ALLENES & ALLENYLPHOSPHONATES IN C-C AND C-X (X = O, S) BOND FORMATION AND CYCLODIPHOSPHAZANE $[\mathrm{ClP}(\mu\text{-N-}t\text{-Bu})]_2$ AS A LIGAND IN CROSS-COUPLING REACTIONS

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

BY

RAMA SURESH RAVI

SCHOOL OF CHEMISTRY

UNIVERSITY OF HYDERABAD

HYDERABAD - 500 046

INDIA

OCTOBER 2011

Dedicated

To

My family

CONTENTS

PART A

ALLENES & ALLENYLPHOSPHONATES IN C-C and C-X (X = O, S) BOND FORMATION

PART B

CYCLODIPHOPHAZANE $[ClP(\mu\text{-N-}t\text{-Bu})]_2$ AS A LIGAND IN CROSS-COUPLING REACTIONS

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
October 2011

R. Rama Suresh

CERTIFICATE

This is to certify that the work described in this thesis entitled "*Allenes & Allenylphosphonates in C-C and C-X (X = O, S) Bond Formation and Cyclodiphosphazane* $[ClP(\mu\text{-}N\text{-}t\text{-}Bu)]_2$ *as a Ligand in Cross-Coupling Reactions* " has been carried out by Mr. R. Rama Suresh, under my supervision and the same has not been submitted elsewhere for any degree.

Hyderabad

October 2011

Prof. K. C. Kumara Swamy

(Thesis supervisor)

Dean

School of Chemistry
University of Hyderabad
Hyderabad 500 046
INDIA

ACKNOWLEDGEMENTS

I express my sincere gratitude to **Prof. K. C. Kumara Swamy,** my research supervisor, for his valuable guidance, encouragement and cooperation. He has been caring and quite helpful in improving my confidence, patience and communication skills.

I thank Prof. M. V. Rajasekharan, Dean, School of Chemistry for providing me the excellent facilities needed for my research. I extend my sincere thanks to former Deans and all the faculty members for their cooperation on various aspects. I thank Prof. D. Basavaiah for his help and counsel in many ways. I also thank Dr. P. Ramu Sridhar for his timely help and useful discussions.

I acknowledge help from my present lab-mates: Anjaneyulu, Sajna, Ramesh, Nagarjuna, Gangadhar, Srinivas, Prasad and Leela Sivakumari and Anil. I am also thankful to former lab-mates Dr. Pavan, Dr. Manab, Dr. Balaraman, Dr. Bhuvan, Dr. Phani and Dr. Venu. All of them have been helpful in creating a pleasant working atmosphere.

Friends are naturally a lot and it is indeed a difficult task to mention them all here. I acknowledge whole-heartedly the contribution of each and every one of them. Even then, my association with N. Purna, N. Ravindra, T. Kishore, V. Narayana, B. Rajesh, B. Suresh, P. Srinu, Ch. Srikanth (chundi), Ch. Sandeep, J. Sridhar (Jetty) from my schooling days to till this date are memorable. I would like to express my sincere gratitude to all my well-wishers particularly Mallibava, Sivanna, Nagarajanna, Sureshanna from Chilakaluripet and N. Sambasiva Rao (Samba) from Kakumanu. I also thank K. Gopi chand (Gopi), D. Ravi, L. Sudha, A. Prasanth, and K. Sridevi who created cheerful atmosphere during my M. Sc at P. B. Siddartha College in Vijayawada. I also thank Majji Durgarao for his help in many ways.

I am thankful to ***everybody else at the school of chemistry*** for helping me with various things. All of them have been very kind, generous, affectionate and helpful. I enjoyed the company of all my friends in UoH.

I also thank all the non-teaching staff of the School of Chemistry for their help in many ways. It is my privilege to acknowledge Mr. Vara Prasad, Mrs. Vijaya Lashmi, Mr. Bhaskar Rao, Mr. Satyanarayana, Mrs. Asia Parwez, Mr. P. Raghavaiah, Mr. Venkataramana, Mr. Rangaiah, Mr. M. Shetty, Mr. A. R. Shetty and Mr. Venkateswara Rao (Venky).

Finally, yet importantly, I would like to express my heartfelt thanks to my beloved parents **R. Nageswara Rao** and **Siva Kumari** and other members of my family for their blessings. I specially thank my sister **A. Aruna** and brother-in-law **V. Subba Rao** for their love and affection for the successful completion of this project.

I thank Council of Scientific and Industrial Research (CSIR, New Delhi) and Department of Science and Technology (DST, New Delhi) for financial support.

R. Rama Suresh

LIST OF PUBLICATIONS

1. Easy and stereoselective synthesis of cyclopropyl substituted phosphonates *via* α-chlorophosphonates
   K. C. Kumara Swamy, K. V. P. Pavan Kumar, **R. Rama Suresh** and N. Satish Kumar *Synthesis* **2007**, *10*, 1485.

2. Molecularly non-stoichiometric crystals in phosphorus compounds
   Manab Chakravarty, **R. Rama Suresh** and K. C. Kumara Swamy *Inorg. Chem*. **2007,** *46***,** 9819.

3. An inexpensive cyclodiphosphazane as an efficient ligand for the palladium-catalyzed amination of aryl bromides and chlorides
   R. Rama Suresh, K. C. Kumara Swamy, *Tetrahedron Lett.* , **2009**, *50*, 6004.

4. Exploring organic reactions using simple cyclodiphosphazanes
   K. C. Kumara Swamy, G. Gangadhararao, **R. Rama Suresh**, N. N. Bhuvan Kumar, Manab Chakravarty. *J. Organmet. Chem*., **2010**, *695*, 1042.

5. Migration of tosyl group of aldimine to allenylphosphonates and allenylsulfones by *N*-Heterocyclic carbenes (NHCs): Synthesis of tosylated allylic phosphonates/phosphine oxides and sulfones
   R. Rama Suresh, K. C. Kumara Swamy (*to be communicated*)

6. Synthesis of phosphono-chromans by $P(n\text{-}Bu)_3$ catalyzed reactions of *N*-thiophosphinyl imines with allenylphosphonates
   R. Rama Suresh, K. C. Kumara Swamy (*to be communicated*)

7. Pd-catalyzed annulation of allenes with indole-2-carboxylic acid derivatives *via* C-H functionalization
   R. Rama Suresh, K. C. Kumara Swamy (*to be communicated*)

Paper presented in symposia

An inexpensive cyclodiphosphazane as an efficient ligand for the palladium-catalyzed C-C and C-N bond formation

R. Rama Suresh and K. C. Kumara Swamy

Chemfest-2010, School of Chemistry, University of Hyderabad, January-2010 (**Poster and Oral Presentation**).

Synopsis

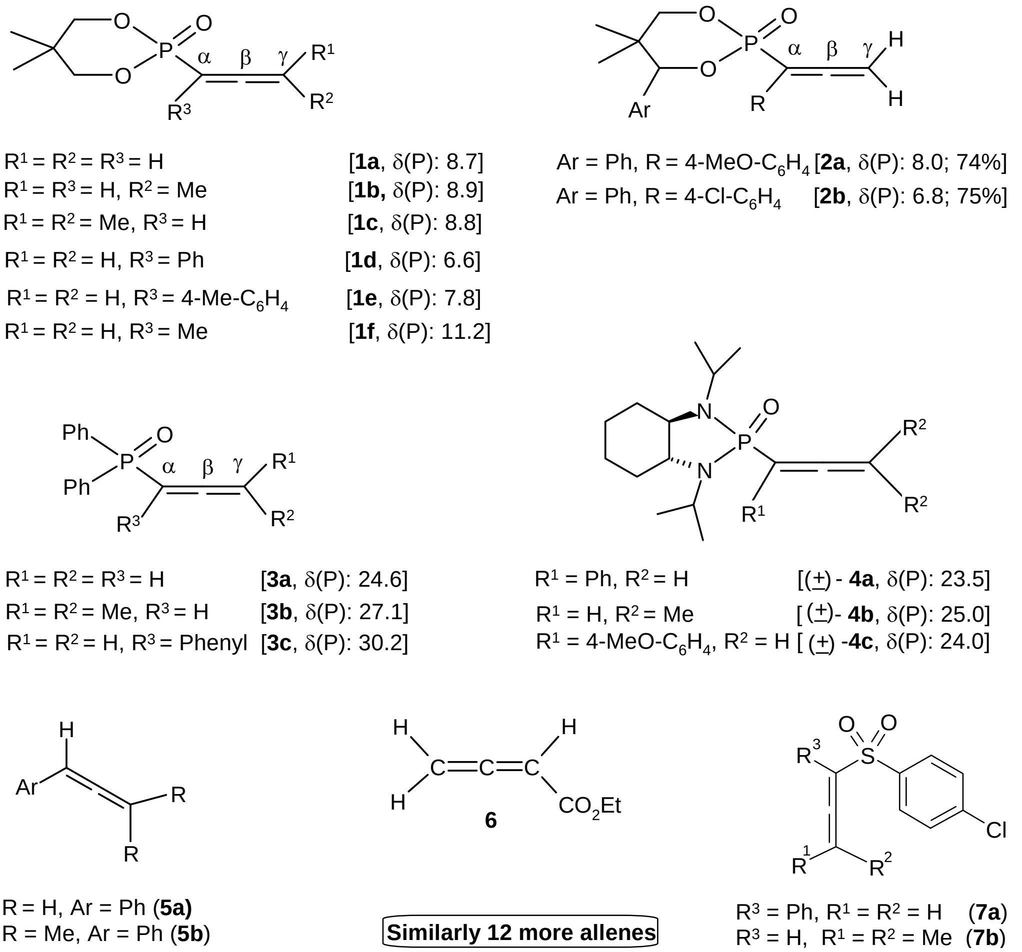
This thesis is divided into two parts: **Part-A** and **Part-B**. **Part-A** deals with investigations on the synthesis and reactivity of allenes. **Part-B** embodies studies on the utility of cyclodiphosphazane $[(t\text{-BuNH})P(\mu\text{-N-}t\text{-Bu})]_2$ as a ligand in Buchwald-Hartwig amination and Suzuki-Miyaura coupling. Each part is subdivided into three chapters: (1) Introduction, (2) Results and Discussion and (3) Experimental Section. Compounds isolated in the present study are, in general, characterized by Mp, IR, NMR, elemental analyses and mass spectra (LC-MS or GC-MS). Wherever feasible, X-ray crystal structures are determined.

PART-A

A review of literature on aspects relevant to this work is presented in Chapter 1. In Chapter 2, the results obtained on the reactions of allenes, in particular (i) those leading to *S*-tosylated allylic compounds catalyzed by *N*-heterocyclic carbenes (NHCs), (ii) base catalyzed reactions with salicyl *N*-thiophosphinyl imines leading to chromans, (iii) palladium catalyzed reactions with indole-2-carboxylic acid derivatives and (iv) cycloaddition reactions of allenylphosphonates with 1,3-diphenylisobenzofuran (IBF) are discussed. Summary is presented at the end of this chapter. Chapter 3 deals with the experimental procedures/ conditions. Pertinent references are compiled after this chapter.

The allenes **1a-f, 2a-b, 3a-c**, **4a-c 5a-b**, **6** and **7a-b** used in the present study are shown in Chart 1. They have been prepared by standard procedures available in the literature, with minor modifications where necessary.

Chart 1



$R^1 = R^2 = R^3 = H$ [**1a**, δ(P): 8.7]
$R^1 = R^3 = H, R^2 = Me$ [**1b,** δ(P): 8.9]
$R^1 = R^2 = Me, R^3 = H$ [**1c**, δ(P): 8.8]
$R^1 = R^2 = H, R^3 = Ph$ [**1d**, δ(P): 6.6]
$R^1 = R^2 = H, R^3 = 4\text{-Me-}C_6H_4$ [**1e**, δ(P): 7.8]
$R^1 = R^2 = H, R^3 = Me$ [**1f**, δ(P): 11.2]

Ar = Ph, R = 4-MeO-C_6H_4 [**2a**, δ(P): 8.0; 74%]
Ar = Ph, R = 4-Cl-C_6H_4 [**2b**, δ(P): 6.8; 75%]

$R^1 = R^2 = R^3 = H$ [**3a**, δ(P): 24.6]
$R^1 = R^2 = Me, R^3 = H$ [**3b**, δ(P): 27.1]
$R^1 = R^2 = H, R^3 =$ Phenyl [**3c**, δ(P): 30.2]

$R^1 = Ph, R^2 = H$ [(±) - **4a**, δ(P): 23.5]
$R^1 = H, R^2 = Me$ [(±)- **4b**, δ(P): 25.0]
$R^1 = 4\text{-MeO-}C_6H_4, R^2 = H$ [(±) -**4c**, δ(P): 24.0]

R = H, Ar = Ph (**5a)**
R = Me, Ar = Ph (**5b**)

6

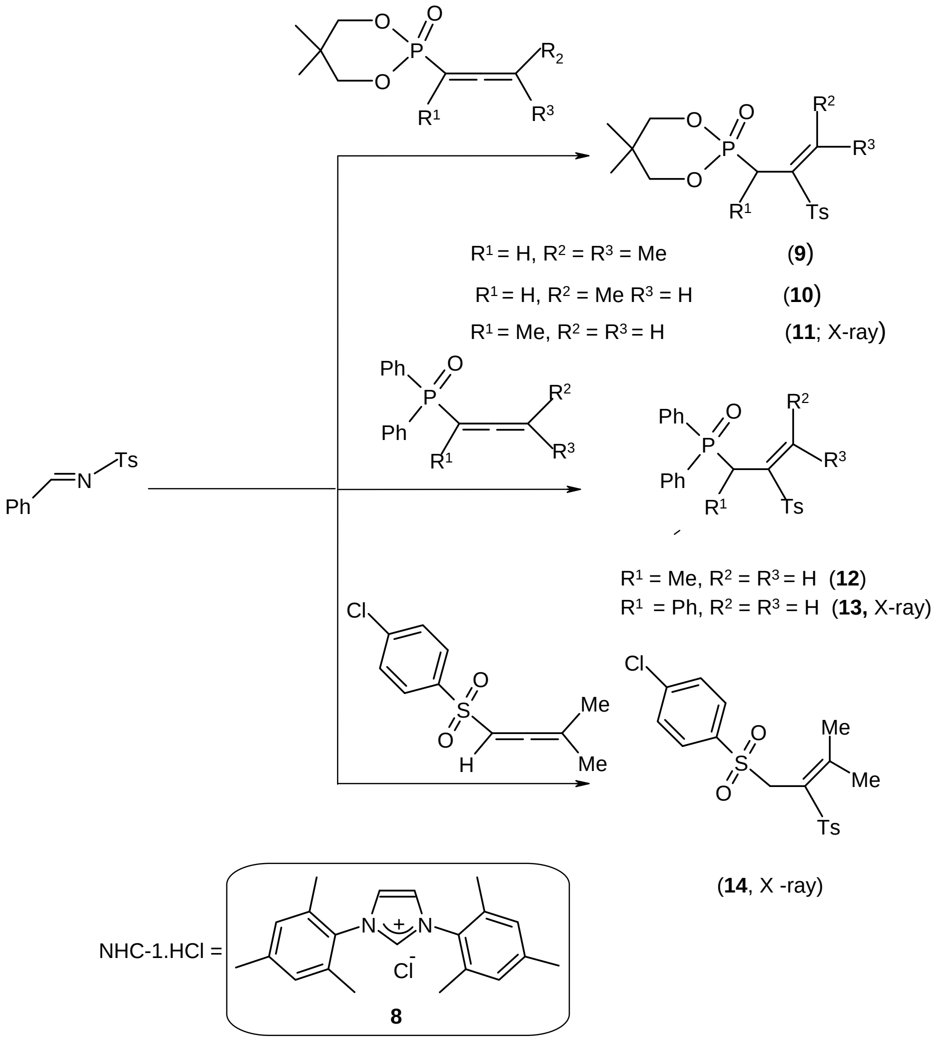
Similarly 12 more allenes

$R^3 = Ph, R^1 = R^2 = H$ (**7a**)
$R^3 = H, R^1 = R^2 = Me$ (**7b**)

(i) Migration of tosyl group of aldimine to allenylphosphonates/ allenylphosphine oxides and allenylsulfones catalyzed by NHCs

We investigated the reactions of allenylphosphonates/ phosphine oxides and allenylsulfones which are catalyzed by NHCs, in an effort to obtain new allylphosphonates that could be subsequently utilized for other organic reactions. Thus, the reaction of allenylphosphonates (**1b-c, 1f**)/ allenylphosphine oxides (**3b-c**) and allenylsulfone (**7b**) with the aldimine PhCH=NTs in the presence of NHC-1.HCl (**8**)/ DBU in toluene at 90 ^{0}C afforded tosylated allylic phosphonates/ phosphine oxides [**9-11**, **12-13**] and sulfone **14** (Scheme 1). The overall isolated yields of the products were moderate to good (43-84%).

Scheme 1



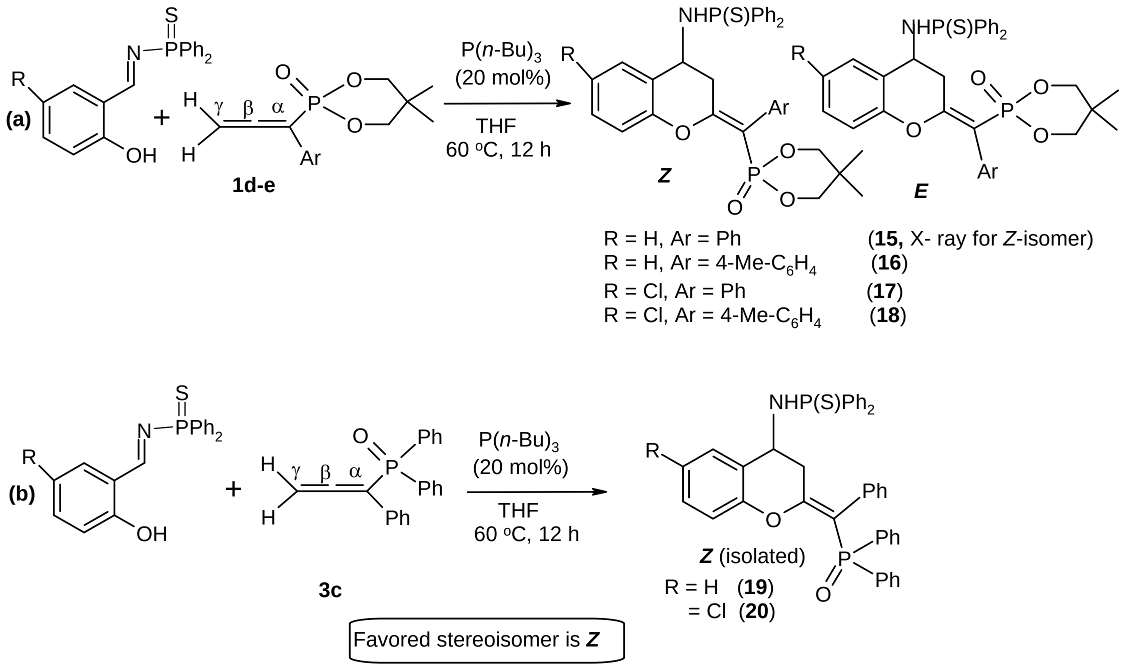
Conditions: 8 (10 mol%), DBU (10 mol%), Toluene (0.25 M), 90 -100 ^{0}C, 12-18 h
Yields (isolated): 43-84%; 66-88%; 65%

It is noteworthy that the tosyl group (-$SO_2C_6H_4CH_3$) has two nucleophilic centers (O and S) and hence can lead to either the ***O***-addition or the ***S***-addition product. But in all our examples, only the ***S***-addition products were observed. The structures of **11**, **13** and **14** are proven by X-ray crystallography.

(ii) Base catalyzed cyclization reactions of allenes with aldimines

Phosphine activated reactions of allenes and alkynes quite often lead to products that are different from transition metal-catalyzed reactions. In an effort to explore routes to phosphono-chromans adapting phosphine catalysis, we have conducted the reactions of allenylphosphonates **1d-e** and allenylphosphine oxide **3c** with salicyl *N*-thiophosphinyl imines that lead to phosphono-chromans **15-18** and **19-20**, after optimizing the experimental conditions [P(*n*-Bu)$_3$/ THF] (Scheme 2). The overall (combined) isolated yields of the two isomers are good (57-78%). Only (β,γ)-cyclized products are formed. The individual isomers have been separated except in the case of **3c**, where only the *Z* isomer could be isolated. The stereochemistry in the case of (*Z*)-**15** is confirmed by X-ray crystallography (Figure 1). Possible mechanistic pathways are also discussed.

Scheme 2



R = H, Ar = Ph (**15,** X- ray for *Z*-isomer)
R = H, Ar = 4-Me-C$_6$H$_4$ (**16**)
R = Cl, Ar = Ph (**17**)
R = Cl, Ar = 4-Me-C$_6$H$_4$ (**18**)

R = H (**19**)
= Cl (**20**)

Favored stereoisomer is ***Z***

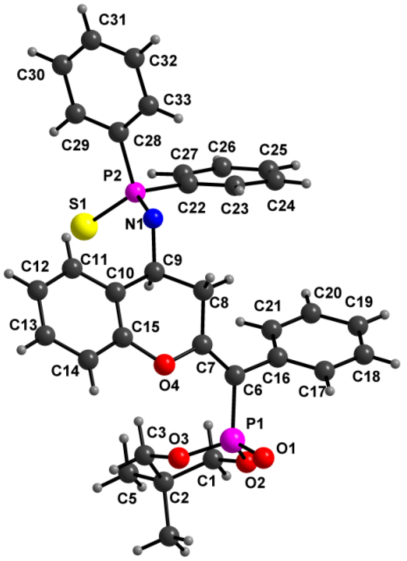
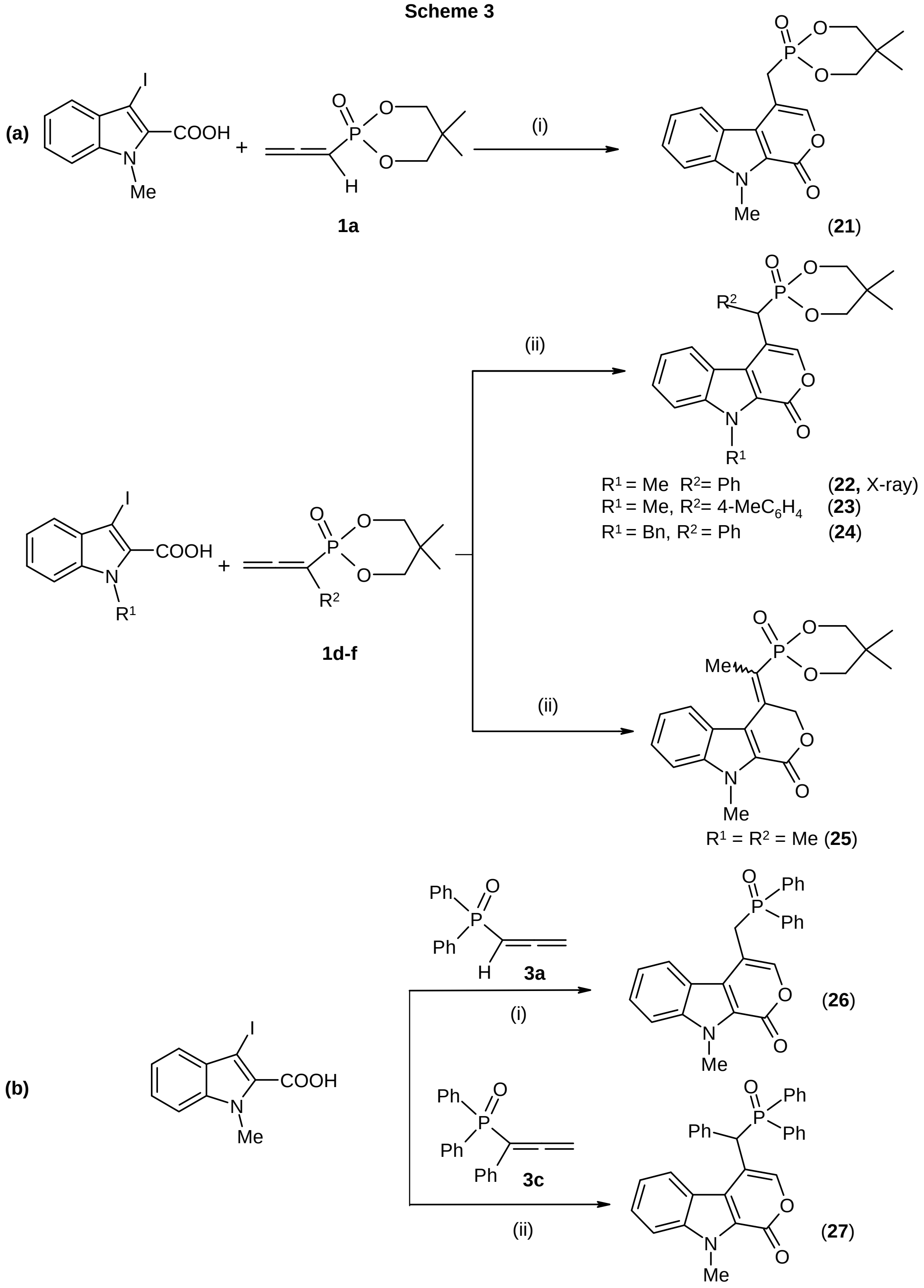


Figure 1. Molecular structure of compound (*Z*)-**15**.

(iii) Pd-catalyzed annulation reactions of allenes with indole carboxylic acids

In view of the significant presence of indole moiety in various pharmaceuticals and other bioactive compounds, we have embarked on a study to incorporate phosphono-moiety onto indole systems. In this context, we investigated the Pd-catalyzed [we use this term to mean reaction catalyzed by palladium complexes] reaction of allenylphosphonate **1d** with 1-methyl-3-iodo-indole-2-carboxylic acid using the system $Pd(OAc)_2/P(o\text{-tol})_3/CsF/DMF$ that lead to the phosphono-pyranone **22** stereoselectively. Under these conditions, treatment of allenylphosphonates, **1e-f** and **3c** with 1-alkyl-3-iodo-indole-2-carboxylic acids also affords pyranone**s 21-27** (Scheme 3). The overall isolated yields of all the compounds were good to excellent (74-94%). In all the cases, the (β,γ)-cyclized products were obtained; one of these (**22**) was characterized by single crystal X-ray structure determination. To avoid the isomerization of **1a** and **3a** to phosphonoalkynes under the conditions used above, we conducted reactions using these allenes in the absence of phosphine. In the case of α-methyl allene **1f** the migration of the proton did not take place and the lactone **25** is formed.

Scheme 3



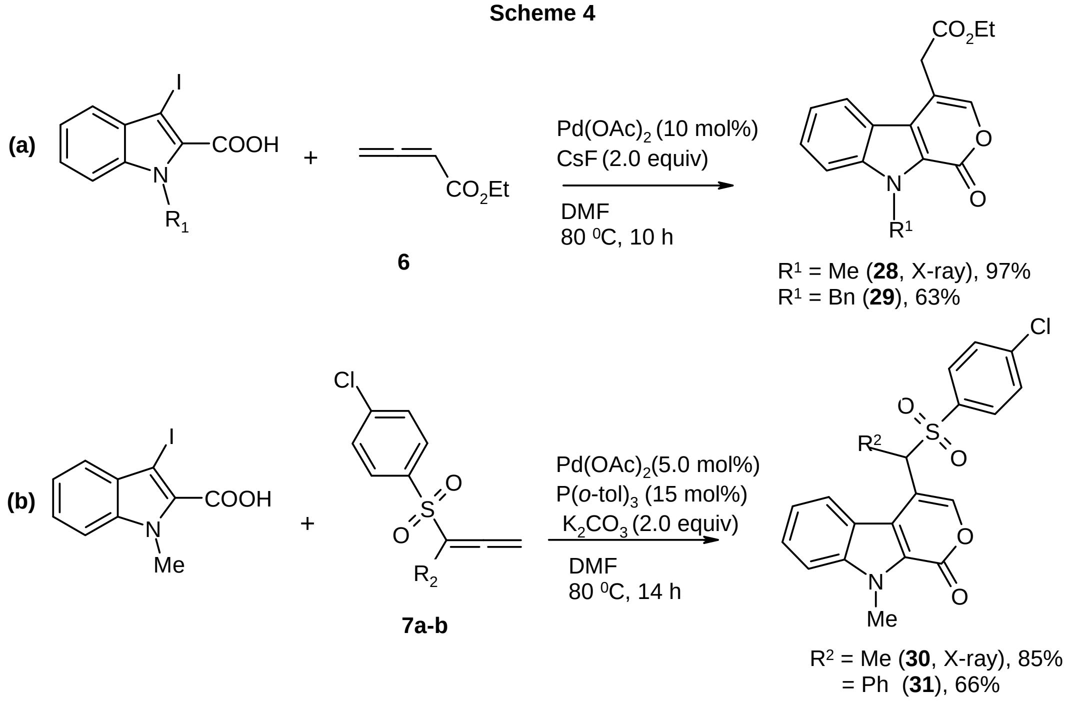
Conditions: (i) $Pd(OAc)_2$ (5 mol%)/ CsF (2.0 equiv)/ DMF/ 80 °C, 14 h

(ii) $Pd(OAc)_2$ (5 mol%)/ $P(o\text{-tol})_3$ (15 mol%)/CsF (2.0 equiv)/ DMF/ 80 °C, 14 h

Yields (isolated): 74-94%

In continuation of the above studies, the Pd-catalyzed annulation reaction of allenyl ester (**6**) with 1-alkyl-3-iodo-indole-2-carboxylic acids afforded pyranones **28-29** (Scheme 4a). The products are (β,γ)-cyclized and are obtained in good to excellent yields (63-97%). The structure of compound **28** was confirmed by X-ray crystallography. A similar reaction with allenylsulfones **7a-b** produced sulfonated pyranoindoles **30** and **31** in good yields (Scheme 4b); X-ray structure of compound **30** has also been determined.

Scheme 4

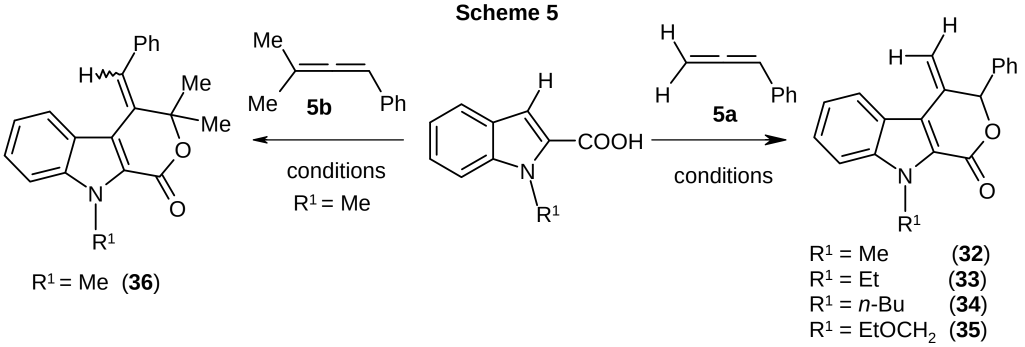


(iv) Pd-catalyzed annulation of allenes with 1-alkyl-indole-2-carboxylic acid *via* C-H functionalization

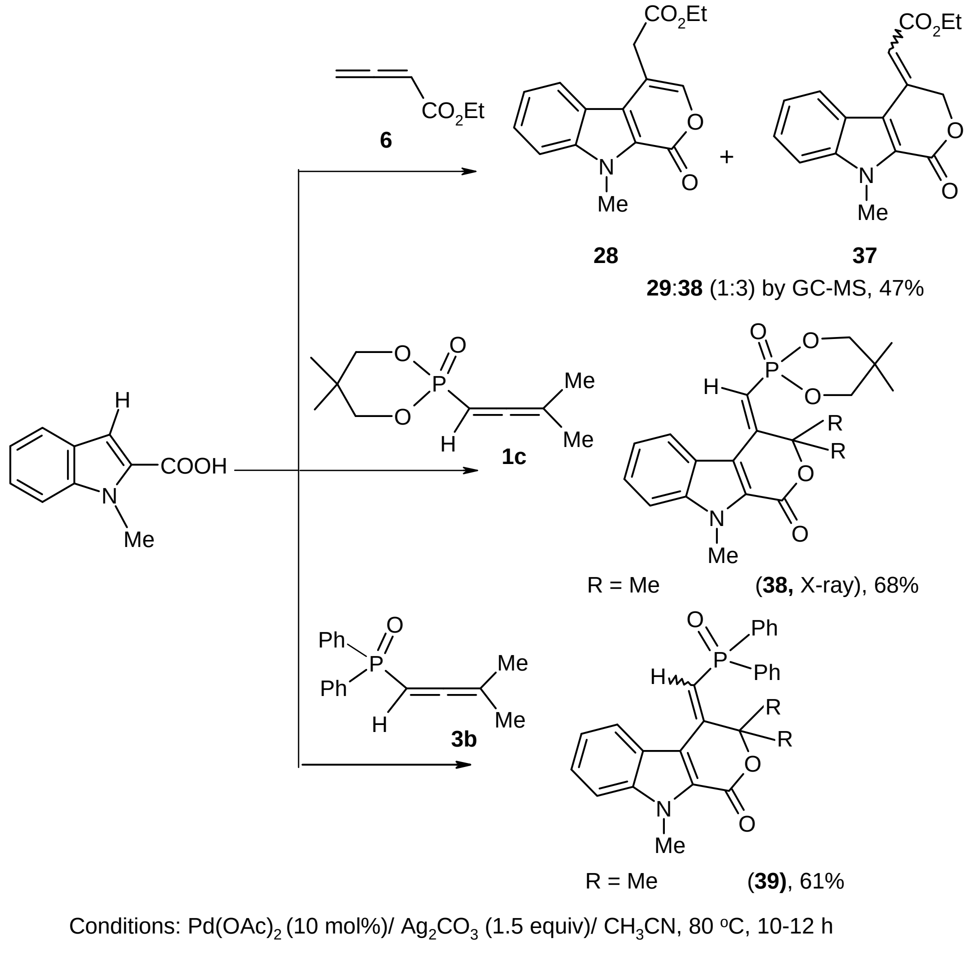
After noting that a direct C-H functionalization at the indole [C$_3$ carbon] may also lead to chromans/ chromenes analogous to those described above in (iii), we investigated the palladium catalyzed oxidative annulations of indole-2-caboxylic acids with allenes *via* direct *C-H functionalization*. This reaction, gratifyingly, produced the corresponding lactones in good yields. Optimization of reaction conditions showed that Pd(OAc)$_2$/ Ag$_2$CO$_3$/ CH$_3$CN is the best combination to obtain good yield of a single product. Under these conditions, we treated the allenes **1c**, **3b**, **5a-b** and **6** with 1-alkyl-indole-2-carboxylic acids for the synthesis of lactones. The allene **5a** gave (α,β)-

cyclized lactones **32-35** while the allenes **5b**, **6**, **1c** and **3b** gave (β,γ)-cyclized products **36**, (**28+37**), **38** and **39** respectively (Scheme 5).

Scheme 5



Conditions: $Pd(OAc)_2$ (10 mol%)/ Ag_2CO_3 (1.5 equiv)/ CH_3CN, 80 °C, 10-12 h

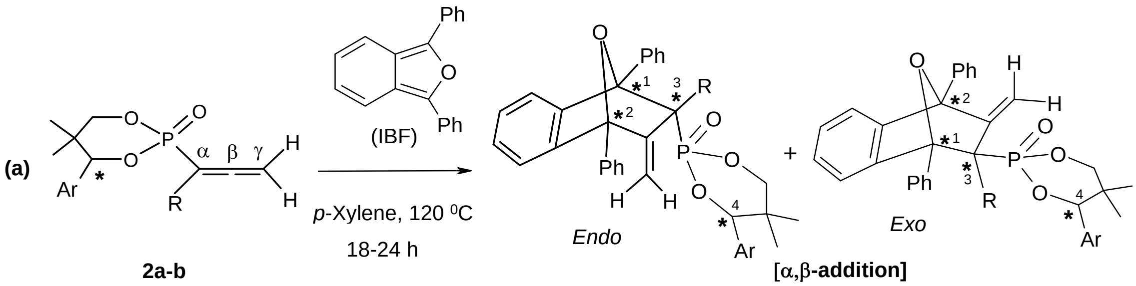


Conditions: $Pd(OAc)_2$ (10 mol%)/ Ag_2CO_3 (1.5 equiv)/ CH_3CN, 80 °C, 10-12 h

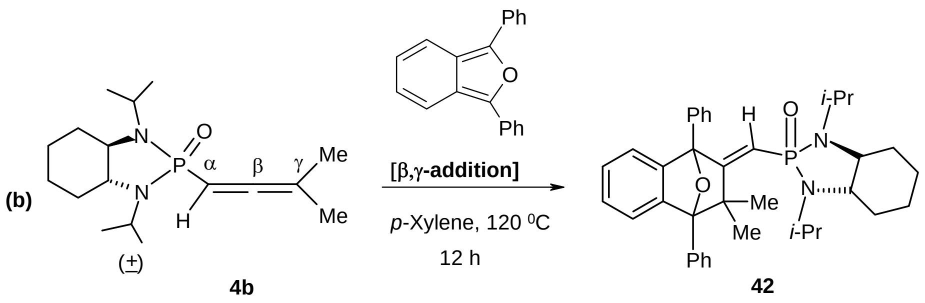
(v) Cycloaddition reactions of allenylphosphonates

The α-aryl allenylphosphonates (**2a-b**) with a remote chiral center and a terminal =CH$_2$ group undergo Diels-Alder reaction with 1,3-diphenyl isobenzofuran (IBF) to give *exo* and *endo* adducts wherein new chiral centers are generated. Our aim here was to identify the different isomers (diastereomers) and where feasible, isolate them. Here, the addition occurs at (α,β) position of the allene and ***we observed at least four diastereomers***. We could isolate the diastereomers **40** and **41** corresponding to the *endo* product in the case of **2a** and **2b**, respectively (Scheme 6a). The allenylphosphoramidate (**4b**) with a terminal =CMe$_2$ group, however, gives (β,γ) addition product (Scheme 6b); The structure of one of the diastereomers (**42**) was confirmed by X-ray crystallography.

Scheme 6



Ar = Ph; R = 4-MeO-C$_6$H$_4$	Ar = Ph, R = 4-Cl-C$_6$H$_4$
Endo (dr:1:1.4)	*Endo* (dr:1:1)
Exo (dr:1.6:1)	*Exo* (dr:1.7:1)
***Endo*:*exo* = ~1:1.5**	***Endo*:*exo* = ~1:1.3**
40 = *Endo*- isomer with δ(P) 16.3	**41** = *Endo*- isomer with δ(P) 15.8

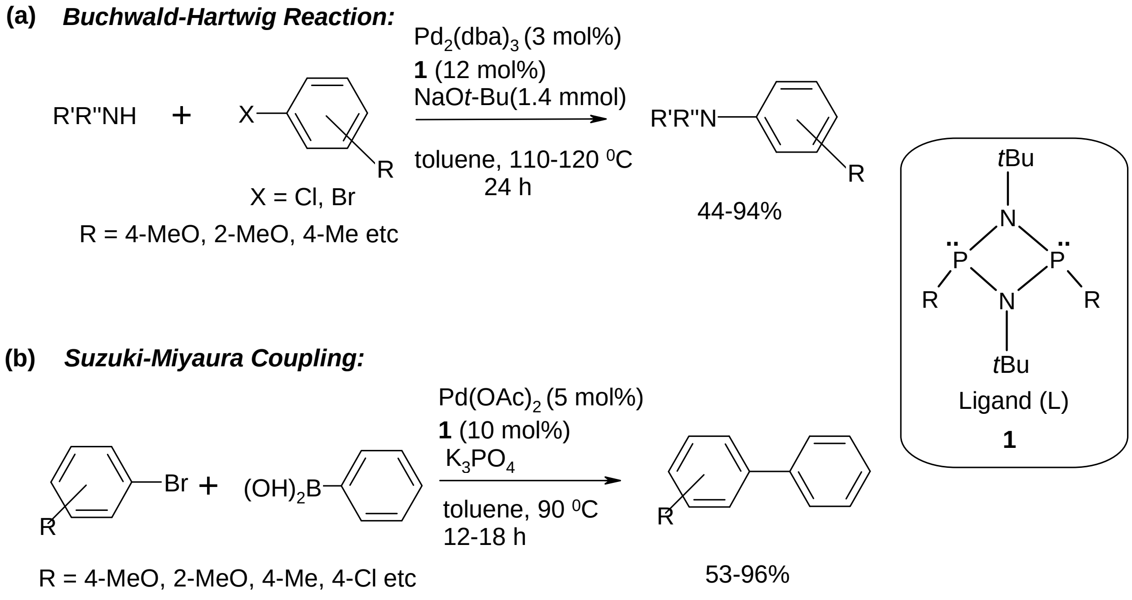


PART-B

This is a small part of the thesis. Here the cyclodiphosphazane [ClPN-*t*-Bu]$_2$ as a ligand in palladium-catalyzed C-N and C-C bond formation has been explored. The focus of Chapter 4 is to briefly review the literature on cross-coupling reactions such as Buchwald-Hartwig amination (C-N) and Suzuki-Miyuara reactions (C-C). Chapter 5 deals with the results obtained in the present study on these aspects. Chapter 6 is the experimental section for this part. Important results of this part are outlined below.

The inexpensive ligand, cyclodiphosphazane [ClPN(*t*-Bu)]$_2$, was introduced in the palladium-catalyzed amination of unactivated aryl halides which allows for the *N*-arylation of aryl chlorides and bromides with secondary cyclic amines and anilines in good yields. Optimization of reaction conditions showed that cyclodiphosphazane [ClPN-*t*-Bu]$_2$ as a ligand (12 mol%) and Pd$_2$dba$_3$ (3 mol%) at 120 ^{o}C in toluene is the best combination. This catalyst also works for the Suzuki [Suzuki-Miyaura] coupling of various unactivated aryl bromides with phenyl boronic acid. The yields vary, but are in the range 44-94% in case of *N*-arylation and 53-96% for the Suzuki coupling.

Scheme 7



PART A

ALLENES & ALLENYLPHOSPHONATES IN C-C and C-X (X = O, S) BOND FORMATION

Chapter 1

INTRODUCTION

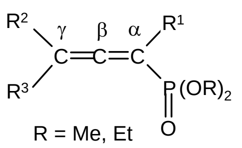
1.1 General Introduction: Allenes

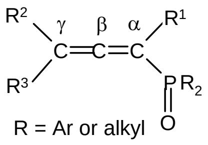
Allenes are carbon compounds with two cumulative double bonds that are orthogonal to each other. For a long period of time, allenes had been considered to be highly unstable. However, many compounds containing the allene group, including natural products and pharmaceuticals, are fairly stable.[2] Because of the diverse biological activities of many allenic natural products, allene moieties are now systematically introduced in steroids, prostaglandins, amino acids and nucleosides.[2] In this perspective, allenes are very versatile precursors for the synthesis of valuable biologically relevant heterocycles such as furanones, γ- and δ- lactones, functionalized dihydrofurans, benzofurans, pyrazoles, chromenes and many more.[1,3,4]

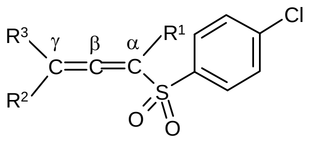
If one of the substituents on allene is the -P(O)(OR)$_2$ moiety, the resulting compound is an allenylphosphonate (phosphorylated allene). In the following sections, a brief literature survey on the synthesis and utility of allenes/ allenylphosphonates will be presented. Wherever possible, comparison will be made between the reactivity of allenylphosphonates, sulfonyl allenes and other allenes.

1.2 Allenylphosphonates (phosphorylated allenes)/ allenylphosphine oxides and allenylsulfones

Allenes of the type **1.1-1.3** are versatile intermediates in organic synthesis for various transformations owing to their ready availability, stability and low cost of preparation. A variety of substituted vinylphosphonates and allylphosphonates, *β*-keto- and *β*-amino-phosphonates and phosphorus substituted heterocycles/ enynes, have been synthesized by starting with allenylphosphonates.[5]







R^1, R^2, R^3 = H, Me, Ar etc

allenylphosphonates
(phosphorylated allenes)
1.1

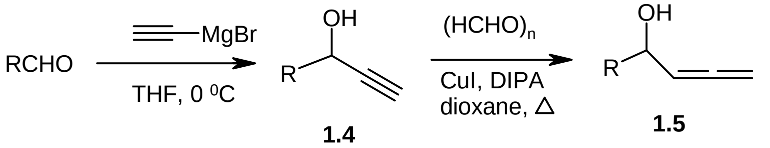
allenylphosphine oxides
1.2

allenyl sulfones
1.3

1.21 Synthesis of allenes/allenylphosphonates/allenyl phosphine oxides and allenylsulfones

There are numerous methods available in the literature for the synthesis of allenes.[6a-l] The best references are the books published by Krause and Hashmi[1a] and Bradsma.[6m] Other recent developments are briefly outlined here. Thus Kazmaier and his coworkers reported the Crabbe homologation[7a] reaction of propargyl alcohols **1.4** to form terminal allenes **1.5** (Scheme 1.1).[7b] The required propargyl alcohols were obtained from the reaction of alkynyl Grignard reagents and an aldehyde.

Scheme 1.1

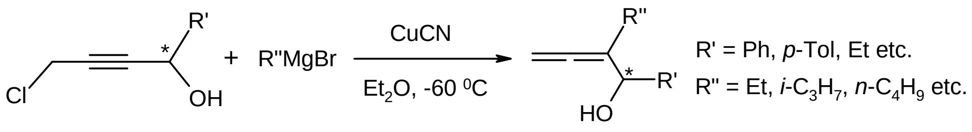


R = Ph, *p*-Tol, Bn etc.

DIPA = Diisopropylamine

Ma and co-workers developed a strategy for the synthesis of optically active secondary 2,3-allenols **1.6** in good yields with up to 99% ee by the reaction of optically active propargyl alcohols with the corresponding Grignard reagents in the presence of CuCN (Scheme 1.2).[8a] As a large number of optically active alcohols are available, a diverse range of optically active allenes can be prepared by this method.

Scheme 1.2

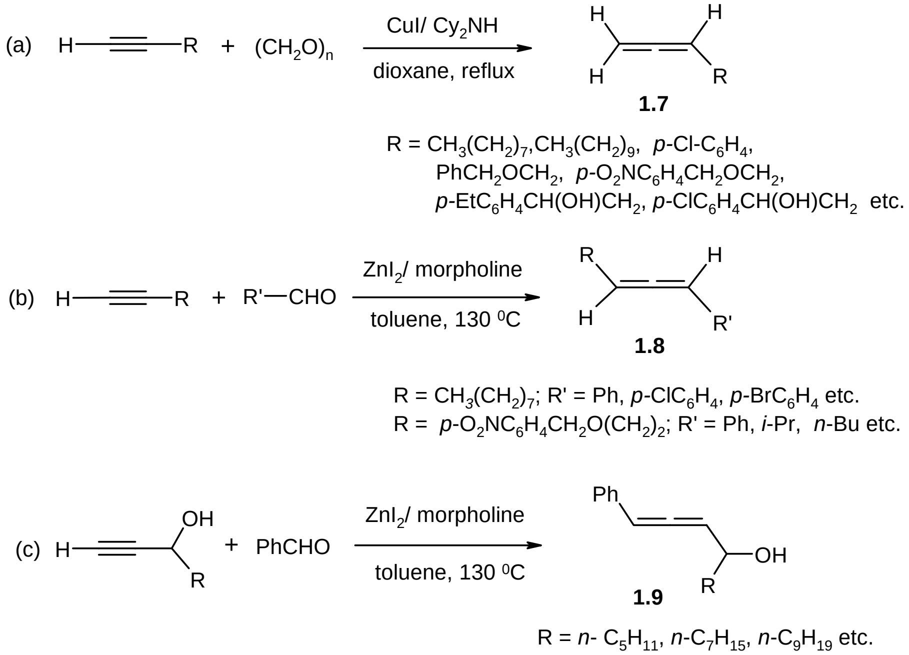


1.6

R' = Ph, *p*-Tol, Et etc.
R" = Et, *i*-C_3H_7, *n*-C_4H_9 etc.

Recently, Kuang and Ma have significantly improved the yields in Crabb homologation by replacing CuBr/ diisopropylamine with CuI/ dicyclohexylamine to obtain the terminal allenes **1.7** (Scheme 1.3a).[8b] Many functional groups such as mesylate, hydroxyl group, amide etc. are tolerated in this reaction. But this method is applicable to only paraformaldehyde; as a consequence only monosubstituted allenes can be synthesized by this method. Very recently, the same group disclosed a method for synthesizing 1,3-disubstituted allenes/ allenols **1.8-1.9** from various aldehydes and terminal alkynes by using ZnI_2 and morpholine (Scheme 1.3b-c).[8c]

Scheme 1.3



1.7

R = $CH_3(CH_2)_7$,$CH_3(CH_2)_9$, *p*-Cl-C_6H_4,
$PhCH_2OCH_2$, *p*-$O_2NC_6H_4CH_2OCH_2$,
p-$EtC_6H_4CH(OH)CH_2$, *p*-$ClC_6H_4CH(OH)CH_2$ etc.

1.8

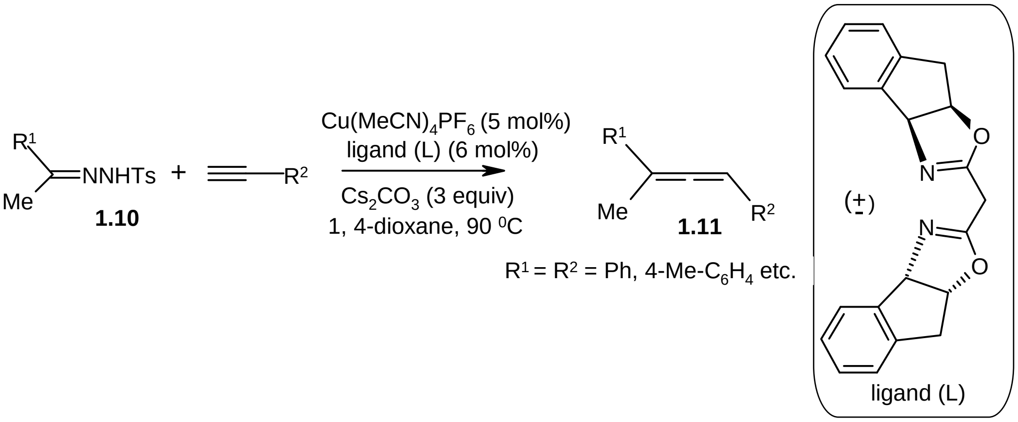
R = $CH_3(CH_2)_7$; R' = Ph, *p*-ClC_6H_4, *p*-BrC_6H_4 etc.
R = *p*-$O_2NC_6H_4CH_2O(CH_2)_2$; R' = Ph, *i*-Pr, *n*-Bu etc.

1.9

R = *n*- C_5H_{11}, *n*-C_7H_{15}, *n*-C_9H_{19} etc.

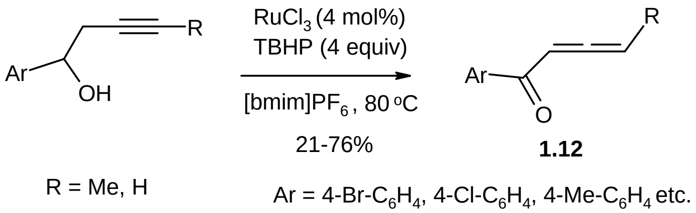
Qing and Wang have developed a novel synthesis of substituted allenes **1.11** from terminal alkynes and tosylhydrazones **1.10** through the copper(I)-catalyzed alkynyl migratory insertion.[9] The scope of this transformation has been studied; it is tolerated for electron rich as well as electron-poor substituents on the aromatic ring of the alkyne and *N*-tosylhydrazones derived from diaryl ketones or aryl aldehydes (Scheme 1.4). The conditions are mild with low catalyst loading and are performed at a moderate temperature.

Scheme 1.4



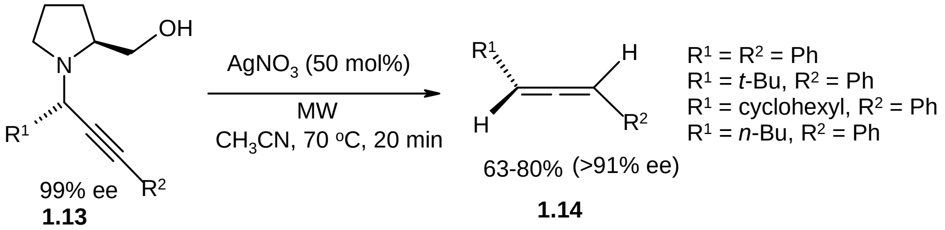
Fan *et al.* reported a green method for the preparation of 1,2-allenic ketones **1.12** through the oxidation of propargyl alcohols with $RuCl_3$ as the catalyst and *t*-butyl hydroperoxide (TBHP) as an oxidant in ionic liquid medium (Scheme 1.5).[10] Many functional groups can be tolerated and the reaction proceeds under mild conditions.

Scheme 1.5



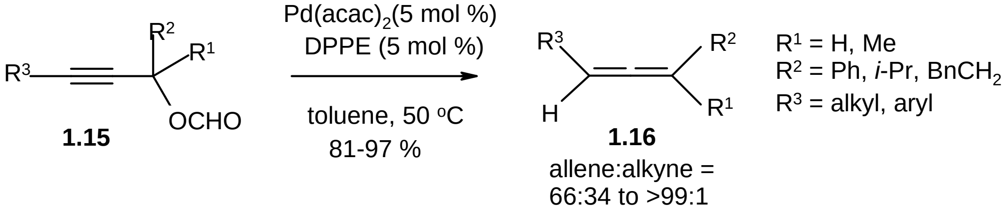
Che *et al.* have developed a novel synthesis of axially chiral allenes **1.14** from optically active propargylamines **1.13** through the silver(I) salts with excellent enantioselectivities (91–99% ee) and without subsequent racemization (Scheme 1.6).[11] This reaction can also be performed under microwave irradiation in a much shorter time than that required under conventional thermal conditions.

Scheme 1.6



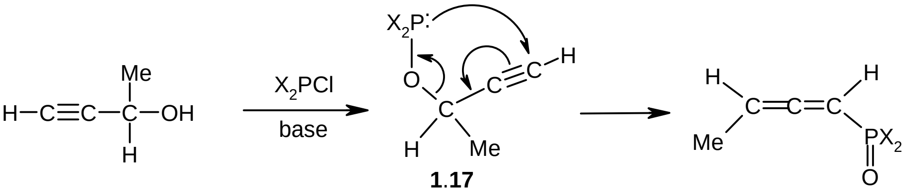
Very recently, Sawamura developed a ligand controlled regioselective palladium-catalyzed decarboxylative hydrogenolysis of propargylic formates **1.15** for the synthesis of allenes or alkynes **1.16**. When DPPE (diphenylphosphinoethane) was used as the ligand, internal allenes were obtained with excellent stereoselectivity (Scheme 1.7).[12] When DPPE was replaced by DPPH, α-selective hydrogenolysis occurred leading to the corresponding alkynes.

Scheme 1.7



In the literature, there are a number of methods available for the synthesis of allenylphosphonates.[13,5a-b] A convenient and common method for the preparation of allenylphosphonates involves the treatment of trivalent phosphorus chloride X_2PCl with the propargyl alcohol [e.g., Me(H)C(OH)C≡CH] in the presence of a base such as pyridine, triethylamine or *N*-methyl morpholine in a suitable solvent like ether, THF or toluene.[13] The intermediate **1.17** undergoes a pseudo-Claisen type rearrangement, usually at temperatures less than 25 ºC, to afford the allenylphosphonates/allenyl phosphine oxides **1.18–1.21** (Scheme 1.8). The conditions used in this method are mild and the yields are moderate to high.

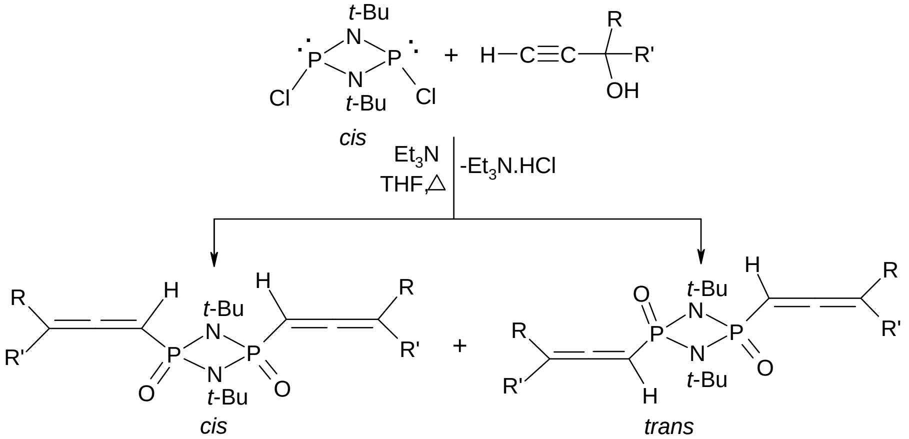
Scheme 1.8



base = pyridine, triethylamine etc X = Ph (**1.18**), OEt (**1.19**), OMe (**1.20**), Cl (**1.21**)

The bis-(allenyl)phosphoramidates *cis*-[(H$_2$C=C=CH)(O)P(μ-N-*t*-Bu)]$_2$ (**1.22**), *cis*- and *trans*-[(Me$_2$C=C=CH)(O)P(μ-N-*t*-Bu)]$_2$ (**1.23a-b**) and *cis*- and *trans*-[(Me)(Et)C=C=CH)(O)P(μ-N-*t*-Bu)]$_2$ (**1.24a-b**) based on a cyclodiphosph(V)azane skeleton have been synthesized in our laboratory by treating *cis*-[ClP(μ-N-*t*-Bu)]$_2$ with the respective propargylic alcohol in the presence of triethylamine (Scheme 1.9).[14]

Scheme 1.9

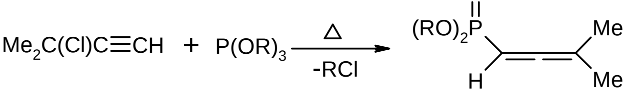


R = R' = H (**1.22**)
R = R' = Me (**1.23a**)
R = Me, R' = Et (**1.24a**)

R = R' = Me (**1.23b**)
R = Me, R' = Et (**1.24b**)

Allenylphosphonates can also be prepared by heating the trialkylphosphites with 3-chloro-3-methyl-1-butyne; thus allenylphosphonates **1.25-1.26** are obtained in moderate to good yields (Scheme 1.10).[15] However, this method is restricted to the use of only terminal alkynes.

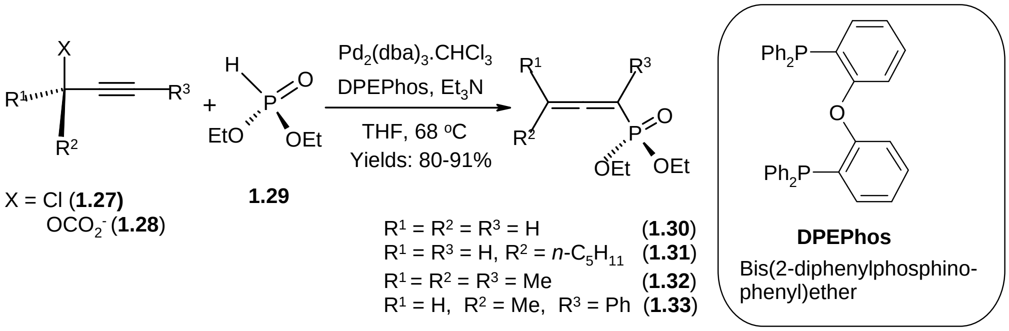
Scheme 1.10



R = Me (**1.25**), Et (**1.26**)

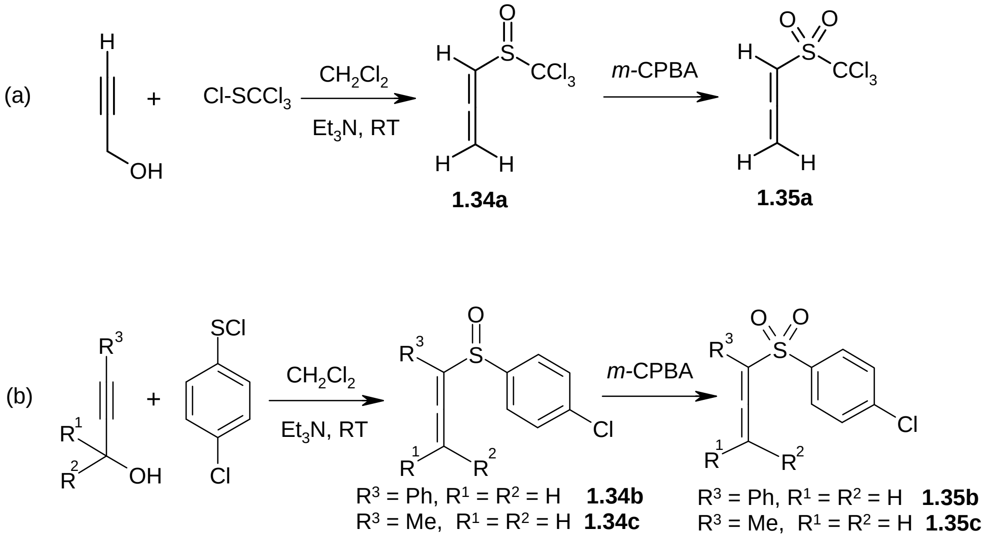
Recently, Stawinski and coworkers reported a novel method for the construction of allenylphosphonates **1.30-1.33** through Pd-catalyzed coupling of propargyl chlorides **1.27** or carbonates **1.28** with *H*-phosphonate $H(O)P(OEt)_2$ (**1.29**) (Scheme 1.11).[16] This reaction proceeds with complete transfer of center to axial chirality and retention of configuration at the phosphorus center.

Scheme 1.11



In a reaction analogous to that for phosphorus, the reaction of sulfenyl chlorides with propargyl alcohol in the presence of triethylamine affords allenylsulfoxides **1.34a-c** which on oxidation by *m*-CPBA leads to allenylsulfones **1.35a-c** (Scheme 1.12) in good yields.[17] Due to ready availability of various propargyl alcohols, we can prepare various allenylsulfones. However, this route has not been explored much in the literature.

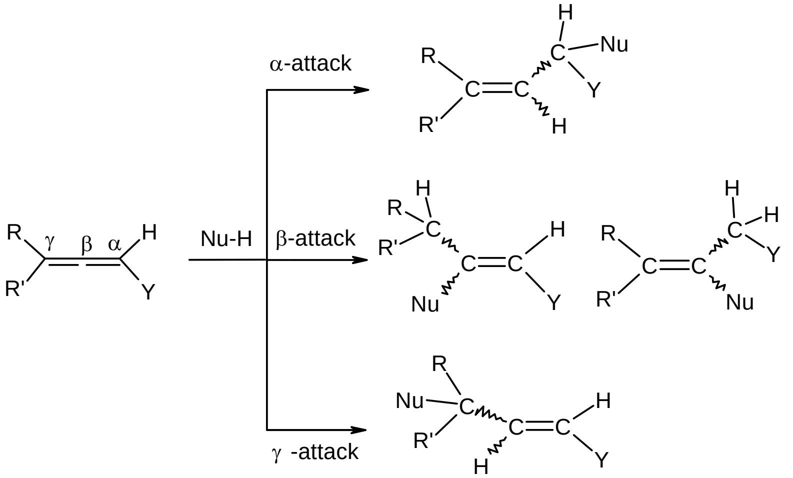
Scheme 1.12



1.22 Nucleophilic addition reactions of allenylphosphonates and other allenes

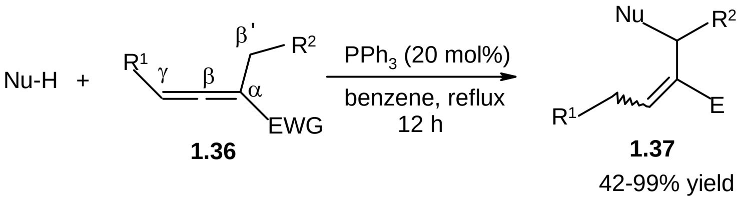
In general, allenes do not have any tendency towards nucleophilic addition reactions. However, this difficulty can be overcome by the activation of the allene skeleton with an electron-withdrawing group (-CO_2R, -$P(O)R_2$, -SO_2R) so that they can undergo nuleophilic addition reactions selectively without any complexity due to the electrophilic nature of the central carbon. Since allene is an unsaturated hydrocarbon having two cumulative double bonds, the incoming nucleophile can attack any one of the three carbon atoms depending on substituents (Scheme 1.13). These reactions can also be initiated by transition metal catalyst or *N*-heterocyclic carbenes (NHCs). Simple reactions of allenes with nucleophiles like amines, alcohols, phenols or thiols lead to addition products where the attack generally takes place at the β-carbon.

Scheme 1.13



Martin and his coworkers reported the first synthesis of highly functionalized alkenes **1.37** through β'-umpolung addition of nucleophile to activated α-disubstituted allenes **1.36** in good to excellent yields with high level of selectivity for the olefin geometry (Scheme 1.14).[18] Various substituents on the allene are compatible under these conditions, which shows the synthetic utility of allenes under the conditions of nucleophilic phosphine catalysis.

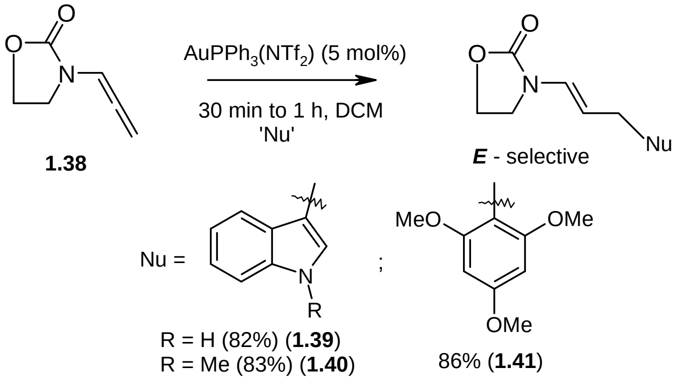
Scheme 1.14



Nu-H = ArOH, RR'NH, $CH_2(CN)_2$, PhSH
R^1 = H, Me; R^2 = H, Ph, 4-pentenyl, CO_2Et; EWG = CN, CO_2Et

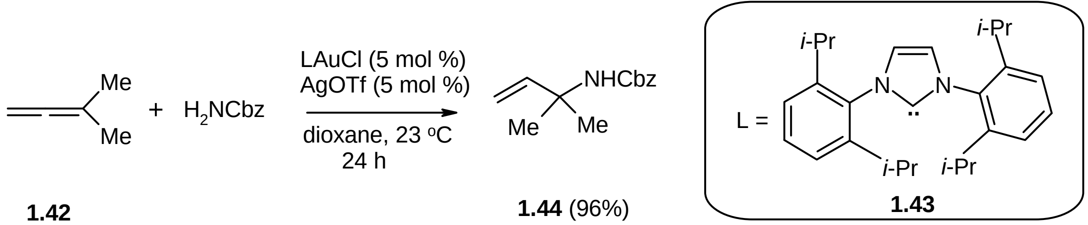
Nucleophilic addition of electron-rich aromatic and heteroaromatics to an allenamide **(1.38)** leads to enamides (**1.39-1.41**) in the presence of gold salt.[19] This intermolecular gold-catalyzed addition of electron-rich aromatics and heteroaromatics to activated allenamides is regioselective and the reaction proceeds under very mild conditions to give desired enamides in good yields (Scheme 1.15).

Scheme 1.15



Unlike activated allenes, unactivated allenes do not participate in nucleophilic addition reactions with amines, but this can be achieved by a transition metal catalyst leading to allylic amines. Very recently, Widenhoefer and co-workers developed a gold(I)-catalyzed protocol for the intermolecular hydroamination of allenes.[20] Thus, treatment of allene **1.42** with benzyl carbamate (H_2Ncbz) catalyzed by a 1:1 mixture of LAuCl (L = *N*-heterocyclic carbene **1.43**) and AgOTf gave single regio- and diastereoisomer of **1.44** in good yield (Scheme 1.16).

Scheme 1.16



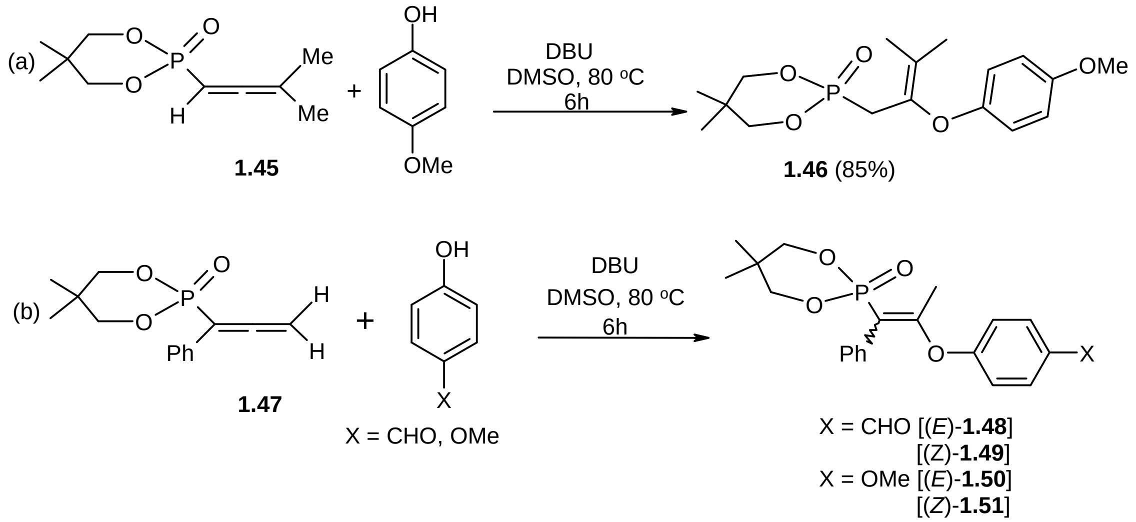
1.42

1.44 (96%)

1.43

Our research group has recently reported that allenylphosphonate (**1.45)** reacts with various phenols to afford multisubstituted allylphosphonate (**1.46**) in good yields (Scheme 1.17a). However, allenylphosphonate **1.47** led to vinyl phosphonates **(1.48-1.51)** (Scheme 1.17b).[21]

Scheme 1.17



1.45

1.46 (85%)

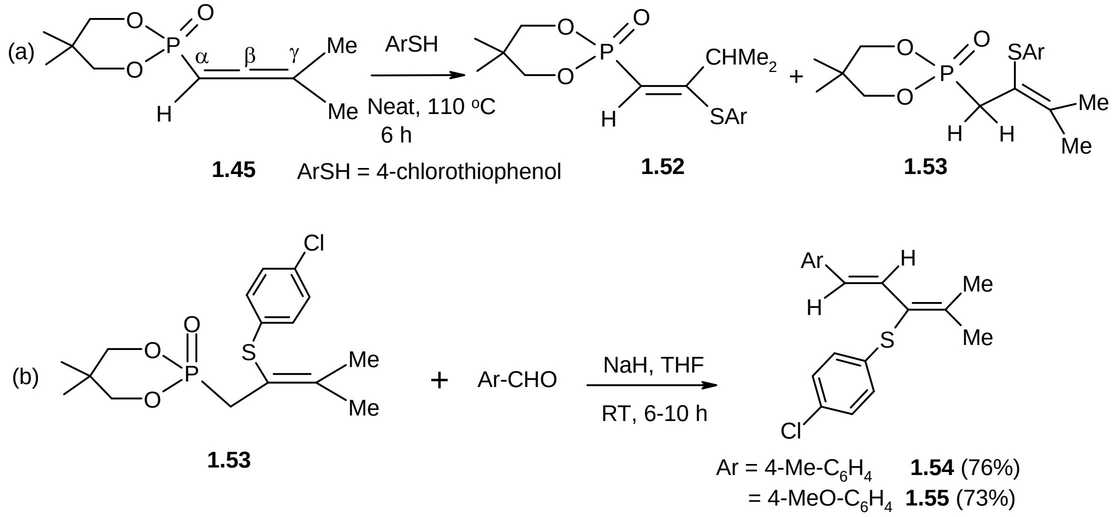
1.47

X = CHO, OMe

X = CHO [(*E*)-**1.48**]
[(Z)-**1.49**]
X = OMe [(*E*)-**1.50**]
[(*Z*)-**1.51**]

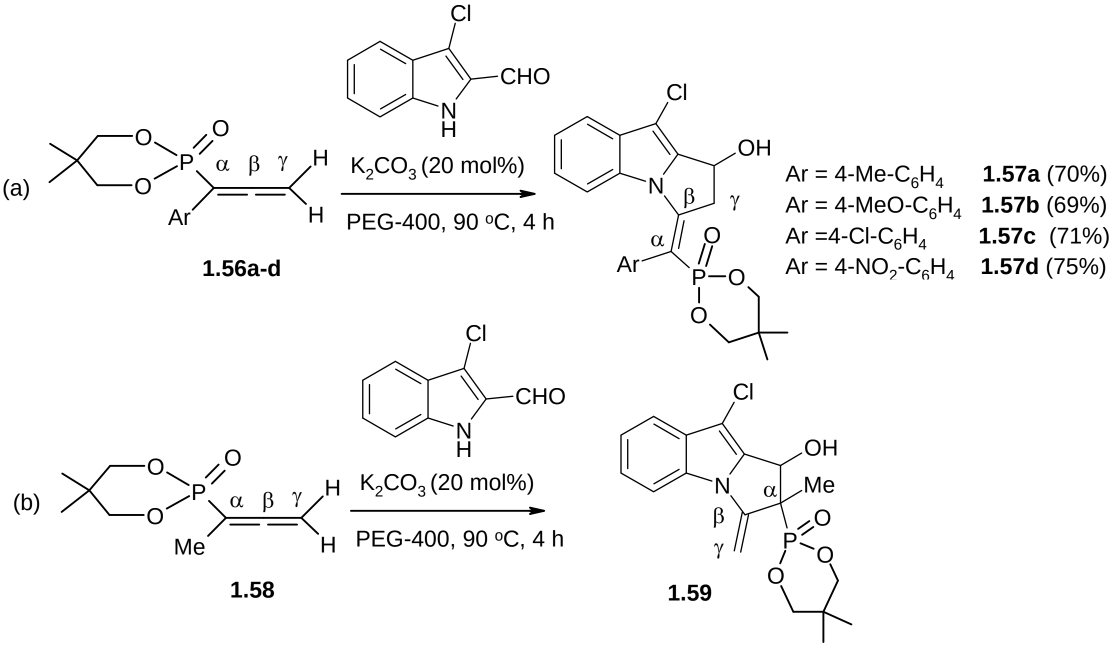
The nucleophilic addition reaction of various thiophenols with allenylphosphonate **1.45** under neat conditions to give vinyl- or allyl-phosphonates **1.52-1.53** has also been reported recently.[22] The allyl-phosphonate thus obtained was utilized in the HWE reaction to give thionyl dienes (**1.54-1.55**) (Scheme 1.18). Interestingly, these reactions did not require the addition of a base. Similar addition reactions take place when allenylphosphonates are treated with nucleobase also.[23]

Scheme 1.18



Very recently, our research group investigated the base catalyzed domino cyclization of allenes with 3-chloro-2-formylindoles in PEG-400 which leads to pyrroloindoles stereoselectively as single products.[24] The structure of the product depends on the type of allene used. In the case of *α-aryl* substituted allenes **1.56a-d,** (*β*,*γ*)-products have been obtained exclusively **1.57a-d** whereas in the case of *α-methyl* substituted allene **1.58**, (*β*,*α*)-attack leading to **1.59** is favored (Scheme 1.19a-b).

Scheme 1.19



1.23 Cycloisomerization reactions of allenes

Allenes bearing a pro-nucleophile (nitrogen, oxygen, sulfur or carbon) can be cyclized on treatment with a wide variety of transition metal catalysts and reagents to give products containing various ring sizes. Thus *N*-aminopyrroles **1.63-1.65** are obtained by the gold(I)-catalyzed cycloisomerization of allenylhydrazones **1.60-1.62** in good to excellent yields (Scheme 1.20).[25] The reaction proceeds through a selective intramolecular 1,2-alkyl or -aryl migration extending the general scope of the reaction under mild conditions with short reaction times.

Scheme 1.20

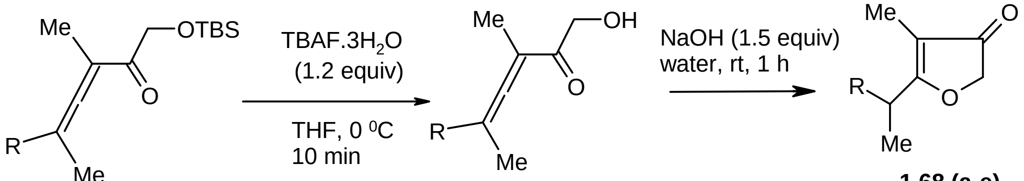
$R^1 = R^2 = Me$ **(1.60)**
$R^1 = R^2 = Ph$ **(1.61)**
$R^1 = Me, R^2 = Ph$ **(1.62)**

1.63-1.65

55-94% yield

3(2H)-Furanones **1.68a-e** can be synthesized by the cycloisomerization of allenic hydroxyl ketones **1.67a-e** (Scheme 1.21) prepared by starting with allenones **1.66a-e**. This cyclization protocol is achieved in water and in the absence of any expensive metal catalyst.[26]

Scheme 1.21



1.66 (a-e)

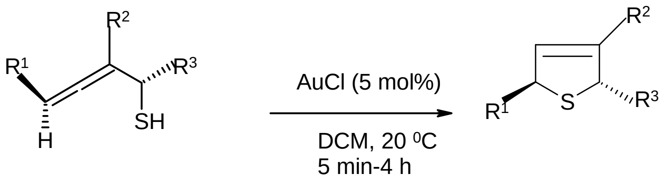
1.67 (a-e)

1.68 (a-e)

R		
i-Pr	**1.67a** (77%)	**1.68a** (61%)
t-Bu	**1.67b** (78%)	**1.68b** (69%)
Allyl	**1.67c** (72%)	**1.68c** (57%)
n-Bu	**1.67d** (78%)	**1.68d** (73%)
Me	**1.67e** (69%)	**1.68e** (69%)

Krause *et al* discovered a highly efficient and stereoselective cycloisomerization of thioallenes **1.69a-d** to 2,5-dihydrothiophenes **1.70a-d**, which is the first example for a gold-catalyzed carbon-sulfur bond formation (Scheme 1.22).[27] Both gold(I) and gold(III) salts can be employed as the precatalysts. The reaction proceeds well in the presence of AuCl and AuI giving the highest yields.

