INVESTIGATIONS ON THE REACTIVITY OF P(III) COMPOUNDS WITH DIALKYL AZODICARBOXYLATES AND UTILITY OF ORGANOPHOSPHONATES

A THESIS

SUBMITTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

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OCTOBER 2006

Dedicated at

the lotus feet of

Bhagawan Sri Sathya Sai Baba

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STATEMENT

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

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

Hyderabad

October 2006

K. V. P. Pavan Kumar

CERTIFICATE

This is to certify that the work described in this thesis entitled "*Investigations on The Reactivity of P(III) Compounds with Dialkyl azodicarboxylates and Utility of Organo Phosphonates*" has been carried out by Mr. K. V. P Pavan Kumar, under my supervision and the same has not been submitted elsewhere for any degree.

Hyderabad

October 2006

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LIST OF PUBLICATIONS

1. Diverse Modes of Reactivity of Dialkyl Azodicarboxylates with P(III) Compounds: Synthesis, Structure, and Reactivity of Products Other than the Morrison-Brunn-Huisgen Intermediate in a Mitsunobu-Type Reaction
   N. Satish Kumar, K. Praveen Kumar, **K. V. P. Pavan Kumar**, Praveen Kommana, J. J. Vittal, and K. C. Kumara Swamy
   J. Org. Chem., **2004**, 69, 1880.

2. Two phosphate-imidazole complexes one with and one without hydrogen bonded guest
   K. V. P. Pavan Kumar and K. C. Kumara Swamy
   Acta Crystallogr. **2005,** *C61*, 0668.

3. Structurally Diverse Penta- and Hexa-coordinate Phosphorus Compounds from the Reaction of Diethyl- or Diisopropyl-Azodicarboxylates with Phosphorus(III) Compounds
   K. V. P. Pavan Kumar, N. Satish Kumar and K. C. Kumara Swamy
   New J. Chem. **2006,** *30*, 717.

4. Mitsunobu and related reactions
   K. C. Kumara Swamy and **K. V. P. Pavan Kumar** (Book chapter*: Submitted*)**.**

5. New Anthracenyl Substituted Phosphonates: Synthesis and Utility
   K. C. Kumara Swamy, Venu Srinivas, **K. V. P. Pavan Kumar** and K. Praveen Kumar. (*Submitted*)

6. First Cationic, Hexacoordinate Phosphorus Compound with S→P←S Double Coordination
   K. V. P. Pavan Kumar and K. C. Kumara Swamy (*Manuscript under preparation*).

7. Facile synthesis of cyclopropyl phosphonates from α-chlorophosphonates
   N. Satish Kumar, **K. V. P. Pavan Kumar** and K. C. Kumara Swamy (*Manuscript under preparation*).

8. Synthesis and Structural Characterization of Inositiol based Pentacoordinate Phosphorane
   K. V. P. Pavan Kumar and K. C. Kumara Swamy (*Manuscript under preparation*).

Work not reported in this thesis:

9. Synthesis and Structure of the Macrocycle $[(OCH_2CEt_2CH_2O)\{P(N\text{-}t\text{-}Bu)_2P\}]_2$
   Praveen Kommana, **K. V. P. Pavan Kumar** and K. C. Kumara Swamy
   Ind. J. Chem. **2003**, 42A, 2371.

10. Formation of phosphonates and pyrophosphates in the reactions of chlorophosphate esters with strong organic bases
    K. V. P. Pavan Kumar, K. Praveen Kumar, M. Vijjulatha and K. C. Kumara Swamy *J. Chem. Sci.* **2004,** *116*, 311.

PAPERS PRESENTED IN SYMPOSIA

1. Synthesis, Structure and Reactivity of Products Other than the Morrison-Brunn-Huisgen Intermediate in a Mitsunobu - Type Reaction
K. V. P. Pavan Kumar, N Satish Kumar, K. Praveen Kumar and K. C. Kumara Swamy
6th National Symposium in Chemistry (CRSI), IIT Kanpur, India, Feb 5-7, 2004.

2. Reaction of Diethyl- or Diisopropyl- Azodicarboxylates with Phosphorus(III) Compounds Leading to Structurally Diverse Penta- and Hexa-coordinate Phosphorus Compounds
K. V. P. Pavan Kumar and K. C. Kumara Swamy
Chemfest-2006, School of Chemistry, University of Hyderabad, Mar 4, 2006.

Synopsis

This thesis is divided into two parts: Part-A and Part-B. **Part-A** embodies various cycloaddition and oxidative addition reactions of phosphorus(III) compounds. **Part-B** deals with the synthesis of organophosphonates and their utility in organic synthesis.

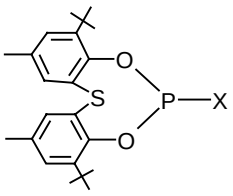
Each part is subdivided into three chapters: (a) Introduction (Literature survey), (b) Results and Discussion and (c) Experimental Section. The compounds obtained in the present study are, in general, characterized by Mp, IR and NMR (^{1}H, ^{13}C & ^{31}P) techniques followed by elemental analysis (of representative compounds) and LC-MS. Wherever feasible, X-ray structure determination is undertaken. Summary as well as references are compiled at the end of each part.

PART-A

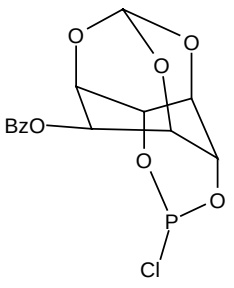
A review of literature on aspects relevant to this part [Mitsunobu reaction, cycloaddition reactions of P(III) compounds, penta- and hexa-coordinate phosphorus compounds, involvement of organophosphates in hydrogen bonding] is presented in Chapter 1. In Chapter 2, the results obtained on the above mentioned aspects are discussed; these are as outlined below.

(i) Phosphite precursors

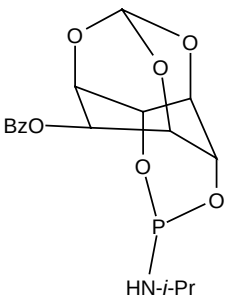
The precursors **1-11** are prepared and used in the present study.



X = Cl [**1;** δ(P): 168.3] OPh [**7**; δ(P): 136.1]
Ph [**2**; δ(P): 167.6] $OCH_2CH_2NMe_2$ [**8**; δ(P): 141.6]
NH*i*-Pr [**3**; δ(P): 137.5]
NHMe [**4**; δ(P): 138.3]
NH*t*-Bu [**5**; δ(P): 138.2]
NCO [**6**; δ(P): 129.4]



10 [δ(P): 140.0; X-ray]



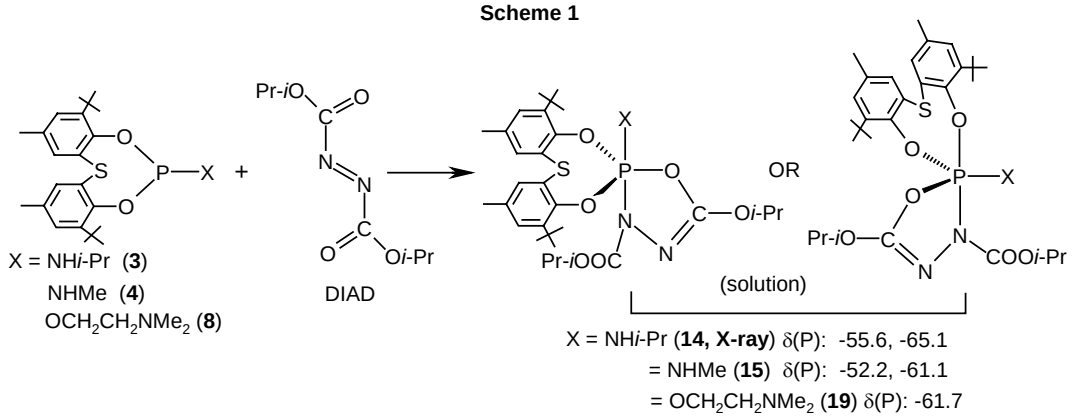
11 [δ(P): 140.6]

(ii) Reactions of phosphorus(III) compounds with dialkyl azodicarboxylates and *o*-chloranil

(a) Formation of pentacoordinate compounds

In the reaction of the cyclic phosphites **3, 4** and **8** with diisopropyl azodicarboxylate (DIAD), pentacoordinate phosphoranes **14, 15 and 19**, rather than the Morrison-Brunn-Huisgen betaine of type $[Ph_3P^+N(CO_2i\text{-}Pr)N^-(CO_2i\text{-}Pr)]$ (**I**), are obtained (Scheme 1). A possible rationale is provided for this observation.

Scheme 1



The equatorial occupancy of the -NH*i*-Pr group in compound **14** (X-ray structure) is on expected lines; however, the N(apical)-O(equatorial) disposition of the five-membered ring in **14** is not consistent with apicophilicity rules according to which a more electronegative and less bulky substituent prefers an apical position of trigonal bipyramidal phosphorus [D. E. C. Corbridge, *Phosphorus 2000: Chemistry, Biochemistry and Technology*, 4th ed.; Elsevier: Amsterdam, 2000; Chapter 13, pp 1137-1142]. The nitrogen (of NCO_2i-Pr group) is apical and oxygen is equatorial. It can be argued that the -C(O)O-*i*-Pr group increases the (group) electronegativity at nitrogen. However, overriding the more electronegative oxygen (which is also sterically less crowded in our system) of the five-membered ring, the nitrogen has occupied the apical position; this was not expected. For comparative purposes the X-ray structure of compound $[CH_2(6\text{-}t\text{-}Bu\text{-}4\text{-}Me\text{-}C_6H_2O)_2P(NC_7H_{14})(1,2\text{-}OC_6Cl_4O)]$ (**17)**, previously reported from our laboratory, has also been determined. Here the amino group occupies an equatorial position of the distorted trigonal bipyramidal (TBP) geometry.

The ^{31}P NMR spectra of **14** in solution changed with temperature [Figure 1]. At low temperatures three peaks at δ -63.7, -63.4 and –54.5 are observed in toluene-

d_8. As the temperature is raised, the two up-field peaks merge and broaden, and a new peak at δ -39.2± 1.0 appears. At 353 K the spectra shows only two peaks, one at δ -39.2± 1.0 and the other at –54.5; upon cooling to 20°C the original pattern was observed. The two closely placed peaks at δ -63.7 and -63.4 are ascribed to the NH*i*-Pr (equatorial) isomers of **14a-b** having the *boat-chair* or *tub* conformation. The remaining two signals for **14** with a large Δδ are then ascribable to either **14c** or **14d**.

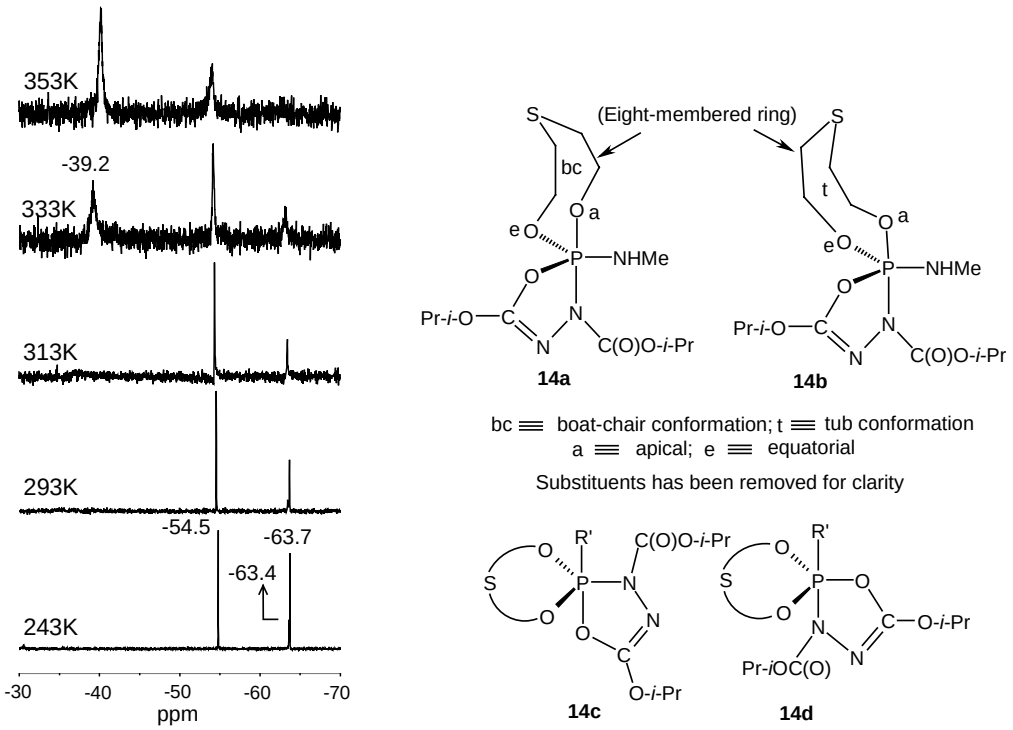


Fig. 1 Variable-temperature ^{31}P NMR spectra of **14**.

Phosphorylated *myo-inositol* derivatives play a significant role in cellular signal transduction and pentacoordinate phosphorus is involved in phosphoryl transfer reactions. In this context, we treated the protected inositol phosphite **10** with DIAD and *o*-chloranil, but there was no apparent reaction [^{31}P NMR]. Then we reacted only **11** with *o*-chloranil (which is more reactive) and obtained the pentacoordinate phosphorane **21** (X-ray) with a TBP structure (Scheme 2). Although the six-membered 1,3,2-dioxaphosphorinane ring has a boat conformation in **21**, it is quite different from the boat conformation found in unrestrained rings investigated before (Fig. 2).

Scheme 2

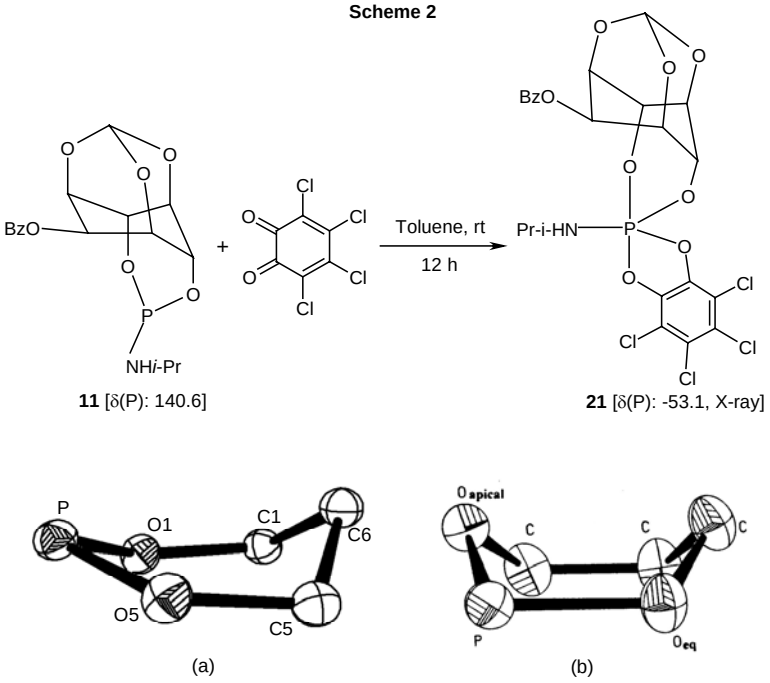
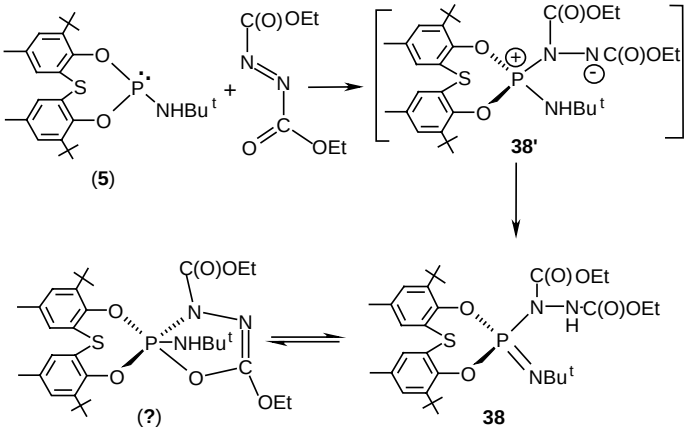


Fig. 2 Plots showing the conformation of the six-membered ring in (a) compound **21** and (b) other pentacoordinate compounds with apical-equatorial disposition of the ring in TBP arrangement.

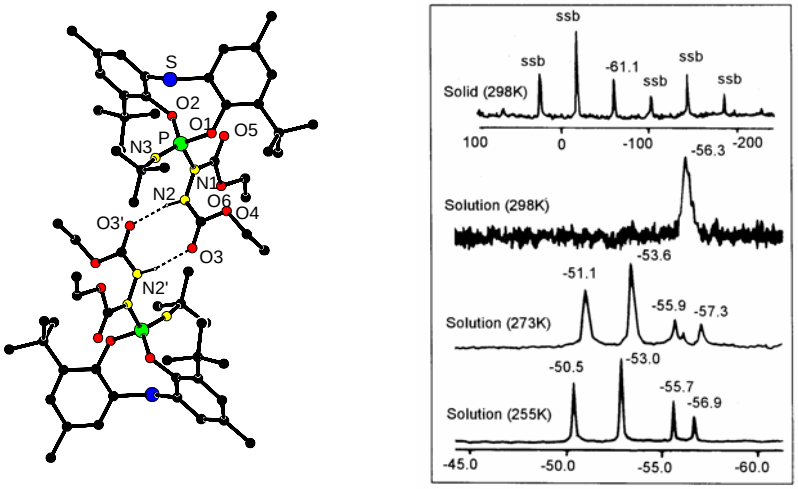
(b) Formation of tetracoordinate compounds with unusual structures

In contrast to the formation of the pentacoordinate compound **14** in the reaction of P^{III}-NH*i*-Pr compound **3** with DIAD discussed above, treatment of the P^{III}-NH*t*-Bu compound **5** with diethyl azodicarboxylate (DEAD) in toluene leads to compound **38** [Scheme 6]. Formation of **38** occurs most likely *via* tautomerization of the betaine **38'** that is analogous to **I**. This is the first example of imino-phosphorus compound (X-ray evidence) that has a structure halfway between the classical MBH betaine **I** and protonated betaine proposed in the Mitsunobu reaction.

Scheme 3



The X-ray structure of **38** (Figure 3a) clearly shows (i) a very short P=N(*t*-Bu) bond [P-N(3) 1.464(4) Å], and (ii) the carbamate type linkage –NH-C(O)OR that is a hydrogen bonded dimer through the NH and the C=O moieties. The IR (KBr) spectrum shows two ν(NH) bands [for **38** at 3262 and 3159 cm^{-1}] consistent with the carbamate- phosphinimine structure; this is different from a single ν(NH) band at 3383 cm^{-1} observed for the pentacoordinate isopropylamino compound **38**. There is also a fairly strong band at 1211cm^{-1} ascribable to ν(P=N). However, the solution and the solid-state ^{31}P NMR spectra of **38** [Figure 3b] appear to be *inconsistent* with the X-ray structure. The δ(P) value of –56.3 [$C_6D_5CD_3$, 298 K, sharpens at higher temperatures] for **38** is clearly in the p*entacoordinate* region (cf. compounds **14** and **15**) and quite upfield to the *tetracoordinate* region.

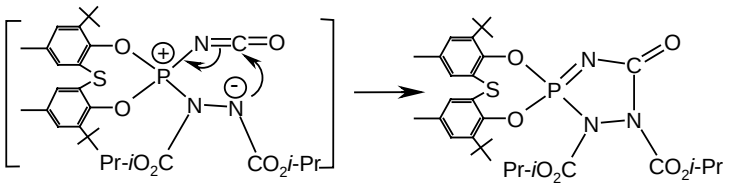


(a) (b)

Fig. 3. (a)A Platon drawing of the hydrogen-bonded dimer of **38**; (b) Solution (VT) and solid-state (5 kHz) ^{31}P NMR spectra for compound **38.**

In contrast to the above, reaction of the P^{III} isocyanate, S(6-*t*-Bu-4-Me-$C_6H_2O)_2$P-NCO (**6**) with DIAD takes an entirely different turn with the formation of the cyclic product **41**, presumably *via* betaine in a step-wise pathway (Scheme 4). The structure of a similar compound prepared in the laboratory [CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$P{N(CO_2Et)N(CO_2Et)-C(O)-N}] [**41;** δ(P): 26.6] has been proven by X-ray crystallography.

Scheme 4

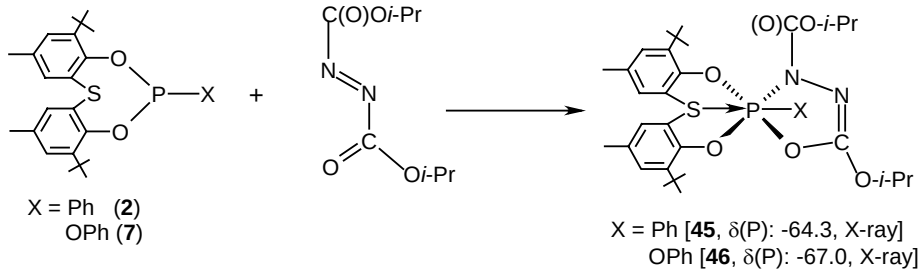


41 [δ(P): 23.6]

(c) Formation of hexacoordinate compounds

Neutral hexacoordinate phosphorus compounds with S→P donor-acceptor bonds by the addition of *o*-chloranil to suitable P(III) precursors have been studied extensively. We were curious to see if hexacoordinate compounds are formed in the cycloaddition reactions using DIAD also. Thus the hexacoordinate compounds **45** and **46** are isolated from the reaction of P^{III} precursors [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(Ph) (**2**), and [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(OPh) (**7**) with DIAD respectively (Scheme 5).

Scheme 5

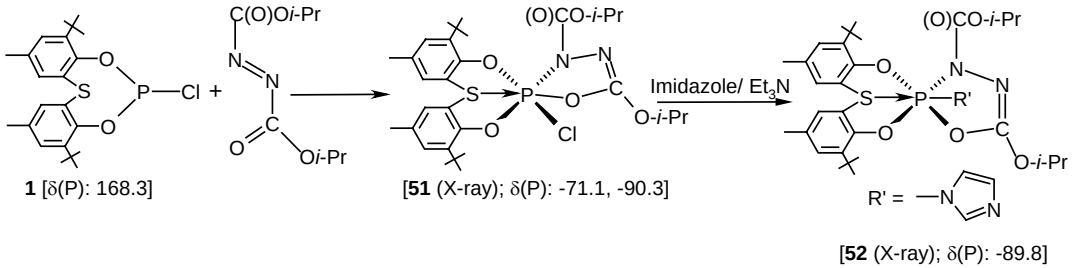


X = Ph (**2**)
OPh (**7**)

X = Ph [**45**, δ(P): -64.3, X-ray]
OPh [**46**, δ(P): -67.0, X-ray]

Similarly, When S(6-*t*-Bu-4-Me-$C_6H_2O)_2$PCl (**1**) is treated with DIAD, the hexacoordinate phosphorus compound **51** is formed; this was further reacted with imidazole to give compound **52** (Scheme 6).

Scheme 6



1 [δ(P): 168.3]

[**51** (X-ray); δ(P): -71.1, -90.3]

[**52** (X-ray); δ(P): -89.8]

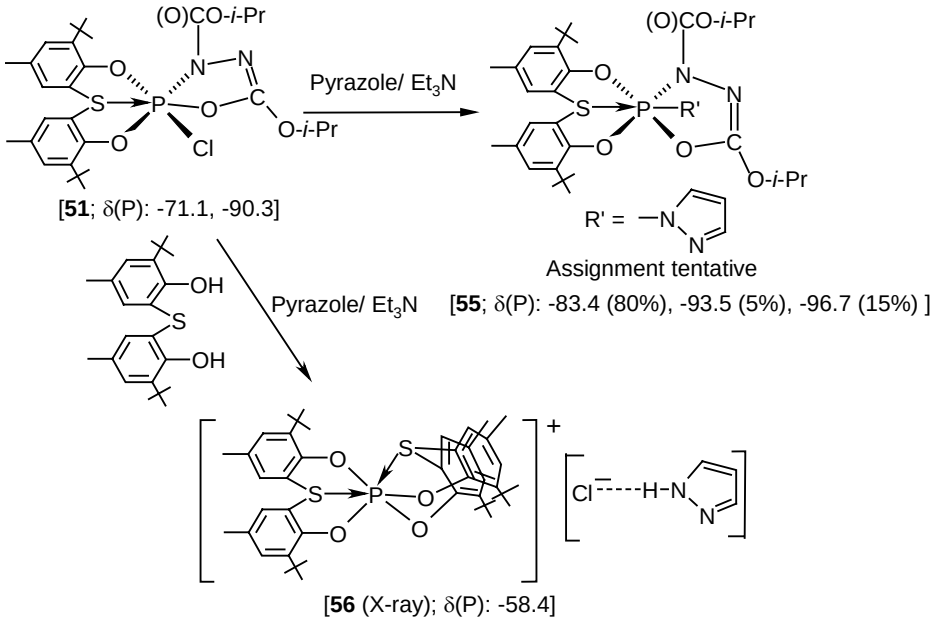
The ^{31}P NMR ($CDCl_3$) spectra for compounds **45, 46** and **52** show a single line, whereas compound **51** [δ -71.1, -90.3] shows two lines at 20°C. The latter

observation is ascribed to S-*trans*-O (as observed in the solid state, shown in Scheme 6 above) and S-*trans*-Cl isomers.

The geometry at phosphorus in all these compounds can be considered to be octahedral, with greater distortion for **51**. The S→P distances are in the range expected for the sulfur coordination to phosphorus. To our knowledge, the S→P donor-acceptor distance (2.317 Å) in **51** is the shortest known for neutral hexacoordinate phosphorus compounds and is pretty close to the covalent bond distance of 2.13-2.14 Å. We have optimized the geometries/ structures of the compounds **14**, **38**, **51** and **52** obtained at B3LYP/6-31G* level using Gaussian 03 program package. These calculations suggest that the compound as isolated is the favored one in most cases.

When a reaction analogous to that shown in Scheme 6 was performed with pyrazole using the *in situ* generated **51**, we obtained a crystalline compound **56** [δ(P): –58.4; X-ray, Figure 4] along with other products (Scheme 7). Compound **56** represents the first example of a hexacoordinate phosphorus compound with S→P←S double coordination.

Scheme 7



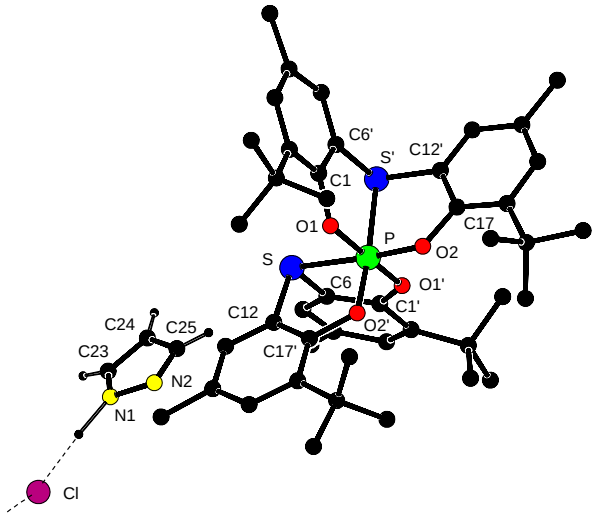
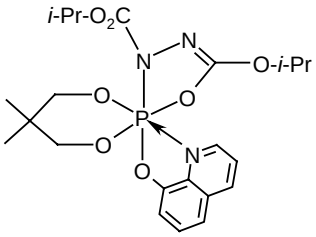


Fig. 4. Molecular structure of **56**

To probe the reaction of P^{III} compounds with DIAD further, we have used [($OCH_2CMe_2CH_2O$)P(oxinate)] (**62**). The ^{31}P NMR spectrum of the reaction mixture suggested the formation of hexacoordinate compound **64** which showed a peak at δ -109.5 via N→P coordination, but so far we have not succeeded in obtaining single crystals.

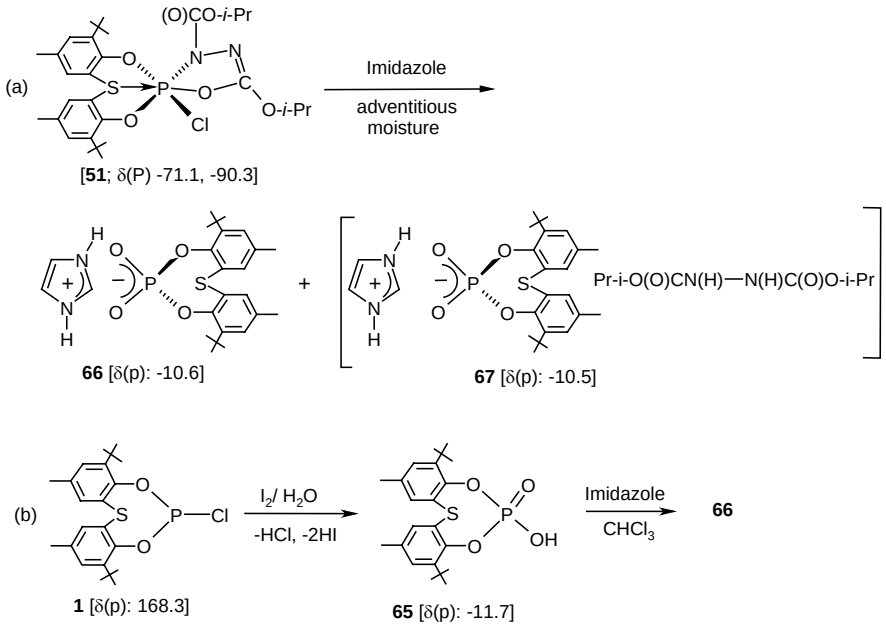


64 [δ(P): -109.5]

(iii) Involvement of cyclic phosphates in hydrogen bonding

Synthesis and X-ray structures of two imidazolyl compounds, [{S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$] (**66**) and [{S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$][$(CH_3)_2$CHO(O)N(H)-N(H)(C(O)O($CH(CH_3)_2$)] (**67**), the latter containing the carboxylate substituted hydrazine as a hydrogen bonded guest are discussed. Compounds **66** and **67** are obtained in the reaction of [{S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}PCl[N(C(O)O($CH(CH_3)_2$)N-C($OCH(CH_3)_2$O-] (**51**) with imidazole in the presence of adventitious moisture (Scheme 8a).

Scheme 8



In compound **66** hydrogen bonding leads to the formation of a chain utilizing the protons on the two-imidazolyl nitrogen atoms and the two phosphate oxygen atoms. The same type of chain is present in **67** also, but in addition, one of the phosphoryl oxygen atom is involved in the 'bifurcate' hydrogen bonding with the additional interaction from the NH hydrogen atoms of the substituted hydrazine residue. Although there is no significant interaction of the NCHN hydrogen with acceptor sites in **66**, there is one such in **67** involving the carbonyl oxygen atom of the substituted hydrazine and the NCHN hydrogen atom in **67**. The C···O distance is pretty short (2.98 Å) and is comparable to that known for strong C-H· ·O hydrogen bonds.

Chapter 3 gives details of experimental procedures.

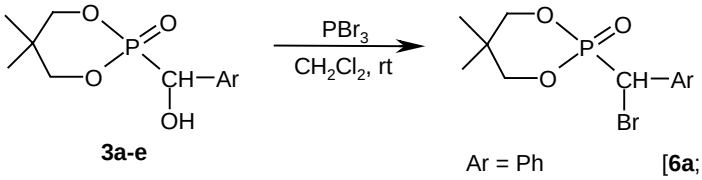
PART-B

The focus of Chapter 4 is to review the literature pertaining to the synthesis and utility of phosphonates. We are also interested in synthesizing substituted anthracenyl derivatives for future use (e.g. in material chemistry) and hence a brief survey of relevant literature on this class of compounds is given. Chapter 5 describes the results obtained in the present study on the above mentioned aspects, as described below.

(i) Synthesis of α-bromophosphonates

Treatment of α-hydroxyphosphonates **3a-e** with phosphorus tribromide (PBr_3) using dichloromethane as the solvent at room temperature afforded the α-bromophosphonates **6a-e** in high yields (80-90%) (Scheme 1). This procedure is much superior to the preparation of various types of α-bromophosphonates using PPh_3/DDQ system in the presence of tetraalkylammonium bromide with regard to the isolation of products.

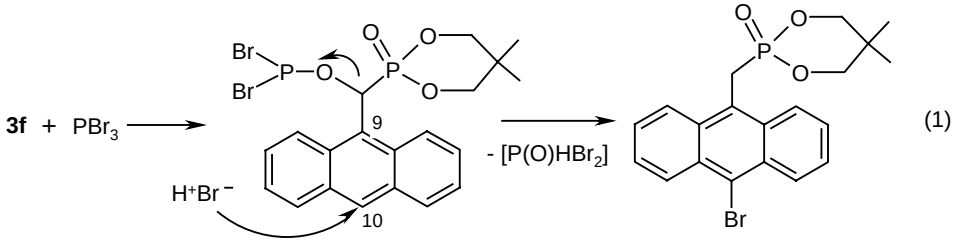
Scheme 1



3a-e

Ar = Ph [**6a**; δ(P): 9.7]
C_6H_4-4-Me [**6b**; δ(P): 9.0]
C_6H_4-4-OMe [**6c**; δ(P): 10.0]
C_6H_4-4-Cl [**6d**; δ(P): 8.4]
C_6H_4-4-Br [**6e**; δ(P): 9.3]

When the anthracenyl phosphonate $(OCH_2CMe_2CH_2O)P(O)CH(OH)$(9-anthryl) (**3f)** was brominated with PBr_3, instead of the expected α-bromophosphonate, we obtained the phosphonate **7** with the Br group at C-10 position of the anthracene moiety (eq. 1). Formation of **7** probably occurs by the attack of the Br^- at C-10 of the anthracene ring *via* an intermediate of type **I**, instead of attack at the carbon α to phosphorus.



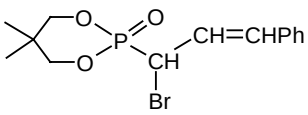
(1)

(**I**)

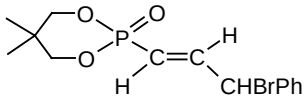
7 (δ(P) 20.3; 80%)

In contrast to the above, the reaction of $(OCH_2CMe_2CH_2O)P(O)CH(OH)(CH{=}CHC_6H_5)$ (**4)** with PBr_3 leads to two products **12** and **13** [δ(P): 8.8 and 10.8] corresponding to α- and γ-bromophosphonates respectively. Formation of brominated products at a position different from α to the

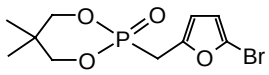
phosphorus was also observed in the case of furfuryl system (e.g. **13**), but this product is not a γ-bromophosphonate.



12 [δ(P) 8.8]



13 [δ(P) 10.8]

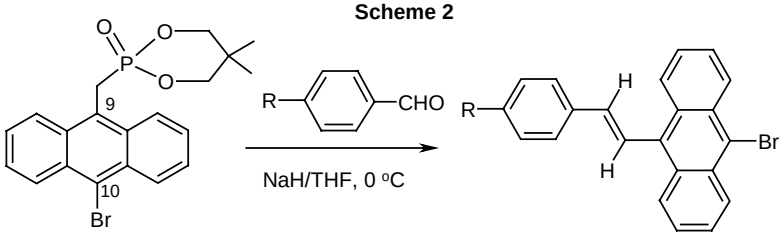


14 [δ(P): 18.1]

(ii) Synthetic utility of phosphonates

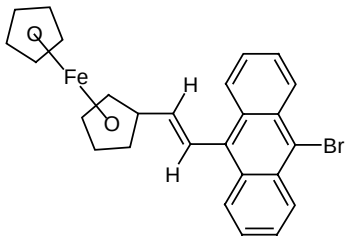
We were interested in systems possessing anthracenyl residue. In this context, when HWE reaction was performed using 10-bromoanthryl phosphonate **8** with various aldehydes, the alkenes **16-19** with anthracenyl moiety were obtained in good yields. The ferrocenyl alkene **20** could also be prepared readily (Scheme 2). When anthraldehyde was used, we were also able to isolate the 1,2-bis(9-anthryl)ethylene (**21**), *albeit* in low yields. The X-ray structure of the HWE product **18** confirms unambiguously the location of bromine at the C-10 of anthracene ring in its precursor **8**.

Scheme 2



8

R = H (**16**), Br (**17**), OMe (**18; X-ray**), NO_2 (**19**)



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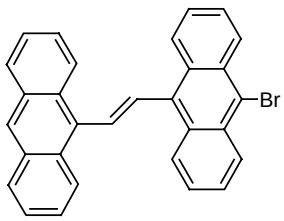
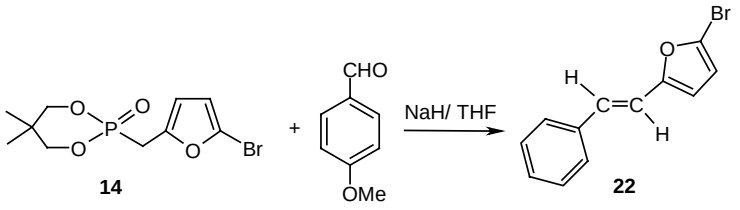


21

In the context of utility of phosphonates synthesized in the present work, when 5-bromofurfuryl phosphonate **14** was reacted with anisaldehyde, we obtained the olefin **22,** which has a *E*-configuration (Scheme 3).

Scheme 3

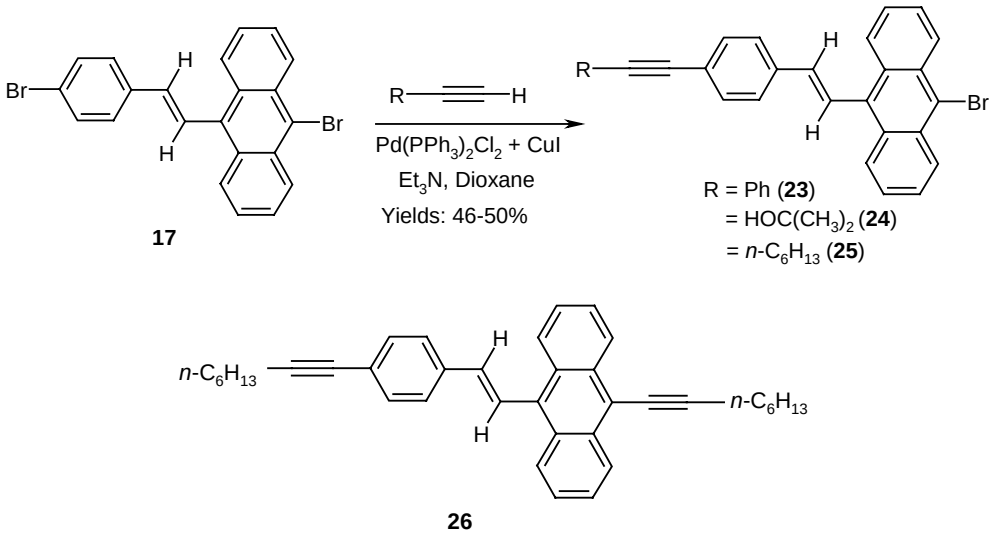


14 **22**

(iii) Sonogashira coupling of compound 17 with terminal alkynes

In connection with our interest in anthracenyl compounds with extended conjugation, we treated the bromoaryl substituted alkene **17** with the terminal acetylenes PhC≡CH, $(HO)(CH_3)_2CC{\equiv}CH$ and n-$C_6H_{13}C{\equiv}CH$ under Sonogashira conditions and obtained the coupled products **23**-**25** in decent yields (Scheme 4). In the reaction using PhC≡CH, we isolated only the mono-coupled product **23** while that using n-$C_6H_{13}C{\equiv}CH$ afforded both the mono- (**25**) and the bis-coupled (**26**) products, although the yield of the latter was quite low.

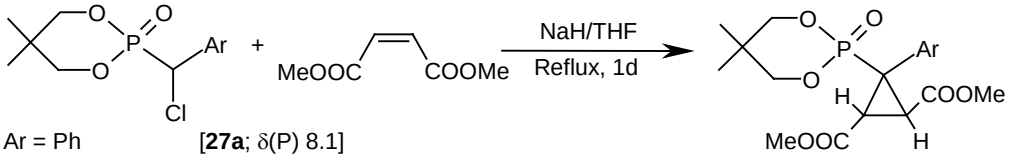
Scheme 4



(iv) Synthesis of cyclopropyl phosphonates from α-chloro/ bromo phosphonates

When α-chlorophosphonates **27a-d** were treated with NaH in THF followed by addition of dimethylmaleate under refluxing conditions we obtained the cyclopropylphosphonates **28a-d** (Scheme 5). This reaction takes place via a Michael addition followed by an intramolecular expulsion of the chlorine to give the cyclopropyl phosphonates. The structure of compound **21c** was confirmed by X-ray crystallography.

Scheme 5



Ar = Ph [**27a**; δ(P) 8.1]
C_6H_4-4-Me [**27b**; δ(P) 8.4]
C_6H_4-4-OMe [**27c**; δ(P) 8.4]
C_6H_4-4-Cl [**27d**; δ(P) 7.5]

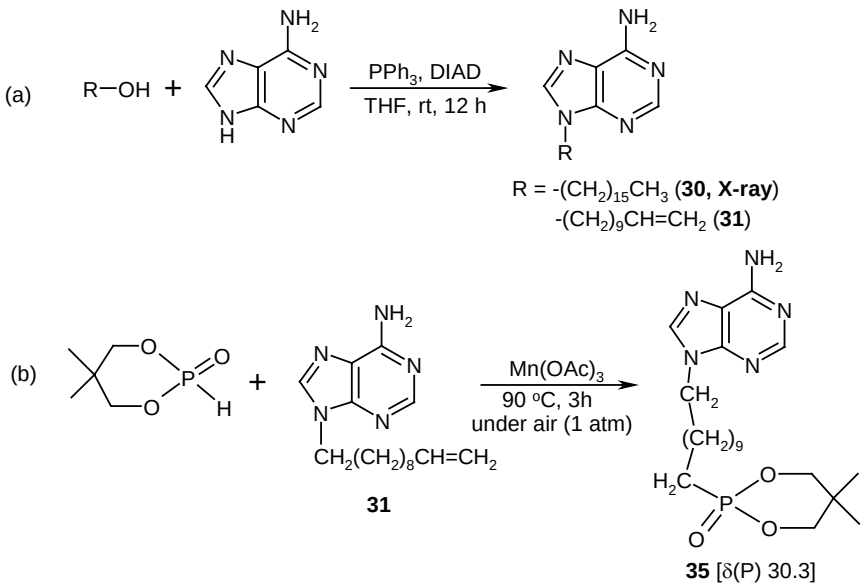
28a-d

Since we had access to the corresponding α-bromophosphonates **7a-d**, we wanted to compare the reactivity of the chloro- and bromo-phosphonates. Thus we treated α-bromophosphonate **7c** with methyl acrylate under similar conditions. The reaction was complete within 5-6 hours compared to α-chlorophosphonates that took 24 h for completion.

(v) Synthetic utility of the Mitsunobu reaction in Phosphonate chemistry

A Mitsunobu protocol was used for synthesis of N-9 alkylated adenine derivatives **30** and **31** (Scheme 6)**.** The terminal double bond in compound **31** underwent hydrophosphorylation with $(OCH_2CMe_2CH_2O)P(O)H$ in the presence of $Mn(OAc)_3$ to give the adenyl phosphonate **35** that could have potential biological activity.

Scheme 6

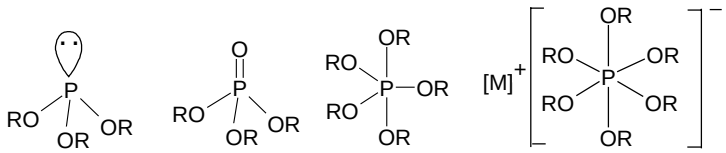


Chapter 6 gives details of the experimental procedures pertaining to this part.

CHAPTER 1

INTRODUCTION

Phosphorus is a vital element in the composition of all living matter and there is no organism in which the chemistry of this element is not utilized. It exists in nature in the form of phosphates and is widely distributed in this form in soils, rocks, in the oceans and in most foods.[1] Phosphorus biochemistry is dominated by two phosphate esters, namely ATP and DNA. There are, however, many other phosphorus compounds which play crucial roles in metabolic processes.[2] Synthetically, P^{III}* compounds 1.**1**** can be oxidized to P^{V} compounds (e.g. 1.**2**-1.**3**) by various routes.[3] These P^{V} derivatives (e.g. 1.**3**) under suitable conditions, can be converted to hexacoordinate derivatives 1.**4**. Penta- and hexa-coordinate species of types 1.**3** and 1.**4** are quite often categorized under hypervalent compounds, although in principle a species like 1.**2** with more than eight valence shell electrons also should be hypervalent.



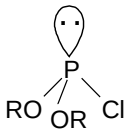
1.**1** 1.**2** 1.**3** 1.**4**

Chlorophosphites 1.**5**, like the phosphite esters 1.**1**, also possess trivalent tricoordinate phosphorus.[2b] By reacting with primary/ secondary amines, they pave way to various phosphoramidites [$(RO)_2$P-NR'R"]. Such chloro and amino

*_Note_: In this thesis, P^{III} refers to phosphorus in trivalent state and P^{V} refers to phosphorus in pentavalent state. Trigonal bipyramidal geometry is represented as TBP.

Numbering of compounds: In the introductory chapters 1 and 4, compounds are numbered as 1.1**, 1.**2**, 4.**5** etc. In other chapters, bold Hindu-Arabic numerals (**1**, **2**, **5**, etc.) are used.

derivatives are valuable intermediates in the synthesis of other tri-, tetra- and pentacoordinate phosphorus compounds.[2b,2c]

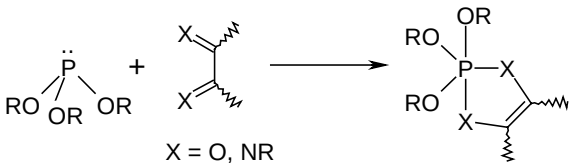


1.**5**

Apart from the presence of a lone pair of electrons on the phosphorus atom, it is the presence of reactive substituents on phosphorus that confer upon P^{III} compounds a high degree of reactivity. In the present work, we restrict ourselves to cycloaddition/ oxidative-addition reactions. Two common ways in which phosphites undergo cycloaddition reactions are the following:

(i) Both the lone pair of electrons as well as other reactive substituents like -CN_2, -N_3, or -NCO present on the phosphorus atom participate in dipolar cycloaddition reactions by reacting with various dipolarophiles.[3] The phosphorus heterocycles initially formed in these reactions need not necessarily be the final products, but can react further or undergo insertion/ elimination reactions leading to new types of compounds.[4]

(ii) Just the lone pair of electrons present on the phosphorus atom is involved in (4+1) cycloaddition with reactants like 1,2-diketones, ketoimines and other *α,β*-unsaturated compounds.[5] The final products formed are the pentacoordinate phosphoranes 1.**6**.[5,6] Hence these reactions are called as oxidative addition reactions, wherein the reactants oxidatively add on to the phosphorus atom. Four atoms from the diketone/ ketoimine, and the phosphorus atom of the phosphite take part in this [4+1] cycloaddition.



1.**6**

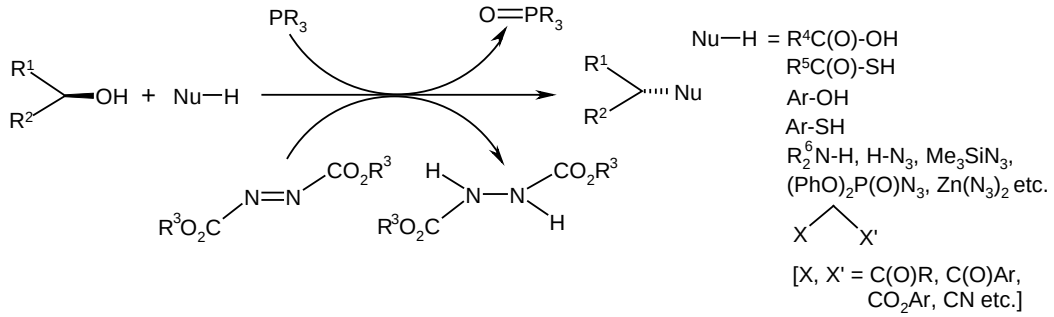
The addition reactions of P^{III} compounds with dialkyl azodicarboxylates (in the context of Mitsunobu reaction) are of interest in this work. In Section **1.1** a survey of relevant literature is presented. Section **1.2** deals with dipolar

cycloaddition reactions of P^{III} compounds. Since in many of these reactions pentacoordinate phosphorus is involved, a brief description of structural features of such compounds is given in Section **1.3** and is followed by literature pertinent to hexacoordinate phosphorus compounds in Section **1.4**. The latter part is related to the fact that if a donor atom is present on the substituents, hexacoordination is possible. During these reactions, hydrolysis of the products (intentionally or inadvertently) leads to phosphates that exhibit interesting hydrogen bonding features. Hence, a brief description of phosphates/ phosphate esters as hydrogen bonding partners is given in section **1.5**.

1.1 Reaction of P^{III} compounds with dialkyl azodicarboxylates

The substitution of primary or secondary alcohols with nucleophiles mediated by the redox combination of a trialkyl- or triaryl- phosphine and a dialkyl azodicarboxylate is popularly known as the Mitsunobu reaction.[7,8] Since its discovery in 1967, this reaction has enjoyed a privileged status in organic synthesis and medicinal chemistry because of its scope, stereospecificity and mild reaction conditions. Apart from esters, a wide range of compounds that include amines, azides, ethers and thioethers can be synthesized using a Mitsunobu protocol (*cf.* Scheme 1.1). Thus this reaction allows C-O, C-S, C-N or C-C bond formation by the condensation of an *acidic component* with a primary or a secondary alcohol in the presence of triphenylphosphine (or another suitable phosphine) and diethyl azodicarboxylate (DEAD) or diisopropyl azodicarboxylate (DIAD).

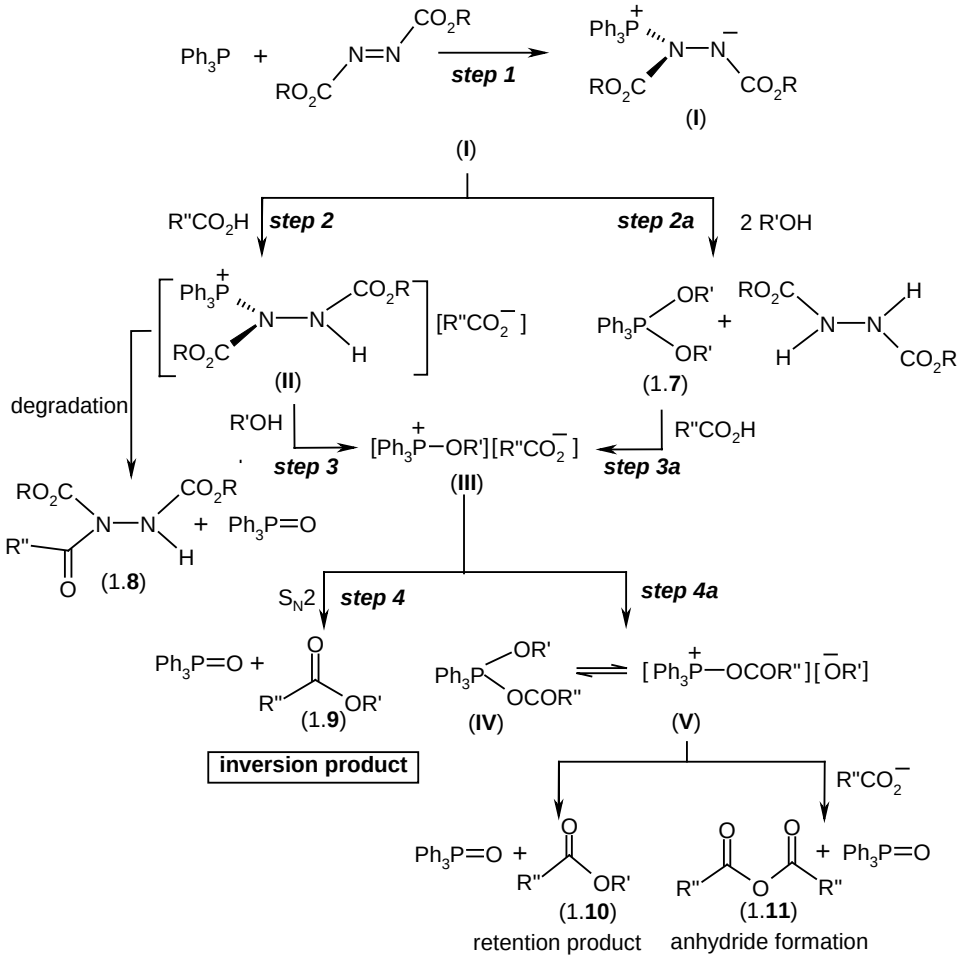
Scheme 1.1



Despite the fact that the Mitsunobu reaction is widely used in synthetic organic chemistry, the mechanistic details particularly at the intermediate stages are

still a subject of debate .[9-11] Possible pathways in the esterification process are shown in Scheme 1.2.

Scheme 1.2

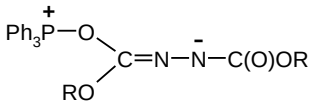


Postulated Mechanism of the Mitsunobu Esterification

EPR spectroscopy shows that the betaine **I** is formed through radical cations of type $RO_2C\text{-}N^{-}\{Ph_3P^{+}\}\text{-}N^{\bullet}\text{-}CO_2R$.[9p] The intensity of the EPR signal varies as *n*-$Bu_3P < Ph_3P < (Me_2N)_3P$ in reactions with DIAD. This observation suggests that the nature of the intermediate in the Mitsunobu reaction could vary depending upon the P^{III} precursor.

It is important to note that altering the electronic environment at P^{III} precursors has a profound effect on the first step in the reaction with DIAD/ DEAD. In earlier literature, Morrison reported that Michael type nucleophilic addition reaction of PPh_3 and DEAD/ DIAD leads to the formation of betaine **I**,[11a] although Ginsburg *et al.* proposed the alternate O-phosphonium salt **VI**.[12] Later, Brunn and Huisgen have conclusively shown the formation of betaine **I** and hence the latter is

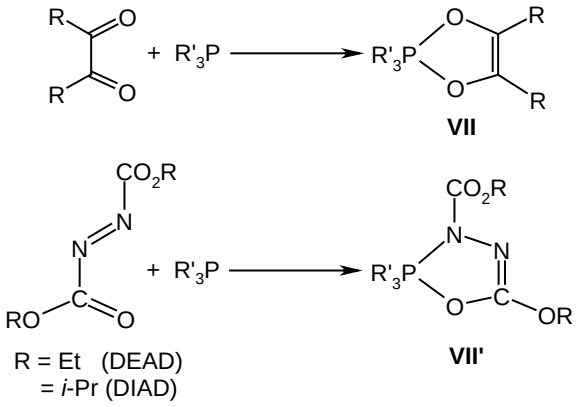
called the Morrison-Brunn-Huisgen [MBH] betaine **I**.[11b] This step is of primary interest in the present work.



VI

However, looking at the same reactants from a different perspective, we note that (i) P^{III} compounds undergo facile cycloaddition reactions with a variety of 1,2-diketones (or ketoimines) to afford pentacoordinate phosphoranes of the type **VII** (Scheme 1.3),[13] and (ii) dialkyl azodicarboxylates are analogous to 1,2-diketones (or the related 1,2-ketoimines). Thus it is possible that in the reaction of P^{III} compounds with dialkyl azodicarboxylates, N,O-cycloaddition could take place to give pentacoordinate phosphorus intermediates **VII'** that are analogous to **VII**.[14] Isolation/ identification of such species could support the possible intermediacy of the P-O bonded tetracoordinate intermediate of the type **VI**.[11b]

Scheme 1.3

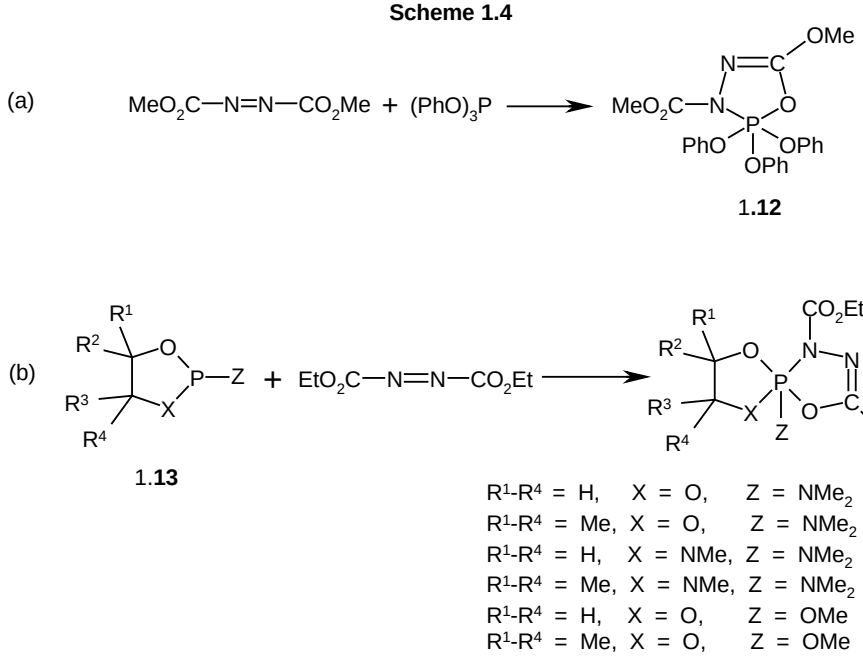


VII

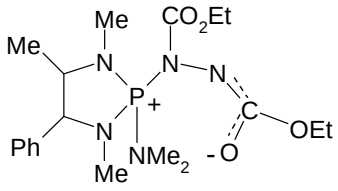
VII'

Earlier literature reveals that there does exist a different mode of addition of DEAD/ DIAD to tricoordinate phosphorus compounds forming products other than the traditional MBH betaine **I**.[9b,14,15] Arbuzov *et al* reported that triphenylphosphite reacts with dimethyl azodicarboxylate *via* N-O cycloaddition to give the pentacoordinate phosphorus compound 1.**12** (Scheme 1.4a).[14a] Later, Gonclaves *et al* prepared a series of pentacoordinate phosphoranes 1.**14**-1.**19** derived from the reaction of DEAD with various phosphites (Scheme 1.4b).[14b]

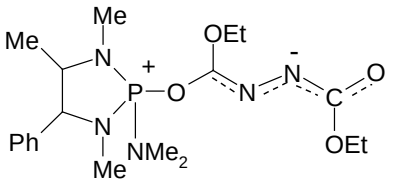
Scheme 1.4



Tetracoordinate species 1.**20** and 1.**21** have also been proposed in the reaction using phosphoramidites, but no X-ray structure is available.[9b] Formation of tetracoordinate (betaine **I**, 1.**20**-1.**21**) and pentacoordinate phosphoranes (1.**14**-1.**19**) in the first step of Mitsunobu reaction suggests that the nature of the intermediates could vary depending upon the electronic environment around the P^{III} precursor.



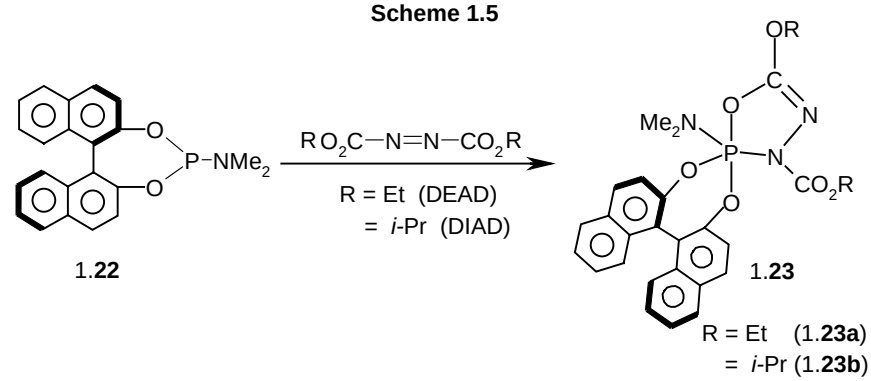
1.**20**



1.**21**

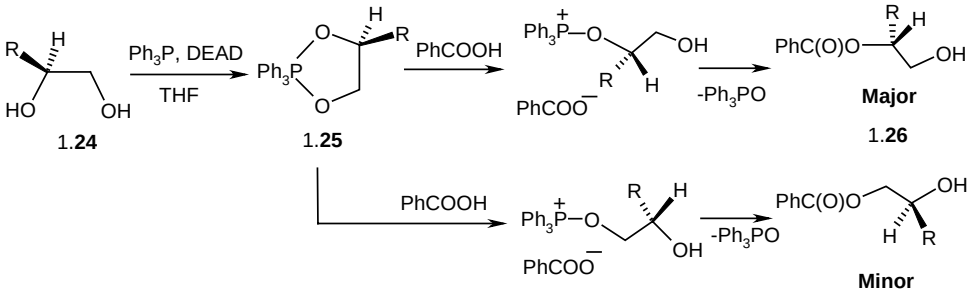
Recently it is also shown that the dimethylamino derivative 1.**22** reacts with DEAD/ DIAD to yield the pentacoordinate phosphoranes 1.**23**, and not the betaine **I** (Scheme 1.5).[15a] This species also has not been characterized by X-ray crystallography. Compound 1.**23** *does participate in the Mitsunobu coupling* between alcohol and acid.[15b]

Scheme 1.5



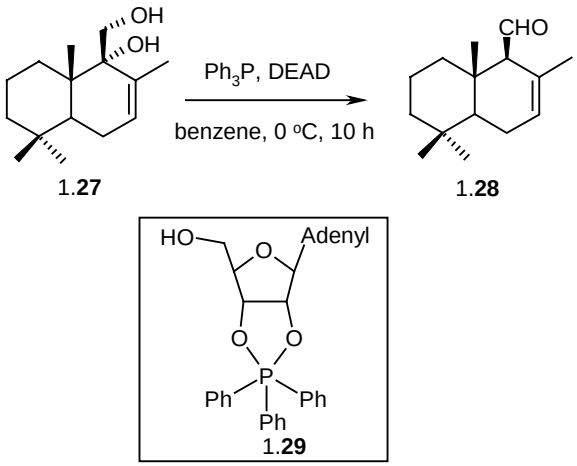
Unsymmetrical 1,2-diols (e.g. 1,2-propanediol and 1-phenyl-1,2-ethanediol) undergo a highly chemoselective monobenzoylation with Ph_3P/DEAD/benzoic acid affording both *kinetically and thermodynamically* least stable secondary benzoate (Scheme 1.6).[9j,17] The 1,3,2-λ^5-dioxaphospholane species 1.**25** is the key intermediate; in its conversion to the oxyphosphonium salt, the proton transfer from the acid occurs predominantly at the least hindered site leading to secondary benzoate 1.**26** as a major product. Similar selectivity has been observed by Voelter and coworkers, and more recently, by Wang and Yue.[18]

Scheme 1.6



In Mitsunobu reaction of 1,1-disubstituted 1,2-diols like 1.**27**, carbonyl compounds (e.g. 1.**28**) may also be formed by dehydration (in addition to epoxides or exclusively; Scheme 1.7).[19a] Similarly 1,1,2-trisubstituted 1,2-diols may give ketones. In a few cases, the covalent pentacoordinate phosphorane (e.g. 1.**29**) intermediate can be isolated.[19b]

Scheme 1.7



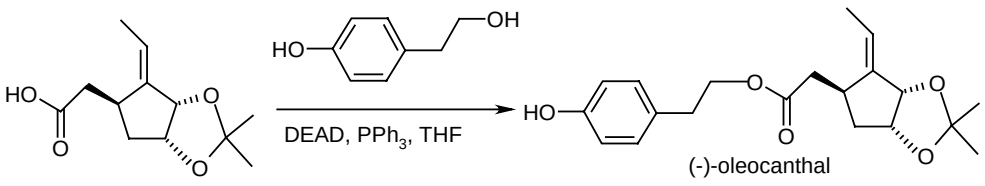
1.**27** 1.**28** 1.**29**

1.11 Synthetic applications of Mitsunobu reaction

The Mitsunobu reaction has found widespread use in many fields because of its high reliability and extensive applicability. Its importance and utility can be gauged from the fact that in *Scifinder*, for 'Mitsunobu reaction', there were 932 citations from 2000-2005 including 83 patents. Only some selected examples are discussed below.

