9090(1) | 2327(1) | -1781(1) | 63(2) |
| C(3) | 8177(1) | 1286(1) | -1784(1) | 69(2) |
| F(1) | 12281(0) | 2302(1) | 3383(1) | 103(2) |
| C(7) | 5936(1) | 1220(0) | 1338(0) | 31(1) |
| C(11) | 3552(1) | 2178(1) | 413(1) | 60(2) |
| C(12) | 5078(1) | 2242(1) | 667(1) | 45(1) |
| C(8) | 5280(1) | 113(1) | 1738(1) | 48(1) |
| C(10) | 2949(1) | 1103(1) | 801(1) | 62(2) |
| C(9) | 3793(1) | 57(1) | 1468(1) | 65(2) |
| C(16) | 7555(1) | 3474(1) | 3176(1) | 64(2) |
| C(21) | 6660(1) | 3351(1) | 3857(1) | 85(3) |
| C(17) | 7617(1) | 4857(1) | 2515(1) | 83(2) |
| C(18) | 6650(1) | 5840(1) | 2634(1) | 122(4) |
| C(20) | 5722(1) | 4430(1) | 4003(1) | 107(4) |
| C(19) | 5760(1) | 5524(2) | 3408(1) | 119(4) |
| C(22) | 6701(1) | 2127(1) | 4487(1) | 85(2) |

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**Compound 35**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I3 | 2668(0) | 7151(0) | 941(0) | 64(0) |
| P3 | 8274(0) | 6811(0) | 1704(0) | 49(1) |
| O5 | 9056(1) | 7084(0) | 953(1) | 57(2) |
| C58 | 5239(1) | 7160(0) | 1061(1) | 49(3) |
| C61 | 4877(1) | 6580(1) | 3085(1) | 65(3) |
| C60 | 5256(1) | 6456(0) | 2203(1) | 49(2) |
| C57 | 6052(1) | 6836(0) | 1598(1) | 50(2) |
| C59 | 5913(1) | 7554(0) | 411(1) | 66(3) |
| C65 | 3882(1) | 5746(0) | 3309(1) | 70(4) |
| C64 | 4191(1) | 5612(0) | 2433(1) | 72(4) |
| C63 | 4892(1) | 5969(0) | 1863(1) | 65(3) |
| C62 | 4177(2) | 6222(0) | 3604(1) | 75(4) |
| I2 | -1803(0) | -416(0) | 5623(0) | 81(0) |
| P2 | 3807(0) | -113(0) | 5623(0) | 48(1) |
| O3 | 4572(1) | -368(0) | 5601(0) | 63(2) |
| C36 | 751(1) | -435(0) | 5720(1) | 53(3) |
| C38 | 797(1) | 253(0) | 6898(1) | 49(2) |