Scheme 1.22

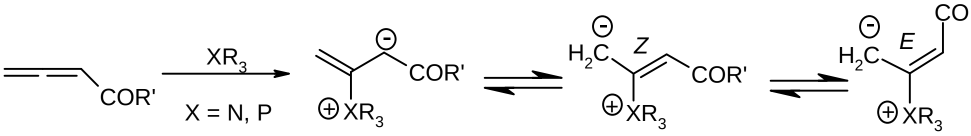


1.69 (a-d) **1.70(a-d)**

R^1	R^2	R^3	d.r.**(1.69)**	*time*	**1.70** (yieid%)
i-Pr	Me	CH_2OBn	95:5	5 min	**1.70a** (87)
i-Pr	Me	$4\text{-}CF_3C_6H_4OCH_2$	>99:1	4 h	**1.70b** (67)
n-hexyl	Me	CH_2OBn	>99:1	2 h	**1.70c** (82)
$CH_2{=}CH(CH_2)_7$	H	H	-	1.5 h	**1.70d** (43)

1.24 Lewis base catalyzed/ promoted reactions of allenes with aldehydes and imines

Lewis base catalysis (often classified as nucleophilic catalysis) employing phosphines and amines, has emerged as a key platform for the generation of molecular complexity. In particular, phosphine/ amine catalysis of allenoates has proven to be useful for the development of new annulation reactions providing various carbo- and hetero-cycles. As illustrated in equation 1, addition of a Lewis base to electrophilic π systems (allenoates) results in the generation of a zwitterionic species. This zwitterion may be depicted as a 1,3-dipole. It can react with aldehydes, α,β-unsaturated ketones, imines, activated alkenes, salicylaldehydes etc. to give diverse products depending on the nature of nucleophile and the substituent on the allenoate.[28] There are several reports on [Au]-mediated annulations reactions,[39] but since the present work does not deal with them, they are not elaborated here.



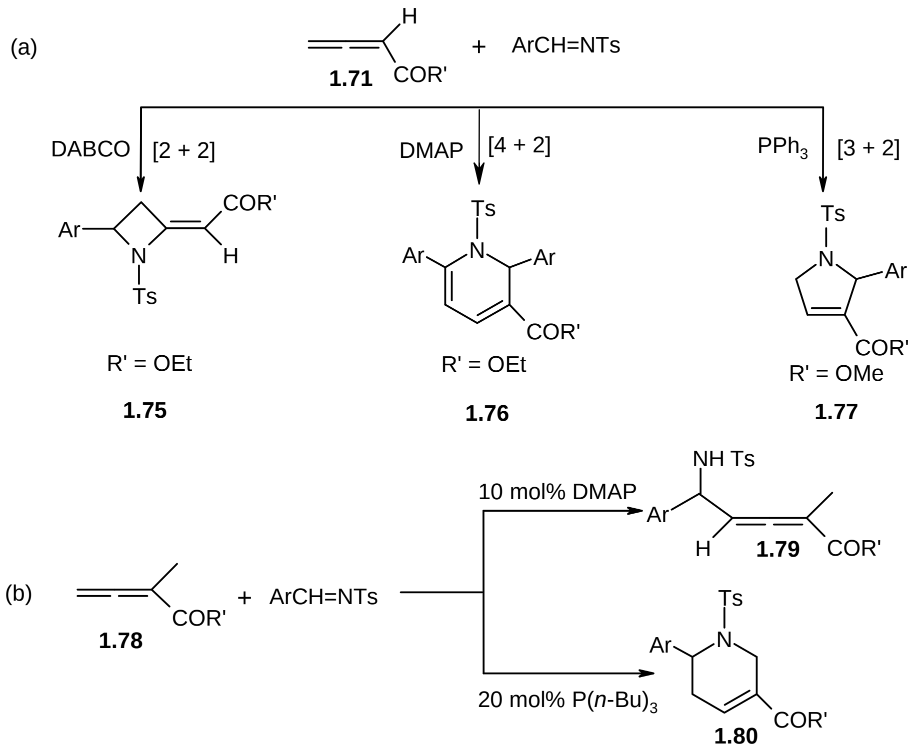
(1)

1.71 **1.72** **1.73** **1.74**

1.241 Reactions with imines

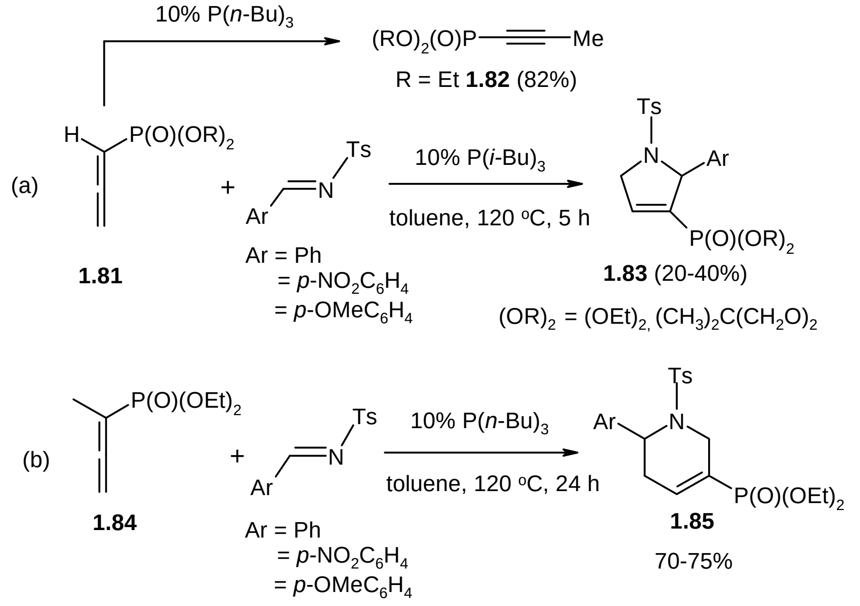
Shi *et* al. reported that under DABCO catalysis, *N*-tosylated imines undergo [2+2] cycloaddition with ethyl 2,3-butadienoate to afford azetidine derivatives (**1.75**) in good yields (Scheme 1.23a). When 4-dimethylaminopyridine (DMAP) was used as a catalyst, the allenoate reacted with two molecules of *N*-tosylated imine to give dihydropyridine **1.76** with the liberation of tosylamine.[29a] Lu and co-workers found that triphenylphosphine catalyzed reaction of methyl 2,3-butadienoate with *N*-tosylated imines led to pyrrolidine derivative **1.77** *via* [3+2] cycloaddition in excellent yield.[29b] If the allene [e.g., **1.78**] had *α*-methyl group, then treatment with *N*-tosylated imines in the presence of the catalyst DMAP in DMSO afforded the corresponding Baylis-Hillman adduct **1.79** (Scheme 1.23b).[29c] When the same reaction was performed in the presence of tri-*n*-butylphosphine (P(*n*-Bu)$_3$), [4+2] cycloaddition took place to give tetrahydropyridine derivatives (**1.80**) in excellent yields with complete regioselectivity.[29d]

Scheme 1.23



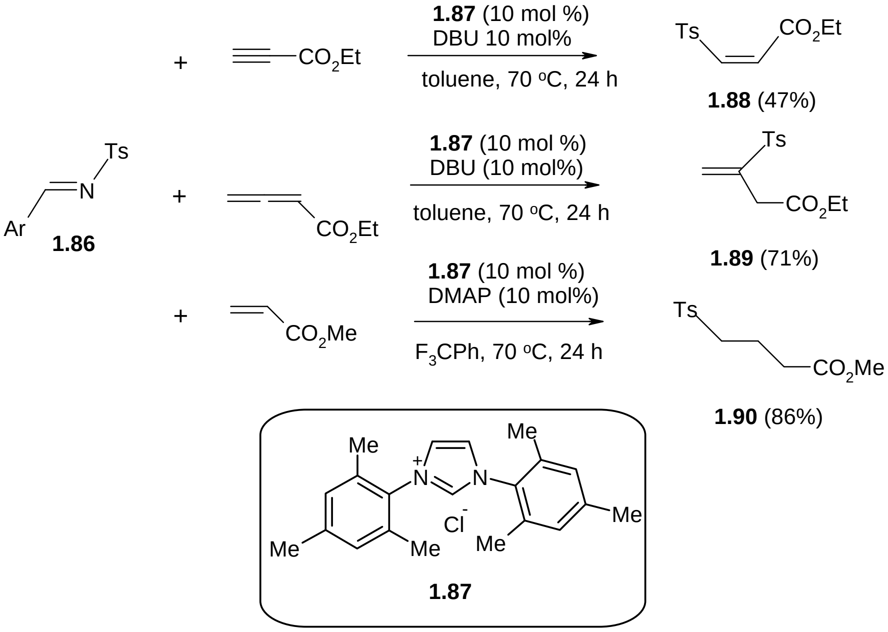
Panossian *et al.* accomplished the synthesis of phosphono-pyrroline and phosphono-tetrahydropyridine from the reaction of allenylphosphonates with *N*-tosylated imines in the presence of various trialkylphosphines.[30] Allenylphosphonate **1.81** isomerized to the corresponding acetylene **1.82** in the presence of $P(n\text{-Bu})_3$ at room temperature (Scheme 1.24a). When they changed the catalyst to $P(i\text{-Bu})_3$, the desired phosphono-pyrrolidine derivatives **1.83** were obtained in moderate yields (Scheme 1.24a). When a similar reaction was performed using α-methyl substituted allenylphosphonate **1.84**, phosphono-tetrahydropyridine **1.85** was obtained in good yields (Scheme 1.24b). If the aromatic group on the imines had electron-withdrawing groups, the yields were very low or in some cases there was no reaction.[30] Also, allenylphosphonates were found to be less reactive when compared to allenyl esters.

Scheme 1.24



N-Heterocyclic carbenes (NHCs) have evoked considerable interest since the isolation of the first stable NHCs by Arduengo and coworkers in 1991.[31] The close analogy of NHCs to phosphines makes them precious as powerful nucleophiles in many synthetically useful reactions.[32] Reactions of electron deficient unsaturated compounds with *N*-tosylimines **1.86** in the presence of catalytic amount of NHC (**1.87**) afforded unexpected tosyl group transfer products **1.88-1.90** in good to high yields, which represents a new reaction pattern for imines as well as for catalysis by NHC (Scheme 1.25).[33]

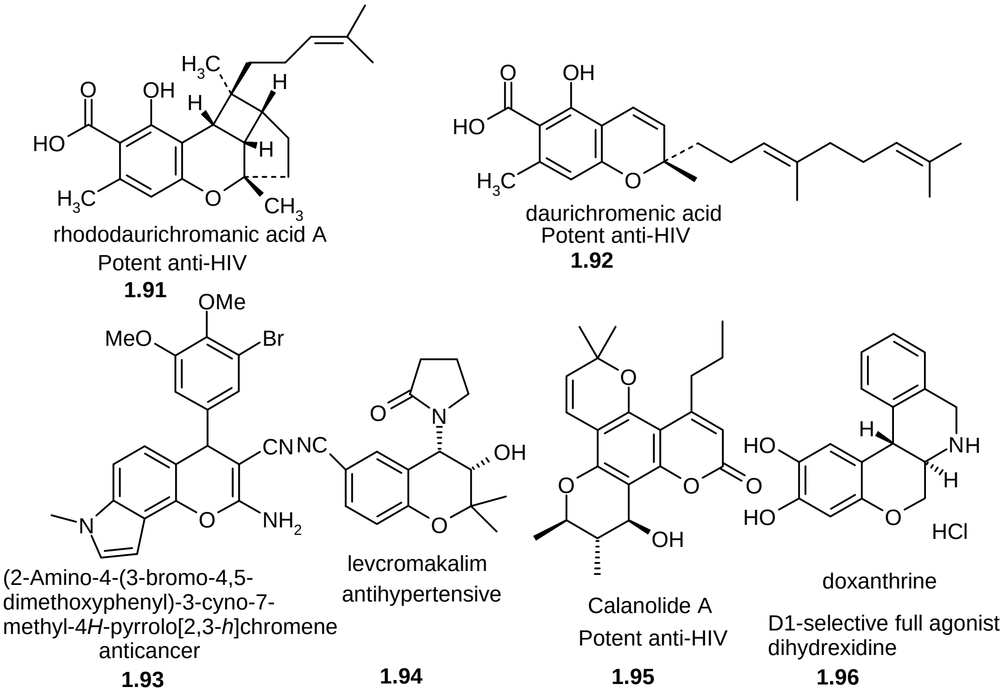
Scheme 1.25



1.242 *Reaction of allenes with substituted salicylaldehydes: Synthesis of chromenes*

Chromenes constitute an important class of oxygenated heterocyclic compounds. They are widespread in natural products and have attracted much attention in diverse areas including physical chemistry (photochromism) and medicinal chemistry (anti HIV, anticancer, antioxidant, inhibitory effect on histamine release, antihypertensive and antiviral activity) and hence a number of research groups have developed different methodologies to synthesize these compounds. Some representative examples (**1.91-1.96**) are shown in Chart 1.[34] In this section, we discuss synthesis of functionalized chromenes, mainly from allenes.

Chart 1



rhododaurichromanic acid A
Potent anti-HIV
1.91

daurichromenic acid
Potent anti-HIV
1.92

(2-Amino-4-(3-bromo-4,5-dimethoxyphenyl)-3-cyno-7-methyl-4*H*-pyrrolo[2,3-*h*]chromene
anticancer
1.93

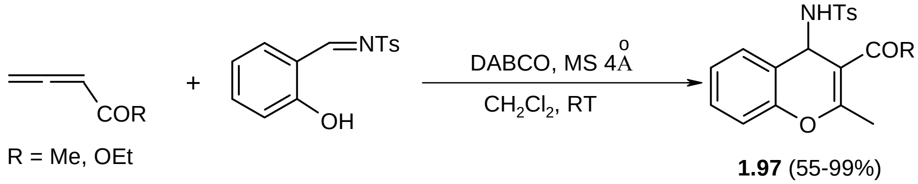
levcromakalim
antihypertensive
1.94

Calanolide A
Potent anti-HIV
1.95

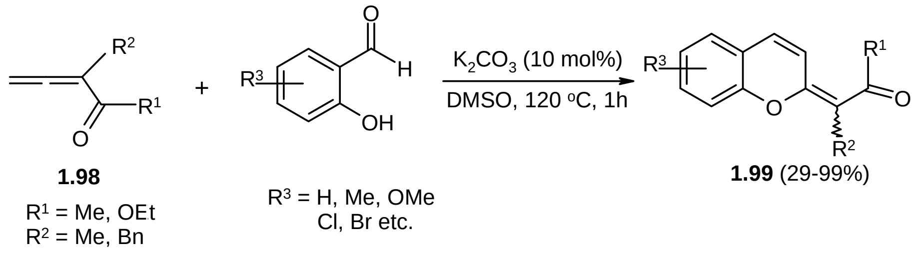
doxanthrine
D1-selective full agonist
dihydrexidine
1.96

Since the pioneering work of Nixon and Scheinmann,[35] several other workers have exploited the reaction of allenes with salicylaldehydes to generate chromenes. For example, Shi and co-workers explored such reactions in the presence of various catalysts (phosphines, amines and inorganic bases) and obtained chromenes of type **1.97** (Scheme 1.26). For these, tertiary amines [DABCO or DBU (1,8-diazabicyclo[5.4.0]undec-7-ene)] or inorganic bases [K_2CO_3 or Na_2CO_3] gave better results than phosphines. They screened several bases/solvents, among which DBU-DMSO combination was shown to be the best.[36b] In continuation of this work, they carried out the reactions of allenones **1.98** also in the presence of K_2CO_3 at high temperature (120 ^{o}C), but in these cases they obtained chromenes (**1.99**) with a different structure (Scheme 1.27).[36c] In a similar way, they have conducted reactions between unsubstituted allenes and salicylaldehydes that afforded the corresponding chromenes.[36d] This is a good example to show that the substituents on the allene and the base/nucleophile are playing a role in determining the course of these reactions. A possible mechanism for the formation of these chromenes has been proposed.[36e]

Scheme 1.26

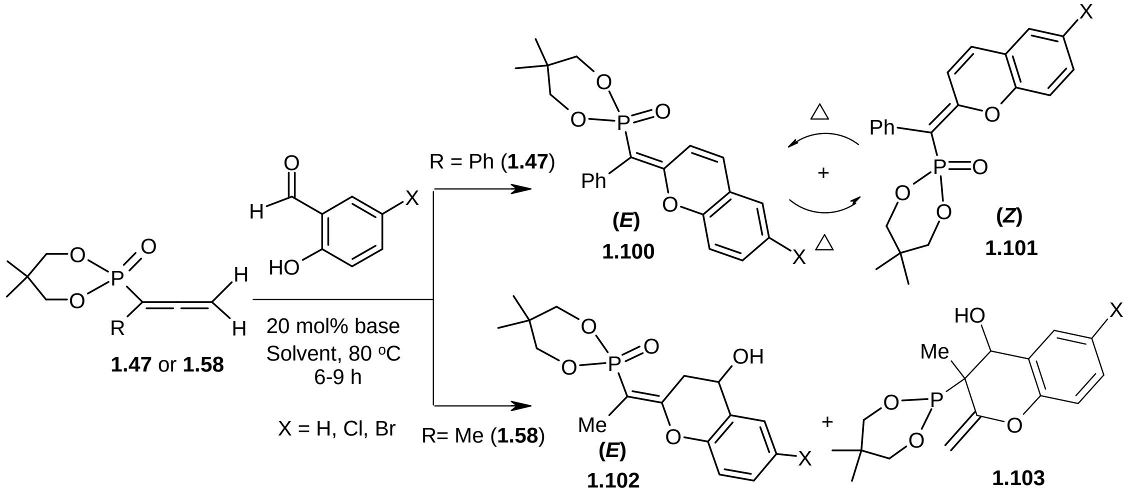


Scheme 1.27



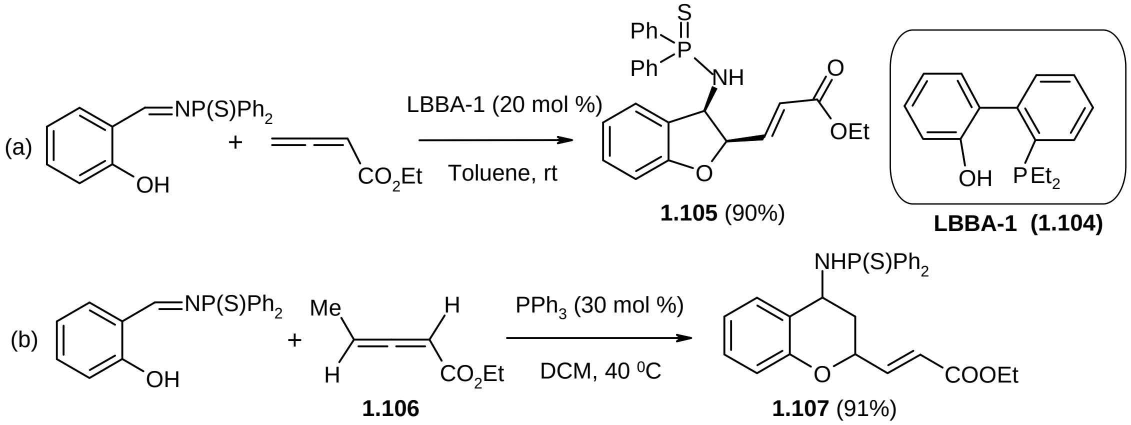
Our research group has recently reported that allenylphosphonates (**1.47** and **1.58**) react with substituted salicylaldehydes in the presence of DBU to afford phosphono-chromenes **1.100-1.103** in good yields (Scheme 1.28).[21] Chromenols such as **102** can undergo dehydration to lead to chromenes.

Scheme 1.28



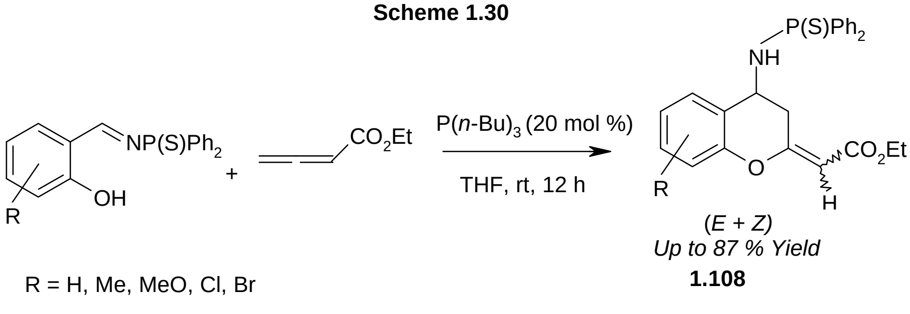
Huang and co-workers reported the novel bifunctional phosphine **1.104** catalyzed aza-MBH/ umpolung addition-domino reaction for the synthesis of *cis*-2,3-dihydrobenzofuran **1.105** with high stereoselectivity from salicyl-*N*-thiophosphinyl imines and allenic ester $EtO_2CCH{=}C{=}CH_2$ (Scheme 1.29a).[37a] The same group described the synthesis of functionalized chroman derivative **1.107** in good yields (Scheme 1.29b) by using PPh_3 catalyzed domino reaction of allene **1.106** with functionalized salicyl-*N*-thiophosphinyl imines. This is the first example in which γ-CH_3 of allene is involved cyclization.[37b]

Scheme 1.29



Very recently, Shi *et al.* reported that the $P(n\text{-}Bu)_3$ catalyzed cyclization reactions of salicyl-*N*-thiophosphinyl imines and salicylaldehydes with ethyl 2,3-butadienoate provide the corresponding functionalized chromans of type **1.108** in good yields in THF under mild conditions (Scheme 1.30).[38]

Scheme 1.30



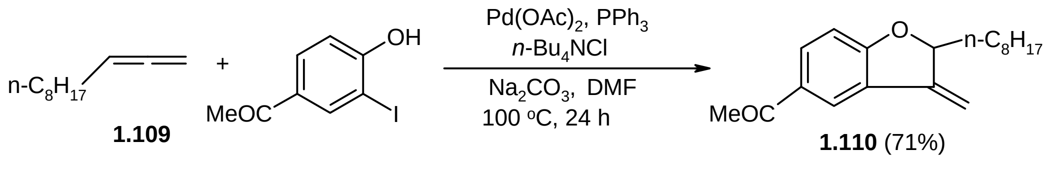
1.3 Pd-Catalyzed annulation reactions of allenes, allenylphosphonates and alkynes: Synthesis of heterocycles/ carbocycles

Annulation processes are among the most significant reactions in organic synthesis.[40] It has been well documented that carbometallation of allenes with an aryl or alkenyl metal halide easily occurs to afford π-allyl complex, which readily undergoes inter- or intra-molecular nucleophilic substitution with various nucleophiles. The feasibility as well as reactivity of these π-allyl species with a wide variety of carbon or heteroatom nucleophiles leads to new bond forming processes.[41] Here, the term *Pd-catalyst* is implied to describe either *a Pd(II) or a Pd(0) complex* that is used in the catalytic reaction. Studies on coupling reactions of allenylphosphonates with iodoarenes are comparatively few in number.[5f,42a-b] Since phosphorus can confer a different electronic constraint relative to an aryl carbon on the intermediates, stereochemistry of the products in palladium-catalyzed coupling using allenylphosphonates and phenyl substituted allenes could be different. Hence coupling reactions of the general allene moiety as relevant to the present work will also be described in this section.

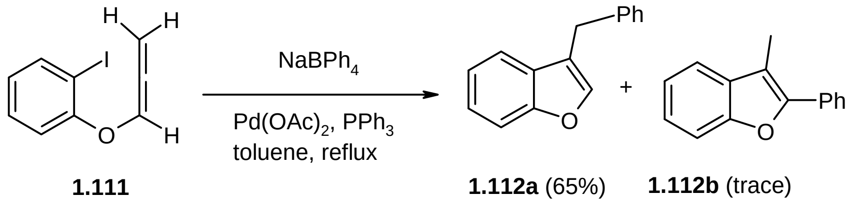
1.31 Synthesis of benzofurans

The Pd-catalyzed heteroannulations of allenes using functionally substituted aryl halides was first reported by Larock and his co-workers in 1991.[43] Thus, treatment of functionalized iodophenol with allene **1.109** in the presence of $Pd(OAc)_2$/ PPh_3/ *n*-Bu_4NCl/ Na_2CO_3 at 100 °C in DMF afforded benzofuran derivative **1.110** in 71 % yield (Scheme 1.31). Grig and co-workers also developed an interesting palladium-catalyzed tandem cyclization-anion capture strategy using allenes as the terminating species.[44a] Thus the allene **1.111** undergoes cyclization leading to five-membered heterocycles **1.112a** and **1.112b** (Scheme 1.32). The same research group has reported the synthesis of benzofurans attached with an azide group as an extension of this reaction.[44b]

Scheme 1.31

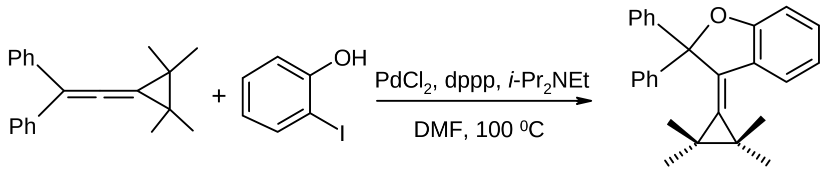


Scheme 1.32



The benzofuran **1.114** was prepared in good yields by the Pd-catalyzed coupling of diarylvinylidenecyclopropane **1.113** with 2-iodophenols (Scheme 1.33).[45] This is a good method for synthesizing cyclopropane appended benzofurans.

Scheme 1.33

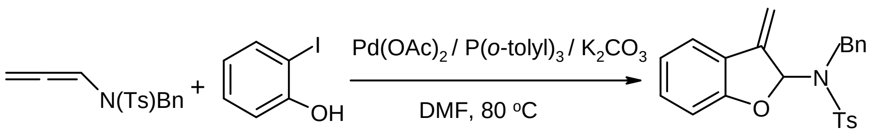


1.113 **1.114** (94%)

dppp = bis(diphenylphosphino)propane

The highly regioselective synthesis of benzofuran **1.116** in moderate yields through the Pd-catalyzed annulation of heteroatom substituted allene **1.115** with 2-iodophenol was reported by Sakamoto and co-workers (Scheme 1.34).[46] However, this method is limited to electron donating substituents on allenes.

Scheme 1.34

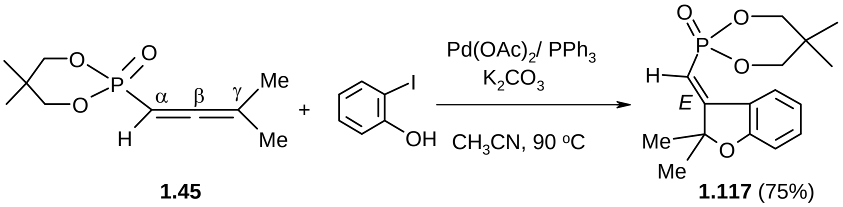


1.115 **1.116** (62%)

Ts = *p*-toluenesulfonyl, Bn = benzyl

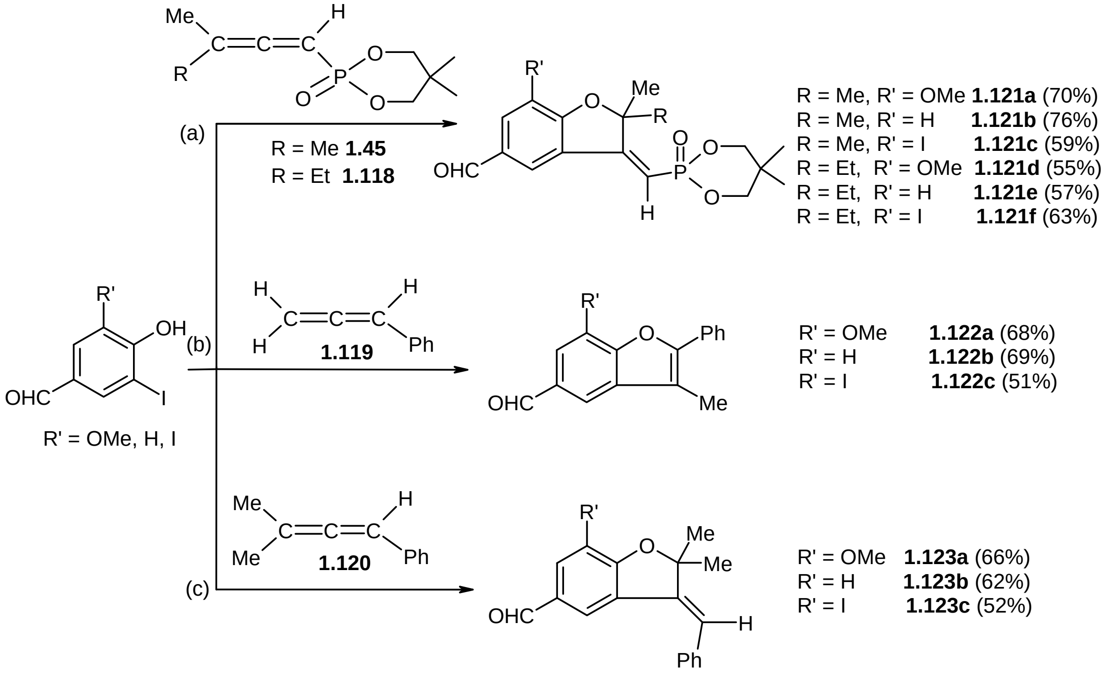
From our research group, various phosphono-benzofurans have been prepared by the coupling reactions of allenylphosphonates with 2-iodophenols in the presence of $Pd(OAc)_2$/ PPh_3 (Scheme 1.35).[47a-b] For example, allenylphosphonate **1.45** reacts with 2-iodophenol in the presence of $Pd(OAc)_2$/ PPh_3 and K_2CO_3 to give the corresponding (*E*)-phosphono-benzofurans **1.117** in good yields. Unlike the reactions of non-phosphorylated allenes which led to only two types of furans, allenylphosphonates afforded at least four different types of phosphono-benzofurans.

Scheme 1.35



As a continuation of the above work on Pd- catalyzed reactions on allenes, various functionalized benzofurans **1.121a-f, 1.122a-c**, and **1.123a-c** have been synthesized by coupling allenyl phosphonates **1.45**, **1.118** or organic allenes **1.119, 1.120** with functionalized iodophenols in PEG-400 as the medium (Scheme 1.36).[47c] This reaction proceeded under green conditions with high regioselectivity and avoided the requirement of additional phosphine as ligand when CsF was used as base in the reactions of =CH_2 terminal allenylphosphonates

Scheme 1.36

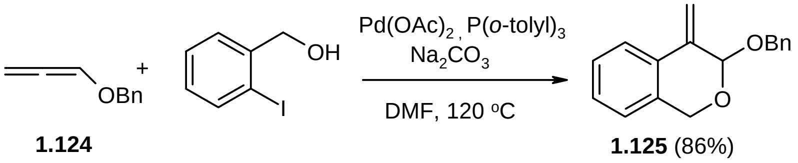


Conditions: $Pd(OAc)_2$ / (*o*-tolyl)$_3$P/ K_2CO_3, PEG-400, 90 °C, 12 h

1.32 Synthesis of benzopyrans and related compounds

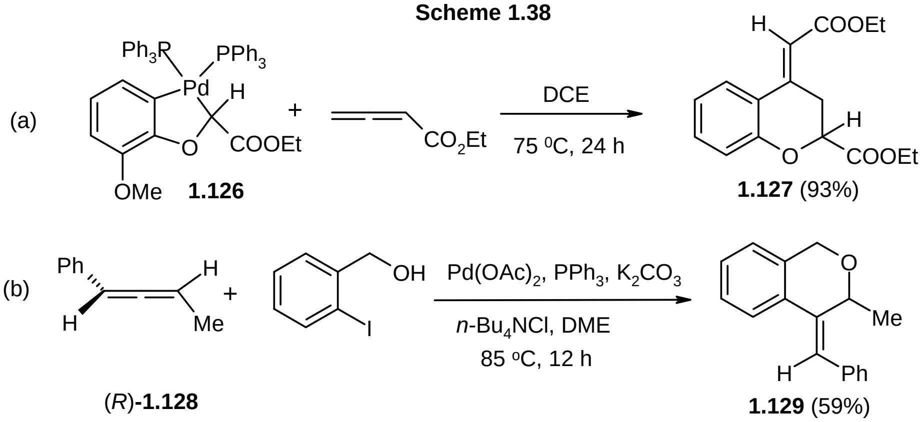
In the literature, there are very few reports on the synthesis of benzopyrans through the Pd-catalyzed annulations using allenes and 2-iodobenzyl alcohol.[43,49] Thus, the reaction of heteroatom substituted allene **1.124** with 2-iodobenzyl alcohol in the presence of $Pd(OAc)_2$/ P(*o*-tol)$_3$/ *n*-Bu_4NCl/ Na_2CO_3 at 120 °C in DMF afforded the benzopyran **1.125** regioselectively in good yield (Scheme 1.37).[50] This is a good method for the synthesis of heteroatom substituted benzopyrans.

Scheme 1.37



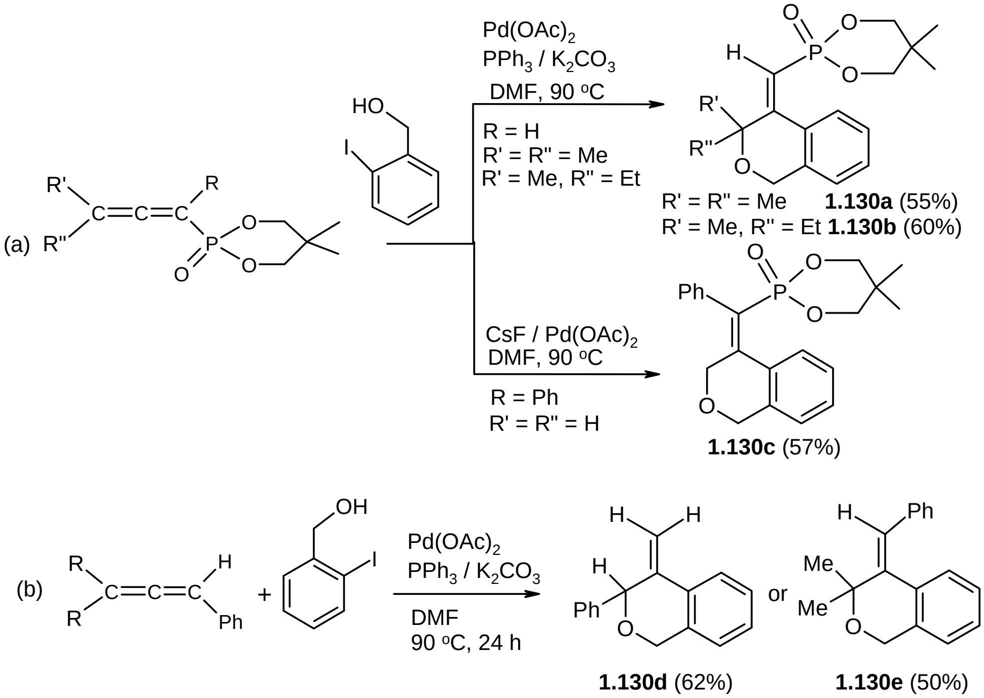
The insertion reaction of allene $H_2C{=}C{=}CH(CO_2Et)$ into benzannulated oxapalladacycle **1.126** at elevated temperatures provides benzopyran **1.127** in high yields (Scheme 1.38a).[51] This reaction works for allenes with either electron deficient or electron donating substituents. In another system, by means of the reaction of 2-iodobenzyl alcohol with the chiral allene (*R*)-**1.128**, the benzopyran derivative **1.129** was prepared in 59 % yield (Scheme 1.38b).[52] However, chirality of the allene could not be preserved under these palladium-catalyzed reaction conditions. Similar reactions were reported by Larock and coworkers earlier.[53]

Scheme 1.38



Recently, our research group reported the synthesis of benzopyran derivatives by the Pd-catalyzed annulations of allenes with 2-iodobenzyl alcohol.[47c] Thus compounds **1.130a-e** were prepared by treating various allenes with 2-iodobenzyl alcohol (Scheme 1.39a-b).

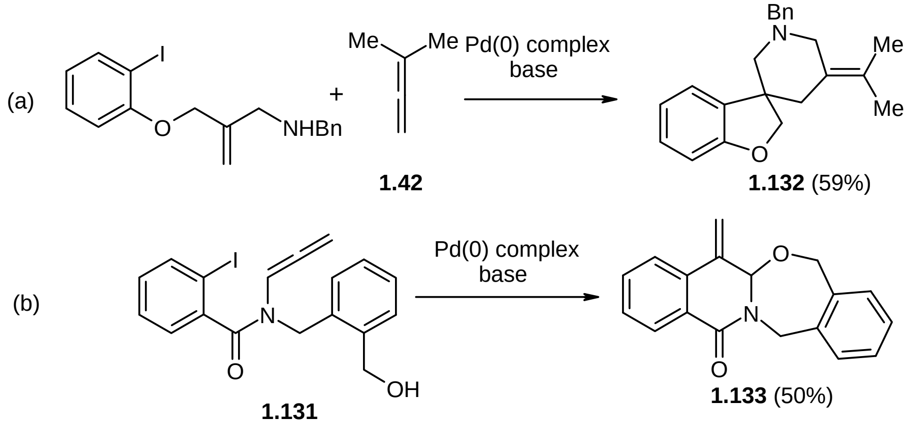
Scheme 1.39



1.33 Synthesis of spirocycles

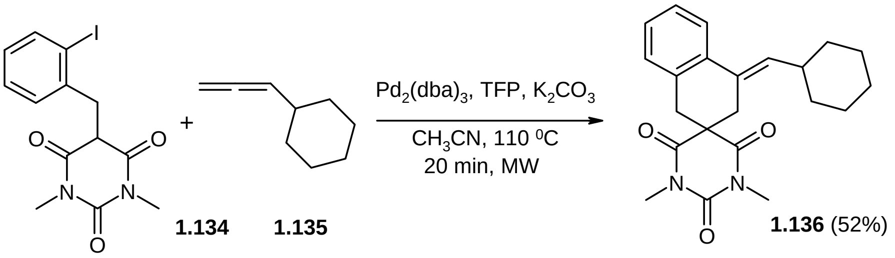
Grigg reported the novel Pd-catalyzed carbo- and hetero-annulation cascade process involving allene **1.42** and **1.131** that affords the unusual compounds **1.132** and **1.133** with spiro- and hetero-cyclic frameworks, respectively (Scheme 1.40).[54]

Scheme 1.40



Spirocyclization of the iodoarene **1.134** with the allene **1.135** by Pd(0)-catalyzed process leads to the formation of six-membered spirocyclic barbiturate **1.136** involving the formation of three C-C bonds (Scheme 1.41).[55] In reactions of allenes such as these, 2-iodobenzamides can also be used in annulation reactions.[56]

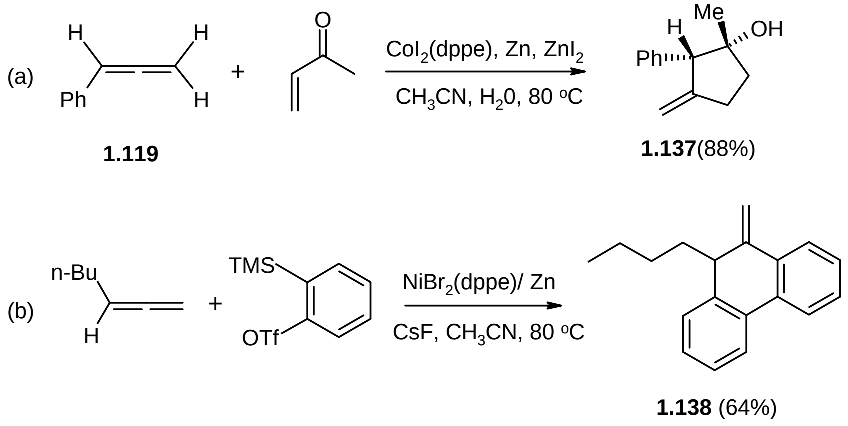
Scheme 1.41



1.34 *Synthesis of carbocycles*

Cheng and co-workers reported a mild and highly diastereoselective cobalt catalyzed intermolecular reductive [3+2] cycloaddition of allene **1.119** with methyl vinyl ketone leading to the five-membered carbocycle **1.137** in good yield (Scheme 1.43a).[57] It may be noted that this reaction can afford a cyclopentane ring system with appended –OH and olefin residues. The same group reported the Ni-catalyzed chemoselective cyclotrimerization of benzyne with allene leading to 10-methylene-9,10-dihydrophenanthrene **1.138** in moderate yield. This method, however, is limited to terminal allenes only (Scheme 1.43b).[58]

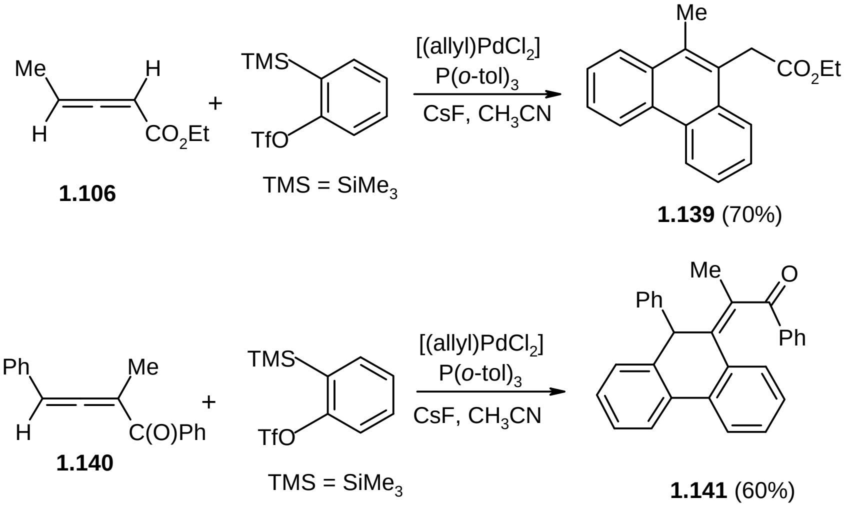
Scheme 1.43



Recently, another group reported the synthesis of phenanthrenes **1.139** and **1.141** by the cyclotrimerization of benzyne with allenes **1.106**, **1.140** catalyzed by a Pd-complex

(Scheme 1.44) [59] This method allows the use of a wide range of allenes, including internal and terminal allenes, in the reaction with arynes.

Scheme 1.44



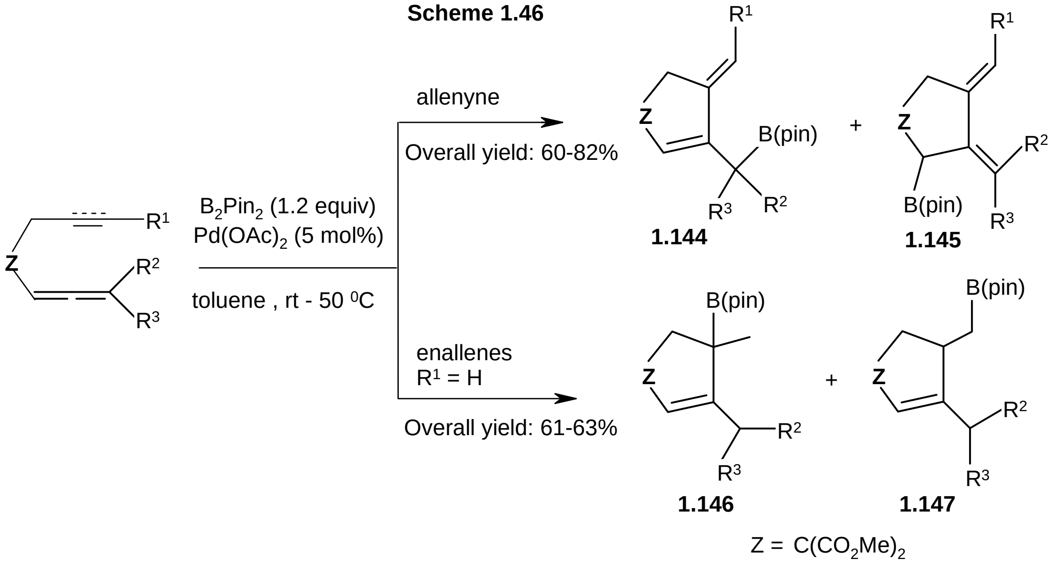
Backvall and co-workers reported that the oxidative cyclization of **1.142** in presence of catalytic amount of Pd(O_2CCF_3)$_2$ to give **1.143** (Scheme 1.45).[60] This is the first example of an allylic oxidation leading to carbon-carbon bond formation employing *catalytic* amounts of palladium(II).

Scheme 1.45

BQ = benzoquinone

Very recently, Cardenas *et al* have prepared the synthetically useful allyl boronates **1.144, 1.146** and alkyl boronates **1.145, 147** through the Pd-catalyzed cyclization of 1,5- and 1,6-allenynes and 1,5-enallenes with bis(pinacolato)diboron in a formal hydroborylative carbocyclization reaction (Scheme 1.46).[61] This is a regioselective process and the obtained boronates can be used in the allylation of aldehydes to give functionalized derivatives.

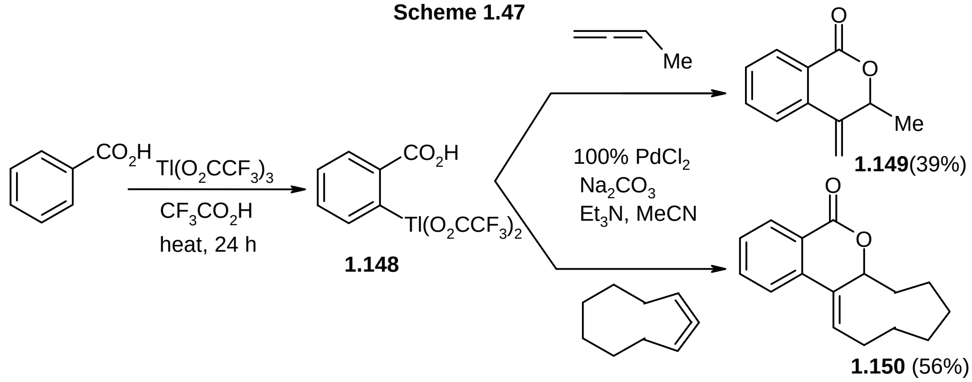
Scheme 1.46



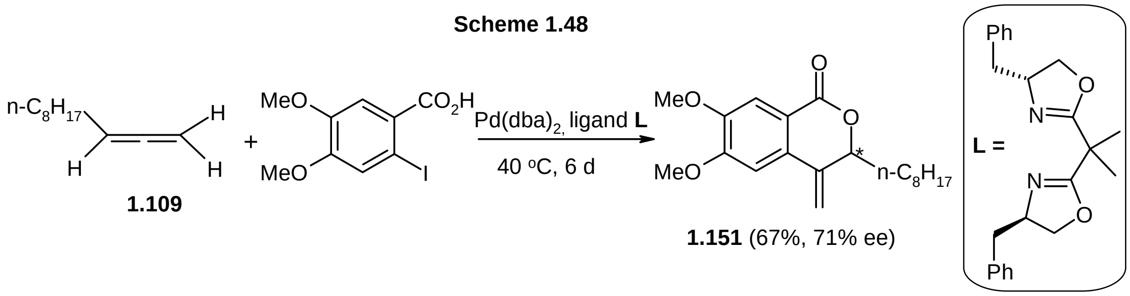
1.35 Synthesis of isocoumarins and related lactones

In 1984, Larock and co-workers reported a *stoichiometric* Pd(II) promoted cyclization of allenes with *ortho*-thallated benzoic acid **1.148** to afford cyclic benzoannulated δ-valerolactones **1.149** and **1.150** (Scheme 1.47).[62] This reaction was the first example where carbon-palladium bond was formed in a *trans*-metallation reaction from thallium to palladium. Later, the chiral isocoumarin derivative **1.151** was synthesized from the reaction of allene **1.109** with 2-iodobenzoic acid using Pd(dba)$_2$ and chiral bisoxazoline ligand (**L**) by the same group (Scheme 1.48).[63] This method is applicable to non-functionalized allenes only.

Scheme 1.47

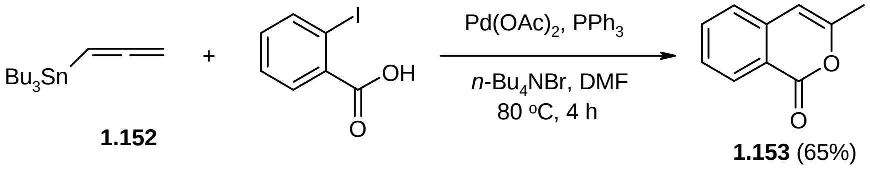


Scheme 1.48



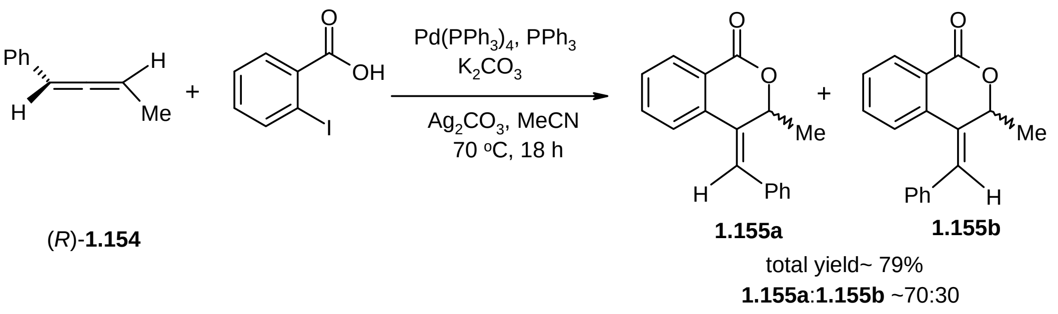
Cherry *et al* developed a convenient regio-selective method for the synthesis of 3-substituted coumarin **1.153** in good yields via Pd-catalyzed coupling of 2-iodobenzoic acid and allenyltributyltin **1.152** (Scheme 1.49).[64] This process is limited in scope because only a limited number of Sn-connected allene precursors are available.

Scheme 1.49



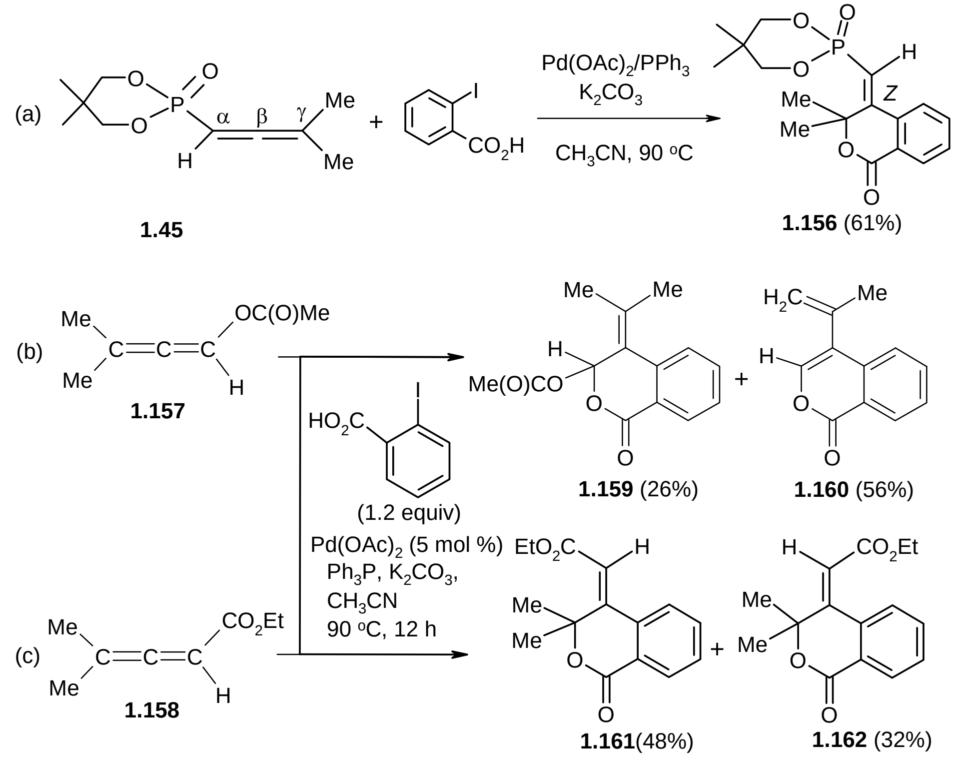
Isomeric lactones have been synthesized by the Pd-catalyzed carboxylation of allenes.[65] Thus, reaction of the chiral allene (*R*)-**1.154** with 2-iodobenzoic acid in the presence of $Pd(PPh_3)_4$/ PPh_3/ K_2CO_3/ Ag_2CO_3 at 70 °C/ 18 h in acetonitrile gives the isocoumarins **1.155a** and **1.155b** (70:30) in good yields (Scheme 1.50). The enantiomeric purity is only ~5 % due to the use of excess of base.

Scheme 1.50



Our research group reported the synthesis of phosphono-isocoumarin **1.156** and isocoumarins **1.159-1.162** by the reaction of allenylphosphonate **1.45** and 3-methylbuta-1,2-dienyl acetate **1.157** and ester allene **1.158** with 2-iodobenzoic acid in the presence of $Pd(OAc)_2$/ PPh_3/ K_2CO_3 in acetonitrile medium (Scheme 1.51a-c).[47a-b] When 4-iodobenzoic acid was used in place of 2-iodobenzoic acid, a normal arylated product with pendant –COOH group was obtained. Vinylic halides with additional functional groups can also undergo similar annulation with allenes to produce five- or six–membered heterocycles.[53, 65]

Scheme 1.51



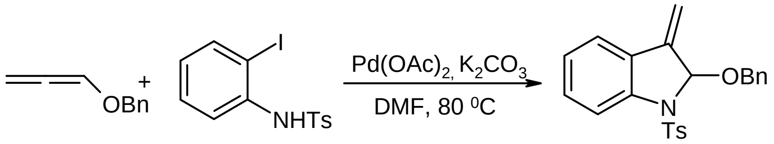
1.4 Synthesis of indole, isoquinoline, and carboline derivatives *via* metal-catalyzed coupling of allenes or alkynes

Mechanistically, Pd-catalyzed annulation reactions of alkynes (acetylenes) and allenes are not much different.[66a-d] Hence a brief discussion on the reactions using alkynes is also included here, along with these of allenes.

1.41 Synthesis of indoles

The highly regioselective synthesis of indole **1.163** through the Pd-catalyzed annulation reaction of heteroatom substituted allenes **1.124** with *N*-tosyl-2-iodoaniline was reported by Sakamoto and co-workers (Scheme 1.52).[66d] This method is limited to terminal allenes and to allenes with electron donating substituents.

Scheme 1.52

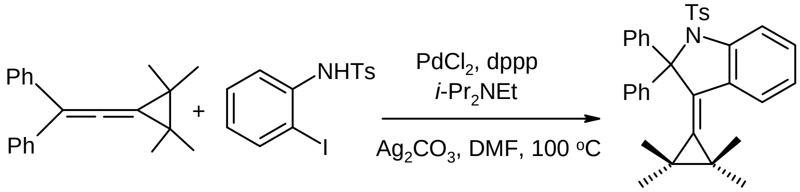


1.124

1.163 (99%)

Li and Shi prepared the cyclopropane appended indole **1.164** in moderate yields by the Pd-catalyzed cross-coupling reaction of diarylvinylidenecyclopropane **1.113** with 2-iodoaniline (Scheme 1.53).[45] This is not a good method for indoles (low yields) although the same route worked well for the benzofurans.

Scheme 1.53

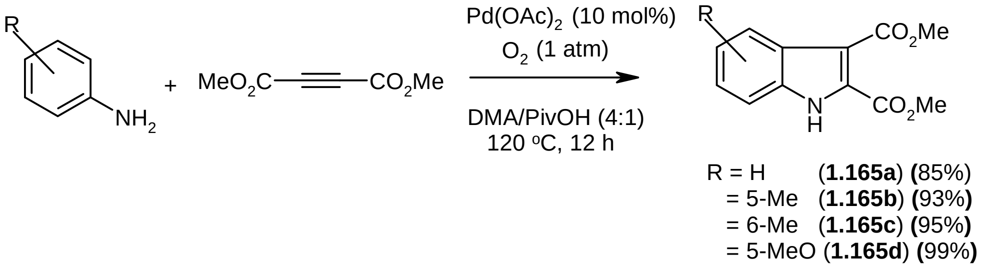


1.164 (58%)

1.113

Recently Jiao and co-workers have discovered a unique and direct approach for compounds with indole skeleton **(1.165a-d)** in good yields from simple and readily available anilines and alkynes by C-H activation (Scheme 1.54). Dioxygen (1 atm) is used as the oxidant in this catalytic cycle. The conditions are mild and do not require the addition of a ligand or base. Using this method, both *N*-unsubstituted and *N*-alkyl anilines can be successfully transformed into the corresponding indoles. [67]

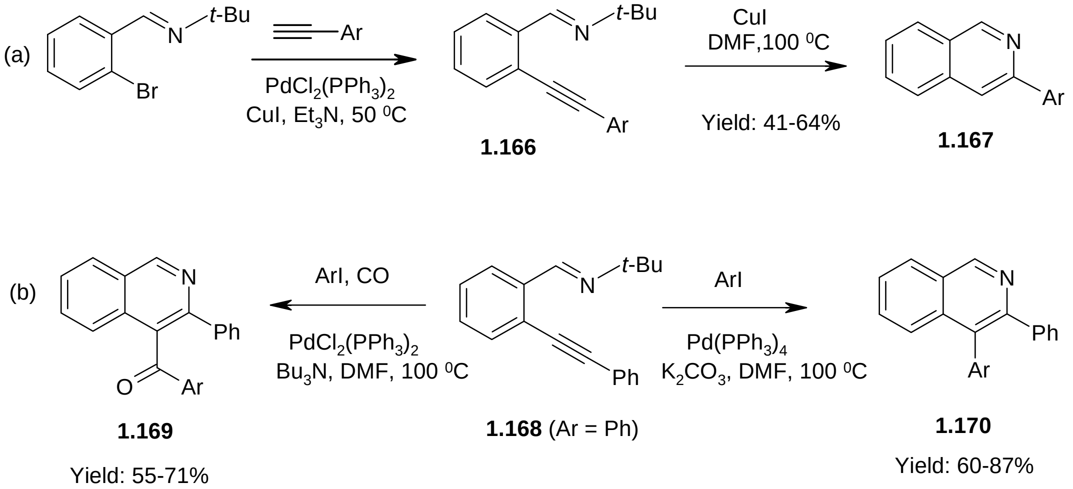
Scheme 1.54



1.42 *Synthesis of isoquinolines*

In the year 1998, Larock and co-workers developed an efficient synthesis of isoquinolines by the Pd-catalyzed annulation of alkynes with aldimines. A wide variety of aryl acetylenes can be applied in this process and the yields are moderate to excellent with high regio-selectivity.[68] Very recently, as an extension of this work, the same group reported the first solution-phase synthesis of isoquinoline scaffolds **1.167** through the copper-catalyzed cyclization of iminoalkynes **1.166** (Scheme 1.55a) and the palladium catalyzed imino-annulation of internal alkyne **1.168** to afford **1.169-1.170** (Scheme 1.55b).[69]

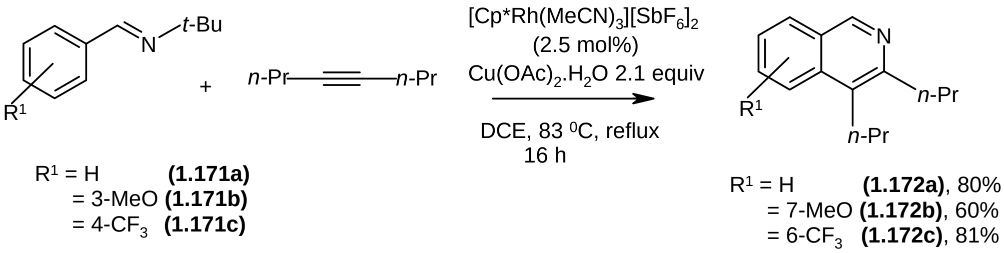
Scheme 1.55



Very recently, Fagnou reported the synthesis of isoquinolines **(1.172a-c)** by the C-H functionalization of aldimines **(1.171a-c)** through rhodium catalyzed cyclization of alkynes. This reaction occurs under mild conditions with high regio-selectivity (Scheme

1.56). A variety of electron-donating or electron-withdrawing groups may be employed on the aldimine coupling partner.[70] Later, the same group disclosed an intermolecular and mechanistically distinct process that affords the isoquinoline motif via Rh(III)-catalyzed annulation of benzhydroxamic acids with alkynes.[71] This is a conceptually new approach to C-N bond formation from benzhydroxamic acid precursors.

Scheme 1.56



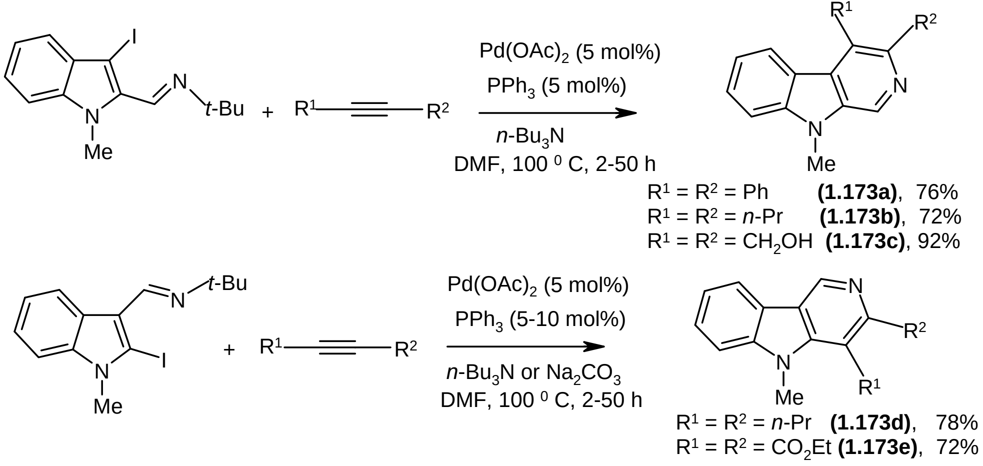
R^1 = H **(1.171a)**
= 3-MeO **(1.171b)**
= 4-CF_3 **(1.171c)**

R^1 = H **(1.172a)**, 80%
= 7-MeO **(1.172b)**, 60%
= 6-CF_3 **(1.172c)**, 81%

1.43 *Synthesis of carbolines*

A variety of substituted *α*- and β- carbolines **(1.173a-e)** have been synthesized in good to excellent yields through the annulation of internal acetylenes with *t*-butylimines of *N*-substituted 3-iodoindole-2-carboxaldehydes and 2-haloindole-3-carboxaldehydes respectively, in the presence of a palladium catalyst (Scheme 1.57).[72] Various substituted acetylenes (such as aryl-, alkyl-, ester-, and hydroxymethyl-) undergo this process in moderate to excellent yields. When unsymmetrical alkynes are employed, mixtures of regioisomers are observed in most cases.

Scheme 1.57

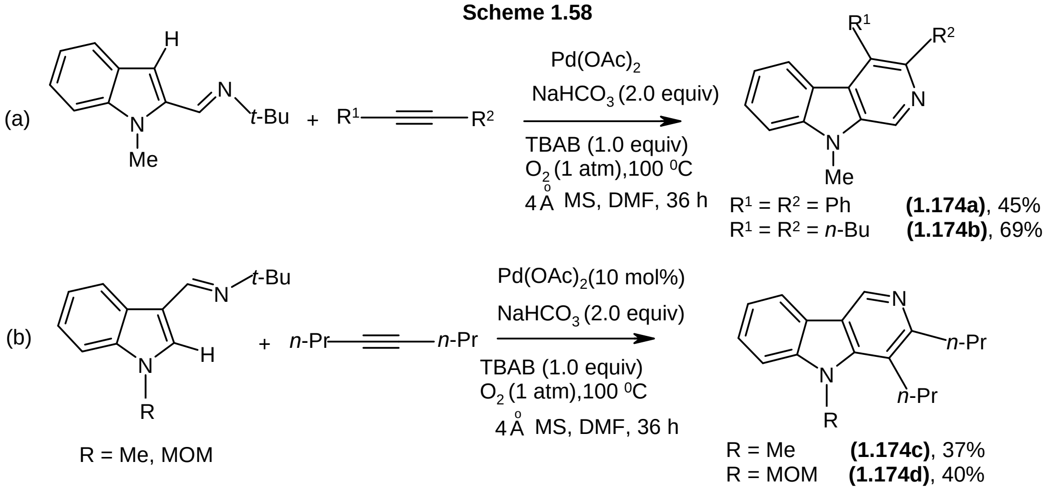


$R^1 = R^2$ = Ph **(1.173a)**, 76%
$R^1 = R^2$ = *n*-Pr **(1.173b)**, 72%
$R^1 = R^2 = CH_2OH$ **(1.173c)**, 92%

$R^1 = R^2$ = *n*-Pr **(1.173d)**, 78%
$R^1 = R^2 = CO_2Et$ **(1.173e)**, 72%

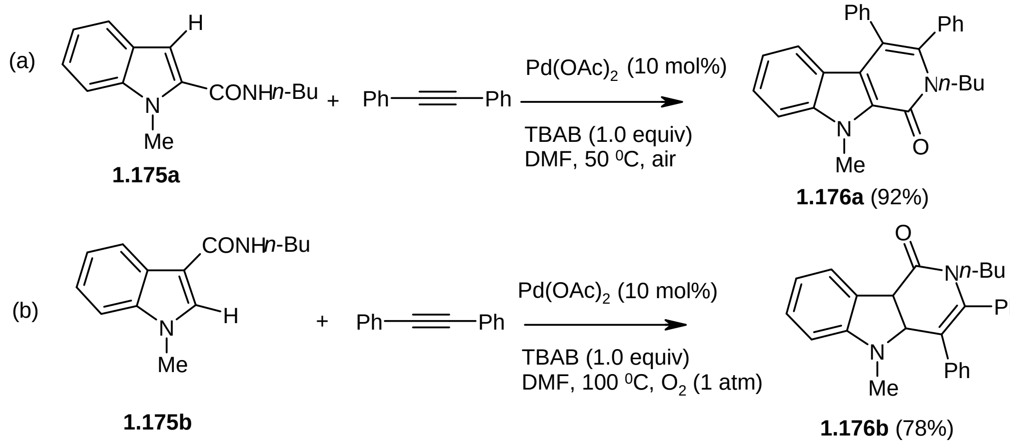
Very recently, Jiao and his co-workers synthesized carboline derivatives **(1.174a-d)** by the Pd(II)-catalyzed direct-dehydrogenative annulation (DDA) of internal alkynes and *tert*-butylimines of *N*-substituted indole carboxaldehydes via direct C-H bond activation (Scheme 1.58a-b).[73] This cyclization protocol is achieved using oxygen as oxidant and in the absence of any expensive ligand or metal oxidant.

Scheme 1.58



As a continuation of the above work, the same group disclosed a novel Pd-catalyzed direct dehydrogenative annulation (DDA) of indole carboxamides **(1.175a-b)** with internal alkynes using air or oxygen as the oxidant (Scheme 1.59a-b). This reaction provides a new strategy for the synthesis of synthetically and medicinally important α- and γ-carbolinone derivatives **(1.176a-b)** via C-H and N-H bond cleavage.[74]

Scheme 1.59

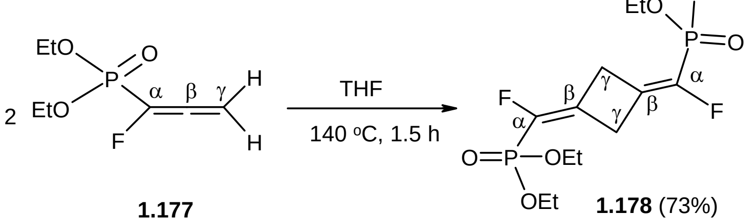


1.5 Cycloaddition reactions involving phosphorylated allenes or related allenes

Allenes are excellent partners for both [2+2] and [4+2] cycloaddition reactions due to their cumulative double bonds.[75] These reactions are subdivided into two parts: inter- and intra-molecular cycloaddition reactions. The following session deals with some of the intermolecular cycloaddition reactions.

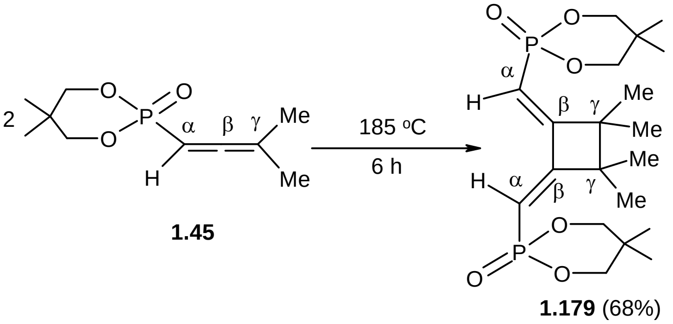
Allene can undergo [2+2] cycloaddition with itself or with another partner (e.g. R'C≡CR') leading to a range of cyclobutanes/cyclobutenes with the nature of the product depending on the electronic and/or steric requirements. For example, the allene, α-fluoroallenylphosphonate **1.177** undergoes [2+2] cycloaddition reaction in a sealed tube provided the tail-to-tail dimer **1.178** exclusively at the β,γ-position (Scheme 1.60).[76] The bulky phosphorus substituent on the allene moiety allowed rotation in the bisallyl diradical intermediate yielding the corresponding dimer **1.178**.

Scheme 1.60



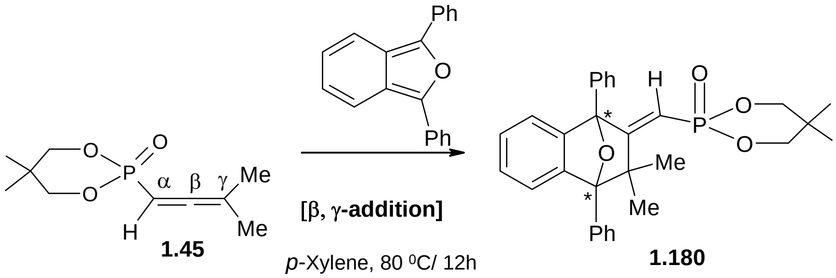
From our laboratory, a head-to-head [2+2] dimerization of the allene **1.45** at the β,γ-position under thermal conditions, which is in contrast to the above reaction, has been reported.[77] The cycloadduct **1.179** was formed exclusively with the defined stereochemistry as shown in Scheme 1.61 via a concerted diradical mechanism.

Scheme 1.61



The cycloaddition reactions of allenylphosphonates with 1,3-diphenylisobenzofuran and anthracene have been recently reported.[78] It is noteworthy that the allene **1.45** undergoes [4+2] cycloaddition with 1,3-diphenylisobenzofuran only at the (β,γ) carbon-carbon double bond (Scheme 1.62) leading to the product **1.180**. Since chiral centers are generated in such a reaction, it would be interesting to see how the reactions go by using allenes that have chiral centers at the ring containing phosphorus.

Scheme 1.62



OBJECTIVES OF THE PRESENT WORK- PART A

The objectives of this part of the work are outlined below.

(i) To study the reactions of allenylphosphonates and allenylsulfones with *N*-tosylaldimine in the presence of *N*-heterocyclic carbenes (NHCs),

(ii) To investigate base-catalyzed reactions of allenylphosphonates and allenylphosphine oxides with *N*-thiophosphinyl imines,

(iii) To investigate Pd-catalyzed annulation reactions of allenes with 3-iodo-indole-2-carboxylic acid derivatives and 1-alkyl-indole-2-carboxylic acids, and

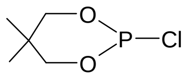
(iv) To study the effect of newly generated chiral centers on the product distribution in cycloaddition reactions involving phosphorus-based allenes.

Chapter 2

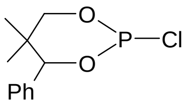
RESULTS AND DISCUSSION

2.1 Synthesis of allenylphosphonates (6a-j, 7a-c)/ allenylphosphine oxides (8a-e) and allenylphosphoramidates (9a-d)

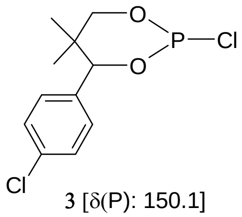
The P^{III}-Cl precursors **1**[79a] and **2**[79b] have been prepared by treating the appropriate diol with phosphorus trichloride under neat conditions. In a similar fashion, the precursor **3** was prepared by using the corresponding diol which itself was prepared by treating isobutyraldehyde with 4-chlorobenzaldehyde (equation 1).[79c] The chlorophosphite **3** is new. The diamine required for the synthesis of **4** was prepared by slightly modifying the literature procedure involving the reaction of *trans*-1,2-diaminocyclohexane with isopropyl bromide/KOH;[79d] the substituted diamine so prepared was treated with PCl_3 in the presence of Et_3N to obtain compound **4**.[79e] The P-Cl functionality present in these compounds is utilized in subsequent reactions as detailed below.



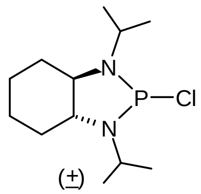
1 [δ(P): 145.8]



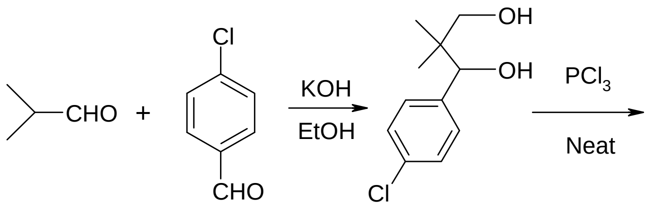
2 [δ(P): 149.6]



3 [δ(P): 150.1]



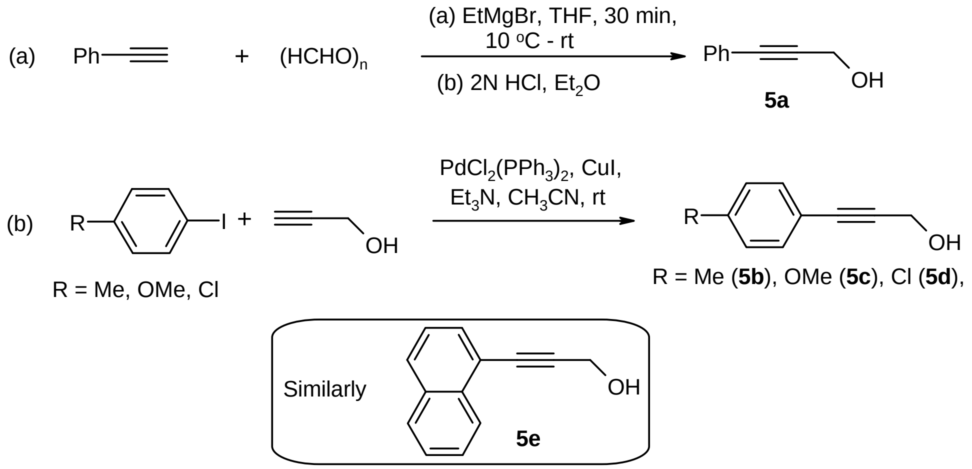
4 [δ(P): 178.8]



3 [b.p. 110 °C/ 2 mm] (1)

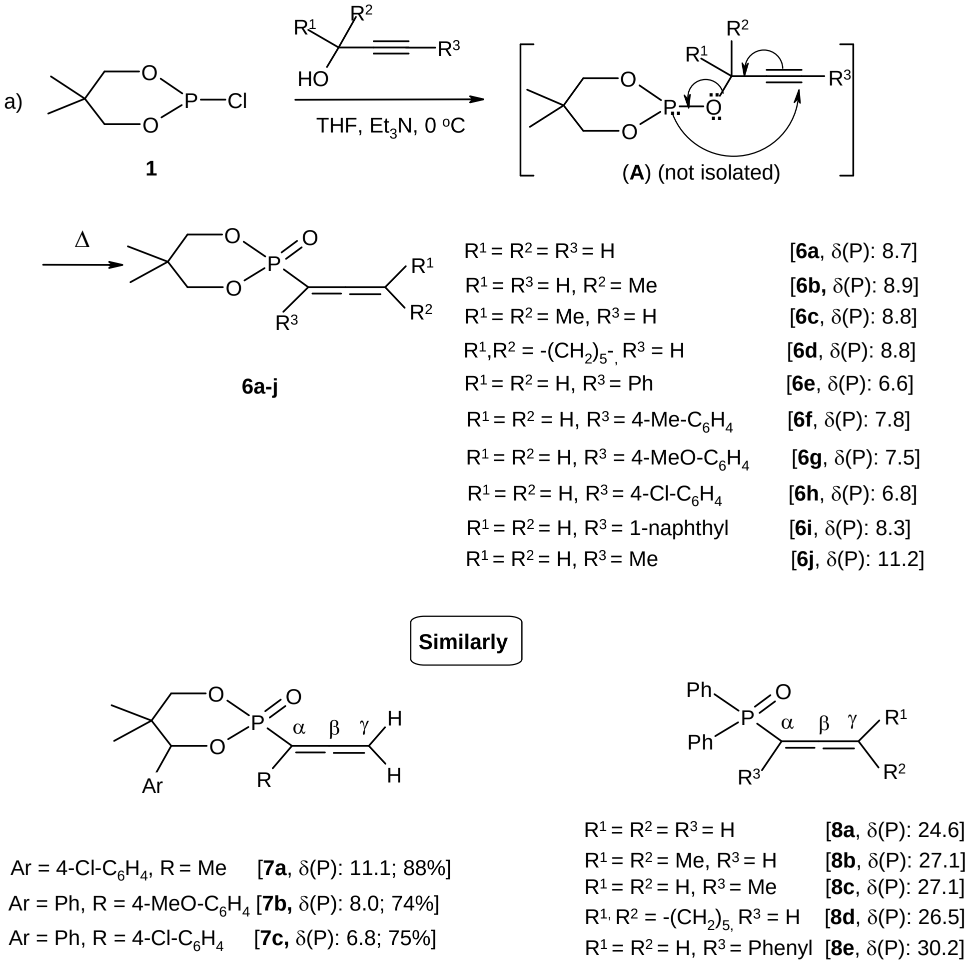
Allenylphosphonates and allenylphosphine oxides can be synthesized more easily than allenoates and keto-allenes.[80,5a] However, only a few references dealing with allenylphosphonates are available in the literature. In this section, we shall discuss a few aspects of the synthesis and stability of different types of phosphorus-based allenes. The propargyl alcohol precursors for the allenes **6a-d**, **6j, 7a, 8a-d** and **9d** are commercially available and the remaining alcohols (**5a-e**) were prepared by using literature procedures (Scheme 1).[81-82]

Scheme 1



Allenylphosphonates **6a-j** [*via* intermediate (**A**)] and **7a-c** as well as allenylphosphine oxides **8a-e** were prepared by the methods previously reported from our laboratory by utilizing appropriate propargyl alcohols (Scheme 2).[17c] Allenes **7a-c** are new. The new allenylphosphoramidates **9a-d** have been obtained by the reaction of chlorophosphoramidite **4** with the corresponding propargyl alcohols (Scheme 3). When we used the chloro precursor prepared by starting with a mixture of the *cis*- and *trans*-diamines corresponding to **9c**, there were four peaks in the ^{31}P NMR spectrum of the reaction mixture [δ 29.2, 28.4, 23.4, 21.8] in the allenylphosphoramidate region. Since this would have led to lot more complications than could be handled by normal chromatographic separation, we continued with only the *trans*-diamine derivative. In the latter case, only the species corresponding to the most downfield signal [δ(P) 29.2 in the reaction mixture when *cis*+*trans* diamine was used; δ(P) 30.0 after purification] was observed.