The Mitsunobu reaction can effectively differentiate alcoholic and phenolic hydroxyls in esterification reactions, thus providing a broadly applicable entry into various phenolics and polyphenolics of biomedical and nutritional relevance.[20] Such discrimination between alcoholic and phenolic hydroxyls has also been recently utilized in the total synthesis of (-)-oleocanthal (1.**31**), a naturally occurring non-steroidal, anti-inflammatory and antioxidant agent (Scheme 1.8).[21]

Scheme 1.8

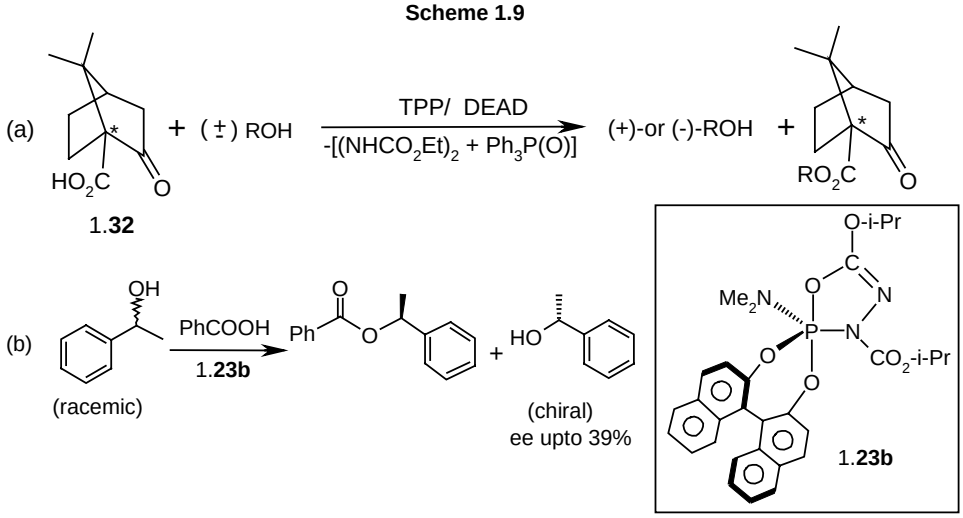


1.**30** (-)-oleocanthal Yield: 92% 1.**31**

It is of some interest to see whether kinetic resolution of secondary alcohols can be affected or not. Thus in the reaction using 0.5 mole equivalents each of Ph_3P, DEAD and (1*S*)-(+)-ketopinic acid (1.**32**) with 1 mole of racemic (±)-PhMeCHOH,

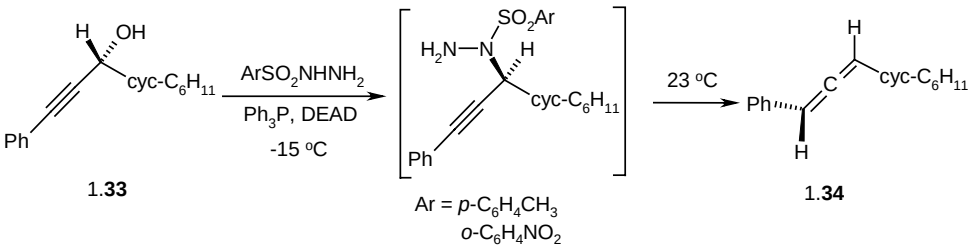
the unreacted alcohol could be obtained in yields of 44% with an *ee* of ~90% (Scheme 1.9a).[22] It is also possible to use the 1,1'-bi-2-naphthoxy based P^{III} compound (+)-(1,1'-$C_{20}H_{12}O_2$)P(NMe_2)(1.**23b**) to effect kinetic resolution as shown by Kellogg and coworkers (Scheme 1.9b).[15a]

Scheme 1.9



Synthesis of a diverse class of substituted allenes (e.g. 1.**34**) has been achieved in a single step starting from propargylic alcohols (e.g. 1.**33**) using a Mitsunobu protocol.[23] This transformation proceeds with complete stereospecificity and provides access to a wide range of optically active allenes since a large number of optically active propargylic alcohols are available (Scheme1.10).

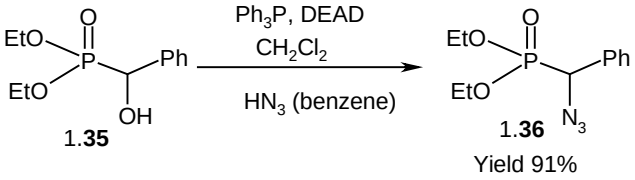
Scheme 1.10



It has been shown earlier that zinc azide along with Ph_3P/ DIAD in toluene is effective in the azidation of secondary alcohols.[24] Catalytic quantities of phenol may activate an alcohol towards azidation by HN_3.[25] The α-hydroxyphosphonates 1.**35** undergo ready azidation *via* Mitsunobu reaction using HN_3 (Scheme 1.11),[26a] these azides (1.**36**) can later be converted to the corresponding α-aminophosphonates that show a wide range of biological activity. Similarly β-hydroxyphosphonates can be

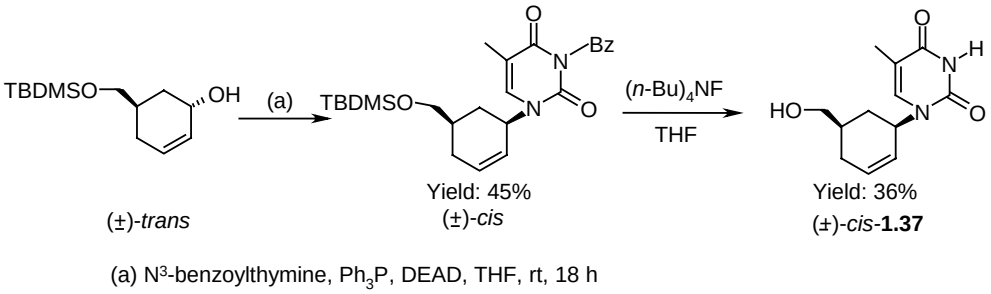
converted to β-azidophosphonates and then to β-aminophosphonates,[26b] many enantiopure β-aminophosphonates could thus be synthesized.

Scheme 1.11



A series of purine and pyrimidine *cis*-substituted cyclohexenyl and cyclohexanyl nucleosides (e.g. 1.**37**), some of which showed moderate antiviral activity against HSV1 and *coxsackie* viruses, were synthesized through a key Mitsunobu step (Scheme 1.12).[27] A similar method was employed to prepare the analogous cytosine and adenine derivatives.

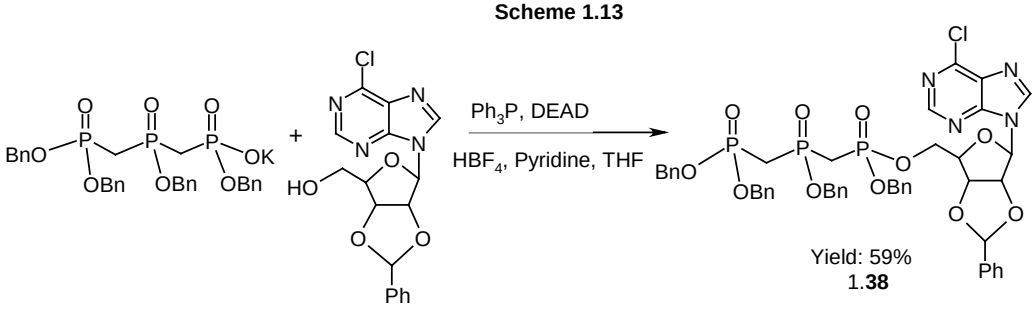
Scheme 1.12



(a) N^3-benzoylthymine, Ph_3P, DEAD, THF, rt, 18 h

It is possible to prepare phosphite esters $(MeO)_2P(OR)$ by starting with phosphites such as $(MeO)_2P(O)H$ and Ph_3P/ DIAD in toluene. Direct esterification of mono- and tri-phosphonic acids using nucleosides as the alcohol components to lead to esters of type 1.**38** is possible under Mitsunobu conditions (Scheme 1.13).[28]

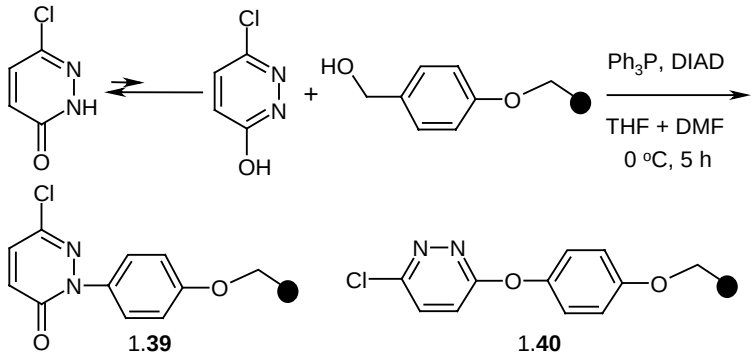
Scheme 1.13



Polymer supports in the Mitsunobu reaction

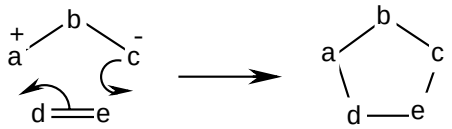
The generation of phosphine oxide and hydrazinecarboxylate as byproducts in the Mitsunobu reaction often prevents the desired compound from being isolated. Many efforts have been directed toward modifying triphenylphosphine or azodicarboxylate reagents to facilitate the isolation and purification of the desired product.[29] The use of polystyryldiphenylphosphine resin (used in excess) can circumvent the problem of removal of Ph_3PO because the resulting oxide is also anchored to the polymer and thus can be readily filtered.[30] Reduction of the oxide back to reusable resin can be effected by treating it with trichlorosilane.[31] Using this methodology, aryl-alkyl ethers can be readily synthesized.[32] Although 3-hydroxypyridazine exists predominantly in the oxo form, it does undergo Mitsunobu coupling with polymer bound benzyl alcohols as shown by Salives *et al* (Scheme 1.14).[33] Both the O-alkylated (1.**39**) and the N-alkylated (1.**40**) products [ratio: 2:3] were obtained.

Scheme 1.14



1.2 Dipolar cycloaddition reactions of P^{III} compounds

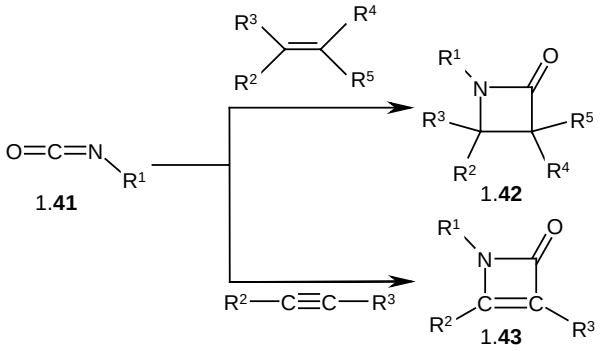
The two most important classical cycloaddition reactions, Diels-Alder and 1,3-dipolar cycloaddition, occur usually through a concerted mechanism. 1,3-Dipolar cycloaddition reactions constitute a large class of synthetically useful processes and offer a remarkably wide range of utility in the construction of five membered heterocycles.[34] Organic isocyanates, azides, nitriles etc are valuable substrates in such cycloadditions and behave typically as 1,3-dipoles toward dipolarophiles.



The classical reactivity of organic functionalities can be dramatically altered by the presence of electron withdrawing groups such as acyl,[35a] sulfonyl[35b] and phosphoryl groups.[36] The lone pair of electrons on the phosphorus atom can participate in the cycloaddition reactions wherein λ^3-phosphorus compounds are converted into λ^5-phosphorus compounds. Thus, the phosphorus substituent is of particular importance as a reactive peripheral functional group in cycloaddition reactions. In some cases, due to the presence of phosphorus, the organic 1,3-dipole transforms into 1,4-dipole. [36]

The organic isocyanate 1.**41** undergoes [2+2] cycloaddition with activated olefins or acetylenes to lead to unstable azetidinone 1.**42** or azetones 1.**43** (Scheme 1.15) as the primary products.[37]

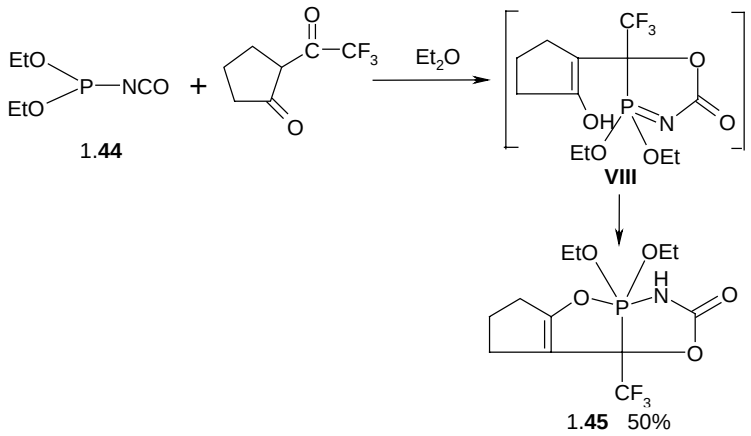
Scheme 1.15



By contrast, dialkyl isocyanatophosphites [$(RO)_2$P-N=C=O] and their isothiocyanato analogues [$(RO)_2$P-N=C=S] act as typical 1,3-(P,C) dipoles in reactions with dipolarophiles.[38-40] In most of the cases this is best explained in terms of nucleophilic attack of the phosphino residue at the electrophilic carbon of the dipolarophiles leading to phosphorus based heterocycles. The diverse reactivity of trivalent phosphorus compounds containing N=C groups makes it possible to synthesize a wide variety of both cyclic and acyclic tetra and pentacoordinate phosphorus compounds.[38]

Diethoxy isocyanatophosphine 1.**44** reacts with a 2-trifluoroacetylcycloalkanes diastereospecifically *via* addition of phosphorus at the trifluoroacetyl group to form azophospholines **VIII** via 1,3-(P,C) dipolar cycloaddition, followed by an additional heterocylization to give pentacoordinate phosphorane 1.**45 (**Scheme 1.16).[46]

Scheme 1.16



It is possible that the P^{III}-NCO compounds undergo reactions with dialkyl azodicarboxylates, but such compounds prior to our work did not exist.

1.3 Pentacoordinate phosphorus compounds

1.31 General Introduction

Many aspects of cellular energetics and biosynthesis involve nucleophilic displacement reactions at a tetracoordinate phosphorus(V) center.[42-43] Enzymatic as well as non-enzymatic hydrolysis of RNA have been of great interest and are shown to take place *via* cyclic pentacoordinate trigonal bipyramidal transition state species.[43] It is assumed that the phosphoryl transfer reactions such as energy transfer and DNA formation *via* ATP also go through the pentacoordinate phosphorus intermediate, which is formed by the nucleophilic attack at the tetracoordinate phosphorus center.[42c] The proposed mechanism for the phosphatidyl inositol cleavage catalyzed by phosphatidylinositol-specific phospholipase (PI-PLC) takes place via a pentacoordinate transition state species (**1X**).[44] In this context, the recent X-ray structure determination of the stabilized pentacovalent phosphorane (**X**) with trigonal bipyramidal geometry in the biochemical phosphoryl group transfer reaction is very significant.[45] Recent investigations have also shown that the inhibition of human α-thrombin by a phosphonate tripeptide goes through *via* a metastable

pentacoordinate phosphorus intermediate.[46] Such an important role played by phosphates in the living world has given rise to numerous kinetic and mechanistic investigations on solvolytic reactions of simple phosphoric acid esters. The emphasis in these studies is on the factors that govern the formation, isomerization, and breakdown of the pentacoordinate intermediate.[1d,42d,47,48] Theoretical calculations have also been useful in understanding the structure of transition states, but the mechanistic speculations based on such calculations need to be proven.[49,50] The behavior of hydroxyphosphoranes and their salts is definitely interesting in this context, but there are only a few well-authenticated examples of such derivatives.[51]

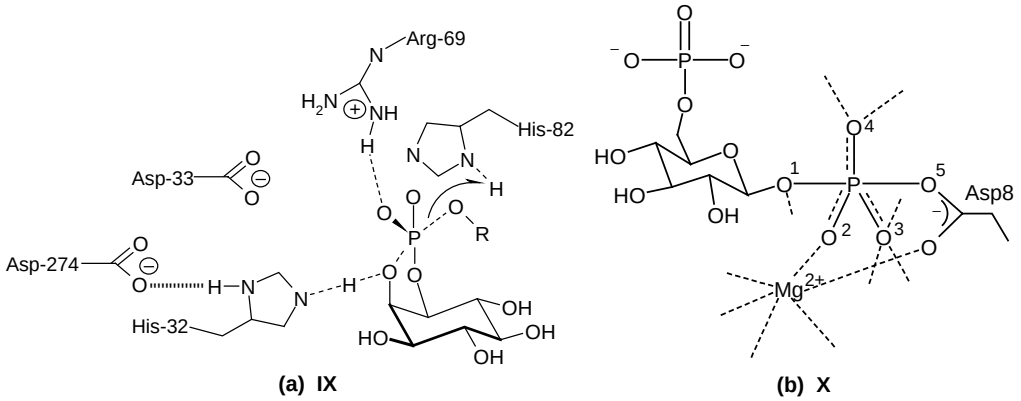
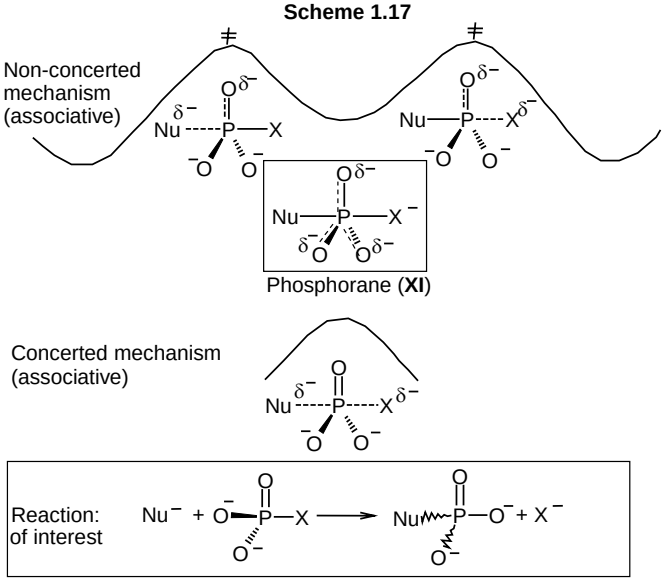


Fig. 1.1. (a) Transition state (**IX**) (drawing taken from ref 45) proposed for the phosphatidylinositol cleavage by PI-PLC. (b) A simplified drawing of the β-glucose-1,6-(bis)phosphate intermediate (**X**) structure in the active site of β-phosphoglucomutase. The extra hatched-line bonds from O(1), O(3) and O(4) at the pentacoordinate phosphorus are hydrogen bonds. Selected bond parameters: P–O(1) 2.0, P–O(2), P–O(3) and P– O(4) 1.7, P–O(5) 2.1Å. O(1)–P–O(5) 174°.

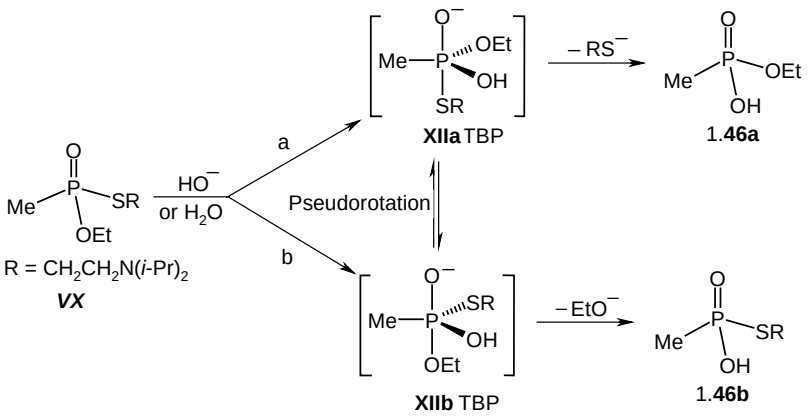
It is possible for the pentacoordinate phosphorus species **XI** (Scheme 1.17, drawing taken from ref 52) that has sufficient lifetime (non-concerted pathway) to undergo intramolecular ligand exchange processes. Thus the relative preference of a substituent to occupy the apical or equatorial site in the more commonly observed trigonal bipyramidal geometry is important as far as the mechanism is concerned.

Scheme 1.17



The apicophilicity of the substituents (relative positioning in trigonal bipyramidal phosphorus) is also significant in the hydrolysis of many organophosphorus poisons.[52] The exceedingly toxic nerve gas agent *VX* [O-ethyl S-(2-diisopropylamino)ethyl methylphosphonothiolate] undergoes hydrolysis in the presence of an alkali via two types of trigonal bypyramidal phosphorus species, (a) with the SR group apical and (b) the OEt group apical (Scheme 1.18). Thus the disposition of the substituents in the transition state species just before its break-up would affect the stereochemistry of the products. In this context, several investigations have been directed at finding apicophilicity of different substituents. Even in neutral molecules, the question of apical/ equatorial preference has been discussed at length by many pioneers.[52]

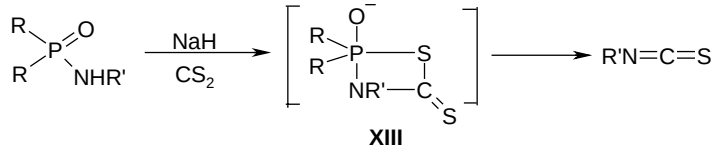
Scheme 1.18



Hydrolysis of **VX** (a chemical warfare agent)

In Wittig, Horner-Wadsworth-Emmons, and Stec reactions (Scheme 1.19) pentacoordinate phosphorus is encountered;[53] even the Mitsunobu esterification can be effected *via* pentacoordinate interemediates.[15a] Numerous other reactions involving P^{III} or tetracoordinate P^{V} compounds also lead to pentacoordinate phosphoranes.[6,54] Thus a knowledge of pentacoordinate phosphorus chemistry is a useful area for research.

Scheme 1.19



XIII

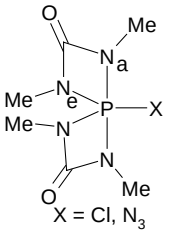
Stec reaction

Apicophilicity, Ring strain and Bent's rule

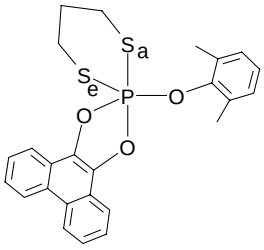
More electronegative substituents prefer apical sites (i.e. more apicophilic) in trigonal bipyramidal phosphorus according to the 3c-4e bonding picture or in terms of Bent's rule.[55] This is perhaps too simplistic a picture without giving due consideration to steric and ring constraints imposed by various groups. In cyclic/ fused ring phosphoranes with a TBP phosphorus, ring constraints generally dominate over the electronegativity effects in apical site occupancy even for highly electronegative substituents (*cf.* Chart 1.1, compounds 1.**47**-1.**50**).[56] In general, 4-7 membered rings at phosphorus prefer apical-equatorial disposition (e.g. 1.**47**-1.**49** and 1.**51**), unless constrained by fused rings (e.g. 1.**50**, 1.**52**).[57] Even when unsaturation is incorporated in the six-membered ring (e.g. 1.**51**), the apical-equatorial disposition of the ring is manifested. Hydrogen bonding can affect ring conformations, but unlike ring strain, is not strong enough to change the apicophilicity of the substituents.[58] High apicophilicity is supposedly favored by high electronegativity, small size and stronger the π-acceptor properties; π-donating and bulkier groups are supposed to occupy the equatorial site.[1d, 59] Based primarily on variable temperature NMR or activation enthalpy different scales of apicophilicity [due to: Trippet, Cambridge and Akiba] are available: (a) F>H>CF_3>OPh> Cl> SMe>OMe>NMe_2> Me>Ph;[1d] (b) OMe ≈ H>COMe ≈ SMe> NMe_2>Me>*n*-Bu[60a]); (c) Ph>CH_2OMe>Me>CH_2Ph>Et>*n*-Pr≈*n*-Bu (in $CDCl_3$) or

Ph>CH_2OMe>CH_2Ph>Me>Et>*n*-Pr>*n*-Bu (in CD_3CN).[60b] Theoretical calculations predict the gas phase apicophilicities in the order F > OH > H > Me > NH_2 for the neutral oxyphosphoranes.[60c]

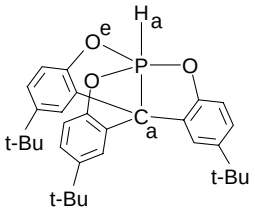
Chart 1.1



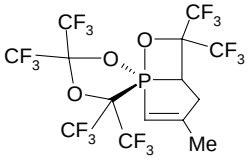
1.**47**



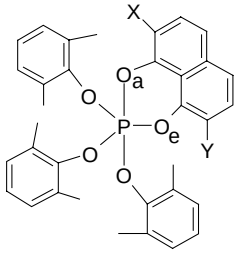
1.**48**



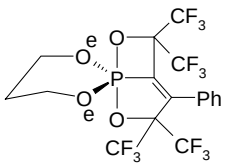
1.**49**



1.**50**



1.**51**

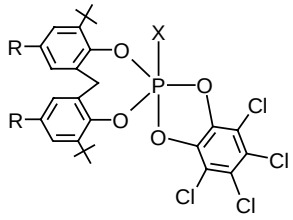


1.**52**

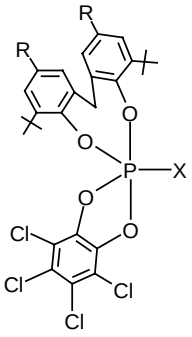
1.32 Reaction of P^{III} compounds with *o*-chloranil – Formation of pentacoordinate phosphorus compounds

The compounds shown in Chart 1.2 are prepared by the reaction of P^{III} compounds with *o*-chloranil. Compounds 1.**54c,** 1.**53**(**a**-**j**)**,** 1.**55(a-e**) and 1.**56** are reported from our laboratory[56g,58b,61] and compounds1.**54a**-1.**54b** are reported by Holmes.[62] In contrast to those in Chart 1.1, the eight-membered 1,3,2-dioxaphosphocin ring for compounds shown in Chart 1.2 can readily occupy either diequatorial or apical-equatorial disposition in a trigonal bipyramid. Investigations from our laboratory clearly revealed that the preference of the fifth ligand to go apical or equatorial drives the eight memebered ring to a-e or e-e positions thus allowing us to determine its relative apicophilicity. It should be noted that without the *t*-butyl group *ortho* to the phenolic oxygen, the eight-membered ring prefers only the apical-equatorial disposition.[56d]

Chart 1.2



R	X
Me	Ph (1.**53a**)
Me	Et (1.**53b**)
Me	*t*-Bu (1.**53c**)
Me	Cl (1.**53d**)
Me	N_3 (1.**53e**)
Me	NCS (1.**53f**)
Me	NMe_2 (1.**53g**)
Me	NMePh (1.**53h**)
Me	$N(i\text{-}Pr)_2$ (1.**53i**)
Me	SC_6H_4-4-Cl (1.**53j**)
t-Bu	Ph (1.**54a**)
t-Bu	Et (1.**54b**)
t-Bu	OC_9H_6N (oxinate) (1.**54c**)

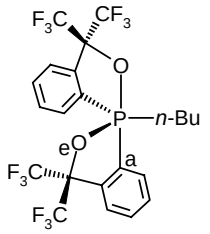


R	X
Me	Me (1.**55a**)
Me	NH_2 (1.**55b**)
Me	NHMe (1.**55c**)
Me	NHPh (1.**55d**)
Me	$N{=}PPh_3$ (1.**55e**)
t-Bu	NHC_6H_{11} (1.**56**)

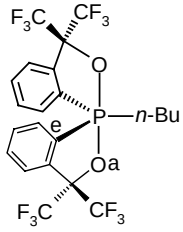
The observed apicophilicity of –Cl, -N_3, -NCS, oxinate and -SC_6H_4-4-Cl is in line with the apicophilicity rules. The higher apicophilicity of an -SR group is also in accordance with the hydrolysis products of the chemical warfare agent *VX* mentioned above. The greater apicophilicity of phenyl group compared to methyl is *opposite* to that given by Corbridge[1d] but consistent with that of Akiba;[60b] The *apical* occupancy of the ethyl group (compound 1.**53b**) compared to the *equatorial* occupancy of methyl (compound 1.**55a**) is different from that observed by Akiba.[60b] It is likely that the *t*-butyl group *ortho* to phenolic oxygen has a role in placing the phenyl/ ethyl group apically in compounds 1.**54a**-1.**54b**[56d] and 1.**53a**-1.**53b**. More significant however, are the (i) *apical* placement of the bulky *t*-butyl group in 1.**53c** compared to *equatorial* placement of the much smaller methyl group in 1.**55a** and similarly, (ii) *apical* placement of –N(i-Pr)$_2$ in 1.**53i** compared to *equatorial* placement of *more electronegative* and *much smaller* –NH_2[63] in 1.**55b**. These are clear cases of 'reversed apicophilicty'. The bulky –N=PPh_3 group in 1.**55e**, however, still prefers the equatorial position.

For many penatcoordinate phosphorus compounds in several instances it has been observed that an aryl/ nonaryl carbon occupies an apical site. Examples include compounds 1.**57**-1.**58**. For 1.**57** and 1.**58**, both C-*apical* and O-*apical* isomers are isolated.[64] Compounds 1.**58a-b** are important as Wittig reaction intermediates.

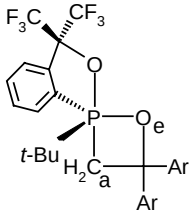
Based on the relative stabilities of these spirophosphoranes, the authors conclude that steric effect is the major cause for stabilization against pseudo-rotation in the isomers that exhibit reversed apicophilicity.



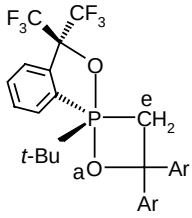
1.**57a** (C-apical)



1.**57b** (O-apical)



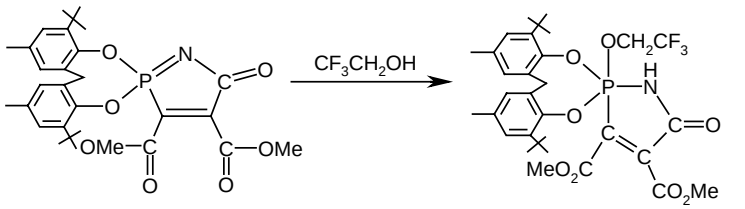
1.**58a** (C-apical)



1.**58b** (O-apical)

Another interesting example of 'reversed apicophilicity' (carbon vs nitrogen) in the 5-membered ring was observed in our laboratory in the spirophosphorane 1.**60** obtained in the reaction of heterocycle 1.**59** with 2,2,2-trifluoroethanol (Scheme 1.20).[65] One may think that the electron-withdrawing carboxyl group increases the group electronegativity at the sp^2 carbon center, but it should be noted that this happens despite the greater steric requirement at the (=)*C*(CO_2R) center relative to NH center.

Scheme 1.20



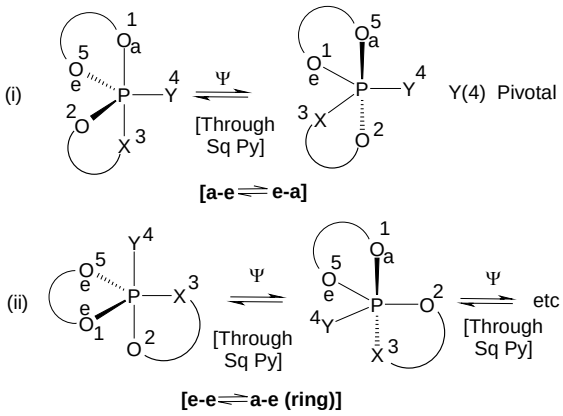
1.**59**; δ(P): 56.7 — 1.**60**; δ(P): -65.0, -72.5; X-ray]

Berry Pseudorotation and Fluxional behavior

Berry pseudorotation is the preferred intramolecular exchange processes in acyclic pentacoordinate phosphoranes.[6a] Even for monocyclic and spirocyclic phosphorane this appears to be a good option, although in principle turnstile

mechanism could also be involved. For the monocyclic/ spirocyclic phosphoranes with a TBP geometry, both a-e ⇔ e-a [process i] and e-e ⇔ a-e [process ii] type of exchange for the rings can be envisaged. Scheme 1.21 depicts this for a set of spirocyclics; the square pyramidal transition state is not shown. Cessation of process (i) for the *o*-chloranil system (*cf.* Chart 1.2) would lead to a single ^{31}P NMR resonance or very closely-spaced signals due to different conformations of the eight-membered ring (boat-chair and tub). For the same *o*-chloranil system, in process ii, the local environment at phosphorus changes significantly and at least two well-separated signals are expected if this is occurring.

Scheme 1.21



Lowering the temperature can inhibit the psuedorotational processes. Thus, one can have an idea of the pseudorotational process involved by recording variable temperature NMR spectra. An example from our laboratory is discussed below.

Variable temperature ^{31}P NMR behavior of compound $[CH_2\{6\text{-}t\text{-Bu-4-Me-}C_6H_2O\}_2]P(NMePh)(1,2\text{-}O_2C_6Cl_4)$[61b] (1.**53h**) is shown in Fig. 1.2. It is clear that at 232 K two peaks are observed at δ -47.0 and -51.7. Upon increasing the temperature (323 K), only one peak at δ -48.1, which is closer to the downfield peak δ -47.0, is seen. Such an unsymmetrical coalescence is new and not reported earlier for pentacoordinate phosphorus compounds. However, pentacoordinate phosphorus compounds showing three or more signals in ^{31}P NMR (at low or room temperature) are rare and the intramolecular exchange aspects of such compounds is still an interesting topic to study.

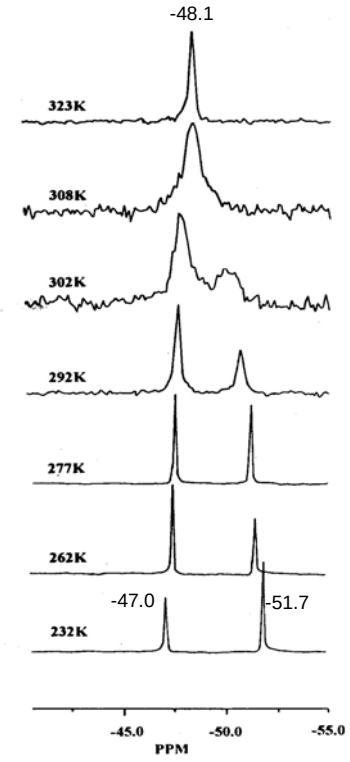
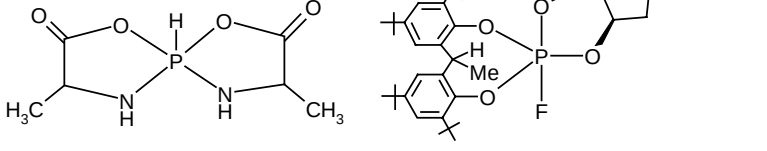


Fig. 1.2 Variable-temperature ^{31}P NMR spectra for 1.**53h**

Developments in the area of pentacoordinate phosphorus that could come up in the future are (i) the isolation/ understanding of phosphoranes of biological relevance/ interest and (ii) use of pentacoordinate compounds as precursors for organic synthesis. Recent reactions of phosphorus trichloride with various amino acids afford pentacoordinate spirophosphoranes, and the reactions were monitored by ^{31}P NMR spectra. The alanine derivative (1.**61**) was characterized by X-ray diffraction. The spirophosphoranes thus prepared showed high tyrosinase inhibition activity.[66a] Recent structural characterization of thymidine based phosphorane (1.**62**) is also relevant in this context.[66b] However, although inositol phosphates are widely found in living systems, not even a single pentacoordinate phosphorane involving inositol has been isolated as yet.



1.**61**

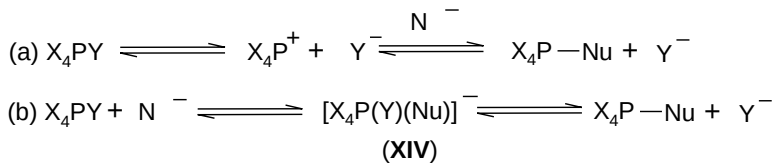
1.**62**

If one visualizes different heteroatoms connected to phosphorus, a large number of pentacoordinate isomers in principle can be formed. This kind of a system, if amenable, will allow us to probe the apicophilicity aspect much deeper.

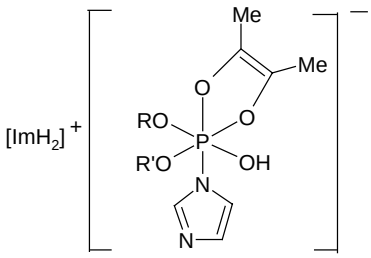
1.4 Hexacoordinate phosphorus compounds

1.41 General Introduction

When we consider substitution at pentacoordinate phosphorus with the formula X_4PY, two different pathways (a) and (b) can be envisaged.[67] The associative mechanism would lead to an anionic hexacoordinate species (**XIV**). This type of mechanism is more common for pentacoordinate phosphorus because of its Lewis acidity, provided that no steric inhibition operates. The existence of such species such as (**XIV**) has been established by Westheimer[68a] as well as Trippett.[68b] In addition to these, Ramirez and coworkers have proposed involvement of the hexacoordination species (**XV**) in the nucleophilic catalysis of the phosphorylation of alcohols R'OH by the cyclic phosphate (RO)P(O)[OC(Me)=C(Me)O] in the presence of imidazole.[69]



(**XIV**)



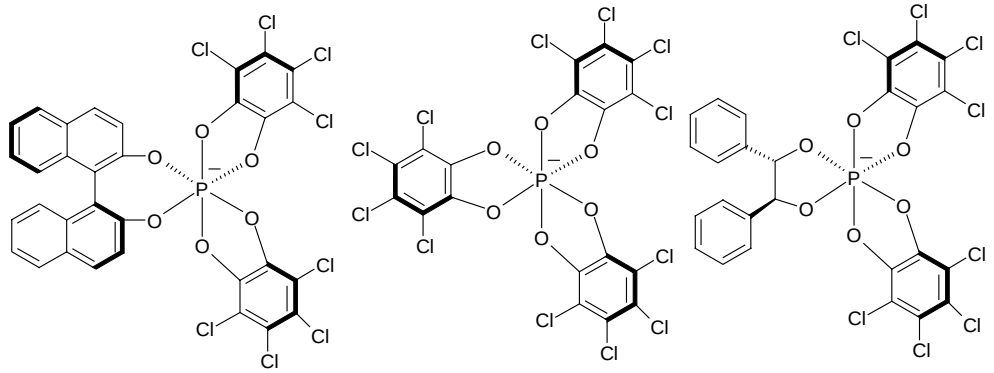
[Im = imidazole]

XV

1.42 Anionic and cationic hexacoordinate phosphorus compounds

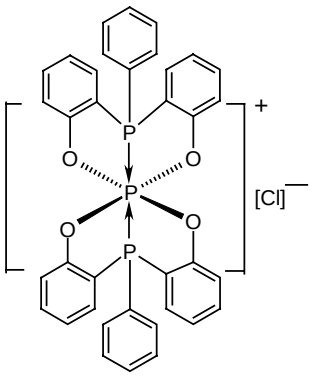
There are quite a number of anionic hexacoordinate phosphorus compounds in literature.[70-71] Recently, chiral hexacoordinate phosphate anions,[72] BINPHAT (bis(tetrachlorobenzenediolato)mono([1,1']binaphthalenyl-2,2'-

diolato)phosphate(V)) (1.**63**), TRISPHAT [tris-(tetrachlorobenzenediolato)phosphate(V)] (1.**64**), and HYPHAT (bis(tetrachlorobenzenediolato)mono(1,2-diphenylethane-1,2-diolato)phosphate(V)) (1.**65**), were shown to be readily prepared in one or two steps from commercially available starting materials.

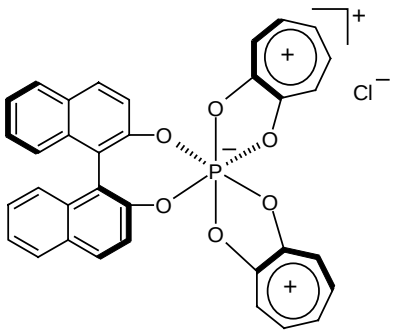


These diamagnetic anions are efficient NMR chiral shift agents, with a preference for cationic metallo-organic and organo-metallic substrates. The efficiency of the anions is explained by the formation of diastereomeric contact ion pairs. In most of the studies, the chiral shift experiments were performed by the addition of $[Bu_3NH][BINPHAT]$ or $[Bu_4N][TRISPHAT]$ to solutions of the chiral cations. However, recent studies have shown that C_2-symmetric 1.**63** and 1.**65** anions often possess better chiral shift properties than 1.**64** when associated with organic cations.[72d]

There are a few studies on cationic hexacoordinate compounds. An example of this type is prepared by treating $[(C_6H_4O_2)_2P]^+[SbCl_6]^-$ with 1,10-phenanthroline.[73] Another interesting compound (1.**66**) with two $P^{III}\rightarrow P^V$ bonds has been reported by Cavell and coworkers.[74] Recently Lacour and coworkers have showed that tropolone, binaphthol and PCl_5 react in one step to give C_2-symmetric hexacoordianted phosphorus cation (1.**67**) which acts as an efficient NMR chiral shift reagent for chiral anionic phosphates and borate anions.[75,71]



1.**66**



BINTROP

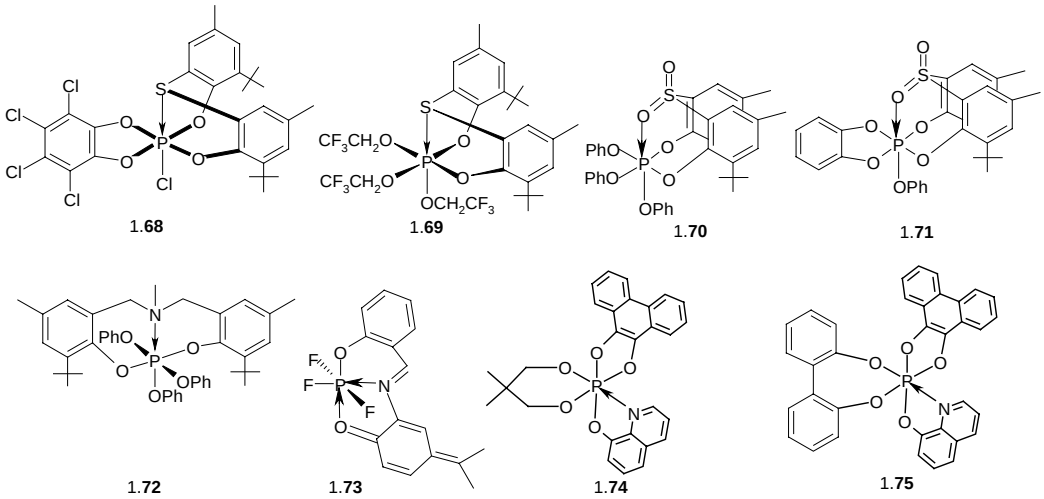
1.**67**

1.43 Neutral hexacoordinate phosphorus compounds

The simplest route to neutral hexacoordinate phosphorus center is to use the Lewis acidity of the halogenophosphorus(V) compounds in combination with simple Lewis base donors. In most cases, the donor atoms are nitrogen and oxygen bases although several sulfur and a few P^{III} donors have been used.[76-78] Cavell and coworkers have characterized various neutral hexacoordinate phosphorus(V) compounds utilizing the chelate effect of one monovalent bidentate ligand to form four-, a five-, or a six-membered chelate ring. Examples include carbamates and thiocarbamtes, 8-oxyquinolates, acetylacetonates, amidinates, 2-oxypyridine and related analogues. In all cases, formation of hexacoordinate phosphorus(V) center is stabilized by rendering it highly acidic using electron withdrawing substitution such as F, Cl or CF_3.[76b]

Recent studies have shown that donor action by sulfur, oxygen and nitrogen atoms incorporated into flexible ring systems may serve to increase the coordination geometry at phosphorus in the tri-, tetra- and pentacoordinate states,[79] this effect strongly depends on the electrophilicity at phosphorus provided by the substituent makeup. Some of the selected hexacoordinate compounds formed by the donor action of sulfur, oxygen and nitrogen are shown in Chart 1.3.[80]

Chart 1.3

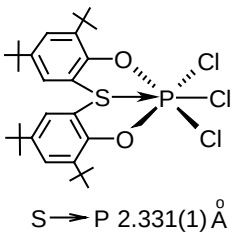


1.**68** 1.**69** 1.**70** 1.**71**

1.**72** 1.**73** 1.**74** 1.**75**

A series of neutral six-coordinate phosphorus(V) compounds using a tridentate ligand H_2L [2,2'-thiobis(4,6,-di-*t*-butylphenol) or 2,2'-thiobis(4,6,-dimethyl-butylphenol)] has been reported by Holmes.[77] By the inclusion of sulfur bridged eight-membered ring in pentaoxyphosphoranes, both penta- and hexacoordinate compounds are formed. These geometries are represented by trigonal bipyramidal (TBP) and octahedral (O_h), respectively. The latter is formed as a result of S→P coordination.

The sum of the covalent radii for P and S is reported as 2.14 Å, while the van der Waals sum is 3.75 Å. The S→P distances vary from 2.36 to 2.88 Å. Cavell extended this range to 2.33 Å in the phosphorane 1.**76** which has three electronegative chlorine substituents.[80b]

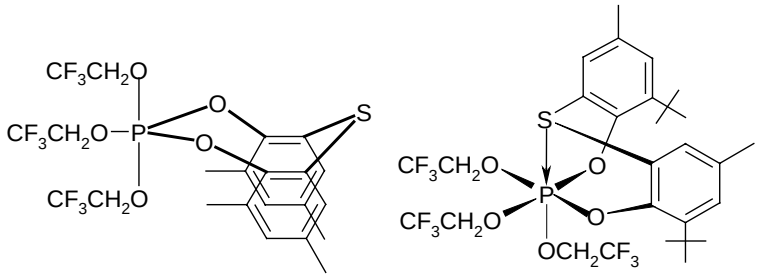


1.**76**

Effect of ring substituents on S→P *donor action*

In a series of compounds, as the ring substituents are varied from methyl groups to *t*-butyl groups, the structure changed from TBP to octahedral.[80a] The methyl groups in compound 1.**77** were replaced with *t*-butyls (*cf* 1.**69)** to ascertain their influence on coordination geometry and ring conformations. The variation of

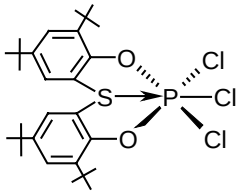
S→P bonding is interpretable in terms of electronic environment. The TBP structure of a cyclic oxyphosphorane (1.**77**) has the diequatorially oriented eight-membered ring in a boat-chair (symmetrical anti) conformation with S→P distance of 3.504 Å. By contrast, the distorted octahedral structure (1.**69**) had analogous ring in a tub conformation with S→P distance of 2.504 Å. The S→P distances decrease with the electron-donating ability of the eight membered ring substituents (*t*-Bu > Me). It is concluded that steric effects of *tert*-groups on the aryl group ortho to the ring oxygen atom bound to phosphorus promote hexacoordination.



Effect of ligands on S→P *donor action*

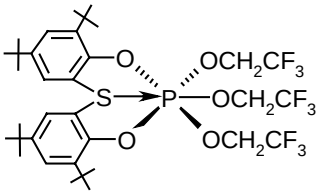
It is of interest to examine the influence of lowering the electrophilicity at phosphorus with use of the less electronegative sulfur atom as the donor atom along with a variation in the substituent electronegativity. This will allow one to ascertain the ease with which phosphorus achieves the hexacoordinate state in neutral compounds.

Despite lowering the electronegativity of the fifth ligand from oxygen (1.**78** and 1.**79**) to nitrogen (1.**80**) or chlorine (1.**76**) in the pentaoxyphosphoranes, hexacoordination occurs via sulfur donor action.[80a-b] The chlorine ligands are more electron withdrawing, a feature that enhances sulfur donor action which leads to greater octahedral character. The trifluoroethoxy and phenoxy ligands have less electronegativity than chlorine leading to longer S→P bond distances. However examination of this trend which have the same eight membered systems reveal an order of decreasing S→P distance that parallels the increasing electron delocalization ability of the ligands: Cl > OCH_2CF_3 > OPh.[80a]



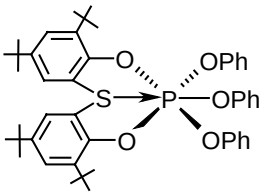
S→P 2.331(1) Å

1.**76**



S→P 2.373(5) Å

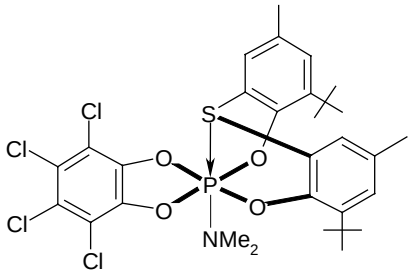
1.**78**



S→P 2.640(2) Å

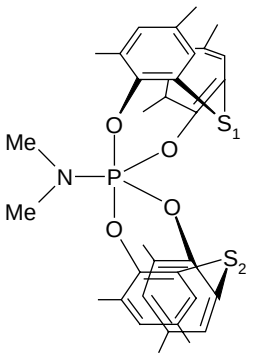
1.**79**

The bicyclic sulfur containing tetraoxyphosphorane 1.**81** that has a Me_2N group as the fifth ligand shows no tendency for S→P coordination even though the rings are in syn boat-boat conformation.[80d] The lack of sulfur donor action is attributed to the P-N π back-bonding which sufficiently reduced the electrophilicity of phosphorus to prevent additional coordination. In the analogous bicyclic tetraoxyphosphorane (1.**80**), the presence of a more electron withdrawing tetrachlorocatecholate ligand increases the Lewis acidity of phosphorus to allow hexacoordination *via* sulfur coordination. Thus the degree of octahedral character is enhanced by increased electronegativity of the ligands and decreased by the presence of the ligand π back-bonding (N to P) at phosphorus.



S→P 2.479(2) Å

1.**80**

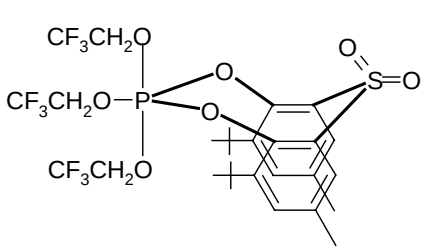


S1.....P 3.652(3) Å

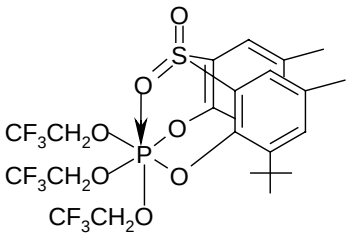
S2.....P 3.485(4) Å

1.**81**

The closeness in energy of the penta- and hexa-coordinate states of phosphorus in these ring systems is indicated by the presence of isomeric forms in solution as demonstrated by ^{31}P NMR for compound 1.**82**.[80e]



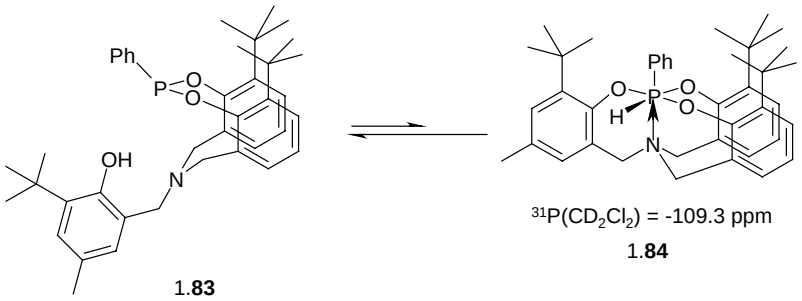
1.**82a**, δ(P): -73.5



1.**82b**, δ(P): -85.4

In literature dealing with spirophosphoranes, conversion and possible equilibria between pentacoordination and hexacoordination has been discussed.[80f] But recently it was shown that $PhPCl_2$ upon treatment with tris(2-hydroxy-3,5-dimethylbenzyl)amine leads to the tricoordinate phosphorus compound 1.**83** (X-ray), which in solution undergoes structural change to hexacoordinate species 1.**84** (Scheme 1.22). This is the first example of conversion of tricoordinate to hexacoordinate phosphorus.

Scheme 1.22

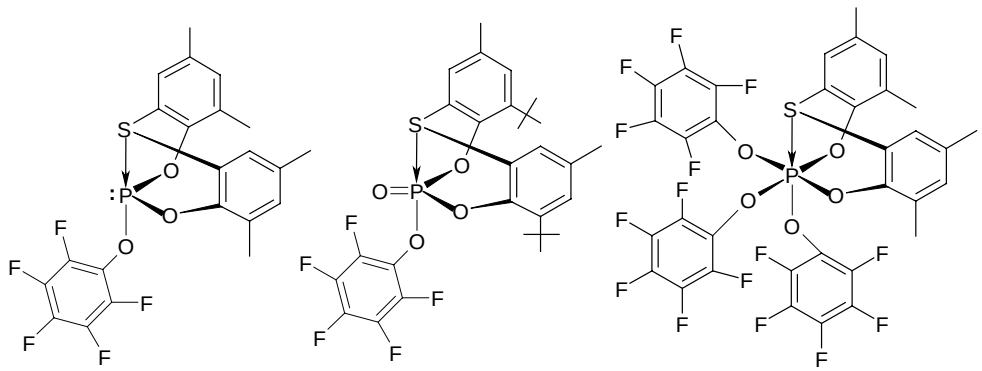


1.**83**
$^{31}P(CD_2Cl_2)$ = 169.3 ppm

$^{31}P(CD_2Cl_2)$ = -109.3 ppm
1.**84**

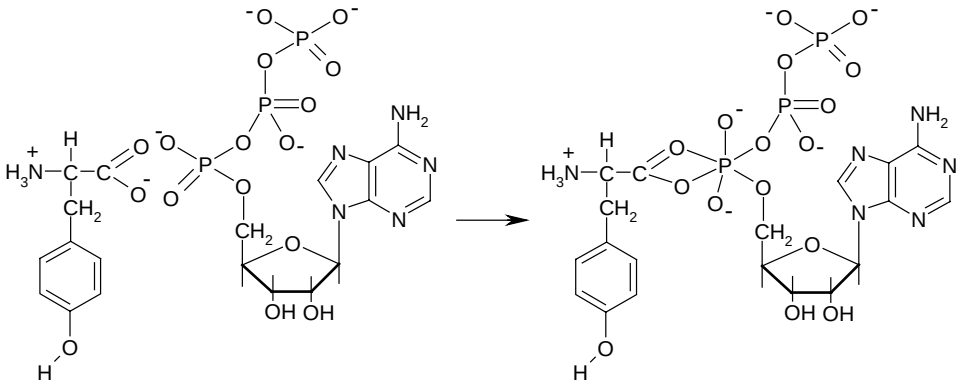
Comparison of S→P *donor action in phosphates and phosphoranes*

For compounds of biological interest, phosphates and pentaoxyphosphoranes comprise model classes that have been demonstrated to undergo coordination changes. Phosphates increase their coordination to five, while pentaoxyphosphoranes approach octahedral geometry as a result of donor action. Holmes provided the first series of cyclic phosphates and phosphates that exhibit sulfur coordination.[81] The tendency of the electron pair donor groups to increase phosphorus atom coordination even for a relatively basic center as found in the cyclic phosphites (e.g. 1.**85**) suggests that this occurrence may be an important consideration in detailing mechanisms of nucloephilic displacement reactions of phosphate esters.



Oxyphosphoranes form hexacoordinate structures via sulfur donor action relative to the lower coordinate phosphorus series, it is in line with increase in phosphorus electrophilicity or Lewis acidity as one proceeds to the higher coordination sites. Increase in coordination usually results in a bond lengthening that would indicate weaker bonds and perhaps a more facile associative type reaction, this phenomenon is well known in silicon chemistry, where five coordinate silicon exhibits enhanced reactivity compared to tetracoordinate silicon.[82] Ligands exhibiting donor action at phosphorus i.e., sulfur, oxygen and nitrogen are the ones present at the active sites of phosphoryl transfer enzymes and in enzyme action involving *c*AMP.[83]

In the mechanism describing the activation of tyrosine in the tyrosyl-tRNA synthetase system,[83] the proposed transition state complex involves formation of an axial P-O bond from the tyrosyl carboxylate group (Figure 1.3). This leads to cleavage of the opposite P-O linkage from a TBP intermediate. It is likely that the carbonyl oxygen atom acts in donor capacity and forms an additional coordinate bond at phosphorus to give a hexacoordinate formulation (**XIV**) as shown. Such added coordination may act as a rate enhancing effect by causing a loosening of the P-O bond undergoing cleavage in forming the enzyme tyrosyl-AMP complex.



XIV

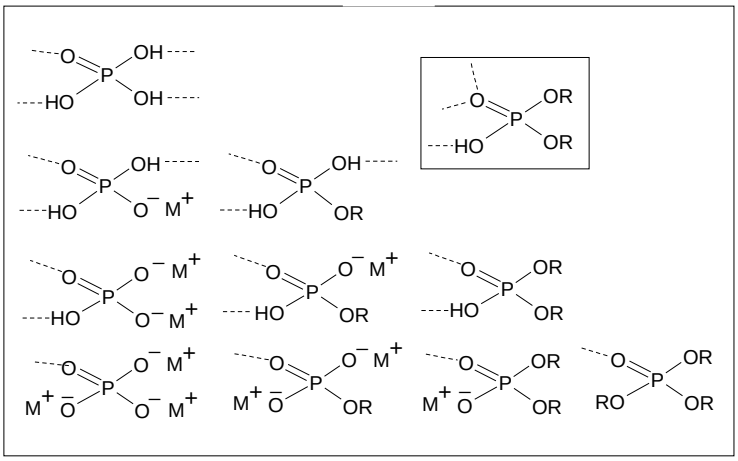
Figure 1.3: Ground state complex and proposed hexacoordinate transition state complex (**XIV**) in the activation of tyrosine by tyrosine-tRNA synthetase.

Thus it is becoming increasingly apparent that hexacoordinate phosphorus should play a role at active sites of phosphoryl transfer enzymes through their formation by coordination with donor atoms of nearby residues.

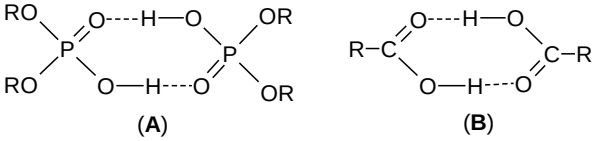
1.5 Organophosphates and their involvement in hydrogen bonding

Phosphates, by virtue of the strong acceptor as well as donor centers present in them, can exhibit strong hydrogen bonds,[84] it has been shown recently that the phosphoryl oxygen of triphenylphosphine oxide [$Ph_3P(O)$] can also engage itself in or facilitate very short C-H…O hydrogen bonds. A phosphorus substrate like H_3PO_4 or $(RO)P(O)(OH)_2$ will have a large number of sites for hydrogen bonding (shown in Chart 1.4). Hence a useful starting point to study hydrogen bonding will be either $(RO)_3PO$ or $(RO)_2P(O)OH$. The dialkyl phosphates $(RO)_2P(O)OH$ are strongly acidic when compared to the monoesters which are in turn stronger than the phosphoric acid itself.[84c]

Chart 1.4



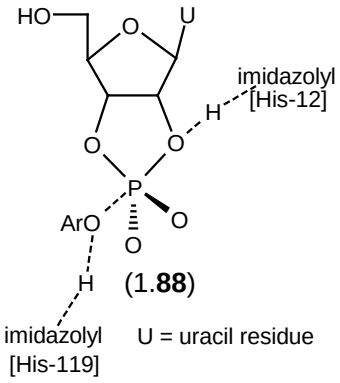
Dialkyl phosphates generally form dimers (Fig. 1.4), wherein the dimeric structure (**A**) is similar to that found in carboxylic acids (**B**).[84e] The hydrogen bond in phosphates is generally stronger than in carboxylic acids because of the greater polarity of the phosphoryl bond compared to the carbonyl linkage which induces a strong electrostatic bond between oxygen and hydrogen in the former.[84]



(**A**) (**B**)

Fig. 1.4 Dimeric structures of dialkyl phosphates and carboxylic acids.

Strong hydrogen bonds exhibited by phosphates are important in the context of proton-transfer reactions in chemical and biological systems, many of which have phosphate as a crucial component (e.g. species 1.**88** in the bovine ribonuclease-A-catalysed cyclization of aryl nucleotides).[85]



(1.**88**)

Flavodoxins are small acidic flavoproteins that utilize riboflavin 5′-monophosphate (FMN) as the only redox active component in a variety of biological electron-transfer reactions.[86] Hydrogen bonding plays a major role in the tight binding of the FMN cofactor in flavodoxins which is important in the context of proton-transfer reactions. Recent NMR investigations on *Desulfo*V*ibrio* V*ulgaris* flavodoxin gave direct experimental evidence for hydrogen bonds involving the phosphate moiety of FMN.

To study the modes of hydrogen bonding in phosphates some work has been done from our laboratory by treating the cyclic phosphate CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2P(O)OH$ (1.**89**) with a variety of hydrogen bonding partners (like imidazole, azopyridine etc).[87] One such compound, [imidazolium]$^+$[CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2PO_2]^-$.MeOH [1.**90**] showed very short C-H$^{\cdots}$O hydrogen bond involving an imidazolyl C-H and methanol in addition to N-H$^{\cdots}$O hydrogen bonds [Fig. 1.5]. This phosphate assisted strong C-H$^{\cdots}$O interaction in 1.**90** could have implications in analyzing biological proton-transfer processes involving histidine residues such as those suggested in structure 1.**88**. It is possible that there could be C-H…O interactions between the imidazolyl N-*CH*-N and the ribosyl –OH group providing temporary 'locking' feature in RNA hydrolysis/cyclization. The azopyridine compound $[HNC_5H_4$-N=N-$C_5H_4NH]_2^+[\{CH_2$(6-*t*-Bu-4-Me-$C_6H_2O)_2PO_2\}_2]_2^-$.$4CH_3CN.H_2O$ (1.**91**) also showed an extremely short N-H…O bond.

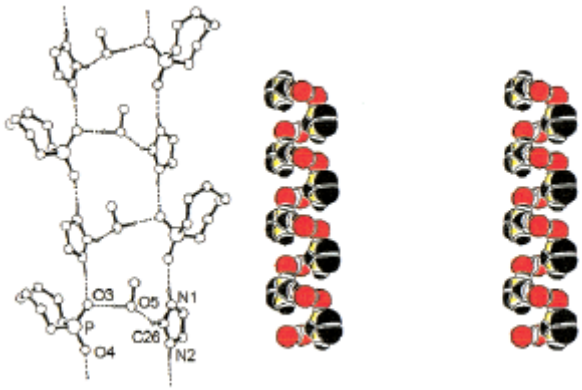


Fig. 1.5 Left: Hydrogen bonding scheme (only selected atoms shown) for compound 1.**90**; Right: CPK model showing the helical structure.

Imidazole forms strong, easily polarizable hydrogen bonds with orthophosphoric acid, trimethyl phosphate and diphenyl phosphate to yield

compounds $[C_3N_2H_5][O_2P(OH)_2]$ (1.**92**),[88a] $[C_3N_2H_5][O_2P(OMe)_2]$ (1.**93**)[88c] and $[C_3N_2H_5][O_2P(OPh)_2]$ (1.**94**)[88b] respectively. Hydrogen bonding pattern of compound 1.**93** and 1.**94** are given in Figure 1.6. In these compounds, the imidazolyl carbon, which is situated between the two nitrogen atoms, is involved in weak but clearly discernible bifurcated C–H…O hydrogen bonds to two oxygen atoms of the same phosphate. However, the original authors missed this point.

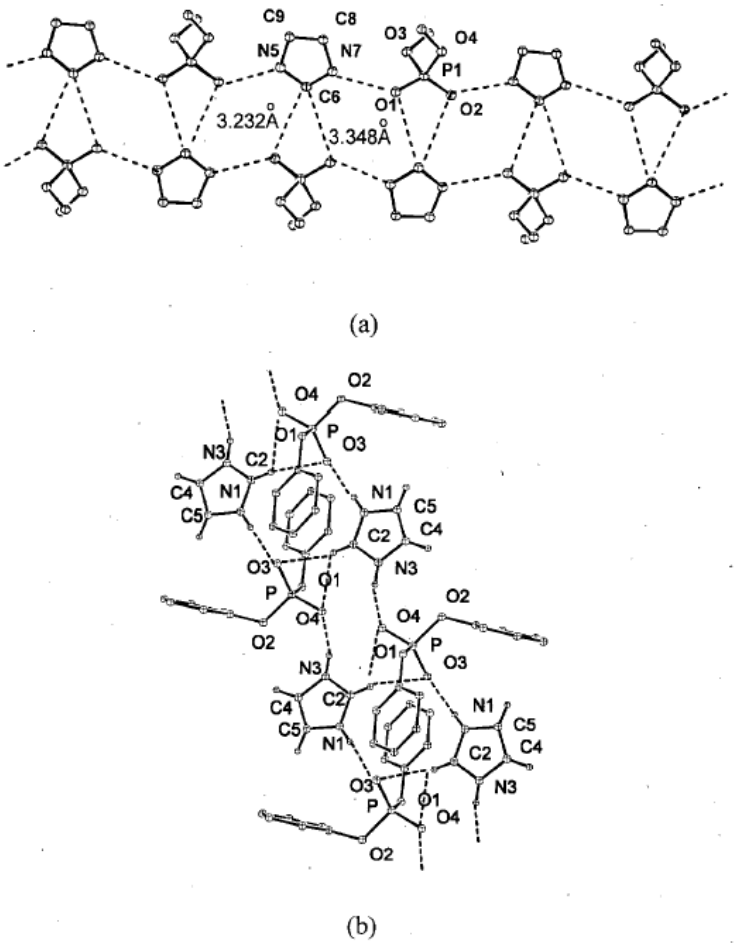


Fig. 1.6. (a) Hydrogen bonding pattern including the C-H···O interactions for compound 1.**93**. Coordinates taken from Cambridge database; hydrogen coordinates not available. There could be weak intermolecular interactions involving C(8) and C(9) {C(8)…O(2) Å; C(9)···O(1) 3.269 Å. (b) Hydrogen bonding pattern including the C-H···O interactions for compound 1.**94**. Coordinates taken form Cambridge database. C-H···O parameters (i) C(2)-H-O(4) 0,873, 2.720, 3.333 Å, 128.3º; (ii) C(2)-H-O(3) 0.873, 2.608, 3.454 Å, 163.6º. The bifurcated mode of C-H···O interactions may be compared to that in (a).