| | | | | |
|---|---|---|---|---|
| C35 | 1605(1) | -126(0) | 6296(1) | 52(3) |
| C37 | 1368(1) | -814(0) | 5037(1) | 61(3) |
| C43 | 651(1) | 162(0) | 7825(1) | 63(3) |
| I(1) | 10976(0) | 3704(0) | 3765(0) | 68(0) |
| P(1) | 5346(0) | 3443(0) | 2975(0) | 51(1) |
| O(1) | 4644(1) | 3695(0) | 3758(0) | 62(2) |
| C(14) | 8416(1) | 3744(0) | 3679(1) | 53(3) |
| C(16) | 8321(1) | 3105(0) | 2419(1) | 49(2) |
| C(13) | 7566(1) | 3452(0) | 3051(1) | 49(2) |
| O(2) | 10415(1) | 2126(0) | 586(1) | 84(3) |
| C(2) | 4186(1) | 2553(1) | 3664(1) | 66(3) |
| C(1) | 4806(1) | 2781(0) | 2890(1) | 52(3) |
| C(15) | 7789(1) | 4094(0) | 4369(1) | 61(3) |
| C(21) | 8680(1) | 3256(1) | 1541(1) | 61(3) |
| C(19) | 9771(1) | 2423(0) | 1229(1) | 59(3) |
| C(4) | 3792(1) | 2042(1) | 3647(1) | 81(4) |
| C(17) | 8765(1) | 2615(1) | 2680(1) | 65(3) |
| C(18) | 9464(2) | 2274(1) | 2091(1) | 69(3) |
| C(20) | 9401(2) | 2920(1) | 948(1) | 65(3) |
| C(6) | 3961(2) | 1749(1) | 2864(1) | 87(4) |
| C(5) | 4523(2) | 1961(1) | 2118(1) | 89(4) |
| C(3) | 4929(2) | 2485(1) | 2118(1) | 76(4) |
| F(1) | 8602(1) | 7986(0) | 396(1) | 119(4) |
| O6 | 3228(1) | 5412(0) | 3941(1) | 110(4) |
| F3 | 5099(1) | 7986(0) | 396(1) | 134(4) |
| F2 | 772(2) | -1272(0) | 5154(1) | 149(5) |
| C(7) | 4778(2) | 3753(0) | 1896(1) | 64(3) |
| O4 | -1132(1) | 1318(0) | 8608(1) | 88(3) |
| C45 | 8842(1) | 7076(0) | 2820(1) | 58(3) |
| C29 | 4445(1) | -408(0) | 7476(1) | 57(3) |
| C(9) | 2930(2) | 3862(1) | 604(1) | 112(7) |
| C(8) | 3454(2) | 3601(1) | 1362(1) | 98(5) |
| C55 | 9809(2) | 5419(1) | 939(1) | 80(4) |
| C51 | 8829(1) | 6144(0) | 1753(1) | 57(3) |
| C49 | 10690(2) | 7108(1) | 4124(1) | 105(6) |
| C41 | -518(1) | 991(0) | 8001(1) | 62(3) |
| C53 | 9031(2) | 5322(1) | 2477(1) | 84(4) |
| C56 | 9424(1) | 5931(1) | 986(1) | 64(3) |
| C34 | 3647(2) | -829(1) | 7793(1) | 76(4) |
| C40 | -407(2) | 1083(1) | 7082(1) | 67(3) |
| C50 | 10199(2) | 6899(1) | 3337(1) | 97(5) |
| C39 | 2761(1) | 712(1) | 6529(1) | 67(3) |
| C33 | 4305(0) | -1079(1) | 8577(1) | 114(7) |
| C(12) | 5565(2) | 4179(1) | 1642(1) | 79(4) |
| C30 | 5931(2) | -251(1) | 7931(1) | 80(4) |
| C52 | 8640(1) | 5829(1) | 2516(1) | 70(3) |
| C42 | -16(2) | 518(1) | 8372(1) | 69(3) |
| C23 | 4346(1) | 552(1) | 6458(1) | 68(3) |
| C44 | -1511(2) | 1820(1) | 8331(1) | 94(5) |
| C66 | 2934(3) | 4937(1) | 3723(1) | 132(8) |

| | | | | |
|---|---|---|---|---|
| C(11) | 5048(2) | 4457(1) | 871(1) | 108(6) |
| C54 | 9649(2) | 5116(1) | 1706(1) | 89(4) |
| C46 | 8002(2) | 7464(1) | 3173(1) | 83(4) |
| C(10) | 3705(3) | 4296(1) | 319(1) | 114(6) |
| C32 | 5771(3) | -915(1) | 9014(1) | 121(8) |
| C28 | 5000(2) | 756(1) | 5686(1) | 111(7) |
| C(22) | 10549(2) | 1595(1) | 769(1) | 100(5) |
| C47 | 8508(3) | 7696(1) | 4000(1) | 109(6) |
| C24 | 4121(2) | 848(1) | 7245(1) | 100(5) |
| C48 | 9859(3) | 7531(1) | 4481(1) | 126(8) |
| C31 | 6427(2) | -517(1) | 8705(1) | 89(5) |
| C25 | 4482(2) | 1376(1) | 7192(3) | 177(15) |
| C27 | 5376(3) | 1302(1) | 5733(2) | 154(13) |
| C26 | 4895(3) | 1585(1) | 6387(3) | 141(11) |