Scheme 2

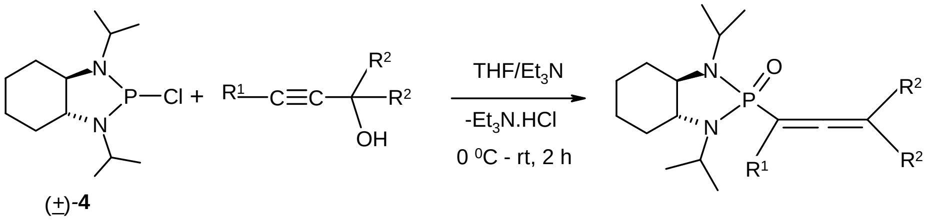


$R^1 = R^2 = R^3 = H$ [**6a**, δ(P): 8.7]
$R^1 = R^3 = H, R^2 = Me$ [**6b,** δ(P): 8.9]
$R^1 = R^2 = Me, R^3 = H$ [**6c**, δ(P): 8.8]
$R^1,R^2 = -(CH_2)_5-, R^3 = H$ [**6d**, δ(P): 8.8]
$R^1 = R^2 = H, R^3 = Ph$ [**6e**, δ(P): 6.6]
$R^1 = R^2 = H, R^3 = 4\text{-Me-}C_6H_4$ [**6f**, δ(P): 7.8]
$R^1 = R^2 = H, R^3 = 4\text{-MeO-}C_6H_4$ [**6g**, δ(P): 7.5]
$R^1 = R^2 = H, R^3 = 4\text{-Cl-}C_6H_4$ [**6h**, δ(P): 6.8]
$R^1 = R^2 = H, R^3 =$ 1-naphthyl [**6i**, δ(P): 8.3]
$R^1 = R^2 = H, R^3 = Me$ [**6j**, δ(P): 11.2]

Ar = $4\text{-Cl-}C_6H_4$, R = Me [**7a**, δ(P): 11.1; 88%]
Ar = Ph, R = $4\text{-MeO-}C_6H_4$ [**7b,** δ(P): 8.0; 74%]
Ar = Ph, R = $4\text{-Cl-}C_6H_4$ [**7c,** δ(P): 6.8; 75%]

$R^1 = R^2 = R^3 = H$ [**8a**, δ(P): 24.6]
$R^1 = R^2 = Me, R^3 = H$ [**8b**, δ(P): 27.1]
$R^1 = R^2 = H, R^3 = Me$ [**8c**, δ(P): 27.1]
$R^1, R^2 = -(CH_2)_5, R^3 = H$ [**8d**, δ(P): 26.5]
$R^1 = R^2 = H, R^3 =$ Phenyl [**8e**, δ(P): 30.2]

Scheme 3



$R^1 = Ph, R^2 = H$ [(±)-**9a**, δ(P): 23.5]
$R^1 = 4\text{-MeO-}C_6H_4, R^2 = H$ [(±)- **9b**, δ(P): 24.0]
$R^1 = C_{10}H_7, R^2 = H$ [(±)-**9c**, δ(P): 30.0]
$R^1 = H, R^2 = Me$ [(±)-**9d**, δ(P): 25.0]

All the allenylphosphonates/allenylphosphine oxides are crystalline solids and are stable under nitrogen. We could preserve them under these conditions for several months. They show a characteristic strong band in the range 1930-1938 cm^{-1} in the IR spectra due to υ(C=C=C) stretch.[80] The ^{31}P NMR spectra show a single peak in the range δ 6.8-11.1 for the new α-aryl allenylphosphonates **7a-c** while the allenylphosphoramidates **9a-d** exhibit a signal in the region δ 23.0-30.0. The observed coupling constants [*J*(P-H) or *J*(P-C)] of allenylphosphine oxides **8a-e** are low compared to allenylphosphonates **6a-j/ 7a-c** as expected.[83] It should be noted that in principle, allenic =CH_2 protons should have been equivalent. The ^{13}C NMR spectra are also quite useful for further analysis. For example, the *α*-carbon appears as a doublet at δ 101.7 [^1J(P-C) = 142.0 Hz] in the ^{13}C NMR spectrum of **9b**. The allenic *β*- and *γ*-carbon nuclei appear around δ 215.6 and 75.5, respectively. Since there are two chiral centers in compound **9c**, and since we planned to explore the effect of these in our later reactions, we have determined the X-ray structure of this allene **9c** [Figure 2]. This structure can be compared with three others (**I-III**) reported from our laboratory (Chart 1).[77] The C=C=C bond angle is expectedly close to linearity although there is a fairly bulky group at one of the ends of allene moiety due to which we expected some bending at the central carbon. Bent allenes have been of current interest in terms of bonding and structure [cf. Chart 2].[84] The P-C bond in **9c** is longer than those observed in **I-III**, perhaps because of the electron releasing nature of the amino substituent on the phosphorus in **9c**. In the ^{1}H NMR spectrum of compound **9b** (and **9a**), an eight line pattern (~AB part of ABX spin system) observed in the region of δ 5.03-5.16 is ascribed to the protons attached to the *γ*-carbon (to phosphorus); in contrast, the naphthyl compound **9c** shows a simple doublet. These features in **9a-b** are due to ^4J(P-H) coupling in addition to ^2J(H-H) for the inequivalent terminal =CH_2 protons. The spectra for **9a-b** show nearly double the lines observed in **9c** suggesting the nonequivalence of several carbon nuclei in **9a-b**. The corresponding ^{13}C NMR spectra also reflect these [Figure 1]. The dihedral angle between the planes containing (i) H(17A), H(17B), C(17) and C(10), and (ii) P1, C(2), C(3) and C(10) in this compound is 89(1)^0 which is expected for orthogonality for allene substituents and is similar to those in **I** and **III**; this value can be contrasted with the angle of 83(1)^o in **II** which is significantly different from the expected orthogonality. Although we were more curious about the compounds **9a-b** because of the unexpected inequivalence of allenic =CH_2 protons, so far we have not been successful in crystallizing these for X-ray structure determination.

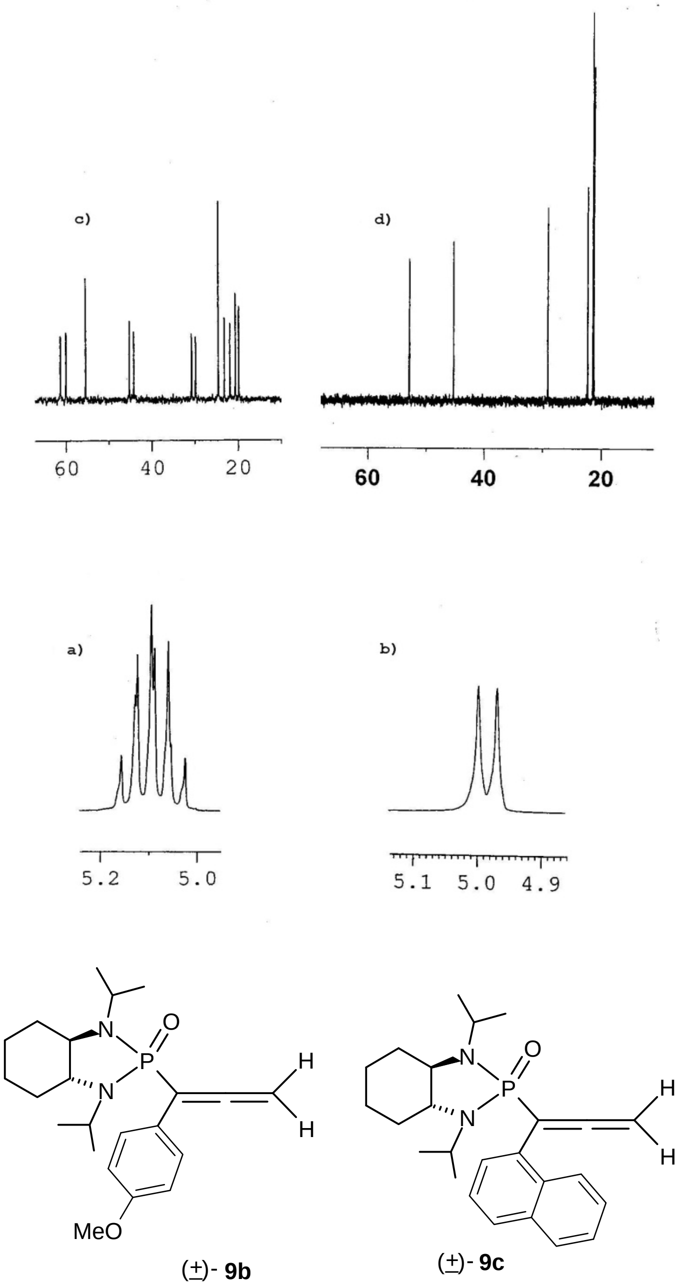


Figure 1. (a) ^{1}H NMR spectrum of **9b** [allenic =CH_2 region] (b) ^{1}H NMR spectrum of **9c** [allenic =CH_2 region], (c) ^{13}C NMR spectrum of **9b** [selected aliphatic region; note the ***splitting*** of N*C*H carbon signals] (d) ^{13}C NMR spectrum of **9c** [selected aliphatic region].

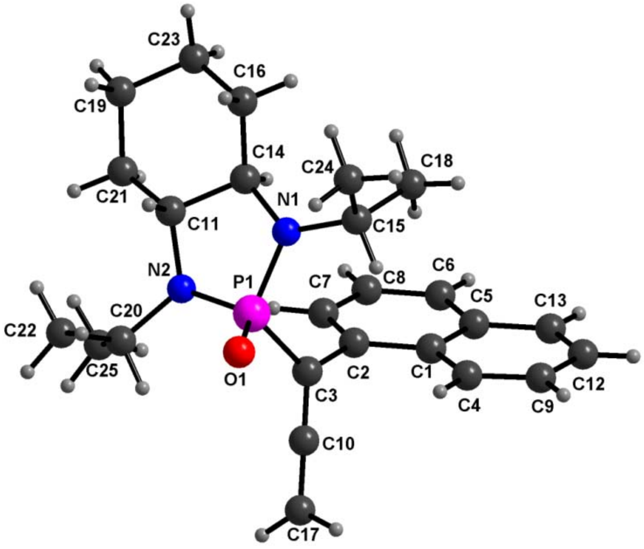
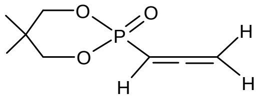
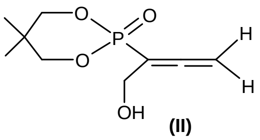


Figure 2. Molecular structure of allene **9c**. Selected bond lengths [Å] with esds in parentheses. P(1)-O(1) 1.474(2), P(1)-C(3) 1.819(3), C(3)-C(10) 1.302(4), C(10)-C(17) 1.307(5), C(2)-C(3) 1.508(3). C(3)-C(10)-C(17) = 178.8(4)°.

Chart 1

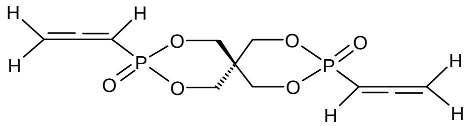


(I)



(II)

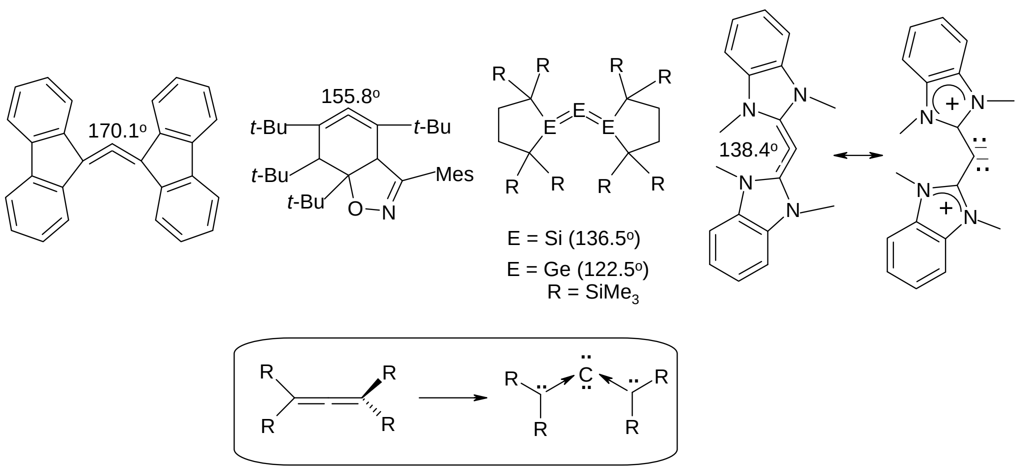
	(I)	(II)
P-C (Å)	1.771(2)	1.779(2)
C(P)=C (Å)	1.288(3)	1.302(2)
C=C (terminal) (Å)	1.280 (4)	1.290(3)
C=C=C (°)	179.1(2)	178.8(2)



(III)

P-C (Å)	1.777(4)
C(P)=C (Å)	1.306(6)
C=C (terminal) (Å)	1.307(6)
C=C=C (°)	178.7(5)

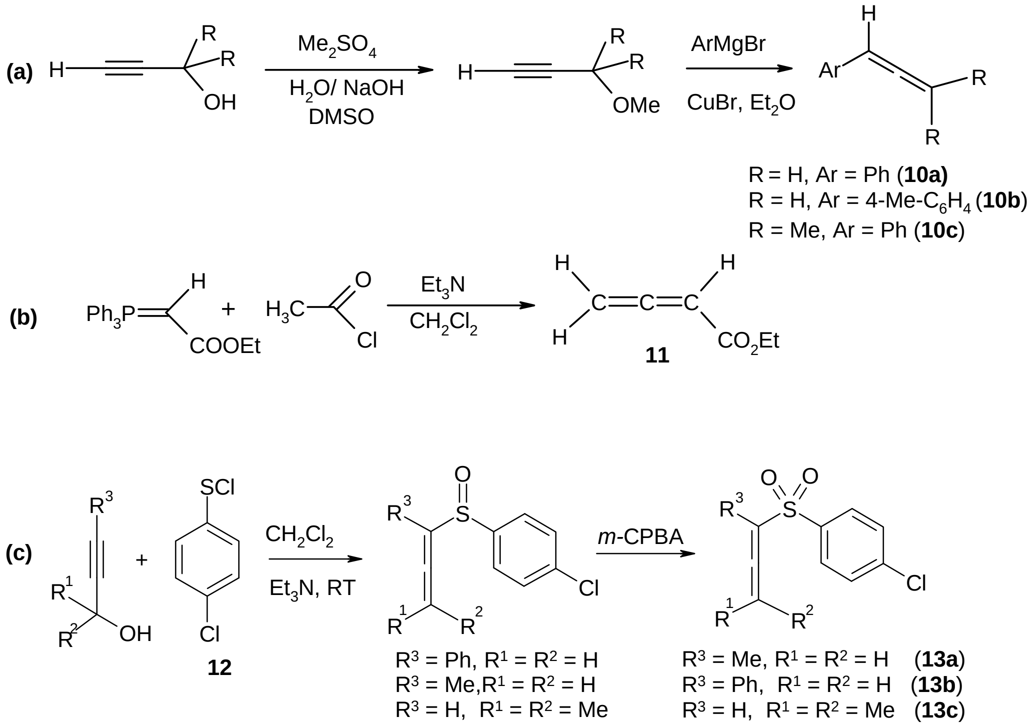
Chart 2: Some 'BENT" allenes and a possible rationale for bending



2.2 Synthesis of phenyl-substituted allenes 10a-c, 1,2-alkadienoate ester (allenoate) 11 and allenylsulfones 13a-c

Aryl substituted allenes (Ar)CH=C=CR_2 (**10a-c**) were prepared by the treatment of methyl propargylic ether (obtained by the methylation reaction of propargyl alcohol) with PhMgBr in the presence of CuBr as a catalyst (Scheme 4a).[6m] After that, the crude reaction mixture had to be distilled (bp 80-85 ^{o}C/ 20 mm) to get pure allenes. They had to be stored under inert atmosphere at low temperature in dark as light and oxygen could induce polymerization.[6m] Allenyl ester (allenoate) **11** could be prepared by the treatment of *α*-phosphoranylidene esters (obtained by the reaction of PPh_3 with *α*-bromoethyl acetate) with acid chlorides in the presence of a base (Scheme 4b).[85] This compound has to be distilled prior to use (bp: 70 ^{o}C/ 15 mm of Hg) and stored in refrigerator. The reaction of 4-chlorophenylsulfenylchloride **12**[86] with the suitable propargyl alcohols in the presence of a base (Et_3N) led to the allenylsulfoxides which are oxidized by *m*-chloroperbenzoic acid (*m*-CPBA) to give allenylsulfones **13a-c** (Scheme 4c).[17] The allenylsulfones **13a-c** are crystalline solids and are stable under nitrogen for several months at low temperature.

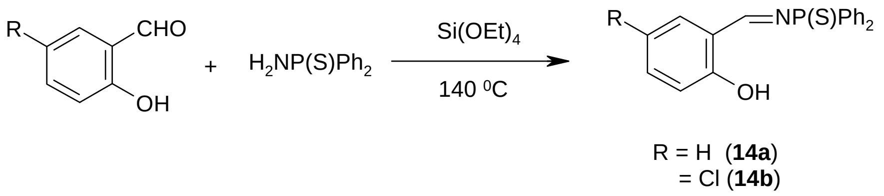
Scheme 4



2.3 Synthesis of salicyl *N*-thiophosphinyl imines 14a-b

Salicyl *N*-thiophosphinyl imines **14a-b** were synthesized by treating the corresponding *o*-hydroxybenzaldehydes (salicylaldehydes) with *P*,*P*-diphenylphosphinothioic amide ($NH_2P(S)Ph_2$) and tetraethoxysilane at 140 °C for 8 h (Scheme 5).[37a] The product was crystallized from ethyl acetate- hexane mixture.

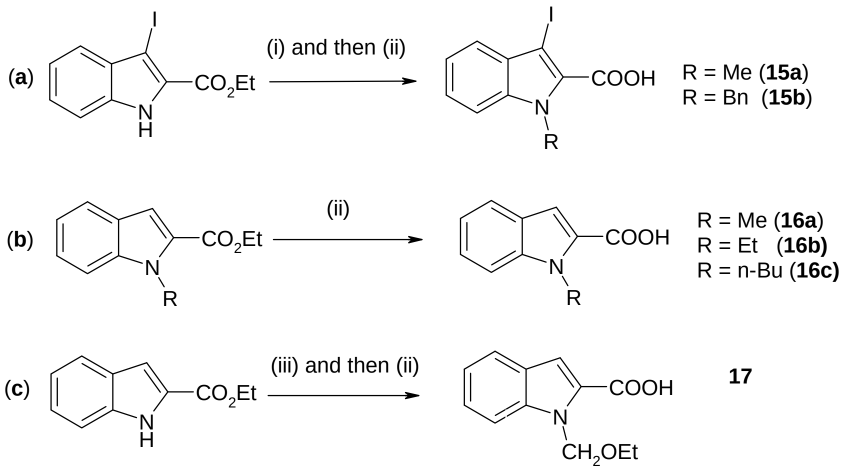
Scheme 5



2.4 Synthesis of indole-2-caboxylic acid derivatives 15a-b, 16a-c and 17

All the indole-2-carboxylic acid derivatives have been synthesized by starting with indole-2-carboxylic acid with slight modification wherever required (Scheme 6).[87] We added tetrabutylammonium bromide (TBAB) that could act as a phase transfer catalyst to increase the yield in the first step. The methylation or benzylation of 3-iodo-2-carboxylate leads to 1-methyl or 1-benzyl-3-iodoindole-2-carboxylate; this upon hydrolysis affords the corresponding carboxylic acids **15a** and **15b**. The alkyl-2-carboxylic acids **16a-c** and **17** are then prepared by the hydrolysis of the respective esters (Scheme 6a-c).

Scheme 6



Condiions: (i) 10 mol% TBAB; K_2CO_3/RX; DMF/rt/12 h

(ii) KOH/ EtOH+H_2O (2:1)/ relux/12 h

(iii) NaH/THF/$ClCH_2OEt$

2.5 Migration of tosyl group of aldimine to allenylphosphonates and allenylsulfones *via* the use of *N*-heterocyclic carbenes (NHCs)

Lewis base-catalyzed reaction between allenes and imines is known to afford functionalized pyrrolines, piperidines and aza-Baylis-Hillman adducts.[28] However, the reaction of allenes in the presence of *N*-heterocyclic carbenes (NHCs) has not been explored much. Hence we wanted to investigate the reactions of allenylphosphonates/ allenylphosphine oxides and allenylsulfones with *N*-tosylaldimine **18** that could lead to the tosylated products based on a recent report on traditional alkynes/allenes.[33] The results of the reaction of *N*-tosylaldimine **18** with the allenylphosphonates/allenylphosphine oxides and allenylsulfones using NHC as catalyst are described herein.

2.51 *Reactions of allenylphosphonates (6b-c, 6e-i)/ allenylphosphine oxides (8b-c, 8e) with PhCH=NTs (18)*

Initially, we examined reaction of allenylphosphonate **6c** with *N*-tosylaldimine **18** in the presence of NHC-1.HCl (**21**)/ DBU in toluene at 60 °C (Scheme 7). To our delight, the desired product **19** was obtained in decent yield (64%) along with the isomer **20** (14%) [Table **1**, entry 1]. But the starting material (allene) was not consumed completely (^{31}P NMR evidence). When the reaction was conducted with DMAP as the base, the yield of **19** was increased to 91% ***selectively*** (entry 2). The yield of **19** was reduced to 84% when NHC-2.HCl (**22**) was used instead of **21** (entry 3); NHC-3.HCl (**23**) was not very effective (entry 4). The yield of **19** was much better (96%) when the reaction was conducted in toluene at 90 °C using 10 mol% each of **21** and DBU (entry 5). Other conditions that we checked did not show any increase in the yield of the product (entries 6-9). Thus, the reaction conditions were optimized to 10 mol% each of **21** and DBU with toluene as the solvent and the temperature being maintained at 90 °C.

Scheme 7

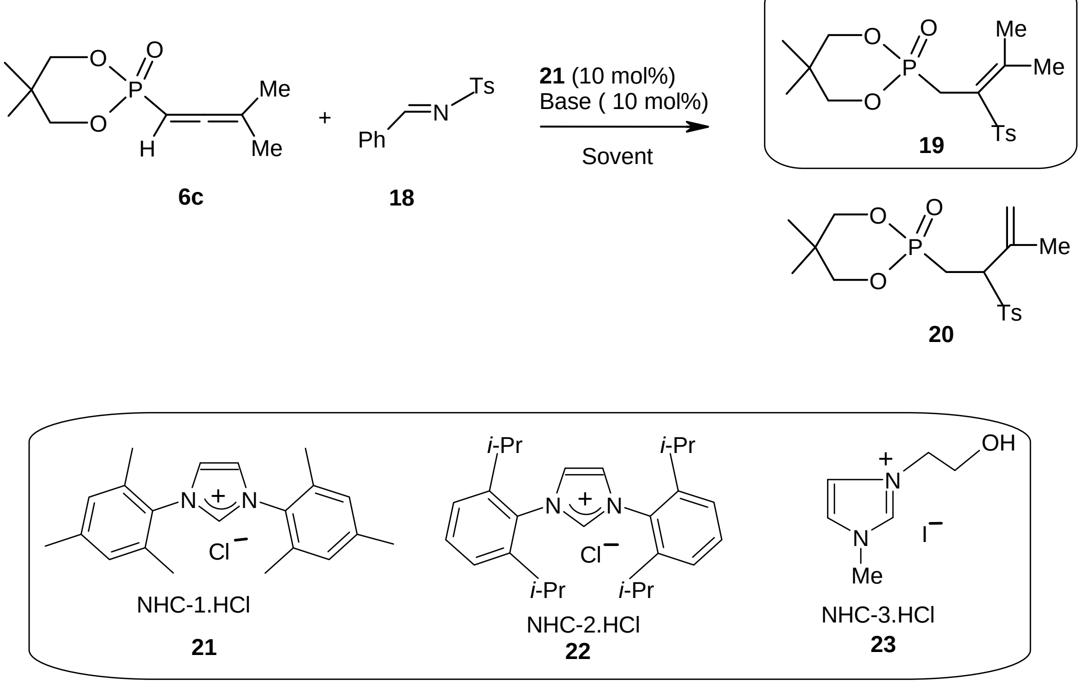


Table 1. Optimization of conditions for the reaction of allenylphosphonate **6c** with imine **18**[a]

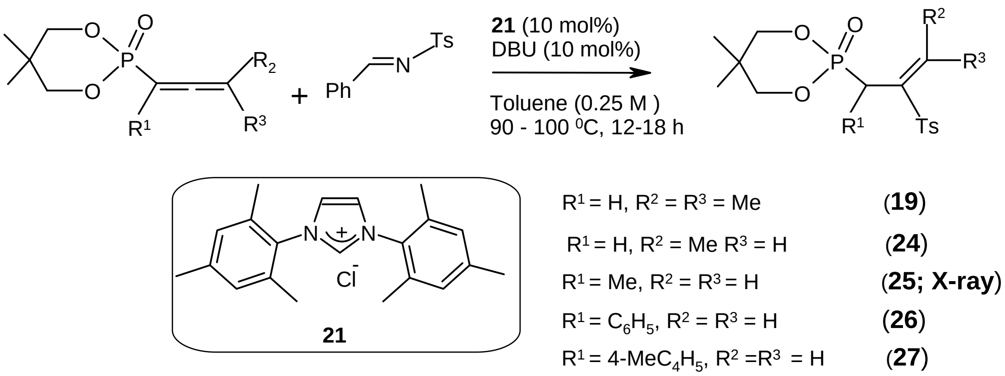
Entry	NHC salt	Base	Solvent	T (°C)	Yield of **19**[b]	Yield of **20**[b]
1	**21**	DBU	Toluene	60	64	14
2	**21**	DMAP	Toluene	80	91	-
3	**22**	DMAP	Toluene	80	84	16
4	**23**	DMAP	Toluene	80	35	-
5	**21**	DBU	Toluene	90	96	-
6	**22**	DBU	Toluene	80	46	54
7	**21**	DBU	THF	60	63	30
8	**21**	DMAP	THF	60	75	-
9	**22**	DMAP	THF	60	6	-

[a] Other parameters: Allene **6c** (0.5 mmol), *N*-tosyl aldimine **18** (0.5 mmol), NHC salt (10 mol%), Base (10 mol%), solvent (0.25M), reaction time 14 h.

[b] Based on ^{31}P NMR analysis (accuracy ± 5%).

Under the above optimized conditions, we were able to generate the tosylated products **24-30** and **31-33** by using allenylphosphonates (**6b, 6e-j**)/ allenylphosphine oxides (**8b-c**, **8e**) and *N*-tosyl aldimine **18** (Schemes 8-9). The yields and ^{31}P NMR chemical shifts for the products are given in Table 2.

Scheme 8



R^1 = H, R^2 = R^3 = Me (**19**)

R^1 = H, R^2 = Me R^3 = H (**24**)

R^1 = Me, R^2 = R^3 = H (**25; X-ray**)

R^1 = C_6H_5, R^2 = R^3 = H (**26**)

R^1 = 4-MeC_4H_5, R^2 =R^3 = H (**27**)

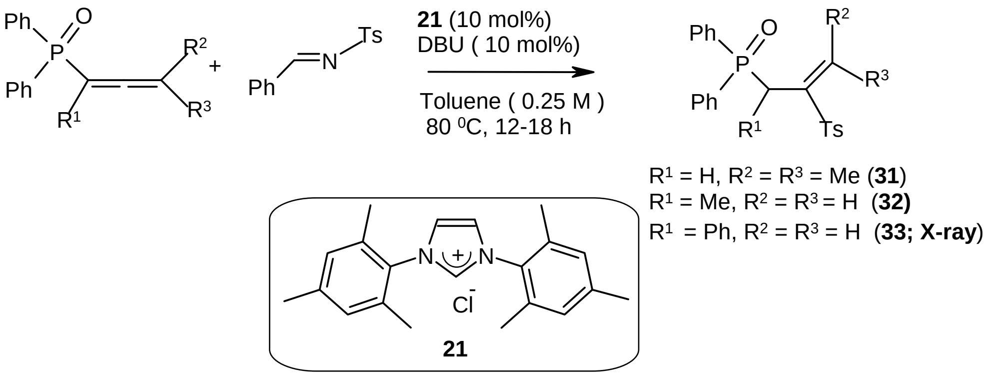
R^1 = 4-MeOC_4H_5, R^2 = R^3 = H (**28**)

R^1 = 4-ClC_4H_5, R^2 = R^3 = H (**29**)

R^1 = $C_{10}H_7$, R_2 = R^3 = H (**30**)

.

Scheme 9



R^1 = H, R^2 = R^3 = Me (**31**)

R^1 = Me, R^2 = R^3 = H (**32**)

R^1 = Ph, R^2 = R^3 = H (**33; X-ray**)

Table 2. Details on the yields and ^{31}P NMR spectra of tosylated products

Entry	Allene	Compound	Yield % (^{31}P NMR^{a}); isolated	^{31}P NMR (δ)
1	**6c**	**19**	(96); 79	18.7
2	**6b**	**24**	(92); 84	18.3
3	**6j**	**25 (X-ray)**	(55); 43	21.7
4	**6e**	**26**	(76); 63	15.1
5	**6f**	**27**	(89); 66	15.3
6	**6g**	**28**	(93); 67	15.4
7	**6h**	**29**	(74); 63	14.6

8	**6i**	**30**	(63); 47	15.5
9	**8b**	**31**	(92); 78	28.7
10	**8c**	**32**	(98); 88	33.1
11	**8e**	**33 (X-ray)**	(76); 66	32.0

[a] Accuracy is ±5%.

All the above compounds **19-20** and **24-33** are characterized by IR, NMR [^{1}H, ^{13}C, ^{31}P] and LC-MS/CHN analyses. The PCH_2 protons of **19** appear as a doublet at δ 3.38 [^{2}J(P-H) =20.4 Hz]. However, the minor isomer **20** shows primarily a doublet of doublet with fine structure at δ 2.59 [^{2}J(P-H), ^{2}J(H-H)], most likely because the two PCH_2 protons are in slightly different environments. In addition, compound **20** shows two singlets at δ 4.90 and 5.12 corresponding to the olefinic protons; this is not shown by compound **19**. Also, compound **20** shows a multiplet at δ 3.97 due to Ts-C*H* proton in the ^{1}H NMR spectrum. The DEPT spectrum is also consistent with the structure as shown. The P-C carbon in both the cases [δ 23-25] shows a ^{1}J(P-C) of ~136 Hz in the ^{13}C NMR. In the ^{1}H NMR spectrum of **25**, the PC*H* proton appears as a multiplet at δ ~3.08 [due to ^{2}J(P-H) and ^{3}J(H-H)]. In the ^{13}C NMR spectrum, the carbon attached to phosphorus shows a doublet at δ 29.0 [^{1}J(P-C) = 135.4 Hz]. In the ^{31}P NMR spectra, all these products show a single peak in the region δ 14-22 [compounds **19** and **24-30**] or 28-33 [phosphine oxides **31-33**]. Finally, the structure of one of these compounds (**25**) is proven by X-ray crystallography [Figure 3]. It shows that the only *S*-attacked products are obtained. The C(8)-S(1) distance of 1.789(3) Å also clearly shows the formation of C-S bond. The location of the double bond C(8)-C(9) is easily discerned by the corresponding bond distance of 1.326(4) Å. Even in the case of phosphine oxides the structure is similar as shown for compound **33 [**Figure 4]; here, a double bond is located between C20 and C21 [1.294(6) Å].

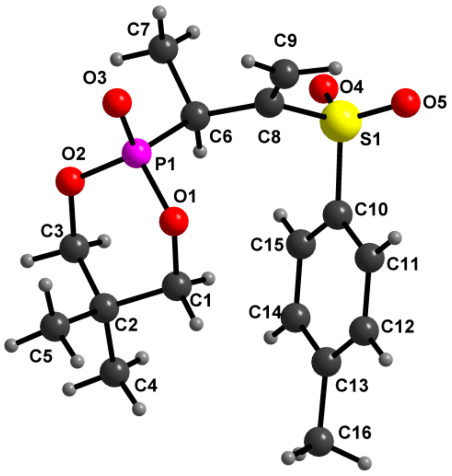


Figure 3. Molecular structure of compound **25**. Selected bond lengths [Å] with esds in parentheses: C(6)-P(1) 1.815(2), C(6)-C(8) 1.524(3), C(8)-C(9) 1.326(4), C(8)-S(1) 1.789(3).

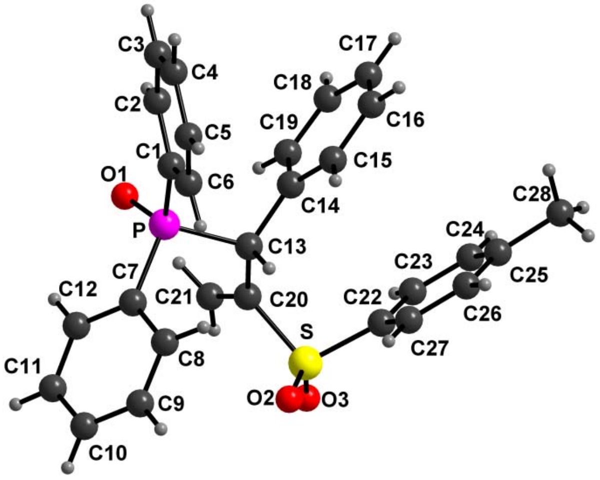
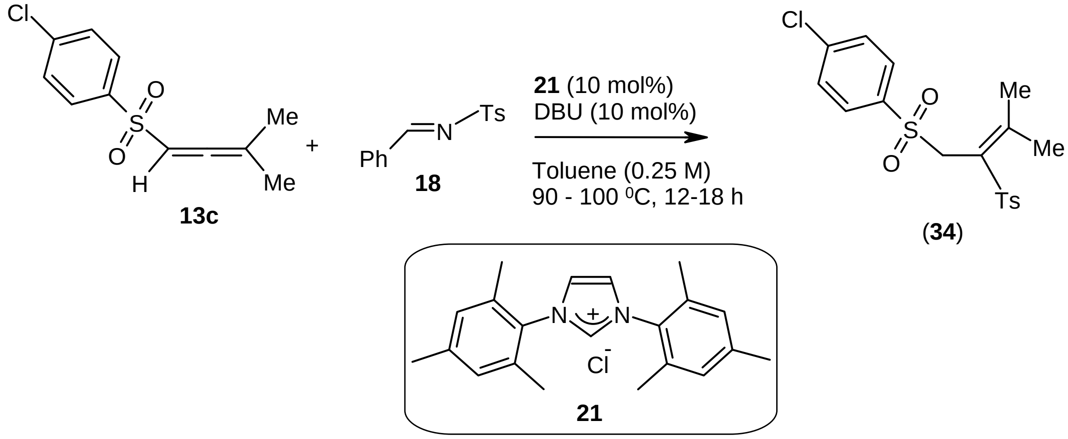


Figure 4. Molecular structure of compound **33**. Selected bond lengths [Å] with esds in parentheses: C(13)-C(20) 1.530(5), S-C(20) 1.795(5), C(20)-C(21) 1.294(6), P-C(13) 1.831(4).

In a manner similar to the above, the reaction of allenylsulfone **13c** with aldimine **18** gives the tosylated product **34** (Scheme 10). Although the NMR spectra are similar to what is described above, since in this case the allene was a sulfone, we determined the structure of compound **34** also by X-ray crystallography [Figure 5]; otherwise there are no additional features. It is noteworthy that the tosyl group (-$SO_2C_6H_4CH_3$) has two nucleophilic centers (O and S) and hence can lead to either the

O-addition or the ***S***-addition product.[33] But in all our examples, only the ***S***-attacked products were observed.

Scheme 10



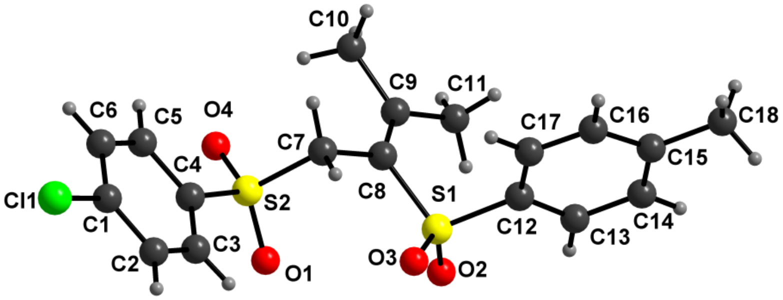
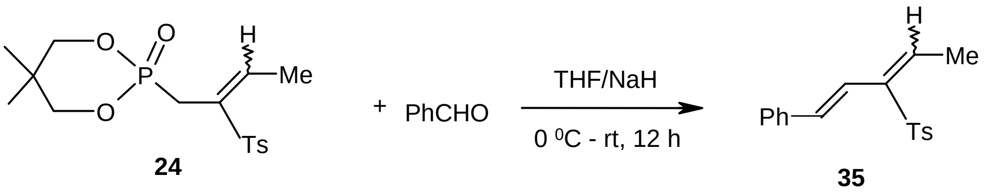


Figure 5. Molecular structure of compound **34**. Selected bond lengths [Å] with esds in parentheses: C(7)-C(8) 1.532(12), C(9)-C(10) 1.523(11), C(9)-C(11) 1.504(14), S(1)-C(8) 1.797(8), S(2)-C(7) 1.780(8).

2.52 Attempted reaction of tosylated compounds as Horner-Wadsworth-Emmons (HWE) reagents

To make the above reactions synthetically useful, we thought of synthesizing substituted 1,3-butadiene derivatives by subjecting them to Horner-Wadsworth-Emmons (HWE) or Wittig reaction with various aldehydes.[88-89] Unfortunately, in only one case using compound **24**, we could isolate the expected product **35** (Scheme 11). In other cases, a mixture of products was obtained [TLC]. The identity of compound **35** is confirmed by NMR [^{1}H, ^{13}C], LC-MS and elemental analyses.

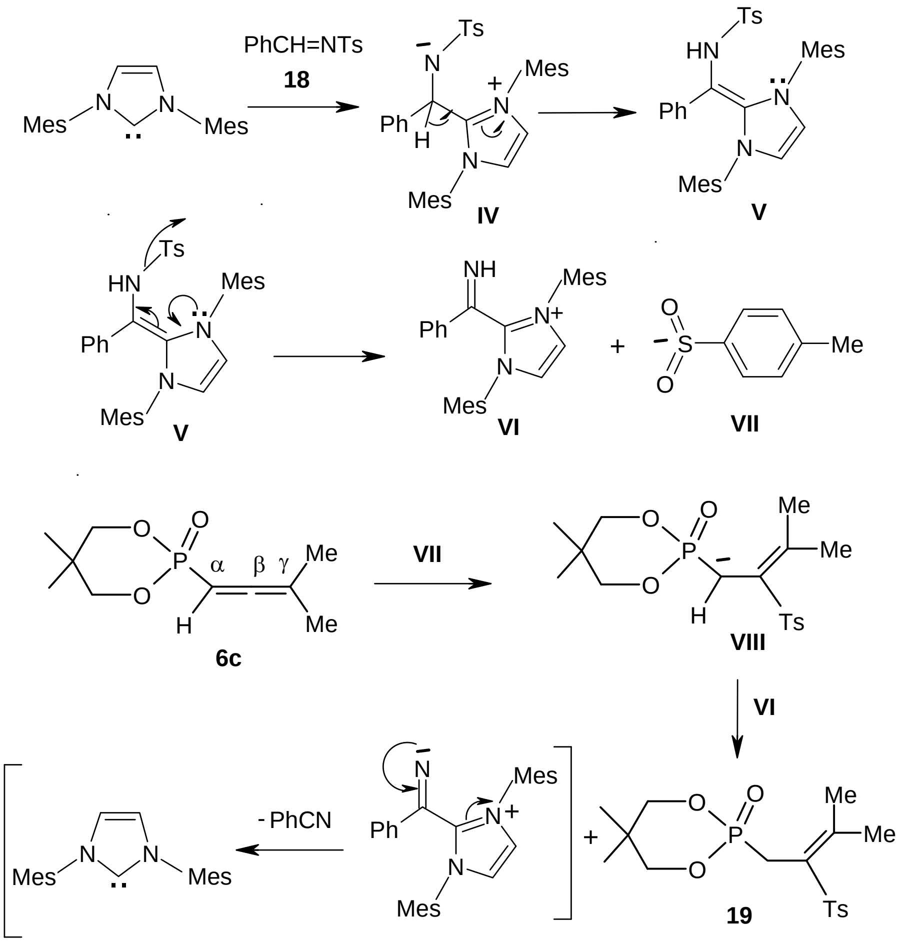
Scheme 11



2.53 Plausible mechanism for the tosyl migration

A plausible mechanism for the transfer of tosyl group based on the available literature[33] is given in Scheme 12. Initially, the imine **18** reacts with the carbene (NHC) generated *in situ* to form the adduct **IV**.[90] This is followed by proton transfer to provide the intermediate **V** which undergoes dissociation to afford the cation **VI** and the tosyl anion **VII**. Anion **VII** then attacks the allenylphosphonate **6c** at β-position of phosphonate from the sulfur end and abstracts a proton from **VI** to afford the final product **19** (*via* intermediate **VIII**) along with benzonitrile (PhCN) and carbene to complete the catalytic cycle.[90d] As far as the allene chemistry is concerned, it is known that in most cases the nucleophiles attack the β-carbon;[21-22] what is proposed herein is consistent with allene chemistry. As is the case with many such studies, we have not attempted to isolate and reuse the NHC salt; although the turnover numbers are not high (10 mol% of carbene is used), this reaction offers a nice synthetic methodology for generating *S*-tosyl substituted allyl-phosphonates/-sulfones.

Scheme 12



2.6 Base catalyzed reactions of allenylphosphonates with salicyl *N*-thiophosphinyl imines-Synthesis of chromans

In a previous work from our laboratory, we reported the Lewis-base catalyzed domino cyclization of salicylaldehydes with allenylphosphonates.[21] Interestingly, in the present work, it was found that the reaction of allenylphosphonates with salicyl *N*-thiophosphinyl imines in the presence of Lewis base also afforded chroman derivatives. This section deals with such reactions. The experimental conditions were standardized by using the allenylphosphonate $(OCH_2CMe_2CH_2O)P(O)C(Ph)=C=CH_2$ (**6e**) and salicyl *N*-thiophosphinyl imine **14a**, because the products could be characterized more readily by ^{31}P NMR spectroscopy.

2.61 Reactions of α-aryl substituted allenylphosphonates $(OCH_2CMe_2CH_2O)P(O)C(Ar)=C=CH_2$ (6e-i) and $Ph_2POC(Ph)=C=CH_2$ (8e) with salicyl N-thiophosphinyl imines 14a and 14b

We treated the allenylphosphonate **6e** with *N*-thiophosphinyl imine **14a** (cf. Scheme 13) in the presence of various bases and in different solvents to optimize the reaction conditions. The results are summarized in the Table 3. It was found that the reaction of allenylphosphonate **6e** with *N*-thiophosphinyl imine **14a** led to the expected product **36** in poor yield using PPh_3 as the base and dimethyl sulfoxide (DMSO) as the solvent (Table 3, entry 1). The reaction was not complete and the ^{31}P NMR of the reaction mixture showed around 50% of the allene **6e** remaining. When the reaction was conducted under the conditions previously reported from our laboratory,[21] instead of the expected product **36**, phosphono-chromenes **37** (*E* and *Z*) were obtained (entry 2). Use of K_2CO_3 or $P(n\text{-}Bu)_3$ as the base also afforded the chromene **37** [^{31}P NMR evidence] (Table 3, entries 3 and 4).

Scheme 13

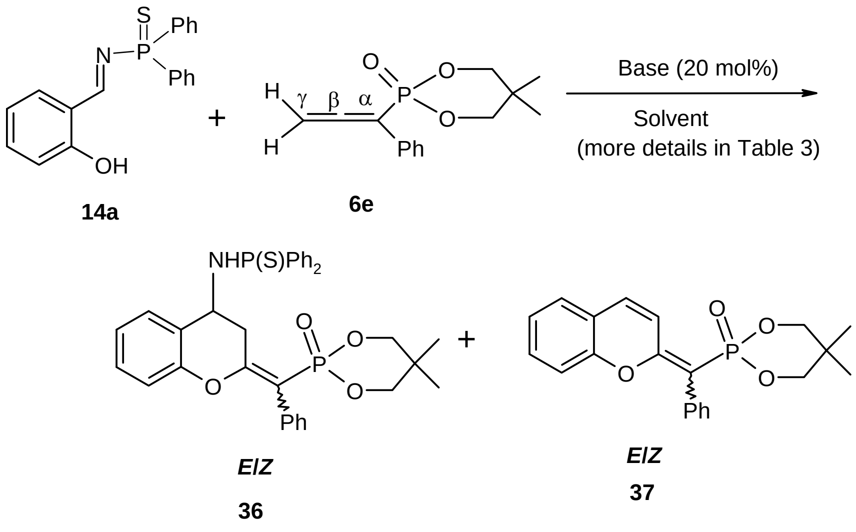


Table 3. Screening of reaction conditions for the optimization of product **36**

Entry	Catalyst	Solvent	Temp. (°C)/ Time (h)	Yield(%)[a]
1	PPh_3	DMSO	80/16	50
2	DBU	DMSO	80/12	-[b]
3	K_2CO_3	DMSO	80/8	-[b]
4	P(*n*-Bu)$_3$	DMSO	80/10	-[b]
5	PPh_3	DCM	40/18	n.r.
6	PPh_3	DMF	80/18	n.r.
7	PPh_3	Toluene	80/18	8
8	PPh_3	THF	50/12	6
9	PPh_3	CH_3CN	80/12	56
10	P(*n*-Bu)$_3$	THF	60/12	78
11	P(*n*-Bu)$_3$	Toluene	60/12	36

[a] Yield of **36 (***E*+*Z***)** based on ^{31}P NMR spectra of the reaction mixtures.

[b] In these cases, chromene **37** (quantitative yield) was obtained.

No desired product was observed by using the base PPh_3 and dichloromethane or dimethyl formamide as the solvent (entries 5 and 6); also the product formation was negligible in toluene or THF (entries 7 and 8). Interestingly, the reaction proceeded well in CH_3CN to lead to the expected product **36** (*E* + *Z*) in moderate yields (entry 9). It is noteworthy that use of P(*n*-Bu)$_3$ as the base in *toluene* medium also led to the product **36** [^{31}P NMR]; however, there were some side products also. Hence, we continued with P(*n*-Bu)$_3$ in *THF* as the medium. As can be seen from Figure 6, the chroman product **36** shows two sets of dominant signals corresponding to the *E* and *Z* isomers, the first one at 58.8/ 10.1 (*Z*-isomer) and the second set at 58.9/ 14.1 (*E*-isomer). There are also additional signals at the thiophosphinate region [δ ~ 48, 57] but these *do not* correspond to the products from the allene; an unassigned minor signal at δ 16.5 is also seen.

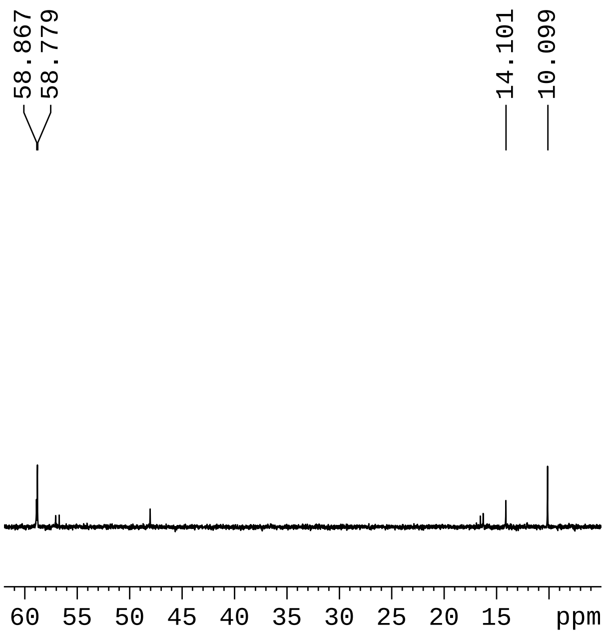


Figure 6. ^{31}P NMR spectrum of the reaction mixture of **6e** with salicyl *N*-thiophosphinyl imine **14a** using P(*n*-Bu)$_3$ as the base in THF at 60 °C/ 10 h. In the plot, only δ values of the product (*E/Z*)-**36** are shown for clarity.

Using the above conditions, we then conducted the reaction of *N*-thiophosphinyl imines **14a** and **14b** with allenylphosphonates **6e-i** and allenylphosphine oxide **8e** for the synthesis of different phosphono-chromans and also for checking the scope and limitations of the reaction (Scheme 14a and b). The yields and *E*/*Z* ratio of the compounds based on the ^{31}P NMR spectra of the reaction mixtures are given in Table 4. We have also separated ***individual isomers in all the cases*** except for **41** and **46**. The major isomer has the ***Z*-configuration** (*vide infra*). In case of **47-48**, the *Z*-isomer was isolated in a pure state.

Scheme 14

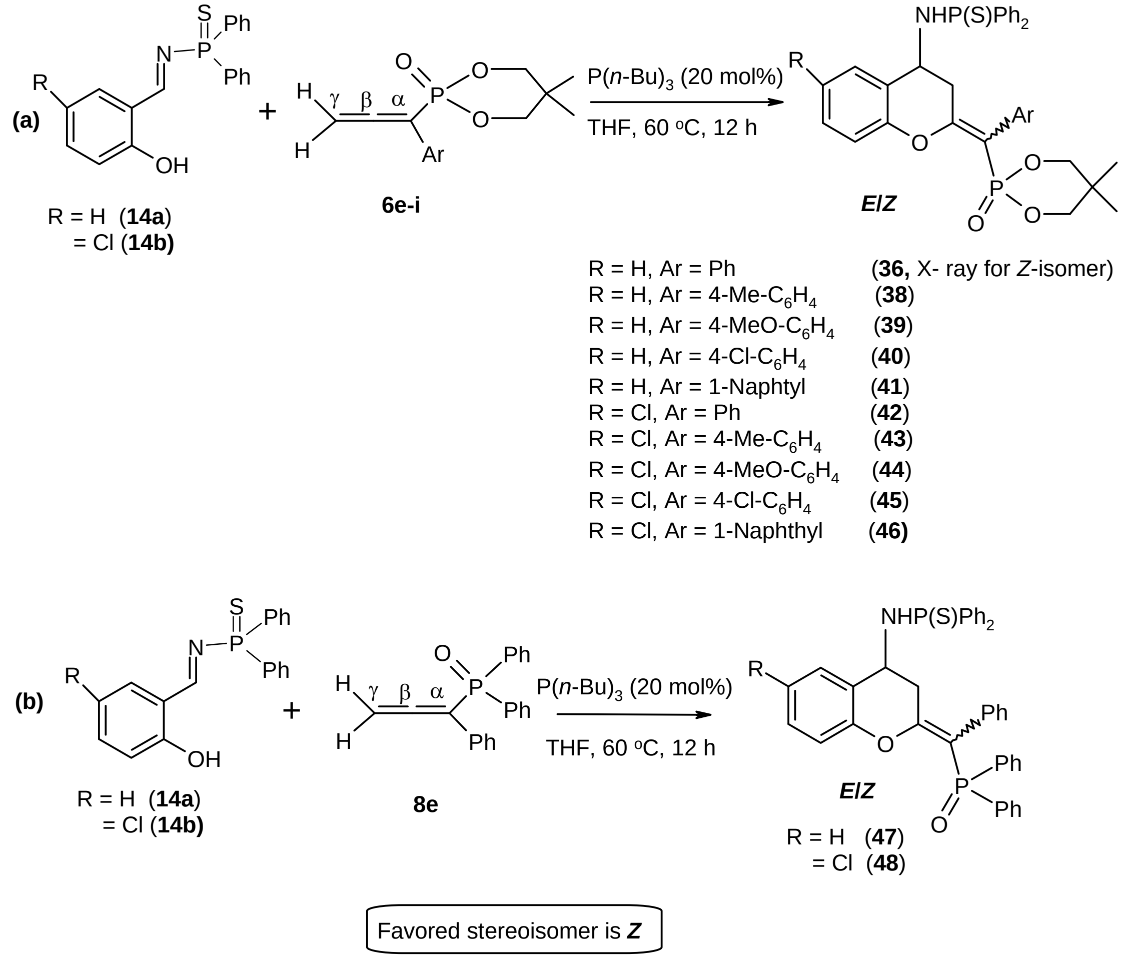


Table 4. ^{31}P NMR data and yields of the compounds **36**, **38-46** and **47-48**

Entry	Compound	δ(P)		Yield (%)^{a}		
		(*E*)	(*Z*)	(*E*)	(Z)	Combined
1	**36**	14.5; 59.1	10.4; 59.3	17	53	70
2	**38**	14.7; 59.1	10.7; 59.3	26	49	75
3	**39**	14.8; 59.1	10.8; 59.3	23	44	67
4	**40**	14.4; 59.1	10.8; 59.2	21	55	76
5	**41**	10.1, 11.0 and 59.0, 59.9		83 (*E*+*Z*)		83
6	**42**	14.1; 59.0	10.0; 59.5	26	35	61
7	**43**	14.3; 59.0	10.3; 59.5	17	45	62
8	**44**	14.3; 59.0	10.3; 59.4	24	33	57

9	**45**	14.0; 59.2	9.5; 59.5	17	45	62
10	**46**	9.3, 10.2 and 59.3,60.2		78 (*E*+*Z*)		78
11	**47**	28.6; 58.1	24.0; 58.9	-	41	41
12	**48**	28.9;57.5	24.4; 59.4	-	31	31

[a]Isolated yields of the pure compounds.

For the identification of *E*- and *Z*-isomers, ^{1}H and ^{13}C NMR spectra were quite useful. In the ^{1}H NMR, signals for the CH_2(CHNP(S)Ph$_2$) protons appear as a multiplet in the region δ 3.02-3.14 for the *E*-isomer; for the Z-isomer, the signals appear up-field [δ ~2.78-2.88] (cf. Figure 7). In the ^{13}C NMR spectra, the ^1J(P-C) value for the *E*-isomer [~195.6 Hz] is higher than that for the *Z*-isomer [~173.4 Hz]. The structure of *Z*-isomer of **36** was determined by X-ray crystallography (Figure 8). The double bond between C6 and C7 is confirmed by the distance [C(6)-C(7) 1.346(8) Å] while the *Z*-stereochemistry at this double bond is clearly shown by the attached substituents. Based on these data, we could assign the ^{31}P NMR chemical shifts for all the other compounds. Thus, the signal for the *E*-isomer [δ(P) = 14.5] appears downfield compared to that for the *Z*-isomer [δ(P) = 10.4].

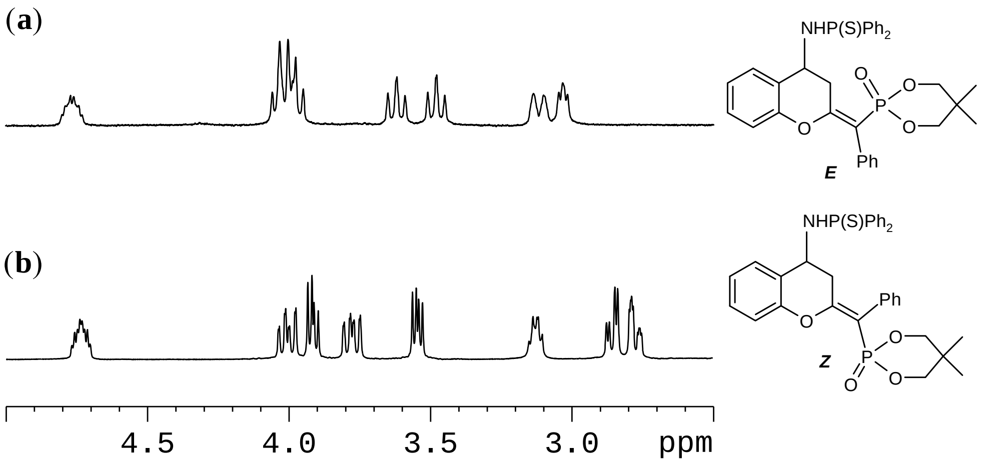


Figure 7. ^{1}H NMR spectra in the region δ 2.0-5.0 for phosphono-thiochromans: (a) (*E*)-**36** and (b) (*Z*)-**36.**

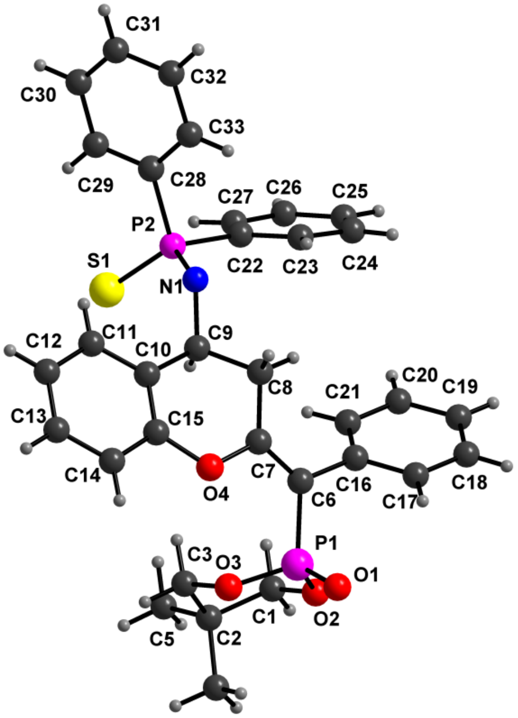
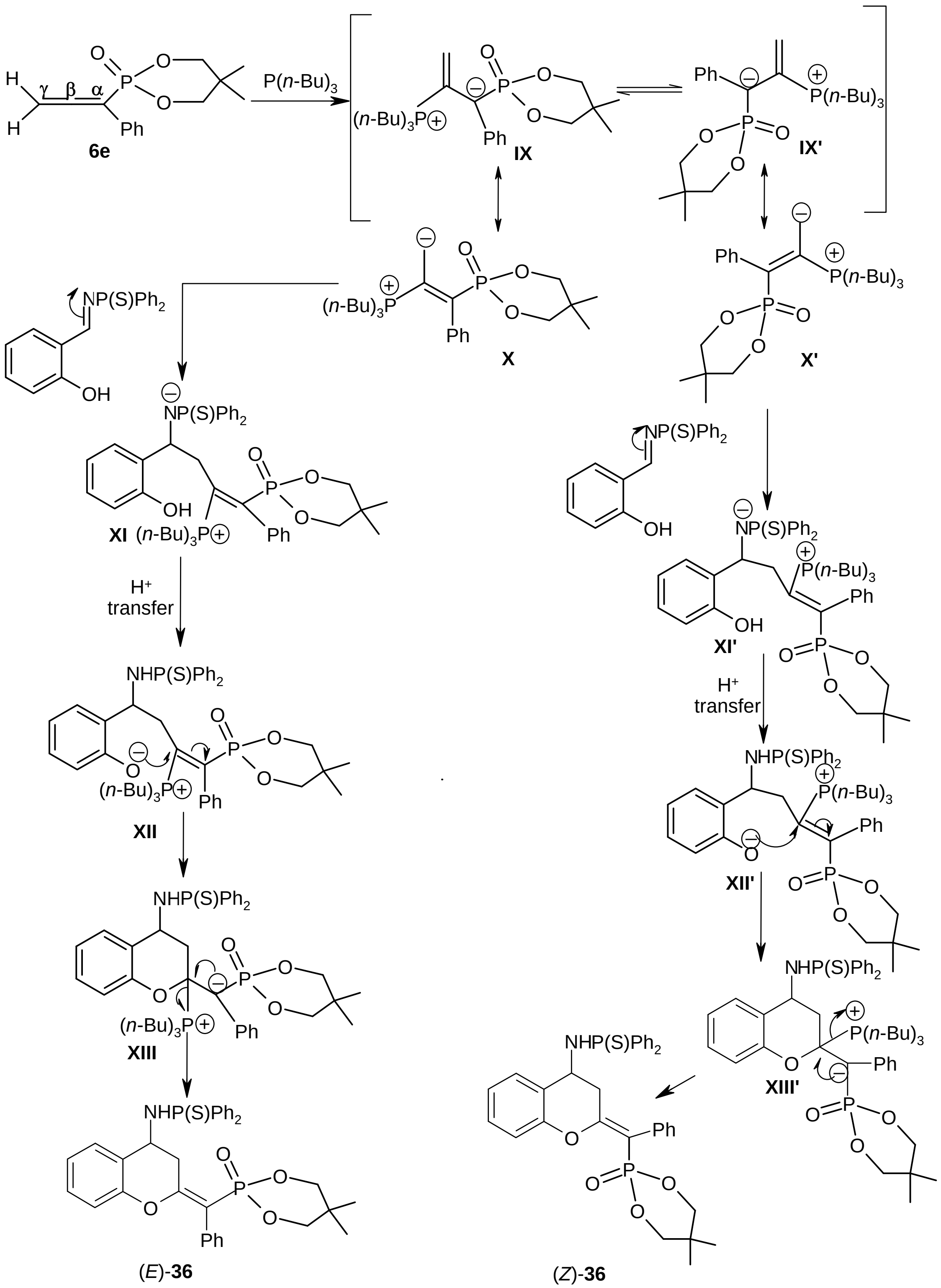


Figure 8. Molecular structure of compound (*Z*)-**36**. Selected bond lengths [Å] with esds in parentheses. O(4)-C(7) 1.365(6), C(8)-C(9) 1.516(8), N(1)-C(9) 1.472(7), C(7)-C(8) 1.488(8), C(6)-C(7) 1.346(8), P(1)-C(6) 1.800(6), C(6)-C(16) 1.504(7).

2.62 Mechanistic pathways for the formation of chroman derivatives

A plausible mechanism for the above reaction, based on the available literature,[36c] is shown in Scheme 15. Initially the Lewis base P(n-Bu)$_3$ attacks the allenylphosphonate **6e** and produces the zwitterionic intermediate **IX** or **X**. The intermediate **IX** is in equilibrium with **IX'** which generates another resonance-stabilized zwitterionic intermediate **X** or **X'**. The intermediate **X** or **X'** undergoes nucleophilic attack with *N*-thiophosphinyl imine **14a** to form the corresponding intermediate **XI** or **XI'** which produces **XII** or **XII'** after the transfer of proton. The cyclization of the resulting intermediates affords **XIII/ XIII'** which is followed by elimination of P(n-Bu)$_3$ to give the final products (***E***)-**36** or (***Z***)-**36**.

Scheme 15



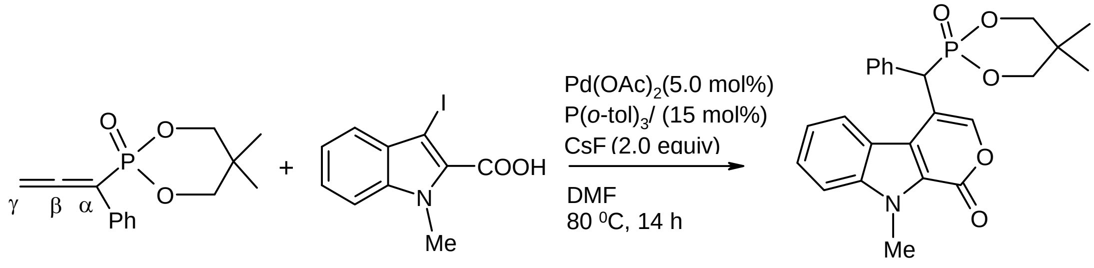
6e
γ β α
P(n-Bu)3
IX
IX'
X
X'
NP(S)Ph2
OH
XI
XI'
H+ transfer
NHP(S)Ph2
XII
XII'
XIII
XIII'
(n-Bu)3P
P(n-Bu)3
Ph
(E)-36
(Z)-36

2.7 Palladium-catalyzed reactions of allenes with indole carboxylic acids

2.71 Reaction of allenylphosphonates (6a, 6e-j)/ allenylphosphine oxides (8a, 8e) with 3-iodo-indole-2-carboxylic acid derivatives (15a and 15b): Formation of pyranoindole derivatives

In two recent papers from our laboratory, reaction of allenylphosphonate and other allenes with iodobenzoic acid under palladium-catalyzed conditions leading to isocoumarin derivatives is described.[47a,47c] Since indole derivatives have a wide range of biological activity,[91] we surmised that an extension of such reactions to 3-iodo-indole-2-carboxylic acids is worthwhile. Thus, we started with the allene $(OCH_2CMe_2CH_2O)P(O)C(Ph)=C=CH_2$ (**6e**) and 1-methyl-3-iodo-indole-2-carboxylic acid (**15a**). Between the two conditions $Pd(OAc)_2$/CsF/PEG-400 and $Pd(OAc)_2/P(o\text{-}tol)_3$/CsF/DMF checked initially, only the latter conditions worked [Scheme 16; ^{31}P NMR spectrum in Figure 9] and afforded the product **49**. The spectroscopic and analytical data are consistent with the structure as given (see also below for a discussion). Its structure was also confirmed by X-ray crystallography [Figure 10]; the C(13)-C(9) distance of 1.527(3) Å clearly shows that the double bond that was initially present at this position (in the allene) is now a single bond as shown in Scheme 16.

Scheme 16



6e **15a** **49**

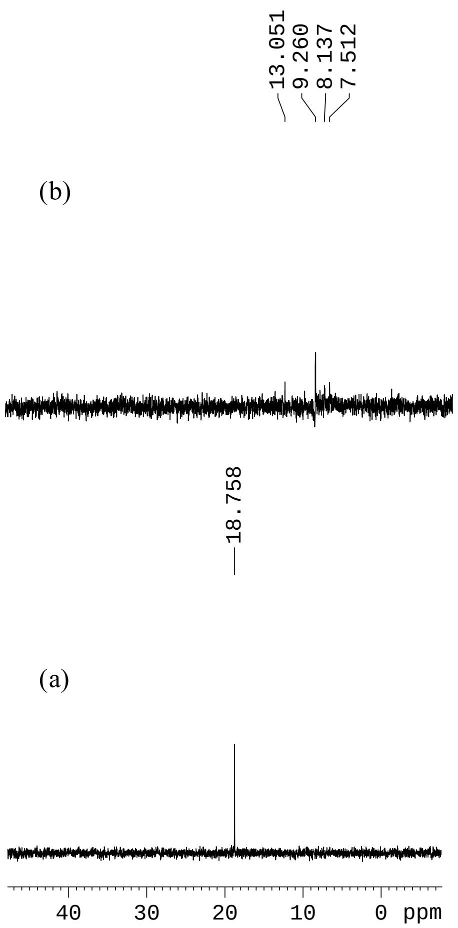


Figure 9. ^{31}P NMR spectra for the reaction mixture of **15a** with α-phenyl allene **6e** in (a) dry DMF at 80 ^{o}C/ 14 h and (b) PEG- 400 at 90 ^{o}C/ 14 h (this is for the reaction mixture and hence the noise level is more).

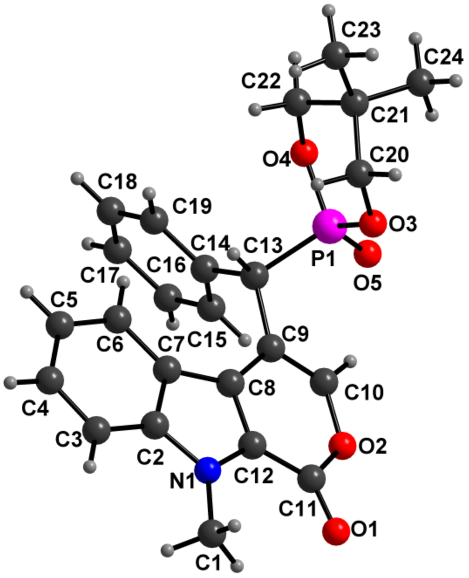


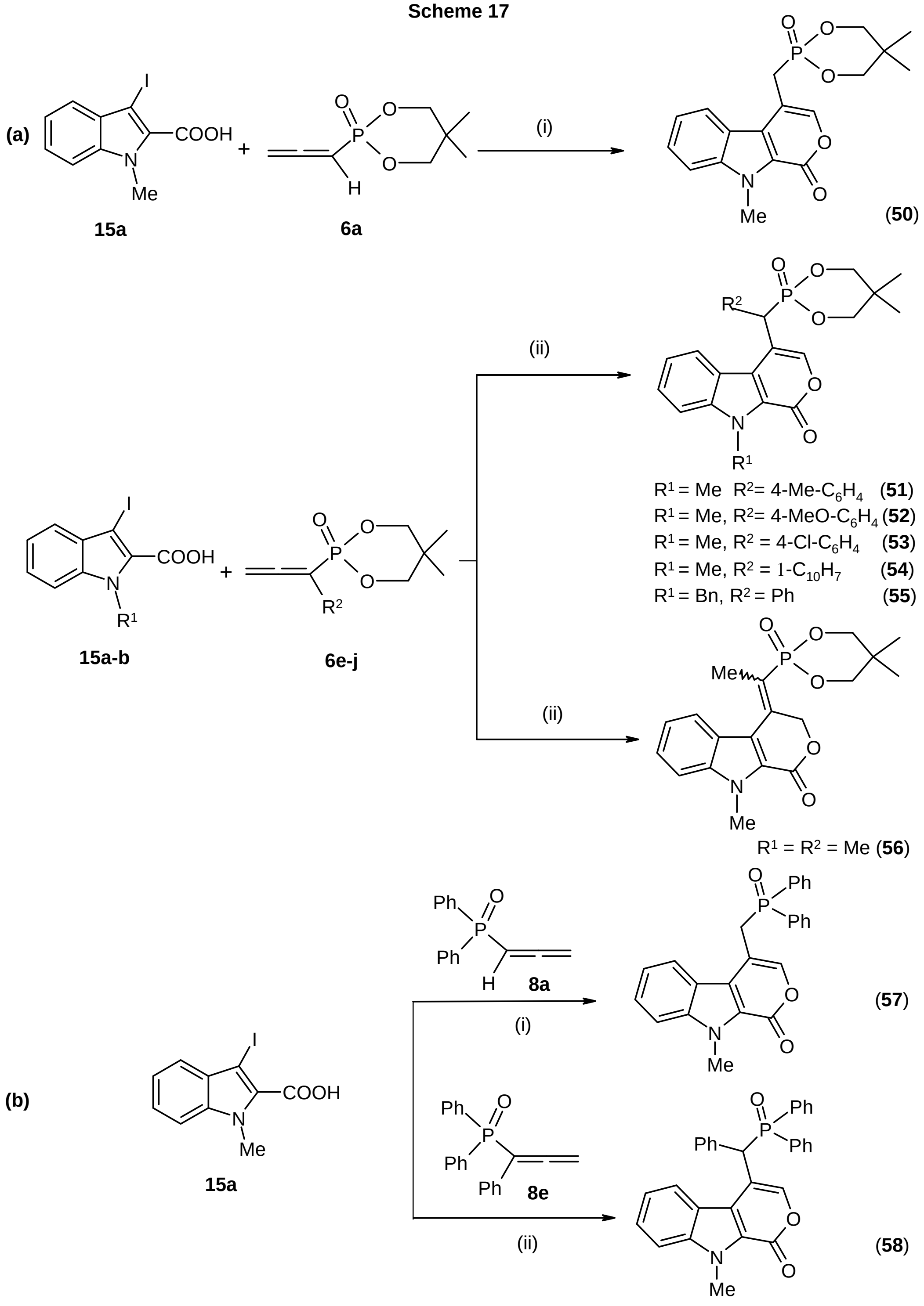
Figure 10. Molecular structure of compound **49**. Selected bond lengths [Å] with esds in parentheses: P(1)-C(13) 1.828(2), C(10)-O(2) 1.380(2), O(1)-C(11) 1.216(2), O(2)-C(11) 1.372(3), C(9)-C(10) 1.337(3), C(13)-C(9) 1.527(3), C(8)-C(9) 1.445(3).

With the above conditions in hand, we explored the scope of this catalytic system for the synthesis of pyranoindole derivatives **50-56** (Scheme 17a). Thus, the reactions of allenylphosphine oxides **8a** and **8e** with **15a** afforded the products **57** and **58** in good yield (Scheme 17b). The reactions were conducted in the absence of P(*o*-tol)$_3$ for the =CH$_2$ terminal allenes **6a** and **8a** to obtain **50** and **57** because of the isomerization of allene to alkyne when phosphine* was used.[30] We were delighted to observe that this system turned out to be broadly applicable. The important feature of this work is that essentially one product is formed regioselectively. In the case of α-methyl allene **6j** the migration of the proton was absent leading to formation of the lactone **56**. The yields, ^{31}P NMR chemical shifts and ^{1}J(P-C) values (from ^{13}C NMR) of all these products are given in Table 5. All these pyranoindoles (**49-58**) are characterized by IR, NMR [^{1}H, ^{13}C, ^{31}P] and LC-MS/CHN analyses.

---

* The reaction is: $R_2P(O)CH{=}C{=}CH_2 \xrightarrow{P(o\text{-tol})_3} R_2P(O)C{\equiv}C{-}CH_3$

Scheme 17



Conditions: (i) $Pd(OAc)_2$ (5 mol%)/ CsF (2.0 equiv)/ DMF/ 80 °C, 14 h

(ii) $Pd(OAc)_2$ (5 mol%)/ $P(o\text{-tol})_3$ (15 mol%)/CsF (2.0 equiv)/ DMF/ 80 °C, 14 h

Table 5. Details on the yields of benzofurans **49-58**

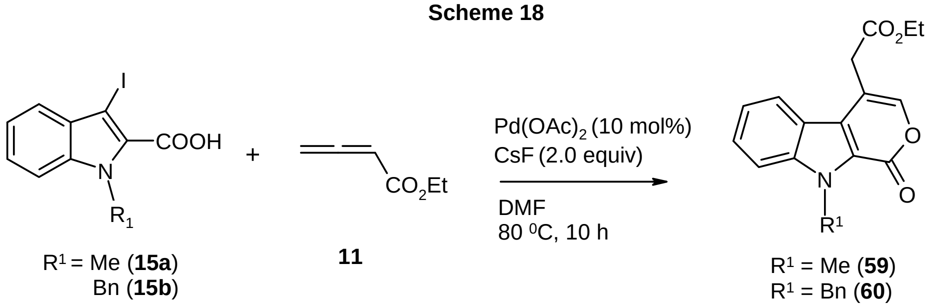
Entry	Allene	Carboxylic acid	Product	Yield % (isolated)	δ (^{31}P) (ppm)	^{1}J(P-C) Hz (^{13}C NMR)
1	**6e**	**15a**	**49**	94	18.8	136.6
2	**6a**	**15a**	**50**	74	21.3	141.0
3	**6f**	**15a**	**51**	77	18.9	137.0
4	**6g**	**15a**	**52**	85	19.1	137.6
5	**6h**	**15a**	**53**	68	18.6	137.1
6	**6i**	**15a**	**54**	81	20.1	139.9
7	**6e**	**15b**	**55**	79	18.7	136.5
8	**6j**	**15a**	**56**	84	15.9	180.0
9	**8a**	**15a**	**57**	92	29.1	67.8
10	**8e**	**15a**	**58**	54	32.3	64.1

As expected, the band corresponding to carbonyl group stretching of the lactone is observed at 1696-1725 cm^{-1} in the IR spectra. In the ^{1}H NMR spectra, the PC*H* proton appears at δ ~5.2 [^{2}J(P-H) ~ 28 Hz] for compounds **49-55** while for **57** and **58** this is observed at δ ~ 4.61 [^{2}J(P-H) ~ 12 Hz]. In the ^{13}C NMR spectrum of **56**, the carbon attached to phosphorus shows a doublet at δ 123.6 [^{1}J(P-C) = 180.0 Hz]. It can be noted that this compound has two possible stereo-isomers; from the data available, it was not possible to distinguish them. The large value of ^{1}J(P-C) is consistent with the sp^{2} hybridized carbon being connected to phosphorus as depicted. In the ^{31}P NMR, these pyranoindoles show a single peak in the region δ 18-22 [for **49-55**] or 29-33 [for **57-58**]. In the case of compound **56**, the δ(P) value of 15.9 was slightly up-field when compared to those for **49-55**. The X-ray structure of **49** has already been discussed above.