OBJECTIVES OF THE PRESENT WORK

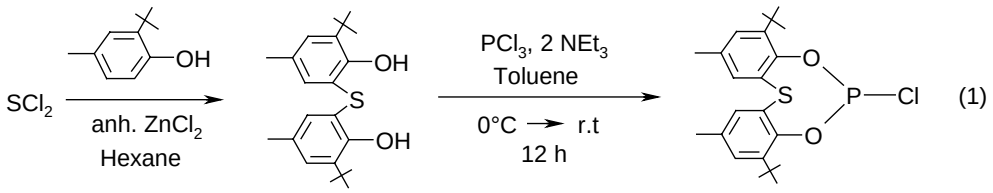
1. To study the reaction of dialkyl azodicarboxylates with different phosphorus(III) substrates in an effort to isolate and characterize compounds analogous to the proposed intermediates in the Mitsunobu reaction,
2. To study the constraints imposed by the secondary atoms, which play a significant role in determining the 'apicophilicity' of a group in pentacoordinate phosphorus compounds with trigonal bipyramidal geometry-usefulness/ limitation of DFT calculations in this context, and
3. To synthesize and study hexacoordinate phosphorus compounds in the context of finding positional isomers.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Synthesis of phosphorus(III) compounds

This part of the present work is essentially based on the key precursor S(6-*t*-Bu-4-Me-$C_6H_2O)_2PCl$ (**1**) that has an eight-membered 1,3,2-dioxaphosphocin ring. In the present study, **1** is prepared by treating 2,2'-thiobis(4-methyl-6-*tert*-butylphenol)[89-90] with phosphorus trichloride (eq. 1).



(1)

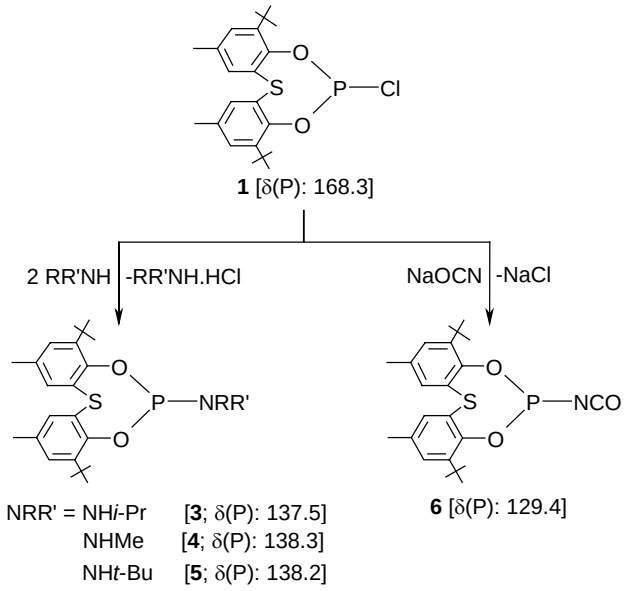
1 [δ(p): 168.3 ppm]

The literature method[91] involves the use of a solvent such as diethyl ether in the presence of triethylamine and subsequent crystallization to give **1** in 54% yield. But in a slightly modified procedure, when toluene was used as solvent, we were able to isolate the product in ~ 95% yield. From the literature, it is known that sulfur atoms in ring containing pentaoxyphosphoranes are capable of donor action which leads to neutral hexacoordinate phosphorus compounds.[79] Taking this into consideration, S(6-*t*-Bu-4-Me-$C_6H_2O)_2PCl$ (**1)** was chosen as the key precursor for this study. The eight-membered phosphocin ring generally remains intact in further reactions under normal conditions. More importantly, **1** possesses sterically encumbered phosphorus, a feature that could facilitate isolation and structural characterization of the products and study their reactivity. The phenyl analogue S(6-*t*-Bu-4-Me-$C_6H_2O)_2PPh$ (**2**) was prepared according to literature procedure.[92]

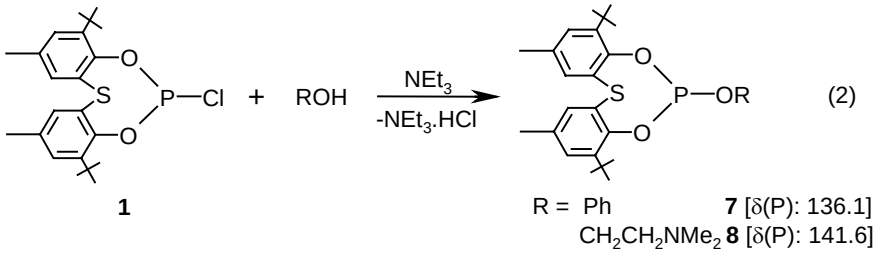
Treatment of **1** with appropriate amines gave the corresponding aminophosphites (phosphoramidites) **3**-**5**. The isocyanato compound **6** has been prepared by treating **1** with an excess of sodium cyanate in acetonitrile. These reactions are shown in Scheme 1. The preference of the phosphorus to bind to

nitrogen end, rather than the oxygen end, of the OCN group is interesting, but we have not probed this aspect in detail. The IR spectra of the methylamino-, *i*-propylamino- or the *t*-butylamino- derivatives show the characteristic N*H* stretch around 3360 cm^{-1}; the isocyanato compound **6** shows a strong band at 2243 cm^{-1}. The ^{31}P NMR spectral chemical shifts of **3**-**5** appear at ~30 ppm up-field of the precursor **1**. This is in line with the previous observations that the compounds $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PNHR$ [R = Me (**4'**), *t*-Bu (**5'**)] which have a CH_2 group in place of S in **4**-**5** exhibit ^{31}P NMR chemical shift values of ~10 ppm upfield compared to their common chloro precursor $CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2PCl$ (**1'**).[93]

Scheme 1

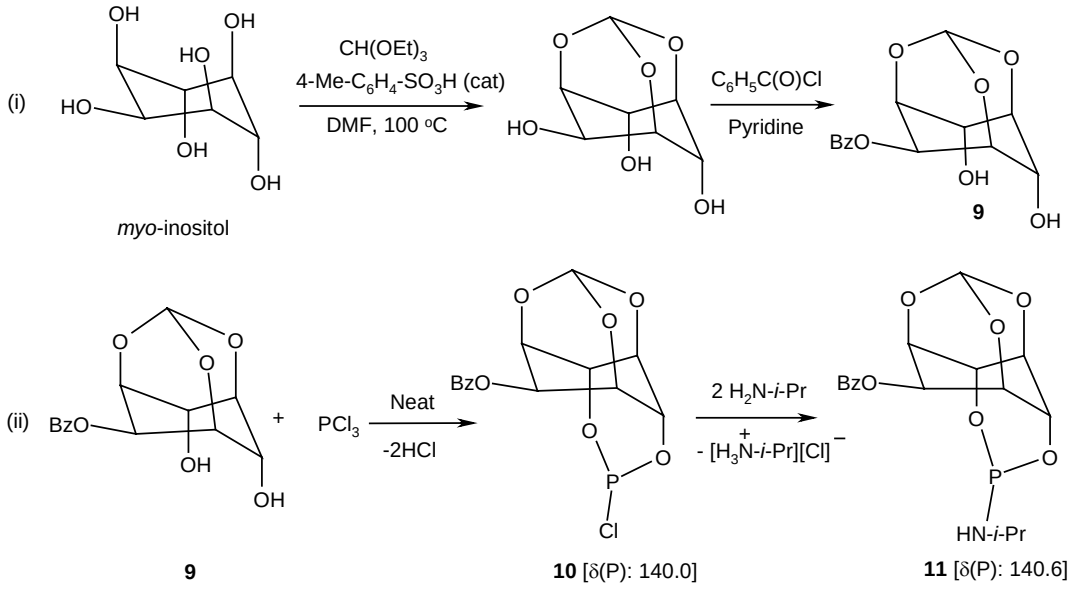


Compounds **7** and **8** were prepared by reacting **1** with phenol and N,N-dimethylaminoethanol respectively in toluene in the presence of triethylamine (eq. 2). The choice of latter precursor was dictated by the possibility of obtaining hypervalent compounds *via* additional N→P coordination.



Inositol phosphates play a significant role in cellular signal transduction.[94] Protected *myo-inositol* derivatives are important precursors for the synthesis of phosphorylated *myo-inositol* derivatives. With this in mind, the monobenzoylated inositol *diol* **9** was prepared by a modification of the literature procedure,[95] which used column chromatography for purification of the compound. In our case, after removal of most of the pyridine [Scheme 2 (i)], ethyl acetate was added; the organic layer was washed with dil. HCl (to remove traces of pyridine) and solvent removed completely. Upon addition of dichloromethane, the monobenzoylated compound **9** crashed out, leaving behind the dibenzoylated derivative in solution. Thus the tedious column chromatography is avoided. This compound was then reacted with PCl_3 under neat condition to lead to the chlorophosphite **10** in good yield [Scheme 2 (ii)]. Further treatment of **10** with isopropyl amine gave the corresponding aminophosphite **11** (Scheme 2(ii)).

Scheme 2



The ^{1}H NMR spectrum of compound **10** showed peaks at δ 4.61 and 5.23 (2H each, m), 5.46 and 5.62 (1H each, m) and a singlet at 5.75 corresponding to -O_3CH protons that are characteristic for the protected inositol ring. The ^{31}P NMR chemical shift for **10** [δ 140.0 ppm] is in the tricoordinate region. The ^{13}C NMR spectrum of this compound showed six peaks in the region δ ~ 60-70 corresponding to the inositol ring carbons and a characteristic peak at δ 102.2 for -O_3CH carbon.

Compound **11** showed similar signals in ^{1}H NMR like **10** in addition to N*H* peak at δ 3.79, a multiplet at 2.87 [NHC*H*$(CH_3)_2$], and a doublet at 1.22 for the methyl protons.

In our laboratory, we have been interested in learning about the conformation of the six-membered 1,3,2-dioxaphosphorinane rings with phosphorus in tri-, tetra-, penta- or hexa-coordinate state.[96] Since compound **10** is the first inositol based cyclic phosphite, we were curious to look at the conformational features of this compound *vis* a *vis* the pentacoordinate derivatives (see later). Hence the X-ray structure of **10** is determined (Fig. 1). Selected bond parameters are given in Figure 1. The six membered 1,3,2-dioxaphosphorinane ring containing phosphorus adapts a *boat* conformation with the phosphorus and C(6) atoms above the mean plane containing the other four atoms in the ring by 0.391 and 0.695 Å respectively. This is quite interesting because for the previously determined structures containing unconstrained phosphorinane rings, a *chair* conformation was found.[96l,97] The unusual *boat* conformation found in **10** is probably because in the chair conformation the phosphorus (or chlorine) may have unfavorable steric interactions with O(7) or C(3)-H.

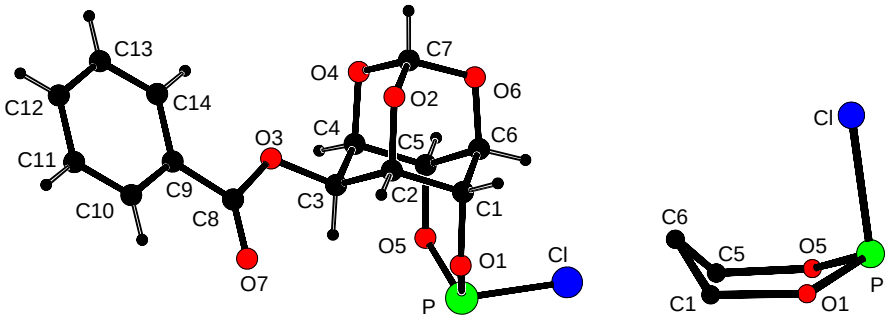
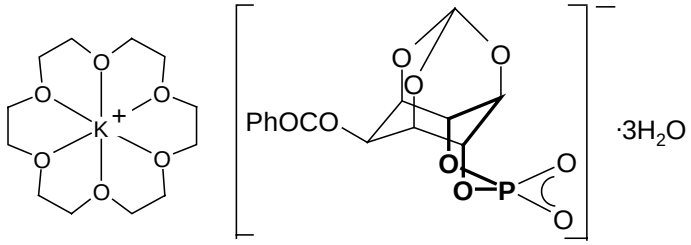


Fig. 1. *Left*: Molecular structure of **10** showing the numbering scheme on selected atoms. *Right*: Drawing showing the conformation of the phosphorinane ring. Selected bond parameters: P-O(1) 1.6025(16), P-O(5) 1.6127(16), P-Cl 2.1227(9) Å, O(1)-P-O(5) 102.11(8), O(1)-P-Cl 100.38(6), O(5)-P-Cl 100.72(7)^o.

That the 1,3,2-dioxaphosphorinane ring system prepared from the protected inositol diol **9** has different conformation compared to the unrestrained ones is also shown by the structure of a cyclic inositol phosphate as a trihydrate of its potassium-

18-crown-6 salt, *viz.* $[K(18\text{-crown-6})]^{+}[myo\text{-}C_6H_6\text{-}3\text{-}\{OC(O)Ph\}\text{-}2,4,6\text{-}(O_3CH)\text{-}\{O_2P(O)O\}]^{-}.3H_2O$ (**12**) reported from our laboratory.[98]

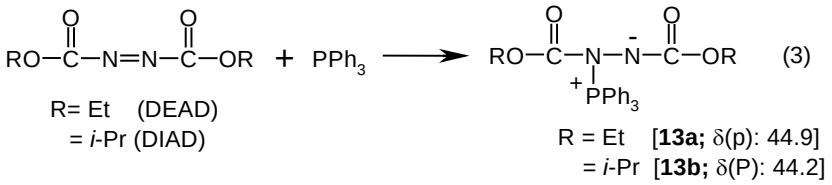


12

2.2 Reactions of P^{III} compounds with dialkyl azodicarboxylates and *o*-chloranil

2.21 Formation of pentacordinate compounds

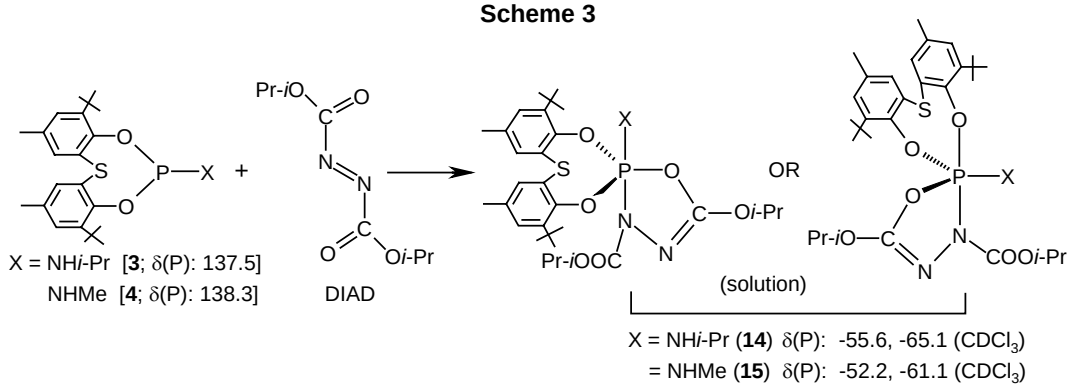
In the original Mitsunobu reaction, as mentioned in Chapter 1, triphenylphosphine that contains three carbons attached to phosphorus is utilized and the Morrison-Brunn-Huisgen (MBH) betaines **13a-b** are proposed as intermediates in the first step (eq. 3). Despite the fact that the Mitsunobu reaction is widely used in synthetic organic chemistry, the mechanistic details particularly at the intermediate stages, are still a subject of debate and intensive studies.[9]



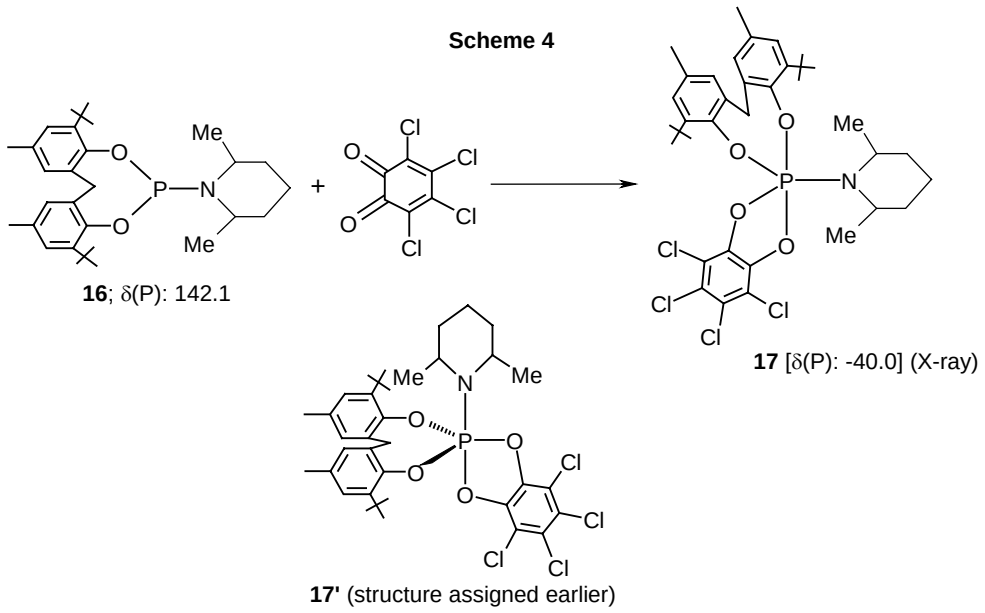
We have been interested in structurally characterizing compounds of type **13a-b**. In this connection, when P^{III} compounds **3** and **4** were treated with diisopropyl azodicarboxylate (DIAD), rather than the intermediate of type **13**, we obtained the pentacoordinate phosphoranes **14** and **15** respectively (^{31}P NMR) (Scheme 3). It is observed from our laboratory that even among the pentacoordinate phosphoranes, there is a significant structural variation with regard to the disposition of the substituents, all of these showing the 'reversed apicophilicity' phenomenon.[61,99] It can be noted that in these compounds, there are four different types of substituents [(a) oxygen atoms of the eight-membered ring, (b) nitrogen of

the five-membered ring, (c) oxygen of the five-membered ring and (d) the fifth substituent] and hence positional isomerism can give input into our knowledge of the apicophilicity in trigonal bipyramidal phosphorus. Although formation of pentacoordinate compounds in analogous reactions has been reported before,[14,15] complete structural characterization was not done. In the present study, compound **14** was characterized by X-ray crystallography. For comparative purposes we have also obtained the X-ray structure of compound **17** previously reported from our laboratory; this compound has a structure that is different from that assigned in the paper (*cf*. Scheme 4; see later for discussion).[61b]

Scheme 3



Scheme 4



When compound **4** was reacted with DIAD, we obtained [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$PNHMe{N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (**15**) that showed a ^{31}P NMR spectrum in pentacoordinate region [δ(P) –52.2, –61.1]**.** But, as this compound could

not be isolated in the pure state, further characterization was not done. The ^{31}P NMR spectrum, however, differs from that of [CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$PNHMe{N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (**18**; structure shown below) [δ(P) – 61.0, –61.7] for which an X-ray structure was obtained by one of my colleagues in the laboratory.[61b]

Treatment of **8** with DIAD led to [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$P($OCH_2CH_2NMe_2$){N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (**19**) that showed a ^{31}P NMR chemical shift of –61.7 ppm which is in the pentacoordinate region. This feature clearly shows that in solution, the nitrogen of the –$OCH_2CH_2NMe_2$ group does not coordinate to phosphorus, probably because of steric hindrance. Interestingly however, the S→P coordination is absent even though four oxygen atoms connected to phosphorus should have made it sufficiently acidic. The ^{1}H NMR spectrum (Figure 2) of **19** clearly showed two *t*-butyl, two methyl, two isopropyl C*H* and four isopropyl methyl signals at room temperature. A similar ^{1}H NMR pattern with two isopropyl and two aromatic methyls was found for a pentacoordinate compound [CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$P(NCS){N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (**20**).[10a]

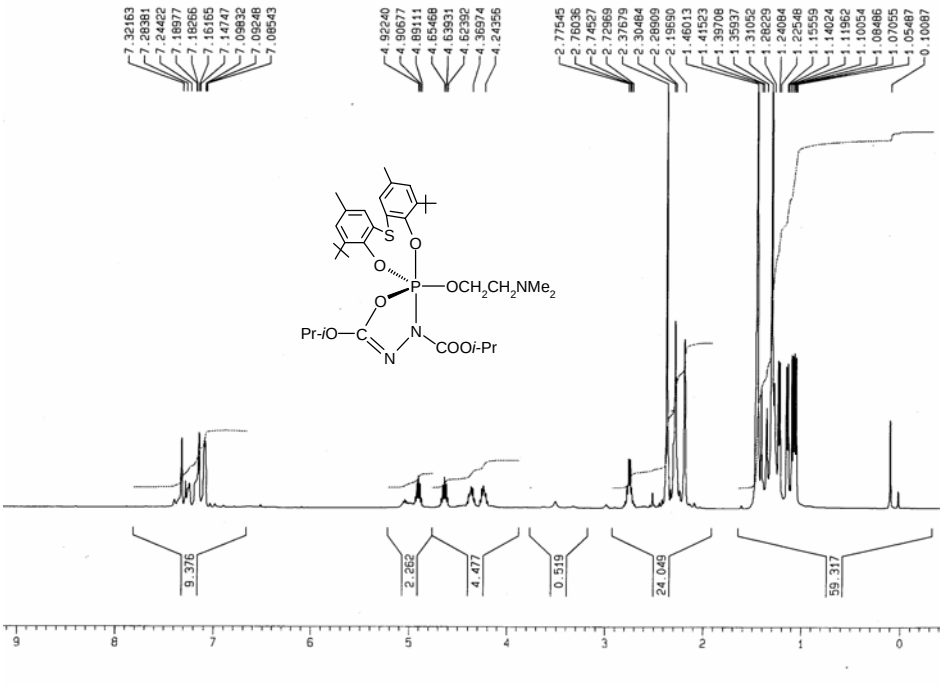
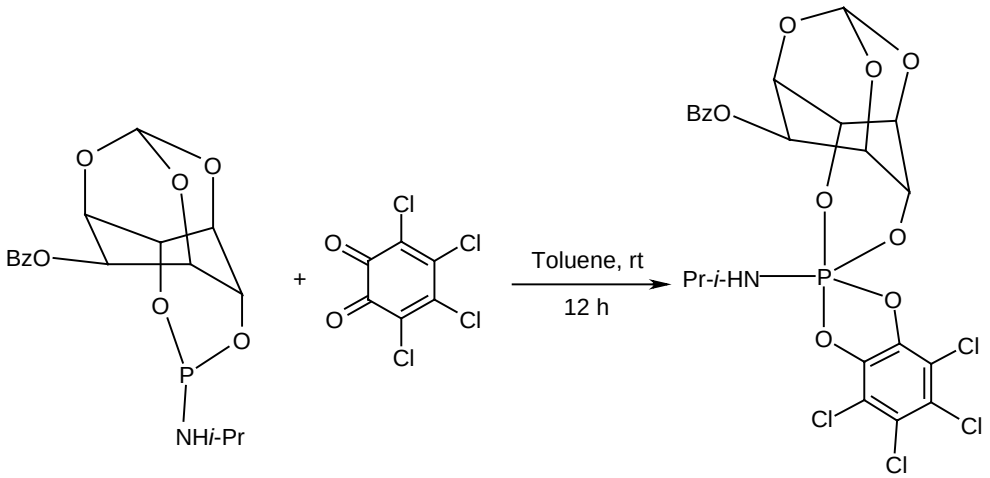


Fig. 2. The ^{1}H NMR spectrum of compound **19**.

As mentioned above phosphorylated *myo-inositol* derivatives play a significant role in cellular signal transduction and pentacoordinate phosphorus is involved in phosphoryl transfer reactions.[94] In this context, we first treated the protected inositol phosphite **10** with DIAD and *o*-chloranil, but there was no apparent reaction [^{31}P NMR]. Then we reacted only **11** with *o*-chloranil (which is more reactive) and obtained the pentacoordinate phosphorane **21** (Scheme 5). Unlike compound **14** which contradicts the Bent's rule, compound **21** is an example of a pentacoordinate phosphorus compound where more electronegative oxygen atoms occupy the apical positions while the less electronegative nitrogen is equatorial in the TBP structure, as expected from Bent's rule.

Scheme 5



11 [δ(P): 140.6] **21** [δ(P): -53.1]

***Solid state structures of* 14, 17 *and* 21**

The molecular structure of **14** is shown in Figure 3; the geometrical parameters are given in Table 1. From the X-ray structure, it can be readily noted that **14** has the PO_3N_2 skeleton and the solid-state structure confirms that this compound possesses slightly distorted trigonal bipyramidal (TBP) geometry, the distortion being more than that observed for similar compounds (**18, 22-24**) from our laboratory.

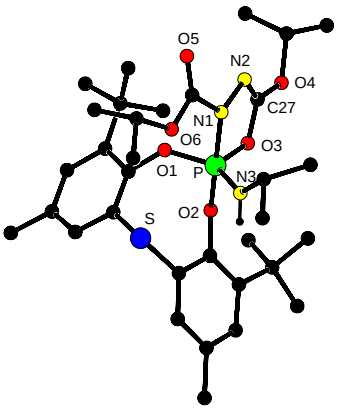
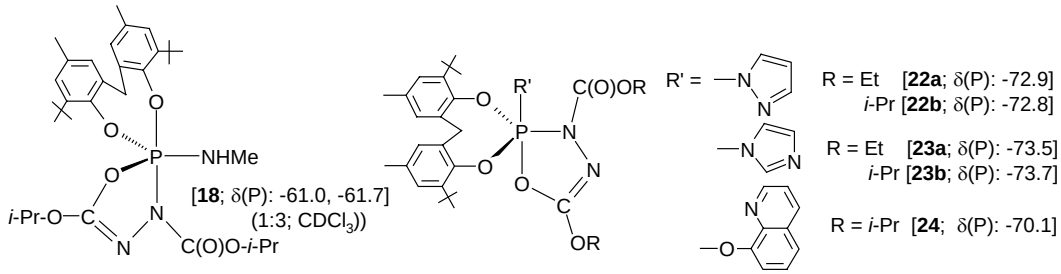


Fig. 3. Molecular structure of **14** showing the numbering scheme on selected atoms.

Table 1. Selected bond lengths [Å] and bond angles [°] for **14** with esd's in parentheses

P-O(1)	1.617(1)	P-N(3)	1.619(2)
P-O(2)	1.680(1)	N(1)-N(2)	1.416(2)
P-O(3)	1.648(1)	N(3)-C(31)	1.477(2)
P-N(1)	1.809(2)		

O(1)-P-O(2)	92.31(6)	O(2)-P-N(1)	171.72(7)
O(1)-P-O(3)	108.84(7)	O(3)-P-N(1)	85.97(6)
O(1)-P-N(1)	85.88(7)	O(3)-P-N(3)	116.34(8)
O(1)-P-N(3)	134.63(8)	N(1)-P-N(3)	93.07(7)
O(2)-P-N(3)	93.94(7)	C(31)-N(3)-P	133.22(1)
O(2)-P-O(3)	86.98(6)	N(2)-N(1)-P	113.15(1)

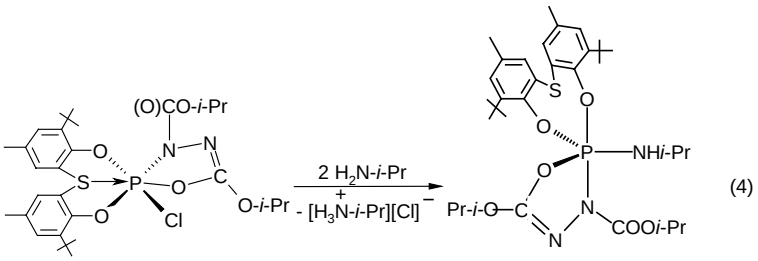


The equatorial occupancy of the NH-*i*-Pr group in compound **14** is on expected lines, because the compound **18** having (i) a –NHMe group and (ii) CH_2 in place of S also has an analogous solid state (X-ray) structure. However, the

N(apical)-O(equatorial) disposition of the five-membered ring in both these compounds is not consistent with apicophilicity rules according to which a more electronegative and less bulky substituent prefers an apical position of trigonal bipyramidal phosphorus.[59,60a] What is observed for the five-membered rings in **14** or **18** is opposite of this: The nitrogen (of NCO_2R group) is apical and oxygen is equatorial. It can be argued that the -C(O)O-*i*-Pr group increases the (group) electronegativity at nitrogen. However, overriding the more electronegative oxygen (which is also certainly sterically less crowded in our system) of the five-membered ring, the nitrogen has occupied the apical position. This was not expected.[59,60]

It can be noted that the flexible eight-membered 1,3,2-dioxphosphocin ring is happy with either a-e or e-e occupancy in trigonal bipyramidal geometry.[61,99] However, it occupies only e-e positions in compounds **22a** and **23b** leaving an apical site to the less electronegative imidazolyl/ pyrazolyl nitrogen. Such a feature also is in contrast to the Bent's rule or in terms of the 3c-4e bonding picture for the apical bonds, according to which more electronegative substituents are expected to prefer apical sites.[100]

The same isomer of **14** was obtained from the reaction of [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$PCl{N(CO_2-*i*-Pr)NC(O-*i*-Pr)-O-}] (**51)** (eq. 4) with an excess of isopropylamine, thus suggesting that it is the favored one; the powder X-ray pattern obtained for the bulk of the sample was essentially identical to the simulated one based on the single crystal data (using the Mercury program) [Figure 4]. The result, nevertheless, is consistent with the previous observations on the *o*-chloranil system (*cf*. Chart 1.2) in that secondary amino groups are more apicophilic compared to primary amino groups in these pentacoordinate compounds. Thus this result contradicts the most often assumed tenet that high apicophilicity is favored by small size and *vice versa*.[59,60] This feature, together with previous results from our laboratory, suggests that one needs to be cautious in using the 'apicophilicity' rules for trigonal bipyramidal phosphorus in larger molecules.



(4)

51 [δ(P): -71.1, -90.3] **14** [δ(P): -55.6, -65.1 ($CDCl_3$)]

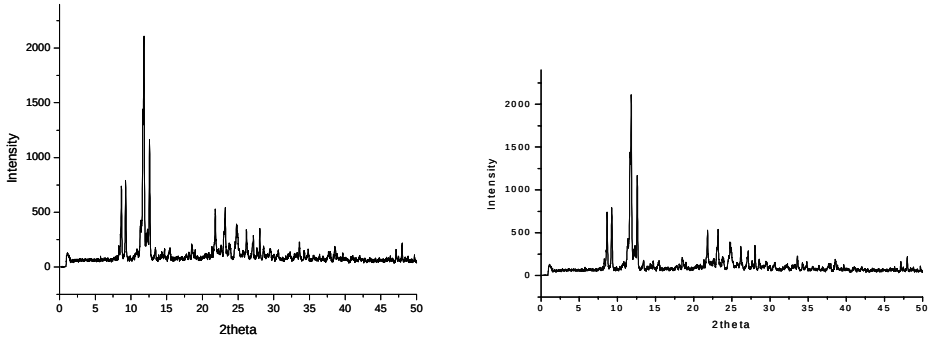


Fig. 4. The left side is the powder diffraction pattern that is recorded one and the right side is simulated one based on the single crystal data for **14.**

The P-N(3) bond is significantly shorter when it is equatorial (**14**) than in a case in which the corresponding nitrogen is apical (**22a**, **23b**). This is in line with the formulation of normal 2c-2e bonds for equatorial substituents and 3c-4e bonds for apical substituents.[101] Interestingly, the apical P-N(1) bond [1.809 Å] in **14** is significantly longer than even the calculated distance using the Schomaker-Stevenson empirical expression* for a P-N single bond [1.77Å].[102]

The sum of the bond angles at N(3) in the three compounds **14, 22a** and **23b** is essentially 360^o (planar). Although it can be argued that the lone pair of electrons on this nitrogen is involved in π-bonding with phosphorus in compound **14** and hence the planarity, a similar argument does not hold water in the case of **22a** and **23b** (here also the sum is ~360^o) because the nitrogen is apical and the P-N bond is longer (hence expected to have less π-interactions with P).[59] At the moment we do not have a good rationalization for this observation. Theoretical calculations done earlier suggest that π-donors prefer equatorial positions, and that their donor orbitals will preferably lie in the equatorial plane.[103] Information regarding the site

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*The Schomaker-Stevenson empirical expression is given below.[102]

$r_{AB} = r_A + r_B - 0.09\ (\chi_A - \chi_B)$ where r_{AB} = distance between the two atoms A and B, r_A and r_B are the covalent radii (Å) and χ_A and χ_B are the electronegativities of the atoms A and B. Any bond shortening beyond that expected (r_{AB}) from electronegativity difference is probably attributable to π character of the bond.

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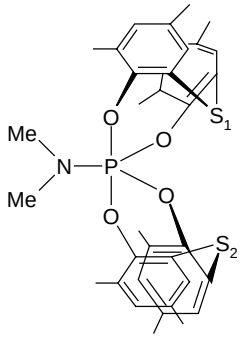
preferences of –NHR and $–NR_2$ groups based on *negative hyperconjugation*[101] involving the nitrogen lone pair and an antibonding orbital of the PO_4N trigonal bipyramid is not available for a more critical assessment of our observation.

The P-N bond distance in **14** [1.619(2) Å] is shorter than that in the bicyclic sulfur containing tetraoxyphosphorane **25**,[91] which has a Me_2N group as the fifth ligand [1.644(7) Å]. These are fairly strong P-N bonds that may sufficiently reduce the electrophilicity of phosphorus to prevent S→P coordination. The S→P distance of 3.287 Å in **14** is lower than the sum of the van der Waals radii [3.65 Å], but is still quite long to say that there is S→P coordination. Thus, the geometry may be treated as only distorted trigonal bipyramid.



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In **14**, P-O the apical bond is about 0.18 Å shorter than that observed for P-O (chloranil) apical bond in $CH_2\{6\text{-}t\text{-Bu-4-Me-}C_6H_2O\}_2P(N{=}PPh_3)(1,2\text{-}O_2C_6Cl_4)$ (**26**).[61a,b] The equatorial disposition of the –NH*i*-Pr group and a-e disposition of the eight-membered ring are analogous to that found in **26**.[61a] The tub conformation of the eight-membered 1,3,2-dioxaphosphocin ring (Figure 5) when located apical-equatorially, has been discussed before.[61.98]

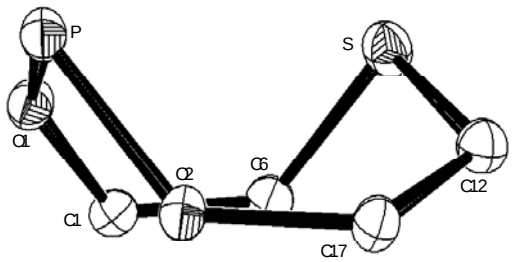
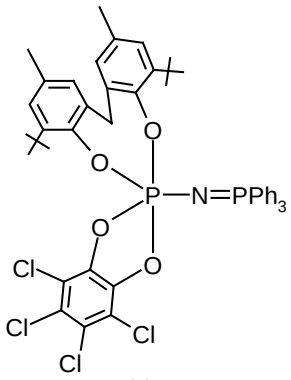


Fig.5. A drawing showing the conformation of the eight-membered ring in **14.**



26

In the structure of **17** [Fig. 6, Table 2], the phosphorus has a severely distorted trigonal bipyramidal geometry with O(2)-P-O(3) bond angle being 166°. This molecule does not show the 'reversed apicophilicity' phenomenon discussed above, but the significant distortion of geometry at phosphorus is an indication that there are additional factors like the two methyl groups of the 2,6-lupetidine group projecting in the same direction that could distort the geometry. The bond distances and angles at phosphorus are in the expected range.

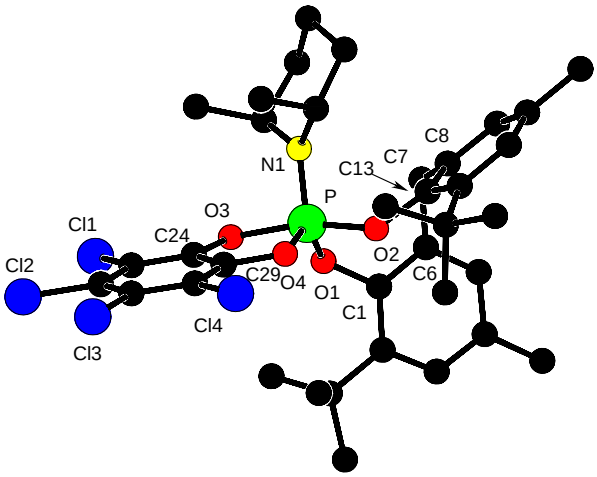


Fig. 6. Molecular structure of **17**.3/2C_4H_8O showing all non-hydrogen atoms; solvent atoms are not shown.

Table 2. Selected bond lengths [Å] and bond angles [°] for **17** with esd's in parentheses

P-O(1)	1.5966(18)	P-O(3)	1.8012(18)
P-O(2)	1.6505(18)	P-O(4)	1.6587(18)
		P-N1	1.644(2)

O(1)-P-O(2)	94.83(9)	O(2)-P-O(4)	83.94(9)
O(1)-P-O(3)	81.03(9)	O(2)-P-N1	101.05(10)
O(1)-P-O(4)	124.99(10)	O(3)-P-O(4)	87.53(9)
O(1)-P-N1	118.85(11)	O(3)-P-N1	92.60(10)
O(2)-P-O(3)	166.02(9)	O(4)-P-N1	115.25(11)

The molecular structure of **21** is shown in Figure 7 and the geometrical parameters are given in Table 3. In TBP structures, P-O bond distances for apical substituents are expected to be longer than the equatorial ones. In compound **21**, one of the P-O(equatorial) bonds [P-O((9) 1.6547(15) Å] is longer than the P-O(apical) bond [P-O(2) 1.6305(14) Å]. Although one can say that O(9) is connected to an aliphatic residue and O(2) belongs to a 5-membered catecholate residue, the fact remains that apical one is *shorter*. Why is it that apical P-O(9) bond is shorter than even the equatorial P-O(2) bond is not satisfactorily explained by the 3c-4e model for the apical bonds in pentacoordinate phosphorus. Although this feature has been observed before, a satisfactory bonding model has not emerged so far.

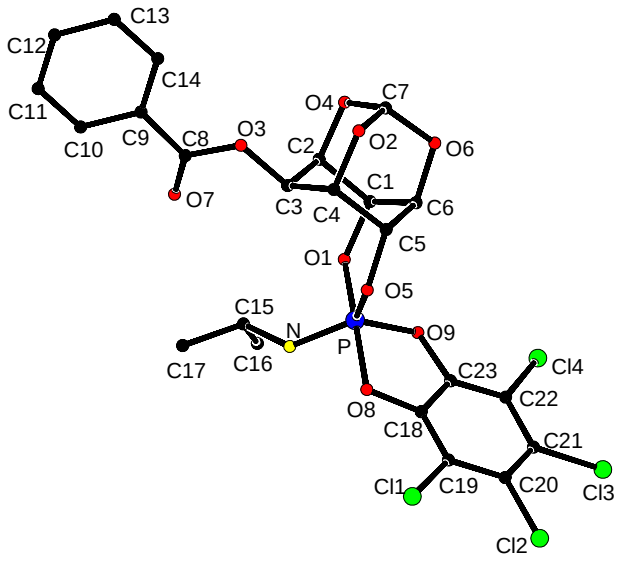


Fig. 7. Molecular structure of **21.**CH_2Cl_2 showing all non-hydrogen atoms. Solvent molecule is not shown.

Table 3. Selected bond lengths [Å] and bond angles [°] for **21.**CH_2Cl_2 with esd's in parentheses

P-O(1)	1.6305(14)	P-O(8)	1.7905(15)
P-O(5)	1.5987(16)	P-O(9)	1.6547(15)
		P-N	1.6166(19)
O(1)-P-O(5)	98.83(8)	O(1)-P-O(9)	89.44(7)
O(5)-P-O(8)	84.65(8)	O(1)-P-N	92.33(9)
O(5)-P-O(9)	112.45(8)	O(8)-P-O(9)	88.86(7)
O(5)-P-N	121.40(9)	O(8)-P-N	86.14(9)
O(1)-P-O(8)	176.50(8)	O(9)-P-N	125.07(9)

The six-membered ring in **21**, which is more rigid because of the adamantane moiety of the inositol, has a boat conformation [Figure 8a]. This is in line with that observed for several other pentacoordinate compounds with 1,3,2-dioxaphosphorinane ring.[96l] However, it should be noted that in those cases the precursor P^{III} compound had a *chair* conformation (e.g. **27**) while our inositol derived P^{III} compound **10** has a *boat* conformation (discussed above). A second point of interest is that the observed boat conformation in **21** [Fig. 8a] is actually different from that observed in other pentacoordinate compounds in that for the latter, one oxygen and a CH_2 carbon are above the mean plane of the other four atoms [e.g. **28**[96l]; Figure 8b]. In **21** the phosphorus and a carbon atom of the inositol residue are above the mean plane of the remaining four atoms.

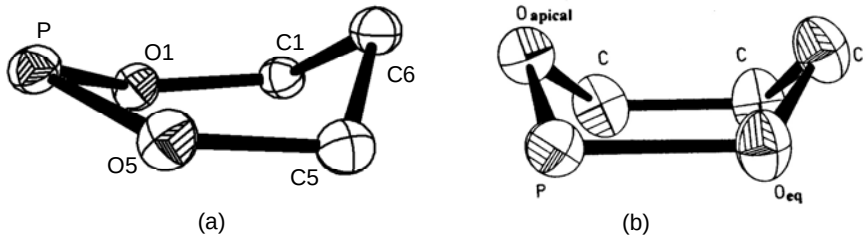
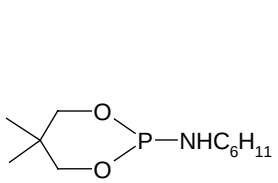
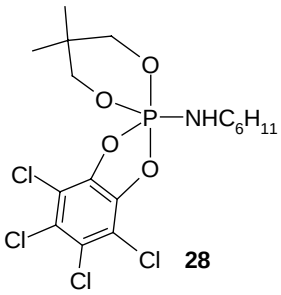


Fig. 8. Plots showing the conformation of the six-membered ring in (a) compound **21** and (b) other pentacoordinate compounds (e.g. **28**) with apical-equatorial disposition of the ring.



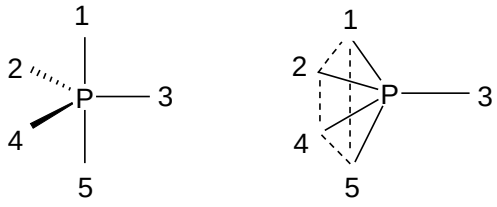
27



28

The extent of distortion from TBP to square pyramidal (SQP) or tetragonal pyramidal geometry is calculated by two means. In the first method, the geometric parameter $\tau = (\beta–\alpha)/60$ (where α and β are the two largest angles) is utilized. For a perfectly tetragonal pyramidal geometry τ is equal to zero, while it becomes unity for perfectly trigonal-bipyramidal geometry. The τ values calculated for **14** [τ = 0.62], **17** [τ = 0.68] and **21** [τ = 0.92] suggest that the phosphorus in **21** is less distorted compared to that in **14** or **17.** However, this is only an approximate calculation since in known square pyramidal pentacoordinate phosphorus compounds the phosphorus atom is slightly above the mean plane of the other four basal atoms.[104]

In the second method, we take one of the substituents as the pivotal atom. The dihedral angle $\delta_{(124,\ 524)}$ is the angle between the normals to the trigonal faces (124) and (524). This value is ~ 53.1^o for ideal trigonal bipyramid (TBP) and 0^o for square pyramid (SQP) by taking the substituent 3 as pivotal. This particular dihedral angle in **14**, **21** and **17** are, 51.2^o [faces (N1, O1, N3) and (O2, O1, N3) with O3 pivotal], 44.4^o [faces (O8, N, O9) and (O1, N, O9) with O5 pivotal] and 35.2^o [faces (O3, O1, O2) and (O2, O1, O4) with N1 pivotal] respectively. These values give a TBP $\rightarrow$ SQP distortion [(53.1 - δ) x 100/53.1] of ~ 3%, 16.4% and 34% for **14**, **21** and **17** respectively. Using a slightly elaborate and more accurate procedure using all the dihedral angles,[105] we obtained distortions of 16.8 %, 15.4 % and 26.6 % respectively for the same compounds. Overall, compound **17** has the maximum distortion, which is also evident from the O2-P-O3 angle of 166.0^o.



TBP ($\delta_{124,\ 524}$) ~53.1° SQP ($\delta_{124,\ 524}$) = 0°

***Solution state NMR behavior of* 14**

The ^{31}P NMR spectra of **14** in solution changed with temperature [Figure 9]. At low temperatures, three peaks at δ -63.7, -63.4 and –54.5 are observed in toluene-d_8.[106] As the temperature is raised, the two up-field peaks merge and broaden, and a new peak at δ -39.2± 1.0 appears. At 353 K the spectra shows only two peaks, one at δ -39.2± 1.0 and the other at –54.5; upon cooling to 20°C the original pattern was observed.

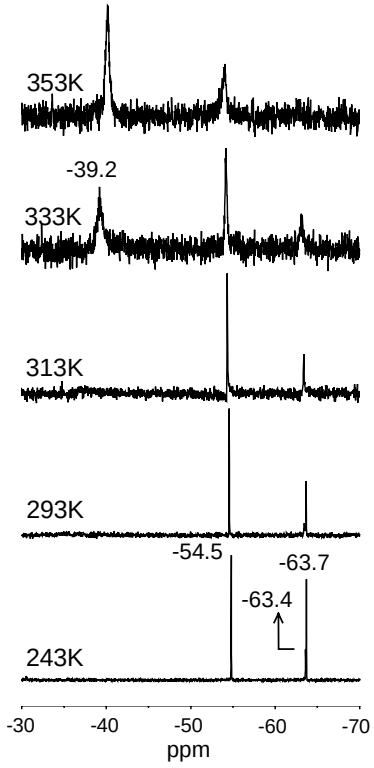
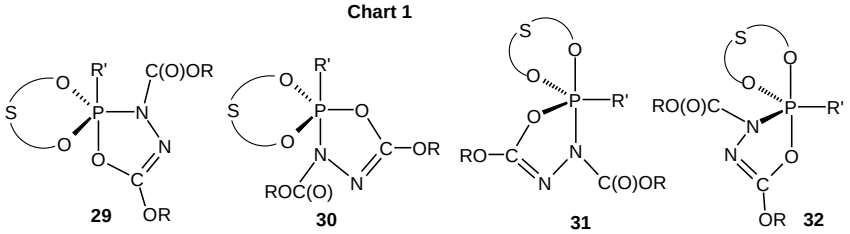


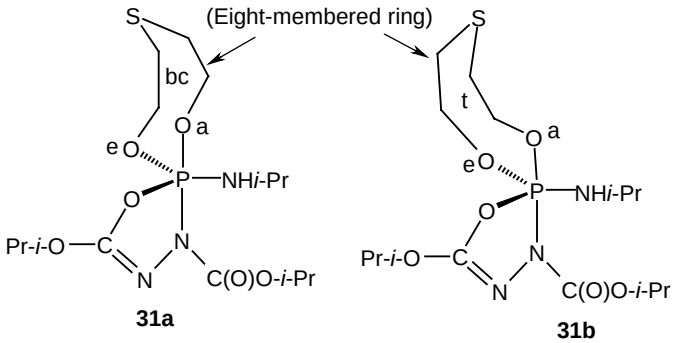
Fig. 9. Variable temperature ^{31}P NMR spectra for **14** in toluene-d_8.

We consider first the structural possibilities **29-35** (Chart 1); a hexacoordinate form **35** and the pentacoordinate form **32** have not been observed in the solid state

(X-ray structure) so far. Based on the chemical shift values, we rule out the hexacoordinate (**33-35**) and tetracoordinate form (see later). The two closely placed peaks at δ -64.7 and -64.4 suggest that the local environment at phosphorus is not changed significantly for these isomers; based on our previous studies e.g. CH_2\{6-*t*-Bu-4-Me-C_6H_2O\}$_2$P(NHR)(1,2-$O_2C_6Cl_4$) [R =H; δ -50.6, –50.9, R = Me; δ -52.2, –52.5],[10a] we ascribe these to the NH-*i*-Pr (equatorial) isomers of **31a-b** having the *boat-chair* or *tub* conformation. We also recorded the ^{31}P NMR spectrum of the closely related CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2$P(NH-*i*-Pr)(N(COOR)-N=C(OR)O-) (**36**), prepared *in situ* in an NMR tube from its P^{III} precursor. Which showed two closely spaced resonances at δ -65.3 and -65.7 (ca 1:4 ratio). These two peaks are similar to the two upfield resonances observed for **14**, no attempt was made to isolate **36** in this study.

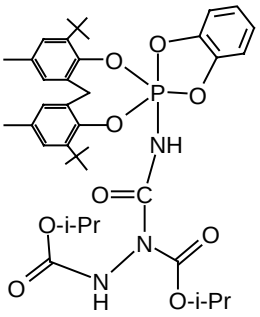
Chart 1





bc ≡ boat-chair conformation; t ≡ tub conformation
a ≡ apical; e ≡ equatorial
Substituents have been removed for clarity

The remaining two ^{31}P NMR signals for **14** [δ: -39.2, -54.5] with a large Δδ are then ascribable to either **29** or **30**. Currently we do not have a way to distinguish these. We only note that in the structure of compound **37**,[107] the NHR group is apical and hence it is possible to have NH-*i*-Pr apical. The variable temperature ^{1}H NMR spectra also showed multiple signals that changed with temperature, but was more complicated for a detailed analysis.

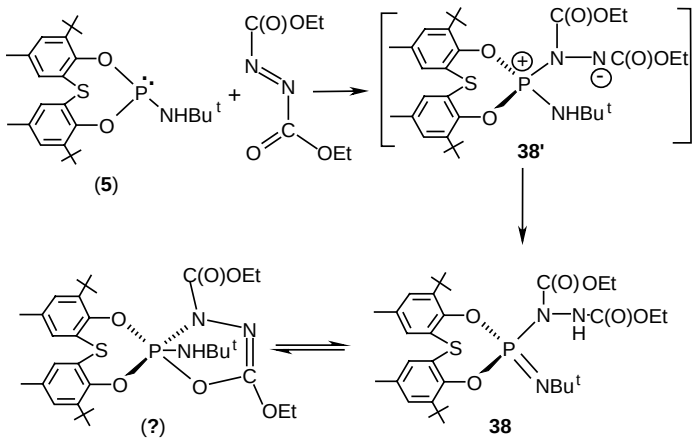


37

2.22 Formation of tetracoordinate compounds with unusual structures

In contrast to the formation of the pentacoordinate compound **14** in the reaction of P^{III}-NH-*i*-Pr compound **3** with DIAD discussed above, treatment of the P^{III}-NH-*t*-Bu compound **5** with diethyl azodicarboxylate (DEAD) in toluene leads to compound **38** [Scheme 6]. Formation of **38** occurs most likely *via* tautomerization of the betaine **38'** that is analogous to **13**. This is the first example of imino-phosphorus compound (X-ray evidence) that has a structure halfway between the classical MBH betaine **13** and protonated betaine proposed in the Mitsunobu reaction.

Scheme 6



The X-ray structure of **38** (Figure 10, geometrical parameters are given in Table 4) clearly shows (i) a very short P=N(*t*-Bu) bond [P-N(3) 1.464(4) Å],[108] and (ii) the carbamate type linkage –NH-C(O)OR that is a hydrogen bonded dimer through the NH and the C=O moieties. There is no S→P interaction in **38**. The IR (KBr) spectrum shows two ν(NH) bands [for **38** at 3262, 3159 cm^{-1}] consistent with the carbamate- phosphinimine structure;[109] this is different from a single ν(NH) band at 3383 cm^{-1} observed for the penta-coordinate isopropylamino compound **14**. There is also a fairly strong band at 1211cm^{-1} for **38** ascribable to ν(P=N). For the question as to why the X-ray structure of –NH*i*-Pr compound **14** shows penta-coordination, whereas the –NH-*t*-Bu compound **38** shows tetra-coordination, the factors responsible could be the bulkiness of the *t*-Bu group resulting in a very strong P=N bond. This, together with the hydrogen bonding involving -NH-C(O) group is the likely driving force for the stability of the phosphinimine-carbamate form compared to the betaine form [*cf.* Scheme 6]. It is important, however, to note that compound **38** can be considered to be tautomeric form of the corresponding betaine $[S\{6\text{-}t\text{-Bu-4-Me-}C_6H_2O\}_2]P^+[\{NH\text{-}t\text{-Bu}\}\{N(CO_2Et)N^-(CO_2Et)\}]$ (**38'**) (*cf.* Scheme 6).

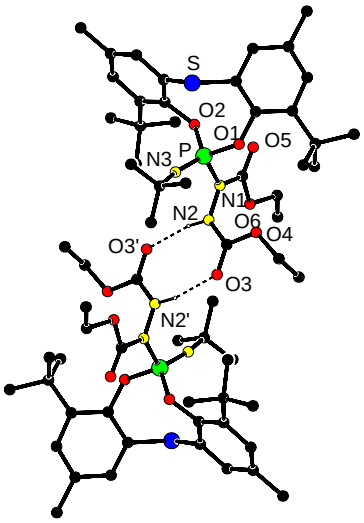
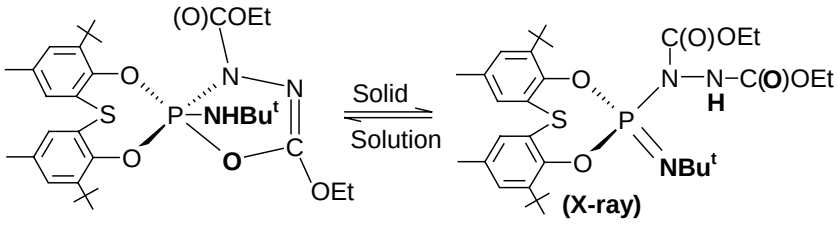


Fig. 10. A Platon drawing of the hydrogen-bonded dimer of **38**.

Table 4. Selected bond lengths [Å] and bond angles [°] for **38** with esd's in parentheses

P-O(1)	1.586(3)	P-N(3)	1.464(4)
P-O(2)	1.593(3)	N(1)-N(2)	1.388(4)
P-N(1)	1.718(4)	N(3)-C(23)	1.422(6)
O(1)-P-O(2)	105.29(16)	O(2)-P-N(1)	101.22(17)
O(1)-P-N(1)	99.46(17)	N(1)-P-N(3)	109.9(2)
O(1)-P-N(3)	117.8(2)	C(23)-N(3)-P	154.8(4)
O(2)-P-N(3)	120.0(2)	N(2)-N(1)-P	117.2(3)

However, the solution and the solid-state ^{31}P NMR spectra of **38** [Figure 11] appear to be *inconsistent* with the X-ray structure. The δ(P) value of –56.3 [$C_6D_5CD_3$, 298 K, sharpens at higher temperatures] for **38** is clearly in the p*enta-coordinate* region (*cf*. compounds **14** and **15**)[10a] and quite upfield to the *tetra-coordinate* region.



The solid-state ^{31}P NMR signal [δ –61.1] is also in the pentacoordinate region.[61] Rather astonishingly, *at least four different signals* could be clearly identified at 255 K [Figure 11]; upon warming to 298 K, the original spectrum was obtained. Based on previously available data,[61,91] these signals can be ascribed to pentacoordinate isomers (**A**)-(**D**) [Chart 2, the extra low intensity peak at 273 K is perhaps due to a conformational isomer involving the eight-membered ring[61a,b]].

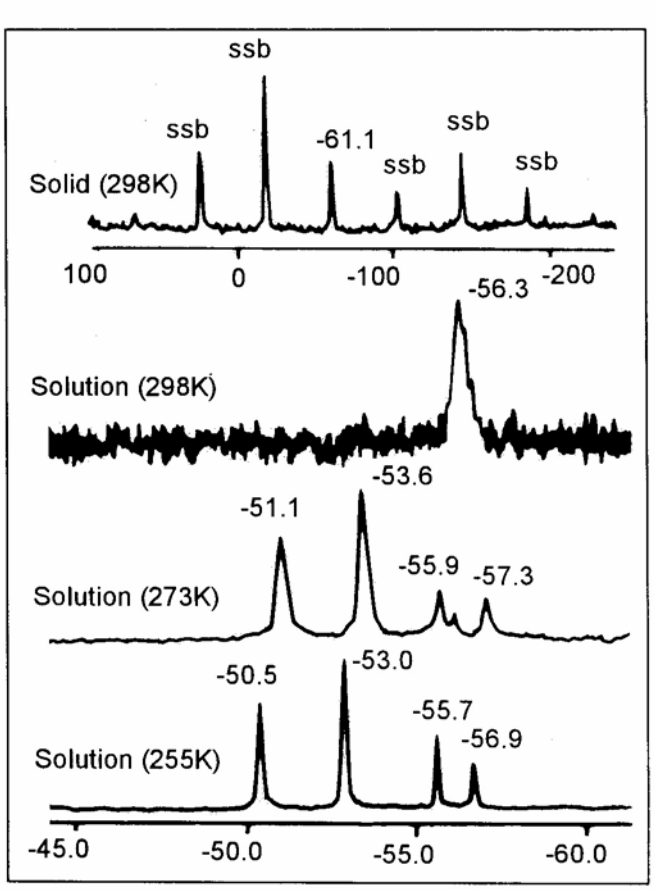
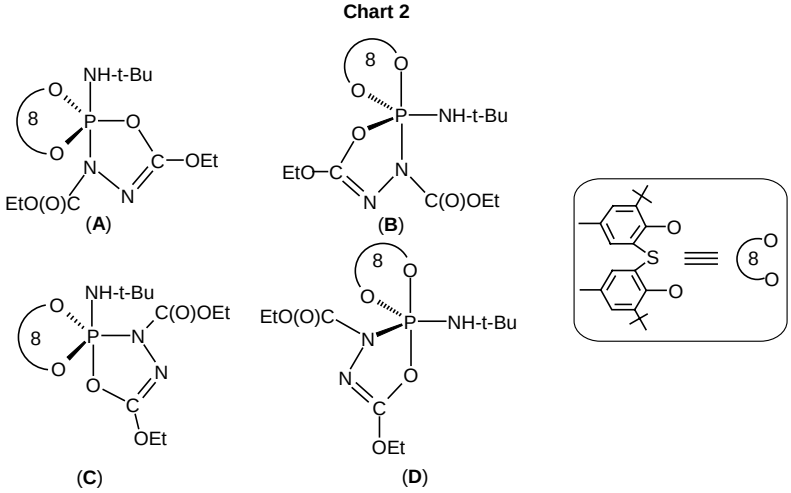


Fig. 11. Solution (VT) and solid-state (5 kHz) ^{31}P NMR spectra for compound **38**; ssb refers to spinning side bands. The spinning side bands were verified by recording the solid-state spectrum at 7 kHz also.

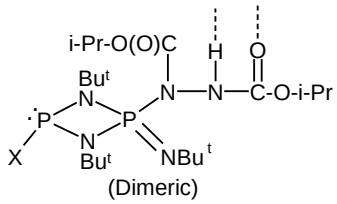
Chart 2



The bulky –NH-*t*-Bu group may not favor significant hexacoordination *via* S→P bond; this assumption is consistent with a similar spectral pattern observed for $[CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P(N\text{-}t\text{-Bu})\{N(CO_2Et)NH(CO_2Et]$. To our knowledge, this is the first ever observation of four distinct isomeric phosphoranes in solution.

When compound **38** was treated with benzoic acid or trifluoroethanol with the intension of getting a pentacoordinate compound by addition across the P=N-*t*-Bu, it gave only a peak in the ^{31}P NMR [δ(P) –8.6] corresponding to tetracoordinate phosphorus, probably by the exclusion of $[NH(CO_2Et)]_2$. Although we could not isolate the phosphorus compound, it is not the hydrolyzed product $[CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P(O)OH$ [δ(P) –11.6[87]].

At the same time as this work was progressing, the cyclophosphazane compounds $XP(\mu\text{-N-}t\text{-Bu})_2P[(N\text{-}t\text{-Bu})\{N\text{-(COO-}i\text{-Pr)-N(H)(COO-}i\text{-Pr)}]$ [X = Cl (**39**), NH-*t*-Bu (**40**)] were also prepared by one of my colleagues. Formation of **39-40** also should have occurred through a betaine in a manner similar to that for **38**. The X-ray structure of **39** shows (i) a very short P=N bond [P-N 1.488(3) Å], and (ii) hydrogen-bonded carbamate NH-C(O)OR dimer; these features are analogous to that observed for **38**. The IR spectrum shows a strong band at 1202 cm^{-1} ascribable to ν(P=N). Thus it appears that in reactions of P(III)–NH-*t*-Bu compounds with DEAD/ DIAD, the imine-carbamate type of structure is favored.



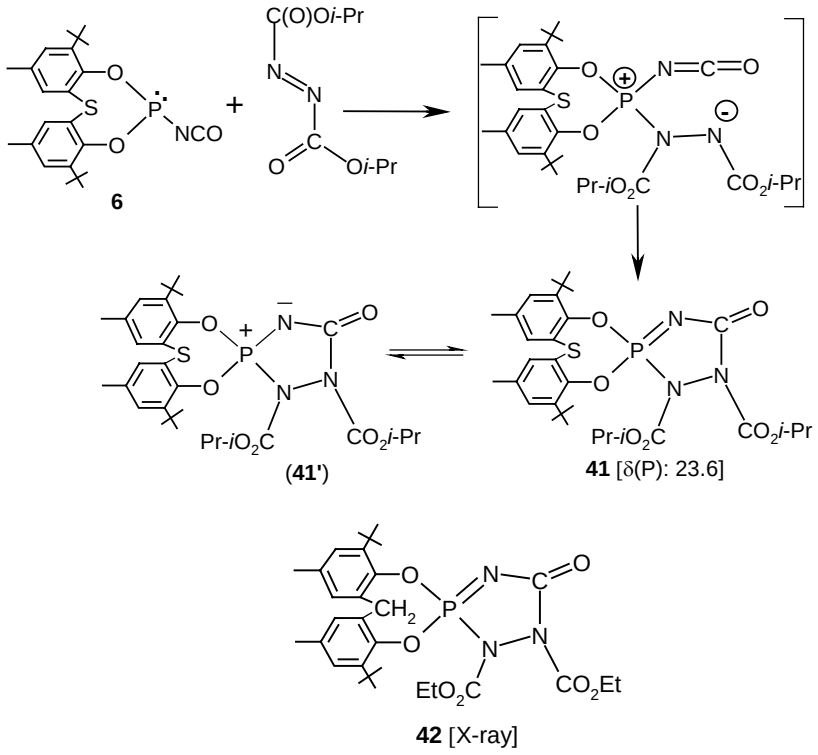
(Dimeric)

X = Cl (**39**), NH-*t*-Bu (**40**)

In contrast to the above, reaction of the P^{III} isocyanate, $S(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P\text{-NCO}$ (**6**) with DIAD takes an entirely different turn with the formation of the cyclic product **41**, presumably *via* betaine in a step-wise pathway (Scheme 7).[10a] The structure of a similar compound prepared by my colleague in the laboratory $[CH_2(6\text{-}t\text{-Bu-4-Me-}C_6H_2O)_2P\{N(CO_2Et)N(CO_2Et)\text{-C(O)-N}\}]$ [**42** δ(P) 26.6] has been proven by X-ray crystallography.[10a] The IR spectrum of **41** (or **42**) exhibits a band at 2266 cm^{-1} due to N-C=O group (surprisingly close to that for the P^{III} compound **6**). The ^{13}C NMR spectrum of **41** showed a doublet at δ 128.6 (d, ^2J(PC)

= 40.0 Hz, N*C*O) for P-C bond coupling in the same region compared to **42** [δ 127.2 (d, ^2J(PC) = 21.0 Hz, N*C*O)]. Since the formal P=N bond in **42** [P-N 1.564(4) Å] is significantly longer than that in **38**, it is likely that there is some phosphonium character in **41** as well as **42** (*cf.* structure **41'** in Scheme 7).

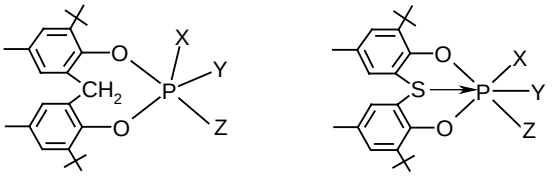
Scheme 7



2.23 Formation of hexacoordinate phosphorus compounds

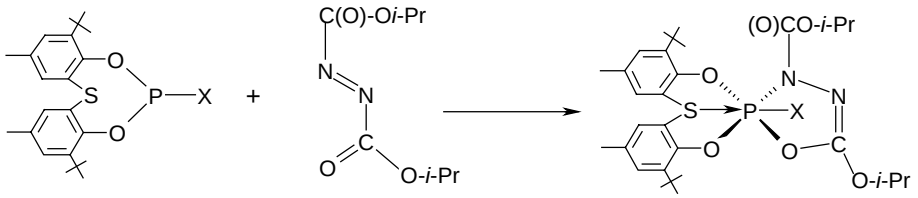
Replacement of the CH_2 moiety (as in **43**) at the eight-membered ring by a donor atom like sulfur (as in **44**) can lead to neutral hexacoordinate phosphorus compounds with S→P donor-acceptor bonds. Such hypervalent compounds obtained by the addition of *o*-chloranil to suitable P^{III} precursors have been studied extensively, as noted in the introduction.[77] We were curious to see if hexacoordinate compounds are formed in the cycloaddition reactions using DIAD also. It may be noted that in this case, the nitrogen of the DIAD residue could lower the acidity at phosphorus leading to weaker (or none) S→P coordination. If hexacoordination occurs, we expect to isolate/ identify positional isomers. Thus we continued our previous studies on the reaction of P^{III} precursors [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(Ph) (**2**), and [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$]P(OPh) (**7**) with DIAD. Indeed we were able to

isolate the hexacoordinate compounds **45** and **46**, respectively, using this reaction (Scheme 8).