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**Compound 36**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| C(21) | 5710(1) | 9232(1) | 1590(0) | 52(1) |
| I(1) | 3376(0) | 11211(0) | 561(0) | 52(0) |
| P(1) | 9076(0) | 10324(0) | 944(0) | 33(0) |
| O(1) | 9749(0) | 11259(0) | 578(0) | 45(1) |
| Cl(1) | 4218(0) | 4995(0) | 1954(0) | 137(1) |
| C(14) | 5957(1) | 11314(1) | 626(0) | 39(1) |
| C(13) | 6844(1) | 10268(1) | 887(0) | 33(1) |
| C(16) | 6122(1) | 8978(1) | 1147(0) | 39(1) |
| C(1) | 9675(1) | 11107(1) | 1518(0) | 43(1) |
| C(7) | 9748(1) | 8307(1) | 950(0) | 35(1) |
| F(1) | 5686(1) | 13874(1) | 332(0) | 149(2) |
| C(15) | 6570(1) | 12610(1) | 34(0) | 57(2) |
| C(12) | 10210(1) | 7703(1) | 544(0) | 49(1) |
| C(2) | 8694(1) | 12141(1) | 1726(0) | 64(2) |
| C(19) | 4924(1) | 6550(1) | 1633(0) | 76(2) |
| C(20) | 5100(1) | 7982(1) | 1834(0) | 70(2) |
| C(18) | 5271(1) | 6275(1) | 1197(0) | 79(2) |
| C(5) | 11800(1) | 11513(1) | 2141(0) | 82(2) |
| C(17) | 5889(1) | 7503(1) | 9577(0) | 56(1) |
| C(11) | 10727(1) | 6164(1) | 531(0) | 74(2) |
| C(6) | 11244(1) | 10806(1) | 1731(0) | 59(2) |
| C(4) | 10826(1) | 12505(1) | 2349(0) | 99(3) |
| C(9) | 10332(1) | 5807(1) | 1309(0) | 75(2) |
| C(10) | 10769(1) | 5227(1) | 911(0) | 83(2) |
| C(8) | 9818(1) | 7349(1) | 1337(0) | 57(2) |
| C(3) | 9268(1) | 12812(1) | 2152(0) | 93(3) |

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**Compound 37**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 4059(0) | 3138(0) | -532(0) | 57(0) |
| P(1) | 1600(0) | 5013(0) | 307(0) | 48(0) |
| C(8) | 3588(0) | 5439(1) | 1981(1) | 50(2) |
| O(2) | 1476(0) | 6891(1) | -124(0) | 51(1) |
| C(6) | 2648(0) | 4612(1) | 214(0) | 39(1) |
| O(3) | 1682(0) | 5150(1) | 1581(0) | 53(1) |
| C(11) | 4034(1) | 8365(1) | 1121(1) | 66(2) |
| C(9) | 4142(1) | 6534(1) | 2624(1) | 64(2) |
| C(14) | 2284(0) | 2148(1) | -1129(1) | 60(2) |
| C(12) | 3470(0) | 7259(1) | 445(1) | 52(2) |
| C(13) | 2849(0) | 3417(1) | -415(0) | 41(1) |
| O(1) | 975(0) | 3825(1) | -267(1) | 81(2) |
| F(1) | 2485(0) | 522(1) | -794(0) | 99(2) |
| C(7) | 3250(0) | 5784(1) | 893(0) | 40(1) |
| C(2) | 1125(0) | 8026(1) | 1533(1) | 53(2) |
| C(5) | 914(0) | 7974(1) | 293(0) | 57(2) |
| C(1) | 1108(0) | 6240(1) | 1974(1) | 59(2) |
| C(10) | 4348(0) | 8004(1) | 2189(1) | 62(2) |
| C(4) | 1943(0) | 8885(1) | 1986(1) | 75(2) |
| C(3) | 434(0) | 9038(0) | 1900(1) | 75(2) |

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**Compound 44**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| I(1) | 4368(0) | 6433(0) | 4123(0) | 48(0) |
| P(1) | 1201(0) | 2995(0) | 3726(0) | 31(0) |
| O(1) | -176(0) | 3511(0) | 3952(0) | 43(1) |
| O(2) | 1434(1) | 6348(0) | 4877(0) | 58(1) |
| C(21) | 2802(1) | 5014(0) | 4199(0) | 29(1) |
| C(13) | 2657(1) | 4164(0) | 3720(0) | 31(1) |
| C(7) | 1014(1) | 2419(0) | 2888(0) | 34(1) |
| C(12) | -159(1) | 2815(1) | 2519(0) | 47(1) |
| C(22) | 2001(1) | 5138(0) | 4835(0) | 39(1) |
| C(1) | 1821(1) | 1683(0) | 4224(0) | 37(1) |
| C(8) | 2001(1) | 1632(0) | 2600(0) | 45(1) |
| C(14) | 3547(1) | 4170(1) | 3117(0) | 50(2) |
| C(11) | -348(1) | 2416(1) | 1864(0) | 66(2) |
| C(6) | 1170(1) | 516(1) | 4134(0) | 59(2) |
| C(9) | 1802(1) | 1243(1) | 1950(0) | 58(2) |
| C(5) | 1529(1) | -488(1) | 4537(0) | 73(2) |