2.72 Pd-catalyzed annulation of allenyl ester (11) with 3-iodo-indole-2-carboxylic acid derivatives (15a-b)

In continuation of the work on indole-2-carboxylic acid derivatives, we treated allenoate **11** with 1-methyl-3-iodo-indole-2-carboxylic acid (**15a**) or *N*-benzyl-3-iodo-indole-2-carboxylic acid (**15b**) in the presence of Pd(OAc)$_2$/CsF in DMF at 80 °C. The reaction was complete in 10 h and led to pyranones **59-60** which are (β,γ)-cyclized products (Scheme 18). The yields are quite good. Spectroscopic and analytical data are consistent with the proposed structure. Compound **59** shows bands centered at 1730 and 1707 cm^{-1} in the IR spectrum corresponding to C=O stretchings of the ester and lactone, respectively. In the ^{1}H NMR, the CH_2CO$_2$Et protons appear as a singlet at δ 3.80. Thus, this compound (as well as **60**) is a (β,γ)-cyclized product. The structure of **59** has also been confirmed by the X-ray crystallography (Figure 11). The C(9)-C(10) [1.324(3) Å] and C(13)-C(9) [1.498(2) Å] bond distances clearly show the location of the C=C and C-C bonds in the molecule as assigned.

Scheme 18



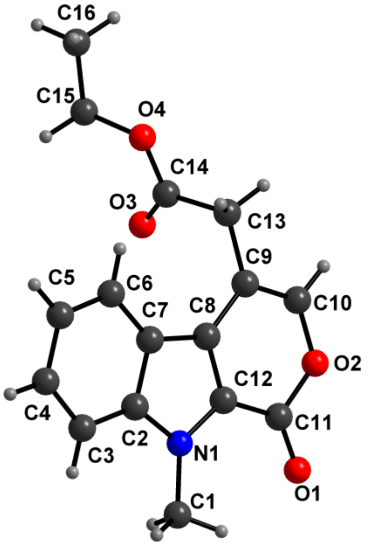
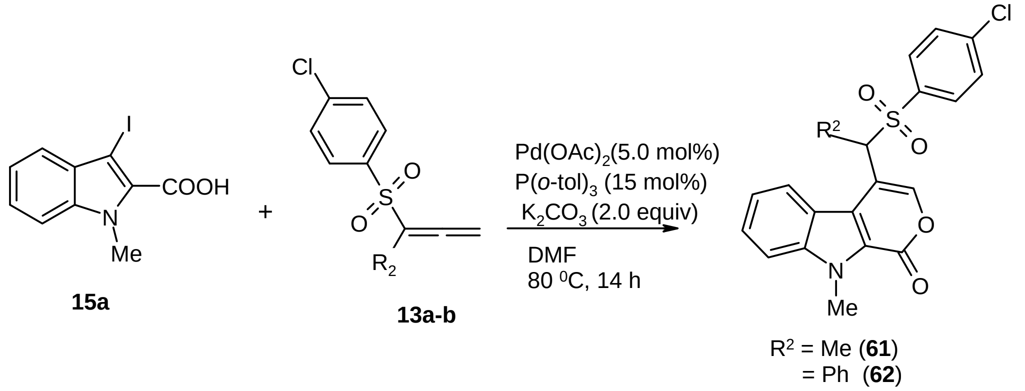


Figure 11. Molecular structure of the compound **59**. Selected bond lengths [Å] with esds in parentheses: C(8)-C(9) 1.432(2), C(9)-C(10) 1.324(3), C(13)-C(9) 1.498(2), O(2)-C(10) 1.363(2), C(11)-O(1) 1.201(2).

2.73 Reaction of allenylsulfones (13a-b) with 3-iodo-1-methyl-indole-2-carboxylic acid (15a)

As an electron withdrawing group, the sulfonyl ($ArSO_2$-) is comparable to the phosphoryl [$(RO)_2P(O)$] or the ester group. Thus we desired to extend the above chemistry to allenes bearing the sulfonyl group and treated the allenylsulfones **13a-b** with 3-iodo-1-methyl-indole-2-carboxylic acid (**15a**), we obtained sulfonated pyranoindoles **61** and **62** in good yields (Scheme 19). Both the allenes **13a** and **13b** gave (β,γ)-cyclized products as expected. This reaction also worked well in the presence of $Pd(OAc)_2$/ CsF without phosphine [P(*o*-tol)$_3$].

Scheme 19



It is noteworthy that the sulfonyl α-methyl allene **13a** afforded the (β,γ)-cyclized chromene product **61** whereas the corresponding reaction of allenylphosphonate **6j** gave **56** wherein there was no isomerization, even though both phosphonyl and sulfonyl groups are electron withdrawing. In order to doubly make sure of our assignment, compound **61** was characterized by single crystal X-ray crystallography (Figure 12). The C(8)-C(9) and C(13)-C(8) bond distances [1.339(5) and 1.519(4) Å, respectively] corroborate the structural assignment.

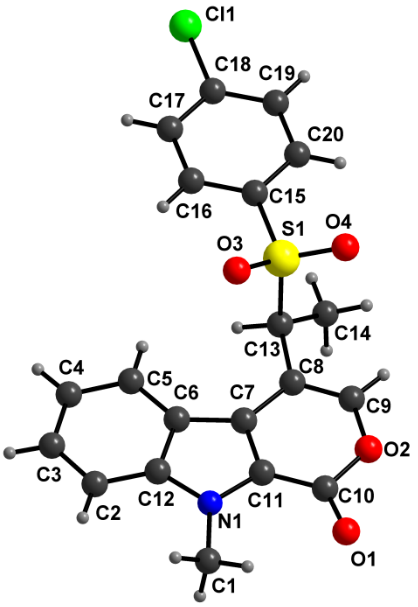
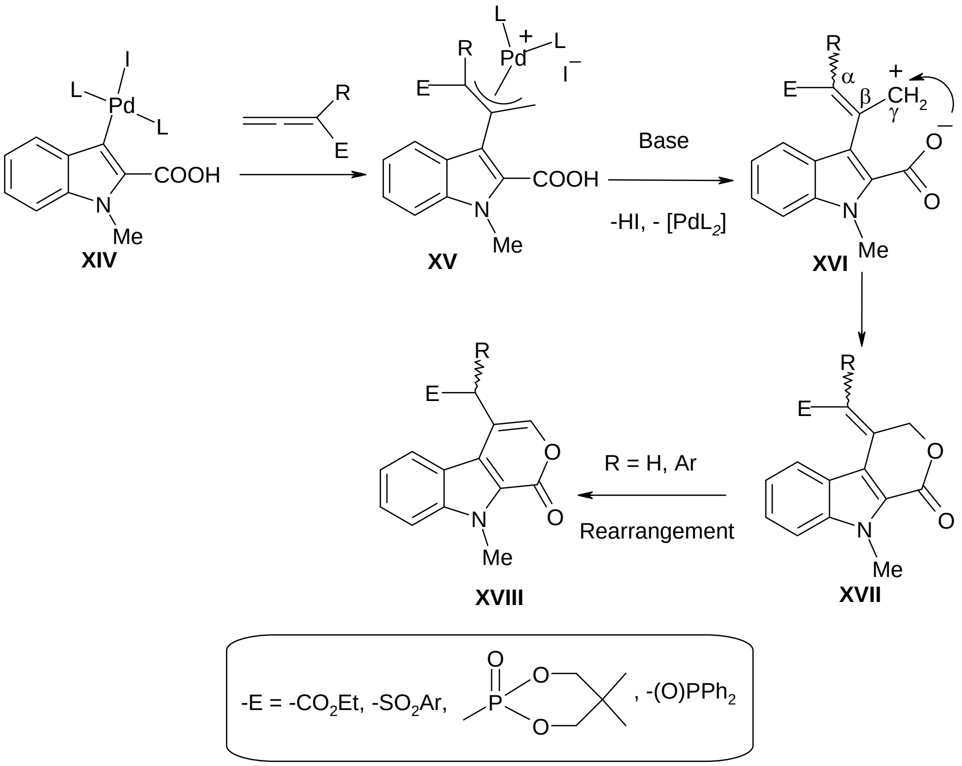


Figure 12. Molecular structure of compound **61**. Selected bond lengths [Å] with esds in parentheses: C(7)-C(8) 1.438(4), C(8)-C(9) 1.339(5), O(2)-C(9) 1.370(4), O(1)-C(10) 1.209(4), C(13)-C(8) 1.519(4).

2.74 Mechanistic pathway for the annulation reaction

Formation of pyranoindole derivatives can be rationalized by the pathway shown in Scheme 20.[47a] The aryl palladium complex **XIV** upon reacting with the allene gives the π-allyl palladium complex **XV** through the insertion reaction at the β-carbon of allene moiety. Elimination of HI (by the base) and the palladium moiety leads to species **XVI**. The cyclization then occurs to provide the compound **XVII**. When R = Me, such a compound has been isolated [cf. compound **56**]. When R = Ph or H, rearrangement takes place to lead to the rearranged product **XVIII** [cf. compounds **49-55, 57-62**].

Scheme 20



Note: The oxidation state of Pd in the intermediate **XV** is not certain and hence is not shown here [L = P(*o*-tol)$_3$ or acetate].

2.8 Pd-catalyzed annulation of allenes with 1-alkyl-indole-2-carboxylic acid *via* C-H functionalization

Transition metal-catalyzed direct C-H functionalization of indole derivatives for the arylation and alkenylation at either C(2)- or C(3)- position of indole have been successfully achieved.[92-93] However, the palladium catalyzed oxidative annulations of indole-2-caboxylic acids with allenes *via* ***direct C-H functionalization*** to produce the corresponding lactones has not yet been established. Interestingly, during our studies on the palladium-catalyzed reactions of allenes, we achieved the cyclization of allenes with indole-2-carboxylic acids by the C-H functionalization that led to lactones. Herein we report, in a preliminary form, the first direct annulations of allenes with indole-2-carboxylic acid derivatives by C-H activation process under palladium catalysis. We first established reaction conditions for the oxidative annulation of indole-2-carboxylic acid **16a** with phenyl allene **10a** (Scheme 21). We were pleased to discover that the reaction was feasible for the formation of **63** along with traces of other isomers, possibly, **64**, **65** and **66** which were detected by GC-MS. Here, the compounds **64-66** (assignment tentative) could not be separated as the R_f values were very close. Hence, the principal challenge in optimization centered upon increasing the yield of **63** at the expense of the other products **64-66**. Initially, the reaction was conducted in the presence of $Pd(OAc)_2$, $Cu(OAc)_2.H_2O$ and LiOAc in dimethyl acetamide (DMA) as the solvent at 120 ^oC for 12 h (Table 6, entry 1). The yield of compound **63** after isolation was 39%. A few other conditions as shown in entries 2-5, 9-10, 13 or 15 did not work well. The selectivity of the lactone **63** was improved by using Ag_2CO_3 as oxidant and CH_3CN as the solvent; the product was isolated in 68 % yield (entry 6). Screening of other palladium salts or oxidants or solvents led to the formation of **63** only in modest yield/ selectivity [entries 7, 8, 11, 12 and 14]. Thus, $Pd(OAc)_2$ as the catalyst, Ag_2CO_3 as the oxidant/ base, CH_3CN as the solvent (0.1M with respect to carboxylic acid), a reaction temperature of 90 ^oC, and a reaction time of 12-14 h were selected as the optimal conditions.

Scheme 21

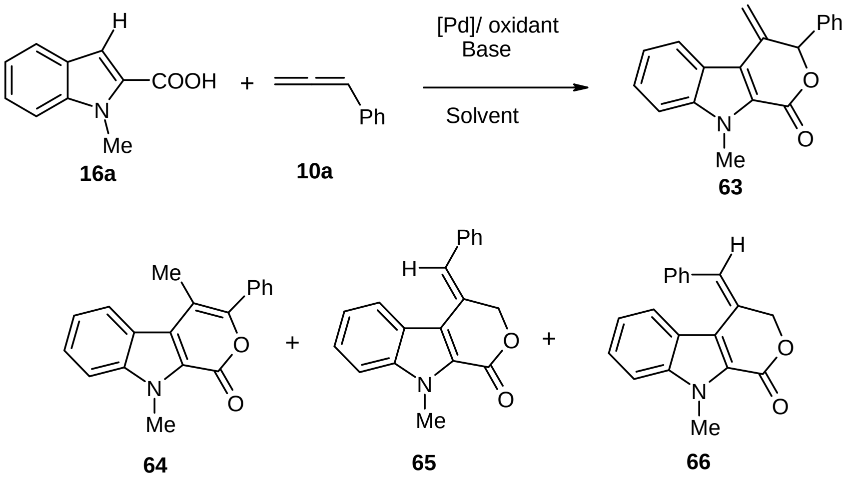


Table 6 Annulation of phenyl allene **10a** with indole carboxylic acid **16a:** Optimization of reaction conditions^{a}

Entry	[Pd]-source	oxidant	Base	Solvent	Temp. (^{o}C)	Yield of **63** (%)^{b}
1	$Pd(OAc)_2$	$Cu(OAc)_2$	LiOAc	DMA	120	39^{c}
2	$Pd(OAc)_2$	Ag_2CO_3	-	DMA	120	28
3	$Pd(OTf)_2$	$Cu(OAc)_2$	LiOAc	DMA	110	43^{c}
4	$Pd(OAc)_2$	Ag_2CO_3		DMF	100	29
5	$Pd(OAc)_2$	$Cu(OAc)_2$	LiOAc	DMA:PivOH	140	17^{c,d}
6	**$Pd(OAc)_2$**	**Ag_2CO_3**		**CH_3CN**	**90**	**68**^{c}
7	$PdCl_2$	$Cu(OAc)_2$	LiOAc	DMA	120	21^{c}
8	$PdCl_2$	Ag_2CO_3	-	DMA	120	51
9	$PdCl_2$	$Cu(OAc)_2$	LiOAc	CH_3CN	80	29^{c}
10	$PdCl_2$	Ag_2CO_3		DMF	120	19^{c}
11	$PdCl_2$	Ag_2CO_3		DMF:DMSO(9:1)	90	29
12	$PdCl_2 (CH_3CN$	Ag_2CO_3		DMA	120	53^{c}
13	$PdCl_2$	$Cu(OAc)_2$	K_2CO_3	DMA	120	15^{c,d}
14	$PdCl_2$	$Cu(OAc)_2$	CsF	DMA	110	14^{c}
15	$PdCl_2$	$CuCl_2$	LiOAc	DMA	110	22^{c}

[a] Reaction conditions: Indole-2-carboxylic acid (0.25 mmol), phenyl allene (0.5 mmol), catalyst (10 mol%), oxidant $Cu(OAc)_2$ (0.5 mmol) or Ag_2CO_3 (0.375 mmol), base (0.5 mmol), solvent (0.1M for carboxylic acid), 10-16 h (reaction time not optimized).

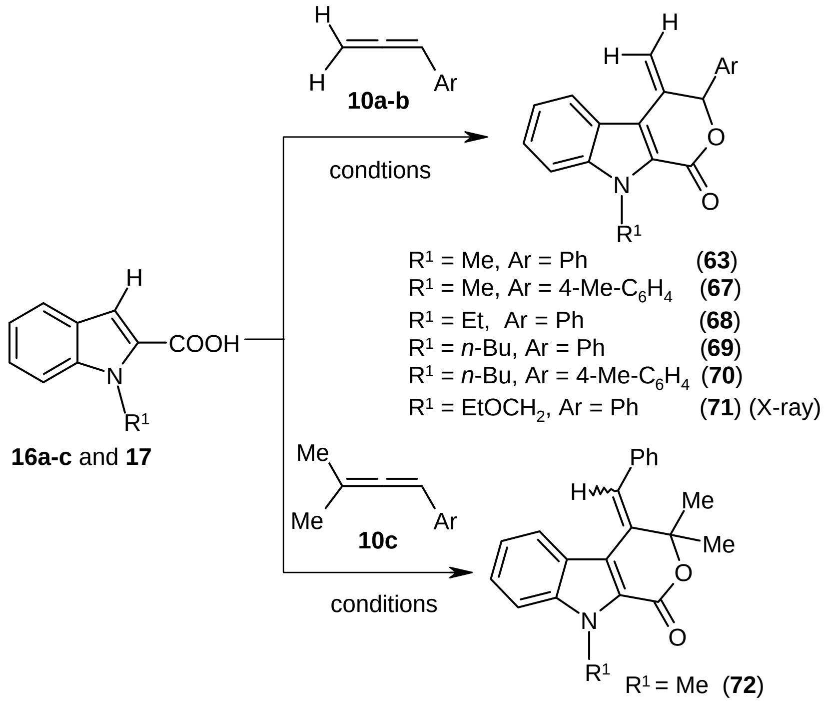
[b] Isolated yield based on the amount of **16a** after column chromatography.

[c] A mixture of products is obtained (GC-MS).

[d] phenyl allege (**10a**) (0.375 mmol)

With the above optimized conditions for the annulation of phenyl allene **10a** with indole-2-carboxylic acid **16a**, we next examined the scope of the reaction with various allenes and indole-2-carboxylic acids. We were able to generate the lactones **67-72** in good yields (Scheme 22). The allenes **10a-b** gave (α,β)-cyclized products **67-71** while the allene **10c** gave (β,γ)-cyclized product **72**.

Scheme 22



Conditions: $Pd(OAc)_2$ (10 mol%)/ Ag_2CO_3 (1.5 equiv)/ CH_3CN, 80 °C, 10-12 h

All the compounds **63** and **67-72** were characterized by spectroscopic and analytical data. As an example, the band corresponding to C=O stretching of lactone **67** appears 1701 cm^{-1} in the IR spectrum. In ^{1}H NMR spectra, the olefinic protons (C=C*H*$_2$) appear at δ ~5.16 and δ ~5.94. In the ^{13}C NMR spectrum, the *C*=O carbon of the lactone appears at δ 159.3. Finally, the structure for the lactone **71** is proven by X-ray crystallography (Figure 13). The C(10)-C(21) distance 1.332(4) Å clearly shows the exocyclic double bond as expected.

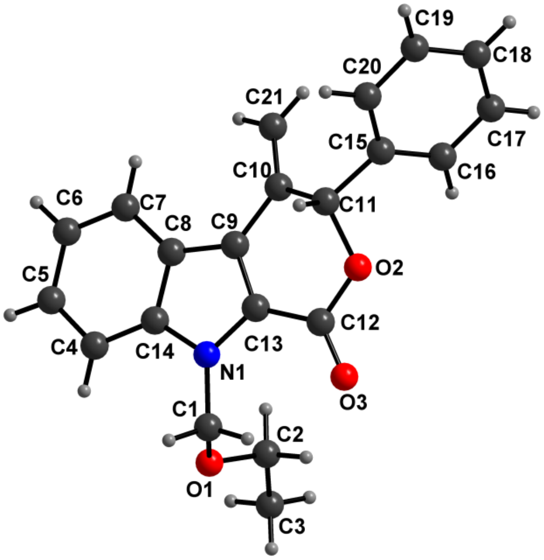
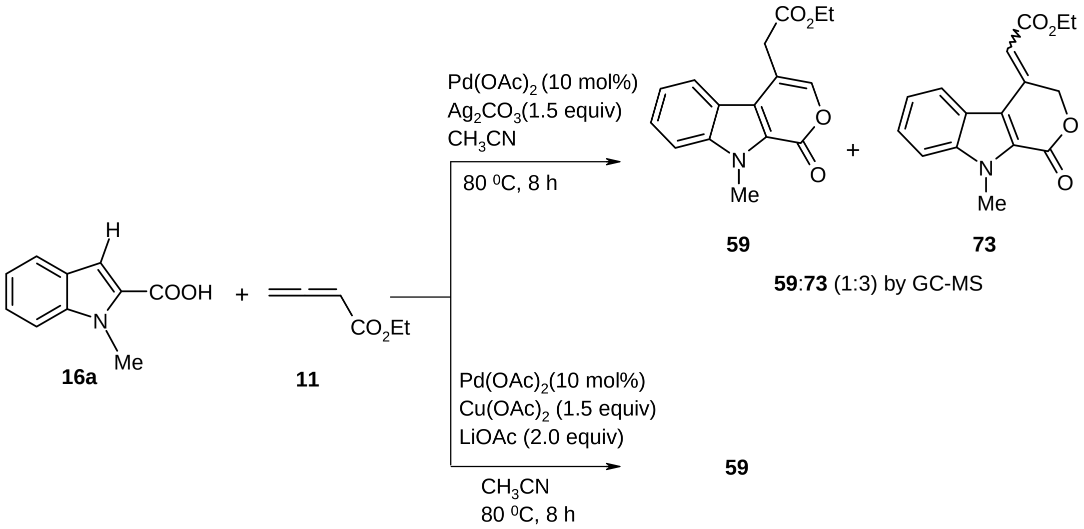


Figure 13. Molecular structure of compound **71**. Selected bond lengths [Å] with esds in parentheses: O(2)-C(11) 1.463(5), O(3)-C(12) 1.204(4), C(10)-C(11) 1.492(5), C(9)-C(10) 1.467(4), C(10)-C(21) 1.332(4), C(11)-H(11) 0.945(10).

2.81 Reaction of allenyl ester (11) with 1-methyl-indole-2-carboxylic acid (16a)

In continuation of the above work*,* we treated allenoate **11** with indole-2-carboxylic acid **16a** (Scheme 22). Interestingly, in this case, the ***cyclization occurs at (β,γ) position*** of allene **11**; the reaction was complete in 8 h, but led to a mixture of products **59** and **73** (*cf.* Scheme 23). However, when the reaction was conducted by using Cu(OAc)$_2$ (1.5 equiv.) as the oxidant in place of Ag$_2$CO$_3$,[94] compound **59** was formed selectively in moderate yields. Currently, we do not have a rationale for this observation. In the ^{1}H NMR spectrum, the C*H*$_2$CO$_2$Et protons appear at δ 3.80 for the isomer **59** and the OC*H*$_2$ protons of **73** appear at δ 5.91. In ^{13}C NMR spectra, the *C*H$_2$CO$_2$Et carbon of **59** appears at δ 34.5 while the carbon of O*C*H$_2$ moiety in **73** appears at δ 70.7. These data are consistent with the structures as written.

Scheme 23



2.82 Reaction of allenylphosphonates (6c-d)/ allenylphosphine oxides (8b, 8d) with 1-methyl-indole-2-carboxylic acid (16a)

Reaction of the allenylphosphonates **6c-d** with 1-methyl-indole-2-carboxylic acid **16a** using Ag_2CO_3 as the oxidant readily afforded the phosphono-lactones **74-75** (Scheme 24). Allenylphosphine oxides **8b** and **8d** led to ***isomeric*** lactones **76-77** as the predominant products; the major isomer was isolated in 95-100% purity. The results are summarized in Table 7. Here, the allenes **6c, 6d, 8b** and **8d** led to ***(β,γ)-cyclized products***. This observation is similar to that for the ester allene **11** but different from that of aryl substituted allenes **10a-c**. Under the same conditions, the reaction was not feasible in the case of α-aryl allenylphosphonate **6e** and hence precursors **6e-i** were not utilized further.

Scheme 24

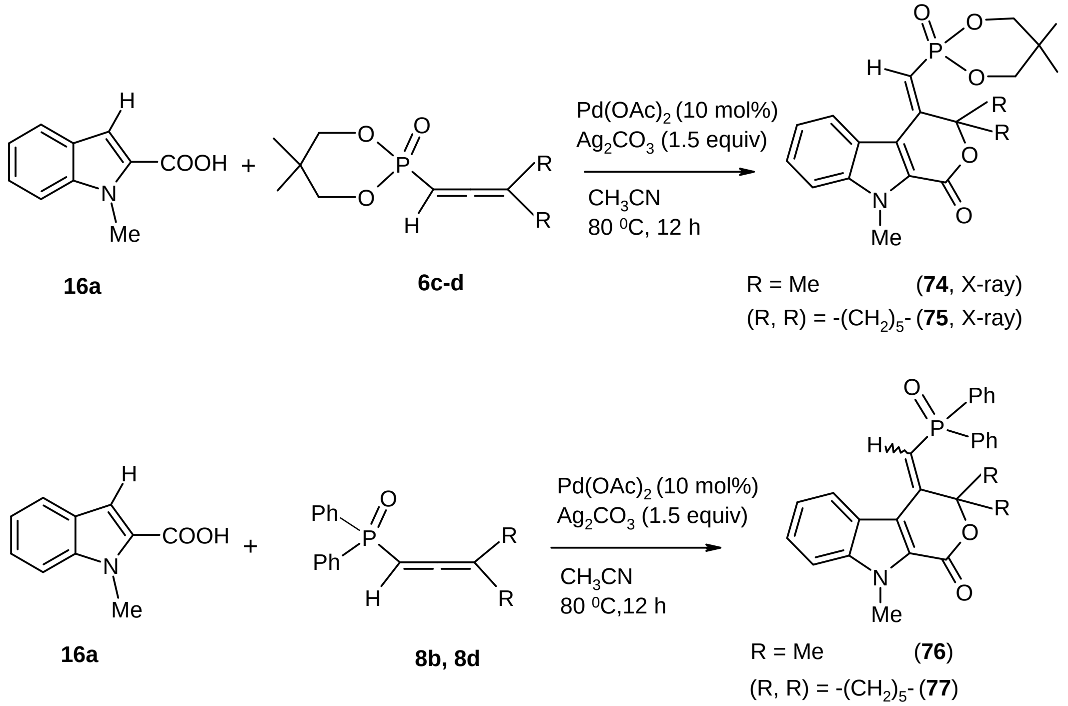


Table 7. Details on the yields of the lactones **75-78**

Entry	Allene	Indole-2-carboxylic acid	Product	Isolated yield (%)	^{31}P NMR (δ ppm)
1	**6c**	**16a**	**74**	68	12.2
2	**6d**	**16a**	**75**	65	11.0
3	**8b**	**16a**	**76**	61[c]	20.7[a]
4	**8d**	**16a**	**77**	51[c]	20.8[b]

[a] Minor product at 18.7; ratio of the major to minor isomer (^{31}P NMR) was 7:3.

[b] Minor product at 18.2; ratio of the major to minor isomer (^{31}P NMR) was 6:4.

[c] Based on ^{31}P NMR spectrum of the reaction mixture, the combined yield was essentially quantitative.

The above lactones **74-77** are characterized by IR, NMR [^{1}H, ^{13}C, ^{31}P] and LC-MS/CHN analyses. In the ^{1}H NMR spectrum of **74**, the PC*H* proton appears at δ ~6.42 (^2J(P-H) ~ 8.4 Hz); the ^{31}P NMR spectrum shows a signal at δ 12.2. In the ^{13}C NMR spectrum, the carbon attached to phosphorus exhibits a doublet at δ 106.4 (^1J(P-C) =

194.7 Hz) which shows that it is of PC=C type. In the ^{31}P NMR, the lactones show a peak in the region δ 11.0-12.0 for **74-75** and at δ 20.0-20.1 (major, 75%) along with δ ~18.0 (minor, 25%) for **76-77** respectively. Finally, the *Z*-configuration around the C=C double bond for **74** and **75** is proven by X-ray crystallography (Figures 14 and 15). The C(9)-C(10) distances of 1.518(3) Å in **74** and 1.512(8) Å in **75** clearly show that the allenes **6c-d** undergo (β,γ)- cyclization.

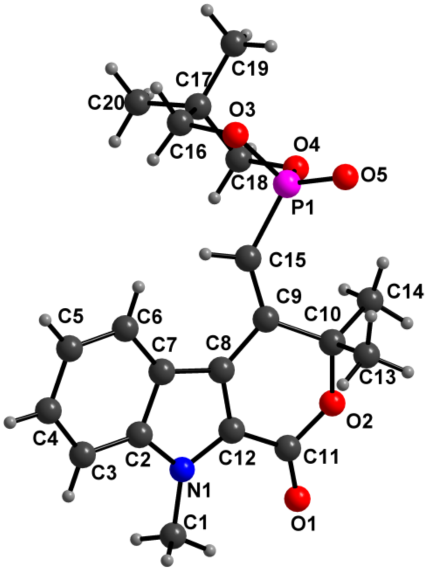


Figure 14. Molecular structure of the compound **74**. Selected bond lengths [Å] with esds in parentheses: P(1)-C(15) 1.7813(19), C(9)-C(10) 1.518(3), C(9)-C(8) 1.457(2), O(2)-C(10) 1.483(3), O(1)-C(11) 1.213(2).

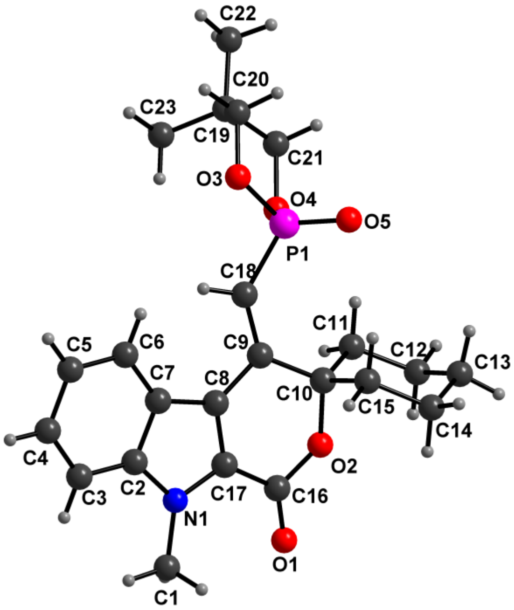
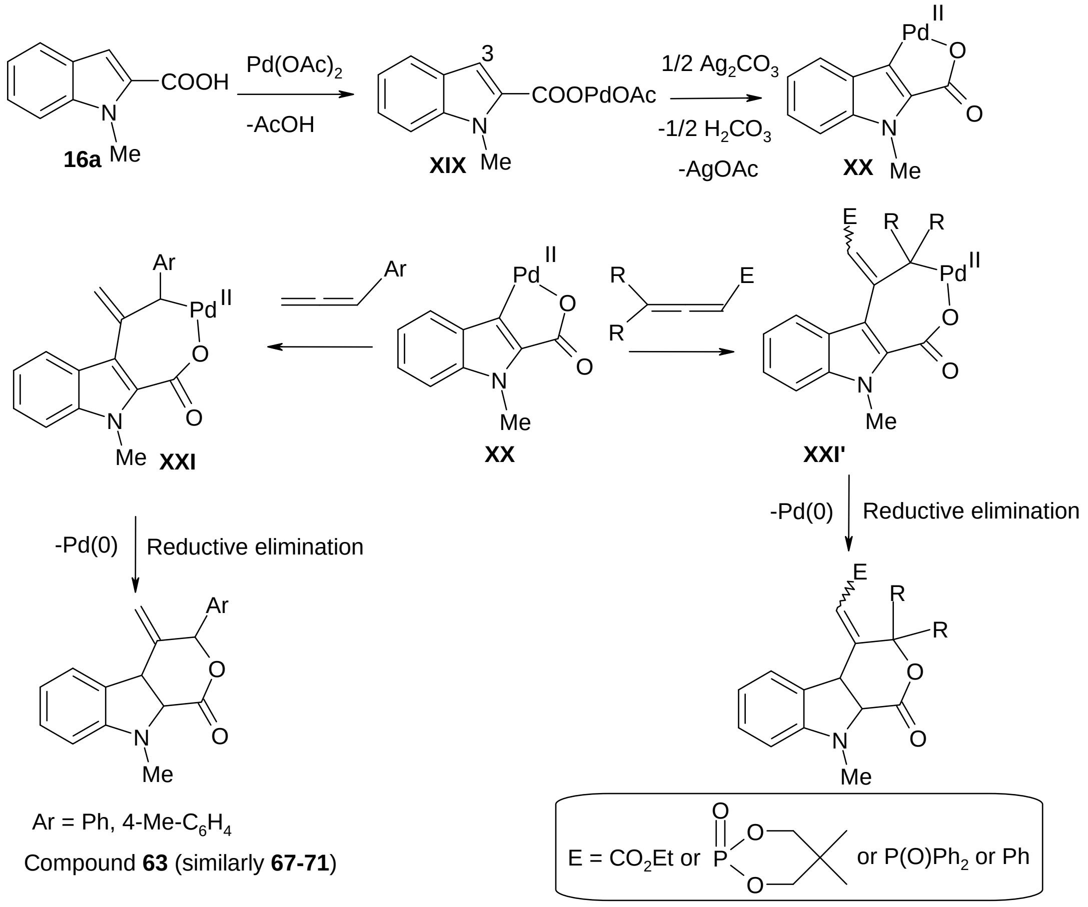


Figure 15. Molecular structure of the compound **75**. Selected bond lengths [Å] with esds in parentheses: P(1)-C(18) 1.764(6), C(9)-C(8) 1.460(7), C(9)-C(10) 1.512(8), O(2)-C(10) 1.461(6), O(1)-C(16) 1.188(7), C(18)-C(9) 1.341(7).

2.83 Mechanistic pathway for the formation of lactones

The exact mechanism of this annulation is still not clear. However, a possible pathway is proposed in Scheme 25 based on the literature reports.[97] Initially, $Pd(OAc)_2$ gets coordinated by the carboxyl oxygen to form the Pd(II) carboxylate **XIX** with the liberation of AcOH which appears to be the key process for this annulation without undergoing decarboxylation in the presence of silver salts.[94-95] Then, the intermediate **XIX** undergoes carbo-palladation at the C(3)-position forming a palladacycle intermediate **XX** which subsequently insert into allenes to produce allylic palladium(II) intermediates **XXI** or **XXI'**. Subsequent reductive elimination of the seven-membered palladacycles **XXI** or **XXI'** generates the lactones as well as Pd(0) species which can be reoxidized to the Pd(II) species by silver or copper salts.

Scheme 25



Ar = Ph, 4-Me-C_6H_4
Compound **63** (similarly **67-71**)

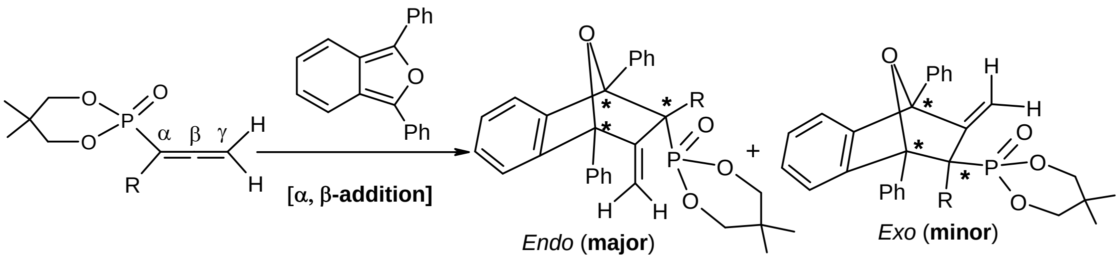
E = CO_2Et or P(O)(OCH$_2$C(Me)$_2$CH$_2$O) or P(O)Ph_2 or Ph

R = H, Me; (R,R) = -$(CH_2)_5$-
Compounds **72-77**

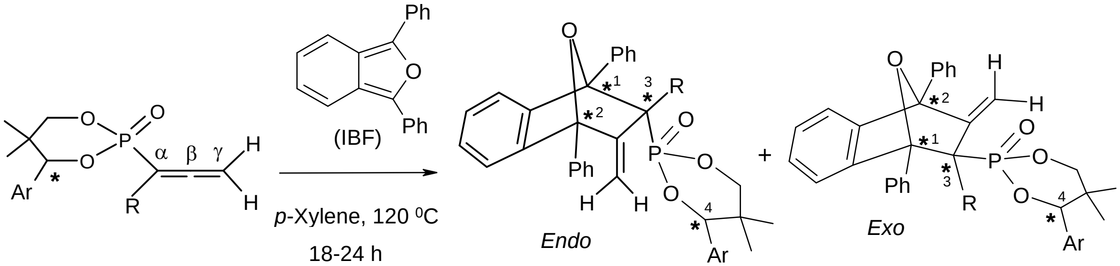
2.9 Cycloaddition reactions of allenylphosphonates (7a-c) with 1,3-diphenylisobenzofuran

Recently from our laboratory, the cycloaddition reactions of allenylphosphonates/ allenylphosphine oxides which involves the reactions of =CH_2 terminal allenylphosphonates with 1,3-diphenylisobenzofuran affording preferentially *endo*-[4+2] cycloaddition products has been reported.[78,96] It can be noted that there are three chiral centers generated during this process (Scheme 26). Hence we surmised that if the ring bearing phosphorus in the allene has chiral centers, several diastereomeric cycloadducts (either exo or endo) may be generated and in favorable cases, individual diastereomers may be isolated. For exploring this aspect, we synthesized the allenylphosphonates **7a-c** and allenylphosphoramidates **9a-d** which already have at least one chiral center. To begin with, we started with racemic system in each case. Assuming that there may not be any change in the stereochemistry at chiral centers corresponding to the bridgehead chiral carbons 1 and 2 (cf. Scheme 27), we expect that at least four diastereomers [(3,4)-*RR*, (3,4)-*RS*, (3,4)-*SR*, (3,4)-*SS*], based on the chiral centers 3 and 4, may result after the cycloaddition in either *exo* or *endo* isomer leading to a total of ***at least eight*** possibilities (cf. Scheme 26). The reaction of **7b-c** with IBF afforded a reaction mixture that showed ***four peaks*** in each case for the cycloaddition products; there was some unreacted allene also. The ^{31}P NMR spectra of the reaction mixtures in the product region in the reactions using **7b** and **7c** are shown in Figure 16. The diastereomer corresponding to δ 16.3 in Figure 16a [**78**] and that corresponding to δ 15.8 in Figure 16b [**79**] have been isolated in pure form. In the ^{1}H NMR spectra of **78** and **79**, the characteristic C=CH_2 protons appear as a double of doublet centered at δ ~5.52 [^{2}J(H-H) ~ 6.5 Hz] which shows that these are (α,β)-cycloaddition products. The carbon attached phosphorus could be identified by a doublet in the aliphatic region (as expected) at δ ~66 (^{1}J(P-C) = 136 Hz). We were fortunate to obtain the X-ray structure of **78** (Figure 17). The C(20)-C(21) distance of 1.306(6) Å clearly shows that this product is an *endo*-(α,β)-cycloadduct. This product crystallizes in the centrosymmetric space group $P\bar{1}$; the other molecule related by inversion symmetry is not shown. The checkcif (IUCr) also suggests the chirality at four centers [C1, C12 C22 and C29] in addition to phosphorus, but since the space group is centrosymmetric, we cannot say much about the other possible configurations.

Scheme 26



Scheme 27



7a-c

[α,β-**addition]**

Ar = 4-Cl-C_6H_4, R = Me	Ar = Ph; R = 4-MeO-C_6H_4	Ar = Ph, R = 4-Cl-C_6H_4
Endo (dr:1.1:1)	*Endo* (dr:1:1.4)	*Endo* (dr:1:1)
Exo (dr:1:1)	*Exo* (dr:1.6:1)	*Exo* (dr:1.7:1)
***Endo:exo* = ~1:3.2**	***Endo:exo* = ~1:1.5**	***Endo:exo* = ~1:1.3**
	78 = *Endo*- isomer with δ(P) 16.3 [see Figure 16 also]	**79** = *Endo*- isomer with δ(P) 15.8

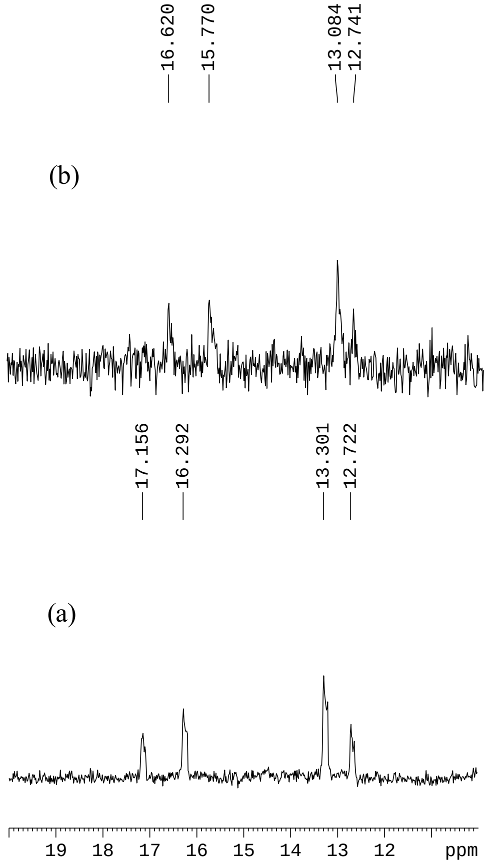


Figure 16. ^{31}P NMR spectra for the reaction mixtures (product region) of allenes **7b** or **7c** with IBF in *p*-xylene at 120 °C/ 20 h. (a) **7b+IBF**, (b) **7c+IBF**.

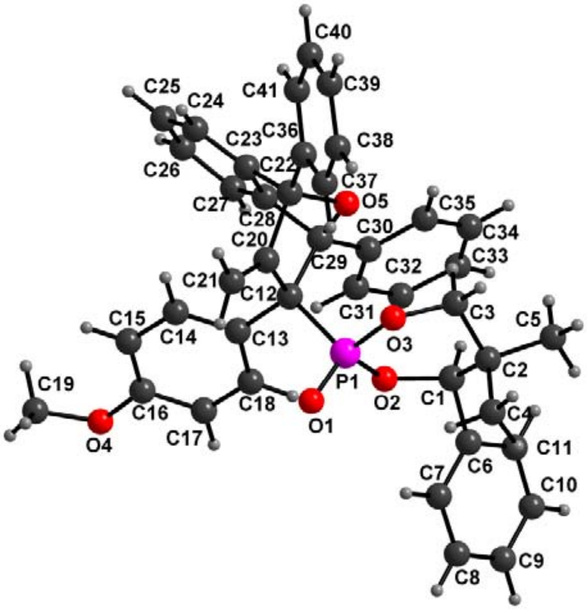
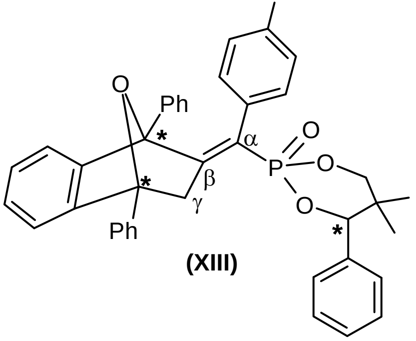


Figure 17. Molecular structure of compound **78**. Selected bond lengths [Å] with esds in parentheses. C(20)-C(21) 1.305(7), C(22)-C(23) 1.510(7), C(28)-C(29) 1.521(6), C(12)-C(20) 1.541(6), C(22)-O(5) 1.457(5), C(29)-O(5) 1.437(5).

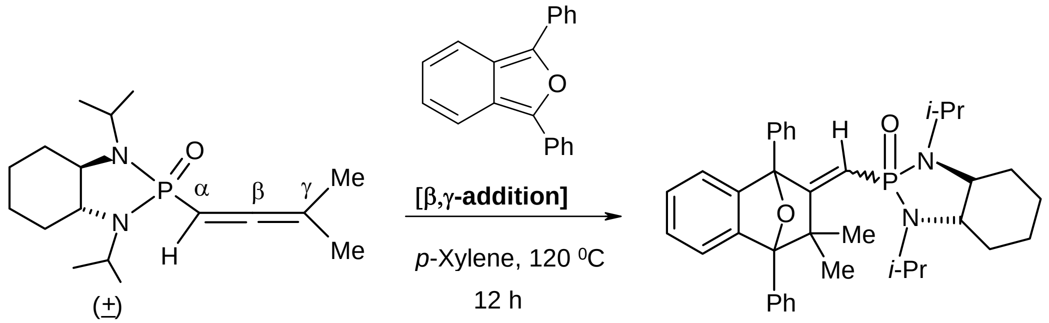
We also isolated a mixture of two components [δ 12.7 and 13.3] corresponding to Figure 16a. The ^{1}H NMR spectrum of this mixture shows peaks centered at δ 5.69, 5.23, 5.00, and 4.65. If they had been (β,γ)-products, peaks in the region δ 2.6-3.5 for the CH_2 protons (cf. structure **XIII**) were expected; the absence of the latter peaks suggest that they are also (α,β)-cycloaddition addition products. It is possible that they are exo-products, but so far, our attempts to separate these have been unsuccessful. It is observed earlier that the *exo* isomer appears up-field to *endo* isomer in the ^{31}P NMR spectrum [Δδ ~ 2.5; region for analogous products δ 18-25].[78]



(XIII)

In a previous work reported from our laboratory, it was also observed that allenes with a terminal =CMe$_2$ group upon reacting with IBF, give (β,γ)-adducts.[78] Thus allene **9d** with =CMe$_2$ group undergoes cyclization at (β,γ) double bond leading to (*E*+*Z*)-**80** (Scheme 28). As expected, two diastereomers were observed [^{31}P NMR: δ 24.2, 23.2; ratio ~ 1:1). In the ^{1}H NMR spectrum (*E*+*Z*)-**80**, the C=C*H* proton appears as two doublets for the two isomers centered at δ 5.15 [^{2}J(P-H) = 11.0 Hz] and 5.18 [^{2}J(P-H) = 11.0 Hz]. Hence both of these appear to be (β,γ)-cycloaddition products. However, we could isolate only one isomer in traces as we faced difficulties in separation, most likely due to hydrolysis at the P-N bond. The X-ray structure of compound (*E*)-**80** is shown in Figure 18. The C(14)-C(13) distance of 1.328(4).Å clearly shows that this is a (β,γ)-cycloadduct. In addition, it also shows that the configuration at the double bond is *E* [P1 and C18 trans to each other]. It can also be noted that in this reaction also new chiral centers [at C18 and C31] are generated, but the compound crystallized in the centrosymmetric space group $P\overline{1}$.

Scheme 28



9d **(*E*+*Z*)-80**

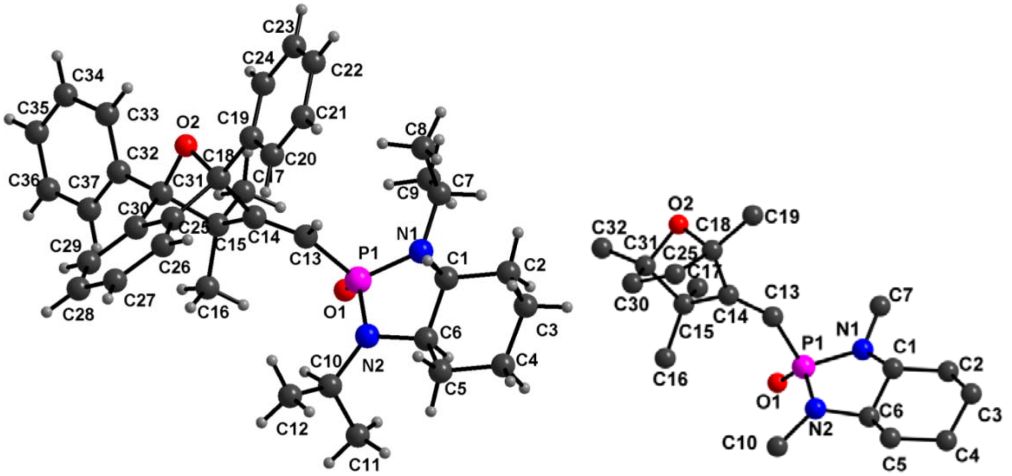


Figure 18. Molecular structure of compound (*E*)-**80.** Selected bond lengths [Å] with esds in parentheses. C(14)-C(13) 1.328(4), C(30)-C(25) 1.392(4), C(18)-C(25) 1.527(5), C(14)-C(18) 1.559(4), C(31)-C(15) 1.588(4), C(14)-C(15) 1.535(4), O(2)-C(31) 1.454(3), O(2)-C(18) 1.446(3).

SUMMARY-PART A

(1) The reaction of allenylphosphonates $(OCH_2CMe_2CH_2O)P(O)C(R)=C=CR'_2$ (**6b-c**, **6e-j**)/ allenylphosphine oxides $(Ph)_2P(O)C(R)=C=CR'_2$(**8b-c** and **8e**) or $4\text{-Cl-}C_6H_4\text{-}SO_2C(R)=C=CMe_2$ (**10c**) with the aldimine PhCH=NTs (**18**) in the presence of a carbene (NHC) afforded tosylated allylic phosphonates/phosphine oxides and or sulfone. This reaction involves a ***C-S bond formation*** and not C-O bond formation.

(2) The reaction of allenylphosphonates and allenylphosphine oxide with *N*-thiophosphinyl imines in the presence of a phosphine leads to a variety of phosphono-chromans. Optimization of reaction conditions reveals that $P(n\text{-}Bu)_3$ (base) in THF (solvent) is the best combination.

(3) Pd-catalyzed regioselective cyclization reactions of allenylphosphonates (**6a, 6e-i**)/ allenylphosphine oxides (**8a** and **8e**) with 3-iodo-indole-2-carboxylic acid derivatives (**15a-b**) lead to pyranoindoles in high yields essentially as single isomers under optimized conditions. The structures of key compounds are confirmed by X-ray crystallography. Similarly allenoate

$EtO_2CCH{=}C{=}CH_2$ (**11)** and allenylsulfones 4-Cl-C_6H_4-$S(O)_2CR{=}C{=}CH_2$ (**13a-b)** also gave pyranoindoles. These results establish that in the formation of phosphono-pyranoindoles, (β,γ)-cyclization is preferred.

(4) Allenes undergo cyclization with indole-2-carboxylic acid derivatives through ***C-H activation*** affording lactones of indole derivatives. Optimization of reaction conditions showed that $Pd(OAc)_2$/ Ag_2CO_3/ CH_3CN is the best combination to obtain good yield of a single product.

(5) α-Aryl allenylphosphonates $[OCHPhCMe_2CH_2O]P(O)C(Ar){=}C{=}CH_2$ [Ar = C_6H_4-4-OMe (**7b**), C_6H_4-4-Cl (**7c**)] with a remote chiral center and a terminal =CH_2 group undergo Diels-Alder reaction with isobenzofuran (IBF) to give *exo* and *endo* adducts wherein new chiral centers are generated. Here, the addition occurs at (α,β) position of the allene. We could isolate the diastereomers **78** and **79** corresponding to the *endo* product in the case of **7b** and **7c**, respectively. An allenylphosphoramidate (**9d**) with a terminal =CMe_2 group, however, gives (β,γ) addition product. The structure of one such diastereomeric product [(*E*)-**80**] is confirmed by X-ray crystallography.

EXPERIMENTAL SECTION

General: Chemicals and solvents were procured from Aldrich/ Fluka or local manufacturers. Further purification was done according to standard procedures wherever required.[97] All operations, unless otherwise specified, were carried out under dry nitrogen atmosphere using standard vacuum line techniques.[98]

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

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

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

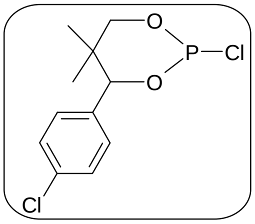
NMR spectroscopy: ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded using 5 mm tubes on a Bruker 400 (unless specified otherwise) or 500 MHz NMR spectrometer [field strengths: 500 400 125 100 162 and 202, MHz respectively] in $CDCl_3$ solution (unless specified otherwise) with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C: $\delta = 0$) and ext. 85% H_3PO_4 (^{31}P: $\delta = 0$) respectively. Spectra for which the 500 MHz equipment is used are specified appropriately. All J values are in Hz. In the ^{13}C NMR data, only ^{1}J(P-C) is specified in this thesis.

LC-MS and GC-MS: LC-MS or GC-MS equipment were 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. GC-MS data were obtained on EI mode using ZB-1 column.

3.1 Synthesis of P(III) compounds 1-4, propargyl alcohols 5a-e and other starting materials 10-17

Some of the precursors are in use in our laboratory and some are previously unknown. In cases where the procedures have been modified for compounds not reported previously, full details along with the spectroscopic data are given. Thus $(OCH_2CMe_2CH_2O)PCl$ [**1**; δ(P) 145.8],[79a] $(OCH(Ph)CMe_2CH_2O)PCl$ [**2**; δ(P) 149.6],[79b-c] $[OCH(C_6H_4\text{-}4\text{-}Cl)CMe_2CH_2O]PCl$ (**3**)[79a,c] and (±)-$[C_6H_{10}(1,2\text{-}(N(i\text{-}Pr))_2]PCl$ (**4**) [δ(P) 178.8][79d-e] were prepared by using literature methods; compound **3** is new. The propargyl alcohols (**5a-e**),[81-82] phenyl-substituted allenes **10a-c**,[87] 1,2-alkadienoate ester (allenoate) **11**,[88] $(4\text{-}Cl\text{-}C_6H_4)SCl$ (**12**),[89] allenylsulfones (**13a-c**),[17] salicyl *N*-thiophosphinyl imines (**14a-b**)[37a] and indole-2-caboxylic acid derivatives (**15a-b**, **16a-c** and **17**)[90] were also prepared by following literature procedures.

$[OCH(C_6H_4\text{-}4\text{-}Cl)CMe_2CH_2O]PCl$ (3)



Yield: 10.5 g (81%) (using 35.83 mmol of diol).

Bp: 110-115 ^{0}C/ 2 mm.

^{1}H NMR: δ 0.79 and 1.05 (2 s, 6H, $C(CH_3)_2$), 3.99 (dd→t, ^3J(P-H) = ^2J(H-H) = 11.2 Hz, 1H, OCH_A), 4.52 (dd, ^2J(H-H) ~ 11.2 Hz, ^3J(P-H) ~ 5.8 Hz, 1H, OCH_B), 5.46 (d, ^3J(P-H) = 5.6 Hz, 1H, OC*H*Ph), 7.24 (d, ^2J(H-H) = 8.4 Hz, 2H, Ar-*H*), 7.34 (d, ^2J(H-H) = 8.4 Hz, 2H, Ar-*H*).

^{13}C NMR: δ 17.9, 22.7, 37.0, 72.6, 82.1 (d, ^2J(P-C) = 10.0 Hz), 128.0, 129.0, 134.2, 134.7.

^{31}P NMR: δ 150.1.

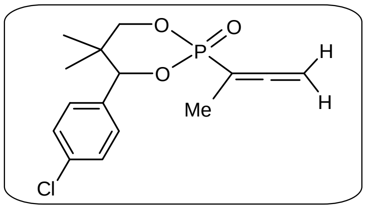
3.2 Synthesis of allenylphosphonates 6a-j and 7a-c

Allenylphosphonates **6a-j** were prepared by following a literature procedure.[79] Compounds **7a-c** are new. General procedure for the synthesis of these compounds is given below.

$[OCH(Ar)CMe_2CH_2O]P(O)(CR^3=C=CH_2)$ (7a-c)

To a solution of substituted propargyl alcohol $R^3C{\equiv}CCR^1R^2OH$ (1.0 equiv) in dry THF (25-40 mL) was added triethylamine (1.0 equiv), the mixture stirred for 5 min, and then $[OCH(Ph)CMe_2CH_2O]PCl$ (**2**) or $[OCH(4\text{-}Cl\text{-}C_6H_4)CMe_2CH_2O]PCl$ (1.0 equiv) in THF (5-10 mL) was added drop-wise (~ 0.5 h) at 0 °C. The contents were brought to room temperature (rt, 30 °C) stirred further for 1 h, and then heated under reflux for 16 h. Triethylamine hydrochloride formed was filtered off and solvent removed *in vacuo* from the filtrate to afford crude allenes **7a-c**. These were purified by column chromatography (silica gel; ethyl acetate-hexane 2:3).

$[OCH(4\text{-}Cl\text{-}C_6H_4)CMe_2CH_2O]P(O)C(Me)=C=CH_2$ (7a)



Yield:	1.50 g (67%) (using 7.17 mmol of **3**).
Mp:	138-140 °C.
IR (KBr):	2975, 1939, 1601, 1493, 1372, 1264, 1046 cm^{-1}.
^1H NMR:	δ 0.78 and 1.08 (2 s, 6H, $C(CH_3)_2$), 1.87-1.92 (td, ^3J(P-H) ~ 14.0 Hz, ^5J(H-H) ~ 2.0 Hz, 3H, CH_3), 3.97 (dd, ^3J(P-H) = 24.0 Hz, ^2J(H-H) = 11.2 Hz, 1H, OCH_A), 4.14-4.16 (m, 1H, OCH_B), 4.94-5.05 (m, 2H, $=CH_2$), 5.06 (s, 1H, OC*H*Ph), 7.26-7.29 (m, 2H, Ar-*H*), 7.34-7.36 (m, 2H, Ar-*H*).
^{13}C NMR:	δ 14.4, 17.1, 21.1, 36.6 (d, *J*(P-C) = 5.0 Hz), 76.1 (d, *J*(P-C) = 15.4 Hz), 78.5 (d, *J*(P-C) = 6.2 Hz), 86.3 (d, ^1J(P-C) ~ 171.1 Hz),

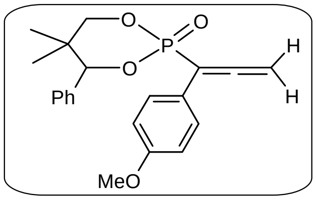
87.2, 128.2, 128.7, 134.1 (d, *J*(P-C) = 8.7 Hz), 134.5, 211.2 (d, *J*(P-C) = 6.0 Hz).

^{31}P NMR: δ 11.1.

LC-MS: *m/z* 313 and 315 $[M]^+$.

Anal. Calcd. for $C_{15}H_{18}ClO_3P$: C, 57.61; H, 5.80. Found: C, 57.65; H, 5.71.

$[OCHPhCMe_2CH_2O]P(O)C(C_6H_4\text{-4-OMe})=C=CH_2$ (7b)



Yield: 2.28 g (79%) (using 6.17 mmol of **2**).

Mp: 152-156 °C.

IR (KBr): 3067, 2969, 1935, 1609, 1514, 1458, 1262, 1043 cm^{-1}.

^{1}H NMR: δ 0.77 and 1.13 (2 s, 6H, $C(CH_3)_2$), 3.77 (s, 3H, OCH_3), 3.95 (dd, *J*(P-H) = 24.4 Hz, ^{2}J(H-H) = 11.2 Hz, 1H, OCH_A), 4.15-4.18 (m, 1H, OCH_B), 5.13 (s, 1H, OC*H*Ph), 5.31-5.35 (d, ^{4}J(P-H) ~ 12.8 Hz, 2H, $=CH_2$), 6.85 (d, ^{3}J(H-H) = 8.8 Hz, 2H, Ar-*H*), 7.33-7.36 (m, 5H, Ar-*H*), 7.54 (d, ^{3}J(H-H) = 8.8 Hz, 2H, Ar-*H*).

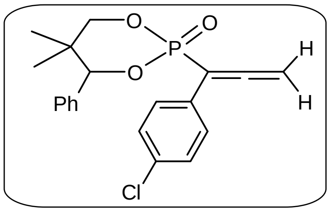
^{13}C NMR: δ 17.4, 21.2, 36.7 (d, *J*(P-C) = 6.0 Hz), 55.3 (s, CH_3), 78.6 (d, *J*(P-C) = 6.2 Hz), 79.0 (d, *J*(P-C) = 14.6 Hz), 88.3 (d, *J*(P-C) = 6.6 Hz), 94.9 (d, ^{1}J(P-C) = 177.7 Hz), 114.3, 122.3 (d, *J*(P-C) = 7.1 Hz), 127.4, 127.9, 128.5, 128.8 (d, *J*(P-C) = 6.2 Hz), 135.5 (d, *J*(P-C) = 8.9 Hz), 159.5, 212.2.

^{31}P NMR: δ 8.0.

LC-MS: *m/z* 371 $[M+1]^+$

Anal. Calcd. for $C_{21}H_{23}O_4P$: C, 68.10; H, 6.26. Found: C, 68.25; H, 6.18.

[$OCHPhCMe_2CH_2O$]P(O)C(C_6H_4-4-Cl-)=C=CH_2 (7c)



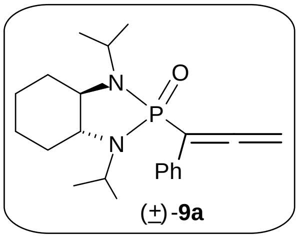
Yield:	0.30 g (74%) (using 1.08 mmol of **2**).
Mp:	128-132 °C.
IR (KBr):	3059, 1930, 1491, 1260, 1044, 870, 803 cm^{-1}.
^{1}H NMR:	δ 0.78 and 1.14 (2 s, 6H, C(C*H*$_3$)$_2$), 3.98 (dd, ^3J(P-H) = 24.4 Hz, ^2J(H-H) = 11.2 Hz, 1H, OC*H*$_A$, 4.14-4.17 (m, 1H, OC*H*$_B$), 5.12 (s, 1H, OC*H*Ph), 5.37-5.40 (d, ^4J(P-H) ~ 12.8 Hz, 2H, =C*H*$_2$), 7.28-7.37 (m, 7H, Ar-*H*), 7.54 (d, ^3J(H-H) = 8.4 Hz, 2H, Ar-*H*).
^{13}C NMR:	δ 17.4, 21.3, 32.8 (d, *J*(P-C) = 5.0 Hz), 78.8 (d, *J*(P-C) = 7.0 Hz), 79.5 (d, *J*(P-C) = 14.0 Hz), 88.6 (d, *J*(P-C) = 6.0 Hz), 94.9 (d, ^1J(P-C) = 175.0 Hz, P*C*), 127.4, 128.0, 128.7, 128.9, 129.0, 129.1, 134.1, 135.4 (d, *J*(P-C) = 9.0 Hz), 212.6 (d, *J*(P-C) = 4.3 Hz).
^{31}P NMR:	δ 6.8.
LC-MS:	*m/z* 375 and 377 $[M]^+$

Anal. Calcd. for $C_{20}H_{20}ClO_3P$: C, 64.09; H, 5.38. Found: C, 64.15; H, 5.31.

3.3 Synthesis of allenylphosphoramidates 9a-d

Allenylphosphoramidates **9a-d** were prepared by a procedure similar to that for allenylphosphonates[79] using (±)-*trans*-**4** (1.0 equiv) and the corresponding propargyl alcohol (1.0 equiv)/Et_3N (1.0 equiv) at room temperature (1 h reaction). These products were purified by column chromatography by using ethyl acetate/hexane (1:1) mixture as the eluent. Compounds **9a-c** are new.

Compound 9a



(±)-**9a**

Yield: 1.00 g (77%, using 3.63 mmol of **4**) (gummy solid).

IR (KBr): 3059, 2934, 2865, 1925, 1717, 1595, 1215, 1020, 762 cm^{-1}.

^{1}H NMR: δ 0.99 and 1.03 (2 d, ^{3}J(H-H) = 6.8 Hz, 6H, CH(C*H*$_3$)$_2$), 1.22-1.41 (m, 10H, cyclohexyl-*H* + CH(C*H*$_3$)$_2$), 1.76-1.83 (m, 2H, cyclohexyl-*H*), 2.00-2.12 (m, 2H, cyclohexyl-*H*), 2.81-2.86 (m, 1H, PNC*H*$_\mathrm{A}$), 3.12-3.17 (m, 1H, PNC*H*$_\mathrm{B}$), 3.39-3.46 (m, 1H, C*H*$_\mathrm{A}$(*i*-Pr)$_2$), 3.53-3.59 (m, 1H, C*H*$_\mathrm{B}$(*i*-Pr)$_2$), 5.06-5.19 (AB qrt coupled to phosphorus, ^{4}J(P-H) ~ 11.6 Hz, ^{2}J(H-H) ~ 13.2 Hz, 2H, =C*H*$_2$), 7.24-7.33 (m, 3H, Ar-*H*), 7.72 (d, ^{3}J(H-H) = 8.0 Hz, 2H, Ar-*H*).

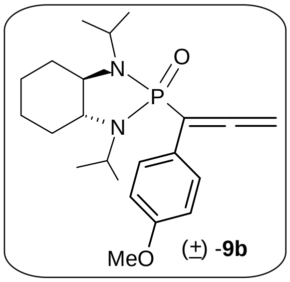
^{13}C NMR: δ 19.0 (NCH*C*H$_3$(A)CH$_3$(B)), 19.9 (NCHCH$_3$(A)*C*H$_3$(B)), 21.0 (NCH*C*H$_3$(C)CH$_3$(D)), 22.4 (NCHCH$_3$(C)*C*H$_3$(D)), 23.8, 29.0 (d, *J*(P-C) = 9.7 Hz, PNCCH*C*H$_2$), 30.1 (d, *J*(P-C) = 7.2 Hz, PNCCH*C*H$_2$), 43.4, 44.5, 59.3 (d, *J*(P-C) = 6.0 Hz, PNC*C*H), 60.5 (d, *J*(P-C) = 7.0 Hz, PNC*C*H), 75.4 (d, *J*(P-C) = 13.0 Hz), 101.8 (d, ^{1}J(P-C) = 150.0 Hz, P-*C*), 126.7, 128.0, 133.5 (d, *J*(P-C) = 11.0 Hz), 158.7, 215.7.

^{31}P NMR: δ 23.5.

LC-MS: *m/z* 360 [M+1]$^{+}$.

Anal. Calcd. for $C_{21}H_{31}N_2OP$: C, 70.36; H, 8.72; N, 7.81. Found: C, 70.25; H, 8.67; N, 7.91.

Compound 9b



(±) -**9b**

Yield: 0.77 g (73%, using 2.73 mmol of **4**) (gummy solid).

IR (KBr): 3057, 2936, 1923, 1605, 1509, 1462, 1296, 1181, 1028 cm^{-1}.

^{1}H NMR: δ 1.01 and 1.03 (2 d, ^3J(H-H) = 6.8 Hz, 6H, CH(CH_3)$_2$), 1.24-1.42 (m, 10H, cyclohexyl-*H* + CH(CH_3)$_2$), 1.75-1.82 (m, 2H, cyclohexyl-*H*), 2.00-2.11 (m, 2H, cyclohexyl-*H*), 2.79-2.84 (m, 1H, PNCH_A), 3.11-3.16 (m, 1H, PNCH_B), 3.39-3.43 (m, 1H, CH_A(*i*-Pr)$_2$), 3.52-3.57 (m, 1H, CH_B(*i*-Pr)$_2$), 3.80 (3H, OCH_3), 5.03-5.16 (AB qrt coupled to phosphorus, ^4J(P-H) ~ 11.6 Hz, ^2J(H-H) ~ 13.2 Hz, 2H, =CH_2), 6.85 (d, ^3J(H-H) = 9.0 Hz, 2H, Ar-*H*), 7.66 (d, ^3J(H-H) = 9.0 Hz, 2H, Ar-*H*).

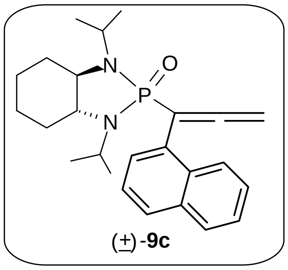
^{13}C NMR: δ 19.7 (NCHCH_3(A)CH$_3$(B)), 20.5 (NCHCH$_3$(A)CH_3(B)), 21.8 (d, *J*(P-C) = 4.0 Hz, NCHCH_3(C)CH$_3$(D)), 23.1 (s, NCHCH$_3$(C)CH_3(D)), 24.5, 29.8 (d, *J*(P-C) = 10.0 Hz, PNCCHCH_2), 30.7 (d, *J*(P-C) = 8.0 Hz, PNCCHCH_2), 44.1 (d, *J*(P-C) = 6.0 Hz, PN*C*H), 45.2, 54.3 (O*C*H$_3$), 59.9 (d, *J*(P-C) = 7.0 Hz, PNC*C*H), 61.1 (d, *J*(P-C) = 8.0 Hz, PNC*C*H), 76.0 (d, *J*(P-C) = 13.0 Hz), 102.0 (d, ^1J(P-C) = 146.0 Hz, P-*C*), 113.7, 126.4 (d, *J*(P-C) = 7.0 Hz), 129.9 (d, *J*(P-C) = 4.0 Hz), 158.9, 216.0 (d, *J*(P-C) = 5.0 Hz, PC=*C*).

^{31}P NMR: δ 24.0.

LC-MS: *m/z* 389 [M+1]$^+$.

Anal. Calcd. for $C_{22}H_{33}N_2O_2P$: C, 68.02; H, 8.56; N, 7.21. Found: C, 68.12; H, 8.51; N, 7.28.

Compound 9c


(±)-**9c**

Yield: 1.34 g (40%; using 8.18 mmol of **4**).

Mp: 88-90 °C (white solid).

IR (KBr): 3048, 2969, 1934, 1740, 1672, 1503, 1223, 1119, 988 cm^{-1}.

^{1}H NMR: δ 0.97 and 0.99 (2 d, ^3J(H-H) = 6.8 Hz, 6H, CH(C*H*$_3$)$_2$), 1.19-1.64 (m, 14H, cyclohexyl-*H* + CH(C*H*$_3$)$_2$), 3.41 (br, 2H, cyclohexyl-C*H*), 3.51-3.57 (m, 2H, PNC*H*(A) + PNC*H*(B)), 4.97-5.00 (d, ^4J(P-H) = 12.0 Hz 2H, =C*H$_2$*), 7.45-7.50 (m, 3H, Ar-*H*), 7.78-7.85 (m, 3H, Ar-*H*), 8.17 (d, ^3J(H-H) = 7.6 Hz, 1H, Ar-*H*).

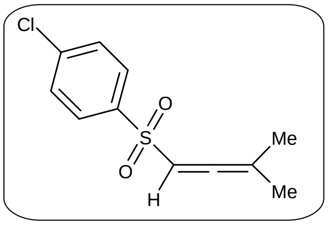
^{13}C NMR: δ 21.3, 21.5, 22.4_0, 22.4_3, 29.1, 29.2, 45.3 (d, *J*(P-C) = 3.4 Hz, PN*C*H(CH$_3$)$_2$), 53.0 (d, *J*(P-C) = 7.0 Hz, PNC*C*H), 74.4 (d, *J*(P-C) = 13.4 Hz), 100.3 (d, ^1J(P-C) = 130.8 Hz, P-*C*), 125.1 (d, *J*(P-C) = 1.9 Hz), 125.6, 125.7, 125.8, 127.7 (d, *J*(P-C) = 2.9 Hz), 127.8, 128.3, 131.3, 132.0 (d, *J*(P-C) = 3.7 Hz), 133.9, 212.4 (d, *J*(P-C) = 4.9 Hz, PC=*C*).

^{31}P NMR: δ 30.0.

LC-MS: *m/z* 409 $[M+1]^+$.

Anal. Calcd. for $C_{25}H_{33}N_2OP$: C, 73.50; H, 8.14; N, 6.86. Found: C, 73.45; H, 8.21; N, 6.81. This compound was crystallized from EtOAc at room temperature (30 °C).

Preparation of allenyl sulfone 13c



A procedure analogous to that for **13a-b**[17]was adapted for **13c** using 4-Cl-C_6H_4-S(O)CH=C=CMe_2 (4.90 g, 21.6 mmol).

Yield: 2.50 g (48%).

Mp: 52-54 ^{o}C (white solid).

IR (KBr): 3048, 2969, 1934, 1740, 1672, 1503, 1223, 1119, 988 cm^{-1}.

^{1}H NMR: δ 1.80 (s, 6H, C(C*H*$_3$)$_2$), 6.03-6.05 (m, 1H, =C*H*), 7.52 (d, ^3J(H-H) = 8.8 Hz, 2H, Ar-*H*), 7.83 (d, ^3J(H-H) = 8.8 Hz, 2H, Ar-*H*).

^{13}C NMR: δ 19.4, 98.7, 107.4, 129.0, 129.4, 139.9, 140.1, 204.1.

LC-MS: *m/z* 243 [M+1]$^+$.

Anal. Calcd. for $C_{11}H_{11}ClO_2S$: C, 54.43; H, 4.57. Found: C, 54.32; H, 4.51.

3.4 Synthesis of indole-2-caboxylic acid derivatives 15a-b, 16a-c and 17

All the indole-2-carboxylic acids derivatives were prepared according to the literature procedures.[82] Hence only general procedures are given below.

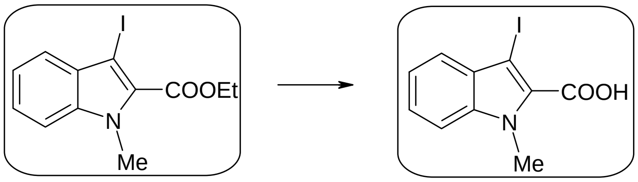
3.41 General procedure for the synthesis of 1-methyl-3-iodo-indole-2-carboxylic acid (15a) and 1-benzyl-3-iodo-indole-2-carboxylic acid (15b)

(a) To a stirred solution of 3-iodo-indole-2-ethylcarboxylate (1.0 equiv) in DMF (0.3M with respect to iodo compound) at rt, tetrabutylammonium bromide (TBAB) (10 mol%) and K_2CO_3 (2.0 equiv) were added. To this, iodomethane (5 equiv) or benzyl chloride (2.0 equiv) was added and the round-bottomed flask (RBF) sealed with a glass stopper. The contents were stirred at rt for 12 h. After the completion of the reaction (tlc), the mixture was diluted with DCM, washed with brine, dried over Na_2SO_4, filtered, and the solvent removed by rotary evaporator. The crude product was purified by column chromatography (hexane/ EtOAc; 9:1) to get the 1-benzyl or 1-methyl-3-iodo-indole-2-ethylcarboxylate pure product in 96 or 85% yield respectively. The spectroscopic data for 1-benzyl-3-iodo-indole-2-ethylcarboxylate is consistent with that reported in the literature.[87d]

(b) The 1-benzyl or 1-methyl-3-iodo-indole-2-ethylcarboxylate as obtained in **(a)** was dissolved in EtOH (0.3M) and the contents heated under reflux before adding of

KOH (3.0 equiv) in water (0.15M). This mixture was heated again under reflux for 16 h, the solvent removed by rotary evaporator and the crude material extracted with ethyl acetate. The organic layer (EtOAc) was dried with anh. Na_2SO_4 and the solvent removed by rotary evaporator to get the carboxylic acid (**15a** or **15b**) in 90% yield. The spectroscopic data for the compound **15b** is consistent with that reported in the literature.[87g]

Compound 15a



15a

The precursor for **15a** is also a new compound but prepared by a literature route[82] [Yield: 2.30 g (88%; using 7.94 mmol of 3-iodo-indole-2-ethylcarboxylate). Mp: 50-52 °C (white solid). IR (KBr): 2980, 1694, 1460, 1379, 1248, 1103, 1011, 741 cm^{-1}. ^1H NMR:δ 1.51 (t, ^3J(H-H) = 7.2 Hz, 3H, CH_2CH_3), 4.02 (s, 3H, N(CH_3)), 4.48 (q, ^3J(H-H) = 7.2 Hz, 2H, CH_2CH_3), 7.24-7.27 (m, 1H, Ar-*H*), 7.34-7.41 (m, 2H, Ar-*H*), 7.58 (d, ^3J(H-H) = 8.4 Hz, 1H, Ar-*H*). ^{13}C NMR:δ 14.3 (OCH_2CH_3), 33.0 (N(CH_3)), 61.3, 110.5, 121.4, 123.9, 126.1, 128.7, 130.3, 139.0, 140.2, 161.4. LC-MS: *m/z* 330 $[M+1]^+$. Anal. Calcd. for $C_{12}H_{12}INO_2$: C, 43.79; H, 3.67; N, 4.26. Found: C, 43.72; H, 3.61, N, 4.32].

Yield (for **15a**):	1.89 g (90%; using 7.00 mmol of 1-methyl-3-iodo-indole-2-ethylcarboxylate).
Mp:	174-176 °C (white solid). Lit.[87e] (177-178 °C).
IR (KBr):	3058, 2924, 2591, 1672, 1501, 1350, 1265, 928 cm^{-1}.
^1H NMR:	δ 4.12 (s, 3H, N(CH_3)), 7.19-7.27 (m, 1H, Ar-*H*), 7.42-7.73 (m, 3H, Ar-*H*).
^{13}C NMR:	δ 31.8 (N(CH_3)), 110.4, 110.7, 112.5, 120.8, 122.9, 124.3, 125.7, 126.9, 167.2.
LC-MS:	*m/z* 302 $[M+1]^+$.

Anal. Calcd. for $C_{10}H_8INO_2$: C, 39.89; H, 2.68; N, 4.65. Found: C, 39.95; H, 2.62, N, 4.61.

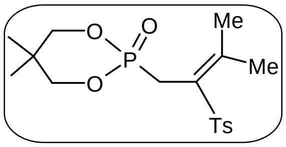
3.5 Migration of tosyl group of aldimine (18) to allenylphosphonates (6b-c, 6e-j, 8b-c and 8e) and allenylsulfone by *N*-heterocyclic carbenes [via NHC salts 21-23]- Synthesis of tosylated phosphonates 19 and 24-34

***3.51 Screening of the reaction conditions*:** In a 25 mL round-bottomed flask (RBF)**,** NHC-1-3. HCl salt (one of **21-23**,[99] 10 mol%) and the solvent [THF or toluene; *ca* 0.5 mL] (0.25M solution with respect to allene) were taken. To this, base [DBU, DMAP; 10 mol%] was added and the mixture stirred at rt for 10 min. After this, *N*-tosylphenylimine **18** (0.5 mmol) followed by allene (0.5 mmol) were added and the stirring continued at the indicated temperature for 14 h. A small sample of the reaction mixture was analyzed by ^{31}P NMR spectrum. Other details are presented in Table 1 in Results and Discussion (Chapter 2).

3.52 General procedure for the tosyl transfer reaction of allenylphosphonates and N-tosylphenylimine to lead to compounds 19 and 24-34

To a stirred solution of NHC salt [**21** (10 mol %)] in dry toluene (0.25M), DBU (10 mol %) was added and the stirring continued for 10-15 min at rt. After this, *N*-tosylphenylimine (**18)** (1.0 equiv) and allenylphosphonate/sulfonyl allene (1.0 equiv) were added and the mixture stirred at 90-100 ^{0}C for 12-18 h. The solvent was removed by rotary evaporator and the reaction mixture directly subjected to column chromatography using ethyl acetate-hexane as eluent (1:1 to 1.5:1) to get the pure product. Compounds **19** and **24-34** were prepared by this procedure.

Compound 19



Yield: 1.00 g (77%; using 3.37 mmol of allene **6c**).

Mp: 124-126 °C (white solid).

IR (KBr): 2967, 1626, 1402, 1277, 1142, 1007, 812 cm^{-1}.

^1H NMR: δ 1.02 and 1.18 (2 s, 6H, $C(CH_3)_2$), 1.96 (d, ^5J(P-H) = 6.0 Hz, 3H, =$C(CH_3$(A)), 2.08 (d, ^5J(P-H) = 4.4 Hz, 3H, =$C(CH_3$(B)), 2.43 (s, 3H, $O_2SC_6H_4CH_3$), 3.38 (d, ^2J(P-H) = 20.4 Hz, 2H, $P(O)CH_2$), 4.04-4.19 (m, 4H, OCH_2(A) + OCH_2(B)), 7.31 (d, ^3J(H-H) = 8.0 Hz, 2H, Ar-*H*), 7.84 (d, *J*(H-H) = 8.0 Hz, 2H, Ar-*H*).