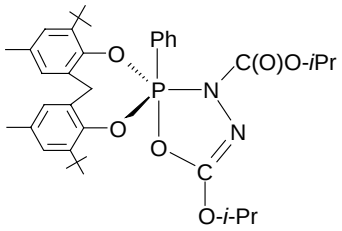


(**43**) (**44**)

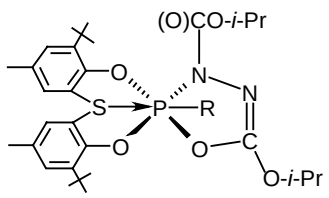
Scheme 8



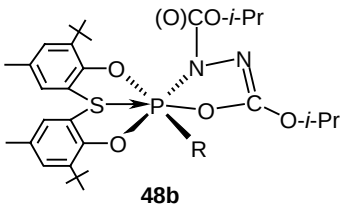
Comparison of the ^{31}P NMR chemical shift of **45** [δ –64.3] to that of the pentacoordinate compound **47** [δ –51.7] prepared earlier in our laboratory[10a] clearly shows an up-field shift of ~12 ppm for compound **45** relative to **47**. Since higher coordination is expected to move the ^{31}P NMR towards higher field, we can say that for compound **47**, the solution state ^{31}P NMR is consistent with hexacoordination.[80c, 110] However, there are at least three possible isomers (**48a-c**). A distinction among these cannot be made *a priori* on the basis of NMR data.



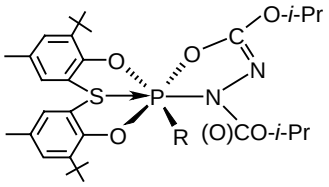
47 [δ(P): -51.7; X-ray]



48a



48b



48c

The ^{1}H NMR spectrum of compound **45** exhibits four distinct doublets [δ 0.95, 1.13, 1.15 and 1.26] for each of the isopropyl C*H*$_3$ protons and two singlets for each of the *t*-butyl [δ 1.20 and 1.40] and Ar-C*H*$_3$ protons [δ 2.22 and 2.28] (Figure 12). Since the ^{31}P NMR spectrum shows a single peak, we assume that a single hexacoordinate isomer [as shown, on the basis of its X-ray structure] is present in solution. Between the two isopropyl groups, one is C-O-*i*-Pr and the other is C(O)O-*i*-Pr. If the structure is rigid (i. e., if the C-C bond rotation is frozen) in solution, we may expect that even the two methyl groups of each of these isopropyl groups to show up as distinct doublets due to coupling to C*H*Me$_2$ (methine) protons, thus giving rise to four doublets. This kind of observation has already been made in pentacoordniate phosphorus compounds.[96e] The two aromatic rings are in different environments as the phenoxy-oxygen atom of one them is *trans* to an oxygen atom of the five-membered ring while the phenoxy oxygen atom of the second aromatic ring is *trans* to the nitrogen atom of the five-membered ring. Thus there are two *t*-butyl and two Ar-C*H*$_3$ signals (at this end C-C bond rotation is not frozen at this temperature).

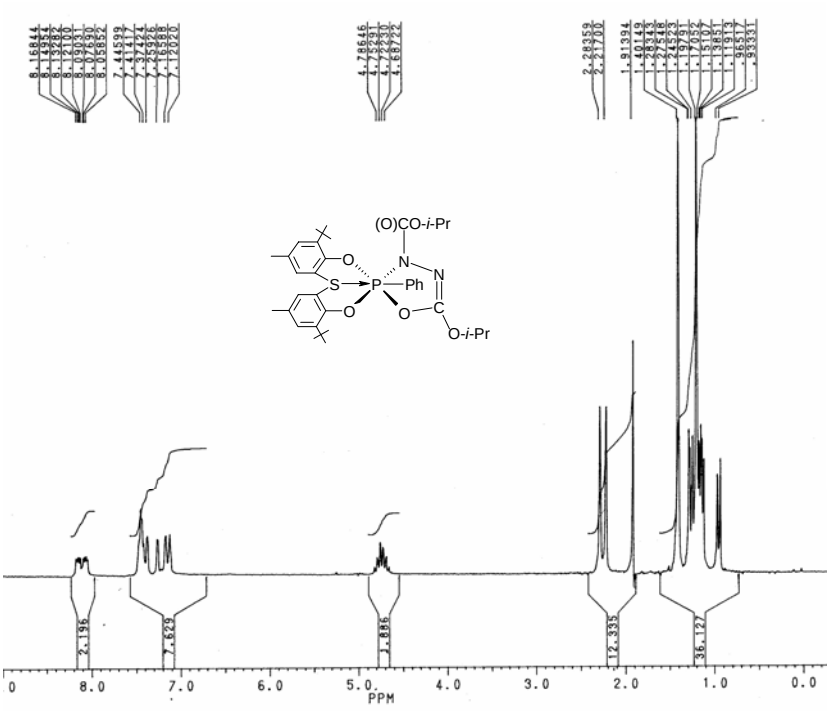


Fig. 12. The ^{1}H NMR spectrum of **45**.CH_3CN, the solvent (CH_3CN) peak appears at δ 1.91.

The molecular structures of **45** and **46** are shown in Figures 13 and 14 respectively. The corresponding bond parameters are given in Tables 5 and 6. Both compounds **45** and **46** have a distorted octahedral structure with S→P distances of 2.628 (2) and 2.794(1) Å respectively. These distances, in particular that of **45**, are longer than those found in the *o*-chloranil compound **49** (see below) [2.594(2) and 2.530(2) Å for the two independent molecules in the unit cell].[80d] It is known from the literature that the S→P distances decrease with the electron-donating ability (*t*-Bu > Me) of the eight membered ring substituents and electronegativity of the ligand.[80a] Compound **45** has three oxygen atoms around phosphorus while compound **49** has four oxygen atoms, and hence the S→P distance is consistent with the expectation. It is, however, interesting to note that in **46**, the S→P bond distance is longer than in **45** even though *four* oxygen atoms are connected to phosphorus in the former (which is expected to make phosphorus more acidic leading to a shorter S→P bond) compared to *three* oxygen atoms in the latter.

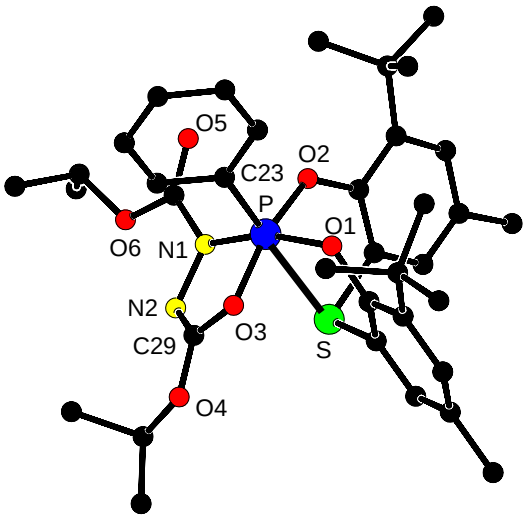
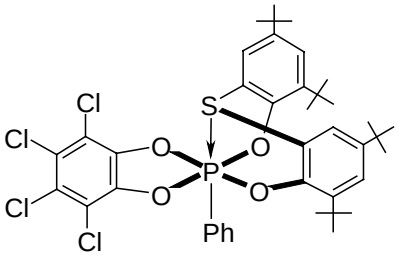


Fig. 13. Molecular structure of **45**.CH_3CN. Solvent atoms are omitted and only selected atoms are labeled.

Table 5. Selected bond lengths [Å] and bond angles [°] for **45**.CH_3CN. with esd's in parentheses

P-O(1)	1.701(3)	P-N(1)	1.791(4)
P-O(2)	1.667(3)	P-C(23)	1.820(4)
P-O(3)	1.715(3)	P-S	2.6284(17)
O(1)-P-O(2)	89.76(15)	O(2)-P-C(23)	97.06(17)
O(1)-P-O(3)	87.81(14)	O(2)-P-S	84.42(11)
O(1)-P-N(1)	162.45(16)	O(3)-P-N(1)	84.61(15)
O(1)-P-C(23)	95.11(17)	O(3)-P-C(23)	97.92(17)
O(1)-P-S	81.40(10)	O(3)-P-S	80.57(10)
O(2)-P-O(3)	164.98(15)	N(1)-P-C(23)	101.59(18)
O(2)-P-N(1)	171.72(7)	N(1)-P-S	81.76(12)
		C(23)-P-S	176.22(15)



49 [δ(P): -54.7; X-ray]

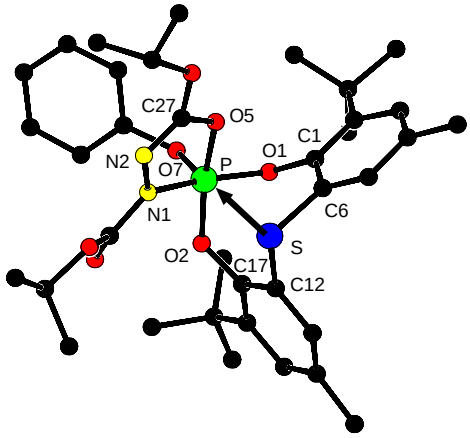


Fig. 14. Molecular structure of **46** showing the numbering scheme on selected atoms.

Table 6. Selected bond lengths [Å] and bond angles [°] for **46** with esd's in parentheses

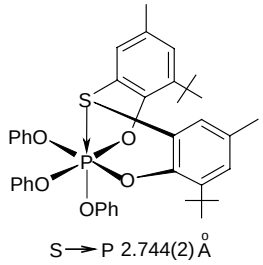
P-O(1)	1.6605(15)	P-N(1)	1.7479(19)
P-O(2)	1.6331(17)	P-O(7)	1.5949(18)
P-O(5)	1.6894(17)	P-S	2.7942(10)
O(1)-P-O(2)	90.64(8)	O(2)-P-O(7)	95.59(10)
O(1)-P-O(5)	87.23(8)	O(2)-P-S	79.52(6)
O(1)-P-N(1)	160.76(10)	O(5)-P-N(1)	85.13(9)
O(1)-P-O(7)	93.97(8)	O(5)-P-O(7)	99.70(10)
O(1)-P-S	75.98(6)	O(5)-P-S	85.24(7)
O(2)-P-O(5)	164.67(9)	N(1)-P-O(7)	104.71(10)
O(2)-P-N(1)	92.08(9)	N(1)-P-S	85.80(8)
		O(7)-P-S	168.66(7)

For compounds exhibiting S→P coordination, ring strain is expected in forming two five membered rings in lieu of the original eight-membered ring that

causes a bond lengthening effect (cf. structures **43** and **44**). The mean P-O distances (in the fused five-membered ring) in **45** and **46** are, respectively 1.684 and 1.647 Å. For comparison, **47** that lack S→P coordination has a mean P-O_{ring} distance of 1.612 Å. Thus the P-O bond lengths differ depending on the ring size. As expected because of higher coordination number, the P-O and P-N distances in **45** [P-N(1) 1.791(4)] are significantly longer than those found in the analogous pentacoordinate compound **47** [P-N(1) 1.701(2)].[10b] The longer P-C bond in **47** [1.843 (2) Å] relative to **45** is consistent with it being at the apical position of the trigonal bipyramid.

In the pentacoordinate compound **47**, the diequatorially oriented eight-membered ring has an *anti* (boat-chair) conformation.[10b] In contrast, in the hexacoordinate compounds **45-46** or **49**, the analogous ring takes *syn* (tub) conformation as a requirement for S→P coordination.

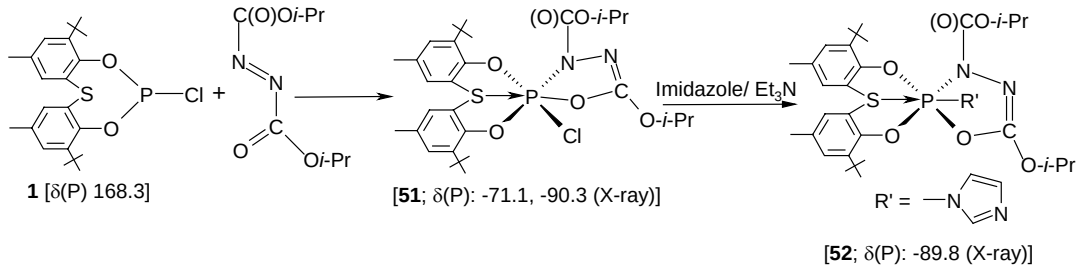
The S→P distance in **46** is slightly longer than that in **50** (which also has a phenoxy substituent) as expected because P is connected to four oxygen atoms (i.e. it is less acidic) in the former compared to five in the latter. The P-O bond lengths in compound **46** are P-O_{mean} (fused ring): 1.647(2) Å and P-O(7) (acyclic *trans* to P-S): 1.595(2) Å. This feature is similar to the *o*-chloranil system like **50**, where also the P-O bond lengths follow the order: P-O (fused ring)>P-O (acyclic *trans* to P-S).[111]



50

When S(6-*t*-Bu-4-Me-$C_6H_2O)_2PCl$ (**1**) is treated with DIAD, the hexacoordinate phosphorus compound **51** is formed; this was further reacted with imidazole to give compound **52** (Scheme 9). The molecular structures of **51** and **52** are shown in Figures 15-16, while the selected bond parameters are given in Table 7 and 8 respectively.

Scheme 9



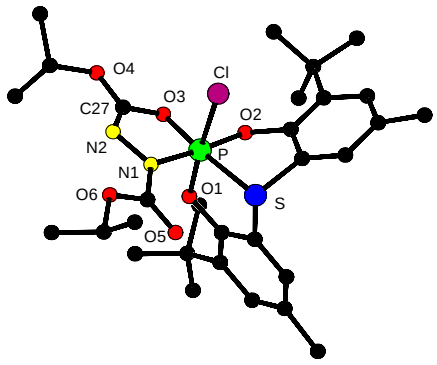


Fig. 15. Molecular structure of **51;** only selected atoms are labeled.

Table 7. Selected bond lengths [Å] and bond angles [°] for **51** with esd's in parentheses

P-O(1)	1.6681(14)	P-N(1)	1.7713(17)
P-O(2)	1.6743(14)	P-Cl	2.2194(8)
P-O(3)	1.6668(14)	P-S	2.3170(8)
O(1)-P-O(2)	91.03(7)	O(2)-P-Cl	90.00(6)
O(1)-P-O(3)	93.70(7)	O(2)-P-S	86.75(5)
O(1)-P-N(1)	91.83(8)	O(3)-P-N(1)	87.14(7)
O(1)-P-Cl	174.03(6)	O(3)-P-Cl	92.18(6)
O(1)-P-S	89.24(5)	O(3)-P-S	175.59(6)
O(2)-P-O(3)	89.91(7)	N(1)-P-Cl	87.44(6)
O(2)-P-N(1)	176.02(8)	N(1)-P-S	96.06(6)
		Cl-P-S	84.95(3)

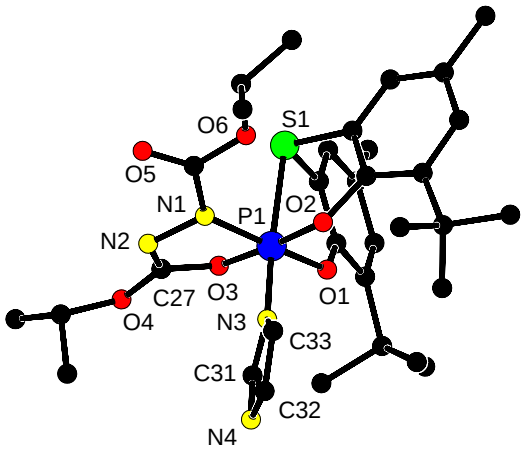


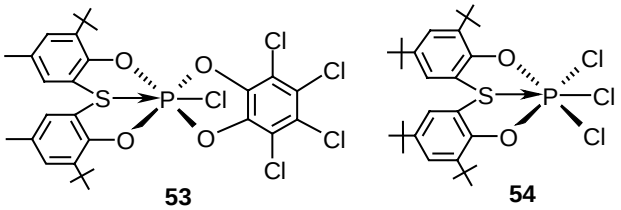
Fig. 16. Molecular structure of **52,** only selected atoms are labeled. There are two molecules in the asymmetric unit, but only one is shown; the other one has similar bond parameters.

Table 8. Selected bond lengths [Å] and bond angles [°] for **52** with esd's in parentheses

P(1)-O(1)	1.6388(16)	P(1)-N(1)	1.789(2)
P(1)-O(2)	1.6760(17)	P(1)-N(3)	1.747(2)
P(1)-O(3)	1.7205(17)	P(1)- S(1)	2.4217(8)
O(1)- P(1)-O(2)	92.90(9)	O(2)- P(1)-N(3)	93.31(9)
O(1)- P(1)-O(3)	175.27(8)	O(2)- P(1)- S(1)	86.67(6)
O(1)- P(1)-N(1)	95.53(9)	O(3)- P(1)-N(1)	84.86(9)
O(1)- P(1)-N(3)	90.79(9)	O(3)- P(1)-N(3)	93.89(9)
O(1)- P(1)-S(1)	86.67(6)	O(3)- P(1)- S(1)	88.62(6)
O(2)- P(1)-O(3)	86.16(8)	N(1)- P(1)-N(3)	93.73(10)
O(2)- P(1)-N(1)	168.94(9)	N(1)- P(1)- S(1)	89.04(7)
		N(3)- P(1)- S(1)	176.41(8)

The geometry at phosphorus in all these compounds can be considered to be octahedral, with greater distortion for **51** compared to **45** and **46**. The S→P distances are in the range expected for the sulfur coordination to phosphorus. To our knowledge, the S→P donor-acceptor distance (2.317 Å) in **51** is the shortest known for neutral hexacoordinate phosphorus compounds and is pretty close to the covalent bond distance of 2.13-2.14 Å.[112] This is a bit surprising since compared to

compounds **53**[80d] or **54**[80b] that have $\mathbf{P}O_4SCl$ or $\mathbf{P}O_2SCl_3$ skeletons respectively, compound **51** has $\mathbf{P}O_3NSCl$ skeleton; the Lewis acidity at the phosphorus center (excluding the S→P bond) should have been lower for **51** when compared to **53** and **54**. This, consequently, should have led to a weaker S→P interaction (i.e. longer bond) in **51**. It is likely that the presence of -CO_2-*i*-Pr group on nitrogen has played a role in the observed shorter distance.



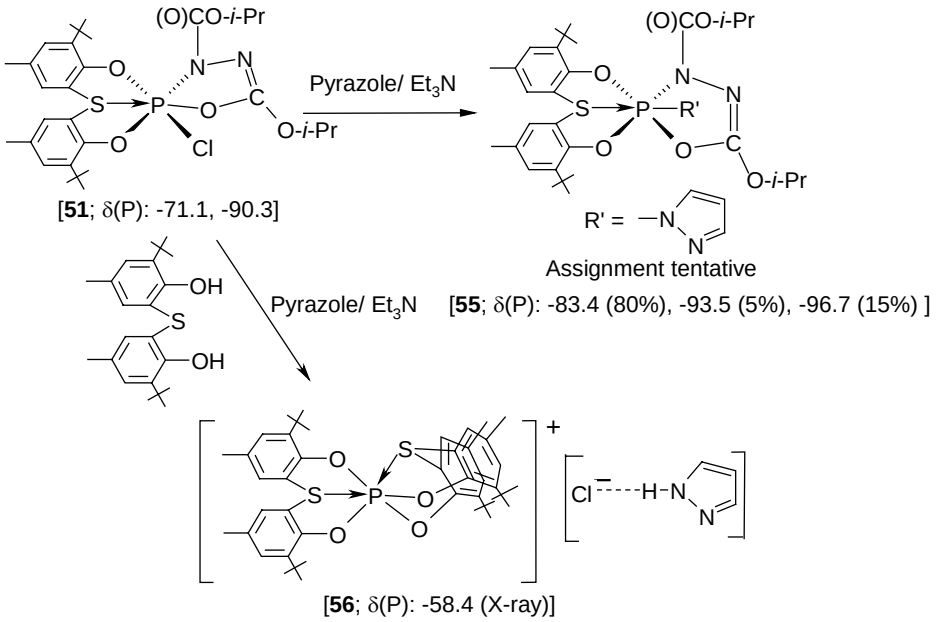
It can be readily seen that in **45**, **46**, **52** and **53** the acyclic substituent (phenyl, phenoxy, imidazolyl or Cl) is the one that is *trans* to the sulfur. This contrasts with **51** in which an oxygen atom of the five-membered ring is *trans* to the sulfur, thus hinting at the possibility of positional isomerism in this class of compounds.[113] As suggested by Cavell, the *facial* coordination observed in these compounds is influenced by the fact that two five-membered rings must be formed and hence the ligand may not be able to span three meridional positions.[78] The fact that the imidazolyl compound **52** is obtained by starting with the chloro compound **51** also suggests that the pentacoordinate-hexacoordinate equilibrium may exist in solution to facilitate the ligand reorganization.

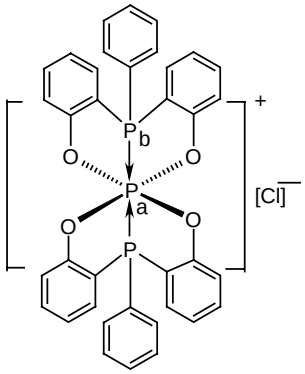
The P-N bond distances in **51** and **52** are in the range [1.747-1.789 Å] expected for the single bond, but still are lower than the P-N(1) apical bond in **14** [1.809 Å]. The P-O distance in the fused ring for **51** [mean 1.671 Å] which is longer than that in **52** [mean 1.657 Å] is the opposite of the trend observed for the in S→P distances in these two compounds. In compounds **45**, **46**, **51** and **52** the phosphorus atom is above the mean plane of the four atoms *cis* to sulfur to an extent of 0.238, 0.247, 0.112, and 0.127 Å respectively. One can roughly estimate the displacement of these structures from square pyramid (that excludes sulfur coordination) to octahedral (that includes sulfur coordination), based on the value of 0.431 Å displacement for phosphorus from the mean plane of the basal atoms in a square pyramidal arrangement with basal angles of 150°.[80d] Thus the order of percentage

displacement from square pyramid to octahedral geometry would be **51** (~ 74%) > **52** (~ 71%) > **45** (~ 45%)> **46** (~ 43%); this is in line with the corresponding S→P distances of 2.317, 2.422, 2.623 and 2.794 Å, respectively. However, one question that remains unanswered is the shorter S→P distance in the *imidazolyl* compound **52** relative to the *phenoxy* compound **46**.

When a reaction analogous to that shown in Scheme 9 was performed with pyrazole using the *in situ* generated **51**, we obtained a solid (labeled as **55**) that showed three peaks in the ^{31}P NMR spectrum [δ -83.4 (80%), -93.5 (5%) and –96.7 (15%)], but in addition, a small quantity of another crystalline compound **56** [δ(P) – 58.4] was isolated (Scheme 10). At the moment we are not sure whether **55** is a pure product or a mixture of products (^{1}H NMR was complicated). However, compound **56** gave clean spectra and could be characterized by X-ray crystallography (Fig. 17, Table 9). In comparison to the P→P←P bonded **57**, reported by Cavell, the δ(P) – 58.4 value in **56** is much downfield,[74] but sulfur connected phosphoranes do appear downfield.[96c]

Scheme 10





57 [δ(P): -107.8 (P_a), -34.8 (P_b)]

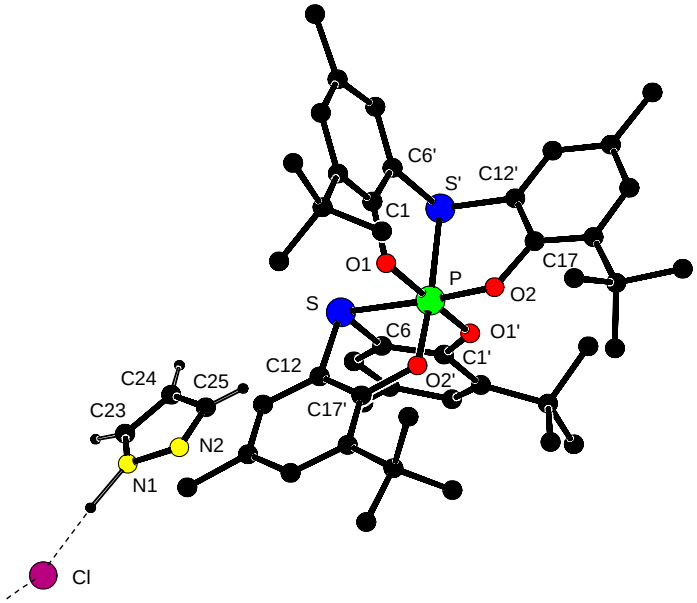


Fig. 17. Molecular structure of **56,** only selected atoms are labeled.

Table 9. Selected interatomic distances [Å] and angles [°] for **56** with esd's in parentheses

P-O(1)	1.6694(16)	P-O(2')	1.6351(17)
P-O(1')	1.6695(16)	P-S	2.3343(9)
P-O(2)	1.6352(17)	P- S'	2.3343(9)
N1-H(N1)	0.86[a]	H(N1)…Cl	2.30[a]
N(1)…Cl	3.140(3)		
O(1)-P-O(1')	173.59(12)	O(2)-P- S'	91.36(6)
O(1)-P-O(2)	94.20(8)	O(1')-P-O(2')	94.20(8)
O(1)-P-O(2')	90.20(8)	O(1')-P-S	88.71(6)

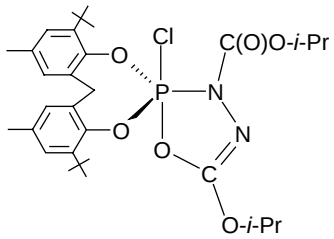
O(1)-P-S	86.53(6)	O(1')-P- S'	86.53(6)
O(1)-P-S'	88.71(6)	S-P-O(2')	91.36(6)
O(2)-P-O(1')	90.20(8)	S-P- S'	83.90(4)
O(2)-P-O(2')	93.39(12)	O(2')-P- S'	175.19(7)
O(2)-P-S	175.19(7)		
N(1)-H(N1)···Cl	166.7[a]		

[a]H(N1) is fixed by geometry and hence for the corresponding distances/ angles esd's are not given.

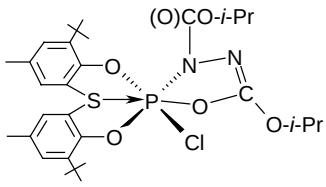
Compound **56** represents the first example of a hexacoordinate phosphorus compound with S→P←S double coordination. All previously known compounds had only one P←S bond. The geometry is essentially octahedral with facial arrangement of the two fused rings, but the two sulfur atoms are *cis* to each other. This arrangement is different from that observed in **57** wherein the two coordinating phosphorus atoms are *trans* to each other. The molecule crystallizes in the *C*2/c space group with only half the molecule in the asymmetric unit. The two equivalent P←S coordinate bonds are quite strong [2.334 (1) Å] and are comparable to that in the chloro precursor **51** [2.317(1) Å]. Between the two sets of the P-O bonds, with O *trans* to S and O *trans* to O, the distances to the former are shorter.

2.24 Solution state NMR spectra of hexacoordinate compounds

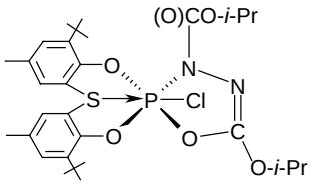
The ^{31}P NMR ($CDCl_3$) spectra compounds **45, 46** and **52** show a single line, whereas compound **51** shows two lines at 20^{o}C. Compound **52** [δ(P) –89.8] has a significantly up-field shift compared to the pentacoordinate compound CH_2(6-t-Bu-4-Me-$C_6H_2O)_2$P(imidazolyl)(N(COO-i-Pr)-N=C(O-i-Pr)O-) [**23b**: δ(P) –73.5] showing that S→P coordination is retained in solution. Observation of two ^{31}P NMR signals for **51** [δ -71.1, -90.3] that are very much up-field to that of **58** [δ(P) -46.0; pentacoordinate] clearly suggests that both the signals for **51** are due to hexacoordinate isomers. We ascribe these to S-*trans*-O (as observed in the solid state) and S-*trans*-Cl [**51'**] isomers. It can be noted that the disposition of substituents in **51'** is similar to that in **52**.



[**58**; δ(P) -46.0]



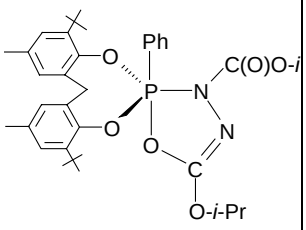
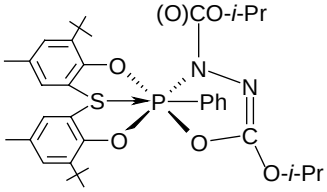
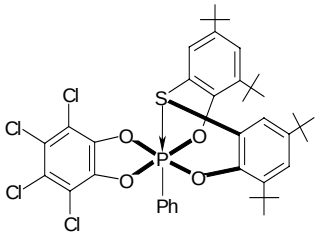
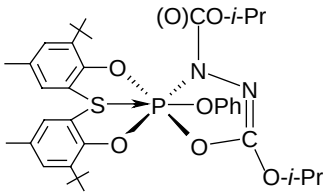
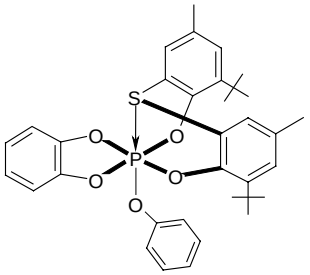
51

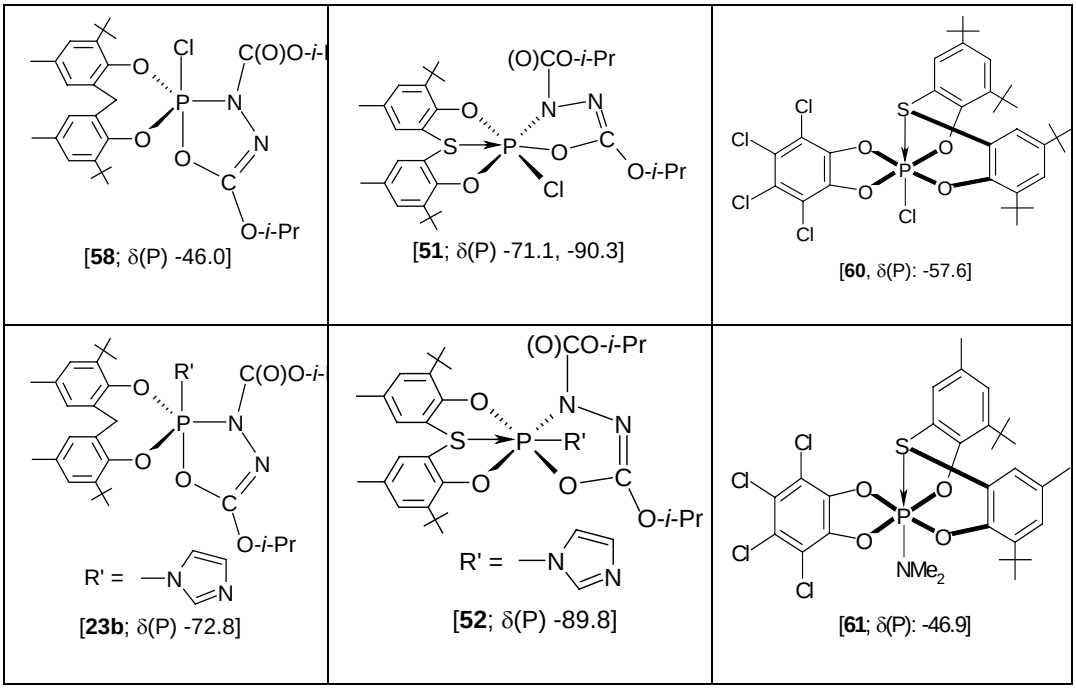


51'

The ^{31}P NMR chemical shift differences (Δδ) between the hexacoordinate compounds (with S→P bond) and their pentacoordinate counterparts (which have CH_2 in place of S in the ring) for the pairs **58**/ **51** (≥ 25.0 ppm), **23b**/ **52** (16.1 ppm), and **47**/ **45** (12.6 ppm) also indicate that S→P bond strength should be in the order **51**> **52** > **45**. This is what is actually observed [S→P distances are, respectively, 2.317(1), 2.422(1) and 2.628(2) Å]. The ^{31}P NMR data are summarized in Table 10 for ready visualization.

Table 10. Comparision of ^{31}P NMR data for the hexacoordinate compounds in this chapter with penta- and hexacoordinate compounds.

Pentacoordinate compounds	Hexacoordinate compounds	Hexacoordinate compounds
 [**47,** δ(P): -51.7]	 [**45**, δ(P): -64.3]	 [**49**, δ(P): -54.6]
	 [**46**, δ(P): -67.0]	 [**59**, δ(P): -58.3]



For compound **52**, we have recorded the variable temperature ^{31}P NMR spectra in toluene-d_8. There was no change in chemical shift value throughout the temperature range studied [233 K to 353 K]; clearly showing that hexacoordination is retained in solution for **52**. In the variable temperature ^{1}H NMR spectra, two *t*-butyl, two methyl and four isopropyl methyl signals are seen till 313 K; while at higher temperatures mainly two isopropyl methyl signals were observed with no change for the methyl or *t*-butyl signals (Figure 18). These data suggests that C-C bond rotation at the isopropyl groups is partially frozen in **52** at room temperature. The chloro compound **51** was hydrolytically not very stable and hence its variable temperature NMR spectra were not recorded.

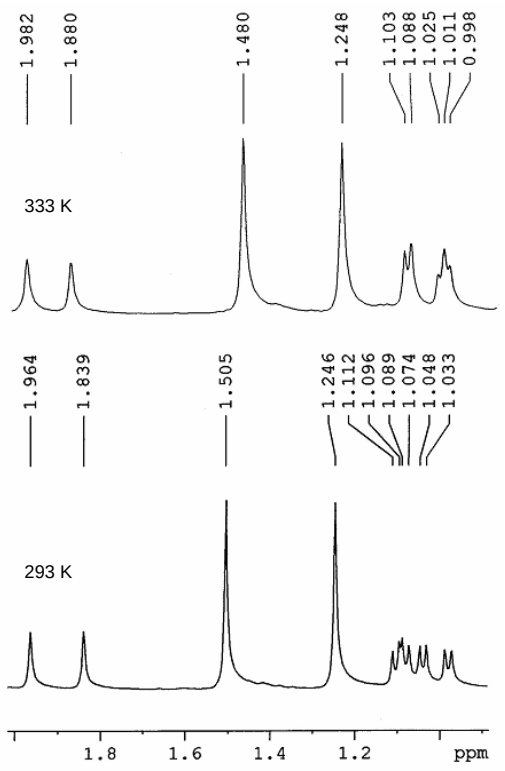
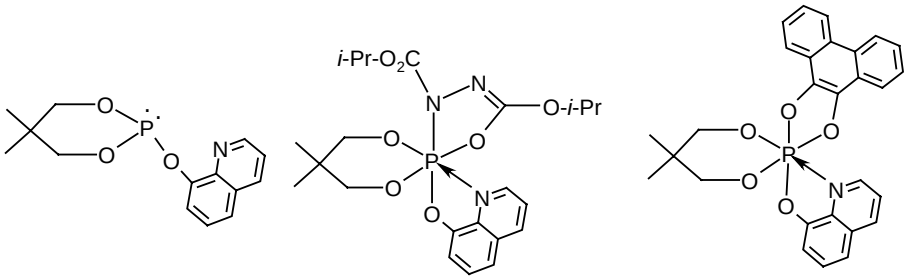


Fig. 18. The ^{1}H NMR spectra of compound **52** at 293 K and 333 K; in the region 0.0-2.0 ppm.

To probe the reaction of P^{III} compounds with DIAD further, we have used $(OCH_2CMe_2CH_2O)P$(oxinate) (**62**).[96l] The ^{31}P NMR spectrum of the reaction mixture suggested the formation of hexacoordinate compound **63** which showed a peak at δ -109.5 *via* N→P coordination (Figure 19). This chemical shift value may be compared with **64** (δ(P): -100.5)[80e] reported from our laboratory. This feature also suggests that in compound **19** discussed earlier, steric factors prevented the formation of the additional N→P coordinate bond.



62 **63** [δ(P): -109.4] **64** [δ(P): -100.5]

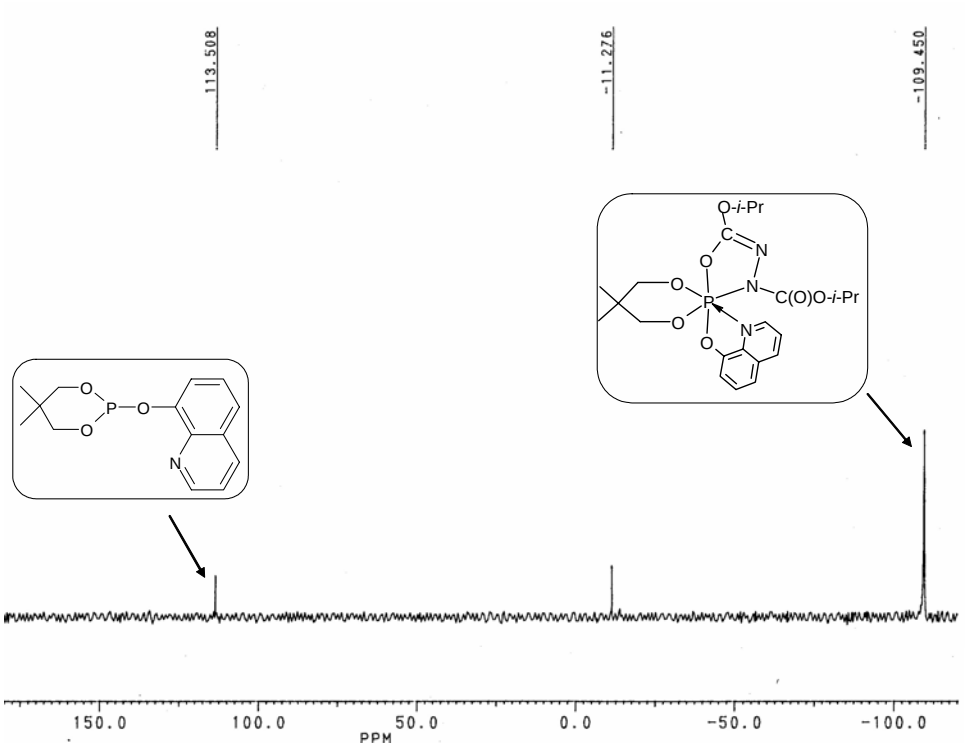


Fig. 19. The ^{31}P NMR spectrum for the reaction mixture obtained by treating **62** with DIAD.

2.25 *Theoretical calculations*

From what has been discussed above, it is clear that depending on the substituents, the reaction of cyclic phosphites with DEAD/ DIAD leads to tetra- (structure **38**), penta- (structures **29-31**; structure **32** is not observed by X-ray so far) or hexacoordinate (structures **33-35**) compounds (Chart 1, see above). In an effort to ascertain the relative stabilities of various configurations particularly for **14**, **38**, **51** and **52**, we did geometry optimization using the known coordinates from the available X-ray structures at B3LYP/6-31G* level using Gaussian 03 program package. For compound **38** which had unusual solution and solid state behavior [tetracoordination in solid state (X-ray) and pentacoordination in solution state (^{31}P NMR)],[10b] optimization showed clearly that tetracoordination is more stable than the penta- or hexa-coordination by at least 17 kJ mol^{-1}. For compound **14** also, theoretically calculated energies justify what is experimentally found, albeit marginally. The observed pentacoordinate isomer **14** is marginally more stable than the tetra- or hexa- or other pentacoordinate structures by ≥ 7 kJ mol^{-1}. The calculated energies for compounds **51** and **52** suggest that the hexacoordinate isomers (**33** and

34) are more stable than their pentacoordinate isomers. Between the two hexacoordinate isomers, the observed structure **34** is the most stable one for **51**; this isomer is marginally more stable (by *ca* 2.5 kJ mol^{-1}) than the observed structure **33** (X-ray) for **52**. Thus, within the errors associated with the calculations, although assessing the stability of individual isomers with a particular coordination number is difficult, prediction of the stability of isomers with different coordination numbers is possible.

We have optimized the structures of the compounds presented in the following Table 11 at B3LYP/6-31G* level[114] using Gaussian 03 program package.[115]

Table 11. Energies (au) of the optimized structures for **14**, **38**, **51** and **52**

Input structure[a]	Total Optimized Energies of the Compounds			
	14	**38**	**51**	**52**
29	-2642.81688	-2603.48652	-2929.11876	-2694.53156
30	-2642.79752	-2603.47500	-2929.12508	-2694.51646
31	-2642.82621	-2603.49209	-2929.12289	-2694.51646
33	-2642.81895	-2603.49488	-2929.12979	-2694.53748
34	-2642.81390	-2603.48600	-2929.13438	-2694.53840
38	-2642.82358	-2603.50296	Not applicable	Not applicable

[a] The coordinates from X-ray structures of **47**, **20**, **14**, **51**, **52** and **38** were used, respectively, for **29**, **30**, **31**, **33**, **34** and **38**. Modification of the substituents (like S replacing CH_2) was then effected and the structure was optimized for minimum energy. Energy in atomic units: 1 a.u. = 627.50 kcal/mol.

2.3 Involvement of cyclic phosphates in hydrogen bonding

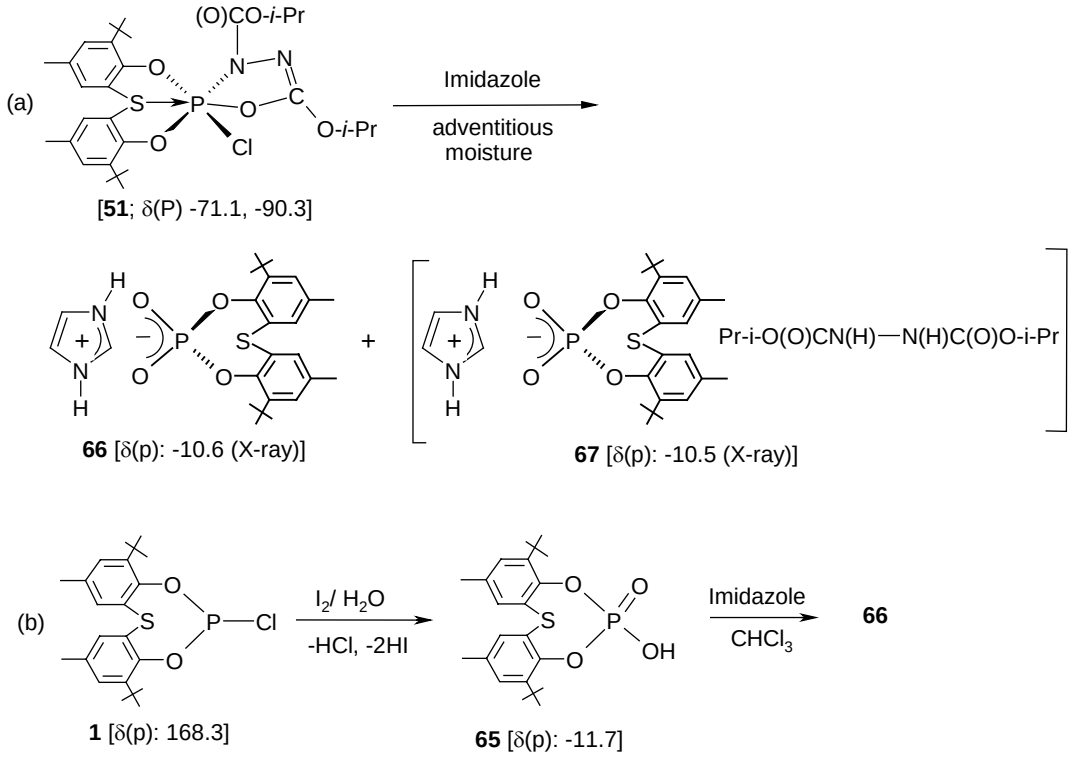
In the reaction of P^{III} compounds with DIAD, one of the problems we encountered was hydrolysis [cf. Fig. 19; peak at δ -11.3]. In fact, in our attempts to crystallize the imidazolyl compound **52**, we ended up in isolating imidazolyl salts of phosphate **65** also. Because the imidazolyl ends of the histidine residue take part (*via*

hydrogen bonding) in the hydrolysis/ cyclization processes of RNA,[85] we have some interest in understanding the hydrogen bonding patterns in these systems. Thus alongside the pentacoordinate and hexacoordinate phosphorus compounds, the hydrogen bonding features involving these phosphates and their salts are also investigated. This aspect is discussed in this section.

In previous reports of the imidazolium salts of phosphates,[88] there were no additional guest molecules except in the one reported from our laboratory.[87] In the latter, a hydrogen bonded methanol molecule exhibiting C—H…O interactions with the imidazolyl CH (located in between the two N atoms) was included as a guest.

In this section, the synthesis and X-ray structures of two imidazolyl compounds, [{S(6-t-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$] (**66**) and [{S(6-t-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$][$(CH_3)_2$CHO(O)N(H)-N(H)(C(O)O(CH$(CH_3)_2$)] (**67**), the latter containing the carboxylate substituted hydrazine as a hydrogen bonded guest are discussed. Compounds **66** and **67** are obtained in the reaction of [{S(6-t-Bu-4-Me-$C_6H_2O)_2$}PCl[N(C(O)O(CH$(CH_3)_2$)N-C(OCH$(CH_3)_2$O-] (**51**) with imidazole in the presence of adventitious moisture (Scheme 11a). The phosphate S(6-t-Bu-4-Me-$C_6H_2O)_2$P(O)OH (**65**) [M.p.: >523 K][116] is also prepared by a procedure similar to that for CH_2(6-t-Bu-4-Me-$C_6H_2O)_2$P(O)OH.[87] When **65** is dissolved in chloroform containing imidazole, a clear solution was obtained initially (Scheme 11b). This is followed by almost immediate crystallization of the salt **66**. From the direct route also we obtained compound **66** by treating the *in situ* prepared phosphate with imidazole. The molecular structures of compound **66** and **67** are given in Figures 20-21, while selected bond parameters are given in Tables 12 and 13, respectively.

Scheme 11



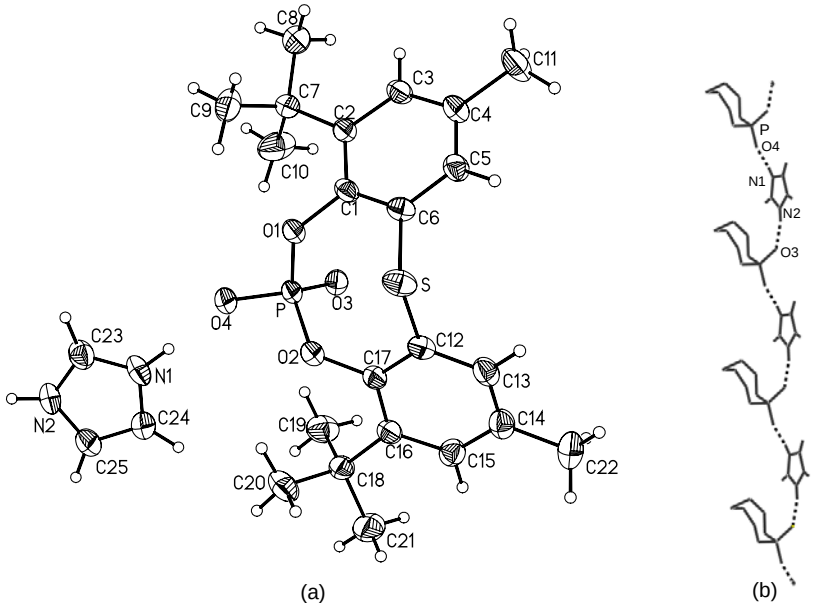


Fig. 20. (a) An ORTEP diagram of **66** showing the numbering scheme, (b) hydrogen bonding scheme in **66** (only selected atoms are shown).

Table 12. Selected interatomic distances [Å] and bond angles [°] for **66** with esd's in parentheses

P-O(1)	1.6077 (15)	P-O(3)	1.4687 (16)
P-O(2)	1.6112 (16)	P-O(4)	1.4688 (15)
N(1)-H(N1)	0.86*	H(N1)···O(4)	1.77*
N(1)...O(4)	2.628 (2)	N(2)-H(N2)	0.86*
H(N2)···O(3)	1.76*	N(2)...O(3)	2.603 (2)
O(1)-P-O(2)	106.03 (9)	O(2)-P-O(4)	105.53 (9)
O(1)-P-O(3)	109.38 (9)	O(3)-P-O(4)	120.85 (10)
O(1)-P-O(4)	104.82 (9)	O(2)-P-O(3)	109.24 (9)
N(1)-H(N1)···O4	173.9*		
N(2)-H(N2)···O3	166.6*		

*H(N1) and H(N2) were fixed by geometry and hence for the corresponding distances/ angles esd's are not given.

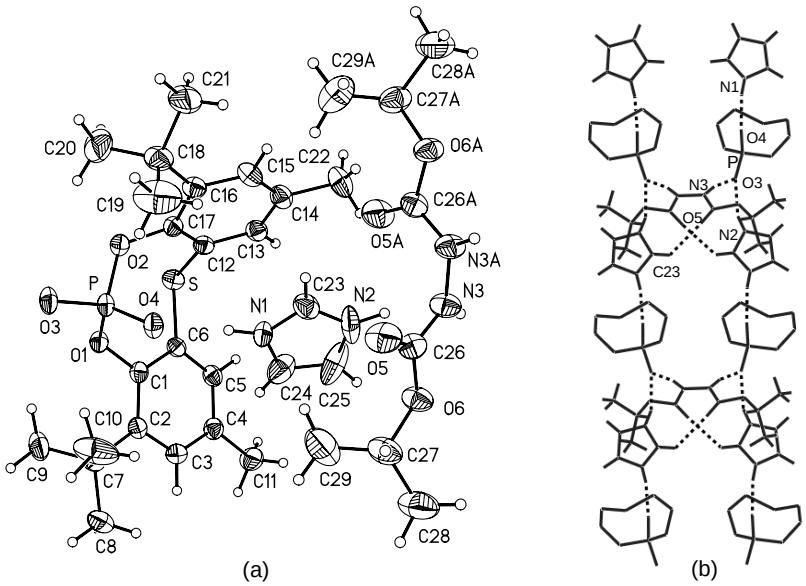


Fig. 21. (a) An ORTEP diagram of **67** showing the numbering scheme, (b) hydrogen bonding scheme in **67** (only selected atoms are shown).

Table 13. Selected interatomic distances [Å] and bond angles [^{o}] for **67** with esd's in parentheses

P-O(1)	1.6125(14)	P-O(2)	1.6095(14)
P-O(3)	1.4759(13)	P-O(4)	1.4741(13)
N(1)-H(N1)	0.86*	H(N1)···O(4)	1.79*
N(1)...O(4)	2.630(2)	N(2)-H(N2)	0.86*
H(N2)···O(3)	1.94*	N(2)...O(3)	2.753(2)
N(3)-H(N3)	0.86(2)	H(N3)···O(3)	2.01(2)
N(3)-O(3)	2.830(2)	C(23)-H(23)	0.93*
H(23)···O(5)	2.30*	C(23)...O(5)	2.980(3)
O(1)-P-O(2)	104.79(7)	O(2)-P-O(3)	105.42 (8)
O(1)-P-O(3)	104.86(7)	O(2)-P-O(4)	109.41 (7)
O(1)-P-O(4)	109.97 (8)	O(3)-P-O(4)	121.15(8)
N(1)-H(N1)···O4	166.3*	N(2)-H(N2)···O	157.9*
N(3)-H(N3) · O3	159 (2)	C(23)-H(23)···O5	129.5

*H(N1) and H(N2) were fixed by geometry and hence for the corresponding distances/ angles esd's are not given.

It is reported that the neutral phosphate **65** exists as a hydrogen-bonded dimer with S→P coordination.[116] When **65** was treated with the amino-diol [CH_2 (C_6H_4)OH]$_2$NMe the anionic phosphate **68**, also having an S→P coordination, was isolated. If we compare **66** or **67** with **68,** the 1,3,2-dioxaphosphocin ring in **66** and **67** has an anti (boat-chair) conformation with S→P distances 3.585 and 3.584 Å respectively implying absence of any S→P coordination (Figure 22) unlike **68** where the ring takes syn (tub) conformation conducive for S→P coordination. Thus in our compounds **66**-**67** containing imidazolyl cations, donor action by sulfur is not present.

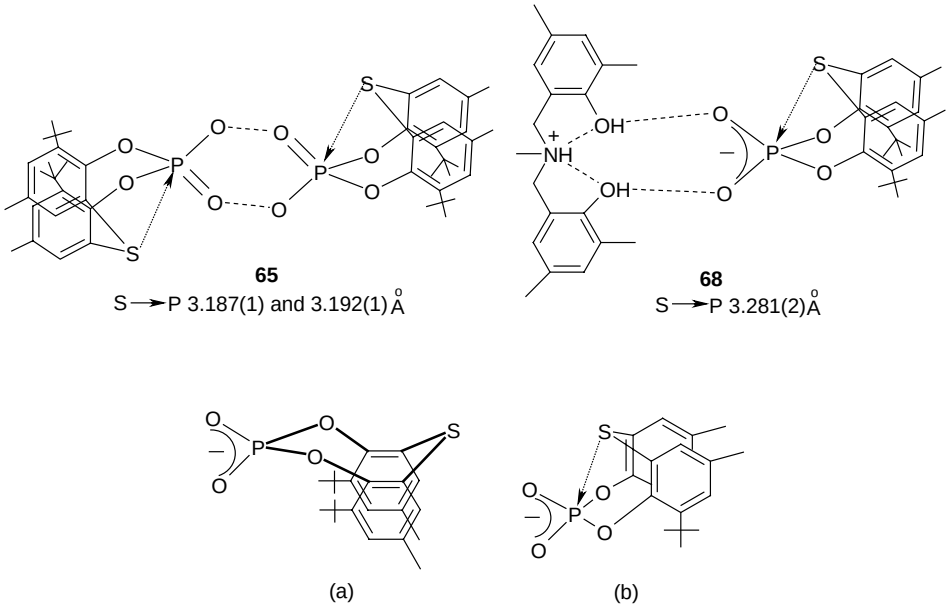


Fig. 22. (a) Ring conformation in compound **66** and **67**, (b) ring conformation in compound **68.**

In compound **66**, hydrogen bonding (Figure 20b) leads to the formation of a chain utilizing the protons on the two-imidazolyl N atoms and the two phosphate oxygen atoms. The same type of chain is present in **67** also, but in addition, one of the phosphoryl O atoms is involved in the 'bifurcate' hydrogen bonding with the additional interaction from the NH hydrogen atoms of the substituted hydrazine residue. This will lead to a 'ladder' type of structure as shown in Figure 21b. The hydrogen bond angles involving the phosphoryl oxygen with the bifurcated hydrogen bonds in **67** are less linear compared to the one at the corresponding oxygen [O(3)] in **67**, as expected. Accordingly, the O…N(imidazolyl) distance in **67** is also lower than that in **66**.

Although there is no significant interaction of the NCHN hydrogen with acceptor sites in **66**, there is one such in **67** involving the carbonyl O atom of the substituted hydrazine and the NCHN hydrogen atom in **67**. The C…O distance is pretty short (2.98 Å) and is comparable to that known for strong C-H…O hydrogen bonds;[87] the angle at hydrogen, however, is quite far from linearity and the H…O distance is 2.30 Å. This 'non-innocent' behavior of the imidazolyl NCHN hydrogen was earlier shown from our group and others. Such a feature may have some implications as regards the hydrolysis of RNA where the hystidine residue comes

close to the active phosphorus site, perhaps with the NCHN hydrogen interacting with the ribosolyl oxygen as pointed out previously.[85]

The eight membered 1,3,2-dioxaphosphocin ring in the phosphates salts **66** and **67** have the same type of ring conformation (can be termed as boat-chair or symmetrical anti) as in [imidazolium]$^{+}$[CH_2(6-*t*-Bu-4-Me-$C_6H_2O)_2PO_2$]$^{-}$.MeOH (**69**) (Figure 23).

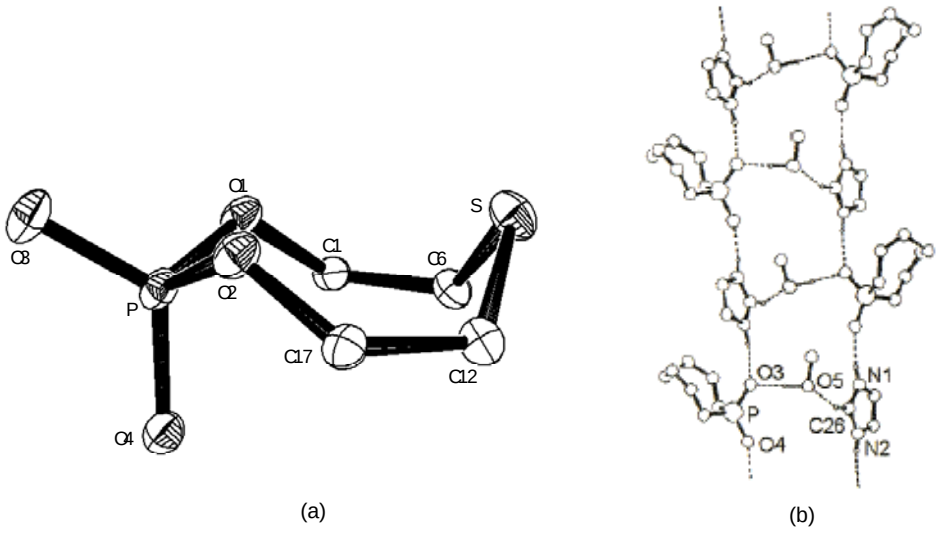


Fig 23. Plots showing conformation of 1,3,2-dioxaphosphocin ring (a) **66** or **67** (boat chair) and (b) **69** (boat chair).

2.4 Summary

1) New pentacoordinate phosphorus compounds that exhibit the 'reversed apicophilicity' phenomenon (compound **14**) and violate the Bent's rule in trigonal bipyramidal geometry are described.

2) Compound **38** (X-ray) is the first example of an imino-phosphorus compound that has a structure halfway between the classical MBH betaine **13** and protonated betaine in the Mitsunobu type reaction. This compound shows an unprecedented solution state behavior in which at least four distinct isomers are present at low temperatures.

3) Existence of positional isomers for neutral penta- and hexa-coordinate phosphorus compounds is established by means of X-ray crystallography and ^{31}P NMR spectroscopy. To our knowledge, the S→P donor-acceptor distance (2.317 Å) in **51** is the shortest known for neutral hexacoordinate phosphorus compounds and is pretty close to the covalent bond distance of 2.13-2.14 Å. In this process compound **56** which represents the first example of a hexacoordinate phosphorus compound with S→P←S double coordination was also obtained.

4) Theoretical calculations suggest that the compound as isolated is the favored one in most cases.

5) Synthesis and X-ray structures of two imidazolyl compounds, [{S(6-t-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$] (**66**) and [{S(6-t-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$][$(CH_3)_2$CHO(O)N(H)-N(H)(C(O)O(CH$(CH_3)_2$)] (**67**), the latter containing the carboxylate substituted hydrazine as a hydrogen bonded guest and with an imidazolyl CH involved in fairly strong C-H…O hydrogen bonding, are discussed.

CHAPTER 3

EXPERIMENTAL SECTION

General: Chemicals and solvents were procured from Aldrich/ Fluka or local manufacturers. Further purification was done according to standard procedures wherever required.[117] All operations, unless otherwise specified, were carried out under dry nitrogen atmosphere using standard vacuum line techniques.[118]

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

Elemental analysis: Elemental analyses were carried out on a Perkin- Elmer 240C CHN analyzer.

Mass spectra: Mass spectra were recorded using a GCMS-QP2010 and LCMS 2010A.

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 200 MHz or 400 MHz NMR spectrometer in $CDCl_3$ solution (unless specified otherwise) with shifts referenced to $SiMe_4$ (^{1}H, ^{13}C; $\delta = 0$) or ext. 85% H_3PO_4 (^{31}P, $\delta = 0$) respectively; *J* values are in Hz.

Absorption and Fluorescence Spectroscopy: Steady state absorption and fluorescence spectra were recorded on UV-Vis-NIR scanning spectrophotometer (Shimadzu, model no. UV-3101PC) and on SPEX FLUOROMAX-3 spectrofluorometer, respectively.

3.1 Preparation of P(III) derivatives

Most of these compounds (although were pure) were moisture sensitive and hence characterization was done mainly by spectroscopy; for stable compounds elemental analyses was performed. Precursors S(6-*t*-Bu-4-Me–$C_6H_2O)_2PCl$ (**1**) and S(6-*t*-Bu-4-Me–$C_6H_2O)_2PPh$ (**2**)[92] were prepared by the literature methods and an improved procedure for **1** is given below.

(a) S(6-*t*-Bu-4-Me-$C_6H_2O)_2PCl$ (1) (*improved procedure*)

To a solution of 2,2'-thiobis(4-methyl-6-*t*-butylphenol)[90] (1.00 g, 2.80 mmol) and triethylamine (0.56 g, 5.55 mmol) in toluene (20 mL) was added PCl_3 in toluene (3 mL) drop-wise over a period of 10 min with continuous stirring at 0 ^oC. On completion of the addition, the mixture was brought to room temperature and stirred for 12 h. The solution was filtered, and the solvent removed in *vacuo* to obtain the title compound.

Yield: 1.00 g (85%).

Mp: 174-176 ^oC [lit 174-176 ^oC[91]].

^1H NMR: δ 1.40 (s, 18 H, Ar-C(CH_3)$_3$), 2.28 (s, 6 H, ArCH_3), 7.14-7.36 (m, 4 H, Ar-*H*).

^{31}P NMR: δ 168.3 [lit 168.4 [91]].

(b) S{6-*t*-Bu-4-Me-C_6H_2O}$_2$P{NHC$(CH_3)_2$} (3)

To a stirred solution of **1** (0.90 g, 2.12 mmol) in toluene (20 mL) was added *iso*-propylamine (0.25 g, 4.25 mmol) drop-wise over a period of 10 min at room temperature. After stirring for 12 h, the precipitate formed was filtered and all the solvent was removed *in vacuo* to obtain the required compound.

Yield: 0.85 g (90%).

Mp: 148-150 ^oC.

IR (KBr): 3360, 2963, 1750, 1595, 1427, 1397, 1360, 1271, 1235, 1207, 1165, 1128, 1105, 1005 cm^{-1}.

^1H NMR: δ 1.30 (d, 6 H, ^3J(H-H) = 6.0 Hz, NH-CH-(CH_3)$_2$), 1.42 (s, 18 H, Ar-C(CH_3)$_3$), 2.25 (s, 6 H, ArCH_3), 3.33 (br, 1 H, *H*N-C$(CH_3)_2$), 3.69 (m, 1 H, NH-C*H*-$(CH_3)_2$), 7.08-7.29 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 20.6 (s, Ar*C*H_3), 26.8 (d, ^3J(P-C) = 5.5 Hz, P-NH-C(*C*H_3)$_2$), 30.2 (s, Ar-C(*C*H_3)$_3$), 35.0 (s, Ar-*C*$(CH_3)_3$), 44.1 (d, ^2J(P-C) = 38.4 Hz, P-NH-H*C*$(CH_3)_2$), 123.3, 128.9, 131.4, 133.7, 140.2, 156.5.

^{31}P NMR: δ 137.5.

(c) S(6-*t*-Bu-4-Me-$C_6H_2O)_2$PNHMe (4)

To a stirred solution of **1** (2.00 g, 4.73 mmol) in toluene (50 mL) at –60^oC was passed an excess of dry methylamine gas for 3 h with continuous stirring. The reaction mixture was stirred further for 0.5 h at the same temperature and filtered

after warming to room temperature. Solvent was completely removed from the filtrate and the residue was crystallized from hexane to give **4**.

Yield: 1.69 g (86%).

Mp: 174-176 ^{o}C.

IR (KBr): 3416, 3349, 1763, 1595, 1564, 1427, 1391, 1359, 1273, 1235, 1209, 1094 cm^{-1}.

^{1}H NMR: δ 1.40 (s, 18 H, Ar-C(CH_3)$_3$), 2.26 (s, 6 H, ArCH_3), 2.89 (dd, ^{3}J(P-H) = 12.0 Hz, ^{3}J(H-H) = 6.0 Hz, 3 H, NHCH_3), 3.17 (br s,1 H, N*H*), 7.10-7.30 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 20.6 (s, Ar*C*H$_3$), 27.6 (d, ^{2}J(P-C) = 30.0 Hz, P-NH-*C*H$_3$), 30.2 (s, Ar-C(*C*H$_3$)$_3$), 35.1 (s, Ar-*C*(CH$_3$)$_3$), 123.2, 126.7, 129.1, 130.3, 131.5, 133.9, 135.2, 140.2, 153.3, 161.7.

^{31}P NMR: δ 138.3.

(d) S{6-*t*-Bu-4-Me-C$_6$H$_2$O}$_2$P(NH-*t*-Bu) (5)

To a stirred solution of **1** (1.17 g, 2.77 mmol) in toluene (20 mL) was added *t*-butylamine (0.40 g, 5.54 mmol) drop-wise over a period of 0.5 h at room temperature. After stirring for 12 h, the precipitate formed was filtered and all the solvent was removed *in vacuo* to obtain the required compound.

Yield: 1.15 g (90%).

Mp: 160-162 ^{o}C.

IR (KBr): 3364, 2959, 1763, 1595, 1427, 1358, 1273, 1209, 1097 cm^{-1}.

^{1}H NMR: δ 1.40 (s, 27 H, Ar-C(CH_3)$_3$ + HN-C(CH_3)$_3$), 2.29 (s, 6 H, ArCH_3), 3.60 (br s, 1 H, *H*N-*t*-Bu), 7.12 (s, 2 H, Ar-*H*), 7.34 (s, 2 H, Ar-*H*).