| | | | | |
|---|---|---|---|---|
| C(10) | 629(1) | 1643(1) | 1583(0) | 64(2) |
| C(4) | 2537(1) | -359(1) | 5016(0) | 78(2) |
| C(2) | 2847(1) | 1782(1) | 4710(0) | 65(2) |
| C(15) | 2904(1) | 4815(1) | 2524(0) | 90(3) |
| C(18) | 5659(1) | 3719(1) | 2460(0) | 89(3) |
| C(19) | 4847(1) | 3667(1) | 3079(0) | 74(2) |
| C(17) | 4970(1) | 4317(1) | 1979(1) | 95(3) |
| C(16) | 3619(1) | 4862(1) | 1959(0) | 108(4) |
| C(20) | 5525(1) | 3091(1) | 3614(0) | 93(3) |
| C(3) | 3208(1) | 766(1) | 5105(0) | 89(3) |

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**Compound 51**

| Atom | x | y | z | U(eq) |
|---|---|---|---|---|
| P(1) | 1470(0) | -2635(0) | 4070(0) | 81(1) |
| P(2) | 849(0) | 2441(0) | 6162(0) | 132(1) |
| O(3) | 1086(0) | -3597(1) | 4369(0) | 92(2) |
| O(2) | 1525(0) | -3183(1) | 3442(0) | 92(2) |
| O(7) | 2185(0) | 2296(1) | 2406(0) | 99(2) |
| C(7) | 1453(0) | -126(1) | 3580(0) | 66(2) |
| O(1) | 1944(0) | -2593(1) | 4361(0) | 102(2) |
| C(20) | 323(0) | 822(1) | 4107(0) | 75(2) |
| C(6) | 1165(0) | -1025(1) | 3993(0) | 71(2) |
| O(5) | 1375(0) | 2589(1) | 6455(0) | 185(5) |
| O(8) | -386(0) | 1952(1) | 3729(0) | 118(2) |
| C(19) | 645(0) | 666(1) | 4577(0) | 65(2) |
| C(3) | 878(0) | -4884(1) | 3496(0) | 96(2) |
| C(17) | 904(0) | 1300(1) | 5568(0) | 83(2) |
| C(8) | 1876(0) | 521(1) | 3746(0) | 72(2) |
| C(9) | 1291(0) | 60(1) | 3016(0) | 84(2) |
| C(21) | -52(0) | 1690(0) | 4146(0) | 87(2) |
| C(12) | 2134(0) | 1330(1) | 3371(0) | 73(2) |
| C(15) | 1320(0) | -447(1) | 5044(0) | 82(2) |
| C(14) | 1049(0) | -289(1) | 4556(0) | 69(2) |
| C(10) | 1549(0) | 880(1) | 2641(0) | 87(2) |
| O(6) | 758(0) | 3880(1) | 5889(0) | 132(2) |
| C(18) | 583(0) | 1433(1) | 5083(0) | 77(2) |
| C(1) | 699(0) | -4208(1) | 4039(0) | 103(3) |
| C(22) | -139(0) | 2398(1) | 4659(1) | 111(3) |
| C(11) | 1968(0) | 1511(1) | 2817(0) | 71(2) |
| C(16) | 1252(0) | 311(1) | 5561(0) | 83(2) |
| C(2) | 1143(0) | -3832(1) | 3144(0) | 120(3) |
| C(25) | -307(0) | 1357(1) | 3192(1) | 137(4) |
| O(4) | 456(0) | 2094(1) | 6567(0) | 226(5) |
| C(26) | 1144(0) | 4527(1) | 5622(1) | 138(4) |
| C(13) | 2583(0) | 3133(1) | 2563(0) | 128(3) |

| | | | | |
|---|---|---|---|---|
| C(4) | 1216(0) | -6031(1) | 3651(1) | 173(5) |
| C(23) | 177(0) | 2262(1) | 5101(0) | 106(3) |
| C(24) | 1582(0) | -104(1) | 6050(0) | 121(3) |
| C(29) | 1365(1) | 5589(1) | 6587(1) | 237(9) |
| C(5) | 414(0) | -5377(1) | 3165(0) | 153(4) |
| C(28) | 1543(1) | 4740(1) | 6042(1) | 170(6) |
| C(27) | 1751(1) | 3351(1) | 6200(1) | 200(7) |
| C(30) | 1933(1) | 5467(2) | 5810(1) | 281(12) |
| O(9) | 9787(0) | 1644(2) | 7294(1) | 160(6) |