^{13}C NMR: δ 21.1, 21.5, 21.8 ($-O_2SC_6H_4CH_3$), 23.1 and 25.3 (2 d, *J*(P-C) = 3.0 Hz, 3.3 Hz =$C(CH_3)_2$), 25.5 (d, ^1J(P-C) = 135.7 Hz, CH_2), 32.6 (d, *J*(P-C) = 6.7 Hz, *C*Me_2), 76.4 (s, OCH_2(A)), 76.5 (s, OCH_2(B)), 127.0, 128.1 (d, *J*(P-C) = 11.2 Hz), 129.6, 139.6, 143.7, 153.5 (d, *J*(P-C) = 10.0 Hz).

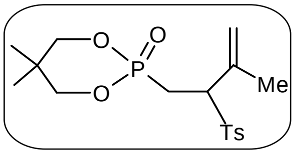
^{31}P NMR: δ 18.7.

LC-MS: *m/z* 373 $[M+1]^+$.

Anal. Calcd. for $C_{17}H_{25}O_5PS$: C, 54.83; H, 6.77. Found: C, 54.75; H, 6.81.

Compound 20

This compound was obtained by using NHC-2.HCl salt **22** instead of **21** **[**Chapter 2, (Table 4, entry 6)]. The residue after removing the solvent from the reaction mixture obtained by using the NHC-2.HCl salt **22** (10 mol%, 0.05 mmol), DBU (10 mol%, 0.05 mmol), allene $(OCH_2CMe_2CH_2O)P(O)(CH{=}C{=}CMe_2)$ (**6c**) (0.5 mmol) and *N*-tosylphenylimine **18** (0.5 mmol in toluene; 5 mL), was subjected to column chromatography (EtOAc/ hexane 1:1.5) to afford the products 1**9** (28%) and **20** (40%). Data for compound **19** is given above.



Yield: 0.074g (40%; using 0.50 mmol of allene **6c** and NHC salt **22**).

Mp: 162-164 °C (white solid).

IR (KBr): 2980, 1642, 1595, 1474, 1271, 1144, 1003, 911 cm^{-1}.

^{1}H NMR: δ 1.04 and 1.07 (2 s, 6H, C(C*H*$_3$)$_2$), 1.80 (s, 3H, =C(C*H*$_3$)), 2.45 (s, 3H, O$_2$SC$_6$H$_4$C*H*$_3$), 2.50-2.70 (m, 2H, P(O)C*H*$_2$), 3.79-3.88 (m, 2H, OC*H*$_2$(A)), 3.95-3.96 (s, 1H, C*H*), 4.09-4.17 (m, 2H, OC*H*$_2$(B)), 4.90 (s, 1H, C=C*H*$_A$), 5.12 (s, 1H, C=C*H*$_B$), 7.33 (d, ^{3}*J*(H-H) = 8.0 Hz, 2H, Ar-*H*), 7.72 (d, ^{3}*J*(H-H) = 8.0 Hz, 2H, Ar-*H*).

^{13}C NMR: δ 21.2, 21.5, 21.6, 21.7, 21.6 (d, ^{1}*J*(P-C) = 138.4 Hz, *C*H$_2$), 32.6 (d, *J*(P-C) = 6.5 Hz, *C*Me$_2$), 66.5 (s, *C*H), 75.6$_1$ (s, O*C*H$_2$(A)), 75.6$_4$ (s, O*C*H$_2$(B)), 121.2, 129.4, 129.7, 133.4, 136.1, 145.2.

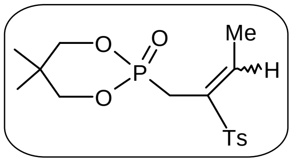
DEPT: δ 20.6, 21.5$_0$, 21.5$_1$, 21.7, 21.8 (d, ^{1}*J*(P-C) = 138.5 Hz, *C*H$_2$), 66.4 (*C*H), 75.5 (s, O*C*H$_2$(A)), 75.6 (s, O*C*H$_2$(B)), 121.1 (=*C*H$_2$), 129.3, 129.6.

^{31}P NMR: δ 22.1.

LC-MS: *m/z* 373 [M]$^+$.

Anal. Calcd. for $C_{17}H_{25}O_5PS$: C, 54.83; H, 6.77. Found: C, 54.92; H, 6.71.

Compound 24



Yield: 0.30 g (84%; using 1.0 mmol of allene **6b**).

Mp: 108-112 °C (white solid).

IR (KBr): 2969, 1642, 1597, 1474, 1252, 1058, 1012, 801, 559 cm^{-1}.

^{1}H NMR: δ 1.00 and 1.05 (2 s, 6H, C(C*H*$_3$)$_2$), 2.02 (m, 3H, =C(C*H*$_3$)), 2.45 (s, 3H, O$_2$SC$_6$H$_4$C*H*$_3$), 3.04 (d, ^{2}*J*(P-H) = 21.6 Hz, 2H, P(O)C*H*$_2$), 3.89 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 11.4 Hz, 2H, OC*H*$_2$(A)), 4.05 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 11.0 Hz, 2H, OC*H*$_2$(B)), 7.14-7.21 (m, 1H, =C*H*), 7.34 (d, ^{3}*J*(H-H) ~ 8.2 Hz, 2H, Ar-*H*), 7.77 (d, ^{3}*J*(H-H) = 8.2 Hz, 2H, Ar-*H*).

^{13}C NMR: δ 15.5 (d, *J*(P-C) = 2.7 Hz, =*C*CH$_3$), 21.3, 21.5 and 21.6 (2*C*H$_3$ + -O$_2$SC$_6$H$_4$*C*H$_3$), 23.3 (d, ^{1}*J*(P-C) = 138.4 Hz, *C*H$_2$), 32.5 (d, *J*(P-C) = 6.6

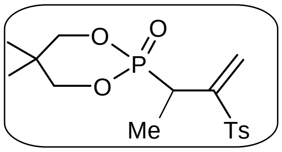
Hz, *C*Me$_2$), 75.8, 75.9, 128.3, 129.8, 133.8 (d, *J*(P-C) = 10.7 Hz), 136.4, 142.2 (d, *J*(P-C) = 8.7 Hz), 144.3.

^{31}P NMR: δ 18.3.

LC-MS: *m/z* 359 [M+1]$^+$.

Anal. Calcd. for $C_{16}H_{23}O_5PS$: C, 53.62; H, 6.47. Found: C, 53.45; H, 6.51.

Compound 25



Yield: 0.154 g (43%; using 1.0 mmol of allene **6j**).

Mp: 129-131 °C (white solid).

IR (KBr): 3098, 2969, 1593, 1474, 1314, 1271, 1163, 835, 799 cm^{-1}.

^{1}H NMR: δ 0.89 and 1.04 (2 s, 6H, C(C*H*$_3$)$_2$), 1.33-1.39 (m, 3H, CHC*H*$_3$), 2.45 (s, 3H, $O_2SC_6H_4$C*H*$_3$), 3.05-3.13 (m, 1H, C*H*CH$_3$), 3.62 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.0 Hz, 1H, OCH_AH$_B$), 3.76 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.0 Hz, 1H, OCH$_A$$H_B$), 3.91 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.4 Hz, 1H, OCH_CH$_D$), 4.05 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.4 Hz, 1H, OCH$_C$$H_D$), 6.43-6.44 (m, 1H, =C$H_XH_Y$), 6.52-6.53 (m, 1H, =CH$_X$$H_Y$), 7.35 (d, ^3J(H-H) = 8.0 Hz, 2H, Ar-*H*), 7.78 (d, ^3J(H-H) = 8.0 Hz, 2H, Ar-*H*).

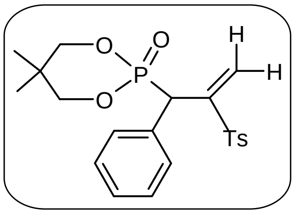
^{13}C NMR: δ 17.3 (d, *J*(P-C) = 5.1 Hz, CH*C*H$_3$), 21.2, 21.5 and 21.6 (2 *C*H$_3$ + $O_2SC_6H_4$*C*H$_3$), 29.0 (d, ^1J(P-C) = 135.4 Hz), 32.4 (d, *J*(P-C) = 6.5 Hz, *C*(CH$_3$)$_2$), 75.8 (d, *J*(P-C) = 6.5 Hz, O*C*H$_2$(A)), 75.9 (d, *J*(P-C) = 6.4 Hz, O*C*H$_2$(B)), 127.3 (d, *J*(P-C) = 6.3 Hz), 128.7, 129.9, 135.2, 144.9, 147.6 (d, *J*(P-C) = 4.9 Hz).

^{31}P NMR: δ 21.7.

LC-MS: *m/z* 360 [M+1]$^+$.

Anal. Calcd. for $C_{16}H_{23}O_5PS$: C, 53.62; H, 6.47. Found: C, 53.75; H, 6.41. This compound was crystallized from a mixture of ethyl acetate, hexane and traces of dichloromethane at 30 °C.

Compound 26



Yield: 0.106 g (63%; using 0.4 mmol of allene **6e**).

Mp: 188-192 °C (white solid).

IR (KBr): 2964, 1597, 1311, 1263, 1157, 1059, 833, 758 cm^{-1}.

^{1}H NMR: δ 0.86 and 1.05 (2 s, 6H, C(C*H*$_3$)$_2$), 2.37 (s, 3H, $O_2SC_6H_4C$*H*$_3$), 3.80-3.87 (m, 2H, OC*H*$_2$(A)), 3.96-4.02 (m, 2H, OC*H*$_2$(B)), 4.42 (d, ^{2}*J*(P-H) = 22.8 Hz, 1H, P(O)C*H*), 6.72 and 6.88 (2 s, 2H, =C*H*$_2$), 7.10-7.27 (m, 7H, Ar-*H*), 7.53 (d, ^{3}*J*(H-H)= 8.0 Hz, 2H, Ar-*H*).

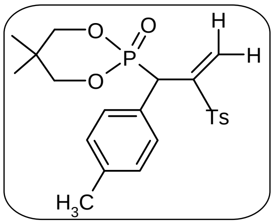
^{13}C NMR: δ 21.0, 21.5, 21.6 (-$SO_2C_6H_4$*C*H_3 + C(*C*H_3)$_2$), 32.5 (d, *J*(P-C) = 6.7 Hz, *C*Me$_2$), 41.4 (d, ^{1}*J*(P-C) = 131.6 Hz, P*C*H), 76.5, 76.6, 127.7 (d, *J*(P-C) = 2.8 Hz), 128.4, 128.5 (d, *J*(P-C) = 2.2 Hz), 128.8 (d, *J*(P-C) = 5.8 Hz), 129.0 (d, *J*(P-C) = 6.4 Hz), 129.5, 132.4 (d, *J*(P-C) = 7.5 Hz), 135.6, 144.4, 145.6.

^{31}P NMR: δ 15.1.

LC-MS: *m/z* 421$[M+1]^+$.

Anal. Calcd. for $C_{21}H_{25}O_5PS$: C, 59.99; H, 5.99. Found: C, 59.86; H, 5.41.

Compound 27



Yield: 0.226 g (66%; using 0.79 mmol of allene **6f**).

Mp: 156-158 °C (white solid).

IR (KBr): 3027, 2963, 1597, 1512, 1267, 1059, 771 cm^{-1}.

^{1}H NMR: δ 0.88 and 1.11 (2 s, 6H, C(C*H*$_3$)$_2$), 2.27 (s, 3H, C_6H_4C*H*$_3$), 2.37 (s, 3H, $O_2SC_6H_4$C*H*$_3$), 3.75-3.88 (m, 2H, OC*H*$_2$(B)), 3.95-4.02 (m, 2H, OC*H*$_2$(A)), 4.39 (d, ^{2}*J*(P-H) = 22.4 Hz, 1H, P(O)C*H*), 6.69-6.70 (m, 1H, =C*H*$_A$H$_B$), 6.87-7.16 (m, 7H, =CH$_A$*H*$_B$ + Ar-*H*), 7.55 (d, ^{3}*J*(H-H) = 8.4 Hz, 2H, Ar-*H*).

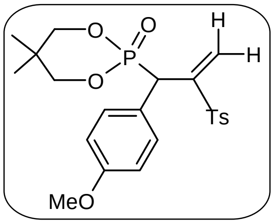
^{13}C NMR: δ 21.0, 21.5 and 21.6 (2 *C*H$_3$ + $O_2SC_6H_4$*C*H$_3$ + C_6H_4*C*H$_3$), 32.5 (d, *J*(P-C) = 6.8 Hz, *C*Me$_2$), 40.9 (d, ^{1}*J*(P-C) = 132.0 Hz, P*C*H), 76.5 (d, *J*(P-C) = 6.8 Hz, O*C*H$_2$(A)), 76.6 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(B)), 128.4, 128.6 (d, *J*(P-C) = 5.9 Hz), 128.8 (d, *J*(P-C) = 6.5 Hz), 129.2 (d, *J*(P-C) = 2.2 Hz), 129.3 (d, *J*(P-C) = 7.4 Hz), 129.5, 135.7, 137.6 (d, *J*(P-C) = 3.1 Hz), 144.4, 145.7.

^{31}P NMR: δ 15.3.

LC-MS: *m/z* 435[M+1]$^+$.

Anal. Calcd. for $C_{22}H_{27}O_5PS$: C, 60.82; H, 6.26. Found: C, 60.75; H, 6.21.

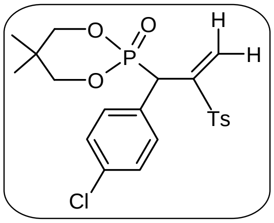
Compound 28



Yield:	0.15 g (67%; using 0.5 mmol of allene **6g**).
Mp:	144-146°C (white solid).
IR (KBr):	2955, 1615, 1512, 1308, 1269, 1059, 1012, 837, 774 cm^{-1}.
^{1}H NMR:	δ 0.88 and 1.10 (2 s, 6H, C(C*H*$_3$)$_2$), 2.37 (s, 3H, O$_2$SC$_6$H$_4$C*H*$_3$), 3.74-3.87 (m, 5H, OC*H*$_2$(A) + OC*H*$_3$), 4.00 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 12.4 Hz, 2H, OC*H*$_2$(B)), 4.38 (d, ^{2}*J*(P-H) = 22.8 Hz, 1H, P(O)C*H*), 6.66-6.69 (m, 3H, =C*H*$_A$H$_B$ + Ar-*H*), 6.85 (s, 1H, =CH$_A$*H*$_B$), 7.07-7.09 (m, 2H, Ar-*H*), 7.15 (d, ^{3}*J*(H-H) ~ 8.2 Hz, 2H, Ar-*H*), 7.55 (d, ^{3}*J*(H-H) ~ 8.2 Hz, 2H, Ar-*H*).
^{13}C NMR:	δ 21.0, 21.5 and 21.6 (2 *C*H$_3$ + SO$_2$C$_6$H$_4$*C*H$_3$), 32.5 (d, *J*(P-C) = 6.7 Hz, *C*Me$_2$), 40.5 (d, ^{1}*J*(P-C) = 132.9 Hz, P*C*H), 55.3 (O*C*H$_3$), 76.4 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(A)), 76.6 (d, *J*(P-C) = 6.9 Hz, O*C*H$_2$(B)), 124.2 (d, *J*(P-C) = 7.3 Hz), 128.4, 128.5 (d, *J*(P-C) = 5.8 Hz), 129.5, 130.1 (d, *J*(P-C) = 6.5 Hz), 133.9 (d, *J*(P-C) = 2.0 Hz), 135.7, 144.4, 145.9, 159.2 (d, *J*(P-C) = 2.7 Hz).
^{31}P NMR:	δ 15.4.
LC-MS:	*m/z* 451[M+1]$^+$.

Anal. Calcd. for $C_{22}H_{27}O_6PS$: C, 58.66; H, 6.04. Found: C, 58.71; H, 6.12.

Compound 29



Yield:	0.143 g (63%; using 0.5 mmol of allene **6h**).
Mp:	156-158 °C (white solid).
IR (KBr):	2922, 1725, 1603, 1491, 1265, 1156, 1057, 1009, 708 cm^{-1}.
^{1}H NMR:	δ 1.00 and 1.12 (2 s, 6H, C(C*H*$_3$)$_2$), 2.39 (s, 3H, O$_2$SC$_6$H$_4$C*H*$_3$), 3.83-3.90 (m, 2H, OC*H*$_2$(A)), 4.00-4.06 (m, 2H, OC*H*$_2$(B)), 4.41(d, ^{2}*J*(P-H) = 24.0

Hz, 1H, P(O)C*H*), 6.74 and 6.88 (2 s, 2H, =CH_A and =CH_B), 7.10-7.54 (m, 8H, Ar-*H*).

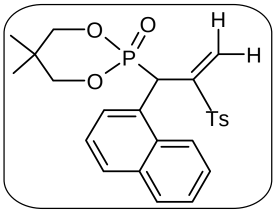
^{13}C NMR: δ 21.0, 21.5 ($O_2SC_6H_4CH_3$ + C(CH_3)$_2$)$_,$ 32.5 (d, *J*(P-C) = 6.7 Hz, *C*Me$_2$), 40.8 (d, ^1J(P-C) = 132.0 Hz, P*C*H), 76.5 (O*C*H$_2$(A)), 76.6 (O*C*H$_2$(B)), 128.4, 128.6 (d, *J*(P-C) = 2.2 Hz), 128.9 (d, *J*(P-C) = 5.7 Hz), 129.6, 130.4 (d, *J*(P-C) = 6.6 Hz), 131.0 (d, *J*(P-C) = 6.8 Hz), 133.9, 135.5, 144.8, 145.4.

^{31}P NMR: δ 14.6.

LC-MS: *m/z* 455 and 457 [M$^+$]

Anal. Calcd. for $C_{21}H_{24}ClO_5PS$: C, 55.45; H, 5.32. Found: C, 55.36; H, 5.38.

Compound 30



Yield: 0.22 g (47%; using 1.0 mmol of allene **6i**).

Mp: 114-116 °C (white solid).

IR (KBr): 3052, 2976, 1595 1455, 1273, 1123, 1059, 808, 666 cm^{-1}.

^{1}H NMR: δ 0.83 and 1.01 (2 s, 6H, C(CH_3)$_2$), 2.09 (s, 3H, $O_2SC_6H_4CH_3$), 3.74 (dd→t, ^3J(P-H) = ^2J(H-H) = 10.8 Hz, 2H, OCH_2(A)), 3.90 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.4 Hz, 1H, OCH_B), 4.01 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 11.8 Hz, 1H, OC$H_{B'}$), 5.41 (d, ^2J(P-H) = 24.0, Hz, 1H, P(O)C*H*), 6.66 (d, ^3J(H-H) = 8.4 Hz, 2H, Ar-*H*), 6.85 (s, 1H, =CH_AH$_B$), 7.06 (s, 1H, =CH$_A$$H_B$), 7.19-7.24 (m, 3H, Ar-*H*), 7.44-7.61 (m, 4H, Ar-*H*), 7.74 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*), 8.00 (d, ^3J(H-H) = 8.4 Hz, 1H, Ar-*H*).

^{13}C NMR: δ 21.1, 21.3 and 21.5 (C(*C*H$_3$)$_2$ + $O_2SC_6H_4CH_3$), 32.5 (d, *J*(P-C) = 6.8 Hz, *C*Me$_2$), 36.4 (d, ^1J(P-C) = 135.0 Hz, P*C*H), 76.3 (d, *J*(P-C) = 6.7 Hz, O*C*H$_2$(A)), 76.8 (d, *J*(P-C) = 7.0 Hz, O*C*H$_2$(B)), 122.6, 125.1 (d, *J*(P-C)

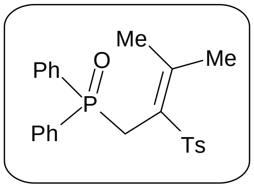
= 3.5 Hz), 125.6, 126.5, 127.7, 127.8 (d, *J*(P-C) = 5.8 Hz), 128.2 (d, *J*(P-C) = 8.7 Hz), 128.3 (d, *J*(P-C) = 3.3 Hz), 128.8, 128.9, 129.1 (d, *J*(P-C) = 5.7 Hz), 131.3 (d, *J*(P-C) = 6.4 Hz), 133.7 (d, *J*(P-C) = 1.5 Hz), 135.3, 143.8, 146.7.

^{31}P NMR: δ 15.5.

LC-MS: *m/z* 471[M+1]$^+$.

Anal. Calcd. for $C_{25}H_{27}O_5PS$: C, 63.82; H, 5.78. Found: C, 63.75; H, 5.71.

Compound 31



Yield: 0.332 g (78%; using 1.0 mmol of allene **8b**).

Mp: 188-190 °C (white solid).

IR (KBr): 3054, 1617, 1437, 1291, 1188, 1134, 816, 781 cm^{-1}.

^{1}H NMR: δ 1.93 and 2.04 (2 d, ^5J(P-H) ~ 4.0 Hz, 6H, C(CH_3)$_2$), 2.38 (s, 3H, $SO_2C_6H_4CH_3$), 3.88 (d, ^2J(P-H) = 12.0 Hz, 2H, P(O)CH_2), 7.17-7.19 (d, ^3J(H-H) = 8.0 Hz, 2H, Ar-*H*), 7.50-7.56 (m, 8H, Ar-*H*), 7.88-7.92 (m, 4H, Ar-*H*).

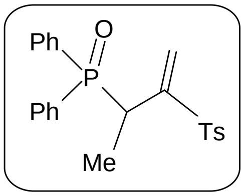
^{13}C NMR: δ 21.5 ($O_2SC_6H_4CH_3$), 23.1 and 26.0 (2 d, *J*(P-C) = 2.0 Hz, C(CH_3)$_2$), 32.5 (d, ^1J(P-C) = 53.4 Hz, CH_2), 126.9, 128.5 (d, *J*(P-C) = 9.4 Hz), 129.0 (d, *J*(P-C) = 7.6 Hz), 129.4, 131.3 (d, *J*(P-C) = 7.3 Hz), 131.9 (d, *J*(P-C) = 2.1 Hz), 132.9 (d, *J*(P-C) = 78.4 Hz), 139.8, 143.4, 153.7 (d, *J*(P-C) = 6.1 Hz).

^{31}P NMR: δ 28.7.

LC-MS: *m/z* 425 [M+1]$^+$.

Anal. Calcd. for $C_{24}H_{25}O_3PS$: C, 67.91; H, 5.94. Found: C, 67.85; H, 5.96.

Compound 32



Yield: 0.18 g (88%; using 0.5 mmol of allene **8c**).

Mp: 120-126 °C (white solid).

IR (KBr): 3063, 2924, 1595, 1439, 1300, 1263, 1157, 1080, 815 cm^{-1}.

^{1}H NMR: δ 1.22-1.28 (m, 3H, CHC*H*$_3$), 2.42 (s, 3H, SO$_2$C$_6$H$_4$C*H*$_3$), 3.49-3.52 (m, 1H, C*H*CH$_3$), 6.29 (s, 1H, = C*H$_A$*H$_B$), 6.73 (s, 1H, = CH$_A$*H$_B$*), 7.23-7.81 (m, 14H, Ar-*H*).

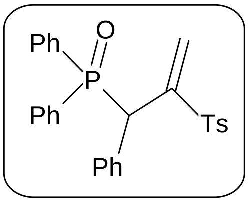
^{13}C NMR: δ 16.8 (d, *J*(P-C) = 2.8 Hz, CH*C*H$_3$), 21.6 (SO$_2$C$_6$H$_4$*C*H$_3$), 32.6 (d, ^{1}*J*(P-C) = 66.7 Hz, *C*H), 127.6 (d, *J*(P-C) = 5.7 Hz), 128.3, 128.4, 128.8 (d, *J*(P-C) = 11.5 Hz), 130.0, 130.4, 130.8 (d, *J*(P-C) = 8.7 Hz), 131.6$_0$ (d, *J*(P-C) = 9.0 Hz), 131.6$_3$ (d, *J*(P-C) = 2.7 Hz), 131.7 (d, ^{1}*J*(P-C) = 57.3 Hz), 131.9 (d, *J*(P-C) = 2.8 Hz), 135.4, 144.7, 148.7 (d, *J*(P-C) = 3.7 Hz).

^{31}P NMR: δ 33.1.

LC-MS: *m/z* 411 [M+1]$^{+}$.

Anal. Calcd. for C$_{23}$H$_{23}$O$_3$PS: C, 67.30; H, 5.65. Found: C, 67.42; H, 5.59.

Compound 33



Yield: 0.17 g (66%; using 0.5 mmol of allene **8e**).

Mp: 204-206 °C (white solid).

IR (KBr): 3061, 1595, 1437, 1312, 1154, 1078, 963 cm^{-1}.

^{1}H NMR: 2.25 (s, 3H, $O_2SC_6H_4CH_3$), 4.70 (d, ^2J(P-H) = 9.6 Hz 1H, PC*H*Ph), 6.56 (s, 1H, =CH_AH$_B$), 6.79-6.98 (m, 7H, Ar-*H*), 7.15 (s, 1H, =CH$_A$$H_B$), 7.19-7.35 (m, 7H, Ar-*H*), 7.52-7.58 (m, 3H, Ar-*H*), 7.95-8.00 (m, 2H, Ar-*H*).

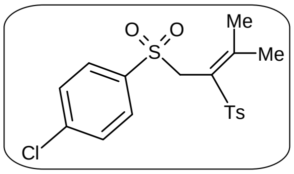
^{13}C NMR: δ 21.5 (-$O_2SC_6H_4CH_3$), 45.7 (d, ^1J(P-C) = 61.7 Hz, *C*H), 127.0, 127.8, 128.1, 128.2$_0$, 128.2$_4$, 128.9 (d, *J*(P-C) = 11.6 Hz), 129.3, 129.4, 129.8 (d, *J*(P-C) = 4.6 Hz), 130.3, 131.0, 131.1, 131.5 (d, *J*(P-C) = 8.7 Hz), 131.7, 132.2, 135.8, 144.2, 147.1.

^{31}P NMR: δ 32.0.

LC-MS: *m/z* 473 $[M+1]^+$.

Anal. Calcd. for $C_{28}H_{25}O_3PS$: C, 71.17; H, 5.33. Found: C, 71.25; H, 5.28.

Compound 34



Yield: 0.13 g (65%; using 0.5 mmol of allene **13c**).

Mp: 180-184 °C (white solid).

IR (KBr): 3005, 1620, 1582, 1396, 1300, 1084, 762 cm^{-1}.

^{1}H NMR: δ 2.07 and 2.16 (2 s, 6H, C=C($CH_3)_2$), 2.45 (s, 3H, $O_2SC_6H_4CH_3$), 4.58 (s, 2H, -O_2SCH_2), 7.32 (d, ^3J(H-H) = 8.4 Hz, 2H, Ar-*H*), 7.57-7.59 (m, 2H, Ar-*H*), 7.84 (d, ^3J(H-H) = 8.0 Hz, 2H, Ar-*H*), 7.94-7.96 (m, 2H, Ar-*H*).

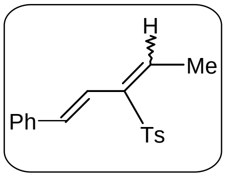
^{13}C NMR: δ 21.6, 23.5 and 26.0 ($C(CH_3)_2$ + -$O_2SC_6H_4CH_3$), 56.4 (O_2SCH_2), 127.4, 127.5, 129.6, 129.7, 130.1, 137.8, 139.2, 140.9, 144.1, 159.2.

LC-MS: *m/z* 400 $[M+1]^+$.

Anal. Calcd. for $C_{18}H_{19}ClO_4S_2$: C, 54.19; H, 4.80. Found: C, 54.36; H, 4.75.

3.53 Utility of tosylated compound 24 in HWE reaction- Synthesis of 1,3-butadiene derivative 35

To a stirred solution of NaH (0.025 g, 0.636 mmol) in dry THF (5 mL) at 0 °C, tosylated compound **24** (0.152 g, 0.424 mmol) was added and the reaction mixture stirred at 0°C to rt for 10 min. To this solution, benzaldehyde (0.045 g, 0.424 mmol) was added. The contents were stirred at rt for 12 h. Water (5 mL) was added and the aqueous layer thoroughly extracted with ether (3 x 15 mL). The combined organic layer was dried over anh. Na_2SO_4, filtered and concentrated to give the crude product that was subjected to column chromatography (hexane/ EtOAc 1:20) to afford the desired product **35**.



Yield:	0.04 g (32%), gummy solid.
IR (KBr):	3059, 2926, 2305, 1719, 1597, 1302, 814 cm^{-1}.
^{1}H NMR:	δ 2.05 (s, 3H, =C(C*H*$_3$)), 2.42 (s, 3H, $O_2SC_6H_4CH_3$), 6.68 (d, 1H, ^3J(H-H) = 16.4 Hz), 6.93 (d, 1H, ^3J(H-H) = 16.4 Hz), 7.15 (d, 1H, ^3J(H-H) = 7.2 Hz), 7.29-7.40 (m, 7H, Ar-*H*), 7.75-7.77 (m, 2H, Ar-*H*).
^{13}C NMR:	δ 14.8, 21.6, 116.7, 126.8, 127.9, 128.6, 128.7, 130.0, 136.3, 136.9, 137.2, 137.6, 140.5, 144.0.
LC-MS:	*m/z* 299 $[M+1]^+$.

Anal. Calcd. for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08. Found: C, 72.35; H, 6.13.

3.6 Base catalyzed reactions of allenylphosphonates with salicyl *N*-thiophosphinylimines-Synthesis of chromans 36 and 38-48

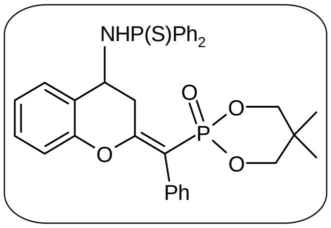
3.61 Standardization of reaction conditions leading to chroman 36 from the allene 6e and salicyl N-thiophosphinyl imine 14a

To a 25 mL RBF containing $(OCH_2CMe_2CH_2O)P(O)C(Ph)=C=CH_2$ (**6e**) (0.132 g, 0.50 mmol) and salicyl *N*-thiophosphinyl imine (**14a**) (0.186 g, 0.55 mmol), the solvent [DMSO, CH_3CN, THF, DMF or DCM; 5 mL] was added and the solution stirred at rt for 2-3 min. To this, base [PPh_3, DBU, K_2CO_3 or P(*n*-Bu)$_3$; 0.10 mmol] was added. The RBF was flushed with N_2 and sealed. The contents were heated at 40-80 ^{o}C for 12 h. After that, a small aliquot was checked by ^{31}P NMR. Other details are presented in Tables 3 in the Results and Discussion (Chapter 2).

3.62 Reaction of α-aryl substituted allenylphosphonates ($OCH_2CMe_2CH_2O$)P(O)C(Ar)=C=CH_2 (6e-i) and $Ph_2POC(Ph)=C=CH_2$ (8e) with salicyl N-thiophosphinyl imines 14a and 14b- Formation of chromans 36 and 38-48

To a 25 mL round-bottomed flask containing allene **6e-i** (0.2-0.5 mmol) and salicyl *N*-thiophosphinyl imine (**14a**) or (**14b**) (0.22-0.55 mmol), was added THF (0.1M with respect to allene, 2.5-5.0 mL). The contents were stirred at rt for 5 min. To this solution, P(*n*-Bu)$_3$ (0.04-0.1 mmol) was added and the round-bottomed flask was sealed after flushing three times with N_2. The reaction mixture was stirred at 60 ^{o}C for 12 h. After that, the solvent was removed by rotary evaporator and the residue subjected to column chromatography (hexane/ EtOAc; 1.5:1) to get the pure product. Compounds **36** and **38-48** were prepared by this procedure. Both *Z* and *E* isomers were formed in most cases. Details on the combined yield of *Z* and *E* isomers are given in Chapter 2 (Table 4) and below.

Compound (*E*)-36 (higher R$_f$)



Yield: 0.210 g (70%, *E*+*Z*); 0.051 g (*E*, isolated, 17%) (using 0.5 mmol of allene **6e**).

Mp: 226-232 ^{o}C.

IR (KBr): 3189, 1630, 1482, 1258, 1231, 1057, 835 cm^{-1}.

^{1}H NMR: δ 0.65 (s, 3H, C*H*$_3$), 0.98 (s, 3H, C*H*$_3$), 3.02-3.14 (m, 2H, CC*H*$_2$), 3.48 (dd→t, ^{3}J(P-H) = ^{2}J(H-H) = 12.2 Hz, 1H, OC*H*$_A$H$_B$), 3.62 (dd→t, ^{3}J(P-H) = ^{2}J(H-H) ~ 12.0 Hz, 1H, OCH$_A$*H*$_B$), 3.95-4.06 (m, 3H, N*H* + OC*H*$_2$), 4.73-4.80 (m, 1H, C*H*NH), 6.63 (d, ^{3}J(H-H) = 8.0 Hz, 1H, Ar-*H*), 6.84 (dd→t, ^{3}J(H-H) ~ 7.4 Hz, 1H, Ar-*H*), 7.05 (dd→t, ^{3}J(H-H) ~ 7.8 Hz, 1H, Ar-*H*), 7.27-7.41 (m, 8H, Ar-*H*), 7.51-7.55 (m, 4H, Ar-*H*), 7.92-7.97 (m, 2H, Ar-*H*), 8.14-8.19 (m, 2H, Ar-*H*).

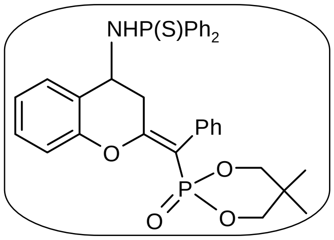
^{13}C NMR (125 MHz): δ 21.2, 21.7, 32.4 (d, *J*(P-C) = 6.3 Hz, *C*(CH$_3$)$_2$), 33.5 (dd, *J*(P-C) ~ 7.3 Hz, 1.6 Hz, *C*H$_2$), 45.4 (NH*C*H), 75.4 (d, *J*(P-C) = 5.9 Hz, O*C*H$_2$(A)), 75.5 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(B)), 109.3 (d, ^{1}J(P-C) = 195.6 Hz, P*C*=C), 116.4, 122.9, 124.5, 127.4 (d, *J*(P-C) = 1.6 Hz), 128.1, 128.3 (d, *J*(P-C) = 13.0 Hz), 128.7 (d, *J*(P-C) = 13.0 Hz), 129.5 (d, *J*(P-C) = 28.3 Hz), 130.7 (d, *J*(P-C) = 4.6 Hz), 131.5 (d, *J*(P-C) = 2.9 Hz), 131.7 (d, *J*(P-C) = 11.1 Hz), 131.8 (d, *J*(P-C) = 2.8 Hz), 132.0 (d, *J*(P-C) = 11.5 Hz), 133.9 (d, *J*(P-C) = 4.8 Hz), 134.0 (d, *J*(P-C) = 22.9 Hz), 134.8 (d, *J*(P-C) = 25.0 Hz), 151.3, 161.0, 161.1.

^{31}P NMR: δ 14.5 and 59.1

LC-MS: *m/z* 602 [M+1]$^+$.

Anal. Calcd. for $C_{33}H_{33}NO_4P_2S$: C, 65.88; H, 5.53; N, 2.33. Found: C, 65.76; H, 5.61; N, 2.30.

Compound (*Z*)-36 (lower R$_f$)



Yield: 0.210 g (70%, *E*+*Z*); 0.051 g (*Z*, isolated, 53%).

Mp: 188-190 °C.

IR (KBr): 3069, 2926, 1645, 1460, 1226, 1055, 826 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.82 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$), 2.78-2.88 (m, 2H, CC*H*$_2$), 3.11-3.15 (m, 1H, N*H*), 3.53-3.56 (m, 1H, OC*H*$_A$H$_B$), 3.75-4.01 (m, 3H, OCH$_A$*H*$_B$ + OC*H*$_2$), 4.70-4.77 (m, 1H, C*H*NH), 6.97-7.00 (m, 1H, Ar-*H*), 7.08 (d, ^{3}J(H-H) = 8.0 Hz, 1H, Ar-*H*), 7.24-7.48 (m, 13H, Ar *H*), 7.71-7.75 (m, 2H, Ar *H*), 7.82-7.86 (m, 2H, Ar *H*).

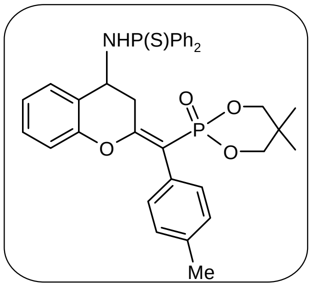
^{13}C NMR (125 MHz): δ 21.1, 22.0, 32.4 (d, *J*(P-C) = 6.0 Hz, *C*(CH$_3$)$_2$), 33.4 (dd, *J*(P-C) ~ 10.2 Hz, *J*(P-C) ~ 4.2 Hz,*C*H$_2$), 44.9 (NH*C*H), 76.0 (d, *J*(P-C) = 6.5 Hz, O*C*H$_2$(A)), 76.1 (d, ^{2}J(P-C) = 6.1 Hz, O*C*H$_2$(B)), 109.1 (d, ^{1}J(P-C) = 173.4 Hz, P*C*=C), 117.0, 123.2, 124.3 (d, *J*(P-C) = 4.5 Hz), 127.9, 128.4 (d, *J*(P-C) = 2.5 Hz), 128.5 (d, *J*(P-C) = 2.4 Hz), 128.7, 128.9, 129.7, 130.8 (d, *J*(P-C) = 4.8 Hz), 131.5 (d, *J*(P-C) = 4.3 Hz), 131.6 (d, *J*(P-C) = 4.4 Hz), 131.7 (d, *J*(P-C) = 2.8 Hz), 131.8 (d, *J*(P-C) = 2.8 Hz), 133.9, 134.0 (d, *J*(P-C) = 22.5 Hz), 134.8 (d, *J*(P-C = 28.0 Hz), 151.4, 160.2.

^{31}P NMR: δ 10.4 and 59.3.

LC-MS: *m/z* 602 [M+1]$^+$.

Anal. Calcd. for $C_{33}H_{33}NO_4P_2S$: C, 65.88; H, 5.53; N, 2.33. Found: C, 65.78; H, 5.49; N, 2.26.

Compound (*E*)-38 (higher R$_f$)



Yield: 0.231 g (75%, *E*+*Z*); 0.080 g (*E*, isolated, 26%) (using 0.5 mmol of allene **6f**).

Mp: 196-198 °C.

IR (KBr): 3239, 1626, 1572, 1437, 1240, 1107, 810 cm^{-1}.

^{1}H NMR: δ 0.68 (s, 3H, C*H*$_3$), 1.00 (s, 3H, C*H*$_3$), 2.39 (s, 3H, C$_6$H$_4$C*H*$_3$), 3.04-3.13 (m, 2H, CC*H*$_2$), 3.47 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) = 11.6 Hz, 1H, OC*H*$_A$H$_B$), 3.62 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 11.6 Hz, 1H, OCH$_A$*H*$_B$), 3.90-4.02 (m, 3H, OC*H*$_2$ + N*H*), 4.73-4.80 (m, 1H, C*H*NH), 6.66 (d, ^{3}*J*(H-H) = 8.4 Hz, 1H, Ar-*H*), 6.83 (dd→t, ^{3}*J*(H-H) = 7.6 Hz, 1H, Ar-*H*), 7.05 (dd→t, ^{3}*J*(H-H) ~ 7.0 Hz, 1H, Ar-*H*), 7.20-7.40 (m, 7H, Ar-*H*), 7.50-7.54 (m, 4H, Ar-*H*), 7.91-7.97 (m, 2H, Ar-*H*), 8.13-8.18 (m, 2H, Ar-*H*).

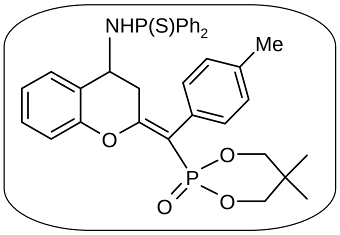
^{13}C NMR (125 MHz): δ 21.3, 21.4 (s, C$_6$H$_4$*C*H$_3$), 21.8, 32.4 (d, *J*(P-C) = 5.8 Hz, *C*(CH$_3$)$_2$), 33.6 (d, *J*(P-C) ~ 7.4 Hz, *C*H$_2$), 45.4 (s, NH*C*H), 75.5 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(A)), 75.6 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(B)), 109.2 (d, ^{1}*J*(P-C) = 192.9 Hz, P*C*=C), 116.5, 122.8, 124.5, 128.3 (d, *J*(P-C) = 13.0 Hz), 128.7 (d, *J*(P-C) = 13.3 Hz), 128.9, 129.5 (d, *J*(P-C) = 29.4 Hz), 130.5 (d, *J*(P-C) = 5.0 Hz), 130.6 (d, *J*(P-C) = 5.1 Hz), 131.5 (d, *J*(P-C) = 2.9 Hz), 131.7 (d, *J*(P-C) = 11.0 Hz), 131.8 (d, *J*(P-C) = 2.8 Hz), 132.0 (d, *J*(P-C) = 11.1 Hz), 134.1 (d, *J*(P-C) = 19.8 Hz), 134.9 (d, *J*(P-C) = 21.0 Hz), 137.0 (d, *J*(P-C) = 1.9 Hz), 151.4, 160.5, 160.7.

^{31}P NMR: δ 14.7 and 59.1.

LC-MS: *m/z* 616 [M+1]$^+$.

Anal. Calcd. for $C_{34}H_{35}NO_4P_2S$: C, 66.33; H, 5.73; N, 2.28. Found: C, 66.15; H, 5.81; N, 2.32.

Compound (*Z*)-38 (lower R$_f$)



Yield: 0.231 g (75%, *E*+*Z*); 0.151 g (*Z*, isolated, 49%).

Mp: 204-210 °C.

IR (KBr): 3214, 2920, 1626, 1597, 1455, 1238, 1059, 831 cm^{-1}.

^{1}H NMR: δ 0.81 (s, 3H, C*H*$_3$), 1.20 (s, 3H, C*H*$_3$), 2.44 (s, 3H, C$_6$H$_4$C*H*$_3$), 2.74-2.88 (m, 2H, CHC*H*$_2$), 3.11-3.14 (m, 1H, N*H*), 3.53-3.56 (m, 1H, OC*H*$_A$H$_B$), 3.73-4.03 (m, 3H, OC*H*$_2$ + OCH$_A$*H*$_B$), 4.72-4.77 (m, 1H, C*H*NH), 6.96-7.44 (m, 14H, Ar-*H*), 7.70-7.71 (m, 2H, Ar-*H*), 7.80-7.83 (m, 2H, Ar-*H*).

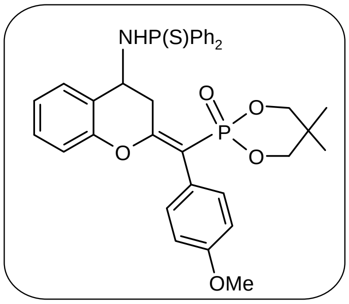
^{13}C NMR (125 MHz): δ 21.0, 21.3 (s, C$_6$H$_4$*C*H$_3$), 22.0, 32.3 (d, *J*(P-C) = 6.1 Hz, *C*(CH$_3$)$_2$), 33.5 (dd, ^{3}*J*(P-C) = 4.3 Hz, 10.3 Hz, *C*H$_2$), 44.9 (s, NH*C*H), 76.0 (d, *J*(P-C) = 7.5 Hz, O*C*H$_2$(A)), 76.1 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(B)), 108.8 (d, ^{1}*J*(P-C) = 172.3 Hz, P*C*=C), 116.9, 123.0, 124.3, 128.3 (d, *J*(P-C) = 2.6 Hz), 128.4 (d, *J*(P-C) = 2.9 Hz), 128.7, 129.4, 129.6, 130.5 (d, *J*(P-C) = 4.8 Hz), 130.7 (d, *J*(P-C) = 6.4 Hz), 131.4$_6$, 131.4$_9$, 131.6 (d, *J*(P-C) = 3.3 Hz), 131.7, 133.9 (d, *J*(P-C) = 32.3 Hz), 134.7 (d, *J*(P-C) = 35.5 Hz), 137.4, 151.4, 159.7.

^{31}P NMR: δ 10.7 and 59.3.

LC-MS: *m/z* 616 [M+1]$^+$.

Anal. Calcd. for $C_{34}H_{35}NO_4P_2S$: C, 66.33; H, 5.73; N, 2.28. Found: C, 66.48; H, 5.70; N, 2.21.

Compound (*E*)-39 (higher R$_f$)



Yield: 0.212 g (67%, *E*+*Z*); 0.049 g (*E*, isolated, 23%) (using 0.5 mmol of allene **6g**).

Mp: 180-184 °C.

IR (KBr): 3478, 3198, 1628, 1510, 1233, 1058, 833 cm^{-1}.

^{1}H NMR: δ 0.69 (s, 3H, C*H*$_3$), 1.00 (s, 3H, C*H*$_3$), 3.04-3.13 (m, 2H, CC*H*$_2$), 3.49 (dd→t, ^{3}J(P-H) = ^{2}J(H-H) = 11.6 Hz, 1H, OC*H*$_A$H$_B$), 3.63 (dd→t, ^{3}J(P-H) ~ ^{2}J(H-H) ~ 12.0 Hz, 1H, OCH$_A$*H*$_B$), 3.86 (s, 3H, C$_6$H$_4$OC*H*$_3$), 3.93-4.04 (m, 3H, OC*H*$_2$ + N*H*), 4.75-4.76 (m, 1H, C*H*NH), 6.66 (d, ^{3}J(H-H) = 8.0 Hz, 1H, Ar-*H*), 6.82-6.94 (m, 3H, Ar-*H*), 7.04-7.07 (m, 1H, Ar-*H*), 7.27-7.56 (m, 9H, Ar-*H*), 7.92-7.97 (m, 2H, Ar-*H*), 8.15-8.17 (m, 2H, Ar-*H*).

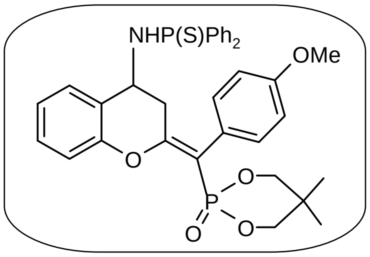
^{13}C NMR: δ 21.3, 21.7, 32.4 (d, *J*(P-C) = 5.8 Hz, *C*(CH$_3$)$_2$), 33.5 (d, *J*(P-C) ~ 6.0 Hz, *C*H$_2$), 45.4 (NH*C*H), 55.3 (O*C*H$_3$), 75.4 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(A)), 75.5 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(B)), 108.8 (d, ^{1}J(P-C) = 195.4 Hz, P*C*=C), 113.6, 116.4, 122.8, 124.5, (d, *J*(P-C) = 2.1 Hz), 125.8 (d, *J*(P-C) = 4.9 Hz), 128.3 (d, *J*(P-C) = 13.3 Hz), 128.5 (d, *J*(P-C) = 13.3 Hz), 128.7 (d, *J*(P-C) = 13.1 Hz), 129.5 (d, *J*(P-C) = 28.8 Hz), 131.3 (d, *J*(P-C) = 11.5 Hz), 131.5 (d, *J*(P-C) = 2.5 Hz), 131.7, 131.8, 132.0 (d, *J*(P-C) = 11.4 Hz), 134.1 (d, *J*(P-C) = 22.4 Hz), 134.9 (d, *J*(P-C) = 23.4 Hz), 151.4, 159.0, 160.7.

^{31}P NMR: δ 14.8 and 59.1.

LC-MS: *m/z* 632 [M+1]$^{+}$

Anal. Calcd. for $C_{34}H_{35}NO_5P_2S$: C, 64.65; H, 5.58; N, 2.22. Found: C, 64.53; H, 5.61; N, 2.27.

Compound (*Z*)-39 (lower R$_f$)



Yield: 0.212 g (67%, *E*+*Z*); 0.093 g (*Z*, isolated, 44%).

Mp: 184-188 °C.

IR (KBr): 3191, 2963, 1628, 1510, 1244, 1061, 772 cm^{-1}.

^{1}H NMR: δ 0.81 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 2.72-2.89 (m, 2H, CHCH_2), 3.13-3.17 (m, 1H, N*H*), 3.52-3.56 (m, 1H, OCH_AH$_B$), 3.77-4.04 (m, 6H, OCH$_A$$H_B$ + OCH_2 + OCH_3), 4.72-4.78 (m, 1H, C*H*NH), 6.91-7.08 (m, 4H, Ar-*H*), 7.21-7.44 (m, 10H, Ar-*H*), 7.70-7.85 (m, 4H, Ar *H*).

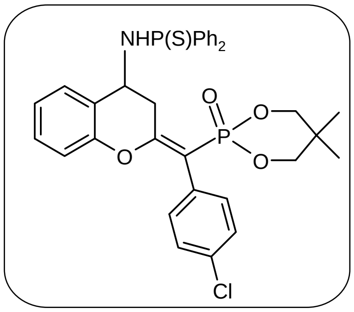
^{13}C NMR: δ 21.0, 22.0, 32.3 (d, *J*(P-C) = 5.6 Hz, *C*(CH$_3$)$_2$), 33.3 (~d, *J*(P-C) ~ 7.4 Hz, *C*H$_2$), 44.9 (NH*C*H), 55.3 (O*C*H$_3$), 76.0 (O*C*H$_2$), 108.5 (d, ^1J(P-C) = 173.1 Hz, P*C*=C), 114.1, 116.9, 123.0, 124.3, 125.8, 128.4, 128.5, 128.7, 129.6, 131.5, 131.6, 131.7, 131.8, 133.9 (d, *J*(P-C) = 32.1 Hz), 134.7 (d, *J*(P-C) = 32.1 Hz), 151.4, 159.2, 159.8.

^{31}P NMR: δ 10.8 and 59.3.

LC-MS: *m/z* 632 [M+1]$^+$

Anal. Calcd. for $C_{34}H_{35}NO_5P_2S$: C, 64.65; H, 5.58; N, 2.22. Found: C, 64.58; H, 5.51; N, 2.26.

Compound (*E*)-40 (higher R$_f$)



Yield: 0.097 g (76%, *E*+*Z*); 0.027 g (*E*, isolated, 21%) (using 0.2 mmol of allene **6h**).

Mp: 188-192 °C.

IR (KBr): 3181, 3058, 1630, 1597, 1485, 1088, 1006 cm^{-1}.

^{1}H NMR: δ 0.70 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 2.98-3.00 (m, 1H, CHCH_AH$_B$), 3.13-3.16 (m, 1H, CHCH$_A$$H_B$), 3.51 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 12.2 Hz, 1H, OCH_AH$_B$), 3.63 (dd→t, ^3J(P-H) = ^2J(H-

H) ~ 12.6 Hz, 1H, OCH_AH_B), 3.95-4.11 (m, 3H, OCH_2 + NH), 4.75-4.76 (m, 1H, CHNH), 6.64 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-H), 6.84-6.88 (m, 1H, Ar-H), 7.05-7.09 (m, 1H, Ar-H), 7.26-7.55 (m, 11H, Ar-H), 7.91-7.96 (m, 2H, Ar-H), 8.13-8.16 (m, 2H, Ar-H).

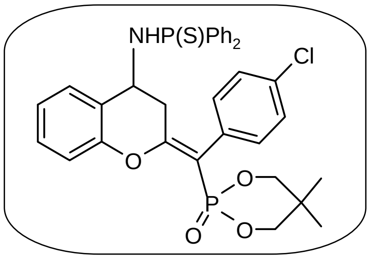
^{13}C NMR (125MHz): δ 21.4, 21.6, 32.4 (d, ^3J(P-C) = 5.9 Hz, $C(CH_3)_2$), 33.4 (d, J(P-C) = 7.3 Hz, CH_2), 45.3 (NHCH), 75.3 (d, J(P-C) = 6.1 Hz, OCH_2(A)), 75.4 (d, J(P-C) = 5.9 Hz, OCH_2(B)), 107.8 (d, ^1J(P-C) = 197.0 Hz, PC=C), 116.4, 123.1, 124.5 (d, J(P-C) = 2.8 Hz), 128.3, 128.4, 128.8 (d, J(P-C) = 13.1 Hz), 129.5 (d, J(P-C) = 4.3 Hz), 131.6 (d, J(P-C) = 2.6 Hz), 131.7 (d, J(P-C) = 17.5 Hz), 131.9 (d, J(P-C) = 2.3 Hz), 132.0 (d, J(P-C) = 11.4 Hz), 132.1 (d, J(P-C) = 4.6 Hz), 132.4 (d, J(P-C) = 5.1 Hz), 133.4 (d, J(P-C) = 2.1 Hz), 133.9 (d, J(P-C) = 24.0 Hz), 134.8 (d, J(P-C) = 24.8 Hz), 151.2, 161.6, 161.8.

^{31}P NMR: δ 14.4 and 59.2.

LC-MS: m/z 636 $[M]^+$ and 638 $[M]^+$.

Anal. Calcd. for $C_{33}H_{32}ClNO_4P_2S$: C, 62.31; H, 5.07; Cl; 5.57; N, 2.20. Found: C, 62.21; H, 5.15; N, 2.26.

Compound (*Z*)-40 (lower R_f)



Yield: 0.097 g (76%, *E*+*Z*); 0.070 g (*Z*, isolated, 55%).

Mp: 176-180 °C.

IR (KBr): 3202, 3058, 1630, 1483, 1242, 1059, 1009, 791 cm^{-1}.

^{1}H NMR: δ 0.83 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 2.76-2.77 (m, 2H, $CHCH_2$), 3.05-3.09 (m, 1H, NH), 3.53-3.58 (m, 1H, OCH_AH_B), 3.79-4.06 (m, 3H, OCH_AH_B + OCH_2), 4.71-4.76 (m, 1H, CHNH), 7.00-7.08 (m, 2H, Ar-*H*), 7.23-7.48 (m, 12H, Ar-*H*), 7.72-7.77 (m, 2H, Ar-*H*), 7.81-7.86 (m, 2H, Ar-*H*).

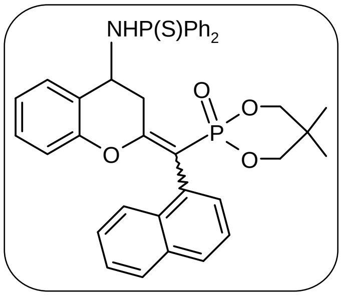
^{13}C NMR: δ 21.2, 22.0, 32.4 (d, *J*(P-C) = 6.5 Hz, *C*(CH_3)$_2$), 33.5 (dd, *J*(P-C) ~ 10.4 Hz, *J*(P-C) ~ 3.4 Hz, *C*H_2), 45.0 (NH*C*H), 76.0 (d, *J*(P-C) = 6.3 Hz, O*C*H_2(A)), 76.1 (d, *J*(P-C) =.6.1 Hz, O*C*H_2(B)), 107.9 (d, ^{1}*J*(P-C) = 174.9 Hz, P*C*=C), 117.1, 123.4, 124.4 (d, *J*(P-C) = 5.4 Hz), 128.5, 128.5_1, 128.5_7, 128.6, 129.0, 129.8, 131.5 (d, *J*(P-C) = 2.3 Hz), 131.6 (d, *J*(P-C) = 1.6 Hz), 131.9, 132.1 (d, *J*(P-C) = 4.8 Hz), 132.5 (d, *J*(P-C) = 6.6 Hz), 133.9 (d, *J*(P-C) = 16.0 Hz), 134.0, 134.7 (d, *J*(P-C) = 18.4 Hz), 151.4, 160.5.

^{31}P NMR: δ 10.1 and 59.3.

LC-MS: *m/z* 634 $[M-2]^+$ and 636 $[M]^+$.

Anal. Calcd. for $C_{33}H_{32}ClNO_4P_2S$: C, 62.31; H, 5.07; Cl; 5.57; N, 2.20. Found: C, 62.21; H, 5.15; N, 2.28.

Compound (*E/Z*)-41



Yield: 0.16 g (83%, *E*+*Z*) (using 0.3 mmol of allene **6i**).

Mp: 210-214 °C.

IR (KBr): 3212, 3058, 1628, 1601, 1453, 1289, 1244, 1060 cm^{-1}.

^{1}H NMR: (E/Z ~ 1:1) δ 0.70 (s, 3H, C*H*$_3$), 0.79 (s, 3H, C*H*$_3$) and 1.10 (s, 6H, C*H*$_3$), 2.51-2.66 (m, 4H), 3.30-3.50 (m, 4H), 3.68-3.76 (m, 2H), 3.93-4.14 (m, 4H), 4.61-4.68 (m, 2H), 6.95-7.00 (m, 4H, Ar-*H*), 7.16-7.82 (m, 37H, Ar-*H*), 8.34 (d, ^{3}*J*(H-H) = 8.4 Hz, 1H, Ar-*H*).

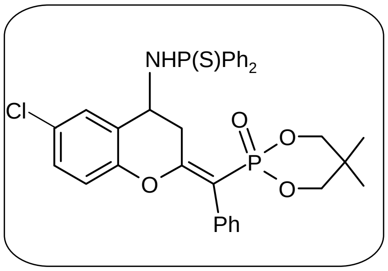
^{13}C NMR: (*E*+*Z*) δ 21.2, 21.3, 21.9, 32.4 (d, *J*(P-C) = 6.0 Hz, *C*(CH$_3$)$_2$), 32.5 (d, *J*(P-C) = 6.2 Hz, *C*(CH$_3$)$_2$), 33.5 (dd, *J*(P-C) ~ 10.2 Hz, *J*(P-C) ~ 5.4 Hz, *C*H$_2$), 33.8 (dd, *J*(P-C) ~ 10.7 Hz, *J*(P-C) ~ 4.2 Hz,*C*H$_2$), 44.3 (d, *J*(P-C) = 4.5 Hz, -NH*C*H), 44.7 (d, *J*(P-C) = 4.9 Hz, -NH*C*H), 75.8 (d, *J*(P-C) = 3.6 Hz, O*C*H$_2$(A)), 76.0 (d, *J*(P-C) =.6.0 Hz, O*C*H$_2$(B)), 76.3, 76.4, 106.4 (d, ^{1}*J*(P-C) = 176.0 Hz, P*C*=C), 107.5 (d, ^{1}*J*(P-C) = 177.0 Hz, P*C*=C), 117.0, 117.1, 123.9 (d, *J*(P-C) = 28.0 Hz), 125.0, 125.5 (d, *J*(P-C) = 13.0 Hz), 126.2, 126.4, 126.6, 126.9, 128.1, 128.3_0, 128.3_2, 128.4_0, 128.4_4, 128.7, 128.9, 129.0, 129.1, 129.2_0, 129.2_4, 129.3, 129.6, 129.7, 130.7, 130.8, 131.4, 131.5, 131.7, 131.9, 132.8, 133.3, 133.6, 133.8, 134.0, 134.3, 134.9 (d, *J*(P-C) = 19.0 Hz), 151.3, 151.4, 161.2, 161.3 [the spectrum was complicated due to the peaks for both the isomers].

^{31}P NMR: δ 10.1, 11.0 and 59.0, 59.9.

LC-MS: *m/z* 650 [M-1]$^+$.

Anal. Calcd. for $C_{37}H_{35}NO_4P_2S$: C, 68.19; H, 5.41; N, 2.15. Found: C, 68.32; H, 5.38; N, 2.21.

Compound (*E*)-42 (higher R$_f$)



Yield: 0.194 g (61%, *E*+*Z*); 0.083 g (*E*, isolated, 26%) (using 0.5 mmol of allene **6e**).

Mp: 260-264 °C.

IR (KBr): 3229, 1624, 1595, 1472, 1250, 1057, 837, 787 cm^{-1}.

^{1}H NMR (500MHz): δ 0.66 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$), 3.08-3.12 (m, 2H, (CHC*H*$_2$), 3.46-3.51 (m, 1H, OC*H*$_A$H$_B$), 3.62-3.67 (m, 1H, OCH$_A$*H*$_B$), 3.97-4.05 (m, 3H, N*H* + OC*H*$_2$), 4.73-4.75 (m, 1H C*H*NH), 6.57 (d, ^3J(H-H) = 9.0 Hz, 1H, Ar-*H*), 6.97-7.00 (m, 1H, Ar-*H*), 7.32-7.54 (m, 12H, Ar-*H*), 7.93-7.97 (m, 2H, Ar-*H*), 8.12-8.17 (m, 2H, Ar-*H*).

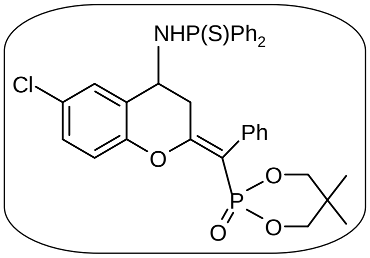
^{13}C NMR (125MHz): δ 21.2, 21.7, 32.3 (d, *J*(P-C) = 6.1 Hz, *C*(CH$_3$)$_2$), 33.0 (d, *J*(P-C) = 8.0 Hz, *C*H$_2$), 45.1 (NH*C*H), 75.5 (d, *J*(P-C) = 6.1 Hz, O*C*H$_2$(A)), 75.6 (d, *J*(P-C) = 6.1 Hz, O*C*H$_2$(B)), 110.0 (d, ^1J(P-C) = 194.6 Hz, P*C*=C), 117.8, 125.8, 127.6 (d, *J*(P-C) = 27.8 Hz), 128.2, 128.3 (d, *J*(P-C) = 13.3 Hz), 129.4 (d, *J*(P-C) = 17.5 Hz), 130.6 (d, *J*(P-C) = 4.6 Hz), 131.6, 131.7_0, 131.7_2, 131.8, 131.9, 133.6 (d, *J*(P-C) = 4.8 Hz), 133.8 (d, *J*(P-C) = 12.5 Hz), 134.6 (d, *J*(P-C) = 10.6 Hz), 149.9, 160.2, 160.4.

^{31}P NMR: δ 14.1 and 59.0.

LC-MS: *m/z* 636 and 638 [M]$^+$.

Anal. Calcd. for $C_{33}H_{32}ClNO_4P_2S$: C, 62.31; H, 5.07; Cl; 5.57; N, 2.20. Found: C, 62.21; H, 5.13; N, 2.27.

Compound (*Z*)-42 (lower R$_f$)



Yield: 0.194 g (61%, *E*+*Z*) 0.111 g (*Z*, isolated, 35%).

Mp: 236-238°C.

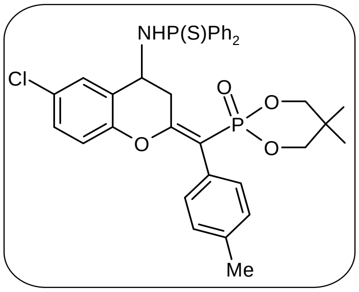
IR (KBr): 3223, 1628, 1476, 1248, 1105, 1060, 828 cm^{-1}.

^{1}H NMR: δ 0.80 (s, 3H, C*H*$_3$), 1.18 (s, 3H, C*H*$_3$), 2.74-2.85 (m, 2H, CHC*H*$_2$), 3.17-4.04 (m, 5H, OC*H*$_2$ + N*H*), 4.68-4.73 (m, 1H C*H*NH), 7.00-7.01 (m, 1H, Ar-*H*), 7.16-7.18 (m, 1H, Ar-*H*), 7.27-7.46 (m, 12H, Ar-*H*), 7.68-7.74 (m, 2H, Ar-*H*), 7.81-7.86 (m, 2H, Ar-*H*).

^{13}C NMR:	δ 21.1, 22.0, 32.4 (d, *J*(P-C) = 6.1 Hz, *C*(CH$_3$)$_2$), 33.1 (dd, *J*(P-C) ~ 10.1 Hz, *J*(P-C) ~ 4.2 Hz, *C*H$_2$), 44.7 (NH*C*H), 76.0$_5$ (d, *J* = 7.0 Hz, O*C*H$_2$(A)), 76.1$_0$ (d, *J* = 6.6 Hz, O*C*H$_2$(B)), 110.0 (d, ^{1}*J*(P-C) = 172.6 Hz, P*C*=C), 118.4, 125.8 (d, *J*(P-C) = 4.8 Hz), 128.0, 128.5 (d, *J*(P-C) = 1.5 Hz), 128.6 (d, *J*(P-C) = 1.8 Hz), 128.8, 129.6, 130.7 (d, *J*(P-C) = 4.8 Hz), 131.4, 131.5, 131.6, 131.7, 131.8 (d, *J*(P-C) = 2.9 Hz), 132.0 (d, *J*(P-C) = 3.0 Hz), 133.6$_8$ (d, *J*(P-C) = 6.1 Hz), 133.6$_9$ (d, *J*(P-C) = 57.8 Hz), 134.5 (d, *J*(P-C) = 54.1 Hz), 150.0, 159.4.
^{31}P NMR:	δ 10.0 and 59.5.
LC-MS:	*m/z* 636 and 638 [M]$^+$.

Anal. Calcd. for $C_{33}H_{32}ClNO_4P_2S$: C, 62.31; H, 5.07; Cl; 5.57; N, 2.20. Found: C, 62.28; H, 5.11; N, 2.15.

Compound (*E*)-43 (higher R$_f$)



Yield:	0.201 g (62%, *E*+*Z*); 0.055 g (*E*, isolated, 17%) (using 0.5 mmol of allene **6f**).
Mp:	216-220 °C.
IR (KBr):	3169, 1624, 1597, 1474, 1250, 1101, 716 cm^{-1}.
^{1}H NMR:	δ 0.68 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$), 2.39 (s, 3H, C$_6$H$_4$C*H*$_3$), 3.05-3.12 (m, 2H, CHC*H*$_2$), 3.46 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 11.4 Hz, 1H, OC*H*$_A$H$_B$), 3.63 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 11.4 Hz, 1H, OCH$_A$*H*$_B$), 3.90-4.04 (m, 3H, OC*H*$_2$ + N*H*), 4.74-4.75 (m, 1H, C*H*NH), 6.57 (d, 1H, ^{3}*J*(H-H) = 8.8 Hz, Ar-*H*), 6.95-6.98

(m,1H, Ar-*H*), 7.18-7.51 (m, 11H, Ar-*H*), 7.90-7.96 (m, 2H, Ar-*H*), 8.10-8.14 (m, 2H, Ar-*H*).

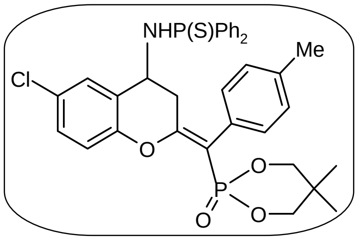
^{13}C NMR (125 MHz): δ 21.2, 21.3 (s, $C_6H_4CH_3$), 21.7, 32.3 (d, *J*(P-C) = 6.0 Hz, *C*$(CH_3)_2$), 33.1 (d, *J*(P-C) ~ 6.1 Hz, *C*H_2), 45.1 (NH*C*H), 75.5 (d, *J*(P-C) = 6.0 Hz, O*C*H_2(A)), 75.6 (d, ^3J(P-C) = 6.1 Hz, O*C*H_2(B)), 109.8 (d, ^1J(P-C) = 193.1 Hz, P*C*=C), 117.7, 125.9, 127.6, 128.2 (d, *J*(P-C) = 13.1 Hz), 128.7 (d, *J*(P-C) = 13.1 Hz), 128.9, 129.3 (d, *J*(P-C) = 17.3 Hz), 130.2_6 (d, *J*(P-C) = 4.6 Hz), 130.3_2, 131.6 (d, *J*(P-C) = 2.1 Hz), 131.7_0, 131.7_4, 131.8, 133.8 (d, *J*(P-C) = 17.5 Hz), 134.6 (d, *J*(P-C) = 15.9 Hz), 137.1, 149.9, 159.7.

^{31}P NMR: δ 14.3 and 59.0.

LC-MS: *m/z* 650 and 652 $[M]^+$

Anal. Calcd. for $C_{34}H_{34}ClNO_4P_2S$: C, 62.82; H, 5.27; Cl; 5.45; N, 2.15. Found: C, 62.75; H, 5.15; N, 2.21.

Compound (*Z*)-43 (lower R_f)



Yield: 0.201 g (62%, *E*+*Z*); 0.146 g (*Z*, isolated, 45%).

Mp: 230-234 °C.

IR (KBr): 3208, 2963, 1630, 1597, 1474, 1254, 1061, 720 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.80 (s, 3H, C*H*$_3$), 1.19 (s, 3H, C*H*$_3$), 2.44 (s, 3H, $C_6H_4CH_3$), 2.72-2.87 (m, 2H, CHC*H*$_2$), 3.26-3.30 (m, 5H, OC*H*$_2$ + N*H*), 4.69-4.75 (m, 1H, C*H*NH), 6.98-7.00 (m, 1H, Ar-*H*), 7.14-7.53 (m, 12H, Ar-*H*), 7.67-7.73 (m, 2H, Ar *H*), 7.80-7.85 (m, 2H, Ar *H*).

^{13}C NMR (125 MHz): δ 21.0, 21.4, 22.0, 32.4 (d, *J*(P-C) = 6.1 Hz, *C*$(CH_3)_2$), 33.0 (d, *J*(P-C) = 14.4 Hz, *C*H_2), 44.7 (NH*C*H), 76.1 (O*C*H_2(A)), 76.2

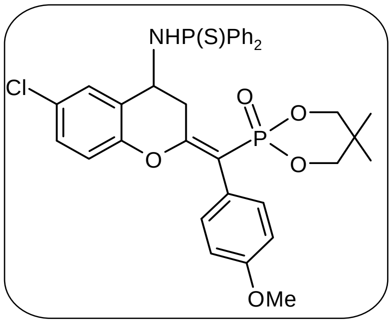
(O*C*H$_2$(B)), 109.9 (d, ^1J(P-C) = 171.1 Hz, P*C*=C), 118.4, 125.7 (d, *J*(P-C) = 4.4 Hz), 128.0, 128.5 (d, *J*(P-C) = 1.3 Hz), 128.6, 128.7, 129.5, 129.6, 130.5 (d, *J*(P-C) = 4.9 Hz), 130.6, 131.5 (d, *J*(P-C) = 11.5 Hz), 131.7 (d, *J*(P-C) = 11.1 Hz), 131.8 (d, *J*(P-C) = 2.9 Hz), 132.0 (d, *J*(P-C) = 2.9 Hz), 133.8 (d, *J*(P-C) = 67.5 Hz), 134.6 (d, *J*(P-C) = 68.5 Hz), 137.9, 150.1, 159.2.

^{31}P NMR: δ 10.3 and 59.5.

LC-MS: *m/z* 650 and 652 $[M]^+$.

Anal. Calcd. for $C_{34}H_{34}ClNO_4P_2S$: C, 62.82; H, 5.27; Cl; 5.45; N, 2.15. Found: C, 62.71; H, 5.35; N, 2.19.

Compound (*E*)-44 (higher R$_f$)



Yield: 0.190 g (57%, *E*+*Z*); 0.080 g (*E*, isolated, 24%) (using 0.5 mmol of allene **6g**).

Mp: 208-210 °C.

IR (KBr): 3229, 2481, 1624, 1596, 1474, 1246, 1057, 839 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.69 (s, 3H, C*H*$_3$), 1.00 (s, 3H, C*H*$_3$), 3.08-3.23 (m, 2H, (CHC*H*$_2$), 3.47 (dd→t, ^3J(P-H) ~ ^2J(H-H) ~ 12.5 Hz, 1H, OC*H*$_A$H$_B$), 3.64 (dd→t, ^3J(P-H) ~ ^2J(H-H) ~ 12.5 Hz, 1H, OCH$_A$*H*$_B$), 3.85 (s, 3H, OC*H*$_3$), 3.91-4.03 (m, 3H, OC*H*$_2$ + N*H*), 4.73-4.76 (m, 1H, C*H*NH), 6.59 (d, ^3J(H-H) = 5.0 Hz, 1H, Ar-*H*), 6.92-6.99 (m, 3H, Ar-*H*), 7.25-7.52 (m, 9H, Ar *H*), 7.92-7.96 (m, 2H, Ar *H*), 8.10-8.15 (m, 2H, Ar-*H*).

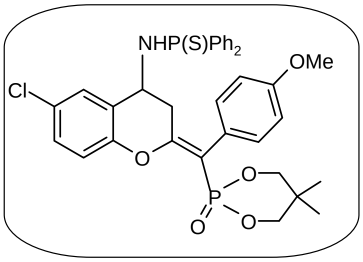
^{13}C NMR (125 MHz): δ 21.1, 22.0, 32.4 (d, *J*(P-C) = 6.3 Hz, *C*(CH$_3$)$_2$), 33.0 (d, *J*(P-C) ~ 10.0 Hz, *C*H$_2$), 44.7 (NH*C*H), 55.4 (C$_6$H$_4$O*C*H$_3$), 76.1_0 (O*C*H$_2$(A)), 76.1_3 (O*C*H$_2$(B)), 109.3 (d, ^{1}*J*(P-C) = 172.5 Hz, P*C*=C), 114.2, 118.3, 125.6 (d, *J*(P-C) = 6.3 Hz), 125.8 (d, *J*(P-C) = 5.0 Hz), 127.9, 128.5, 128.6, 129.6, 131.4, 131.5, 131.6, 131.7_0, 131.7_4, 131.8, 131.9, 133.8 (d, *J*(P-C) = 13.7 Hz), 134.6 (d, *J*(P-C) = 12.5 Hz), 150.0, 159.3.

^{31}P NMR: δ 14.3 and 59.0.

LC-MS: *m/z* 664 [M-2]$^+$ and 666 [M]$^+$.

Anal. Calcd. for $C_{34}H_{34}ClNO_5P_2S$: C, 61.31; H, 5.14; Cl; 5.32; N, 2.10. Found: C, 61.25; H, 5.19; N, 2.18.

Compound (*Z*)-44 (lower R$_f$)



Yield: 0.190 g (57%, *E*+*Z*); 0.110 g (*Z*, isolated, 33%).

Mp: 228-232 °C.

IR (KBr): 3235, 1632, 1601, 1439, 1057, 1009, 756 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.81 (s, 3H, C*H*$_3$), 1.19 (s, 3H, C*H*$_3$), 2.74-2.86 (m, 2H, CHC*H*$_2$), 3.22-3.26 (m, 1H, N*H*), 3.53 (dd, ^{3}*J*(P-H) = 12.5 Hz, ^{2}*J*(H-H) = 7.5 Hz, 1H, OC*H*$_A$H$_B$), 3.74-4.02 (m, 6H, OCH$_A$*H*$_B$ + OC*H*$_2$ + C$_6$H$_4$OC*H*$_3$), 4.70-4.75 (m, 1H, C*H*NH), 6.92-7.00 (m, 3H, Ar-*H*), 7.15-7.49 (m, 10H, Ar-*H*), 7.71-7.76 (m, 2H, Ar-*H*), 7.82-7.86 (m, 2H, Ar-*H*).

^{13}C NMR (125 MHz): δ 21.2, 21.7, 32.3 (d, *J*(P-C) = 5.9 Hz, *C*(CH$_3$)$_2$), 33.1 (d, *J*(P-C) ~ 6.9 Hz, *C*H$_2$)), 45.2 (NH*C*H), 55.3 (O*C*H$_3$), 75.5 (d, *J*(P-C) = 6.1 Hz, O*C*H$_2$(A)), 75.6 (d, *J*(P-C) = 6.3 Hz, O*C*H$_2$(B)), 109.4 (d, ^{1}*J*(P-C) = 193.9 Hz, P*C*=C), 113.6, 117.7, 125.5 (d, *J*(P-C) = 5.1

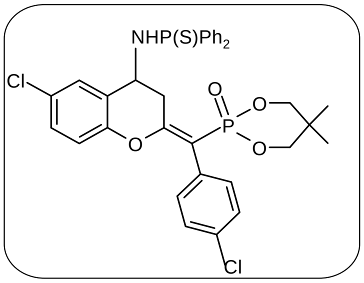
Hz), 125.9 (d, *J*(P-C) = 1.9 Hz), 127.6, 128.2 (d, *J*(P-C) = 12.9 Hz), 128.7 (d, *J*(P-C) = 12.9 Hz), 129.3 (d, *J*(P-C) = 16.6 Hz), 131.6$_0$, 131.6$_3$, 131.6$_7$, 131.8, 131.9, 133.8 (d, *J*(P-C) = 14.1 Hz), 134.6 (d, *J*(P-C) = 12.5 Hz), 149.9, 158.9, 159.9, 160.2.

^{31}P NMR: δ 10.3 and 59.4.

LC-MS: *m/z* 666 and 668 [M]$^+$.

Anal. Calcd. for $C_{34}H_{34}ClNO_5P_2S$: C, 61.31; H, 5.14; Cl; 5.32; N, 2.10. Found: C, 61.35; H, 5.09; N, 2.18.

Compound (*E*)-45 (higher R$_f$)



Yield: 0.208 g (62%, *E*+*Z*); 0.057 g (*E*, isolated, 17%) (using 0.5 mmol of allene **6h**).

Mp: 186-190 ^{o}C.

IR (KBr): 3200, 1628, 1474, 1250, 1059, 789 cm^{-1}.

^{1}H NMR: δ 0.70 (s, 3H, C*H*$_3$), 0.96 (s, 3H, C*H*$_3$), 3.06-3.14 (m, 2H, CHC*H*$_2$), 3.50 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 12.7 Hz, 1H, OC*H*$_A$H$_B$), 3.64 (dd→t, ^{3}*J*(P-H) = ^{2}*J*(H-H) ~ 12.7 Hz, 1H, OCH$_A$*H*$_B$), 3.95-4.12 (m, 3H, OC*H*$_2$ + N*H*), 4.70-4.77 (m, 1H, C*H*NH), 6.56 (d, ^{3}*J*(H-H) = 8.8 Hz, 1H, Ar-*H*), 6.98-7.00 (m, 1H, Ar-*H*), 7.26-7.52 (m, 11H, Ar-*H*), 7.90-7.96 (m, 2H, Ar-*H*), 8.08-8.14 (m, 2H, Ar-*H*).