^{13}C NMR: δ 20.7 (s, Ar*C*H$_3$), 30.3 (s, Ar-C(*C*H$_3$)$_3$), 33.2 (d, ^{3}J(P-C) = 10.2 Hz, P-NH-C(*C*H$_3$)$_3$), 35.0 (s, Ar-*C*(CH$_3$)$_3$), 51.0 (d, ^{2}J(P-C) = 19.4 Hz, P-NH-*C*(CH$_3$)$_3$), 123.2, 128.2, 128.9, 131.3, 133.8, 140.2, 153.5.

^{31}P NMR: δ 138.2.

(e) S(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$PNCO (6)

Sodium cyanate (previously dried by evacuating in vacuum for 1 h; 0.71 g (10.94 mmol)) was added to solution of **1** (1.54 g, 3.65 mmol) in acetonitrile (20 mL) with continuous stirring and the mixture stirred further for 2 d. The solvent was removed *in vacuo*, heptane (15 mL) added to the residue and the mixture was

filtered. The solvent was completely removed from the filtrate and the residue crystallized from acetonitrile to give **6**.

Yeild: 1.25 g (85%).

Mp: 152-154 ^{o}C.

IR (KBr): 1595, 1429, 1362, 1271, 1227, 1094 cm^{-1}.

^{1}H NMR: δ 1.44 (s, 18 H, Ar-C(C*H*$_3$)$_3$), 2.31 (s, 6 H, ArC*H*$_3$), 7.15-7.35 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 20.7 (s, Ar*C*H$_3$), 29.9 (s, Ar-C(*C*H$_3$)$_3$), 35.1 (s, Ar-*C*(CH$_3$)$_3$), 122.3, 129.8, 133.2, 140.8, 152.9.

^{31}P NMR: δ 129.4.

(f) S(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$POPh (7)

To a stirred solution of **1** (1.06 g, 2.50 mmol) in toluene (20 mL) was added phenol (0.24 g, 2.50 mmol) in toluene drop-wise at 0 ^{o}C over a period of 10 min. After stirring for 12 h, the precipitate formed was filtered and all the solvent was removed *in vacuo* to obtain the required compound.

Yeild: 1.02 g (85%).

Mp: 114-116 ^{o}C.

IR (KBr): 1595, 1493, 1427, 1362, 1271, 1120, 1094, 1024 cm^{-1}.

^{1}H NMR: δ 1.46 (s, 18 H, Ar-C(C*H*$_3$)$_3$), 2.30 (s, 6 H, ArC*H*$_3$), 7.10-7.50 (m, 9 H, Ar-*H*).

^{13}C NMR: δ 20.8 (s, Ar*C*H$_3$), 30.0 (s, Ar-C(*C*H$_3$)$_3$), 35.2 (s, Ar-*C*(CH$_3$)$_3$), 120.4, 120.6, 122.9, 123.3, 128.3, 129.1, 129.4, 129.7, 132.7, 133.2, 140.8, 152.9, 153.4, 153.6.

^{31}P NMR: δ 136.1.

(g) S(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$POCH$_2$CH$_2$NMe$_2$ (8)

To a stirred solution of **1** (1.27 g, 3.00 mmol) in toluene (20 mL) at 0 ^{o}C was added triethylamine (0.30 g, 3.0 mmol) and N,N-dimethylethanolamine (0.27 g, 0.22 mL, 3.00 mmol) in toluene drop-wise over a period of 10 min. After stirring for 12 h, filtration followed by the removal of solvent afforded **8** as a white solid.

Yield: 1.28 g (90%).

Mp: 106-108 ^{o}C.

IR (KBr): 1595, 1429, 1273, 1235, 1209, 1096, 1032 cm^{-1}.

^{1}H NMR: δ 1.42 (s, 18 H, Ar-C(C*H*$_3$)$_3$), 2.29 (s, 6 H, ArC*H*$_3$), 2.42 (s, 6 H, N(C*H*$_3$)$_2$) 2.79 (m, 2 H, OCH$_2$C*H*$_2$N(*C*H$_3$)$_2$), 4.27-4.29 (m, 2 H, OC*H*$_2$CH$_2$NMe$_2$), 7.13 and 7.35 (2 s, 4 H, Ar-*H*).

^{13}C NMR: δ 20.7 (s, Ar*C*H$_3$), 30.0 (s, Ar-C(*C*H$_3$)$_3$), 35.1 (s, Ar-*C*(CH$_3$)$_3$), 45.9 (s, OCH$_2$CH$_2$N(*C*H$_3$)$_2$), 60.1 (s, OCH$_2$*C*H$_2$N(CH$_3$)$_2$), 60.4 (d, ^{2}*J*(PC) = 25.3 Hz, PO*C*H$_2$CH$_2$N(CH$_3$)$_2$), 123.1, 125.3, 128.2, 129.0, 129.2, 132.2, 133.4, 140.6, 153.5.

^{31}P NMR: δ 141.6.

Preparation on protected inositol diol 9

Myo-inositol (2.70 g, 15.0 mmol), triethylorthoformate (2.40 g, 22.5 mmol), p-toluenesulfonic acid monohydrate (0.25 g, 1.31 mmol) and dry DMF (20 mL) were mixed and heated at 100 ºC with stirring for 3 h. The clear solution was cooled to room temperature. Then triethylamine (1 mL) was added to the mixture and low boiling components were removed *in vacuo*. Dry toluene was added and the solvent again removed *in vacuo* (2 × 5 mL). This operation was useful in removing traces of DMF. The residue was cooled to 0 ºC and then pyridine (10 mL) followed by benzoyl chloride (2.20 g, 15.0 mmol) were added drop-wise over a period of 30 min. The reaction mixture was brought to room temperature and stirred for 8 h. After removal of most of the pyridine, ethyl acetate was added; the organic layer was washed with dil. HCl (to remove traces of pyridine) and solvent removed completely. Upon addition of dichloromethane, the monobenzoylated compound **9** [Mp: 206-208 ^{o}C (lit. 209 ^{o}C [94b])] precipitated out, leaving behind the dibenzoylated derivative in solution.

(h) {[*myo*-C$_6$H$_6$-3-[OC(O)Ph]-2,4,6-(O$_3$CH)-[1,5-O$_2$PCl]} (10)

An excess of PCl_3 (20 mL) was added to **9** (1.20 g, 4.08 mmol) and the mixture was heated under reflux for 1 d. Excess PCl_3 was removed by distillation to obtain a white solid. The residue was crystallized from toluene to give **10**.

Mp: 130-132 ^{o}C.

IR (KBr): 1726, 1603, 1454, 1408, 1277, 1165 cm^{-1}.

^{1}H NMR: δ 4.61 (m, 2 H, inosityl-*H*), 5.23 (m, 2 H, inosityl-*H*), 5.46 (m, 1 H, inosityl-*H*), 5.62 (m, 1 H, inosityl-*H*), 5.75 (s, 1 H, O$_3$C*H*), 7.45-8.18 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 60.9, 61.1, 63.3, 68.9, 69.5, 102.1 (d, ^{5}J (P-C) = 13.9 Hz, O_3CH), 128.2, 128.6, 129.0, 129.2, 130.0, 133.7, 165.8 (Ph-*C*(O)O-) (Fig. 1).

^{31}P NMR: δ 140.0.

X-ray structural analysis was performed on this compound.

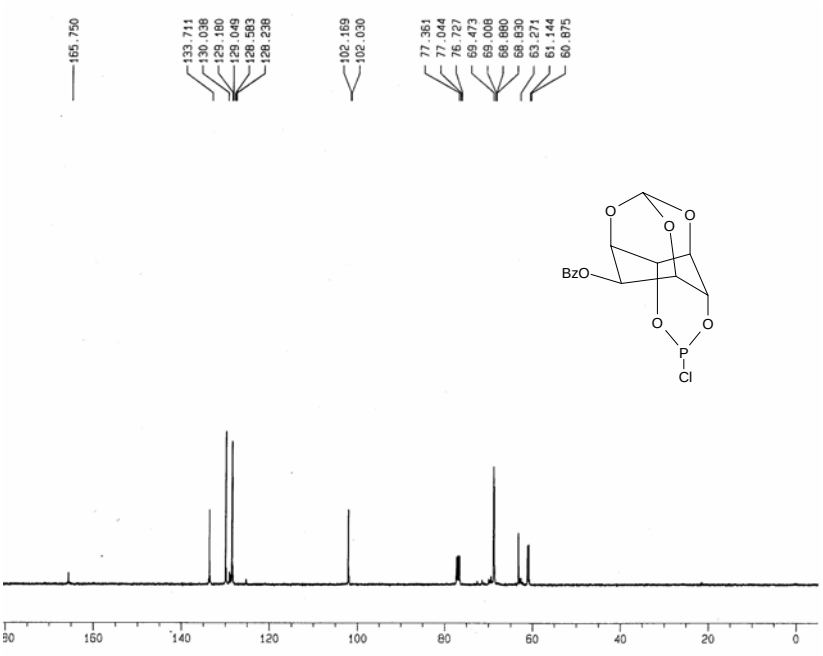


Fig. 1. The ^{13}C NMR spectrum of compound **10**.

(i) {[*myo*-C_6H_6-3-[OC(O)Ph]-2,4,6-(O_3CH)-[1,5-$O_2PNHCH(CH_3)_2$]} (11)

To a stirred solution of **10** (0.60 g, 1.60 mmol) in toluene (20 mL) at room temperature (25 ^{o}C) was added *iso*-propylamine (0.20 g, 3.30 mmol) drop-wise over a period of 10 min. After stirring for 12 h, filtration followed by the removal of solvent afforded **11** as a white solid.

Mp: 114-116 ^{o}C.

IR (KBr): 3414, 1620, 1408, 1167 cm^{-1}.

^{1}H NMR: δ 1.22 (d, 6 H, ^{3}J (H-H) ~ 6.2 Hz, NHCH(CH_3)$_2$), 2.87 (m, 1 H, NHC*H*(CH_3)$_2$), 3.79 (br s, 1 H, N*H*), 4.50 (m, 2 H, inosityl-*H*), 5.07 (m, 2 H, inosityl-*H*), 5.18 (m, 1 H, inosityl-*H*), 5.56 (m, 1 H, inosityl-*H*), 5.93 (m, 1 H, O_3CH), 7.48-8.20 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 26.7 (d, ^{3}J(P-C) = 4.0 Hz, PNCH(*C*H_3)$_2$), 42.0 (d, ^{2}J(P-C) = 12.0 Hz, PNH*C*(CH_3)$_2$), 64.1, 64.4, 64.8, 68.9, 70.0, 102.6 (O_3CH), 128.2, 128.5, 129.0, 129.6, 130.0, 133.4, 166.0 (Ph-*C*(O)O-).

^{31}P NMR: δ 140.6.

3.2 Reactions of P^{III} compounds with DIAD/ DEAD and *o*-chloranil: Reactivity of the products

3.21 Formation of pentacoordinate compounds

Synthesis of [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$PNH*i*Pr{N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (14)

To a solution of **3** (0.69 g, 1.53 mmol) in dry toluene (15 mL), DIAD (0.31 g, 1.53 mmol) was added drop-wise over a period of 3 min through syringe and the mixture stirred for 24 h at room temperature. The solvent was removed and the residue crystallized from heptane (*ca* 2 mL) containing traces of dichloromethane to afford **14**. The same compound was also obtained by reacting **51** with *iso*-propylamine.

Yield: 0.77 g (78%).

Mp: 118-120 ^{o}C.

IR (KBr): 3383, 1728, 1676 cm^{-1}.

^{1}H NMR: δ 1.00-1.48 (many lines, 36 H, CH(C*H*$_3$)$_2$ + Ar-C(C*H*$_3$)$_3$ + NCH(C*H*$_3$)$_2$), 2.22 and 2.32 (2 s, 6 H, ArC*H*$_3$), 2.95 and 3.30 (m, together 1 H, NHC*H*(CH$_3$)$_2$), 3.50 and 3.68 (br, together 1 H, -N*H),* 4.45 and 4.90 as well as 5.05 and 5.16 (two sets of m, total 2 H, -OC*H*(CH$_3$)$_2$), 7.00-7.40 (many lines, 4 H, Ar-*H*). Two major groups of signal are thus seen. The variable temperature ^{1}H NMR spectra were recorded but were too complicated for a detailed analysis.

^{13}C NMR: δ 20.7, 21.8, 22.2, 26.4, 29.7, 30.3, 30.5, 34.6, 34.9, 44.5, 45.9, 68.3, 72.4, 73.0, 128.5, 129.0, 130.0, 131.5, 133.4, 133.6, 135.7. The *C*=O signals were too broad.

^{31}P NMR: δ –55.6, –65.1 (1:2); a minor signal (*ca* 5% of the other two put together) at –64.7 was also observed. The variable temperature ^{31}P NMR spectra were recorded; details are discussed in Chapter 2.

Anal. Calcd for $C_{33}H_{50}N_3O_6PS$: C, 61.18; H, 6.48; N, 7.78. Found: C, 59.93; H, 7.75; N, 6.52.

X-ray structural analysis was performed on this compound.

Synthesis of [CH_2(6-*t*-Bu-4-Me-C_6H_2O)$_2$P(NC_7H_{14})(1,2-OC_6Cl_4O)] (17)

Compound **17** was prepared by treating the corresponding P(III) precursor **16** (*cf* Chapter 2) [Mp: 222-224 °C; δ(P): 142.1] with an equimolar quantity of *o*-chloranil. Data for **17** are as follows.

Mp: 276-278 °C (dec).

^{1}H NMR: δ 1.14 (d, ^3J(H-H) = 7.6 Hz, 6 H, CHCH_3), 1.31 (s, 18 H, Ar-C(CH_3)$_3$), 1.20-1.80 (br, 6 H, (CH_2)$_3$), 2.27 (s, 6 H, ArCH_3), 3.41 (d, ^2J(H-H) = 13.9 Hz, 1 H, (Ar)$_2$CH_AH$_X$), 4.08 (br m, 2 H, C*H*-N), 4.66 (d, ^2J(H-H) = 13.9 Hz, 1 H, (Ar)$_2$CH$_A$$H_X$), 6.88 and 6.99 (2 s, 4 H, Ar-*H*).

^{31}P NMR: δ -40.0.

Anal. Calcd for $C_{36}H_{44}Cl_4NO_4P$: C, 59.43; H, 6.10; N, 1.94. Found: C, 59.65; H, 6.14; N, 1.98.

X-ray structural analysis was performed on this compound.

Synthesis of [S(6-*t*-Bu-4-Me-C_6H_2O)$_2$P($OCH_2CH_2NMe_2$){N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}] (19)

To a solution of **8** (1.20 g, 2.52 mmol) in dry toluene (15 mL) DIAD (0.51 g, 2.52 mmol) was added drop-wise over a period of 3 min through syringe and the mixture was stirred for 24 h at room temperature. The solvent was removed and the residue was crystallized from toluene (*ca* 2 mL).

Yield: 0.77 g (78%).

Mp: 122-124 ^{o}C.

IR (KBr): 2969, 1715, 1658, 1282 cm^{-1}.

^{1}H NMR: δ 1.06, 1.09, 1.13 and 1.23 (d each, 12 H, ^3J(H-H) ~ 8.0 Hz, HC(CH_3)$_2$), 1.31 and 1.46 (2 s, 18 H, Ar-C(CH_3)$_3$), 2.19 and 2.30 (2 s, 6 H, Ar-CH_3), 2.76 (m, 2 H, OCH$_2$CH_2N(CH$_3$)$_2$), 2.38 (s, 6 H, N(CH_3)$_2$) 4.24 and 4.37 (m each, 2 H, OC$H_A$$H_BCH_2$N(CH$_3$)$_2$), 4.64 and 4.91 (m each, 2 H, OC*H*(CH$_3$)$_2$), 7.09-7.32 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 20.7, 20.8, 20.9, 21.5, 21.6, 21.8 (6 s, Ar*C*H$_3$ + OCH(*C*H$_3$)$_2$), 29.4 and 29.5 (2 s, Ar-C(*C*H$_3$)$_3$), 34.7 and 34.9 (2 s, *C*(CH$_3$)$_3$), 46.0 (s, N(*C*H$_3$)$_2$), 59.1 (d, ^2J(P-C) = 12.3 Hz, OCH$_2$*C*H$_2$NMe$_2$), 65.6 (d, ^2J(P-C) = 8.9 Hz, O*C*H$_2$CH$_2$NMe$_2$), 69.6 and 72.4 (2 s, O*C*H(CH$_3$)$_2$),

119.0, 119.1, 124.2, 124.3, 125.3, 128.2, 129.0, 129.8, 130.3, 131.3, 131.5, 137.7, 137.8, 138.1, 138.2, 151.9, 152.0, 152.5, 152.6, 154.2, 154.3, 154.5, 154.7.

^{31}P NMR: δ –61.2.

Anal. Calcd for $C_{34}H_{52}N_3O_7PS$: C, 60.24; H, 7.73; N, 6.19. Found: C, 60.30; H, 7.73; N, 6.16.

Synthesis of {[*myo*-C_6H_6-3-[OC(O)Ph]-2,4,6-(O_3CH)-[1,5-O_2PNHCH(CH_3)$_2$]}{OC_6Cl_4O)}.CH_2Cl_2 (21)

To a solution of **11** (0.40 g, 1.11 mmol) in toluene (10 mL), *o*-chloranil (0.27 g, 1.11 mmol) was added and the solution heated at 50-60 ºC for 10 min. Later the reaction mixture was allowed to come to room temperature and stirred overnight. The solvent was removed and the residue crystallized from dichloromethane and traces of hexane.

Mp: 150-152 ^{o}C.

IR (KBr): 3383, 1726, 1232, 1107 cm^{-1}.

^{1}H NMR: δ 1.23 (br s, 6 H, NHCH(C*H*$_3$)$_2$), 3.21 (m, 1 H, NHC*H*(CH_3)$_2$), 3.84 (br s, 1 H, N*H*), 4.63 (br s, 2 H, inosityl-*H*), 4.82 (br s, 1 H, inosityl-*H*), 5.03 (br s, 2 H, inosityl-*H*), 5.30 (s, C*H*$_2$Cl$_2$), 5.58 (br s, 1 H, inosityl-*H*), 5.71 (br s, 1 H, O_3C*H*), 7.50-8.19 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 20.8 and 21.3 (2 s, NCH(*C*H$_3$)$_2$), 47.3 (s, N*C*H(CH_3)$_2$), 61.5, 61.7, 63.4, 70.0, 101.9 (s, O_3*C*H), 125.2, 127.4, 127.8, 127.9, 128.1, 128.4, 128.9, 129.2, 129.9, 133.5, 165.7 (s, Ph-*C*(O)O-).

^{31}P NMR: δ –53.1.

X-ray structural analysis was performed on this compound.

3.22 Formation of tetracoordinate compounds

Synthesis of [S{6-*t*-Bu-4-Me-C_6H_2O}$_2$]P[{NC(CH_3)$_3$}{N(CO_2Et)NH(CO_2Et)}] (38)

To a stirred solution of **2** (1.23 g, 2.68 mmol) in toluene (15 mL) was added diethyl azodicarboxylate (DEAD) (0.46 g, 2.68 mmol) drop-wise over a period of 10 min. After stirring for 1 d, the solution was concentrated to (*ca* 4 mL) and heptane (*ca* 1 mL) added to obtain a crystalline solid.

Yield: 1.35 g (80%).

Mp: 170-171 ^{o}C.

IR (KBr): 3261, 3159, 2964, 2361, 1718, 1421, 1286, 1211, 1097 cm^{-1}.

^{1}H NMR: δ.1.11 (d, ^{4}J(P-H) ~ 2.0 Hz, 9 H, P-N-C(CH_3)$_3$), 1.25 and 1.46 (2 s, 18 H, ArC(CH_3)$_3$), 1.32 (t, ^{3}J(H-H) = 7.0 Hz, 6 H, OCH$_2$CH_3), 2.25 and 2.32 (2 s, 6 H, ArCH_3), 4.30 (q, ^{3}J(H-H) = 7.0 Hz, 4 H, OCH_2CH$_3$), 6.45 (br, 1 H, N*H*-CO$_2$Et), 7.08-7.31 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 14.7 (s, OCH$_2$*C*H$_3$), 20.5 and 20.8 (2 s, Ar*C*H$_3$), 30.1 and 31.3 (2 s, Ar-C(*C*H$_3$)$_3$), 33.5 (d, ^{3}J(P-C) = 10.2 Hz, PNC(*C*H$_3$)$_3$), 34.4 and 35.9 (2 s, Ar-*C*(CH$_3$)$_3$), 51.2 (br s, PN*C*(CH$_3$)$_3$), 61.9 and 62.8 (2 s, O*C*H$_2$CH$_3$), 128.0, 130.3, 133.1, 133.7, 135.8, 155.9.

^{31}P NMR: δ -56.3 (br).

Anal. Calcd for $C_{32}H_{48}N_3O_6N_3PS$: C, 60.64; H, 7.63; N, 6.63. Found: C, 60.58; H, 7.66; N, 6.67.

X-ray structural analysis was performed on this compound.

Synthesis of [S(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$P{N(CO$_2$-*i*-Pr)N(CO$_2$-*i*-Pr)-C(O)-N-}] (41)

DIAD (0.47 g, 2.33 mmol) was added in one lot to a solution of **6** (1.0 g, 2.33 mmol) in dry toluene (20 mL) and the mixture stirred for 24 h at room temperature. The solution was concentrated (~ 2 mL) and heptane (~ 2 mL) added to get the crystals of the title compound.

Yield: 1.18 g (80%).

Mp: 58-60 ^{o}C.

IR (KBr): 2268, 1711, 1661 cm^{-1}.

^{1}H NMR: δ 1.33 (d, ^{3}J(H-H) = 6.2 Hz, 6 H, CH(CH_3)$_2$), 1.35 (s, 9 H, ArC(CH_3)$_3$), 1.40 (d, ^{3}J(H-H) = 6.1 Hz, 6 H, CH(CH_3)$_2$), 1.43 (s, 9 H, ArC(CH_3)$_3$), 2.32 (s, 6 H, ArCH_3), 4.80-5.12 (m, 2 H, C*H*Me$_2$), 7.24 and 7.40 (2 s, 4 H, Ar-*H*).

^{13}C NMR: δ 20.7 (s, Ar*C*H$_3$), 21.6 (s, CH(*C*H$_3$)$_2$), 30.4 (s, C(*C*H$_3$)$_3$), 35.1 (s, *C*Me$_3$), 72.4, 72.6 (2 s, O*C*HMe$_2$), 122.0, 125.3, 128.6 (d, ^{2}J(P-C) = 40.0 Hz, N*C*O), 131.4, 133.3, 135.9, 140.2, 149.6, 152.5, 149.0, 154.0 (^{2}J(P-C) = 10.0 Hz, *C*O$_2$R).

^{31}P NMR: δ 23.6.

Anal. Calcd for $C_{31}H_{42}N_3O_7PS$: C, 58.93; H, 6.65; N, 6.65. Found: C, 58.92; H, 6.75; N, 6.62.

3.23 Formation of Hexacoordinate compounds

Synthesis of [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$P{N(CO_2*i*-Pr)NC(O-*i*-Pr)O}(Ph)] (45)

To a stirred solution of **2** (0.94 g, 2.0 mmol) in toluene (20 mL) was added DIAD (0.40 g, 2.0 mmol) drop-wise over a period of 0.5 h. Upon stirring for 2 d and removal of all the solvent, compound **45** was obtained as a light yellow solid. This was crystallized from acetonitrile-dichloromethane (2:1) mixture.

Yield: 1.07 g (80%).

Mp: 199-200 ^oC.

IR (KBr): 1714, 1655, 1103 cm^{-1}.

^1H NMR: δ 0.95, 1.13, 1.15 and 1.26 (d each, 12 H, ^3J(H-H) ~ 6.3 Hz, HC(CH_3)$_2$), 1.20 and 1.40 (2 s, 18 H, Ar-C(CH_3)$_3$), 2.22 and 2.28 (2 s, 6 H, ArCH_3), 4.62-4.80 (m, 2 H, CH(CH_3)$_2$), 7.10-7.45 and 8.10-8.17 (2 m, 9 H, Ar-*H*). The CH_3CN peak in the spectrum of crystals appeared at δ 1.91.

^{13}C NMR: δ 20.6, 20.7, 21.5, 21.7 and 21.9 (5 s, ArCH_3 + OCH(CH_3)$_2$), 29.5 and 30.6 (2 s, C(CH_3)$_3$), 34.7 and 35.2 (2 s, C(CH_3)$_3$), 69.1 and 72.6 (2 s, OCH(CH_3)$_2$), 117.6, 117.9, 122.8, 122.9, 127.1, 127.4, 129.4, 129.8, 129.9, 130.6, 130.8, 131.0, 131.3, 131.7, 132.0, 136.6, 137.7, 137.9, 138.6, 138.8, 141.3, 151.1, 151.4, 151.7, 152.9, 153.1, 154.4, 154.6.

^{31}P NMR: δ –64.3.

Anal. Calcd for $C_{36}H_{47}N_2O_6PS$: C, 64.84; H, 7.11, N, 4.20. Found: C, 64.21; H, 7.10; N, 4.83.

X-ray structural analysis was performed on this compound.

Synthesis of {S{6-*t*-Bu-4-Me-C_6H_2O}$_2$}P OPh {N(CO_2*i*-Pr)NC(O*i*-Pr)O} (46)

To a solution of **7** (0.84 g, 1.75 mmol) in toluene (15 mL) was added diisopropyl azodicarboxylate (DIAD) (0.35 g, 1.75 mmol) drop-wise over a period of 10 min. After stirring for 1 d, the solution was concentrated (*ca* 3 mL) and heptane (*ca* 0.5 mL) added to obtain a crystalline solid.

Yield: 0.96 (80%).

Mp: 178-180 ^{o}C.

IR (KBr): 2961, 1721, 1672, 1593, 1437, 1408, 1277, 1209, 1107, 1049 cm^{-1}.

^{1}H NMR: δ 1.01, 1.05, 1.07 and 1.43 (d each, 12 H, ^{3}J (H-H) ~ 6.2 Hz, HC(CH_3)$_2$), 1.42 and 1.47, (2 s, 18 H, Ar-C(CH_3)$_3$), 2.21 and 2.31 (2 s, 6 H, Ar-CH_3), 4.54 and 4.85 (2 m, 2 H, CH(CH$_3$)$_2$), 7.07-7.40 (m, 9 H, Ar-H).

^{13}C NMR: δ 20.8, 21.5, 21.7,21.9 (4 s, ArCH$_3$ + OCH(CH$_3$)$_2$), 29.6 and 29.9 (2 s, C(CH$_3$)$_3$), 34.8 and 34.9 (2 s, C(CH$_3$)$_3$), 69.5 and 69.9 (2 s, OCH(CH$_3$)$_2$), 118.4, 118.6, 122.2, 122.3, 124.1, 124.3, 129.0, 129.6, 130.0, 130.7, 131.1, 131.4, 131.6, 137.8, 138.0, 138.7, 138.9, 151.8, 152.1, 152.4, 152.6, 153.6, 153.8.

^{31}P NMR: δ –67.0.

Anal. Calcd for $C_{36}H_{47}N_2O_7PS$: C, 63.35; H, 6.93; N, 4.10. Found: C, 63.66; H, 7.13; N, 4.29.

X-ray structural analysis was performed on this compound.

Synthesis of [S(6-*t*-Bu-4-Me-C$_6$H$_2$O)$_2$PCl{N(CO$_2$-*i*-Pr)NC(O-*i*-Pr)-O-}] (51)

To a stirred solution of **1** (0.92 g, 2.2 mmol) in toluene (20 mL) at –78 ^{o}C was added DIAD (0.45 g, 2.2 mmol) drop-wise through a syringe over a period of 5 min. The reaction mixture was brought to room temperature and stirred for 12 h; then the solvent was evaporated and the residue crystallized from heptane-dichloromethane (2 + 0.5 mL) mixture.

Yield: 0.95 g (70%).

Mp: 156-158 ^{o}C.

IR (KBr): 1747, 1651, 1593, 1373, 1225 cm^{-1}.

^{1}H NMR: δ 0.92-1.60 (many lines, 30 H, CH(CH_3)$_2$ + Ar-C(CH_3)$_3$), 2.35 (br s, 6 H, ArCH_3), 4.90-5.20 (m, 2 H, CHMe$_2$), 7.20-7.44 (m, 4 H, Ar-H).

^{13}C NMR: δ 20.7, 20.9, 21.0, 21.8, 21.9, 29.2, 29.5, 30.4, 31.2, 34.5, 35.8, 69.3, 69.7, 70.4, 72.2, 73.1, 73.9, 121.6, 125.5, 127.7, 128.1, 129.8, 130.3, 130.8, 131.2, 131.6, 132.1, 133.2, 134.5, 134.7, 135.0, 135.3, 137.3, 137.5, 141.0, 147.3, 150.1, 150.1, 153.1,160.5, 173.1.

^{31}P NMR: δ –71.0, -90.3 (br). The compound hydrolyzes rapidly and a peak at δ -7.0 appears within 0.5 h.

Anal. Calcd for $C_{30}H_{42}ClN_2O_6PS$: C, 57.64; H, 6.77; N, 4.48, S, 5.13. Found C, 57.78; H, 6.81; N, 4.62; S, 5.04.

X-ray structural analysis was performed on this compound.

Synthesis of [S(6-*t*-Bu-4-Me-$C_6H_2O)_2$P{N(CO_2-*i*-Pr)NC(O-*i*-Pr)O-}(NCH=NCH=CH-)] (52)

To a stirred solution of **51** (1.38 g, 2.19 mmol) in dichloromethane (20 mL) was added imidazole (0.15 g, 2.19 mmol) and triethylamine (0.22 g, 2.19 mmol) in dichloromethane drop-wise over a period of 0.5 h. at 0 ^{o}C. The mixture was stirred at room temperature for 12 h, dichloromethane removed *in vacuo*, dry toluene (15 mL) added and the mixture filtered. The residue was crystallized from dichloromethane-hexane (4:1) mixture (2 mL).

Yield: 0.54 g (85%).

Mp: 192-194 ^{o}C.

IR (KBr): 1717, 1651, 1599 cm^{-1}.

^{1}H NMR: δ 1.03, 1.10, 1.17 and 1.25 (d each, ^{3}J(H-H) = 6.4 Hz, 12 H, CH(CH_3)$_2$), 1.34 and 1.41 (2 s, 18 H, Ar-C(CH_3)$_3$), 2.23 and 2.31 (2 s, 6 H, ArCH_3), 4.83 (m, 2 H, OCH(CH$_3$)$_2$), 7.20-7.57 (m, 5 H, Ar-*H* + imidazolyl-*H*), 7.46 and 8.23 (s, 2 H, imidazolyl-*H*).

^{13}C NMR: δ 20.9, 21.5 and 21.6 (3 s, Ar*C*H$_3$ + CH(*C*H$_3$)$_2$), 29.5 and 29.8 (2 s, C(*C*H$_3$)$_3$), 34.8 and 35.0 (2 s, *C*(CH$_3$)$_3$), 69.8 and 73.1 (2 s, O*C*HMe$_2$), 118.1, 118.2, 120.3, 120.4, 121.4, 121.5, 128.0, 128.1, 128.2, 128.3, 131.7, 131.8, 131.9, 132.2, 137.5, 137.6, 138.2, 138.3, 140.2, 140.3, 149.8, 150.0, 151.1, 151.2, 154.4.

^{31}P NMR: δ –89.8.

Anal. Calcd for $C_{33}H_{45}N_4O_6PS$: calcd C, 60.34; H, 6.90; N, 8.55. Found C, 60.50; H, 7.10; N, 8.61.

X-ray structural analysis was performed on this compound.

Synthesis of [S{6-*t*-Bu-4-Me-C_6H_2O}$_2$]$_2$$P^+Cl^-$.($C_3H_4N_2$) (56)

When a reaction pyrazole was performed with using the *in situ* generated **51**, the compound **56** was obtained as a crystalline material.

^{1}H NMR: δ 1.02 and 1.53 (2 s, 36 H, Ar-C(C*H*$_3$)$_3$), 2.36 (s, 12 H, ArC*H*$_3$), 4.83 (m, 2 H, OC*H*(CH$_3$)$_2$), 6.38 (br s, 1 H, pyrazolyl-*H*) 7.23-7.64 (m, 5 H, Ar-*H*), 8.03 and 8.12 (2 br s, 2 H, pyrazolyl-*H*).

^{13}C NMR: δ 21.6 (s, Ar*C*H$_3$), 29.0 and 29.4 (2 s, C(*C*H$_3$)$_3$), 34.9 and 35.3 (2 s, *C*(CH$_3$)$_3$), 129.0, 129.1, 129.5, 133.1, 133.7, 134.4, 135.5, 137.8.

^{31}P NMR: δ –58.4.

X-ray structural analysis was performed on this compound.

3.3 Synthesis of phosphate salts

Synthesis of {S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}P(O)OH (65)

To a stirred solution of **1** (1.33 g, 3.14 mmol) in dichloromethane (20 mL) was added iodine (0.88 g, 3.45 mmol) in small portions and the mixture stirred at room temperature for 72 h. The solution was washed with 10% aq. $Na_2S_2O_3$ until the organic layer was colorless. After removing dichloromethane, the resulting solid was crystallized from toluene-heptane (or $CHCl_3$-acetonitrile) to afford **65**.

Yield: 0.66 g (50%).

Mp: >250 ^{o}C.

^{1}H NMR: δ 1.38 (s, 18 H, Ar-C(C*H*$_3$)$_3$), 2.27 (s, 6 H, Ar-C*H*$_3$), 7.14 and 7.32 (2 s, 4 H, Ar-*H*).

^{31}P NMR: δ –15.5 [lit. –11.57[115]].

Synthesis of {S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$] (66)

To a partially soluble solution of **65** (0.20 g, 0.48 mmol) in chloroform, imidazole (0.03, 0.48mmol) was added. Immediately the solution became clear; after a few minutes, compound **66** precipitated out.

Mp: >270 ^{o}C.

IR (nujol): 3158 (sharp), 1460, 1253 cm^{-1}.

^{1}H NMR (DMSO-d$_6$): δ 1.35 (s, 18 H, Ar-C(C*H*$_3$)$_3$), 2.19 (s, 6 H, Ar-C*H*$_3$), 7.08, 7.29 and 7.46 (s each, 6 H, Ar-*H* + imidazolyl-*H*), 8.71 (s, 1 H, imidazolyl-*H*).

The signal for imidazolyl N*H* proton was very broad. The solubility was too low for recording a satisfactory ^{13}C NMR.

^{31}P NMR (DMSO-d_6): δ −10.6.

X-ray structural analysis was performed on this compound.

Synthesis of [{S(6-*t*-Bu-4-Me-$C_6H_2O)_2$}P(O)(O)][$C_3N_2H_5$][$(CH_3)_2$CHO(O)N(H)-N(H)(C(O)O(CH$(CH_3)_2$)] (67)

To a stirred solution **1** (0.92 g, 2.2 mmol) in toluene, diisopropyl azodicarboxylate (0.45 g, 2.2 mmol) was added drop-wise at -78 ºC and the contents stirred overnight. Imidazole (0.15 g, 2.2 mmol) and triethylamine (0.22 g, 2.2mmol) in toluene (5 mL) were then added. The mixture was stirred further for 12 h, filtered and the solvent evaporated *in vacuo*. The residue upon crystallization from dichloromethane-hexane mixture in air yielded compound **67** (0.30 g, 21.4 %; a small quantity of **66** also crystallized, which could be separated by hand-picking).

Mp: 190-192 ^{o}C (charring).

IR (nujol): 3223 (br), 3152, 1732, 1711, 1464, 1256.

^1H NMR (DMSO-d_6): δ 1.15 (d, ^3J(H-H) = 5.2 Hz, 12 H, (CH(CH_3)$_2$)), 1.34 (s, 18 H, Ar-C(CH_3)$_3$), 2.18 (s, 6 H, Ar-CH_3), 2.48 (s, 2 H, N-*H*), 4.74 (m, 2 H, C*H*(CH_3)$_2$), 7.07 and 7.45 (s each, 5 H, Ar-*H* + imidazolyl-*H*), 8.65 and 8.84 (s each, 2H, imidazolyl-*H*). The signal for imidazolyl N*H* proton was very broad.

The solubility was too low for recording a satisfactory ^{13}C NMR.

^{31}P NMR (DMSO-d_6): δ −10.5.

X-ray structural analysis was performed on this compound.

3.4 X-ray crystallography

A suitable crystal of **10, 14**, **17**.3/2C_4H_8O**, 21**.CH_2Cl_2**, 38, 45.**CH_3CN**, 46, 51, 52, 56, 66** or **67** was inserted into a Lindemann capillary and X-ray data collected at 293 K on an Enraf-Nonius MACH3 or on a Bruker AXS-SMART diffractometer using Mo-K_α radiation (λ = 0.71073 Å). Structures were solved and refined using standard methods.[119] Crystal data are summarized in Tables 14-16.

Table 14. Crystal data for compounds **10, 14, 17** and **21**

Compound	**10**	**14**	**17**.3/2C_4H_8O	**21**.CH_2Cl_2
Emp. formula	$C_{14}H_{12}ClO_7P$	$C_{33}H_{50}N_3O_6PS$	$C_{84}H_{112}Cl_8N_2O_{11}P_2$	$C_{24}H_{22}Cl_6NO_9P$
Formula weight	358.66	647.79	1671.30	712.10
Crystal system	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space group	*P2₁*	*P2₁/n*	*C2/c*	$P\bar{1}$
a /Å	7.4207(8)	11.9655(9)	21.978(5)	9.8167(8)
b /Å	10.9150(12)	22.0001(17)	13.464(3)	10.2887(9)
c /Å	9.2807(10)	13.9870(11)	31.081(7)	15.3489(13)
α/deg	90	90	90	89.1900(10)
β/deg	100.854(2)	94.2570(10)	96.074(4)	83.7880(10)
γ/deg	90	90	90	72.9990(10)
V /Å^3	738.26(14)	3671.8(5)	9146(4)	1473.6(2)
Z	2	4	4	2
D_{calc} /g cm^{-3}]	1.613	1.172	1.214	1.605
μ /mm^{-1}	0.402	0.175	0.336	0.689
F(000)	368	1392	3536	724
Data/ restraints/ parameters	3393/ 1/ 208	6468 / 0/ 411	8026/ 7/ 493	6868/ 0/ 376
S	1.038	1.014	1.067	1.054
R1 [I>2σ(I)]	0.0325	0.0404	0.0598	0.0432
wR2 [all data]	0.0817	0.1163	0.1944	0.1230
Max./min. residual electron dens. [eÅ^{-3}]	0.284/ -0.222	0.233/ -0.302	0.708/ -0.412	0.408 / -0.300

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

Table 15. Crystal data for compounds **38, 45, 46** and **51**

Compound	**38**	**45**.CH_3CN	**46**	**51**
Emp. formula	$C_{32}H_{48}N_3O_6PS$	$C_{38}H_{50}N_3O_6PS$	$C_{36}H_{47}N_2O_7PS$	$C_{30}H_{42}ClN_2O_6PS$
Formula weight	633.76	707.84	682.79	625.14
Crystal system	Triclinic	Monoclinic	Monoclinic	Triclinic
Space group	$P\bar{1}$	$P2_1/n$	$P2_1/c$	$P\bar{1}$
a /Å	10.681(9)	9.274(2)	20.7843(12)	10.4788(7)
b /Å	10.761(3)	17.798(3)	10.6218(6)	10.8660(7)
c /Å	17.409(4)	24.057(7)	16.7361(10)	16.3413(11)
α/deg	74.34(7)	90	90	92.567(1)
β/deg	72.41(5)	96.367(15)	99.0500(10)	103.1120(10)
γ/deg	71.50(11)	90	90	111.9970(10)
V /Å^3	1775.1(16)	3946.2(16)	3648.8(4)	1662.80(19)
Z	2	2	4	2
D_{calc} /g cm^{-3}]	1.186	1.191	1.243	1.249
μ /mm^{-1}	0.180	0.169	0.181	0.268
F(000)	680	1512	1456	664
Data/ restraints/ parameters	6237/ 0/ 405	6872/ 0/ 455	6433/ 0/ 436	5836/ 0/ 382
S	1.009	1.046	1.008	0.962
R1 [I>2σ(I)]	0.0629	0.0575	0.0534	0.0418
wR2 [all data]	0.2057	0.1938	0.1632	0.1125
Max./min. residual electron dens. [eÅ^{-3}]	0.481/ -0.343	0.626/ -0.356	0.486/ -0.533	0.321 / -0.198

Table 16. Crystal data for compounds **52, 56, 66** and **67**

Compound	**52**	**56**	**66**	**67**
Emp. formula	$C_{33}H_{45}N_4O_6PS$	$C_{25}H_{32}Cl_{0.50}N_2O_2P_{0.50}S$	$C_{25}H_{33}N_2O_4PS$	$C_{29}H_{41}N_3O_6PS$
Formula weight	656.76	457.80	488.56	590.68
Crystal system	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$	$C2/c$	Cc	$C2/c$
a /Å	19.6085(11)	22.8081(13)	7.6466(6)	29.333(2)
b /Å	19.8928(11)	15.0379(9)	17.0714(12)	9.9415(7)
c /Å	19.3009(11)	16.0253(10)	19.7596(14)	23.3483(17)
α/deg	90	90	90	90
β/deg	111.8530(10)	113.1990(10)	98.0600(10)	112.5420(10)
γ/deg	90	90	90	90
V /Å^3	6987.7(7)	5052.0(5)	2553.9(3)	6288.5(8)
Z	8	8	4	8
D_{calc} /g cm^{-3}]	1.249	1.204	1.271	1.248
μ /mm^{-1}	0.186	0.236	0.222	0.198
F(000)	2800	1952	1040	2520
Data/ restraints/ parameters	12295/ 0/ 835	4452 / 0/ 289	5940 / 2 / 306	7424 / 0/ 375
S	1.031	1.055	0.929	0.947
R1 [I>2σ(I)]	0.0484	0.0501	0.0393	0.0484
wR2 [all data]	0.1445	0.1480	0.0865	0.1348
Max./min. residual electron dens. [eÅ^{-3}]	0.662/ -0.369	0.484 / -0.265	0.294 / -0.223	0.392/ -0.243

References

1) D. E. C. Corbridge, *Phosphorus 2000: Chemistry, Biochemistry and Technology*, 4th ed.; Elsevier: Amsterdam, 2000; Chapter 1, pp 16-31.

2) a) D. J. H. Smith, *in Comprehensive Organic Chemistry*; D. H. R. Barton, V. D. Ollis, Eds; Vol. 2, I. O. Sutherland, Vol. Ed.; Pergamon: Exeter, 1979, pp. 1189; b) J. Emsley and D. Hall, *The Chemistry of Phosphorus*, Harper and Row, London, 1976, 379; c) F. H. Osman and F. A. El-Samahy, *Chem. Rev.* 2002, **102**, 629.

3) a) R. Francke and G. V. Röschenthaler, *Z. Anorg. Allg. Chem*. 1989, **572**, 135; b) T. Facklam, O. Wagner, H. Heydt and M. Regitz, *Angew. Chem. Int. Ed.* 1990, **29**, 314; c) G. Bertrand, *Angew. Chem. Int. Ed.* 1998, **37**, 270; d) R. Francke, J. Heine and G. V. Röschenthaler, *Phosphorus, Sulfur, Silicon* 1990, **49/50**, 377.

4) a) M. Regitz, *Chem. Rev*. 1990, **90**, 191; b) G. Bertrand and R. Reed, *Coord. Chem. Rev*. 1994, **137**, 323; c) C. Buron, H. Gornitzka, V. Romanenko and G. Bertrand, *Science* 2000, **288**, 834; d) E. Niecke, A. Fuchs, F. Baumeister, M. Nieger and W. W. Schoeller, *Angew. Chem. Int. Ed.* 2000, **34**, 951.

5) R. R. Holmes, *Pentacoordinated Phosphorus - Structure and Spectroscopy* (Vol. I) and *Reaction Mechanisms* (Vol. II), ACS Monographs 175 and 176 respectively, American Chemical Society, Washington, DC; 1980.

6) a) W. S. Sheldrick, *Top. Curr. Chem.* 1978, **73**, 1; b) R. R. Holmes, R. O. Day, J. M. Deiters, K. C. Kumara Swamy, J. M. Holmes, J. Hans, S. D. Burton and T. K. Prakasha, *in Phosphorus Chemistry-Development in American Science*, ACS Symposium Series 486, E. N. Walsh, E. J. Griffith, R. W. Parry and L. D. Quin, Eds, 1992, Chapter 2, and references cited therein; c) K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day and R. R. Holmes, *Phosphorus, Sulfur and Silicon* 1990, **53**, 437; d) V. G. Ratner, E. Lork, K. I. Pashkevich and G. V. Röschenthaler, *J. Fluorine Chem.* 2000, **102**, 73; e) F. H. Osman and F. A. El-Samahy, *Chem. Rev.* 2002, **102**, 629;f) Y. V. Rassukana, K. O. Davydova, P. P. Onys'ko and A. D. Sinitsa, *J. Fluorine Chem.* 2002, **117**, 107; g) F. H. Osman and F. A. El-Samahy, *Chem. Rev.* 2002, **102**, 629.

7) a) O. Mitsunobu, M. Yamada, *Bull. Chem. Soc. Jpn*. 1967, **40**, 2380; b) O. Mitsunobu, M. Yamada, T. Mukaiyama, *Bull. Chem. Soc. Jpn*. 1967, **40**, 935.

8) Reviews: a) O. Mitsunobu, *Synthesis* 1981, 1; b) B. R. Castro, *Org. React.* 1983, **29**, 1; c) D. L. Hughes, *Org. React.* 1992, **42**, 335; d) D. L. Hughes*, Org. Prep. Proced. Int*. 1996, **28**, 127; e) J. A. Dodge, S. A. Jones, *Rec. Res. Dev. Org. Chem.* 1997, **1**, 273; f) C. Simon, S. Hosztafi, S. Makleit, *J. Heterocycl. Chem.* 1997, **34**, 349; g) K. Wisniewski, A. S. Koldziejczyk, B. Falkiewicz, *J. Peptide Science* 1998, **4**, 1; h) S. Ito, *Yakugaku Zasshi* 2001, **121**, 567; i) S. Lawrence, *PharmaChem* 2002, **1**, 12; j) N. M. Paul, C. J. Gabriel, J. R. Parquette, *Chemtracts* 2002, **15**, 617; k) D. H. Valentine, Jr., J. H. Hillhouse, *Synthesis* 2003, 317.

9) a) R. D. G. Guthrie, I. D. Jenkins, *Aust. J. Chem.* 1982, **35**, 767; b) A. Heesing, H. Steinkamp, *Chem. Ber.* 1982, **115**, 2854; c) E. Grochowski, B. D. Hilton, R. J. Kupper, C. J. Michejda, *J. Am. Chem. Soc.* 1982, **104**, 6876; d) W. Adam, N. Narita, Y. Nishizawa, *J. Am. Chem. Soc.* 1984, **106**, 1843; e) M. Von Itzstein, I. D. Jenkins, *J. Chem. Soc., Perkin Trans. 1* 1986, 437; f) M. Varasi, K. A. M. Walker, M. L. Maddox, *J. Org. Chem.* 1987, **52**, 4235; g) M. Von Itzstein, I. D. Jenkins, *J. Chem. Soc., Perkin Trans. 1* 1987, 2057; h) D. L. Hughes, R. A. Reamer, J. J. Bergan, E. J. J. Grabowski, *J. Am. Chem. Soc.* 1988, **110**, 6487; i) D. Crich, H. Dyker, R. J. Harris, *J. Org. Chem.* 1989, **54**, 257; j) A. Pautard-Cooper, S. A. Evans Jr., *J. Org. Chem.* 1989, **54**, 2485; k) D. Camp, I. D. Jenkins, *J. Org. Chem.* 1989, **54**, 3049; l) D. Camp, I. D. Jenkins, *J. Org. Chem.* 1989, **54**, 3045; m) D. Camp, I. D. Jenkins, *Aust. J. Chem*. 1992, **45**, 47; n) S. R. Wilson, J. Perez, A. Pasternak, *J. Am. Chem. Soc.* 1993, **32**, 72; o) J. E. Macor, J. M. Wehner, *Heterocycles* 1993, **35**, 349; p) D. Camp, G. R. Hanson, I. D. Jenkins, *J. Org. Chem*. 1995, **60**, 2977; q) D. L. Hughes, R. A. Reamer, *J. Org. Chem.* 1996, **61**, 2967; r) J. Moravcova, P. Rollin, C. Lorin, V. Gardon, J. Capkova, J. Mazac, *J. Carbohydr. Chem.* 1997, **16**, 113; s) P. J. Harvey, M. von Itzstein, I. D. Jenkins, *Tetrahedron* 1997, **53**, 3933; t) L. Eberson, O. Persson, J. O. Svensson, *Acta Chem. Scand.* 1998, **52**, 1293; u) T. Watanabe, I. D. Gridnev, T. Imamoto, *Chirality* 2000, **12**, 346; v) C. Ahn, R. Correia, P. DeShong, *J. Org.*

Chem. 2002, **67**, 1751; w) K. E. Elson, I. D. Jenkins, W. A. Loughlin, *Org. Biomol. Chem.* 2003, **1**, 2958; x) S. Schenk, J. Weston, E. Anders, *J. Am. Chem. Soc.* 2005, **127**, 12566.

10) a) N. S. Kumar, P. Kommana, J. J. Vittal, K. C. Kumara Swamy, *J. Org. Chem.* 2002, **67**, 6653; b) N. S. Kumar, K. P. Kumar, K. V. P. P. Kumar, P. Kommana, J. J. Vittal, K. C. Kumara Swamy, *J. Org. Chem.* 2004, **69**, 1880; c) K. C. Kumara Swamy, K. P. Kumar, N. N. Bhuvan Kumar, *J. Org. Chem.* 2006, **71**, 1002.

11) a) D. C. Morrison, *J. Org. Chem.* 1958, **23**, 1072; b) E. Brunn, R. Huisgen, *Angew. Chem. Int. Ed. Engl.* 1969, **8**, 513; *Angew. Chem.* 1969, **81**, 534; c) M. Von Itzstein, I. D. Jenkins, *Aus. J. Chem.* 1983, **36**, 557.

12) A. Ginsburg, M. N. Vasileva, S. S. Dubov and A. Y. Yakubovich, *Zh. Obshch. Khim.* 1960, **30**, 2854.

13) a) K. C. Kumara Swamy, J. M. Holmes, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6092; b) D. J. H. Smith, In *Comprehensive Organic Chemistry*; D. H. R. Barton, V. D. Ollis, Eds.; I. O. Sutherland, Vol. Ed.; Pergamon: Exeter, 1979; Vol. 2, pp 1233-1256; c) K. C. Kumara Swamy, C. Muthiah, S. Kumaraswamy and M. A. Said, *Proc. Indian Acad. Sci. (Chem Sci.),* 1999, **111**, 489.

14) For earlier literature on the formation of pentacoordinate compounds from the reactions of P(III) species with DEAD/ DIAD, see: a) B. A. Arbuzov, N. A. Polezhaeva and V. S. Vinogradova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1968, 2525, b) H. Gonclaves, J. R. Domroy, Y. Chapleur, B. Castro, H. Faudet and R. Burgada, *Phosphorus Sulfur* 1980, 147.

15) a) R. Hulst, A. van Basten, K. Fitzpatrick, R. M. Kellogg, *J. Chem. Soc., Perkin Trans. 1* 1995, 2961; b) Z. Li, Z. Zhou, L. Wang, Q. Zhou and C. Tang, *Tetrahedron: Asymmetry* 2002, **13**, 145.

16) E. Grochowski, B. D. Hilton, R. J. Kupper and C. J. Michejda, *J. Am. Chem. Soc***.** 1982, **104**, 6876.

17) A. Pautard-Cooper and S. A. Evans, Jr., *J. Org. Chem.* 1988, **53**, 2300.

18) a) M. Saeed, T. Ilg, M. Schick, M. Abbas and W. Voelter, *Tetrahedron Lett.* 2001, **42**, 7401; b) F. D. Wang and Jian-Min Yue, *Eur. J. Org. Chem*. 2005, 2575.

19) a) A. F. Barrero, E. J. A.-Manzaneda and R. Chahboun, *Tetrahedron Lett.* 2000, **41**, 1959; b) R. Mengel and M. Bartke, *Angew. Chem. Int. Ed. Engl.* 1978, **17**, 679; *Angew. Chem.* 1978, **90**, 725.

20) G. Appendino, A. Minassi, N. Daddario, F. Bianchi and G. C. Tron, *Org. Lett.* 2002, **4**, 3839.

21) A. B. Smith III, Q. Han, P. A. S. Breslin and G. K. Beauchamp, *Org. Lett.* 2005, **7**, 5075.

22) S. Chandrasekhar and G. Kulkarni, *Tetrahedron: Asymmetry* 2002, **13**, 615.

23) A. G. Myers and B. Zheng, *J. Am. Chem. Soc.* 1996, **118**, 4492.

24) M. C. Viaud and P. Rollin, *Synthesis* 1990, 130.

25) C. M. Afonso, M. T. Barros, L. S. Godinho, C. D. Maycock, *Tetrahedron* 1994, **50**, 9671.

26) a) T. Gajda and M. Matusiak, *Synthesis* 1992, 367; b) C. Xu and C. Yuan, *Eur. J. Org. Chem*. 2004, 4410.

27) a) K. Barral, P. Halfon, G. Pèpe and M. Camplo, *Tetrahedron Lett.* 2002, **43**, 81; b) K. Barral, J. Courcambeck, G. Pèpe, J. Balzarini, J. Neyts, E. De Clercq and M. Camplo, *J. Med. Chem.* 2005, **48**, 450.

28) M. Saady, L. Lebeau and C. Mioskowski, *SynLett*. 1995, 643.

29) a) T. Tsunoda, H. Kaku and S. Itô, *TCIMeru* 2004, 2; b) S. Dandapani and D. P. Curran, *Chem. Eur. J.* 2004, **10**, 3130.

30) R. Dembinski, *Eur. J. Org. Chem.* 2004, 2763 and the references cited there in.

31) R. A. Amos, R. W. Emblidge and N. Havens, *J. Org. Chem*. 1983, **48**, 3598.

32) A. R. Tunoori, D. Dutta and G. I. Georg, *Tetrahedron Lett.* 1998, **39**, 8751.

33) R. Salives, G. Dupas, N. Plé, G. Quéguiner, A. Turck, P. George, M. Sevrin, J. Frost, A. Almario and A. Li, *J. Comb. Chem.* 2005, **7**, 414.

34) a) A. Padwa, *1,3-Dipolar Cycloaddition Chemistry*, Volumes 1 and 2, Wiley Interscience, New York, 1984; b) A. Padwa, in *Comprehensive Organic Synthesis*, *Vol. 4* (Eds: B. M. Trost, I. Fleming, Volume Editor: M. F.

Semmelhack), Pergamon, Oxford, 1991, pp. 1069-1168; c) F. A. Carey, R. J. Sundberg, *Advanced Organic Chemistry*, Part A: Structure and Mechanisms and Part B: Reactions and Synthesis, Plenum Press, New York, 1990, pp. 635-640 and pp. 300-306 respectively; d) R. Huisgen, *Angew. Chem. Int. Ed. Engl.* 1963, **2**, 565; e) K. Banert and F. Köhler, *Angew. Chem. Int. Ed. Engl.* 2001, **40**, 174.

35) a) B. A. Arbuzov and N. N. Zobova, *Synthesis* 1974, 461; b) A. G. M. Barrett, M. J. Betts and A. Fenwick, *J. Org Chem*. 1985, **50**, 169.

36) a) M. Granier, A. Baceiredo, M. Nieger and G. Bertrand, *Angew. Chem. Int. Ed. Engl.* 1990, **29**, 1123; b) T. Facklam, O. Wagner, H. Heydt and M. Regitz, *Angew. Chem. Int. Ed. Engl.* 1990, **29**, 314.

37) a) F. P. Cossio, G. Roa, B. Lecea and J. M. Ugalde, *J. Am. Chem. Soc.* 1995, **117**, 12306; b) M. A. Pericas, F. Serratosa and E. Valenti, *J. Chem. Soc. Perkin Trans II.* 1986, 961.

38) A. N. Pudovik, I.V. Konovalova and L. A. Burnaeva, *Synthesis* 1986, 793.

39) a) R. I. Tarasova, N. M. Kislitsina and A. N. Pudovik, *Zh. Obshch. Khim.* 1971, **41**, 1972; b) R. I. Tarasova, T. V. Zykova, M. V. Alparova, N. I. Sinitsina and R. A Salakhutdinov, *Zh. Obshch. Khim.* 1980, **50**, 757; c) R. I. Tarasova, T. A. Davoinishnikova, N. I. Sinitsina, T. V. Zykova, R. I. Tarasova and M. V. Alparova, *Zh. Obshch. Khim.* 1983, **53**, 1254; d) R. I. Tarasova, N. I. Sinitsina, T. A. Davoinishnikova and V.V. Moskva, *Zh. Obshch. Khim.* 1983, **53**, 694; e) R. I. Tarasova, N. I. Sinitsina, T. A. Davoinishnikova, A. B. Remizov, M. V. Alparova, T. V. Zykova and V.V. Moskva, *Zh. Obshch. Khim.* 1984, **54**, 6656.

40) a) I. V. Konovalova, R. D. Gareev, L. A. Burnaeva, T. A. Faskhutdinova, O. A. Molchanova and A. N. Pudovik, USSR Patent 1977, 635101; b) J. Bvierley, I. J. Dichstein and S. Trippett, *Phosphorus Sulfur* 1979, **7**, 167; c) G. Bauhadir, k. Bieger, P. Livotto, R. Rèau, H. Gornitzka, F. Dahan and G. Bertrand, *J. Orgmet. Chem.* 1997, **529**, 79.

41) D. V. Sevenard, E. Lork, K. I. Pashkevich and G.-V. Röschenthaler, *Heteroatom Chem.* 2002, **13**, 97.

42) a) J. A. Gerlt, *The Enzymes*, 3rd ed.; Sigman, D. S., Ed.; Academic Press: New York, 1992; Vol. XX, pp 95-139; b) P. A. Frey, *The Enzymes*, 3rd ed.; Sigman,

D. S., Ed.; Academic Press: New York, 1992; Vol. XX, pp 141-186; c) D. Voet, J. G. Voet, C. W. Pratt, *Fundamentals of Biochemistry*, John Wiley and Sons: New York, 1998; (d) Z.-Y. Zhang, *Acc. Chem. Res.* 2003**, 36**, 385.

43) Selected references: a) D. M. Perreault and E. V. Anslyn, *Angew. Chem. Int. Ed. Engl.* 1997, **36**, 432; b) R. T.Raines, *Chem. Rev.* 1998, **98**, 1045; (c) Y. Takagi, M. Warashina, W. J. Stec, K. Yoshinari and K. Taira, *Nucleic Acids Res.* 2001, **29**, 1815.

44) R. J. Hondal, Z. Zhao, S. R. Riddle, A. V. Kravchuk, H. Liao, K. S. Bruzik and M.-D. Tsai, *J. Am. Chem. Soc.* 1997, **119**, 9933.

45) a) S. D. Lahiri, G. Zhang, D. Dunaway-Mariano and K. N. Allen, *Science* 2003, **299**, 2067; b) K. C. Kumara Swamy and N. Satish Kumar, *Curr. Sci.* 2003, **85**, 101; c) L. W. Tremblay, G. Zhang, J. Dai, D. Dunaway-Mariano and K. N. Allen, *J. Am. Chem Soc.* 2005, **127**, 5298.

46) E. Skordalakes, G. G. Dodson, D. St C. Green, C. A. Goodwin, M. F. Scully, H. R. Hudson, V. V. Kakkar and J. J. Deadman, *J. Mol. Biol.* 2001, **311**, 549.

47) P. K. Grzyska, P. G.Czyryca, J. Golightly, K. Small, P. Larsen, R. H. Hoff and A. C. Hengge, *J. Org. Chem.* 2002, **67***,* 1214.

48) Selected references: a) W. S. Sheldrick, *Top. Curr. Chem.* 1978, **73**, 1.; b) R. R. Holmes, *Pentacoordinated Phosphorus- Reaction Mechanisms*, Vol. II; ACS Monograph 176, American Chemical Society: Washington, DC. 1980; c) R. R. Holmes, *Chem. Rev*. 1996, **96**, 927 and the references cited therein.

49) See for example: a) R. R. Holmes and J. A. Deiters, *Inorg. Chem.* 1994, **33**, 3235; b) T.Uchimaru, M. Uebayasi, T. Hirose, S. Tsuzuki, A. Yliniemela, K. Tanabe and K. Taira, *J. Org. Chem.* 1996, **61**, 1599; c) X. Lopez, M. Schaefer, A. Dejagere and M. Karplus, *J. Am. Chem. Soc.* 2002, **124**, 5010.

50) a) A. Yliniemela, T. Uchimaru, K. Tanabe and K. Taira, *J. Am. Chem. Soc.* 1993, **115**, 3032; b) C. S. Lopez, O. N. Faza, A. R. de Lera and D. M. York, *Chem. Eur. J.* 2005, **11**, 2081.

51) D. Dubourg, R. Roques, J. P. Declercq, D. Boyer, L. Lamande, A. Munoz and R. Wolf, *Phosphorus Sulfur* 1983**, 17**, 97.

52) a) P. Vayron, P.-Y. Renard, F. Taran, C. Cre´minon, Y .Frobert, J. Grassi and C. Mioskowski, *Proc. Nat. Acad. Sci. (USA)*, 2000, **97**, 7058; b) H. Morales-Rojas and R. A. Moss, *Chem. Rev.* 2002, **102***,* 2497.

53) a) O. I. Kolodiazhnyi, *The Wittig reaction and related methods*, in Phosphorus Ylides: Chemistry and Application in Organic Synthesis, Wiley-VCH, Weinheim, 1999; (b) P. Savignac, B. Iorga, *Modern Phosphonate Chemistry*, CRC Press, Boca Raton, 2003; (c) L. A. Wozniak and A. Okruszek, *Chem. Soc. Rev.* 2003, **32**, 158.

54) a) T. Kawashima, R. Okazaki and R. Okazaki, *Angew. Chem. Int. Ed. Engl.* 1997, **36**, 2500; b) P Kommana and K. C. Kumara Swamy, *Inorg. Chem.* 2000, **39**, 4384; c) E. Vedejs and P. L. Steck, *Angew. Chem. Int. Ed. Engl.* 1999, **38**, 2788; d) M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *J. Am. Chem. Soc.* 1996, **118**, 9841; e) K. Praveen Kumar, M. Chakravarty and K. C. Kumara Swamy, *Z. Anorg. Allg. Chem*. 2004, **630**, 2063.

55) (a) H. A. Bent, *J. Chem. Edn.* 1960, **37**, 616; b) J. E. Huheey, *Inorganic Chemistry- Principles of Structure and Reactivity*, 3rd Edn, Harper & Row Publishers, Inc., 1983, pp. 230-232; c) G. Wulfsberg, *Inorganic Chemistry*, University Science Books, Sausalito, California (USA), 2000, p. 110.

56) Some key references: a) D. Schomburg, U. Wermuth and R. Schmutzler, *Chem. Ber.* 1987, **120**, 1713; b) K. C. Kumara Swamy, J. M. Holmes, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6092; c) S. D. Burton, K. C. Kumara Swamy, J. M. Holmes, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6104; d) R. R. Holmes, K. C. Kumara Swamy, J. M .Holmes and R. O. Day, *Inorg. Chem.* 1991, **30**, 1052; e) T. Kawashima, H. Takami and R. Okazaki, *J. Am. Chem. Soc.* 1994, **116**, 4509; f) S. Vollbrecht, A. Vollbrecht, J. Jeske, P. G. Jones, R. Schmutzler and W. W. Du Mont, *Chem. Ber./Recueil* 1997, **130**, 819; g) C. Muthiah,; M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *Polyhedron* 2000, **19**, 63; h) J. Kobayashi, K. Goto, T. Kawashima, M. W. Schmidt and S. Nagase, *J. Am. Chem. Soc.* 2002, **124**, 3703.

57) Y. Huang, A. M. Arif and W. G. Bentrude, *J. Am. Chem. Soc.* 1991, **113**, 7800.

58) See, for example: a) R. O. Day, K. C. Kumara Swamy, L. Fairchild, J. M. Holmes and R. R. Holmes, *J. Am. Chem. Soc.* 1991, **113**, 1627; b) M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *Inorg. Chem.* 1997, **36**, 2044.

59) S. Trippett, *Phosphorus Sulfur* 1976, **1**, 89.

60) a) D. E. C. Corbridge, *Phosphorus 2000: Chemistry, Biochemistry and Technology*, 4th ed.; Elsevier: Amsterdam, 2000; Chapter 13, pp 1137-1142; b) M. Nakamoto, S. Kojima, S. Matsukawa, Y. Yamamoto and K. –y. Akiba, *J. Organomet. Chem.* 2002, **643-644**, 441; c) S. Matsukawa, K. Kajiyama, S. Kojima, S. –y. Furuta, Y. Yamamoto and K. –y. Akiba, *Angew. Chem. Int. Ed. Engl.* 2002, **41**, 4718; *Angew. Chem.* 2002, ***114***, 4912-4916 (apicophilicity scale); d) B. D. Wladkowski, M. Krauss and W. J. Stevens, *J. Phys. Chem.* 1995, **99**, 4490; e) S. Kojima, K. Kajiyama, M. Nakamoto, S. Matsukawa and K. –y. Akiba, *Eur. J. Org. Chem.* 2006, 218.