^{13}C NMR: δ 21.4, 21.6, 32.4 (d, *J*(P-C) = 5.6 Hz, *C*(CH$_3$)$_2$), 33.0 (dd→d, *J*(P-C) ~ 7.2 Hz, *C*H$_2$)), 45.0 (NH*C*H), 75.3 (d, *J*(P-C) = 5.9 Hz, O*C*H$_2$(A)), 75.5 (d, *J*(P-C) = 6.1 Hz, O*C*H$_2$(B)), 108.4 (d, ^{1}*J*(P-C) = 196.3 Hz, P*C*=C), 117.7, 125.9, 128.0, 128.3, 128.4, 128.8 (d, *J*(P-C) = 13.0 Hz), 129.4 (d, *J*(P-C) = 3.8 Hz), 131.7, 131.8,

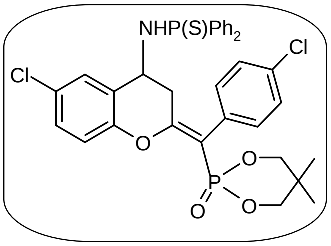
131.9_0, 131.9_4, 132.0, 132.1, 133.5 (d, *J*(P-C) = 9.7 Hz), 134.6 (d, *J*(P-C) = 7.4 Hz), 149.7, 155.9, 160.9, 161.2.

^{31}P NMR: δ 14.0 and 59.2.

LC-MS: *m/z* 670, 672 and 674 $[M]^+$.

Anal. Calcd. for $C_{33}H_{31}Cl_2NO_4P_2S$: C, 59.11; H, 4.66; N, 2.09. Found: C, 59.23; H, 4.61; N, 2.15.

Compound (*Z*)-45 (lower R_f)



Yield: 0.208 g (62%, *E*+*Z*); 0.151 g (*Z*, isolated, 45%).

Mp: 232-236 °C.

IR (KBr): 3187, 3058, 1628, 1474, 1248, 1059, 791 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.84 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 2.75-2.81 (m, 2H, CHCH_2), 3.12-3.16 (m, 1H, N*H*), 3.53-3.56 (m, 1H, OCH_AH$_B$), 3.82-4.06 (m, 3H, OCH$_A$$H_B$ + OCH_2), 4.69-4.76 (m, 1H, C*H*NH), 7.01 (d, ^{3}*J*(H-H) = 9.0 Hz, 1H, Ar-*H*), 7.19-7.22 (m, 3H, Ar-*H*), 7.35-7.52 (m, 9H, Ar *H*), 7.74-7.78 (m, 2H, Ar *H*), 7.84-7.88 (m, 2H, Ar *H*).

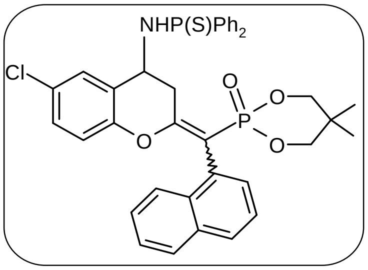
^{13}C NMR (125 MHz): δ 21.2, 21.9, 32.4 (d, *J*(P-C) = 6.3 Hz, *C*(CH$_3$)$_2$), 33.1 (dd, *J*(P-C) ~ 10.4 Hz, *J*(P-C) ~ 3.8 Hz,*C*H$_2$), 44.8 (s, NH*C*H), 76.0 (d, *J*(P-C) = 6.4 Hz, O*C*H$_2$(A)), 76.1 (d, *J*(P-C) =.6.0 Hz, O*C*H$_2$(B)), 108.7 (d, ^{1}*J*(P-C) = 174.6 Hz, P*C*=C), 118.4, 126.0 (d, *J*(P-C) = 5.4 Hz), 128.3, 128.6 (d, *J*(P-C) = 6.1 Hz), 128.7 (d, *J*(P-C) = 5.6 Hz), 129.0, 129.7, 131.5 (d, *J*(P-C) = 11.1 Hz), 131.6 (d, *J*(P-C) = 11.4 Hz), 132.0 (d, *J*(P-C) = 3.5 Hz), 132.1 (d, *J*(P-C) = 2.9 Hz), 132.2 (d, *J*(P-C) = 6.3 Hz), 133.5, 133.9, 134.1 (d, *J*(P-C) = 2.0 Hz), 134.3, 134.7, 150.0, 159.9.

^{31}P NMR: δ 9.8 and 59.5.

LC-MS: *m/z* 670, 672 and 674 $[M]^+$.

Anal. Calcd. for $C_{33}H_{31}Cl_2NO_4P_2S$: C, 59.11; H, 4.66; N, 2.09. Found: C, 59.25; H, 4.56; N, 2.15.

Compound (*E/Z*)-46



Yield: 0.27 g (78%, *E*+*Z*; using 0.5 mmol of allene **6i**).

Mp: 240-244 °C.

IR (KBr): 3198, 2963, 1628, 1472, 1258, 1057, 806 cm^{-1}.

^{1}H NMR (500MHz): (E/Z = ~1:1). Major isomer: δ 0.67 (s, 3H, C*H*$_3$), 0.71 (s, 3H, C*H*$_3$), 2.23-2.60 (m, 2H, CHC*H*$_2$), 3.06-4.06 (m, 5H, OC*H*$_2$(A) + OC*H*$_2$(B) + N*H*), 4.59 (br m, 1H, C*H*NH), 7.03-7.95 (m, 19H, Ar-*H*), 8.24-8.26 (m, 1H, Ar-*H*). Minor isomer: δ 1.07 (s, 6H, 2 C*H*$_3$); remaining peaks were merged with peaks due to the major isomer.

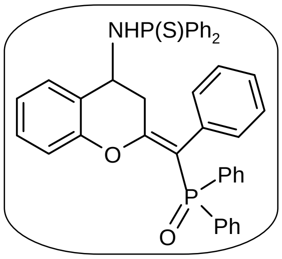
^{13}C NMR (125 MHz): δ 21.1, 21.2, 21.8_7, 21.8_8, 32.4 (d, *J*(P-C) = 6.3 Hz, *C*(CH$_3$)$_2$) and 32.5 (d, *J*(P-C) = 6.3 Hz, *C*(CH$_3$)$_2$), 33.2 (dd, *J*(P-C) ~ 10.1 Hz, *J*(P-C) ~ 5.6 Hz,*C*H$_2$) and 33.4 (dd, *J*(P-C) ~ 10.7 Hz, *J*(P-C) ~ 4.7 Hz,*C*H$_2$), 44.2 (NH*C*H) and 44.5 (NH*C*H), 75.8_1 (d, *J*(P-C) = 5.9 Hz, O*C*H$_2$(A)), 75.8_3 (d, *J*(P-C) =.6.0 Hz, O*C*H$_2$(B)), 76.0 (d, *J*(P-C) = 6.1 Hz, O*C*H$_2$(A)), 76.4 (d, *J*(P-C) = 6.5 Hz, O*C*H$_2$(B)), 107.3 (d, ^{1}*J*(P-C) = 176.3 Hz, P*C*=C) and 108.3 (d, ^{1}*J*(P-C) = 176.8 Hz, P*C*=C), 118.4_1, 118.4_3, 124.5, 125.3, 125.4, 125.5, 125.6, 126.2 (d, *J*(P-C) = 16.6 Hz), 126.6, 126.9, 127.0, 128.1, 128.2, 128.3, 128.4_0 128.4_1, 128.4, 128.5, 128.9, 129.0, 129.1_0, 129.1_1, 129.2_0, 129.2_3, 129.6_5, 129.6_7, 130.5 (d, *J*(P-C) = 5.6 Hz), 131.4 (d, *J*(P-C) = 11.1 Hz), 131.5$_5$, 131.5$_7$, 131.6$_2$, 131.6$_4$, 131.7$_1$, 131.7$_3$, 131.9, 132.6 (d, *J*(P-C) = 4.8 Hz), 133.1, 133.3, 133.4 (d, *J*(P-C) = 2.5 Hz), 133.5, 133.9, 134.0 (d, *J*(P-C) = 5.5 Hz), 134.1, 134.3, 134.8, 149.9, 150.0, 160.5, 160.6 [the spectrum was complicated due to the peaks for both the isomers].

^{31}P NMR: δ 9.3, 10.2 and 59.3, 60.2.

LC-MS: *m/z* 686 and 688 $[M]^+$.

Anal. Calcd. for $C_{37}H_{34}ClNO_4P_2S$: C, 64.77; H, 4.99; N, 2.04. Found: C, 64.85; H, 4.91; N, 2.12.

Compound (*Z*)-47 (lower R$_f$)



Yield: 0.134 g (41%; using 0.5 mmol of allene **8e**).

Mp: 248-250 °C.

IR (KBr): 3187, 3058, 1628, 1474, 1248, 1059, 791 cm^{-1}.

^{1}H NMR: δ 2.65-2.70 (br d, ^3J(H-H) ~ 12.0 Hz, 1H, CHCH_A), 2.85-2.90 (dd, ^3J(H-H) ~ 14.8 Hz, ^4J(P-H) = 4.1 Hz, 1H, CHCH_B), 3.35-3.39 (dd, ^3J(H-H) ~ 6.4 Hz, ^4J(P-H) ~ 6.8 Hz, 1H, N*H*), 4.66-4.72 (m, 1H, C*H*NH), 6.14 (d, ^3J(H-H) = 7.6 Hz, 1H, Ar-*H*), 6.83-6.85 (m, 1H, Ar-*H*), 7.01-7.18 (m, 1H, Ar *H*), 7.23-7.46 (m, 18H, Ar-*H*), 7.68-7.85 (m, 8H, Ar *H*).

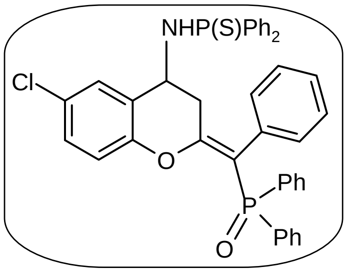
^{13}C NMR: δ 33.5 (dd→t, *J*(P-C) ~ *J*(P-C) ~ 5.5 Hz, *C*H$_2$), 44.8 (s, NH*C*H), 115.1 (d, ^1J(P-C) = 95.6 Hz, P*C*=C), 116.1, 122.9, 124.3 (d, *J*(P-C) = 4.1 Hz), 127.4, 128.0, 128.1, 128.2, 128.3$_0$, 128.3$_1$, 128.3$_4$, 128.4, 128.5, 128.8, 129.3, 130.9, 131.0$_2$, 131.0$_6$, 131.0$_9$, 131.1$_1$, 131.1$_4$, 131.1$_8$, 131.2$_2$, 131.4$_3$, 131.4$_4$, 131.4$_5$, 131.5, 131.6, 131.7, 132.6, 133.7, 133.8, 133.9, 134.2, 134.3, 134.6, 134.8, 134.9, 135.6, 150.6, 158.1 [the spectrum was complicated].

^{31}P NMR δ 24.7 and 59.2.

LC-MS: *m/z* 654 $[M+1]^+$.

Anal. Calcd. for $C_{40}H_{33}NO_2P_2S$: C, 73.49; H, 5.09; N, 2.14. Found: C, 73.38; H, 5.15; N, 2.19

Compound (*Z*)-48 (lower R_f)



Yield: 0.107 g (31%; using 0.5 mmol of allene **8e**).

Mp: 190-194 ^{o}C.

IR (KBr): 3113, 3058, 1630, 1474, 1265, 1165, 926 cm^{-1}.

^{1}H NMR: (500 MHz): δ 2.65-2.70 (m, 1H, CHC*H*$_A$), 2.87-2.91 (m, 1H, CHC*H*$_B$), 3.66-3.71 (m, 1H, N*H*), 4.66-4.73 (m, 1H, C*H*NH), 6.08 (d, ^{3}J(H-H) = 8.8 Hz, 1H, Ar-*H*), 7.16-7.48 (m, 19H, Ar-*H*), 7.64-7.86 (m, 8H, Ar-*H*).

^{13}C NMR (125 MHz): δ 33.3 (dd→t, *J*(P-C) ~ *J*(P-C) ~ 6.1 Hz, *C*H$_2$), 44.5 (NH*C*H), 115.8 (d, ^{1}J(P-C) = 95.1 Hz, P*C*=C), 117.5, 125.7_5, 125.7_9, 127.5, 127.7, 128.0, 128.1, 128.2_6, 128.3_0, 128.3_8, 128.4_3, 128.5, 128.6, 129.2, 130.8, 130.9, 131.0, 131.1, 131.2, 131.4, 131.4_7, 131.5_1, 131.6, 131.8, 132.3, 133.4, 133.9, 134.0, 134.1, 134.4, 134.5, 134.9, 135.4, 149.2, 157.8 [the spectrum was complicated].

^{31}P NMR δ 24.7 and 59.3.

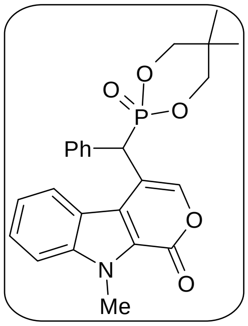
LC-MS: *m/z* 688 and 690 $[M]^+$.

Anal. Calcd. for $C_{40}H_{32}ClNO_2P_2S$: C, 69.81; H, 4.69; N, 2.04. Found: C, 69.73; H, 4.61; N, 2.08.

3.7 Palladium catalyzed annulation of indole-2-carboxylic acid derivatives with allenes to lead to compounds 49-62- General procedure

In an oven dried 25 mL round-bottomed flask, Pd(OAc)$_2$ (5.0 mol%), P(*o*-tol)$_3$ (15 mol %), 3-iodo-1-methylindole-2-carboxylic acid **15a** or **15b** (0.55 mmol), CsF (or K$_2$CO$_3$) (1.0 mmol) and DMF (5.0 mL) were added and the mixture was kept stirring at rt for 5 min. After that, allene (0.5 mmol) was added. The RBF was flushed with N$_2$ and sealed. Then the contents were heated at 80 ^{o}C with stirring for 10-14 h. After the completion of the reaction (TLC), the mixture was cooled to rt, diluted with ethyl acetate (30 mL), washed with brine (3x10 mL), dried over anh. Na$_2$SO$_4$, filtered, and the solvent removed by rotary evaporator. The crude products were purified by column chromatography (hexane/ EtOAc; 1:1.5) to get the pure products in 54-97 % yield Compounds **49-62** were prepared by this method.

Compound 49



Yield: 0.158 g (94%; using 0.5 mmol of allene **6e**).

Mp: 222-224 ^{o}C.

IR (KBr): 2965, 1696, 1476, 1262, 1020, 874, 799 cm^{-1}.

^{1}H NMR: δ 0.79 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$), 3.68-3.77 (m, 2H, OC*H*$_2$(A)), 4.23-4.28 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 5.16 (d, 1H, ^{2}*J*(P-H) = 26.8 Hz, P(O)C*H*), 7.18-7.58 (m, 8H, Ar-*H*), 7.90 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*), 8.02 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*).

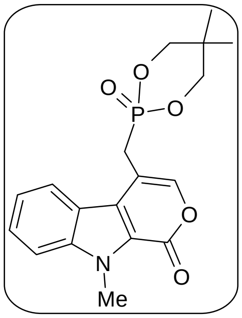
^{13}C NMR: δ 21.4, 21.5, 31.5 (N*C*H$_3$), 32.7 (d, *J*(P-C) = 6.5 Hz, *C*(CH$_3$)$_2$), 43.3 (d, ^{1}*J*(P-C) = 136.6 Hz, P*C*H), 75.9 (d, *J*(P-C) = 6.8 Hz, O*C*H$_2$(A)), 76.0 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(B)), 110.9, 112.8 (d, *J*(P-C) = 3.3 Hz), 120.3, 121.3, 122.2, 122.6, 123.5 (d, *J*(P-C) = 14.5 Hz), 127.5, 128.1 (d, *J*(P-C) = 3.3 Hz), 128.9 (d, *J*(P-C) = 2.8 Hz), 129.7 (d, *J*(P-C) = 5.8 Hz), 133.8 (d, *J*(P-C) = 7.7 Hz), 141.1, 143.0 (d, *J*(P-C) = 7.3 Hz), 157.0.

^{31}P NMR: δ 18.8.

LC-MS: *m/z* 438 $[M+1]^+$.

Anal. Calcd. for $C_{24}H_{24}NO_5P$: C, 65.90; H, 5.53; N, 3.20. Found: C, 65.82; H, 5.46; N, 3.28.

Compound 50



Yield: 0.13 g [74%; using 0.5 mmol of allene **6a** without P(*o*-tol)$_3$].

Mp: 216-218 °C.

IR (KBr): 3081, 2971, 1705, 1607, 1476, 1267, 1065, 735 cm^{-1}

^{1}H NMR: δ 0.89 (s, 3H, C*H*$_3$), 0.93(s, 3H, C*H*$_3$), 3.51 (d, ^{2}*J*(P-H) = 20.4 Hz, 2H, P(O)C*H*$_2$), 3.67 (dd, ^{3}*J*(P-H) = 16.6 Hz, ^{2}*J*(H-H) ~ 11.0 Hz, 2H, OC*H*$_2$(A)), 4.20-4.23 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 7.28-7.33 (m, 2H, Ar-*H*), 7.48-7.56 (m, 2H, Ar-*H*), 8.12 (d, ^{3}*J*(H-H) = 8.4 Hz, 1H, Ar-*H*).

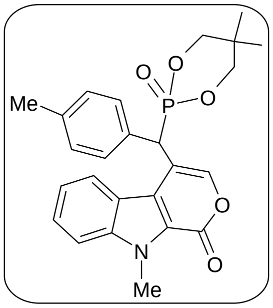
^{13}C NMR: δ 21.3, 21.6, 25.6 (d, ^{1}*J*(P-C) = 141.0 Hz, P*C*H$_2$), 31.4 (N*C*H$_3$), 32.6 (d, *J*(P-C) = 6.0 Hz, *C*(CH$_3$)$_2$), 75.1_0 (O*C*H$_2$(A)), 75.1_4 (O*C*H$_2$(B)), 108.5 (d, *J*(P-C) = 11.0 Hz), 110.7, 120.9, 121.4_0, 121.4_5, 123.1, 123.8 (d, *J*(P-C) = 4.0 Hz), 127.8, 141.2, 141.6 (d, *J*(P-C) = 11.0 Hz), 157.0.

^{31}P NMR: δ 21.3.

LC-MS: *m/z* 361 $[M]^+$.

Anal. Calcd. for $C_{18}H_{20}NO_5P$: C, 59.83; H, 5.58; N, 3.88. Found: C, 59.76; H, 5.65; N, 3.81.

Compound 51



Yield: 0.052 g (77%; using 0.15 mmol of allene **6f**).

Mp: 216-218 °C.

IR (KBr): 2967, 1711, 1512, 1474, 1277, 1061, 831 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.85 (s, 3H, C*H*$_3$), 1.00 (s, 3H, C*H*$_3$), 2.30 (s, 3H, C_6H_4C*H*$_3$), 3.67-3.77 (m, 2H, OC*H*$_2$(A)), 4.23-4.27 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 5.12 (d, 1H, ^{2}*J*(P-H) = 26.5 Hz, P(O)C*H*), 7.16-7.23 (m, 3H, Ar-*H*), 7.43-7.51 (m, 4H, Ar-*H*), 7.92 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*), 8.02 (s, 1H, Ar-*H*).

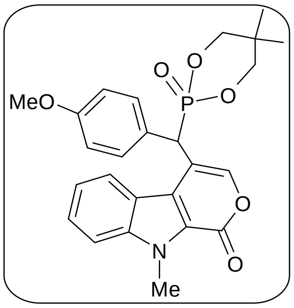
^{13}C NMR (125 MHz): δ 21.1, 21.5 (C*C*H$_3$ + C_6H_4*C*H$_3$), 31.5 (N*C*H$_3$), 32.7 (d, *J*(P-C) = 6.2 Hz, *C*(CH$_3$)$_2$), 42.8 (d, ^{1}*J*(P-C) = 137.0 Hz, P*C*H), 75.9 (d, *J*(P-C) = 6.5 Hz, O*C*H$_2$(A)), 76.0 (d, *J*(P-C) = 6.8 Hz, O*C*H$_2$(B)), 110.9, 113.0 (d, *J*(P-C) = 2.9 Hz), 120.4, 121.3, 122.3, 122.7, 123.6 (d, *J*(P-C) = 14.4 Hz), 127.4, 129.6_0 (d, *J*(P-C) = 6.0 Hz), 129.6_4 (d, *J*(P-C) = 2.6 Hz), 130.6 (d, *J*(P-C) = 7.6 Hz), 137.9 (d, *J*(P-C) = 3.4 Hz), 141.1, 143.0 (d, *J*(P-C) = 7.3 Hz), 157.0.

^{31}P NMR: δ 18.9.

LC-MS: *m/z* 451 $[M]^+$.

Anal. Calcd. for $C_{25}H_{26}NO_5P$: C, 66.51; H, 5.80; N, 3.10. Found: C, 66.45; H, 5.85; N, 3.18.

Compound 52



Yield: 0.20 g (85%; using 0.5 mmol of allene **6g**).

Mp: 230-232 °C.

IR (KBr): 3058, 2955, 1719, 1613, 1510, 1246, 1051, 735 cm^{-1}.

^{1}H NMR (500 MHz): δ 0.85 (s, 3H, C*H*$_3$), 1.00 (s, 3H, C*H*$_3$), 3.67-3.79 (m, 5H, OC*H*$_2$(A) + C_6H_4OC*H*$_3$), 4.23-4.28 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 5.10 (d, 1H, ^2J(P-H) = 33.0 Hz, P(O)C*H*), 6.87-6.89 (m, 2H, Ar-*H*), 7.19-7.23 (m, 1H, Ar-*H*), 7.44-7.51 (m, 4H, Ar-*H*), 7.89 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*), 8.02 (s, 1H, Ar-*H*).

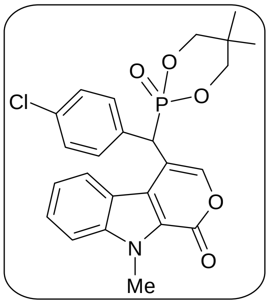
^{13}C NMR (125 MHz): δ 21.5 (C(*C*H$_3$)$_2$), 31.5 (N*C*H$_3$), 32.7 (d, *J*(P-C) = 6.4 Hz, *C*(CH$_3$)$_2$), 42.3 (d, ^1J(P-C) = 137.6 Hz, P*C*H), 55.3 (C_6H_4O*C*H$_3$), 75.8 (d, *J*(P-C) = 6.8 Hz, O*C*H$_2$(A)), 75.9 (d, *J*(P-C) = 6.7 Hz, O*C*H$_2$(B)), 110.9, 133.0 (d, *J*(P-C) = 2.7 Hz), 114.3 (d, *J*(P-C) = 2.7 Hz), 120.3, 121.3, 122.2, 122.7, 123.5 (d, *J*(P-C) = 14.5 Hz), 125.4 (d, *J*(P-C) = 14.5 Hz), 127.4, 130.8 (d, *J*(P-C) = 5.7 Hz), 141.1, 142.8 (d, *J*(P-C) = 7.1 Hz), 157.0, 159.4 (d, *J*(P-C) = 3.3 Hz).

^{31}P NMR: δ 19.1.

LC-MS: *m/z* 467 $[M]^+$.

Anal. Calcd. for $C_{25}H_{26}NO_6P$: C, 64.24; H, 5.61; N, 3.00. Found: C, 64.41; H, 5.56; N, 3.07.

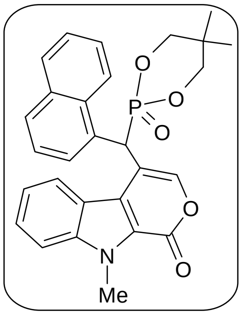
Compound 53



Yield:	0.16 g (68%; using 0.5 mmol of allene **6h**).
Mp:	212-216 °C.
IR (KBr):	2957, 1715, 1617, 1489, 1339, 1285, 1057, 785 cm^{-1}.
^{1}H NMR:	δ 0.87 (s, 3H, C*H*$_3$), 0.98 (s, 3H, C*H*$_3$), 3.70-3.82 (m, 2H, OC*H*$_2$(A)), 4.23-4.32 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 5.12 (d, 1H, ^{2}*J*(P-H) = 26.8 Hz, P(O)C*H*), 7.19-7.23 (m, 1H, Ar-*H*), 7.32-7.34 (m, 2H, Ar-*H*), 7.46-7.52 (m, 4H, Ar-*H*), 7.82 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*), 8.01 (s, 1H, Ar-*H*).
^{13}C NMR:	δ 21.4, 21.6, 31.5 (N*C*H$_3$), 32.8 (d, *J*(P-C) = 5.9 Hz, *C*(CH$_3$)$_2$), 42.5 (d, ^{1}*J*(P-C) = 137.1 Hz, P*C*H), 75.7 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(A)), 75.8 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(B)), 111.0, 112.4, 120.2, 121.4, 122.2, 122.3, 123.1 (d, *J*(P-C) = 14.1 Hz), 127.6, 129.1 (d, *J*(P-C) = 2.7 Hz), 131.0 (d, *J*(P-C) = 5.8 Hz), 132.4 (d, *J*(P-C) = 7.4 Hz), 134.1 (d, *J*(P-C) = 4.2 Hz), 141.1, 143.1 (d, *J*(P-C) = 7.1 Hz), 156.8.
^{31}P NMR:	δ 18.6.
LC-MS:	*m/z* 471 and 473 [M]$^{+}$.

Anal. Calcd. for $C_{24}H_{23}ClNO_5P$: C, 61.09; H, 4.91; N, 2.97. Found: C, 61.22; H, 4.98; N, 2.91.

Compound54



Yield: 0.197 g (81%; using 0.5 mmol of allene **6i**).

Mp: 278-280 ^{o}C.

IR (KBr): 3104, 1725, 1609, 1470, 1238, 1061, 743 cm^{-1}.

^{1}H NMR: δ 0.73 (s, 3H, C*H*$_3$), 0.91 (s, 3H, C*H*$_3$), 3.37-3.57 (m, 2H, OC*H*$_2$(A)), 4.15-4.21 (m, 5H, NC*H*$_3$ + OC*H*$_2$(B)), 6.02 (d, 1H, ^{2}*J*(P-H) = 26.0 Hz, P(O)C*H*), 7.05-7.09 (m, 1H, Ar-*H*), 7.45-7.56 (m, 5H, Ar-*H*), 7.74-8.00 (m, 5H, Ar-*H*), 8.18 (d, ^{3}*J*(H-H) = 7.6 Hz, 1H, Ar-*H*).

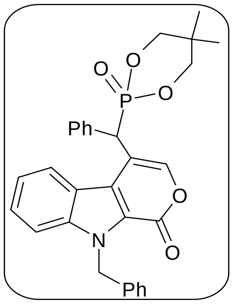
^{13}C NMR: δ 21.3 (C(*C*H$_3$)$_2$), 31.4 (N*C*H$_3$), 32.5 (d, *J*(P-C) = 6.5 Hz, *C*(CH$_3$)$_2$), 39.3 (d, ^{1}*J*(P-C) = 139.9 Hz, P*C*H), 75.6 (d, *J*(P-C) = 3.0 Hz, O*C*H$_2$(A)), 75.7 (d, *J*(P-C) = 2.9 Hz, O*C*H$_2$(B)), 110.8, 113.6 (d, *J*(P-C) = 5.6 Hz), 120.5, 121.2, 121.8, 122.8, 123.2, 123.5 (d, *J*(P-C) = 10.1 Hz), 125.4 (d, *J*(P-C) = 2.6 Hz), 125.9, 126.8, 127.4, 127.8 (d, *J*(P-C) = 6.4 Hz), 129.0 (d, *J*(P-C) = 2.2 Hz), 129.3, 130.2 (d, *J*(P-C) = 4.9 Hz), 131.6 (d, *J*(P-C) = 8.5 Hz), 134.3, 141.0, 144.1 (d, *J*(P-C) = 7.6 Hz), 156.8.

^{31}P NMR: δ 20.1.

LC-MS: *m/z* 487 [M]$^{+}$.

Anal. Calcd. for $C_{28}H_{26}NO_5P$: C, 68.99; H, 5.38; N, 2.87. Found: C, 68.79; H, 5.31; N, 2.95.

Compound 55



Yield: 0.162 g (79%; using 0.4 mmol of allene **6e**).

Mp: 224-228 ^{o}C.

IR (KBr): 3058, 2971, 1717, 1613, 1462, 1277, 1059, 741 cm^{-1}.

^{1}H NMR (500MHz): δ 0.79 (s, 3H, C*H*$_3$), 0.99 (s, 3H, C*H*$_3$), 3.68-3.77 (m, 2H, OC*H*$_2$(A)), 4.24-4.28 (m, 2H, OC*H*$_2$(B)), 5.19 (d, 1H, ^{2}*J*(P-H) = 27.0 Hz, P(O)C*H*), 5.90 (d, ^{2}*J*(H-H) = 16.0 Hz, 1H, C*H*$_A$H$_B$C$_6$H$_5$), 6.04 (d, ^{2}*J*(H-H) = 16.0 Hz, 1H, CH$_A$*H*$_B$C$_6$H$_5$), 7.18-7.27 (m, 7H, Ar-*H*), 7.36-7.44 (m, 4H, Ar-*H*), 7.58-7.59 (m, 2H, Ar-*H*), 7.93 (d, ^{3}*J*(H-H) = 8.5 Hz, 1H, Ar-*H*), 8.07 (s, 1H, Ar-*H*).

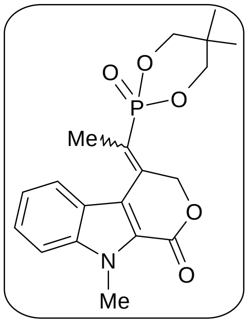
^{13}C NMR (125MHz): δ 21.4, 21.5, 32.7 (d, *J*(P-C) = 6.4 Hz, *C*(CH$_3$)$_2$), 43.4 (d, ^{1}*J*(P-C) = 136.5 Hz, P*C*H), 48.1 (N*C*H$_2$C$_6$H$_5$), 75.9 (d, *J*(P-C) = 6.8 Hz, O*C*H$_2$(A)), 76.0 (d, *J*(P-C) = 6.6 Hz, O*C*H$_2$(B)), 111.7, 112.8 (d, *J*(P-C) = 3.3 Hz), 120.8, 121.5, 121.9, 122.7, 124.1 (d, *J*(P-C) = 14.0 Hz), 127.1, 127.6 (d, *J*(P-C) = 3.1 Hz), 128.1 (d, *J*(P-C) = 3.1 Hz), 128.8, 128.9 (d, *J*(P-C) = 2.6 Hz), 129.8_0, 129.8_1, 129.8 (d, *J*(P-C) = 5.9 Hz), 133.8 (d, *J*(P-C) = 7.5 Hz), 137.3, 140.7, 143.4 (d, *J*(P-C) = 7.3 Hz), 156.7.

^{31}P NMR: δ 18.7.

LC-MS: *m/z* 513 [M]$^{+}$.

Anal. Calcd. for $C_{30}H_{28}NO_5P$: C, 70.17; H, 5.50; N, 2.73. Found: C, 70.08; H, 5.56; N, 2.81.

Compound 56



Yield: 0.156 g (84%; using 0.5 mmol of allene **6j**).

Mp: 140-146 ^{o}C.

IR (KBr): 2924, 1715, 1609, 1507, 1252, 1055, 785 cm^{-1}.

^{1}H NMR (500 MHz): δ 1.01 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 2.34 (d, ^{3}J(P-H) = 15.0 Hz, 3H, C=CCH_3), 3.88 (dd, ^{3}J(P-H) ~ 17.0 Hz, ^{2}J(H-H) ~ 11.0 Hz, 2H, OCH_2(A)), 4.14 (s, 3H, NCH_3), 4.41 (dd, ^{2}J(H-H) ~ 11.0 Hz, ^{3}J(P-H) ~ 6.0 Hz, 2H, OCH_2(B)), 5.55 (s, 2H, C=CCH_2), 7.28-7.47 (m, 3H, Ar-*H*), 7.66 (d, ^{3}J(H-H) = 8.5 Hz, 1H, Ar-*H*).

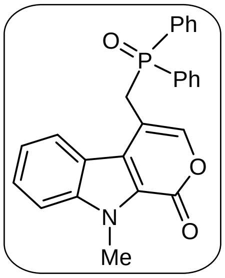
^{13}C NMR (125 MHz): δ 20.0 (d, *J*(P-C) = 8.4 Hz, C=C*C*H$_3$), 21.5, 22.2, 31.3 (N*C*H$_3$), 32.7 (d, *J*(P-C) = 5.5 Hz, *C*(CH$_3$)$_2$), 71.6 (d, *J*(P-C) = 7.6 Hz, C=C*C*H$_2$), 74.8 (d, *J*(P-C) = 5.9 Hz, O*C*H$_2$(A)), 77.3 (O*C*H$_2$(B)), 120.2, 120.4, 122.5 (d, ^{1}J(P-C) = 180.0 Hz, P*C*=C), 121.9, 122.2, 123.7, 124.1, 126.2, 139.7, 140.0 (d, *J*(P-C) = 15.5 Hz), 160.0.

^{31}P NMR: δ 15.9.

LC-MS: *m/z* 375 [M]$^{+}$.

Anal. Calcd. for $C_{19}H_{22}NO_5P$: C, 60.80; H, 5.91; N, 3.73. Found: C, 60.91; H, 5.88; N, 3.65.

Compound 57



Yield: 0.19 g [92%; using 0.5 mmol of allene **8a** without P(*o*-tol)$_3$].

Mp: 248-252 ^{o}C.

IR (KBr): 2948, 1707, 1435, 1331, 1183, 1030, 847, 735 cm^{-1}.

^{1}H NMR (500MHz): δ 3.90 (d, ^{2}*J*(P-H) = 12.5 Hz, 2H, PC*H*$_2$), 4.16 (s, 3H, NC*H*$_3$), 7.07 (d, ^{3}*J*(H-H) = 4.0 Hz, 1H, Ar-*H*), 7.21-7.24 (m, 1H, Ar-*H*), 7.42-7.55 (m, 8H, C=C*H* + Ar-*H*), 7.78-7.82 (m, 4H, Ar-H), 8.05 (d, ^{3}*J*(H-H) = 8.5 Hz, 1H, Ar-*H*).

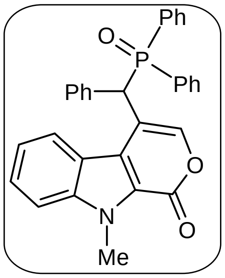
^{13}C NMR (125MHz): δ 30.0 (d, ^{1}*J*(P-C) = 67.8 Hz, P*C*H$_2$), 31.3 (N*C*H$_3$), 108.6 (d, *J*(P-C) = 8.1 Hz), 110.7, 121.0, 121.2, 121.6, 122.9, 124.2 (d, *J*(P-C) = 4.5 Hz), 127.5, 128.8 (d, *J*(P-C) = 11.8 Hz), 131.1 (d, *J*(P-C) = 9.1 Hz), 131.7, 132.2 (d, *J*(P-C) = 2.3 Hz), 132.4, 141.1, 141.7 (d, *J*(P-C) = 8.0 Hz).

^{31}P NMR: δ 29.1.

LC-MS: *m/z* 413 [M]$^+$.

Anal. Calcd. for $C_{25}H_{20}NO_3P$: C, 72.63; H, 4.88; N, 3.39. Found: C, 72.81; H, 4.83; N, 3.32.

Compound 58



Yield: 0.133g (54%; using 0.5 mmol of allene **8e**).

Mp: 288-292 ^{o}C.

IR (KBr): 3056, 1701, 1599, 1476, 1206, 1036, 739, 511 cm^{-1}.

^{1}H NMR (500 MHz): δ 4.20 (s, 3H, NC*H*$_3$), 5.32 (d, ^{2}J(P-H) = 11.0 Hz, 1H, PC*H*), 7.17-7.18 (m, 3H, Ar-*H* + C=C*H*), 7.25-7.29 (m, 2H, Ar-*H*), 7.36-7.53 (m, 11H, Ar-*H*), 7.83-7.87 (m, 2H, Ar-*H*), 8.06 (d, ^{3}J(H-H) = 8.5 Hz, 1H, Ar-*H*), 8.48 (s, 1H, Ar-*H*).

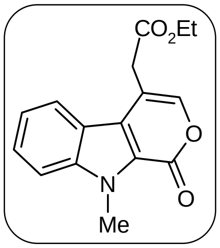
^{13}C NMR (125 MHz): δ 31.5 (s, N*C*H$_3$), 45.5 (d, ^{1}J(P-C) = 64.1 Hz), 111.1, 114.9 (d, *J*(P-C) = 3.5 Hz), 120.5, 121.4, 122.3$_0$, 122.3$_1$, 123.4 (d, *J*(P-C) = 10.1 Hz), 127.5, 127.6 (d, *J*(P-C) = 2.6 Hz), 128.3, 128.4, 129.0 (d, *J*(P-C) = 11.3 Hz), 130.3 (d, *J*(P-C) = 4.6 Hz), 131.2 (d, *J*(P-C) = 8.4 Hz), 131.4 (d, *J*(P-C) = 9.0 Hz), 131.9 (d, *J*(P-C) = 2.8 Hz), 132.0 (d, *J*(P-C) = 2.5 Hz), 132.2 (d, ^{1}J(P-C) = 57.1 Hz), 132.6, 133.1 (d, *J*(P-C) = 5.8 Hz), 141.1, 143.8 (d, *J*(P-C) = 7.8 Hz), 157.0.

^{31}P NMR: δ 32.3.

LC-MS: *m/z* 489 [M]$^{+}$.

Anal. Calcd. for $C_{31}H_{24}NO_3P$: C, 76.06; H, 4.94; N, 2.86. Found: C, 76.15; H, 5.06; N, 2.81.

Compound 59



Yield: 0.138 g [97%; using 0.5 mmol of allene **11** without P(*o*-tol)$_3$].

Mp: 106-110 ^{o}C.

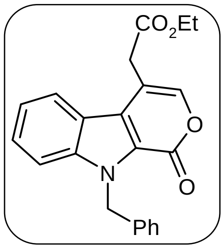
IR (KBr): 3083, 1730, 1707, 1624, 1478, 1275, 1017, 737 cm^{-1}.

^{1}H NMR: 1.23 (t, ^{3}J(H-H) ~ 7.0 Hz, 3H, OCH$_2$C*H*$_3$), 3.80 (s, 2H, C*H*$_2$CO$_2$Et), 4.16-4.21 (m, 5H, OC*H*$_2$ + NC*H*$_3$), 7.24-7.28 (m,

	2H, Ar-*H*), 7.45-7.53 (m, 2H, Ar *H*), 7.91 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*).
^{13}C NMR:	14.2 (OCH_2CH_3), 31.3 (NCH_3), 34.5 (CH_2CO_2Et), 61.5 (OCH_2CH_3), 110.8, 111.0, 120.8, 121.3, 121.5, 122.4, 124.0, 127.6, 141.1, 141.3, 157.2, 170.5.
GC-MS:	*m/z* 285 $[M]^+$.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.21; H, 5.36; N, 4.85.

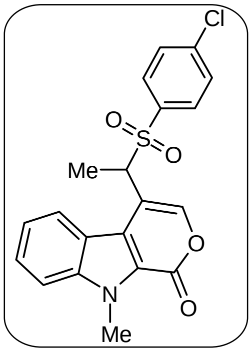
Compound 60



Yield:	0.068 g [63%; using 0.3 mmol of allene **11** without P(*o*-tol)$_3$].
Mp:	216-222°C.
IR (KBr):	3034, 2980, 1730, 1707, 1622, 1495, 1277, 1022, 741 cm^{-1}.
^{1}H NMR:	1.25 (t, ^3J(H-H) = 7.2 Hz, 3H, OCH_2CH_3), 3.85 (s, 2H, CH_2CO_2Et), 4.19-4.24 (q, ^3J(H-H) = 7.2 Hz, 2H, OCH_2CH_3), 5.98 (s, 2H, $CH_2C_6H_5$), 7.20-7.30 (m, 7H, Ar-*H*), 7.46-7.51 (m, 2H, Ar-*H*), 7.97 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*).
^{13}C NMR:	14.2 (OCH_2CH_3), 34.5 (CH_2CO_2Et), 48.0 ($CH_2C_6H_5$), 61.6 (OCH_2CH_3), 111.1, 111.7, 121.3, 121.6, 122.6, 124.7, 126.5, 127.1, 127.6, 127.9, 128.8, 137.4, 140.7, 141.7, 157.0, 170.5.
GC-MS:	*m/z* 361 $[M]^+$.

Anal. Calcd. for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.32; H, 5.38; N, 3.81.

Compound 61



Yield: 0.17 g (85%; using 0.5 mmol of allene **13a**).

Mp: 204-208 °C.

IR (KBr): 3117, 1721, 1707, 1615, 1476, 1314, 1146, 1024, cm^{-1}.

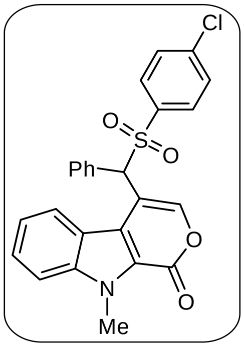
^{1}H NMR (500 MHz): δ 1.80 (d, ^3J(H-H) = 9.0 Hz, 3H, CHC*H*$_3$), 4.24 (s, 3H, NC*H*$_3$), 5.09-5.10 br, 1H, C*H*CH$_3$), 7.24-7.39 (m, 4H, Ar-*H* + C=C*H*), 7.49-7.59 (m, 2H, Ar-*H*), 7.69-7.72 (m, 2H, Ar-*H*), 8.00 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*).

^{13}C NMR (125 MHz): δ 14.9 (CH*C*H$_3$), 31.5 (N*C*H$_3$), 59.1 (*C*HCH$_3$), 111.1, 112.5, 120.4, 121.3, 121.6, 122.8, 123.0, 127.9, 129.3, 131.1, 134.7, 141.0, 141.3, 143.0, 156.5.

LC-MS: *m/z* 402 and 404 [M]$^+$.

Anal. Calcd. for $C_{20}H_{16}ClNO_4S$: C, 59.78; H, 4.01; N, 3.49. Found: C, 59.65; H, 4.08; N, 3.55.

Compound-62



Yield: 0.152 g (66%; using 0.5 mmol of allene **13b**).

Mp: 156-160 °C.

IR (KBr): 3063, 2924, 1609, 1476, 1319, 1148, 702 cm^{-1}.

^{1}H NMR (500 MHz): δ 4.21 (s, 3H, N*CH_3*), 5.03 (s, 1H, C*H*SO$_2$), 7.16-7.56 (m, 10H, Ar-*H* + C=C*H*), 7.68-7.70 (m, 2H, Ar-*H*), 7.85 (d, ^{3}*J*(H-H) = 8.4 Hz, 1H, Ar-*H*), 8.27 (s, 1H, Ar-*H*).

^{13}C NMR (125 MHz): δ 31.5 (N*C*H$_3$), 69.1 (*C*HC$_6$H$_5$), 111.1, 111.3, 120.0, 121.7, 122.0, 122.4, 127.7, 129.1, 129.5, 129.7, 130.2, 130.6_0, 130.6_4, 136.4, 140.9, 141.1, 143.1, 156.4.

LC-MS: *m/z* 464 and 466 [M]$^+$.

Anal. Calcd. for $C_{25}H_{18}ClNO_4S$: C, 64.72; H, 3.91; N, 3.02. Found: C, 64.82; H, 3.85; N, 3.12.

3.8 Pd-catalyzed annulation of allenes with 1-alkyl-indole-2-carboxylic acids *via* C-H functionalization- Synthesis of compounds 63, 67-77

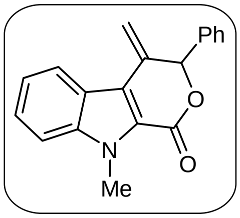
3.81 Standardization of reaction conditions

An oven dried 10 mL RBF was charged with the Pd(II) complex (10 mol%), oxidant [Ag_2CO_3 or Cu(OAc)$_2$; 0.375-0.500 mmol], 1-methyl-indole-2-carboxylic acid **16a** (0.25 mmol) and the base [LiOAc, CsF or K_2CO_3]. The RBF was evacuated for 5 min and filled with N$_2$. To this, solvent [CH$_3$CN, DMF or dimethyl acetamide; 2.5 mL] was added and the contents were stirred at rt for 5 min. After this, allene **10a** was added *via* a micropipette. The RBF was flushed with N$_2$ and sealed. The contents were stirred in preheated oil bath (90-120 ^{0}C) for the indicated period of time. After the completion of the reaction (GC-MS), the mixture was cooled to rt, diluted with ethyl acetate (15 mL), washed with brine (3x5 mL), dried over Na$_2$SO$_4$, filtered, and the solvent removed from the filtrate. The crude product was purified by column chromatography (silica gel, ethyl acetate-hexane) to get the pure product (**63**). Other details are presented in Tables 6 in the Results and Discussion (Chapter 2).

3.82 Standardized procedure

In an oven dried 25 mL RBF, silver carbonate (0.75 mmol) was taken and dried *in vacuo* while heating with hot air gun for 0.5 h. After cooling (5 min), Pd(OAc)$_2$ (10 mol%), 1-alkylindole-2-carboxylic acid (0.5-0.55 mmol) and CH$_3$CN (5.0 mL) were added. The mixture was kept stirring at rt for 5 min. After that, allene (0.50-0.75 mmol) was added and the RBF was sealed with a stopper. The resulting mixture was heated with stirring at 80 °C (oil bath) for 10-12 h. After the completion of the reaction (GC-MS), the solvent was removed by rotary evaporator and the mixture subjected to flash chromatography [silica gel, ethyl acetate/ hexane 1:19] to obtain the pure products in 43-68% yield. Compounds **63**, **67-77** were prepared by this procedure.

Compound 63



Yield: 0.097 g [67%; using **10a** (0.75 mmol) and **16** (0.50 mmol)].

Mp: 154-156 °C.

IR (KBr): 3036, 2932, 1701, 1480, 1308, 1096, 733 cm^{-1}.

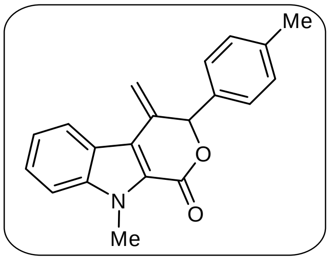
^{1}H NMR: 4.11 (s, 3H, NC*H*$_3$), 5.16 (s, 1H, C=C*H*$_A$H$_B$), 5.94 (s, 1H, C=CH$_A$*H*$_B$), 6.19 (s, 1H, OC*H*), 7.27-7.36 (m, 4H, Ar-*H*), 7.43-7.49 (m, 4H, Ar-*H*), 7.95 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*).

^{13}C NMR: 31.4 (N*C*H$_3$), 85.1 (O*C*H), 111.0, 113.2, 120.6, 122.0, 122.7, 126.7, 127.3, 128.3, 128.5, 128.7, 129.0, 136.6, 138.0, 140.6, 159.3.

GC-MS: *m/z* 289 [M]$^+$.

Anal. Calcd. for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.72; H, 5.18; N, 4.92.

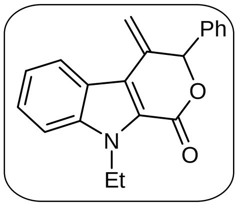
Compound 67



Yield:	0.096 g [63%; using **10b** (0.75 mmol) and **16a** (0.50 mmol)].
Mp:	126-130 °C.
IR (KBr):	2955, 1703, 1478, 1308, 1229, 1200, 1090, 808, 735 cm^{-1}.
^{1}H NMR:	δ 2.34 (s, 3H, $C_6H_4CH_3$), 4.11 (s, 3H, NC*H*$_3$), 5.17 (s, 1H, C=C*H*$_A$H$_B$), 5.93 (s, 1H, C=CH$_A$*H*$_B$), 6.16 (s, 1H, OC*H*), 7.15-7.17 (m, 2H, Ar-*H*), 7.27-7.30 (m, 1H, Ar-*H*), 7.35-7.37 (m, 2H, Ar *H*), 7.42-7.49 (m, 2H, Ar-*H*), 7.95 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*).
^{13}C NMR:	δ 21.2 ($C_6H_4CH_3$), 31.4 (N*C*H$_3$), 85.1 (O*C*H), 111.0, 113.1, 120.6, 121.9$_6$, 122.0$_0$, 122.7, 126.6, 127.2, 129.2, 129.3, 135.1, 136.6, 138.5, 140.6, 159.8.
GC-MS:	*m/z* 303 [M]$^+$.

Anal. Calcd. for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.32; H, 5.75; N, 4.56.

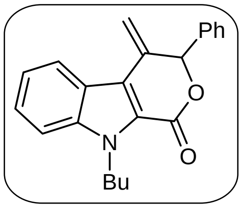
Compound 68



Yield:	0.094 g [62%; using **10a** (0.75 mmol) and **16b** (0.50 mmol)].
Mp:	130-134 °C.
IR (KBr):	2924, 1707, 1466, 1231, 1092, 905, 735 cm^{-1}.
^{1}H NMR:	1.43 (t, ^3J(H-H) = 7.2 Hz, 3H, CH$_2$C*H$_3$*), 4.65 (m, 3H, C*H$_2$*CH$_3$), 5.14 (s, 1H, C=C*H*$_A$H$_B$), 5.93 (s, 1H, C=CH$_A$*H*$_B$), 6.19 (s, 1H, OC*H*), 7.27-7.49 (m, 8H, Ar-*H*), 7.96 (d, ^3J(H-H) = 8.4 Hz, 1H, Ar-*H*).
^{13}C NMR:	15.5 (s, NCH$_2$*C*H$_3$), 39.7 (N*C*H$_2$CH$_3$), 85.1 (O*C*H), 111.0, 113.1, 120.8, 122.0, 122.1, 122.2, 126.6, 127.3, 128.5, 128.7, 136.8, 138.0, 139.6, 159.4.
GC-MS:	*m/z* 303 [M]$^+$.

Anal. Calcd. for $C_{20}H_{17}NO_2$: C, 79.19; H, 5.65; N, 4.62. Found: C, 79.32; H, 5.71; N, 4.55.

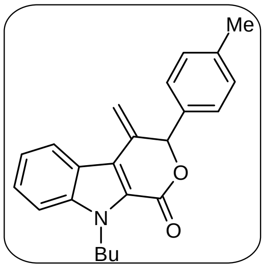
Compound 69



Yield:	0.103 g [62%; using **10a** (0.75 mmol) and **16c** (0.50 mmol)].
Mp:	94-98 °C.
IR (KBr):	2955, 1713, 1522, 1471, 1341, 1184, 698 cm^{-1}.
^{1}H NMR:	0.93 (t, ^3J(H-H) = 7.2 Hz, 3H, $(CH_2)_3CH$), 1.34-1.38 (m, 2H, C*H*$_2$), 1.78-1.82 (m, 2H, C*H*$_2$), 4.60-4.63 (m, 2H, C*H*$_2$), 5.17 (d, ^3J(H-H) = 1.6 Hz, 1H, C=CH_AH_B), 5.94 (d, ^3J(H-H) = 1.2 Hz, 1H, C=CH$_A$*H$_B$*), 6.19 (s, 1H, OC*H*), 7.27-7.50 (m, 8H, Ar-*H*), 7.96 (d, ^3J(H-H) = 8.4 Hz, 1H, Ar-*H*).
^{13}C NMR:	13.9, 20.1, 32.5, 44.5, 85.1 (O*C*H), 111.3, 113.1, 120.6, 121.9, 122.0$_5$, 122.0$_9$, 122.3, 126.5, 127.2, 128.5, 128.6, 136.8, 138.1, 139.9, 159.4.
GC-MS:	*m/z* 331 $[M]^+$.

Anal. Calcd. for $C_{22}H_{21}NO_2$: C, 79.73; H, 6.39; N, 4.23. Found: C, 79.65; H, 6.31; N, 4.18.

Compound 70

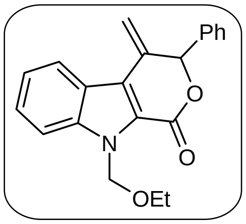


Yield:	0.112 g [65%; using **10b** (0.75 mmol) and **16c** (0.50 mmol)].
Mp:	100-104 °C.

IR (KBr):	2955, 1705, 520, 1472, 1237, 1190, 1098, 741 cm^{-1}.
^{1}H NMR:	0.94 (t, ^3J(H-H) = 7.5 Hz, 3H, (CH$_2$)$_3$CH_3), 1.35-1.37 (m, 2H, CH_2), 1.79-1.82 (m, 2H, CH_2), 2.36 (s, 3H, C$_6$H$_4$CH_3), 4.60-4.63 (m, 2H, CH_2), 5.17 (s 1H, C=CH_AH$_B$), 5.92 (s, 1H, C=CH$_A$$H_B$), 6.17 (s, 1H, OC*H*), 7.17-7.28 (m, 3H, Ar-*H*), 7.36-7.38 (m, 2H, Ar-*H*), 7.46-7.47 (m, 2H, Ar-*H*), 7.96 (d, ^3J(H-H) = 8.0 Hz, 1H, Ar-*H*).
^{13}C NMR:	13.9, 20.1, 21.2, 32.5 (NCH_2), 44.5, 85.1 (O*C*H), 111.3, 112.9, 120.7, 121.9, 122.1, 122.2, 122.4, 126.4, 127.2, 129.3, 135.2, 137.0, 138.4, 139.9, 159.5.
GC-MS:	*m/z* 345 [M]$^+$.

Anal. Calcd. for $C_{23}H_{23}NO_2$: C, 79.97; H, 6.71; N, 4.05. Found: C, 79.85; H, 6.63; N, 4.12.

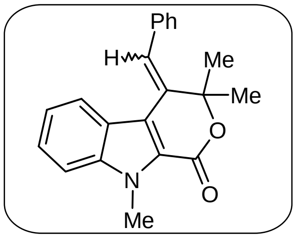
Compound 71



Yield:	0.072 g [43%; using **10a** (0.75 mmol) and **17** (0.50 mmol)].
Mp:	100-104 °C.
IR (KBr):	2975, 1703, 1464, 1337, 1196, 1096, 999, 749 cm^{-1}.
^{1}H NMR:	1.11 (t, ^3J(H-H) ~ 7.0 Hz, 3H, OCH$_2$CH_3), 3.46-3.54 (m, 2H, OCH_2CH$_3$), 5.23 (s, 1H, C=CH_AH$_B$), 5.99 (s, 1H, C=CH$_A$$H_B$), 6.03-6.10 (m, 2H, NC$H_2OCH_2CH_3$), 6.20 (s, 1H, OC*H*), 7.31-7.39 (m, 4H, Ar-*H*), 7.47-7.67 (m, 4H, Ar-*H*), 7.95 (d, ^3J(H-H) = 8.4 Hz, 1H, Ar-*H*).
^{13}C NMR:	15.0 (s, OCH$_2$*C*H$_3$), 64.1 (O*C*H$_2$CH$_3$), 73.5 (N*C*H$_2$OEt), 85.0 (O*C*H), 112.4, 114.4, 121.9, 122.2, 122.5, 122.7, 127.2, 128.5, 128.7, 136.5, 137.8, 140.4, 159.5.
GC-MS:	*m/z* 333 [M]$^+$.

Anal. Calcd. for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.48; H, 5.65; N, 4.31. It was crystalized from chloroform at 30 ^{0}C.

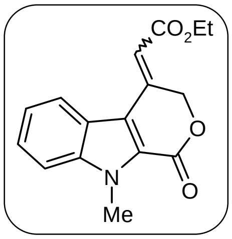
Compound 72



Yield:	0.101 g [64%; using allene **10c** (0.75 mmol) and **16a** (0.50 mmol)].
Mp:	134-138 °C.
IR (KBr):	3058, 2984, 1701, 1509, 1483, 1267, 1090, 747 cm^{-1}.
^{1}H NMR:	1.75 (s, 6H, C(C*H*$_3$)$_2$), 4.16 (s, 3H, NC*H*$_3$), 6.36 (d, ^{3}*J*(H-H) = 8.4 Hz, 1H, Ar-*H*), 6.74-6.78 (m, 1H, Ar-*H*), 6.85 (s, 1H, C=C*H*), 7.21-7.55 (m, 7H, Ar-*H*).
^{13}C NMR:	27.7 (C(*C*H$_3$)$_2$), 31.4 (N*C*H$_3$), 87.7 (O*C*H), 110.3, 119.6, 120.6, 122.1, 124.0, 124.5, 125.3, 125.7, 127.5, 128.4, 129.5, 133.6, 137.6, 140.1, 160.4.
GC-MS:	*m/z* 317 [M]$^+$.

Anal. Calcd. for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.36; H, 6.12; N, 4.51.

Compound 73



Yield:	Combined yield (**59**+**73**) 0.089 g [47%; using **11** (0.75 mmol) and **16a** (0.50 mmol)]; isolated yield for **73** was 0.022 g (15%).
Mp:	120-122 °C.

IR (KBr): 2961, 1717, 1697, 1601, 1489, 1262, 1030 cm^{-1}.

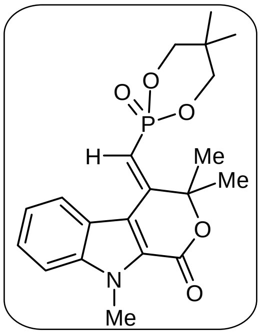
^{1}H NMR: 1.38 (t, ^3J(H-H) = 9.0 Hz, 3H, OCH$_2$C*H*$_3$), 4.20 (s, 3H, NC*H*$_3$), 4.27 (q, ^3J(H-H) = 9.0 Hz 2H, OC*H*$_2$CH$_3$), 5.91 (s, 2H, OC*H*$_2$), 6.58 (s, 1H, C=C*H*), 7.36-7.38 (m, 1H, Ar-*H*), 7.53-7.54 (m, 2H, Ar-*H*), 8.03 (d, ^3J(H-H) = 10.5 Hz 1H, Ar-*H*).

^{13}C NMR: 14.4 (OCH$_2$*C*H$_3$), 31.7 (N*C*H$_3$), 60.4 (O*C*H$_2$CH$_3$), 70.7 (=CO*C*H$_2$), 111.3, 118.2, 121.6, 122.2, 123.2, 124.0, 127.0, 140.3, 143.3, 158.9, 166.4.

GC-MS: *m/z* 285 [M]$^+$.

Anal. Calcd. for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.22; H, 5.36; N, 4.85.

Compound 74



Yield: 0.132 g [68%; using **6c** (0.50 mmol) and **16a** (0.55 mmol)].

Mp: 118-122 °C.

IR (KBr): 2965, 2884, 1715, 1586, 1269, 1059, 745 cm^{-1}.

^{1}H NMR: 1.14 (s, 6H, C(C*H*$_3$)$_2$), 2.01 (s, 6H, OC(C*H*$_3$)$_2$), 3.96 (dd, ^3J(P-H) = ^2J(H-H) = 12.0 Hz, 2H, OC*H*$_2$(A)), 4.19 (s, 3H, NC*H*$_3$), 4.26 (dd→t, ^3J(P-H) = ^2J(H-H) ~ 10.0 Hz, 2H, OC*H*$_2$(B)), 6.42 (d, *J* = 8.0 Hz, 1H, C=C*H*), 7.37-7.54 (m, 3H, Ar-*H*), 8.00 (d, *J* = 8.0 Hz, 1H, Ar-*H*).

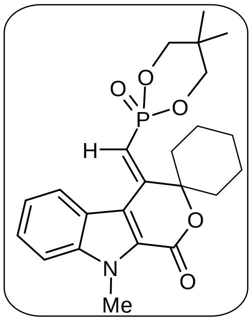
^{13}C NMR: 21.6, 21.7, 29.0 (OC(*C*H$_3$)$_2$), 31.7 (N*C*H$_3$), 32.7 (d, *J*(P-C) = 5.3 Hz, *C*(CH$_3$)$_2$), 75.6 (O*C*H$_2$(A)), 75.7 (O*C*H$_2$(B)), 88.5 (d, *J*(P-C) = 5.8 Hz, O*C*(CH$_3$)$_2$), 106.4 (d, ^1J(P-C) = 194.7 Hz, P*C*=C), 111.6, 118.7 (d, *J*(P-C) = 24.5 Hz), 121.7, 122.3, 123.3, 124.0, 126.8, 140.7, 155.5 (d, *J*(P-C) = 7.2 Hz), 158.5.

^{31}P NMR: δ 12.2.

LC-MS: *m/z* 389 [M]$^+$.

Anal. Calcd. for $C_{20}H_{24}NO_5P$: C, 61.69; H, 6.21; N, 3.60. Found: C, 61.58; H, 6.26; N, 3.71.

Compound 75



Yield: 0.14 g [65%; using **6d** (0.50 mmol) and **16a** (0.55 mmol)].

Mp: 198-200 °C.

IR (KBr): 2932, 1713, 1609, 1485, 1273, 1057, 822 cm^{-1}.

^{1}H NMR: δ 0.75 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.67-2.12 (m, 10H, -(CH_2)$_5$-), 3.58-3.69 (m, 4H, OCH_2), 4.16 (s, 3H, NCH_3), 5.92 (d, ^{2}*J*(P-H) = 9.6 Hz, 1H, C=C*H*), 7.33-7.45 (m, 3H, Ar-*H*), 8.54 (d, ^{3}*J*(H-H) = 8.0 Hz, 1H, Ar-*H*).

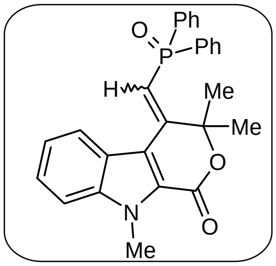
^{13}C NMR: 20.7, 21.7, 21.8, 25.2, 31.4 (N*C*$\mathrm{H_3}$), 32.3 (d, *J*(P-C) = 7.0 Hz, *C*($\mathrm{CH_3}$)$_2$), 35.5, 76.6 (O*C*$\mathrm{H_2}$(A)), 77.2 (O*C*$\mathrm{H_2}$(B)), 88.1 (d, *J*(P-C) = 21.0 Hz, O*C*($\mathrm{CH_2}$)$_2$), 109.2 (d, ^{1}*J*(P-C) = 179.0 Hz, P*C*=C), 110.2, 117.7 (d, *J*(P-C) = 9.0 Hz), 122.3, 123.4, 123.8, 124.7, 126.6, 139.7, 152.2, 159.2.

^{31}P NMR: δ 11.0.

LC-MS: *m/z* 429 [M]$^+$.

Anal. Calcd. for $C_{23}H_{28}NO_5P$: C, 64.33; H, 6.57; N, 3.26. Found: C, 64.48; H, 6.65; N, 3.18.

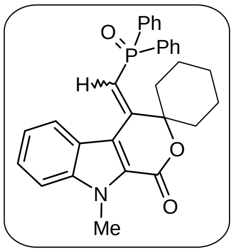
Compound 76



Yield:	0.135 g [61%; using allene **8b** (0.50 mmol) and **16a** (0.55 mmol)].
Mp:	156-160 °C.
IR (KBr):	3058, 2988, 1715, 1563, 1485, 1254, 1094, 721 cm^{-1}.
^{1}H NMR:	δ 1.99 (s, 6H, C(C*H*$_3$)$_2$, 4.18 (s, 3H, NC*H*$_3$), 6.89 (d, ^{3}*J*(H-H) = 15.6 Hz, 1H, C=C*H*), 7.25-7.27 (m, 1H, Ar-*H*), 7.50-7.56 (m, 8H, Ar-*H*), 7.70-7.84 (m, 5H, Ar-*H*). There was also a minor isomer: δ 1.69, 4.01, 6.45(d) [other peaks were buried in the signals due to the major isomer].
^{13}C NMR:	δ 29.8 (C(*C*H$_3$)$_2$), 31.7 (NC*H*$_3$), 89.1 (O*C*(CH$_3$)$_2$), 111.5, 113.7 (d, ^{1}*J*(P-C) = 103.3 Hz, P*C*=C), 121.5, 122.4, 123.2, 126.6, 128.9 (d, *J*(P-C) = 12.0 Hz), 130.9 (d, *J*(P-C) = 9.7 Hz), 131.8, 135.1, 136.1, 140.7, 158.7.
^{31}P NMR:	δ 20.7 [major, ca 75%], 18.7 [minor, ca 25%].
GC-MS:	*m/z* 441 [M]$^+$.

Anal. Calcd. for $C_{27}H_{24}NO_3P$: C, 73.46; H, 5.48; N, 3.17. Found: C, 73.56; H, 5.41; N, 3.22.

Compound 77



Yield:	0.123 g [51%; using allene **8d** (0.50 mmol) and **16a** (0.55 mmol)].
Mp:	210-212 °C.
IR (KBr):	2926, 1707, 1561, 1437, 1350, 1267, 1098, 828 cm^{-1}.
^{1}H NMR:	δ 1.56-1.98 (m, 8H, -(CH_2)$_4$-), 2.75-2.82 (m, 2H, -(CH_2)-), 4.18 (s, 3H, NCH_3), 6.84 (d, ^{2}J(P-H) = 15.6 Hz, 1H, C=C*H*), 7.46-7.56 (m, 9H, Ar-*H*), 7.68 (d, ^{3}J(H-H) = 8.4 Hz, 1H, Ar-*H*), 7.81-7.86 (m, 4H, Ar-*H*).
^{13}C NMR:	δ 21.5, 23.9, 31.6 (NCH_3), 37.0, 89.8 (d, *J*(P-C) = 3.6 Hz, O*C*(CH$_2$)$_2$), 111.4, 113.4 (d, ^{1}J(P-C) = 105.0 Hz, P*C*=C), 119.4 (d, *J*(P-C) = 19.0 Hz), 121.4, 121.6, 122.4, 123.0, 123.5, 126.4, 128.1 (d, *J*(P-C) = 11.0 Hz), 128.8 (d, *J*(P-C) = 13.0 Hz), 130.7, 130.9 (d, *J*(P-C) = 9.0 Hz), 131.2, 131.6, 135.1, 136.2, 140.6, 155.0, 158.0.
^{31}P NMR:	δ 21.5.
LC-MS:	*m/z* 481 [M]$^{+}$.

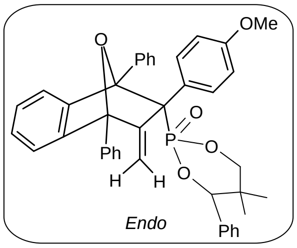
Anal. Calcd. for $C_{30}H_{28}NO_3P$: C, 74.83; H, 5.86; N, 2.91. Found: C, 74.65; H, 5.81; N, 2.99.

3.9 Reaction of allenylphosphonates (7a-c) with 1,3-diphenylisobenzofuran

3.91 General procedure for the cycloaddition reactions

A mixture of allenylphosphonate **7a-c** (1.0 equiv) and 1,3-diphenylisobenzofuran (1.2 equiv) in *p*-xylene (3 mL) was heated at 120 °C for 20 h. The solvent was removed under reduced pressure and the crude product/s was isolated by using silica gel column chromatography [acetone/ hexane (1:9)].

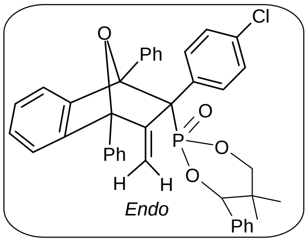
Compound 78



Yield (isolated):	0.028 g (8%; using 0.54 mmol of allene **7b**).
Mp:	180-182 °C.
IR (KBr):	3065, 2969, 1607, 1510, 1460, 1296, 1059, 997 cm^{-1}.
^{1}H NMR	δ 0.58 and 1.04 (2 s, 6H, C(CH_3)$_2$), 3.56 (d, ^3J(P-H) = 3.6 Hz (assignment not certain), 1H, OCH_A), 3.75 (s, 3H, OCH_3), 3.84 ((dd, ^3J(P-H) ~ 22.8 Hz, ^2J(H-H) ~ 12.2 Hz, 1H, OCH_A), 4.60 (d, ^3J(P-H) = 10.4 Hz, 1H, OC*H*Ph), 5.52 (s, 1H, CH_A), 5.53 (d, ^2J(H-H) = 4.0 Hz, 1H, CH_B), 6.52-6.60 (m, 3H, Ar-*H*), 6.81-6.82 (m, 1H, Ar-*H*), 6.99-7.14 (m, 3H, Ar-*H*), 7.32-7.71 (m, 14H, Ar-*H*), 8.07-8.10 (m, 2H, Ar-*H*).
^{13}C NMR :	δ 18.8, 21.7, 36.7 (d, *J*(P-C) = 8.9 Hz), 55.1 (s, O*C*H$_3$), 66.0 (d, ^1J(P-C) = 137.9 Hz), 77.1, 88.9 (d, *J*(P-C) = 10.1 Hz), 91.2, 91.6, 112.5, 113.9 (d, *J*(P-C) = 6.2 Hz), 120.0, 123.0, 126.4, 126.6, 127.1, 127.6, 127.9, 128.0 (d, *J*(P-C) = 4.5 Hz), 128.4, 128.6, 128.9, 129.9, 130.7, 131.6, 131.7, 134.4, 136.9, 137.8, 143.8, 147.0 (d, *J*(P-C) = 11.1 Hz), 152.6 (d, *J*(P-C) = 8.2 Hz), 158.5.
^{31}P NMR:	δ 16.4.
LC-MS:	*m/z* 641 $[M+1]^+$.

Anal. Calcd. for $C_{41}H_{37}O_5P$: C, 76.86; H, 5.82. Found: C, 76.98; H, 5.81. It was crystallized from chloroform at 25 °C.

Compound 79



Yield (isolated):	0.023 g (9%; using 0.416 mmol of allene **7c**).
Mp:	200-202 °C.
IR (KBr):	3069, 2976, 1601, 1495, 1373, 1258, 1063 cm^{-1}.

^{1}H NMR: δ 0.58 and 1.04 (2 s, 6H, C(C*H*$_3$)$_2$), 3.58 (d, ^3J(P-H) = 3.6 Hz (assignment not certain), 1H, OC*H*$_A$), 3.82 (dd, ^3J(P-H) ~ 20.6 Hz, ^2J(H-H) ~ 10.6 Hz, 1H, OC*H*$_A$), 4.59 (d, ^3J(P-H) = 10.8 Hz, 1H, OC*H*Ph), 5.52 (d, ^2J(H-H) ~ 5.2 Hz, 1H, C*H*$_A$), 5.54 (d, ^2J(H-H) ~ 5.2 Hz, 1H, C*H*$_B$), 6.54 (d, ^3J(H-H) = 7.6 Hz, 1H, Ar-*H*), 6.83-6.85 (m, 2H, Ar-*H*), 7.01-7.12 (m, 5H, Ar-*H*), 7.33-7.66 (m, 13H, Ar-*H*), 8.05-8.08 (m, 2H, Ar-*H*).

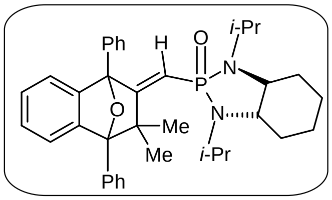
^{13}C NMR (125 MHz): δ 18.8, 21.7, 36.8 (d, *J*(P-C) = 7.3 Hz), 66.2 (d, ^1J(P-C) = 139.0 Hz), 77.1, 89.1 (d, *J*(P-C) = 10.1 Hz), 91.2, 91.7, 114.0, 114.1, 120.1, 123.0, 126.5, 126.6, 127.3, 127.5, 127.6, 128.0, 128.1$_0$, 128.1$_3$, 128.4, 128.6, 128.8, 128.9, 131.9 (d, *J*(P-C) = 7.5 Hz), 133.3, 134.2, 136.7 (d, *J*(P-C) = 4.6 Hz), 137.4, 137.5, 146.6 (d, *J*(P-C) = 8.7 Hz), 152.3 (d, *J*(P-C) = 7.6 Hz).

^{31}P NMR: δ 15.5

LC-MS: *m/z* 645 and 647 [M]$^+$.

Anal. Calcd. for $C_{40}H_{34}ClO_4P$: C, 74.47; H, 5.31. Found: C, 74.36; H, 5.38.

Compound (*E*+*Z*)-80



Yield (isolated): 0.162 g (78% *E*+*Z*; using 0.36 mmol of allene **9d**).

IR (KBr): 3030, 2926, 2855, 1640, 1497, 1300, 1061, 928 cm^{-1}.

^{1}H NMR: (E/Z = ~1:1). δ 0.80-1.34 (m, 18H, cyclohexyl-*H* + CH(C*H*$_3$)$_2$ + (C*H*$_3$)$_2$), 1.45-1.47 (m, 3H, cyclohexyl-*H*), 1.72-1.74 (m, 3H, cyclohexyl-*H*), 1.96-1.99 (m, 2H, cyclohexyl-*H*), 5.15 (d, ^2J(P-H) ~ 11.6 Hz, =C*H*), 7.21-7.38 (m, 2H, Ar-*H*), 7.44-7.58 (m, 8H, Ar-*H*), 7.73-7.80 (m, 2H, Ar-*H*), 7.87-7.90 (m, 2H, Ar-*H*).

^{13}C NMR: δ 19.9, 20.5, 22.2, 22.3, 23.0, 24.0$_7$, 24.1$_0$, 24.3, 24.4, 30.6, 43.7, 43.8, 44.1, 49.6$_0$, 49.6$_3$, 59.3, 59.4, 61.0, 61.0$_3$, 91.5, 92.1, 115.2 (d, ^1J(P-C) = 152.0 Hz, P-*C*) and 120.7 (d, ^1J(P-C) = 158.0 Hz, P-*C*), 125.8, 126.5, 127.0, 127.3, 127.9, 128.2, 128.4, 129.1, 130.2, 130.9, 133.3, 135.5, 136.3, 136.8, 137.1, 143.0, 143.1, 147.4, 150.3, 154.6, 156.4, 167.9 [the spectrum was complicated due to the peaks for both the isomers].

^{31}P NMR: δ 23.2 and 24.2.

LC-MS: *m/z* 582 [M+1]$^+$.

Anal. Calcd. for $C_{35}H_{45}N_2O_2P$: C, 76.52; H, 7.81; N, 4.82. Found: C, 76.68; H, 7.75; N, 4.76. X-ray crystal structure was determined for (*E*)-isomer.

3.10 X-ray crystallography

A suitable crystal was mounted on a glass fiber (for **9c, 25, 33,34, (*Z*)-36, 49, 59, 61, 71, 74, 75, 78** and **80**) and X-ray data were collected at 293 K on an OXFORD diffractometer or on a Bruker AXS-SMART diffractometer using Mo-K$_\alpha$ radiation (λ = 0.71073 Å). Structures were solved and refined using standard methods.[100] 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 1-4. In the structure of **79.**1/2H_2O.$CHCl_3$, there is hydrogen bonding between the solvent water (O7) and phosphoryl oxygen (O1), but because of the half occupancy and disorder at O7 the hydrogen bond parameters are not given. However, the main structure is fully refined.

Table 1. Crystal data for compounds **9c, 25, 33 and 34**[a]

Compound	**9c**	**25**	**33**	**34**
Emp. formula	$C_{25}H_{33}N_2OP$	$C_{16}H_{22}O_5PS$	$C_{28}H_{25}O_3PS$	$C_{17}H_{19}ClO_4S_2$
Formula wt	408.50	357.38	472.52	386.89
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	*P2(1)/n*	*P2(1)/c*	*P2(1)/c*	*C2/c*
a /Å	12.7972(6)	9.866(3)	10.029(2)	26.87(2)
b /Å	13.9345(6)	11.350(3)	20.917(4)	10.533(3)
c /Å	13.1009(5)	18.154(5)	12.214(3)	14.124(6)
α/deg	90	90	90	90
β/deg	95.799(4)	114.75(2)	110.81(3)	105.41
γ/deg	90	90	90	90
V /Å^3	2324.22(18)	1846.1(9)	2395.1(9)	3854(3)
Z	4	4	4	8
D_{calc} /g cm^{-3}]	1.167	1.286	1.310	1.334
μ /mm^{-1}	0.936	0.282	0.230	0.432
F(000)	880	756	992	1616
Data/ restraints/ parameters	3966/0/274	3774/0/224	2508/0/299	3382/0/229
S	1.029	0.898	0.693	1.390
R1 [I>2σ(I)]	0.0612	0.0442	0.0458	0.1413
wR2 [all data]	0.1676	0.1078	0.0530	0.4458
Max./ min. residual electron dens. [eÅ^{-3}]	0.735/ -0.360	0.202/ -0.219	0.196/ -0.175	0.603/ -0.930

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{0.5}$

Table 2. Crystal data for compounds (*Z*)-**36, 49, 59** and **61**[a]

Compound	(*Z*)-**36**	**49**	**59**	**61**
Emp. formula	$C_{33}H_{32}NO_4P_2S$	$C_{24}H_{24}NO_5P$	$C_{16}H_{15}NO_4$	$C_{21}H_{18}C_{l3}NO_4S$
Formula wt	600.61	437.41	285.29	486.79
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	*P2(1)/c*	*P2(1)/c*	*P2(1)/c*	$P\bar{1}$
a /Å	13.459(3)	11.2790(3)	13.362(3)	9.1437(8)
b /Å	15.365(3)	13.8867(4)	13.883(3)	9.3147(7)
c /Å	16.616(3)	14.0971(4)	7.849(2)	12.784(2)
α/deg	90	90	90	92.975(8)
β/deg	112.72(2)	95.564	103.842(3)	95.650(9)
γ/deg	90	90	90	91.661(6)
V /Å^3	3170(1)	2197.6(1)	1413.7(6)	1081.5(2)
Z	4	4	4	2
D_{calc} /g cm^{-3}]	1.259	1.322	1.340	1.495
μ /mm^{-1}	0.240	0.161	0.097	0.549
F(000)	1260	920	600	500
Data/ restraints/ parameters	4578/0/372	3876/0/284	2484/0/193	3802/0/274
S	0.911	1.042	1.032	1.063
R1 [I>2σ(I)]	0.0831	0.0451	0.0501	0.0536
wR2 [all data]	0.2295	0.1233	0.1351	0.1581
Max./ min. residual electron dens. [eÅ^{-3}]	0.541/ -0.310	0.518/ -0.235	0.237/ -0.168	0.392/ -0.378

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{0.5}$

Table 3. Crystal data for compounds **71, 74, 75** and **78**[a]

Compound	**71**	**74**	**75**	**78**.1/2H_2O.$CHCl_3$
Emp. formula	$C_{21}H_{19}NO_3$	$C_{20}H_{24}NO_5P$	$C_{23}H_{28}NO_5P$	$C_{41}H_{36}O_5P$. 1/2H_2O.$CHCl_3$
Formula wt	333.39	389.37	429.43	768.04
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	*P2(1)/c*	*P2(1)/c*	*P2(1)/c*	$P\bar{1}$
a /Å	13.077(2)	13.8122(6)	7.1222(9)	11.588(1)
b /Å	16.069(2)	13.1379(4)	17.729(2)	13.838(1)
c /Å	8.6435(9)	11.7893(6)	16.957(2)	13.898(1)
α/deg	90	90	90	69.460(2)
β/deg	105.02(1)	112.165(6)	93.189	67.759(2)
γ/deg	90	90	90	65.710(2)
V /Å^3	1754.3(4)	1981.2(2)	2137.9(5)	1829.2(3)
Z	4	4	4	2
D_{calc} /g cm^{-3}]	1.262	1.305	1.334	1.394
μ /mm^{-1}	0.084	0.169	0.164	0.342
F(000)	704	824	912	800
Data/ restraints/ parameters	3093/1/230	3475/0/250	3772/0/274	7119/1/475
S	0.784	1.030	1.201	1.131
R1 [I>2σ(I)]	0.0583	0.0416	0.1213	0.1010
wR2 [all data]	0.1277	0.1046	0.2163	0.2108
Max./ min. residual electron dens. [eÅ^{-3}]	0.206/ -0.159	0.212/ -0.281	0.215/ -0.212	1.423/ -1.377

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{0.5}$

Table 4. Crystal data for compounds **80** [a]

Compound	**80**
Emp. formula	$C_{17}H_{25}N_2O_2P_2$
Formula wt	351.33
Crystal system	Triclinic
Space group	$P\bar{1}$
a /Å	10.6243(6)
b /Å	11.5554(6)
c /Å	14.4508(8)
α/deg	79.955
β/deg	82.201
γ/deg	70.764
V /Å^3	1643.5(2)
Z	4
D_{calc} /g cm^{-3}]	1.420
μ /mm^{-1}	0.276
F(000)	748
Data/ restraints/ parameters	5792/0/386
S	1.053
R1 [I>2σ(I)]	0.0710
wR2 [all data]	0.1969
Max./ min. residual electron dens. [eÅ^{-3}]	0.502/ -0.315

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{0.5}$

References

1) (a) Krause, N.; Hashmi, A. S. K. Modern Allene Chemistry Eds.; Wiley-VCH: Weinheim, 2004; Vols. 1, 2. (b) Wang, K. K. *Chem. Rev*. **1996**, *96*, 207. (c) Marshall, J. A. *Chem. Rev*. **2000**, *100*, 3163. (d) Ma, S. *Acc. Chem. Res.* **2003**, *36*, 701. (e) Sydnes, L. K. *Chem. Rev*. **2003**, *103*, 1133. (f) Brandsma, L.; Nedolya, N. A. *Synthesis* **2004**, 735. (g) Tius, M. A. *Acc. Chem. Res.* **2003**, *36*, 284. (h) Ma, S. in *Palladium-Catalyzed Two or Three-Component Cyclization of Functionalized Allenes in Palladium in Organic Synthesis*: Tsuji, J., Ed.; Springer: Berlin, Heidelberg, 2005 pp 183-210. (i) Ma, S. *Aldrichimica Acta* **2007**, *40*, 91. (j) Brasholz, M.; Reissig, H.-U.; Zimmer, R. *Acc. Chem. Res.* **2009**, *42*, 45. (k) Ma, S. *Acc. Chem. Res.* **2009**, *42*, 1679.