61) a) S. Kumaraswamy, C. Muthiah and K. C. Kumara Swamy, *J. Am. Chem. Soc.* 2000, **122**, 964; b) P. Kommana, S. Kumaraswamy, J. J. Vittal and K. C. Kumara Swamy, *Inorg. Chem.* 2002, **41**, 2356; c) S. Kumaraswamy and K. C. Kumara Swamy, *Polyhedron*, 2002, **21**, 1155; d) P. Kommana, N. Satish Kumar, J. J. Vittal, E. G. Jayasree, E. D. Jemmis and K. C. Kumara Swamy, *Org. Lett.* 2004, **6**, 145.

62) N. V. Timosheva, A. Chandrasekaran, T. K. Prakasha, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1996, **35**, 6552 and the references cited therein.

63) Pauling electronegativities of $-NMe_2$ and $-NH_2$ are, respectively, 2.37 and 2.50. The Mulliken electronegativities of some relevant groups are as follows: –N(*i*-Pr)$_2$ 8.37, –N(Me)Et 8.37, $–NHCH_3$ 8.53, $–NH_2$ 8.76 and –NCS 11.74. See ref. 15a, p. 156 and: D. Bergmann, J. Hinze, In *Struct. Bonding*, *66*, *Electronegativity;* K. D. Sen, , C. K. Jørgensen, Eds.; Springer-Verlag: Heidelberg, 1987; pp 145-190.

64) a) S. Kojima, M. Sugino, S. Matsukawa, M. Nakamoto and K-y. Akiba, *J. Am. Chem. Soc.* 2002, **124**, 7674 and references cited therein; b) T. Kawashima, K. Kato and R. Okazaki, *J. Am. Chem. Soc.* 1992, **114**, 4008.

65) S. Kumaraswamy, P. Kommana, N. Satish Kumar and K. C. Kumara Swamy, *Chem. Commun.* 2002, 40.

66) a) N. V. Timosheva, A. Chandrasekaran and R. R. Holmes, *J. Am. Chem. Soc.* 2005, **127**, 12474; b) L. Yu, Z. Liu, H. Fang, Q. L. Zeng, and Y. F. Zhao, *Amino Acids* 2005, **28**, 369.

67) J. Michalski, A. Skowronska and R. Bodalski, *in Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis* (eds J. G. Verkade and L. D. Quinn), VCH, 1987, Chapter 8, pp. 255-296.

68) a) C. Lerman and F. H. Westheimer, *J. Am. Chem. Soc.* 1976, **98**, 179; b) S. Trippett and R. E. L. Waddling, *Tetrahedron Lett*. 1979, 193.

69) F. Ramirez, J. F. Marecek and H. Okazaki, *J. Am. Chem. Soc.* 1976, **98**, 5310.

70) a) Hellwinkel, *Chem. Ber.* 1965, **98**, 576; b) H. R. Allcock and E. C. Bissell, *J. Am. Chem. Soc.* 1973, **95**, 3154; c) D. Hellwinkel and H. –J. Wilfanger, *Chem. Ber.* 1970, **103**, 1056; d) M. Koenig, A. Klaebe, A. Munoz and R. Wolf, *J. Chem. Soc., perkin Trans. 2*, 1976, 955; e) G. E. Rychketwitch and J. M. Garret, *J. Chem. Soc.* 1968, **90**, 7234; f) T. Ito, A, Kobayashi, F. Marumo and Y. Saito, *Inorg. Nucl. Chem. Lett.* 1971, **7**, 1097; g) D. Hellwinkel, *Angew. Chem. Int. Ed. Engl.* 1965, **4**, 356;

71) S. Constant and J. Lacour, *Top Curr Chem*. 2005, **250**, 1 and references cited there in.

72) a) C. Chuit, R. J. P. Corriu, P. Monforte, C. Reye, J. –P. Declercq and A. Dubourg, *Angew. Chem. Int. Ed. Engl.* 1993, **32**, 1430; b) J. Lacour, A. Londez, C. Goujon-Ginglinger, V. Buss, and G. Bernardinelli, *Org. Lett.* 2000, **2**, 4185; c) J. Lacour, L. Vial and C. Herse, *Org. Lett.* 2002, **4**, 1351; d) V. Hebbe, A. Londez, C. Goujon-Ginglinger, F. Meyer, J. Uziel, S. Juge´ and J. Lacour, *Tetrahedron Lett.* 2003, **44**, 2467.

73) K. B. Dillon, A. W. G. Platt and T. C. Waddington, *J. Chem. Soc., Dalton Trans.* 1978, 1465.

74) V. Luo, R. McDonald and R. G. Cavell, *Angew. Chem. Int. Ed. Engl.* 1998, **37**, 1098.

75) J. Lacour, L. Vial and G. Bernardinelli, *Org. Lett.* 2002, **4**, 2309.

76) a) C. Y. Wong, D. K. Kennepohl and R. G. Cavell, *Chem. Rev.* 1996, **96**, 1917 and references cited there in.

77) R. R. Holmes, *Acc. Chem. Res.* 1998, **31**, 535 and references cited there in.

78) K. C. Kumara Swamy, S. Kumara swamy, M. A. Said, R. S. Krishna Kishore, R. Herbst-Irmer and M. Pülm, *Current Science* 2000, **78**, 473.

79) P. Sood, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1998, **37**, 6329.

80) a) T. K. Prakasha, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1993, **115**, 2690; b) C. Y. Wong, R. McDonald and R. G. cavell, *Inorg. Chem.* 1996, **35**, 325; c) M. A. Said, M. Pülm, R. Herbst-Irmer and K. C. Kumara Swamy, *J. Am. Chem. Soc.* 1996, **118**, 9841; d) D. J. Sherlock, A. Chandrasekaran, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1997, **119**, 1317; e) A. Chandrasekaran, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1997, **119**, 11434; f) N. V. Timosheva, A. Chandrasekaran and R. R. Holmes, *Inorg. Chem.* 2004, **43**, 7403.

81) D. J. Sherlock, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1997, **36**, 5082.

82) K. C. Kumara Swamy, C. Sreelatha, R. O. Day, J. Holmes and R. R. Holmes, *Inorg. Chem.* 1991, **30**, 3126.

83) N. V. Timosheva, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1998, **37**, 7403.

84) See for example: a) J. Emsley, N. M. Reza, H. M. Dawes and M. B. Hursthouse, *Chem. Commun.* 1985, 1459; b) C. A. Poutasse, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1984, **106**, 3814; c) J. Emsley, *Chem. Soc. Rev.* 1980, **9**, 91.

85) a) M. Page, A. Williams, *Organic and Bioorganic Mechanisms*, Longman, Singapore, 1997, p. 156; b) R. J. Kubiak, R. J. Hondal, X. Yue, M. –D. Tsai and K. S. Bruzik, *J. Am. Chem. Soc.* 1999, **121**, 488.

86) F. Lohr, S. G. Mayhew and H. Ruterjans, *J. Am. Chem. Soc.* 2000, **122**, 9289.

87) K. C. Kumara Swamy, S. Kumaraswamy and P. Kommana, *J. Am. Chem. Soc.* 2001, **123**, 12642.

88) a) R. H. Blessing and E. L. McGandy, *J. Am. Chem. Soc.* 1972, **94**, 4034; b) J. H. Clark, M. Green, R. Madden, C. D. Reynolds and Z. Dauter, *J. Am. Chem.*

Soc. 1984, **106**, 4056; c) R. R. Holmes, R. O. Day, Y. Yoshida and J. M. Holmes, *J. Am. Chem. Soc.* 1992, **114**, 1771.

89) Preparation of Dichloromonosulfane (SCl_2): G. Brauer, Handbook of Preparative Inorganic Chemsitry, Volume 1, 2nd ed.; Academic Press, New York, 1963, pp 370-371.

90) T. K. Prakasha, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1993, **115**, 2690.

91) D. J. Sherlock, A. Chandrasekaran, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1997, **119**, 1317.

92) S. D. Pastor, J. D. Spivack and L. P. Steinhuebel, *J. Heterocyclic Chem.* 1984, **21**, 1285.

93) P. Kommana, S. Kumaraswamy, J. J. Vittal and K. C. Kumara Swamy,. *Inorg. Chem.* 2002, **41**, 2356.

94) a) B. V. L.Potter and& D. Lampe, *Angew. Chem. Int. Ed. Engl.* 1995, **34**, 1933; b)

95) U. Samanta, V. G. Puranik, P. Chakrabarti, P. Thoniyot and M. S. Shashidhar, *Acta Cryst. C54*, 1998, 1289.

96) a) K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day and R. R. Holmes, *Phosphorus. Sulfur. Silicon.* 1990, **49**, 367; b) Review: K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day and R. R. Holmes, *Phosph. Sulf. Silicon.* 1990, **53**, 437; c) K. C. Kumara Swamy, J. M. Holmes, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6092; d) K. C. Kumara Swamy, R. O. Day, J. M. Holmes and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6095; e) K. C. Kumara Swamy, S. D. Burton, J. M. Holmes, R. O. Day and R. R. Holmes, *J. Am. Chem. Soc.* 1990, **112**, 6104; f) R. R. Holmes, K. C. Kumara Swamy, J. M. Holmes and R. O. Day *Inorg. Chem.* 1991, **30**, 1052; g) R. O. Day, K. C. Kumara Swamy, L. Fairchild, J. M. Holmes and R. R. Holmes, *J. Am. Chem. Soc.* 1991, **113**, 1627; h) M. A. Said, K. C. Kumara Swamy, K. C. Mohan and N. V. Lakshmi, Tetrahedron 1994, **50**, 6989; i) M. A. Said, K. C. Kumara Swamy, M. Veith and V. Huch, *J. Chem, Soc., Perkin Tran, 1* 1995, 2945; j) M. A. Said, K. C. Kumara Swamy, R. –H. Irmer and K. C. Kumara

Swamy, *J. Am. Chem. Soc.* 1996, **118**, 9841; k) M. A. Said, K. C. Kumara Swamy, M. Veith and V. Huch, *Inorg. Chem.* 1996, **35**, 6627; l) M. A. Said, M. Pülm, R. –H. Irmer and K. C. Kumara Swamy, *Inorg. Chem.* 1997, **36**, 2044; k) K. C. Kumara Swamy, M. A. Said, K. Sudha, R. –H. Irmer and M. Pülm, *Polyhedron* 1998, **17**, 3643; l) K. C. Kumara Swamy, C. Muthiah, K. Sudha and M. A. Said, *Proc. Indian. Acad. Sci. (Chem. Sci.)* 1999, **111**, 489; m) K. C. Kumara Swamy, K. Sudha, M. A. Said, R. –H. Irmer and M. Pülm, *Current Science* 2000, **78**, 473.

97) (a) B. E. Maryanoff, R. O. Huchins, C. A. Maryanoff, *Top.Stereochem.* 1979, **11**, 187; b) Y. Huang, N. N. Mullah, A. E. Sopchik, A. M. Arif and W. G. Bentrude, *Tetrahedron Lett.* 1991, **32**, 899; c) M. J. Gallagher, In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH: Deerfield Beach, FL, 1987; Chapter 9; d) W. G. Bentrude, W. N. Setzer, In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH: Deerfield Beach, 1987; Chapter 11 and references cited therein; e) D. E. Schiff, J. W. Richardson Jr., R. A. Jacobson, A. H. Cowley, J. Lasch, J. G. Verkade, *Inorg. Chem.* 1984, **23**, 3373.

98) K. C. Kumara Swamy and S. Kumaraswamy, *Acta Cryst. C57*, 2001, 1147.

99) For other interesting examples with 'reversed apicophilicity', see: a) N. V. Timosheva, T. K. Prakasha, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1995, **34**, 4525. b) T. K. Prakasha, A. Chandrasekaran, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1995, **34**, 1243; (c) N. V. Timosheva, A. Chandrasekaran, T. K. Prakasha, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1996, **35**, 6552; (d) S. Kojima, K. Kajiyama, M. Nakamoto and K.-y. Akiba, *J. Am. Chem. Soc.* 1996, **118**, 12866; (e) K. Kajiyama, M. Yoshimune, M. Nakamoto, S. Matsukawa, S. Kojima and K.-y. Akiba, *Org. Lett.* 2001, **3**, 1873; (f) J. Kobayashi, K. Goto and T. Kawashima, *The Ninth International Symposium on Inorganic Ring Systems*, Saarbrücken, Germany, July 23-28, 2000, Abstract No. P-115. (g) S. Kojima, M. Sugino, S. Matsukawa, M. Nakamoto and K. –y. Akiba, *J. Am. Chem. Soc.* 2002, **124**, 7674; (h) K. V. P.

Pavan Kumar, N. Satish Kumar and K. C. Kumara Swamy, *New J. Chem.* 2006, 717.

100) See, for example: a) J. E. Huheey, E. A. Keiter and R. L. Keiter, *Inorganic Chemistry- Principles of Structure and Reactivity*, 4th Edn, Addison-Wesley Publishing Company (Harper Collins College Publishers), 1993, p. 227; b) G. Wulfsberg, *Inorganic Chemistry*, University Science Books, Sausalito, California (USA), 2000, p. 110.

101) a) A. E. Reed, P. von and R. Schleyer, *J. Am. Chem. Soc.* 1990, **112**, 1434; b) M. Lattman, in *Hypervalent Compounds* in *Encyclopedia of Inorganic Chemistry*, Vol. 3 (Ed: R. B. King), John Wiley & Sons, Chichester, England, 1994, pp 1496-1511.

102) See ref. 1, p. 69; we have used the Pauling electronegativity for this calculation.

103) Selected references: a) R. Hoffmann, J. M. Howell and E. L. Muetterties, *J. Am. Chem. Soc.* 1972, **94**, 3047; b) T. Uchimaru, W. J. Stec and K. Taira, *J. Org. Chem*. 1997, **62**, 5793; c) H. Wasada and K. Hirao, *J. Am. Chem. Soc*. 1992, **114**, 16; d) H. Wasada and Y. Tsutsui, *Chem. Lett*. 1995, 825; e) J. A. Deiters and R. R. Holmes, *Organometallics* 1996, **15**, 3944-3956.

104) A. W. Addison, T. N. Rao, J. Reedijk, J. C. Rijn and G. C. Verschoor, *J. Chem. Soc., Dalton Trans.* 1984, 1349.

105) R. R. Holmes and J. A. Deiters, *J. Am Chem. Soc.* 1977, **99**, 3318.

106) Previously, we have shown that the ^{31}P NMR spectrum recorded at low temperature immediately upon dissolution also shows the same pattern as the one obtained by dissolved at room temperature and then lowering the temperature. See ref. 10a.

107) K. Sudha, K. Senthil Kumar, N. S. Kumar and K. C. Kumar Swamy, *J. Chem. Soc., Dalton Trans.* 2005, 1847.

108) The P=N bond length in $Ph_3P{=}NC_6H_4Br$ is 1.57 Å. See: D. E. C. Corbridge, *Phosphorus- An Outline of its Chemistry, Biochemistry and Technology*, 4th Edn, Elsevier, Amsterdam, 1990, p. 47.

109) Generally it is expected that amides show two or more bands for the *NH*-C(O) group due to hydrogen-bonded oligomers; we believe that our compounds also

behave similarly. See: D. H. Williams, I. Fleming, *Spectroscopic Methods in Organic Chemistry*, 4th Edn, Tata McGraw-Hill, New Delhi, pp. 60-61 (Figures 2.13a-c).

110) R. G. Cavell, In *Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH: Deerfield Beach, FL, 1987; Chapter 7.

111) R. R. Holmes, T. K. Prakasha and R. O. Day, *Inorg. Chem.* 1993, **32**, 4360.

112) See ref. 10, p. 72 and: D. F. Shriver and D. W. Atkins, *Inorganic Chemistry*, 3rd Edn, Oxford University Press, Oxford, 1999, p. 24 and p. 71.

113) In most of the compounds using the same type of sulfur containing ligand, sulfur is *trans* to the acyclic substituent except in S{4,6-(*t*-Bu)$_2$C$_6$H$_2$O}$_2$P(OCH$_2$CF$_3$)[2,2'-O$_2$(C$_6$H$_4$)$_2$]. See reference 80 and: T. K. Prakasha, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1992, **31**, 3391-3397.

114) a) A. D. Becke, *J. Chem. Phys.* 1993, **98**, 5648; b) A. D. Becke, *Phys. Rev. A*. 1988, **38**, 2398; c) C. Lee, W. Yang and R. G. Parr, *Phys. Rev. B*. 1988, **37**, 785.

115) Gaussian 03, Revision C.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson,W. Chen,M. W. Wong, C. Gonzalez and J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

116) A. Chandrasekaran, P. Sood, R. O. Day and R. R. Holmes, *Inorg. Chem.* 1999, **38**, 3952.

117) D. D. Perrin, W. L. F. Armarego and D. R. Perrin, *Purification of Laboratory Chemicals*, Pergamon, Oxford, 1986.

118) D. F. Shriver and M. A. Dresdzon, *The Manipulation of Air Sensitive Compounds*, 2nd Edn, Wiley Interscience, New York, 1986.

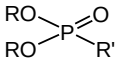
119) a) G. M. Sheldrick, *SHELXS-90*, *Acta Crystallogr., Sect. A*, 1990, **46**, 467; b) G. M. Sheldrick, *SHELXL-93*, University of Göttingen 1993; c) G. M. Sheldrick, *SHELX-97*, University of Göttingen, 1997; d) G. M. Sheldrick, *SHELXTL*. Version 6.12; University of Göttingen, Germany, 1997.

CHAPTER 4

INTRODUCTION

4.1 General Introduction

Phosphonates 4.**1** are similar to phosphates except that they have one carbon-phosphorus bond in place of an oxygen-phosphorus linkage. Due to their structural similarity to phosphate esters, phosphonates often act as inhibitors of enzymes. In fact, the phosphonate and phosphonic acid moieties may be accepted by enzymes as false substrates and hence interfere with biological processes.[1] A number of phosphonates are used as anti-viral agents and antibiotics.[1c,1d] Organophosphonates are esters of phosphonic acids and are versatile intermediates in organic synthesis. In particular, phosphonate stabilized carbanions have traditionally found wide application in C-C bond forming reactions *via* the Horner-Wadsworth-Emmons (HWE) reaction.[2-3] Thus, owing to the synthetic and biological significance, there is a great deal of interest in the chemistry of phosphonates.[2-4] The focus of this chapter is to review the literature pertaining to the synthesis and utility of phosphonates. We are also interested in synthesizing substituted anthracenyl derivatives for future use (e.g. in material chemistry) and hence a brief survey of relevant literature on this class of compounds is given in section 4.4.



Phosphonate

(4.**1**)

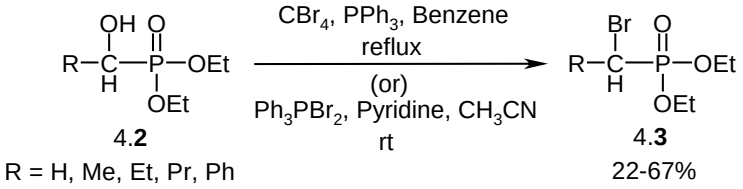
4.2 Synthesis of α-bromo- and α-chloro-phosphonates

4.21 Synthesis of α-bromophosphonates

The precursors, dialkyl α-hydroxyphosphonates, are prepared by reaction of dialkylphosphites with aldehydes in the presence of a base by the Pudovik reaction.[5] The α-bromophosphonates $RCHBrP(O)(OEt)_2$ (4.**3**) can be prepared by treating the α-hydroxyphosphonates $RCH(OH)P(O)(OEt)_2$ (4.**2**) with Ph_3P and CBr_4 in refluxing

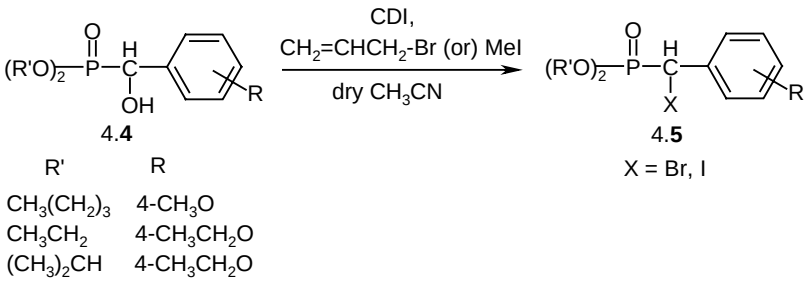
benzene, or with Ph_3PBr_2 and pyridine in acetonitrile at room temperature (Scheme 4.1).[6]

Scheme 4.1



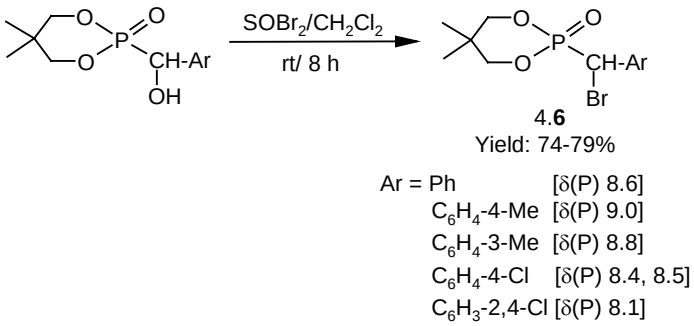
O,O-dialkyl α-hydroxybenzylphosphonates (4.**4**) may be converted to their corresponding α-halobenzylphosphonates (4.**5**) by using N,N'-carbonyldiimidazole (CDI) in the presence of excess allyl bromide or methyl iodide at room temperature in anhydrous acetonitrile (Scheme 4.2). The alkoxycarbonylimidazole intermediate formed at room temperature by the reaction of the α-hydroxyphosphonate and CDI is quaternized with reactive halide (e.g. allyl bromide or methyl iodide) to form a substituted imidazole phosphonate salt. Heating this intermediate to 150°C was found to favor formation of a phosphonate carbenium ion with decarboxylation, which readily combines with halide ions to give the α -halophosphonate.[7]

Scheme 4.2



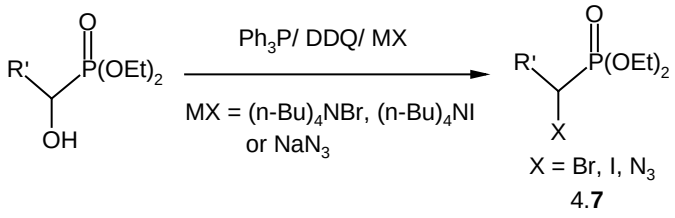
α-Bromophosphonates (4.**6**) have been prepared readily by treating the corresponding α-hydroxyphosphonates with thionyl bromide in good yields in our laboratory.[8] Formation of α-bromophosphonates occurs by the attack of the Br^- ion on the carbon α to phosphorus (Scheme 4.3).

Scheme 4.3



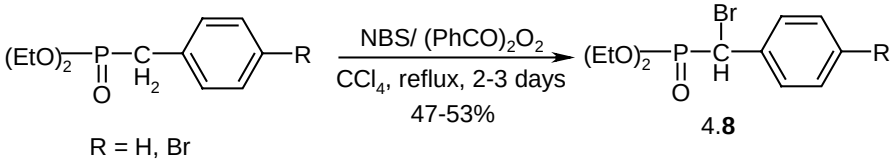
The mixture of triphenylphosphine (PPh_3) and 2,3-dichloro-5,6-dicyanobenzquinone (DDQ) as a neutral system has been used for the preparation of various types of diethyl α-bromo, α-iodo and α-azidophosphonates (4.**7**) from their corresponding diethyl α- hydroxyphosphonates in the presence of *n*-Bu_4NBr, *n*-Bu_4NI and NaN_3 as nucleophilic sources under mild reaction conditions in good to excellent yields (Scheme 4.4).[9] In order to show the unique behavior of PPh_3/DDQ system for the preparation of α-functionalized phosphonates, bromination and iodination of α- hydroxyphosphonates with *n*-Bu_4NBr and *n*-Bu_4NI in the presence of PPh_3/DEAD was done. The results indicate that under these reaction conditions, besides the formation of the desired products in low yields, alkylated hydrazine derivatives $[(EtO)_2P(O)CH\{N(CO_2Et)NH(CO_2Et)\}Ph]$ are also formed as byproducts. The major disadvantage of this procedure is the separation of the byproduct triphenylphospine oxide which is difficult (as it is water insoluble).[9]

Scheme 4.4



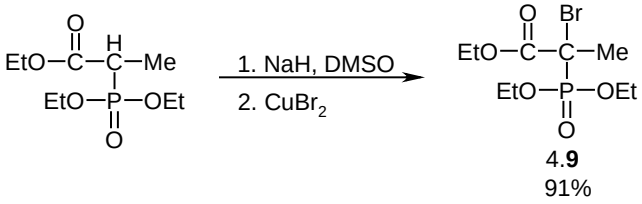
Diethyl α-bromobenzylphosphonate (4.**8**) was prepared by radical bromination using NBS in the presence of benzoyl peroxide (Scheme 4.5).[10] However, the reaction was very slow, requiring CCl_4 at reflux and long reaction times (2-3 days). The yields were also only moderate (47-53%).

Scheme 4.5



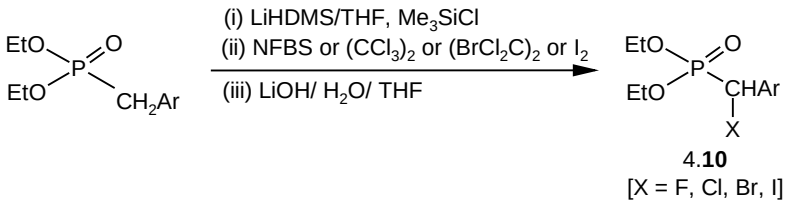
When various stabilized ester enolates of 2-keto, 2-(alkoxycarbonyl), 2-phosphoryl, and 2-(benzenesulfonyl) were reacted with cupric chloride or cupric bromide, 2-halo esters 4.**9** were obtained in good to excellent yields under mild conditions. One such example is given in Scheme 4.6.[11]

Scheme 4.6



The diethyl α-monohalogenobenzylphosphonates (4.**10**) (X=F, Cl, Br, I) have been obtained in pure form by starting with diethyl benzylphosphonates in a one-pot procedure. This high yielding method implies the reaction of intermediate benzyl anion with TMSCl followed by halogenation with an electrophilic halogenating reagent (Scheme 4.7).[12] However, a number of expensive reagents need to be used and hence this route may not be preferable on a large scale.

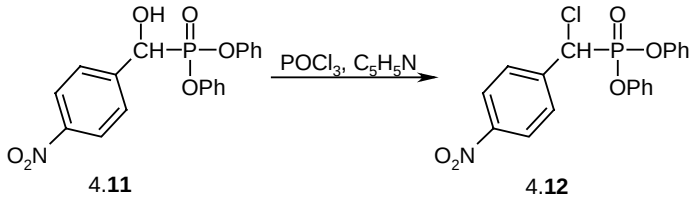
Scheme 4.7



4.22 Synthesis of α-chlorophosphonates

The hydroxyphosphonate (4.**11)** can be smoothly converted into the corresponding chlorophosphonate (4.**12)** using pyridine/ phosphorus oxychloride system (Scheme 4.8).[13] This method is simple but utilizes the not so friendly pyridine.

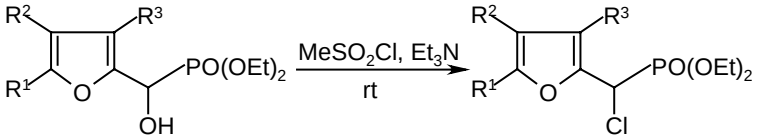
Scheme 4.8



4.**11** 4.**12**

2-Furylchloromethylphosphonate (4.**14**) was readily prepared by the reaction of the corresponding hydroxyphosphonate (4.**13** with methanesulfonyl chloride ($MeSO_2Cl$) in the presence of triethylamine under dry conditions at room temperature (Scheme 4.9).[14] It is possible that if R^1 is H, the reaction may yield a mixture of products or chlorination could take place preferentially at the furan ring (*vide infra*).

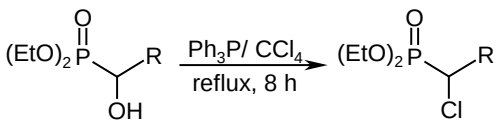
Scheme 4.9



4.**13** 4.**14**

A convenient synthesis of diethyl 1-chloroalkyl phosphonates (4.**15**) from diethyl 1-hydroxyalkyphosphonates utilizing triphenylphosphine/carbon tetrachloride system was achieved in high yield (Scheme 4.10).[15] The best results are obtained when 50% molar excess of triphenylphosphine is used, but this method is limited to primary and secondary alkylhydroxyphosphonates. Use of triphenylphosphine also means that the byproduct $Ph_3P(O)$ should be removed at some stage, which acts as a limitation.

Scheme 4.10

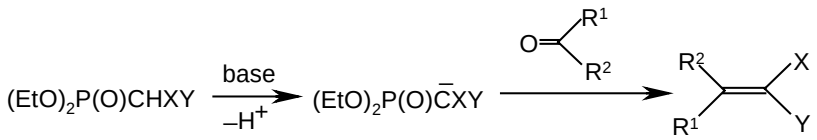


4.**15**

4.3 Synthetic utility of phosphonates

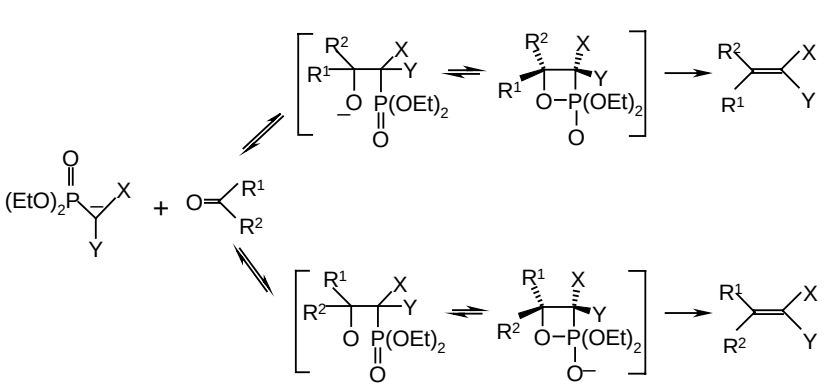
Phosphonates with a hydrogen at the α-carbon undergo a Wittig like reaction with aldehydes and ketones to lead to alkenes described as Horner-Wadsworth-Emmons (HWE) reaction (Scheme 4.11).[16] The main advantage of this method is that the byproduct (a salt of phosphate esters) is water soluble and hence the separation of the product is very easy when compared to Wittig reaction in which the byproduct $Ph_3P(O)$ is water insoluble [and hence the separation of product is not convenient].

Scheme 4.11



As regards mechanistic pathway, the addition of phosphonate anions to ketones/aldehydes [$R^1R^2C(O)$] gives a mixture of the *erythro* and *threo* isomeric β-hydroxyphosphonates as anionic intermediates (Scheme 4.12).[17] These intermediates lead to four-membered phosphetanes which will then decompose by *syn* elimination of phosphate (or phosphinate) to give the alkenes. The elimination is stereospecific, with the *erythro* form producing one isomer and *threo* form producing the other.

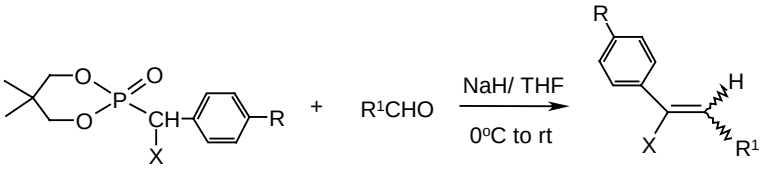
Scheme 4.12



A convenient route to aryl substituted chloro and bromo olefins 4.**17** by HWE reaction of α-chloro/bromophosphonates 4.**16** with aldehydes was reported from our laboratory (Scheme 4.13).[18] The *E* and *Z* isomers were formed in the ratio

of 3:2.[8] Normally *E*-isomer is exclusively formed in the HWE reaction but in this case it is interesting to note that both *E* and *Z* isomers are formed in comparable quantities.

Scheme 4.13



4.**16**

X = Cl, Br

R = H, 4-Me, 4-OMe

R^1= 4-Me-C_6H_4, PhCH=CH, 4-MeOC_6H_4

4.**17**

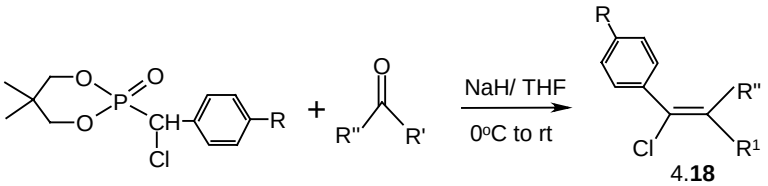
X = Cl, yield 60-90%

X = Br, yield 20-30%

Z and *E* isomers (1:1 to 1:2)

The reaction of α-chloro/ bromophosphonates with ketones was studied previously in our laboratory. It was shown that the reaction of α-chlorophosphonates with ketones in the presence of NaH in THF give trisubstituted vinyl halides 4.**18** in good yields. The corresponding α-bromophosphonates failed to react with ketones under the same conditions but gave the unsymmetrical acetylenes 4.**19** using NaH/ DMSO (Scheme 4.14).[19] Formation of the latter products is probably due to the formation of a more powerful dimsyl anion when DMSO is used.

Scheme 4.14

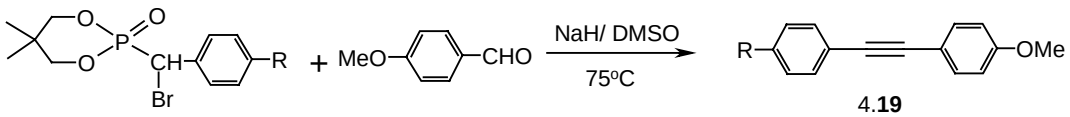


4.**18**

R= H, 4-Me, 4-OMe

R'',R'= Ph, 4-Me-C_6H_4,4-OMe-C_6H_4

yield 65-96%

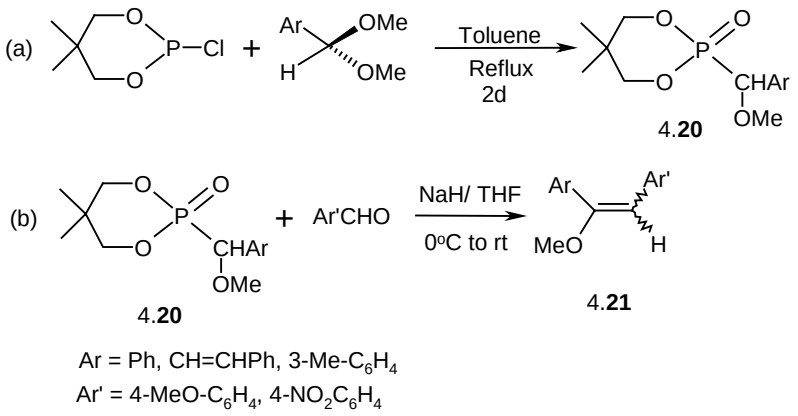


4.**19**

R= H, 4-Me, 4-OMe

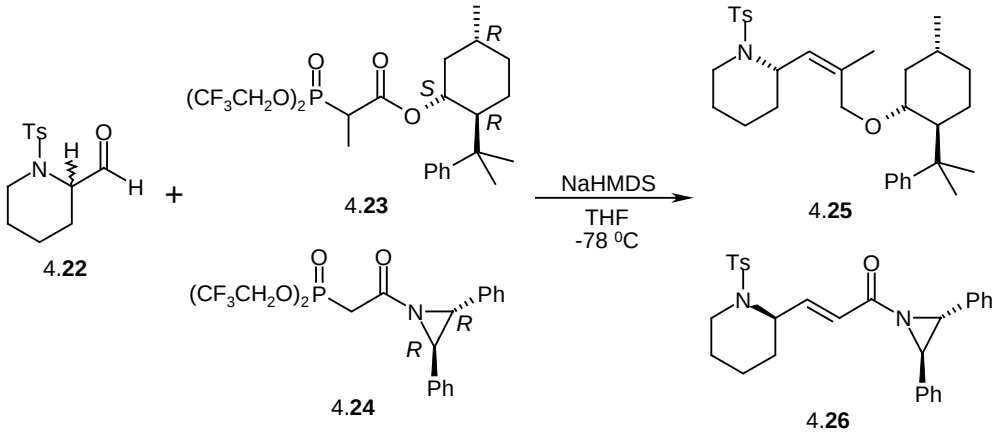
Synthesis of vinyl ethers 4.**21** by the HWE reaction of methoxyphosphonates (4.**20**) with aldehydes in the presence of NaH (Scheme 4.15) was also reported recently from our laboratory.[20] This is perhaps the most convenient method to prepare the methoxy substituted olefins.

Scheme 4.15



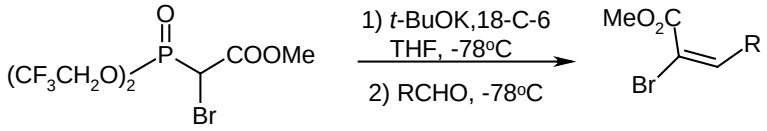
When the racemic aldehyde 4.**22** was reacted simultaneously with two different chiral phosphonates 4.**23** and 4.**24** differing in structure, it undergoes parallel kinetic resolution leading to two different synthetically useful chiral products 4.**25** and 4.**26** (Scheme 4.16).[21]

Scheme 4.16



A novel reagent, bis(2,2,2-trifluoroethoxy)bromophosphonoacetate 4.**27**, was prepared by Tago *et al* to synthesize (*E*)-α-bromoacrylates 4.**28** by the HWE reaction of various aldehydes with 4.**27** in the presence of *t*-BuOK and 18-crown-6 (Scheme 4.17).[22]

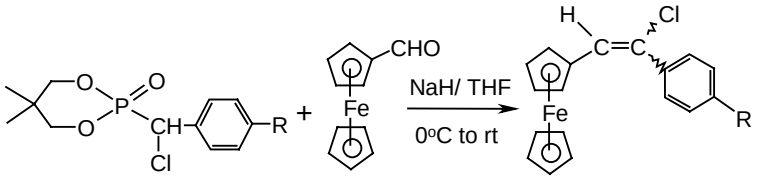
Scheme 4.17



4.**27** 4.**28**

In the literature, a number of methods have been reported for the synthesis of ferrocenyl alkenes. In most of these methods, $Pd(OAc)_2$ or SmI_2 is used as a catalyst.[23] An alternative method developed in our laboratory uses the HWE reaction of α-chlorophosphonates for the synthesis of ferrocenyl substituted chlorostilbenes 4.**29a-d** (Scheme 4.18).[24]

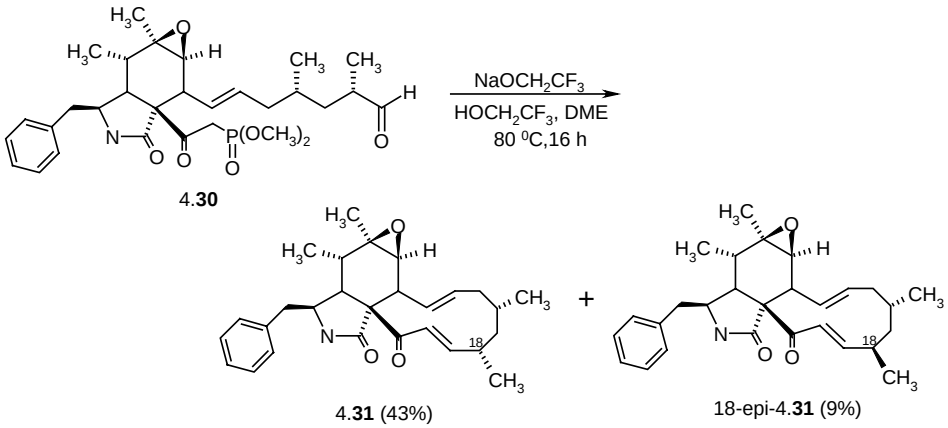
Scheme 4.18



Compound		Yield (%)
R = H	(4.**29a**)	80
4-Me	(4.**29b**)	81
4-MeO	(4.**29c**)	85
Cl	(4.**29d**)	78

In a synthetic route to natural products of cytochalasin family, intramolecular HWE reaction done using a unusual base sodium trifluoroethoxide (slightly less than 1 equiv) in 1,2-dimethoxyethane (DME) at 80 ºC (16 h) proved to be the optimal condition to maximize the yield of cyclized product 4.**31** while minimizing epimerization at the stereocenter adjacent to aldehyde group (Scheme 4.19).[25]

Scheme 4.19



4.**30**

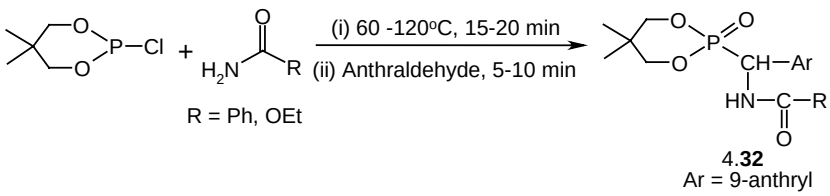
4.**31** (43%) 18-epi-4.**31** (9%)

4.4 Synthesis of anthracene derivatives with extended conjugation

Anthracene and its derivatives are of immense interest in materials chemistry as organic semiconductors[26] and photoswitches.[27] Many of these compounds are highly fluorescent and thermochromic or photochromic.[28] They can also act as light induced electron donors or acceptors and can undergo photodimerization.[29] Their applications in optical, electronic, or magnetic switches incorporated in polymers, films, or crystals are quite often based on this photo-dimerization property. Because of effective blocking on one side, the carbenes with carbon attached to C-9 of anthracene are quite stable in the triplet form.[30] Anthracene based compounds are also useful for probing DNA cleavage and related studies on biological systems.[31] Recently, Celik and co-workers.[32] have prepared several interesting epoxy-anthracene derivatives. In view of these applications, we have been interested in systems possessing the antracenyl residue.

One of the ways by which anthracenyl group can be introduced is by using the Horner-Wadsworth-Emmons (HWE) reaction *via* a suitable phosphonate and an aldehyde. The anthracenyl moiety may be present in either of the two, but to our knowledge, phosphonates with anthracenyl residue are too few in number. One such example of α-aminophosphonate of the type $(OCH_2CMe_2CH_2O)P(O)CH(NHCO_2R)$(9-anthryl) (4.**32**) has been synthesized in our laboratory by a three-component reaction using $(OCH_2CMe_2CH_2O)PCl$, benzamide (or urethane) and anthraldehyde without using any catalyst under solvent-free conditions (Scheme 4.20).[33]

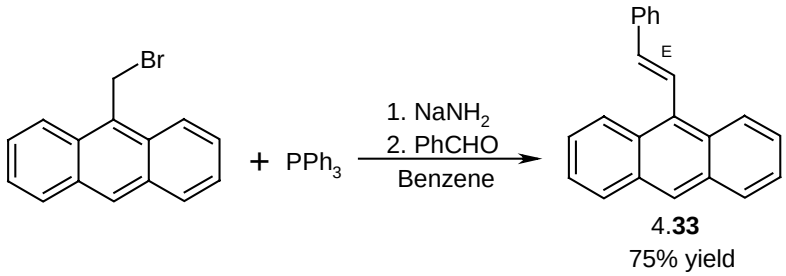
Scheme 4.20



A new semi-stabilized phosphonium ylide, 9-anthrylmethylene triphenylphosphorane, generated by the action of sodium hydride or sodamide in benzene or sodium methoxide in methanol on (9-anthrylmethyl) triphenylphosphonium bromide, has been reacted with substituted aromatic

aldehydes to give exclusively the *trans*-1-(9-anthryl)-2-substituted-arylethylenes 4.**33** (Scheme 4.21).[34]

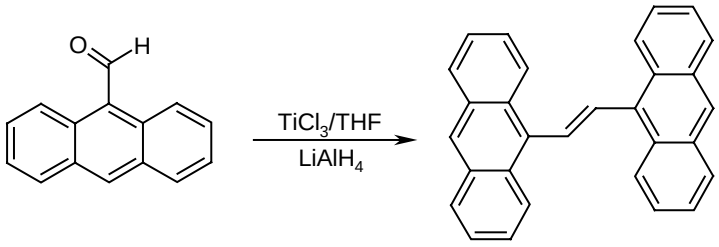
Scheme 4.21



4.**33**
75% yield

A one step route to (*E*)-1,2-bis(9-anthryl)ethane (4.**34**) involving a coupling reaction of low-valent titanium with 9-anthraldehyde is reported (Scheme 4.22). Photochemical properties of 9-anthrylethylenes thus synthesized in terms of geometrical isomerization and intermolecular cycloaddition have been investigated.[35]

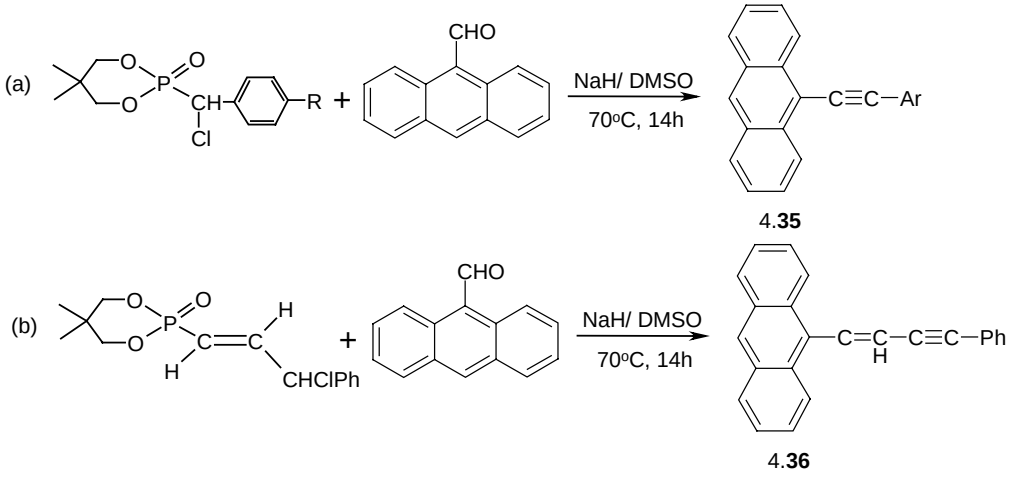
Scheme 4.22



4.**34**
53% yield

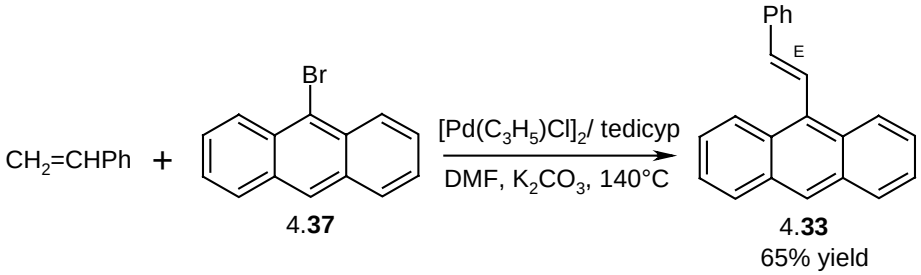
When α-chloro and γ-chlorophosphonates were reacted with anthraldehyde in the presence of NaH in DMSO under refluxing conditions, anthracenyl alkynes 4.**35** and enynes 4.**36**, respectively, are formed (Scheme 4.23).[36]

Scheme 4.23



The Heck reaction is one of the most widely used palladium-catalyzed methodologies in organic synthesis.[37] Tetradentate ligand Tedicyp with palladium complex $\{[PdCl(C_3H_5)]_2\}$ system efficiently catalyses the Heck reaction of aryl halides (4.**37**) with styrene and vinyl ether derivatives. One such example that leads to anthracenyl derivative 4.**33** is shown in Scheme 4.24.[38]

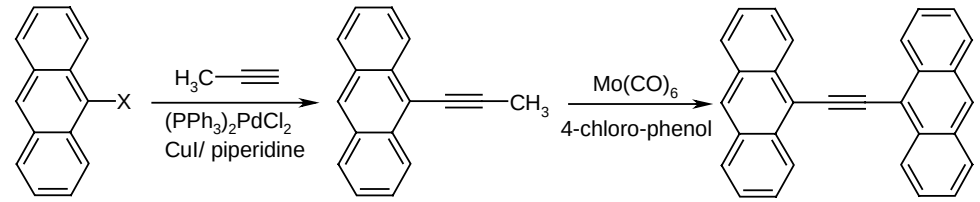
Scheme 4.24



tedicyp = cis,cis,cis-1,2,3,4-Tetrakis(diphenylphosphinomethyl)cyclopentane

Sonogashira conditions were used for coupling of bromo/iodo anthracene (4.**38**) with a measured quantity of propyne gas. Further, the product 4.**39** when reacted with $Mo(CO)_6$/ 4-chlorophenol in 1,2-dichlorobenzene catalyzes the dimerization of propynylated arene to give 4.**40** (Scheme 4.25).[39] However the yields are very low.

Scheme 4.25



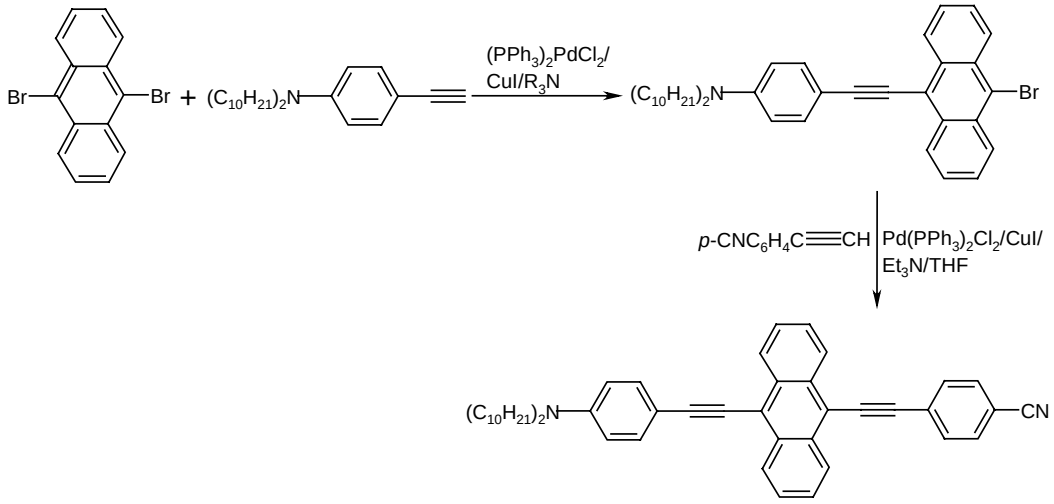
4.**38**
X = I or Br

4.**39**
5% yield

4.**40**
10% yield

A series of 9,10-bis(arylethynyl)anthracene derivatives (4.**41**) were synthesized under Sonogashira conditions and their two-photon absorption (TPA) cross sections were measured. One representative example is given in the Scheme 4.26.[40]

Scheme 4.26



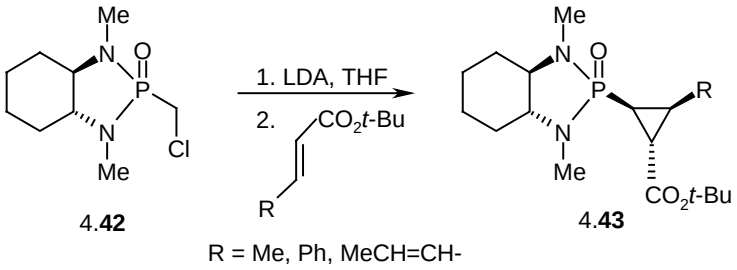
4.**41**
32% yield

4.5 Addition of phosphonates to α,β-unsaturated esters– Formation of cyclopropyl P substituted phosphonate derivatives

Conformationally constrained rings like cylcopropane have received particular attention due to their pharmalogical and biological activities.[41] The asymmetric synthesis of cyclopropanes has been a topic of considerable interest and challenge over the past two decades.[42] A novel method for the synthesis of fully functionalized cyclopropanes 4.**43** has been found by Hanessian based on *trans*-*N,N*-dimethyl-1,2-diaminocylohexane derived phosphonamide 4.**42**.[43] This involves the stereocontrolled synthesis of 1,2,3-trisubstituted cyclopropane phosphonic acids utilizing a method that capitalizes on the highly diastereofacial addition of the anion

of an α-chloromethylphosphonamide to an α,β-unsaturated ester as shown in Scheme 4.27. The intermediate α-chlorophosphonamide esters undergo intramolecular displacement by the incipient enolate to give the corresponding cyclopropanes. The additions to an α,β-unsaturated esters were highly diastereoselective, particularly when the γ-substituent was bulky or electronically biased. This method uses the rather expensive LDA.

Scheme 4.27

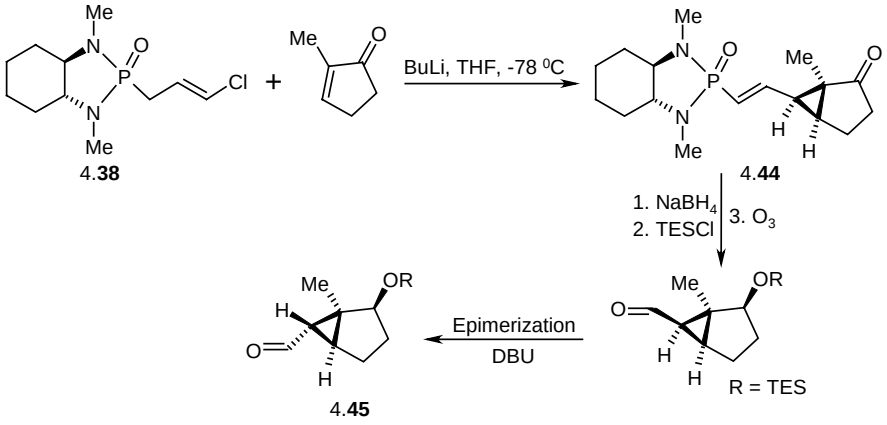


4.**42** 4.**43**

R = Me, Ph, MeCH=CH-

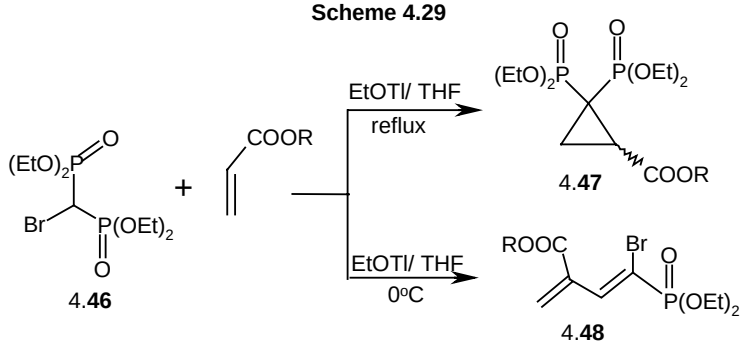
In a similar way, a versatile protocol for the synthesis of diastereomerically pure and highly enriched substituted cyclopropane derivatives (4.**44**) from *trans*-chloroallyl phosphonamide endowed with functional diversity was reported (Scheme 4.28).[44]

Scheme 4.28



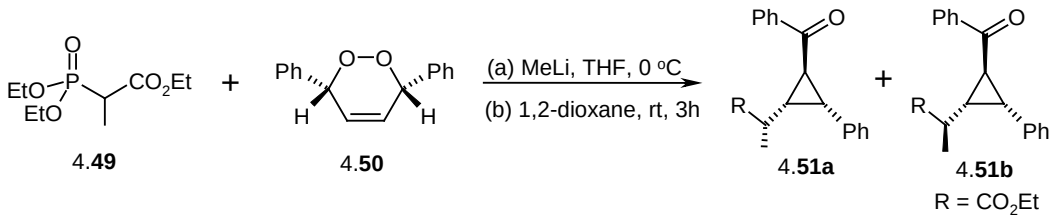
The reaction of bromomethylene bis(phosphonates) 4.**46** with electron deficient alkenes as Michael acceptors in the presence of thallium(I) ethoxide under refluxing condition leads to cyclopropanyl bis(phosphonates) 4.**47**, but at 0°C it gives mostly the monophosphonates 4.**48** (Scheme 4.29).[45]

Scheme 4.29



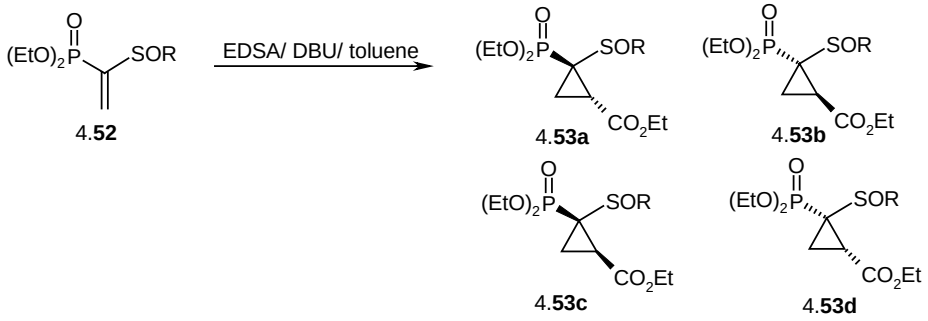
Stabilized ylides and 1,2-dioxines were used in the synthesis of diastereomerically pure tri-substituted cyclopropanes.[46] Recently, addition of stabilized HWE phosphonates (4.**49**) to substituted 1,2-dioxines (4.**50**) to lead to diastereomerically pure di- and trisubstituted cyclopropanes (4.**51**) in high yields has been reported (Scheme 4.30).[47] Thus, this route represents a viable alternative to the one using ylides.

Scheme 4.30



The reaction of 1-(diethoxyphosphoryl)vinyl *p*-tolyl sulfoxide with ethyl (dimethylsulfuranylidene) acetate (EDSA) was stereoselective (Scheme 4.31).[48] The reaction affords diastereomeric cyclopropanes with facial stereoselectivity and the stereochemical outcome is strongly dependent on the conditions used.

Scheme 4.31



In connection with above observations, it will be interesting to study the reaction of α,β-unsaturated esters with functionalized phosphonates, such as *α*-chlorophosphonates to see whether the reaction takes place in 1,4-Michael addition followed by cyclization to cyclopropyl derivatives) or 1,2-fashion.

Objectives of the present work

The objectives of this part of the work are given below:

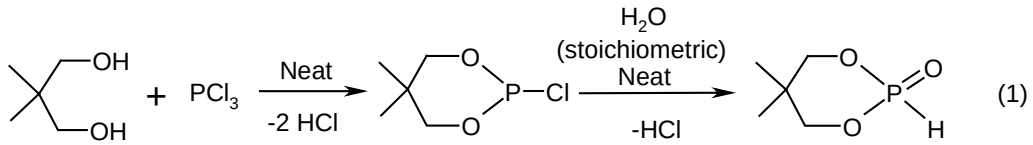
1) To transform α-hydroxyphosphonates to α-bromophosphonates,
2) To synthesize anthracenyl substituted alkenes by HWE reaction *via* the reaction of a suitable phosphonate with an aldehyde,
3) To synthesize cyclopropyl phosphonates from the reaction of α-chlorophosphonates with α,β-unsaturated esters, and
4) To synthesize N-alkylated adenine derivatives using Mitsunobu protocol for further use in phosphonylation reactions.

CHAPTER 5

RESULTS AND DISCUSSION

5.1 Synthesis of phosphites

This part of the present work is essentially based on the key precursor $(OCH_2CMe_2CH_2O)PCl$ (**1**) which has a six-membered 1,3,2-dioxaphosphorinane ring.[49] In the present study, **1** was prepared by treating 2,2-dimethyl-1,3-propanediol with phosphorus trichloride under neat conditions (eq. 1). As is the case with many P^{III} compounds containing a residual P-Cl bond, **1** can be readily hydrolyzed by water to give the H-phosphonate **2** (eq. 2). Compound **2**, although can be distilled in vacuum, was used as such for further reactions in the present study without any difficulty, thus making it comparable in cost to the commercially available diethylphosphite $(EtO)_2P(O)H$.



1
[b.p. 40°C/ 1mm, δ(P) 145.8]
Yield: 85 - 95%

2 [δ(P) 2.3]
Yield: Quantitative

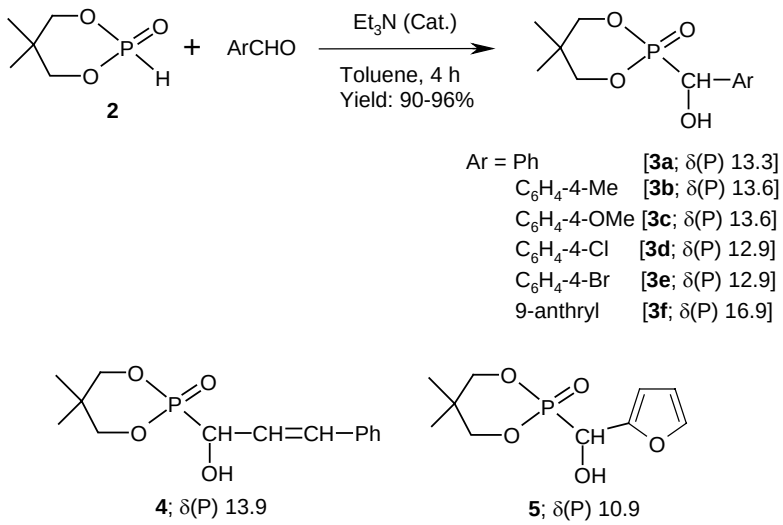
(1)

5.2 Synthesis of phosphonates

5.21 Synthesis of α-hydroxyphosphonates

The α-hydroxyphosphonates **3a-f,** have been synthesized by the route developed from our laboratory from the reaction of **2** with aromatic aldehydes (Pudovik reaction) (Scheme 1);[8,36] compounds **4** and **5** are also similarly obtained by treating **2** with cinnamaldehyde and furfuraldehyde respectively. Compound **3e** is new.

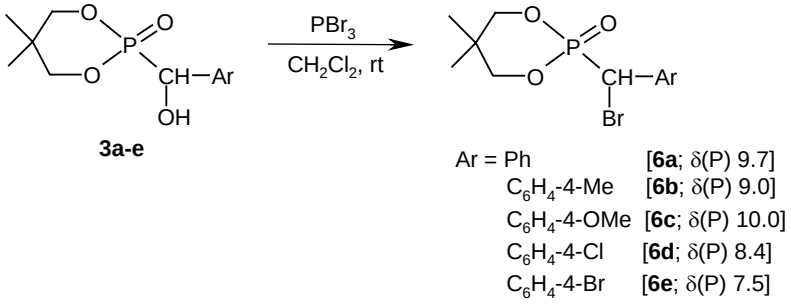
Scheme 1



5.22 Synthesis of bromophosphonates

Treatment of α-hydroxyphosphonates **3a-e** with phosphorus tribromide (PBr_3) using dichloromethane as the solvent at room temperature afforded the α-bromophosphonates **6a-e** (Scheme 2) in high yields (80-90%).

Scheme 2

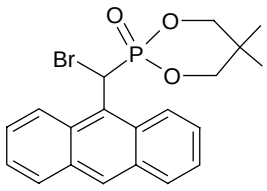


Compounds **6a-e** are air stable solids. It is likely that the presence of the six-membered ring in our systems has facilitated the high yields. This procedure is much superior to the preparation of various types of α-bromophosphonates using PPh_3/ DDQ system in the presence of tetraalkylammonium bromide with regard to the isolation of products.[9] Also, DDQ is quite expensive. The $Ph_3P(O)$ side product formed in the latter reaction is not water-soluble and requires chromatography to isolate the pure products. The other disadvantage of the literature procedure is that the R_f value (TLC) of the phosphine oxide formed in the reaction is close to that of

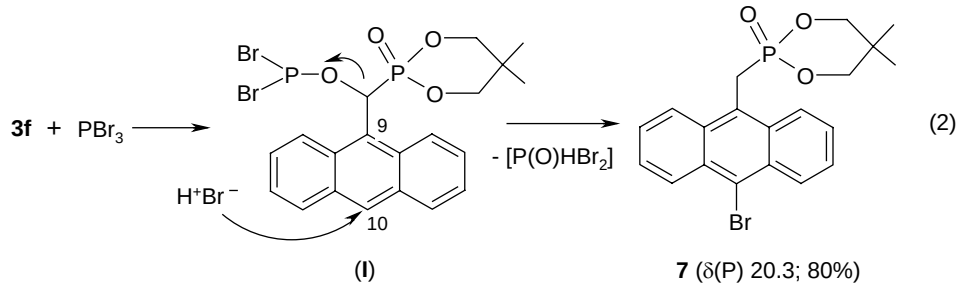
phosphonate **6a** and hence isolation of pure product is hampered. In our route, isolation of products is very easy as the side products formed are water-soluble and can be removed by a thorough water wash of the organic layer. Isolation of the pure product does not require column chromatography. In addition, the PBr_3 route gave better yields of phosphonates than the one using thionyl bromide previously reported from our laboratory.[8] Cost-wise, both PBr_3 and $SOBr_2$ are comparable, but the former is more readily available than the latter; only one caution that is to be exercised is that both of these reagents are moisture sensitive and hence require dry atmosphere.

The ^{31}P NMR spectra of **6a-e** showed peaks upfield to α-hydroxyphosphonates (*cf.* Scheme 1 and 2), and the peaks are in the expected region compared to those for similar compounds prepared from our laboratory using the thionyl bromide ($SOBr_2$) route.[8] The ^{1}H NMR spectra of these compounds exhibit a characteristic peak at δ ~ 5.0 as a doublet for P-C*H*Br due to ^{2}J(P-H) coupling; similarly P-*C*HBr carbon appears as a doublet at δ ~ 40.0 in the ^{13}C NMR. In the case of **6b**, we obtained a single peak [δ(P) 9.0], which is unlike that for the products using thionyl bromide which showed two isomers [δ(P) 9.0 (major), 8.5 (minor), possibly due to the different disposition (axial or equatorial) of the substituents in the dioxaphosphorinane ring].[8]

When the anthracenyl substituted phosphonate **3f** was brominated with PBr_3, instead of the expected α-bromophosphonate **6f**, we obtained phosphonate **7** with the -Br group at C-10 position of the anthracene moiety (eq. 2). Formation of **7** probably occurs by the attack of the Br^- at C-10 of the anthracene ring *via* an intermediate of type **I**, instead of attack at the carbon α to phosphorus (*cf.* Scheme 2). The P-CH_2 protons of **7** exhibited a characteristic doublet at δ 4.37 (Figure 1) in the ^{1}H NMR spectrum and the corresponding carbon appeared as a doublet at 27.1 [^{1}J (P-C) = 137 Hz] in the ^{13}C NMR.