2) (a) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196. (b) Hu, G.; Liu, K.; Williams, L. J. *Org. Lett.* **2008**, *10*, 5493. (c) Wang, S.; Mao, W.; She, Z.; Li, C.; Yang, D.; Lin, Y.; Fu, L. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2785. (d) Lyakhova, E. G.; Kalinovsky, A. I.; Dmitrenok, A. S.; Kolesnikova, S. A.; Fedorov, S. N.; Vaskovsky, V. E.; Stonik, V. A. *Tetrahedron Lett.* **2006**, *47*, 6549.

3) (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed.* **2000**, *39*, 3590. (b) Bates, R.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12.

4) For recent reviews on the synthesis of allenes, see: (a) Brummond, K. M.; Deforrest, J. E. *Synthesis* **2007**, 795. (b) Ogasawara, M. *Tetrahedron: Asymmetry* **2009**, *20*, 259. (c) Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671.

5) (a) Satish Kumar, N. "*Studies on the Synthesis, Reactivity and Utility of Cyclic Phosphorus(III) Compounds and Organophosphonates*", Ph.D. thesis, 2004, University of Hyderabad, India. (b) Zapata, A. J.; Gu, Y.; Hammond, G. B. *J. Org. Chem.* **2000**, *65*, 227. (c) Zhao, C. Q.; Han, L. B.; Tanaka, M. *Organometallics* **2000**, *19*, 4196. (d) Rubin, M.; Markov, J.; Chuprakov, S.; Wink, D. J.; Gevorgyan, V. *J. Org. Chem*. **2003**, *68*, 6251. (e) Ma, S.; Guo, H.; Yu, F. *J. Org. Chem.* **2006**, *71*, 6634. (f) Chakravarthy, M.; Bhuvan Kumar, N. N.; Sajna, K. V.; Kumara Swamy, K. C. *Eur. J. Org. Chem*. **2008**, 4500.

6) (a) Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318. (b) Marshall, J. A.; Wolf, M. A.; Wallace, E. M. *J. Org. Chem*. **1997**, *62*, 367. (c) Ibrahim-Quali, M.; Sinibaladi, M.-E.; Troin, Y.; Gardette, D.; Gramain, J.-C. *Synth. Commun*. **1997**, *27*, 1827 (d) Ma, S.; Shi, Z.; Li, L. *J. Org. Chem.* **1998**, *63*, 4522. (e) Kumar, K.; Kaur, S.; Ishar, M. P. S. *Synlett* **1999**, 1237. (f) Ma, S.; Shi, Z.; Yu, Z. *Tetrahedron Lett.* **1999**, *40*, 2393. (g) Yamazaki, J.; Watanabe, T.; Tanaka, K. *Tetrahedron: Asymmetry* **2001**, *12*, 669. (h) Ma, S.; Jiao, N.; Zhao, S.; Hou, H. *J. Org. Chem*. **2002**, *67*, 2837. (i) Ogata, A.; Nemoto, M.; Kobayashi, K.; Tsubouchi, A.; Takeda, T. *Chem. Eur. J.* **2007**, *13*, 1320. (j) Li, C.-Y.; Wang, X.-B.; Sun, X.-L.; Tang, Y.; Zheng, J.-C.; Xu, Z.-H.; Zhou, Y.-G.; Dai, L.-X. *J. Am. Chem. Soc*. **2007**, *129*, 1494. (k) Li, C.-Y.; Zhu, B.-H.; Ye, L.-W.; Jing, Q.; Sun, X.-L.; Tang, Y.; Shen, Q. *Tetrahedron* **2007**, *63*, 8046. (l) Yua, S.; Ma, S. *Chem. Commun.* **2011**, *47*, 3528. (m) Brandsma, L. *Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques*; Elsevier: Kidlington, Oxford, UK, 2004**.** (n) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943.

7) (a) Crabbe, P.; Fillion, H.; Andre, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859. (b) Kazmaier, U.; Lucas, S.; Klein, M. *J. Org. Chem.* **2006**, *71*, 2429.

8) (a) Li, J.; Kong, W.; Fu, C.; Ma, S. *J. Org. Chem.* **2009**, *74*, 5104. (b) Kuang, J.; Ma, S. *J. Org. Chem.* **2009**, *74*, 1763. (c) Kuang, J.; Ma, S. *J. Am. Chem. Soc.* **2010**, *132*, 1786.

9) Xiao, Q.; Xia, Y.; Li, H.; Zang, Y.; Wang, J. *Angew. Chem., Int. Ed*. **2011**, *50*, 1114

10) Fan, X.; Qu, Y.; Wang, Y.; Zhang, X.; Wang, J. *Tetrahedron Lett*. **2010**, *51*, 123.

11) Lo, V. K.-Y.; Zhou, C.-Y.; Wong, M.-K.; Che, C.-M. *Chem. Commun*. **2010**, *46*, 213.

12) Ohmiya, H; Yang, M.; Yamauchi, Y.; Ohtsuka, Y.; Sawamura, M. *Org. Lett.* **2010**, *12*, 1796.

13) (a) Mukai, C.; Ohta, M.; Yamashita, H.; Kitagaki, S. *J. Org. Chem.* **2004**, *69*, 6867. (b) Brel, V. K.; Belsky, V. K.; Stash, A. I.; Zavodnik, V. E.; Stang, P. J. *Eur. J. Org. Chem.* **2005**, 512.

14) Bhuvan Kumar, N. N.; Kumara Swamy, K. C. *Polyhedron* **2006**, *26*, 883.

15) Pudovik, A. N. *J. Gen. Chem*. **1950**, *29*, 97.

16) Kalek, M.; Johansson, T.; Jezowska, M.; Stawinski, J. *Org. Lett.* **2011**, *12*, 4702.

17) (a) Scheufler, F.; Maier, M. E. *Eur. J. Org. Chem.* **2000**, 3945. (b) Braverman, S.; Lior, Z. *Tetrahedron Lett.* **1994**, *35*, 6725. (c) Phani Pavan, M. "*New Phosphono-Heterocycles Through Allenylphosphonates*", Ph.D. thesis, 2010, University of Hyderabad, India.

18) Martin, T. J.; Vakhshori, V. G.; Tran, Y. S.; Kwon, O. *Org. Lett.* **2011**, *13*, 2586.

19) Kimber, M. C. *Org. Lett.* **2010**, *12*, 1128.

20) Kinder, R. E.; Zhang, Z.; Widenhoefer, R. A. *Org. Lett.* **2008**, *10*, 3157.

21) Bhuvan Kumar, N. N.; Nagarjuna Reddy, M.; Kumara Swamy, K. C. *J. Org. Chem.* **2009**, *74*, 5395.

22) Chakravarthy, M.; Kumara Swamy, K. C. *Synthesis* **2007**, 3171.

23) Kumara Swamy, K. C.; Balaraman, E.; Satish Kumar, N. *Tetrahedron* **2006**, *62*, 10152.

24) Phani Pavan, M.; Kumara Swamy, K. C. *Synlett.* **2011**, 1288.

25) Benedetti, E.; Lemiere, G.; Chapellet, L.-L.; Penoni, A.; Palmisano, G.; Malacria, M.; Goddard, J.-P.; Fensterbank, L. *Org. Lett.* **2010**, *12*, 4396.

26) Poonath, M.; Krause, N. *J. Org. Chem.* **2011**, *76*, 1934.

27) Morita, N.; Krause, N. *Angew. Chem., Int. Ed.* **2006**, *45*, 1897.

28) (a) Cowen, B. J.; Miller, S. J. *Chem. Soc. Rev.* **2009**, 3102. (b) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res.* **2001**, *34*, 535.

29) (a) Zhao, G.-L.; Huang, J.-W.; Shi, M. *Org. Lett.* **2003**, *5*, 4737. (b) Xu, Z.; Lu, X. *J. Org. Chem.* **1998,** *63,* 5031. (c) Zhao, G.-L.; Shi, M. *Org. Biomol. Chem.* **2005**, *3*, 3686. (d) Zhu, X.-F.; Lan, J.; Kwon, O. *J. Am. Chem. Soc.* **2003**, *125*, 4716.

30) Panossian, A.; Fleury-Brégeot, N.; Marinetti, A. *Eur. J. Org. Chem.* **2008**, 3826.

31) Arduengo, III. A. J.; Harlow, R. L.; Kline, M. *J. Am. Chem. Soc.* **1991**, *113*, 361.

32) Nair, V.; Bindu, S.; Sreekumar, V. *Angew. Chem., Int. Ed*. **2004**, *43*, 5130.

33) Chen, D.-D.; Hou, X.-L.; Dai, L.-X. *J. Org. Chem.* **2008**, *73*, 5578.

34) (a) Frigoli, M.; Mehl, G. H. *Chem. Commun.* **2004**, 2040. (b) Liu, K.; Chougnet, A.; Woggon, W.-D. *Angew. Chem., Int. Ed.* **2008**, *47*, 5827. (c) Lee, Y. R.; Choi, J. H.; Yoon, S. H. *Tetrahedron Lett.* **2005**, *46*, 7539. (d) Lee, Y. R.; Wang, X. *Org. Biomol. Chem.* **2005**, *3*, 3955. (e) Flavin, M. T.; Rizzo, J. D.; Khilevich, A.; Kucherenko, A.; Sheinkman, A. K.; Vilaychack, V.; Lin, L.; Chen, W.; Greenwood, E. M.; Pengsuparp, T.; Pezzuto, J. M.; Hughes, S. H.; Flavin, T. M.; Cibulski, M.; Boulanger, W. A.; Shone, R. L.; Xu, Z.-Q. *J. Med. Chem.* **1996**, *39,* 1303. (f) Cueva, J. P.; Giorgioni, G.; Grubbs, R. A.; Chemel, B. R.; Watts, V. J.; Nichols, D. E. *J. Med. Chem.* **2006**, *49*, 6848. (g) Kemnitzer, W.; Drewe, J.; Jiang, S.; Zhang, H.; Crogan-Grundy, C.; Labreque, D.; Bubenick, M.; Attardo, G.; Denis, R.; Lamothe, S.; Gourdeau, H.; Tseng, B.; Kasibhatla, S.; Cai, S. X. *J. Med. Chem.* **2008,** *51*, 417. (h) Bulman Page, P. C.; Buckley, B. R.; Heaney, H.; Blacker, A. J. *Org. Lett.* **2005**, *7*, 375. (i) Shi, Y.-L.; Shi, M. *Org. Biomol. Chem.* **2007**, *5*, 1499. (j) Liu, F.; Evans, T.; Das, B. C. *Tetrahedron Lett.* **2008**, *49*, 1578.

35) Nixon, N. S.; Scheinmann, F. *Tetrahedron Lett.* **1983**, *24*, 597.

36) (a) Shi, Y.-L.; Shi, M. *Org. Lett.* **2005**, *7*, 3057. (b) Zhao, G.-L.; Shi, Y.-L.; Shi, M. *Org. Lett.* **2005**, *7*, 4527. (c) Shi, M.; Dai, L.-Z.; Shi, Y.-L.; Zhao, G.-L. *Adv. Synth.*

Catal. **2006**, *348*, 967. (d) Dai, L.-Z.; Shi, Y.-L.; Zhao, G.-L.; Shi, M. *Chem. Eur. J.* **2007**, *13*, 3701. (e) Shi, Y.-L.; Shi, M. *Org. Biomol. Chem.* **2007**, *5*, 1499.

37) (a) Meng, X.; Huang, X.; Chen, R. *Org. Lett.* **2009**, *11,* 137. (b) Meng, X.; Huang, Y.; Zhao, H.; Xie, P.; Ma, J.; Chen, R. *Org. Lett.* **2009,** *11,* 991.

38) Sun, Y.-W.; Guan, X.-Y.; Shi, M. *Org. Lett.* **2010,** *12,* 5664.

39) Watanabe, T.; Oishi, S.; Fujii, N.; Ohno, H. *Org. Lett*. **2007**, *9*, 4821.

40) (a) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285. (c) Larock, R. C. *Pure. Appl. Chem.* **1999**, *71*, 1435.

41) Selected recent reviews: (a) Yamamoto, Y.; Radhakrishnan, U. *Chem. Soc. Rev.* **1999**, *28*, 199. (b) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067. (c) Wei, L.-L.; Xiong, H.; Hsung, R. P. *Acc. Chem. Res.* **2003**, *36*, 773. (d) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.

42) (a) Zhao, C. Q.; Han, L. B.; Tanaka, M. *Organometallics* **2000**, *19*, 4196. (b) Nishimura, T.; Hirabayashi, S.; Yasuhara, Y.; Hayashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 2556.

43) Larock, R. C.; Berrios-Peña, N. G.; Fried, C. A. *J. Org. Chem*. **1991**, *56*, 2615.

44) (a) Grigg, R. *J. Heterocycl. Chem.* **1994**, *31*, 631. (b) Gardiner, M.; Grigg, R.; Sridharan, V.; Vicker, N. *Tetrahedron Lett*. **1998**, *39*, 435.

45) Li, W.; Shi, M. *Eur. J. Org. Chem.* **2009**, 270.

46) Inamoto, K.; Yamamoto, A.; Ohsawa, K.; Hiroya, K.; Sakamoto, T. *Chem. Pharm. Bull.* **2005**, *53*, 1502.

47) (a) Chakravarty, M.; Kumara Swamy, K. C. *J. Org. Chem.* **2006**, *71*, 9128. (b) Manab Chakravarthy. "*Investigations on Catalytic and Noncatalytic Reactions of Allenylphosphonates, α-Methoxy Phosphonates and Phosphazanes possessing N-P=X [X= O, S, Se] Skeleton*", Ph.D. thesis, 2007, University of Hyderabad, India. (c) Phani Pavan, M.; Chakravarty, M.; Kumara Swamy, K. C. *Eur. J. Org. Chem.* **2009**, 5927.

48) (a) Rozhkov, R. V.; Larock, R. C. *J. Org. Chem.* **2010**, *75*, 4131.

49) Kato, F.; Hiroi, K. *Chem. Pharm. Bull.* **2004**, *52*, 95.

50) Inamoto, K.; Yamamoto, A.; Ohsawa, K.; Hiroya, K.; Sakamoto, T. *Chem. Pharm. Bull.* **2005**, *53*, 1502.

51) Lu, G.; Malinakova, H. C. *J. Org. Chem.* **2004**, *69*, 8266.

52) Kato, F.; Hiroi, K. *Chem. Pharm. Bull.* **2004**, *52*, 95.

53) Larock, R. C.; He, Y.; Leong, W. W.; Han, X.; Refvik, M. D.; Zenner, J. M. *J. Org. Chem*. **1998**, *63*, 2154.

54) Grigg, R.; Koppen, I.; Rasparini, M.; Sridharan, V. *Chem. Commun.* **2001**, 964.

55) Lofberg, C.; Grigg, R.; Keep, A.; Derrick, A.; Sridharan, V.; Kilnera, C. *Chem. Commun.* **2006**, 5000.

56) Grigg, R.; Kordes, M. *Eur. J. Org. Chem*. **2001**, 707.

57) Chang, H.-T.; Jayanth, T. T.; Cheng, C.-H. *J. Am. Chem. Soc.* **2007**, *129*, 4166.

58) Hsieh, J.-C.; Rayabarapu, D. K.; Cheng, C.-H. *Chem. Commun.* **2004**, 532.

59) Liu, Y.-L.; Liang, Y.; Pi, S.-F.; Huang, X.-C.; Li, J.-H. *J. Org. Chem.* **2009**, *74*, 3199.

60) Franzen, J.; Backvall, J-.E. *J. Am. Chem. Soc.* **2003**, *125*, 6056.

61) Pardo-Rodriguez, V.; Marco-Martinez, J.; Bunuel, E.; Cardenas. D. J. *Org. Lett.* **2009,** *11,* 4548.

62) Larock, R. C.; Varapath, S.; Lau, H. H.; Fellows, C. A. *J. Am. Chem. Soc.* **1984**, *106*, 5274.

63) Larock, R. C.; Zenner, J. M. *J. Org. Chem*. **1995**, *60*, 482.

64) Cherry, K.; Parrain, J.-L.; Thibonnet, J.; Duchene, A.; Abarbri, M. *J. Org. Chem.* **2005**, *70*, 6669.

65) Kato, F.; Hiroi, K. *Chem. Pharm. Bull.* **2004**, *52*, 95.

66) (a) Zeni, G.; Larock, R. C. *Chem. Rev.* **2006**, *106*, 4644. (b) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (c) Kundu, N. G.; Pal, M.; Mahanty, J. S.; De, M. *J. Chem. Soc.*, *Perkin Trans. I* **1997**, 2815. (d) Inamoto, K.; Yamamoto, A.; Ohsawa, K.; Hiroya, K.; Sakamoto, T. *Chem. Pharm. Bull.* **2005**, *53*, 1502.

67) Shi, Z.; Zhang, C.; Li, S.;Pan, D.; Ding, S.; Cui, Y.; Jiao, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 4572.

68) Roesch, K. R.; Larock, R. C. *J. Org. Chem*. **1998**, *63*, 5306.

69) Roy, S.; Roy, S.; Neuenswander, B.; Hill, D.; Larock, R. C. *J. Comb. Chem.* **2009,** *11,* 1061.

70) Guimond, N.; Fagnou, K. *J. Am. Chem. Soc.* **2009**, *131*, 12050.

71) Guimond, N.; Gouliaras, C.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 6908.

72) Zhang, H.; Larock, R. C. *Org. Lett.* **2001,** *3,* 3083.

73) Ding, S.; Shi, Z.; Jiao, N. *Org. Lett.* **2010,** *12,* 1540.

74) Shi, Z.; Cui, Y.; Jiao, N. *Org. Lett.* **2010,** *12,* 2908.

75) (a) Weinreb, S. M.; Scola, P. M. *Chem. Rev*. **1989**, *89,* 1525. (b) Back, T. G.; Clary, K. N.; Gao, D. *Chem. Rev.* **2010**, *110*, 4498. (c) Croatt, M. P.; Wender, P. A. *Eur. J. Org. Chem.* **2010**, 19. (d) Henderson, J. R.; Chesterman, J. P.; Parvez, M.; Keay, B. A. *J. Org. Chem.* **2010**, *75*, 988. (e) Hayashi, R.; Feltenberger, J. B.; Hsung, R. P. *Org. Lett.* **2010**, *12*, 1152.

76) Gu, Y.; Hama, T.; Hammond, G. B. *Chem. Commun*. **2000**, 395.

77) Bhuvan Kumar, N. N.; Chakravarty, M.; Satish Kumar, N.; Sajna, K. V.; Kumara Swamy, K. C. *J. Chem. Sci*. **2009**, *121*, 23.

78) Sajna, K. V.; Kotikalapudi, R.; Chakravarty, M.; Bhuvan Kumar, N. N.; Kumara Swamy, K. C. *J. Org. Chem.* **2011**, *76*, 920.

79) (a) Muthiah, C.; Praveen Kumar, K.; Aruna Mani, C.; Kumara Swamy, K. C. *J. Org. Chem*. **2000**, *65*, 3733. (b) Weener, J.-W.; Versleijen, J. P. G.; Meetsma, A.; ten Hoeve, W.; Van Leusen, A. M. *Eur. J. Org. Chem*. **1998**, 1511. (c) Hoeve, W.t.; Wynberg H. *J. Org. Chem*. **1985**, *50*, 4508 (d) M. Padmaja, *“Synthesis and applications of chiral amines and quaternary ammonium salts containing trans-1,2-cyclohexyl moiety”*, Ph. D. thesis, 2005, University of Hyderabad, India. (e) Krysiak, J.; Lyon, C.; Baceiredo, A.; Gornitzka, H.; Mikolajczyk, M.; Bertrand, G. *Chem. Eur. J.* **2004**, *10*, 1982.

80) (a) Enchev, D. D.; Kirilov, M. *Phosphorus, Sulfur, and Silicon* **2005**, *180*, 2269. (b) Guo, H.; Qian, R.; Guo, Y.; Ma, S. *J. Org. Chem.* **2008**, *73*, 7934.

81) Fuji, K.; Morimoto, T.; Tsutsumi, K.; Kakiuchi, K. *Chem. Commun*. **2005**, 3295.

82) Tang, Y.; Deng, L.; Zhang, Y.; Dong, G.; Chen, J.; Yang, Z. *Org. Lett.* **2005**, *7*, 1657.

83) Venu Srinivas. “*Synthetic Studies on Organophosphonates and 9-Chloroacridines*”, Ph.D. thesis, 2010, University of Hyderabad, India.

84) (a) Patel, D.S.; Bharatam, P. V. *J. Org. Chem.* **2011**, *76*, 2558. (b) Dyker, C. A.; Lavallo, V.; Donnadieu, B.; Bertrand, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 3206.

85) (a) Lang, R. W.; Hansen, H.-J. *Organic Syntheses Coll. Vol. 7,* p. 232. (b) Ma, S.; Jiao, N.; Zhao, S.; Hou, H. *J. Org. Chem.* **2002**, *67*, 2837.

86) Edward, A. R.; Andrew, B. E.; Patent WO2005121141, 2005; *Chem. Abstr*. **2005**, *144*, 51458.

87) (a) Putey, A.; Joucla, L.; Picot, L.; Besson, T.; Joseph, B. *Tetrahedron* **2007**, *63*, 867. (b) Sechi, M.; Derudas, M.; Dallocchio, R.; Dessi A.; Bacchi, A.; Sannia, L.; Carta, F.; Palomba, M.; Ragab, O.; Chan, C.; Shoemaker, R.; Sei, S.; Dayam, R.; Neamati, N. *J. Med. Chem.* **2004**, *47*, 5298. (c) Poriel, C.; Lachia, M.; Wilson, C.; Davies, J. R.; Moody C. J.; *J. Org. Chem.* **2007**, *72*, 2978. (d) Achab, S.; Guyotb, M.; Potierb, P. *Tetrahedron Lett.* **1995**, *36*, 2615. (e) Johnson, J. R.; Hasbroucjka, R. B.; Dutcher, J. D.; Bruce, W. F. *J. Am. Chem. Soc.* **1945**, *67*, 423. (f) Aktiengesellschaft, H. U. S. Patent

US5852046, **1998**. (g) Ngi, S. I.; Guilloteau, V.; Abarbri, M.; Jerome, T. *J. Org. Chem.* ASAP (DOI: 10.1021/jo201528u).

88) (a) Kumaraswamy, S.; Selvi, R. S.; Kumara Swamy, K. C. *Synthesis* **1997**, 207. **(**b) Praveen Kumar, K.; Muthiah, C.; Kumaraswamy, S.; Kumara Swamy, K. C. *Tetrahedron Lett*. **2001**, *42*, 3219. (c) Kumara Swamy, K. C.; Srinivas, V.; Pavan Kumar, K. V. P.; Praveen Kumar, K. *Synthesis* **2007**, 893.

89) Wittig, G.; Schoellkopf, U. *Org. Synth.* **1960**, *40*, 66.

90) (a) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418. (b) He, M.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3131. (c) He, L.; Jian, T. Y.; Ye, S. *J. Org. Chem.* **2007**, *72*, 7466. (d) Nair, V.; Augustine, A.; Suja, T. D. *Synthesis* **2002**, 2259.

91) (a) Gribble, G. W. *J. Chem. Soc.*, *Perkin Trans. 1*, **2000**, 1045. (b) Tois, J.; Franzen, R.; Koskinen, A. *Tetrahedron* **2003**, *59*, 5395.

92) (a) Joucla, L.; Djakovitch, L. *Adv. Synth. Catal*. **2009**, *351*, 673. (b) Cornella, J.; Lu, P.; Larrosa, I. *Org. Lett*. **2009**, *11*, 5506. (c) Ruiz-Rodríguez, J.; Albericio, F.; Lavilla, R. *Chem. Eur. J*. **2010**, *16*, 1124. (d) Ackermann, L.; Dell Acqua, M.; Fenner, S.; Vicente, R.; Sandmann, R. *Org. Lett*. **2011**, *13*, 2358.

93) (a) Capito, E.; Brown, J. M.; Ricci, A. *Chem. Commun*. **2005**, 1854. (b) Rimster, N. P.; Gauntlett, C.; Godfrey, C. R. A.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 3125. (c) Maehara, A.; Tsurugi, H.; Satoh, T.; Miura, M. *Org. Lett*. **2008**, *10*, 1159. (d) García-Rubia, A.; Arrayas, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed*., **2009**, 48, 6511. (e) Jia, C.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Org. Lett*. **1999**, *1*, 2097.

94) Yamashita, M.; Horiguchi, H.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7481.

95) Wang, C.; Rakshit, S.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 14006. and the references in this journal.

96) Sajna, K. V. *"Cycloaddition/ Cyclization Reactions of Allenylphosphonates/ Related Allenes and Palladium-Catalyzed Diarylation of Alkynes"*, Ph. D. thesis, 2011, University of Hyderabad, India.

97) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, Pergamon, Oxford, 1986.

98) Shriver, D. F.; Dresdzon, M. A. *The Manipulation of Air Sensitive Compounds*, 2nd Ed, Wiley Interscience, New York, 1986.

99) (a) Voges, M. H.; Romming, C.; Tilset, M. *Organometallics* **1999,** *18,* 529. (b) Arduengo, III, A. J.; Krafczyk, R.; Schmutzler, R. *Tetrahedron* **1999**, *55*, 4523. (c) He, J.; Tang, S.; Liu, J.; Su, Y.; Pan, X.; She, X. *Tetrahedron* **2008**, *64*, 8797.

100) (a) Sheldrick, G. M. *SADABS, Siemens Area Detector Absorption Correction*, University of Göttingen, Germany, **1996**. (b) Sheldrick, G. M., SHELX-97- *A program for crystal structure solution and refinement*, University of Göttingen, **1997**. (c) Sheldrick, G. M. *SHELXTL NT Crystal Structure Analysis Package*, Bruker AXS, Analytical X-ray System, WI, USA, **1999**, version 5.10.

PART B

CYCLODIPHOPHAZANE [ClP(*μ*-N-*t*-Bu)]$_2$ AS A LIGAND IN CROSS-COUPLING REACTIONS

INTRODUCTION

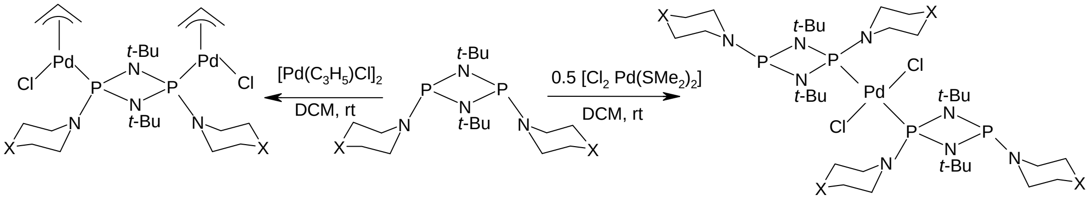
Cyclodiphosph(III)azanes are compounds with a saturated four-membered ring of the type $[XP(\mu\text{-}NR)]_2$ containing alternating phosphorus(III) and nitrogen atoms.[1] A variety of cyclodiphosphazane derivatives have been prepared by nucleophilic substitution reactions of $[ClP(\mu\text{-}NR)]_2$ and their applications have been investigated.[2] Several groups studied the possibility of using these compounds as highly versatile ligands as well as macrocyclic precursors.[3,4] It is noteworthy that in these compounds, both phosphorus and nitrogen are trivalent and it is the lone pair of phosphorus that takes part in reactions in the majority of cases. In the course of our efforts to utilize such compounds we have found molecularly non-stoichiometric compounds[5] wherein a phosphoryl oxygen interchanges its position with a lone pair of electrons on phosphorus. Use of cyclophosphazane as a nucleophile and as a ligand in transition metal-catalyzed reactions is not explored in detail.[6] A brief survey of recent literature on some aspects of cyclodiphosphazane chemistry is presented below.

4.1 *Coordination chemistry of cyclodiphosphazanes*

The P(III) center in cyclodiphosph(III)azanes is known to coordinate to transition metals readily. In the year 1992, the palladium complexes $[PdCl_2L_2]$ [L = *cis*-[*t*-BuNP(OPh)]$_2$] were reported.[7] Their structures was ascertained mainly from ^{31}P NMR spectroscopic data. Subsequently, several other complexes were prepared and structurally characterized.[2a-b,3] Recently, a stable dipalladium(II) complex possessing a Pd-P σ bond has also been reported by Balakrishna's group.[8] Other studies include the reaction of $[t\text{-}BuHN(t\text{-}BuNP)_2OCH_2]_2$ with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ that afforded $[\{Pd(\eta^3\text{-}allyl)Cl\}_4\{t\text{-}BuHN(t\text{-}BuNP)_2OCH_2\}_2]$; in contrast, the reaction between $[t\text{-}BuHN(t\text{-}BuNP)_2OCH_2]_2$ and $[Pd(PEt_3)Cl_2]_2$ leads to $[\{Pd(PEt_3)Cl\}_2\{t\text{-}BuHN(t\text{-}BuNP)_2OCH_2\}_2$.[9] The reactions of *cis*-$[(t\text{-}BuN\text{-}\mu)_2(PNC_4H_8O)_2]$ and *cis*-$[(t\text{-}BuN\text{-}\mu)_2(PNC_4H_8NMe)_2]$ with $[PdCl_2(SMe_2)_2]$ produced exclusively the mononuclear *trans*-[PdCl$_2${(*t*-BuN-

$\mu)_2(PNC_4H_8X)_2\}_2]$ [X =O (**4.1**), NMe (**4.2**)], whereas the reactions with $[Pd(\mu\text{-}Cl)(\eta^3\text{-}C_3H_5)]_2$ afforded the bimetallic complexes $[\{PdCl(\eta^3\text{-}C_3H_5)\}_2(t\text{-}BuN\text{-}\mu)_2(PNC_4H_8X)_2\}]$ [X = O (**4.3**), NMe (**4.4**)] in good yields (Scheme 4.1).[10] However, use of these complexes catalytic activity such have been tested only recently. There are a couple of reports on the use of palladium complexes of cyclodiphosphazanes,[11] but since these reports appeared subsequent to our work,[12] they will be discussed in the Results and Discussion section.

Scheme 4.1



X = O, **4.3**
NMe, **4.4**

X = O, **4.1**
NMe, **4.2**

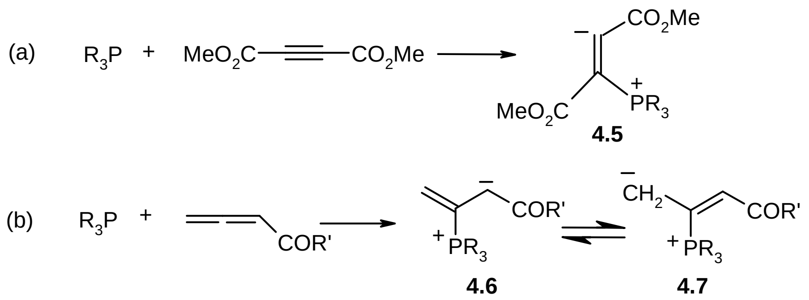
4.2 Other reactions of cyclodiphosph(III)azanes from the recent literature

Aminocyclodiphosph(III)azanes are fairly strong bases. Their utility in analyzing organic reaction mechanism has also been of some interest. This aspect is briefly discussed in the following two subsections.

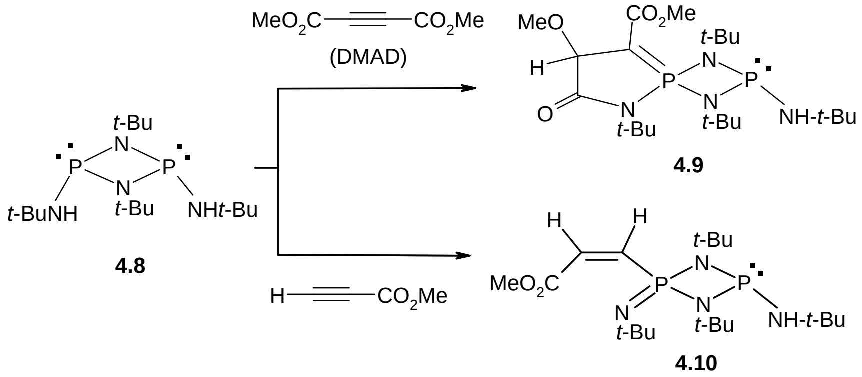
4.21 Reaction of cyclodiphosphazane [(t-BuNH)P(μ-N-t-Bu)]₂ with C=C and C≡C bonded systems

Several important organic transformations of allenes/ alkenes and alkynes are catalyzed by phosphines.[13] In these systems, the key intermediates are the phosphonium salts (betaines) of the types **4.5-4.7** shown in Scheme 4.2. In a study directed at isolating such species, when compound $[(t\text{-}BuNH)P(\mu\text{-}N\text{-}t\text{-}Bu)]_2$ (**4.8**) was treated with dimethylacetylene dicarboxylate (DMAD), instead of the expected phosphonium salt like **4.5**, the novel five-membered ring heterocycle **4.9** was obtained. However, use of methyl propiolate afforded the tautomeric form **4.10** of the expected phosphonium salt (Scheme 4.3).[14] Although species **4.9** or **4.10** is not a phosphonium salt, the formation of P-C bond suggests the involvement of the postulated intermediates shown in Scheme 4.2.

Scheme 4.2

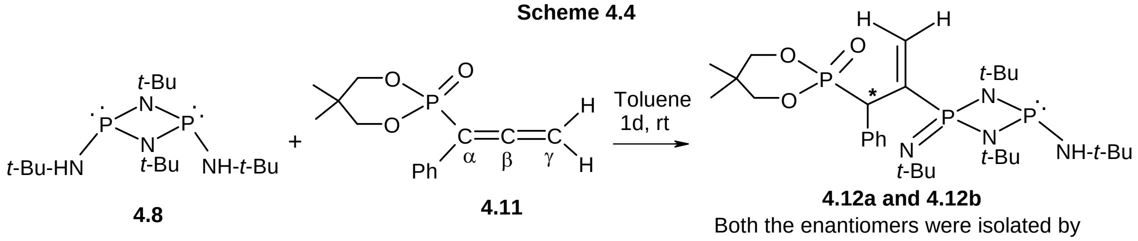


Scheme 4.3



The reaction of allenylphosphonate **4.11** with cyclodiphosphazane [(*t*-BuNH)P(*μ*-N-*t*-Bu)]$_2$ (**4.8**) leads to enantiomers **4.12a/4.12b** which could be isolated (spontaneous resolution; Scheme 4.4).[15] These results clearly show that the initial attack of the P(III) species occurs at the central carbon of the allene part giving a reasonable proof for the proposed intermediate of the type **4.6** or **4.7** shown in Scheme 4.2. Similar compounds were prepared in a later work also.[16] In a more recent work, our group has shown that the reaction of **4.8** with dimethyl maleate also leads to P-C bonded species, but in this case, there is no transfer of the N*H*-*t*-Bu proton.[17]

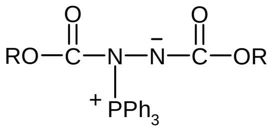
Scheme 4.4



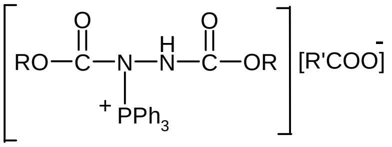
Both the enantiomers were isolated by crystallization (spontaneous resolution)

4.22 *Reaction of cyclodiphosphazanes with dialkyl azodicarboxylates- Implications for the mechanism of Mitsunobu reaction*

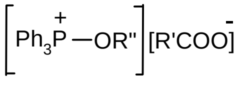
The Mitsunobu reaction allows the conversion of primary and secondary alcohols to a variety of functional groups, such as an ester, using triphenyl phosphine and diethyl azodicarboxylate (DEAD). As the reaction proceeds with clean inversion in case of secondary alcohols, it can be considered as a powerful method for the inversion of stereogenic centers in natural product synthesis. Various intermediates (e.g., **4.13-4.15**) have been proposed in this synthetically useful reaction.[13b] Detailed characterization of these or analogous species had not been documented prior to work from our research group.[18] By making use of the cyclodiphosphazane **4.8**, several important compounds **4.16-4.17** have been structurally characterized (Scheme 4.5). Hence a reasonable (though not exact) evidence for the proposed first stage intermediate in the Mitsunobu reaction is provided from our group.[16]



4.13

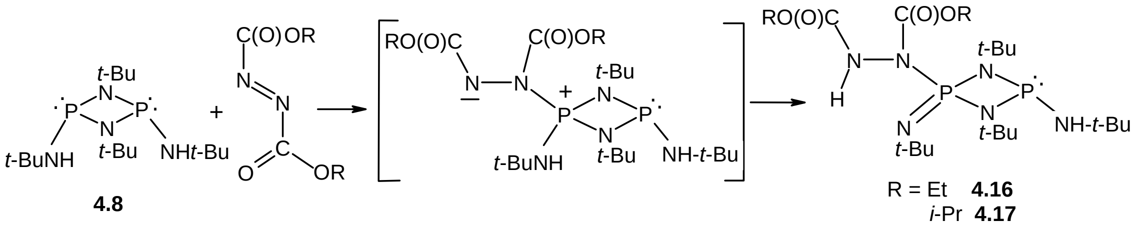


4.14



4.15

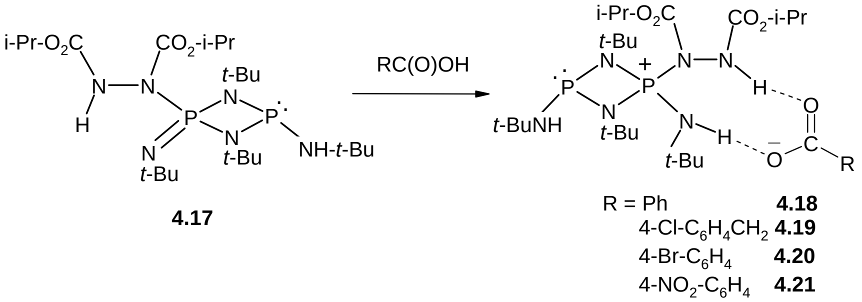
Scheme 4.5



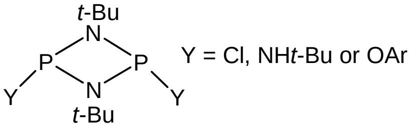
R = Et **4.16**
i-Pr **4.17**

In the second stage of the Mitsunobu reaction, species of type **4.14** are the proposed intermediates. Here our group could isolate the compounds **4.18-4.21** by the addition of carboxylic acids to **4.8**. Interestingly, these compounds undergo the Mitsunobu esterification and thus lend credence to the postulated intermediate like **4.14** (Scheme 4.6).[17c]

Scheme 4.6



In furtherance to the above work, we have been interested in utilizing cyclodiphosph(III)azanes **4.22** in organic reactions, in particular Pd-catalyzed coupling reactions that are briefly discussed below.

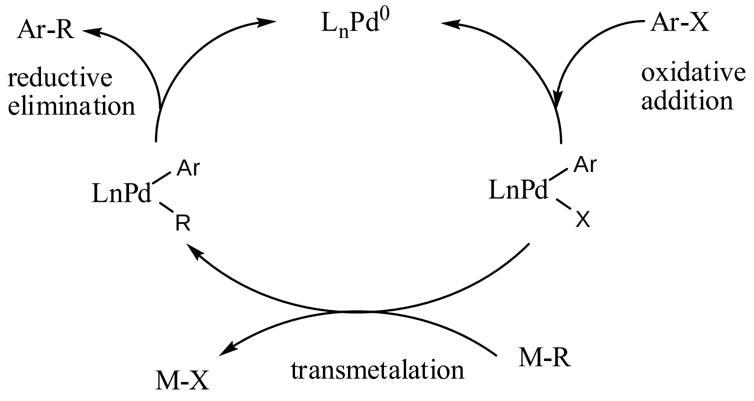


4.22

4.3 Palladium- catalyzed C-C and C-N bond formation

Transition-metal-catalyzed cross-coupling reactions for C-C and C-N bond formation have become some of the most powerful tools in organic synthesis.[18] Of the metals commonly employed in organic synthesis, palladium has arguably stood alone as the most versatile for the formation of carbon-carbon and carbon-heteroatom bonds in reactions such as Suzuki–Miyaura, Sonogashira, Heck, Buchwald-Hartwig amination, Negishi, Stille, Hiyama and Kumada cross-couplings. Among these, Suzuki–Miyaura coupling and Buchwald–Hartwig amination are the preeminent methods for formation of C-C and C-N bonds and have been used in numerous synthetic ventures.[19] A lot of recent work has been directed towards the development of new catalyst systems that capably process demanding substrates such as aryl chlorides,[20] hindered aryl boronic acids and hindered amines under mild reaction conditions with low catalyst loadings.[21] The recent insight of new active catalyst systems can be attributed to an increased focus on ligand design. During this process, a number of ligands including electron-rich alkyl-substituted tertiary phosphines, phosphines having aryl groups at suitable positions and various *N*-heterocyclic carbenes have been recently examined for palladium catalysis.[22,23] A brief discussion regarding these aspects has been presented here.

In general, the coupling reactions occurs through a mechanism that involves three characteristic steps shown in Figure 1.[24] First, oxidative addition of an aryl/ alkenyl halide to Pd(0) affords a Pd(II) intermediate. Transmetalation between this complex and some nucleophilic group (carbon- or heteroatom-based) affords a new Pd(II) intermediate. Reductive elimination regenerates the active Pd(0) catalyst while forming the desired bond of the product. In this process, the rate determining step depends upon the nature of the aryl halide. For aryl chlorides and unactivated aryl bromides, it is found that the oxidative addition step is the rate determining step.



R = carbon or hetroatom based nucleophile

M = alkali metal, X = halogen

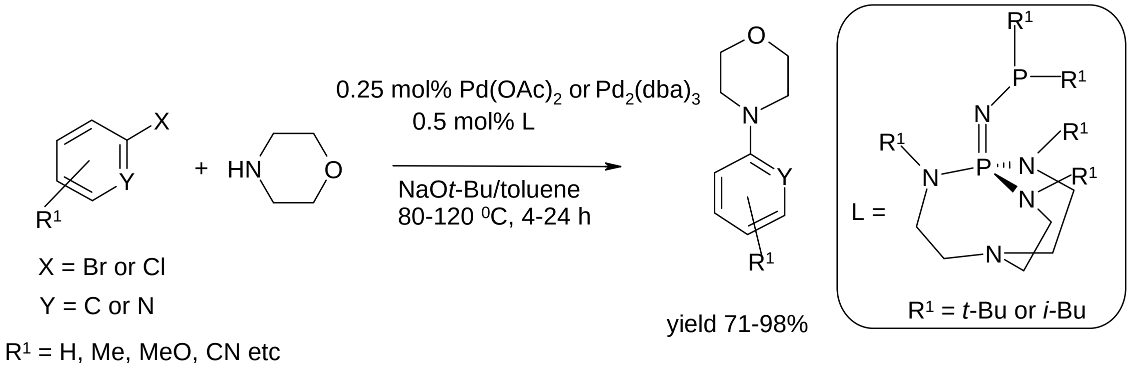
Figure 1. Generalized mechanism for palladium-catalyzed cross-coupling reactions.

4.31 Buchwald-Hartwig Reaction (*C-N bond formation*)

As a result of the pioneering efforts of the groups of Buchwald and Hartwig, palladium-catalyzed C-N bond formation from aryl halides and triflates has recently emerged as an extremely powerful tool for the synthesis of aniline derivatives which are important to a diverse array of fields, such as pharmaceuticals, agrochemicals and photography.[25] Activated aryl bromides and iodides can be successfully transformed to the corresponding aryl amines by employing simple copper[26] or (recently) iron salts[27] with various ligands as catalysts and also under ligand-free conditions. However, application of a similar method using unreactive aryl chlorides, especially possessing deactivated substituents on benzene ring, require special attention because of their easy availability and cost efficiency that necessitates an exclusive catalyst design for thriving coupling reaction.[20,28] To achieve this goal, new classes of ligands have been designed for the amination process.[22-23] They include 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) and 1,1'-bis(diphenylphosphino)ferrocene (DPPF) or 1,1'-bis(di-*t*-butylphosphino) ferrocene (D*t*-BPF).[29] However, these ligands do not give good results in case of unactivated aryl chlorides. Later, Koie and co-workers reported tri-*t*-butylphosphine as a ligand for the coupling of aryl chlorides. But this is not stable to air and moisture.[30] Buchwald and co-workers have developed a series of biarylphosphine ligands which are more stable in air and allow reactions to proceed with short reaction times, low catalyst loadings for the amination of aryl chlorides at room temperature.[31]

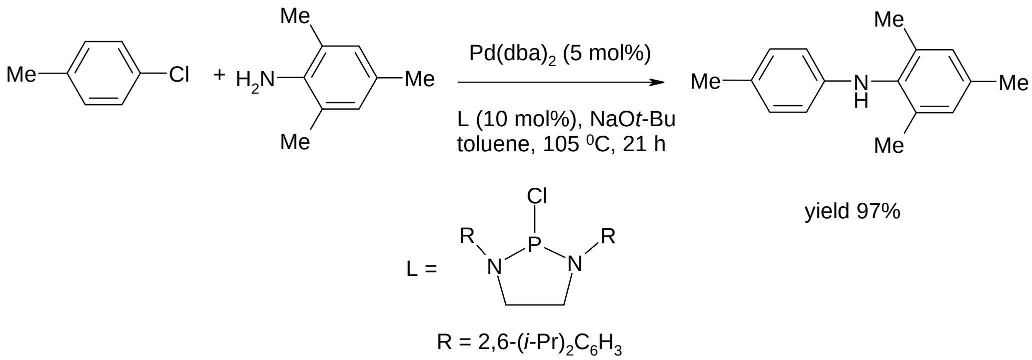
Hartwig and co-workers developed a bulky ligand with one di-*tert*-butylphosphinyl and one dicyclohexylphosphinyl group [Josiphos ligand] for the amination of heteroaryl chlorides with primary amines and related nucleophiles in high yield at room temperature or with mild heating.[32] This ligand is air stable and the turnover numbers are very high with loadings of metal salt and ligand between 10 and 50 ppm. Monodentate *N*-substituted heteroarylphosphines have been used for the coupling of aryl and heteroaryl chlorides by Beller and co-workers.[33] This was the first report for the palladium-catalyzed amination of aryl halides in the presence of *N*-substituted heteroarylphosphines and the turnover numbers are up to 8000. Verkade and co-workers designed a new ligand which can be applied for the coupling of aryl and heteroaryl halides with base sensitive functional groups for the amination of bulky aryl amines in good to excellent yields.[34] For the first time, vinyl bromides have been successively coupled with a variety of amines to produce imines and enamines at room temperature by this catalytic system (Scheme 4.7).

Scheme 4.7



Ackerman *et al* have reported the use of a cyclic diaminochlorophosphine as a ligand for the palladium-catalyzed C-N bond formation.[35] By making use of this phosphine, sterically hindered amines were successively coupled with unactivated aryl chlorides. Thus the amination of *p*-chlorotoluene with mesityl amine in the presence of Pd(dba)$_2$ and chlorophosphine as ligand affords the coupled product in good yield (Scheme 4.8). However, the chlorophosphine ligand is not that cheap and therefore, avenues exist for exploring inexpensive ligands.

Scheme 4.8

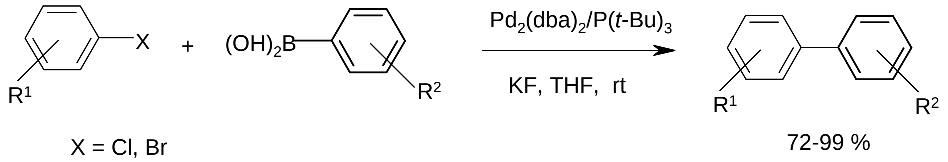


4.32 *Suzuki-Miyaura Coupling*

The Suzuki cross-coupling reaction is an efficient method for carbon-carbon bond formation and has been applied to a variety of reactions, ranging from natural-products synthesis to materials chemistry, including large-scale production. Among the attractive features of the Suzuki reaction are the wide availability, stability to air, moisture and low toxicity of boronic acids, as well as the facile removal of the boron-containing side products. Most important of all, the coupling proceeds with high regio- and stereo-selectivity, and is little affected by steric hindrance.[36] Various catalysts/ligands have been designed to facilitate the coupling. Some of these are discussed here.

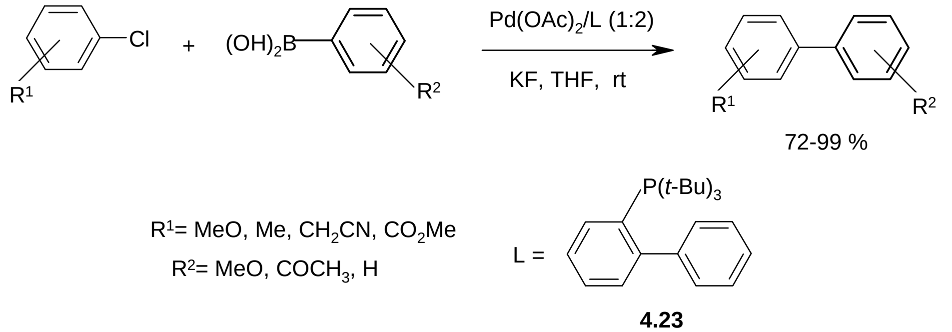
Fu and co-workers developed an efficient catalytic system for aryl and vinyl halides and triflates under mild conditions with good yields.[37] With these versatile catalysts, electronically and sterically diverse reactants, including electron-rich aryl chlorides, can be cross-coupled at room temperature (Scheme 4.9). The steric bulk and the electron-richness of the phosphine are the keys to activate these systems.

Scheme 4.9



Buchwald and his co-workers have prepared a series of dialkylbiarylphosphines which are applicable to a wide variety of Pd-catalyzed cross-coupling reactions.[38] Aryl bromides, unactivated aryl chlorides, aryl tosylates, a variety of hetero aryl systems and very much hindered substrates can be employed in conjunction with these ligands with low catalyst loadings at room temperature. For example, conditions aryl chlorides can be coupled with boronic acids under mild reaction conditions in the presence of ligand **4.23** (Scheme 4.10) to afford coupled products in very good yields.[31]

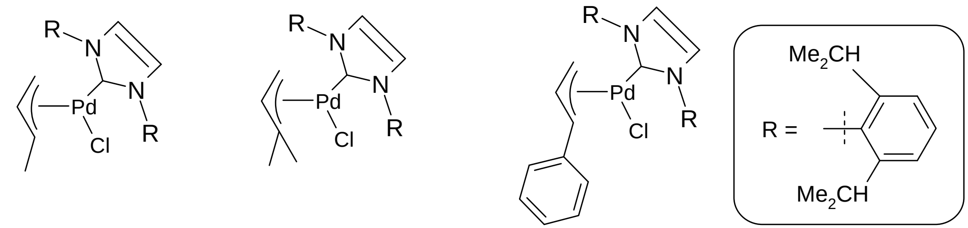
Scheme 4.10



4.23

Later, the same group reported that the addition of *ortho*-substituents on the bottom ring of the biarylphosphine lead to significant increase in activity and stability by preventing palladacycle formation.[39] Several water soluble alkylphosphines and sulfonated phosphines have also been prepared to facilitate the Suzuki and Sonogashira couplings in aqueous or organic/water biphasic solvent systems.[40] But these systems are not general and the range of substrate scope is limited. However, the water soluble sulfonated ligands have been used for a wide variety of substrates, including highly functionalized aryl chlorides or heteroaryl halides with either aryl or alkyl boronic acids in aqueous media in Suzuki and Sonagashira couplings.[41]

Nolan *et al* have developed a new class of (NHC)Pd(R-allyl)Cl complexes (**4.24a-c**; Figure 2) which can be applied to a variety of cross-coupling reactions under mild conditions. The complexes are highly stable to air and moisture. A wide range of aryl bromides, chlorides and triflates can be coupled with boronic acids at room temperature at extremely low catalyst loadings (0.05 mol %) (Scheme 4.11). The loading of the catalyst depends upon the temperature.[21b] The complexes (NHC)Pd(R-allyl)Cl (**4.23a-c**) can also be used in *N*-aryl amination.



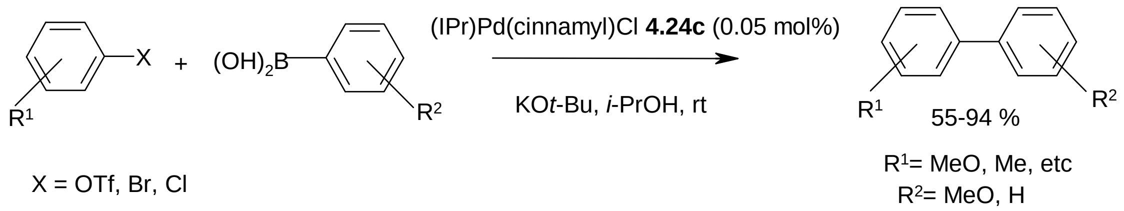
(IPr)Pd(crotyl)Cl **4.24a**
crotyl = 3-methylallyl

(IPr)Pd(prenyl) Cl **4.24b**
prenyl = 3,3-dimethylallyl

(IPr)Pd(cinnamyl)Cl **4.24c**
cinnamyl = 3-phenylallyl

Figure 2. Structures of (NHC)Pd(II) pre-catalysts efficient in Suzuki-Miyaura and/or Buchwald-Hartwig reactions.

Scheme 4.11



Thus it can be seen that developing new ligand systems for Pd-catalyzed cross-coupling reactions is still a fertile area for exploration.

OBJECTIVES OF THE PRESENT WORK-PART B

The main objective of this part of the work was to study the use of the inexpensive cyclodiphosphazane $[ClPN(t\text{-}Bu)]_2$ as a ligand in the palladium-catalyzed cross-coupling reactions such as Buchwald-Hartwig amination and Suzuki [also referred to as Suzuki-Miyaura] reactions with aryl halides (X = Cl, Br).

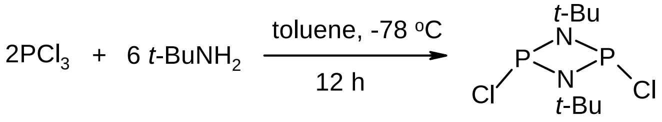
Chapter 5

RESULTS AND DISCUSSION

5.1 Synthesis of cyclodiphosph(III)azane [ClPN-*t*-Bu]$_2$ (1)

The main precursor cyclodiphosph(III)azane [ClPN-*t*-Bu]$_2$ [δ(P) 207.9] was prepared by using a literature procedure[41] and purified by vacuum distillation (110 ^{o}C/ 3 mm of Hg) (Scheme 1).

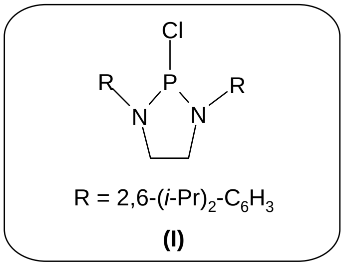
Scheme 1



1 [δ(P): 207.9]

5.2 Cyclodiphosphazane [ClPN-*t*-Bu]$_2$ as a ligand in palladium-catalyzed C-N and C-C bond formation- Rationale for its usage

Aromatic C-C and aromatic C-N bond formation by organometallic catalysts are among the most significant reactions in organic chemistry. Even if outstanding progress has been made, there are still significant challenges in utilizing substrates such as aryl chlorides, hindered aryl halides and hindered amines under economically viable reaction conditions. In this context, a number of palladium-based catalytic systems have been examined for cross-coupling reactions.[21-22] However, the ligands being used in most of these coupling reactions are very expensive. In one of the papers [*Angew. Chem., Int. Ed.* **2006**, *45*, 7627], Ackermann and his coworkers utilized the cyclic chloro-phosphorus ligand (**I**) that requires the preparation of rather expensive substituted 1,2-diaminoethane. Since we use very inexpensive precursors [PCl$_3$ and *t*-butylamine] to synthesize cyclodiphosphazane [ClPN(*t*-Bu)]$_2$ (**1**) that has been very frequently used in our laboratory[15, 16c] and since this P^{III} compound can act as a ligand, we became curious to see if it can be used to activate N-C/C-C bond formation in [Pd] catalyzed reactions. The results are reported herein.

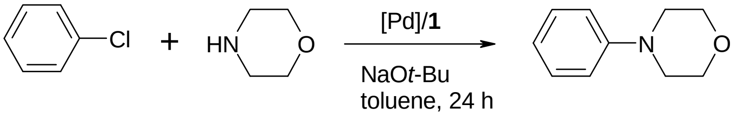


(I)

5.3 Buchwald-Hartwig amination of chloro- and bromo-arenes

Our initial experiments were focused on the coupling of chlorobenzene with morpholine. In the absence of ligand $[ClPN(t\text{-}Bu)]_2$ **(1)**, the reaction did not proceed to give the coupled product, *N*-phenyl morpholine (Table 1 entry 1). However, in the presence of ligand (12 mol%) and Pd_2dba_3 (3 mol%) at 80 °C, the product was obtained in 25% yield. No significant improvement in the yield was observed by changing the Pd-catalyst or by increasing the temperature (Table 1, entries 3-6). Interestingly, increasing temperature to 120 °C resulted in obtaining 71% of the coupled product (Table 1, entry 7) even when the concentration of the catalyst/ligand was a bit low.

Table 1. Optimization of reaction conditions for the amination of chlorobenzene with morpholine[a]

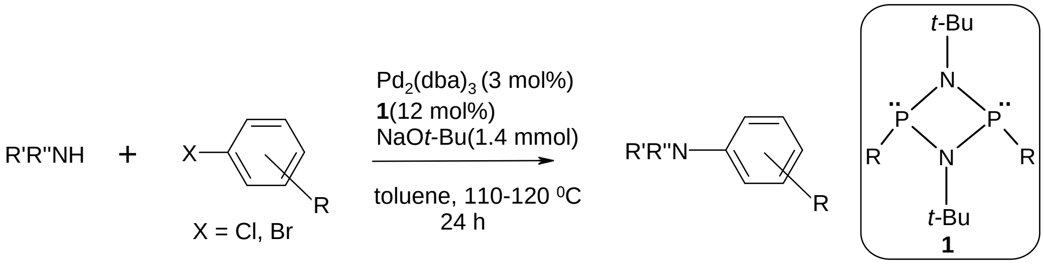


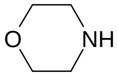
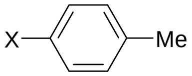
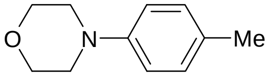
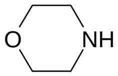
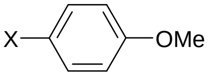
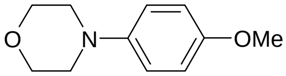
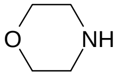
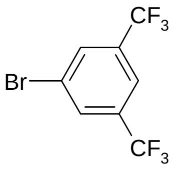
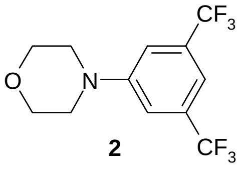
Entry	Pd source (mol%)	Ligand (**1**) (mol%)	T (°C)	Yield (%)^{b}
1	Pd_2dba_3 (3)	-	120	nr
2	Pd_2dba_3 (3)	12	80	25
3	$Pd(dba)_2$ (5)	10	110	38
4	$Pd(dba)_2$ (6)	12	110	43^{c}
5	$Pd(OAc)_2$ (6)	12	110	31
6	$[Pd(allyl)Cl]_2$(3)	12	110	28
7	Pd_2dba_3 (2)	8	120	71
8	Pd_2dba_3 (2.5)	10	90	27
9	Pd_2dba_3 (2.5)	10	120	80
10	Pd_2dba_3 (3)	12	120	94^{c}

[a]Reaction conditions: chlorobenzene (1.0 mmol), morpholine (1.2 mmol), NaO*t*-Bu (1.4 mmol), toluene (3 mL), 24 h (reaction times not optimized). [b]Yields were established by GC-MS with hexadecane as internal standard. [c]Isolated yield.

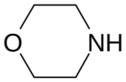
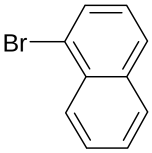
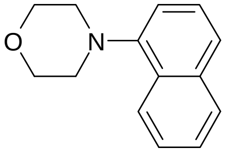
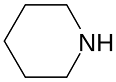
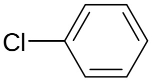
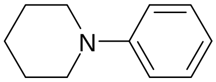
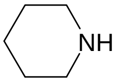
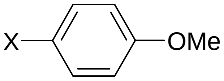
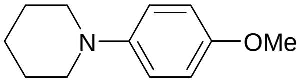
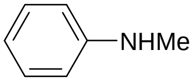
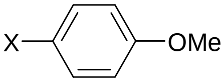
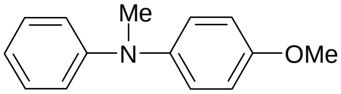
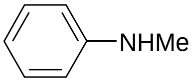
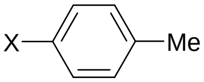
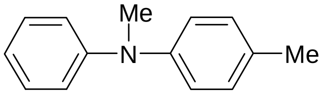
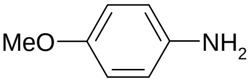
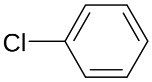
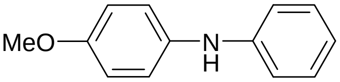
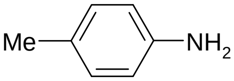
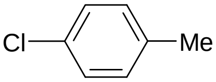
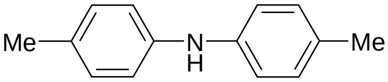
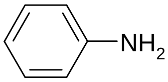
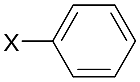
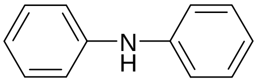
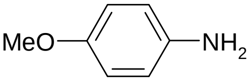
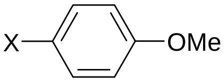
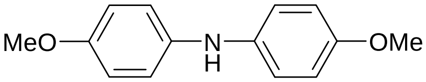
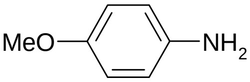
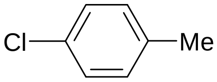
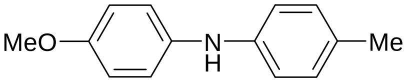
As expected, decreasing the temperature to 90 °C drastically decreased the yield (Table 1, entries 8-9). Finally, the reaction conditions were optimized by keeping the temperature constant at 120 °C and slightly increasing the concentration of catalyst and ligand to produce the coupled product up-to 94% isolated yield (Table 1, entry 10). On the basis of this, the coupling between a variety of aryl chlorides/ bromides and amines were investigated. As shown in Table 2, morpholine was coupled with several deactivated aryl chlorides and bromides to produce the *N*-aryl morpholine derivatives in good yield (entries 1-2). It is worth mentioning that 3,5-trifluoromethyl phenyl bromide upon coupling with morpholine under our optimized reaction conditions gave the coupled product (**2**) in 68% yield (entry 3; see Figure 1 for X-ray structure). We were also able to couple the bulkier bromide (1-bromonaphthalene) with morpholine using our new ligand system (entry 4). Piperidine was also coupled with electron rich chlorides and bromides to give the desired aryl amines in good yields (entries 5-6). Reaction of *N*-methyl aniline with aryl chlorides and bromides afforded the desired products in moderate to good yields (entry 7-8). Substituted anilines couple with chlorobenzene and 4-chlorotoluene to give the desired products in moderate to good yields (entries 9-11). Self coupling also occurs when the amine component is cyclohexylamine, as revealed by GC-MS. This is a limitation. *p*-Anisidine gave lower yields with 4-chlorotoluene and 4-chloroanisole (entries 12-13). These results are also summarized in Table 2. It is heartening to note that subsequent to the publication of our work, another group in the school also could perform N-C coupling, although other coupling agents (but more expensive) worked better.[42]

Table 2. *N*-aryl-amination of aryl chlorides and bromides.[a]



Entry	amine	Ar-X	Product	Yield [b] (%)
1				75 (X = Cl) 80 (X = Br)
2		 X = Br, Cl		73 (X = Cl) 75 (X = Br)
3			 **2**	68

Contd.....

4				56
5				73[c]
6		 X = Br, Cl		63[c] (X = Cl) 66 (X = Br)
7		 X = Br, Cl		55 (X = Cl) 61 (X = Br)
8		 X = Br, Cl		62 (X = Cl) 68 (X = Br)
9				60
10				56
11				51[d] (X = Cl) 54[d] (X = Br)
12				40 (X = Cl) 48 (X = Br)
13				44

[a]Reaction conditions: chlorobenzene (1.0 mmol), morpholine (1.2 mmol), Pd_2dba_3 (3.0 mol %), **1** (12 mol %), NaO-*t*-Bu (1.4 mmol) and toluene (3 mL) were heated at 120 °C (oil bath), with continuous stirring for 24 h under N_2 atmosphere.

[b]Isolated yields.

[c]Reaction scaled up to 5 mmol in 8 mL toluene. [d]Yields were established by GC-MS with hexadecane as internal standard.

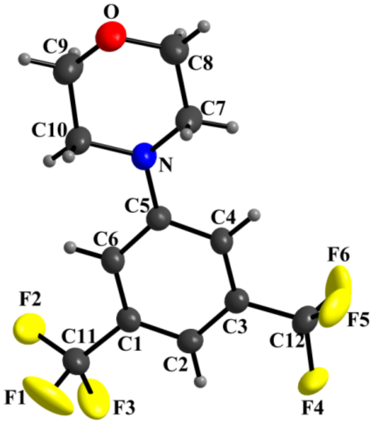
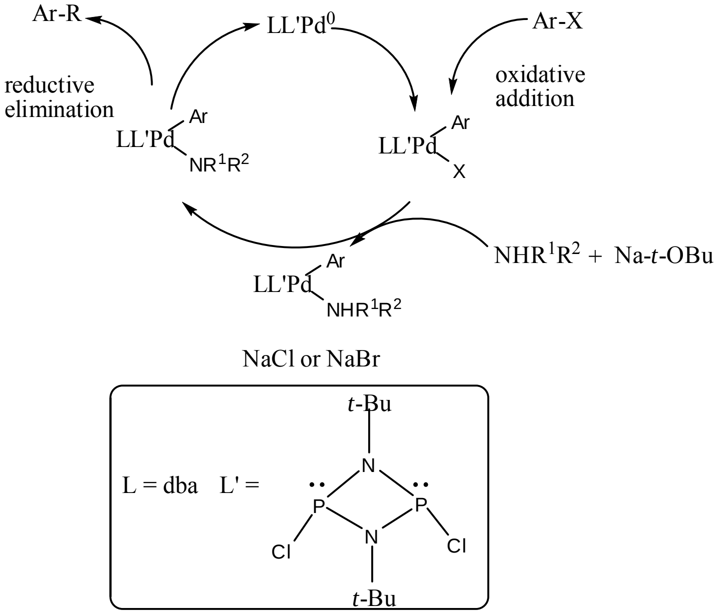


Figure 1. Molecular structure of compound **2** (Table 2, entry 3). Selected bond lengths [Å] with esd's in parentheses. N-C(5) 1.386(5), N-C(10) 1.453(5), N-C(7) 1.459(5), O-C(9) 1.411(5), O-C(8) 1.413(5). The CF_3 groups show some disorder.

A possible concise pathway for this N-C bond formation is given below in Scheme 2 wherein the coordination of ligand **1** to palladium is indicated. The ^{31}P NMR spectrum of the mixture of **1** and Pd_2dba_3 showed a peak at δ(P) 318.9 (along with many other peaks), consistent with the formation of a Pd-cyclophosphazane complex which might be responsible for this catalytic activity. However, we have not succeeded in isolating this species because of the presence of other products. Due to the hydrolytic instability of **1** we have not proceeded with further characterization.

Scheme 2

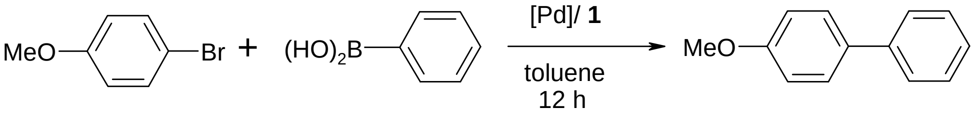


L and L' stoichiometry variable

5.4 Suzuki coupling

As a standard Suzuki (Suzuki-Miyaura) cross-coupling reaction for screening purposes, the coupling of 4-bromoanisole with phenyl boronic acid has been examined under different conditions (Table 3). In the absence of ligand (**1**), using Pd(OAc)$_2$ (5 mol%) and K$_3$PO$_4$ as base at 90 ^{0}C the coupled product 4–methoxy biphenyl was obtained in 31% yield (Table 3, entry 1). However, in the presence of ligand (10 mol%) and KO*t*-Bu, the yield was increased to 71% (entry 2). No significant improvement was observed by using Pd(dba)$_2$/NaO-*t*-Bu (entry 3) or Pd(OAc)$_2$/Cs$_2$CO$_3$ (entry 4). Interestingly, with 5 mol% of Pd(OAc)$_2$ as catalyst and K$_3$PO$_4$ (two equiv) as the base, the yield was increased to 92% (entry 5). As expected, decreasing the load of Pd(OAc)$_2$, or ligand (**1**) concentration resulted in somewhat lower yield (76%) of the coupled product (entry 6). The yield was increased to 80% when 5 mol% each of Pd(OAc)$_2$ and ligand were used (entry 7). It is noteworthy that the reaction proceeds well when Pd(OAc)$_2$ was replaced by Pd$_2$(dba)$_3$ (entry 8). As can be seen from the table, increasing the concentration of Pd$_2$(dba)$_3$ and ligand furnishes the coupled product in good yield (entry 9). Thus cyclophosphazane (**1**) in combination with Pd(OAc)$_2$ or Pd$_2$(dba)$_3$ and K$_3$PO$_4$ (base) in toluene provided an improved catalytic system for this transformation (entries 5 and 8). We chose conditions corresponding to entry 5 for further reactions; a few reactions using conditions corresponding to entry 8 were also conducted since a Pd(0) catalyst is used in this case. The results are summarized in Table 3.

Table 3. Various reaction conditions used for the Suzuki cross-coupling of 4-bromo anisole with phenylboronic acid in this work[a]



Entry	Pd source (mol %)	Ligand (**1**) (mol %)	Base	Yield (%)[b]
1	$Pd(OAc)_2$ (5)	-	K_3PO_4	31
2	$Pd(OAc)_2$ (5)	10	KO*t*-Bu	71
3	$Pd(dba)_2$ (5)	10	NaO*t*-Bu	65
4	$Pd(OAc)_2$ (5)	10	Cs_2CO_3	65
5	**$Pd(OAc)_2$ (5)**	**10**	**K_3PO_4**	**92**
6	$Pd(OAc)_2$ (2)	4	K_3PO_4	76
7	$Pd(OAc)_2$ (5)	5	K_3PO_4	80[d]
8	Pd_2dba_3 (1)[c]	4	K_3PO_4	80
9	$Pd_2(dba)_3$ (2.5)[c]	10	K_3PO_4	92[d]

[a] Reaction conditions: 4-bromoanisole (0.5 mmol), phenylboronic acid (0.75 mmol), Base (1.0 mmol), toluene (2 mL), 12 h (reaction time not optimized), temperature 90-100 °C (oil bath).

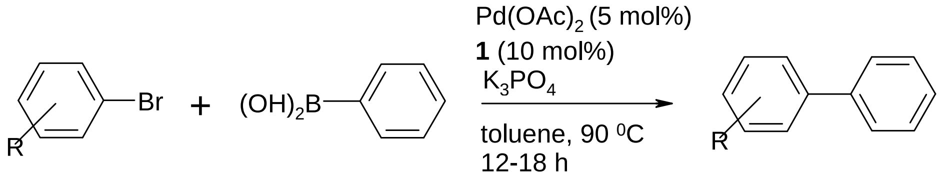
[b] Isolated yield.

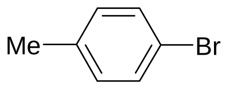
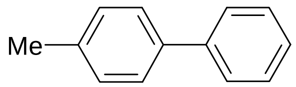
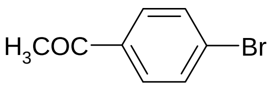
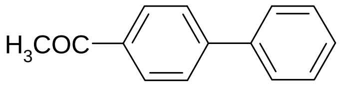
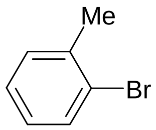
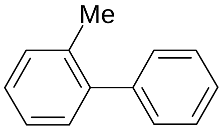
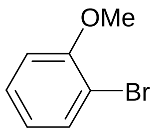
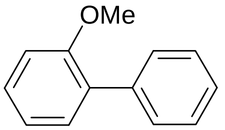
[c] Corresponds to two palladium atoms per molecule.

[d] Yields established by GC-MS with hexadecane as an internal standard.

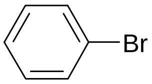
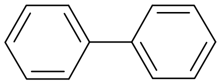
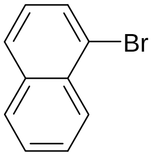
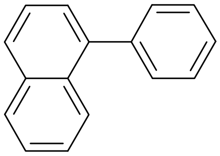
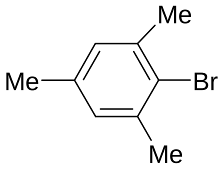
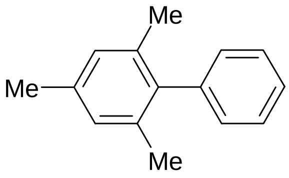
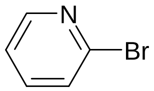
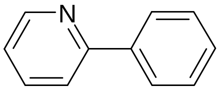
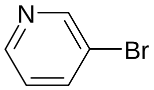
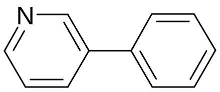
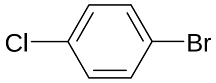
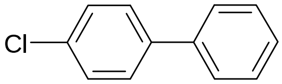
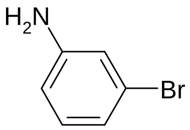
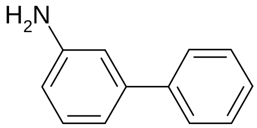
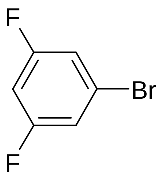
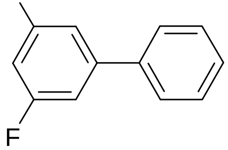
We were pleased to find that the above protocol afforded high yields of the coupled products with aryl bromides bearing a variety of substituents (Table 4, entries 1-5). We were also able to couple the bulkier bromides (1-bromonaphthalene and mesityl bromide) with **2** using our conditions to give the desired products in decent yields (entries 6-7). It is worth mentioning that the hetero-aryl bromides such as 2-bromo pyridine and 3-bromo pyridine upon coupling with phenylboronic acid afforded the products in very good yields (entries 8-9). In addition, aryl halides which bear NH_2, F and Cl are tolerated under the cross-coupling conditions (entries 10-12) and the yields of the coupled products are excellent. The mechanism is along the standard lines[17] and hence is not elaborated here.

Table 4. Suzuki reaction of phenylboronic acid with different aryl and hetero-aryl bromides^{a}



Entry	Ar-X	Product	Yield ^{b} (%)
1			82
2			85
3			75
4			53

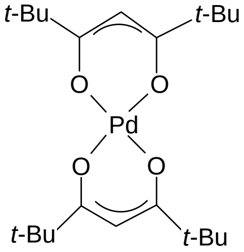
Contd….

5			85
6			65
7			62[c]
8			87
9			80
10			96[c]
11			86[c]
12			82[c]

---

[a]Reaction conditions: Aryl bromide (1.0 equiv), amine (1.2 equiv), K_3PO_4 (2.0 equiv.), toluene (0.25 M), 90 ^{0} C, 12 - 18 h. [b]Isolated yields. [c]Pd_2dba_3 (2 mol %) and **1** (8.0 mol%) were used.