6f (**Not obtained**)



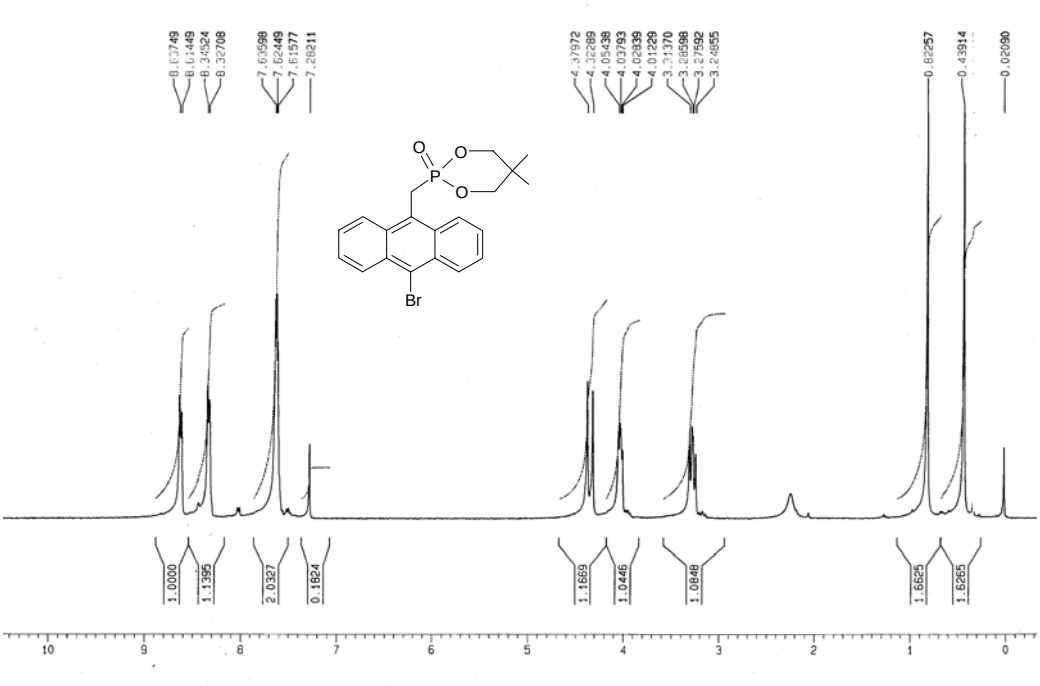
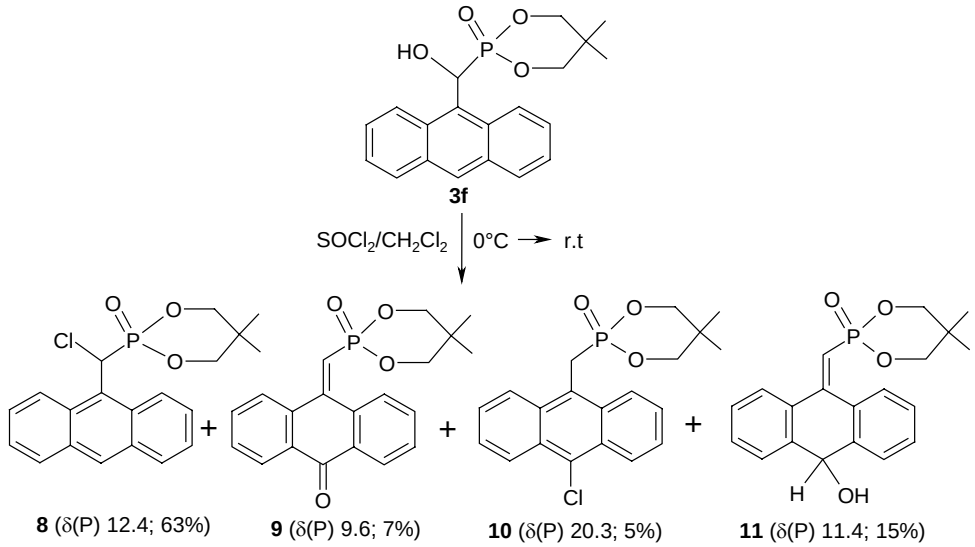


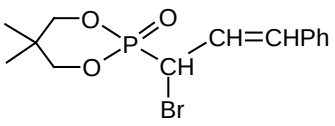
Fig. 1. ^{1}H NMR spectrum of compound **7**

It is interesting to note that when **3f** was treated with thionyl chloride ($SOCl_2$) by my colleague, it gave rise to four distinct products **8**-**11** (Scheme 3) including the α-chloro and 10-Cl phosphonates that were separated by column chromatography.[50] Even with PCl_3, the same products, albeit in a different ratio, were observed. Thus the bromination and chlorination reactions of α-hydroxyphosphonates appear to lead to different arrays of products.

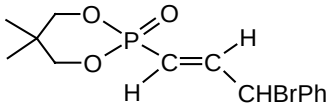
Scheme 3



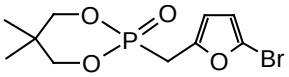
In contrast to the above, the reaction of cinnamyl compound **4** with PBr_3 leads to two products **12** and **13** [δ(P) 8.8 and 10.8] corresponding to α- and γ-bromophosphonates respectively. Formation of brominated products at a position different from α to the phosphorus was also observed in the case of furfuryl system (e.g. **14**), but this product is not a γ-bromophosphonate. The structures of compounds **12** and **13** are proven by NMR spectroscopy. The ^{1}H NMR spectrum of **12** showed a characteristic multiplet at δ 4.77 corresponding to P-C*H*(Br) while **13** exhibited a multiplet at δ 5.94 for the P-C*H*=C proton, with the expected integrated intensities. Also, in the ^{13}C NMR spectrum [Figure 2], compound **13** shows a doublet at δ 117.2 [^1J(PC) = 185.6 Hz] for the P-*C*H carbon that is much downfield to that observed for **6a-e** [δ ~ 40]. The NMR spectra of **13** is comparable to that of the chloro analogue ($OCH_2CMe_2CH_2$)P(O)CH=CH-CH(Cl)Ph (**15**), the structure of which was proved by the X-ray crystallography.[36] It may be noted that the reaction of **4** with thionyl bromide is reported to give two products [δ(P) 6.4, 12.5] in the earlier literature, but no pure product could be isolated.[8]



12 [δ(P) 8.8]



13 [δ(P) 10.8]



14 [δ(P): 18.1]

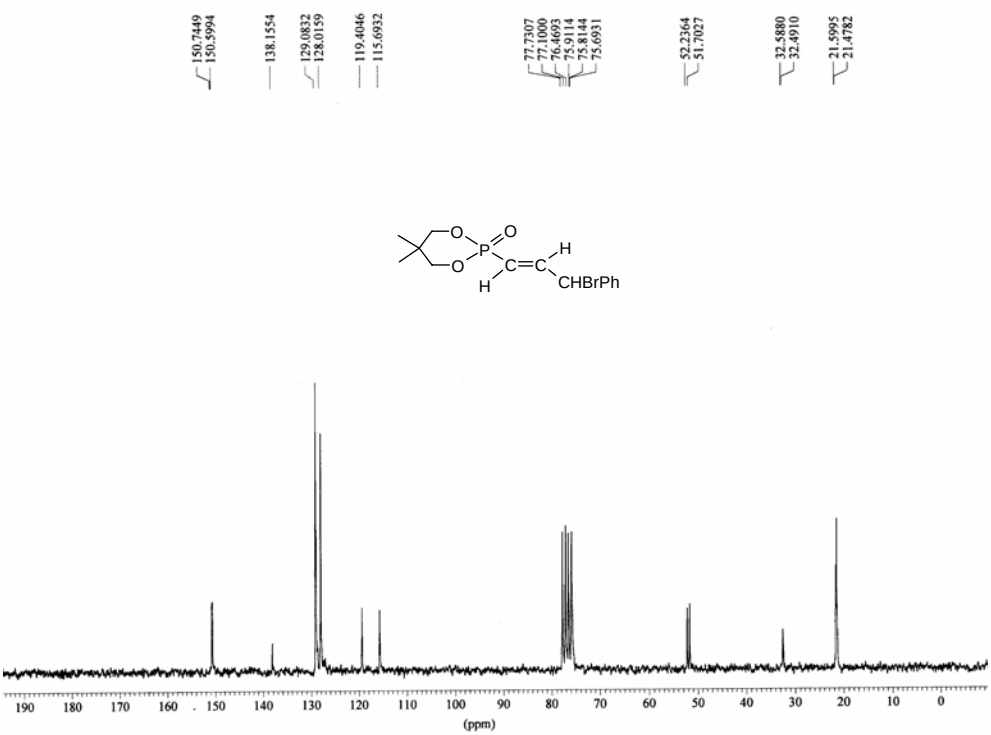
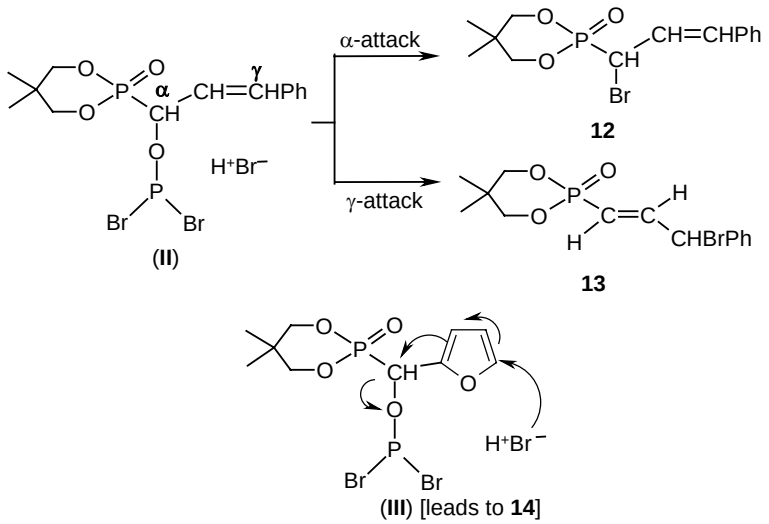


Fig. 2. The ^{13}C NMR spectrum of compound **13**

The ^{1}H NMR spectrum of compound **14** showed a doublet at δ 3.38 for the P-CH_2 proton clearly showing that it is not an α-bromophosphonate; also, consistent with the proposed structure, only two aromatic protons are observed.

A possible pathway for the formation of **12** and **13** via the intermediate (**II**) is given in Scheme 4. The proposed γ-attack is similar to that shown in eq. 2 for the formation of the anthracene derivative **7**. Formation of **14** also would involve a similar intermediate (**III**). Overall, the species [Br_2P(O)H] (which possibly undergoes further hydrolysis during work-up] is also eliminated.

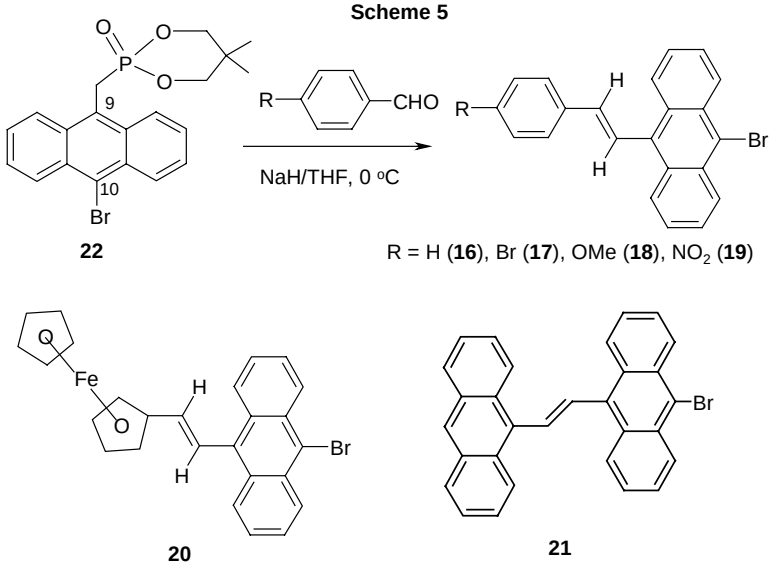
Scheme 4



5.3. Synthetic Utility of phosphonates

As discussed in the introductory chapter 4, we were interested in systems possessing anthracenyl residue [for exploring their photochemical properties later]. One of the ways by which anthracenyl group can be introduced is by using the Horner-Wadsworth-Emmons (HWE) reaction *via* a suitable phosphonate with an aldehyde. In this context, when HWE reaction was performed using 10-bromoanthracenyl substituted phosphonate **7** with various aldehydes, the alkenes **16-19** with anthracenyl moiety were obtained in good yields. The ferrocenyl alkene **20** could also be prepared readily (Scheme 5). When anthraldehyde was used, we were also able to isolate the 1,2-bis(9-anthryl)ethylene (**21**), *albeit* in low yields. Compounds of type **21** (but without the bromine substituent at the 10th position were prepared earlier by coupling anthraldehyde using a titanium reagent.[35] Our route represents the first example utilizing the HWE reaction and offers scope for extending the conjugation *via* coupling using the 10-bromo substituent.

Scheme 5



The ^{1}H NMR spectrum of **21** showed a characteristic peak at δ 6.90 with ^{3}J(H-H) of 16.0 Hz for the olefinic proton PhC*H*=CH(9-anthryl) showing that the phenyl and anthryl group are *trans* (*E*-isomer) to each other. This feature is in line with the general HWE reaction wherein *E*-products are the predominant isomers.[17] The other alkene proton connected to the anthryl ring appears more downfield along with the aromatic protons. The ^{1}H NMR spectrum of **16** is shown in Figure 3.

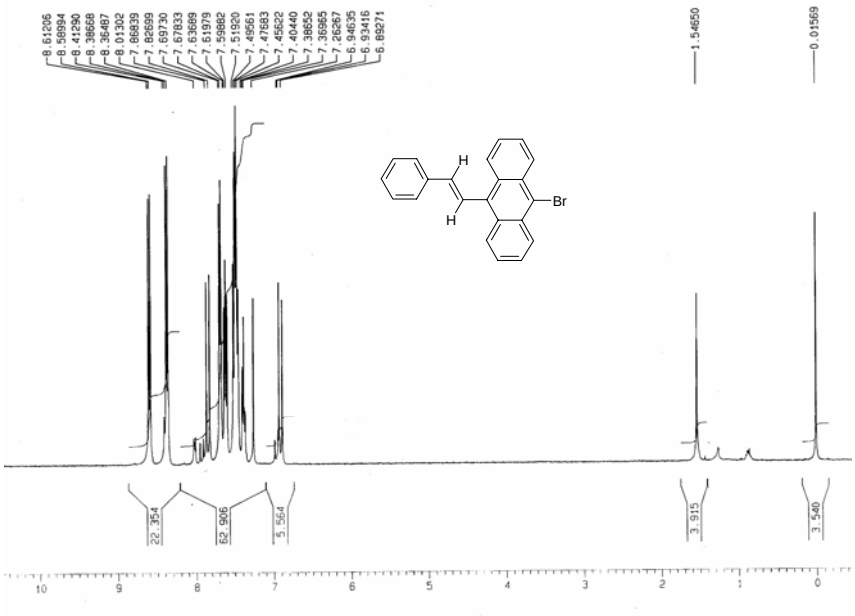


Fig. 3. The ^{1}H NMR spectrum of compound **16**.

The X-ray structure of the HWE product **18** [Figure 4] also confirms unambiguously the location of bromine at the C-10 of anthracene ring in its precursor **7**. It may be noted that a specific route for anthracenyl substituted alkenes involving a 4,4'-dimethyl-2,2'-bipyridyl ligand by the dehydration of the precursor alcohol is reported recently.[31b] Our route offers a general entry to a large number of alkenes with anthracenyl residue.

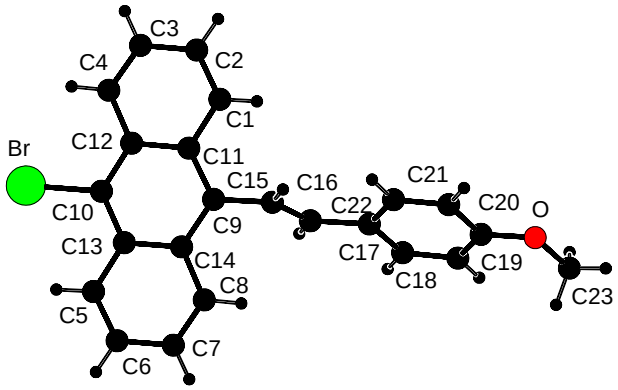
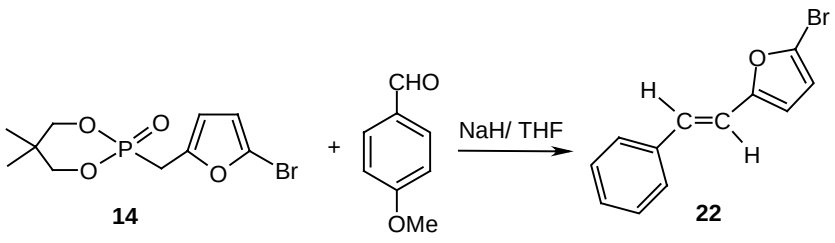


Fig.4. A PLATON drawing showing the molecular structure of compound **18.**

In the context of utility of phosphonates synthesized in the present work, when 5-bromofurfuryl phosphonate **14** was reacted with anisaldehyde, we obtained the olefin **22** as the *E* isomer (Scheme 6). The ^{3}J(H-H) value of the *trans*-olefinic protons is 16.0 Hz, as expected.

Scheme 6

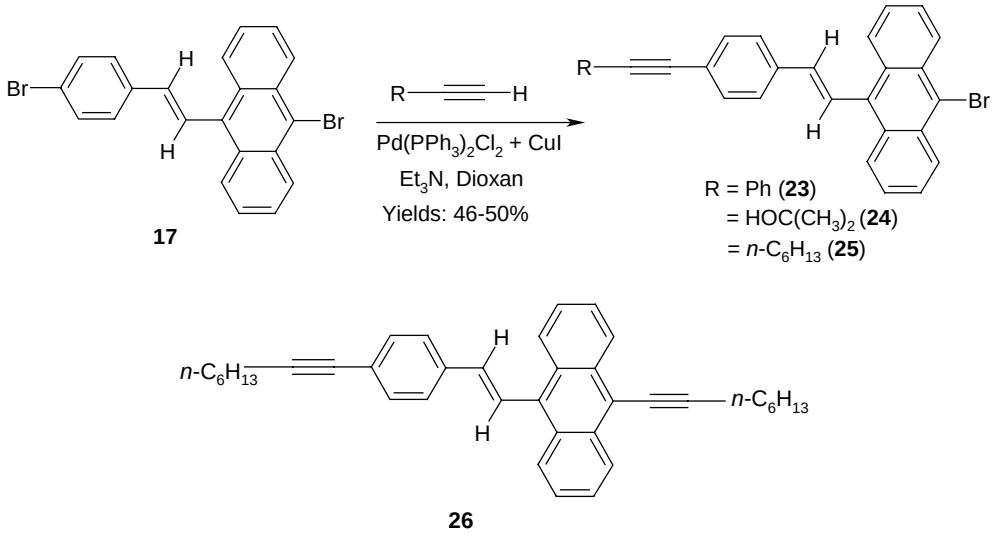


5.4. Sonogashira coupling of compound 17 with terminal alkynes

In continuation of our work on anthracenyl compounds with extended conjugation, we noted that Sonogashira coupling of arylbromides with terminal

alkynes is one of the convenient routes that can lead to such derivatives. Towards this end, we treated the bromoaryl substituted alkene **17** with the acetylenes PhC≡CH, (HO)$(CH_3)_2$CC≡CH and *n*-C_6H_{13}C≡CH under Sonogashira conditions[51] and obtained the coupled products **23**-**25** in decent yields (Scheme 7). As is common with most palladium-catalyzed reactions, the presence of an -OH group did not pose any problem (cf. compound **24**). In the reaction using PhC≡CH, we isolated only the mono-coupled product **23** while that using *n*-C_6H_{13}C≡CH afforded both the mono- (**25**) and the bis-coupled (**26**) products, although the yield of the latter was quite low. We have not made attempts to maximize the yields, but the results clearly demonstrate the utility of the bromoanthracenyl alkenes prepared in this work.

Scheme 7



The ^{1}H NMR spectrum of **23** does not differ much from its precursor in the aliphatic region, as there is no extra proton in the aliphatic region. But the ^{13}C NMR spectrum of **23** clearly showed two peaks at δ 86.6 and 101.3 corresponding to the acetylinic carbons (Figure 5).

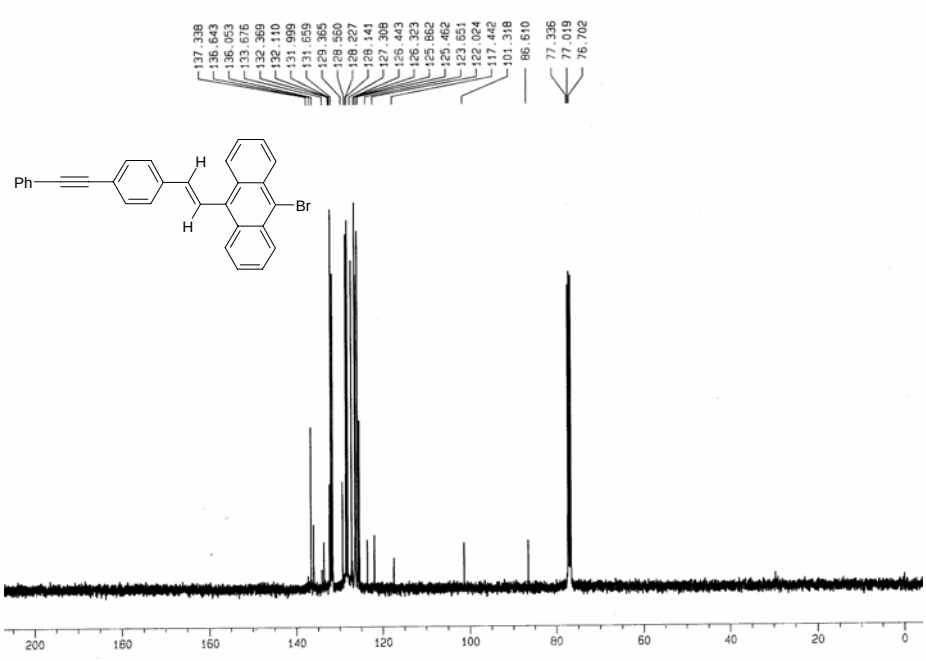


Fig. 5. ^{13}C NMR spectrum of compound **23**

As the compounds **23-25** have bromine substituents, they must have two peaks at [M] and [M+2] of almost equal in intensity because of ^{79,81}Br isotopes. For compound **26** as there is no bromine atom, we have no [M+2] peak. The details of the mass spectra are given in Table 1.

Table 1. Mass spectrometric details of compounds **23-26**

Compd	m/z
23	459 [M], 461 [M+2]
24	423 (M-18), 425 [(M-18)+2]
25	467 [M], 469 [M+2]
26	497 [M]

5.41 Fluorescence spectroscopy of anthracenyl derivatives

As mentioned above, we were interested to study the fluorescence behavior of compounds **20** and **23-26** that have anthracene as the fluorophore moiety. We have recorded the steady state absorption and emission spectra for all these compounds in a non-polar solvent cyclohexane and in a moderately polar solvent acetonitrile (Figures 6 and 7). The absorption maxima for all these compounds in cyclohexane and acetonitrile (having different polarities) did not change much (see

Table 2). But in compound **20** there is an additional broad hump in the absorption spectrum, in both the solvents, which starts at 550 nm and extends up to 450 nm.

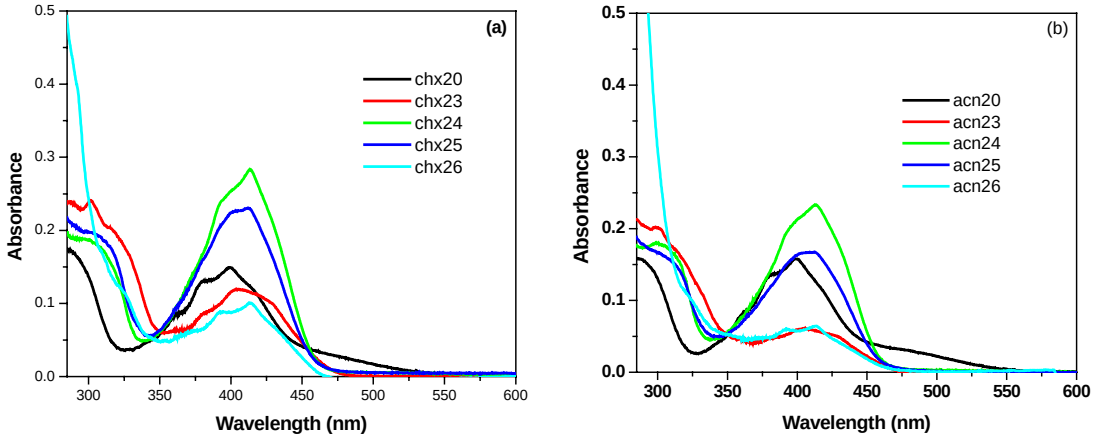


Fig 6. Absorption spectra for compounds **20** and **23-26** in cyclohexane (a) and acetonitrile (b).

Table.2 Absortion and emission maxima of **20** and **23-26** in cyclohexane and acetonitrile.[a]

Compd.	λ_{max}^{abs}		λ_{max}^{fluo}	
	Cyclohexane	Acetonitrile	Cyclohexane	Acetonitrile
20	362, 380, 400, 416	362, 380, 400	No observable emission	No observable emission
23	360, 380, 405, 429	380, 405, 429	436, 522	437, 466, 544
24	393, 413, 430	393, 413, 430	506	514
25	380, 400, 412	401, 413	518	518
26	374, 393, 414	372, 392, 413	419, 445, 518	419, 445, 519

[a]Wavelength maximum values are in nm.

Although compound **20** has significant absorption at 400 nm, it did not show any considerable emission. Compound **23** has a dual emission, one anthracene type structured band around 420-430 nm and another broad band around 505-520 nm. Anthracene type structured band did not show Stokes shift on changing the polarity (cyclohexane to acetonitrile), but the broad band shows 10-20 nm Stokes shift on changing the polarity This phenomenon is indicative of charge transfer nature of the species responsible for this broad emission.

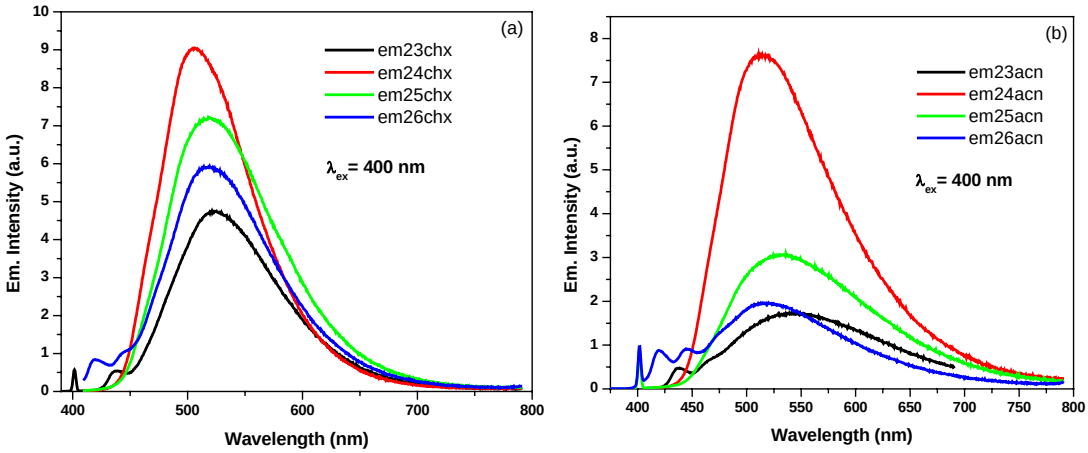


Fig.7. Emission spectra for compounds **23-26** in cyclohexane (a) and acetonitrile (b).

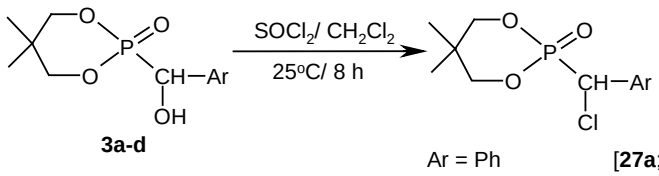
Compounds **24** and **25** show a single emission band; the anthracene type band as observed in the case of **23** is not so clearly observable, but there is a broad charge transfer band (above 500 nm) that shows 10-12 nm Stokes shift on changing the polarity from cyclohexane to acetonitrile. Compound **26** showed dual emission but in contrary to what is observed in **23**, the broad emission band at 518 nm did not show any Stokes shift on changing the polarity. Further studies on similar compounds having different electron donating groups at one end are on the way to understand convincingly the origin of the dual emission for these types of molecules.

5.5. Synthesis of cyclopropyl phosphonates from α-chloro/ bromo phosphonates

Synthesis of α-chlorophosphonates

The α-chlorophosphonates (**27a-d**) have been synthesized from α-hydroxyphosphonates (**3a-d**) by the route developed in our laboratory (Scheme 8).[8]

Scheme 8

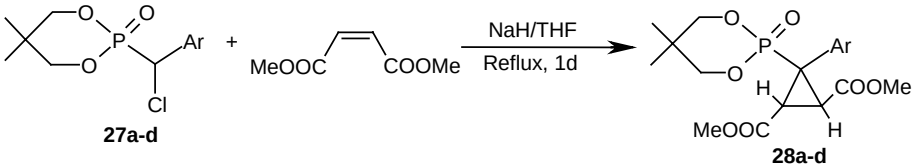


Ar = Ph [**27a**; δ(P) 8.1]
C_6H_4-4-Me [**27b**; δ(P) 8.4]
C_6H_4-4-OMe [**27c**; δ(P) 8.4]
C_6H_4-4-Cl [**27d**; δ(P) 7.5]

Reaction of α-chlorophosphonates with dimethyl maleate

Taking cue from the synthesis of fully functionalized cyclopropanes based on *trans*-*N*,*N*-dimethyl-1,2-diaminocylohexane derived phosphonamide,[43] we were interested in studying the conjugate addition of anions derived from α-chlorophosphonates to α,β-unsaturated esters. In this regard, when α-chlorophosphonates **27a-d** were treated with NaH in THF followed by addition of dimethylmaleate under refluxing conditions we obtained the cyclopropylphosphonates **28a-d**. This reaction takes place via a Micheal addition followed by an intramolecular expulsion of the chlorine to give the cyclopropyl phosphonates (Scheme 9, Table 3).

Scheme 9



Mechanism

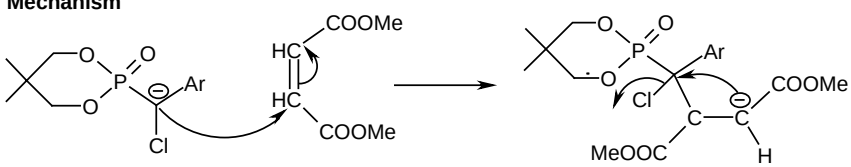


Table 3. ^{31}P NMR data and yields for **28a-d**

Entry	Compd	Ar	δ(P)	Yield (%)
1	**28a**	Ph	15.4	65
2	**28b**	4-Me-C_6H_4	15.4	60
3	**28c**	4-MeO-C_6H_4	15.8	66
4	**28d**	4-Cl-C_6H_4	15.0	60

Compounds **28a-d** are air-stable solids. The ^{31}P NMR spectrum of each of these compounds shows a single peak at δ ~15.0. The ^{1}H NMR spectra exhibit two characteristic multiplets around δ 3.00 and 3.30 corresponding to the C(*H*)(COOMe) proto of the cyclopropyl moiety (Figure 8). The ^{13}C NMR spectra showed a characteristic doublet at δ 35.0 [d, ^{1}J(PC) ~ 186.0 Hz] for the α-carbon attached to the phosphorus (Figure 9).

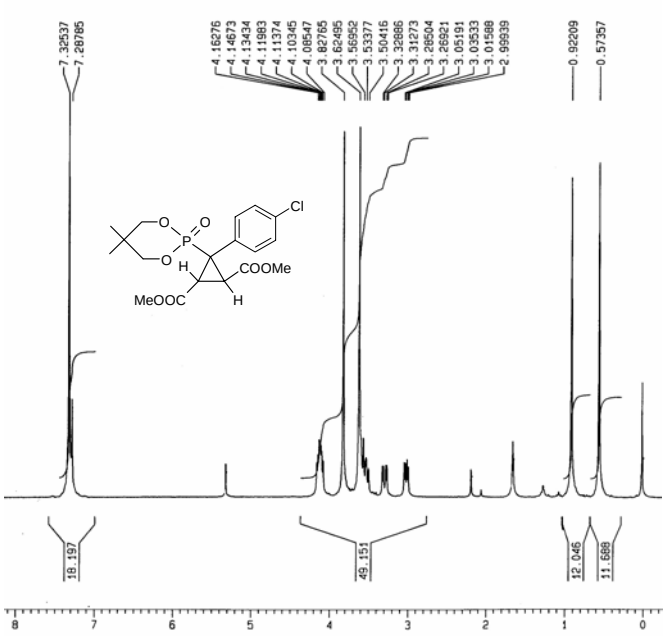


Fig. 8. The ^{1}H NMR spectrum of compound **28d**

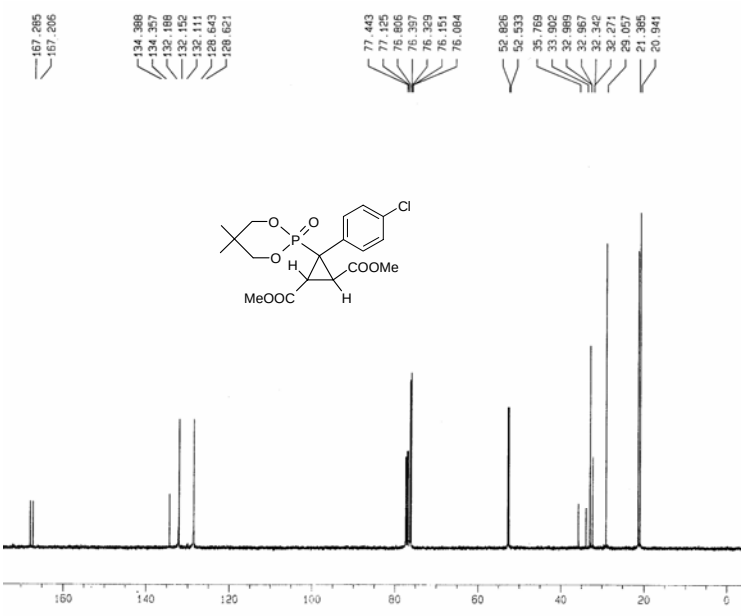


Fig.9. The ^{13}C NMR spectrum of compound **28d**

It can be noted that as per the proposed mechanistic pathway shown in Scheme 9, *cis* and *trans* isomers can be formed in the above reaction. We had obtained a single isomer in our reaction [^{31}P NMR evidence]. Since the protons are attached to two saturated cyclopropyl carbons and are coupled to phosphorus, assignment of configuration is not straightforward. Hence the structure of compound **28c** was confirmed by X-ray crystallography (Figure 10). The *trans*- configuration of the two CO_2Me groups can be readily recognized from the ORTEP drawing.

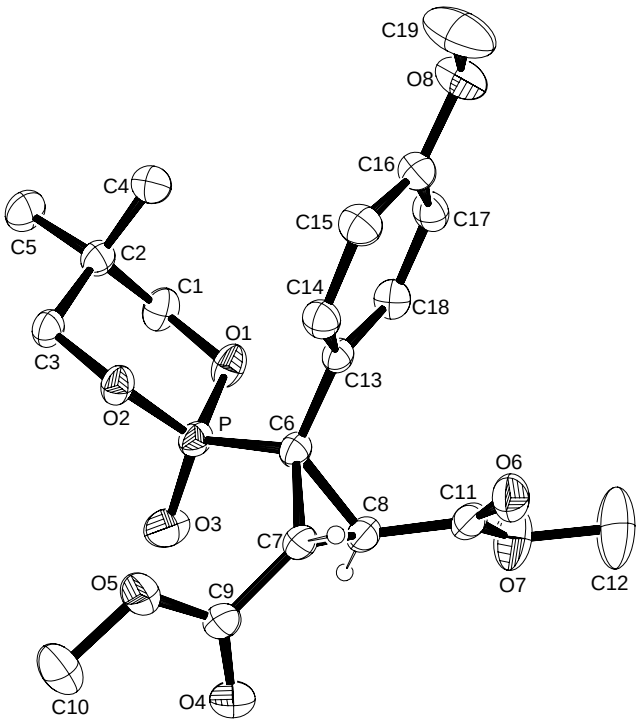
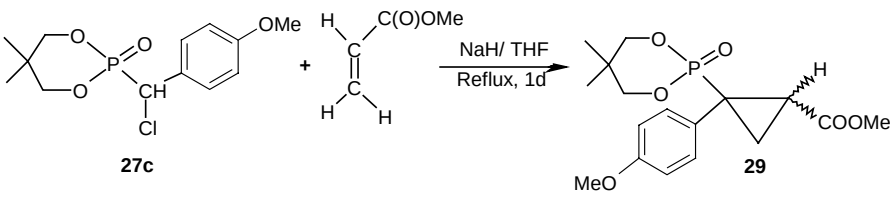


Fig. 10. Molecular structure of **28c** showing the numbering scheme.

The NMR details of the above compounds are analogous to those of similar cylcopropyl compounds synthesized in our laboratory from the reaction of α-chlorophosphonates with alkyl acrylates (instead of dimethyl maleate). One such example with methyl acrylate is given in Scheme 10.[52] Since we had access to the corresponding α-bromophosphonates **6a-d**, we wanted to compare the reactivity of the chloro- and bromo-phosphonates. Thus we treated α-bromophosphonate **6c** with methyl acrylate under similar conditions. The reaction was complete within 5-6 h compared to chloro phosphonates, which took 24 h for completion. Both the precursors gave cyclopropyl phosphonate (**29**) in modest yields. The structure of **29** was also established by X-ray crystallography (Figure 11)

Scheme 10



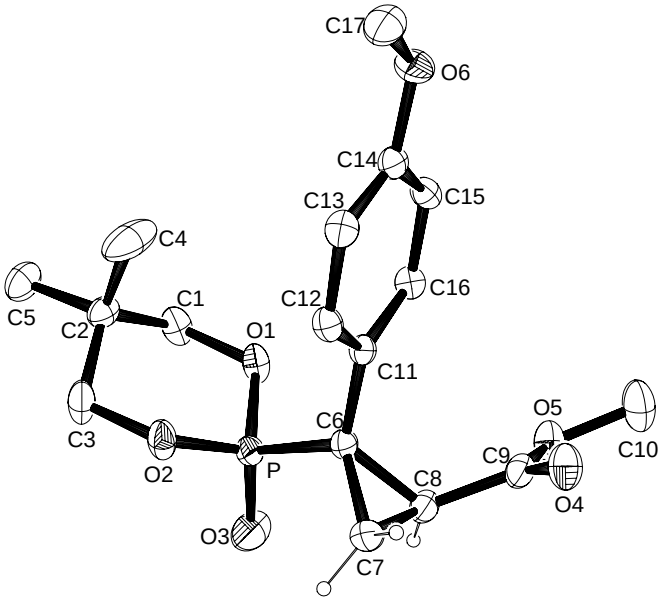


Fig. 11. Molecular structure of compound **29**

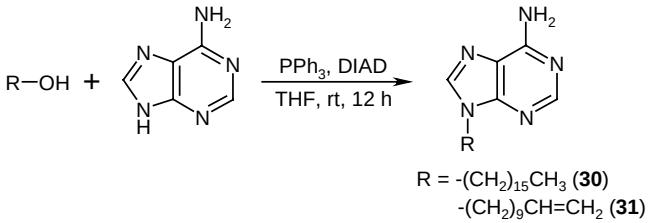
5.6. Synthetic utility of Mitsunobu reaction in phosphonate chemistry

In addition to probing the mechanistic aspects of the Mitsunbu reaction (*cf*. Chapter 1) we were also interested in using this reaction for alkylation of adenine. The final target was to use this to prepare compounds with a terminal double bond to be utilized for catalytic phosphonylation that could show interesting biological activity. In the literature, to alkylate adenine, the corresponding alkyl alcohol is generally converted to the bromide and then is coupled with adenine in presence of a base.[53] The advantage of the Mitsunobu protocol is that we can directly synthesize regioselective N-9 alkylated product using unprotected adenine in one pot synthesis under mild conditions.

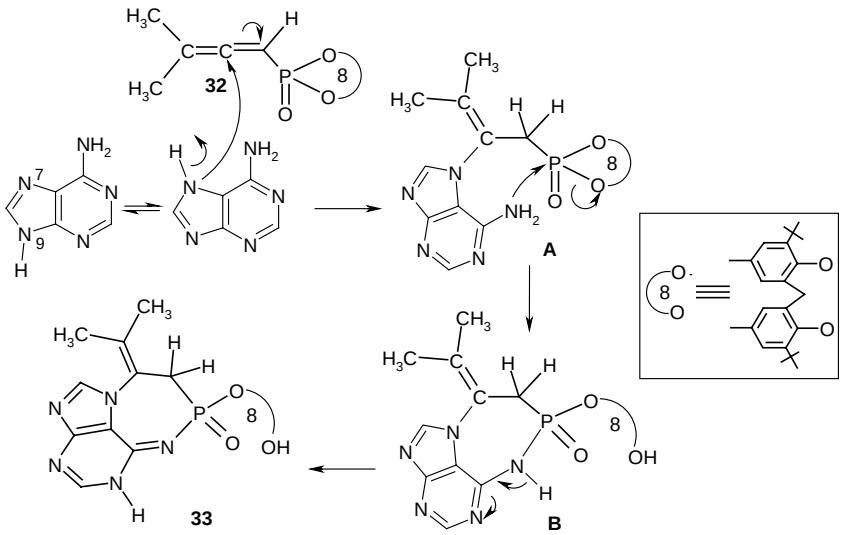
In the above context, we obtained the alkylated adenine derivatives **30** and **31** respectively in moderate yields by treating cetyl- or undecenyl-alcohol with adenine in the presence of PPh_3 and DIAD in THF at room temperature (Scheme 11). The products could be easily separated by column chromatography. The ^{1}H NMR spectrum of **30** exhibited peaks at δ 0.87 and 4.19 (triplets each) for -$(CH_2)_{15}CH_3$ and -N-$CH_2(CH_2)_{14}CH_3$ protons; it also showed two peaks at 7.79 and 8.37 characteristic of adenine protons. The ^{13}C NMR spectrum of **30** showed peaks at δ 44.0 for N-CH_2- and 119.7, 140.4, 150.1, 152.9 and 155.5 corresponding to adenine carbons. The spectral details of compound **31** are consistent with those

available in the literature.[53b-c] In most cases, the N-9 alkylated products are formed and attack at N-7 are rare; an example of the latter type was observed in our laboratory in the formation of unusual ring compound **33** from the reaction of a phosphorylated allene **32** and adenine where initial attack occurs at N-7 of adenine followed by cyclization involving the attack of the adenine-NH_2 (Scheme 12).[54]

Scheme 11



Scheme 12



The structure of compound **30** is proven by X-ray crystallography (Figure 12). Molecules of **30** in the crystal are held by N–H…N hydrogen bonds involving the two hydrogen atoms of the N(5) with N(2) and N(4). These N–H…N interactions are mainly responsible for the formation of two dimensional zig-zag tapes. This feature is similar to the one observed earlier for an analogous compound.[53b] Since the molecule contains a long hydrophobic chain and a hydrophilic polar head, it may behave in a manner similar to that of micelle, where polar heads come together connected by hydrogen bonds and the hydrophobic chains are held by weak van der Waals interactions. It is interesting to note that the monosubstituted adenyl phosphonate **34** synthesized in our laboratory is a hydrogen bonded dimer (Fig. 13).[54] We ascribe this difference to the accessibility of hydrogen

bonding partners (which s less in **34**); the hydrogen bond involving the nitrogen of the six-membered ring of the adenyl group is absent in **34**.

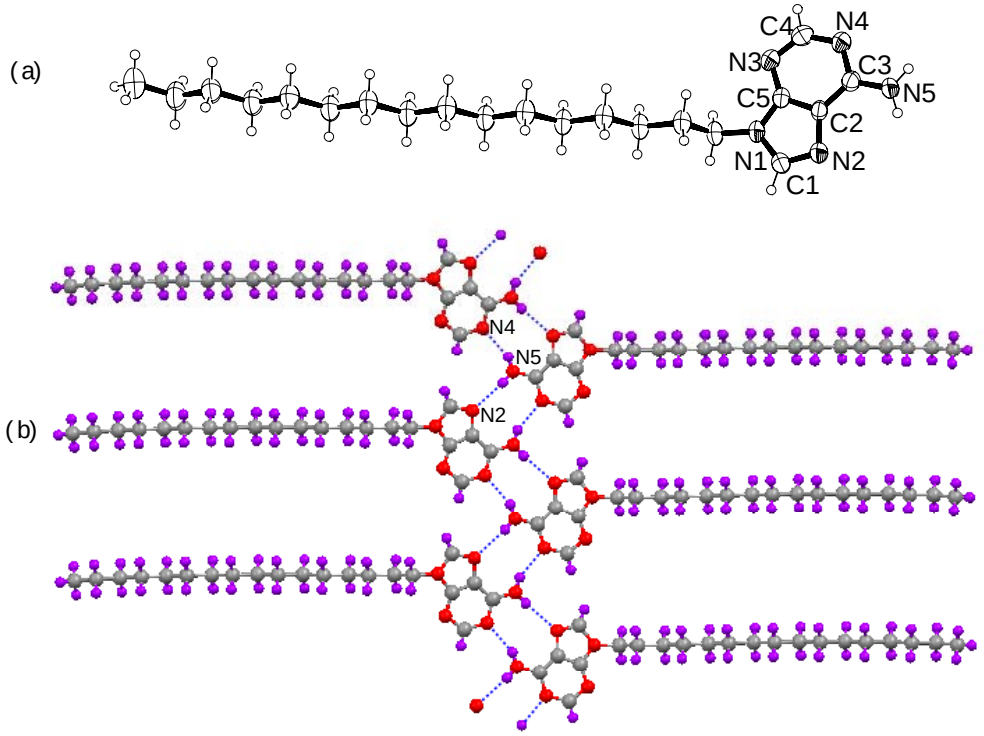


Fig. 12 (a) An ORTEP drawing of **30** showing the numbering scheme on selected atoms. Adenine ring numbering is also shown. (b) Diagram showing the hydrogen bonding pattern involving N–H···N atoms in **30**. Hydrogen bond (D-H…A) parameters; N(5)-H(5A)…N(2') 0.86, 2.29, 3.119(2)Å, 162.7°; N(5)-H(5B)…N(4') 0.86, 2.17, 2.971(3)Å, 154.1°.

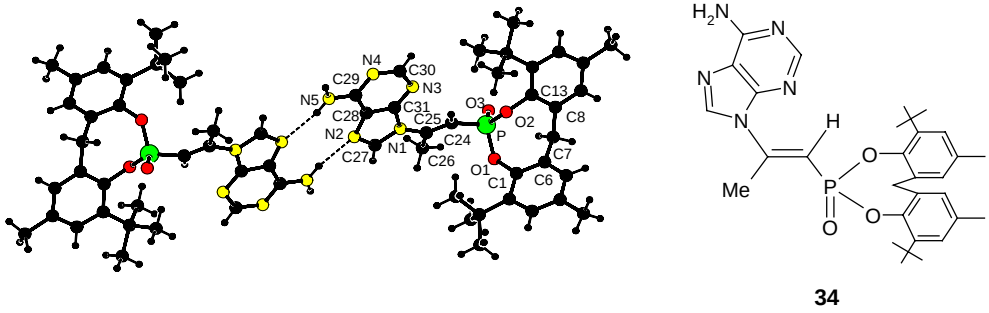
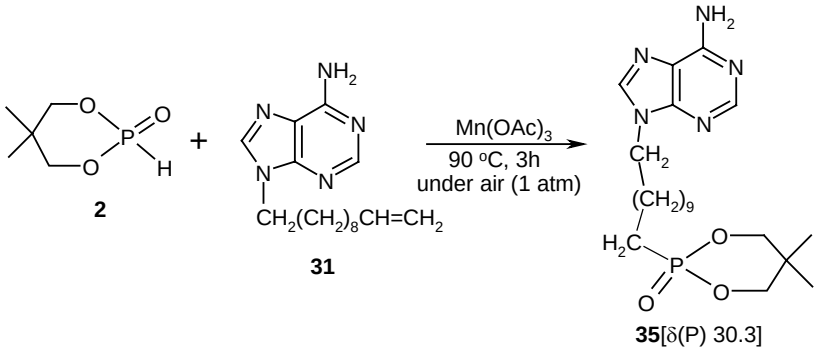


Fig. 13. Molecular structure of **34** showing the *dimeric* formulation; on the right is shown the conventional drawing of the molecule. Relevant hydrogen bond (D-H…A) parameters: N5-H5A…N2' 0.90(3), 2.09(3), 2.940(4) Å, 157(3)°

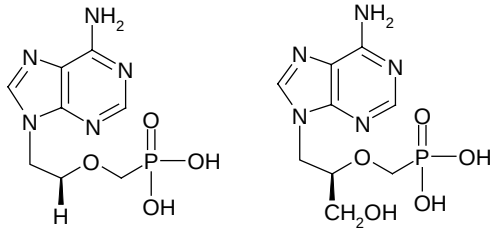
In the literature, an efficient method for hydrophosphorylation of alkenes and alkynes with dialkyl phosphites in presence of $Mn(OAc)_3$ in air was demonstrated by Ishii *et al*.[55] We did hydrophosphorylation using the H-phosphonate **2** on alkene **30** using similar conditions (Scheme 13) and isolated the phosphorylated product **35**.

Scheme 13



2 **31** **35**[δ(P) 30.3]

The ^{1}H NMR spectrum of **35** showed peaks at δ 0.96 and 1.17 (singlet each), 3.72-3.79 (m) and 4.25-4.29 (m) corresponding to the 1,3,2-dioxaphosphorinane ring. The protons attached to the α-carbon to phosphorus (PC*H*$_2$) appear as a multiplet that is merged with the other aliphatic protons. The ^{31}P NMR spectrum of **35** shows a peak at δ 30.3. Although we have not been able to get single crystals of this compound, it is worth noting that such a compound could have potential biological activities (say for example, as an anti-HIV agent; these studies are planned under collaboration for the future). Compounds **36-37** are two such adenyl phosphonates that are active as anti-HIV agents.[56]



36 **37**

5.7. Summary

1) A better and convenient chromatography-free synthesis of α-bromophosphonates (**6a-e**) from the reaction of α-hydroxyphosphonates with phosphorus tribromide in high yields has been developed. Bromination of **3f** (anthracenyl hydroxyphosphonate) with phosphorus tribromide afforded the bromophosphonate **7** with bromine at the 10^{th} position of anthracenyl moiety. In contrast, the reaction of **4** with phosphorus tribromide leads to two products, the α- and γ-bromophosphonates **12** and **13**.

2) The bromophosphonate **7** has been used in the HWE reaction with various aldehydes leading to a large number of alkenes with anthracenyl residue. Utility of the bromoanthracenyl alkenes thus obtained has been shown by the synthesis of anthracenyl alkenes with extended conjugation by treating them with terminal acetylenes under Sonogashira conditions.

3) A facile synthesis of cyclopropyl phosphonates from the reaction of α-chlorophosphonates with dimethyl maleate in the presence of sodium hydride has been accomplished. Here the reaction takes place via a Michael addition of dimethyl maleate to the phosphonate carbanion, followed by expulsion of the chloride ion, to give the cyclopropyl phosphonates.

4) A Mitsunobu protocol was used for synthesis of N-9 alkylated adenine derivatives **30** and **31.** The terminal double bond in compound **31** underwent hydrophosphorylation with $(OCH_2CMe_2CH_2O)P(O)H$ in the presence of $Mn(OAc)_3$ to give the adenyl phosphonate **35** that could be pharmacologically active.

CHAPTER 6

EXPERIMENTAL SECTION

6.1. Synthesis of α-hydroxy phosphonates

The procedure was the same as that reported from our laboratory.[8] Compounds **3a-d**, **3f** and **4-5** are reported in the literature; the ^{31}P NMR chemical shifts and melting point data are summarized below. Data for the new compound **3e** is given below the table.[8,36,50]

Sl. No	Compound	Mp (°C)	δ(P), ppm
1	$(OCH_2CMe_2CH_2O)P(O)CH(OH)Ph$ (**3a)**	151-153	13.3
2	$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4$-4-Me) (**3b**)	164	13.6
3	$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4$-4-OMe) (**3c**)	164	13.6
4	$(OCH_2CMe_2CH_2O)P(O)CH(OH)$ (C_6H_4-4-Cl) (**3d)**	174-176	12.9
5	$(OCH_2CMe_2CH_2O)P(O)CH(OH)$(9-anthryl) (**3f**)	156-158	16.9
6	$(OCH_2CMe_2CH_2O)P(O)CH(OH)(CH{=}CHCH_5)$ (**4**)	141-142	13.9
7	$(OCH_2CMe_2CH_2O)P(O)CH_2(C_4H_3O)$ (**5**)	104-106	10.9

$(OCH_2CMe_2CH_2O)P(O)CH(OH)(C_6H_4$-4-Br) (3e)

Yield: 2.68 g (80%).

Mp: 158 ^oC.

IR (KBr): 3397 (ν(OH)), 1483, 1242, 1061 cm^{-1}.

^{1}H NMR: δ 0.85 and 1.12 (2 s, 6 H, $C(CH_3)_2$), 3.98-4.17 (m, 4 H, 2 OCH_2), 4.50 (br, 1 H, O*H*), 5.12 (d, ^2J(P-H) = 12.5 Hz, PC(*H*)OH), 7.36 and 7.48 (d each, 4 H, ^3J(H-H) = 8.0 Hz, Ar-*H*).

^{13}C NMR: δ 20.8 and 21.8 (2 s, $C(CH_3)_2$), 32.7 (d, ^3J(P-C) = 7.5 Hz, $C(CH_3)_2$), 71.4 (d, ^1J(P-C) = 158.1 Hz, P*C*), 77.6 and 77.9 (d each, ^2J(P-C) = 7.2 Hz, OCH_2), 122.2, 128.7, 131.5, 135.7.

^{31}P NMR: δ 13.6.

6.2 Synthesis and utility of bromophosphonates

6.21 Synthesis of bromophosphonates 6a-e, 7 and 12-14

To a solution of **3a-e**, **4** or **5** (14.0 mmol) in dichloromethane (80 mL) maintained at 0 ^{o}C was added PBr_3 (35.1 mmol) drop-wise under nitrogen atmosphere over a period of 30 min and the mixture was maintained at 0 ^{o}C for another 0.5 h. After stirring for 12 h at room temperature, the reaction mixture was quenched with ice-cold water and the dichloromethane layer thoroughly washed with water (3 X 20 mL), dried over anhydrous Na_2SO_4 and solvent removed to obtain the bromophosphonates **6a-e**, **7** and **12-14**.

$(OCH_2CMe_2CH_2O)P(O)CH(Br)(C_6H_5)$ (6a)

Yield: 6.35 g (85%).

Mp: 164-166 ^{o}C.

IR (KBr): 1269, 1057, 1011 cm^{-1}.

^{1}H NMR: δ 0.97 and 1.15 (2 s, 6 H, C(C*H*$_3$)$_2$), 4.02-4.23 (m, 4 H, 2 OC*H*$_2$), 5.06 (d, ^{2}J(P-H) = 16.0 Hz, PC(*H*)Br), 7.35-7.61 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 21.2, 21.7 (2 s, C(*C*H$_3$)$_2$), 32.7 (d, ^{3}J(P-C) = 7.5 Hz, *C*(CH$_3$)$_2$), 40.7 (d, ^{1}J(P-C) = 155.5 Hz, P*C*), 76.4 and 77.0 (2 s, O*C*H$_2$), 128.8, 129.2, 129.5, 129.6, 134.1.

^{31}P NMR: δ 9.7.

Anal. Calcd for $C_{12}H_{16}O_3BrP$: C, 45.16; H, 5.05. Found: C, 45.16; H, 5.04.

$(OCH_2CMe_2CH_2O)P(O)CH(Br)(C_6H_4\text{-}CH_3)$ (6b)

Yield: 6.4 g (87%).

Mp: 196-198 ^{o}C.

IR (KBr): 1273, 1055, 1007 cm^{-1}.

^{1}H NMR: δ 0.97 and 1.14 (2 s, 6 H, C(C*H*$_3$)$_2$), 2.35 (s, 3 H, Ar-C*H*$_3$), 4.03-4.20 (m, 4 H, 2 OC*H*$_2$), 5.07 (d, ^{2}J(P-H) = 12.0 Hz, PC(*H*)Br), 7.17 and 7.48 (d each, 4 H, ^{3}J(H-H) = 8.0 Hz, Ar-*H*).

^{13}C NMR: δ 21.2 (s, C(CH_3)$_2$), 21.7 (s, Ar-CH_3), 32.7 (d, ^3J(P-C) = 7.4 Hz, C(CH$_3$)$_2$), 40.5 (d, ^1J(P-C) = 155.1 Hz, PC), 76.5 and 77.1 (2 s, OCH_2), 129.3, 129.5, 131.0, 139.3.

^{31}P NMR: δ 9.0.

Anal. Calcd for $C_{13}H_{18}O_3BrP$: C, 46.87; H, 5.45. Found: C, 46.86; H, 5.48.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Br)(C$_6$H$_4$-OCH$_3$) (6c)

Yield: 6.7 g (92%).

Mp: 170 ^{o}C.

IR (KBr): 1271, 1055, 1007 cm^{-1}.

^{1}H NMR: δ 1.00 and 1.14 (2 s, 6 H, C(CH_3)$_2$), 3.80 (s, 3 H, Ar-OCH_3), 4.05-4.19 (m, 4 H, 2 OCH_2), 5.05 (d, ^2J(P-H) = 12.0 Hz, PC(H)Br), 6.88 and 7.51 (d each, 4 H, ^3J(H-H) = 8.0 Hz, Ar-H).

^{13}C NMR: δ 21.2 and 21.7 (2 s, C(CH_3)$_2$), 32.7 (d, ^3J(P-C) = 7.4 Hz, C(CH$_3$)$_2$), 40.5 (d, ^1J(P-C) = 156.7 Hz, PC), 55.3 (s, OCH_3), 76.4 and 77.0 (2 s, OCH_2), 114.3, 126.0, 130.8, 131.0, 160.3.

^{31}P NMR: δ 10.0.

Anal. Calcd for $C_{13}H_{18}O_4BrP$: C, 44.72; H, 5.20. Found: C, 44.74; H, 5.19.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Br)(C$_6$H$_4$-Cl) (6d)

Yield: 5.5 g (90%).

Mp: 170-172 ^{o}C.

IR (KBr): 1269, 1055, 1011 cm^{-1}.

^{1}H NMR: δ 1.02 and 1.16 (2 s, 6 H, C(CH_3)$_2$), 4.09-4.26 (m, 4 H, 2 OCH_2), 5.02 (d, ^2J(P-H) = 12.7 Hz, PC(H)Br), 7.35 and 7.53 (d each, 4 H, ^3J(H-H) = 8.0 Hz, Ar-H).

^{13}C NMR: δ 21.2 and 21.7 (2 s, C(CH_3)$_2$), 32.8 (d, ^3J(P-C) = 8.5 Hz, C(CH$_3$)$_2$), 39.7 (d, ^1J(P-C) = 154.0 Hz, PC), 76.4 and 77.0 (2 s, OCH_2), 129.0, 130.9, 132.8,135.2.

^{31}P NMR: δ 8.4.

Anal. Calcd for $C_{12}H_{15}O_3ClBrP$: C, 40.76; H, 4.28. Found: C, 40.78; H, 4.29.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH(Br)(C$_6$H$_4$-Br) (6e)

Yield: 1.6 g (90%).

Mp: 156-158 ^{o}C.

IR (KBr): 1269, 1055, 1009 cm^{-1}.

^{1}H NMR: δ 1.02 and 1.16 (2 s, 6 H, C(C*H*$_3$)$_2$), 4.09-4.24 (m, 4 H, 2 OC*H*$_2$), 5.00 (d, ^{2}J(P-H) = 12.8 Hz, PC(*H*)Br), 7.47 and 7.51 (d each, 4 H, ^{3}J(H-H) = 8.0 Hz, Ar-*H*).

^{13}C NMR: δ 21.2 and 21.9 (2 s, C(*C*H$_3$)$_2$), 32.8 (d, ^{3}J(P-C) = 7.7 Hz, *C*(CH$_3$)$_2$), 39.6 (d, ^{1}J(P-C) = 154.0 Hz, P*C*), 76.8 and 77.1 (2 s, O*C*H$_2$), 123.4, 128.8, 131.1, 131.9, 133.1.

^{31}P NMR: δ 9.3.

Anal. Calcd for $C_{12}H_{15}O_3Br_2P$: C, 36.21; H, 3.80. Found: C, 36.29; H, 3.82.

(OCH$_2$CMe$_2$CH$_2$O)P(O)CH$_2$(C$_{14}$H$_8$)Br [C$_{14}$H$_8$ = 9-anthryl] (7)

Yield: 6.6 g (80%).

Mp: 168-170 ^{o}C.

IR (KBr): 1260, 1061, 1007 cm^{-1}.

^{1}H NMR: δ 0.44 and 0.83 (2 s, 6 H, C(C*H*$_3$)$_2$), 3.29 and 4.04 (m each, 4 H, OC*H*$_2$), 4.37 (dd, 2 H, ^{2}J(P-H) = 14.8 Hz, ^{2}J(H-H) = 8.0 Hz, P-C*H*$_2$), 7.51-8.64 (m, 8 H, Ar-*H*).

^{13}C NMR: δ 21.1 and 21.3 (2 s, C(*C*H$_3$)$_2$), 27.1 (d, ^{1}J(P-C) = 137.0 Hz, P*C*H$_2$), 32.3 (d, ^{3}J(P-C) = 6.0 Hz, *C*(CH$_3$)$_2$), 75.3 (d, ^{2}J(P-C) = 7.5 Hz, 2 O*C*H$_2$), 124.1, 124.8, 125.2, 126.5, 127.0, 128.7, 129.1, 130.4, 131.1, 131.2 (all aromatic *C*) (Fig. 1).

^{31}P NMR: δ 20.3.

Anal. Calcd for $C_{20}H_{20}O_3BrP$: C, 57.29; H, 4.81. Found: C, 57.24; H, 4.80.

LC-MS: 419 [M], 421 [M+2] (^{79,81}Br).

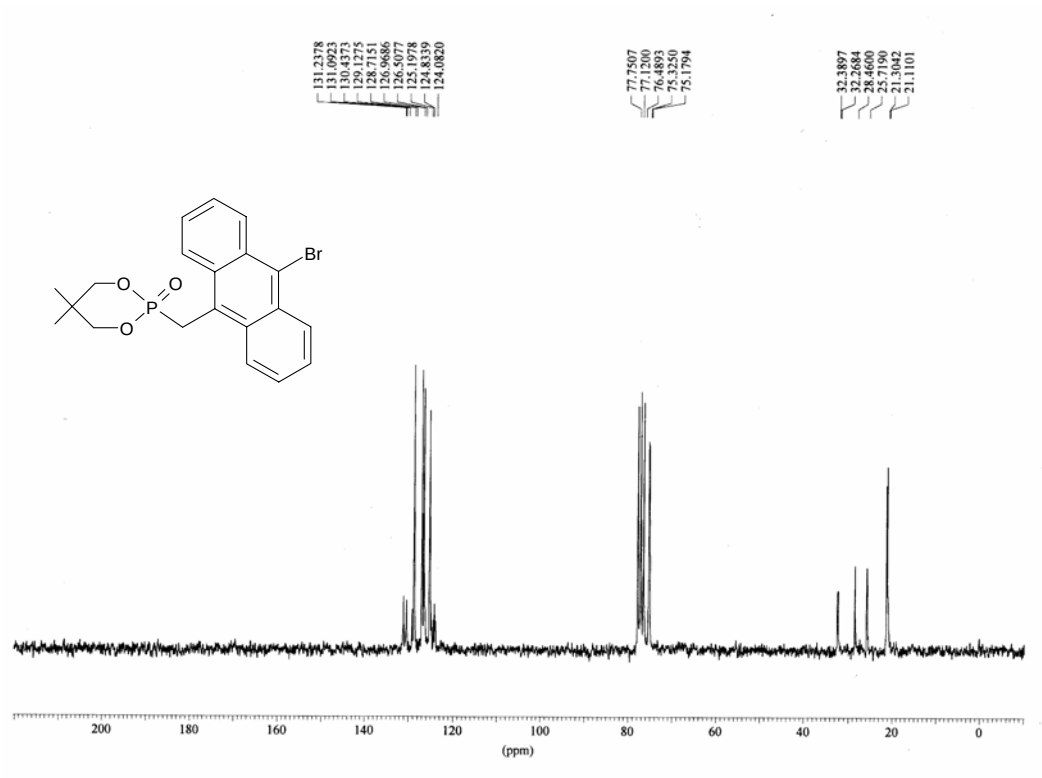


Fig. 1. The ^{13}C spectrum of compound **7**

Compounds 12 and 13

The overall yield of the compound obtained was 80%. There are two isomers, **12** and **13** in the ratio 3:2 [^{1}H NMR integrated intensities]. First, compound **13** was obtained by using ethyl acetate-hexane (1:1) mixture. The residue after removal of all solvent was crystallized from dichloromethane-hexane (2:1) mixture to obtain **12**.