Our conditions as given above may be compared with that of Bhanage *et al* who utilized the Pd-complex **II** along with K_2CO_3.[43] With bromobenzene, they have reported an yield of 92%, while in our case the corresponding yield was 85% which is comparable. We do admit that there are several other [Pd]-systems that work fairly well for this cross-coupling using aryl bromides,[44] but the ligand used in the present study is relatively easily prepared and affordable. We believe that this is a highlighting point. The results were better in N-C couplings as discussed above.



II

SUMMARY-PART B

We have demonstrated the use of a very inexpensive cyclodiphosphazane as a ligand in the palladium catalyzed *N*-arylation of various amines with aryl halides (X = Cl, Br) and Suzuki [Suzuki-Miyaura] coupling of various aryl bromides with phenyl boronic acid. The yields vary, but are in the range 51-94% in case of *N*- arylation and 62-96% for the Suzuki coupling.

EXPERIMENTAL SECTION

As mentioned earlier, essentially all the compounds, including the cyclodiphosphazane [ClPN-*t*-Bu]$_2$ [δ(P) 207.9][41] reported in this part of the study are known. The compounds Pd$_2$(dba)$_3$ and Pd(dba)$_2$ have been prepared by following the literature procedures.[45] General experimental conditions have already been described in Chapter 3. In this part, typical procedures adapted for the Buchwald-Hartwig amination and Suzuki coupling involving **1** are described.

6.1 General procedure for the Buchwald-Hartwig amination using the cyclodiphosphazane [ClPN(*t*-Bu)]$_2$ (1)

All the compounds reported here are well-known. Hence only representative procedures are given.

In an oven dried Schlenk tube, 1 mL of ligand [ClPN(*t*-Bu)]$_2$ (**1**) (R = Cl) (33 mg, 0.12 mmol, 12 mol%) of 0.120M solution in toluene, Pd$_2$dba$_3$ (28 mg, 0.03 mmol, 3 mol%) and 2 mL toluene were taken and stirred at room temperature for 30 min. To this solution, NaO*t*-Bu (135 mg, 1.4 mmol) and aryl halide (1.0 mmol) were added successively. After 15 min, amine (1.2 mmol) was added and the tube was sealed using a suba-seal septum. The mixture was stirred at 120 ^{o}C (oil bath) for 24 h. Subsequently, the reaction mixture was allowed to cool to room temperature and then quenched by adding EtOAc (4 mL). It was then filtered through a plug of celite and analyzed by GC-MS by using hexadecane as internal standard. Further purification of the product was achieved by silica gel column chromatography (eluent: hexane/EtOAc).

6.2 General procedure for the Suzuki coupling using cyclodiphosphazane [ClPN(*t*-Bu)]$_2$ (1)

All the compounds reported here also are well-known. In an oven dried Schlenk tube, 0.41 mL of ligand **1** (14 mg, 0.05 mmol, 10 mol%) of 0.120M solution in toluene,

$Pd(OAc)_2$ (5.6 mg, 0.025 mmol, 5 mol%) or [$Pd_2(dba)_3$ (9.2 mg, 0.01 mmol, 2 mol%)] and **1** (11 mg, 0.036 mmol, 8 mol%) of 0.120M solution in toluene and 1.6 mL toluene were taken and stirred at 90 ^{0}C for 30 min. To this solution, K_3PO_4 (212 mg, 1.0 mmol), aryl bromide (0.5 mmol) and phenylboronic acid (92 mg, 0.75 mmol) were added successively and the tube was sealed. The mixture was stirred at 90 ^{o}C (oil bath) for 12-18 h. Subsequently, it was allowed to cool to room temperature and then diluted by adding EtOAc (3 mL). It was then filtered through a plug of celite and the solvent removed by rotary evaporator. The crude material was purified by silica gel column chromatography (eluent: hexane/EtOAc).

6.3 X-ray structure of compound 2

Single crystal X-ray data for compound **2** were collected at 298 K on a Bruker AXS-SMART diffractometer using Mo-K_α radiation (λ = 0.71073 Å). The structure was solved and refined using standard methods.[46] All non-hydrogen atoms were refined anisotropically; hydrogen atoms were fixed by geometry or located by a Difference Fourier and refined isotropically; there was some disorder on the trifluoromethyl fluorine atoms but the overall structure was fine. Crystal data are summarized in Table 5.

Table 5. Crystal data for compound **2**[a]

Compound	**2**
Emp. formula	$C_{12}H_{11}F_6NO$
Formula weight	299.22
Crystal system	Monoclinic
Space group	*P2(1)/n*
a /Å	9.338
b /Å	7.752
c /Å	17.542
α/deg	90
β/deg	98.38
γ/deg	90
V /Å^3	1256.3
Z	4
D_{calc} /g cm^{-3}]	1.582
μ /mm^{-1}	0.161
F(000)	608
Data/ restraints/ parameters	2212/0/235
S	0.956
R1 [I>2σ(I)]	0.0843
wR2 [all data]	0.2530
Max./ min. residual electron dens. [eÅ^{-3}]	0.627/-0.187

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ and $wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{0.5}$

References

1) Balakrishna, M. S. *J .Organomet. Chem.* **2010**, *695*, 925.
2) (a) Reddy, V. S.; Krishnamurthy, S. S.; Nethaji, M. *J. Chem. Soc., Dalton Trans.* **1994**, 2661 and references cited therein. (b) Vijjulatha, M.; Kumara Swamy, K. C. Vittal, J. J.; Koh, L. L. *Polyhedron* **1999**, *18*, 2249.
3) (a) Lief, G. R.; Carrow, C. J; Stahl, L.; Staples, R. J. *Chem. Commun.* **2001**, 1562. (b) Briand, G. G.; Chivers, T.; Parvez, M.; Schatte, G. *Inorg. Chem.* **2003**, *42*, 525. (c) Balakrishna, M. S;. Mague, J. T. *Organometallics* **2007**, *26*, 4677. (d) Chandrasekaran, P.; Mague, J. T.; Balakrishna, M. S. *Polyhedron* **2008**, *27*, 80.
4) (a) Gonce, F.; Caminade, A. M.; Boutonnet, F.; Majoral, J. P. *J. Org. Chem.* **1992**, *57*, 970. (b) Kommana, P.; Kumara Swamy, K. C. *Inorg. Chem.* **2000**, *39*, 4384. (c) Kommana, P.; Pavan Kumar, K. V. P.; Kumara Swamy, K. C. *Indian J. Chem.* **2003**, *42A*, 2371. (d) Garcia, F.; Goodman, J. M.; Kowenicki, R. A.; McPartlin, M.; Riera, L.; Silva, M. A.; Wirsing, A.; Wright, D. S. *Dalton Trans*. **2005**, 1764. (e) Chandrasekaran, P.; Mague, J. T.; Balakrishna, M. S. *Dalton Trans*. **2009**, 5478.
5) (a) Chakravarty, M.; Kommana, P.; Kumara Swamy, K. C. *Chem. Commun.* **2005**, 5396. (b) Chakravarty, M.; Rama Suresh, R.; Kumara Swamy, K. C. *Inorg. Chem.* **2007**, *46*, 9819.
6) Balakrishna, M. S.; Krishnamurthy, S. S. *J. Organomet. Chem*. **1992**, *424*, 243.
7) Balakrishna, M. S.; Venkateswaran, R.; Mague, J. T. *Dalton Trans*. **2010**, 11149.
8) Balakrishna, M. S.; Venkateswaran, R.; Mague, J. T. *Inorg. Chem.* **2009**, *48*, 1398.
9) Balakrishna, M. S.; Suresh, D.; Mague, J. T. *Eur. J. Inorg. Chem*, **2010**, 4201.
10) Balakrishna, M. S.; Mohanty, S. *J. Chem. Sci*. **2010**, *122*, 137.
11) Rama Suresh, R.; Kumara Swamy, K. C. *Tetrahedron Lett*. **2009**, *50*, 6004.
12) (a) Lu, X.; Zhang, C.; Xu, Z. *Acc. Chem. Res*. **2001**, *34*, 535. (b) Kumara Swamy, K.C.; Bhuvan Kumar, N. N.; Balaraman, E.; Pavan Kumar, K. V. P. *Chem. Rev*. **2009**, *109*, 2551.
13) Bhuvan Kumar, N. N.; Chakravarty, M.; Kumara Swamy, K. C. *New J. Chem.* **2006**, 30, 1614.
14) Bhuvan Kumar, N. N.; Kumara Swamy, K. C. *Tetrahedron Lett*. **2008,** *49*, 7135.
15) Kumara Swamy, K. C.; Gangadhara Rao, G.; Rama Suresh, R.; Bhuvan Kumar, N. N.; Chakravarty, M. *J. Organomet. Chem*, **2010**, *695*, 1042.
16) (a) Satish Kumar, N.; Praveen Kumar, K.; Pavan Kumar, K. V. P.; Kommana, P.; Vittal, J. J.; Kumara Swamy, K.C. *J. Org. Chem.* **2004**, *69*, 1880. (b) Praveen Kumar, K.; Chakravarty, M.; Kumara Swamy, K.C. *Z. Anorg. Allg. Chem*. **2004**, *630*, 2063. (c) Kumara Swamy, K. C.; Praveen Kumar, K.; Bhuvan Kumar, N. N. *J. Org. Chem.* **2006**, *71*, 1002.
17) (a) Heck, R. F. In Comprehensive Organic Synthesis, Vol. 4 (Eds.: Trost, B. M. Fleming, I.), Pergamon, Oxford, 1991; (b) Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457. (c) Sambasivarao, K.; Kakali, L.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.
18) (a) Miyaura, N. *Top. Curr. Chem*. **2002**, *219*, 11. (b) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.
19) For a review on Pd-catalyzed coupling reactions of aryl chlorides, see Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed*. **2002**, *41*, 4176.
20) (a) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685. (b) Marion, N.; Navarro, O.; Mei, J.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101.
21) (a) Zim, D.; Buchwald, S. L. *Org. Lett.* **2003**, *5*, 2413. (b) Strieter, E. R.; Blackmond, D. G.; Buchwald, S. L. *J. Am. Chem. Soc*. **2003**, *125*, 13978. (c) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed*. **1999**, *38*, 2413. (d) Huang, X.; Anderson, K. W.; Zim, D.;

Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653. (e) Li, G. Y; Zheng, G.; Noonan, A. F. *J. Org. Chem.* **2001**, *66*, 8677. (g) Li, G. Y. U.S. Patent 20040147392, 2004; *Chem. Abstr.* **2004**, *141*, 142192.

22) (a) Marion, N.; Navarro, O.; Mei, J.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101. (b) Suzuki, K.; Hori, Y.; Kobayashi, T. *Adv. Synth. Catal.* **2008**, *350*, 652. (c) Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 15914. (d) Dogan, O.; Demira, S.; Ozdemira, I.; Cetinkaya, B. *Appl. Organometal. Chem.* **2011**, *25*, 163. (e) Lu, B.; Li, P.; Fu, C.; Xue, L.; Lin, Z.; Ma, S. *Adv. Synth. Catal.* **2011**, *353*, 100.

23) Christmann, U; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366.

24) For some general reviews of palladium-catalyzed C-N bond formation, see (a) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046. (b) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125.

25) Selected examples for copper catalyzed amination: (a) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3096. (b) Xu, H.; Wolf, C. *Chem. Commun.* **2009**, 1715. (c) Ma, D.; Zhang, Y.; Yao, J.; Wu, S.; Tao, F. *J. Am. Chem. Soc.* **1998**, *120*, 12459. (d) Zhang, H.; Cai, Q.; Ma, D. *J. Org. Chem.* **2005**, *70*, 5164. (e) Rout, L.; Jammi, S.; Punniyamurthy, T. *Org. Lett.* **2007**, *9*, 3397. (f) Xia, N.; Taillefer, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 337.

26) (a) Correa, A.; Bolm, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 8862. (b) Correa, A.; Bolm, C. *Chem. Eur. J.* **2008**, *14*, 3527. (c) Correa, A.; Bolm, C. *Adv. Synth. Catal.* **2008**, *350*, 391.

27) (a) Li, G. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513. (b) Chen, G.; Lam, W. H.; Fok, W. S.; Lee, H. W.; Kwong, F. Y. *Chem. Asian J.* **2007**, *2*, 306. (c) Shen, Q.; Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6586.

28) Schlummer, B.; Scholz, U. *Adv. Synth. Catal.* **2004**, *346*, 1599.

29) Nishiyama, M.; Yamamoto, T.; Koie, Y.; *Tetrahedron Lett.* **1998**, *39*, 617.

30) Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413.

31) Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2005**, *44*, 1371.

32) Rataboul, F.; Zapf, A.; Jackstell, R.; Harkal, S.; Riermeier, T.; Monsees, A.; Dingerdissen, U.; Beller, M. *Chem. Eur. J.* **2004**, *10*, 2983.

33) Reddy, Ch. V.; Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2008**, *73*, 3047.

34) Ackermann, L.; Spatz, J. H.; Gschrei, C. J.; Born, R.; Althammer, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 7627.

35) Suzuki, A. *Chem. Commun.* **2005**, 4759.

36) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020.

37) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.

38) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685.

39) (a) Moore, L. R.; Shaughnessy, K. H. *Org. Lett.* **2004**, *6*, 225. (b) Western, E. C.; Daft, J. R.; Johnson II, E. M.; Gannett, P. M.; Shaughnessy, K. H. *J. Org. Chem.* **2003**, *68*, 6767. (c) Gulyas, H.; Szollosy, A.; Szabo, P.; Halmos, P.; Bakos, J. *Eur. J. Org. Chem.* **2003**, 2775. (d) DeVasher, R. B.; Moore, L. R.; Shaughnessy, K. H. *J. Org. Chem.* **2004**, *69*, 7919.

40) Anderson, K. W.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2005**, *44*, 6173.

41) Allcock, H. R. *Inorg. Synth.* **1972**, *25*, 8.

42) Sateesh Kumar, A.; Nagarajan, R. *Org. Lett.* **2011**, *13*, 1398.

43) Nandurkar, N.S.; Bhanage, B. M. *Tetrahedron* **2008**, *64*, 3655.

44) (a) Godoy, F.; Segarra, C.; Poyatos, M.; Peris, E. *Organometallics* **2011**, *30*, 684. (b) Escarcega-Bobadilla, M. V.; Teumaa, E.; Masdeu-Bulto, A. M.; Gomez, G. *Tetrahedron* **2011**, *67*, 421. (c) Fan, X.-H.; Yang, L.-M. *E. J. Org. Chem.* **2011**, 1467.

45) (a) Fairlamb, I. J. S.; Kapdi, A. R.; Lee, A. F. *Org. Lett.* **2004**, *6*, 4435. (b) Takahashi, Y.; Ito, Ts.; Sakai, S.; Ishii, Y. *J. Chem. Soc. D*, **1970**, 1065. (c) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J.J.; Ibers, J. A. *J. Organomet. Chem*. **1974**, *65*, 253.

46) (a) Sheldrick, G. M. *SADABS, Siemens Area Detector Absorption Correction*, University of Göttingen, Germany, **1996**. (b) Sheldrick, G. M., SHELX-97- *A program for crystal structure solution and refinement*, University of Göttingen, **1997**. (c) Sheldrick, G. M. *SHELXTL NT Crystal Structure Analysis Package*, Bruker AXS, Analytical X-ray System, WI, USA, **1999**, version 5.10.

A) Copies of $^1H/^{13}C$ NMR spectra for representative compounds

PART A: Compounds 25, (*E*)-36, (*Z*)-36, 49, 59, 71, 74, and 79.

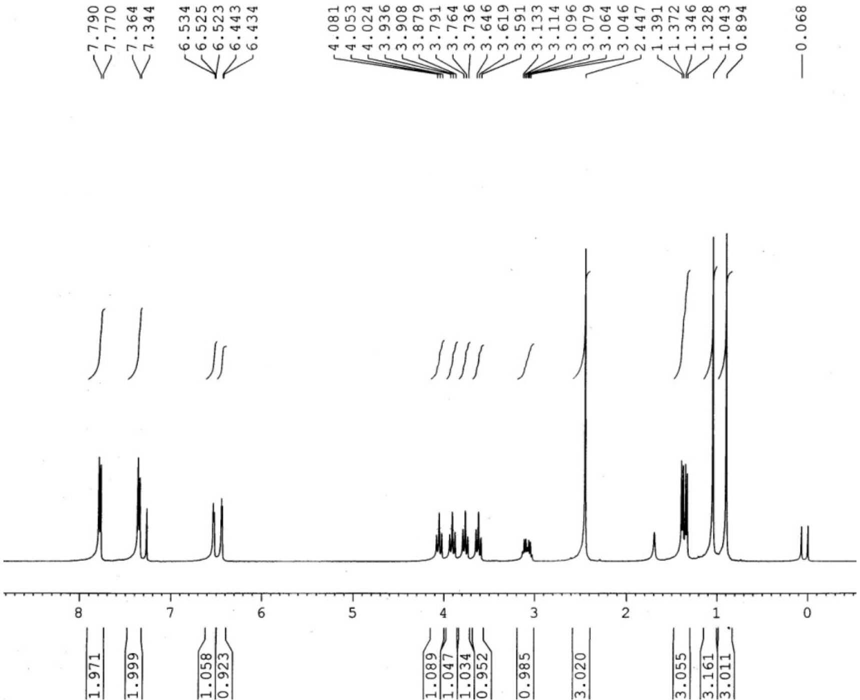


Fig. A1. ^1H NMR spectrum of compound **25**

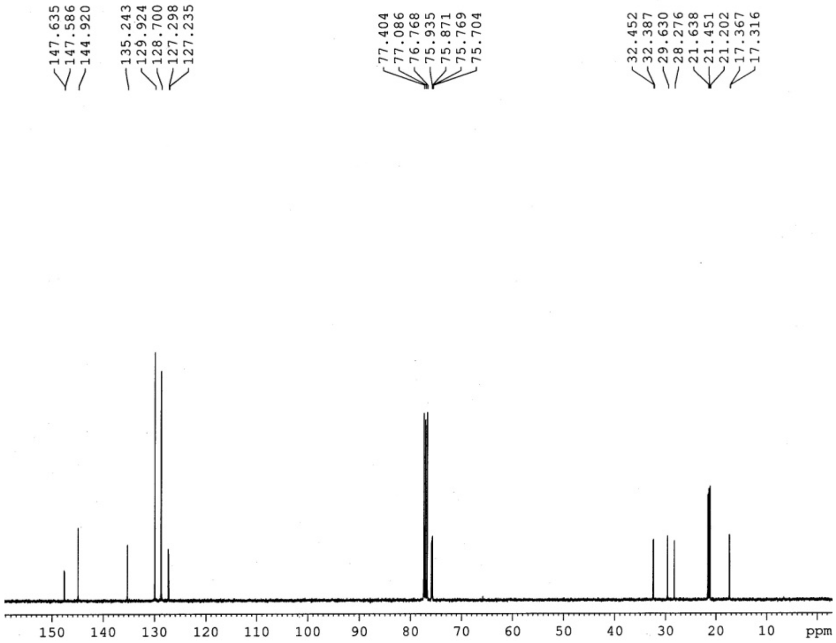


Fig. A2. ^{13}C NMR spectrum of compound **25**

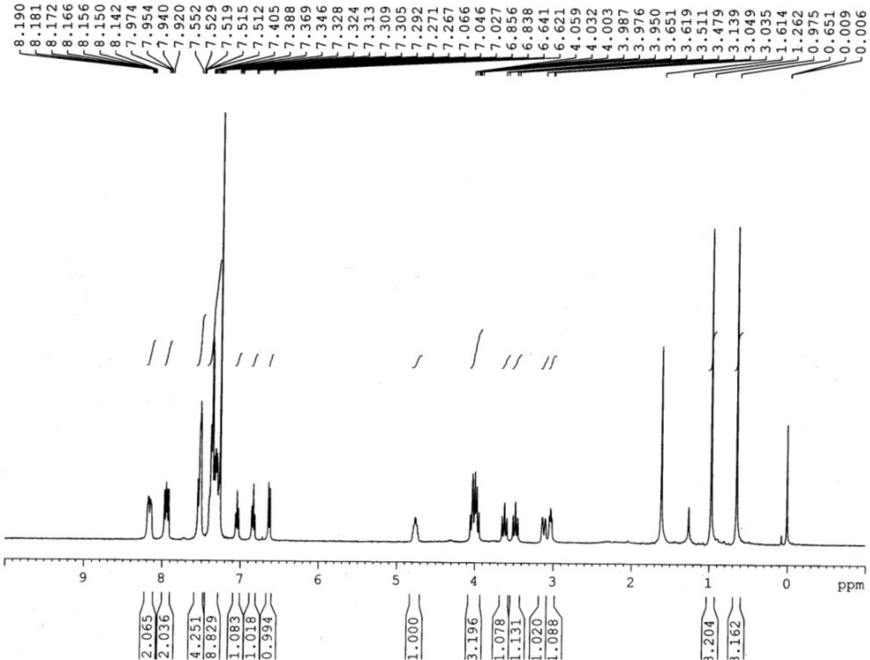


Fig. A3. ^{1}H NMR spectrum of compound **(*E*)-36**

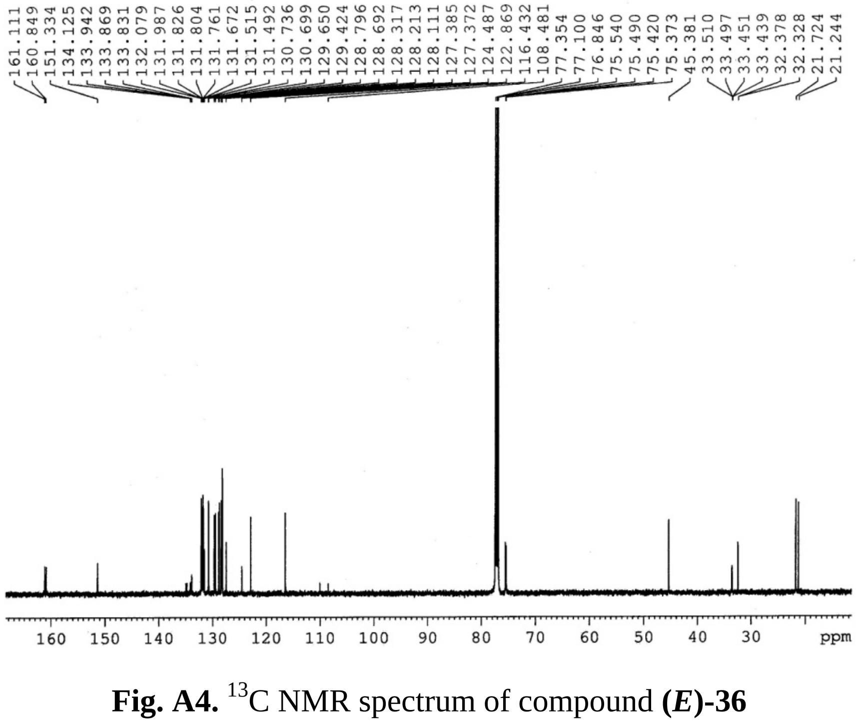


Fig. A4. ^{13}C NMR spectrum of compound **(*E*)-36**

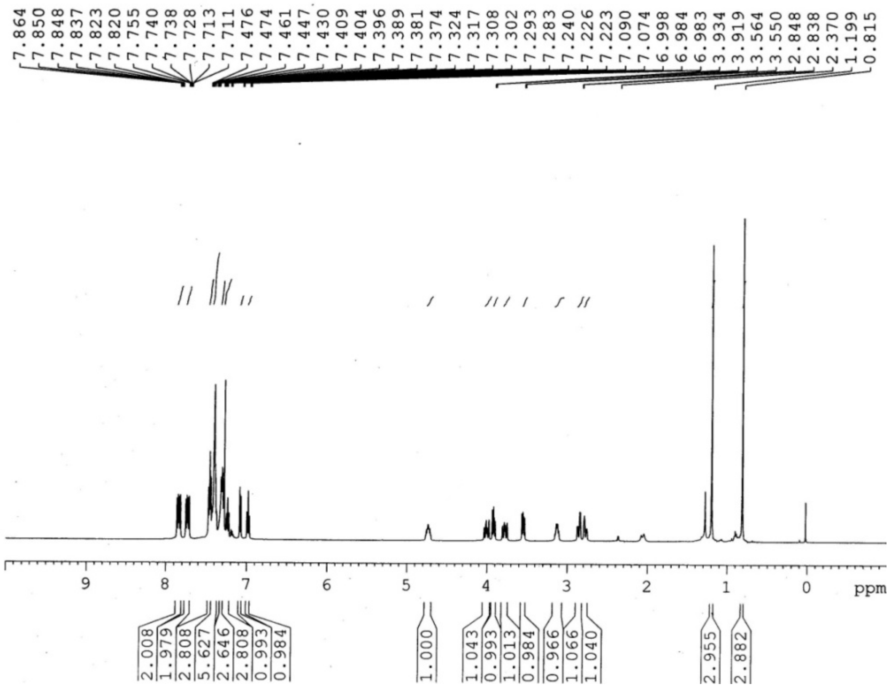


Fig. A5. ^{1}H NMR spectrum of compound **(*Z*)-36**

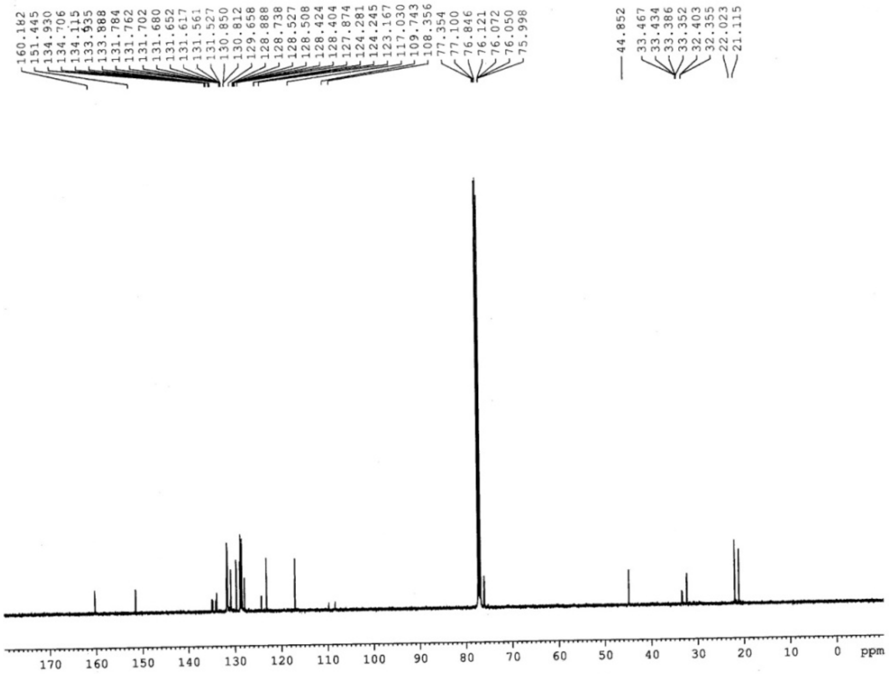


Fig. A6. ^{13}C NMR spectrum of compound **(*Z*)-36**

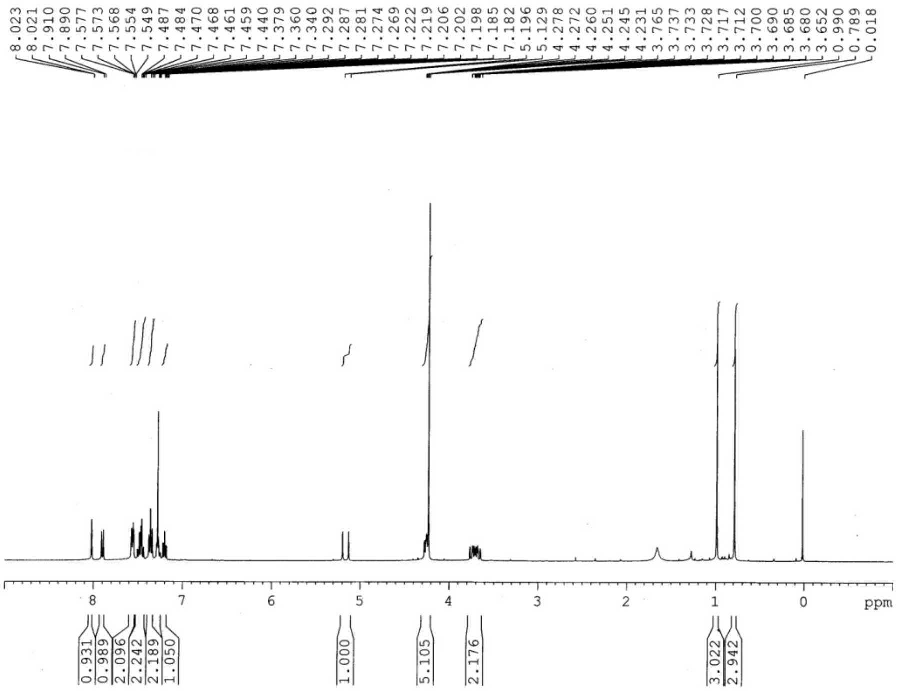


Fig. A7. ^{1}H NMR spectrum of compound **49**

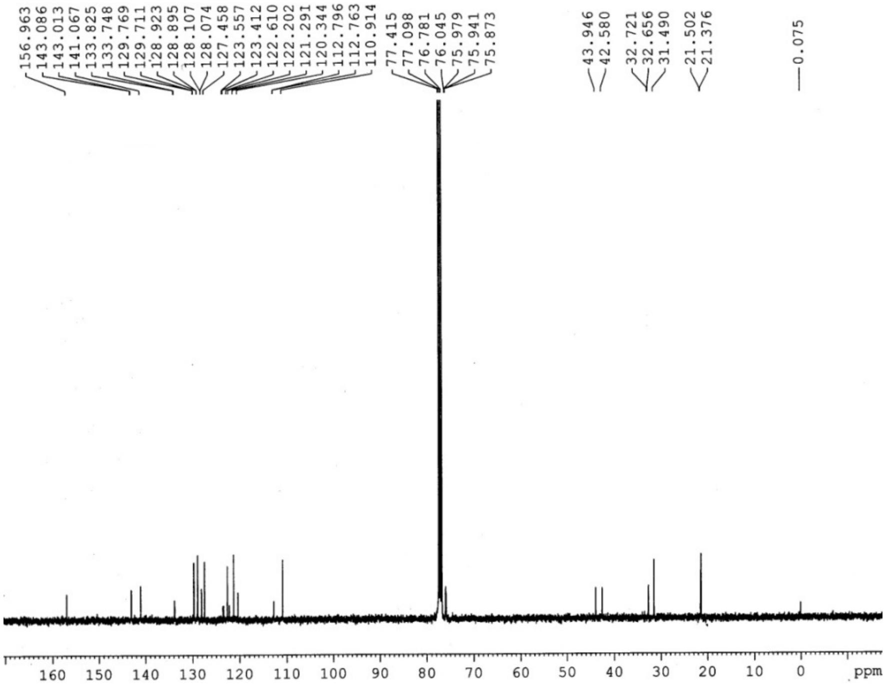


Fig. A8. ^{13}C NMR spectrum of compound **49**

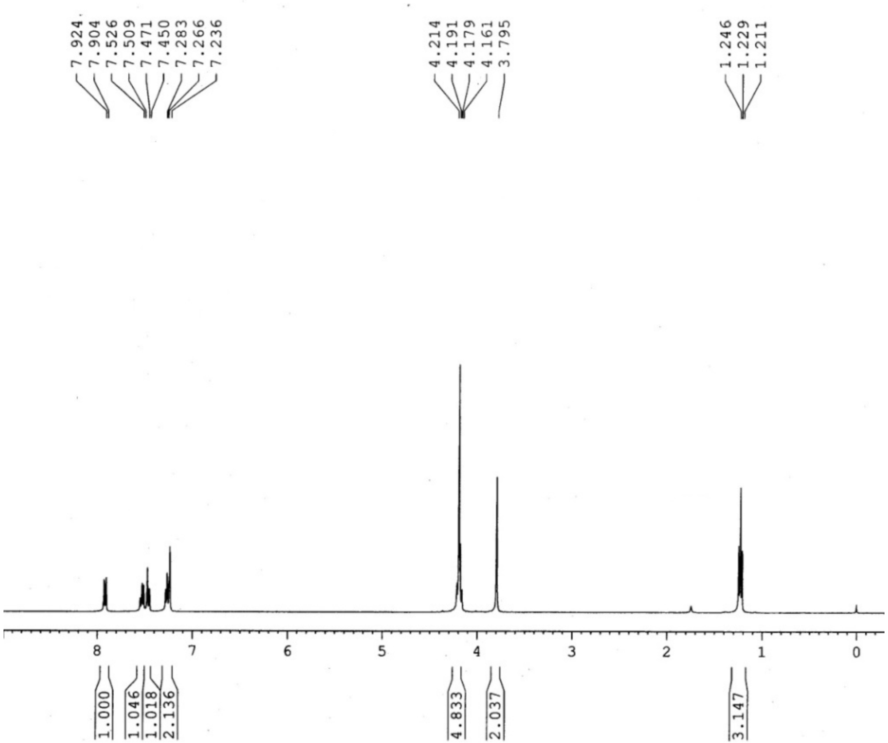


Fig. A9. ^{1}H NMR spectrum of compound **59**

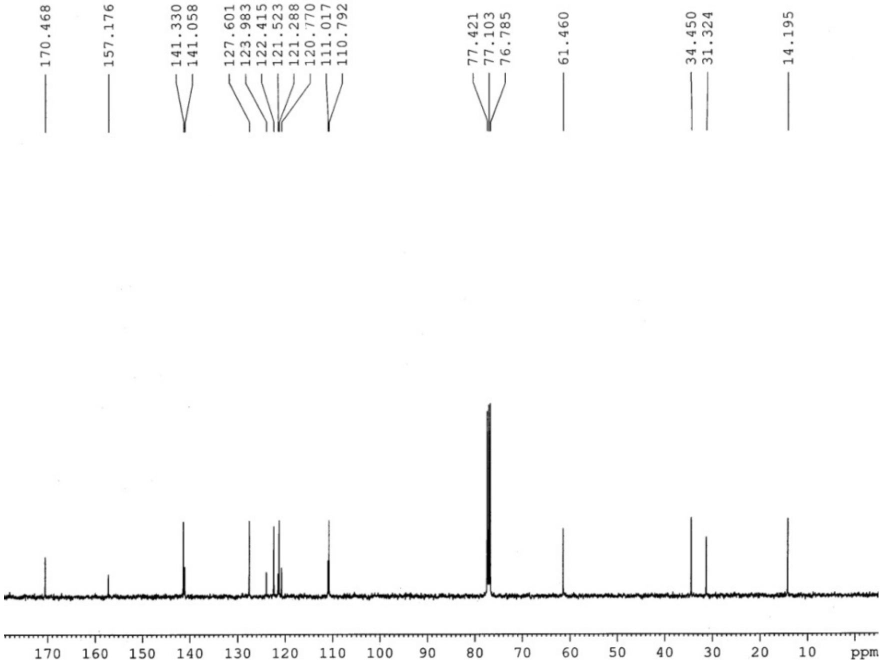


Fig. A10. ^{13}C NMR spectrum of compound **59**

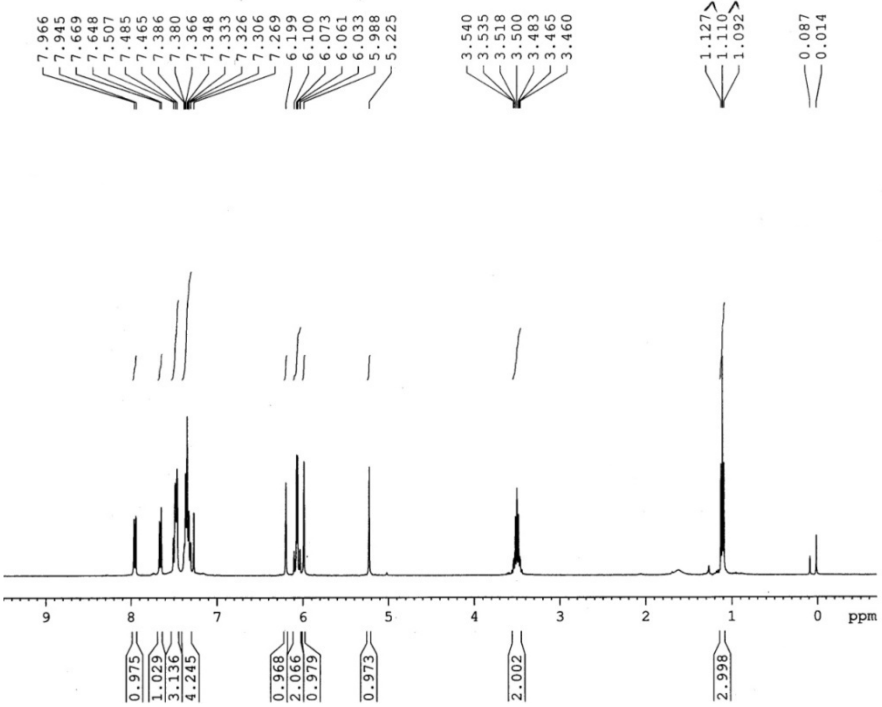


Fig. A11. ^{1}H NMR spectrum of compound **71**

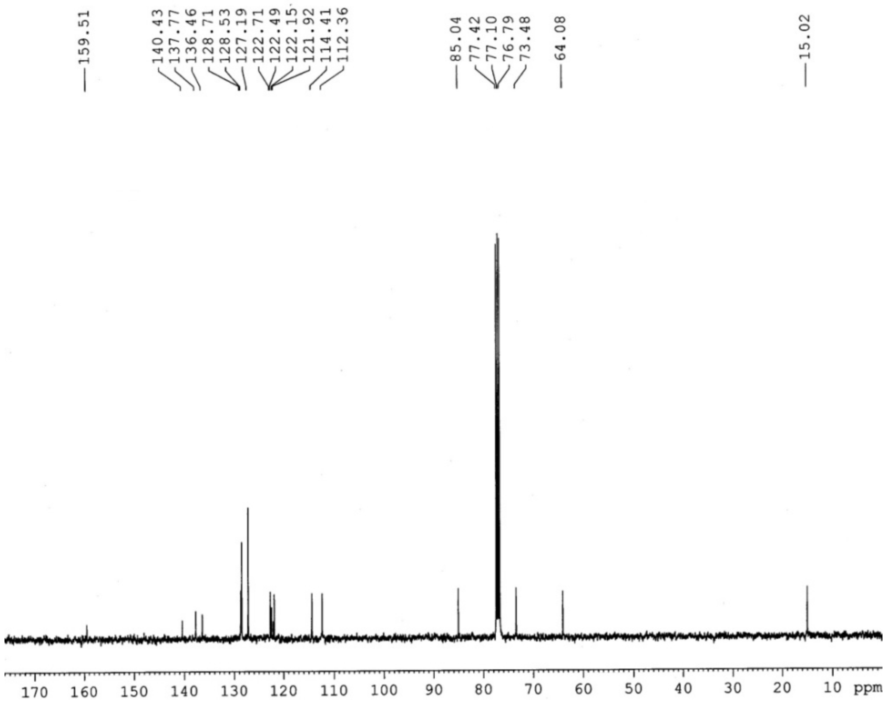


Fig. A12. ^{13}C NMR spectrum of compound **71**

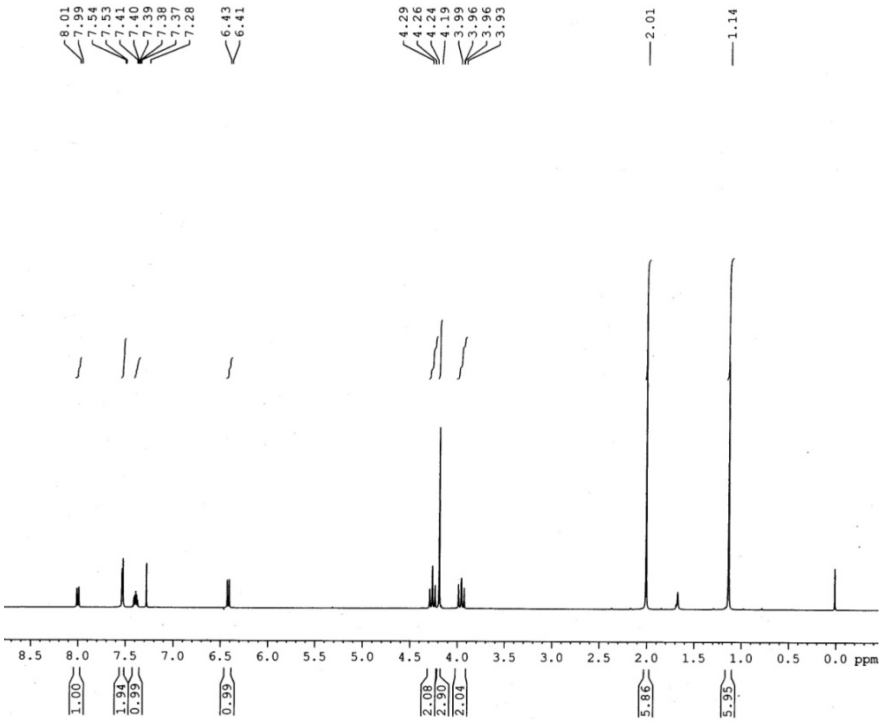


Fig. A13. ^{1}H NMR spectrum of compound **74**

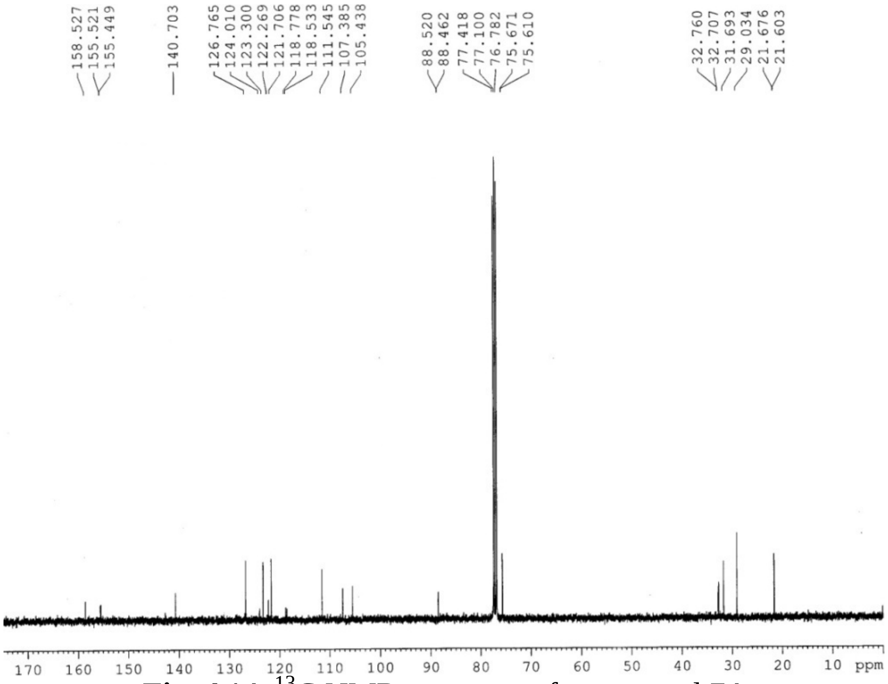


Fig. A14. ^{13}C NMR spectrum of compound **74**

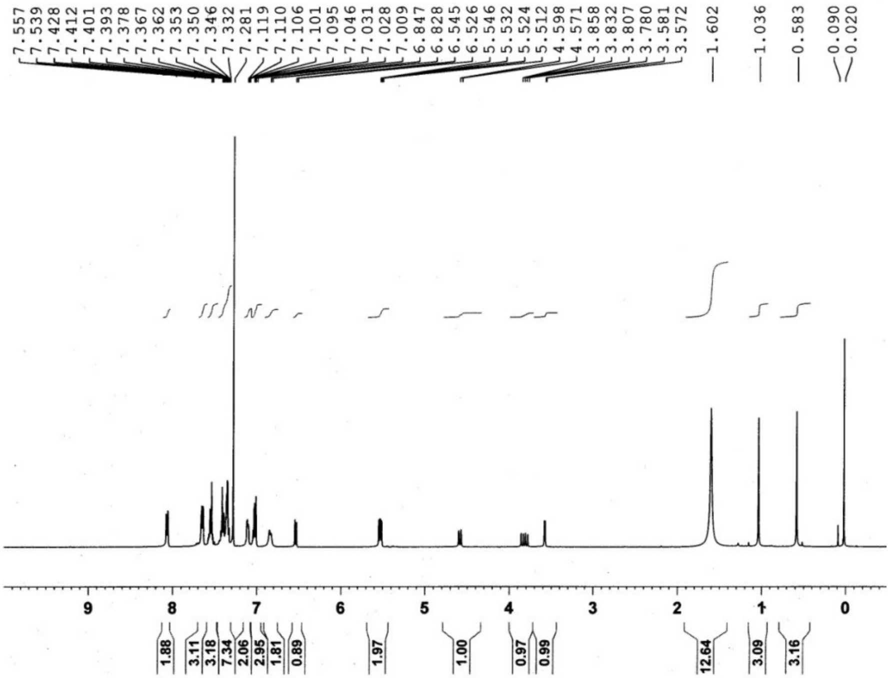


Fig. A15. ^{1}H NMR spectrum of compound **79**

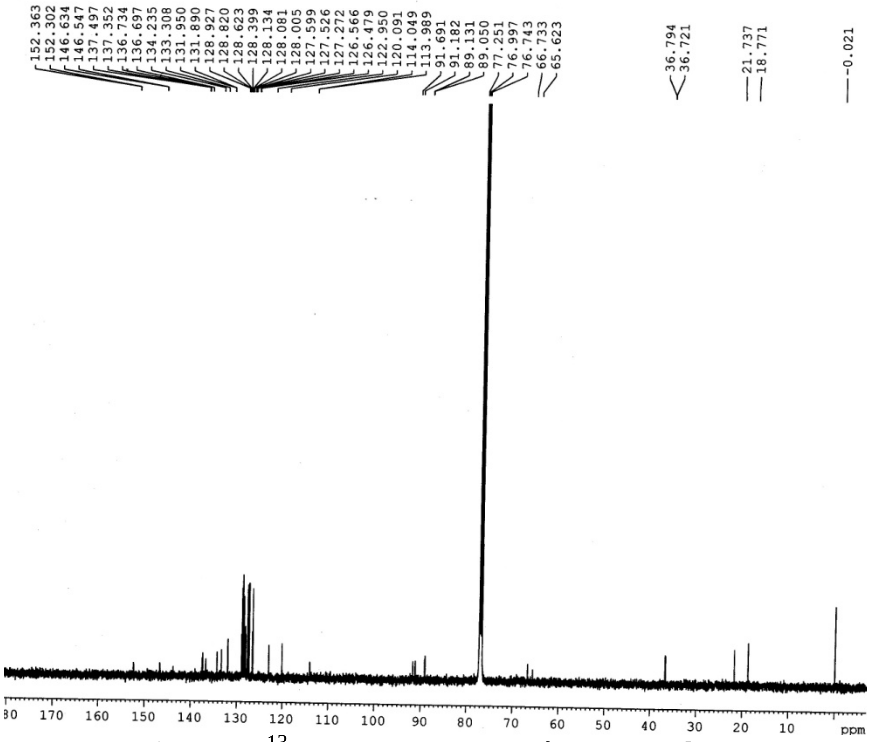


Fig. A16. ^{13}C NMR spectrum of compound **79**

B) Publication numbers and atomic coordinates for X-ray structures reported in this thesis

I. PART A: Compounds 9c, 25, 33, 34, (*Z*)-36, 49, 59, 61, 71, 74, 75, 78.1/2H_2O.CHCl$_3$ and (*E*)-80

PART B: Compound 2

Publication no. 3 (Contents, p. x)

II. Selected atomic coordinates for compounds 9c, 25, 33, 34, (*Z*)-36, 49, 59, 61, 71, 74, 75, 78.1/2H_2O.CHCl$_3$ and (*E*)-80 from PART A and compound 2 from PART B .

Atomic coordinates (x 10^4) and equivalent isotropic displacementparameters (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 9c

Atom	x	y	z	U(eq)
P(1)	3699(1)	1902(1)	943(1)	39(1)
C(1)	894(2)	1993(2)	1968(2)	35(1)
C(2)	1960(2)	1700(2)	2216(2)	35(1)
C(3)	2568(2)	1299(2)	1386(2)	36(1)
N(2)	4681(2)	1749(2)	1861(2)	47(1)
O(1)	3813(2)	1559(2)	-104(2)	58(1)
C(4)	388(2)	1995(2)	957(2)	44(1)
C(5)	318(2)	2329(2)	2773(2)	41(1)
C(6)	805(2)	2360(2)	3786(2)	49(1)
C(7)	2409(2)	1760(2)	3204(2)	43(1)
C(8)	1825(3)	2083(3)	3993(2)	53(1)
C(9)	-621(3)	2309(3)	756(3)	59(1)
N(1)	3621(2)	3070(2)	1106(2)	44(1)
C(10)	2310(2)	474(2)	966(2)	46(1)
C(11)	5208(3)	2664(2)	2084(3)	58(1)
C(12)	-1190(3)	2630(3)	1560(3)	63(1)
C(13)	-735(2)	2635(3)	2533(3)	55(1)
C(14)	4357(2)	3414(2)	1950(3)	57(1)
C(15)	2784(3)	3633(2)	533(3)	61(1)
C(16)	4802(3)	4404(3)	1944(3)	76(1)
C(17)	2056(4)	-363(3)	564(4)	70(1)
C(18)	2116(3)	4174(3)	1233(4)	84(1)
C(19)	6399(3)	3811(3)	3030(3)	74(1)
C(20)	5245(3)	815(3)	1915(3)	69(1)
C(21)	5963(3)	2803(3)	2975(4)	85(1)
C(22)	6191(3)	787(3)	1321(4)	98(2)
C(23)	5575(3)	4582(3)	2838(3)	79(1)
C(24)	3207(4)	4275(3)	-273(3)	92(1)
C(25)	5387(5)	461(4)	2981(5)	135(2)

Compound 25

Atom	**x**	**y**	**z**	**U(eq)**
C(1)	1937(2)	9110(2)	1517(1)	51(1)
C(2)	3159(2)	8920(2)	2365(1)	50(1)
C(3)	2434(2)	8592(2)	2923(2)	59(1)
C(4)	4100(3)	7860(2)	2326(2)	77(1)
C(5)	4126(3)	10024(2)	2664(2)	89(1)
C(6)	-1279(2)	8811(2)	1748(2)	49(1)
C(7)	-2093(3)	8698(3)	2305(2)	81(1)
C(8)	-2365(2)	9004(2)	866(2)	57(1)
C(9)	-2986(3)	10019(4)	533(2)	82(1)
C(10)	-1304(2)	7198(2)	196(2)	53(1)
C(11)	-893(3)	7669(2)	-381(2)	61(1)
C(12)	433(3)	7320(2)	-404(2)	62(1)
C(13)	1369(2)	6503(2)	145(2)	54(1)
C(14)	922(3)	6027(2)	712(2)	54(1)
C(15)	-408(3)	6362(2)	742(2)	53(1)
C(16)	2834(3)	6157(3)	127(2)	80(1)
O(1)	893(2)	10027(1)	1501(1)	53(1)
O(2)	1367(2)	9485(1)	2931(1)	54(1)
O(3)	-461(2)	11104(1)	2206(1)	77(1)
O(4)	-3374(2)	6842(2)	723(1)	96(1)
O(5)	-4012(2)	8030(2)	-534(1)	114(1)
P(3)	125(1)	9961(1)	2108(1)	49(1)
S(1)	-2953(1)	7699(1)	263(1)	74(1)

Compound 33

Atom	**x**	**y**	**z**	**U(eq)**
S	6736(2)	4217(1)	7655(2)	54(1)
P	4790(2)	2653(1)	5410(1)	48(1)
O(1)	4663(3)	2790(2)	4183(3)	60(1)
O(2)	7417(3)	3718(2)	8480(3)	61(1)
O(3)	7598(3)	4734(1)	7469(3)	75(1)
C(1)	3375(5)	2118(2)	5446(5)	39(2)
C(2)	2217(6)	2065(2)	4422(5)	56(2)
C(3)	1141(6)	1643(3)	4365(6)	76(2)
C(4)	1202(6)	1289(3)	5317(7)	76(2)
C(5)	2348(7)	1340(3)	6347(6)	71(2)
C(6)	3418(5)	1767(3)	6412(5)	59(2)
C(7)	6510(5)	2341(2)	6283(5)	42(1)
C(8)	6948(6)	2240(2)	7483(5)	54(2)
C(9)	8314(7)	2043(2)	8106(5)	67(2)
C(10)	9270(6)	1969(3)	7535(7)	77(2)
C(11)	8869(8)	2082(3)	6357(7)	85(2)
C(12)	7479(7)	2257(2)	5726(5)	68(2)
C(13)	4669(5)	3366(2)	6240(4)	40(1)
C(14)	3164(5)	3656(2)	5787(5)	44(2)
C(15)	2225(6)	3525(2)	6355(5)	59(2)
C(16)	859(7)	3780(3)	5972(6)	70(2)

C(17)	467(6)	4176(3)	5035(6)	74(2)
C(18)	1367(7)	4320(3)	4450(5)	69(2)
C(19)	2714(6)	4049(2)	4821(5)	59(2)
C(20)	5839(5)	3841(2)	6265(5)	39(2)
C(21)	6261(5)	4000(2)	5418(5)	62(2)
C(22)	5334(5)	4542(3)	8023(5)	40(2)
C(23)	4616(6)	5081(3)	7461(5)	59(2)
C(24)	3475(7)	5303(2)	7722(6)	65(2)
C(25)	3000(6)	5001(3)	8520(6)	55(2)
C(26)	3762(6)	4475(3)	9082(4)	52(2)
C(27)	4901(5)	4242(2)	8838(5)	44(2)
C(28)	1719(5)	5249(2)	8760(5)	89(2)

Compound 34

Atom	**x**	**y**	**z**	**U(eq)**
S(1)	1548(1)	8287(2)	1604(2)	102(1)
S(2)	2984(1)	8154(2)	2579(3)	115(1)
Cl(1)	4550(1)	10637(3)	611(3)	135(1)
C(4)	3440(4)	8780(7)	1999(7)	81(3)
O(2)	1427(4)	6987(6)	1752(5)	130(3)
C(12)	995(3)	9201(8)	1505(6)	88(3)
C(7)	2502(3)	9356(7)	2399(7)	85(3)
C(9)	1949(4)	8820(7)	3562(7)	85(3)
C(8)	2024(3)	8845(7)	2670(6)	72(2)
C(5)	3864(5)	9478(9)	2578(9)	119(4)
C(2)	3707(3)	9222(9)	574(7)	92(3)
C(6)	4202(4)	10037(10)	2138(8)	100(3)
C(1)	4119(3)	9897(8)	1149(8)	92(3)
C(17)	1013(4)	10513(10)	1374(8)	111(4)
O(3)	1718(3)	8561(7)	756(5)	128(3)
C(15)	111(5)	10705(13)	1234(7)	113(4)
C(10)	2342(4)	9370(9)	4449(6)	100(3)
C(3)	3367(3)	8686(8)	1024(8)	88(3)
C(13)	539(5)	8644(11)	1461(7)	109(4)
C(16)	583(5)	11233(11)	1231(8)	133(5)
C(14)	90(5)	9399(15)	1337(8)	126(4)
C(11)	1474(4)	8301(11)	3798(7)	107(3)
O(1)	2755(4)	7087(6)	2000(9)	163(4)
C(18)	-367(5)	11490(13)	1121(7)	137(5)
O(4)	3235(4)	8013(8)	3602(7)	151(4)

Compound (*Z*-) 36

Atom	**x**	**y**	**z**	**U(eq)**
S(1)	9125(2)	1395(1)	4650(1)	78(1)
P(1)	6284(2)	5795(1)	3524(1)	59(1)
P(2)	8129(1)	1190(1)	3450(1)	52(1)
O(1)	5301(4)	6251(3)	3016(3)	96(2)
O(2)	7308(4)	6343(3)	3650(3)	69(1)
O(3)	6366(4)	5638(3)	4476(3)	66(1)
O(4)	5810(3)	3987(3)	3899(3)	65(1)
N(1)	6940(4)	1658(3)	3173(3)	55(1)
C(1)	8312(6)	6098(6)	4309(5)	91(2)
C(2)	8253(6)	6046(6)	5212(5)	89(2)

C(3)	7377(7)	5393(5)	5147(4)	85(2)
C(4)	7998(7)	6937(6)	5490(5)	111(3)
C(5)	9356(8)	5702(9)	5867(6)	174(5)
C(6)	6462(4)	4794(4)	3032(3)	49(2)
C(7)	6185(5)	4012(4)	3245(3)	53(2)
C(8)	6216(5)	3161(4)	2827(3)	52(2)
C(9)	6829(5)	2512(4)	3532(3)	48(1)
C(10)	6266(4)	2466(4)	4174(3)	48(2)
C(11)	6239(5)	1724(4)	4642(4)	60(2)
C(12)	5748(5)	1746(5)	5242(4)	72(2)
C(13)	5299(5)	2491(5)	5389(4)	65(2)
C(14)	5318(5)	3236(5)	4924(4)	64(2)
C(15)	5805(5)	3206(4)	4323(3)	50(2)
C(16)	6903(5)	4898(4)	2332(4)	54(2)
C(17)	6420(6)	5464(5)	1642(4)	74(2)
C(18)	6841(8)	5564(6)	999(5)	91(2)
C(19)	7718(8)	5129(6)	1029(5)	85(2)
C(20)	8227(6)	4581(5)	1727(5)	80(2)
C(21)	7816(5)	4485(5)	2373(4)	68(2)
C(22)	8716(5)	1534(4)	2693(3)	51(2)
C(23)	8099(6)	1906(5)	1898(4)	81(2)
C(24)	8569(7)	2193(6)	1334(5)	95(3)
C(25)	9636(8)	2066(6)	1542(6)	103(3)
C(26)	10269(7)	1684(6)	2331(6)	107(3)
C(27)	9813(6)	1442(5)	2890(4)	82(2)
C(28)	7777(5)	66(4)	3191(3)	54(2)
C(29)	8245(8)	-549(6)	3782(5)	113(3)
C(30)	7961(12)	-1457(7)	3569(9)	162(5)
C(31)	7257(9)	-1672(6)	2824(7)	126(4)
C(32)	6765(7)	-1066(7)	2225(6)	105(3)
C(33)	7021(6)	-171(6)	2411(5)	95(2)

Compound 49

Atom	**x**	**y**	**z**	**U(eq)**
P(1)	1850(1)	4331(1)	1092(1)	38(1)
C(8)	4492(2)	4346(1)	3299(1)	32(1)
N(1)	6237(2)	4014(1)	4184(1)	39(1)
C(6)	4786(2)	6224(2)	3443(2)	40(1)
C(13)	2629(2)	4828(2)	2181(2)	35(1)
C(7)	5068(2)	5243(2)	3562(1)	33(1)
C(12)	5228(2)	3626(2)	3705(2)	35(1)
C(9)	3387(2)	4081(2)	2757(2)	34(1)
C(22)	1788(2)	5796(2)	-121(2)	45(1)
C(14)	1722(2)	5356(2)	2725(2)	38(1)
C(15)	993(2)	4861(2)	3297(2)	46(1)
C(20)	3413(2)	4630(2)	-144(2)	48(1)
C(3)	6931(2)	5702(2)	4516(2)	44(1)
C(5)	5554(2)	6904(2)	3851(2)	47(1)
C(10)	3099(2)	3148(2)	2769(2)	42(1)
C(19)	1554(2)	6344(2)	2611(2)	49(1)
C(21)	2511(2)	5215(2)	-769(2)	46(1)
C(18)	686(2)	6822(2)	3061(2)	59(1)
C(4)	6622(2)	6643(2)	4381(2)	48(1)
C(16)	123(2)	5348(2)	3742(2)	60(1)
C(24)	1707(3)	4565(2)	-1419(2)	74(1)
C(23)	3211(3)	5923(3)	-1333(3)	89(1)
C(17)	-25(2)	6328(2)	3628(2)	65(1)
O(2)	3802(1)	2447(1)	3234(1)	45(1)
O(3)	2846(2)	3973(1)	468(1)	48(1)
O(4)	1231(1)	5208(1)	553(1)	41(1)
O(1)	5513(2)	1939(1)	3965(1)	56(1)
O(5)	1010(2)	3570(1)	1276(1)	59(1)
C(11)	4925(2)	2627(2)	3662(2)	40(1)
C(2)	6147(2)	5005(2)	4113(2)	36(1)
C(1)	7231(2)	3509(2)	4702(2)	59(1)

Compound 59

Atom	**x**	**y**	**z**	**U(eq)**
O(4)	10736(1)	704(1)	2167(2)	62(1)
C(13)	9211(1)	1392(1)	556(2)	53(1)
C(8)	7443(1)	1009(1)	1155(2)	49(1)
O(3)	9745(1)	1399(1)	3705(2)	82(1)
C(14)	9905(1)	1174(1)	2325(2)	50(1)
O(2)	6889(1)	2898(1)	529(2)	76(1)
N(1)	5959(1)	597(2)	1864(2)	74(1)
C(9)	8146(1)	1672(1)	666(2)	49(1)
C(12)	6511(1)	1343(2)	1371(2)	58(1)
C(7)	7473(2)	-3(1)	1513(2)	56(1)
C(10)	7824(2)	2572(2)	366(3)	62(1)
C(2)	6542(2)	-227(2)	1945(3)	71(1)
C(11)	6190(2)	2318(2)	1080(3)	74(1)
O(1)	5410(1)	2691(2)	1253(3)	115(1)
C(15)	11498(2)	465(2)	3771(3)	73(1)
C(6)	8176(2)	-742(2)	1482(3)	72(1)
C(16)	12457(2)	188(2)	3299(3)	85(1)
C(3)	6305(3)	-1167(3)	2351(3)	106(1)
C(4)	7014(4)	-1863(2)	2307(4)	126(1)
C(1)	4975(2)	678(3)	2370(4)	107(1)
C(5)	7931(3)	-1654(2)	1870(4)	103(1)

Compound 61

Atom	**x**	**y**	**z**	**U(eq)**
Cl(1)	-4866(1)	120(1)	6566(1)	73(1)
S(1)	794(1)	4098(1)	6939(1)	38(1)
O(3)	1129(2)	4522(3)	8030(2)	50(1)
C(15)	-800(3)	2954(3)	6817(3)	37(1)
O(4)	575(3)	5199(2)	6203(2)	50(1)
C(7)	4594(3)	3833(3)	7796(2)	36(1)
C(13)	2265(3)	2984(4)	6543(3)	42(1)
O(2)	5322(3)	5701(3)	6302(2)	63(1)
C(8)	3678(3)	3883(4)	6818(3)	40(1)
C(6)	4546(3)	3050(3)	8727(3)	38(1)
C(18)	-3283(4)	1212(4)	6654(3)	47(1)
C(19)	-2985(4)	1998(4)	5817(3)	50(1)
C(16)	-1109(4)	2164(4)	7659(3)	46(1)
C(17)	-2370(4)	1272(4)	7572(3)	52(1)
C(11)	5859(3)	4721(4)	7945(3)	42(1)
C(14)	1957(4)	2447(4)	5389(3)	55(1)
N(1)	6588(3)	4535(3)	8915(2)	47(1)
C(20)	-1730(3)	2884(4)	5898(3)	45(1)
C(12)	5803(4)	3531(4)	9407(3)	44(1)
O(1)	7316(3)	6543(4)	7261(3)	86(1)
C(10)	6269(4)	5710(4)	7211(3)	54(1)
C(9)	4095(4)	4808(4)	6128(3)	54(1)
C(5)	3603(4)	2014(4)	9068(3)	51(1)
C(2)	6099(4)	3018(4)	10408(3)	56(1)
C(3)	5151(5)	2016(5)	10708(4)	69(1)
C(1)	7988(4)	5227(5)	9370(3)	64(1)
C(4)	3914(5)	1498(4)	10054(4)	67(1)
Cl(2)	363(2)	8913(1)	8922(1)	95(1)
Cl(3)	1473(2)	9029(2)	6891(2)	130(1)
C(21)	284(5)	8190(5)	7645(4)	94(2)

Compound 71

Atom	**x**	**y**	**z**	**U(eq)**
O(2)	4204(2)	8575(2)	1713(3)	71(1)
O(3)	5170(2)	8643(2)	4205(3)	97(1)
C(9)	6011(3)	8621(2)	542(4)	48(1)
C(10)	4970(3)	8668(2)	-616(4)	56(1)
N(1)	7121(3)	8516(2)	3013(3)	58(1)
O(1)	8122(2)	9165(2)	5385(3)	78(1)
C(8)	7058(3)	8627(2)	379(4)	48(1)
C(13)	6064(3)	8555(2)	2150(4)	58(1)
C(6)	8579(3)	8646(2)	-644(5)	70(1)
C(14)	7733(3)	8555(2)	1929(4)	51(1)
C(15)	2992(3)	8409(3)	-868(5)	61(1)
C(5)	9233(3)	8565(2)	915(5)	71(1)
C(7)	7513(3)	8674(2)	-922(4)	57(1)
C(21)	4789(3)	8911(2)	-2137(4)	87(2)
C(11)	4138(4)	8301(3)	76(5)	78(1)
C(4)	8829(3)	8522(2)	2221(5)	65(1)
C(1)	7548(3)	8462(2)	4748(4)	68(1)
C(12)	5156(4)	8591(3)	2809(5)	68(1)
C(20)	2564(4)	7857(3)	-2058(5)	78(1)
C(18)	947(3)	8593(4)	-2702(6)	92(2)
C(16)	2400(4)	9067(3)	-606(5)	79(1)
C(19)	1551(4)	7954(3)	-2983(6)	95(2)
C(17)	1362(5)	9150(3)	-1525(7)	93(2)
C(2)	7548(4)	9905(3)	5251(5)	94(2)
C(3)	8168(4)	10566(3)	6274(6)	133(2)

Compound 74

Atom	**x**	**y**	**z**	**U(eq)**
P(1)	4402(1)	5903(1)	3233(1)	46(1)
O(3)	5394(1)	5863(1)	4467(2)	53(1)
O(4)	4523(1)	6942(1)	2629(1)	46(1)
N(1)	150(1)	6391(1)	4217(2)	42(1)
C(9)	2292(2)	5992(1)	3178(2)	35(1)
C(8)	1637(1)	6051(1)	3897(2)	34(1)
C(7)	1850(2)	5910(1)	5174(2)	36(1)
C(12)	599(2)	6327(1)	3360(2)	37(1)
C(15)	3341(2)	6019(1)	3733(2)	40(1)
O(2)	649(1)	6350(1)	1382(1)	56(1)
C(18)	4813(2)	7833(2)	3424(2)	46(1)
O(1)	-806(1)	6842(2)	1557(2)	76(1)
C(10)	1678(2)	5829(2)	1820(2)	48(1)
O(5)	4369(1)	5034(1)	2457(2)	78(1)
C(2)	900(2)	6129(1)	5326(2)	41(1)
C(17)	5833(2)	7674(2)	4501(2)	46(1)
C(16)	5723(2)	6764(2)	5229(2)	54(1)
C(6)	2716(2)	5604(2)	6205(2)	45(1)
C(11)	77(2)	6520(2)	2066(2)	48(1)
C(3)	801(2)	6053(2)	6459(2)	55(1)
C(1)	-912(2)	6699(2)	4044(2)	57(1)
C(19)	6724(2)	7517(2)	4047(3)	67(1)
C(5)	2613(2)	5531(2)	7312(2)	57(1)
C(4)	1670(2)	5756(2)	7438(2)	64(1)
C(20)	6046(2)	8616(2)	5325(3)	80(1)
C(14)	2165(2)	6287(2)	973(2)	75(1)
C(13)	1445(2)	4696(2)	1591(3)	80(1)

Compound 75

Atom	**x**	**y**	**z**	**U(eq)**
P(1)	4715(3)	4765(1)	1598(1)	52(1)
O(4)	6733(6)	5124(2)	1586(2)	58(1)
N(1)	2376(6)	5277(3)	5142(3)	52(1)
O(3)	5064(6)	3899(2)	1484(2)	57(1)
O(5)	3342(7)	5096(3)	1033(2)	73(1)
C(18)	4174(8)	4772(4)	2600(3)	50(2)
C(9)	3431(8)	5284(3)	3075(3)	45(2)
O(1)	2286(7)	6891(3)	4734(3)	73(1)
C(16)	2500(9)	6406(4)	4265(4)	53(2)
O(2)	2711(6)	6586(2)	3511(2)	65(1)
C(8)	3008(8)	5065(3)	3876(3)	44(2)
C(17)	2608(7)	5606(4)	4422(3)	43(2)
C(7)	2987(8)	4359(4)	4279(3)	48(2)
C(20)	8191(9)	4042(3)	993(3)	49(2)
C(10)	2807(8)	6071(3)	2841(3)	46(2)
C(19)	6291(9)	3668(3)	877(4)	56(2)
C(21)	7918(9)	4875(3)	964(3)	57(2)
C(6)	3133(9)	3601(4)	4062(4)	61(2)
C(3)	2452(9)	3954(5)	5616(4)	66(2)
C(15)	853(9)	6037(4)	2447(4)	66(2)
C(2)	2601(8)	4517(4)	5063(4)	51(2)
C(22)	9392(10)	3812(4)	307(4)	72(2)
C(12)	3361(13)	7266(4)	2075(5)	88(3)
C(5)	2991(9)	3046(4)	4615(5)	71(2)
C(11)	4128(10)	6490(4)	2328(4)	74(2)
C(14)	80(12)	6809(4)	2215(6)	99(3)
C(13)	1384(16)	7216(5)	1707(5)	109(3)
C(4)	2664(9)	3231(5)	5392(5)	72(2)
C(1)	1963(9)	5659(4)	5872(3)	66(2)
C(23)	9195(10)	3807(4)	1772(4)	79(2)

Compound 78.1/2H_2O.$CHCl_3$

Atom	**x**	**y**	**z**	**U(eq)**
C(1)	-1122(4)	8992(4)	3337(4)	24(1)
C(2)	-1733(5)	8721(4)	2691(4)	24(1)
C(3)	-653(5)	8355(4)	1724(4)	26(1)
C(4)	-2379(5)	7847(4)	3339(4)	31(1)
C(5)	-2727(5)	9780(4)	2270(5)	35(1)
C(6)	-1978(4)	9100(4)	4453(4)	24(1)
C(7)	-1941(5)	8198(5)	5312(4)	33(1)
C(8)	-2771(6)	8323(5)	6310(5)	41(1)
C(9)	-3614(5)	9311(5)	6480(5)	43(2)
C(10)	-3643(5)	10205(5)	5646(5)	43(2)
C(11)	-2821(5)	10108(4)	4624(5)	34(1)
C(12)	2623(5)	7384(4)	2217(4)	25(1)
C(13)	3346(5)	7088(4)	3053(4)	25(1)
C(14)	4682(5)	6510(4)	2869(4)	29(1)
C(15)	5359(5)	6261(4)	3598(4)	26(1)
C(16)	4717(5)	6600(4)	4537(4)	23(1)
C(17)	3383(5)	7179(4)	4744(4)	28(1)
C(18)	2710(5)	7413(4)	4021(4)	25(1)
C(19)	6596(5)	5688(4)	5216(4)	29(1)
C(20)	3294(4)	6631(4)	1432(3)	21(1)
C(21)	3680(5)	5568(4)	1661(4)	26(1)
C(22)	3481(4)	7390(4)	320(4)	21(1)

C(23)	4608(4)	7738(4)	217(4)	22(1)
C(24)	5924(5)	7434(4)	-295(4)	27(1)
C(25)	6712(5)	7876(4)	-156(4)	32(1)
C(26)	6178(5)	8581(4)	504(4)	34(1)
C(27)	4855(5)	8864(4)	1060(4)	26(1)
C(28)	4084(4)	8439(4)	895(3)	21(1)
C(29)	2638(4)	8526(4)	1370(4)	21(1)
C(30)	1708(4)	9595(4)	1651(4)	23(1)
C(31)	1686(5)	9885(4)	2514(4)	29(1)
C(32)	842(5)	10875(4)	2745(4)	32(1)
C(33)	25(5)	11585(4)	2111(4)	32(1)
C(34)	78(5)	11312(4)	1234(4)	29(1)
C(35)	921(4)	10318(4)	1004(4)	24(1)
C(36)	3466(4)	7038(4)	-580(4)	20(1)
C(37)	2720(5)	6398(4)	-394(4)	26(1)
C(38)	2710(5)	6076(4)	-1230(4)	28(1)
C(39)	3444(5)	6403(4)	-2250(4)	29(1)
C(40)	4166(5)	7052(4)	-2445(4)	26(1)
C(41)	4183(4)	7371(4)	-1621(4)	21(1)
C(44)	9760(6)	4991(5)	2312(5)	45(2)
Cl(1)	8962(2)	4104(2)	3278(2)	129(1)
Cl(2)	8729(2)	5962(1)	1531(2)	53(1)
Cl(3)	11196(2)	4266(2)	1516(2)	71(1)
O(1)	1150(4)	6124(4)	3596(3)	59(1)
O(2)	121(3)	8153(3)	3453(3)	39(1)
O(3)	345(3)	7353(3)	2017(3)	26(1)
O(4)	5290(3)	6442(3)	5294(3)	31(1)
O(5)	2371(3)	8366(2)	517(2)	20(1)
O(7)	239(10)	4607(8)	4338(6)	57(3)
P(1)	1004(1)	7201(1)	2882(1)	28(1)

Compound (*E*)-80

Atom	x	y	z	U(eq)
P(1)	7769(1)	1974(1)	2241(1)	56(1)
O(2)	7180(2)	-2225(2)	2131(1)	48(1)
C(32)	9402(3)	-3742(3)	2144(2)	50(1)
C(30)	8007(3)	-2762(3)	3574(2)	47(1)
N(1)	6738(3)	3177(2)	1632(2)	52(1)
C(31)	8465(3)	-2600(3)	2526(2)	46(1)
C(14)	7431(3)	-430(3)	2463(2)	46(1)
C(18)	6472(3)	-1232(3)	2677(2)	45(1)
C(13)	6985(3)	786(3)	2468(2)	52(1)
C(19)	5068(3)	-629(3)	2382(3)	52(1)
C(15)	8828(3)	-1348(3)	2274(2)	49(1)
O(1)	9162(2)	1542(2)	1844(2)	81(1)
C(25)	6749(3)	-1887(3)	3676(2)	47(1)
C(6)	6638(3)	3915(3)	3065(2)	60(1)
N(2)	7435(3)	2609(3)	3228(2)	68(1)
C(1)	5848(4)	4021(3)	2256(2)	59(1)
C(36)	11516(4)	-5367(4)	2105(3)	79(1)
C(33)	8985(4)	-4303(3)	1531(2)	62(1)
C(26)	6072(4)	-1767(3)	4556(3)	62(1)
C(29)	8593(4)	-3536(3)	4341(3)	61(1)
C(17)	9295(4)	-1158(3)	1222(3)	70(1)
C(16)	9870(3)	-1281(3)	2878(3)	70(1)
C(24)	4769(4)	-732(4)	1524(3)	86(1)
C(37)	10684(3)	-4282(3)	2424(3)	65(1)
C(2)	5132(4)	5318(3)	1876(3)	77(1)
C(28)	7900(4)	-3425(4)	5227(3)	74(1)
C(34)	9820(4)	-5398(4)	1231(3)	80(1)
C(35)	11082(5)	-5917(4)	1509(3)	82(1)
C(20)	4066(4)	75(4)	2949(3)	85(1)
C(27)	6673(4)	-2555(4)	5329(3)	75(1)
C(7)	6343(4)	3191(4)	695(3)	78(1)
C(22)	2502(4)	502(4)	1784(5)	107(2)
C(5)	5828(5)	4568(4)	3849(3)	93(1)

C(8)	5123(5)	2774(4)	730(3)	94(1)
C(23)	3498(5)	-168(4)	1227(4)	113(2)
C(10)	8370(5)	2071(5)	3962(3)	110(2)
C(21)	2788(5)	634(5)	2648(5)	114(2)
C(3)	4322(5)	6031(4)	2647(4)	102(2)
C(4)	5071(5)	5882(4)	3481(4)	97(2)
C(11)	9276(5)	2800(5)	4031(4)	109(2)
C(12)	7882(6)	1451(6)	4789(4)	140(2)
C(9)	7408(5)	2694(7)	36(4)	157(3)

Compound 2

Atom	x	y	z	U(eq)
N	3785(3)	3162(4)	6221(2)	63(1)
O	2433(3)	3377(4)	7572(2)	82(1)
C(1)	4288(4)	2447(5)	4202(2)	50(1)
C(2)	5749(5)	2310(5)	4245(2)	56(1)
C(3)	6566(4)	2410(5)	4962(2)	50(1)
C(4)	5926(4)	2632(5)	5615(2)	53(1)
C(5)	4426(4)	2801(5)	5574(2)	51(1)
C(6)	3632(4)	2676(5)	4846(2)	53(1)
C(7)	4575(5)	2828(7)	6987(2)	81(2)
C(8)	3908(5)	3803(7)	7591(3)	92(2)
C(9)	1676(5)	3813(8)	6841(3)	90(2)
C(10)	2247(5)	2843(7)	6199(3)	80(2)
C(11)	3348(6)	2356(9)	3437(3)	71(1)
C(12)	8173(5)	2299(8)	5057(3)	71(1)
F(1)	2870(40)	840(20)	3240(10)	142(11)
F(1A)	3999(18)	1720(50)	2890(9)	148(8)
F(2)	2173(19)	3280(40)	3409(11)	131(11)
F(2A)	2310(20)	1290(40)	3445(10)	130(9)
F(3)	3950(16)	2980(40)	2871(7)	119(6)
F(3A)	2750(40)	3750(20)	3211(14)	176(13)
F(4)	8653(11)	1670(30)	4457(7)	140(6)
F(4A)	8729(15)	2970(40)	4495(12)	131(8)
F(5)	8729(8)	1310(20)	5604(8)	106(3)
F(5A)	8636(17)	727(19)	5090(30)	158(8)
F(6)	8789(9)	3768(11)	5231(12)	128(6)
F(6A)	8781(15)	2890(70)	5682(16)	240(17)