$(OCH_2CMe_2CH_2O)P(O)(CH(Br)CH=CHPh)$ (12)

^{1}H NMR: δ 1.07 and 1.16 (2 s, 6 H, $C(CH_3)_2$), 4.14-4.22 (m, 4 H, 2 OCH_2), 4.78 (m, 1 H, PC(*H*)Br), 6.38-6.42 (m, 1 H, Ph-CH=C*H*), 6.80 (d, 1 H, ^{3}J(H-H) = 15.6 Hz, Ph-C*H*=CH), 7.26-7.42 (m, 5 H, Ar-*H*) (Fig. 2).

^{31}P NMR: δ 8.8.

This compound could be isolated only in small quantities and was not stable in solution. Hence the other data were not obtained.

$(OCH_2CMe_2CH_2O)P(O)(CH=CH-CH(Br)Ph)$ (13)

Mp: 114-116 ^oC.

IR (KBr): 1618, 1265, 1057, 1008 cm^{-1}.

^1H NMR: δ 1.08 and 1.10 (2 s, 6 H, $C(CH_3)_2$), 3.83-3.91 and 4.17-4.23 (m each, 4 H, 2 OCH_2), 5.64 (d, ^3J(H-H) = 4.0 Hz, PhC(*H*)Br), 5.94 (m, 1 H, P-C*H*=CH), 7.12 (m, 1 H, P-CH=C*H*), 7.33-7.42 (m, 5 H, Ar-*H*) (Fig. 2).

^{13}C NMR: δ 21.5 and 21.6 (2 s, $C(CH_3)_2$), 32.5 (d, ^3J(P-C) = 9.7 Hz, $C(CH_3)_2$), 52.0 (d, ^3J(P-C) = 26.7 Hz, P-CH=CH-*C*(H)Br), 75.7 and 75.9 (2 s, OCH_2), 117.6 (d, ^1J(P-C) = 185.6 Hz, P*C*) 128.0, 129.1, 138.2,150.7(d, ^2J(P-C) = 14.6 Hz, P-CH=*C*H-).

^{31}P NMR: δ 10.8.

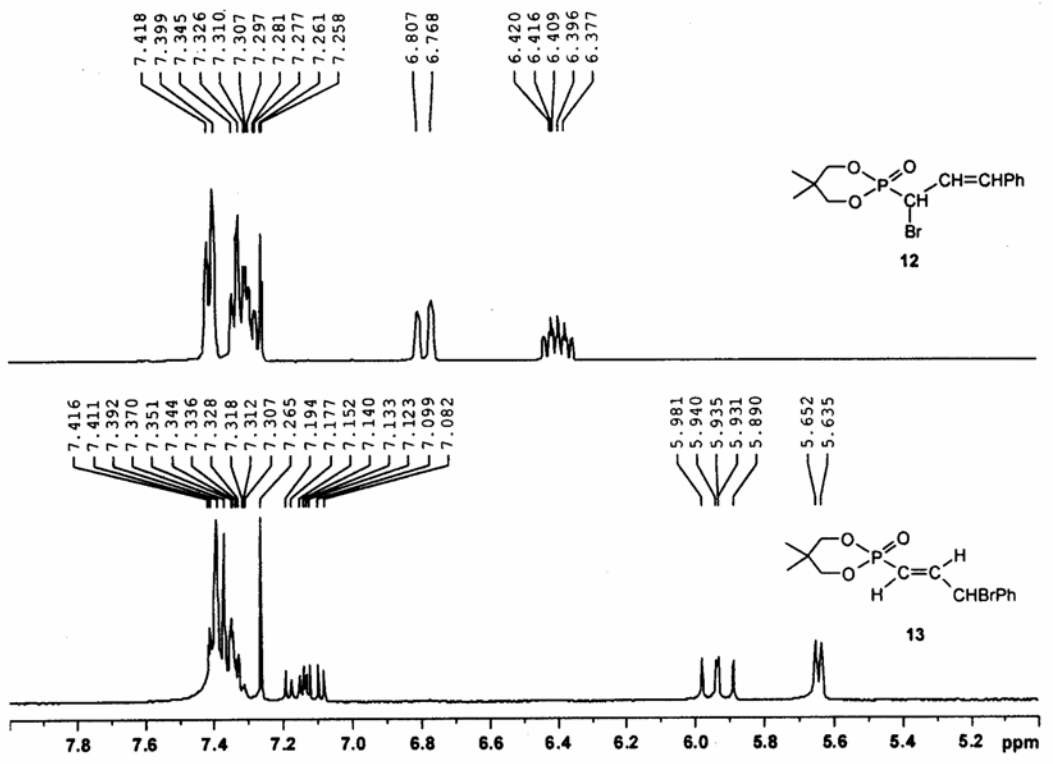


Fig. 2. ^1H NMR spectra of compounds **12** and **13** in the region 5.0-8.0 ppm.

$(OCH_2CMe_2CH_2O)P(O)(5\text{-}BrC_4H_2O)$ (14)

Gummy solid

Yield: 1.8 g (75%).

IR (neat): 1474, 1277, 822 cm^{-1}.

^{1}H NMR: δ 0.91 and 1.04 (2 s, 6 H, C(C*H*$_3$)$_2$), 3.75-3.80 and 4.12-4.17 (m each, 4 H, 2 OC*H*$_2$), 4.37 (d, ^{2}*J*(P-H) = 11.8 Hz, 2 H, , P-C*H*$_2$) 6.28 and 6.35 (each br s, 2 H, furfuryl ring protons).

^{13}C NMR: δ 21.2 and 21.5 (2 s, C(*C*H$_3$)$_2$), 25.8 (d, ^{1}*J*(P-C) = 140.3 Hz, P*C*), 32.5 (d, *C*(CH$_3$)$_2$), 75.9 (s, O*C*H$_2$), 111.0, 111.6, 112.6, 142.1.

^{31}P NMR: δ 18.1.

LC-MS: 309 [M], 311 [M+2] (^{79,81}Br).

6.22 HWE reaction of the bromophosphonate 7 with aldehydes

To a suspension of NaH (0.14 g, 60% suspension, 5.72 mmol) in THF (20 mL) stirred at 0 ^{o}C was added 10-bromophosphonate **7** (0.54 g, 1.28 mmol) at once, the mixture was stirred for 30 min, aldehyde (1.28 mmol) was added *via* syringe, the contents brought to room temperature and stirred further for 12 h. Then crushed ice was added, the product extracted with ether and chromatographed over silica gel using hexanes to afford the alkenes.

PhC(H)=C(H)(C$_{14}$H$_8$Br) (16)

Yield: 0.43 g (70%).

Mp: 154-156 ^{o}C.

IR (KBr): 1614, 1435, 1339, 1254, 963, 903, 748 cm^{-1}.

^{1}H NMR: δ 6.91 (d, 1 H, ^{3}*J*(H-H) = 16.4 Hz, Ph-C(*H*)=), 6.95-8.61 (m, 14 H, Ar*H* + Ph-C(H)=C(*H*)-).

^{13}C NMR: δ 122.7, 124.6, 125.2, 125.7, 126.1, 126.6, 127.7, 128.2, 129.0, 130.4, 130.5, 133.7, 137.1, 138.0.

LC-MS: 359 [M], 361 [M+2] (^{79,81}Br).

Anal. Calcd for C$_{22}$H$_{15}$Br: C, 73.55; H 4.21. Found: C, 73.66; H 4.26.

(4-Br-C$_6$H$_4$)C(H)=C(H)(C$_{14}$H$_8$Br) (17)

Yield: 1.67 g (80%).

Mp: 206-208 ^{o}C.

IR (KBr): 1487, 1435, 1337, 1071, 1005, 972, 949, 903, 837, 799, 775, 752 cm^{-1}.

^{1}H NMR: δ 6.84 (d, 1 H, ^3J(H-H) = 16.0 Hz, Ar-C(*H*)=), 7.47-8.61 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 122.1, 122.9, 125.4, 125.8, 126.4, 127.1, 128.1, 128.2, 128.8, 130.4, 132.0, 133.2, 135.9, 136.8.

Anal. Calcd for $C_{22}H_{14}Br_2$: C, 60.31; H, 3.22. Found: C, 60.44; H, 3.21.

(4-MeO-C_6H_4)C(H)=C(H)($C_{14}H_8$Br) (18)

Yield: 0.43 g (70%).

Mp: 160-162 ^{o}C.

IR (KBr): 1603, 1508, 1441, 1250, 1173, 1028, 748 cm^{-1}.

^{1}H NMR: δ 3.89 (s, 3 H, C*H*$_3$), 6.84 (d, 1 H, ^3J(H-H) = 16.4 Hz, Ph-C(*H*)=), 7.0-8.6 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 55.5, 114.3, 122.2, 122.6, 125.2, 125.4, 125.5, 126.2, 126.8, 127.0, 127.8, 127.9, 128.1, 128.7, 129.9, 130.4, 130.6, 134.1, 136.7, 137.4, 159.6, 159.8.

Anal. Calcd for $C_{23}H_{17}OBr$: C 70.96, H 4.40. Found C 70.98, H 4.40.

X-ray structural analysis was performed on this compound.

(4-NO_2-C_6H_4)C(H)=C(H)($C_{14}H_8$Br) (19)

Yield: 0.30 g (58%).

Mp: 196-198 ^{o}C.

IR (KBr): 1591, 1514, 1339, 1262, 1105, 1017, 885, 850, 802, 734 cm^{-1}.

^{1}H NMR: δ 7.05 (d, 1 H, ^3J(H-H) = 16.0 Hz, Ar-C(*H*)=), 7.50-8.50 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 124.3, 125.4, 125.5, 126.0, 126.2, 127.1, 127.4, 128.5, 128.9, 129.7, 129.9, 131.3, 131.5, 135.1, 143.6.

Anal. Calcd for $C_{22}H_{14}NO_2Br$: C, 65.36; H, 3.50; N, 3.46. Found: C, 65.38; H, 3.56; N, 3.56.

$C_5H_5FeC_5H_4CH$=CH($C_{14}H_8$Br) (20)

Yield: 0.34 g (65%).

Mp: 166-168 ^{o}C.

IR (KBr): 1616, 1437, 1327, 1254, 1105, 1044, 999, 955, 903, 822, 799, 766, 748 cm^{-1}.

^{1}H NMR: δ 4.30, 4.40 and 4.63 (3 s, 9 H, ferrocenyl-*H*), 6.67 (d, 1 H, ^{3}J(H-H) = 16.0 Hz, FeC_5H_4-C(*H*)=), 7.41-8.60 (m, 9 H, Ar*H* + -C(H)=C(*H*)-).

^{13}C NMR: δ 67.2, 69.3 and 69.6 (ferrocenyl-*C*), 83.2 (*C*(ferrocenyl)CH=CH), 121.5, 122.0, 125.5, 126.2, 126.7, 127.0, 128.2, 128.8, 130.5, 134.4, 136.5 (Fig. 3).

LC-MS: 467 [M], 469 [M+2] (^{79,81}Br).

Anal. Calcd for $C_{26}H_{19}BrFe$: C, 66.84; H, 4.10. Found: C, 66.92; H, 4.07.

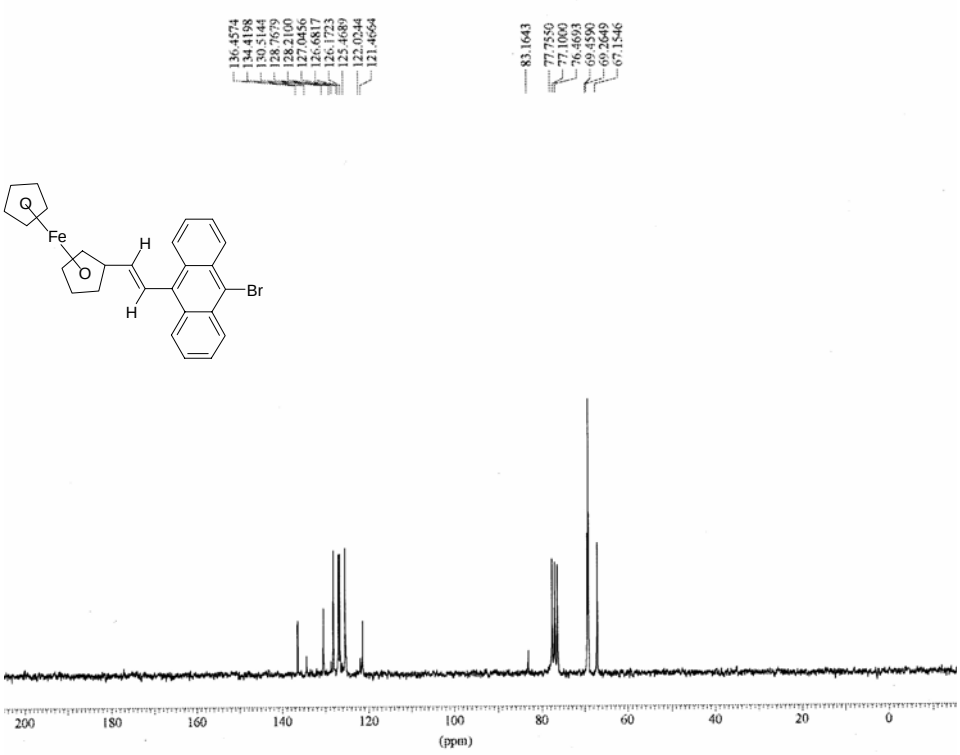


Fig. 3. The ^{13}C spectrum of compound **20**

$(C_{14}H_9)C(H)=C(H)(C_{14}H_8Br)$ (21)

Yield: 0.13 g (20%).

Mp: 216-218 ^{o}C.

IR (KBr): 1618, 1516, 1439, 1348, 1253, 981, 952, 905, 885 cm^{-1}.

^{1}H NMR: δ 7.53-8.69 (m, 19 H, Ar*H* + Ar-C(*H*)=C(*H*)-).

^{13}C NMR: δ 125.3, 125.7, 126.0, 126.2, 126.4, 127.1, 128.4, 129.0, 129.7, 130.5, 131.6, 132.3, 133.2, 134.5.

Reaction of 14 with anisaldehyde

(C_6H_4-4-OCH_3)C(H)=C(H)(5-Br-C_4H_2O) (22)

Yield: 0.2 g (50%).

Mp: 152-154 ^oC.

IR (KBr): 1604, 1510, 1458, 1248, 1175, 1111, 1030, 963 cm^{-1}.

^1H NMR: δ 3.85 (s, 3 H, C*H*$_3$), 6.33 and 6.43 (br s each, 2 H, furfuryl ring protons), 6.79 (d, ^3J(H-H) = 16.0 Hz, -CH=C*H*-C_4H_2OBr), 6.91 (d, 2 H, ^3J(H-H) = 8.0 Hz, Ar-*H*), 7.02 (d, ^3J(H-H) = 16.0 Hz, Ar-C*H*=CH-), 7.43 (d, 2 H, ^3J(H-H) = 8 Hz, Ar-*H*).

^{13}C NMR: δ 55.3 (O*C*H$_3$), 107.7, 109.8, 111.6, 113.3, 113.6, 113.8, 114.2, 114.7, 126.8, 127.4, 127.6, 127.8, 129.9, 141.8, 153.6, 159.3.

6.23 Sonogashira coupling of compound 17 with terminal alkynes

Representative procedure: To previously evacuated mixture of **17** (0.30 g, 0.68 mmol), $Pd(PPh_3)_2Cl_2$ (2 mol %) and CuI (4 mol %) in dry dioxane (3 mL), triethylamine (0.57 mL, 4.09 mmol) was added followed by slow addition of terminal acetylene (2.05 mmol) in dry dioxane (1 mL) over a period of 40 min. After the addition is complete the reaction was heated at 80 ^oC for 12 h, solvent was removed *in vacuo* and the residue was purified by column chromatography using hexane/ethyl acetate to obtain the required compound.

$C_6H_5C\equiv C$-(C_6H_4)CH=CH($C_{14}H_8Br$) (23)

Yield: 0.16 g (50%).

Mp: 110-112 ^oC.

IR (KBr): 1694, 1483, 1435, 1381, 1271, 1159, 1069, 1007, 953, 847, 795, 760 cm^{-1}.

^1H NMR: δ 6.84 (d, 1 H, ^3J(H-H) = 16.6 Hz, Ar-C(*H*)=), 7.36-8.76 (m, 18 H, Ph-C≡C + Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 86.6, 101.3, 117.4, 122.0, 123.7, 125.5, 125.9, 126.3, 126.4, 127.3, 128,1, 128.2, 128.6, 129.4, 131.7, 132.0, 132.1, 132.4, 133.7, 136.1, 136.6, 137.3.

LC-MS: 459 [M], 461 [M+2] (^{79,81}Br).

Anal. Calcd for $C_{30}H_{19}Br$: C, 78.44; H, 4.17. Found: C, 78.51; H 4.12.

(HO)(CH$_3$)$_2$CC≡C-(C$_6$H$_4$)CH=CH(C$_{14}$H$_8$Br) (24)

Yield: 0.14 g (46%).

Mp: 134-136 ^{o}C.

IR (KBr): 3455, 1671, 1593, 1487, 1441, 1283, 1069, 808, 754 cm^{-1}.

^{1}H NMR: δ 1.88 (s, 6 H, -C(C*H*$_3$)$_2$), 6.84 (d, 1 H, ^{3}J(H-H) = 16.6 Hz, Ar-C(*H*)=), 7.36-8.76 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 31.6, 31.9, 66.3, 79.1, 105.8, 116.8, 122.0, 125.2, 125.4, 125.5, 125.8, 126.3, 126.5, 127.1, 128.1, 128.2, 129.2, 130.4.

LC-MS: 423 [M-18], 425 [(M-18)+2] (^{79,81}Br).

Anal. Calcd for $C_{27}H_{21}BrO$: C, 73.48; H, 4.80. Found: C, 73.38; H 4.86.

(*n*-C$_6$H$_{13}$)C≡C-(C$_6$H$_4$)CH=CH(C$_{14}$H$_8$Br) (25)

Yield: 0.15 g (48%).

Mp: 96-98 ^{o}C.

IR (KBr): 1483, 1379, 1071, 1007, 965, 801, 752 cm^{-1}.

^{1}H NMR: δ 0.93-2.80 (m, 13 H, Aliphatic-*H*), 6.90 (d, 1 H, ^{3}J(H-H) = 16.0 Hz, Ar-C(*H*)=), 7.49-8.66 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 14.1, 19.6, 20.3, 22.6, 28.8, 31.5, 80.6, 102.8, 118.8, 119.1, 121.9, 125.0, 125.7, 126.0, 126.2, 126.5, 127.0, 127.5, 128.1, 129.4, 130.5, 132.0, 132.4, 133.5, 136.2, 136.4, 137.5.

LC-MS: 467 [M], 469 [M+2] (^{79,81}Br).

Anal. Calcd for $C_{30}H_{27}Br$: C, 77.08; H, 5.82. Found: C, 77.12; H, 5.81.

(*n*-C$_6$H$_{13}$)C≡C-(C$_6$H$_4$)C(H)=C(H)(C$_{14}$H$_8$)-C≡C(*n*-C$_6$H$_{13}$) (26)

Yield: 0.03 g (10%).

Mp: 116-118 ^{o}C.

^{1}H NMR: δ 0.94-2.81 (m, 26 H, Aliphatic-*H*), 6.92 (d, 1 H, ^{3}J(H-H) = 16.0 Hz, Ar-C(*H*)=), 7.48-8.66 (m, 13 H, Ar*H* + Ar-C(H)=C(*H*)-).

^{13}C NMR: δ 14.1, 19.6, 20.2, 22.6, 28.2, 28.6, 28.8, 29.1, 30.2, 31.4, 31.8, 80.6, 91.7, 102.7, 118.5, 123.2, 123.7, 124.8, 124.9, 125.2, 125.6, 125.9,

126.3, 126.4, 126.5, 126.8, 127.4, 129.4, 132.0, 132.4, 132.8, 136.3, 137.1.

LC-MS: 497 [M].

6.3 Synthesis of cyclopropyl phosphonates

To a stirred suspension of NaH (2.5 mmol) in dry THF (30 mL) at 0 ^{o}C was added the *a*-chlorophosphonate **27a-d** (1.0 mmol). After 0.5 h, dimethyl maleate (1.0 mmol) was added drop-wise *via* syringe. The mixture was allowed to come to room temperature and then heated under reflux for 1 d. After cooling and quenching with cold water (20 mL), the mixture was extracted with dichloromethane (3 x 15 mL). The dichloromethane layer was dried (Na_2SO_4), the solvent removed, and the crude product obtained was purified by column chromatography (silical gel, hexane-ethyl acetate).

[(OCH$_2$CMe$_2$CH$_2$O)P(O){C(Ph){C(H)(COOMe)}$_2$-}] (28a)

Yield: 0.90 g (65%).

Mp: 104-106 ^{o}C.

IR (KBr): 1748, 1732, 1607, 1437, 1341, 1271, 1219, 1169, 1057, 1005 cm^{-1}. There was a weak band at 3461 cm^{-1} (most likely an overtone of the band at 1732 cm^{-1}).

^{1}H NMR: δ 0.50 and 0.94 (2 s, 6 H, C(C*H*$_3$)$_2$), 3.03-3.09 and 3.27-3.28 (m each, 2 H, C(*H*)(COOMe)), 3.46-3.57 (m, 2 H, OC*H*$_A$H$_B$), 3.59 and 3.82 (2 s, 6 H, COOC*H*$_3$), 4.00-4.08 (m, 2 H, OCH$_A$*H*$_B$), 7.28-7.38 (m, 5 H, Ar-*H*).

^{13}C NMR: δ 20.8 and 21.5 (2 s, C(*C*H$_3$)$_2$), 29.2 (s, *C*(H)(COOMe)), 32.2 (d, ^{3}J(P-C) = 10.0 Hz, *C*(CH$_3$)$_2$), 33.0 (s, *C*(H)(COOMe)), 35.8 (d, ^{1}J(P-C) = 184.4 Hz, P*C*), 52.3 and 52.7 (2 s, COO*C*H$_3$), 76.4 and 76.6 (2 s, O*C*H$_2$), 128.4, 130.1, 133.6, 167.6 and 168.0 (2 s, *C*OOMe).

^{31}P NMR: δ 15.4.

Anal. Calcd for $C_{18}H_{23}O_7P$: C, 56.54; H, 6.06. Found: C, 56.49; H, 6.06.

[(OCH$_2$CMe$_2$CH$_2$O)P(O){C(4-Me-C$_6$H$_4$){C(H)(COOMe)}$_2$-}] (28b)

Yield: 0.82 g (60%).

Mp: 172-174 ^{o}C.

IR (KBr): 1750, 1732, 1516, 1439, 1341, 1263, 1217, 1167, 1055, 1003 cm^{-1}.

^{1}H NMR: δ 0.54 and 0.97 (2 s, 6 H, C(C*H*$_3$)$_2$), 2.34 (s, 3 H, Ar-C*H*$_3$), 3.00-3.06 and 3.25-3.29 (m each, 2 H, C(*H*)(COOMe)), 3.44-3.58 (m, 2 H, OC*H*$_A$H$_B$), 3.61 and 3.82 (2 s, 6 H, COOC*H*$_3$), 3.99-4.05 (m, 2 H, OCH$_A$*H*$_B$), 7.14 and 7.27 (d each, 4 H, ^{3}J (H-H) = 8.0 Hz, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.2 (2 s, C(*C*H$_3$)$_2$), 21.8 (s, Ar-*C*H$_3$), 29.2 (s, *C*(H)(COOMe)), 32.2 (d, ^{3}J(P-C) = 7.2 Hz, *C*(CH$_3$)$_2$), 33.0 (s, *C*(H)(COOMe)), 35.6 (d, ^{1}J(P-C) = 186.1 Hz, P*C*), 52.4 and 52.8 (2 s, COO*C*H$_3$), 76.5 and 76.8 (2 s, O*C*H$_2$), 129.2, 130.8, 138.1, 167.6 and 168.1 (2 s, *C*OOMe).

^{31}P NMR: δ 15.4.

Anal. Calcd for $C_{19}H_{25}O_7P$: C, 57.66; H, 6.35. Found: C, 57.66; H, 6.34.

[(OCH$_2$CMe$_2$CH$_2$O)P(O){C(4-MeO-C$_6$H$_4$){C(H)(COOMe)}$_2$-}] (28c)

Yield: 0.80 g (66%).

Mp: 118-120 ^{o}C.

IR (KBr): 1750, 1734, 1615, 1514, 1437, 1339, 1262, 1215, 1163, 1057, 1003 cm^{-1}.

^{1}H NMR: δ 0.56 and 0.95 (2 s, 6 H, C(C*H*$_3$)$_2$), 3.00-3.04 and 3.23-3.29 (m each, 2 H, C(*H*)(COOMe)), 3.47-3.57 (m, 2 H, OC*H*$_A$H$_B$), 3.60 (s, 3 H, COOC*H*$_3$), 3.81 (br s, 6 H, Ar-OC*H*$_3$ + COOC*H*$_3$), 4.00-4.09 (m, 2 H, OCH$_A$*H*$_B$), 6.85 and 7.29 (d each, 4 H, ^{3}J (H-H) = 8.0 Hz, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.5 (2 s, C(*C*H$_3$)$_2$), 29.2 (s, *C*(H)(COOMe)), 32.2 (d, ^{3}J(P-C) = 7.3 Hz, *C*(CH$_3$)$_2$), 33.1 (s, *C*(H)(COOMe)), 35.1 (d, ^{1}J(P-C) = 187.1 Hz, P*C*), 52.4 and 52.7 (2 s, COO*C*H$_3$), 55.2 (s, Ar-O*C*H$_3$), 76.4 and 76.6 (2 s, O*C*H$_2$), 114.0, 125.1, 132.0, 159.5, 167.6 and 168.1 (2 s, *C*OOMe).

^{31}P NMR: δ 15.8.

Anal. Calcd for $C_{19}H_{25}O_8P$: C, 55.34; H, 6.11. Found: C, 55.32; H, 6.10.

X-ray structural analysis was performed on this compound.

[$(OCH_2CMe_2CH_2O)P(O)\{C(4\text{-}Cl\text{-}C_6H_4)\{C(H)(COOMe)\}_2\text{-}\}$] (28d)

Yield: 0.80 g (60%).

Mp: 174-176 ^oC.

IR (KBr): 1748, 1730, 1516, 1439, 1341, 1263, 1217, 1167, 1055, 1003 cm^{-1}.

^1H NMR: δ 0.57 and 0.92 (2 s, 6 H, $C(CH_3)_2$), 3.00-3.05 and 3.27-3.33 (m each, 2 H, C(*H*)(COOMe)), 3.50-3.57 (m, 1 H, OCH_AH_B), 3.62 and 3.83 (2 s, 6 H, $COOCH_3$), 4.09-4.16 (m, 1 H, OCH_AH_B), 7.29-7.33 (m, 4 H, Ar-*H*).

^{13}C NMR: δ 21.0 and 21.4 (2 s, $C(CH_3)_2$), 29.1 (s, *C*(H)(COOMe)), 32.3 (d, ^3J(P-C) = 7.1 Hz, $C(CH_3)_2$), 33.0 (s, *C*(H)(COOMe)), 34.8 (d, ^1J(P-C) = 186.7 Hz, P*C*), 52.5 and 52.8 (2 s, $COOCH_3$), 76.1 and 76.2 (2 s, OCH_2), 128.6, 132.1, 134.4, 167.2 and 167.9 (2 s, *C*OOMe).

^{31}P NMR: δ 15.0.

Anal. Calcd for $C_{18}H_{22}O_7PCl$: C, 51.86; H, 5.32. Found: C, 51.88; H, 5.36.

6.4 Alkylation of adenine using Mitsunobu reaction

To a solution of alcohol (2.06 mmol), adenine (2.06 mmol) and PPh_3 (2.47 mmol) in THF (15 mL) was added DIAD (2.47 mmol) at room temperature drop-wise over a period of 45 min. After the addition, the reaction mixture was stirred for 12 h. The solvent was removed in *vacuo* and the crude product obtained was purified by column chromatography (silical gel, hexane-ethyl acetate).

$C_{21}H_{37}N_5$ (30)

Yield: 0.44 g (60%).

Mp: 86-88 ^oC.

^1H NMR: δ 0.83 (t, 3 H, ^3J(H-H) = 8.0 Hz, CH_3), 1.24-1.32 (m, 26 H, CH_2), 1.89 (m, 2 H, NCH_2CH_2-), 4.19 (t, 2 H, ^3J(H-H) = 8.0 Hz, NCH_2-) 5.79 (br s, 2 H, NH_2), 7.79 and 8.37 (2 s, 2 H, Adenyl-*H*).

LC-MS: 360 [M+1].

X-ray structural analysis was done on this compound

$C_{16}H_{25}N_5$ (31)

Yield: 0.52 g (62%).

Mp: 100-102 ^{o}C [105 ^{o}C[53c]]

^{1}H NMR: δ 1.26-1.35 (m, 12 H, 6 CH_2) 1.87-2.05 (m, 4 H, 2 CH_2), 4.19 (t, 2 H, ^{3}J(H-H) = 8.0 Hz, NCH_2-), 4.91-5.01 (m, 2 H, CH_2=), 5.77-5.81 (m, 1 H, -C*H*=CH$_2$), 6.57 (br s, 2 H, NH_2), 7.81 and 8.31 (2 s, 2 H, Adenyl-*H*).

LC-MS: 288 [M+1].

Hydrophosphorylation of alkene 31 using H-phosphonate 2

To **2** (2.08 mmol) and Mn(OAc)$_3$ (5 mol%) alkene (**31**) (0.69 mmol) was added, the mixture was stirred at 90 ºC for 3 h in air. The reaction was monitored by thin layer chromatography (TLC). After disappearance of alkene, the crude product was purified by column chromatography (silical gel, hexane-ethyl acetate).

(OCH$_2$CMe$_2$CH$_2$O)P(O)(CH$_2$)$_{10}$CH$_2$(C$_5$H$_5$N$_5$) (35)

Yield: 0.12 g (40%).

^{1}H NMR: δ 0.96 and 1.17 (s each, C(CH_3)$_2$), 1.26-1.40 (m, 12 H, 6 CH_2), 1.65-1.68 (m, 2 H, CH_2) 1.80-1.91 (m, 4 H, CH$_2$ + P(O)CH_2-), 3.72-3.79 (m, 2 H, OCH_2), 4.21 (t, 2 H, ^{3}J(H-H) = 8.0 Hz, NCH_2-), 4.25-4.29 (m, 2 H, OCH_2), 6.67 (br s, 2 H, NH_2), 7.84 and 8.32 (2 s, 2 H, Adenyl-*H*).

^{31}P NMR: δ 30.3.

LC-MS: 438 [M+1].

6.5 X-ray crystallography

A suitable crystal was mounted on a glass fibre (for **18, 28c, 29 and 30**) X-ray data were collected at 293 K on a Bruker AXS-SMART diffractometer using Mo-K$_\alpha$ radiation (λ = 0.71073 Å). Structures were solved and refined using standard methods. Crystal data are summarized in Table 1.

Table 1. Crystal data for compounds **18, 28c, 29 and 30**

Compound	**18**	**28c**	**29**	**30**
Emp. formula	$C_{23}H_{17}BrO$	$C_{19}H_{25}O_8P$	$C_{17}H_{23}O_6P$	$C_{21}H_{37}N_5$
Formula weight	389.28	412.36	354.32	359.56
Crystal system	Triclinic	Monoclinic	Monoclinic	Monoclinic
Space group	$P\bar{1}$	*P2₁/c*	*C2/c*	*P2₁/c*
a /Å	8.3283(7)	11.5535(7)	38.155(2)	22.836(3)
b /Å	9.2291(8)	8.7141(6)	5.8878(3)	8.1778(9)
c /Å	12.8143(11)	21.4828(14)	17.5994(9)	11.5773(13)
α/deg	80.2920(10)	90	90	90
β/deg	71.5650(10)	92.3740(10)	112.9260(10)	94.290(2)
γ/deg	68.6200(10)	90	90	90
V /Å^3	868.51(13)	2161.0(2)	3641.3(3)	2156.0(4)
Z	2	4	8	4
D_{calc} /g cm^{-3}]	1.489	1.267	1.293	1.108
μ /mm^{-1}	2.374	0.167	0.179	0.067
F(000)	396	872	1504	792
Data/ restraints/ parameters	4037/ 0/ 227	3807 / 0/ 258	3187 / 0 / 221	3792 / 0 / 236
S	1.023	1.028	1.091	0.998
R1 [I>2σ(I)]	0.0372	0.0437	0.0568	0.0590
wR2 [all data]	0.1046	0.1210	0.1378	0.1673
Max./min. residual electron dens. [eÅ^{-3}]	0.340/ -0.304	0.224/ -0.294	0.311 / -0.420	0.223 / -0.135

References

1. a) R. Engel, *Chem. Rev*. 1977, **77**, 349; b) R. L. Hilderbrand, *The Role of Phosphonates in Living Systems*, CRC Press, Boca Raton, FL, 1982; c) M. Takeuchi, M. Nakajima, T. Ogita, M. Inukai, K. Kodama, K. Furuya, H. Nagaki and T. Haneishi, *J. Antibiot.* 1989, **42**, 198; d) R. L. Rawls, *Chem. Engg. News* 1998 (Aug.17), p 38. (e) Corbridge, D. E. C. *Phosphorus 2000: Chemistry, Biochemistry and Technology*, 4th ed.; Elsevier: Amsterdam, 2000; Chapter 2, pp 16-31.
2. a) L. Horner, *Chem. Ber.* 1958, **83**, 733; b) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.* 1961, **83**, 1733.
3. Reviews: a) W. S. Wadsworth, Jr., *Org. Reactions* 1977, **25**, 73; b) B. E. Maryanoff and A. B. Reitz, *Chem. Rev.* 1989, **89**, 863; c) E. Vedejs, M. Peterson. *J. Top. Stereochem.* 1994, **21**, 1.
4. Selected recent references: a) Z. Trela, H. Kleszczyńska and J. Sarapuk, *Z. Naturforsch.C* 2001, **56**, 838; b) P. Kafarski and B. Lejczak, *Curr. Med. Chem.-Anti-Cancer Agents* 2001, **1**, 301; c) B. C. Ranu and A. Hajra, *Green Chemistry* 2002, **4**, 551; d) M. R. Saide, N. Azizi, *Synlett*. 2002, 1347; e) J. S. Yadav, B. V. S. Reddy and P. Sreedhar, *Green Chemistry* 2002, **4**, 436; f) R. J. Cohen, D. L. Fox, J. F. Eubank and R. N. Salvatore, *Tetrahedron Lett.* 2003, **44**, 8617; g) B.-An Song, Y.-Lan Wu, S. Yang, De.-Yu Hu, X.-Qiong He and L.-Hong Jin, *Molecules* 2003, **8**, 186; h) E. D. Matveeva, T. A. Podrugina, E. V. Tishkovskaya, L. G. Tomilova and N. S. Zefirov, *Synlett* 2003, **15**, 2321; i) N. Azizi and M. R. Saidi, *Eur. J. Org. Chem.* 2003, **23**, 4630.; j) A. Manjula, B. V. Rao and P. Neelakantan, *Synth. Commun.* 2003, **33**, 2963; k) T. Akiyama, M. Sanada and K. Fuchibe, *Synlett* 2003, **10**, 1463; l) D. R. Carmela, D. Perrone, A. Dondoni, G. P. Pollini and V. Bertolasi, *Eur. J. Org. Chem.* 2003, **10**, 1904; m) B. Kaboudin and F. Saadati, *Synthesis* 2004, 1249; n) M. Amedjkouh, K. Westerlund, *Tetrahedron Lett.* 2004, **45**, 5175; o) F. A. Davis, S. H. Lee, H. Seung, H. Xu, *J. Org. Chem.* 2004, **69**, 3774; p) T. Rammeloo, C. V. Stevens and B. Soenen, *Eur. J. Org. Chem.* 2004, **6**, 1271.
5. R. Engel, in *Synthesis of Phosphorus-Carbon Bonds*; CRC Press; Boca Raton, FL, 1988, pp 1-136.
6. T. Gajda, *Phosphorus Sulfur Silicon Relat. Elem*. 1990, **53**, 327.

7. D. Green, S. Elgendy, G. Patel, J. A. Baban, E. Skordalakes, W. Husman, V. V. Kakkar and J. Deadman, *Tetrahedron* 1996, **52**, 10215.
8. S. Kumaraswamy, R. S. Selvi and K. C. Kumara Swamy, *Synthesis* 1997, 207.
9. H. Firouzabadi, N. Iranpoor and S. Sobhani, *Tetrahedron* 2004, **60**, 203.
10. S. K. Chakraborty and R. Engel, *Syn. Commun.* 1991, **21**, 1039.
11. X. Shi and L. Dai, *J. Org. Chem.* 1993, **58**, 4596.
12. B. Iorga, F. Eymery and P. Savignac, *Tetrahedron* 1999, **55**, 2671.
13. M. J. Gallagher and H. Noerdin, *Aust. J. Chem.* 1985, **38**, 997.
14. E. Castagnino, M. D. Auria, A. De Mico, F. D. Onofrio and G. Piancatelli, *J. Chem. Soc., Chem. Commun.* 1987, 907.
15. T. Gajda, *Synthesis* 1990, 717.
16. L. Horner, H. Hoffmann, H. G. Wippel and G. Klahre, *Chem. Ber.* 1959, **92**, 2499.
17. *S. E. Kelly, in* Comprehensive Organic synthesis*; M. B. Trost and I. Flemming, Editors; S. L. Schreiber, volume Ed.; Pergamon; Oxford, 1991, Vol. **1**, p 762.*
18. S. Kumaraswamy and K. C. Kumara Swamy, *Tetrahedron Lett.* 1997, **38**, 2183.
19. C. Muthiah, K. Praveen Kumar, S. Kumaraswamy and K. C. Kumara Swamy, *Tetrahedron* 1998, **54**, 14315.
20. M. Chakravarty, B. Srinivas, C. Muthiah and K. C. Kumara Swamy, *Synthesis* 2003, 2368.
21. T. M. Pedersen, J. F. Jensen, R. E. Humble, T. Rein, D. Tanner, K. Bodmann and O. Reiser, *Org. Lett.* 2000, **2**, 535.
22. K. Tago and H. Kogen, *Org. Lett.* 2000, **2**, 1975.
23. a) S. J. Jong and J. M. Fang, *J. Org. Chem.* 2001, **66**, 3533; b) P. Debroy and S. Roy, *Ind. J. Chem. Sect.A.* 2003, **42A**, 2416; c) B. Konig, H. Zieg, P. Bubenitschek and P. G. Jones, *Chem. Ber.* 1994, **127**, 1811.
24. K. Senthil kumar and K. C. Kumara Swamy, *J. Organomet. Chem*. 2001, **637-639**, 616.
25. L. K. Blasdel and A. G. Myers, *Org. Lett.* 2005, **7**, 4281.
26. a) Y. -H. Kim, D. –C. Shin, S. –H. Kim, C. –H. Ko, H. –S. Yu, Y. –S. Chae and S. –K. Kwon, *Adv. Mater.* 2001, **13**, 1690; b) K. Ito, T. Suzuki, Y.

Sakamoto, D. Kubota, Y. Inoue, F. Sato and S. Tokito, *Angew. Chem. Int. Ed.* 2003, **42**, 1159; c) S. Ando, J.-i. Nishda, E. Fujiwara, H. Tada, Y. Inoue, S. Tokito and Y. Yamashita, *Chem. Mater.* 2005, **17**, 1261; d) H. Sasaki, Y. Wakayama, T. Chikyow, E. Barrena, H. Dosch and K. Kobayashi, *Appl. Phys. Lett.* 2006, **88**, 081907(1)-081907(3); e) W. Cui, X. Zhang, X. Jiang, H. Tian, D. Yan, Y. Geng, X. Jing and F. Wang, *Org. Lett.* 2006, **8**, 785.

27. a) C. Schafer and J. Mattay, *Photochem. Photobiol. Sci.* 2004, **3**, 331 (photoswitches); b) J. F. Callan, A. P. de Silva and N. D. McClenaghan, *Chem. Commun*. 2004, 2048 (switch). c) P. Raghunath, M. A. Reddy, C. Gouri, K. Bhanuprakash and V. Jayathirtha Rao, *J. Phys. Chem. A* 2006, **110**, 1152.

28. a) A. Samanta, K. Bhattacharya and M. Chowdhury, *J. Phys. Chem.* 1987, **91**, 4671; b) S. Sengupta and P. Purkayastha, *Org. Biomol. Chem.* 2003, 436; c) D. Bailey and V. E. Williams, *Chem. Commun*. 2005, 2569; d) S. Bantia and A. Samanta, *J. Phys. Chem. B.* 2006, **110**, 6437.

29. a) H. D. Becker, *Chem Rev*. 1993, **93**, 145; b) H. B.-Laurent, A. Castellan, J.-P. Desvergne and R. Lapouyade, *Chem. Soc. Rev*. 2000, **29**, 43; b) H. Ihmels, D. Leusser, M. Pfeifferb, D. Stalke, *Tetrahedron* 2000**, 56**, 6867; c) S. Jones and J. C. C. Atherton, *Tetrahedron: Asymmetry* 2001, **12**, 1117; d) J. C. C. Atherton and S. Jones, *Tetrahedron Lett.* 2002, **43**, 9097; e) R. A. Bawa and S. Jones, *Tetrahedron* 2004, **60**, 2765 (Diels-Alder reaction); f) J. C. C. Atherton and S. Jones, *Tetrahedron* 2003, **59**, 9039; g) M. Horiguchi and Y. Ito *J. Org. Chem.* 2006, **71**, 3608.

30. E. Iwamoto, K. Hirai and H. Tomioka, *J. Am. Chem. Soc.* 2003, **125**, 14664.

31. a) W. B. Tan, A. Bhambhani, M. R. Duff, A. Rodger and C. V. Kumar, *Photochem Photobiol*. 2006, **82**, 20 (DNA cleavage); b) T. Ghosh, B. G. Maiya, A. Samanta, A. D. Shukla, D. A. Jose, D. K. Kumar and A. Das, *J Biol Inorg Chem* 2005**, 10**, 496; c) F. Marques, A. Paulo, M. P. Campello, S. Lacerda, R. F. Vitor, L. Gano, R. Delgado and I. Santos, *Rad. Prot. Dosimetry* 2005, **116**, 601.

32. O. Cakmak; R. Erenler; A. Tutar and N. Celik, *J. Org. Chem.* 2006**, 71**, 1795.

33. K. C. Kumara Swamy, S. Kumaraswamy, K. S. Kumar and C. Muthiah, *Tetrahedron. Lett.* 2005, **46**, 3347.

34. K. C. Gupta, P. K. Pathak, B. K. Saxena and N. Srivastava, *Indian J. Chem.* 1986, **25B**, 196.

35. M. J. Cravey and D. J. Doss, *J. Org. Chem.* 1988, **53**, 5963.

36. C. Muthiah, K. Praveen Kumar, C. Aruna Mani and K. C. Kumara Swamy, *J. Org. Chem*. 2000, **65**, 3733.

37. For reviews on the palladium-catalysed Heck reaction, see: (a) R. F. Heck, *Palladium Reagents in Organic Syntheses*; A. R. Katritzky, O. Meth-Cohn, C. W. Rees, Eds.; Academic Press: London, 1985; p. 2; (b) R. F. Heck, In *Comprehensive Organic Synthesis*; B. M. Trost, I. Fleming, Eds. Vinyl Substitution with Organopalladium Intermediates; Pergamon: Oxford, 1991; Vol. 4; (c) J.-L. Malleron, J.-C. Fiaud, J.-Y. Legros, *Handbook of Palladium-Catalysed Organic Reactions*; Academic Press: London, 1997; (d) M. T. Reetz, In *Transition Metal Catalysed Reactions*; S. G. Davies, S.-I. Murahashi, Eds.; Blackwell: Oxford, 1999; (e) I. Beletskaya, A. Cheprakov, *Chem. Rev*. 2000, **100**, 3009; (f) N. Withcombe, K. K. Hii (Mimi), S. Gibson, *Tetrahedron* 2001, **57**, 7449.

38. M. Feuerstein, H. Doucet and M. Santelli, *Tetrahedron. Lett.* 2002, **43**, 2191.

39. N. G. Pschirer and Uwe H. F. Bunz, *Tetrahedron. Lett.* 1999, **40**, 2481.

40. W. J. Yang, C. H. Kim, M.-Y. Jeong, S. K. Lee, M. J. Piao, S. -J. Jeon and B. R. Cho, *Chem. Mater.* 2004, **16**, 2783.

41. a) N. Sitachitta and W. H. Gerwick, J. Nat. Prod. 1998, **61**, 681; b) B. Cao, D. Xiao and M. M. Joullie, *Org. Lett*. 1999, **1**, 1799; c) A. Esposito, P. P. Piras, D. Ramazzotti, and M. Taddei, *Org. Lett*. 2001, **3**, 3273; d) S. Ono, K. Ogawa, K. Yamashita, T. Yamamoto, Y. Kazuta, A. Matsuda, and S. Shuto, *Chem. Pharm. Bull.* 2002, **50**, 966; e) Y. Kazuta, A. Matsuda, and S. Shuto, *J. Org. Chem.* 2002, **67**, 1669; f) B. Frydman, A. V. Blokhin, S. Brummel, G. Wilding, Y. Maxuitenko, A. Sarkar, S. Bhattacharya, D. Church, V. K. Reddy, J. A. Kink, L. J. Marton, A. Valasinas, and H. S. Basu, *J. Med. Chem.* 2003**, 46**, 4586; g) J. M. Janjic,a, Y. Mu, C. Kendall, C. R. J. Stephenson, R. Balachandran, B. S. Raccor, Y. Lu, G. Zhu, W. Xie, P. Wipf and B. W. Day, *Bioorg. Med. Chem.* 2005, **13**, 157; h) A. Reichelt and S. F. Martin, *Acc. Chem. Res*. 2006, **3**, 433.

42. a) W. B. Motherwell and C. J. Nutley, *Contemp. Org. Synth.* 1994**, 1,** 219; b) M. P. Doyle, *Catalytic Asymmetric Synthesis;* I. Ojima, Ed.; VCH

Publishers: New York, 1993; pp 63-99; (d) J. Salaun, *Chem. Rev.,* 1989, **89**, 1247.

43. S. Hanessian, L. –D. Cantin, S. Roy, D. Andreotti and A. Gomtsyan, *Tetrahedron. Lett.*, 1997, **38**, 1103.
44. S. Hanessian, D. Andreotti and A. Gomtsyan, *J. Am. Chem. Soc.* 1995, **117**, 10393.
45. C. Yuan, C. Li and Y. Ding, *Synthesis* 1991, 854.
46. a) T. A. Avery, T. D. Haselgrove, T. J. Rathbone, D. K. Taylor and E. R. T. Tiekink, *J. Chem. Soc., Chem. Commun.* 1998, 333; b) T. A. Avery, D. K. Taylor and E. R. T. Tiekink, *J. Org. Chem.* 2000, **65**, 5531; c) T. A. Avery, B. W. Greatrex, D. K. Taylor and E. R. T. Tiekink, *J. Chem. Soc., Perkin Trans. 1* 2000, 1319; d) T. A. Avery, G. Fallon, B. W. Greatrex, S. M. Pyke, D. K. Taylor and E. R. T. Tiekink, *J. Org. Chem.* 2001, **66**, 7955.
47. M. C. Kimber and D. K. Taylor, *J. Org. Chem.* 2002, **67**, 3142.
48. W. H. Midura, *Phosphorus, Sulfur, Silicon* 2005, **180**, 1285.
49. A. Zwierzak, *Can. J. Chem*. 1967, **45**, 2501.
50. K. C. Kumara Swamy, V. Srinivas, K. V. P. P. Kumar and K. P. Kumar, (*Submitted for publication*).
51. a) K. Sonogashira, Y. Tohda and N. Hagihara, *Tetrahedron Lett*. 1975, 4467; b) E. Negishi and L. Anastasia, *Chem. Rev.* 2003, **103**, 1979.
52. N. Satish Kumar, Thesis entitled "*Studies On The Synthesis, Reactivity and Utility Of Cyclic Phosphorus(III) Compounds and Organophosphonates*", April 2004.
53. a) J. Michas, C. M. Paleos, A. Skoulios and P. Weber, *Mol. Cryst. Liq. Cryst.* 1994, **239**, 245; b) Q. Zeng, C. Wang, S. Xu, P. Wu, X. Qiu and C. Bai, *J. Indian. Chem. Soc*. 2000, **77**, 599; c) J. J. E. Moreau, B. P. Pichon, G. Arrachart, M. W. Chi Man and C. Bied, *New. J. Chem.* 2005, **29**, 653.
54. K. C. Kumara Swamy, E. Balaraman and N. Satish Kumar, *Tetahedron* 2006, **62**, 10152.
55. O. Tayama, A. Nakano, T. Iwahama, S. Sakaguchi and Y. Ishii, *J. Org. Chem.* 2004, **69**, 5494.
56. J. Balzarini, C. Pannecouque, E. De Clercq, S. Aquaro, C.-F. Perno, H. Egberink, and A. Holy, *Antimicrob. Agents Chemother.* 2002, **46**, 2185.

APPENDIX

CCDC Reference codes/ publication numbers and atomic coordinates for X-ray structures reported in this thesis

I. CCDC Reference codes or publication numbers of the published compounds

PART A

Compound	CCDC Reference code	Publication no. (Contents, pp. viii)
14		**3**
38	**EVELAS**	**1**
45.CH_3CN	-	**3**
46 -	**EVEMIB**	**1**
51 -		**3**
52		**3**
66	**WAWPOA**	**2**
67	**WAWPUG**	**3**

PARTB

Compound	CCDC No.	publication no. (Contents, pp. viii)
18	-	**5**

II. Selected atomic coordinates for compounds 10, 17 $3/2C_3H_8O$, 21.CH_2Cl_2 and 56 from PART A and for compounds 28, 29 and 30 from PART B

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for 4. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

PART A

Compound 10

Atom	x	y	z	U(eq)
P(1)	13738(1)	10447(1)	7657(1)	43(1)
Cl(1)	14745(1)	11899(1)	9108(1)	60(1)
O(1)	13608(2)	9374(1)	8811(2)	38(1)
O(2)	9518(2)	8208(1)	10015(2)	43(1)
O(3)	8710(2)	7501(1)	7081(2)	45(1)
O(4)	7652(2)	9536(1)	8439(2)	44(1)
O(5)	11620(2)	10847(1)	7163(2)	42(1)
O(6)	9644(2)	10287(1)	10453(2)	42(1)
O(7)	10851(2)	6323(2)	6367(2)	53(1)
C(1)	12221(3)	9291(2)	9716(2)	33(1)
C(2)	10932(3)	8236(2)	9143(2)	34(1)
C(3)	10035(3)	8444(2)	7547(2)	35(1)
C(4)	8961(3)	9644(2)	7487(2)	37(1)
C(5)	10231(3)	10717(2)	8053(2)	34(1)
C(6)	11080(2)	10458(2)	9647(2)	34(1)
C(7)	8514(3)	9300(2)	9891(3)	43(1)
C(8)	9327(3)	6446(2)	6589(2)	36(1)
C(9)	7869(3)	5492(2)	6355(2)	36(1)
C(10)	8330(3)	4319(2)	5957(2)	43(1)
C(11)	7013(4)	3412(2)	5711(3)	54(1)
C(12)	5251(4)	3659(3)	5881(3)	55(1)
C(13)	4781(3)	4809(3)	6297(3)	53(1)
C(14)	6090(3)	5732(2)	6541(2)	43(1)

Compound 17

Atom	x	y	z	U(eq)
P(1)	2897(1)	5877(1)	1110(1)	36(1)
Cl(1)	4193(1)	6262(1)	-47(1)	80(1)
Cl(2)	5554(1)	6569(1)	371(1)	94(1)
Cl(3)	5833(1)	6717(1)	1372(1)	93(1)
Cl(4)	4748(1)	6512(1)	1960(1)	80(1)
O(1)	2442(1)	6632(1)	842(1)	40(1)
O(2)	2571(1)	5983(1)	1562(1)	41(1)
O(3)	3318(1)	6063(1)	650(1)	44(1)
O(4)	3527(1)	6201(1)	1420(1)	42(1)
O(5)	4401(5)	-440(13)	404(6)	467(14)
O(6)	0	6673(12)	2500	740(50)
N(1)	2819(1)	4681(2)	1015(1)	44(1)
C(1)	1928(1)	7150(2)	958(1)	41(1)
C(2)	1939(1)	8190(2)	953(1)	45(1)
C(3)	1407(2)	8657(2)	1039(1)	59(1)
C(4)	878(2)	8154(3)	1112(1)	67(1)
C(5)	889(1)	7130(3)	1110(1)	62(1)
C(6)	1410(1)	6617(2)	1030(1)	47(1)
C(7)	1420(1)	5496(2)	1049(1)	50(1)
C(8)	1591(1)	5145(2)	1505(1)	46(1)
C(9)	1181(1)	4560(2)	1705(1)	54(1)
C(10)	1282(1)	4303(2)	2136(1)	58(1)
C(11)	1794(1)	4693(2)	2375(1)	56(1)
C(12)	2224(1)	5288(2)	2196(1)	48(1)
C(13)	2124(1)	5453(2)	1750(1)	42(1)
C(14)	2505(2)	8789(2)	856(1)	52(1)
C(15)	3031(2)	8620(2)	1216(1)	68(1)
C(16)	2701(2)	8513(2)	412(1)	67(1)
C(17)	2365(2)	9909(2)	838(1)	74(1)
C(18)	294(2)	8714(4)	1187(2)	112(2)
C(19)	836(2)	3664(3)	2348(2)	84(1)
C(20)	2750(2)	5774(3)	2493(1)	62(1)
C(21)	2680(2)	5589(4)	2974(1)	91(1)
C(22)	3364(2)	5340(4)	2409(1)	92(1)
C(23)	2747(2)	6895(3)	2423(1)	96(1)
C(24)	3909(1)	6207(2)	770(1)	42(1)
C(25)	4373(1)	6303(2)	503(1)	52(1)
C(26)	4967(1)	6459(2)	696(1)	56(1)
C(27)	5093(1)	6528(2)	1137(1)	56(1)
C(28)	4619(1)	6439(2)	1406(1)	49(1)
C(29)	4043(1)	6286(2)	1210(1)	42(1)
C(30)	2972(2)	3949(2)	1372(1)	56(1)
C(31)	2529(2)	3081(3)	1329(2)	84(1)
C(32)	2435(2)	2644(3)	874(2)	94(1)
C(33)	2251(2)	3447(3)	547(2)	83(1)
C(34)	2719(2)	4286(2)	564(1)	57(1)
C(35)	3654(2)	3629(3)	1405(1)	76(1)
C(36)	3302(2)	3957(3)	365(1)	74(1)
C(37)	4204(5)	663(12)	431(7)	375(18)
C(38)	4242(6)	1004(9)	932(8)	450(20)
C(39)	4467(4)	156(12)	1259(5)	295(9)
C(40)	4556(4)	-693(6)	888(6)	250(9)
C(41)	567(6)	7346(10)	2382(3)	308(9)
C(42)	275(5)	8428(8)	2452(5)	245(10)

Compound 21. CH_2Cl_2

Atom	x	y	z	U(eq)
P	7366(1)	6325(1)	2688(1)	32(1)
Cl(1)	8530(1)	8695(1)	112(1)	67(1)
Cl(2)	11645(1)	7115(1)	-715(1)	86(1)
Cl(3)	13339(1)	4422(1)	124(1)	81(1)
Cl(4)	11895(1)	3327(1)	1803(1)	63(1)
O(1)	7178(2)	5448(1)	3562(1)	33(1)
O(2)	7092(2)	6265(2)	5871(1)	43(1)
O(3)	4517(2)	8132(2)	5439(1)	41(1)
O(4)	7246(2)	8422(2)	5496(1)	43(1)
O(5)	7533(2)	7647(1)	3147(1)	36(1)
O(6)	9184(2)	6520(2)	5161(1)	42(1)
O(7)	3047(2)	7249(2)	4793(1)	64(1)
O(8)	7574(2)	7200(2)	1688(1)	42(1)
O(9)	8929(2)	5194(1)	2389(1)	38(1)
N	5844(2)	6291(2)	2394(1)	41(1)
C(1)	7767(2)	5474(2)	4370(1)	31(1)
C(2)	6520(2)	6108(2)	5072(1)	34(1)
C(3)	5668(2)	7494(2)	4772(1)	35(1)
C(4)	6677(2)	8367(2)	4675(1)	36(1)
C(5)	7958(2)	7739(2)	4004(1)	34(1)
C(6)	8770(2)	6356(2)	4314(1)	34(1)
C(7)	7978(3)	7110(2)	5754(2)	43(1)
C(8)	3234(2)	7932(2)	5360(2)	41(1)
C(9)	2134(2)	8638(2)	6074(2)	40(1)
C(10)	706(3)	8862(3)	5945(2)	60(1)
C(11)	-350(3)	9539(3)	6580(2)	78(1)
C(12)	-5(3)	9935(3)	7349(2)	74(1)
C(13)	1403(3)	9705(3)	7488(2)	58(1)
C(14)	2480(3)	9070(2)	6840(2)	45(1)
C(15)	4819(2)	5570(2)	2765(2)	42(1)
C(16)	3335(3)	6355(3)	2555(2)	66(1)
C(17)	5270(3)	4123(3)	2424(2)	60(1)
C(18)	8893(2)	6695(2)	1276(1)	39(1)
C(19)	9494(3)	7209(3)	550(2)	46(1)
C(20)	10880(3)	6499(3)	199(2)	52(1)
C(21)	11639(3)	5302(3)	568(2)	52(1)
C(22)	11025(2)	4798(2)	1319(2)	44(1)
C(23)	9671(2)	5528(2)	1653(1)	37(1)
C(24)	4789(4)	9940(4)	1394(3)	103(1)
Cl(5)	4049(1)	8855(1)	853(1)	112(1)
Cl(6)	4119(1)	10221(1)	2490(1)	95(1)

Compound 56

Atom	x	y	z	U(eq)
P	5000	2445(1)	2500	37(1)
S	4260(1)	3599(1)	1983(1)	36(1)
Cl	0	543(1)	2500	51(1)
O(1)	4895(1)	2507(1)	3472(1)	41(1)
O(2)	5566(1)	1699(1)	2880(1)	43(1)
C(1)	5216(1)	3089(2)	4159(2)	36(1)
C(2)	5123(1)	3054(2)	4974(2)	40(1)
C(3)	5417(1)	3724(2)	5593(2)	42(1)
C(4)	4197(1)	4386(2)	-458(2)	41(1)
C(5)	4077(1)	4359(2)	320(2)	38(1)
C(6)	4372(1)	3700(2)	957(2)	35(1)
C(7)	4743(1)	2302(2)	5180(2)	51(1)
C(8)	4041(2)	2347(2)	4532(3)	84(1)
C(9)	4800(2)	2352(2)	6164(3)	96(1)
C(10)	5018(2)	1400(2)	5075(2)	66(1)
C(11)	3916(1)	5099(2)	-1165(2)	57(1)
C(12)	3630(1)	2822(2)	1718(2)	37(1)
C(13)	3006(1)	3101(2)	1431(2)	45(1)
C(14)	2528(1)	2472(2)	1235(2)	52(1)
C(15)	2704(1)	1581(2)	1353(2)	54(1)
C(16)	6668(1)	1274(2)	3340(2)	46(1)
C(17)	6202(1)	1930(2)	3161(2)	39(1)
C(18)	1838(1)	2749(2)	895(3)	76(1)
C(19)	6502(1)	278(2)	3234(2)	61(1)
C(20)	6053(2)	77(2)	2259(3)	98(1)
C(21)	7101(2)	-296(2)	3453(3)	99(1)
C(22)	6186(2)	31(2)	3890(3)	92(1)
N(1)	1445(2)	1093(2)	3303(2)	86(1)
N(2)	1932(2)	517(3)	3686(3)	126(1)
C(23)	1651(2)	1872(4)	3156(4)	139(2)
C(24)	2275(2)	1840(5)	3499(5)	162(3)
C(25)	2429(2)	951(5)	3795(4)	141(2)

PART B

Compound 28

Atom	x	y	z	U(eq)
P(1)	8833(1)	8170(1)	704(1)	43(1)
O(1)	9554(1)	6884(2)	386(1)	45(1)
O(2)	7767(1)	8459(2)	240(1)	53(1)
O(3)	9476(2)	9542(2)	890(1)	69(1)
O(4)	10323(1)	9019(2)	2331(1)	76(1)
O(5)	10921(1)	7019(2)	1787(1)	65(1)
O(6)	6718(1)	6621(2)	2493(1)	64(1)
O(7)	6183(2)	9013(2)	2287(1)	89(1)
O(8)	5268(1)	2220(2)	687(1)	71(1)
C(1)	9744(2)	7023(2)	-283(1)	45(1)
C(2)	8605(2)	7142(2)	-653(1)	48(1)

C(3)	7955(2)	8532(3)	-431(1)	56(1)
C(4)	8871(2)	7404(3)	-1341(1)	67(1)
C(5)	7897(2)	5671(3)	-585(1)	66(1)
C(6)	8226(2)	7183(2)	1347(1)	39(1)
C(7)	8943(2)	7187(2)	1955(1)	41(1)
C(8)	7924(2)	8232(2)	1900(1)	44(1)
C(9)	10121(2)	7880(2)	2041(1)	48(1)
C(10)	12095(2)	7573(4)	1869(2)	102(1)
C(11)	6894(2)	7829(2)	2258(1)	49(1)
C(12)	5142(3)	8729(5)	2633(2)	136(2)
C(13)	7464(2)	5835(2)	1188(1)	38(1)
C(14)	6345(2)	6058(2)	941(1)	47(1)
C(15)	5645(2)	4839(2)	781(1)	50(1)
C(16)	6043(2)	3350(2)	858(1)	50(1)
C(17)	7156(2)	3103(2)	1096(1)	52(1)
C(18)	7851(2)	4347(2)	1262(1)	46(1)
C(19)	5583(3)	698(3)	813(2)	108(1)

Compound 29

Atom	x	y	z	U(eq)
P(1)	1854(1)	7972(1)	2247(1)	52(1)
O(1)	1712(1)	10176(3)	1729(1)	59(1)
O(2)	1971(1)	6360(3)	1685(1)	68(1)
O(3)	2149(1)	8333(6)	3062(1)	107(1)
O(4)	765(1)	5947(4)	2942(2)	77(1)
O(5)	962(1)	9530(4)	3227(1)	75(1)
O(6)	136(1)	7158(4)	-726(1)	70(1)
C(1)	2190(1)	7313(5)	1239(2)	75(1)
C(2)	1978(1)	9252(5)	699(2)	56(1)
C(3)	1918(1)	11038(5)	1243(2)	66(1)
C(4)	2228(1)	10281(7)	284(2)	81(1)
C(5)	1598(1)	8462(10)	54(2)	133(2)
C(6)	1431(1)	6692(4)	2264(2)	45(1)
C(7)	1498(1)	4737(5)	2864(2)	61(1)
C(8)	1394(1)	6980(5)	3097(2)	55(1)
C(9)	1006(1)	7355(5)	3079(2)	56(1)
C(10)	596(1)	10181(7)	3217(3)	104(1)
C(11)	1084(1)	6725(4)	1477(1)	41(1)
C(12)	855(1)	8654(4)	1246(2)	47(1)
C(13)	544(1)	8741(5)	514(2)	50(1)
C(14)	454(1)	6897(5)	-18(2)	50(1)
C(15)	680(1)	4983(5)	196(2)	52(1)
C(16)	991(1)	4910(4)	940(2)	48(1)
C(17)	18(1)	5273(7)	-1277(2)	81(1)

Compound 30

Atom	x	y	z	U(eq)
N(1)	1026(1)	4027(2)	872(2)	46(1)
N(2)	537(1)	3020(2)	-727(2)	48(1)
N(3)	1040(1)	6891(2)	376(2)	59(1)
N(4)	526(1)	7426(2)	-1489(2)	54(1)
N(5)	117(1)	5414(2)	-2688(2)	54(1)
C(1)	794(1)	2700(3)	298(2)	50(1)
C(2)	602(1)	4708(3)	-821(2)	39(1)
C(3)	408(1)	5819(3)	-1688(2)	43(1)
C(4)	828(1)	7826(3)	-491(2)	64(1)
C(5)	901(1)	5329(3)	153(2)	44(1)
C(6)	1308(1)	4096(3)	2044(2)	52(1)
C(7)	1967(1)	4075(3)	2114(2)	53(1)
C(8)	2221(1)	4096(3)	3365(2)	56(1)
C(9)	2883(1)	4052(3)	3528(2)	57(1)
C(10)	3118(1)	4042(3)	4786(2)	56(1)
C(11)	3780(1)	3999(3)	4988(2)	59(1)
C(12)	4008(1)	3988(3)	6247(2)	56(1)
C(13)	4667(1)	3966(3)	6464(2)	57(1)
C(14)	4889(1)	3966(3)	7725(2)	58(1)
C(15)	5547(1)	3974(3)	7947(2)	57(1)
C(16)	5766(1)	3976(3)	9212(2)	59(1)
C(17)	6422(1)	4008(3)	9445(2)	58(1)
C(18)	6635(1)	4019(3)	10710(2)	61(1)
C(19)	7287(1)	4095(3)	10976(2)	60(1)
C(20)	7475(1)	4140(4)	12255(2)	75(1)
C(21)	8118(1)	4266(4)	12548(3)	92(1)